

ADVANCES IN
CARBENE CHEMISTRY

Editor: UDO H. BRINKER

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Wien, Austria

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PREFACE

Beginning as chemical curiosities, carbenes are now solidly established as reactive intermediates with fascinating and productive research areas of their own. Six decades of divalent carbon chemistry have provided us with a vast repertoire of new, unusual, and surprising reactions. Some of those reactions, once classified as exotic, have become standard methods in organic synthesis. These highly reactive carbene species have been harnessed and put to work to achieve difficult synthetic tasks other reactive intermediates cannot easily perform.

The fruitful relationship between experiment and theory has pushed carbene chemistry further toward the direction of reaction control; that is, regio- and stereoselectivity in intra- and intermolecular addition and insertion reactions. The interplay between experiment and modern spectroscopy has led to the characterization of many carbenes that are crucial to both an understanding and further development of this field.

Monographs devoted entirely to carbenes appeared in the late 1960's, such as the classic works of Hine and of Kirmse. Second-generation surveys published in the seventies consisted of the series of three volumes edited by Jones and Moss. At the end of the eighties, the status of such knowledge was collected into the two imposing volumes of Houben-Weyl (*Methoden der Organischen Chemie*; Regitz, editor).

Our understanding of carbene chemistry has advanced dramatically, especially in the last two decades, and new developments continue to emerge. Some of the recent exciting findings have been collected in the first and second volumes of *Advances in Carbene Chemistry*. With the third volume, the series will continue to provide a periodic coverage of carbene chemistry in its broadest sense.

Udo H. Brinker
Series Editor

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CARBENE PROTONATION

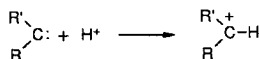
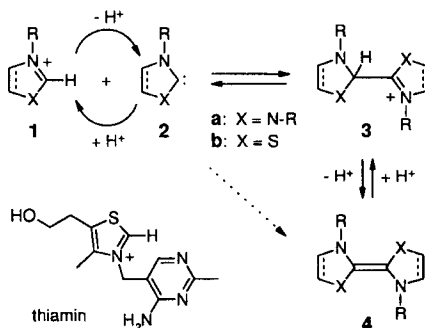
Wolfgang Kirmse

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I. INTRODUCTION

Carbenes are neutral, divalent derivatives of carbon.¹ The carbene carbon has two electrons not involved in bonding which can be spin-paired (singlet state) or unpaired (triplet state). The electron pair of a singlet carbene can accept a proton (or other electrophile) with formation of a carbocation (Scheme 1). Current nomenclature defines carbenium ions (trivalent carbocations) and carbenes as acid–base pairs,^{2,3} although the generic names were devised from a different perspective (the name carbene was coined to fit a *carbon* with the same degree of “unsaturation” as an *alkene*).⁴

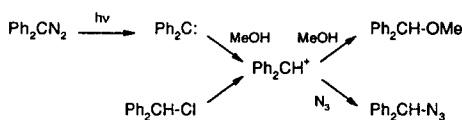
For years, the acid–base relationship of carbenium ions and carbenes was regarded as a purely formal concept which would not materialize. However,

**Scheme 1.****Scheme 2.**

experimental verification was foreshadowed by Breslow's pioneering work on the mechanism of thiamine action.^{5,6} It was observed that imidazolium (1a) and thiazolium salts (1b) exchange hydrogen at C-2 for deuterium under extraordinarily mild conditions.^{5a,7} Base converts 1 into a carbene *dimer* 4 which reverts to 1 on treatment with acid (Scheme 2).⁸ Although these processes are likely to be mediated by 2 and 3, the protonation of 2 was conclusively demonstrated only after the advent of persistent, monomeric imidazolylidenes (see Section V).⁹

Suggestive evidence for the protonation of diphenylcarbene was uncovered in 1963.¹⁰ Photolysis of diphenyldiazomethane in a methanolic solution of lithium azide produced benzhydryl methyl ether and benzhydryl azide in virtually the same ratio as that obtained by solvolysis of benzhydryl chloride. These results pointed to the diphenylcarbenium ion as an intermediate in the reaction of diphenylcarbene with methanol (Scheme 3). However, many researchers preferred to explain the O-H insertion reactions of diarylcarbenes in terms of electrophilic attack at oxygen (ylide mechanism),¹¹ until the intervention of carbocations was demonstrated by time-resolved spectroscopy (see Section III).¹²

As exemplified above, the chemistry of carbenes in protic media raised the prospect that carbocations could be formed. Experiments were designed to identify the intervening species by means of product and/or label distributions (Section II). The results thus obtained set the stage for the application of

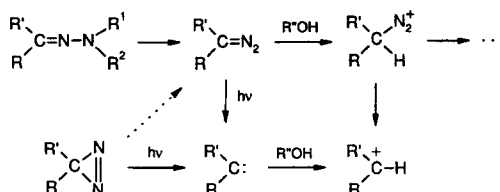
**Scheme 3.**

spectroscopic techniques, based on the laser flash photolysis (LFP) of carbene precursors (Sections III and IV). Some of the earlier work has been reviewed,¹³ in the context of O–H insertion reactions. In view of recent advances, an account focusing on carbene protonation appears to be timely.

II. CHEMICAL EVIDENCE FOR CARBENE PROTONATION

The experiments described in this section involve the generation of carbenes in protic solvents, with the aim of detecting carbocations. The section is divided according to the concepts and methods that were applied. First of all, carbenes and carbocations are not readily differentiated as both species feature a vacant p orbital. If that problem has been solved, the origin of the carbocation must be scrutinized. Most often, carbene protonation is not the only possible route to carbocations. Diazo compounds, which are widely used carbene precursors, can give rise to carbocations by way of diazonium ions (Scheme 4).¹⁴ The basicity of diazo compounds is known to decrease in the order $R, R' = \text{alkyl} > \text{H} > \text{aryl} > \text{carbonyl} > \text{sulfonyl}$. Diazoalkanes are readily protonated by alcohols whereas some diazo ketones tolerate even carboxylic acids. In order to obtain meaningful results on carbene protonation, the $RR'CN_2/R''OH$ mixtures employed must be stable in the dark. This simple criterion is not applicable to labile diazo compounds which are generated *in situ* from hydrazone precursors. Fortunately, some diazonium ions undergo reactions not shown by the analogous carbocations (e.g., the norbornyl $\rightarrow$ norpinyl rearrangement).¹⁵ The absence of diazonium-derived products is a strong argument supporting the carbene route to carbocations.

Diazirines, which are stable in protic solvents, might be regarded as the precursors of choice for studies on carbene protonation. However, photolyses of diazirines proceed, in part, by way of the isomeric diazo compounds.¹⁶ If potent dipolarophiles are present in the reaction mixture, the diazo compounds can be scavenged faster than protonation occurs. Thus the intervention of diazonium ions is avoided, and the carbene route is singled out (for examples, see below). This short survey indicates that nitrogen is a widely applicable but tricky leaving group. Although non-nitrogenous sources of carbenes are available, few of them



Scheme 4.

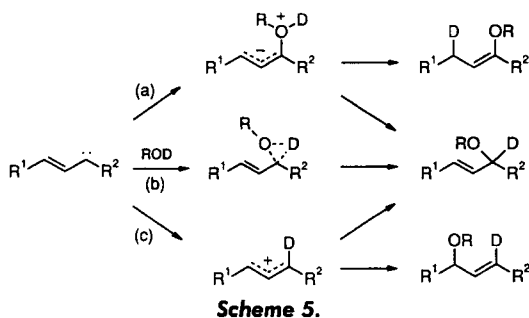
are compatible with protic media. Some approaches, limited in scope, will be discussed in due course.

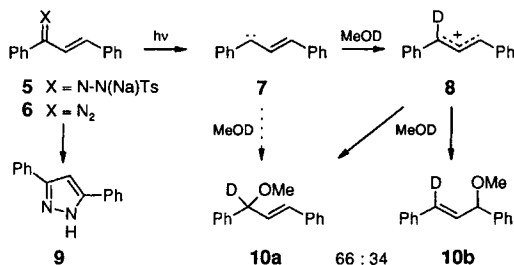
A. Generation of Delocalized Carbocations

The reaction of carbenes with alcohols can proceed by various pathways, which are most readily distinguished if the divalent carbon is conjugated to a π system (Scheme 5). Both the ylide mechanism (a) and concerted O–H insertion (b) introduce the alkoxy group at the originally divalent site. On the other hand, carbene protonation (c) gives rise to allylic cations, which will accept nucleophiles at C-1 and C-3 to give mixtures of isomeric ethers. In the case of $R^1 = R^2$, deuterated alcohols will afford mixtures of isotopomers.

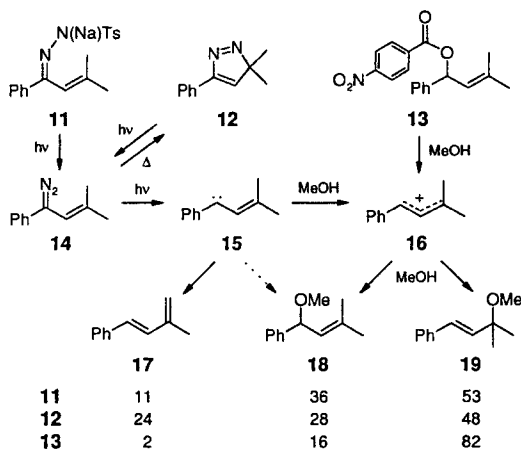
Vinylcarbenes. The use of diazoalkenes as vinylcarbene precursors is often precluded by rapid cyclization, with formation of pyrazoles. However, on photochemical generation of the diazoalkenes *in situ*, cyclization and nitrogen extrusion can proceed competitively. Photolysis of 1,3-diphenylpropenone tosylhydrazone sodium salt (**5**) in MeOD afforded 3,5-diphenylpyrazole (**9**) and 1,3-diphenyl-3-methoxypropene (**10**) in similar amounts.¹⁷ If **10** is formed by way of the 1,3-diphenylallyl cation (**8**), the deuterium should be distributed between C-1 and C-3 of **10** (Scheme 6). The observed ratio of **10a** to **10b** was 66 : 34; the methoxy group is bound preferentially to the deuterated site, which originates from the divalent carbon of **7** (for a discussion of this effect, see below).

3,3-Dimethyl-1-phenylpropenylidene (**15**) was generated from the tosylhydrazone sodium salt **11** as well as from 3,3-dimethyl-5-phenylpyrazole (**12**), by way of the diazo compound **14**.^{17,18} The reaction of **15** with methanol gave a mixture of the isomeric ethers **18** and **19**, pointing to intervention of the allylic cation **16** (Scheme 7). In order to assess the regioselectivity of **16**, the solvolysis of the 4-nitrobenzoate in methanol was also studied. Although **19** prevailed in each case, the **19** : **18** ratio obtained from **11** (1.5) and from **12** (1.7) was inferior to that obtained from **13** (5.1).





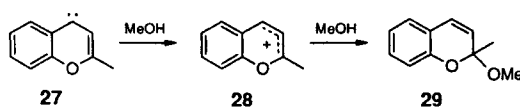
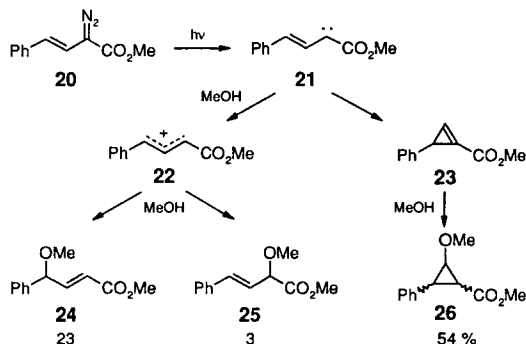
Scheme 6.



Scheme 7.

The reactions of the vinylcarbenes **7** and **15** with methanol clearly involve delocalized intermediates. However, the product distributions deviate from those of “free” (solvated) allyl cations. Competition of the various reaction paths outlined in Scheme 5 could be invoked to explain the results. On the other hand, the effect of charge delocalization in allylic systems may be partially offset by ion pairing. Proton transfer from alcohols to carbenes will give rise to carbocation–alkoxide ion pairs; that is, the counterion will be closer to the carbene-derived carbon than to any other site. Unless the paired ions are rapidly separated by solvent molecules, collapse of the ion pair will mimic a concerted O–H insertion reaction.

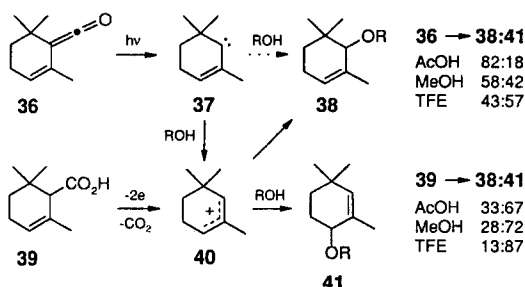
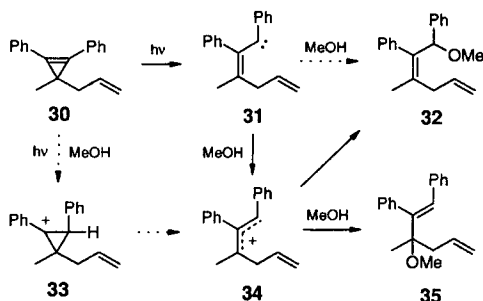
The ratio of isomeric ethers is strongly affected by polar substituents which induce an asymmetric distribution of charge in allylic cations. Photolysis of methyl 2-diazo-4-phenyl-3-butenolate (**20**) in methanol produced **24** in large excess over **25** as the positive charge of **22** resides mainly α to phenyl (Scheme 8).¹⁹ As would be expected, proton transfer to the electron-poor carbene **21** proceeds reluctantly; intramolecular addition with formation of the cyclopropene



23 and, eventually, **26** was the major reaction. On the other hand, the carbene **27** should be readily protonated to give the stable benzopyrylium ion **28**. In fact, the acetal **29** was obtained as the only product when **27** was generated by photolysis of the analogous tosylhydrazone in MeOH–MeONa (Scheme 9).²⁰ Both carbenes, **21** and **27**, add methanol predominantly in a 1,3 fashion: H is bound to the divalent carbon, and OMe to the γ position. The data exclude significant contributions of a non-ionic reaction path.

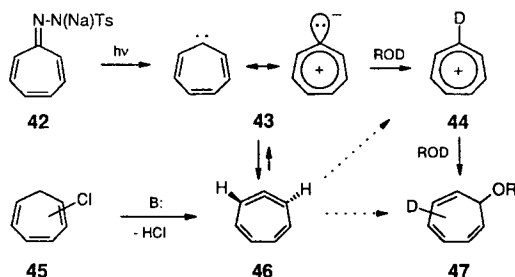
The elusive diazoalkenes **6** and **14** are unlikely to react with methanol as their basicity should be comparable to that of diphenyldiazomethane. However, since the formation of diazonium ions cannot be rigorously excluded, the protonation of vinylcarbenes was to be confirmed with non-nitrogenous precursors. Vinylcarbenes are presumedly involved in photorearrangements of cyclopropenes.²¹ In an attempt to trap the intermediate(s), **30** was irradiated in methanol. The ethers **32** and **35** (60 : 40) were obtained,²² pointing to the intervention of the allylic cation **34** (Scheme 10). Protonation of the vinylcarbene **31** is a likely route to **34**. However, **34** could also arise from protonation of photoexcited **30**, by way of the cyclopropyl cation **33**. The photosolvolysis of alkenes is a well-known reaction which proceeds according to Markovnikov's rule and is, occasionally, associated with skeletal reorganizations.²³ Therefore, cyclopropenes are not the substrates of choice for demonstrating the protonation of vinylcarbenes.

Ketenes are useful sources of carbenes in the gas phase but are rarely applied in solution, owing to their tendency to dimerize and to accept nucleophiles. However, the sterically encumbered ketene **36**, derived from cyclogeranium

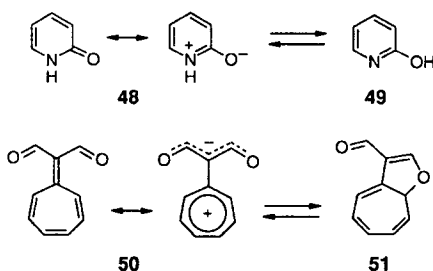


acid (**39**), does not react with OH groups at ambient temperature. Photolysis of **36** in protic solvents gave mixtures of allylic ethers or esters, **38** and **41**, which are indicative of the delocalized intermediate **40** (Scheme 11).²⁴ Oxidative decarboxylation of **39** served as an alternative source of **40**. Although the solvent effect on both reactions was qualitatively similar, the fraction of rearranged product **41** from the ketene **36** was always inferior to that from the carboxylic acid **39**. The increase of **41** with increasing *polarity* of the solvent supports the formation of ion pairs from **37**. If competing reactions of the carbene, **37** → **38** and **37** → **40**, were involved, increasing *acidity* of the solvent should lead to enhanced rearrangement. The opposite effect was observed (cf. MeOH vs. AcOH).

Cycloheptatrienyliidenes. Photolysis of tropone tosylhydrazide sodium salt (**42**)²⁵ as well as base-induced elimination of hydrogen chloride from chlorocycloheptatrienes (**45**)²⁶ generate an intermediate that was first regarded as cycloheptatrienylidene (**43**) but is now thought to be 1,2,4,6-cycloheptatetraene (**46**). In the presence of ROD, both methods afforded 7-alkoxycycloheptatrienes (**47**) with random distribution of deuterium among all positions of the seven-membered ring (Scheme 12).²⁷ The intervention of tropylium ions (**44**) is obvious, but their origin remains to be scrutinized.



Scheme 12.

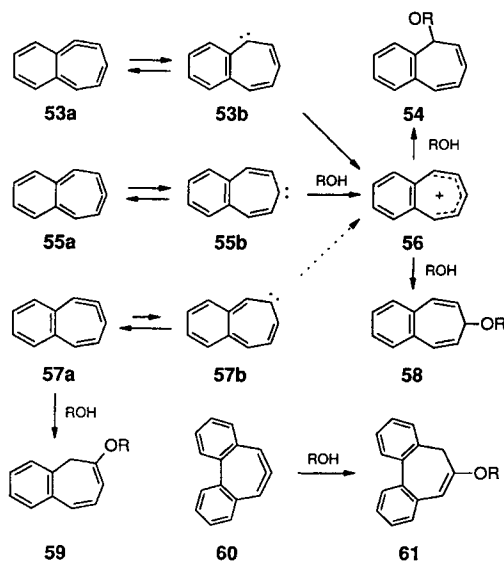


Scheme 13.



Scheme 14.

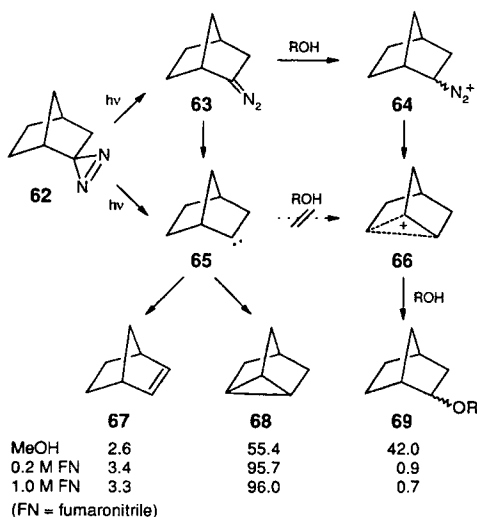
The non-planar, chiral allene **46** was identified by IR spectroscopy in matrix isolation studies aimed at **43**.²⁸ At all levels of theory, singlet ($^1A_1$) **43** is well above **46** in energy.²⁹ According to some computational methods, **43** is the transition structure interconverting the enantiomers of **46** while others assign a local minimum to **43**.²⁹ It should be recalled that these findings refer to the gas phase (theory) or to nonpolar media (matrix), which favor the hydrocarbon-like allene **46** over the π -delocalized, dipolar carbene **43**. Solvation is expected to stabilize **43** relative to **46**. The tautomerism of strongly polar 2-pyridone (**48**) with weakly polar 2-hydroxypyridine (**49**) provides the classical example for solvent effects (Scheme 13).³⁰ The gas-phase equilibrium constants differ from those in aqueous solution by as much as 10^4 . More closely related to the present case, the dipolar 8,8-diformylheptafulvene (**50**) was found to predominate in D_2O and CD_3OD whereas the less dipolar 8aH-cyclohepta[b]furan-3-carbaldehyde (**51**) prevailed in CCl_4 .³¹ In view of these observations, the protonation of **43** to give **44** should not be dismissed *a priori*.



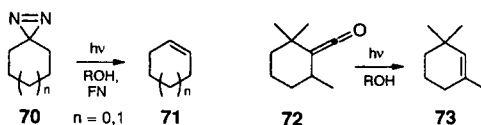
Scheme 15.

Can tropylium ions (**44**) originate from 1,2,4,6-cycloheptatetraene (**46**)? As a rule, allenes are protonated to give 2-propenyl rather than allyl cations, despite the greater thermodynamic stability of the latter.³² The reason for this is stereo-electronic: protonation of the center carbon leads to a twisted structure which is devoid of allylic conjugation (Scheme 14). However, it is questionable that these considerations apply to strained cyclic allenes such as **46**. For an experimental approach to the problem, the effect of benzoannulation on the relative stabilities of **43** and **46** was exploited. 1,2- and 3,4-benzoannulation narrows the energy gap between allenes (**53a**, **55a**) and carbenes (**53b**, **55b**), although the computed gas-phase energies of the singlet carbenes are still above those of the allenes.³³ Both species, **53** and **55**, were found to give identical mixtures of the benzocycloheptatrienyl ethers **54** and **58**, by way of the benzotropylium ion (**56**).³⁴ 2,3-Benzoannulation, on the other hand, stabilizes the allene **57a** and destabilizes the carbene **57b**. Only a minor fraction of **57** reacted via **56** while the major product was the vinyl ether **59** (Scheme 15). Appropriate annelation of a second benzene ring widens the energy gap between allene and carbene even further, the consequence being exclusive formation of **61** from **60**.³⁴ It appears that 1,2,4,6-cycloheptatetraenes accept the alkoxy group, rather than the proton, of alcohols at the *sp*-hybridized carbon. Protonation of cycloheptatrienylenes remains the most plausible route to tropylium ions.

Bicycloalkylidenes. σ -Delocalization in bicyclic carbocations provides the opportunity to detect the protonation of bicycloalkylidenes. An obvious choice was the 2-norbornyl cation (**66**), for which symmetrical bridging (equivalence



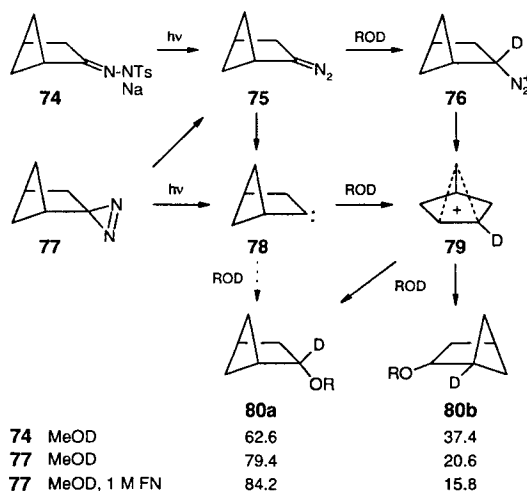
Scheme 16.



Scheme 17.

of positions 1 and 2) has been amply demonstrated.³⁵ Photolyses of the diazirine **62** in the presence of alcohols afforded mixtures of norbornene (**67**), nortricyclane (**68**), and 2-alkoxynorbornanes (**69**) (Scheme 16).³⁶ The *exo:endo* ratios of **69**, as well as deuterium distributions from photolyses in ROD, matched those obtained with 2-diazonorbornane (**63**). These data suggested that the diazonium ion route, $62 \rightarrow 63 \rightarrow 64 \rightarrow 66$, was responsible for the formation of **69**. On addition of fumaronitrile, the fraction of **69** dropped to <1%, due to interception of **63** by the powerful dipolarophile. It appears that the intramolecular C–H insertion reactions of 2-norbornylidene, $65 \rightarrow 67 + 68$, are too fast for proton transfer to compete. The behavior of **65** is paralleled by that of cyclopentylidenes and cyclohexylidenes. The formation of ethers from the diazirines **70** was quenched by added dipolarophiles,³⁷ and photolysis of the ketene **72** afforded 1,3,3-trimethylcyclohexene (**73**) exclusively (Scheme 17).²⁴ The intervening carbenes undergo 1,2-H shifts in strong preference to the reaction with ROH.

Bicyclo[2.1.1]hex-2-ylidene (**78**) is expected to be longer lived than 2-norbornylidene (**65**), owing to the enhanced ring strain of the intramolecular products. Although vacuum thermolysis of the tosylhydrazone salt **74** gives bicyclo[2.1.1]hex-2-ene,³⁸ intermolecular reactions of **78** prevail in solution.³⁶

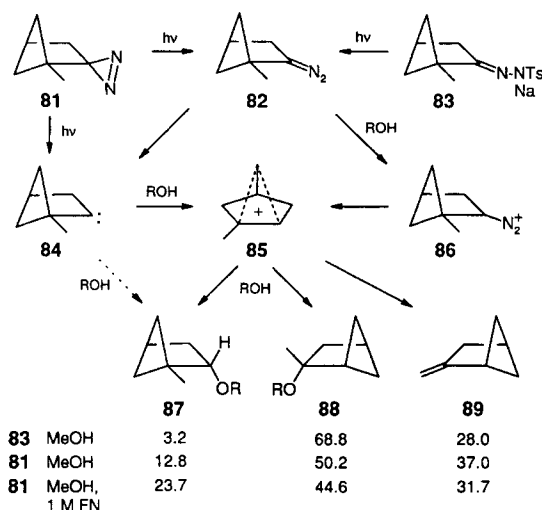


Scheme 18.

Photolysis of the diazirine **77** in the presence of alcohols afforded the ethers **80**, the azine $R_2C=N-N=CR_2$ being the only additional product (Scheme 18). With increasing concentrations of dipolarophiles, the yield of **80** decreased to a limiting value of *ca.* 60%. Analogy with the norbornyl case suggests that, with 1 M fumaronitrile, the diazo compound **75** should be scavenged, and **80** should arise only from the carbene **78**. In the presence of MeOD, the isotopomers **80a** and **80b** (84:16) were obtained, pointing to intervention of the bicyclo[2.1.1]hex-2-yl cation (**79**).³⁶ The complex degeneracy of **79**, described earlier,³⁹ does not affect the present conclusions.

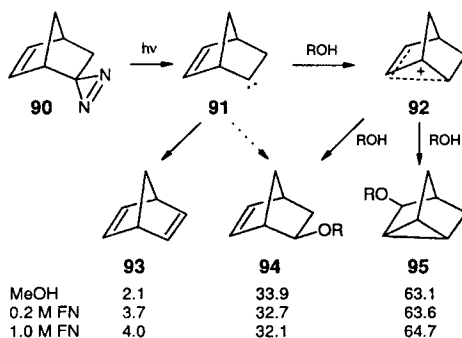
As discussed above for allylic systems, the uneven distribution of deuterium can be attributed to competing reactions of the carbene, or to ion pairing. The effect of a methyl group in the bridgehead position (**84** vs. **78**) on carbene partitioning should be small. On the other hand, the nature of the carbocation **79** is changed profoundly by a methyl group at C-1: **85** is highly unsymmetrical, with the positive charge residing largely at the tertiary carbon. As a consequence, the diazonium ion route, **83** → **82** → **86** → **85**, afforded only 3% of the secondary ether **87** (Scheme 19). Although the carbene route, **81** + FN → **84** → **85**, gave more of **87**, the tertiary ether **88** and the alkene **89** predominated.³⁶ A fivefold increase in rearrangement was observed with **84**, relative to **78**. Therefore, protonation is thought to be the major reaction path of both **78** and **84**, while the product distributions are controlled by the tightness of the intervening ion pairs.

Bicycloalkenylidenes. The vacant p orbitals of 5-norbornen-2-ylidene (**91**) and of 2-norbornen-7-ylidene (**100**) interact with the π bonds, thus enhancing the nucleophilicity of the divalent carbon.⁴⁰ Protonation of these carbenes leads

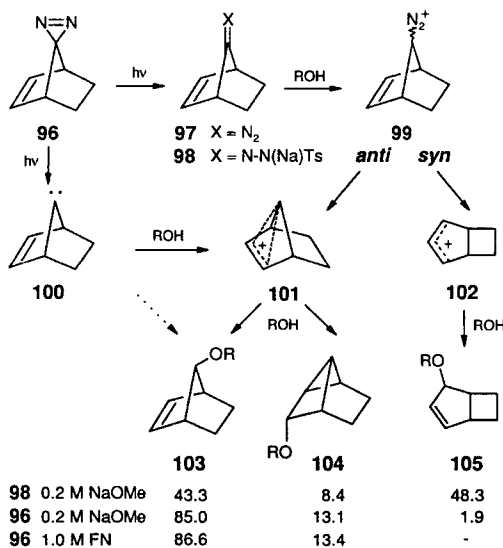


Scheme 19.

to homoconjugated cations which give rise to tricyclic as well as bicyclic products.⁴¹ Photolysis of the diazirine **90** in methanol afforded the ethers **94** and **95** in the ratio of about 1: 2, which is characteristic of the 5-norbornen-2-yl cation (**92**) (Scheme 20).⁴² A small amount of norbornadiene (**93**) was also obtained. The insignificant effect of added fumaronitrile suggests that little, if any, diazo compound is formed on irradiation of **90**. For the generation of 2-norbornen-7-ylidene (**100**) from the diazirine **96**, the role of the diazo compound **97** is more clearly defined (Scheme 21). Protonation of **97** produces a mixture of the epimeric diazonium ions *anti*-**99** and *syn*-**99** which decompose by distinct reaction paths.⁴³ The *anti* species gives rise to the 2-norbornen-7-yl cation (**101**) whereas vinyl shift of the *syn* isomer leads to the bicyclo[3.2.0]hept-3-en-2-yl cation (**102**). In the photolysis of the tosylhydrazone sodium salt **98**, which proceeds entirely by way of **97**, the bicyclo[3.2.0] heptenyl ether **105** accounted for 48% of the products. Only 2% of **105** was obtained on photolysis of the diazirine **96**, and the formation of **105** was quenched completely by added fumaronitrile. Under these conditions, the ethers **103** and **104** must originate from the carbene **100**. These ethers are formed stereospecifically, in a ratio depending on the concentration of methoxide. Analogous results were reported for the carbocation **101**, as generated by solvolysis of 2-norbornen-7-yl tosylate.⁴⁴ Obviously, the formation of **103** and **104** from **100** involves proton transfer to give **101**. The data obtained by photolysis of the diazirine **96** confirm the results of earlier work in which **100** was generated by way of the Skattebøl rearrangement.⁴⁵



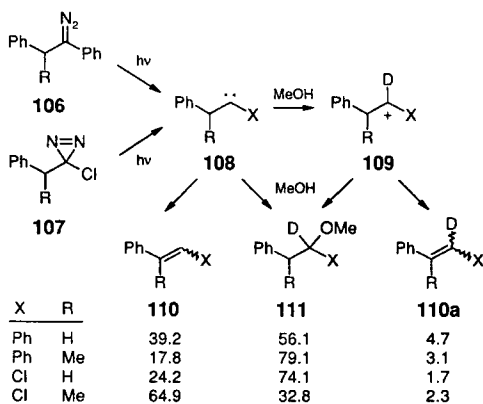
Scheme 20.



Scheme 21.

B. Protonation-Deprotonation Route to Alkenes

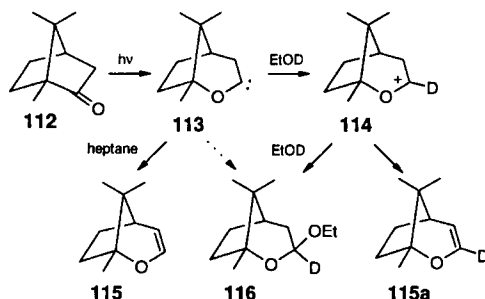
Many carbenes bearing hydrogen vicinal to the divalent carbon undergo 1,2-H shifts to the exclusion of intermolecular reactions (see Scheme 17). Stabilizing substituents, such as aryl, halogen, or alkoxy, raise the barrier to hydrogen migration.⁴⁶ In the presence of alcohols, protonation of the carbene with subsequent elimination of a proton from the β position must then be considered as an alternative route to alkenes. The carbenic and cationic pathways are readily distinguished in deuterated solvents (Scheme 22). When benzylphenylcarbenes (**108**, X = Ph) were generated from the diazo compounds **106** in MeOD, the



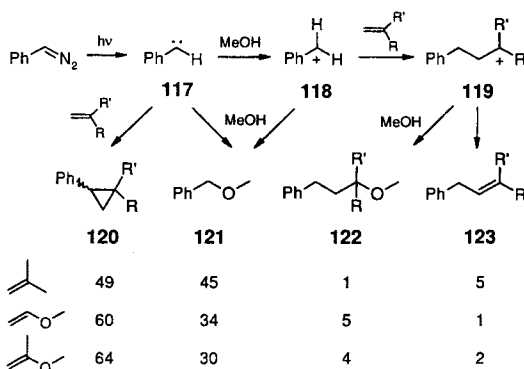
Scheme 22.

alkenes **110** were formed with incorporation of deuterium (10.6% for R = H and 14.8% for R = Me).⁴⁷ Similar results were obtained with benzylchlorocarbenes (**108**, X = Cl), generated from the diazirines **107**. With R = H, the incorporation of deuterium into **110** (X = Cl) increased from 6.7% in MeOD to 20.4% in AcOD.⁴⁸ The modest yields of **110a** can be due to (i) slow protonation of the carbenes (**108** → **109**), relative to the 1,2-H shift (**108** → **110**), and/or (ii) unfavorable partitioning of the carbocations **109** between elimination (→ **110a**) and substitution (→ **111**).

Protonation should be more efficient for the oxycarbenes arising from photochemical ring expansion of cyclobutanones and, to a lesser extent, bicyclo[2.2.1]heptanones (see also Section IV).⁴⁹ Most of these species do not give enol ethers, but **113**, generated from camphor (**112**), affords **115** (Scheme 23).⁵⁰ In the presence of EtOD, the fully deuterated enol ether **115a** was obtained along with the acetal **116**. When this work was performed in the 1960s, the results were not discussed in terms of carbene protonation. With hindsight, the intervention of the cation **114** appears most likely.



Scheme 23.

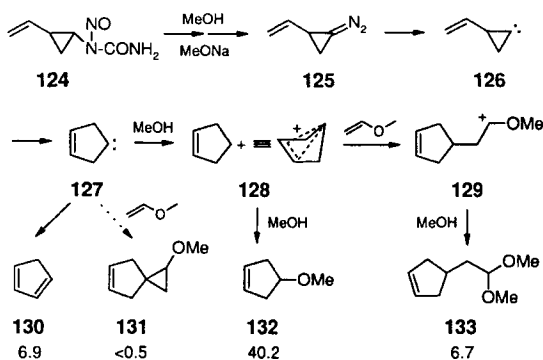


Scheme 24.

C. Addition to Alkenes

Alkenes are scavengers that are able to differentiate between carbenes (cycloaddition) and carbocations (electrophilic addition). The reactions of phenylcarbene (**117**) with equimolar mixtures of methanol and alkenes afforded phenylcyclopropanes (**120**) and benzyl methyl ether (**121**) as the major products (Scheme 24).⁵¹ Electrophilic addition of the benzyl cation (**118**) to alkenes, leading to **122** and **123** by way of **119**, was a minor route (*ca.* 6%). Isobutene and enol ethers gave similar results. The overall contribution of **118** must be more than 6% as (part of) the ether **121** also originates from **118**. Alcohols and enol ethers react with diarylcarbenium ions at about the same rates (*ca.* $10^9 \text{ M}^{-1} \text{ s}^{-1}$), somewhat faster than alkenes (*ca.* $10^8 \text{ M}^{-1} \text{ s}^{-1}$).⁵² By extrapolation, diffusion-controlled rates and indiscriminate reactions are expected for the “free” (solvated) benzyl cation (**118**). In support of this notion, the product distributions in Scheme 24 only respond slightly to the nature of the π bond (alkene *vs.* enol ether). The formation of “free” benzyl cations from phenylcarbene and methanol is thus estimated to be in the range of 10–15%. However, the major route to the benzyl ether **121**, whether by ion-pair collapse or by way of an ylide, cannot be identified.

Enol ether additives were used to probe the protonation of 3-cyclopentenylidene (**127**). Treatment of *N*-nitroso-*N*-(2-vinylcyclopropyl)urea (**124**) with sodium methoxide generates 2-vinylcyclopropylidene (**126**) by way of the labile diazo compound **125** (Scheme 25). For simplicity, products derived directly from **126** (allene, ether, cycloadduct) are not shown in Scheme 25. The Skat-tebøl rearrangement of **126** generates **127** whose protonation leads to the 3-cyclopentenyl cation (**128**). In the presence of methanol, cyclopentadiene (**130**) and 3-methoxycyclopentene (**132**) were obtained.⁵³ With an equimolar mixture of methyl vinyl ether and methanol, cycloaddition of **127** ($\rightarrow$ **131**)



Scheme 25.

and electrophilic addition of **128** ($\rightarrow$ **129** $\rightarrow$ **133**) were also observed, in a 1 : 14 ratio. Thus the carbocation **128** is the major species trapped by the vinyl ether, in contrast to the phenylcarbene case discussed above. The protonation of **127** appears to be promoted by p– π interaction. Owing to the nonplanar, homoconjugated structure of **128**, the ether **132** is formed stereospecifically from an appropriately labeled substrate.

III. SPECTROSCOPIC EVIDENCE FOR CARBENE PROTONATION

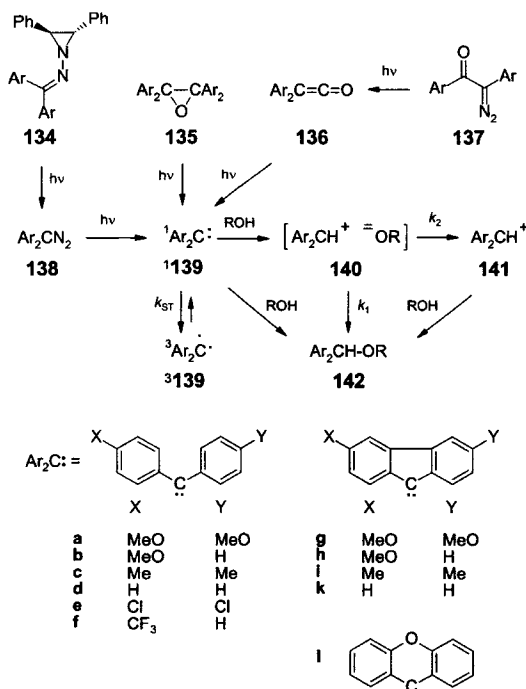
The advent of the pulsed laser has made available for optical detection many reactive intermediates, including carbenes^{46,54} and carbocations.⁵⁵ Most of the carbene work was performed in the nanosecond (ns) regime although a few picosecond (ps) studies were reported. In an ideal proton transfer experiment, the decay of the carbene as well as the growth of the carbocation absorption would be monitored, and the rates compared. In order to obtain such data, *both* intermediates must be long-lived, relative to the duration of the laser pulse, and their extinction coefficients must be similar. These conditions are rarely, if ever, fulfilled. With increasing acidity of the solvent, the lifetime of carbocations is enhanced whereas that of singlet carbenes is shortened. Moreover, the lifetimes of many singlet carbenes are controlled by intrinsic factors, such as intersystem crossing. In view of these limitations, two sets of reaction conditions have been routinely employed:

(a) The carbene is generated in neat ROH, or a solvent mixture rich in ROH, in order to achieve rapid proton transfer. The absorption spectrum of the carbocation is observed, with maximum intensity immediately after the laser pulse. The rate of carbocation decay can be adjusted by the choice of ROH. The results of such studies are summarized in the present section.

(b) The carbene is generated and monitored in an “unreactive” solvent. The effect of ROH, typically in submolar concentrations, on the rate of carbene decay is estimated. The kinetic data thus obtained will be reviewed in Section IV.

A. Diarylcarbenes

Laser flash photolysis (LFP) of diaryldiazomethanes (**138**) generates diarylcarbenes initially in their singlet states (¹**139**) (Scheme 26). As a rule, singlet diarylcarbenes are “invisible” in the ns regime as they undergo rapid intersystem crossing to the triplet ground states (³**139**). Exceptions include 3,6-dimethoxyfluorenylidene (**139g**) and 9-xanthylidene (**139l**) which have singlet ground states.⁵⁶ For diphenylcarbene (**139d**) at 300 K, k_{ST} ranges from $3.2 \times 10^9 \text{ s}^{-1}$ in acetonitrile to $1.05 \times 10^{10} \text{ s}^{-1}$ in isooctane.⁵⁷ The rate constant for the reaction of ¹**139d** with methanol in acetonitrile, $k \approx 6 \times 10^9 \text{ M}^{-1} \text{ s}^{-1}$, is close to the diffusion limit.⁵⁸ For $[\text{MeOH}] < 1 \text{ M}$, spin inversion of ¹**139d** and capture by methanol can compete, while at sufficiently high concentrations, reaction of ¹**139d** with the alcohol becomes the only significant route of decay. The “slow” reaction of ³**139d** with MeOH in MeCN, $k = 2.4 \times 10^7 \text{ M}^{-1} \text{ s}^{-1}$, is



Scheme 26.

Table 1. Decay Kinetics and Yields for Various Carbocations **141** Produced by Protonation of Diarylcarbenes **139**

	Solvent	$\tau = 1/k$ (ns)	$\lambda_{\max}$ (nm)	Φ_{141}	Ref.
141a	H ₂ O–MeCN (2 : 1)	8.3×10^3	500	0.120	12
	TFE–MeCN (1 : 1)	2×10^5	500		62
141b	H ₂ O–MeCN (4 : 1)	4.3×10^2	455	0.056	12
	TFE–MeCN (1 : 1)	3×10^4	460		62
141c	H ₂ O–MeCN (2 : 1)	2.4×10^1	462	0.016	12
	TFE–MeCN (1 : 1)	4.5×10^3	465		62
141d	TFE–MeCN (1 : 1)	1.3×10^2	435	0.007	62
	TFE	3.1×10^2	435		12
141e	TFE–MeCN (1 : 1)	1.7×10^2	470	0.003	62
141f	TFE	2.7×10^1	425		18
141g	H ₂ O–MeCN (2 : 1)	8.3×10^1	490		65
141h	H ₂ O–MeCN (2 : 1)	1.9×10^1	480		65
	TFE	6.4×10^3	480		65
141i	TFE	6.6×10^1	520		65

widely thought to proceed by way of **139d** (pre-equilibrium mechanism).^{13,56} Alternatively, spin inversion could occur *after* the triplet carbene has begun to interact with the alcohol (surface crossing mechanism).^{54b,59}

The transient absorption spectra of diarylcarbenium ions (**141**) were detected following nanosecond LFP of **138a–c** in H₂O–MeCN and of **138d–f** in TFE–MeCN.¹² Comparison with data from photoheterolyses of Ar₂CH–X makes the characterization of these intermediates straightforward.⁶⁰ The lifetimes of Ar₂CH⁺ are strongly affected by the solvent ($\tau_{\text{H}_2\text{O}} : \tau_{\text{TFE}} \approx 1 : 10^2$) and by *para* substituents. Moreover, the diphenylmethyl cations **141a–c** are longer lived than the analogous 9-fluorenyl cations **141g–i** (Table 1). The problem of short cation lifetimes can be solved by enhanced time resolution. Following picosecond LFP of **138d**, the diphenylcarbenium ion (**141d**) was detected in H₂O–MeCN, 2-propanol, ethanol, and methanol, with lifetimes ($1/k$) of 750, 85, 70, and 40 ps, respectively.⁶¹ With nanosecond LFP, the reactivity of **141** dictates the choice of the solvent. Unfortunately, many diazo precursors, such as **138a–d**, are readily decomposed by TFE; **138i** is even decomposed by water. Stopped-flow techniques were applied to **138a–e** in order to overcome these difficulties.⁶² Alternatively, diarylcarbenes were generated from aziridinylienes **134** in a biphotonic process, **134** → **138** → **139** (Figure 1).^{63,64} The aziridinyliene method was used to demonstrate the protonation of xanthyliene (**139l**) by water, and the protonation of fluorenylidene (**139k**) by hexafluoro-2-propanol (HFIP).⁶⁴ The cations **141l** ($\text{p}K_{\text{R}^+} = -0.85$) and **141k** ($\text{p}K_{\text{R}^+} = -16.6$) bracket the range of the diarylcarbenium ions that have been obtained by carbene protonation. LFP of tetraphenyloxirane (**135d** → Ph₂C: + Ph₂CO)¹²

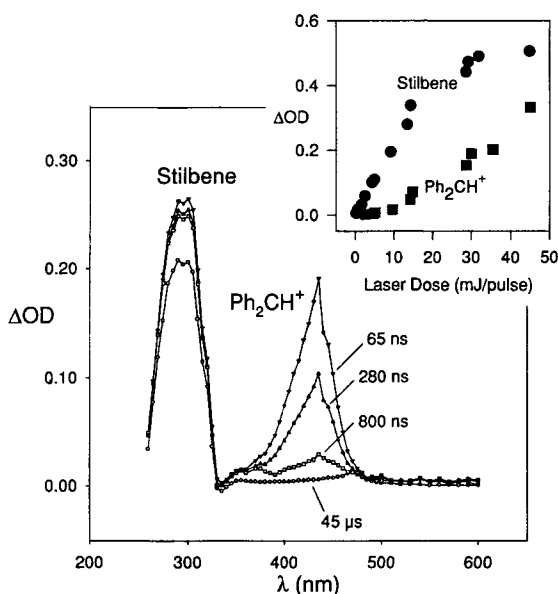
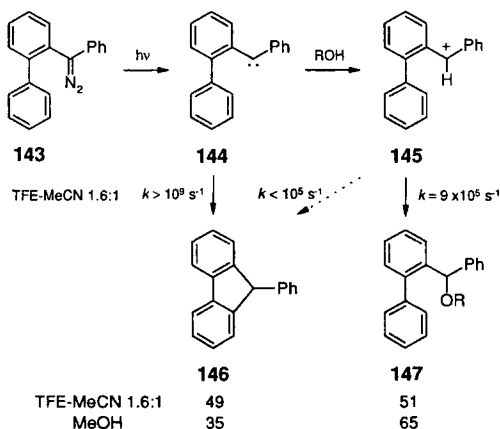


Figure 1. Time-dependent absorption spectra obtained after laser excitation (248 nm, 20 ns) of benzophenone (*trans*-2,3-diphenylaziridin-1-yl)imine (**134d**) in oxygen-saturated TFE.⁶⁴ Inset: influence of the laser dose on the yields of stilbene (monophotonic) and diphenylmethyl cation (biphotonic).

and 2-diazo-1,2-diphenylethanone (**137d** $\rightarrow$ $\text{Ph}_2\text{C}=\text{C}=\text{O} \rightarrow \text{Ph}_2\text{C} \cdot + \text{CO}$)⁶⁴ in TFE was also found to generate **141d**. The results with non-nitrogenous precursors exclude the idea that excited diazo compounds could be involved in the formation of **141** from **138**.

Quantum yields for the formation of **141** from **138** in TFE–MeCN were estimated by transient absorption actinometry (Table 1).⁶² The data refer to solvated carbocations (**141**) since ion pairs (**140**) are too short-lived for detection on the ns time scale. The modest to poor yields of **141** could be due to predominant ion-pair recombination (**140** $\rightarrow$ **142**), or to parallel protonation (**139** $\rightarrow$ **140**) and insertion (**139** $\rightarrow$ **142**). Picosecond LFP studies on photoheterolyses of $\text{Ar}_2\text{CH}-\text{X}$ in MeCN revealed that the ratio of collapse to escape (k_1/k_2) for $[\text{Ar}_2\text{CH}^+ \text{X}^-]$ is slightly affected by *p*-substituents (H, Me, OMe) and by X (Cl, Br).⁶⁶ In contrast, Φ_{141} was found to increase by a factor of 17 as *p*-H (**138d**) was replaced with *p*-OMe (**138a**).⁶² Hence the ion-pair hypothesis seems difficult to reconcile with the effect of *p*-substituents on Φ_{141} , unless the strong nucleophile RO^- in **140** behaves differently from the weakly nucleophilic halide ions.

Some direct information on ion pairing comes from picosecond LFP of **138a** in ROH–MeCN mixtures.⁶⁷ In the presence of EtOH, the transient absorption of **139a**, $\lambda_{\text{max}} \approx 400$ nm, was apparent at 50 ps. At 150 ps, the 400 nm



Scheme 27.

absorption had decreased, and a new absorption, $\lambda_{\text{max}} \approx 470 \text{ nm}$, had appeared, which was assigned to **140a**. At later times, this new absorption red-shifted to 500 nm, due to the escape of **141a** from the ion pair. The estimated ratios of collapse to escape (k_1/k_2) were 91, 42, and 6 for EtOH, MeOH, and TFE, respectively. Clearly, k_1/k_2 is strongly affected by the polarity of the solvent and the nucleophilicity of the counterion. The data for TFE–MeCN, $\Phi_{141a} = 0.12$ ⁶² and $k_1/k_2 = 6$,⁶⁷ give $\Phi_{140a} = 0.84$, which compares well with $\Phi_{\text{N}_2} = \Phi_{139} = 0.78$ for **138b** and **138d**.⁶⁸ Thus, virtually complete protonation of **139a** is indicated.

The diarylcarbenes discussed so far do not undergo intramolecular reactions. By contrast, 2-biphenyl(phenyl)carbene (**144**) cyclizes to give eventually 9-phenylfluorene (**146**). In the presence of alcohols, **146** and the ethers **147** are formed competitively from **144** (Scheme 27).⁶⁹ The transient absorption of the carbocation **145** ($\lambda_{\text{max}} = 435, 525 \text{ nm}$) was detected, following LFP of **143** in TFE–MeCN. The rate of decay for **145** ($k = 9.2 \times 10^5 \text{ s}^{-1}$) was the same as that of the 4-biphenyl analogue ($k = 9.3 \times 10^5 \text{ s}^{-1}$). Solvent capture appears to be the only significant route for the decay of **145** in TFE, although cyclization occurs in more acidic conditions (e.g., on treatment of **147-OH** with concentrated sulfuric acid). The divergent intramolecular reactivities of **144** and **145** are astounding as both species feature vacant p orbitals and cyclize by analogous 4e processes (pentadienyl $\rightarrow$ cyclopentenyl).

B. Miscellaneous Arylcarbenes

Aryl(cyclopropyl)carbenes. The potential of the cyclopropyl group for conjugation⁷⁰ suggests that the nucleophilicity of carbenes should not be strongly

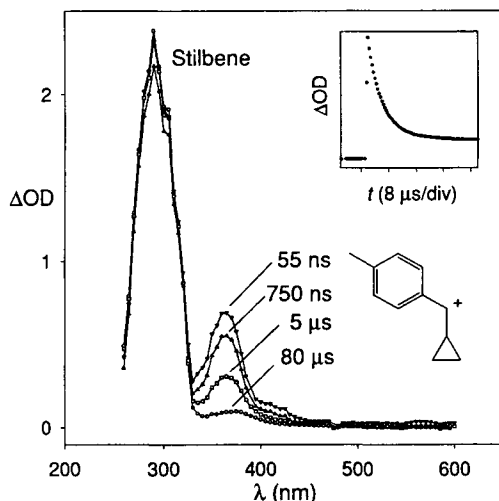
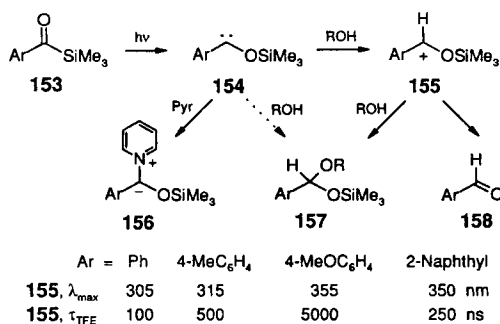
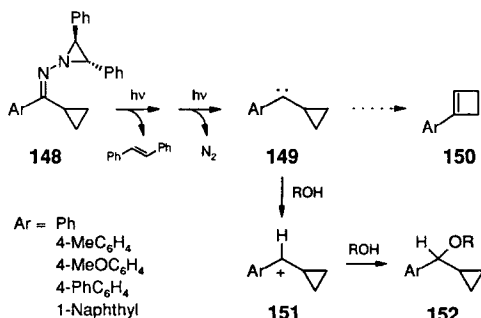


Figure 2. Time-dependent absorption spectra obtained after laser excitation (248 nm, 20 ns, 95 mJ/pulse) of **148** (Ar = 4-MeC₆H₄) in oxygen-saturated TFE.⁷¹ Inset: decay of the carbocation (**151**, Ar = 4-MeC₆H₄) absorption at 370 nm.

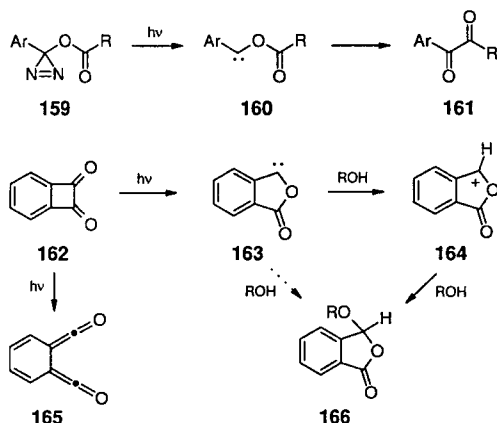
affected by replacing phenyl with cyclopropyl. In view of the rapid decay of aryl(cyclopropyl)diazomethanes in protic solvents, the carbenes **149** were generated from the aziridinylienes **148** (Scheme 28).⁷¹ Under aprotic conditions, the rearrangement of **149** to give 1-arylcyclobutenes (**150**) predominates.⁷² In the presence of alcohols, the ethers **152** (41–68%) were obtained along with minor amounts (2–9%) of **150**. LFP of **148** in TFE gave rise to transient absorption spectra of the carbocations **151** (Figure 2). The absorption maxima of **151** are blue-shifted by 75–100 nm relative to those of ArPhCH⁺ while the rates of nucleophilic capture of **151** and ArPhCH⁺ are similar in magnitude. In contrast to ArPhCH⁺, the cations **151** are not accessible by photoheterolysis of **152** (R = H, Ac). Thus carbene protonation was helpful to settle the long-standing dispute on the cation stabilizing abilities of cyclopropyl and phenyl groups.⁷⁰

Aryl(trimethylsiloxy)carbenes. Acylsilanes (**153**) undergo a photoinduced C → O silyl shift leading to aryl(trimethylsiloxy)carbenes (**154**).^{73,74} The carbenes **154** can be captured by alcohols to form acetals (**157**)⁷³ or by pyridine to give transient ylides (Scheme 29).⁷⁵ LFP of **153** in TFE produced transient absorptions of the carbocations **155** which were characterized by their reactions with nucleophiles.⁷⁶ The cations **155** are more reactive than ArPhCH⁺, but only by factors < 10. Comparison of **154** and **155** with Ar(RO)C: and Ar(RO)CH⁺, respectively, would be of interest. Although LFP was applied to generate methoxy(phenyl)carbene and to monitor its reaction with alcohols,⁷⁷ no attempt was made to detect the analogous carbocation.



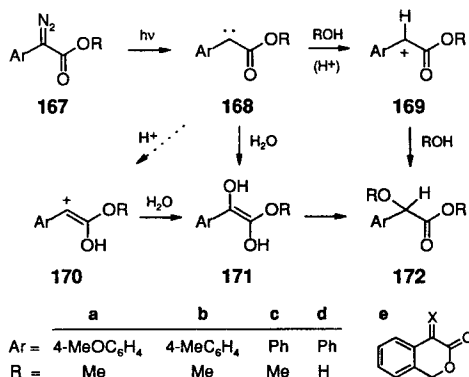
Acyloxy(aryl)carbenes. Various carbenes of the general structure **160** have been generated from diazirine precursors (**159**).⁷⁸ LFP studies with **160** did not include O–H insertion reactions but focused on the acyl shift leading to 1,2-diketones, **160** → **161** (Scheme 30). The reverse rearrangement, 1,2-diketone → acyloxycarbene, was induced by photoexcitation of benzocyclobutenedione (**162**). The carbene **163** was trapped with alcohols as well as alkenes.⁷⁹ Two processes were found to compete in the LFP of **162**.⁸⁰ One leads to formation of the long-lived bisketene **165** (λ_{max} = 380 nm). The other process generates the oxacarbene **163** which was monitored indirectly, using adamantanethione or pyridine as probes. In the presence of alcohols, a short-lived intermediate (λ_{max} ≈ 370 nm, τ = 400 ns in 6 M MeOH–MeCN) was observed, in addition to **165**. Assignment of the short-lived component as the carbocation **164** is supported by rapid reactions with anionic nucleophiles (bromide and azide). However, **164** was not detected in TFE, which is the preferred solvent for related carbocations, such as **155**.

Aryl(carbonyl)carbenes. The mechanism of proton transfer to the carbenes **168** was found to respond sensibly to the ΔpK_a of the reactants. LFP of **167a** generated **168a** (λ_{max} = 355 nm) whose absorption was quenched rapidly by



Scheme 30.

the addition of low concentrations of perchloric acid in MeCN with 1.0 M water.⁸¹ Concomitant with the acid quenching was the formation of a transient, $\lambda_{\max} = 325$ nm, which was assigned to the carbocation **169a** (Scheme 31). In neat water or TFE, the 325 nm transient was the only species observed, with lifetimes of 50 and 5900 ns, respectively. These lifetimes decreased rapidly upon the addition of nucleophiles such as methanol ($k_{\text{MeOH}} = 3 \times 10^6 \text{ M}^{-1} \text{ s}^{-1}$) and bromide ($k_{\text{Br}^-} = 6.0 \times 10^9 \text{ M}^{-1} \text{ s}^{-1}$). The rate of decay in 1 : 1 TFE–H₂O ($k = 1.2 \times 10^7 \text{ M}^{-1} \text{ s}^{-1}$) was close to the rate ($k = 1.4 \times 10^7 \text{ M}^{-1} \text{ s}^{-1}$) estimated for **169a** by an indirect method (“azide clock”).⁸² The more reactive cations **169b** ($\lambda_{\max} = 335$ nm) and **169c** ($\lambda_{\max} = 330$ nm) were not detected in the presence of water but could be readily observed in HFIP.⁸¹ Flash photolysis of **167c–e** in aqueous solution gave rise to longer-lived transients which were identified as the enols **171** by characteristic rate-pH profiles for ketonization (**171** → **172**).⁸³



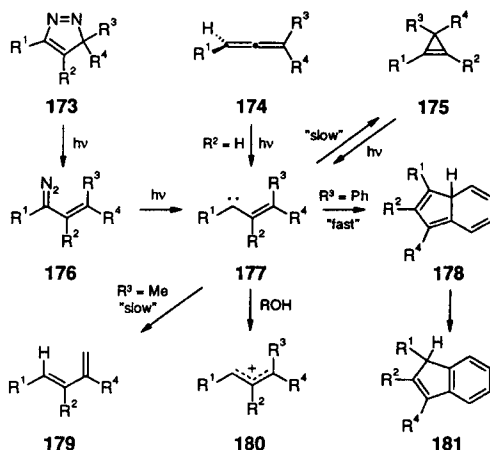
Scheme 31.

Acid catalysis was observed in the formation of **171** from **168**, and the enol cation **170** was proposed as an (invisible) intermediate.^{83c}

C. Vinylcarbenes

Allylic cations (**180**) were observed as transients following LFP of 3*H*-pyrazoles (**173**) in protic media.^{18,84} Photolysis of **173** is known to generate vinylcarbenes (**177**) by way of diazoalkenes (**176**) (Scheme 32).⁸⁵ Accordingly, the cations **180** were found to arise from **173** in biphotonic processes. The protonation of **177** competes with 1,3-cyclization to give cyclopropenes (**177** → **175**) and 1,4-H shifts from *Z*-3-Me groups (**177** → **179**). On the other hand, protonation of **177** is slow relative to 1,5-cyclization with *Z*-3 phenyl groups ($R^3 = \text{Ph}$), which leads to indenenes (**177** → **178** → **181**). Thus, **173a** afforded ethers which are derived from **180a** but not from the geometric isomer ($R^3 = \text{Ph}$, $R^4 = \text{Me}$). Analogous observations were made with **173d** and **173e**. Therefore, the transient absorption spectra were assigned to the cations **180a,d,e**, respectively, bearing Ph in the *E*-3 position. With $R^3 = R^4 = \text{Ph}$, no evidence for the intervention of an allylic cation was obtained.

Allylic cations (**180**) were also generated by LFP of allenes (**174**) in TFE.⁸⁶ Deuterium labels revealed that the cations **180** originate predominantly from vinylcarbenes (**177**), which are formed from **174** by way of a 1,2-H shift. Protonation at the central carbon of the photoexcited allenes⁸⁷ is a minor reaction path with **174a,b,d**. Vinylcarbenes are also known to arise in photolyses of cyclopropenes, **175** → **177**.^{85b,88} However, LFP of **175** in protic media proved to be rather inefficient in generating allylic cations, presumably due to low quantum yields.



Scheme 32.

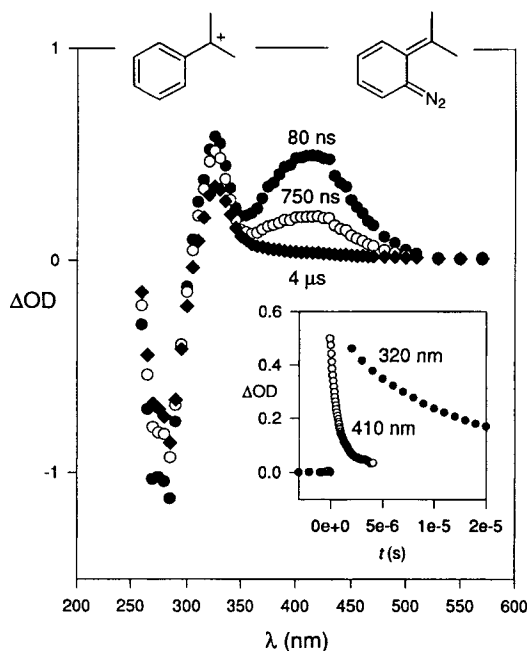
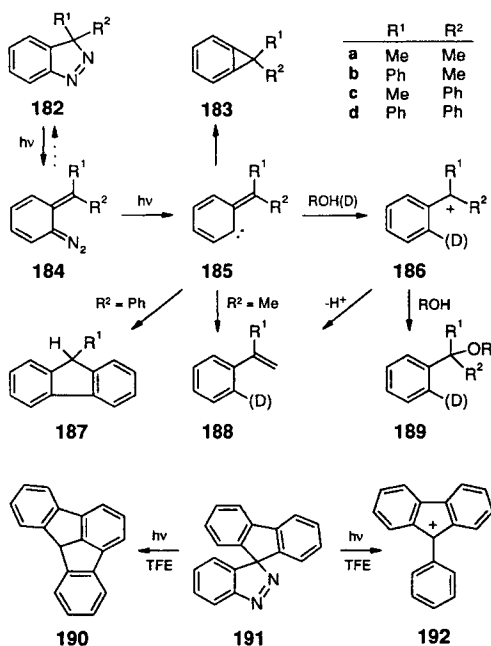


Figure 3. Time-dependent absorption spectra obtained after laser excitation (248 nm, 20 ns, 110 mJ/pulse) of 3,3-dimethyl-3*H*-indazole (**182a**) in oxygen-saturated HFIP.⁹⁰ Inset: decay of the diazo compound **184a** (at 410 nm) and of the cumyl cation **186a** (at 320 nm).

Photolyses of 3*H*-indazoles (**182**) afford products (**183**, **187**, **188**) that are indicative of 2-methylene-3,5-cyclohexadienylidenes (**185**) as intermediates (Scheme 33).⁸⁹ In the presence of alcohols, benzylic ethers (**189**) were obtained as additional products. With ROD, the *ortho* position of **189** was fully deuterated.⁹⁰ Following LFP of **182a** in HFIP, the diazo compound **184a** ($\lambda_{\text{max}} = 410$ nm) and the cumyl cation (**186a**, $\lambda_{\text{max}} = 325$ nm) were observed as transients (Figure 3). The photolysis of **182b** = **182c** is thought to proceed by a mixture of the isomeric carbenes **185b** ($\rightarrow$ **188b** + **189b**) and **185c** ($\rightarrow$ **187c**). Employing LFP of **182b,c** in TFE, a transient cation ($\lambda_{\text{max}} = 430$ nm) was detected and assigned as **186b**. Rapid 1,5-cyclization, eventually leading to 9-phenylfluorene (**187d**), was found to preclude protonation of the carbene **185d**. By contrast, photolysis of **191** in TFE gave rise to the 9-phenylfluorenyl cation (**192**, $\lambda_{\text{max}} = 490$ nm) along with the hydrocarbon **190**. Due to the ring strain of **190**, the cyclization of the intervening carbene appears to be retarded. Thus protonation is reestablished as a competing reaction path.



Scheme 33.

IV. KINETIC EVIDENCE FOR CARBENE PROTONATION

Proton transfer to carbenes is indicated by the following kinetic data: (i) the rates of X–H insertion reactions increase with increasing acidity of the proton donor HX; (ii) “normal” deuterium kinetic isotope effects are observed, $k_{\text{HX}} > k_{\text{DX}}$; (iii) alcohols react faster than ethers. However, mechanistic conclusions cannot be drawn from rates that are close to the diffusion limit. Thus, $k_{\text{HX}} \approx k_{\text{DX}}$ and $k_{\text{ROH}} \approx k_{\text{ROR}}$ argue against carbene protonation, and for the ylide mechanism, if $k \leq 10^8 \text{ M}^{-1} \text{ s}^{-1}$, but not if $k \geq 10^9 \text{ M}^{-1} \text{ s}^{-1}$.

Rate measurements are straightforward if the carbenes can be monitored directly. As a rule, the decay of carbene absorption is (pseudo) first-order, due to rearrangement and/or reaction with the solvent. In the presence of a quencher, the decay is accelerated (Eq. 1), and the rate constant k_q is obtained from a plot of k_{obs} versus $[Q]$. Curved plots were often observed with proton donors (HX) as quenchers, particularly for high concentrations of weakly acidic alcohols. Although these effects have been attributed to oligomerization of the alcohols,⁹¹ the interpretation of curved plots remains a matter of dispute.⁷⁶ Therefore, the rate constants reported in Tables 2–4 are taken from linear (regions of) k_{obs} –HX plots, or refer to a specified concentration of HX.

$$k_{\text{obs}} = k_0 + k_q[Q] \quad (1)$$

Table 2. Relative Rates of Singlet Carbenes Obtained by Stern–Volmer Methods

Carbene	Solvent	Y:	Reactant	$k_q\tau$	Ref.
$\text{H}-\ddot{\text{C}}-\text{H}$	MeCN	MeCN	MeOH	1.89	94
			MeOD	1.49	
			CD_3OD	1.53	
			Et_2O	1.21	
			THF	1.12	
$\text{H}-\ddot{\text{C}}-\text{CO}_2\text{Et}$ 193	Me_2CO	Me_2CO	<i>i</i> -PrOH	0.10	95
			MeOH	0.09	
			MeOD	0.10	
			Et_2O	0.17	
			THF	0.19	
 194	EtOAc	EtOAc	<i>i</i> -PrOH	2.5	96
			MeOH	3.4	
			TFE	5.0	
			HFIP	8.8	
			THF	0.73	
$\text{H}-\ddot{\text{C}}-\text{Ph}$ 117	MeCN	MeCN	<i>i</i> -PrOH	2.7	97
			EtOH	7.8	
			MeOH	11.9	
			MeOD	4.3	
			TFE	27.7	
$\text{H}-\ddot{\text{C}}-\text{C}_6\text{F}_5$ 195	MeCN	MeCN	<i>i</i> -PrOH	1.05	97
			EtOH	1.99	
			MeOH	3.58	
			MeOD	1.29	
			TFE	4.04	
$\text{Ph}-\ddot{\text{C}}-\text{OSiMe}_3$ 154	Cyclohexane	6.2 M Py	<i>i</i> -PrOH	2.1	75
			EtOH	2.7	
			EtOD	1.4	
			MeOH	4.4	
			MeOD	1.7	
			TFE	23.4	
			HFIP	13.6	

Spectroscopically “invisible” carbenes can be monitored by the “ylide method”.⁹² Here, the carbene reacts with a nucleophile Y: to form a strongly absorbing and long-lived ylide, competitively with all other routes of decay. Although pyridine (Py) stands out as the most popular probe, nitriles and thiones have also been used. In the presence of an additional quencher, the observed pseudo-first-order rate constant for *ylide formation* is given by Eq. 2.^{92,93} A plot of k_{obs} vs. $[\text{Q}]$ at constant $[\text{Y}]$ will provide k_q . With $\text{Q} = \text{HX}$, complications can arise from protonation of Y: and/or the derived ylides. The available data indicate that *alcohols* are compatible with the pyridine-ylide probe technique.

Table 3. Absolute Rate Constants for Reactions of Singlet Carbenes with Proton Donors

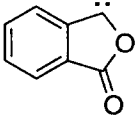
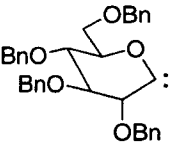
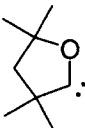
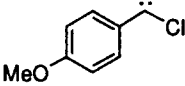
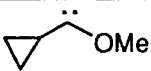
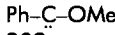
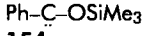
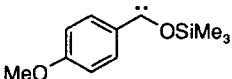
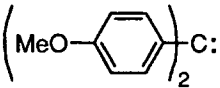
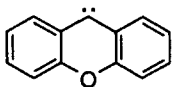
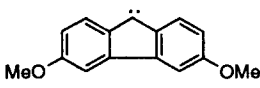
Carbene	Solvent	Species monitored	Reactant	k_q ($M^{-1} s^{-1}$)	Ref.
$F-\ddot{C}-OMe$ 196	MeCN	Carbene	HFIP (1 M)	9.1×10^3	99
			AcOH (1 M)	2.0×10^7	
	Pentane		AcOH	1.7×10^7	
			AcOD	8.7×10^6	
$MeO-\ddot{C}-OMe$ 197	MeCN	Carbene	EtOH (1 M)	3.2×10^4	99
			MeOH (1 M)	8.8×10^4	
			Cl(CH ₂) ₂ OH (1 M)	9.1×10^5	
			F(CH ₂) ₂ OH (1 M)	2.3×10^6	
			TFE (1 M)	6.3×10^7	100
			HFIP (1 M)	6.7×10^8	
			HOAc (1 M)	2.4×10^9	
	Pentane		MeOH	6.36×10^6	
			MeOD	1.95×10^6	
			AcOH	2.91×10^9	
			AcOD	2.84×10^9	
	Toluene	Py-Ylide	<i>i</i> -PrOH	1.7×10^5	80
			EtOH	3.5×10^5	
			MeOH	3.6×10^5	
		R ₂ C=S-Ylide	TFE	1.2×10^8	
	MeCN	Py-Ylide	EtOH	1.2×10^6	101
			MeOH	1.3×10^7	
			TFE	6.9×10^8	
			HFIP	2.9×10^9	
	MeCN	Carbene	TFE	6.4×10^8	102c
			HFIP	2.6×10^9	
			HClO ₄	7.3×10^9	
$Ph-\ddot{C}-Cl$ 200	MeCN	Carbene	AcOH	1.8×10^9	91b
			CF ₃ CO ₂ H	2.4×10^9	59b
	Isooctane		2,3-Butanediol	5.4×10^7	
	MeCN	Carbene	MeOH	6.5×10^6	91
			AcOH	2.2×10^9	
	Isooctane		<i>t</i> -BuOH	2.3×10^8	
			AcOH	5.1×10^9	

Table 3. (continued)

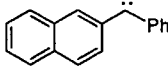
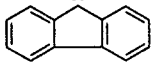
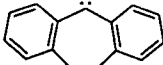
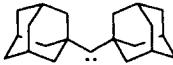
Carbene	Solvent	Species monitored	Reactant	k_q ($M^{-1} s^{-1}$)	Ref.
 202	Pentane	Carbene	MeOH	2.1×10^8	103
 203	Pentane	Carbene	<i>t</i> -BuOH	2.7×10^8	77
 154a	MeCN	Carbene	H ₂ O MeOH TFE HFIP AcOH	9.3×10^7 3.0×10^8 1.5×10^9 1.6×10^9 1.1×10^9	76
 154c	MeCN	Carbene	H ₂ O MeOH TFE HFIP AcOH	1.0×10^8 3.8×10^8 1.5×10^9 1.6×10^9 1.0×10^9	76
 129d	MeCN	Triplet carbene	2-Pentanol MeOH MeOH	2.0×10^9 5.0×10^9 3.0×10^9	58a
 139a	MeCN	Carbene	<i>t</i> -BuOH EtOH MeOH	6.0×10^8 2.8×10^9 4.7×10^9	67
 139l	Pentane	Carbene	<i>t</i> -BuOH EtOH	3.4×10^9 5.1×10^9	104
 139g	Benzene	Carbene	<i>t</i> -BuOH MeOH MeOD	4.1×10^9 5.6×10^9 4.8×10^9	105

However, care should be exercised with more acidic proton donors.

$$k_{\text{obs}} = k_o + k_y[Y:] + k_q[Q] \quad (2)$$

If the growth of ylide absorption is too fast to be monitored, *relative* rates can still be obtained by a Stern–Volmer approach, Eq. 3. The yield of ylide, measured as the change in optical density (ΔOD), decreases in the presence of

Table 4. Mechanistically Relevant Rates of Spin-Equilibrated Carbenes

Carbene	Solvent	Species monitored	Reactant	$k_q K$ ($M^{-1} s^{-1}$)	Ref.
Ph ₂ C: 139	PhCl	Carbene	MeOH	2.8×10^7	59a
			Et ₂ O	7.1×10^4	112
	Benzene		MeOH	2.0×10^7	59a
			THF	1.4×10^5	113
 205	Benzene	Carbene	MeOH	3.0×10^7	114
			MeOD	2.2×10^7	
 139k	C ₆ F ₆	Carbene	MeOH	6.3×10^8	115
			MeOD	4.6×10^8	
			CD ₃ OH	7.5×10^8	
			CD ₃ OD	5.3×10^8	
	MeCN		<i>t</i> -BuOH	1.6×10^8	116
			<i>t</i> -BuOD	4.2×10^7	
 206	Toluene	Carbene	MeOH	2.5×10^6	117
	Benzene		THF	8.8×10^4	
 207	Cyclohexane	Carbonyl oxide	MeOH	2.0×10^7	118
			TFE	1.7×10^8	

a carbene quencher. By plotting $1/\Delta OD$ as a function of $[Q]$, the ratio k_q/k_y $[Y:]$ can be derived. This ratio corresponds to the $k_q \tau$ term of the Stern–Volmer equation. Here, τ is the lifetime of the carbene in the absence of Q . By means of $k_q \tau$, the reactivity of an individual carbene toward various proton donors can be established, but different carbenes cannot be compared.

$$\frac{\Delta OD_0}{\Delta OD} = 1 + \frac{k_q [Q]}{k_y [Y:]} = 1 + k_q \tau [Q] \quad (3)$$

A. Singlet Carbenes

Relative rates of some prototypical carbenes, obtained by Stern–Volmer methods, are listed in Table 2. Although many of these carbenes have triplet ground states, reaction with nucleophiles $Y:$ occurs prior to spin equilibration. Most often, ylide formation with solvent molecules was analysed in terms of Eq. 3. The pyridine-ylide served as the probe for **154**.

The results for methylene confirm the indiscriminate nature of the parent carbene. A small deuterium isotope effect is apparent for MeOH vs. MeOD,

but similar reaction rates with alcohols and ethers point to carbene attack at oxygen.⁹⁴ Ethoxycarbonylcarbene (**193**) and tetrachlorocyclopentadienylidene, both strongly electrophilic species, were found to react faster with ethers than with alcohols.^{95,96} The reverse holds for cyclopentadienylidene (**194**) and fluorenylidene which also show a slight increase in rate with increasing acidity of the alcohol.⁹⁶ Substantial rate enhancements (*i*-PrOH : EtOH : MeOH : TFE = 1 : 2.9 : 4.4 : 10.3) and a sizeable isotope effect ($k_{\text{MeOH}}/k_{\text{MeOD}} = 2.8$) were observed for phenylcarbene (**117**).⁹⁷ The kinetic data corroborate the proton transfer to phenylcarbene (Section II.C). The rate enhancement, but not the isotope effect, is attenuated by replacing the phenyl group with pentafluorophenyl (**195**).⁹⁷ Interestingly, the response of phenyl(trimethylsiloxy) carbene (**154**) to the acidity of ROH is about the same as that of **117**,⁷⁵ although the benzyl cation (**118**, $k_{\text{HFIP}} > 10^6 \text{ s}^{-1}$)⁹⁸ is less stable than the phenyl(trimethylsiloxy)carbenium ion (**155**, $k_{\text{HFIP}} = 10^4 \text{ s}^{-1}$).⁷⁶ The reaction rate of **154**, as estimated by the Stern–Volmer method, *decreases* from TFE to HFIP. Direct monitoring of **154** did not confirm this effect (see Table 3).⁷⁶ For the pyridine-ylide technique, HFIP ($\text{p}K_{\text{a}} = 9.3$) may be too acidic to give reliable results.

Absolute rate constants for reactions of singlet carbenes with proton donors were obtained from the rates of decay of the carbenes (Eq. 1), or from the rates of ylide formation (Eq. 2). In the case of diphenylcarbene, the growth of the triplet absorption was monitored.⁵⁸ In Table 3, the carbenes are arranged in the order of increasing reactivity. Fluoro(methoxy)carbene (**196**) proved to be surprisingly “inert” to alcohols.⁹⁹ Methanol and TFE failed to quench the carbene at 1 M ROH in MeCN. Nevertheless, the increase in rate from HFIP to HOAc, and a significant isotope effect ($k_{\text{AcOH}}/k_{\text{AcOD}} = 1.95$), argue in favor of proton transfer from acidic donors. The reactivity of dimethoxycarbene (**197**) with alcohols spans four orders of magnitude.⁹⁹ A sizeable isotope effect was observed with MeOH ($k_{\text{MeOH}}/k_{\text{MeOD}} = 3.3$) but not with AcOH whose rate of reaction is close to the diffusion limit. Since some of the data were taken from curved plots, the apparent solvent effect (MeOH in MeCN *vs.* MeOH in pentane) should not be overstressed. The alkoxy(alkyl)carbenes **198** and **199** are clearly more reactive than **197**. The glycosylidene **198** was generated from a diazirine precursor and studied by means of the pyridine-ylide technique.¹⁰¹ Photochemical ring expansion of 2,2,4,4-tetramethylcyclobutanone led to **199**,^{102a} which was monitored directly ($\lambda_{\text{max}} = 360 \text{ nm}$).^{102b} In spite of the different experimental methods, the reaction rates of **198** and **199** with TFE agree closely (the reaction rates with MeOH cannot be compared as **199** gave a curved plot).^{102c}

Linear dependencies of k_{obs} on [ROH] are also rare for the aryl(chloro)carbenes **200** and **201**;⁹¹ hence the “ranking” of these carbenes is somewhat uncertain. The aryl(oxy)carbenes **203**, **154a**, and **154c** are clearly superior to their alkyl(oxy) counterparts (**198**, **199**) as proton acceptors.^{76,77} The 4-OMe

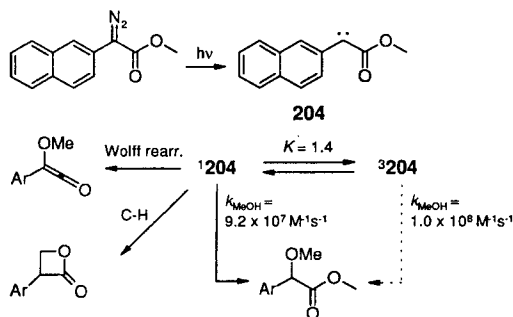
group of **154c** does not significantly enhance the reactivity relative to **154a**, although the rates for water and MeOH do not approach the diffusion limit. Diarylcarbenes (**139**) rank at the upper end of the reactivity scale. Even the rate constant for the reaction of diphenylcarbene (**139d**) with methanol is close to diffusion-controlled.^{58a} Therefore, electron donation to the aryl rings, as in **139a**,⁶⁷ **1**,¹⁰⁴ and **g**,¹⁰⁵ is anticipated (and found) to be without effect. The carbenes **139i** and **139g** have singlet ground states, in contrast to **139a** and **139d**. Monitoring of ¹**139a**, prior to spin inversion, was achieved on the ps time scale,⁶⁷ while k_q for ¹**139d** was derived from the growth of ³**139d**.^{58a} The close agreement of the data attests to the reliability of these diverse methods. However, as pointed out above, diffusion-controlled rates provide little mechanistic insight.

For carbenes reacting with alcohols by way of proton transfer, the rate constants would be expected to correlate with proton affinities, which measure the thermodynamic driving force for protonation in the gas phase. Unfortunately, *experimental* proton affinities (see Section IV) are available only for carbenes that have not been studied kinetically, with the exception of dimethoxycarbene. However, the order of reactivities, $\text{F(MeO)C:} < (\text{MeO})_2\text{C:} < \text{Ph}_2\text{C:}$, is consistent with the *computed* proton affinities for F(HO)C: (199.3 kcal/mol), $(\text{HO})_2\text{C:}$ (217.3 kcal/mol), and $\text{Ph}_2\text{C:}$ (275.0 kcal/mol).¹⁰⁶ The reaction rates of carbene protonation do *not* correlate with the stabilities of the resulting carbocations. The cation stabilizing ability of methoxy groups exceeds that of phenyl groups.¹⁰⁷ Yet the order of carbene reactivities is $(\text{MeO})_2\text{C:} < \text{R(MeO)C:} < \text{Ph(MeO)C:} < \text{Ph}_2\text{C:}$ (Table 3). Moreover, methoxy groups in the 4-position strongly affect the rates and equilibria of arylcarbenium ions,^{60,108} but not those of arylcarbenes.

The reactivities of carbenes toward alkenes have been correlated with the inductive and resonance effects of the carbene substituents, $\log k = a\Sigma\sigma_I + b\Sigma\sigma_{R+} + c$.¹⁰⁹ Analogous correlations cannot be obtained for the reaction rates of carbenes with alcohols, neither with the substituent parameters used by Moss,¹⁰⁹ nor with related sets.¹¹⁰ In particular, the substituent parameters do not describe the strong, rate-enhancing effect of aryl groups. For a detailed analysis, see the discussion of proton affinities (Section V.A).

B. Spin-Equilibrated Carbenes

Triplet arylcarbenes have long been thought to react with alcohols by way of their singlet counterparts (pre-equilibrium mechanism).^{13,56} This notion was recently supported in a series of papers on methoxycarbonyl(2-naphthyl)carbene (**204**).¹¹¹ The spin states of **204** are nearly degenerate, with the triplet slightly favored ($K_{ST} = 1.4$, $\Delta G_{ST} = 0.2$ kcal/mol at 21°C). The planar triplet and the twisted singlet state of **204** show distinct IR spectra. Time-resolved IR studies revealed that ¹**204** and ³**204** were quenched by methanol at the same rate,



Scheme 34.

within experimental error (Scheme 34).^{111b} Obviously, the singlet–triplet spin equilibration of **204** is rapid relative to the reaction with methanol.

For a spin-equilibrated carbene, the effect of a *singlet* quencher on the rate of *triplet* decay, k_{obs} , is given in Eq. 4; $K = [\text{S}]/[\text{T}]$ is the equilibrium constant. “Invisible” triplets can be trapped with oxygen to give strongly absorbing carbonyl oxides. The rate of *formation* of the carbonyl oxide, k_{obs} , is given in Eq. 5. As a rule, saturated solutions of oxygen in organic solvents were employed to keep $[\text{O}_2]$ constant. Under these conditions, $k_q K$ can be obtained by plotting k_{obs} vs. $[\text{Q}]$.

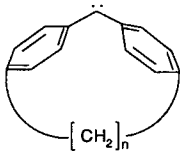
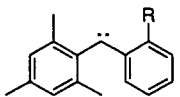
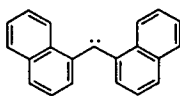
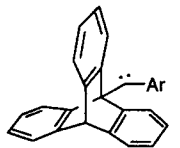
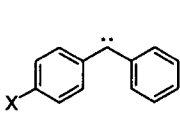
$$k_{\text{obs}} = k_0 + k_q K [\text{Q}] \quad (4)$$

$$k_{\text{obs}} = k_0 + k_{\text{ox}} [\text{O}_2] + k_q K [\text{Q}] \quad (5)$$

If the reaction rates of a specific carbene with various quenchers are studied in the same solvent, and with small concentrations of Q, K will be constant. Relative reactivities for the singlet state of a spin-equilibrated carbene can thus be derived. However, few researchers have varied the acidity of ROH, estimated kinetic isotope effects, and compared alcohols with ethers (Table 4). The data indicate proton transfer to diarylcarbenes (**139d**, **139k**, **205**, **206**)^{112–117} and diadamantylcarbene (**207**).¹¹⁸

If the singlet reaction rates are close to the diffusion limit ($k_q \approx \text{constant}$), as appears to be the case for many diarylcarbenes, the only variable will be K . Factors influencing the singlet–triplet equilibrium can thus be examined (Table 5). Contraction of the carbene bond angle is expected to narrow the singlet–triplet gap, relative to diphenylcarbene (**139d**). For experimental verification, the cyclophane-derived carbenes **208** were studied, that is, the 4,4′-positions of diphenylcarbene were connected by a polymethylene chain. As the “tether” is shortened, $k_q K$ increases.¹¹⁹ Conversely, repulsive interaction of *ortho* substituents, as in **209**, leads to expansion of the bond angle,

Table 5. Rate Constants for Reactions of Triplet Diarylcarbenes with Methanol

Carbene	Solvent	$k_q K$ ($M^{-1} s^{-1}$)	ΔG_{ST}^a (kcal/mol)	Ref.
Ph ₂ C: 139d	Isooctane	6.4×10^6	3.9	59a
	Benzene	2.0×10^7	3.3	
	PhCl	2.1×10^7	3.2	
	MeCN	2.2×10^7	3.2	
	THF	6.3×10^6	3.9	119
	THF	2.0×10^8	1.9	119
208		2.1×10^8	1.8	
		6.8×10^8	1.2	
		2.0×10^9	0.5	
	Isooctane	8.2×10^4	6.5	120
209		2.1×10^4	7.3	
	Benzene	3.1×10^5	5.7	121
210				
	Benzene	3.2×10^5	5.7	121
211		2.1×10^5	6.0	
		1.2×10^4	7.7	
	Cyclohexane	1.2×10^7	3.6	123
212		7.9×10^6	3.8	
		1.3×10^6	4.9	
		8.7×10^5	5.1	

Note: ^a Assuming $k_q = 5 \times 10^9 M^{-1} s^{-1}$.

with concomitant decrease of $k_q K$.¹²⁰ Analogous observations were made with di(1-naphthyl)carbene (**210**) and aryl(9-trypticyl)carbenes (**211**).¹²¹ Quenching of triplet dimesitylcarbene with alcohols does not compete detectably with dimerization while the singlet state reacts rapidly with methanol ($k > 2 \times 10^7 M^{-1} s^{-1}$).¹²² The results imply that the singlet–triplet gap is substantially greater for dimesitylcarbene than for the diarylcarbenes in Table 5. Modest rate effects

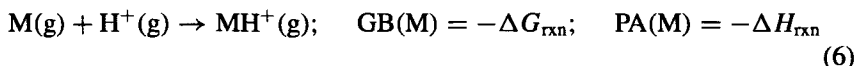
were found with p acceptor substituents in the 4-position of diphenylcarbene, as illustrated by **212**. These groups help to delocalize an unpaired electron of the triplet carbene while destabilizing the singlet state; k_qK varies accordingly.¹²³ However, substituent effects on k_q , although unlikely (see Section IV.A), cannot be excluded.

V. BASICITY OF CARBENES

Considering the abundant evidence for carbene protonation, some quantitative estimate for the base strength of carbenes is clearly desirable. The conventional spectrometric or potentiometric methods of determining the pK_a in solution are not applicable, with the exception of some onium ions **1** and their conjugate bases **2** (Section V.B). In favorable cases, equilibria of carbenes with the conjugate carbenium ions have been studied in the gas phase. Proton affinities of various carbenes can be obtained from their enthalpies of formation, and by *ab initio* computation (Section V.A). Kinetic data have been evaluated to obtain the pK_a of carbenes in solution (Section V.B).

A. Gas Phase Basicities and Proton Affinities

The gas phase basicity (GB) of a species M is the negative of the Gibbs free energy change for the hypothetical gas phase protonation reaction of M, Eq. 6. The proton affinity (PA) is the negative of the corresponding enthalpy change. The relationship between gas basicity and proton affinity is given in Eq. 7, where ΔS_p is the entropy of protonation of M.



$$GB(M) = PA(M) + T \Delta S_{rxn} = PA(M) + T[\Delta S_p(M) - S(H^+)] \quad (7)$$

The gas phase basicity of M is obtained experimentally by investigating proton transfer equilibria, Eq. 8, between M and reference species R whose gas phase basicities have been established.¹²⁴ The ratio of the ions MH^+ and RH^+ can be measured using an ion cyclotron resonance spectrometer (ICR), a high pressure mass spectrometer (HPMS), or a flowing afterglow apparatus (FA, 100–1000 Pa). For elusive species, upper and lower bounds of the basicity can be estimated through a technique known as “bracketing”. If proton transfer occurs from MH^+ to R_1 , but does not occur from MH^+ to R_2 , the basicity of M is taken to be between the basicities of R_1 and R_2 . The bracketing technique was applied to a series of halocarbenes, $MH^+ = CXYH^+$ (Table 6).¹²⁵ The *relative* gas basicities thus derived lead to *relative* proton affinities if the entropy change of reaction 8 is known (from measurements of K over a wide temperature range)

Table 6. Experimental Gas Phase Basicities (GB) and Proton Affinities (PA) of Carbenes and Reference Compounds (298 K)

Carbene	Method ^a	GB (kcal/mol)	PA (kcal/mol)	Ref.
:CF ₂	bracketing	163 ^b	(171) ^d	125
:CClF	bracketing	177 ^b	(185) ^d	125
:CCl ₂	bracketing	183 ^b	(191) ^d	125
	bracketing	203 ^b	(211) ^d	126
:CHF	bracketing	183 ^b	(191) ^d	125
:CHCl	bracketing	201 ^b	(209) ^d	125
	threshold	(220) ^c	227	127
CH ₂ O		163	170	124
(CH ₃) ₂ O		183	189	124
NH ₃		196	204	124
(CH ₃) ₃ N		219	227	124
(Me ₂ N) ₂ C=NMe		243	250	124

Notes: ^a See text.^b Evaluated gas phase basicities from Ref. 124 were used for the bracketing compounds given in Ref. 125.^c Calculated from the PA by means of Eq. 7, using ΔS_p from Ref. 124.^d Calculated from the GB by means of Eq. 7, using ΔS_p from Ref. 124. The results differ slightly from the data reported in Ref. 125.

or can be reliably estimated (from statistical mechanics treatments or *ab initio* computations).¹²⁴



Alternatively, the translational energy threshold for endothermic proton transfer from MH^+ to R can be measured using a flowing afterglow triple quadrupole instrument.¹²⁷ These data define the proton affinity of M, relative to that of R. Thus, the PA of cyclopropenylidene was found to exceed that of ammonia by 23.3 ± 1.8 kcal/mol (Table 6).¹²⁸ In order to obtain *absolute* proton affinities, the enthalpies of formation of both the base and the conjugate acid must be known from other measurements (Eq. 9). Numerous reference compounds with known absolute PA are available.¹²⁴

$$PA(M) = \Delta H_f(M) + \Delta H_f(H^+) - \Delta H_f(MH^+) \quad (9)$$

The proton affinity of a carbene can be derived by means of Eq. 9 ($M = RR'C:$) if ΔH_f of the carbene and of the corresponding carbocation have been estimated independently (Table 7). Appearance potentials (AP) are convenient, although sometimes inaccurate, sources of $\Delta H_f(RR'CH^+)$.¹²⁹ Adiabatic ionization energies (IE_a) of free radicals, in combination with dissociation enthalpies

Table 7. Proton Affinities (PA) of Carbenes from Experimental Enthalpies of Formation^a

Carbene	ΔH_f (RR'C:)		ΔH_f (RR'CH ⁺)		PA kcal/mol
	kcal/mol	Ref.	kcal/mol	Ref.	
:CF ₂	-44.0	b	145.0	b	177
:CClF	7.4	b	187.4	b	186
:CCl ₂	55.0	b	214.2	b	206
:CHF	34.2	b	200.6	b	199
:CHCl	78.0	b	230.1	b	214
:CH ₂	102	131-133	262	139	206
:C=CH ₂	102	135	262	140	206
:C(OMe) ₂	-54	99	97	141	215
:CH-CH=CH ₂	103 ^c	133	227	142	242
:CH-Ph	107 ^d	133	215	143	258

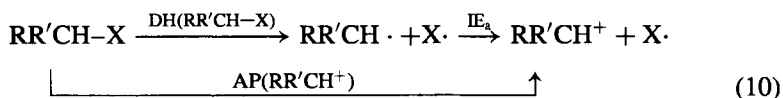
Notes: ^a Eq. 9, M = :CR'R; ΔH_f (H⁺) = 365.7 kcal/mol. All data refer to 298 K.

^b Recommended enthalpies of formation from Ref. 134b; ± 2 kcal/mol.

^c To ΔH_f (³:CH-CH=CH₂) = 93 kcal/mol was added ΔE_{ST} = 10 kcal/mol. The calculated singlet-triplet gap of 13.3 kcal/mol (B3LYP/cc-pVTZ) from Ref. 133 was corrected by 3 kcal/mol, which is the difference between the experimental and computed (B3LYP/cc-pVTZ) ΔE_{ST} for methylene.

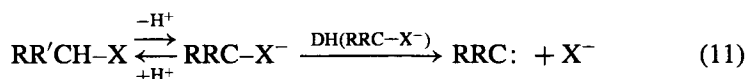
^d To ΔH_f (³:CH-Ph) = 103 kcal/mol was added ΔE_{ST} = 4 kcal/mol. The calculated singlet-triplet gap of 7.7 kcal/mol (B3LYP/cc-pVTZ) from Ref. 133 was corrected by 3 kcal/mol, which is the difference between the experimental and computed (B3LYP/cc-pVTZ) ΔE_{ST} for methylene.

(DH), are thought to provide more precise data (Eq. 10).¹³⁰

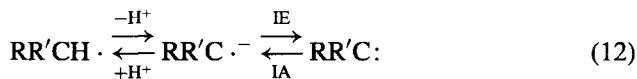


$$\begin{aligned} \Delta H_f(\text{RR'CH}^+) &= \Delta H_f(\text{RR'CH-X}) - \Delta H_f(\text{X} \cdot) + \text{AP(RR'CH}^+) \\ &= \Delta H_f(\text{RR'CH} \cdot) + \text{IE}_a(\text{RR'CH} \cdot) \end{aligned}$$

Enthalpies of formation for the singlet and triplet states of methylene were obtained from the photodissociation of ketene.¹³¹ The data for CH₂ (³B₁) were recently confirmed by methods which do not rely on ketene.^{132,133} In a widely applicable procedure, threshold collision energies for the loss of halide ion from RR'C-X⁻ were combined with gas phase acidities of RR'CH-Cl to give ΔH_f (RR'C:) (Eq. 11).¹³⁴ Similarly, gas phase acidities of the radicals RR'CH· were combined with ionization energies of the radical anions RR'C⁻, or electron affinities of the carbenes RR'C: (Eq. 12).^{135,136}



$$\begin{aligned}\Delta H_f(\text{RR}'\text{C}:) &= \text{DH}(\text{RR}'\text{C}-\text{X}^-) + \Delta H_f(\text{RR}'\text{C}-\text{X}^-) - \Delta H_f(\text{X}^-) \\ &= \text{DH}(\text{RR}'\text{C}-\text{X}^-) + \Delta H_f(\text{RR}'\text{CH}-\text{X}) + \Delta H_{\text{acid}}(\text{RR}'\text{CH}-\text{X}) \\ &\quad - \Delta H_f(\text{HX}) - \Delta H_{\text{acid}}(\text{HX})\end{aligned}$$



$$\begin{aligned}\Delta H_f(\text{RR}'\text{C}:) &= \Delta H_f(\text{RR}'\text{C} \cdot) + \text{IE}(\text{RR}'\text{C} \cdot) \\ &= \Delta H_f(\text{RR}'\text{CH} \cdot) + \Delta H_{\text{acid}}(\text{RR}'\text{CH} \cdot) - \Delta H_f(\text{H}^+) + \text{IE}(\text{RR}'\text{C} \cdot)\end{aligned}$$

The methods summarized by Eqs. 8 and 9 have both been applied to halocarbenes. The proton affinities obtained by ICR bracketing¹²⁵ (Table 6) are consistently lower than those derived from enthalpies of formation (Table 7). The case of dichlorocarbene, with a difference in ΔH_f of 15 kcal/mol), is particularly disturbing and has been analysed in some detail.^{134a} Notably, the PA of :CCl_2 from an earlier bracketing experiment¹²⁶ was closer to the enthalpy-derived PA. The discrepant results from similar experiments^{125,126} indicate that HCCl_2^+ is not a good substrate for proton transfer studies.

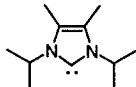
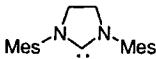
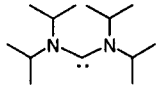
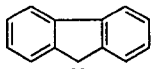
Photoacoustic calorimetry (PAC)¹³⁷ has also been utilized to probe the energetics of carbenes. If the carbene under investigation reacts “slowly” with methanol ($k < 10^5 \text{ M}^{-1} \text{ s}^{-1}$), flash photolysis of the corresponding diazo compound or diazirine in neat MeOH results in two time-resolved heat depositions that reflect carbene formation, ΔH_{dec} , and subsequent O–H insertion, ΔH_{ins} (Eq. 13). For more reactive carbenes ($k_{\text{MeOH}} > 10^6 \text{ M}^{-1} \text{ s}^{-1}$), a single heat deposition, reflecting $\Delta H_{\text{dec}} + \Delta H_{\text{ins}}$, is observed. Here, ΔH_{dec} can be extracted from the rapid heat deposition measured in acetonitrile or pentane. ΔH_{ins} is obtained as the difference of the data from protic and aprotic solvents, the neglect of solvent effects being a potential source of error. In order to derive $\Delta H_f(\text{RR}'\text{C}:)$, either $\Delta H_f(\text{RR}'\text{CN}_2)$ or $\Delta H_f(\text{RR}'\text{CH}-\text{OMe})$ is required. Most of the PAC results were combined with MNDO calculations for the ΔH_f of products.¹³⁸ While trends are disclosed by this approach, the absolute values of $\Delta H_f(\text{RR}'\text{C}:)$ are questionable and have not been compiled here. An exception is dimethoxycarbene whose thermochemistry can be based on the *experimental* ΔH_f of HC(OMe)_3 (Table 7).⁹⁹



$$\begin{aligned}\Delta H_f(\text{RR}'\text{C}:) &= \Delta H_f(\text{RR}'\text{CHN}_2) + \Delta H_{\text{dec}} \\ &= \Delta H_f(\text{RR}'\text{CH}-\text{OMe}) - \Delta H_f(\text{MeOH}) - \Delta H_{\text{ins}}\end{aligned}$$

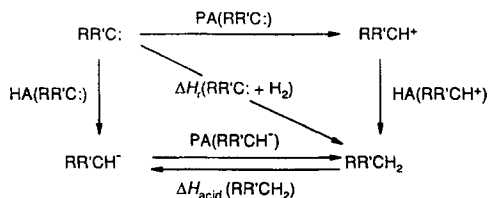
The proton affinities listed in Table 7 range from 177 kcal/mol for difluorocarbene to 258 kcal/mol for phenylcarbene. The PA of dimethoxycarbene exceeds that of methylene by only 9 kcal/mol, but vinyl or phenyl substituents

Table 8. Computed Gas Phase Basicities (GB) and Proton Affinities (PA) of Carbenes

Carbene	Method	GB (kcal/mol)	PA (kcal/mol)	Ref.
:CF ₂	G2(MP2)	170	177	106
:CF(OH)	G2(MP2)	192	200	106
:CCl ₂	G2(MP2)	202	210	106
:CH ₂	G2(MP2)	200	207	106
:C(OH) ₂	G2(MP2)	210	217	106
:C(NH ₂)OH	B3LYP/6-311G		236	144
:CH-NH ₂	RCCSD(T)		242	145
	MP2/DZ		257	146
	AM1		255	147
	AM1		252	147
	AM1		254	147
	MP2/DZ	265	272	106
:CPh ₂	MP2/DZ	267	275	106

enhance the PA strongly. While the PA of methylene is similar to that of ammonia (Table 6), phenylcarbene compares with one of the strongest nitrogen bases, pentamethylguanidine. Although experimental data are lacking for diphenylcarbene, computational studies indicate that the second phenyl group raises the PA even further.¹⁰⁶ Proton affinities from theory (Table 8) and experiment (Table 7) are in good agreement for those carbenes that have been studied in both ways. Computation also reveals that amino groups enhance the PA of carbenes more strongly than hydroxy groups.^{144–146} The much disputed “aromaticity” of imidazolylidenes (Arduengo carbenes)^{8,9} does not affect the PA as the imidazolium ions formed on protonation of these species are likewise aromatic.¹⁴⁶ The PA of diaminocarbenes, whether cyclic or acyclic, is similar to that of phenylcarbene but inferior to that of diarylcarbenes. The computed PA of Ph₂C: ranks at the top of neutral organic bases¹²⁴ (but below that of the diphenylmethyl anion, by *ca.* 90 kcal/mol).

The thermochemistry of carbenes¹⁴⁸ is summarized in Scheme 35. The enthalpy of hydrogenation, ΔH_r (RR'C: + H₂), is a measure of the ther-

**Scheme 35.**

modynamic stability of carbenes, relative to the hydrocarbons $\text{RR}'\text{CH}_2$. The acid–base (electrophilic–nucleophilic) properties of carbenes are measured by hydride affinities (HA) and proton affinities (PA), respectively. $\text{HA}(\text{RR}'\text{C:})$ is estimated from $\Delta H_f(\text{RR}'\text{C:})$ and $\Delta H_f(\text{RR}'\text{CH}^-)$, the latter being obtained from $\Delta H_f(\text{RR}'\text{CH}_2)$ and $\Delta H_{\text{acid}}(\text{RR}'\text{CH}_2)$. Aside from the trivial fact that $\text{PA}(\text{RR}'\text{C:}) + \text{HA}(\text{RR}'\text{CH}^+) = \text{HA}(\text{RR}'\text{C:}) + \text{PA}(\text{RR}'\text{CH}^-)$, the enthalpies of reaction in Scheme 35 vary independently (Table 9). $\text{PA}(\text{RR}'\text{C:})$ does not correlate with $\text{PA}(\text{RR}'\text{CH}^-)$, although in both processes the proton is accepted by a nonbonding electron pair on carbon. The divergence is particularly obvious for p-conjugated systems. Due to resonance stabilization, the PA of the benzyl anion is smaller than that of the methyl anion. In phenylcarbene, the nonbonding electron pair is situated in the plane of the benzene ring, and does not interact with the p system. The interaction of the vacant p orbital of phenylcarbene with the benzene ring involves charge *separation*, as opposed to charge *delocalization* in the case of the benzyl cation.¹⁴⁹ Hence the resonance stabilization *increases* on protonation, and the PA of phenylcarbene exceeds that of methylene.

Numerous gas phase equilibria have been analyzed in terms of substituent polarizability (σ_a), field (σ_F), and resonance (σ_{R^+}) effects.¹⁵⁰ Substituent polarizability (σ_a) accounts for short-range dipole interactions between substituent and the reaction center, which are anticipated to play an important role in car-

Table 9. Thermochemical Data for Scheme 35 (298 K, kcal/mol)

Carbene	ΔH_f ($\text{RR}'\text{CH}_2$)	ΔH_f ($\text{RR}'\text{C:} + \text{H}_2$)	HA ($\text{RR}'\text{C:}$)	ΔH_f ($\text{RR}'\text{CH}^-$)	PA ($\text{RR}'\text{CH}^-$)
:CF ₂	-108.1	64.1	75.6	-84.9	389.0
:CClF	-63.1	70.5	—	—	—
:CCl ₂	-22.9	77.9	103.8	-14.1	374.5
:CHF	-56.8	91.0	81.6	-12.7	409.0
:CHCl	-19.6	97.6	102.0	10.7	399.6
:CH ₂	-17.8	119.8	103.6	33.1	416.7
:C=CH ₂	12.5	89.5	80.5	56.2	409.4
:C(OMe) ₂	-83.2	29.2	—	—	—
:CH-CH=CH ₂	4.8	98.2	107.9	29.8	390.7
:CH-Ph	12.0	95.0	114.8	26.9	380.6

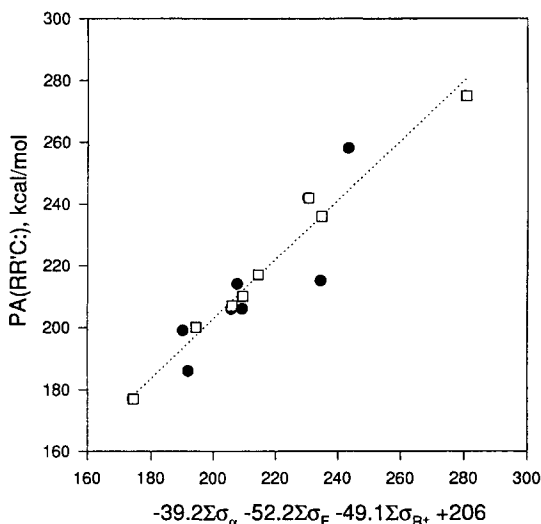
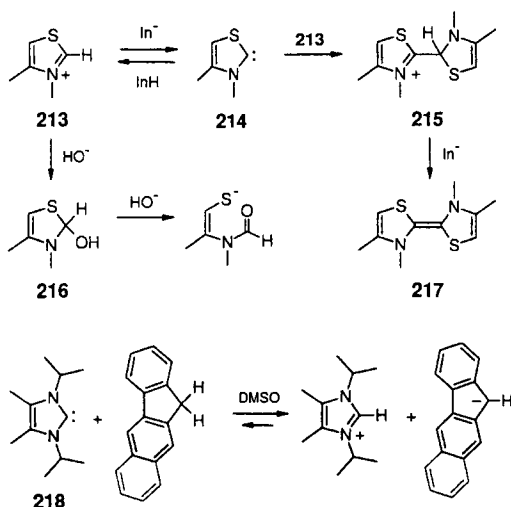


Figure 4. Proton affinities (PA) of carbenes from Table 7 (circles) and Table 8 (squares) as a function of Taft parameters for proton transfer equilibria.^{110,150} The coefficients for $\Sigma\sigma_\alpha$, $\Sigma\sigma_F$, and $\Sigma\sigma_{R+}$ were optimized, with $PA(:CH_2) = 206$ kcal/mol constant ($r^2 = 0.897$).

bene protonation. The reported^{110,150} substituent parameters were applied to the reactions in Scheme 35, using methylene, methyl cation, and methyl anion, respectively, as points of reference. A diagram for $PA(RR'C:)$, which includes data from Tables 7 and 8, is shown in Figure 4. The correlation is fair ($r^2 = 0.897$), as is that for $HA(RR'CH^+)$ ($r^2 = 0.918$). By contrast, an excellent correlation ($r^2 = 0.998$) was found for $\Delta H_f(RR'C: + H_2)$. These observations suggest that the data for $\Delta H_f(RR'C:)$ (Table 7) are rather accurate, and that the scatter in Figure 4 results mainly from experimental errors in $\Delta H_f(RR'CH^+)$. This notion is supported by the fact that computed proton affinities of carbenes (Table 8) are correlated much better ($r^2 = 0.985$) than the experimental data (Table 7, $r^2 = 0.881$). The errors in $\Delta H_f(RR'CH^-)$ appear to be smaller, as indicated by correlation coefficients of $r^2 = 0.955$ for $HA(RR'C:)$ and $r^2 = 0.973$ for $PA(RR'CH^-)$.

B. The pK_a of Carbene Conjugates in Solution

Equilibrium studies. Acidities of thiazolium cations, such as **213**, cannot be measured in basic aqueous solution because the hydroxyl adduct ("pseudobase") **216** of the thiazolium cation is formed rapidly and is subject to base-catalyzed ring opening (Scheme 36).¹⁵¹ In DMSO, formation of the carbene dimer **217** from **213** and **214** is a complicating factor.⁸ If indicator anion (In^-) was added to a solution of **213**, a very rapid drop in absorbance was followed by a somewhat



Scheme 36.

slower decrease (In = fluorenone 4-chlorophenylhydrazone, $pK_a = 14.15$). Most likely, the rate of establishment of the acid–base equilibrium $\text{213} + \text{In}^- \rightleftharpoons \text{214} + \text{InH}$ is faster than the rate of dimerization. Extrapolation of the absorbance back to t_0 gave the equilibrium concentration of In^- , which led to an estimate of $pK_a = 16.5$ for **213**.¹⁵²

The ability of the stable carbene **218** to deprotonate acidic hydrocarbons was examined by NMR in $(\text{CD}_3)_2\text{SO}$.¹⁵³ Indene ($pK_a = 20.1$) was completely converted to its anion whereas 9-phenylxanthene ($pK_a = 27.7$) was not measurably deprotonated. The NMR spectra of 1 : 1 mixtures of **218** with fluorene ($pK_a = 22.9$) and 2,3-benzofluorene ($pK_a = 23.5$) showed separate absorptions for the hydrocarbons and their anions. From the integration of these spectra, $pK_a = 24.0$ for **218** was derived. In THF, **218** failed to deprotonate fluorene but almost completely deprotonated indene. The proton transfer from hydrocarbons to **218** creates ions (ion pairs) from neutral species, which will be less favorable in solvents of lower polarity.

Evaluation of kinetic data. Rate constants were determined for 2-H exchange from 3-R-4-methylthiazolium ions, catalyzed by D_2O (pseudo first order) and DO^- (second order).¹⁵⁴ The observed rate constants for the pD-independent exchange reaction were corrected for the solvent isotope effect ($k_{\text{H}_2\text{O}}/k_{\text{D}_2\text{O}} = 2.6$), and the reverse protonation of the carbene by H_3O^+ was assumed to be diffusion-controlled ($k = 2 \times 10^{10} \text{ M}^{-1} \text{ s}^{-1}$). A similar analysis was performed for the exchange catalysed by DO^- . The results agreed nicely, giving $pK_a = 18.9$ for **213** and $pK_a = 18.0$ for thiamine.¹⁵⁴ The thiazolium ion **213** seems to be less acidic in water¹⁵⁴ than in DMSO¹⁵² ($\Delta pK_a = 2.4$). Aside from the

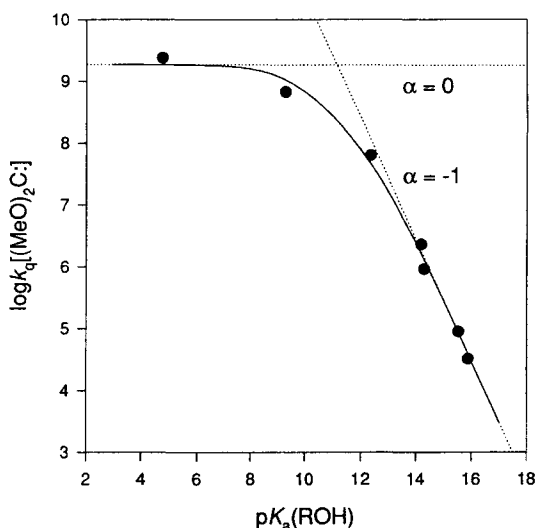


Figure 5. Rate constants ($\log k_q$) for quenching of dimethoxycarbene (**197**) with ROH (Table 3)⁹⁹ as a function of pK_a (ROH).¹⁵⁶ A theoretical Eigen curve (solid line) was fitted to the data points (circles). The dotted lines are extrapolated from the portions of the Eigen curve where $\alpha = 0$ and $\alpha = -1$. These dotted lines cross at pK_a (ROH) = pK_a [(MeO)₂C:].¹⁵⁵

influence of solvent polarity, the equilibria studied in water (**213** + H₂O = **214** + H₃O⁺) and in DMSO (**213** + In[−] = **214** + InH) differ. In the latter case, annihilation of opposite charges is expected to shift the equilibrium to the right, thus enhancing the apparent acidity of **213**.

Proton transfer reactions between “normal” acids and bases show biphasic Brønsted plots ($\log k$ vs. ΔpK_a), which are commonly called *Eigen curves*.¹⁵⁵ The slopes α are equal to zero when proton transfer is exergonic, with rates being controlled by diffusional encounter of the reactants. When proton transfer is thermodynamically unfavorable then diffusion-controlled separation of the products is rate limiting and the slope α equals one. There is an intermediate, curved region near $\Delta pK_a = 0$ where proton transfer is partially rate limiting. The Brønsted plots for O–H insertion reactions of phenyl(trimethylsiloxy)carbene (**154a**)⁷⁶ and dimethoxycarbene (**197**)⁹⁹ (Figure 5) conform to this description. The carbenes are thus classified as “normal” bases which undergo protonation with minimal structural and electronic reorganization. A detailed treatment in terms of Eigen and Marcus theory yields intrinsic barriers for proton transfer near 1 kcal/mol.¹⁵⁶ Tangents to the $\alpha = 1$ and $\alpha = 0$ regions of Eigen curves intersect at $\Delta pK_a = 0$ ($\alpha = 0.5$). Thus pK_a values of 14.8 ± 0.6 and 11.2 ± 0.2 were estimated for the conjugate acids of **154a** and **197**, respectively.¹⁵⁶

The basicity of dimethoxycarbene (**197**) in solution is similar to that of pyrrolidine ($pK_a = 12.3$). The gas phase proton affinity of pyrrolidine, 227

kcal/mol,¹²⁴ is intermediate between the PA of **197** from Table 7 (215 kcal/mol) and that taken from the correlation line of Figure 4 (234 kcal/mol). The basicity of phenyl(trimethylsiloxy)carbene (**154a**) in solution exceeds that of pentamethylguanidine ($pK_a = 13.8$); the PA of **154a** (257 kcal/mol, from Figure 4) and that of pentamethylguanidine (250 kcal/mol) rank accordingly. It appears that solvation influences the basicities of carbenes and amines similarly. However, more data are needed for a thorough analysis of solvent effects.

VI. Conclusion and Outlook

Carbene protonation has been amply demonstrated by product studies, time-resolved spectroscopy, and kinetic measurements. The ability of singlet carbenes to accept a proton is not adequately described by the traditional scale of carbene philicities, which is based on addition reactions with alkenes. In particular, aryl- and diarylcarbenes excel as proton acceptors but would traditionally be classified as electrophiles.

Most often, hydroxyl groups (alcohols, phenols, carboxylic acids) have been used as proton donors. However, the role of ROH oligomers has not been clearly defined, and a generally accepted picture of the proton transfer from ROH to singlet carbenes has not come forth.¹⁵⁷ Substantial evidence points to the formation of ion pairs which subsequently recombine or dissociate. Spectroscopic and kinetic investigations of carbene-derived ion pairs, with ps resolution, are still in their infancy. This approach would complement the generation of (radical) ion pairs by light-induced charge transfer.¹⁵⁸

Gas phase proton affinities have been estimated, by experiment and/or computation, for a considerable number of carbenes. The (computed) PA of diphenylcarbene exceeds that of the strongest nitrogen bases. When compared with amines or carbanions, singlet carbenes respond differently to substituent effects. For a better understanding of these phenomena, in particular the PA-enhancing influence of aryl groups, the arguments presented in Section V need further investigation. So far, pK_a values of carbenes in solution are extremely rare. Eigen curves could be fitted to the O–H insertion rates of dimethoxycarbene ($pK_a = 11.2$) and phenyl(trimethylsiloxy)carbene ($pK_a = 14.8$). Both species behave as “normal” bases, in contrast to carbanions (enolates, nitronates), most of which are abnormally slow to accept protons. For analogous studies of (di)arylcarbenes, weak proton donors must be found which react with Ar(R)C: at sub-diffusional rates.

Singlet carbenes are a unique class of carbon bases whose nature has yet to be fully revealed. Although substantial progress has recently been made, challenging problems remain to be solved.

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KINETICS OF INTRAMOLECULAR CARBENE REACTIONS

Dina C. Merrer and Robert A. Moss

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I. INTRODUCTION

The past decade has witnessed extraordinary progress in the quantitative understanding of the intramolecular rearrangements of singlet alkylcarbenes, particularly the ubiquitous 1,2-H shift. Fast kinetic methodologies, especially nanosecond laser flash photolysis (LFP), together with powerful computational capabilities, have generated a cornucopia of new kinetic and mechanistic information about these fundamental carbene reactions. Much of the new knowledge has been summarized in a number of excellent reviews.¹⁻⁸

This chapter has three principal themes: (1) the relative importance of rearrangements in the excited states (RIES) of carbene precursors versus carbene-alkene complexes (CAC) as secondary intermediates in carbenic rearrangements; (2) quantum mechanical tunneling (QMT) in carbenic rearrangements (especially 1,2-H shifts); and (3) the influence of substituents on the rates of hydrogen and carbon shifts. Although reference will be made to work appearing throughout the 1988-1999 period, our emphasis will fall on material appearing after our 1994 review.¹

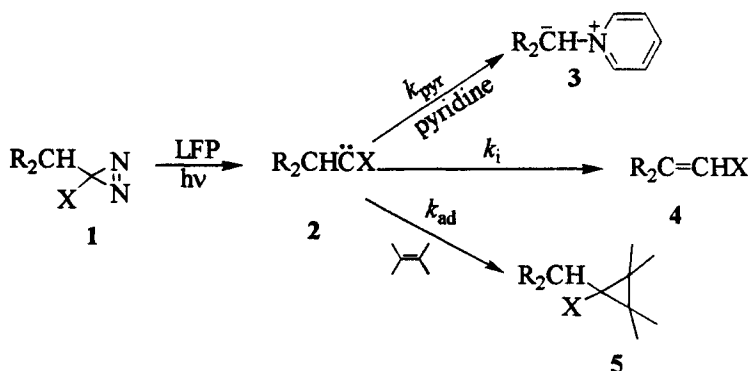
II. THE YLIDE METHOD

LFP gives us the time resolution needed to follow the kinetic evolution of many carbenic reactions.⁹ However, if the carbene lacks a readily accessible UV chromophore, its reactions must either be followed indirectly or, as has recently become practical, by LFP with IR detection of the carbenic intermediates.¹⁰

In the 1988-1999 period, almost all absolute kinetic studies of carbenic reactions employed LFP with UV detection. Carbenes that contain a UV chromophore (e.g., PhCCl) are easily observed, and their decay kinetics during reaction can be readily followed by LFP.¹¹ However, alkyl, alkylhalo, and alkylacyloxy-carbenes are generally transparent in the most useful UV region. To follow their kinetics, Jackson et al. made use of the "ylide method,"¹² in which the laser-generated carbene (**2**) is competitively captured by (e.g.) pyridine, forming a chromophoric ylide (**3**, cf. Scheme 1). The observed pseudo first order rate constants (k_{obs}) for the growth of ylide **3** at various concentrations of pyridine are monitored by UV spectroscopy, and obey Eq. 1.

$$k_{\text{obs}} = k_o + k_{\text{pyr}}[\text{pyr}] \quad (1)$$

k_{obs} is directly proportional to pyridine concentration. Therefore a plot of k_{obs} vs. [pyridine] is linear, with a slope (k_{pyr}) equal to the second order rate constant for ylide formation, and an intercept (k_o) equal to the sum of all processes that destroy the carbene in the absence of pyridine: (e.g.) intramolecular reactions, carbene dimerization, reactions with solvent, and, in the case of diazirine or diazo carbene precursors, azine formation.



Scheme 1.

In order to safely identify k_o with intramolecular carbenic reactions (e.g., k_i and the formation of alkene 4 in Scheme 1), product analysis should demonstrate that the yield of intramolecular products exceeds 90%, while dimer, azine, and solvent-derived (intermolecular) carbene products should be absent or minimal. If these conditions are not met, mechanistic interpretation is often ambiguous, a result that is well illustrated by the saga of benzylchlorocarbene (see below, Section IV.C). Less desirably, k_o can be “corrected” for competitive intermolecular carbenic reactions. Bimolecular reactions like dimerization and azine formation can be minimized by working at low carbene precursor concentrations, and careful experimental practice should include quantitative product studies at several precursor concentrations to highlight potential product contamination by intermolecular processes.

Knowledge of the intramolecular product distribution may allow for the partitioning of k_o between competitive intramolecular reactions, but one must be certain that noncarbenic routes to the products do not compete with the carbenic pathways. In particular, we must be concerned with the possible intervention of RIES (cf. Section III.C), especially when diazirines or diazoalkanes are the carbene precursors. Again, corrections for RIES can be made to quantitate the carbenic routes; see, for example, the discussion of the cyclobutylhalocarbene rearrangements (Section III.C.1).

Although we are not specifically concerned here with k_{pyr} and the kinetics of carbene–pyridine ylide formation, we note that the magnitude of k_{pyr} is directly related to the structure and reactivity of the carbene. k_{pyr} ranges from $\sim 10^5 \text{ M}^{-1} \text{ s}^{-1}$ for ambiphilic alkoxy-carbenes to $\sim 10^9\text{--}10^{10} \text{ M}^{-1} \text{ s}^{-1}$ for electrophilic halocarbenes or alkylcarbenes. Very nucleophilic carbenes (MeOCOMe) do not react with pyridine.¹³

The pyridine ylide method also allows determination of the rate constants for the intermolecular reactions of carbenes with alkenes, alcohols, or other carbene

traps.⁹ Thus, when an alkene is added to the pyridine/precursor/solvent solution in which carbene **2** is generated, the observed rate constant for ylide formation will follow Eq. 2.

$$k_{\text{obs}} = k_o + k_{\text{pyr}}[\text{pyr}] + k_{\text{ad}}[\text{alkene}] \quad (2)$$

Here the alkene and pyridine will compete for the carbene; at a constant concentration of pyridine the observed pseudo first order rate constant for ylide formation will *increase* with increasing alkene concentration. A plot of k_{obs} vs. $[\text{alkene}]$ will be linear with a slope of k_{ad} , which is the rate constant for the carbene/alkene addition reaction affording cyclopropane **5** (Scheme 1).

The pyridine ylide method depends on the effective trapping of the carbene by pyridine. At high pyridine concentrations every carbene produced by the laser pulse will be trapped as ylide, and the ylide's absorbance (A_y) will "saturate" or reach a plateau (A_y^∞). The magnitude of A_y^∞ will vary with carbene structure; it will decrease with both the increasing ease of carbene rearrangement and the intervention of RIES during carbene generation.³

Equation 1 cannot be used to extract k_o for carbenic rearrangements in the region of A_y^∞ . There, however, a Stern-Volmer analysis can be applied wherein the optical yield of ylide as a function of pyridine concentration is used to obtain k_o .⁴ The optical yield of ylide formation, A_y , is defined in Eq. 3,

$$A_y = \phi_y A_y^\infty \quad (3)$$

where ϕ_y is the quantum yield of ylide formation and A_y^∞ is the maximum obtainable (saturated) ylide yield. As shown in Eq. 4, the quantum yield of ylide formation (ϕ_y) depends directly on the quantum yield of carbene formation, ϕ_c , resulting from the reaction of the carbene with pyridine ($k_{\text{pyr}}[\text{pyr}]$), and is inversely proportional to the other processes that destroy the carbene (k_o).

$$\phi_y = \phi_c \left(\frac{k_{\text{pyr}}[\text{pyr}]}{k_o + k_{\text{pyr}}[\text{pyr}]} \right) \quad (4)$$

Substitution of Eq. 4 into Eq. 3 and rearrangement produces Eq. 5. A plot of $1/A_y$ vs. $1/[\text{pyr}]$ will be linear, and division of the slope by the intercept will afford the ratio k_o/k_{pyr} ; Eq. 6.

$$\frac{1}{A_y} = \frac{1}{\phi_c A_y^\infty} + \frac{1}{[\text{pyr}]} \left(\frac{k_o}{\phi_c A_y^\infty k_{\text{pyr}}} \right) \quad (5)$$

$$\frac{\text{slope}}{\text{intercept}} = \frac{k_o}{k_{\text{pyr}}} \quad (6)$$

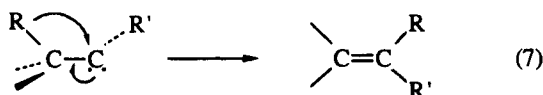
Substitution of a measured or estimated value of k_{pyr} (e.g., $\sim 10^9$ for alkylcarbenes), affords the value of k_o for those processes that destroy the carbene other than ylide formation. The *inverse* of k_o can be taken as τ_o , the lifetime of the

carbene under the given experimental conditions and in the absence of pyridine.⁴ Note that the conditions described above for the validity of k_o continue to apply. It is also possible to curve-fit variants of Eq. 5 to solve for k_o/k_{pyr} without using double reciprocal plots such as Eq. 5.¹⁴

III. REARRANGEMENTS IN THE EXCITED STATE VS. CARBENE-ALKENE COMPLEXES

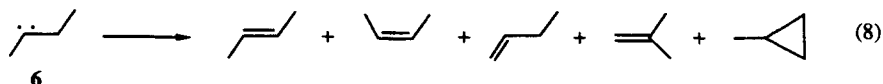
A. Introduction

1,2-Hydrogen and 1,2-carbon migrations are the most common singlet carbene rearrangements. They involve simple shifts of substituents from an adjacent carbon to the carbenic center, affording an alkene product; Eq. 7.



However, there have long been suspicions that carbenes may not be the only intermediates leading to the products.¹⁵

For example, methylethylcarbene (**6**) appears to rearrange to *trans*- and *cis*-2-butene and 1-butene by 1,2-H shifts, to 2-methylpropene (1,2-C shift), and to methylcyclopropane (1,3-CH insertion); Eq. 8.^{15b}

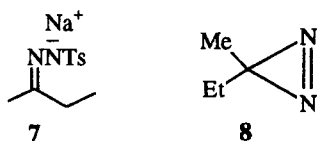


As shown in Table 1, however, the product distribution depends on the method of "carbene" generation. Whereas thermolysis of either tosylhydrazone salt (**7**) or methylethyldiazirine (**8**) affords essentially the same product distribution (in which ~95% of the products are the 2-butenes), photolysis of diazirine **8** is quite different.

Table 1. Experimental Product Distributions for the Decomposition of Various Precursors of **6**^a

Precursor	Conditions					
7	Δ	67	28	5	0.5	0.0
8	Δ	66.6	29.5	3.3	0.5	0.0
8	$h\nu$	38.0	34.7	23.2	3.7	0.3

Note: ^a See reference 15b.



Now the 2-butenes comprise only 73% of the products, while 1-butene, a minor thermolytic product, increases to 23%. It is at least conceivable that some of the 1-butene here derives from an excited state of diazirine **8**, rather than exclusively from carbene **6**.^{3,15} Computational studies indicate that the 1,2-H shifts of **6** leading to the 2-butenes are preferred to the 1,2-H shift that yields 1-butene by a $\Delta\Delta G^\ddagger$ of 2.6–3.3 kcal/mol. This again suggests that the substantial yield of 1-butene obtained from the photolysis of **8** is not simply derived from carbene **6**.¹⁶

Additional evidence for a “second intermediate” in supposed carbene reactions comes from numerous studies.^{17–29} In the earliest experimental approach, the carbene precursor, frequently a diazirine, was photolyzed in the presence of increasing quantities of an alkene, which trapped the carbene with the formation of a cyclopropane (**5** in Scheme 1). If carbene **2** were the sole product-forming intermediate, as depicted in Scheme 1, then the ratio of its alkene addition product (**5**) to its 1,2-H shift rearrangement product (**4**) would vary *linearly* with alkene concentration; Eq. 9.

$$\frac{\text{addn}}{\text{rearr}} = \frac{[\mathbf{5}]}{[\mathbf{4}]} = \frac{k_{\text{ad}}}{k_i} [\text{alkene}] \quad (9)$$

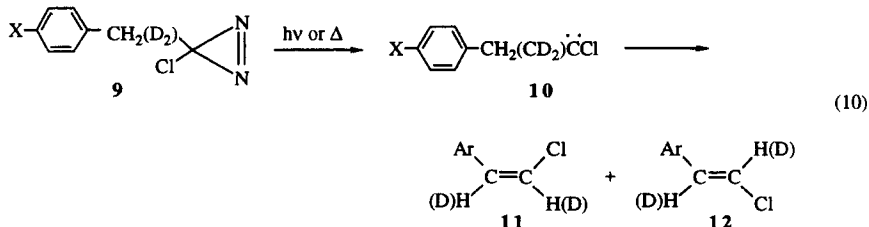
However, it is often observed that the correlation of addn/rearr vs. [alkene] is not linear, but curved.^{17–20,25–28} On the other hand, a double inverse plot of [4]/[5] (rearr/addn) vs. 1/[alkene] is linear! These results can be understood if a second intermediate, besides the carbene, contributes to the formation of product **4**. The kinetic and mechanistic formulation of this scenario appears below (Section III.B).

The second intermediate’s identity has been debated since the mid-1980s. In 1984, Liu and Tomioka suggested that it was a carbene–alkene complex (CAC).¹⁷ Similar complexes had been previously postulated to rationalize the negative activation energies observed in certain carbene–alkene addition reactions.^{11,30} A second intermediate is not limited to the CAC, however. In fact *any* other intermediate, in addition to the carbene, will satisfy the kinetic observations; i.e., that a correlation of addn/rearr vs. [alkene] is curved, whereas the double reciprocal plot is linear.³¹ Proposed second intermediates include the CAC,¹⁷ an excited carbene,³¹ a diazo compound,²³ or an excited diazirine.^{22,26} We will consider the last three proposals collectively below as “rearrangements in the excited state” (RIES).

We now review the CAC and RIES mechanisms in greater detail, including recent definitive work of Platz et al., which demonstrates that RIES chemistry is, in fact, responsible for the unanticipated curvature in correlations of addn/rearr vs. [alkene].^{24,25}

B. Carbene-Alkene Complexes (CAC)

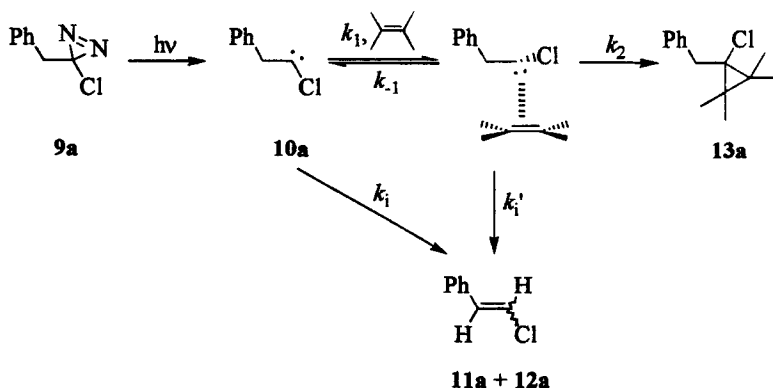
The chemistry of benzyldichlorocarbene is central to discussions of CAC, RIES, and QMT. The thermolysis and photolysis of 3-chloro-3-benzyl-diazirine, **9a**, in benzene and CCl₄ gave (*Z*)- and (*E*)-2-chlorostyrene, **11a** and **12a**; Eq. 10.



a, X = H; **b**, X = H (D₂); **c**, X = CH₃; **d**, X = OCH₃; **e**, X = Cl; **f**, X = CF₃; **g**, X = CCl₃. These 1,2-H shift products were formed in *Z/E* ratios of 0.125 and 0.33 via thermolysis or photolysis, respectively, with the variation in isomer ratios attributed to product photoisomerization.³²

Quantitative studies of the photolysis of **9a** or **9c-g** in the presence of alkenes provided evidence for the participation of a second reactive intermediate, in addition to carbenes **10a** or **10c-g**, because the addn/rearr ratio was not linearly dependent on [alkene]; cf. Section III.A and Scheme 2.

If carbenes **10** were the only product-forming intermediates in these reactions, a linear correlation of addn/rearr ([**13**]/[**11** + **12**]) vs. [alkene] should



Scheme 2.

have been observed; cf. Scheme 1 and Eq. 9. Tomioka, however, found that the irradiation of **9c-g** in cyclohexane-*cis*-4-methyl-2-pentene mixtures afforded curved correlations.¹⁷ Similarly curved correlations were obtained by Liu for the photolysis of **9a** in isooctane with added tetramethylethylene (TME) or diethyl fumarate.^{19,33} The curvature was particularly apparent upon photolytic decompositions of the diazirine carbene precursors.²⁰ With thermolytic decomposition, as in the reactions of *n*-propylchlorodiazirine in isooctane and TME at 79, 84, 90, and 97°C, the curvature was much less obvious; straight lines can fit the published data²⁰ (which may reflect the *absence* of a second intermediate in the thermolytic reactions).

The additional reactive intermediate responsible for the curvature was postulated^{17,33} to be a CAC.³⁰ The mechanism of Scheme 2 was proposed, in which carbene **10a** was in equilibrium with the CAC. Thus, styrenes **11a** and **12a** can be formed by two pathways: from the free carbene (k_i) and from the CAC (k'_i). A steady-state kinetic analysis of Scheme 2 affords Eq. 11, which predicts that a correlation of *rearr*/*addn* with $1/[\text{alkene}]$ should be linear; the behavior actually observed by Tomioka and Liu.^{17,33} The CAC mechanism also accounts for the observation that the **11a/12a** product ratio depends upon the identity and concentration of the added alkene; both k'_i and k_2 , which define the Y-intercept of Eq. 11, depend on the added alkene. The dependence has been observed,^{19,33-37} albeit with only small variations in the Y-intercepts.

$$\frac{\text{rearr}}{\text{addn}} = \frac{[\mathbf{11} + \mathbf{12}]}{[\mathbf{13}]} = \frac{k'_i}{k_2} + \frac{k_i(k_{-1} + k'_i + k_2)}{k_1 k_2 [\text{alkene}]} \quad (11)$$

There are, however, difficulties with the CAC mechanism. Although it rationalizes the kinetic results,^{17,33} no direct evidence for a CAC intermediate has yet been provided. CACs were originally postulated as intermediates in carbene-alkene addition reactions to account for the negative activation energies observed in some of these reactions.^{11,30} However, Houk presented a persuasive alternative analysis, in which the negative activation energies stemmed from the great exothermicity of the additions, with ΔH continually decreasing as the carbene and alkene reacted. In this model, a very unfavorable $\Delta S^\ddagger$, caused by the required restriction of reactant vibrational and rotational modes during the bimolecular reaction was responsible for an observed, mildly positive free energy of activation, $\Delta G^\ddagger$.³⁸ The Houk model nicely accounts for the experimental observations¹¹ without the need to invoke a CAC.

Moreover, *ab initio* calculations indicate that additions of chlorocarbenes to ethylene or TME lead to cyclopropanes either without the intermediacy of CACs,³⁹ or via broad shallow wells for complexes that might occur in the reaction enthalpy profile but are not minima on the free energy surface.⁴⁰ More recent calculations confirm these conclusions; CACs are not predicted to be im-

portant for additions of (e.g.) CCl_2 , MeCCl , or ClCH_2CCl to alkenes.^{41,42} On the other hand, weakly interacting but thermally stable π complexes are predicted to be formed from (e.g.) CCl_2 or MeCCl and benzene;^{42,43} 1:1 or 2:1 (aromatic: carbene) complexes may modulate the intramolecular and intermolecular chemistry of alkylhalocarbenes occurring in aromatic solvents.^{42–44}

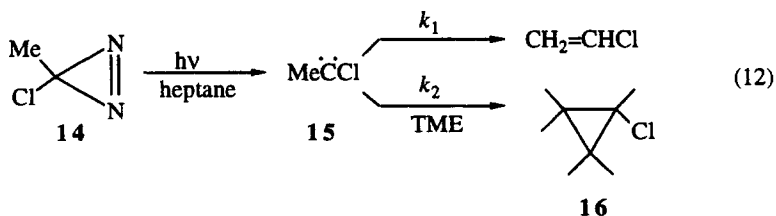
These computational findings agree with experimental work showing that the extent of rearrangement of carbene **10a** increases relative to its addition to TME in aromatic solvents. With $[\text{TME}] = 0.25 \text{ M}$, $[\mathbf{11a} + \mathbf{12a}]/[\mathbf{13a}]$ is about 1.2 in isooctane, but increases to 2.5 or 3.7 in benzene or anisole, respectively. For $n\text{-PrCCl}$, the rearrangement/addition ratio increases from 2.7 in isooctane to 18.2 or 26.6 in benzene or anisole. Complexation with an aromatic solvent is suggested to interfere with addition of the carbene to the alkene, thereby providing the carbene with a greater opportunity for intramolecular rearrangement.⁴³

C. Rearrangement in the Excited State (RIES)

1. Diazirines

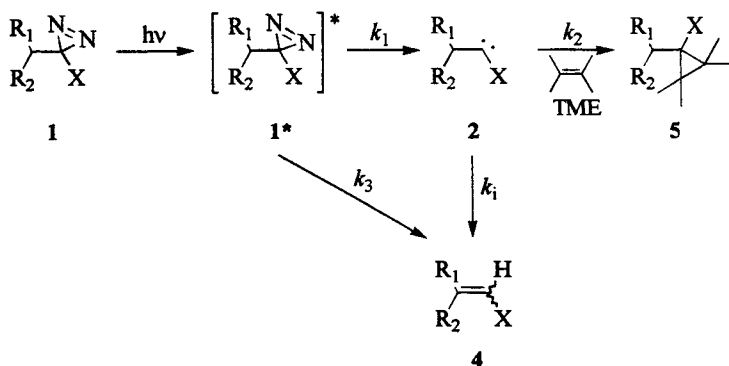
In the absence of direct evidence for CACs other second intermediates have been proposed to rationalize the curvature observed in correlations of addn/rearr vs. [alkene]. A particularly viable candidate is an excited state (or species derived therefrom) of the carbene precursor, a suggestion that is quite apposite when the precursor is a photolytically decomposed diazirine.

In 1990, Goodman described a photoacoustic calorimetric study of the rearrangement of MeCCl in heptane;²⁶ Eq. 12.



Photolysis of diazirine **14** gave >90% of vinyl chloride, but, in accord with the observations of Tomioka, Liu, and Bonneau,^{17–20} photolyses in the presence of increasing quantities of TME led to a strongly curved correlation of addn/rearr vs. [TME]. And, carbene **15** was trapped by TME with, at most, ~66% efficiency, so that about a third of the diazirine was converted to vinyl chloride by a 1,2-H shift that seemed to “bypass” the carbene.

Goodman suggested that an excited diazirine was the culprit and offered Scheme 3 and Eq. 13 to rationalize the results.^{1,26}



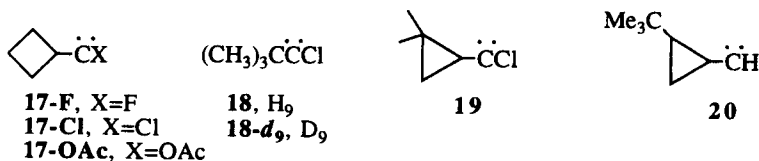
Scheme 3.

$$\frac{4}{5} = \frac{k_3}{k_1} + \frac{k_1(k_1 + k_3)}{k_1 k_2 [\text{alkene}]} \quad (13)$$

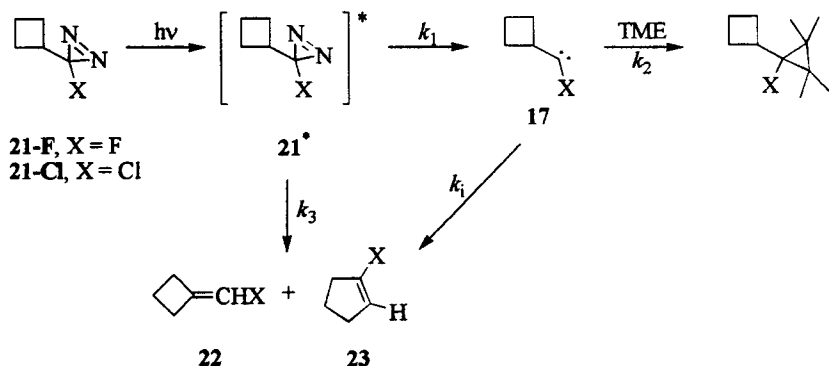
Indeed, plotted according to Eq. 13, the experimental data afforded a straight line.²⁶

Although the RIES mechanism of Scheme 3 fits the overall kinetic results, and is strongly supported by spectroscopic and chemical evidence presented below, there are "loose ends". For example, k_3/k_1 , the Y-intercept of Eq. 13, gives the partition between rearrangement of the excited diazirine (1^*) and its loss of nitrogen to carbene 2. It is difficult to see why this should depend on alkene identity, yet small dependences have been observed.^{19,33-37} The behavior can be understood in terms of the CAC mechanism (Scheme 2, Eq. 11), where the Y-intercept is dependent on the rate of rearrangement of the CAC. On the other hand, there are reports that the Y-intercept does not vary in experiments with benzylchlorocarbene and (e.g.) 1-hexene, α -chloroacrylonitrile, or TME.²³

The RIES mechanism provides a particularly good framework for several reaction systems. Examples include the C and H migrations of cyclobutyl-halocarbenes **17-F** and **17-Cl**,²⁸ the methyl migration and 1,3-CH insertion of *t*-butylchlorocarbene, **18**,²⁷ and the fragmentations of 2,2-dimethylcyclopropyl-chlorocarbene, **19**,⁴⁵ and *trans*-*t*-butylcyclopropylcarbene, **20**.⁴⁶



Photolysis of diazirines **21-Cl** or **21-F** in the presence of varying concentrations of TME or 2-methyl-1-butene gave the 1,2-H and 1,2-C products **22**



Scheme 4.

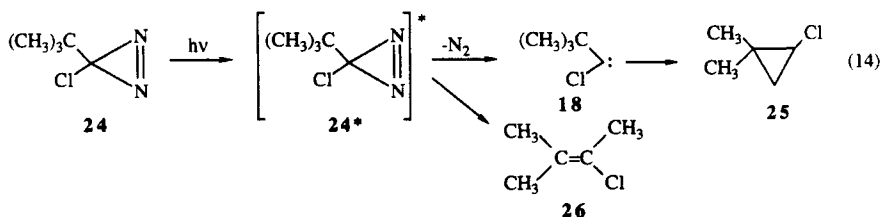
and **23**, along with the corresponding cyclopropane adducts. The correlations of addn/rearr with [alkene] were curved, but the reciprocal correlations of rearr/addn vs. $1/[\text{alkene}]$ were linear, and the RIES mechanism of Scheme 4 was offered.²⁸

The Y-intercept (k_3/k_1 ; Eq. 13) of the reciprocal correlation for the photolysis of diazirine **21-Cl** in TME was 2.18, which translated into a 68% incursion of diazirine excited state in the genesis of the rearrangement products, **22-Cl** and **23-Cl**; carbene **17-Cl** only accounted for ~32% of these products.²⁸ A similar conclusion followed from the ratio of rearr/addn (68:32) at a high concentration (6.7 M) of TME in pentane, where carbene **17-Cl** was almost completely diverted to the cyclopropane, and **22** and **23** were exclusively derived from the excited diazirine.²⁸

One can correct the observed distribution of 1,2-C and 1,2-H products so as to reflect only the carbenic pathway.²⁸ The corrected 1,2-C/1,2-H ratio (4.8), coupled with a pyridine ylide absolute rate constant for overall carbene rearrangement ($k_c + k_H = 6.8 \times 10^7 \text{ s}^{-1}$), gives the partitioned rate constants $k_c = 5.6 \times 10^7 \text{ s}^{-1}$ and $k_H = 1.2 \times 10^7 \text{ s}^{-1}$.²⁸ The dominance of 1,2-C over 1,2-H in this system will be discussed below.

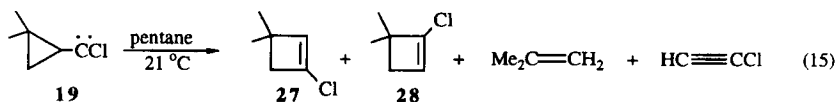
In the cyclobutylfluoro system, the excited diazirine, **21-F***, is considerably less involved. A parallel analysis indicates that only about 12% of **22-F** and **23-F** arise from excited diazirine, while 88% of those products descend from carbene **17-F**.²⁸ The increased carbene involvement in the photolysis of **21-F** presumably reflects the greater stability of fluorocarbene **17-F** over its chloro analogue **17-Cl** and, consequently, a more favorable partition (k_1/k_3) of excited diazirine **21-F*** to the carbene.

An especially strict partition between carbene and excited state diazirine rearrangements occurs in the photolysis of *t*-butylchlorodiazirine, **24**; Eq. 14.²⁷



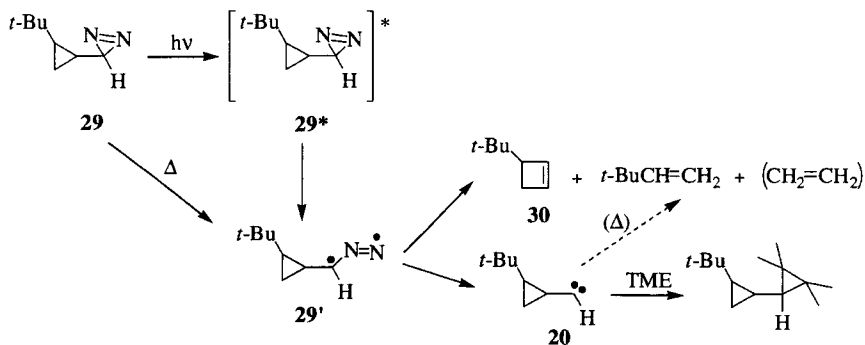
In pentane, the distribution of 1,3-insertion product **25** to 1,2-Me shift product **26** is 91:9. Upon addition of 2-methyl-1-butene, the yield of **25** smoothly decreases (to 19% with 4 M alkene), but the yield of **26** is *unaffected*.²⁷ Moreover, correlation of addn/1,3-CH insertion (to **25**) for **18** is nicely *linear*. The simplest interpretation is that **25** comes directly from carbene **18**, whereas the 1,2-Me shift product **26** comes from the excited diazirine.²⁷ Interestingly, *thermolysis* of **24** at 79°C produces 90% of **25** and 10% of **26**, but now the yields of both products smoothly decrease in the presence of an alkene. In thermolysis the (electronically) excited diazirine is unavailable, both **25** and **26** stem from the carbene, and their formation is suppressed by the alkene's interception of the carbene. A pyridine ylide kinetic study gave the 1,3-CH insertion rate constant (**18** → **25**) as $9.3 \times 10^5 \text{ s}^{-1}$.^{27,47}

Photolytic generation of carbene **19** from a precursor diazirine afforded cyclobutenes **27** (68%) and **28** (14%) via CH_2 and CMe_2 migrations, respectively; cf. Eq. 15.⁴⁵



In addition, 18–19% of isobutene and chloroacetylene formed via fragmentation. Photolysis of the diazirine in up to 9 M trimethylethylene in pentane led to a sharp decrease in **27** and **28** (to 32% and 8.5%), along with 40% of cyclopropanes formed via the capture of **19**. However, the yield of isobutene and chloroacetylene was *unchanged*, indicating that these products did not stem from the carbene, but arose directly by fragmentation of its excited diazirine precursor.⁴⁵

When the diazirine was decomposed thermally, avoiding its electronically excited state, the yield of fragmentation products dropped to 1–2%. Further analysis revealed that, under photolytic conditions, cyclobutenes **27** and **28** were formed from both the carbene (63%) and directly from the excited diazirine (17%); fragmentation accounted for the remainder of the material balance. LFP studies by the pyridine ylide method gave rate constants for **19** → **27** ($1.3 \times 10^6 \text{ s}^{-1}$) and **19** → **28** ($2.5 \times 10^5 \text{ s}^{-1}$), with the 5-fold preference for CH_2 migration to **27** over CMe_2 migration to **28** attributed to differential steric effects.⁴⁵



Scheme 5.

Related observations were reported for *trans*-*t*-butylcyclopropylcarbene, **20**.⁴⁶ Photolysis of diazirine **29** in freon-113 gave *t*-butylcyclobutene, **30** (46–49%), as well as ~20% of *t*-butylethene (and ethene) fragmentation products; Scheme 5.

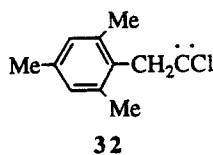
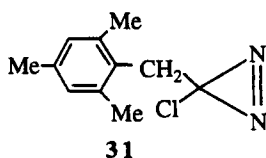
Addition of up to 0.42 M TME did not much affect the yields, even though up to 37% of the cyclopropane adduct of carbene **20** formed, presumably at the expense of freon–carbene (C–Cl) insertion products which form in the absence of TME. The yield of **30**, but not *t*-butylethene, was also minimally affected by TME when the diazirine was thermally decomposed at 100°C.⁴⁶

The mechanism of Scheme 5 accounts for these observations. Both excited diazirine **29*** and carbene **20** are regarded as product precursors. A strict partition is postulated, whereby cyclobutene **30** comes only from **29***, while the carbene reacts only intermolecularly, either with the freon solvent or added alkene. In Scheme 5, the excited diazirine pathway is expanded by interposition of the opened diazirine biradical, **29'**, as the proximate partitioning intermediate.^{46,48} Of course either an excited diazirine or a diazirine-derived biradical, would satisfy the need for a “second intermediate” in cases where curved correlation of addn/rearr vs. [alkene] require expansion of the kinetic scheme.

Fragmentation of **29*** or **29'** accounts for *t*-butylethene formation during the photolysis of **29**. In thermolytic experiments, however, the yield of this olefin decreases as TME is added and carbene **20** is trapped. The inference is that fragmentation during thermolysis at 100°C is, at least partly, a reaction of carbene **20**,⁴⁶ with continued contribution from the fragmentation of **29'**.

RIES is also important in the decomposition of mesitylmethylchlorodiazirine, **31**, which generates mesitylmethylchlorocarbene, **32**, upon photolysis.²⁹ Both excited **31** and carbene **32** are involved in the chemistry of this benzylchlorocarbene analogue, which will be described in detail below (Section IV.C).

A number of recent studies use the RIES mechanism (Scheme 3) rather than



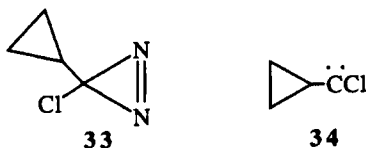
the CAC rationale to explain product formation from a second intermediate. Reasons for this preference include the observation that *thermal* decomposition of (e.g.) methylchlorodiazirine in the presence of TME results in a linear correlation between addn/rearr and [alkene], consistent with a single (carbene) intermediate.²⁶ Thermolysis bypasses an electronically excited diazirine (although it could yield an open diazirine biradical). In contrast, the CAC mechanism should be operative for both thermal and photolytic diazirine decompositions, as long as an alkene is present. Additionally, various carbene traps afford similar Y-intercepts in double reciprocal correlations of rearr/addn vs. 1/[alkene].^{23,26} The RIES mechanism predicts that the identity of the trapping agent should not affect the Y-intercept. To be fair, however, the CAC mechanism makes the opposite prediction and is supported by small, trap-dependent variations of the Y-intercept in some cases.^{19,33-37}

Another line of support for the RIES mechanism is provided by White and Platz, who focus on the structural dependence of the carbene yield in the photolytic decomposition of diazirines.²³ In the presence of pyridine, the carbenes generated by LFP of the diazirines are captured to produce ylides; see Scheme 1, $1 \rightarrow 2 \rightarrow 3$. At high [pyridine], all of the carbenes generated by the laser pulse are diverted to ylide, maximizing the latter's yield and absorbance, A_y^∞ . Both A_y^∞ and carbene yield vary with diazirine structure in a predictable fashion that is readily understood in terms of a RIES mechanism.^{3,23} Thus, for diazirine **1** ($X=\text{Cl}$ or Br^{21}), the yield of trappable carbene upon LFP depends on the strength of the α -CH bond (i.e., its bond dissociation energy). If the α -CH bond is strong (e.g., cyclopropyl C-H), or nonexistent (*t*-butylchlorodiazirine, **24**), the carbene yield, and hence the yield of ylide, (A_y^∞), is greater than if the α -CH bond is weak (isopropyl C-H). Indeed, the ratio of A_y^∞ values for *t*-butyl:methyl:isopropyl chlorodiazirines (**24**, **14**, **1** with $\text{R}=\text{Me}$, $\text{X}=\text{Cl}$) is 10:2:1.²³

These observations are easily understood in terms of RIES, Scheme 3: excited state diazirine (**1**^{*}) undergoes 1,2-H shift in concert with nitrogen loss (k_3) and in competition with carbene formation (k_1). Excited diazirines with weaker α -CH bonds give more 1,2-H shift associated with N_2 loss (RIES), less carbene, and hence less ylide. Conversely, a diazirine with a stronger α -CH bond affords a greater yield of carbene and more ylide. In fact, there is a linear correlation between A_y^∞ and α -CH bond dissociation energies for alkylhalodiazirines **1** ($\text{X}=\text{Cl}^{23}$ or Br^{21}).

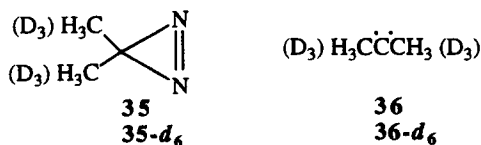
For **1**, X=F, however, A_y^∞ is independent of the bond dissociation energies. The greater carbene-stabilizing ability of F²⁸ (vs. Cl or Br) drives the partition of excited alkylfluorodiazirines mainly to carbene, thus minimizing the RIES pathway. In the case of the cyclobutylhalodiazirine **21-X** photolyses (Scheme 4), RIES accounted for 68% of reaction when X=Cl, but only 12% when X=F; the balance of reaction was due to carbene in each case.²⁸

Cyclopropylchlorodiazirine **33** seems to give cyclopropylchlorocarbene about as efficiently as *t*-butylchlorodiazirine **24** gives carbene **18**; chlorocyclobutene, the 1,2-C shift product of **34** is very largely formed from the carbene, and not from excited diazirine **33**.²³



Why then does excited cyclobutylchlorodiazirine (**21***, Scheme 4) so readily undergo 1,2-C RIES?²⁸ Presumably, the difference is in the energetics of the 1,2 shifts. Ring expansion of **21-Cl*** (or **17-Cl**) to chlorocyclopentene relieves about 20 kcal/mol of ring strain, but the analogous conversion of **33*** or **34** to chlorocyclobutene actually increases ring strain by ~2 kcal/mol.²¹

Diazirine fluorescence provides additional support for RIES.²² Excited dialkyldiazirines (but not alkylhalodiazirines) fluoresce, and the fluorescence intensity increases with decreasing temperature, suggesting the existence of a barrier to nitrogen loss from the excited diazirine.²² For example, dimethyldiazirine (**35**) and **35-d₆** fluoresce upon pulsed laser excitation, with emission due to the excited diazirines.

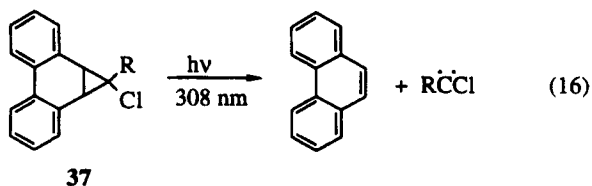


The fluorescence is not quenched by pyridine (i.e., the excited diazirines do not react with pyridine), although the carbenes do react with pyridine to form ylides. Importantly, the fluorescence from diazirine **35-d₆** is 50% stronger than that of **35**, and the pyridine-trappable yield of carbene **36-d₆** (from **35-d₆**) is 50% greater than that of **36** from diazirine **35**. These results parallel deuterium kinetic isotope effects on RIES.²²

Thus, excited diazirine **35-d₆** less efficiently undergoes 1,2-D migration with nitrogen loss compared to the analogous 1,2-H shift process in excited **35**; accordingly, excited **35-d₆** more frequently decays by fluorescence than does

excited **35**. Consequently, excited **35-d₆** more efficiently affords the carbene by simple nitrogen loss than does excited **35**, where the energetically preferred 1,2-H shift more readily occurs with loss of nitrogen.²² Excited diazirines decay by fluorescence, carbene formation, or 1,2-H(D) migration coupled with N₂ loss. C–D bonds are stronger than C–H bonds, so that deuteration retards the latter pathway and therefore RIES, leading to an increase in both fluorescence and carbene formation from **35-d₆**.^{3,22}

Compelling evidence for the RIES mechanism comes from studies of non-nitrogenous phenanthrene precursors for RCCl; cf. **37** in Eq. 16. Comparisons of RCCl generated by LFP from **37** with RCCl generated from the diazirine reveal key features of their reactions that are consistent with the RIES but not the CAC mechanism.



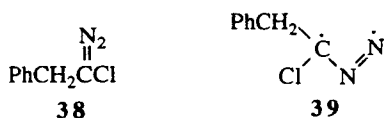
Cyclopropanated phenanthrenes revert to phenanthrene and carbenes on photolysis; CH₂,⁴⁹ CCl₂,⁵⁰ CBr₂,⁵¹ CBrCl,⁵¹ and *t*-BuCH^{15d} have been generated this way. Platz et al.²⁵ used **37** (R=PhCH₂) to generate benzylchlorocarbene (**10a**) for comparison with **10a** generated from diazirine **9a**; cf. Scheme 2.

Repetition²⁵ of the **9a** photolysis in the presence of TME in either isooctane or CH₂Cl₂ confirmed that correlations of addn/rearr vs. [TME] were indeed curved, as previously observed.^{17,19,33} However, generation of PhCH₂CCl from **37** by photolysis at 308 nm gave *linear* correlations of addn/rearr vs. [TME].²⁵ Thus, curvature in the addn/rearr correlations is precursor dependent, and is not due to the intervention of a CAC. If such a complex does form, it must continue on to cyclopropane faster than it reverts or rearranges to β-chlorostyrene by 1,2-H shift. Indeed, the most recent calculations indicate no barrier to the collapse of a MeCCl/TME “complex”; such a species is not located on the electronic energy surface.⁴⁵

If Scheme 2 accurately represented the PhCH₂CCl chemistry, curvature in the addn/rearr vs. [alkene] correlation would persist when the carbene was generated from **37**. The absence of curvature in this case counts against Scheme 2 (and the CAC mechanism), but accords with the RIES mechanism, Scheme 3. Elimination of the diazirine precursor eliminates the diazirine excited state. From **37**, both cyclopropane formation and 1,2-H rearrangement proceed from a single (carbene) intermediate, and addn/rearr vs. [alkene] is linear.²⁵

Time resolved (LFP) infrared spectroscopy of diazirine **9a** showed a low efficiency ($\Phi \approx 0.075$) isomerization to diazo compound **38**, but **38** was not

considered responsible for the addn/rearr curvature in the diazirine experiments because it was not formed in sufficient quantity.²⁵

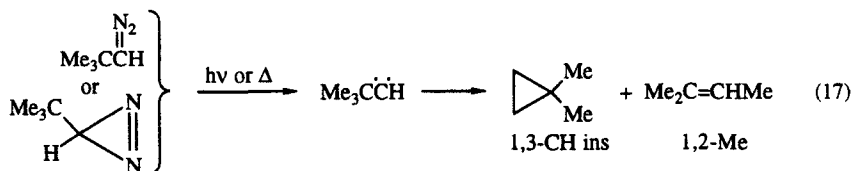


Rather, the second intermediate responsible for RIES was suggested to be **39**, the open diazirine biradical derived from the electronically excited diazirine.^{25,48}

Studies of RCCl photogenerated from **37** in the presence of pyridine permitted comparisons of A_y^∞ for carbene-ylide formation with this parameter as observed for the diazirine-generated carbenes.²⁴ When R was *t*-Bu, CD₃, CH₃, PhCH₂, Et, or *i*-Pr, and the carbene precursor was the diazirine, the efficiency of carbene formation measured by A_y^∞ was dependent on R. In accord with RIES, those diazirines with weak α -CH bonds gave substantial rearrangement in their excited states, less carbene, and lower values of A_y^∞ (see above). However, when RCCl was generated from **37**, A_y^∞ was much less dependent on the α -CH bond strength.²⁴ These results also argue against carbene-pyridine complexes as product-determining branch points. If formed, such complexes must efficiently proceed to ylides.²⁴ Indeed, the observed A_y^∞ values linearly correlate with the phenanthrene yields in Eq. 16.²⁴

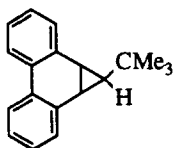
2. Diazo compounds

Diazo compounds are classic precursors of carbenes.⁵² Given that RIES is an important feature of carbene generation via diazirine photolysis, we might expect a similar complication during the photolysis of diazo compounds. Product distribution changes as a function of precursor and generative conditions were useful in alerting us to RIES intervention with diazirine precursors¹⁵ (see above, Section III.A). Analogous evidence is available for diazoalkanes.^{15d} Consider, for example, the competitive 1,3-CH insertion and 1,2-Me migration reactions of *t*-butylcarbene, Eq. 17.



The 1,3-ins/1,2-Me ratio is 89:11 when the carbene is generated by thermolysis (130°C) of *t*-butyldiazomethane and 87.6:12.4 when the diazirine is pyrolyzed at 145°C.^{15d} Similarly, a 90:10 distribution is obtained by photolysis of the phenanthrene precursor (**40**) at 25°C.^{15d} However, photolyses of the ni-

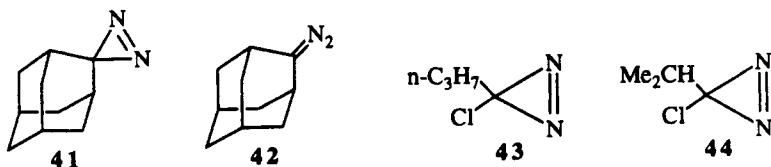
trogenous precursors at 25°C give distributions of only 50:50 or 44.7:55.3, respectively.^{15d}



40

It is suggested that the “real” carbene, generated by thermolysis of the diazo or diazirine precursors or photolysis of **40**, gives mostly 1,3-insertion, whereas photolysis of either the diazoalkane or diazirine yields much 1,2-Me migration directly from precursor excited states.^{15d} An analogous intervention of 1,2-Me migration via RIES was also observed in the photolytic decomposition of *t*-butylchlorodiazirine (**24**) to *t*-butylchlorocarbene (**18**); cf. Eq. 14.²⁷

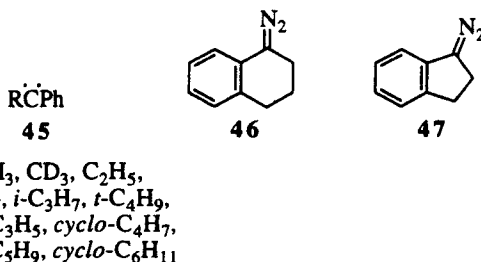
An additional complication is the known (and theoretically expected⁵³) photoisomerization of diazirines to their “open” diazo isomers. Thus, benzylchlorodiazirine **9a** photoisomerizes with low efficiency to its diazo isomer **38**,^{23,25} and adamantyldiazirine **41** has long been known to photoisomerize to diazoadamantane, **42**.⁵⁴



Bonneau and Liu studied the LFP decomposition of *n*-propylchlorodiazirine (**43**), *i*-propylchlorodiazirine (**44**), and adamantyldiazirine (**41**) in isooctane at 25°C.⁵⁵ Transient UV spectra with $\lambda_{\max}$ 235–240 nm and lifetimes of ~ 0.5 s were observed from **43** and **44** and attributed to the respective diazo isomers; diazoadamantane (**42**) from **41** was longer-lived with $\tau \approx 1$ –1.5 h.⁵⁵ Activation parameters for decompositions of the diazo isomers of **43** and **44** were $E_a \approx 17$ kcal/mol and $\log A = 12.7$ s⁻¹.⁵⁵

The quantum yield of diazo compound formation from diazirines **43** and **44** was only ~ 0.10 – 0.13 , however, so that RIES was not considered an important product source during the diazirine photolysis. In the case of **44**, for example, the substantial RIES contribution to chloroisobutene formation stems from excited **44**, not from the excited state of its diazo isomer.⁵⁵ The situation is analogous to the RIES formation of α -chlorostyrene during the photolysis of benzylchlorodiazirine.²⁵

When, however, carbenes are directly generated from diazoalkanes, RIES becomes significant.⁵⁶ Photolytic generation of carbene **45** from diazoalkane precursors in the presence of >1.5 M pyridine gave A_y^∞ values for the derived pyridinium ylides.



As in experiments with diazirine **1**, the maximum yields of the ylides, and hence of the carbenes, increased with increasing strength of the alkyl group's α -CH bond.⁵⁶ For example, the relative yields of carbene **45** from diazoalkane photolysis were 100% for $\text{R}=\text{cyclo-C}_3\text{H}_5$, 96% for $\text{R}=t\text{-C}_4\text{H}_9$, and 72% for $\text{R}=\text{CH}_3$; the relative carbene yields decreased to 14% with $\text{R}=\text{C}_2\text{H}_5$ and to only 7% with $\text{R}=i\text{-C}_3\text{H}_7$.

The yields of carbene (and pyridinium ylide) are thus controlled by competition between "simple" nitrogen loss to the carbene or 1,2-H (or 1,2-C) shift linked to nitrogen loss in the excited state of the diazoalkane precursor.⁵⁶ When $\text{R}=i\text{-C}_3\text{H}_7$, the α -CH bond is weak, there is much RIES upon diazoalkane photolysis, and carbene production is inefficient. When $\text{R}=t\text{-C}_4\text{H}_9$ (no α -CH bond) or $\text{R}=\text{cyclo-C}_3\text{H}_5$ (strong α -CH bond), diazoalkane photolysis gives little RIES and much carbene.⁵⁶

RIES from diazoalkanes is also sensitive to the dihedral angle between the migrating α -H and the C-N bond of the diazo moiety.⁵⁷ For example, the A_y^∞ values for the pyridine capture of the photolytically generated carbenes from **46** and **47** are in the ratio of $\sim 1.7:1$. Similarly, the carbene from **46** is more efficiently generated and trapped in methanol, whereas the photolysis of **47** in methanol affords twice as much olefin (by 1,2-H RIES) compared to the photolysis of **46**. These phenomena are attributed to conformational factors that favor RIES during the photolysis of **47**, with the proximal excited state represented as a pyramidalized 1,3-C-N=N diradical.⁵⁷

Clearly, rearrangements do occur in the excited states of diazirine and diazo carbene precursors. Kinetic studies of carbenic rearrangements need to consider the possible intervention of RIES when absolute rate constants are partitioned between competitive rearrangement pathways on the basis of product distributions.²⁸

IV. QUANTUM MECHANICAL TUNNELING

A. Overview

The second of our principal concerns is the contribution of quantum mechanical tunneling (QMT) to singlet carbene 1,2-H shifts and related reactions. There is strong evidence that QMT is important in the low temperature matrix reactions of (e.g.) *t*-butylchlorocarbene (**18**)⁵⁸ and benzylchlorocarbene (**10a**).⁵⁹

In a nitrogen matrix at 11 K, photolysis of *t*-butylchlorodiazirine (**24**) generates carbene **18**, characterized by IR and UV spectroscopy.⁵⁸ Significantly, **18** undergoes slow 1,3-CH insertion to cyclopropane **25** (Eq. 14) even at 11 K, where the reaction proceeds with $k \approx 4 \times 10^{-4}$ to $3 \times 10^{-5} \text{ s}^{-1}$ and exhibits little temperature dependence in the matrix between 11 and 30 K. In contrast, *t*-butylchlorocarbene-*d*₉ is stable to 1,3-CD insertion under these conditions even after 2 days at 30 K.⁵⁸ The "flat" temperature dependence of the 11–30 K 1,3-CH insertion of **18**, together with the very strong isotopic dependence of **18-d**₉ (no C–D insertion), implicates 1,3-H tunneling in the former case. Moreover, because a C–C bond is formed in this insertion reaction, heavy atom tunneling might also be involved.⁵⁸

The photolyses of diazirines **9a** and **9b** were similarly studied in Ar matrices at 10–34.5 K;⁵⁹ Eq. 10. Benzylchlorocarbene (**10a**) and its α,α -*d*₂ analogue (**10b**) were observed by UV or IR (**10b**) spectroscopy, and their decay to styrenes **11** and **12** could be monitored. Tunneling in these 1,2-H(D) shifts was indicated by (a) much higher rates of carbene decay at 10 K than could be anticipated from extrapolation of the 298 K LFP kinetic data, (b) a kinetic isotope effect (KIE) for the 1,2-H(D) shifts estimated at ~ 2000 , and (c) little temperature dependence of the rate at low temperature.⁵⁹ Accepting that QMT is important in the very low temperature H shifts of carbenes **10** and **18**, the obvious question becomes: is QMT important at higher or even ambient temperatures?

Goodman proposed that QMT was responsible for the observed curvature in Arrhenius correlations of the 1,2-H(D) shifts of MeCCl (**15**),⁶⁰ MeCBr,⁶¹ and their *d*₃ analogues. Arrhenius curvature usually signals the active competition of two or more reaction channels characterized by differing activation energies. When QMT intrudes into a classically activated process, the Arrhenius plot of $\log k$ vs. $1/T$ becomes nonlinear, with the curvature tending toward zero activation energy at low temperature.⁶²

The 1,2-H shift of MeCCl was studied by LFP over temperature ranges of –25 to 70°C in dichloroethane and –70 to 80°C in heptane; Arrhenius correlations were curved.⁶⁰ Moreover, the KIE for the 1,2-H(D) shifts of MeCCl and MeCCl-*d*₃ increased with increasing temperature. For example, $k_{\text{H}}/k_{\text{D}}$ was 0.9 at 248 K, but 1.8 at 343 K;⁶⁰ comparable KIEs were observed for MeCBr.⁶¹

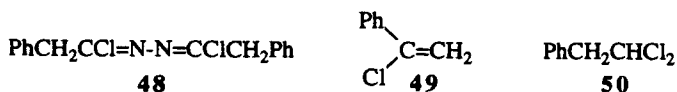
An unusually negative entropy of activation (-16.1 e.u.) was also observed for the 1,2-H shift.⁶⁰

Three possibilities were considered to account for the curved Arrhenius plots and unusual KIEs: (a) the 1,2-H shift might feature a variational transition state due to the low activation energy (4.9 kcal/mol⁶⁰) and quite negative activation entropy; (b) MeCCl could react by two or more competing pathways, each with a different activation energy (e.g., 1,2-H shift and azine formation by reaction with the diazine precursor); (c) QMT could occur.⁶⁰ The first possibility was discounted because calculations by Storer and Houk indicated that the 1,2-H shift was adequately described by conventional transition state theory.⁶³ Option (b) was excluded because the Arrhenius curvature persisted after correction of the 1,2-H shift rate constants for the formation of minor side products (azine).⁶⁰

Goodman concluded that QMT dominated the 1,2-H shifts of MeCCl or MeCBr at low temperatures. At higher temperatures, the classical (activated) mechanism with $E_a = 4.9$ kcal/mol, became important, but even at 298 K, QMT was considered to account for $>85\%$ of the reaction.⁶⁰ Theoretical studies supported the incursion of QMT in these 1,2-H rearrangements, accounting for both the KIE and entropic peculiarities.⁶³ However, calculations implied that the classical mechanism overtook QMT at quite low temperatures (>200 K), so that the 1,2-H shift would be very largely classical at ambient temperature.⁶³ It was also deemed possible that QMT could be important in 1,2-C shifts.⁶³

The studies of MeCCl refocused attention on benzylchlorocarbene (**10a**). Earlier studies of **10a**, over a temperature range of 0 – 31°C , afforded linear Arrhenius correlations for the 1,2-H shift, with $E_a = 4.5$ – 4.8 kcal/mol and $\log A \approx 11.2$ s⁻¹.³⁶ Additionally, LFP studies of *p*-CF₃ and *p*-Cl substituted benzylchlorocarbenes (**10f** and **10g**) in isooctane over a temperature range of -3 to 47°C gave linear Arrhenius correlations with E_a (4.9 and 4.5 kcal/mol) and $\log A$ (10.9 s⁻¹) values comparable to those found for parent carbene **10a**.⁶⁴

Of some concern is the report that photolysis of neat benzylchlorodiazirine (**9a**) gave 40% of azine **48** as well as 40% of chlorostyrenes **11a** and **12a**, 10% of α -chlorostyrene (**49**, the product of a 1,2-Ph shift in carbene **10a**), and 10% of 1,1-dichloro-2-phenylethane (**50**, the product of HCl addition to carbene **10a**).⁶⁵



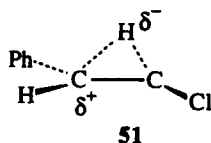
However, it was emphasized that azine **48** was not observed as a product at the 10 – 34 mM diazine concentrations used in the LFP kinetics experiments.^{64,65}

B. Benzylchlorocarbene at Lower Temperatures

The Arrhenius curvature found for the rearrangement of MeCCl prompted a reinvestigation of benzylchlorocarbene reactivity over a wider temperature range.⁶⁶ Indeed, LFP studies in isooctane with diazirine **9a** and its dideuterio analogue (**9b**) from -80 to 60°C afforded curved Arrhenius correlations for the rearrangements of carbenes **10a** and **10b**; Eq. 10. The Arrhenius curves leveled off at -40°C for parent carbene **10a** and at -10°C for its dideuterio analogue, **10b**, where a convergent, limiting rate constant ($\sim 1 \times 10^7 \text{ s}^{-1}$) was reached for carbene rearrangement.⁶⁶ As with MeCCl,⁶⁰ the KIE for **10a/10b** also increased with increasing temperature; e.g., $k_{\text{H}}/k_{\text{D}} \approx 0.87$ at -60°C and 2.62 at 30°C .⁶⁶

The Arrhenius curvature could be attributed to the occurrence of two competing reactions with different activation energies. However, photolysis of **9a** at -80°C afforded only β -chlorostyrenes **11a** and **12a**; no carbene-solvent insertion product was detected, and reaction of the carbene with diazirine to give azine was considered unimportant at the diazirine concentrations employed.

In the more polar solvent, chloroform, *linear* Arrhenius correlations were observed for the rearrangements of both **10a** and **10b** from -55 to 60°C . Arrhenius parameters were $E_{\text{a}} = 3.6 \text{ kcal/mol}$ and $\log A = 10.4 \text{ s}^{-1}$ for **10a**, and $E_{\text{a}} = 4.05 \text{ kcal/mol}$ and $\log A = 10.3 \text{ s}^{-1}$ for **10b**.⁶⁶ These results accord with the idea that polar solvents stabilize the polar 1,2-H shift, hydride-like transition state (**51**), accelerating this reaction at the expense of potential competitors.^{4,22}



Explanations offered for the marked difference between the Arrhenius correlations for benzylchlorocarbene in isooctane and chloroform are either that the carbene reacts with the isooctane or that QMT plays a role at lower temperatures.⁶⁶ The first idea was preferred, with the contention that carbene **10a** did not live long enough to react with CHCl_3 , so that a linear Arrhenius correlation was obtained in that solvent, reflecting only the 1,2-H shift. In contrast, the lifetime of **10a** in isooctane was deemed long enough to permit solvent insertion to compete with the 1,2-H shift, thus leading to Arrhenius curvature. A carbene-solvent complex was postulated in which the vacant carbenic p orbital interacted with an isooctane C-H bond; the complex could lead to insertion or decay via 1,2-H shift.⁶⁶ Although a carbene-solvent product was not identified, the LFP kinetics were "corrected" for a **10a**-CH insertion reaction with $k = 9 \times 10^6 \text{ s}^{-1}$, affording linearized Arrhenius correlations with

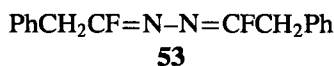
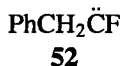
E_a (**10a**) = 5.78 kcal/mol, $\log A = 11.86 \text{ s}^{-1}$, and E_a (**10b**) = 6.68 kcal/mol, $\log A = 11.98 \text{ s}^{-1}$.⁶⁶

Of course carbene C–H insertion reactions are well known; absolute kinetics have been reported for the insertions of ArCCl into isooctane, cyclohexane, and *n*-hexane,⁶⁷ and of PhCCl into Si–H, Sn–H, and C–H bonds.⁶⁸ More recently, detailed studies have appeared of PhCCl insertions into a variety of substrates bearing tertiary C–H bonds, especially adamantane derivatives.⁶⁹ Nevertheless, because QMT is considered important in the low temperature solution reactions of MeCCl,^{60,63} and is almost certainly involved in the cryogenic matrix reactions of benzylchlorocarbene,⁵⁹ its possible intervention in the low temperature solution reactions of the latter is a real possibility. We are therefore faced with two alternative explanations for the Arrhenius curvature exhibited by benzylchlorocarbene in solution at temperatures < 0°C: either other classical reactions (besides 1,2-H shift) become competitive (e.g., solvent insertion, azine formation), or QMT becomes significant.^{7,59,66}

C. Benzylchlorocarbene: Intermolecular Reactions at Lower Temperatures

The possible intervention of classical, competitive reactions in the low temperature solution chemistry of benzylchlorocarbene (**10a**) requires careful investigation. There are reasons to suspect azine (**48**) formation: Goodman reported minor yields of azine in analogous MeCCl experiments,⁶⁰ and Liu et al. found 40% of **48** in the photolysis of neat diazine **9a**.⁶⁵ Perhaps azine formation is also significant at low temperature in hydrocarbon solvents. If so, the intervention of bimolecular azine formation, in competition with the unimolecular carbene 1,2-H shift, could lead to a nonlinear temperature dependence for the disappearance of **10a**. Arrhenius curvature could then be explained without invoking QMT.

Further cause for concern comes from experiments with benzylfluorocarbene (**52**)⁷⁰ and mesitylmethylchlorocarbene (**32**).²⁹



Ambient temperature photolysis of benzylfluorodiazirine in hydrocarbon solvents generated carbene **52** which produced β -fluorostyrenes by 1,2-H shift, and up to 38% of azine **53** via the reaction of **52** with its precursor diazine.⁷⁰ The azine yield reached 70% when the reaction was done at –55°C. In *sym*-tetrachloroethane, where azine formation was only 14% at –5°C, a linear Arrhenius correlation (–7 to 68°C) was obtained for the 1,2-H shift of **52**: $E_a = 3.2 \pm 0.3 \text{ kcal/mol}$ and $\log A = 9.5 \pm 0.2 \text{ s}^{-1}$.⁷⁰

Similarly, photolysis of mesitylmethylchlorodiazirine (**31**) in hydrocarbon

solvents affords carbene **32**, and leads to significant quantities of azine at low temperatures, as well as to curved Arrhenius correlations for the 1,2-H shifts of **32** and **32- α,α - d_2** .²⁹ Azine formation is minimized by lowering the concentration of the diazirine precursor, whereupon *linear* Arrhenius correlations are obtained down to -70°C ($E_a = 4.8$ kcal/mol, $\log A = 10.7$ s⁻¹ for **32**).²⁹ These results suggest that the curved Arrhenius correlations observed with PhCH_2CCl could also be due to mundane competing reactions like azine formation rather than QMT.²⁹

Accordingly, a re-examination of the benzylchlorocarbene system was performed, with close attention paid to the products formed at low temperature.⁷¹ Carbene **10a** was photolytically generated from diazirine **9a** in isooctane, methylcyclohexane, and tetrachloroethane at temperatures ranging from ~ 30 to -75°C . At -70°C in isooctane, the products included 47% of β -chlorostyrenes **11a** and **12a**, 2.4% of α -chlorostyrene (**49**), 2% of dichloride **50**, 5.5% of a C-H insertion product of **10a** and isooctane, 4% of the dimers of **10a**, and 30% of azine **48**.⁷¹ The sum of the intermolecular products at -70°C was thus $\sim 41.5\%$, of which azine was the principal component.

The significant incursion of intermolecular products implies that the kinetic data previously obtained for the disappearance of **10a** at low temperatures⁶⁶ is biased and should not be used in Arrhenius treatments of the 1,2-H shift reaction. Therefore, the curved Arrhenius correlations do not require a QMT rationalization.

Photolytic decomposition of diazirine **9a** in methylcyclohexane led to substantial C-H insertion of PhCH_2CCl into the solvent, although azine was a minor product. At 25°C , there were 74% of 1,2-H shift products and 14% of C-H insertion. Insertion increased to 44% at -75°C . Here too, a curved Arrhenius correlation reflected the competition of two classical reactions, not the incursion of QMT.⁷¹

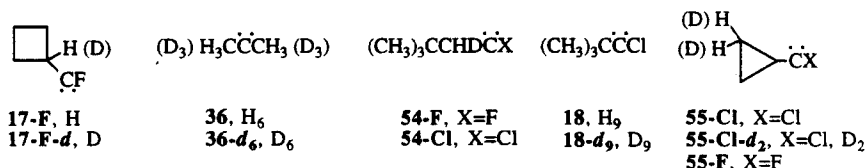
In tetrachloroethane (as in chloroform⁶⁶), however, clean H-shift reactions of **10a** were obtained, even at -71°C .⁷¹ A linear Arrhenius correlation (-71 to 3°C) gave $E_a = 3.2$ kcal/mol and $\log A = 10.0$ s⁻¹,⁷¹ similar to the values obtained in chloroform (3.6 kcal/mol, 10.4 s⁻¹).⁶⁶ In accord with polar solvent stabilization of the transition state (**51**), the activation energy for the rearrangement of **10a** is 3.2–3.6 kcal/mol in the halogenated solvents, but 4.5–4.8 kcal/mol in isooctane (0 – 31°C).³⁶

The totality of evidence suggests that QMT does not play a major role in the 1,2-H rearrangement of benzylchlorocarbene at ambient or near ambient temperatures in solution. At temperatures below -70°C , however, QMT may become important; after all, by -243°C (in Ar matrices) QMT is dominant.⁵⁹ The key question is: at what temperature does QMT first significantly intervene in the *solution* chemistry of benzylchlorocarbene? The practical answer may be “never”, unless very low activation energy intermolecular reactions such as

azine formation can be inhibited. In solution, these reactions become important at low temperatures where the classically activated 1,2-H shift is slowed. At present, only the 1,2-H shift of MeCCl has suggestive evidence for QMT contributions in solution near ambient temperatures.^{60,63}

V. KINETIC ISOTOPE EFFECTS

The unusual temperature dependence of the KIEs observed for both benzylchlorocarbene⁶⁶ and methylchlorocarbene⁶⁰ (see Section IV.A) have been attributed to QMT. Here we will review the KIEs associated with intramolecular carbenic rearrangements, so that the KIEs of PhCH₂CCl and MeCCl can be viewed in context. KIEs will be examined for rearrangements of cyclobutylfluorocarbene (**17-F**),⁷² dimethylcarbene (**36**),^{4,22,73} neopentylfluorocarbene and neopentylchlorocarbene (**54-F** and **54-Cl**),^{2,74,75} *t*-butylchlorocarbene (**18**),^{58,76} and cyclopropylchlorocarbene (**55-Cl**).⁷⁷ KIEs for these carbenes are collected in Table 2.



QMT is considered important in the 1,2-H shift reaction of MeCCl,^{60,63}

Table 2. KIEs for 1,2-H(D) Migrations in Singlet Carbenes

Carbene	Solvent	<i>T</i> range (°C)	<i>k_H</i> / <i>k_D</i> range	Cause of KIE trend	Ref.
MeCCl	ClCH ₂ CH ₂ Cl	−25 to +70	0.9 to 1.8	QMT	60
	calculated	−173 to −73	2.91 to 3.06	QMT	63
MeCBr	heptane	−50 to +70	0.92 to 1.35	QMT	61
10a	Ar, Xe matrices	−263 and −253	~2000	QMT	59
	isooctane	−60 to +30	0.87 to 2.62	reaction with solvent	66
32	isooctane	−68 to +25	4.5	classical mechanism	29
54-F	CDCl ₃	−30 to +22	6.6 to 5.0	classical mechanism	2,74
54-Cl	pentane	+20	3.5	classical mechanism	2,75
	CDCl ₃	+60	2.6	classical mechanism	2,75
18	N ₂ matrix	−262 to −243	→ ∞	QMT	58
	CDCl ₃	−12 to +118	3.25 to 2.14	classical mechanism	76
55-Cl	CDCl ₃	−30 to +60	1.28 to 1.18	classical mechanism	2,77
	calculated	−30 to +60	1.10 to 1.07	classical mechanism	2,77
17-F	decane	−15 to 138	1.67 to 2.50	classical mechanism	72
36	pentane	+25	3.2	QMT	22
	perfluorohexane	−30 to 0	3.07 ^a	QMT	73

Note: ^a Δ*E*₀ for 1,2-D shift minus 1,2-H shift in kcal/mol.

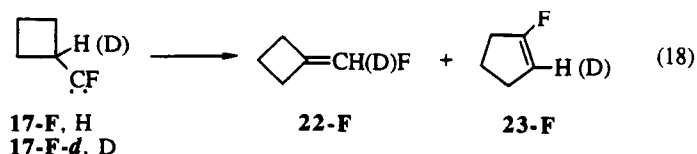
where the experimental values of E_a and $\Delta S^\ddagger$ (4.9 kcal/mol and -16.7 e.u.)⁶⁰ differ greatly from the theoretical ones (11.5 kcal/mol and -3.1 e.u., without tunneling corrections).⁷⁸ Temperature-dependent LFP kinetic studies of the MeCCl 1,2-H(D) shifts revealed curved Arrhenius correlations and a small KIE which increased from 0.9 at -25°C to 1.8 at 70°C .⁶⁰ Previously, it was generally accepted that QMT afforded very large KIEs in solution at low temperature, approaching infinity in cryogenic matrices. To account for the unusual trend with MeCCl, tunneling corrections were included in the computations, predicting a KIE of 2.91 at -173°C that increased slightly to 3.06 at -73°C .⁶³ The computed KIE was reduced with the inclusion of QMT because the tunnel correction for deuterium exceeded that for protium, and the computed activation parameters for the 1,2-H shift ($E_a = 7.7$ kcal/mol, $\Delta S^\ddagger = -14.9$ e.u.) now more closely approached the experimental values.⁶³

These results support the idea that Arrhenius curvature in the rearrangements of MeCCl⁶⁰ (and MeCBr⁶¹) may be associated with QMT, although the theoretical analysis found that QMT dominated the 1,2-H(D) shift only below -73°C ; at higher temperatures, the classical process became more important.⁶³ The benzylchlorocarbene case is less clear. QMT is clearly important in matrices at 10–34 K, where the KIE for 1,2-H(D) shift is ~ 2000 ;⁵⁹ cf. Section IV.A. However, the nonlinear Arrhenius behavior exhibited by **10a** or **10b** in solution is largely due to the intervention of intermolecular reactions (Section IV.C) which obscure any contribution of QMT.⁷¹

We must also consider the increase in KIE with increasing temperature reported for **10a/10b**: $k_{\text{H}}/k_{\text{D}}$ varies from 0.87 to 2.62 over -60 to 30°C in isooctane.⁶⁶ However, these results may be suspect at lower temperatures because k_{H} and k_{D} were obtained by interpolations on smooth curves⁶⁶ drawn through experimental rate constants that are now known to have been “contaminated” by intermolecular reactions.⁷¹

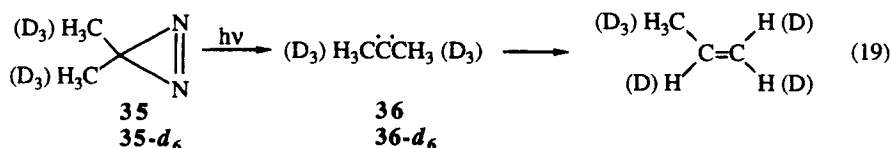
For the related mesitylmethylchlorocarbene (**32** and **32- α,α - d_2**), the KIE also appears to increase with increasing temperature (to 4.8 at 25°C). However, this behavior is also biased by intermolecular chemistry: when the precursor diazine concentration is lowered so as to exclude the intermolecular reactions, the KIE settles at a temperature-independent value of ~ 4.5 for the 1,2-H(D) shift.²⁹

The KIE also increased with increasing temperature for cyclobutylfluorocarbene (**17-F**), where $k_{\text{H}}/k_{\text{D}}$ was measured for a 1,2-H(D) shift from a tertiary migration origin; Eq. 18.⁷²



The KIEs were evaluated from -15 to 138°C from product studies in decane; the shift of H was preferred to D by ratios of 1.67 to 2.50.⁷² Although the KIE increased with increasing temperature, as with MeCCl ,⁶⁰ its magnitude was within the range expected for a classical 1,2-H(D) shift from a tertiary carbon atom. Therefore, the contribution of QMT to these KIEs was unclear.⁷²

The case of dimethylcarbene (**36**) is clearer; Eq. 19. Platz et al. determined that the lifetime in pentane of **36-d₆** (67 nanoseconds) was 3.2 times greater than that of the parent **36** (21 ns) at 25°C ,²² a difference that was attributed to QMT.^{4,22}



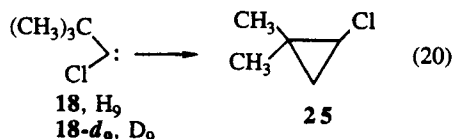
A more recent study of **36** in perfluorohexane lent support to this conclusion.⁷³ Firstly, the experimental barrier to 1,2-H migration in **36** was much smaller than predicted by *ab initio* calculations (2.56 vs. 7.4 kcal/mol), whereas the measured E_a for the rearrangement of **36-d₆** compared well with the computed 5.6 kcal/mol. Secondly, the observed activation parameters revealed large KIEs: $(E_a^D - E_a^H) = 3.18$ kcal/mol, and $A^D/A^H = 158$. These results support the operation of QMT in the 1,2-H shift of **36**.⁷³

Some carbenes exhibit unusually large intramolecular KIEs but seem to react by classical 1,2-H(D) shifts; e.g., neopentylfluorocarbene (**54-F**)^{2,74} and its chloro analogue (**54-Cl**).^{2,75} For **54-F**, k_H/k_D ranged from 6.6 at -30°C to ~ 5.0 at 22°C , as determined from product distributions. These values were corroborated by the LFP-based KIE of 6.5 at 20°C in pentane.⁷⁴ Although the chemistry of **54-Cl** is complicated by the participation of its excited diazine precursor, k_H/k_D could be determined by LFP as 3.5 at 20°C , using the pyridine ylide method.⁷⁵ A similar KIE (2.8) was measured by product analysis for the 1,2-H(D) shifts attending the decomposition of excited neopentylchlorodiazirine.⁷⁵

Methylchlorocarbene exhibits a small KIE that increases with increasing temperature; QMT is considered important in its 1,2-H shift.^{60,63} The KIEs of **54-F** and **54-Cl** are larger, and that of **54-F** decreases with increasing temperature. QMT has not been invoked for these rearrangements, at least at the temperatures studied. However, it is possible that QMT could intervene at lower temperatures (e.g., <200 K, as calculated for MeCCl ⁶³) or in cryogenic matrices.^{58,59}

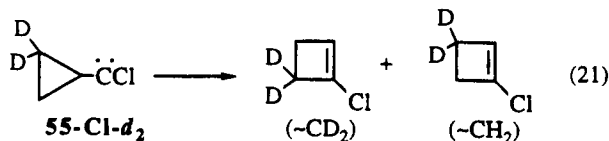
As discussed in Section IV.A, both the 1,2-H shift of benzylchlorocarbene⁵⁹ and the 1,3-CH insertion reaction of *t*-butylchlorocarbene (**18**)⁵⁸ occur via QMT in low temperature matrices. At 11–30 K, the conversion of **18** to cyclopropane

25 is temperature independent, with $k \approx 0.3$ to $4 \times 10^{-4} \text{ s}^{-1}$, whereas **18-d₉** shows no C–D insertion over 40 h at 14 K or 48 h at 30 K.⁵⁸ These results indicate that the KIE approaches infinity. Together, the temperature independence of the C–H insertion rate, and the enormous KIE, give clear evidence for tunneling in the matrix; Eq. 20.



In solution, however, the 1,3-CH insertion reaction of **18** → **25** demonstrates KIEs of “normal” magnitude and temperature dependence. From -12 to $+118^\circ\text{C}$, $k_{\text{H}}/k_{\text{D}}$ ranges from 3.25 to 2.14.⁷⁶ This trend is consistent with that shown by the neopentylhalocarbenes,^{74,75} but contrasts with that reported for methylchlorocarbene⁶⁰ in similar temperature regimes. Based on these comparisons, **18** was assumed to undergo 1,3-CH insertion by QMT at matrix temperatures, but to revert to the classical mechanism at higher temperatures.⁷⁶

Finally, consider the secondary KIE associated with the 1,3-C rearrangement of cyclopropylchlorocarbene (**55-Cl**);^{2,77} Eq. 21. The experimental $k_{\text{H}}/k_{\text{D}}$ for the ring expansion varies from 1.28 at -30°C to 1.18 at 60°C . In *ab initio* calculations, the KIE ranges from 1.10 (-30°C) to 1.07 (60°C).

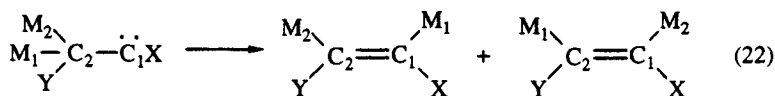


These are reasonable KIEs for a secondary isotope effect in a 1,2-C migration, and originate from the hybridization changes at the migrant carbon ($\text{sp}^{2.6} \rightarrow \text{sp}^{2.4}$); QMT is therefore not invoked.⁷⁷

VI. SUBSTITUENT EFFECTS ON SINGLET CARBENE REARRANGEMENTS

A. Introduction and Definitions

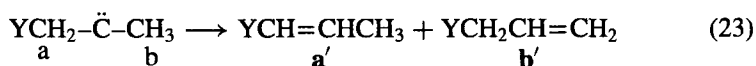
We have seen that 1,2-H migrations in singlet carbenes may be affected by (e.g.) the participation of carbene precursor excited states, QMT, stabilization of the hydride shift transition state by polar solvents, and temperature. Here, we consider our third principal theme, the effect of substituents on the kinetics of carbenic rearrangements. We first examine the influence of “bystander” and “spectator” substituents (as defined in Eq. 22) on 1,2-H rearrangements of alkyl, alkylchloro, and alkylacetoxycarbenes.



where M = migrant group; Y = bystander substituent; X = spectator substituent. The electronic effects of spectator substituents have been analyzed by Evensen and Houk,⁷⁸ and will be elaborated below.

The most common fate of a singlet carbene (at C₁) generated adjacent to saturated carbon C₂ is a 1,2-shift to give an alkene, as in Eq. 22. If two migrant groups (M₁ and M₂) are present on C₂, their relative migration rates can be determined from the product distribution of Eq. 22. From such "competitions", the generally accepted order of inherent migratory aptitudes is H > Ph > Me.^{8,78-80} Nickon, however, suggests that the facility of migration is determined not only by migratory aptitude, but also by the influence of the bystander substituent (Y) present on C₂. When Y enhances the migration of M, the effect is termed "bystander assistance." Indeed, taking account of bystander effects, Nickon concludes that the order of intrinsic migratory aptitudes is actually Ph > H > Me,⁸ a conclusion shared by Keating et al. (KGH) on theoretical grounds.⁸⁰

Using literature data, bystander assistance factors, B[Y], could be calculated for a number of substituents. For example, the thermolysis of certain ketone tosylhydrazone salts afforded dialkylcarbenes which gave competitive 1,2-H shifts, Eq. 23, where either H_a or H_b migrated.



The product ratio a'/b' (statistically corrected for the number of competing H migrants), gives the relative migration rate of H_a vs. H_b, or k_{Ha}/k_{Hb}. The rate constant for the migration of H_a corresponds to the intrinsic migratory aptitude of H_a (M[H]) multiplied by the bystander assistance factor for Y, B[Y]. The carbon atom that bears H_b has no bystander substituent, so that k_{Hb} is simply M[H]. We thus obtain Eq. 24.

$$\frac{k_{\text{H}_a}}{k_{\text{H}_b}} = \frac{M[\text{H}]}{M[\text{H}]} (B[\text{Y}]) \quad (24)$$

Both M[H]s cancel, so that the bystander assistance factor, B[Y], for any substituent, Y, is simply the corrected product ratio a'/b'.⁸ In Eqs. 23 and 24, bystanders Y were found to enhance H-shifts in the order MeO > alkyl > Ph; quantitative data appear in Table 3.⁸

The bystander substituent (Y) exerts a direct influence on the migrant group (M) at the *migration origin*. In contrast, a spectator substituent (X in Eq. 22)

Table 3. Bystander Assistance Factors for Hydrogen Migration in Dialkylcarbenes^a

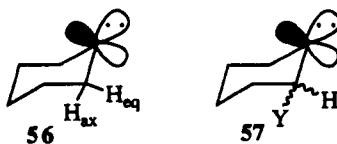
Y	B[Y]
Ph	9.2
Me	28.5
Et	32.3
Allyl ^b	28.1
MeO	73.5

Notes: ^a At 150°C.^b At 100°C.

is bonded to the carbenic center, thereby affecting the electronic environment at the *migration terminus*.⁸¹ Variation of spectator substituents will modulate the lifetime, electrophilicity, and reactivity of a carbene, but should not alter the order of migratory aptitudes or bystander assistance effects operative at the adjacent carbon atom.

Spectator effects were examined computationally in methylcarbene derivatives, MeCX, where it was found that the activation energies for 1,2-H shifts from the Me group were linearly related to the electron donating power of spectator X, as represented by the σ_R^0 substituent constant of X.⁷⁸ MeCX with X = MeO, HO, F, Cl, vinyl, and H were considered. Because electron donation from X modulates the E_a for the 1,2-H shift (E_a increases as donation increases), the spectator also affects the lifetime of MeCX, which therefore increases with increasing electron donation by X.⁷⁸

A more detailed analysis of bystander substituent effects considers rearrangements in cyclic systems; e.g., cyclohexylidene, **56**.⁸

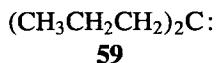
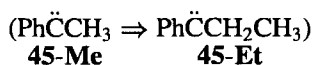
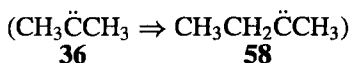


Although stereoelectronic considerations suggest a better alignment of H_{ax} than H_{eq} with the vacant carbenic p orbital, implying $M[H_{ax}] > M[H_{eq}]$, the experimentally observed advantage, ~ 1.7 , is relatively small.⁸ This is not true for the bystander effect of the axial or equatorial group, Y, in **57**. Experimental results from conformationally anchored cyclohexylidenes indicate that an equatorial methoxy bystander promotes 1,2-H migration ~ 23 times more than an axial methoxy bystander.⁸ With Y = Ph, the eq > ax bystander advantage is only ~ 1.6 , but with the rotationally symmetric Me bystander, this ratio rises to ~ 4.6 .⁸²

The effectiveness of equatorial vs. axial bystanders at promoting the 1,2-H shift ($\text{MeO} > \text{Me} > \text{Ph}$) may be related to their ability to stabilize the partial positive charge that arises at the migration origin during the 1,2-H shift. In this scenario, the lone pairs of the MeO group are superior to the hyperconjugative and inductive properties of Me, whereas the conformationally dependent π -electron release of Ph is the least effective.

B. Substituent Effects in Dialkylcarbenes

By stabilizing partial positive charge development at the migration origin during 1,2-H (hydride) shifts, electron releasing alkyl groups enhance the rates of singlet alkylcarbene rearrangements and decrease the lifetimes of these species. Substitution of an ethyl group for a methyl group of dimethylcarbene (**36**) transforms it to ethylmethylcarbene (**58**), and reduces the lifetime from 21 to ~ 2 ns in pentane.²²

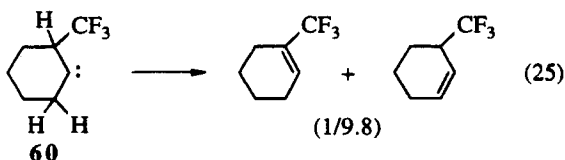


This reflects an enhancement of the 1,2-H shift rate constant from $\sim 4.8 \times 10^7 \text{ s}^{-1}$ to $5 \times 10^8 \text{ s}^{-1}$. Similarly, the rate constant for the 1,2-H migration of phenylmethylcarbene (**45-Me**) increases 60-fold (to $\sim 3.6 \times 10^8 \text{ s}^{-1}$) upon Me substitution to phenylethylcarbene, **45-Et**.⁸³

In the same vein is the observation that the lifetime of dipropylcarbene (**59**) in CH_2Cl_2 or cyclohexane is ~ 0.3 ns,⁸⁴ which, after statistical correction is ~ 48 times less than the lifetime (~ 21 ns) of Me_2C in pentane.²² This reflects promotion by the propyl bystander groups of **59** of the 1,2-H shift to Z- and E-3-heptene.⁸⁴ (Dipropylcarbene can be photolytically generated from either an oxadiazoline (diazalkane)⁸⁴ or diazirine⁸⁵ precursor, but RIES lowers the efficiency of carbene production in either case.) Recently reported LFP lifetimes for Et_2C and MeCEt in cyclohexane or benzene are 0.6–3 ns (cyclohexane) or 1–5 ns (benzene),¹⁴ in accord with the lifetimes of **58**²² and **59**.⁸⁴ The rate constants for carbene disappearance in cyclohexane ($\sim 3 \times 10^8$ to $2 \times 10^9 \text{ s}^{-1}$) are presumably limited by 1,2-H shifts.¹⁴

LFP affords the lifetime of cyclohexanylidene (**56**) in cyclohexane as ~ 0.1 – 0.7 ns ($k_{\text{H}} \approx 0.14$ to $1.0 \times 10^{10} \text{ s}^{-1}$),¹⁴ so that transformation of dimethylcarbene (**36**) to **56** elicits a lifetime decrease similar to that observed in the analogous **36** $\Rightarrow$ **59** change. Of particular interest is the finding that the competitive 1,2-H

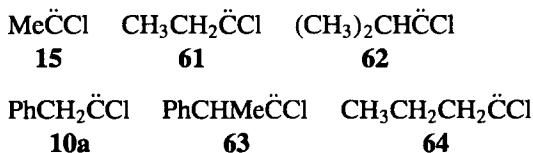
shifts of 2-trifluoromethylcyclohexanylidene (**60**) favor migration of H from the unsubstituted β -carbon, rather than the CF_3 -substituted carbon atom; Eq. 25.¹⁴



The 10-fold disadvantage of the latter 1,2-H migration can be attributed to destabilization of the corresponding transition state by the inductively electron-withdrawing CF_3 bystander.¹⁴

C. Alkylchlorocarbenes

Bystander effects are also known for a variety of alkylchlorocarbenes.^{60,80,86–88} Absolute rate constants for the rearrangements of MeCCl (**15**), EtCCl (**61**), and $i\text{-PrCCl}$ (**62**), as determined by photoacoustic calorimetry were reported by LaVilla and Goodman.⁶⁰



The lifetime of **15** (740 ns) was reduced to less than 10 ns by substitution of one or two Me groups on the methyl carbon atom; i.e., the 1,2-H shifts of **61** and **62** were strongly promoted by methyl bystander substituents.⁶⁰

LFP with ps time resolution gave more precise kinetic data for carbene **62**, as well as PhCH_2CCl (**10a**), α -methylbenzylchlorocarbene (**63**), and $n\text{-PrCCl}$ (**64**).^{86,87} Rate constants for the 1,2-H migrations of these carbenes in isooctane solution are compiled in Table 4. Taking MeCCl (**15**) as the reference carbene, substitution of a phenyl (to **10a**) or an alkyl substituent (to **61** or **64**) increases the rate of 1,2-H migration by 20–30 times, whereas substitution of two bystander substituents, e.g., methyl plus phenyl (**15** to **63**), yields an increase of ~ 165 times. Indeed, with two methyl bystanders (**15** to **62**) the 1,2-H shift is too rapid to measure, even at -90°C .⁸⁷ In general, rate enhancements promoted by methyl bystanders reflect decreased activation energies for the 1,2-H shifts (Table 4). Early MNDO and MINDO/3 calculations on carbenes **10a**, **62**, **63**, and **64** support this conclusion.

Keating, Garcia-Garibay, and Houk (KGH) provided an elegant and extensive theoretical survey of the 1,2-H and 1,2-Ph rearrangements of eight alkylchlorocarbenes at the B3LYP/6-311G^{*}//B3LYP/6-31G^{*} level.⁸⁰ Included were carbenes **15**, **61**, **62**, **63**, **64**, **10a**, fluoromethylchlorocarbene (**65-F**), and

Table 4 Rate Constants and Activation Parameters for Alkylchlorocarbene Rearrangements at 25°C in Isooctane^a

Carbene	Type of shift	$k_{H,25}$ (s ⁻¹)	E_a (kcal mol ⁻¹)	$\Delta G_{25}^\ddagger$ (kcal mol ⁻¹)	$\Delta S_{25}^\ddagger$ (e.u.)	Ref.
15 (MeCCl)	1,2-H	3.0×10^6	9.4 ^b		-3.5 ^b	86
		1.4×10^6	4.9			60
			11.5 ^b	12.2 ^b	-3.8 ^b	78,80
61 (EtCCl)	1,2-H	$>10^8$ ^b				60,86
		1.3×10^8 ^b	6.0 ^b		-3.1 ^b	86
			4.9 ^c			80
			6.9 ^d	7.3 ^c	-2.2 ^d	80
64 (<i>n</i> -PrCCl)	1,2-H	5.9×10^7	3.6		-12.8	87
		8.6×10^7 ^b				86
62 (<i>i</i> -PrCCl)	1,2-H	$>10^8$ ^e	~2			87
		8.8×10^7 ^b	2.5		-3.8	86
			3.9 ^b	4.4 ^b	-2.3 ^b	80
18 (Me ₃ CCCl)	1,2-Me	1.1×10^7	1.0 ^b			12,86
65-Cl (ClCH ₂ CCl)	1,2-H	2×10^7		7.5		20
			10.9 ^b	11.7 ^b	-3.7 ^b	80
65-F (FCH ₂ CCl)	1,2-H		9.0 ^b	9.4 ^b	-2.4 ^b	80
10a (PhCH ₂ CCl)	1,2-H	6.2×10^7	4.5-4.8		-8.9	36
			4.3 ^b		-3.6 ^b	86
			5.5 ^b	6.2 ^b	-3.3 ^b	80
	1,2-Ph		9.2 ^b	10.5 ^b	-6.0 ^b	80
63 (PhCHMeCCl)	1,2-H	$\sim 5 \times 10^8$ ^f	2.85-3.0		-11.7	87
			2.3 ^b			86
			5.1 ^b	5.5 ^b	-1.7 ^b	80
	1,2-Ph		8.2 ^b	9.4 ^b	-5.1 ^b	80
66^g (Ph ₂ CHCCl)	1,2-H and 1,2-Ph	2.2×10^7 ^g	1.65 ^h		-21	88

Notes: ^a Experimental values unless otherwise indicated.^b Calculated or *ab initio* values.^c ΔH value, from E.J. Dix, Ph.D. Thesis, University of Rochester, New York, 1994.^d Average, calculated from *cis*- and *trans*-isomers.^e Estimated, at -90°C.^f Estimated value.^g 2.1×10^7 s⁻¹ for 1,2-H and 1.5×10^6 s⁻¹ for 1,2-Ph shifts (in pentane).^h In tetrachloroethane.chloromethylchlorocarbene (**65-Cl**).**65-F**, X=F; **65-Cl**, X=Cl

KGH provide ground state and rearrangement transition state structures and energies for these carbenes, as well as activation energies for their 1,2-H

shifts.⁸⁰ As summarized in reference 88, highlights of the KGH analysis include the following. (a) The generally accepted migratory aptitude in 1,2-carbenic rearrangements ($H > Ph > Me$) is strongly influenced by bystander effects.^{8,82} (b) The *innate* barrier opposing a 1,2-Ph shift (computed as 9.2 kcal/mol in **10a**) is actually *lower* than that for a 1,2-H shift (computed as 11.5 kcal/mol in **15**); i.e., the intrinsic migratory aptitudes are $Ph > H$. One observes 1,2-H migration in **10a** because the Ph bystander lowers the E_a for the 1,2-H shift from 11.5 kcal/mol in (**15**) to 5.5 kcal/mol in **10a**, which is then more favorable than the 1,2-Ph shift ($E_a \approx 9.2$ kcal/mol). (c) As bystander substituents, Ph exceeds Me at promoting a 1,2-H shift, but only if steric factors do not inhibit Ph conjugation with the developing $C=C$; steric inhibition can render Ph less effective than Me.^{80,82} (d) The desired alignment of Ph can be disrupted by a second C_2 substituent; e.g., a *gem*-Me prevents Ph from maintaining planarity with the developing $C=C$, and lessens its stabilizing effect. Bystander substituent effects are therefore not simply additive; two Me groups promote a 1,2-H shift more than one Ph and one Me.

The activation parameters computed for 1,2-shifts by KGH are included in Table 4.⁸⁰ In general, bystander substituents are computed to accelerate 1,2-H shifts in the order $Ph > Me > F > Cl > H$. Methyl bystanders also promote the 1,2-Ph shift. Substitution of Me for a proton of $MeCCl$ (**15** to **61**) lowers the E_a for 1,2-H migration by 4.6 kcal/mol; an additional Me bystander (**61** to **62**) further reduces E_a by 3.0 kcal/mol; the Me bystander effects are not strictly additive.^{8,80} The Ph bystander effect is computed to exceed that of Me; the 1,2-H shift E_a is reduced by 6.0 kcal/mol when **15** is transformed to **10a** by Ph substitution. (Compare with $\Delta E_a = 4.6$ kcal/mol for the **15** to **61** Me substitution.)

Interestingly, comparison of the barriers for 1,2-H migration in $MeCCl$ and 1,2-Ph migration in $PhCH_2CCl$ gives the inherent migratory aptitudes free of bystander effects.⁸⁰ The 1,2-Ph shift ($E_a = 9.2$ kcal/mol) is preferred to the 1,2-H shift (11.5 kcal/mol). (However, the unfavorable $\Delta S^\ddagger$ associated with Ph migration lowers the differential $\Delta G^\ddagger$ to about 1.7 kcal/mol.) Bystander effects can thus cause the dominance of 1,2-H shifts observed in experiment.⁸⁰ With $PhCH_2CCl$, for example, 1,2-H shift is aided by the Ph bystander, but there is no bystander to promote the inherently more favorable 1,2-Ph shift. QMT⁶³ may also accentuate the dominance of 1,2-H over 1,2-Ph shifts; the latter would not be expected to benefit from QMT.⁸⁰

A fluorine bystander is more effective at promoting the 1,2-H shift than a chlorine bystander (**15** to **65-F** vs. **15** to **65-Cl**); the F for H bystander substitution lowers the E_a by 2.5 kcal/mol. The advantage of fluorine is due to more effective donation of its 2p lone pair electrons toward the developing positive charge at the migration origin during the 1,2-H (hydride) shift.⁸⁰

These bystander accelerations of 1,2-migrations generally operate by reduc-

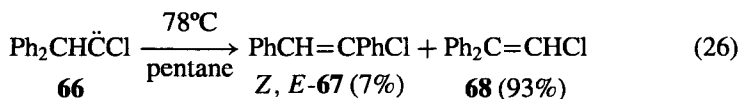
tion of enthalpies of activation,^{80,86,87} entropic factors are less significant. It is noteworthy, however, that the computed entropies of activation for the 1,2-H shifts (-2 to -4 e.u.)⁸⁰ are much more positive than the experimentally measured values, which are quite negative¹ (e.g., $\Delta S^\ddagger = -16$ e.u. for MeCCl⁶⁰). A very similar value, $\Delta S^\ddagger = -17$ e.u., is estimated for the 1,2-H shift of methylcarbene to ethylene.⁸⁹ The unfavorable $\Delta S^\ddagger$ is presumably associated with the need of the migrant H to navigate a 90° turn away from its original trajectory after traversing the transition state to the product, resulting in a small transmission coefficient expressed as a very unfavorable $\Delta S^\ddagger$.⁸⁹

Inspection of the activation energy data in Table 4 reveals that, generally, the computed E_a s are higher than the corresponding experimental values; e.g., for MeCCl, E_a is computed at 11.5 kcal/mol whereas the observed value is ~ 5 kcal/mol. The discrepancies could be due to imprecision in the calculations; larger basis sets yield lower E_a s. Additionally, the actual 1,2-H shift E_a s may be lowered by QMT.⁸⁰

Bystander-induced reductions in the activation barriers for 1,2-Ph migrations were also computed.⁸⁰ For instance, α -Me substitution on PhCH₂CCl (**10a** to **63**) decreased the E_a for a 1,2-Ph shift by ~ 1 kcal/mol (9.2 vs. 8.2 kcal/mol in Table 4). A methyl bystander thus promotes 1,2-Ph shifts, but not as strongly as 1,2-H shifts, where ΔE_a is computed as 4.6 kcal/mol for the 1,2-H shifts of MeCCl vs. EtCCl.⁸⁰

An interesting case is that of diphenylmethylchlorocarbene, **66**. Although calculations are lacking, KGH note that steric interactions between the *gem*-C₂ phenyl groups would prevent effective bystander stabilization of a 1,2-H shift transition state, although good alignment of a single Ph bystander with the developing alkene's π -system might significantly accelerate a 1,2-Ph shift. Therefore, rearrangement of **66** might include a substantial 1,2-Ph shift component.⁸⁰

Experimental results for the rearrangement of **66** appear in Eq. 26, where the 7% of **67** corresponds to the 1,2-Ph shift and the 93% of **68** to the 1,2-H shift.⁸⁸



Clearly, Ph migration is the minor pathway; correcting the product distribution for the 2 : 1 statistical advantage of Ph over H, the 1,2-H migration is ~ 27 times more prevalent. The (uncorrected) LFP kinetic results are $k_H = 2.1 \times 10^7 \text{ s}^{-1}$ and $k_{Ph} = 1.5 \times 10^6 \text{ s}^{-1}$ at 25°C in pentane.⁸⁸

Note, from Table 4, that k_H for PhCH₂CCl is $\sim 6 \times 10^7 \text{ s}^{-1}$, about 3 times greater than k_H for Ph₂CHCCl. This underscores the previously noted non-additivity of bystander effects on rate constants; in going from **10a** to **66**, the second Ph bystander actually slows the 1,2-H shift. The KGH analysis provides a solution to this conundrum. Steric effects in **66** cause the second Ph to adopt

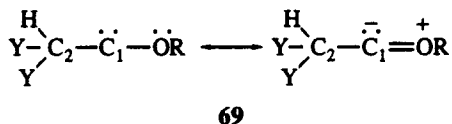
a conformation in which it cannot stabilize the developing positive charge at the migration origin by π -electron donation. Rather it destabilizes that charge by a mild electron-withdrawing inductive effect.

The rearrangement of **66** was also studied in tetrachloroethane (TCE) where the **67/68** product distribution was 12 : 88 at 78°C, indicating a slight increase in 1,2-Ph shift in the more polar solvent.⁸⁸ The measured E_a for (mainly) the 1,2-H shift of **66** was 1.6 kcal/mol,⁸⁸ just half of the 3.2 kcal/mol observed for this process with PhCH₂CCl in TCE.⁷¹ However, the reduced E_a of Ph₂CHCCl was offset by a less favorable pre-exponential factor ($\log A = 8.6 \text{ s}^{-1}$ for **66** vs. 10.0 s^{-1} for **10a**), demonstrating that in terms of $\Delta G^\ddagger$ for these rearrangements, a second phenyl bystander both giveth and taketh away.

D. Acetoxycarbenes

The intramolecular 1,2-H shifts of alkylchlorocarbenes are often very rapid making it difficult to relate structure with reactivity in terms of absolute rate constants. For example the k_H values of Me₂CHCCl, PhCHMeCCl, and EtCCl exceed 10^8 s^{-1} in hydrocarbon solvents at 25°C (Table 4).^{60,86,87} However, due to the stabilizing effect of the oxa *spectator* substituent, acetoxycarbenes react at much reduced rates relative to their chlorocarbene analogues,^{90,91} thus providing kinetically accessible results for a wide array of bystander-substituted alkylacetoxycarbenes.^{81,92}

Spectator substituents, bonded to the carbene's migration terminus (C₁), directly influence the lifetime and philicity of the carbene, but they do not primarily alter the migratory aptitudes of migrants on C₂. Oxa spectator substituents stabilize singlet carbenes by electron donation to the vacant carbenic p orbital (LUMO); cf. resonance hybrid **69**.



Indeed, such donation is calculated to stabilize singlet dimethoxycarbene by 76 kcal/mol relative to the corresponding triplet.⁹³ The electron donation also modulates carbenic reactivity;⁷⁸ a strong electron donor on C₁ raises both the carbene's HOMO and LUMO energies, thereby increasing the carbene's nucleophilicity while rendering its LUMO less accessible to nucleophiles (decreasing its electrophilicity).⁹⁴ These consequences are illustrated by **69** and the related structures in Scheme 6.

The nucleophilicity of oxacarbenes can be fine-tuned by adjusting the oxa substituent's donor potential.⁹¹ For instance, due to its inductively withdrawing CF₃ unit, the trifluoroethoxy group ($\sigma_R^+ = -0.56$) is less electron donating

Substituent	Resonance contributors		Trend
CH ₃ O-	$\text{R}-\ddot{\text{C}}-\ddot{\text{O}}\text{CH}_3$	$\longleftrightarrow \text{R}-\ddot{\text{C}}=\overset{+}{\text{O}}\text{CH}_3$	↑ nucleophilic
CF ₃ CH ₂ O-	$\text{R}-\ddot{\text{C}}-\ddot{\text{O}}\text{CH}_2\text{CF}_3$	$\longleftrightarrow \text{R}-\ddot{\text{C}}=\overset{+}{\text{O}}\text{CH}_2\text{CF}_3$	
CH ₃ COO-	$\text{R}-\ddot{\text{C}}-\ddot{\text{O}}-\overset{\text{O}}{\parallel}\text{CCH}_3$	$\longleftrightarrow \text{R}-\ddot{\text{C}}=\overset{+}{\text{O}}-\overset{\text{O}}{\parallel}\text{CCH}_3 \longleftrightarrow \text{R}-\ddot{\text{C}}-\overset{+}{\text{O}}=\overset{-}{\text{O}}\text{CCH}_3$	↑ electrophilic
X-	$\text{R}-\ddot{\text{C}}-\ddot{\text{X}}$	$\longleftrightarrow \text{R}-\ddot{\text{C}}=\overset{+}{\text{X}}$	

Scheme 6. Resonance contributors of oxacarbenes.

than methoxy ($\sigma_{\text{R}}^+ = -0.66$), so that trifluoroethoxycarbenes are more reactive and less nucleophilic than corresponding methoxycarbenes (Scheme 6).⁹⁵ An acetoxy substituent ($\sigma_{\text{R}}^+ = -0.26$) is a still weaker electron donor than trifluoroethoxy, as suggested by the acetoxycarbene formulation in Scheme 6. Here, an oxygen lone pair is delocalized over both the carbenic center and the acetoxy carbonyl group. Considering only substituent resonance donation, as represented by σ_{R}^+ , acetoxy-substituted carbenes ($\sigma_{\text{R}}^+ = -0.26$) should be closer in reactivity to the analogous chlorocarbenes ($\sigma_{\text{R}}^+ = -0.21$) than to methoxycarbenes ($\sigma_{\text{R}}^+ = -0.66$).⁹¹

Nevertheless, acetoxycarbenes are less reactive than analogous chlorocarbenes, as shown by the data in Table 5, where we compare 1,2-H shift rate constants for phenoxymethyl-, cyclobutyl-, and isopropyl halo and acetoxy carbenes. Decreased rates of 1,2-H shifts are observed, due to the influence of the acetoxy spectator substituents, with the kinetic suppression reaching a factor > 900 for the comparison of cyclobutylacetoxycarbene with cyclobutylchlorocarbene.⁸¹

Table 5. Rate Constants for 1,2-H Shifts of Halo and Acetoxycarbenes in Hydrocarbon Solvents^a

Carbene	k_{H} (s ⁻¹)	$k_{\text{H}}(\text{X})/k_{\text{H}}(\text{OAc})$	Ref.
PhOCH ₂ CCl	3.6×10^7 ^b	8.8	96
PhOCH ₂ CF	1.3×10^7 ^b	3.2	96
PhOCH ₂ COAc	4.1×10^6	—	90
CbCCl ^c	1.2×10^7	923	28
CbCF ^c	5.3×10^5	41	96
CbCOAc ^c	1.3×10^4	—	81
<i>i</i> -PrCCl	$\sim 10^8$ ^d	~ 25	87
<i>i</i> -PrCOAc	4.0×10^6	—	81

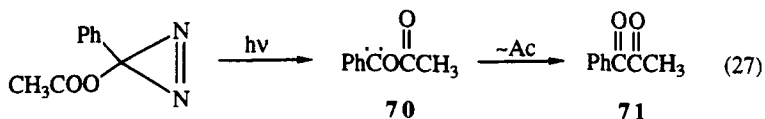
Notes: ^a 20–25°C.

^b At –32°C.

^c Cb = cyclobutyl; cf., structures 17.

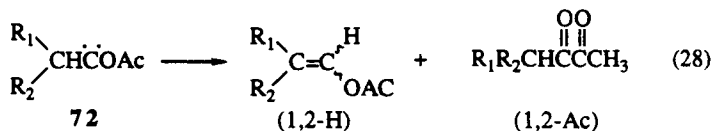
^d At –90°C.

The signature reaction of acetoxy-carbenes is the 1,2-acetyl migration, illustrated for phenylacetoxy-carbene (**70**) in Eq. 27.⁹⁰ At 25°C, LFP (pyridine ylide method) affords $k_{Ac} = 1.3 \times 10^5 \text{ s}^{-1}$ for rearrangement of **70** to dione **71**.



The kinetics, activation parameters, and substituent effects attending the acyl rearrangements of acyloxy-carbenes have been analyzed in detail from both the experimental and theoretical viewpoints; further discussion will appear below in Section VII.D.

If the second substituent of an acetoxy-carbene (or acyloxy-carbene) can undergo a 1,2-H shift, then there may be an intracarbenic competition between this rearrangement and the expected 1,2-acetyl migration; Eq. 28 provides an example where carbene **72** affords both 1,2-H and 1,2-Ac migrations.



The kinetics of alkylacetoxy-carbene rearrangements provides another opportunity to observe the influence of bystander substituents on 1,2-H shifts. Carbenes **73–77** undergo the competitive rearrangements of Eq. 28 with the product distributions and associated LFP rate constants shown in Table 6 (with k_H and k_{Ac} partitioned according to the product distributions).^{88,92}

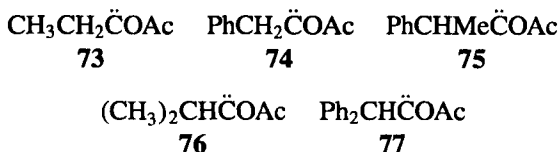


Table 6. Rearrangements of Alkylacetoxy-carbenes, RCOAc^a

<i>R</i> in RCOAc	1,2-Ac (%)	1,2-H (%)	$10^{-5} k_{Ac}, \text{ s}^{-1}$	$10^{-5} k_H, \text{ s}^{-1}$	Ref.
MeCH ₂ (73)	82.2	17.8	0.74	0.16	92
PhCH ₂ (74)	82.6	6.8 ^b	6.8	0.57	92
PhCHMe (75)	37.6	62.4	0.96	1.6	92
Me ₂ CH (76)	5.2	94.8	1.1	19.0	92
Ph ₂ CH (77)	88.6	11.4	56.0	7.2	88

Notes: ^a In tetrachloroethane (TCE) at 25°C.

^b Carbene dimer (10.6%) also formed; rate constants are corrected for dimer formation.

Although the carbenes are generated by diazirine photolysis, RIES is an unlikely complication because the alkylacetoxycarbenes (e.g., **76**) can be almost completely scavenged by added alkenes, with the suppression of rearrangement products.⁸¹

A detailed analysis of the data in Table 6 supports the operation of bystander effects on the 1,2-H shifts of RCOAc.⁹² For example, substitution of an α -Me group on EtCOAc (**73**) gives Me₂CHCOAc (**76**), and increases the H/Ac migration ratio from 18/82 to 95/5. The corresponding rate constants indicate that the gain in 1,2-H migration accompanying introduction of an additional Me bystander is due to a 121-fold enhancement in k_H , slightly offset by a 1.4-fold increase in k_{Ac} .⁹²

Parallel substitution of α -Ph on **73** gives PhCHMeCOAc (**75**), where k_H increases by 9.9 times while k_{Ac} increases only 1.3 times. Note that the α -Me bystander is ~ 12 times ($121/9.9$) more effective than an α -Ph bystander substituent at driving the 1,2-H shift. A similar conclusion emerges upon comparison of the k_H values of **77** vs. **76**, where an α -Me is substituted for an α -Ph group and k_H increases by a factor of 12.⁹²

The 1,2-H shift promotion due to α -Me substitution, and the superiority of bystander Me over Ph with the alkylacetoxycarbenes, are similar to observations for the alkylchlorocarbenes discussed above in Section IV.C.^{8,60,80,86,87} However, this conclusion is tempered by the behavior of Ph₂CHCOAc (**77**), where k_H ($7.2 \times 10^5 \text{ s}^{-1}$) exceeds k_H for both PhCHMeCOAc and PhCH₂COAc ($5.7 \times 10^4 \text{ s}^{-1}$), although it remains inferior to k_H for Me₂CHCOAc ($1.9 \times 10^6 \text{ s}^{-1}$). Thus, for RCOAc (as for RCCl), two α -Me bystanders promote a 1,2-H shift more than two α -Ph groups,⁸⁸ while with RCOAc (but *not* RCCl) one α -Me and one α -Ph together are less effective than two α -Ph bystanders.^{88,92} With Ph₂CHCOAc *no* 1,2-Ph migration is observed, while 12% of this process occurs in TCE at 78°C with Ph₂CHCCl.⁸⁸

Activation parameters measured for the aggregate 1,2-H and 1,2-Ac rearrangements of carbenes **73–76** ranged from $E_a = 13.4 \text{ kcal/mol}$, $\log A = 14.8 \text{ s}^{-1}$ for **73** to $E_a = 2.5 \text{ kcal/mol}$, $\log A = 7.7 \text{ s}^{-1}$ for **74**. There was an underlying compensation between E_a and $\log A$, with a decrease in E_a opposed by a decrease in $\log A$. Similar compensation was noted in the Eyring parameters, $\Delta H^\ddagger$ and $\Delta S^\ddagger$; carbene structural changes that led to lower, more favorable $\Delta H^\ddagger$ also engendered opposing entropic changes.⁹²

Kinetic effects of solvent polarity are also observed with the alkylacetoxycarbenes. Polar solvents promote 1,2-H shifts,^{22,83} and the 1,2-H/1,2-Ac migration ratio of **76** increases from 50/50 to 95/5 as the solvent is changed from isooctane to TCE; a parallel alteration (26/74 to 62/38) occurs with carbene **75**.⁹² Thus, bystander substituents or a polar solvent exert positive effects on the 1,2-H shifts of alkylacetoxycarbenes.⁹²

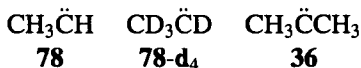
VII. KINETICS OF 1,2-REARRANGEMENTS

A. Introduction

The principal themes of this chapter (RIES, QMT, and bystander substituent effects) were considered in previous sections. This concluding section will survey the signature 1,2-rearrangements of singlet alkylcarbenes in a somewhat wider context. Carbene lifetimes, the kinetics of rearrangement, and migration preferences will be surveyed for alkyl, dialkyl, and alkylhalocarbenes, as well as phenylacyloxy-carbenes, various cycloalkylcarbenes, and cycloalkylenes. An **Appendix** is included, which summarizes rate constants and activation parameters for the rearrangements discussed in this chapter.

B. Alkyl, Dialkyl, and Alkylhalocarbenes

The simplest carbene capable of a 1,2-H shift, methylcarbene (**78**) is very difficult to study experimentally. Theoretical studies suggest that the carbene is a ground state triplet lying ~ 5 kcal/mol below the singlet.⁹⁷



Generation of **78** by thermolysis or photolysis of a diazoalkane or diazirine precursor, however, affords the singlet carbene, whose 1,2-H shift to ethene is opposed by a barrier of only 0.6⁷⁸ to 1.2⁹⁸ kcal/mol. Consequently, even in cryogenic matrices, singlet **78** rearranges more rapidly than it intersystem crosses to the triplet, which has therefore not been detected by UV or ESR in either an Ar matrix at 8 K or a Xe matrix at 15 K.⁹⁹ The lifetime of singlet **78** at ambient temperature has been estimated at <0.5 ns.^{89,98b} (Note the enormous spectator substituent effect of Cl: the lifetime of MeCCl is ~ 740 ns,⁶⁰ at least 1500 times longer than that of MeCH.)

Despite its fleetingness, **78** has been captured by CO in a matrix at 10 K, affording low yields of ketene.⁹⁹ Modarelli and Platz were unable to observe the formation of a pyridine ylide upon LFP generation of **78** in pyridine/pentane at -40°C . However, with perdeuterated methylcarbene (**78-d₄**) a weak pyridine ylide signal was detected, and the rate constant of the 1,2-D shift could be estimated as $k_D \approx 2 \times 10^9 \text{ s}^{-1}$ ($\tau \approx 0.5$ ns) using a Stern–Volmer analysis (see Eqs. 3–6 in Section II).⁸⁹ The activation energy for this 1,2-D shift was estimated at 2.3 kcal/mol, assuming $A \approx 10^{11} \text{ s}^{-1}$.⁸⁹ However, it seems likely that both E_a and A are somewhat lower, with $A \approx 10^8$ to 10^9 s^{-1} ($\Delta S^\ddagger \approx -17$ e.u.).⁸⁹

Substitution of a second Me substituent at the carbenic center of **78** furnishes dimethylcarbene (**36**), the simplest dialkylcarbene. A significant spectator effect attends the change of H to Me: the lifetime of **36** is ~ 21 ns ($k_H \approx 5 \times 10^7 \text{ s}^{-1}$),

more than 40 times longer than that of **78-d₄**, and the lifetime of Me₂C-d₆ is ~67 ns, 134 times longer than that of **78-d₄** (while manifesting a KIE of ~3.2 for its 1,2-D shift vs. the 1,2-H shift of **36**).^{22,89}

Computational studies on Me₂C suggest that the singlet carbene, stabilized by methyl group C–H hyperconjugative electron release to the carbenic p orbital (LUMO), is now the ground state by ~1.5 kcal/mol.^{100,101} Methyl substituent stabilization of the singlet over the triplet state of the simplest carbenes is roughly additive, with ($E_S - E_T$) ~9 kcal/mol for CH₂, 3¹⁰⁰ to 5⁹⁷ kcal/mol for MeCH, and –1.5 kcal/mol for Me₂C.^{100,101} Further discussion of the 1,2-H rearrangement of Me₂C⁷³ appears above in Section V.

In general, substituted methylcarbenes, MeCX, undergo 1,2-H shifts with $k_H = 10^7$ to 10^8 s^{–1} in hydrocarbon solvents when X = alkyl,²² and ~10⁶ s^{–1} when X = Ph ($k_H \approx 6 \times 10^6$ s^{–1})⁸³ or halogen (e.g., MeCCl).^{26,60,61,83,86} As expected, their 1,2-H migrations are accelerated in polar solvents (e.g., MeCN), with k_H increasing 3–5 times for Me₂C and MeCPh (where E_a is reduced by ~2.3 kcal/mol).^{22,83} We should remember, however, that the rearrangements of some of these carbenes are complicated by RIES and/or QMT (MeCCl, MeCBr, Me₂C).^{4,60,61}

In Section VI.C, we saw that alkyl bystander substituents promoted 1,2-H shifts. In isooctane, k_H for Me₂CHCCl and EtCCl (>10⁸ s^{–1}), as well as *n*-PrCCl (5.9×10^7 s^{–1}) were increased by 1–2 orders of magnitude over k_H for MeCCl (3×10^6 s^{–1}).^{86,87} Similarly, for PhCEt, which is formally derived from PhCMe by addition of a Me bystander substituent, k_H is enhanced ~60 times (to 3.6×10^8 s^{–1}), while E_a is reduced by ~2.5 kcal/mol by the methylation.⁸³

The stabilizing effect of the acetate substituent was described in Section VI.D. Although the 1,2-H shifts of alkyl and alkylhalocarbenes span the 10⁶ to 10⁸ s^{–1} range, the analogous rate constants for alkylacetoxycarbenes are on the order of 10⁵ s^{–1}.^{81,88,92}

In general, 1,2-C shifts do not compete effectively with the 1,2-H shifts of acyclic alkyl and alkylhalocarbenes. However, *t*-butylchlorocarbene (**18**) lacks the α-H needed for a 1,2-H shift, and so affords 1,3-CH insertion and 1,2-Me migration; Eq. 14. Note that only for the thermally generated **18** is the 1,2-Me shift product (**26**) derived from the carbene. Photolytic generation of **18** from diazirine **24** gives only 1,3-CH insertion to dimethylchlorocyclopropane **25**; in this case, the 1,2-Me shift product is formed by RIES of the diazirine.²⁷ Based on the rate constant for the 1,3-CH insertion of *t*-BuCCl at 25°C (9.3×10^5 s^{–1}), we can estimate $k \approx 10^5$ s^{–1} for the 1,2-Me shift at 78°C.

C. Benzylhalocarbenes

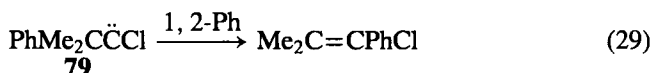
Of all the carbenes considered in this chapter, benzylchlorocarbene (**10a**) has produced the most debate, from carbene–alkene complexes vs. excited state

chemistry, to QMT. Nevertheless, comprehensible kinetic trends are discernable, especially as determined by the pyridine ylide method (Section II), which tracks only the carbene.

The simple 1,2-H shifts of benzylhalo- and benzylacetoxycarbenes manifest the anticipated bystander and spectator substituent effects. The rate constants for 1,2-H migrations of **10a**, its *p*-substituted analogues (**10c–10g**), Eq. 10, and mesitylmethylchlorocarbene (**32**) range from 2×10^7 to 2×10^8 s⁻¹ in both hydrocarbon and halogenated solvents.^{29,36,64,66} Parent benzylchlorocarbene ($k_H \approx 5$ to 6×10^7 s⁻¹ in isooctane)^{36,86} rearranges at a comparable rate to benzylbromocarbene ($k_H = 5.6 \times 10^7$ s⁻¹),^{34,86} but faster than benzylfluorocarbene (9.2×10^6 s⁻¹ in TCE)⁷⁰ or benzylacetoxycarbene (5.7×10^4 s⁻¹ in TCE),⁹² where the stabilizing spectator effects of the first row electron donor substituents (F and O) are significant.

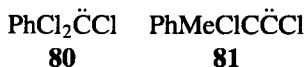
The activation energies for these rearrangements depend on solvent: in hydrocarbon, the benzylhalocarbenes exhibit $E_a \approx 4$ –5 kcal/mol,^{29,36,64,66,102} but these values are reduced to 3.2–3.6 kcal/mol in more polar solvents.^{66,70,71,92} The minimal E_a is represented by Ph₂CHCCl which, in TCE, affords $E_a = 1.65$ kcal/mol.⁸⁸ With regard to bystander effects, k_H for PhCH₂CCl ($\sim 6 \times 10^7$ s⁻¹)³⁶ increases to ($\sim 5 \times 10^8$)⁸⁷ upon α -Me substitution to PhCHMeCCl. Conversely, α -Ph substitution (to Ph₂CHCCl) reduces k_H to 2.1×10^7 s⁻¹;⁸⁸ see Section VI.C.

KGH predicted the activation barriers for the 1,2-Ph shifts of PhCH₂CCl and PhCHMeCCl to be ~ 4 kcal/mol higher than those of their alternative hydride migrations.⁸⁰ Because the H-shifts of these carbenes are so rapid, little or no Ph migration has been detected experimentally.⁷¹ 1,2-Ph shifts have been studied for Ph₂CHCCl, Ph₂CHCOAc, and carbene **79**, Eq. 29.



In isooctane at 25°C, **79** underwent 1,2-Ph shift with $k_{\text{Ph}} = 2 \times 10^7$ s⁻¹ and $E_a \approx 5$ kcal/mol (assuming $\log A = 11$ s⁻¹).¹⁰³ The diphenymethylchlorocarbene, Ph₂CHCCl, was studied in hydrocarbon solvent or TCE, where k_{Ph} was 1.5×10^6 or 3.1×10^6 s⁻¹, respectively, at 25°C.⁸⁸

The rate constants for 1,2-Cl shifts were measured for carbenes **80** and **81**.



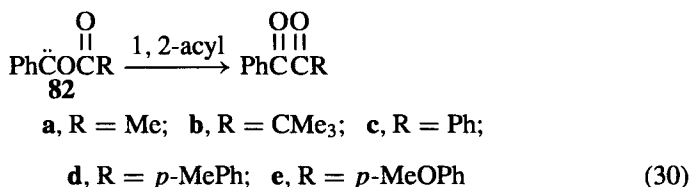
The lifetime of **80** in isooctane at 25°C was 33 ns ($k_{\text{Cl}} = 3 \times 10^7$ s⁻¹),¹⁰⁴ whereas carbene **81** rearranged more rapidly, with $\tau = 3.5$ ns and $k_{\text{Cl}} \approx 2.9 \times 10^8$ s⁻¹.¹⁰⁵ The 10-fold increase in 1,2-Cl shift between **80** and **81** can be reasonably attributed to the Cl to Me α -substituent change; i.e., to a methyl bystander effect. The activation parameters for the 1,2-Cl shift of **81** were $E_a = 3.4$

kcal/mol and $\log A = 11 \text{ s}^{-1}$.¹⁰⁵ Note that the 1,2-Cl shift of **81** is kinetically similar to the 1,2-H shift of PhCHMeCCl (**63**), where $k_H \approx 5 \times 10^8 \text{ s}^{-1}$, with $E_a \approx 2.8\text{--}3.0 \text{ kcal/mol}$.⁸⁷

The barriers to 1,2-shifts of fluorine are, not surprisingly, greater than those for 1,2-Cl migration. The experimental gas phase E_a for the rearrangement of CF₃CH to CF₂=CHF is $29 \pm 4 \text{ kcal/mol}$, with $\log A = 11\text{--}12.7 \text{ s}^{-1}$.¹⁰⁶ The calculated E_a s for the 1,2-F shift range from 21 to 24 kcal/mol,^{107,108} in reasonable agreement with experiment. Although CF₃CH is computed to be a triplet ground state carbene (by 8.5–13 kcal/mol),^{107,108} the 1,2-F shift most likely occurs from the carbene's singlet state because the triplet state rearrangement is endothermic by 6 kcal/mol, while the singlet state reaction is exothermic by 60 kcal/mol.¹⁰⁷ The computed E_a for the triplet rearrangement, however, is uncertain, with divergent reported values of 16¹⁰⁷ or 50¹⁰⁸ kcal/mol.

D. Phenylacyloxycarbenes

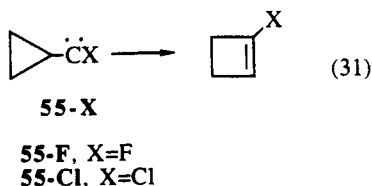
The synthesis of acetoxydiazirines⁹⁰ made available a number of precursors for acetoxy and acyloxycarbenes.^{81,91,92} The 1,2-H shifts of alkylacetoxy-carbenes were discussed above, in Section VI.D. Here, we consider phenylacyloxy-carbenes, **82**, which rearrange only by 1,2-acyl migrations to diones, Eq. 30.



Oxa spectator groups stabilize carbenes so that the O → C acyl group shifts all fall in the range, $k_{Ac} = 10^5$ to 10^6 s^{-1} .⁹¹ Alkyl- and benzylacetoxy-carbenes exhibit rather similar 1,2-acyl shift rate constants (Table 6). For **82**, the rate of acyl rearrangement depends on the electron donating properties of the migrant group. For instance, with **82c–e**, $10^5 k_{acyl} = 6.7, 9.2,$ and 12.4 , respectively; the rate of acyl migration increases as the electron donating ability of the acyl migrant increases,⁹¹ consistent with migration to an electrophilic carbenic center. The activation parameters for the rearrangement of **82c** to benzil are $E_a = 8.4 \text{ kcal/mol}$ and $\log A = 12.1 \text{ s}^{-1}$.⁹¹

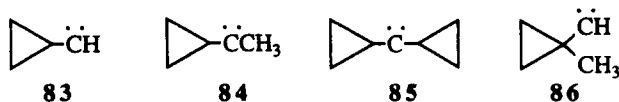
E. Cycloalkylcarbenes

Cyclopropylchloro (**55-Cl**) and cyclopropylfluorocarbene (**55-F**) undergo 1,2-C migrations leading to ring expanded 1-halocyclobutene products; Eq. 31.



The kinetics of these rearrangements have been reviewed in detail:¹ the most consistent measurements provide $k_c \approx 1 \times 10^6 \text{ s}^{-1}$ for **55-Cl**, with $E_a \approx 3 \text{ kcal/mol}$ and $\log A \approx 8 \text{ s}^{-1}$ ($\Delta S^\ddagger \approx -20$ to -24 e.u.).¹⁰⁹ The comparable data for **55-F** are $k_c = 1.4 \times 10^5 \text{ s}^{-1}$, $E_a = 4.2 \text{ kcal/mol}$, and $\log A = 8.3 \text{ s}^{-1}$.^{1,96} Cyclopropylfluorocarbene ring expands about 7 times more slowly than its chloro analogue. This difference, due to a slightly higher E_a ($\sim 1 \text{ kcal/mol}$), reflects the larger spectator substituent stabilization by the better electron donor, fluorine.

It is of interest to compare the cyclopropylhalocarbenes to the parent cyclopropylcarbene (**83**) and its alkyl derivatives (**84–86**).^{110–113}

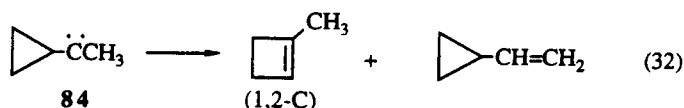


Pyridine ylide/LFP studies of **83–85** in pentane or isooctane afforded carbene lifetimes of 21–24 ns ($k \approx 4$ to $5 \times 10^7 \text{ s}^{-1}$), similar to the lifetime of dimethylcarbene under these conditions. Unfortunately, these lifetimes are limited by reactions with the hydrocarbon solvents; the lifetime of **83** is 1.5 times longer in cyclohexane- d_{12} than in cyclohexane. The observation that the lifetimes of **55-Cl** ($\sim 1000 \text{ ns}$) and **55-F** ($\sim 7000 \text{ ns}$) are considerably longer than those of **83** and **84** could reflect the superior stabilization provided by the halogen spectator substituents of **55**, but this conclusion is tentative in the absence of definitive intramolecularly controlled lifetimes for **83–85**.

Surprising is the absence of evidence for additional stability of **85** over **83**. Electron donation from the electron-rich σ bonds of the cyclopropyl ring to the carbene's vacant p orbital is widely believed to stabilize cyclopropylcarbenes.⁴ One would therefore expect **85**, with an additional cyclopropyl substituent, to react more slowly than either parent carbene **83** or dimethylcarbene, but all three lifetimes are comparable. The lifetimes of **83–85** need to be redetermined in inert (fluorocarbon) solvents in order to reveal their innate differences. Note, however, that the effect of cyclopropyl substitution is apparent upon comparison of **83** ($\tau \approx 24 \text{ ns}$) to MeCH ($\tau < 0.5 \text{ ns}$).^{89,110}

There are further complications in the chemistry of cyclopropylcarbenes. Although **84** is widely accepted to undergo a 1,2-C shift ring expansion as its principal intramolecular reaction, reinvestigations indicate that the 1,2-H shift product, cyclopropylethene, is important and, under some circumstances,

dominant; Eq. 32.¹¹¹

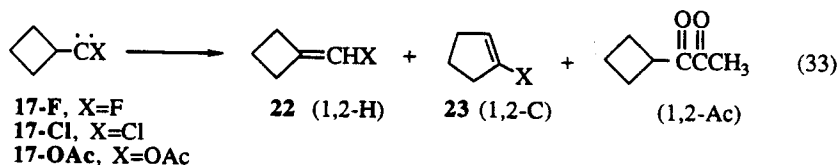


Thus, the 1,2-C pathway dominates when **84** is generated by the thermolysis of a tosylhydrazone salt, but a 1,2-H shift to cyclopropylethene is the major pathway when **84** is generated from either a hydrocarbon precursor or via the atomic carbon abstraction of oxygen from cyclopropylmethylketone at -196°C .¹¹¹

A LFP kinetic study of 1-methylcyclopropylcarbene (**86**), generated from a phenanthrene precursor, gave (mostly) 1,2-C rearrangement to 1-methylcyclobutene with $k_c = 8.3 \times 10^7 \text{ s}^{-1}$ ($\tau = 12 \text{ ns}$) in 1,1,2-trichlorotrifluoroethane.¹¹² The lifetime of **86** was not limited by reaction with solvent, and was slightly shorter than those of **83–85**. Computational comparison of **86** with **83** revealed that the free energies of activation for the 1,2-C shifts were 2.0 and 6.0 kcal/mol, respectively. The lower barrier confronting **86** reflects the ability of the Me group to stabilize the positive charge that develops on the cyclopropyl carbon during the ring expansion.¹¹²

A caveat in cyclopropylcarbene rearrangements is the possibility that, at least in certain systems, rearrangements may occur in stepwise fashion via diradical intermediates.¹¹³ Whether such complications intrude with the simplest cyclopropylcarbenes (**83–86**) is not yet clear.

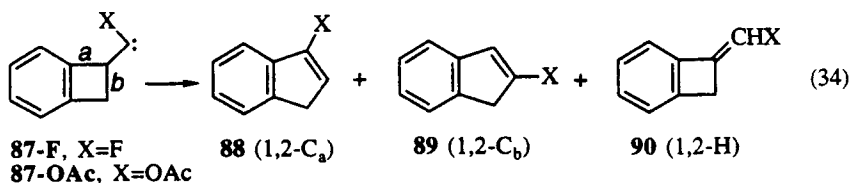
Cyclobutylcarbenes **17** rearrange by both 1,2-H and 1,2-C migrations, with the 1,2-C shift favored by 2.5–4.8 times over the 1,2-H shift; Eq. 33.^{1,96}



Above (Section III.C.1), we have discussed problems of RIES when **17-Cl** and **17-F** are photolytically generated from diazirine precursors. Rate constants for these rearrangements are: (**17-Cl**), $k_c = 5.6 \times 10^7 \text{ s}^{-1}$, $k_H = 1.2 \times 10^7 \text{ s}^{-1}$, and (**17-F**), $k_c = 1.8 \times 10^6 \text{ s}^{-1}$, $k_H = 5.3 \times 10^5 \text{ s}^{-1}$.^{28,96} The $\text{F} > \text{Cl}$ spectator substituent effect is apparent for each reaction channel. For **17-OAc**, the 1,2-acetyl shift dominates both 1,2-C and 1,2-H migrations: the rate constants are $k_{Ac} = 4.0 \times 10^5 \text{ s}^{-1}$, $k_c = 3.2 \times 10^4 \text{ s}^{-1}$, and $k_H = 1.3 \times 10^4 \text{ s}^{-1}$, although 1,2-C migration is still preferred to the 1,2-H shift.⁸¹ In these systems, 1,2-C ring expansion provides strain relief, whereas the 1,2-H shift to methylenecyclobutanes does not.

Benzocyclobutenylcarbenes (**87**) display a striking preference for carbon migration; no hydride shift product (**90**) appears upon photolysis or thermolysis of

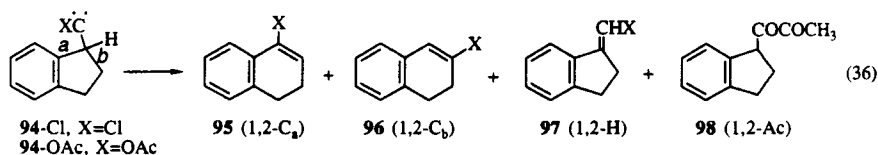
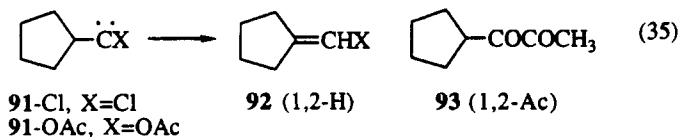
the diazirine precursors to carbene **87**,¹¹⁴ cf. Eq. 34. Indeed, 1,2-acyl migration is also suppressed for **87-OAc**.¹¹⁴



Fluorocarbene **87-F** rearranges in pentane to fluoroindenes **88-F** and **89-F** in a ratio of 95.3 : 4.7.¹¹⁴ The LFP rate constant for the dominant **87-F** → **88-F** rearrangement is $3.75 \times 10^7 \text{ s}^{-1}$, which is 21 times faster (42 times faster on a per bond basis) than the analogous ring expansion of the nonbenzannulated cyclobutylfluorocarbene, **17-F** → **23-F**, where $k_c = 1.8 \times 10^6 \text{ s}^{-1}$; Eq. 33.^{28,96}

Similarly, in the acetoxycarbene series, **87-OAc** rearranges to **88-OAc** with $k_c = 8.5 \times 10^6 \text{ s}^{-1}$, 265 times faster than **17-OAc** ring expands to **23-OAc** ($3.2 \times 10^4 \text{ s}^{-1}$).⁸¹ These rapid and dominant “phenyl” carbon 1,2-C shifts of **87** to **88** (bond *a*), rather than “benzyl” carbon (bond *b*) 1,2-C shifts to **89**, are attributed to π orbital mediation by the phenyl group; in effect an electrophilic attack of the carbenic carbon on the aromatic ring. *Ab initio* calculations support this view.¹¹⁴

In contrast to the cyclopropyl- and cyclobutylhalo- (and acetoxy)carbenes, the cyclopentylhalo- and acetoxycarbenes (**91**), and their corresponding benzo derivatives, the indanylcarbenes (**94**), prefer 1,2-H shifts over 1,2-C shifts; Eqs. 35 and 36.¹¹⁵ In the absence of strain relief to drive ring expansion, as with the cyclobutylcarbenes, **17**, where k_c exceeds k_H , the 1,2-H shift is preferred.¹¹⁵



Rate constants for the 1,2-H shifts of **91-Cl** and **91-OAc** to **92-Cl** and **92-OAc** are 2.2×10^7 and $2.9 \times 10^6 \text{ s}^{-1}$, respectively. (In the latter case, $k_{Ac} = 2.4 \times 10^6 \text{ s}^{-1}$ for **91-OAc** → **93**.)

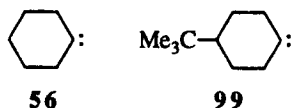
For the indanylcarbenes (**94**), two 1,2-C shifts and a 1,2-H migration compete, affording products **95**–**97**. With **94-Cl**, $k_{Ca} = 1.5 \times 10^6 \text{ s}^{-1}$, $k_{Cb} = 4.5 \times 10^4 \text{ s}^{-1}$, and $k_H = 1.4 \times 10^7 \text{ s}^{-1}$. The analogous rate constants for carbene **94-OAc**

are 1.6×10^4 , 4.7×10^3 , and $1.4 \times 10^5 \text{ s}^{-1}$, respectively (with $k_{\text{Ac}} = 8.5 \times 10^4 \text{ s}^{-1}$). Note that the 1,2- C_a rearrangement of the benzocyclobutylacetoxycarbene (**87-OAc**) is 531 times faster than the corresponding reaction of the benzocyclopentylacetoxycarbene (**94-OAc**), while the 1,2-H shifts, suppressed for **87**, dominate with **94**.

Nevertheless, π mediation persists in the 1,2-C rearrangements of **94-Cl** and **94-OAc**, where the migrations of C_a exceed those of C_b by factors of 33 or 3.4, respectively.¹¹⁵ Moreover, comparisons of **94** with **91** reveal significant 1,2- C_a shift accelerations, consistent with π mediation.

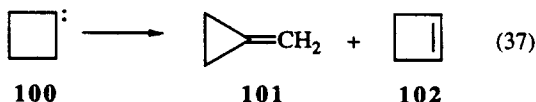
F. Cycloalkylidenes, Bicycloalkylidenes, Adamantanylidene and Homocubylidene

LFP studies furnish lifetimes of 0.1–0.7 ns and 0.3–2 ns ($k_H = 0.14$ to 1.0×10^{10} and 5.8×10^8 to $3 \times 10^9 \text{ s}^{-1}$) for cyclohexanylidene (**56**) and 4-*t*-butylcyclohexanylidene (**99**) in cyclohexane, respectively.¹⁴ The lifetimes are independent of solvent deuteration (i.e., cyclohexane- d_{12}), so that each carbene's disappearance is due to 1,2-H shift and not to reaction with solvent.



The similarity in lifetimes of **56** and **99** suggests that these 1,2-H shifts are not particularly sensitive to conformational effects in the 6-membered ring. The lifetimes are not markedly longer in benzene; π complexes of **56** and benzene (see Section III.B) do not seem to be kinetically significant. The lifetime of **56** in cyclohexane is similar to that of dipropylcarbene ($\sim 0.3 \text{ ns}$),⁸⁴ as would be expected from the fact that they are both dialkylcarbenes.

In other cases, however, the chemistry of the cycloalkanylidenes can be governed by the geometric constraints inherent in the system. Strain can raise the activation barrier to the 1,2-H shift, permitting the intervention of other rearrangements. The reaction of cyclobutylidene (**100**) is a case in point; Eq. 37.^{16,116}

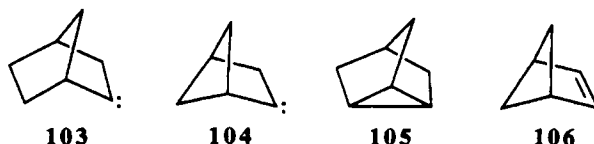


Generated from diazocyclobutane, and corrected for $\sim 80\%$ of RIES by experiments in the presence and absence of a TME carbene trap, **100** affords methylenecyclopropane (**101**) by a 1,2-C shift and cyclobutene (**102**) by a 1,2-H shift. The LFP rate constants are $k_C = 5 \times 10^7$ to $2.5 \times 10^8 \text{ s}^{-1}$ and $k_H = 8 \times 10^6$ to $4 \times 10^7 \text{ s}^{-1}$ in cyclohexane. The 1,2-C shift is therefore ~ 6 times faster

than the 1,2-H shift. In acetonitrile, the lifetime of **100** is reduced from ~ 4 –20 ns (cyclohexane) to < 1 ns, with both the 1,2-C and 1,2-H shifts exhibiting comparable polar solvent accelerations.¹¹⁶

Although experiment reveals 1,2-C to be preferred to 1,2-H for **100**,¹¹⁶ *ab initio* calculations suggest that the 1,2-H migration should dominate: calculated $\Delta G^\ddagger$ values are 1,2-C, 10.5 kcal/mol, and 1,2-H, 9.7 kcal/mol.¹⁶ (The transannular 1,3-CH insertion of **100** to bicyclobutane has a computed barrier of 14.6 kcal/mol, however, and should not be competitive.¹⁶) The discrepancy between experiment and theory might be relieved with the use of a larger basis set and a higher computational level. Note that the computed $\Delta G^\ddagger$ for the 1,2-C shift of **100** (10.5 kcal/mol) is ~ 8 kcal/mol less than $\Delta G^\ddagger$ for the 1,2-C shift of methylethylcarbene (**6**); the latter must undergo a large geometrical change to reach the 1,2-C shift transition state, whereas cyclobutylidene's ground state structure is already close to that of the 1,2-C transition state.¹⁶

Although 2-norbornanylidene (**103**) and bicyclo[2.1.1]hexan-2-ylidene (**104**) are structurally related, their reactivities are quite distinct.¹¹⁷

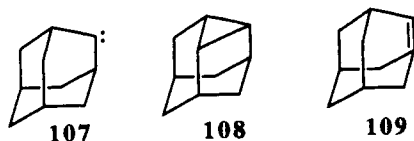


Carbene **103** undergoes 1,3-CH insertion to nortricyclene (**105**), but this reaction is either too rapid for LFP measurement by the pyridine ylide method ($\tau < 0.1$ ns), or the insertion occurs by RIES of the precursor 2-norbornyldiazirine. Theoretically, a short lifetime is expected for **103**; $\Delta G^\ddagger$ for the carbene insertion into the 6-*endo*-CH bond (**103** $\rightarrow$ **105**) is computed at 5.2 kcal/mol, about 6.7 kcal/mol less than the (unobserved) *exo*-1,2-H shift to norbornene.¹⁶

In contrast, 1,2-H shift to olefin **106** is the dominant reaction of carbene **104**, and this process is slow enough to be measured by LFP: $\tau = 300$ ns in cyclohexane and 560 ns in pentane at 25°C.¹¹⁷ There is a polar solvent effect; the lifetime decreases to 52 ns in acetonitrile. However, at least in the case of cyclohexane, the lifetime is solvent limited, with a KIE of 1.5 on the lifetime in cyclohexane-*d*₁₂ (460 ns). Carbene **104** is much longer-lived than dimethylcarbene ($\tau \approx 21$ ns in pentane) or methylcarbene (< 1 ns).^{22,89}

Computed values of $\Delta G^\ddagger$ are in qualitative agreement with the experimental findings for **104**. Thus, $\Delta G^\ddagger$ computed for the 1,2-H shift (16.2 kcal/mol) is 6.4 kcal/mol lower than the $\Delta G^\ddagger$ calculated for the (unobserved) 1,3-CH insertion.¹⁶ The high $\Delta G^\ddagger$ calculated for the 1,2-H shift suggests that **104** should have a relatively long lifetime in pentane, as is observed. No doubt strain in both product **106** and in the unobserved 1,3-CH insertion product contribute to their high $\Delta G^\ddagger$ values.¹⁶

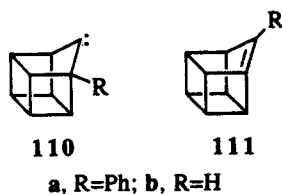
The reaction kinetics of 2-adamantanylidene (**107**) have been carefully investigated.^{118,119} Carbene **107** is computed to have a singlet ground state lying ~ 4.8 kcal/mol below the triplet.¹²⁰



Isolated in an argon matrix at 10 K, singlet **107** displays an absorbance at 620 nm due to a lone pair to p orbital transition; irradiation at 620 nm converts **107** to its 1,3-CH insertion product, dehydroadamantane, **108**.¹²⁰ This product is much less strained than the alternative, *anti*-Bredt, 1,2-H shift alkene, **109**.

Using the pyridine ylide methodology, the lifetime of **107**, generated by LFP from the diazirine, was 19–20 ns in cyclohexane^{118,119} (83 ns in isooctane)¹¹⁹ and 553¹¹⁸ or 725¹¹⁹ ns in benzene. The lifetime was very sensitive to traces of water and oxygen in the solvents.^{118,119} The dramatic shortening of the **107** lifetime in cyclohexane, as compared to benzene, can be attributed to a combination of intermolecular carbene C–H insertion in the cyclohexane, together with carbene stabilization by π complexation^{42–44} in the benzene. From the lifetimes observed in benzene, we infer that the **107** $\rightarrow$ **108** 1,3-CH insertion occurs with $k \approx 1.4$ to 1.8×10^6 s⁻¹.

We conclude by noting the extraordinary equilibration by 1,2-C migration of the homocub-9-ylidenes (**110**), and the exceedingly strained *anti*-Bredt homocubenes (**111**), Eq. 38.^{121–126}



Chemical trapping experiments with TME or methanol, as well as LFP studies of **110b** (pyridine ylide method) with methanol, permit an estimate of ~ 1 for the equilibrium constant between **110b** and **111b**.¹²⁴ *Ab initio* calculations afford a free energy difference of ~ 1.1 kcal/mol in favor of the carbene, in reasonable agreement with experiment, and singlet **110b** is computed to be the carbene's ground state by ~ 1.6 kcal/mol.¹²⁵ Moreover, the rates of isomerization of **110b** and **111b** are considerably faster than the rates of their interception by MeOD,¹²⁴ so that k_C for **110b** $\rightarrow$ **111b** exceeds 10^9 s⁻¹.

ACKNOWLEDGEMENTS

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APPENDIX

This Appendix contains a summary of rate constants and activation parameters published for singlet intramolecular carbene reactions between 1989 and 1999. It may be regarded as an updated and expanded version of the listing published as the Appendix to reference 1. Both experimental and computed data are included in Table 7, and although we do not claim completeness, most of the extant data are included. In many cases, divergent rate constants are included for the identical reaction. Usually, the later values are better, reflecting advances in technology over the past decade. The Appendix does not comment on which of the several values are to be preferred, although the text often discusses what, in our opinion, is the "best" value.

Table 7. Kinetics of Singlet Carbene Rearrangements

<i>R</i> (in <i>R</i> -C-X)	<i>X</i>	Type of rearr.	Solvent	<i>T</i> (°C)	<i>k_T</i> (s ⁻¹)	<i>E_a</i> (kcal mol ⁻¹)	log <i>A</i> (s ⁻¹)	Ref.
CH ₃	H	1,2-H	calc.	-273		0.6		4
			calc.	-273		1.2		98a
	CH ₃	1,2-H	pentane	25	4.76 × 10 ⁷			22
			cyclohexane	25	0.5–2.4 × 10 ⁸			14
			TFT ^a	25	3.70 × 10 ⁷			22
			CH ₃ CN	25	1.25 × 10 ⁸			22
			CD ₃ CN	25	1.11 × 10 ⁸			22
			CHCl ₃	25	1.47 × 10 ⁸			22
			CDCl ₃	25	1.37 × 10 ⁸			22
			pentane	25	5 × 10 ⁸			22
	CH ₂ CH ₃	1,2-H	cyclohexane	25	0.3–2 × 10 ⁹			14
			isooctane	25	3.0 × 10 ⁶			86
	Cl	1,2-H		22	1.4 × 10 ⁶	4.9	9.7	60
			DCE ^b	21	1.21 × 10 ⁶	6.8	10.7	60
			calc.			11.5	12.4	80
			isooctane	22	5.26 × 10 ⁶			26
	Ph	1,2-H	hydrocarbon	25	<6 × 10 ⁶	≥4.3	10 ^c	1
			heptane	25	1.20 × 10 ⁶			83
			benzene	25	1.64 × 10 ⁶			83
			TFT ^a	25	1.68 × 10 ⁶			83
			CH ₃ CN	25	6.15 × 10 ⁶	2.1–2.3	8.3–10	83
			heptane	25	2.49 × 10 ⁶			83
	<i>p</i> -CF ₃ Ph	1,2-H	heptane	25	2.11 × 10 ⁶			83
	<i>p</i> -BrPh	1,2-H	heptane	25	3.23 × 10 ⁶			83
	<i>p</i> -CH ₃ OPh	1,2-H	heptane	25				83

Table 7. (continued)

R (in R-C-X)	X	Type of rearr.	Solvent	T (°C)	k _T (s ⁻¹)	E _a (kcal mol ⁻¹)	log A (s ⁻¹)	Ref.	
CD ₃	D	1,2-D	pentane	25	2 × 10 ⁹	2.3	10 ^c	89	
			calc.	-273		1.5		98a	
	CD ₃	1,2-D	pentane	25	1.49 × 10 ⁷			22,89	
	Ph	1,2-H	heptane	25	1.74 × 10 ⁶			83	
			TFT ^a	25	1.87 × 10 ⁶			83	
benzene			25	1.13 × 10 ⁶			83		
ClCH ₂	Cl	1,2-H	isooctane	25	2 × 10 ⁷	7.5 ^d		20	
			calc.			10.9	12.4	80	
CF ₃	F	1,2-H	calc.			9.0	12.7	80	
	H	1,2-F	gas phase			29 ± 4	11-12.7	106	
			calc.			24		107	
			calc.			21.5		108	
CH ₃ CH ₂	CH ₃ CH ₂	1,2-H	cyclohexane	25	0.3-2 × 10 ⁹	14			
		1,2-H	isooctane	25	1.28 × 10 ⁸	2.4	9.7	56,86	
		1,2-H	isooctane	25		4.89 ^e		80	
			calc.			6.9	12.7	80	
			calc.	25		15.4		86	
			heptane	25	3.64 × 10 ⁸	2.0	10 ^c	83	
			pentane	25	8.40 × 10 ⁶			56	
	OAc	1,2-H	TCE ^f	25	1.59 × 10 ⁴	13.4 ^g	14.8 ^g	92	
		1,2-Ac	TCE ^f	25	7.35 × 10 ⁴	13.4 ^g	14.8 ^g	92	
	CH ₃ (CH ₂) ₂	CH ₃ (CH ₂) ₂	1,2-H	cyclohexane	25	~3.3 × 10 ⁹			84
		Cl	1,2-H	isooctane	25	5.9 × 10 ⁷			87
		Ph	1,2-H	pentane	25	8.77 × 10 ⁶			56

Table 7. (continued)

<i>R</i> (in <i>R</i> -C-X)	<i>X</i>	Type of rearr.	Solvent	<i>T</i> (°C)	<i>k_T</i> (s ⁻¹)	<i>E_a</i> (kcal mol ⁻¹)	log <i>A</i> (s ⁻¹)	Ref.
(CH ₃) ₂ CH	Cl	1,2-H	isooctane	-90	>1.0 × 10 ^{8h}	~2 ^h	10.3 ^h	87
			calc.		8.85 × 10 ⁷	2.5	12.4	86
			calc.			3.9	12.7	80
	OAc	1,2-H	isooctane	25	4 × 10 ⁶	10.8 ^g	13.4 ^g	81,92
			TCE ^f	25	1.93 × 10 ⁶	5.78	10.6	92
		1,2-Ac	isooctane	25	4 × 10 ⁶	10.8 ^g	13.4 ^g	81,92
			TCE ^f	25	1.06 × 10 ⁵	5.78	10.6	92
(CH ₃) ₃ C	Cl	g	isooctane	25	1.11 × 10 ^{7g}	1.0 ⁱ		86
			pentane	20	9.3 × 10 ⁵			27
(CH ₃) ₃ CCH ₂	Cl	1,2-H	hydrocarbon	20	1.4 × 10 ⁷			96
	F	1,2-H	pentane	20	2.6 × 10 ⁶	3.3	8.9	96, ¹²⁷
	OCH ₃	1,2-H	pentane	0	≤1 × 10 ⁴			74,127
PhCH ₂	Cl	1,2-H	isooctane	25	6 × 10 ⁷			86
			isooctane	24	6.2 × 10 ⁷	4.5-4.8	11.1-11.3	36
			isooctane			5.8	11.9	66
			CHCl ₃	25	2.2 × 10 ⁷	3.6	10.4	66
			calc.			5.5	12.5	80
			TCE ^f	0	2.7 × 10 ⁷	3.2	10.0	71
	F	1,2-H	calc.			9.5	11.9	80
			TCE ^f	26	9.2 × 10 ⁶	3.2	9.5	70
			isooctane	25	5.6 × 10 ⁷	4.7-6.6 ^h		34,86
			TCE ^f	25	5.66 × 10 ⁴	2.49 ^g	7.7 ^g	92
			TCE ^f	25	6.85 × 10 ⁵	2.49 ^g	7.7 ^g	92
			isooctane	24	2.2 × 10 ⁷	4.9	10.9	64
<i>p</i> -CF ₃ PhCH ₂	Cl	1,2-H	isooctane	25	4.2 × 10 ⁷	4.5	10.9	64
<i>p</i> -ClPhCH ₂	Cl	1,2-H	isooctane	24	1.2 × 10 ⁸			64
<i>p</i> -CH ₃ PhCH ₂	Cl	1,2-H	isooctane	24	1.7 × 10 ⁸			64

Table 7. (continued)

R (in R-C-X)	X	Type of rearr.	Solvent	T (°C)	k _T (s ⁻¹)	E _a (kcal mol ⁻¹)	log A (s ⁻¹)	Ref.
MesCH ₂	Cl	1,2-H	isooctane	20	1.8×10^7	4.8	10.7	29
MesCD ₂	Cl	1,2-D	isooctane	21	3.7×10^6	4.6	10.2	29
PhCH(CH ₃)	Cl	1,2-H	isooctane	25	$\sim 5 \times 10^8$	2.85-3.0	10.7	87
			calc.			2.3		86
			calc.			5.1	12.9	80
		1,2-Ph	calc.			8.2	12.1	80
	OAc	1,2-H	TCE ^f	25	1.58×10^5	5.1 ^g	9.17 ^g	92
		1,2-Ac	TCE ^f	25	9.55×10^4	5.1 ^g	9.17 ^g	92
Ph ₂ CH	Cl	1,2-H	pentane	25	2.1×10^7			88
			TCE ^f	25	2.3×10^7	1.65 ^g	8.6 ^g	88
		1,2-Ph	pentane	25	1.5×10^6			88
			TCE ^f	25	3.1×10^6	1.65 ^g	8.6 ^g	88
	OAc	1,2-H	TCE ^f	25	7.2×10^5	2.97 ^g	8.9 ^g	88
		1,2-Ac	TCE ^f	25	5.6×10^6	2.97 ^g	8.9 ^g	88
PhC(CH ₃) ₂	Cl	1,2-Ph	isooctane	25	2.0×10^7	~ 5		103
PhCH ₂ C(Cl)	Cl	1,2-Cl	isooctane	25	2.86×10^8	3.39	11.0	105
PhCCl ₂	Cl	1,2-Cl	isooctane	25	3.0×10^7			104
PhOCH ₂	Cl	1,2-H	hydrocarbon	-32	3.6×10^7			96
			isooctane	25	1.11×10^8	2.8	10.1	128
	F	1,2-H	hydrocarbon	-32	1.3×10^7			96
	OCH ₃	1,2-H	pentane	-32	$\leq 1 \times 10^4$			95
	OAc	1,2-H	pentane	25	4.1×10^6			90
Ph	OAc	1,2-Ac	isooctane	20	1.33×10^5			91
p-CF ₃ Ph	OAc	1,2-Ac	isooctane	20	2.56×10^5			91
p-ClPh	OAc	1,2-Ac	isooctane	20	2.44×10^5			91

Table 7. (continued)

R (in R-C-X)	X	Type of rearr.	Solvent	T (°C)	k _r (s ⁻¹)	E _a (kcal mol ⁻¹)	log A (s ⁻¹)	Ref.
Ph	O ₂ CC(CH ₃) ₃	1,2-Piv ⁱ	isooctane	20	4.9 × 10 ⁵			91
Ph	O ₂ CPh	1,2-Bz ^k	isooctane	20	6.7 × 10 ⁵	8.4	12.1	91
	O ₂ C(p-CH ₃ Ph)	1,2-Bz ^k	isooctane	20	9.24 × 10 ⁵			91
	O ₂ C(p-CH ₃ OPh)	1,2-Bz ^k	isooctane	20	1.24 × 10 ⁶			91
c-C ₃ H ₅ ^l	H	1,2-C	pentane	25	4.17 × 10 ⁷			4,110
			C ₆ H ₁₂	25	7.14 × 10 ⁷			4,110
			C ₆ D ₁₂	25	4.76 × 10 ⁷			4,110
			CD ₃ CN	25	7.14 × 10 ⁷			4,110
			CDCl ₃	25	2.50 × 10 ⁸			4,110
	CH ₃	1,2-C	pentane	25	4.76 × 10 ⁷			4,110
	c-C ₃ H ₅ ^l	1,2-C	pentane ^m	25	4.55 × 10 ⁷			4,110
			pentane ⁿ	25	3.13 × 10 ⁷			4,110
	Cl	1,2-C	hydrocarbon	25	6 × 10 ⁵			86
			hydrocarbon	23	3.8 × 10 ⁵	7.4	11.1	129
			isooctane	20	0.9–1.5 × 10 ⁶	3.0	8.2	109
	F	1,2-C	pentane	23	1.4 × 10 ⁵	4.2	8.3	96
	Ph	1,2-H	pentane	25	7.81 × 10 ⁶			56
	OMe	1,2-C			<3 × 10 ³			130
(CH ₃) ₂ -c-C ₃ H ₃	Cl	1,2-CH ₂	pentane	25	1.3 × 10 ⁶			45
		1,2-CMe ₂	pentane	25	2.5 × 10 ⁵			45
1-MeC ₃ H ₅	H	1,2-C		25	8.3 × 10 ⁷			112
c-C ₄ H ₇ ^o	Cl	1,2-H	pentane	20	2.1 × 10 ⁷			96
			pentane	25	1.2 × 10 ⁷			28
		1,2-C	pentane	20	4.6 × 10 ⁷			96
			pentane	25	5.6 × 10 ⁷			28
	F	1,2-H	pentane	23	5.3 × 10 ⁵	3.8	8.5	96
		1,2-C	pentane	23	1.8 × 10 ⁶	2.3	8.0	96
	Ph	1,2-H	pentane	25	7.46 × 10 ⁶			56

Table 7. (continued)

R (in R-C-X)	X	Type of rearr.	Solvent	T (°C)	k _r (s ⁻¹)	E _a (kcal mol ⁻¹)	log A (s ⁻¹)	Ref.
Bz-c-C ₄ H ₃ ^p	OAc	1,2-H	pentane	25	1.3 × 10 ⁴			81
		1,2-C	pentane	25	3.2 × 10 ⁴			81
		1,2-Ac	pentane	25	4.0 × 10 ⁵			81
	F	1,2-C(Ph)	pentane	24	3.75 × 10 ⁷			114
	OAc	1,2-C(Ph)	pentane	25	8.5 × 10 ⁶			114
c-C ₅ H ₉ ^q	OAc	1,2-C(Bz)	pentane	25	<8.5 × 10 ⁴			114
		1,2-H	pentane	25	2.2 × 10 ⁷			115
	Ph	1,2-H	pentane	25	4.15 × 10 ⁶			56
	OAc	1,2-H	pentane	25	2.9 × 10 ⁶			115
		1,2-Ac	pentane	25	2.4 × 10 ⁶			115
Bz-c-C ₅ H ₅ ^r	Cl	1,2-H	pentane	25	1.4 × 10 ⁷			115
		1,2-C(Ph)	pentane	25	1.5 × 10 ⁶			115
		1,2-C(Bz)	pentane	25	4.5 × 10 ⁴			115
	OAc	1,2-H	pentane	25	1.4 × 10 ⁵			115
		1,2-C(Ph)	pentane	25	1.6 × 10 ⁴			115
		1,2-C(Bz)	pentane	25	4.7 × 10 ³			115
		1,2-Ac	pentane	25	8.5 × 10 ⁴			115
		1,2-H	pentane	25	3.13 × 10 ⁶			56
		1,2-H	pentane	25	2.20 × 10 ⁶			56
c-C ₆ H ₁₁ ^s	Ph	1,2-H	pentane	25	0.8-4 × 10 ⁷			116
Bz-c-C ₆ H ₆ [†]	-	1,2-H	cyclohexane	25				16
c-C ₄ H ₆ : ^u	-	1,2-H	calc.			9.7 ^d		16
		1,3-H	calc.			14.6 ^d		16
		1,2-C	cyclohexane	25	0.5-2 × 10 ⁸			116
			calc.			10.5 ^d		16
C ₆ H ₁₀ ^v	-	1,2-H	cyclohexane	25	0.14-1.0 × 10 ¹⁰			14
4- <i>t</i> -BuC ₆ H ₁₀ ^v	-	1,2-H	cyclohexane	25	0.5-3 × 10 ⁹			14
Ad ₂ C: ^w	-	1,2-C	cyclohexane	25	<5 × 10 ⁶			4
2-bicyclo	-	1,2-H	cyclohexane	25	3.33 × 10 ⁶			4,117
[2.1.1]			cyclohexane	25	2.17 × 10 ⁶			4,117

Table 7. (continued)

R (in R-C-X)	X	Type of rearr.	Solvent	T (°C)	k_T (s ⁻¹)	E_a (kcal mol ⁻¹)	log A (s ⁻¹)	Ref.
hexanylidene			pentane	25	1.79×10^6			4,117
			CH ₃ CN	25	1.92×10^7			4,117
			CD ₃ CN	25	1.19×10^7			4,117
			CCl ₄	25	4.55×10^6			4,117
			toluene	25	9.09×10^6			4,117
			toluene-d ₈	25	4.35×10^6			4,117
			calc.			16.2 ^d		16
2-norborn-anylidene	-	1,3-H endo-1,3-H	pentane		$>1 \times 10^{10}$	22.6 ^d		16
			calc.			5.2 ^d		16
		exo-1,2-H	calc.			11.9 ^d		16
		endo-1,2-H	calc.			14.4 ^d		16
		1,2-H	calc.			17.9 ^d		16
		bridge-1,3-H	calc.			25.3 ^d		16
		1,3-H	cyclohexane		$5.0-5.3 \times 10^7$			118,119
Ad: ^γ	-		isooctane		1.2×10^7			119
			benzene		$1.4-1.8 \times 10^6$			118,119
Cub: ^z	-	1,2-C	CH ₂ Cl ₂		$>1 \times 10^9$			124

Notes: ^a TFT = α,α,α-trifluorotoluene.^b DCE = 1,2-dichloroethane.^c Assumed value.^d ΔG[‡].^e ΔH[‡] value, from E.J. Dix, Ph.D. Thesis, University of Rochester, New York, 1994.^f TCE = sym-tetrachloroethane.^g Composite values for all processes.^h Estimated.ⁱ Calculated value.^j Piv = pivaloyl.^k Bz = benzoyl.^l c-C₃H₅ = cyclopropyl.^m By pyridine ylide method.ⁿ By direct observation.^o c-C₄H₇ = cyclobutyl.^p Bz-c-C₄H₃ = benzocyclobutenyl.^q c-C₅H₉ = cyclopentyl.^r Bz-c-C₅H₅ = benzocyclopentenyl.^s c-C₆H₁₁ = cyclohexyl.^t Bz-c-C₆H₆ = benzocyclohexenylidene.^u c-C₄H₆ = cyclobutylidene.^v C₆H₁₀ = cyclohexenylidene.^w Ad₂C: = diadamantylcarbene; data is for triplet state.^x 1,1,2-trichlorotrifluoroethane.^y Ad: = 2-adamantanylidene.^z Cub: = homocub-9-ylidene.

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CARBENES IN MATRICES: SPECTROSCOPY, STRUCTURE, AND PHOTOCHEMICAL BEHAVIOR

Günther Maier and Hans Peter Reisenauer

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I. INTRODUCTION

Matrix isolation is a very suitable technique for the synthesis and detection of highly reactive molecules. This method allows spectroscopic studies of the target species with routine spectroscopic instrumentation (IR, UV, ESR) without making use of fast time-resolved techniques. As postulated by Porter¹ and Pimentel et al.² in 1954, the reactive species are prevented from any chemical reaction by embedding them in a solid, if three conditions are fulfilled: (a) the solid has to be chemically inert, (b) isolation of the single molecules must be achieved by choosing concentrations which are sufficiently low, and (c) diffusion in the solid has to be suppressed by applying low temperatures during the experiments. In this way the kinetic instability inherent to the isolated molecules is counteracted. In general, there are two possibilities to create a solid with the desired properties, the so-called *matrix*. The molecules of interest can be generated from suitable precursors by reactions in the gas phase and codeposited with an excess of host material on the cold matrix holder. The second way is to produce the reactive species *in situ* by photolysis after isolating the precursor molecules in the matrix material. For detailed information on the development of matrix isolation methods and their application range the reader is referred to several monographs³⁻⁸ and reviews.⁹⁻¹³

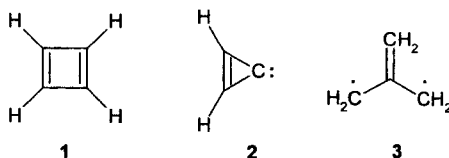
The properties of the matrix material determine the spectroscopic methods that can be applied. The use of solid rare gases like argon and xenon or solid nitrogen is well established, since they are optically transparent in the commonly observed spectral ranges. The fact that there is nearly no interaction between the host lattice and the enclosed guest species and that the rotational movements are frozen has an important effect on the IR spectra; under ideal conditions the recorded infrared spectra are reduced to spectra consisting of very narrow lines ($<1\text{ cm}^{-1}$). Each of them originates from the respective vibrational transition. UV/VIS spectra are also obtained easily and are useful for the structural elucidation of unknown species as well. What is even more important: the UV absorptions allow the selection of the appropriate wavelengths for the induction of photochemical reactions, which under matrix conditions are often reversible. The multiplicity of the expected electronic ground state of the matrix-isolated molecule can be derived from MO calculations. Experimental evidence for a triplet species is accessible by recording the electron spin resonance (ESR) spectrum of the matrix-isolated compound.

It is obvious, that matrix isolation spectroscopy is the method of choice for the study of carbenes. The large number of carbenes identified by matrix isolation illustrates the strength of this analytical tool, as demonstrated by an excellent review on this topic by Sander et al. in 1993¹⁴. In this comprehensive article all the work carried out until that date has been summarized. The goal of our review is to report on our own contributions to this field and to complete Sander's overview — taking over his classification of individual carbenes — by results achieved by us in this subject matter during the most recent epoch.

II. BACKGROUND

A. Carbenes as Transient Intermediates

Our interest in carbenes is closely related to our work on conjugated hydrocarbons containing four electrons. The parent molecules of three completely different families within this category are 1,3-cyclobutadiene (**1**), cyclopropenylidene (**2**), and trimethylenemethane (**3**).



1,3-Cyclobutadiene (**1**)¹⁵ is the first member of the series of cyclic conjugated hydrocarbons (Kekulé compounds); cyclopropenylidene (**2**), of cyclic conjugated carbenes; trimethylenemethane (**3**), of the non-Kekulé hydrocarbons.

During a very early study on tetramethylcyclobutadiene¹⁶ it was anticipated by one of us that 2,2,4,4-tetramethyl-1,3-dicarbenacyclobutane formed in the pyrolysis of dry di-sodium salt of 2,2,4,4-tetramethyl-1,3-cyclobutanedione-bis-tosylhydrazone might be a reasonable precursor for the cyclobutadiene derivative. But the only product — isolated in a cooling trap — was tetramethylbutatriene.

Our next experience with a carbene was associated with the attempt to get 1,2-diphenylcyclobutadiene by photolysis of diphenylcyclopropenyldiazomethane¹⁷. It was found that the (diphenylcyclopropenyl)carbene splits mainly into diphenylacetylene and acetylene and rearranges only to a very small extent to the wanted cyclobutadiene.

The same procedure was later effectively used by Masamune^{15b,18} to prepare *tert*-butylated cyclobutadienes. Regitz¹⁹ widely employed the *Masamune cyclopropenylcarbene route* in his studies on the properties of the *tert*-butylester of tri-*tert*-butylcyclobutadiene carboxylic acid. We also used several differently

substituted cyclopropenyldiazomethanes as precursor molecules for cyclobutadienes and/or tetrahedranes²⁰. By these means it was possible to synthesize a whole series of tetrahedranes (bearing at least three *tert*-butylgroups).^{20b-h} But in none of these studies the corresponding cyclopropenylcarbene could be detected directly as an intermediate.

B. Matrix Isolation of Carbenes

During all these studies on cyclobutadienes and tetrahedranes formed via carbenes as *transient* species we wondered whether matrix isolation IR spectroscopy might be a good tool for the direct observation of cyclopropenyldiene (2) and trimethylenemethane (3). This is indeed the case.

Cyclopropenyldiene (2) was assumed to fulfill the requirements for a successful isolation in a rare gas matrix. (a) Carbene 2 is stabilized by cyclic conjugation. (b) Promising educt molecules were known. (c) Cyclopropenyldiene (2) was expected to have a singlet ground state. (d) Molecule 2 should represent the global minimum on the C₃H₂ potential-energy hypersurface and therefore it should not be thermally transformed in a matrix into one of the other isomers. Keeping in mind these prerequisites we selected cyclopropenyldiene to be the target molecule in our first attempt²¹ to identify a carbene directly by using matrix isolation techniques.

The third member, trimethylenemethane (3), had some relevance to our studies on carbenes, since besides methylene and its simply substituted derivatives trimethylenemethane 3 is one of the few molecules having a triplet ground state.²² Also the experience with 3 could be of help in order to deal with the singlet/triplet differentiation in matrix-isolated carbenes. We learned that, if the calculated IR spectra of the singlet and triplet molecule are sufficiently different, it might be possible to determine the multiplicity of the matrix-isolated species by comparison with the experimental IR spectrum. In this context it is also worth mentioning that we were able to measure the matrix IR spectrum of 3, but a special technique (irradiation in halogen-doped xenon matrices) had to be developed in order to achieve a concentration of 3 sufficient for its IR detection.²³

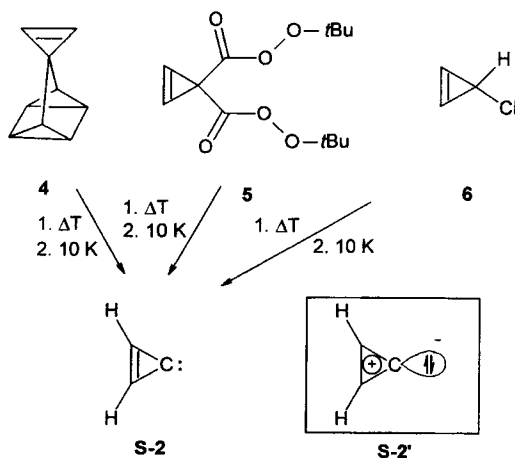
III. INDIVIDUAL CARBENES

A. Cyclic Carbenes

1. Cyclopropenyldiene

Molecule 2 is of considerable theoretical interest.²⁴ At the time of our success in generating 2 by flash pyrolysis of quadricyclane derivative 4²¹ in combination

with matrix isolation, only indirect evidence for the existence of some derivatives of **2** had been described.²⁵



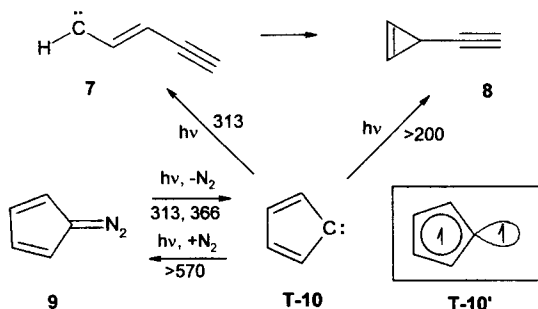
Carbene **2** was identified by comparison with the calculated IR spectrum.^{24h} At that time we were not yet able to carry out own calculations and therefore we gratefully accepted Prof. Schaefer's offer to help us in this respect. Cyclopropenylidene (**2**) has, as predicted²⁴ a singlet electronic ground state. The molecule can best be described as a cyclopropenylum ylide with the structure **S-2'**.

Later we found that diprester **5** is a much better precursor for the preparation of **2**.²⁶ But the easiest way of generating **2** is the thermal HCl elimination from 3-chlorocyclopropene (**6**).^{27,28} This reaction is astonishing and is probably due to the resonance stabilization of **2** in the singlet ground state, as the thermal elimination of HCl (in the absence of a base) does not work with ordinary halides. It should be added that **2** has been detected in interstellar clouds and it is claimed that **2** may be one of the most abundant hydrocarbons in interstellar space.²⁹

2. Cyclopentadienylidene

Cyclopentadienylidene (**10**) has an even longer history than cyclopropenylidene (**2**).¹⁴ Carbene **10** possesses a triplet ground state. Its ESR spectrum indicates a structure with C_{2v} symmetry. One electron is localized at the carbenic center, the other unpaired electron is delocalized over the five-membered ring (structure **T-10'**).³⁰ The IR and UV spectra of **10** are also known.³¹

We were intrigued by Lewars' recently published calculations on the C_5H_4 singlet hypersurface³² and therefore decided to study cyclopentadienylidene (**10**) once more.³³ As reported,^{14,31} diazocompound **9** generates triplet-**10** upon irradiation in argon at 10 K. With light of the wavelength $\lambda = 366 \text{ nm}$ only **10** can be detected IR spectroscopically. The experimental spectrum is in accor-



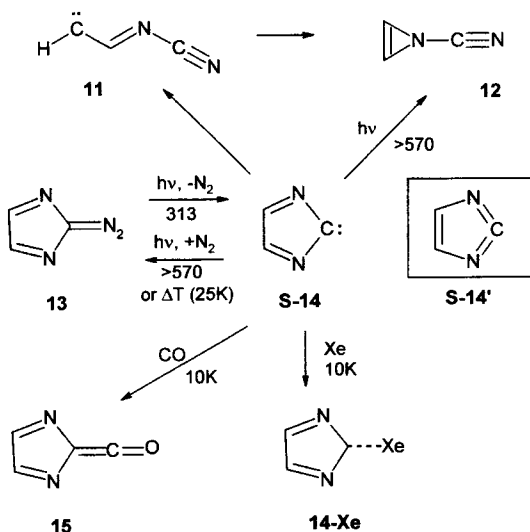
dance with earlier calculations by Schaefer.³⁴ With $\lambda > 570$ nm the nitrogen still present in the same matrix cage as **10** can be recaptured and diazocompound **9** is reformed. In this context it is no surprise that in a $^{15}\text{N}_2$ matrix the nitrogen in **9** can be exchanged upon short-time irradiation with $\lambda = 366$ nm. The mechanism of the known isomerization **T-10** $\rightarrow$ **8** ($\lambda > 200$ nm)³¹ can be elucidated by irradiating with $\lambda = 313$ nm. One sees the bands of carbene **7** ($\nu_{\text{C,H}} = 3328.6$ cm^{-1}), which upon further photoexcitation with $\lambda = 436$ nm gives a trace of ethynylallene ($\nu_{\text{C}=\text{C}=\text{C}} = 1953$ cm^{-1}) and mainly 3-ethynylcyclopropene (**8**) ($\nu_{\text{C,H}} = 3334.1$ cm^{-1}), which on irradiation with $\lambda = 254$ nm in a xenon matrix rearranges to 1,5-pentadiyne.

Our own calculations (B3LYP/6-311+G(d,p)) not only were in agreement with the published relative energies of **T-10** and **S-10** ($^1\text{A}_2$) ($\Delta E_{\text{S-T}} = 4.3$ kcal mol $^{-1}$) but could also be used to show that the experimental IR spectrum fits better for **T-10** than for **S-10** and to identify carbene **7**, which is also characterized by a strong UV absorption at 238/245 nm. Calculations also verify the isotopic shift of the diazo band in **9** compared to $^{15}\text{N}_2$ -**9** (exp.: -65 cm^{-1} ; calc.: -73 cm^{-1}).

3. 2H-Imidazol-2-ylidene (2,5-Diazacyclopentadienylidene)

Experiments to trap 2H-imidazol-2-ylidene (**14**), a diaza derivative of cyclopentadienylidene (**10**), generated by thermolysis or photolysis of 2-diazo-2H-imidazole (**13**) indicated, that **14** should be regarded as a highly reactive carbene with a strong singlet diradical character and a very electrophilic carbon atom.³⁵ Matrix isolation of **14**, carried out by us, together with *ab initio* calculations (MP4SDTQ(fc)/6-311+G(dp)//B3LYP/6-311+G(dp)) confirm that **14** possesses a singlet ground state with an unusual structure.³⁶

Its formation can be observed after short irradiation with a wavelength of $\lambda = 313$ nm in argon at 10 K. It is possible to use the comparison of the experimental IR spectrum with the calculated spectra for the singlet and triplet carbene to determine the singlet multiplicity of the isolated molecule. Its structure cannot easily be described by normal valence formulas. The calculated



bond lengths in the NCN framework suggest the presence of a cumulenic unit. On the other hand, the situation is quite different from that of an open-chain carbodiimide structure. The two bonds between the nitrogen atoms and the backbone carbon atoms cannot be perpendicular but are forced into an eclipsed orientation by the rigid structure (C_{2v} symmetry) of the five-membered ring. The molecule can best be interpreted by formula **S-14'**.

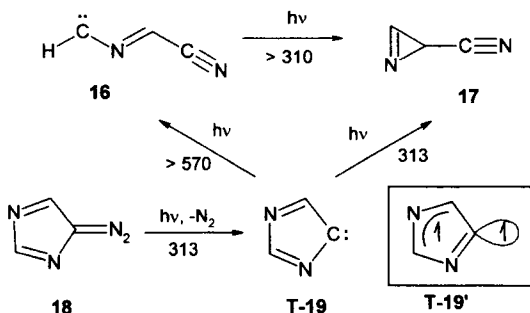
As proposed **S-14** is a very reactive electrophile, as demonstrated, firstly, by the thermal addition of nitrogen at 25 K to give **13** back, secondly, by the addition of CO to yield 2H-imidazol-2-ylideneketene (**15**) (**T-10** reacts in a similar fashion³¹), and thirdly, by formation of a complex **14-Xe** of the carbene with xenon. In a xenon matrix complexes of this type were also found by Sander et al.³⁷ for difluorovinylidene and by Maier and Lautz³⁸ for C_2 .

Subsequent irradiation of **S-14** with $\lambda > 570$ nm in the presence of a nitrogen molecule in the same matrix cage results as in the case of **T-10** in the recapture of nitrogen (which is also possible by annealing the matrix at 25 K). Parallel to this reaction, a photochemically induced rearrangement of **S-14** to *N*-cyano-1H-azirene (**12**) — perhaps via the ring-opened carbene **11** — and *N*-cyanoketenimine occurs.

4. 4H-Imidazol-4-ylidene (2,4-Diazacyclopentadienylidene)

Based on studies of the fragmentation of 4-diazo-4H-imidazole (**18**) in solution Amick and Shechter³⁹ argued that **19** has to be regarded as an electrophilic carbene with a singlet ground state. Later calculations either predicted a very small S/T-gap⁴⁰ or preferred the triplet.⁴¹ Our own B3LYP/6-311+G(d,p) cal-

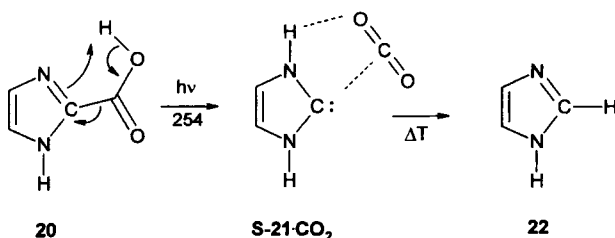
culations demand for **S-19** a cumulenic type of structure like in **S-14'**. The more stable triplet molecule is best described by a geometry given in structure **T-19'** with one electron localized at the carbenic center and the other one in an allylic type segment.^{33b}



The IR spectrum which can be measured in argon at 10 K after irradiation of diazo compound **18** with $\lambda = 313$ nm is relatively complex. But the absorptions of **19** can be extracted by a subsequent irradiation with $\lambda > 570$ nm. The signals of **19** decrease in intensity during this secondary irradiation. They fit much better with the bands calculated for **T-19** than for **S-19**. The product formed under these conditions ($\lambda > 570$ nm) is the ring-opened carbene **16**, which in this case can directly be detected and shows an IR spectrum which is in agreement with that of **S-16**. Intermediate **16** can be transferred photochemically to 2-cyano-2H-azirene (**17**) with $\lambda > 313$ nm, which is the main product in the primary irradiation of diazo compound **18** with this wavelength.

5. 2,3-Dihydroimidazol-2-ylidene

In 1991 Arduengo and co-workers⁴² reported the isolation and characterization of the first stable carbene, 1,3-di(1-adamantyl)-2,3-dihydroimidazol-2-ylidene. Since that time many substituted nucleophilic carbenes have been prepared.⁴³ From *ab initio* studies it can be shown that cyclic electron delocalization is partly responsible for the extraordinary stability of 2,3-dihydroimidazol-2-ylidenes.⁴⁴



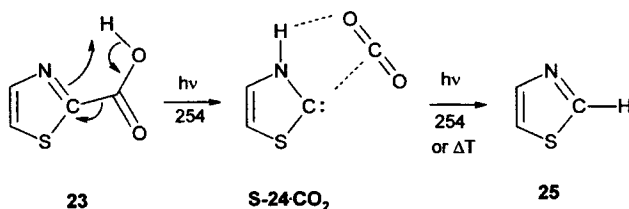
It was obvious, that the parent carbene **21** should be isolable in an argon matrix at 10 K. The barrier for the isomerization of **21** to imidazole **22** is calculated (B3LYP/6-311G(d,p)) to be rather high (41.5 kcal mol⁻¹).⁴⁵ Because of the interaction of the nitrogen lone pairs with the empty p-orbital of the carbenic center, carbene **21** should be a singlet molecule (S/T-gap = 81.6 kcal mol⁻¹).

The only problem for the matrix-isolation of **21** consisted in the non-availability of a reasonable diazo precursor molecule suited for this technique. But since we already had experience with the preparation of 2,3-dihydrothiazol-2-ylidene⁴⁶ (see below) by photofragmentation of thiazole-2-carboxylic acid we tried the same method with imidazole-2-carboxylic acid (**20**). Indeed, irradiation of **20** with a wavelength of 254 nm leads to decarboxylation and the formation of a complex between carbene **21** and CO₂. This is shown by the observation that the experimental IR spectrum fits only with the calculated spectrum of complex **21**·CO₂ (calculated stabilization energy relative to its fragments 4.3 kcal mol⁻¹). The type of fixation of CO₂ to **21** is indicated in the formula **S-21**·CO₂.

Carbene **21** should isomerize upon further irradiation to imidazole **22**, which is calculated to be 26.3 kcal mol⁻¹ more stable than **21**. This reaction could not be observed. But the trapped product after pyrolysis (400°C) of educt **20** was only imidazole **22**, probably formed via carbene **21** as an intermediate.

6. 2,3-Dihydrothiazol-2-ylidene

The ring system **24** especially exemplifies a nucleophilic carbene, since, as Breslow showed already more than 40 years ago,⁴⁷ it is the structural element that is responsible for the activity of vitamin B₁.⁴⁸



Calculations allow an assessment of electronic and geometric properties of the target molecule and the probability of isolating it in a matrix. In spite of the fact that singlet carbene **24** is 34.0 kcal mol⁻¹ (MP4SDTQ(fc)/6-311G(d)//MP2(fc)/6-31-G(d) calculation⁴⁶) higher in energy than thiazole **25** the isomerization **24** → **25** has — like **21** (see above) — a considerable energy barrier of 42.3 kcal mol⁻¹. Bond lengths and partial charges of planar **24** indicate partial “aromatic” character of **S-24**.

The standard methods for generating nucleophilic carbenes (deprotonation of

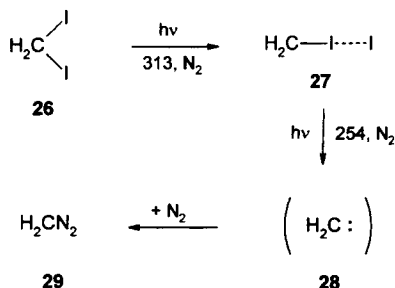
the corresponding H salts) are not suitable for matrix isolation of unsubstituted carbene **24**. But it turned out that thiazole-2-carboxylic acid (**23**) is an ideal candidate for the generation of **24**.⁴⁶ Upon irradiation of **23** in argon at 10 K with $\lambda = 254$ nm loss of CO_2 occurs and carbene **24** is formed (N–H band at 3410.0 cm^{-1}). During prolonged photolysis the absorptions of **24** diminish and the known bands of thiazole **25** appear. A detailed analysis of the IR spectra revealed that the species generated from **23** is not free **24** but a complex with CO_2 . The interaction of CO_2 with **24** is calculated to stabilize the carbene by 5.9 kcal mol^{-1} . The orientation of the CO_2 molecule is presented in formula **S-24-CO₂**. This arrangement can be regarded as a model for the catalytic activity of 2,3-thiazol-2-ylidenes in benzoin condensations of aliphatic aldehydes, since it uncovers both, the nucleophilic attack by the carbenic center and the electrophilic behavior of the proton at the nitrogen.

B. Acyclic Carbenes

1. Methylene

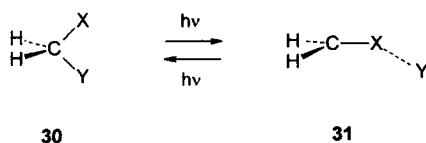
The first — flash photolytic — evidence of triplet^{49a,b,d} and singlet methylene^{49b,c} is to be found in the pioneering work of Herzberg. Furthermore, triplet methylene has been isolated in a noble gas matrix and characterized by ESR⁵⁰ and IR spectroscopy.⁵¹ No information is available, however, for the matrix isolation of singlet methylene. This is no surprise, since the singlet molecule is $9.05\text{ kcal mol}^{-1}$ higher in energy than the triplet ground state molecule.⁵²

Is the failure to isolate singlet CH_2 in matrix experiments perhaps due to the wrong choice of the precursor (diazomethane, diazirene)? In order to shed light on this matter, we irradiated diiodomethane (**26**) in argon or nitrogen at 10 K.⁵³ The result was a violet colored matrix. However, this is only apparently an indication for the splitting off of iodine. We found that **26** upon irradiation with $\lambda = 313$ nm is transformed into a violet “isodiiodomethane” **27**. If **27** is subsequently irradiated in a nitrogen matrix with $\lambda = 254$ nm, then diazomethane is formed! It is reasonable to assume, that photoexcitation of **27** generates methylene **28** (S or T), which then is trapped by the nitrogen used as



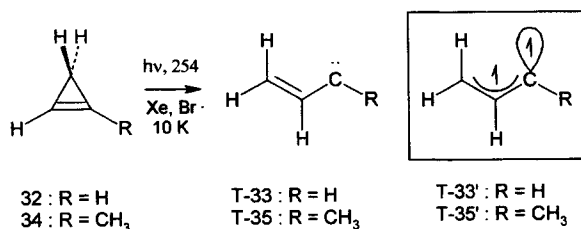
matrix material. Such a trapping of methylene (**28**) by nitrogen in a matrix at 10 K is already known since the early labeling experiments with diazomethane by Milligan and Pimentel.^{51b} As a result of this recapture of N₂ diazomethane **29** is apparently photostable under matrix conditions.

The isomerization of methylene iodide (**26**) can be expanded to other dihalomethanes **30** with X, Y = Cl, Br, I (not with F)⁵⁴ and polyhalomethanes.⁵⁵ If two different halogen atoms X and Y are present, it is the heavier one that migrates. This selectivity can be explained by a homolytic cleavage of the weaker C–Y bond in **30** as the primary step. The radical pair (Y· + ·CH₂X) formed from **30** prefers to re-add Y· with formation of the isodihalomethane **31**, instead of splitting off the second halogen atom X· and giving methylene (**28**).



2. Vinylcarbene

Photolysis of vinyl diazomethane in an organic glass at 6 K leads to vinylcarbene in its triplet ground state,^{14,56,57} which — as is indicated by the ESR spectra — forms a pair of the *s-cis* and *s-trans* isomer. The delocalization of one unpaired electron in the π -system is similar to that of the allyl radical, while the other unpaired electron is localized in a sp^2 -orbital at the carbenic C atom (see formula **T-33'**).⁵⁸



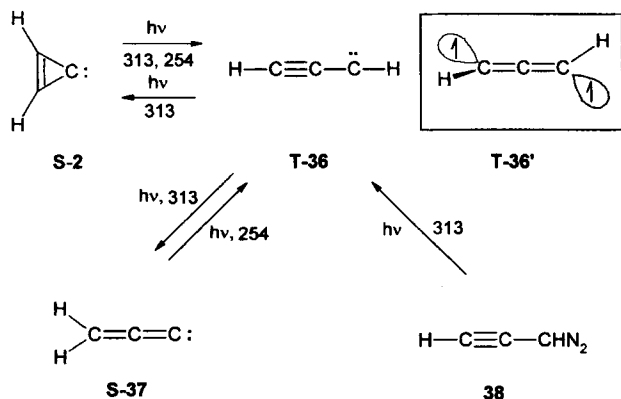
Vinylcarbene is known to close to cyclopropene.⁵⁹ The reverse reaction is also possible: Triplet-propene-1,3-diyl (**trans-T-33'**) can be generated from cyclopropene **32** by irradiation in a bromine-doped xenon matrix at 10 K; 1-methylcyclopropene (**34**) yields triplet-2-butene-1,3-diyl (**trans-T-35'**).^{60–62} The concentration of **35** under these conditions is high enough to be able to detect this diradical IR spectroscopically. The experiments suggest that even the parent vinyl carbene **33** is detectable.^{61,62} Calculations ((U)B3LYP/6-31G*)^{61,62} not only allow the comparison of theoretical and experimental IR spectra but also

reveal that the reactions $32 \rightarrow 33$ and $34 \rightarrow 35$ are the lowest energy ground state pathways for the ring opening of **32** and **34**, respectively.

3. Ethynylcarbene (Propargylene)

In 1987 we reported²⁶ that the three possible C_3H_2 isomers **S-2**, **T-36**, and **S-37** can be transformed into each other under photochemical conditions. For several reasons propargylene (**36**) attracted our attention: On the one hand the first C_3H_2 parent species, identified by direct spectroscopic methods, was triplet propargylene (**T-36**). Its ESR spectrum was published in 1965,⁶³ and, based on the zero-field-splitting parameters, a linear or nearly linear structure was derived. On the other hand, the structural elucidation of **36** by comparison of the calculated and experimental IR spectra turned out to be rather difficult.⁶⁴

In 1972 a matrix-isolation study on the photolysis of diazopropyne (**38**) and some IR bands of propargylene (**36**) were reported in a doctoral thesis.⁶⁵ In 1974, **36** was identified as one of the products of the vacuum UV irradiation of matrix-isolated propyne and allene.⁶⁶



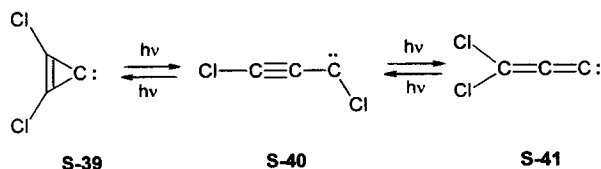
A complete analysis of the vibrational spectrum had to wait until we were able to prepare **T-36** via the photoisomerization of **S-2**. Even if an anharmonic approximation was taken in account in the calculation (UMP2/6-31G**) the IR spectrum was still in poor agreement with the observed spectrum.⁶⁴ But one thing was clear: formula **T-36** does not represent the real structure of propargylene, since no IR band in the expected region for the C,C triple bond vibration of an acetylene was found, but a C,C stretching vibration at 1620 cm^{-1} was registered instead.

The C_3H_2 potential energy surface continued to find attention, computationally and experimentally. It was Herges and Mebel,⁶⁷ who reported in 1994, that the experimental and calculated IR spectra of **T-36** agree quite well if a more sophisticated treatment including configuration interaction (QCISD/6-31G*) is

used. This theoretical treatment indicates that propargylene possesses a bent allenic 1,3-diradical structure with C_2 symmetry (formula **T-36'**).⁶⁷ This result was confirmed by McMahon et al.,^{68,69} who used differently ^{13}C -labeled diazopropynes **38** as precursor molecules. These authors also were able to measure the UV spectrum of **T-36**. All three isomers, **S-2**, **T-36**, and **S-37** were used by Chen et al.⁷⁰ as target molecules for the spectroscopic determination of thermochemical quantities of carbenes.

4. Halogenated Ethynylcarbenes

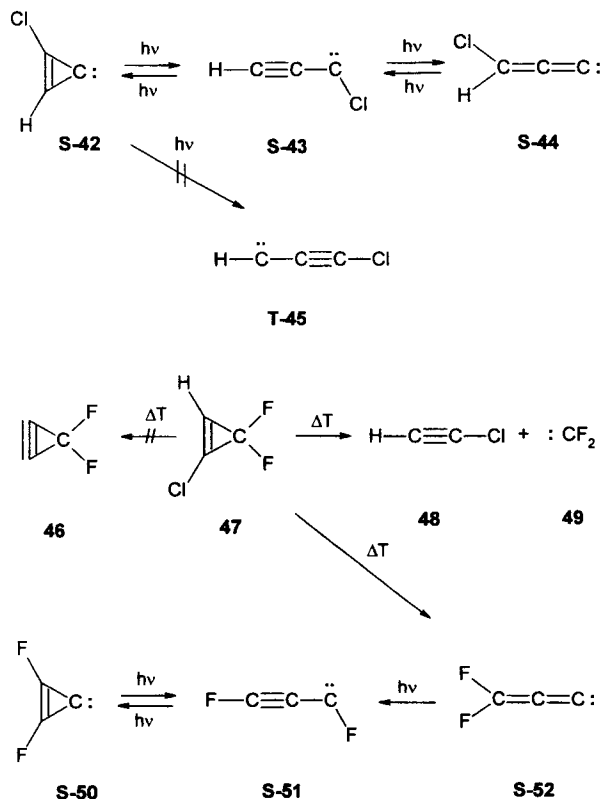
The problem which arose in the structural elucidation of triplet propargylene **T-36'** should not exist in the case of halogenated derivatives with singlet electronic ground states. Indeed, when dichlorocyclopropenylidene (**39**) was generated by high-vacuum pyrolysis from 1,2,3- or 1,3,3-trichlorocyclopropene (thermal HCl elimination) and subsequently photoisomerized into dichloropropargylene (**40**) and dichlorovinylidenecarbene (**41**), the identification of all three carbenes could easily be carried out by comparison of the calculated and experimental spectra of **S-39**, **S-40**, and **S-41**.²⁷



The same is true for the series of monochlorinated derivatives **S-42**, **S-43**, and **S-44**. The main structural information can again be drawn from the IR spectra.

In contrast to the unsubstituted propargylene **T-36'** not only the chlorinated cyclopropenylidenes and vinylidenecarbenes but also dichloro- and monochloropropargylene have singlet ground states showing IR spectra for species with "fixed" C,C triple and C,C single bonds. The other possible monochloropropargylene (**45**), for which a triplet ground state is expected, could not be detected as a photoproduct of **S-42**.

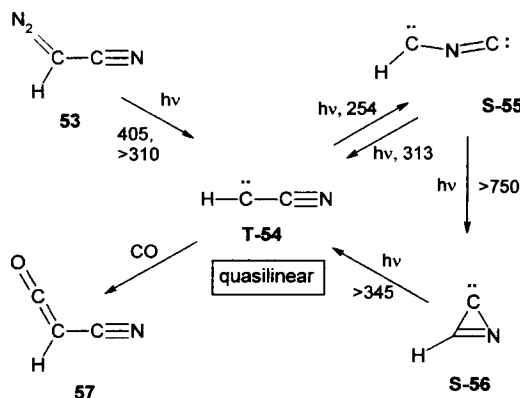
Entry into the C_3F_2 series was found by an unusual route. One might not expect the formation of cyclopropyne **46** (such a compound has been identified during the study of C_2SiH_2 isomers,⁷¹⁻⁷³ see Section IV.A) upon pulsed flash pyrolysis of cyclopropene **47**. What really happens upon thermolysis of **47** is the formation of chloroacetylene (**48**) together with difluoromethylene (**49**), and via a parallel pathway the generation of difluorovinylidene-carbene (**52**). By subsequent photoisomerization one gets singlet difluoropropargylene (**S-51**) and difluorocyclopropenylidene (**S-50**).⁷⁴ The identification of the free carbenes was quite simple, by comparison with the vibrational spectra calculated by Frenking et al.⁷⁵



5. Cyano- and Isocyanocarbenes

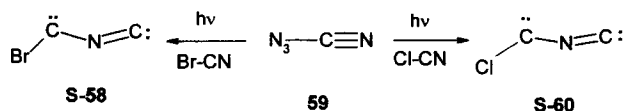
The first detection of cyanocarbene (**54**) goes back to 1964, when Bernheim et al.⁷⁶ measured the ESR spectrum of matrix-isolated **54**. From the early ESR,^{76,77} matrix IR,⁷⁸ and microwave⁷⁹ studies a triplet ground state and a linear or nearly linear structure were derived, in contrast to many theoretical calculations that predicted a bent structure.⁸⁰ Since then additional results from microwave⁸¹ and gas phase IR⁸² studies, and *ab initio* calculations⁸³ have led to the *quasilinearity* of cyanocarbene (**T-54**) being generally accepted.

We generated **T-54**, as reported,⁷⁸ from diazoacetonitrile **53** by irradiation in argon or nitrogen at 10 K and found that cyanocarbene (**T-54**) can be isomerized to isocyanocarbene (**55**) and azacyclopropenylidene (**56**), both possessing singlet ground states, by irradiation with light of selected wavelengths.⁸⁴ The identification of both carbenes **S-55** and **S-56** is once more based on the good agreement between the experimental and theoretical IR spectra, which were obtained by density functional calculations (B3LYP/6-311++G**).⁸⁴ Cyanocarbene (**T-54**) and isocyanocarbene (**S-55**) are peculiar isomers in so far that they



differ in their multiplicity and therefore in their chemical behavior.⁸⁵ Compound **T-54** has a triplet ground state and is a quasilinear molecule. It reacts with carbon monoxide under irradiation to form cyanoketene (**57**). In contrast, **S-55** is a singlet molecule with a rigid structure and is inert against carbon monoxide. The differences are reflected in the diverging geometries and spectroscopic (IR, UV) properties of **T-54** and **S-55**. The third isomer, azacyclopropenyldiene (**S-56**), is not the transition state in the nitrile/isonitrile rearrangement **T-54** $\rightarrow$ **S-55**, but a real energy minimum, which can also be identified spectroscopically.

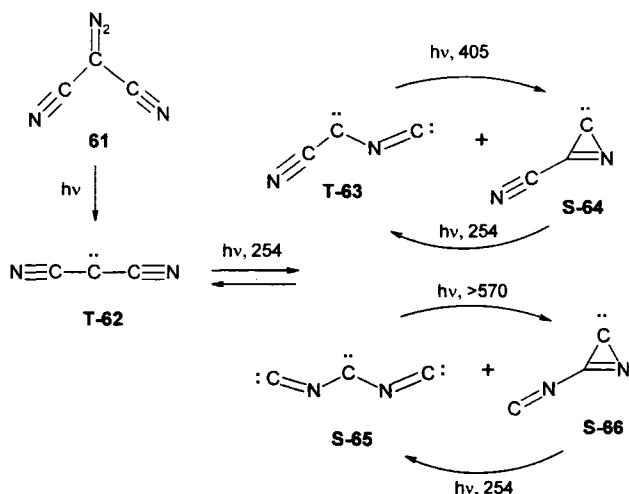
By accident we also found an entry to the potential-energy surfaces of the systems C_2BrN and C_2ClN .⁸⁶ If the photolysis of cyanogen azide (**59**), which was studied by Milligan and Jacox in 1965,⁸⁷ is carried out in the presence of cocondensed BrCN , the formerly unknown singlet bromoisocyanocarbene (**S-58**), a strongly bent molecule, can be identified by comparison of the experimental and theoretical (B3LYP/6-311++G**) IR spectra.



Similar observations were made when BrCN was replaced by ClCN . Then the chlorine analogue **S-60** was observed. Probably we were also successful in transferring photochemically both isocyanocarbenes **58** and **60** into the corresponding halogenated cyanocarbenes. But their identification has to remain tentative, since only two IR bands could be found for each of the new cyanocarbenes.

Dicyanocarbene (**62**) has a similar history as the monocyano derivative. Waserman et al.⁸⁸ reported the ESR spectrum of **T-62** in 1965. Smith and Leroy⁸⁹ published a matrix IR study in 1969, which was partly corrected by Dunkin and McCluskey.⁹⁰ Many other calculations have also been published.^{88,91} All theo-

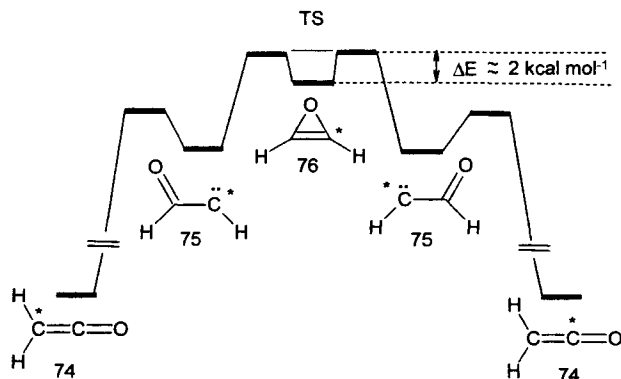
retical treatments agreed insofar that dicyanocarbene possesses a triplet ground state, but the predictions for the geometry of **T-62** differed.



In combination with the work discussed above and due to the still existing inconsistencies in the experimental and theoretical studies on **T-62** we decided to study **62** in more detail.⁹² B3LYP/6-311+G* calculations confirm the triplet ground state of **62** with a linear geometry, which is characterized by a rather high spin density at the nitrogen atoms. The calculated IR spectrum gives only a poor agreement with the experimental data published earlier.^{89,90} Our own findings can be summarized as follows. Photolysis of dicyanodiazomethane (**61**)⁹³ with light of wavelength $\lambda > 385$ nm in argon at 10 K leads to an IR spectrum (most intense bands: 1747.6 (vs), 1508.1 (s), 387 (s) cm^{-1}), which fits much better with the calculated absorptions for **T-62** than for **S-62**. In accordance with the literature⁹⁰ we observe for **T-62** two UV absorptions at $\lambda_{\text{max}} = 340$ and 268 nm (with vibrational fine structure). Irradiation into these UV maxima allow the photoisomerization of carbene **T-62** to a mixture of four additional isomers **63–66**. The experimentally detected photochemical connectivities are shown in the reaction scheme given above. In all cases the identification is based on the comparison of the measured and calculated IR spectra. It is worth mentioning that in cyanoisocyanocarbene (**63**) the cyano group (stabilization of the triplet) wins against the isocyano group (stabilization of the singlet multiplicity).

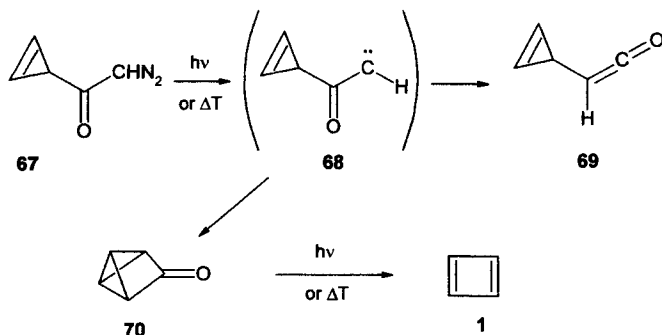
C. Ketocarbenes

Our interest in ketocarbenes originated from the aim to matrix-isolate oxirene (**76**) (Scheme 1), the oxygen-containing hetero analog of cyclobutadiene (**1**)

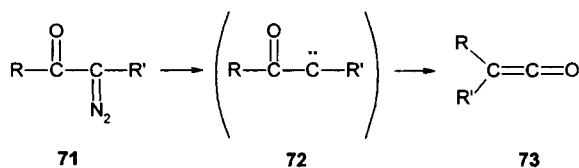


Scheme 1. Reaction coordinate for the isomerization of labeled ketene **74** via oxirene **76**.

(cyclic delocalization of 4π electrons). So already in 1982 we not only tried to generate oxirene **76** by photochemically induced cycloreversion of suitable precursor molecules⁹⁴ but also undertook a systematic study of a variety of diazoketones.⁹⁵ Our hope was that we might find a specific diazoketone which yields a ketocarbene in such a concentration, that its IR or UV spectroscopic detection as well as an experimental proof for its isomerization into the corresponding oxirene might be possible. Triplet ketocarbenes have been observed in matrices by measuring the ESR spectra.⁹⁶ Further spectroscopic studies were prevented by the fast Wolff rearrangement into the related ketenes. But there are many indirect indications that triplet and/or singlet ketocarbenes are formed upon photochemical N_2 elimination from diazoketones. Just one example. Tricyclopentanone **70**,^{97,98} the best starting molecule for cyclobutadiene (**1**), is formed upon matrix photolysis of diazoketone **67**,⁹⁸ together with ketene **69**. It is tempting to assume that ketocarbene **68** is formed in the first step and then not only undergoes a Wolff rearrangement but also an intramolecular carbene addition under formation of **70**.

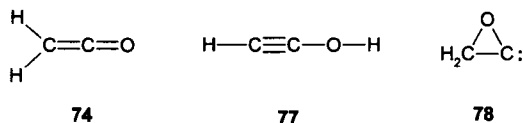


In the list of diazoketones studied by us⁹⁵ mostly derivatives were included which have in solution no or only a small tendency for a Wolff rearrangement. Nevertheless we found not a single diazoketone **71** which enabled us to identify a ketocarbene **72**, only the corresponding ketenes **73** could be detected. The same observation was made when we studied in collaboration with Yannoni et al.⁹⁹ the photochemically induced deazotation of 1-diazo-2-propanone in an organic matrix at 77 K, using ¹³C CPMAS NMR spectroscopy as the analytical tool.

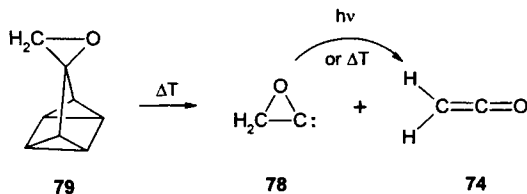


As far as the oxirene problem¹⁰⁰ is concerned, we concluded in 1982⁹⁵ that Scheme 1 would illustrate the interconversions between ketene **74**, formylcarbene (**75**), and oxirene (**76**). The basic statement was that it might be difficult to decide whether oxirene (**76**) has to be regarded as an intermediate or a transition state on the reaction coordinate.

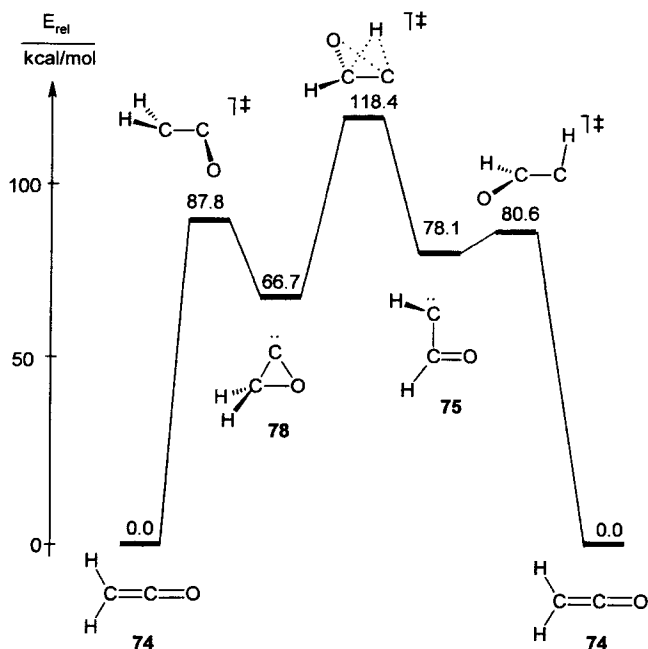
In the meantime several theoretical¹⁰¹ and experimental¹⁰² papers dealing with this subject have been published. Recent calculations^{101c} have shown that oxirene (**76**) is a true minimum on the C₂H₂O energy surface. An unequivocal verification of this prediction, however, is still missing.¹⁰³



But there is also good news about the members of the C₂H₂O family and that is the matrix isolation of oxiranylidene (**78**). Besides ketene **74** and ethynol (**77**)¹⁰⁴ carbene **78** should be a minimum on the C₂H₂O potential surface¹⁰¹ with a considerable barrier to isomerization. Indeed, oxiranylidene **78** is observable under matrix conditions.¹⁰⁵



When quadricyclane derivative **79** was pyrolyzed by Hoffmann and Schüttler¹⁰⁶ they detected ketene **74** as the only product. But the combination of flash

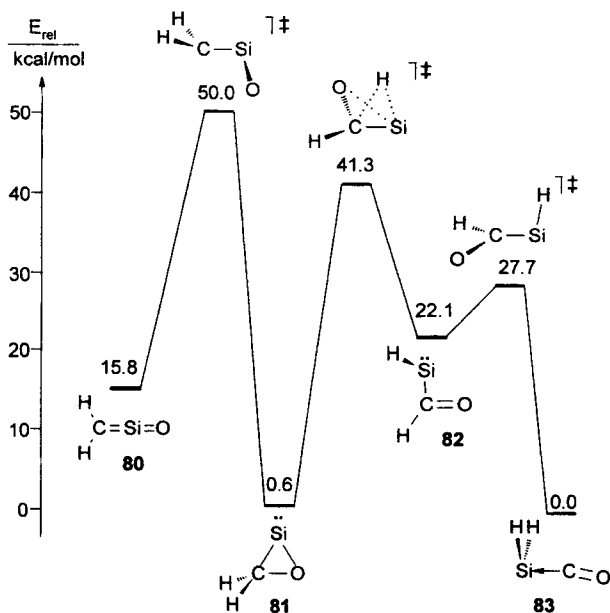


Scheme 2. Relevant cutouts for the calculated $\text{C}_2\text{H}_2\text{O}$ energy hypersurface (B3LYP/6-311++G**).

pyrolysis and matrix isolation allows also the identification of **78**.¹⁰⁵ Its structure can be elucidated by the comparison of the experimental with the calculated (MP2/6-311++G**) IR spectrum. Thermal or photochemical excitation of **78** yields ketene **74**.

The investigation of carbene **78** was of interest to us also because of our attempts to matrix-isolate the corresponding silicon species of the elemental composition CH_2OSi .¹⁰⁷ The comparison of the relevant cutouts of the two calculated energy hypersurfaces (B3LYP/6-31G**) $\text{C}_2\text{H}_2\text{O}$ (Scheme 2) and CH_2OSi (Scheme 3) illustrates the characteristic differences — and analogies — if one carbon is replaced by a silicon atom.¹⁰⁷

The reaction coordinates are in principle similar. But there are two main differences. First, silaoxiranylidene **81** is — as also shown experimentally — more stable than the planar silaketene **80**. The opposite is true for the system **74/78**. Second, the global minima are different; formylcarbene **75** leads, via a small barrier, to ketene **74**, and formylsilylene (**82**) gives, in accordance with experiment¹⁰⁷, the pyramidal $\text{H}_2\text{Si}\cdot\text{CO}$ complex **83**.



Scheme 3. Relevant cutouts for the calculated CH_2OSi energy hypersurface (B3LYP/6-31G**).

D. Unsaturated Carbenes

1. Vinylidenecarbene

As has already been discussed (Section III.B.3) we were able to demonstrate that the three C_3H_2 isomers cyclopropenylidene (**2**), propargylene (**36**), and vinylidenecarbene (**37**), interconvert photochemically in low-temperature matrices. Unlike **36** vinylidenecarbene (**37**) was predicted to be a singlet.^{108–110} To aid the spectroscopic identification of **S-37** we calculated (MP2/6-31G**) IR frequencies and intensities of this species.²⁶ Comparison with the experimental IR spectrum (most intense band at 1952 cm^{-1}) confirmed the allenic structure **S-37**. For **T-37** a completely different IR spectrum was expected. An additional structural proof for **S-37** was its reversible transformation into the other two C_3H_2 isomers **S-2** and **T-36**.

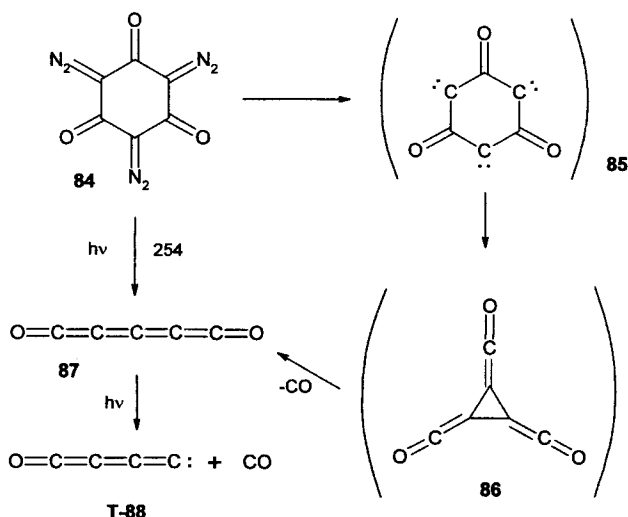
McMahon et al. contributed to this field not only by revealing the electronic spectrum of **S-37**¹¹¹ but also by elucidating — on the basis of studies with labeled compounds — the complex mechanism of the automerizations and isomerizations of the three C_3H_2 species **S-2**, **T-36** and **S-37**.^{69,112} A complete record, including high level calculations, was published by McMahon.⁶⁹

2. Halogenated Vinylidenecarbenes

The entries to chlorovinylidenecarbene **S-44**, dichlorovinylidenecarbene **S-41**, and difluorovinylidenecarbene **S-52** and their photochemical interconversions into the corresponding propargylenes and cyclopropenylidenes have already been discussed (Section III.B.4). All these halogenated vinylidenecarbenes have singlet ground states.²⁷ The chlorinated derivatives can be generated photochemically from their cyclopropenylidene isomers.²⁷ For difluorovinylidenecarbene we had to use an unusual route, namely flash pyrolysis of cyclopropene derivative **47**. There are two reasons why this procedure works at all. First, the weakest bond is the one neighbored to the double bond (see also Section III.B.2) leading to a vinylcarbene upon breakage. Second, in the C_3H_2 and in the chlorinated series the global minima are represented by the cyclopropenylidene isomers. On the C_3F_2 potential energy surface the vinylidenecarbene isomer is the most stable one.⁷⁵

3. Carbon Oxides $C_n=O$ and Carbon Sulfides $C_n=S$

The amazing discovery that carbenes like cyclopropenylidene (**2**)²⁹ (Section III.A.1), vinylidenecarbene (**37**)¹¹³, as well as butatrienylidene¹¹⁴ are present in interstellar clouds, inspired us to search for further highly reactive compounds that might be found to exist as "molecules between the stars". Based on the experience gathered so far,¹¹⁵ possibilities include systems with polycumulated double bonds. Realizing this, we resumed an earlier study (1979) of the photobehavior of tris(diazo)ketone **84**¹¹⁶, which we had begun¹¹⁷ in the hope, that **84** might form trisketene **86** via a threefold Wolff rearrangement of tris(ketocarbene) **85**.



Indeed, **84** undergoes on irradiation in argon at 10 K a clean elimination of nitrogen, as can be derived from the fast disappearance of the diazo band in the IR spectrum and the emergence of two predominant ketene bands at 2213 and 2059 in the intensity ratio of about 3 : 1. At the time of this first experiment¹¹⁷ we were not able to correlate this spectrum to a certain compound, for instance trisketene **86**. So the structural proof for the isolated molecule had to wait until a semiempirical calculation (MNDO) became possible.^{116,118} The comparison of the experimental and calculated IR spectrum¹¹⁹ made it clear that the photoproduct of **84** was 1,2,3,4-pentatetraene-1,5-dione (**87**). In agreement with the prognosis^{120,121} that carbon oxides C_nO_2 having an odd number of C atoms should be more stable than those having an even number, it was possible to prepare **87** also on a preparative scale.¹¹⁶ Probably the three-membered ring compound **86**, which could have been formed from **84** via tris(ketocarbene) **85**, is an intermediate of the photocleavage of **84**.

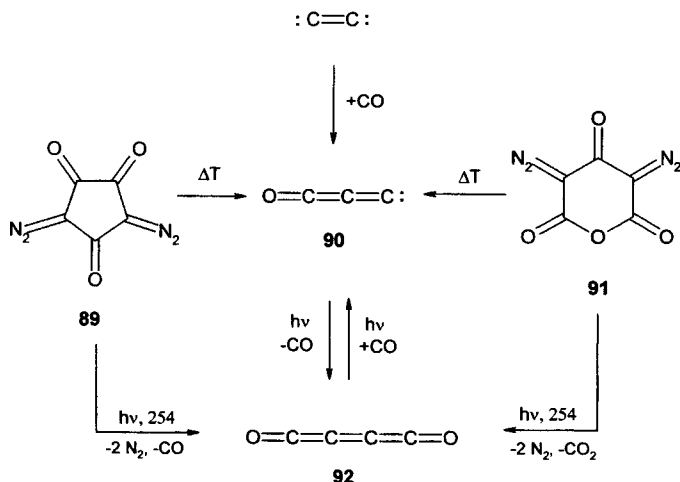
In practice the investigation of the photochemistry of tris(diazoketone) (**84**) became for us the starting point not only for the use of calculated IR spectra in the elucidation of structures of matrix-isolated molecules, but also for the detailed study of a whole series of chalcogeno heterocumulenes $X=C_n=Y$ ($X = O, S$) including formal carbenes $C_n=O$ and $C_n=S$. At the time when we began our investigation only a few carbon oxides and sulfides had been identified. Within a few years we were successful in filling the many white spots on the map of chalcogeno heterocumulenes.¹²¹

As far as the multiplicity of the carbenic species $C_n=O$ and $C_n=S$ is concerned, the following rules can be used as a guideline. As in the case of the heterocumulenes $X=C_n=Y$ also the carbon oxides $C_n=O$ and sulfides $C_n=S$ possess, supposing a linear structure, as HOMOs doubly degenerated π -orbitals. For even n these orbitals are half-filled, resulting according to Hund's rule in a triplet ground state. In the case of odd n the HOMOs are fully occupied, with a singlet state as the consequence.¹²¹ Thus with growing chain length the multiplicity of the electronic ground state of the chalcogeno heterocumulenes alternates between singlet and triplet.

a. Carbon Monoxides. When matrix-isolated C_5O_2 **87** was irradiated in argon with light of the wavelength 230 nm, CO was cleaved off and a new species was found. Again the comparison of the experimental and theoretical IR spectrum (MNDO) helped to identify the photofragment as oxobutatrienyli-dene (**88**). As calculated for a linear triplet molecule,¹²³ five bands were observed in the matrix IR spectrum corresponding to four stretching modes and one bending vibration. Weltner et al.¹²⁴ found, that C_4O is also formed by photochemical reaction of carbon monoxide with matrix-isolated graphite vapor by selective excitation of C_3 . They showed the triplet character of **T-88** by ESR spectroscopy as well as the linear structure with cumulene-like bonding by use

of ^{13}C and ^{17}O isotopomers. We detected the same ESR signal upon irradiation of **87**.

Having detected oxobutatrienylidene (**T-88**) we became interested in lower and higher members of the series $\text{C}_n=\text{O}$. In order to generate oxopropadienylidene (**90**) via dioxide C_4O_2 , we synthesized butatrienedione (**92**) by photolysis of the cyclic diazoketones **89** and **91**.¹²⁵ These photoreactions are crucially depending on the wavelength of the irradiating light. With $\lambda = 254$ nm the main product is dione **92**. This compound was the first dioxide of carbon with an even number of carbon atoms and was characterized by both, its two IR-active stretching modes and one bending vibration. Since C_4O_2 has an even-membered carbon chain, **92** is expected to be a linear molecule with a triplet ground state.^{121,126} But there is no experimental verification for this prediction.



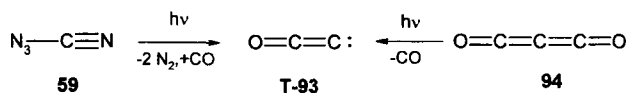
With wavelengths >300 nm dione **92** splits off carbon monoxide and oxopropadienylidene C_3O (**90**) is formed, whose preparation can also be achieved by pyrolysis of the educt molecules **89** and **91**.¹²⁵ Quite recently³⁸ we found that C_3O **90** is also formed when C_2 is trapped by carbon monoxide in a matrix at 10 K.

Based on these results, the detailed IR spectrum of **90** was treated in a comprehensive theoretical study by Botschwina and Reisenauer.¹²⁷

C_3O was observed in a matrix by DeKock and Weltner in 1971.¹²⁸ Later (1985) Brown et al.¹²⁹ found several other pathways to **90** and added further spectroscopic information on the molecule.

The next lower member, oxoethenylidene C_2O (**93**), played already an important role in the history of matrix isolation of cumulenenic carbenes. Jacox et al.¹³⁰ generated oxoethenylidene **93** by reaction of carbon atoms obtained from

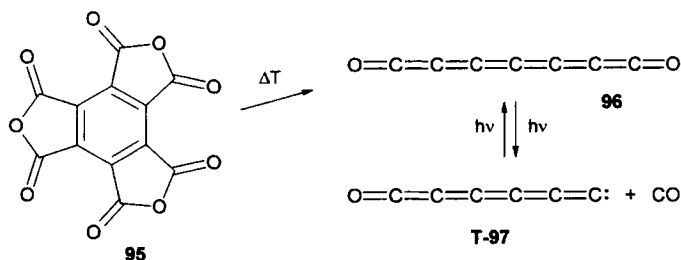
cyanogen azide (**59**) with carbon monoxide and by vacuum UV photolysis of matrix-isolated carbon suboxide C_3O_2 (**94**).



The linear structure of **93** was derived from experiments with labeled precursor molecules and by correlation of vibrational frequencies calculated from estimated force constants with the recorded IR absorptions. The three fundamentals were observed as well as the UV/VIS spectrum,¹³¹ which was resolved and analyzed by gas phase measurements.¹³² The predicted triplet ground state was confirmed by recording the ESR spectrum of **93** isolated in various matrices.¹³¹

Our goal to isolate the next higher member of C_4O , namely oxopentatetraenylidene C_5O , could not be achieved. Following the routine procedure it would be necessary to generate the dioxide C_6O_2 , which should be a triplet molecule of high reactivity. Therefore it is no surprise that we failed in our attempts to prepare C_6O_2 and/or C_5O .

The situation is expected to be better for dione C_7O_2 **96**. Therefore we studied the pyrolysis and matrix photolysis of mellithic acid trianhydride (**95**).¹³³ In these investigations we found, that in the matrix spectrum of the flash pyrolysis products several IR bands are observed, which can be ascribed to heptahexaenedione C_7O_2 (**96**), representing the longest matrix-isolated heterocumulene detected so far. The four IR active stretching vibrations predicted for **96** were observed. Combination bands indicated a centrosymmetric molecule and gave a hint to two additional fundamentals.



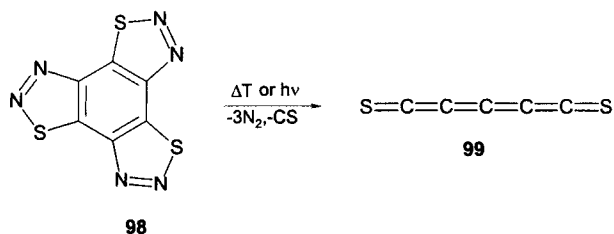
The correlation of the recorded IR spectrum with semiempirical calculations and the reversible cleavage into oxohexapentaenylidene (**97**) and carbon monoxide give a consistent picture for both, dione **96** and carbene **97**. The spectrum of **97** correlates with scaled *ab initio* vibrational frequencies.¹²³ C_6O **97** should be a triplet molecule. Indeed, Weltner et al.¹²⁴ observed during the experiment concerning C_4O **T-88** another triplet ESR signal which they ascribed to **T-97**.

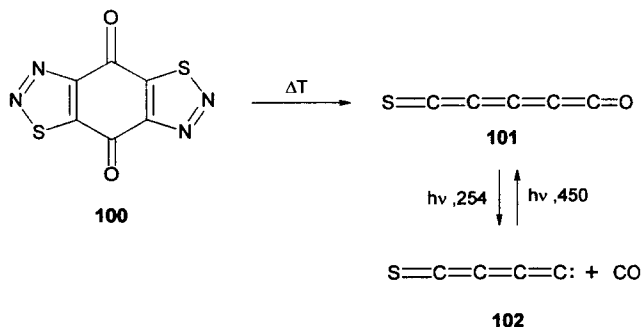
In order to complete the list of carbon oxides $C_n=O$ ($n = 1-9$) it should be mentioned that, as it was already discussed for C_5O , also the higher members C_7O , C_8O , and C_9O have not been yet isolated in a matrix, but they could be generated by Endo et al.^{134,135} in the gas phase by an electric discharge in a mixture of C_3O_2 and argon. The reaction products were analyzed by rotational spectra, from which the linear cumulenic structure and the bond lengths were derived.

In conclusion it can be said that all the "carbenes" C_nO with $n = 1-9$ are known. As predicted by theory the multiplicity alternates depending on the number of n (odd n : singlets; even n : triplets). The calculated $C=C$ bond lengths in the higher members vary between 1.27 and 1.30 Å.¹²¹ This small alternation fits to our traditional habit to regard the species $C_n=O$ as cumulenic carbenes, but — as is stressed by Janoschek¹²¹ — the high dipole moments with a positive charge at the oxygen atom demand a strong π -electron delocalization from the oxygen atom to the carbenic center at the end of the chain.

b. Carbon Monosulfides. Having prepared pentatetraenedione (**87**) and oxobutatrienylidene (**88**) starting from tris(diazoketone) **84** (see above) it was tempting to apply the same strategy to the corresponding sulfur derivatives.

Already in the first experiment of this series (1990) we found¹³⁶ that photolysis or pyrolysis of benzotris(thiadiazole) **98** leads to pentatetraenedithione (**99**), the third carbondisulfide beyond the already known low members CS_2 and C_3S_2 . The long-chain derivative **99** can be kept in a solution even at room temperature for some time without polymerization.



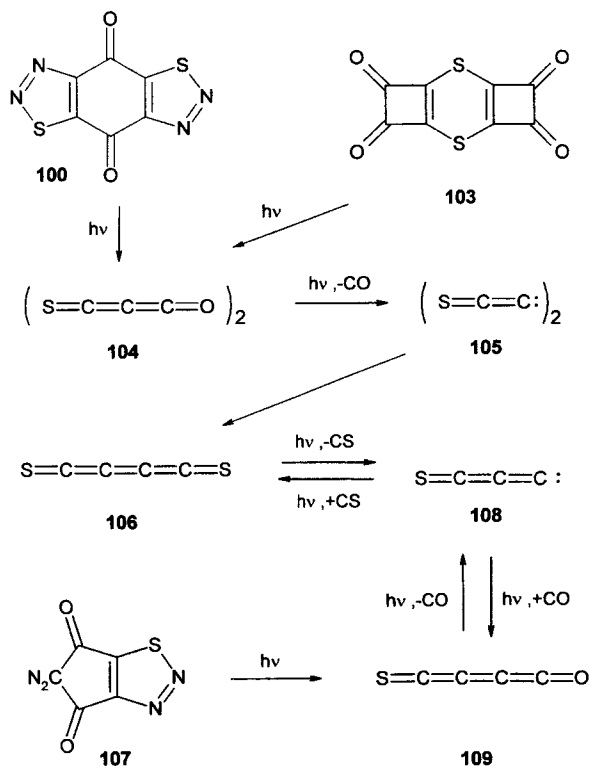


of sulfur-containing carbenes of the type $\text{C}_{n-1}=\text{S}$ starting from sulfide oxides $\text{O}=\text{C}_n=\text{S}$. For instance, photochemical cleavage of matrix-isolated C_5OS yields thioxobutatrienylydene C_4S (**102**).¹³⁷ The UV spectrum of **102**, expected to be a triplet molecule, shows two maxima at 240 and 450 nm. Therefore, upon irradiation with light of the wavelength $\lambda = 450\text{ nm}$ carbene **102** recaptures the carbon monoxide, which is still present in the same matrix cage, and sulfide oxide **101** is reformed.

Analogous procedures can be used to prepare thioxopropadienylydene (**108**). Relevant precursor molecules would be butatrienedithione C_4S_2 (**106**) or thioxobutatrienone C_4OS (**109**). Our studies in this respect were published in 1991.¹³⁹ C_4S_2 (**106**) is formed upon matrix photolysis of the polycyclic compounds **100** (behavior on pyrolysis see above) and **103**. The generation of C_4S_2 from **100** and **103** was surprising at first glance, since these molecules, on the other hand, proved also to be very good photochemical or pyrolytic precursors of C_3OS . However, because two molecules are, as indicated in formula **104**, embedded in the same matrix cage during the photolysis of **100** or **103**, the generation of an association **105** of two molecules of $\text{S}=\text{C}=\text{C}$ by splitting off CO is believed to be the crucial step. The two encapsulated molecules then dimerize and give C_4S_2 **106**.

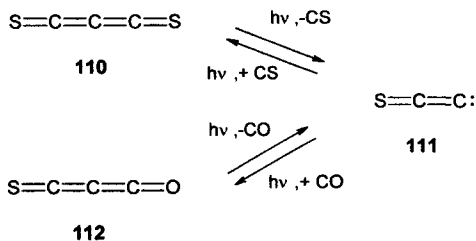
Strangely enough, thioxobutatrienone C_4OS (**109**) is observed as a photo-product of thiadiazole **107**.¹³⁹ Both chalcogeno cumulenes **106** and **109** are fragmented upon matrix irradiation into thioxopropadienylydene C_3S (**108**) and carbon monosulfide or carbon monoxide.¹³⁹ It is noteworthy that in the case of **109** only CO and no CS is split off. C_3S **108** was identified by three vibrational bands corresponding to stretching modes on the basis of semiempirical calculations. Reversible photochemical readdition of CO or CS embedded in the same matrix cage can be achieved by selective irradiation with $\lambda = 366\text{ nm}$ into the observed UV maximum ($\lambda_{\text{max}} = 378\text{ nm}$) of C_3S **108**.

Similar to C_3O , Botschwina et al.¹⁴⁰ published comprehensive theoretical calculations on C_3S **108** and compared their results with experimental values,



including a state-of-the-art IR spectrum of **108**. These high level calculations confirm that C_3S **108** should possess a singlet electronic ground state.

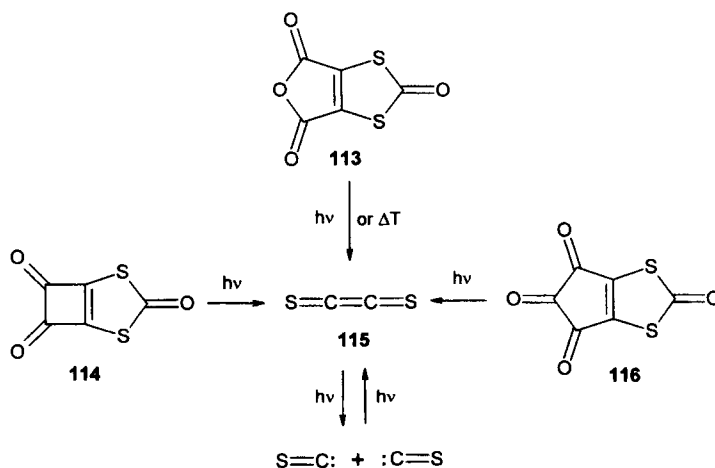
The next lower member in the $\text{C}_n=\text{S}$ series is thioxoethynylidene C_2S (**111**). It took a couple of years from its detection in interstellar space by microwave spectroscopy^{141,142} to its first isolation and identification in a matrix.⁹²



The target molecule C_2S **111** was generated by laser-induced photolysis of matrix-isolated C_3S_2 **110** or C_3OS **112**. Two of the three fundamental vibrations of **111** are observed directly at 1666.6 and 862.7 cm^{-1} , and from an overtone and a combination vibration the position of the missing bending mode in the

far infrared region can be derived (*ca.* 234 cm^{-1}). The correlation was carried out on the basis of density functional theory calculations, which predict a linear molecule with a triplet electronic ground state.^{92,121}

In the series $\text{C}_n=\text{X}$ ($\text{X} = \text{O}, \text{S}$) with $n = 1$ it is certainly not the parent molecule CO or CS, which is of interest. The important question in this case is, whether the monomeric entities can photochemically be dimerized to the corresponding chalcogeno cumulenes containing only two carbon atoms. Nothing was known in this respect when we began our studies described below.

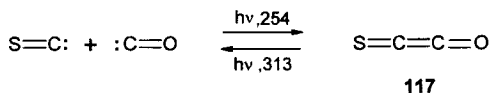


In 1990 we showed that ethenedithione (115) is a stable molecule under matrix conditions. It can be prepared by photolysis of the matrix-isolated precursors 113, 114, and 116.¹⁴³ Different pathways to 115 have been found by Wentrup et al.¹⁴⁴ The matrix IR spectrum of 115 shows one absorption corresponding to the only IR active stretching mode. The IR active bending vibration is expected to appear in the for us unobservable far infrared region. The position of both IR inactive stretching vibrations were derived from two observed combination bands. The IR spectra allow no decision about the multiplicity of 115, since calculations show, that the equilibrium geometries of both states are almost identical. Recent calculations^{121,145} favor the triplet state.

C_2S_2 , isolated in argon at 10 K, gives rise to a UV band with pronounced vibrational fine structure between 382 and 350 nm and to an additional intense end absorption beginning at about 230 nm. Due to the long wavelength absorption of 115, irradiation with $\lambda > 300$ nm leads to a photoexcitation of 115 which results in a dissociation into two molecules of CS.¹⁴³ Since they remain embedded in the matrix cage the reverse reaction $\text{CS} + \text{CS} \rightarrow \text{C}_2\text{S}_2$ can be triggered upon irradiation with the appropriate wavelength (excitation of CS ($\lambda_{\text{max}} = 257$ nm) with light of the wavelength $\lambda = 254$ nm).¹⁴⁶

It should be added that ethenedithione (**115**) can also be prepared by an electric discharge in a mixture of CS₂ and argon.¹⁴⁷ As in the photo-dimerization of CS it can be assumed that in both cases one CS molecule is excited to the triplet state and then adds another singlet CS to form triplet C₂S₂ **T-115**.

As it is shown above for many cases, dioxides, sulfide oxides and disulfides of carbon decompose upon irradiation into two carbene type fragments. They can recombine if a wavelength is used, which is absorbed by one of the fragments. According to the recombination of two molecules of CS it should also be possible to synthesize S=C=C=O **117**, if CS is photochemically excited in the presence of carbon monoxide.



Indeed, access to matrix-isolated thioxoethenone C₂OS (**117**) was gained by us in 1997.¹⁴⁸ As proposed the photochemical addition of CS, generated by a microwave discharge in CS₂, to CO was achieved by selective excitation ($\lambda = 254$ nm) of CS. This reaction could be reversed completely by changing the excitation wavelength to $\lambda = 313$ nm.

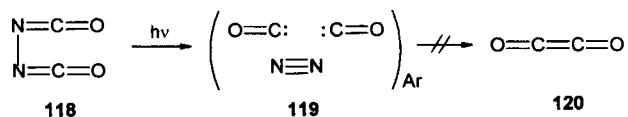
Density functional theory calculations were carried out for the identification of **117**, resulting in a very good agreement of theoretical prediction and observed IR spectra.¹⁴⁸ The experimental bands represent two of three expected stretching modes, the third was calculated from combination vibrations. Experiments using ¹³CO together with calculated isotopic frequency shifts demonstrated the linear geometry of the molecule. Thus, C₂OS **117** very likely possesses a triplet ground state, since the lowest computed singlet state is a transoidally bent species.

To sum up it can be said that all monosulfides C_n=S with $n = 1-4$ have been matrix-isolated and identified. The next member C₅S has been prepared by electric discharge in a mixture of CS₂, C₂H₂ and argon and observed by its rotational spectrum.¹⁴⁹ The expected multiplicities and spectral data^{121,122,150} are verified by the experimental observations.

c. A Special Remark on C₂O₂. As mentioned above, ten years ago only a few carbon oxides and sulfides had been identified and many missing chalcogeno heterocumulenes had yet to be discovered. Matrix isolation turned out to be the method of choice for the preparation and identification of this kind of elusive molecules. Today all the candidates X=C_n=Y (X = O,S) and C_n=X(Y) with $n = 2-5$ (and even some with $n > 5$) are known. There is only one exception, namely C₂O₂ **120**.

The C₂O₂ problem has a long history.¹⁵¹ Many attempts to generate or matrix-isolate **120** using "routine" methods were not successful so far.^{152,153} Neutralization of the radical cation in the gas phase also failed.^{154,155}

With the successful preparation of C_2S_2 **115** and C_2OS **117** by photoaddition of CS to CS or CO in mind, it was tempting to try the same with CO alone. The prerequisite would be, to have only two CO molecules in the same matrix cage without any other molecule which might also absorb photoenergy. For this purpose we synthesized diisocyanate (**118**).¹⁵⁶ Upon irradiation of **118** in an argon matrix at 10 K N_2 is eliminated and an association **119** of two molecules of CO and one molecule of N_2 in solid argon is formed.



In spite of this ideal situation for the dimerization of CO no C_2O_2 **120** could be detected. If one of the CO molecules would be excited to the triplet state, the reaction would directly lead to triplet C_2O_2 . According to calculations^{151,155} this molecule should — in contrast to singlet C_2O_2 — be thermally stable enough to survive under matrix conditions. In reality upon irradiation of **118** with $\lambda = 185$ and 193 nm — which should allow the singlet–triplet excitation of carbon monoxide — only the formation of CO can be observed. Thus, either no addition ${}^3\text{CO} + \text{CO} \rightarrow {}^3\text{C}_2\text{O}_2$ occurs, or this species is formed but is *apparently* non-existent, since ${}^3\text{C}_2\text{O}_2$ may absorb at a similar wavelength as CO and is therefore immediately split back by the irradiating light.

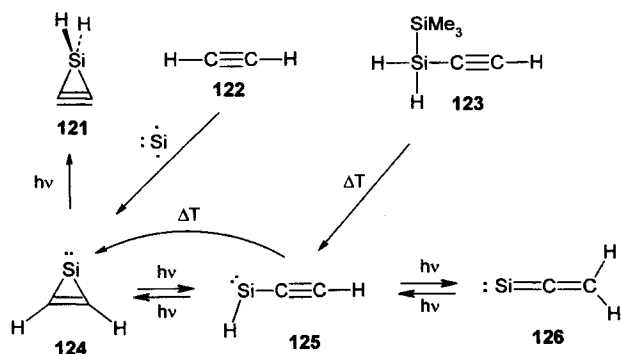
IV. ANALOGS OF CARBENES

A. Silylenes

Silylenes are the silicon analogs of carbenes, and most of what we have learned about carbenes also applies to them. There are even some advantages of silylenes compared to carbenes. First, silylenes always (at least as far as we know today) possess singlet electronic states. According to calculations, the singlet state of the parent silylene SiH_2 lies 21 kcal mol^{-1} lower than the first triplet state.¹⁵⁷ Second, carbenes isomerize whenever possible (e.g., presence of a hydrogen atom in α -position) to compounds containing doubly bonded carbon atoms even under the conditions of matrix isolation. In contrast, silylenes are thermodynamically about as stable as the corresponding systems with doubly bonded silicon atoms. For example, methylsilylene lies — due to calculations — only 4 kcal mol^{-1} above silaethene, whereas the difference between methylcarbene and ethene is as high as 70 kcal mol^{-1} .^{158–160} Third, silicon does not want to undergo hybridization. In addition to pairing energy and electronic effects, the small extent of s,p mixing in silicon seems to play an important role.¹⁶¹ The last factor is manifested not only in the large stabilization

of the singlet state but also in the bond angle of SiH_2 calculated to be as small as 93.4° .¹⁶² This is a consequence of the relatively large difference in the sizes of the 3s and 3p orbitals compared with the difference between 2s and 2p.¹⁶³

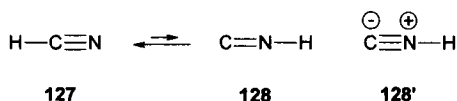
In view of these facts it is no surprise that matrix isolation studies of silylenes have been carried out with the same intensity as was applied to carbenes. A comprehensive survey on these efforts has recently been published.¹⁶⁴ Therefore only one example is given in order to illustrate the close correlation between carbenes and their silicon analogs. Similar to the carbon series $\text{S-2} \rightleftharpoons \text{T-36} \rightleftharpoons \text{S-37}$ (see above) it is also possible to prepare and to matrix-isolate the silicon species **124**, **125**, and **126**, which again exist in a photoequilibrium. Our first entry to 1-silacyclopropenylidene (**124**) was the pulsed flash pyrolysis of 2-ethynyl-1,1,1-trimethyldisilane (**123**).^{71,72} Even though the structure of educt molecule **123** suggests formation of ethynylsilylene (**125**), the isolated product was **124**. Obviously **125** had already thermally isomerized to the most stable isomer **124** before the products were condensed at 10 K.



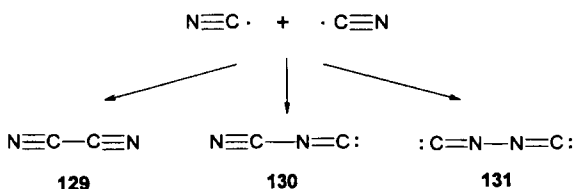
Two things are remarkable in this context. On the one hand, subsequent photolysis of **124** not only led to the two “conventional” isomers **125** and **126**, but also to silacyclopropyne (**121**) with a “formal” triple bond in a three-membered ring!^{71,72} On the other hand, we were able to open a second route to **124** by addition of matrix-isolated silicon atoms to acetylene (**122**).⁷³ An analogous addition of carbon atoms to acetylene under formation of cyclopropenylidene (**2**) was not achieved. Propargylene (**T-36**) was found instead.¹⁶⁵ Finally it should be mentioned, that the reaction of matrix-isolated silicon atoms turns out to be a very promising route to all kinds of silylenes,^{107,166–169} as it was shown already in the pioneering work of Margrave et al.,¹⁷⁰ Skell et al.,¹⁷¹ and Weltner et al.¹⁷² A similar reaction of butadiene with recoil silicon atoms in the gas phase was proposed by Gaspar et al.¹⁷³

B. Isonitriles, Silaisisonitriles

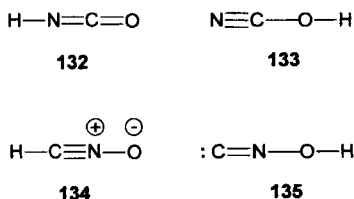
In the equilibrium $127 \rightleftharpoons 128$ the nitrile form is preferred.¹⁷⁴ Nevertheless the linear isonitrile isomer **128**, which is isoelectronic with carbon monoxide, is expected to have a high thermodynamic stability. The carbenic resonance structure **128'** makes only a small contribution. Similar to CO the iso form **128** of hydrogen cyanide is best described by the dipolar resonance structure **128'** with a real triple bond between carbon and nitrogen.



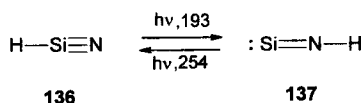
Therefore, isonitriles are stable molecules under standard conditions. Matrix isolation techniques are only rarely necessary to trap those isonitriles, which otherwise cannot be detected.



One example is the series of the linear C_2N_2 isomers **129**, **130**, and **131**. Upon flash pyrolysis of norbornadienone azine, an educt molecule similar to **4** and **79**, which promised to lead to C_2N_2 isomers, Bickelhaupt et al.¹⁷⁵ observed besides the long known cyanogen (**129**) also a new isomer. This species was identified as monoisocyanogen (**130**).^{176,177} Later we found¹⁷⁸ that cyano radicals, generated by microwave discharge of a mixture of acetylene and nitrogen, recombine not only to **129** and **130**, but also to diisocyanogen (**131**). The diiso form showed in the matrix an IR spectrum a band at 1997 cm^{-1} , which is in accordance with the calculated¹⁷⁹ antisymmetric CN stretching vibration of linear diisocyanogen (**131**). The upshot of this study was, that **131** in contrast to the normal isocyanides is extremely reactive, but is capable of existence under matrix isolation conditions.¹⁷⁸



Another investigation^{180,181} can be taken as a lesson about the borderline in elucidating structures by comparison of experimental and calculated IR spectra. In the hope that dibromoformoxime may give carboxime (isofulminic acid) (**135**) (the only missing member in the series **132–135**) upon irradiation in a similar manner to the dehalogenation of diiodomethane (see Section III.B.1), we carried out such an experiment. At first glance it looked as if the anticipated reaction had occurred.¹⁸⁰ It needed a lot of effort to show that in reality the photochemistry of matrix-isolated dihaloformoximes is very complex.¹⁸¹



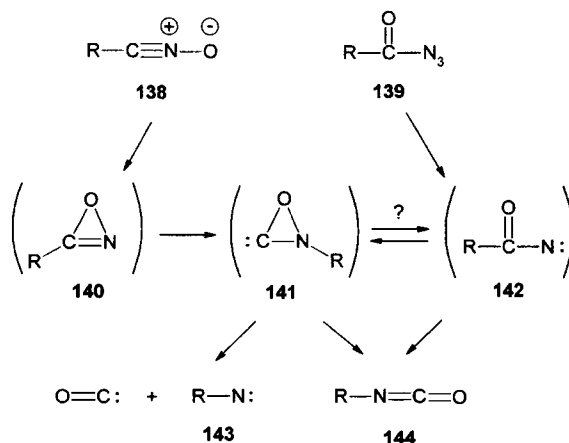
The equilibrium **127** $\rightleftharpoons$ **128** is expected to be reversed in the sila series. According to *ab initio* calculations^{158,182} the silane nitrile form **136** is 65^{182f} kcal mol⁻¹ higher in energy than the also linear isonitrile isomer **137**. The already known¹⁸³ iminosilylene (silaisonitrile) (**137**) was trapped in an argon matrix as a photoproduct ($\lambda = 254$ nm) of silylazide.^{183,184} If the wavelength is changed ($\lambda = 193$ nm) also silane nitrile (**136**) can be identified.¹⁸⁵ Thus, the first compound with a Si $\equiv$ N triple bond of the nitrile type could be isolated. This study also shows once more how dramatic the change in relative energies can be when a carbon atom is exchanged by silicon.

C. Nitrenes, Isonitroso Compounds

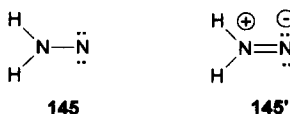
Nitrenes, the nitrogen analogs of carbenes, are too reactive for isolation under ordinary conditions. The ground state of :NH, and of most nitrenes, is a triplet. Aryl nitrenes have been trapped at 77 K,¹⁸⁶ the more reactive alkyl nitrenes in matrices at 4 K.¹⁸⁷

We entered this field when we studied the photoisomerization of simply substituted nitrile oxides **138** (R = Cl, Br, CN).¹⁸⁸ Matrix irradiation yields the corresponding isocyanates **144**. In the case of chloronitrile oxide besides the absorptions of chloroisocyanate¹⁸⁹ the bands of chloronitrene¹⁹⁰ also appear. It can be assumed that the nitrile oxide-isocyanate rearrangement starts with the ring closure **138** $\rightarrow$ **140**.^{191,192}

In remembrance of the isolation of carbene **78** (Section III.C) it seems acceptable that **141**, formed from **140** by a [1,2]-migration of the substituent, functions as a second intermediate. Carbene **141** can subsequently fragment into a nitrene **143** and carbon monoxide or open to an isocyanate **144**, which alternatively may also be generated from an acid azide via acylnitrene **142**. In comparison to calculated reaction pathways **75** $\rightleftharpoons$ **78** and **82** $\rightarrow$ **81** (Schemes 2 and 3; ring closure and synchronous [1,2]-migration of an hydrogen atom)



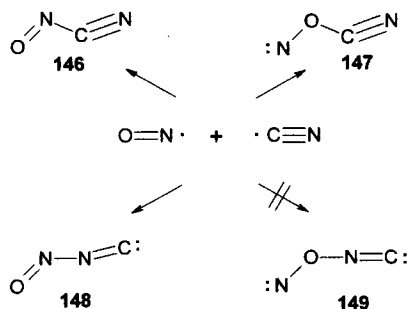
it can be rationalized that also interconversions of the type $142 \rightleftharpoons 141$ play a role in the isomerizations of CONR species. It depends on the R group in **144**, whether upon matrix irradiation a fragmentation of the isocyanate into a nitrene **143** and carbon monoxide occurs. For instance, cyanoisocyanate (**144**, R = CN) is photostable.¹⁸⁸ On the contrary, aminoisocyanate (**144**, R = NH₂) is rapidly split upon irradiation ($\lambda = 254$ nm) into aminonitrene (**145**) and carbon monoxide.^{193,194}



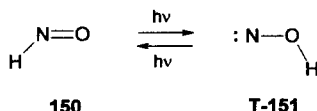
Aminonitrene (isodiazene) (**145**) is the least stable of all isomers of the elemental composition N₂H₂ and was isolated in an argon matrix for the first time in 1984.¹⁹⁵ Theoreticians also gave much attention to aminonitrene (**145**).¹⁹⁶ This molecule is exceptional in so far, that it is one of the few nitrenes with a singlet electronic ground state and is best described by the dipolar structure **145'**.

Irradiation of the oxide of cyanoisocyanate (**144**, R = C≡N→O) gives again another result upon irradiation in a matrix. The product formed with light of the wavelength $\lambda = 254$ nm is nitrosyl cyanide (**146**).¹⁹⁷ When an ArF laser ($\lambda = 193$ nm) was used, a new species with a strong IR absorption at 1837 cm⁻¹ was generated instead of **146**. A study of the photochemistry of **146** showed that the new compound was isonitrosyl cyanide (**147**), the first member of the class of isonitroso compounds (which can be regarded as nitrenes). To sum up, it has been found that the radical pair O=N·/·CN can recombine under photochemical conditions not only to nitrosyl cyanide (**146**) and nitrosyl isocyanide (**148**), but

also to isonitrosyl cyanide (**147**). Only isonitrosyl isocyanide (**149**), which has the highest relative energy on the CN_2O energy hypersurface, is not detected in the photoequilibrium.¹⁹⁷

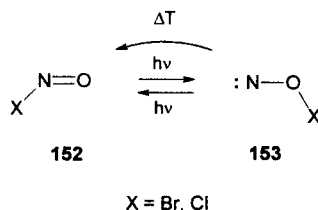


The same kind of isomerization can also be enforced in the parent compound, namely nitrosohydrogen **HNO** (**150**).¹⁹⁸ Matrix irradiation of **150** leads to isonitroso hydrogen **NOH** (**151**). Calculations of the potential-energy surface of the system **HNO/HON** show a singlet ground state for **HNO** **150**, which is also the global minimum.^{199,200} However, for **HON** **151** a triplet ground state is predicted. Indeed, the experimental IR spectrum of **151** fits much better the calculated spectrum of the triplet. Thus, the isomerization $\text{150} \rightleftharpoons \text{151}$ involves a change in multiplicity. Last but not least the calculated structural data (bent molecule with a typical O–H bond length and a very long N–O bond) indicate that isonitrosohydrogen **NOH** should be regarded as a *hydroxy nitrene*.



Our latest results in this field stem from a matrix-spectroscopic study of the isomerization of nitrosyl halides (**152**) and isonitrosyl halides (**153**).²⁰¹ Irradiation of nitrosyl bromide (**152**; $\text{X} = \text{Br}$) and nitrosyl chloride (**152**; $\text{X} = \text{Cl}$) leads to the corresponding isomers isonitrosyl bromide (**153**; $\text{X} = \text{Br}$) and isonitrosyl chloride (**153**; $\text{X} = \text{Cl}$). Both compounds, **NOBr** and **NOCl**,²⁰² have again been identified by comparison of the experimental and calculated (BLYP/6-311+ G^*) IR spectra. The back-reactions $\text{153} \rightarrow \text{152}$ can be initiated by UV, visible or IR light. Astonishingly, this retransformation also occurs spontaneously even in the matrix at 10 K under exclusion of any UV/VIS or IR radiation.

An additional surprise is, that the reaction rates of these spontaneous back-reactions $\text{153} \rightarrow \text{152}$ ($\text{X} = \text{Br}, \text{Cl}$) are temperature-independent between 8.5 and 25 K. In our opinion this unusual kinetic behavior might be the outcome of a double “two-state reaction involving a surface crossing with the triplet state of



the nitroso isomers **152**. If this is true, this finding would once more illustrate the power of matrix isolation techniques, allowing us to study phenomena which are otherwise not accessible.

V. CONCLUSION

Matrix isolation techniques have been applied for the generation and spectroscopic detection of a variety of carbenes. The structural elucidation of the matrix-isolated molecules is mostly based on the comparison of the experimental and calculated IR spectra. This interplay between theory and experiment is the characteristic feature of all the studies mentioned in this review.

ACKNOWLEDGEMENTS

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REACTIONS OF 2,5-CYCLOHEXADIENYLIDENES INVESTIGATED BY DIRECT SPECTROSCOPIC METHODS

Wolfram Sander and Holger F. Bettinger

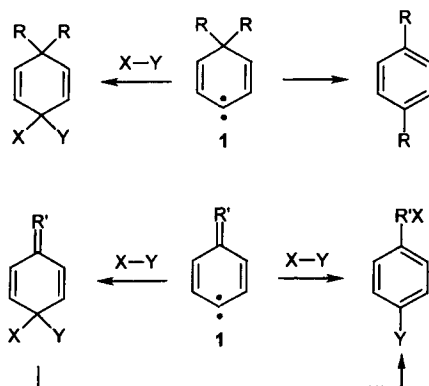
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I. INTRODUCTION

2,5-Cyclohexadienylidenes **1** are a remarkable class of highly reactive carbenes which during their reactions can be transformed into either aromatic or quinoid systems (Scheme 1). The parent 2,5-cyclohexadienylidene (**1**, R = H) is an unstable isomer of benzene that is expected to rapidly rearrange via hydrogen migration. Introduction of R substituents with a lower migratory aptitude in the 4-position of **1** increases the stability and allows the isolation of these carbenes in low-temperature matrices. A considerable activation barrier is required for the rearrangement to benzene derivatives, and this type of reaction is predominantly observed at higher temperatures. An even more efficient stabilization of **1** is the introduction of a double bond in the 4-position such as in 4-oxo-2,5-cyclohexadienylidene (**1a**) (R' = O).

The major techniques used for the direct spectroscopic characterization of carbenes are matrix isolation^{1,2} and nanosecond time resolved UV/vis absorption spectroscopy (laser flash photolysis, LFP).³⁻⁷ Matrix isolation allows determination of the IR, UV/vis, and ESR spectra of carbenes. IR spectra with a high spectral resolution provide valuable information on the structure and electronic properties of carbenes.^{8,9} IR spectroscopy requires the use of inert gas matrices — such as argon or nitrogen — which are transparent in the desired spectroscopic range, while UV/vis and EPR spectra can also be obtained in organic glasses (MTHF etc.).^{10,11} While the preparation of organic glasses is less technically demanding than matrix isolation in inert gases, highly electrophilic carbenes such as **1a** are reactive to most solvents even at 4 K and can only be stabilized in noble gas matrices.

During recent years the combination of matrix IR spectroscopy — using highly sensitive FTIR spectrometers — and the accurate calculation of vibrational data with *ab initio* or density functional theory (DFT) methods has



Scheme 1.

dramatically improved the power of matrix isolation. In particular DFT calculations allow reproduction of the IR spectra of carbenes with high accuracy.¹² Comparison of the experimental and calculated spectra provides detailed insight into structure, binding properties, and ground state multiplicity of carbenes.

Since most of the carbenes **1** have triplet ground states, ESR spectroscopy allows to “see” the unpaired electrons and determine the local symmetry at the carbene center and the amount of spin delocalization.^{13–18} Most of the ESR spectra of carbenes reported in the literature have been recorded in organic glasses or powder samples at temperatures between 4 and 77 K. Many carbenes are slightly colored and exhibit characteristic absorptions extending to the visible region of the spectrum. UV/vis spectroscopy not only provides information on the excited states of carbenes, which in many cases are the reactive species during precursor photolyses, but also links low temperature spectroscopy to LFP in solution at room temperature.

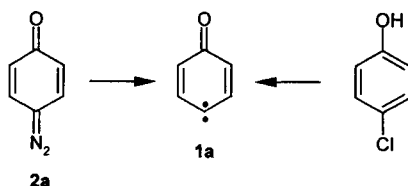
Both matrix isolation and LFP have been used to investigate carbene reactions, although under entirely different conditions. Matrix isolation allows to study reactions of carbenes with small molecules (e.g., O₂, CO, HCl) by doping the matrix with these trapping reagents.⁹ After the photochemical generation of the carbene at very low temperatures (4–10 K), where the diffusion of trapped molecules is extremely slow, the matrix is warmed up to 30–50% of its melting point (in argon matrices typically 35–45 K). Under these conditions small molecules diffuse rapidly and thermal reactions can be monitored at low temperatures. This technique allows the characterization of primary reaction products which in many cases are short lived in solution at higher temperatures. Reactions in matrices are solid state reactions and it is thus very difficult to abstract meaningful kinetic data from these experiments. LFP in solution, on the other hand, provides kinetic data under “ordinary” laboratory conditions (solvents, temperature), however, the spectroscopic information is much more limited than with matrix isolation. The combination of both methods provides an in-depth insight into the structure and properties of carbenes. The emphasis of this chapter is on recent literature dealing with the characterization and investigation of the chemistry of carbenes of type **1** using direct spectroscopic methods.

II. 4-OXOCYCLOHEXA-2,5-DIENYLIDENE AND DERIVATIVES

A. 4-Oxocyclohexa-2,5-dienylidene (**1a**)

Oxocyclohexadienylidene (**1a**) and derivatives are highly reactive, electrophilic carbenes. Suitable precursors of these carbenes are quinone diazides

2, which are readily synthesized by diazotization of *p*-hydroxyanilines or from the corresponding quinones. A compilation of the solution chemistry of quinone diazides and the carbenes derived from these precursors was published by Nikiforov et al. in 1981.¹⁹ The parent quinone diazide **2** was characterized by X-ray crystallography²⁰ and has been the subject of several matrix isolation^{21–24} and LFP studies.²⁵ An alternative route to **1a** in solution is the UV photolysis of 4-chlorophenol, which has been used to study the chemistry of **1a** in aqueous solution by nanosecond LFP.^{26–28}



1. Electronic structure computations

The identification of unknown chemical compounds isolated in inert gas matrices is nowadays facilitated by comparison of the measured IR spectra with those computed at reliable levels of *ab initio* or density functional theory (DFT). Furthermore, the observed reactivity of matrix isolated species can in some instances be explained with the help of computed reaction energies and barriers for intramolecular rearrangements. Hence, electronic structure methods developed into a useful tool for the matrix isolation community. In this chapter, we will give an overview of the various theoretical methods and their limitations when employed in carbene chemistry. For a more detailed qualitative description of the merits and drawbacks of commonly used electronic structure methods, especially for open-shell systems, the reader is referred to the introductory guide of Bally and Borden.²⁹

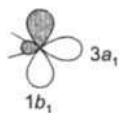
a. Electronic structure of carbenes. The prototype carbene, methylene CH₂, is among the computationally best studied molecules.^{30–33} The bent triplet ($\phi_{\text{H-C-H}} = 136^\circ$) with the electronic configuration

$$(1a_1)^2(2a_1)^2(1b_2)^2(3a_1)^1(1b_1)^1 \quad (1)$$

is the ground state, $\tilde{X}^3B_1$. The $\tilde{a}^1A_1$ singlet state ($\phi_{\text{H-C-H}} = 102.4^\circ$) is 9.2 kcal mol⁻¹ higher in energy. In Hartree–Fock molecular orbital theory, which uses a single Slater determinant to describe the electronic state of interest, the $\tilde{a}^1A_1$ state is given by the electronic configuration:

$$(1a_1)^2(2a_1)^2(1b_2)^2(3a_1)^2 \quad (2)$$

The $3a_1$ and $1b_1$ orbitals, which are symmetric (σ) or antisymmetric (π) with respect to the molecular plane, comprise the “special” carbene orbitals.



Due to the low lying $1b_1$ LUMO (the p orbital centered on the carbon atom), the doubly excited configuration

$$(1a_1)^2(2a_1)^2(1b_2)^2(1b_1)^2 \quad (3)$$

is needed in addition to the Hartree–Fock configuration for a reliable computational description of the $\tilde{a}^1A_1$ state. The singlet–triplet energy separation (ΔE_{ST}) between the $\tilde{X}^3B_1$ and $\tilde{a}^1A_1$ states of methylene is therefore a sensitive probe for the ability of a theoretical method to deal with the two-configuration nature of the $\tilde{a}^1A_1$ state. Hence, the systematic study of the performance of various electronic structure methods on the singlet–triplet energy splitting is enlightening, especially if these results can be compared to the correct solution of the Schrödinger equation as provided by *full* configuration interaction (full CI) computations. In a full CI calculation all Slater determinants are included which arise from all the electron excitations that are possible out of the occupied molecular orbitals (MOs) into the unoccupied MOs. Such benchmark studies have been performed for CH_2 by Sherrill et al.^{34,31} using either DZP or TZ2P basis sets in full CI treatments. Note that the difference between the exact *ab initio* (full CI) result (12.7 kcal mol⁻¹) for ΔE_{ST} and experiment (9.4 kcal mol⁻¹) is sizable (Table 1), even with a basis set as large as TZ2P (11.1 kcal mol⁻¹). This demonstrates that larger basis sets are needed to predict results of chemical accuracy for quantitative comparison with experimental ΔE_{ST} val-

Table 1. The Energy (ΔE_{ST}) Difference Between the $\tilde{X}^3B_1$ and $\tilde{a}^1A_1$ States of Methylene (in kcal mol⁻¹) Using Various Electronic Structure Methods and a DZP Basis Set. Taken from Ref. 36

Method	ΔE_{ST}
HF	26.4
TC-SCF	13.6
MP2	18.6
CASPT2 ^a	15.4
CISD	15.5
(TC)CISD	12.6
B3LYP	13.6
CCSD	13.6
CCSD(T)	12.9
full CI	12.7
Experiment	9.4

Note: ^a The 6-31G(d) basis set was used. Including zero-point energy corrections.

ues. Nonetheless, the full CI/DZP data allows to judge the performance of approximate electronic structure methods.

Hartree–Fock [HF, also called self-consistent field (SCF)] theory uses the single Slater determinant arising from configuration (2).³⁵ This results in an inadequate description of the singlet state and as a consequence, the ΔE_{ST} value is much too large (Table 1). However, a significantly better ΔE_{ST} value is obtained if a two-configuration self-consistent field (TC-SCF) wave function derived from configurations (2) and (3) is employed for the description of the singlet state. Note that the TC-SCF wave function is equivalent to a complete active space (CAS) SCF wave function with two electrons in two orbitals and the generalized valence bond (GVB) description of the singlet state. All these theoretical approaches are capable of treating the nondynamic correlation arising from the near-degeneracy of the $3a_1$ and $1b_1$ MOs well. If dynamic electron correlation (to correct for the overestimation of electron repulsion in SCF theory) is included in the calculation of ΔE_{ST} by construction of a CI wave function with single and double excitations (CISD) based on the two configurations (2) and (3), agreement with the exact result is obtained. The CASPT2 method was developed to account for dynamic electron correlation based on a CASSCF wave function by second-order perturbation theory. This approach, however, deteriorates the CASSCF result for ΔE_{ST} of methylene due to an overestimation of the stabilization of the triplet with respect to the singlet state.³⁶

Although multiconfiguration treatments are the theoretically sound approach for dealing with near-degeneracies, there are some practical limitations to these methods. The selection of the active space in CASSCF or the references in multireference CI (MRCI) calculations is sometimes problematic, especially if different parts of a potential energy surface need to be investigated. Besides the demand in computational resources, the restricted availability or lack of gradient techniques (needed for geometry optimizations) and second derivatives (needed for prediction of vibrational spectra) limits the application of such methods to rather small molecules.

Hence, in practice correlation procedures based on a single electronic configuration are often considered to be more convenient. A popular way to improve on HF theory by considering dynamic electron correlation is to apply second-order many body perturbation theory, often in the framework of the Møller–Plesset formulation (MP2). This approach assumes that the perturbation of the trial wave function, i.e., the Hartree–Fock wave function, is small. But in the case of the $\tilde{a}^1A_1$ states of methylene this is clearly not the case as the Hartree–Fock wave function completely neglects configuration (3). Consequently, MP2 gives much too large ΔE_{ST} values. Coupled cluster theory,^{37,38} an infinite-order perturbation method, with single and double excitations (CCSD) out of the single reference, is surprisingly reliable even if this reference has some deficiencies due to modest amounts of non-dynamic correlation. When the triple excitations

are accounted for in a perturbative way [CCSD(T)] a ΔE_{ST} value of 12.9 kcal mol⁻¹ is obtained in very good agreement with full CI. Indeed, it has been found for larger systems with moderate amounts of nondynamic correlation, e.g., the three didhydrobenzenes, that CCSD(T) gives reasonable agreement with experimental singlet–triplet energy splittings, although the coupled cluster treatment is based on the Hartree–Fock determinant. However, such good performance is not observed for systems with significant nondynamic correlation, and improved results are expected if multiconfiguration treatments are employed for such cases.

Density functional theory (DFT) is an alternative to the wave function methods discussed above for solving the electronic Schrödinger equation. According to the first Hohenberg–Kohn theorem, the potential and the wave function are uniquely determined by the electron density $\rho(r)$, i.e., they are functionals of $\rho(r)$. In the Kohn–Sham formulation of DFT the exact Hartree–Fock exchange is replaced by an exchange–correlation functional of the density. This introduces some amount of electron correlation into the DFT treatment. The successful hybrid HF/DFT methods, use a combination of HF exchange and some exchange–correlation functionals. Especially Becke's³⁹ three parameter hybrid functional in conjunction with the correlation functional of Lee et al.⁴⁰ (B3LYP) is extremely popular among the many available functionals. Although the accuracy of this approach is below that of highly correlated single or multiconfiguration wave function techniques, it was found that B3LYP performs remarkably well for various carbenes.^{12,41,42} Thus, systems of chemical interest, for which many of the high accuracy methods are prohibitively expensive, can be studied reliably with DFT. The major drawback of DFT is that it is not possible to improve the result systematically.

b. The singlet–triplet energy separations in alkyl and vinyl carbenes. The singlet–triplet energy separation in carbenes depends decisively on the substituents and geometry at the divalent carbon atom.^{43,12} Using isodesmic equations, it was found that alkyl substituents hyperconjugatively stabilize the singlet state more than the triplet state.⁴⁴ The closed-shell singlet states of carbenes resemble carbocations whereas the open-shell triplet states can be compared with radicals, and it is well known that carbocations are stabilized better by alkyl groups than are radicals. As a consequence, the singlet and triplet states are almost isoenergetic for dimethylcarbene; in fact the singlet state is found to be more stable than the triplet state by 1–2 kcal mol⁻¹ according to B3LYP and CCSD(T)/TZ2P + f//CISD/TZ2P+f calculations.^{42,44–46}

It is well known that double bonds have a different effect on the singlet–triplet energy separation and thus on the reactivity of the carbene than alkyl groups. The description of the electronic structure of such carbenes is rendered more difficult by the fact that several low-lying electronic states are possible. For

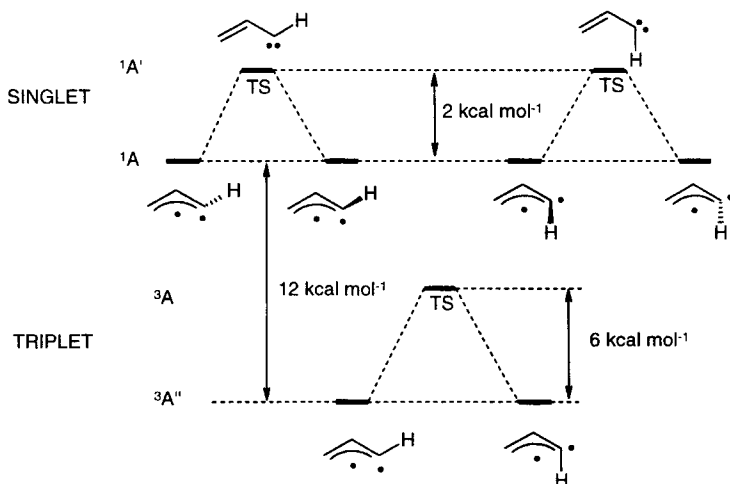


Figure 1. Energetic ordering of vinylcarbene conformers and electronic states according to the MRCI/DZP//MCSCF/4-31G computations of Yoshimine et al.⁴⁷

some of these, single determinant methods are not suited. A linear combination of Slater determinants is needed for a correct zeroth-order description of an open-shell singlet state as a single open-shell Slater determinant is not an eigenfunction of the S^2 operator.

The prototype α,β unsaturated carbene, vinylmethylene C_3H_4 , was studied comprehensively by Yoshimine and co-workers employing multireference configuration interaction methods (MRCI/DZP//MCSCF/4-31G).^{47,48} Both, the *trans* and *cis* conformers of vinylmethylene have triplet $^3A''$ ground states (Fig. 1). The C_s geometries of these $^3A''$ states are allylic, i.e., the two C–C bonds almost have the same lengths as the three π electrons are delocalized over the three carbon centers similar to the allyl radical. The *cis* and *trans* isomers are isoenergetic.^{47,49} Hutton et al. have observed these two isomers by ESR spectroscopy after photolysis of vinyldiazomethane isolated in organic glasses at 6–15 K.¹¹ The lowest *cis* and *trans* singlet states are also isoenergetic but 12 kcal mol⁻¹ higher in energy than the triplets. Due to a pseudo-Jahn–Teller distortion, these singlet states are asymmetric (C_1 point group) with the terminal hydrogen above or below the C–C–C plane. In addition, their π systems are also allyl radical-like. Hence, they have open-shell singlet states; for these, two determinants are necessary for the theoretically sound description of their electronic wave functions.³⁵ The closed-shell C_s symmetric σ^2 carbenes depicted conventionally for vinylmethylene are transition states for the degenerate isomerization of the asymmetric *cis* or *trans* structures.

The vinylmethylene–cyclopropene rearrangement on the singlet PES has been the subject of several investigations, primarily due to its importance in

combustion processes. Yoshimine et al.⁴⁷ arrived at a barrier of 5 kcal mol⁻¹ using MRCI/DZP, although they could not obtain a reliable transition state geometry from their partial geometry optimizations due to the flatness of the energy profile between *trans*-vinylmethylene and the TS for ring closure. There is a *direct* reaction path from *cis*-vinylmethylene to cyclopropene. The ring closure barrier of the *cis* form is lower (only 1 kcal mol⁻¹) than for the *trans* isomer according to MRCI/DZP. A similar value (0.3 kcal mol⁻¹, zero-point corrected) was obtained ten years later by Davis et al. using G2 theory in conjunction with B3LYP geometries and harmonic vibrational frequencies.⁵⁰

Endocyclic carbenes with multiple conjugated double bonds can have several low-lying states. Cyclopentadienylidene has a ³B₁ ground state, but the open-shell ¹A₂ singlet and the ³A₂ triplet states are only 6.3 and 6.8 kcal mol⁻¹ higher in energy.^{51,52} The conventional closed-shell singlet (¹A' state) is found to be C_s symmetric with a puckered ring. This state is energetically 10–12 kcal mol⁻¹ above the triplet ground state. A similar multitude of low-lying states is also found for cycloheptatrienylidene, for which the ³A₂ and ³B₁ states are almost isoenergetic.^{53,54} The ¹A₂ state is slightly below the ³A₂ state and corresponds to the transition state for the degenerate isomerization of cycloheptatetraene. The σ² carbene structure (¹A₁ state) is most probably also a transition state [at DFT levels, but not with CASSCF(8,8)] for this isomerization and is 4–10 kcal mol⁻¹ above the ¹A₂ and 26–30 kcal mol⁻¹ above the cycloheptatetraene ground state.

2. The electronic structure of **1a**

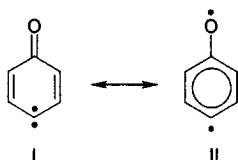
Following initial computational investigations of Sander and co-workers (up to HF/6-31G(d)),²³ the electronic structure and the excited states of 4-oxocyclohexa-2,5-dienylidene (**1a**) were studied comprehensively by Solé et al. in 1995 at the (two-configuration) configuration interaction [(TC)-CISD/6-31G(d)//MCSCF/6-31G(d)] level of theory (Table 2).⁵⁵ In agreement with electron spin resonance (ESR) studies, the theoretical investigations find that a triplet (³B₁) is the ground state of **1**. The geometry of this state exhibits significant C–C bond length alternation (0.089 Å) and a rather short C–O distance of 1.230 Å at the CASSCF(8,8)/6-31G(d) level. In addition, the unpaired π-electron density at the O atom is small (0.2050). Hence, Solé et al. concluded that the ground state of **1** is better considered to have a quinoid (I) rather than an aromatic structure (II). Schleyer et al.⁴² introduced the nucleus-independent chemical shift (NICS) as a probe for ring currents arising from cyclic electron delocalization. Whereas negative NICS values indicate aromaticity, positive NICS value can be associated with antiaromaticity. Systems lacking cyclic electron delocalization show NICS values close to zero.

The NICS value of benzene computed in the center of the ring is –9.7 at the B3LYP/6-31G(d) level of theory. For the ³B₁ state of **1a** we obtain a very

Table 2. The Relative Energies of Various Electronic States of **1a** at the CISD + Q/6-31G(d)/(MC)SCF/6-31G(d) and B3LYP/6-31G(d) Levels of Theory

State	CISD+Q/6-31G(d) ^a	B3LYP/6-31G(d)
³ B ₁	0	0
¹ B ₁	10.9	—
¹ A ₁	23.3	31.1
¹ A'	17.5	16.6
³ A ₂	62.6	86.8
¹ A ₂	63.1	—
³ B ₂	70.1	—
¹ B ₂	92.0	—

Note: ^a The CISD energies, which include Davidson correction for unlinked quadruple excitations, were obtained at the MCSCF/6-31G(d) optimized geometries and used a TC-SCF reference for closed-shell singlet states and a single configuration reference for triplet and open-shell singlet states. The SCF/6-31G(d) geometry was employed for the ¹A' state. See Ref. 55.



small NICS value of -1.3 in the center of the six-membered ring. This result indicates that ³B₁-**1a** is largely quinoid rather than aromatic, in agreement with the conclusions of Solé et al.

The lowest singlet state of **1a** is an open-shell singlet of B₁ symmetry, which is 10 kcal mol^{-1} (CISD+Q/6-31G(d)/CASSCF(8,8)/6-31G(d)) higher in energy than the ³B₁ state. In agreement with the longer C–O bond (1.272 Å) and the reduced C–C bond length alternation (0.047 Å), the unpaired π -electron density on the O atom is about twice as large as in the ³B₁ state.

As the topology of the π system does not favor a cyclic conjugation as in cyclopentadienylidene and cycloheptatrienylidene, the A₂ states are found to be much higher in energy than in these cyclic carbenes. In particular the $\tilde{A}^3$ A₂ state is 63 kcal mol^{-1} above the ground state (Fig. 2). Assuming that the longest wavelength absorption band observed in the UV spectra at 530 nm (i.e., 54 kcal mol^{-1}) corresponds to the ³A₂ $\leftarrow$ ³B₁ transition, Solé et al. concluded that their approach yields good agreement with experiment for the excitation which is believed to be responsible for the photochemistry of **1** (*vide infra*). Note that the B3LYP/6-31G(d) energy of the ³A₂ state is significantly higher than that obtained at the CISD+Q level.

The closed-shell C_{2v} symmetric ¹A₁ state is a transition state, similar to the closed-shell singlet state of cyclopentadienylidene discussed above. Note

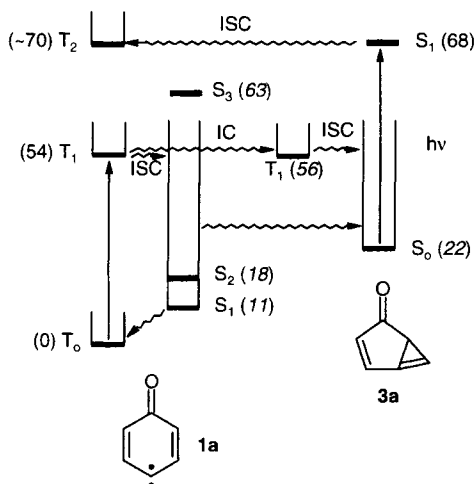


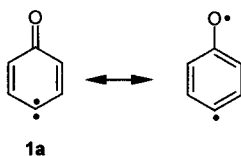
Figure 2. Jablonski diagram for the photochemical interconversion of **1a** and **3a**. The energies (in kcal/mol) of various electronic states were obtained from spectroscopic data or by quantum chemical calculations (in italics) using CISD+Q/6-31G(d) and B3LYP/6-31G(d) calculations for T_1 -**3a**.

that the CISD+Q/6-31G(d) energy of this state differs significantly from the B3LYP/6-31G(d) result. At the latter level of theory, an unusually large imaginary vibrational frequency of $6244i\text{ cm}^{-1}$ (B_1) is obtained for the ring puckering mode. This renders the B3LYP/6-31G(d) data unreliable, as such a large frequency indicates an “instability volcano” of the force constants due to a very small eigenvalue of the molecular orbital Hessian.^{38,56} The σ^2 carbene distorts to C_s symmetry ($^1A'$ state) with a folded six-membered ring (folding angle 31.1° at HF/6-31G(d)). The $^1A'$ state is the second lowest state of **1a** as it is 17–18 kcal mol⁻¹ above the $^3B_1$ ground state, and therefore 7 kcal mol⁻¹ above the $^1B_1$ state. In contrast to the $^1A_1$ state, CISD+Q/6-31G(d)//CASSCF(8,8)/6-31G(d) and B3LYP/6-31G(d) agree very well for the $^1A'$ state.

3. Spectroscopic characterization of **1a**

a. Matrix isolation of carbene 1a. The photochemistry of diazo compound **2a** was investigated in solid Ar, Kr, Xe, or N_2 matrices at 8–10 K.²³ Visible light irradiation ($\lambda > 495\text{ nm}$) produces carbene **1a** in high yields which was characterized by IR, UV/vis, and ESR spectroscopy. The ESR spectra, which had been previously recorded by Wasserman and Murray in a powder sample at 4 K,⁵⁷ clearly demonstrates the triplet ground state of **1a**,^{21,23} in accordance with the theoretical results. The UV/vis spectrum of **1a** in argon at 10 K shows a strong and broad absorption at 290 nm, a very sharp absorption of medium intensity at 379 nm, and a broad and weak absorption at 530 nm.²³ The

latter absorption maximum in the visible region leads to the pale violet color of matrices containing **1a**.



The matrix IR spectra of **1a** and several isotopomers (d_4 -**1a**, ^{18}O -**1a**) reveal details of the electronic structure of the carbene.²³ In particular the red-shift of the C=O stretching vibration (compared to *p*-benzoquinone) below 1500 cm^{-1} indicates a substantial contribution of the phenoxyl/phenyl resonance structure to the wave function of **1a**. The C_{2v} symmetry of the carbene was experimentally revealed by measuring the IR dichroism of partially oriented samples of matrix-isolated **1a**. The orientation of **1a** in an argon matrix was achieved by irradiation with linearly polarized light.

b. Comparison of measured and computed IR spectra of 1a and other carbenes. The vibrational frequencies are generally computed within the harmonic approximation.⁵⁸ As a consequence, the calculated vibrational frequencies for the $3N-6$ normal modes of the molecule are often systematically found to be too high compared to experiment, but method and basis set dependant scaling factors allow for a comparison between theoretical normal mode vibrational frequencies ω_i and measured vibrational frequencies.⁵⁹ The scaling factors of 0.87 for HF/6-31G(d) and 0.91 for MP2/6-31G(d) indicate that with these as well as with other low-level *ab initio* methods a reliable assignment of, and comparison with experimental vibrational frequencies is problematic.

Not surprisingly, the experimental vibrational spectrum of **1a** proved to be difficult to reproduce computationally. An unusually strong absorption at 1496 cm^{-1} was initially assigned to the C=O stretching vibration of the carbene, but the UHF/6-31G(d) level of theory predicted the C=O stretching vibration at 1246 cm^{-1} (after applying the usual scaling factor of 0.87), 250 cm^{-1} shifted to the red. Later, Olivella and coworkers used CASSCF(8,8)/6-31G(d) theory to calculate the IR spectrum of **1a**.⁵⁵ Although the theoretical value was now in perfect agreement with the experimental 1496 cm^{-1} absorption (after scaling by 0.87), the agreement with other vibrations in the spectrum was not convincing.

During recent years DFT methods have been used to reproduce vibrational frequencies and IR intensities (dipole moment derivatives) with high accuracy (scaling factors are close to unity).^{29,60,61} We therefore used the B3LYP and BLYP functionals to calculate the spectra of **1a** and its isotopomers, and indeed the calculated frequencies, isotopic shifts, and intensities are now in excellent agreement with the experimental values (Fig. 3).⁶² A careful reexamination

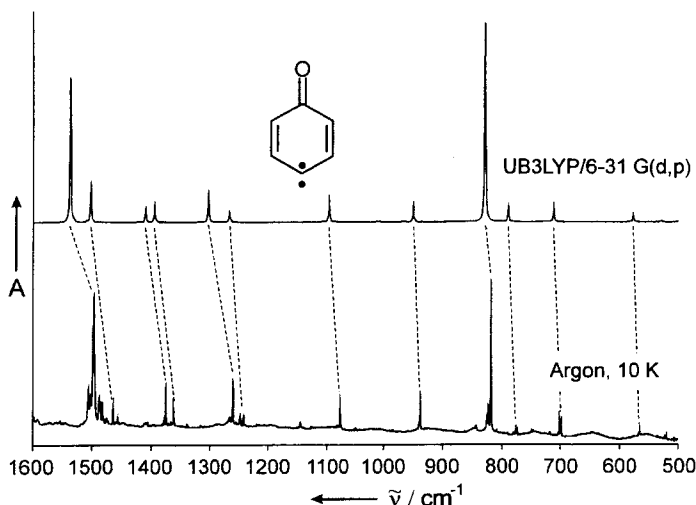


Figure 3. Infrared spectrum of carbene **1a**, matrix isolated in argon at 10 K (bottom) compared to the spectrum calculated at the B3LYP/6-31 G(d) level of theory.

of the spectra clearly shows that the intense absorption at 1496 cm^{-1} has to be assigned to a C=C rather than the C=O stretching vibration. The C=O stretching vibration is found at 1482 cm^{-1} and is only of low intensity.

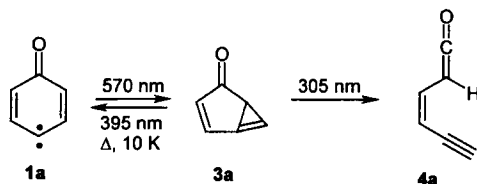
c. LFP studies of **1a.** The carbene **1a** was also generated in solution at room temperature from **2a** using time-resolved laser flash photolysis (LFP).²⁵ This technique allows the observation of reactive intermediates if (i) the lifetime is in the order of ns or longer and (ii) the species exhibit strong and characteristic absorptions, not masked by other constituents in the solution. Since the visible absorption of **1a** is of very low intensity and the UV absorptions overlap strongly with that of starting material **2a** and reaction products, the carbene could not be directly monitored. However, the addition of quenchers such as molecular oxygen, cyclohexane, or methanol resulted in the formation of intermediates which could be detected in the visible range of the spectrum. From extrapolation of the quenching plot to zero quencher concentration a lifetime of **1a** in Freon-113 of $1.65\text{ }\mu\text{s}$ was deduced.

The direct spectroscopic characterization of **1a** in an LFP experiment was achieved by using a different precursor. LFP of *p*-chlorophenol in aqueous solution produces, at the end of the laser pulse, a transient with absorption maxima at 250, 370, and 384 nm.²⁶ These absorptions are in reasonable agreement with the strong and medium intensity absorptions of **1a** in argon at 10 K (290 and 379 nm), especially if a solvent shift of the highly polar **1a** in water compared to argon is taken into account. The assignment of the transient

species to **1a** was confirmed by trapping studies with molecular oxygen to give quinone *O*-oxide **7a** and with hydrogen donors to give the well known phenoxyl radical (Section II.A.4). The exceptional stability of **1a** in water is attributed to the very high O–H bond energy in the water molecule.

4. Intramolecular reactions of **1a**

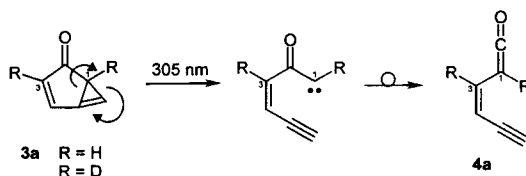
The most striking property of carbene **1a** is the photochemical rearrangement to the highly strained 1*H*-bicyclo[3.1.0]hexa-3,5-dien-2-one (**3a**) on visible light irradiation ($\lambda = 543$ nm) (Fig. 2).²³ The cyclopropene **3a** is formed in a photostationary equilibrium, and shorter wavelength irradiation ($\lambda > 395$ nm) results in the complete recovery of carbene **1a**. Moreover, even at temperatures as low as 10 K **3a** is thermally labile and rearranges back to **1a** with a half-life time of several hours. This clearly shows that the cyclopropene **3a** lies in a very shallow minimum and is energetically less stable than the carbene. Since **1a** has a triplet ground state and **3a** a singlet ground state, the rearrangement is a formally spin-forbidden reaction that requires an intersystem crossing (ISC) along the reaction coordinate. The rate for the **3a** $\rightarrow$ **1a** rearrangement depends on the matrix, and in Xe at 10 K the rearrangement is 37 times faster than in Ar at the same temperature. In Kr and N₂ much smaller matrix effects are observed. The rate enhancement in solid Xe might be a matrix site effect caused by the larger matrix cavities, or result from the external heavy atom effect of the Xe atoms, which enhances the ISC rates.



In all matrices investigated curved Arrhenius plots are obtained, and at very low temperature the rates become virtually independent of temperature.²³ An explanation of this unusual behavior is quantum mechanical tunneling (QMT) which competes with the classical thermal reaction at very low temperature. The simple model of a parabolic barrier in a modified Arrhenius equation developed by Bell⁶³ allows reproduction of the kinetic data. The **3a** $\rightarrow$ **1a** rearrangement requires only very small geometric changes, and if the mass of the tunneling particle is set to 12 (carbon atom), a tunneling distance of 0.4 Å and an activation barrier of 2.6 kcal/mol is estimated.²³ The rates for the **3a** $\rightarrow$ **1a** rearrangement drastically increase on IR irradiation, which is in line with a model of vibrationally enhanced QMT.

UV irradiation ($\lambda > 305$ nm) of cyclopropene **3a** results in the ring-opening and formation of ketene **4a**. Two reaction pathways for the **3a** $\rightarrow$ **4a** rearrange-

Pathway I:

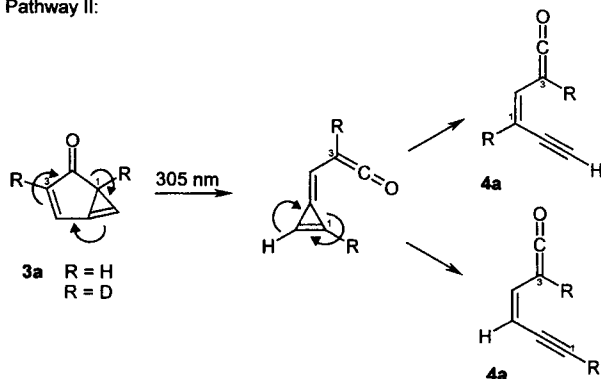
**Scheme 2.**

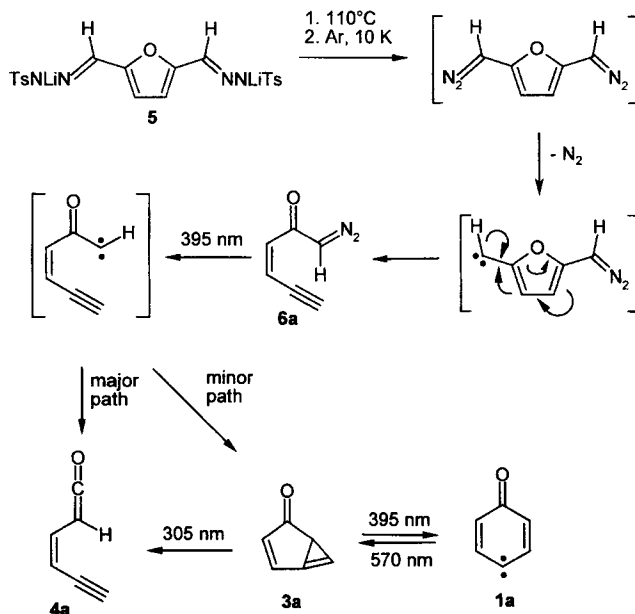
ment are conceivable.⁶⁴ Pathway I requires the rupture of two bonds in the cyclopropane ring and formation of a ketocarbene as short-lived intermediate (Scheme 2). The ketocarbene subsequently undergoes a Wolff rearrangement to ketene **4a**.

In Pathway II the first step is the opening of the five-membered ring and formation of a methylenecyclopropene (Scheme 3). The methylenecyclopropene should be thermally stable under the conditions of matrix isolation. However, since this species is photolabile, only very low concentrations accumulate during the 305 nm irradiation, and it is thus not directly observed. Pathway I and II can be distinguished by selective deuteration of the carbon atoms 1 and 3 of **3a**. Pathway I results in no label at the terminal acetylenic carbon atom, while in Pathway II the cleavage of the methylenecyclopropane should lead to a 50% deuteration of this position, which is in agreement with the experimental observation. Thus, ketene **4a** is formed via α -cleavage of **3a** and secondary photochemical rearrangement of the methylenecyclopropene according to Pathway II (Scheme 3).

A further proof for the structure of **3a** is the independent synthesis of this cyclopropane via intramolecular addition of a carbene carbon atom to the triple

Pathway II:

**Scheme 3.**



Scheme 4.

bond (Scheme 4).⁶⁴ Thermolysis of the dilithium salt **5** and subsequent trapping of the products in argon at 10 K leads to matrix-isolated diazoketone **6**. The formation of **6** requires loss of one nitrogen molecule of the primary bisdiazofuran to give a diazofurfurylidene. Furfurylidenes are known to be labile and readily rearrange to vinylacetylenes (Hoffman–Shechter rearrangement).^{65,66} On irradiation, diazoketone **6** loses the second nitrogen molecule and produces a ketocarbene, which is unstable even under the conditions of matrix isolation. The major route of the ketocarbene is the Wolff rearrangement to ketene **4a**. However, the ketocarbene is long-lived enough to be intramolecularly trapped by the triple bond to give the cyclopropene **3a** as a minor product (Scheme 4). This reaction sequence not only proves the structure of **3a**, but also provides an independent synthesis of ketene **4a**, the product of the UV photolysis of **3a**.

The reaction of **1a** to **3a** was studied theoretically by Solé et al.⁵⁵ as well as in our research group (at B3LYP/6-31G(d)).⁶² The asymmetric cyclopropene **3a** (^1A electronic state) is found to lie $9.1 \text{ kcal mol}^{-1}$ above $1\text{a-}^1\text{B}_1$ and hence 19 kcal mol^{-1} higher in energy than the $1\text{a-}^3\text{B}_1$ ground state. Our B3LYP/6-31G(d) energy difference between $1\text{a-}^3\text{B}_1$ and **3a** of $22.2 \text{ kcal mol}^{-1}$ agrees well with the earlier result. The transition state for ring opening of **3a** on the singlet PES is clearly reactant-like, as the bond between bridgehead carbons is stretched from 1.530 (1.512 , B3LYP/6-31G(d)) Å in **3a** to only 1.837 (1.802) Å in the TS. The barrier for ring opening was found to be $6.7 \text{ kcal mol}^{-1}$

at CASPT2/6-31G(d) including zero-point vibrational energy corrections (from MCSCF/6-31G(d) harmonic vibrational frequencies). A slightly lower energy barrier of 5.0 kcal mol⁻¹ was found at the B3LYP/6-31G(d) level of theory. Solé et al.⁵⁵ computed the activation energy at 60 K to be 6.8 kcal mol⁻¹ (5.1 kcal mol⁻¹ at B3LYP/6-31G(d)),⁶² significantly higher than the 2.6 kcal mol⁻¹ experimentally obtained by Sander et al. in the 40–70 K temperature range in a Xe matrix.²³ With the theoretical activation entropy, Solé et al. computed the Arrhenius pre-exponential *A* factor of log *A* (60 K) = 12.6 s⁻¹ (12.5 s⁻¹ at B3LYP/6-31G(d)) for the ring opening of **3a** to **1a**-¹B₁.⁵⁵ As the experimental log *A* value was only 4.9 ± 1 s⁻¹, Solé et al. concluded that the intersystem crossing (ISC) from the ¹B₁ to the ³B₁ state of **1a** should be the rate limiting step of the **3a** → **1a** rearrangement. As the spin-orbit coupling (SOC) between the ¹B₁ and the ³B₁ states of **1a** is zero by symmetry, the singlet state should have a sufficiently long life time to be observable, but in the matrix isolation experiments the formation of such a species could not be detected.

Since the lifetime of **3a** at room temperature is very short and in addition **3a** does not show any characteristic UV/vis absorptions, it is not detected in the LFP experiments.

5. Intermolecular reactions

Reactions of carbene **1a** were investigated by annealing matrices containing the carbene and a trapping reagent. The first step in a typical reaction sequence is to generate the carbene by photolysis of diazo compound **2a** in matrices doped with 0.5–2% of the trapping reagent at very low temperature (8–10 K). Under these conditions the diffusion of matrix isolated species is completely suppressed. Both the diazo compound (ca. 0.1%) and the trapping reagent are distributed statistically in the matrix, and a reaction can only occur if the carbene is generated in close proximity to the trapping reagent. The second step is the annealing of the matrix at higher temperatures (depending on the matrix, e.g., Ar at 30–40 K) which allows the diffusion and thus thermal reaction of small molecules. It is important to note that the photochemical synthesis of the carbene and the subsequent thermal reaction with small molecules are subsequent reactions that can be easily followed by spectroscopic methods (in most cases IR, but UV/vis, ESR, fluorescence etc. are also possible).⁹

A highly characteristic reaction of triplet carbenes is the oxygenation with molecular oxygen ³O₂.⁶⁷ The primary thermal product is a carbonyl *O*-oxide, which in the case of **1a** is quinone *O*-oxide **7a** (Scheme 5). Carbonyl oxides are easily identified by (i) their intense absorptions in the visible spectrum (λ_{max} ca. 400–500 nm), which results in a yellow to red color of the matrix, and (ii) the very strong O–O stretching vibration in the IR spectrum around 900 cm⁻¹, which is in general the most intense IR absorption. Thus, warming an argon matrix containing carbene **1a** and doped with 0.5% O₂ from 10 K to

35 K within several minutes results in an intense yellow coloring of the matrix and appearance of a strong absorption in the visible region of the spectrum with $\lambda_{\text{max}} = 462$ nm assigned to **7a**.^{22,68} This absorption exhibits a dominant vibrational progression of 780 cm^{-1} due to the O–O stretching vibration of the excited state of **7a**. The ground state O–O stretching vibration is easily identified in the IR spectrum of **7a** as the most intense absorption at 1034 cm^{-1} , which shows the expected large isotopic shift (-57 cm^{-1}) on $^{18}\text{O}_2$ labeling. Thus, the O–O stretching vibration was observed in both the ground state and in the lowest lying excited state of **7a**. Obviously, the O–O bond is considerably weaker in the excited state.

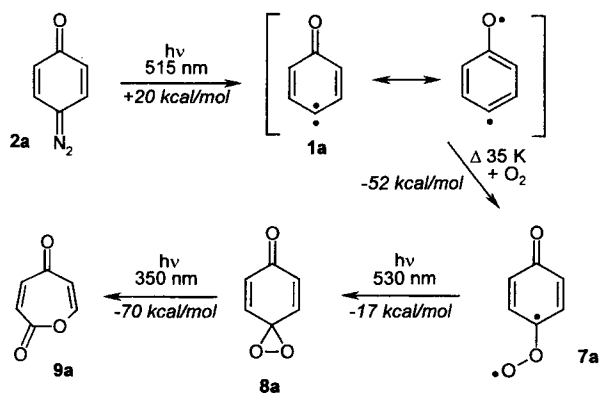
RHF-based methods including MP2 fail to reliably reproduce the vibrational spectra of carbonyl oxides,⁶⁹ and therefore at the time when **7a** was synthesized for the first time²² the calculation of its IR spectrum was beyond the computational capabilities. DFT calculations (B3LYP/6-31G(d,p)) now permit the reproduction of the IR spectrum of **7a** with high accuracy even on a personal computer, and thus confirm the earlier assignment.

The formation of **7a** was also observed in solution using laser flash photolysis (LFP) with nanosecond time resolution.^{25,26} In Freon-113 **7a** shows an absorption maximum at 470 nm, and a life-time of longer than 20 μs .²⁵ The rate of $2.9 \times 10^9\text{ M}^{-1}\text{ s}^{-1}$ for this reaction is almost the diffusion limit and implies a very small or absent barrier. In aqueous solution the rate constant for the reaction of **1a** with $^3\text{O}_2$ is $3.5 \times 10^9\text{ M}^{-1}\text{ s}^{-1}$, and the absorption maximum of **7a** was determined as 460 nm.²⁶ This clearly demonstrates that the oxidation of carbene **1a** in solid argon and in solution follows the same reaction pathway.

According to the B3LYP calculations, the formation of **7a** from **1a** and $^3\text{O}_2$ is exothermic by 52 kcal/mol.⁶² Despite the large excess energy released in this reaction and despite its thermal and photochemical lability, the carbonyl oxide **7a** is formed in high yield. Irradiation with red light ($\lambda > 630\text{ nm}$) very rapidly results in the complete photolysis of **7a** and formation of the spirodioxirane **8a** (Scheme 5). The dioxirane **8a** was identified by its subsequent photochemistry and by comparison of the experimental with the DFT calculated IR spectrum. The **7a** $\rightarrow$ **8a** rearrangement is calculated to be exothermic by 17 kcal/mol.

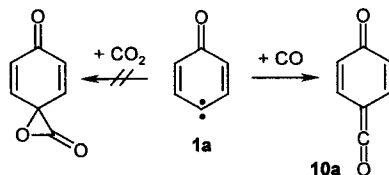
The dioxirane **8a** is much less labile than the carbonyl oxide **7a**, and UV irradiation ($\lambda > 400\text{ nm}$) is required to induce the rearrangement to lactone **9a**. With 70 kcal/mol this is the most exothermic step in the whole reaction sequence from **1a** to **9a**. All of these reaction intermediates were generated in subsequent steps in high yields and characterized by matrix IR spectroscopy.

Another reaction of carbene **1a** in an argon matrix is the carbonylation with CO to give ketene **10a**.²³ The carbonylation obviously proceeds with a very small barrier even at low temperature. The carboxylation with CO_2 , on the other hand, which is also a characteristic reaction of many carbenes, is not observed.⁷⁰ The primary and rate-determining step of this reaction is the nucleophilic attack



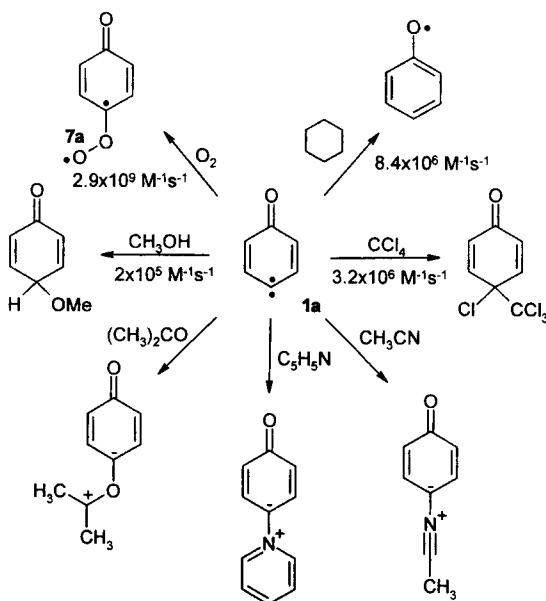
Scheme 5.

of the carbene center at the CO_2 carbon atom, and therefore the reactivity depends on the nucleophilicity of the carbene. Electrophilic carbenes, such as **1a**, show only a reduced or no reactivity towards CO_2 , while less electrophilic carbenes, such as diphenylcarbene, react rapidly.⁷⁰

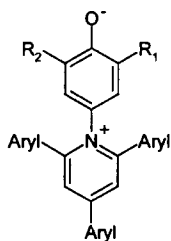


Several intermolecular reactions of **1a** were investigated in solution at room temperature via LFP.^{25,26} The reaction with cyclohexane as a hydrogen atom donor results in the formation of the phenoxyl radical with a characteristic UV spectrum.²⁵ In a hydrocarbon as solvent and in the absence of oxygen this reaction determines the lifetime of the carbene. The rate of the reaction with CCl_4 is about half that of the hydrogen abstraction from cyclohexane, while the rate of the reaction with Freon-113, which was used as the solvent, is almost two orders of magnitude slower. The reaction rate with methanol, determined by competitive quenching of the reaction with molecular oxygen, was determined to be $2 \times 10^5 \text{ M}^{-1} \text{ s}^{-1}$. This is, within the large uncertainties of these experiments, in reasonable agreement with the kinetic data of the methanol reaction in aqueous solution ($1 \times 10^6 \text{ M}^{-1} \text{ s}^{-1}$).²⁶

Other interesting reactions of **1a** are the formation of ylides with acetone, pyridine, and acetonitrile (Scheme 6).²⁵ These ylides are intensely colored with absorption maxima in Freon-113 at 500, 560, and 540 nm, respectively, and thus easily detected spectroscopically. Interestingly, transient species with absorption maxima around 620 nm and lifetimes in the order of ms are found in all three

**Scheme 6.**

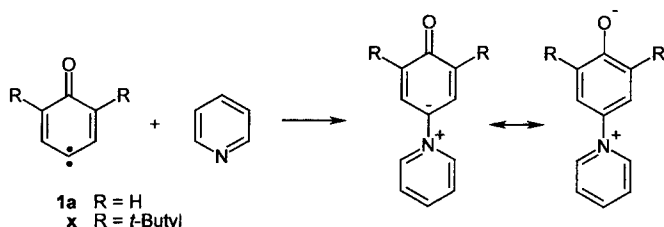
reactions. The decay of these transients matches the growth of the ylides, which clearly demonstrates that the 620 nm transients are precursors of the ylides. Since the absorption maximum of the transient species is almost independent of which reactant is used, the chromophore must be mainly located at that part of the molecule originating from the carbene **1a**. An explanation of these experimental findings is the formation of a triplet adduct as the primary product which subsequently decays to the ylide.

**Dimroth-Reichardt Dye**

The pyridine ylide of **1a** is the parent compound of the Dimroth–Reichardt betaine dyes used to probe solvent polarity.^{71,72} These dyes show a very pronounced solvatochromism, and the shifts of the absorption maxima as a function of the solvent polarity has been used to establish the quantitative ET₃₀ scale.

The Dimroth–Reichardt betaines are synthesized by reactions of *p*-aminophenols with pyrylium salts bearing aryl substituents in *ortho* position.

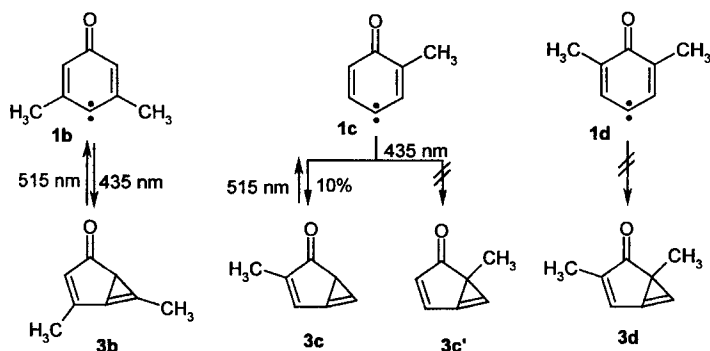
The reaction of carbenes **1**, generated either thermally or photochemically from the corresponding quinone diazides **2**, with pyridine results in the formation of the deeply colored betaines which can be isolated in substance from the reaction mixture.^{73,62} This alternative synthesis of the betaines opens a general route to pyridine ylides unsubstituted at the pyridine ring.



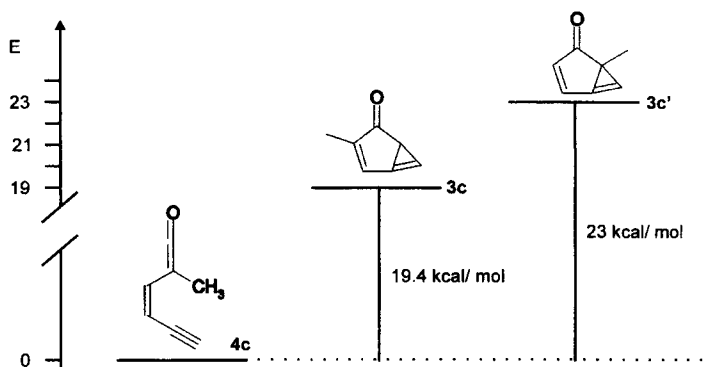
B. Methylated Derivatives

The methylated carbenes **1b–d** are easily generated in argon matrices by photolysis of the corresponding diazo compounds.²⁴ The IR and UV/vis spectra are very similar to that of **1a**. In addition, the carbenes were chemically characterized by their reaction with molecular oxygen to give the corresponding quinone *O*-oxides **7b–d**.

The methyl substitution in carbenes **1b–d** has a pronounced influence on the yield of the bicyclic isomers **3**.^{24,74} Thus, visible light irradiation of the 2,6-dimethylated carbene **1b** rapidly and with very high yield produces the cyclopropene **3b** (Scheme 7). The yield is significantly higher than in the case of the parent system **3a**. In contrast, methyl substitution in 3-position as in **1c** drastically reduces the yield of the cyclopropene **3c** to approximately 10%.



Scheme 7.



Scheme 8.

Two isomers of the cyclopropene, **3c** and **3c'** with the methyl group in 3- and 1-position, respectively, have to be considered. Although the number of IR absorptions suggests that only one isomer is formed and the experimental spectrum is better matched by the spectrum calculated for **3c**, the theoretical IR spectra of the two isomers are too similar to allow for a definitive assignment. According to DFT calculations, the isomer **3c** is by 3.6 kcal/mol more stable than the isomer **3c'** with the methyl group at the bridgehead carbon atom, which is in line with the preferential formation of **3c** (Scheme 8).

Rearrangement of the 3,5-dimethylated carbene **1d** would yield the destabilized cyclopropene **3d** with a methyl group in the bridgehead position 1, and consequently no detectable amount of cyclopropene **3d** is formed during irradiation of **1d**. Indeed, whereas the 3,5-dimethyl substituted carbene **1d** is 3.4 kcal mol⁻¹ more stable than the 2,6-dimethyl isomer **1b**, the stability is reversed for the cyclopropenes, as **3d** is found to be 6.5 kcal mol⁻¹ higher in energy than **3b** at the B3LYP/6-31G(d) level of theory (Table 3).

Consequently, the reaction from **1d** to **3d** is significantly more endothermic, +25 kcal mol⁻¹, than the rearrangement of **1b** to **3b** (+15 kcal mol⁻¹). The approximately 10 kcal mol⁻¹ energy advantage for **1b** is also partially preserved in the TS for ring closure, which is found to be 7.4 kcal mol⁻¹ lower for the formation of **3b** compared to **3d** (see Table 4).

Table 3. B3LYP/6-31G(d) Energies ($E_{rel}/\text{kcal mol}^{-1}$) of the 2,6-Dimethyl-substituted Species **1b**, **3b** and the Transition State Relative to the 3,5-Dimethyl-substituted Species **1d**, **3d**

Substitution	Carbene, ³ B ₁	Carbene, ¹ A'	TS, ¹ A	Cyclopropene, ¹ A
3,5-dimethyl, d	0	0	0	0
2,6-dimethyl, b	+3.4	+2.2	-4.0	-6.5

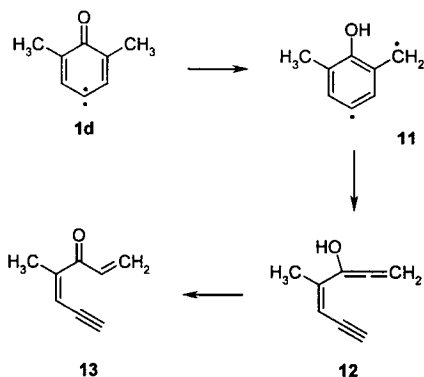
Table 4. The B3LYP/6-31G(d) Energies of Bicyclic Compounds **3a,b,d**, and of the Transition Structures for their Formation Relative to Carbenes **1a,b,d**

Isomer	E_{rel} (kcal mol ⁻¹)	Isomer	E_{rel} (kcal mol ⁻¹)	Isomer	E_{rel} (kcal mol ⁻¹)
1a , ³ B ₁	0	1b , ³ B ₁	0	1d , ³ B ₁	0
1a , ¹ A'	16.6	1b , ¹ A'	14.5	1d , ¹ A'	15.6
TS, ¹ A	27.2	TS, ¹ A	20.7	TS, ¹ A	28.1
3a , ¹ A	22.2	3b , ¹ A	15.1	3d , ¹ A	24.9

Compared to the parent system **3a**, the barrier for formation of **3d** is the highest in this series whereas the formation of **3b** should be the most facile according to our computations. Although the reactions of carbenes **1a–c** are initiated photochemically, the observed reactivity seems to be in line with the computed ground state properties. Thus, while methyl substitution in 3- and 5-position inhibits the vinylcarbene–cyclopropene rearrangement, methyl substitution in 2- and 6-position has the opposite effect.

UV irradiation ($\lambda > 360$ nm, argon, 10 K) is required to rearrange carbene **1d**, and in this case a reaction path entirely different from the photochemistry of **1a–c** is followed.⁷⁴ At least three photoproducts are formed in consecutive steps. To identify these products and to assign the IR spectra, the methyl-perdeuterated isotopomer d₆-**1d** was also investigated. The primary reaction product **11** exhibits a strong phenolic OH stretching vibration which was characteristically red-shifted on deuteration. This clearly indicates that the primary photoreaction of **1d** is the transfer of a hydrogen atom from one of the methyl groups to the carbonyl oxygen atom. The vibrational spectrum of the ¹A'' singlet **11** was computed using the 6-31G(d,p) basis set and the *restricted open shell theory for low spin states* (ROSS) formulation of DFT with a modified BLYP functional to correctly account for the two-determinant form of the wave function of the singlet ground state.⁷⁴ Comparison of the theoretical and experimental IR spectra allowed identification of the phenol **11** as a α ,3-didehydrocresol, the first derivative of a α ,3-didehydrotoluene that could be isolated and characterized spectroscopically (Scheme 9).

Derivatives of α ,3-didehydrotoluene are the key intermediates in the *in vivo* action of neocarzinostatin and related eneyne-allene antibiotics,^{75–77} and thus there currently is considerable interest in studying the physical–organic properties of such biradical intermediates. The parent α ,3-didehydrotoluene is known from collision-induced dissociation threshold energy measurements of the corresponding haloanions to have a ¹A'' singlet ground state with a small energy separation ($\Delta E_{ST} = -3.0$ kcal mol⁻¹) to the ³A'' triplet state.^{78–80} Note that α ,2- and α ,4-didehydrotoluene have triplet ground states with open-shell singlets lying 7.4 and 8.1 kcal mol⁻¹ higher in energy, respectively.⁷⁸



Scheme 9.

The reaction from **1d** to **11**-³A'' is endothermic by 16.2 kcal mol⁻¹ at B3LYP/6-31G(d), and assuming $\Delta E_{ST} \approx -3$ kcal mol⁻¹ as in the parent system, an overall endothermicity of 13 kcal mol⁻¹ is estimated for the formation of the **11**-¹A'' ground state. The barrier for the hydrogen atom migration is calculated to be 39.4 kcal mol⁻¹ on the lowest triplet energy surface, which can easily be overcome by photochemical activation. The experiments do not allow to decide whether the reaction proceeds on an excited state surface or via hot ground state molecules. Interestingly, a related intramolecular hydrogen atom transfer yielding the 2,4-didehydrophenol biradical has been previously observed in our laboratory (see Section II.D).⁸¹ The hydrogen transfer and CO₂ elimination from 2,5-cyclohexadien-1-one-2-carboxylic acid-4-ylidene **1i** occurs upon 600–700 nm irradiation, whereas UV light ($\lambda > 360$ nm) has to be employed to convert **1d** into **11**. The different reactivities of these biradical precursors are due to the different distances between the oxygen and the migrating hydrogen atoms. The much shorter distance in the acid derivative results in a lower barrier for hydrogen transfer (Fig. 4).

The second photoproduct was identified as ene-yne-allene **12** with highly characteristic IR absorptions. The **11** $\rightarrow$ **12** ring-opening is the reverse of a Myers cyclization,^{75,82} the reaction that produces diradicals similar to **11** in biological systems. Due to the formation of a biradical intermediate, the reliable computational modeling of the Myers reaction or the competitive C²–C⁶ ("Schmittel") cyclization^{83,84} is challenging,^{85,86} but Schreiner and Prall have demonstrated that pure DFT methods give surprisingly reliable results for the energetics of these reactions.⁸⁷ Hughes and Carpenter recently concluded from competitive trapping experiments that the Myers cyclization of eneyne-allenes proceeds by two different mechanisms.⁸⁸ Besides the one involving biradicals of the type discussed here, a dipolar reaction path with a nonplanar cyclic allene might be competitive. The asymmetric cyclic allene is 2 to 7 kcal mol⁻¹

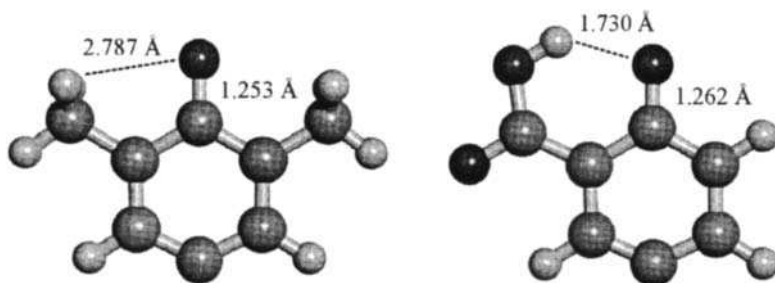
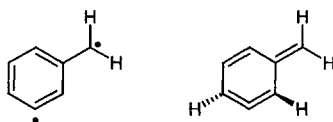


Figure 4. Structures of carbenes **1d** (left) and **1i** (right) according to B3LYP/6-31G(d) calculations. The strong OH $\cdots$ O hydrogen bridge in **1i** with a non-bonding H $\cdots$ O distance of 1.730 Å is much more favorable for the hydrogen migration than the 2.787 Å distance in **1d**.

less stable than the biradical according to MP2/6-31G(d) and CASPT2(8,8)/6-31G(d)//CASSCF(2,2)/6-31G(d) computations.



Compound **12** contains a vinylic hydroxyl group and thus is expected to be unstable at higher temperatures in solution. Under the conditions of matrix isolation, however, it is perfectly stable and a third photochemical activation is required to induce the tautomerization to the unsaturated ketone **13**.

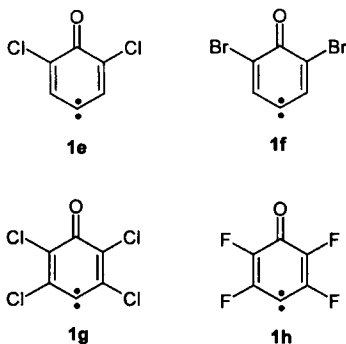
Laser flash photolysis (LFP) of quinone diazide **2d** in Freon-113 at room temperature produces carbene **1d**, which could be monitored indirectly by addition of trapping reagents.²⁵ At 2.0 μ s the lifetime of **1d** is slightly longer than that of **1a** (1.65 μ s), otherwise the reactivities of these carbenes are very similar. The **1d** $\rightarrow$ **11** rearrangement is not observed in the LFP experiments. All trapping products with a variety of reagents (O_2 , acetonitrile, pyridine etc.) are derived from carbene **1d**.

C. Halogenated Derivatives

Halogen substitution is expected to increase the electrophilicity of the carbenes, and in particular **1h** with four fluorine substituents is expected to be highly electrophilic and of unusual reactivity. All the carbenes **1e–g** could be matrix-isolated by irradiation of their corresponding quinone diazides **2** in argon at 8–10 K.^{24,68,62} Again, the thermal reaction in O_2 -doped matrices results in the formation of quinone oxides **7**, which show the expected photochemical rearrangement to the spiro dioxiranes **8** and finally lactones **9**.

The halogen substitution results in a systematic modification of the spectro-

scopic properties of compounds **7–9**.⁶⁸ For example, the visible transition of **7e** is red-shifted by 22 nm and that of **7f** by 26 nm compared to **7a**. Since the COO moiety in carbonyl oxides can be described as an electron rich 3-center 4-electron π -system, the strength of the O–O bond increases with increasing electron demand of the ring. This stabilization leads to a significant shift of the O–O stretching vibration to higher frequencies in **7e** and **7f** compared to **7a**.

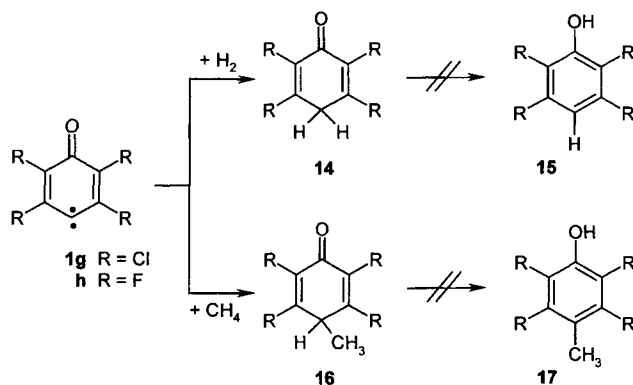


The vinylcarbene–cyclopropene rearrangement of carbenes **1e–h** was also investigated. Whereas visible irradiation of the dihalogenated carbenes **1e** and **1f** yields **3e** and **3f** in clean and completely reversible reactions,²⁴ the cyclopropenes **3g** and **3h** are not accessible from the corresponding carbenes. This finding is remarkable, since, according to B3LYP/6-31G(d) computations, **3g** and **3h** are thermodynamically more stable with respect to their triplet carbenes than **3a** (see Table 5). However, the ring opening of **3h** is predicted to be very facile (barrier of only 1.7 kcal mol^{−1}). If formed at all during irradiation, **3h** is expected to rearrange rapidly even at temperatures as low as 10 K.

The perhalogenated carbenes **1g** and **1h** are of unusual reactivity towards molecular hydrogen and hydrocarbons.⁶² Annealing of H₂- or CH₄-doped argon matrices containing the carbenes **1g** or **1h** at 30–45 K rapidly results in the formation of insertion products (Scheme 10). With H₂ 2,5-cyclohexadienone (**14**) is formed and with CH₄ the 4-methyl-2,5-cyclohexadienone (**16**). The

Table 5. The B3LYP/6-31G(d) Energies of Bicyclic Compounds **3a** and **3g–h**, and of the Transition Structures for their Formation Relative to Carbenes **1a** and **1g–h**

Isomer	E_{rel} (kcal mol ^{−1})	Isomer	E_{rel} (kcal mol ^{−1})	Isomer	E_{rel} (kcal mol ^{−1})
1a , ³ B ₁	0	1g , ³ B ₁	0	1h , ³ B ₁	0
1a , ¹ A'	16.6	1g , ¹ A'	12.4	1h , ¹ A'	9.1
TS, ¹ A	27.2	TS, ¹ A	18.5	TS, ¹ A	17.9
3a , ¹ A	22.2	3g , ¹ A	13.3	3h , ¹ A	16.2

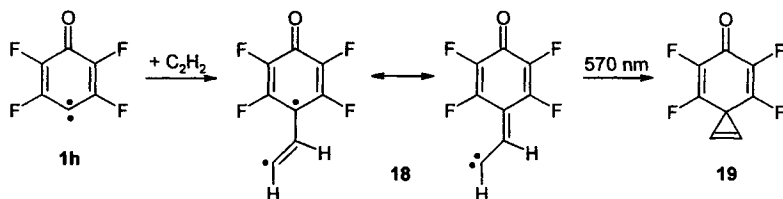


Scheme 10.

tautomerization to the thermodynamically more stable phenols **15** and **17**, respectively, is kinetically inhibited under the conditions of matrix isolation. Both carbenes **1g** and **h** also insert into D_2 and CD_4 . In contrast, carbene **1a** (and most other carbenes) are completely unreactive with both H_2 and CH_4 in low temperature matrices, which demonstrates the enormous electrophilicity and reactivity of **1g** and **h**. The insertion reactions of the fluorinated carbene **1h** are faster and the yields of products are higher than in the case of the chlorinated carbene **1g**. This indicates that low-barriers in the insertion reactions correlate with a high electrophilicity of the carbenes.

The mechanism of the insertion is not clear, however, since both carbenes have triplet ground states, an abstraction-recombination mechanism with radical pairs as intermediates is most likely. The only other triplet carbene that has been reported to insert into CH_4 in low temperature matrices is methylene.^{89,90} However, in this case it is not completely clear if the insertion is a thermal or photochemical reaction.

The thermal reaction of matrix-isolated **1h** with acetylene leads to the formation of the intensely red-colored vinylcarbene **18** as the primary product.⁶² This carbene, which can also be formulated as a 1,3-diradical, has a triplet ground state and is thus formed in a spin-allowed reaction from triplet carbene **1h** (Scheme 11)



Scheme 11.

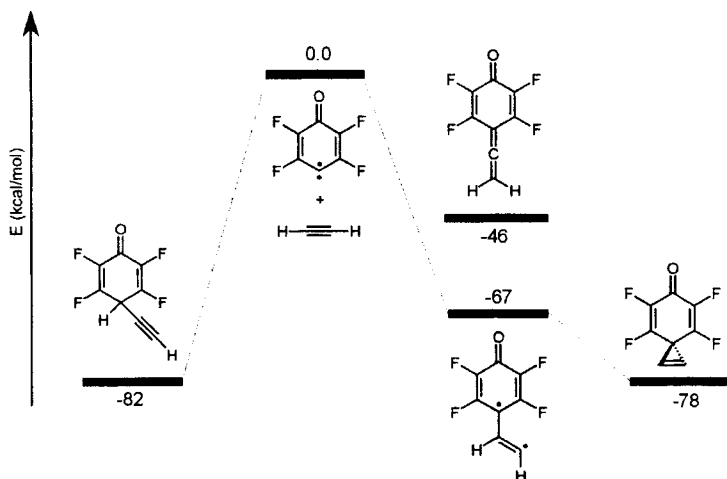


Figure 5. Reaction of carbene **1h** with acetylene, relative energies calculated at the B3LYP/6-31G(d) level of theory.

11, Fig. 5). A photochemical activation (irradiation into the visible absorption of carbene **18**) is required to induce the ring-closure to the spiro-cyclopropene **19**. Both **18** and **19** could be identified by comparison of the experimental with DFT-calculated IR spectra.

D. Carboxylic Acid Derivatives

The quinone diazides **2i–2m** bearing carboxylic acid functions adjacent to the carbonyl groups exhibit pronounced red shifts of the C=O (ring) stretching vibrations, and in the ^1H NMR spectra the acidic protons are shifted downfield to 11–17 ppm. These spectroscopic findings indicate strong OH $\cdots$ O hydrogen bridges between the carboxyl OH and ring carbonyl groups, which is confirmed by X-ray crystal structure analyses of the quinone diazides **2i** (Fig. 6) and **2l**. The distance between the OH and ring C=O oxygen atoms in **2i** was determined to 2.475 Å, and that in **2l** even to only 2.442 Å.

The carboxylic acid derivatives **1i–1m** can only be matrix-isolated if the corresponding quinone diazides **2i–2m** are irradiated with monochromatic blue light ($\lambda = 436\text{ nm}$).^{81,91,92} UV or broad-band visible irradiation rapidly results in the decarboxylation of the carbenes. As expected, the IR and UV/vis spectra of the carbenes are very similar to that of **1a**. Oxygen trapping results in the formation of the photolabile carbonyl oxides **7**. Thus, the carbenes **1i–1m** were identified both spectroscopically and by their characteristic reaction with molecular oxygen.

The IR spectrum of carbene **1i** indicates a very strong hydrogen bridge between the carboxyl hydrogen atom and the ring carbonyl group.⁹² The red shift

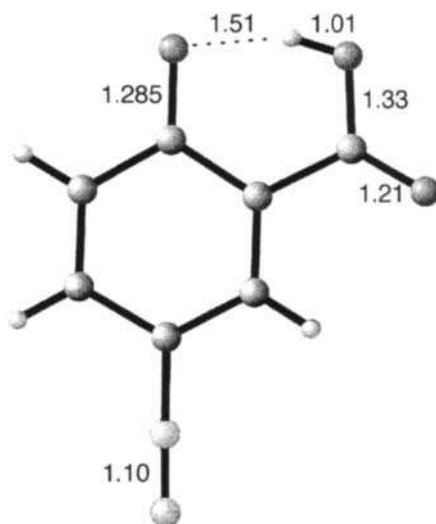
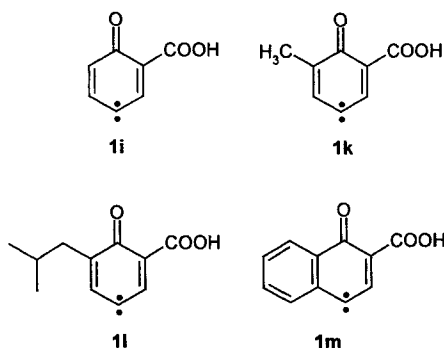
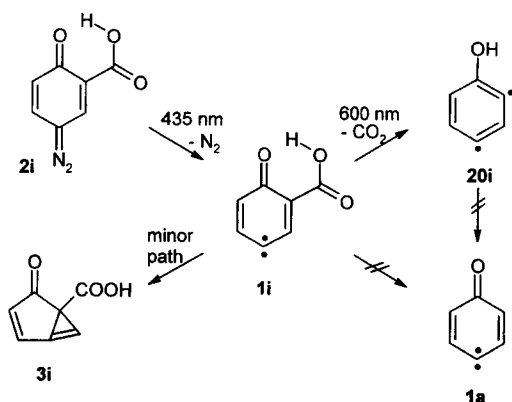


Figure 6. X-ray structure of quinone diazide **2i** with some bond distances.



of the C=O stretching vibration of the ring carbonyl group in **1i** compared to **1a** is even larger than that of **2i** compared to **2a**. Visible light irradiation ($\lambda > 600$ nm) of **1i** produced only traces of the cyclopropene **3i**. The major products are CO_2 and a novel compound with strong IR absorptions at 3612, 1516, 641, and 519 cm^{-1} . Deuteration of the COOH group in **2i** results in a very large red-shift of the 3612 cm^{-1} absorption, which allows to assign this vibration to a phenolic OH stretching vibration.⁸¹ Thus, during the decarboxylation a hydrogen atom is transferred from the carboxyl group to the carbonyl group of **1i** (Scheme 12). The most reasonable structure for the newly formed compound is that of 2,4-didehydrophenol (**20i**), a derivative of *m*-benzynes.⁹³

Our initial calculations of the IR spectrum of **20i** at the GVB level of theory reproduced the experimental spectrum only partially, and in particular the



Scheme 12.

calculated low frequency ring deformation modes involving the radical centers showed a large deviation from the experimental data.⁸¹ However, coupled cluster and DFT calculations give a very nice agreement of experiment and theory and clearly confirm the assignment of the structure (Fig. 7) of **20i**.^{92,93} The decarboxylation of carbene **1i** was estimated to be exothermic by 18 kcal/mol,⁹² and the excitation with red light is sufficient to overcome the small activation barrier.

Due to the high polarity of **2i** and the exclusive formation of intra- rather than intermolecular hydrogen bridges, its solubility in almost all solvents is very low. To investigate the photochemistry of carboxylic acids of type **2i**, alkyl chains were introduced as substituents.⁹² The isobutyl derivative **2i** is soluble in MTHF, a solvent that generates a transparent organic glass on cooling to liquid

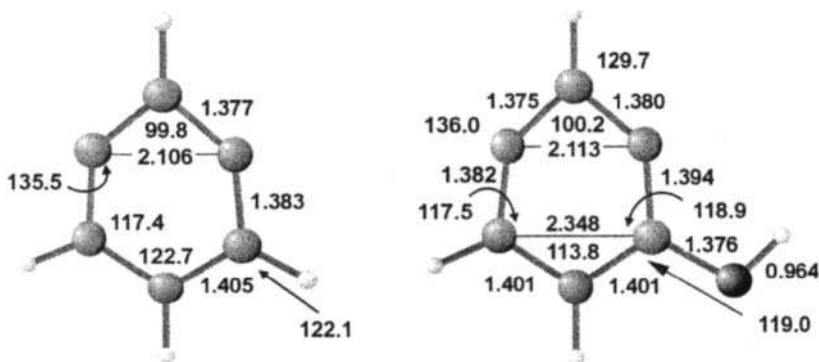
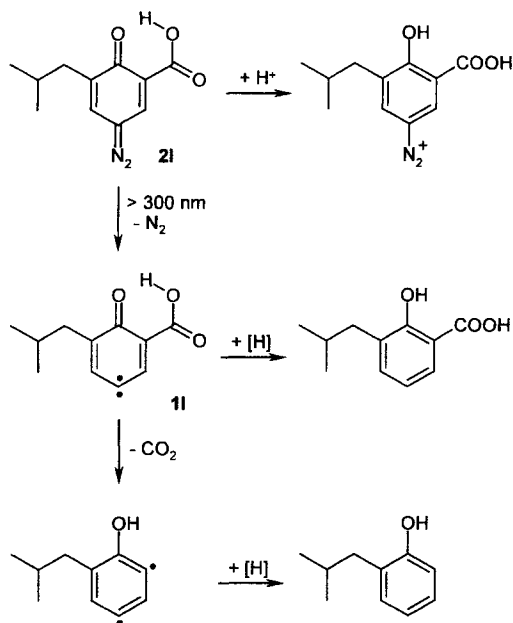


Figure 7. Some calculated (CCSD(T)) geometric data of *m*-benzynes (left) and didehydrophe-nol **20i** (right). The introduction of the OH group in **20i** results in an only small distortion of the ring.



Scheme 13.

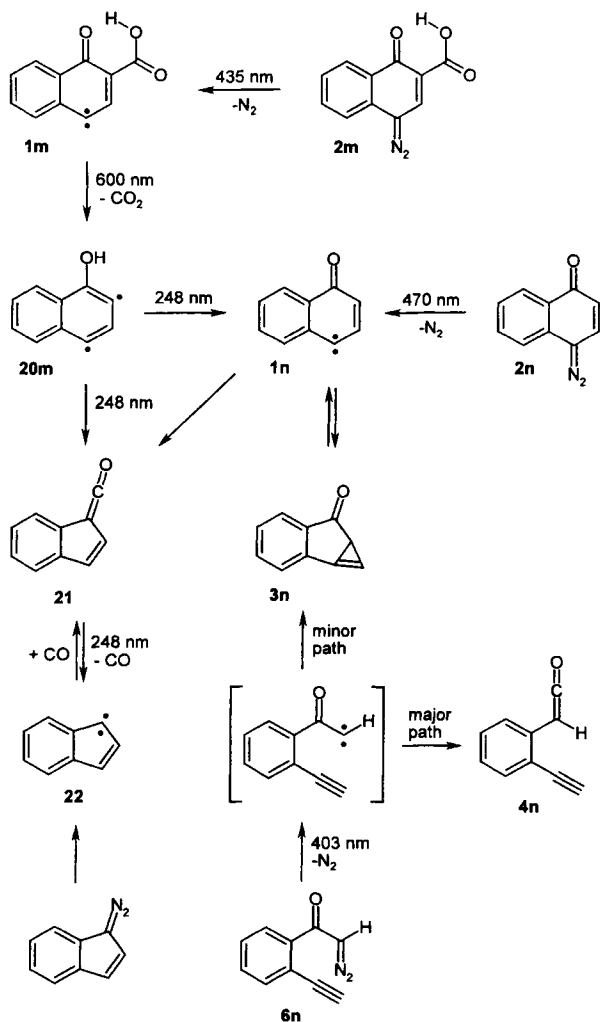
nitrogen temperature. Irradiation ($\lambda > 300$ nm) of **2I** in MTHF at 77 K produces mixtures of the corresponding salicylic acid and phenol derivatives (Scheme 13). While the former are trapping products of carbene **1I**, the latter are formed from the didehydrophenol **20I**. Salicylic acid is not photochemically decarboxylized under the reaction conditions, and therefore the ratio salicylic acid/phenol corresponds to a yield of 20–30% of dehydrophenol **20I**. Since the formation of **20I** from **2I** is a two step photochemical process — loss of N_2 followed by loss of CO_2 requiring one photon each — the yield of **20I** depends much on experimental conditions such as intensity and frequency of the irradiating light, solvent, and temperature. Nevertheless, these experiments clearly reveal that carbene **1I** is long-lived enough to undergo secondary photolysis to **20I**. In acidic media (e.g., trifluoroethanol) a large fraction of the diazo compound **2I** is protonated to give the diazonium ion. Loss of N_2 from this species results in the formation of products derived from phenyl cations.

Dehydrophenol **20i** is a tautomeric form of carbene **1a**, and a [1,3]-H migration should in principal interconvert these species. However, under the conditions of matrix isolation the benzyne **20i**–**1** are thermally and photochemically stable towards rearrangement to the corresponding carbenes. UV irradiation of **20i** results in a ring-opening and formation of so far unidentified acetylenic products.

The photolysis of benzo-annellated quinone diazides such as **2m** should preferentially lead to products with intact benzene rings. Monochromatic irradiation

of **2m** with $\lambda = 435$ nm produces carbene **1m** in quantitative yield. The carbene **1m** shows the expected IR spectrum (carbonyl and carboxyl group are easily identified) and was chemically identified by its thermal reaction with molecular oxygen to give carbonyl oxide **7m**.⁹² Similar to the related carbenes **1i**–**1l**, carbene **1m** is rapidly decarboxylated on long-wavelength irradiation ($\lambda > 600$ nm) yielding didehydronaphthol **20m** with the OH stretching vibration at 3608 cm^{-1} (Scheme 14).

UV irradiation ($\lambda = 248$ nm, KrF Excimer Laser) of benzyne **20m** produces a mixture of indeneketene **21**, CO, and indenylidene **22**. Indenylidene **22** was



Scheme 14.

independently matrix-isolated by photolysis of diazoindene, which in CO-doped matrices is trapped to give ketene **21**.⁹⁴ A reasonable mechanism for the formation of **22** from diradical **20m** during UV photolysis is a [1,3]-H migration to give carbene **1n** as the first step. Carbene **1n** is labile towards the intense 248 nm irradiation and a second [1,3]-H shift followed by Wolff-rearrangement finally produces ketene **21**. However, since none of these intermediates was observed, this mechanism remains speculative.

E. Benzoannulation

1. The naphtho-system

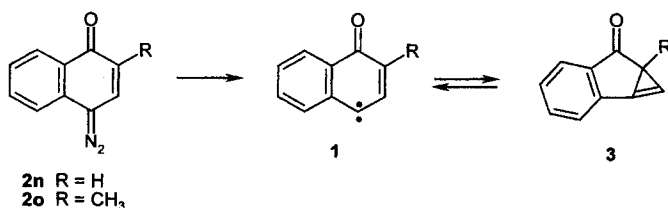
The quinone diazide **2o** was investigated using LFP in solution at room temperature.²⁵ As with **1a**, the carbene **1o** does not show characteristic absorptions in the UV/vis region and therefore could not be directly monitored during the LFP experiments. By extrapolation of quenching plots to zero quencher concentration the life-time of **1o** in Freon-113 was determined to 2.5 μ s, slightly longer than that of **1a** with 1.65 μ s.

The matrix photochemistry of **2n**²⁴ and **2o**⁹² is completely analogous to that of **2a**. The primary irreversible loss of nitrogen from **2** produces carbenes **1** in photostationary equilibria with cyclopropenes **3** (Scheme 15). The relative amounts of **1** and **3** formed in the matrix depends very much on the wavelength used for the irradiation. Both carbenes **1n** and **1o** were chemically identified by oxygen trapping. UV irradiation (248 nm) of **1n** produces a mixture of indeneketene **21**, CO, and indenylidene **22** (Scheme 14).

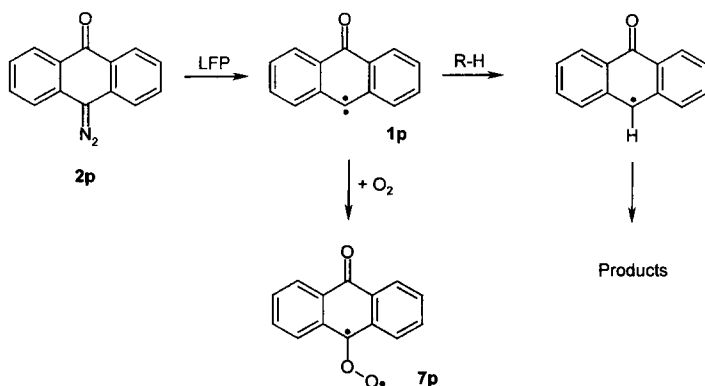
2. Anthronylidene

The ESR spectrum of triplet anthronylidene **1p** was recorded after UV irradiation of **2p** at 77 K.⁹⁵⁻⁹⁷ At 0.365 cm^{-1} the zero field parameter *D* in **1p** is larger than that in **1a**, which indicates that the delocalization of the unpaired π -electron in **1p** is less efficient — despite the larger π -system — than in **1a**. Obviously the phenoxy resonance structure in **1a** is more favorable than in **1p**.

The photochemistry of diazoanthrone **2p** in solution at room temperature



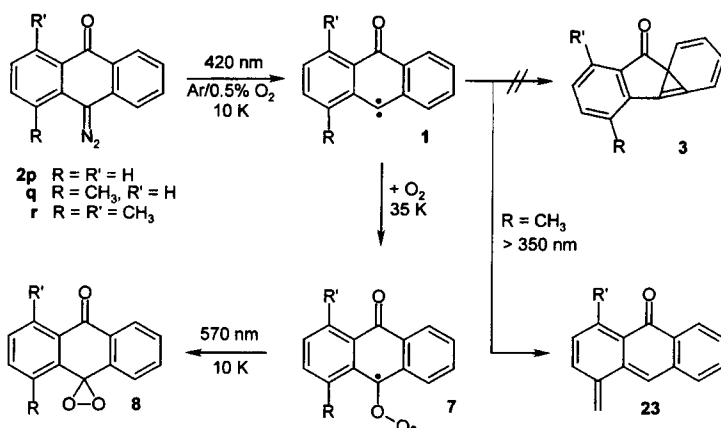
Scheme 15.



Scheme 16.

was studied by LFP and product studies, and a transient with three prominent maxima at 354, 521, and 561 nm was attributed to carbene **1p** (Scheme 16).⁹⁸ The reactivity of **1p** is that of a typical triplet ground state carbene: fast reaction with $^3\text{O}_2$, loss of the stereochemistry in cyclopropanation reactions, and formation of the anthranyl radical in cyclohexane as solvent. The products isolated from the photolysis of **2p** in a variety of solvents are the formal insertion products (C–H insertion in hydrocarbons and O–H insertion in alcohols), anthrone from the reaction with traces of oxygen, and the dimer of the anthranyl radical. From trapping experiments with methanol and pyridine *N*-oxide a singlet–triplet splitting of $\Delta G_{\text{ST}} = 5.8 \pm 0.6$ kcal/mol is estimated.

The anthronylidenes **1p–1r** are easily matrix-isolated by photolysis of the corresponding diazo compounds **2** (Scheme 17).⁹⁹ The reaction of the carbenes with molecular oxygen results in the formation of anthraquinone *O*-oxides **7**,

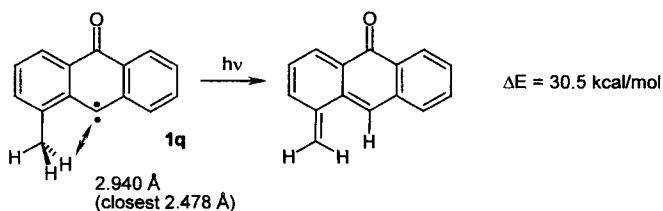


Scheme 17.

which on 400 nm irradiation rearrange to dioxiranes. As expected, anthronylidene **1p** and its derivatives **1q** and **1r** do not rearrange to the very highly strained cyclopropenes **3p-r**.

While carbene **1p** is completely stable towards irradiation with visible or UV light, carbenes **1q** and **1r** bearing methyl groups in the *peri*-position adjacent to the carbene center slowly rearrange on irradiation with $\lambda > 420$ nm.⁹⁹ During this photolysis the color of the matrix changes from yellow (carbene) to purple. By comparison of the experimental with the DFT-calculated IR spectrum the purple compound was identified as 5-methylene-5*H*-anthracene-1-one (**23**) with an extended π -system that is responsible for the intense color.

The migration of a hydrogen atom from the methyl group to the carbene center in **1q** was calculated to be exothermic by 30.5 kcal/mol. The distance the hydrogen atom has to cross is 2.94 Å in the minimum conformation of **1q**, and the shortest distance possible by rotation of the methyl group is 2.48 Å.⁹⁹ In **1r** an alternative hydrogen migration from the second methyl group is in principal possible. However, this rearrangement, yielding an energetically unfavorable carbene, is not found.



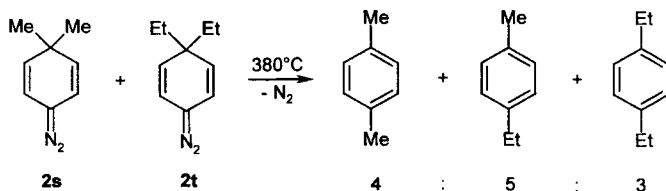
III. OTHER CYCLOHEXADIENYLIDENES

While the 4-oxo derivatives are the cyclohexadienylidenes investigated most, several other derivatives without a carbonyl group in 4-position have been reported in literature.

A. 4,4-Disubstituted Cyclohexa-2,5-dienylidenes

2,5-Cyclohexadienylidenes, disubstituted at the 4-position are expected to be kinetically more stable than the parent carbene, however, the rearrangement to benzene derivatives is still very exothermic. The gas phase chemistry of 4,4-dimethyl-2,5-cyclohexadienylidene **1s** was investigated by Jones et al.^{100,101} The gas phase pyrolysis of the diazo compound **2s** produces a mixture of *p*-xylene and toluene, and by crossover experiments it was demonstrated that the methyl group transfer occurs intermolecularly via free radicals. Thus, the pyrolysis of a mixture of the dimethyl and the diethyl derivative **2s** and **2t**

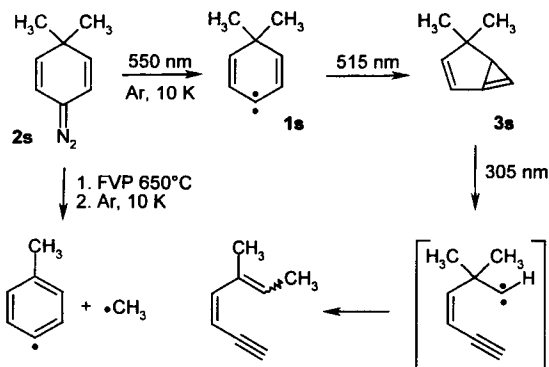
yields *p*-ethylmethylbenzene as the major product. From these experiments no evidence for the vinylcarbene–cyclopropene rearrangement to **3s** and **3t**, respectively, is obtained.



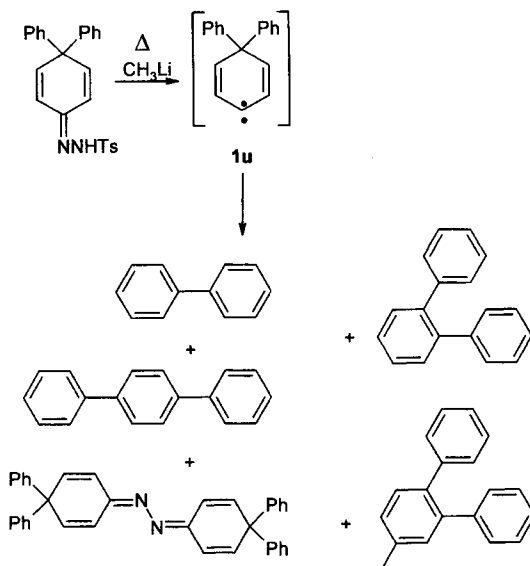
The radical mechanism was confirmed by matrix isolation of the pyrolysis products of **2s**.¹⁰² Flash vacuum pyrolysis of **2s** with subsequent trapping of the products in argon at 10 K produces methyl radicals, which are easily identified by IR spectroscopy.

The photolysis of matrix-isolated **2s** in argon at 10 K gives high yields of the carbene **1s** (Scheme 18) with the strongest IR absorption at 733 cm^{-1} , in good agreement with theoretical predictions.¹⁰² Oxygen trapping of **2s** results in the formation of carbonyl oxide **7s** which shows the expected photochemistry — rearrangement to dioxirane **8s** — on visible light irradiation. The O–O stretching vibration of carbonyl oxide **7s** is found at 893 cm^{-1} , close to that of benzophenone *O*-oxide (896 cm^{-1}),^{103,104} but considerably red-shifted compared to that of quinone oxide **7a** (1034 cm^{-1}).²² This is in line with the qualitative description of the C–O–O moiety as an electron-rich 3-center 4-electron π -system. A π electron acceptor — such as the carbonyl group in **7a** — will thus stabilize the carbonyl oxide and lead to higher O–O stretching frequencies.¹⁰⁵

Carbene **1s** proved to be photolabile, and long-wavelength irradiation ($\lambda > 515\text{ nm}$) results in the irreversible formation of the strained cyclopropene **3s**. The methyl shift to give *p*-xylene, which is energetically much more favorable, is not



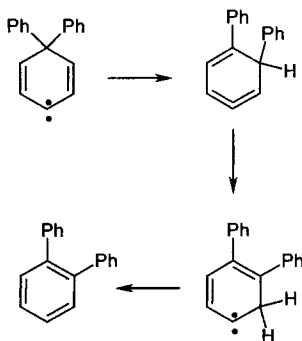
Scheme 18.

**Scheme 19.**

observed. At the UMP2/6-31G(d) level of theory the **3s** $\rightarrow$ **1s** rearrangement is calculated to be exothermic by 8 kcal/mol, considerably less than the 19 kcal/mol calculated for the **3a** $\rightarrow$ **1a** rearrangement. Obviously, the transition state for the former rearrangement is now large enough to prevent the thermal isomerization under the conditions of matrix isolation at low temperature. The differences in the energies of the vinylcarbene–cyclopropene rearrangements result mainly from the better stabilization of carbene **1a** compared to **1s** due to the better delocalization of the unpaired π electron in **1a**. At 77.6 and 74.7 kcal/mol the strain energies of **3a** and **3s**, respectively, are very similar and approximately 20 kcal/mol higher than that of cyclopropene.

The thermochemistry of 4,4-diphenylcyclohexa-2,5-dienylidene (**1u**) in solution was investigated by Freeman and Pugh (Scheme 19).¹⁰⁶ The thermal decomposition of the diazo compound **2u** (produced *in situ* from the corresponding tosylhydrazone lithium salt) produces a complex product mixture with the azine as the major product (51%). Volatile monomeric products biphenyl and several terphenyls were also formed in low yields.

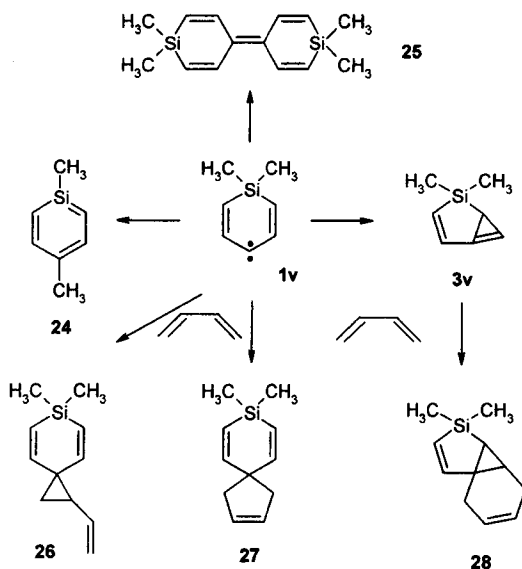
The formation of *o*-terphenyl is of special interest, and by isotopic labeling it was shown that this compound is formed by consecutive phenyl and hydrogen migrations. The key intermediate in this sequence of rearrangements is the formation of a highly strained isobenzene (Scheme 20). Several alternative mechanisms are not compatible with the observed distribution of isotopes and could thus be ruled out.¹⁰⁶



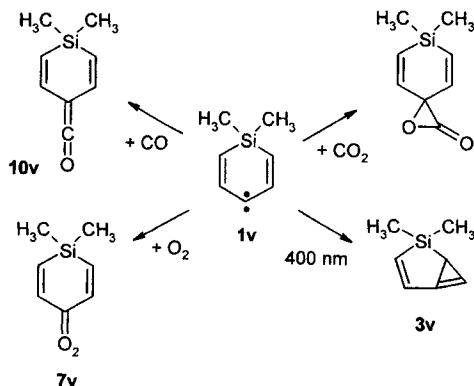
Scheme 20.

B. 4-Silacyclohexadienylidenes

4,4-Dimethyl-4-silacyclohexadienylidene (**1v**) is of interest as a potential source of silaxylene **24**, however, all attempts to convert the carbene into an aromatic compound failed.¹⁰⁷ The only isolated product from gas phase reactions is the dimer **25**. In solution, carbene **1v** was found to add stereospecifically to *cis*-2-butene. With butadiene as trapping reagent both the products of the 1,2- and 1,4-addition **26** and **27**, respectively, are observed (Scheme 21).¹⁰⁷ In addition, silacyclopentene **28** is formed, which is the trapping product of cyclo-



Scheme 21.



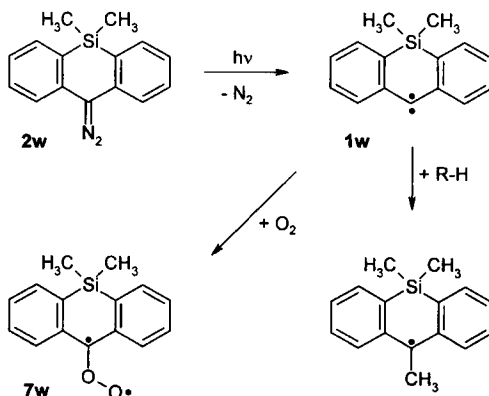
Scheme 22.

propene **3v**. This indicates a thermal vinylcarbene–cyclopropene rearrangement with carbene **1v** and cyclopropene **3v** being of similar energy.

The matrix photochemistry of **2v** proved to be fairly complicated.¹⁰⁸ The primary product of the photolysis of **2v** is carbene **1v**, which was identified by ESR spectroscopy. Under the conditions of matrix isolation the carbene showed the expected reactivity towards molecular oxygen (formation of carbonyl oxide **7v**) and carbon monoxide (formation of ketene **10v**) (Scheme 22). In contrast to the oxocyclohexadienylidenes (**1a** and derivatives) carbene **1v** slowly reacted with CO₂ to give an α -lactone with the characteristic C=O stretching vibration at 1896 cm⁻¹. The latter reaction indicates that **1v** is — as expected — more nucleophilic than **1a**.

Carbene **1v** is photolabile, and 400 nm irradiation produces a mixture of products.¹⁰⁸ By comparison with calculated IR spectra the major product was identified as cyclopropene **3v**. The formation of **3v** is irreversible, and it cannot be thermally (by annealing the matrix) nor photochemically converted back to carbene **1v**. The **1v** → **3v** rearrangement is calculated (B3LYP/6-31G(d) + ZPE) to be endothermic by only 5.4 kcal/mol with an activation barrier of 18.2 kcal/mol. Due to the two Si–C bonds in the five-membered ring of **3v** this cyclopropene is less strained than **3s**, which is reflected by the smaller destabilization relative to carbene **1v**. The thermal energy available at temperatures below 40 K is much too low to overcome the calculated barrier of 12.8 kcal/mol for the rearrangement of **3v** back to **1v**, and consequently **3v** is stable under the conditions of matrix isolation.

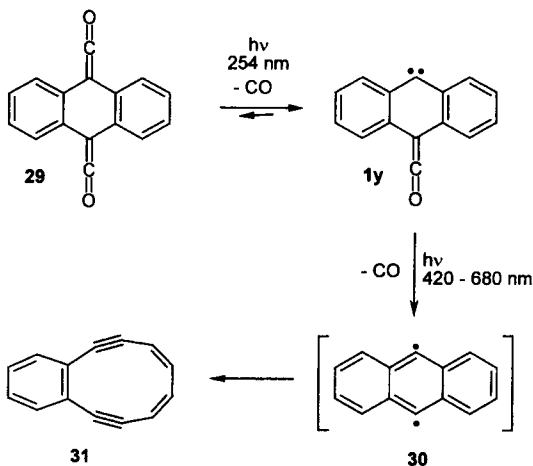
10-Silaanthracene-9(10H)-ylidene (**1w**) was investigated at room temperature in a LFP study and at 77 K in an organic glass (Scheme 23).^{109–111} Photolysis of diazo compound **2w** in an EPA glass at 77 K gives rise to an intense ESR signal of a triplet species which was assigned to carbene **1w**. The visible spectrum recorded under the same conditions exhibited a characteristic absorption with

**Scheme 23.**

a maximum at 510 nm. LFP of **2w** in degassed cyclohexane produces **1w**, which was identified by comparison of the transient UV/vis spectrum with that obtained in an EPA glass at 77 K. In solution the lifetime of **1w** is limited by hydrogen abstraction reactions with the solvent to 100 ns. In the presence of molecular oxygen carbene **1w** is trapped as carbonyl oxide **7w** with an absorption maximum at 425 nm.¹¹⁰

C. 4-Carbonyldibenzocyclohexadienylidene **1y**

9,10-Dihydro-9,10-dicarbonylanthracene (**29**) was proposed as a precursor for the matrix isolation of 9,10-didehydroanthracene (**30**) (Scheme 24).¹¹² In

**Scheme 24.**

a later study it was shown that **30** is not stable under these conditions and during irradiation of the precursor rearranges to the 10-annulene **31**.¹¹³ At higher temperatures the **30** $\rightarrow$ **31** rearrangement is reversible,¹¹⁴ and **31**, which is estimated to be thermodynamically less stable than **30** by 6–8 kcal/mol, is formed in low equilibrium concentrations. As a diradical, **30** is much more reactive towards hydrogen atom donors than **31** and thus is rapidly trapped by the solvent to give anthracene.¹¹⁴ The identification of matrix-isolated **31** was achieved by independent synthesis and by calculation of the IR spectra with DFT methods.¹¹³

The decarbonylation of bisketene **29** proceeds in two consecutive steps with carbonylcarbene **1y** being the key intermediate. By using monochromatic UV irradiation (254 nm) for the decarbonylation of **29**, substantial yields of **1y** are obtained in the matrix. Carbene **1y** exhibits several long-wavelength absorptions in the red (558, 572 nm) and blue (436 nm) region of the spectrum and thus proved to be highly labile towards broad-band visible irradiation, which leads to loss of the second CO molecule and formation of **31**. Annealing a matrix containing **1y** and CO to 35–40 K results in a thermal reaction with CO and formation of the starting material **29**. The carbonylation of **1y** was estimated to be exothermic by 54.4 kcal/mol.

According to DFT calculations, the singlet and triplet states of **1y** are almost degenerate, and after taking the errors of ΔE_{ST} for other carbenes at this level of theory into account, the singlet state is estimated to be 2 kcal/mol more stable than the triplet state. Since the IR spectrum calculated for the closed shell singlet state nicely reproduces the experimental spectrum, carbene **1y** is assigned a singlet ground state. Thus, carbene **1y** is the only derivative of a 2,5-cyclohexadienylidene with a singlet ground state observed experimentally.

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DIFFERENCES BETWEEN PHENYLCARBENE AND PHENYLNITRENE AND THE RING EXPANSION REACTIONS THEY UNDERGO

William L. Karney and Weston Thatcher Borden

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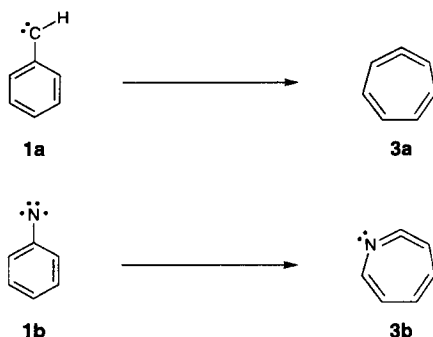
I. INTRODUCTION

The intriguing chemistry of carbenes and nitrenes has inspired a vast and impressive body of research. Arylcarbenes and arylnitrenes have been of particular interest, because they undergo intramolecular reactions that lead to other exotic species.^{1,2} The parent systems, phenylcarbene (**1a**) and phenylnitrene (**1b**), have attracted considerable attention from both experimentalists and theoreticians, with the result being that we now understand a great deal about the fascinating chemistry of these species.³ Both molecules undergo ring expansion to cyclic cumulenes.⁴ As shown in Scheme 1, phenylcarbene (**1a**) rearranges to 1,2,4,6-cycloheptatetraene (**3a**),¹ and phenylnitrene (**1b**) rearranges to 1-aza-1,2,4,6-cycloheptatetraene (**3b**).²

In this chapter we describe experimental studies on the ring expansion reactions of phenylcarbene and phenylnitrene and the calculations that have been performed in order to try to explain the experimental results. Our aim is to show how theory can rationalize these observations and can also serve to stimulate additional experiments by predicting their outcome. We will attempt to demonstrate that an understanding of the fundamental differences between the electronic structures of phenylcarbene and phenylnitrene can explain the many differences in the chemistry of these reactive intermediates.

II. EXPERIMENTAL AND EARLY THEORETICAL STUDIES

Before discussing recent studies on the ring expansion reactions of phenylcarbene and phenylnitrene, we will describe some of the earlier experimental and theoretical work on these molecules. Our purpose here is to give a brief overview, in order to provide a context for the discussion of more recent results. For detailed descriptions of the chemistry of arylcarbenes and arylnitrenes, we refer the reader to the many excellent reviews in this area.^{1,2}



Scheme 1.

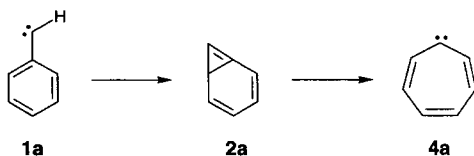
A. Ring Expansion of Phenylcarbene

Experiments. Experiments in the 1960s established that high-temperature gas-phase pyrolysis of phenyldiazomethane yields a ring-expanded product.⁵ The product was initially thought to be a seven-membered-ring carbene, cycloheptatrienylidene (**4a**),⁵ which perhaps arose via ring opening of a bicyclic cyclopropene intermediate (**2a**, Scheme 2).⁶

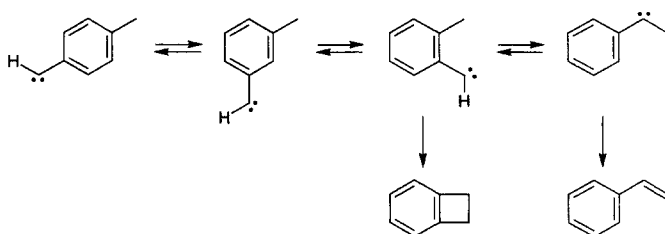
It was also found that the ring expansion could be accomplished photochemically, from either phenyldiazomethane or triplet phenylcarbene.⁷ Both the thermal and photochemical ring expansions were found to be reversible,^{5c,7} thus providing rare examples of carbene-to-carbene interconversions. One remarkable example of this reversibility is the interconversion of the isomeric tolylcarbenes upon pyrolysis — the ultimate products of which include styrene and benzocyclobutene (Scheme 3).^{6,8,9}

Another example of the reversibility of the ring expansion — one of special relevance to this chapter — is found in the interconversion of the isomeric pyridylcarbenes, and their conversion to phenylnitrene (Scheme 4).^{10,11}

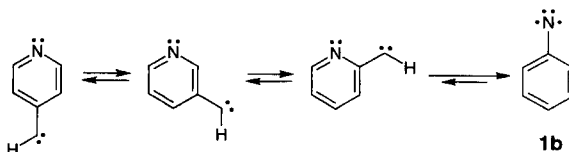
In both of these examples, the interconversions were thought to occur via methylcycloheptatrienylidene or azacycloheptatrienylidene intermediates analo-



Scheme 2.



Scheme 3.



Scheme 4.

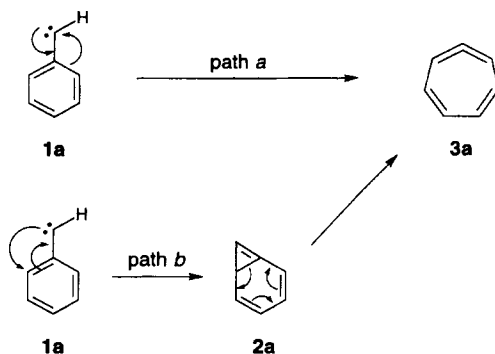
gous to **4a**.^{8a,10} In the 1980s, however, Orville Chapman and co-workers employed matrix isolation spectroscopy to show that the product of ring expansion of phenylcarbene is not carbene **4a**, but rather the cyclic allene, 1,2,4,6-cycloheptatetraene (**3a**),⁷ shown in Scheme 1. Chapman and co-workers then went on to show that the same type of cyclic allene is the key intermediate connecting the isomeric tolylcarbenes.⁹ Warmuth and co-workers have recently carried out the photochemical ring expansion of phenylcarbene inside a hemicarcerand host, and have obtained the NMR spectrum of **3a**.¹²

With the identity of the ring-expanded product established with some confidence, several important questions about phenylcarbene (**1a**) still remained. These included:

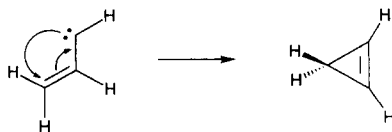
- (i) the magnitude of the singlet–triplet energy gap in **1a**,
- (ii) the precise mechanism of the ring expansion of the singlet carbene,
- (iii) the role, if any, of the cyclic carbene, cycloheptatrienyldiene (**4a**), in this reaction.

Triplet phenylcarbene (³**1a**) has been characterized spectroscopically in low-temperature matrices,^{7,13} and its heat of formation has been determined in the gas phase.¹⁴ ESR has established the triplet as the ground state.¹³ In contrast, the singlet state of **1a** has so far eluded direct detection. The fact that the solution chemistry of phenylcarbene is dominated by the singlet state suggests that this state is fairly close in energy to the triplet.¹⁵ This energy difference has been estimated to be approximately 2–5 kcal/mol.^{1h,2e,15} Using data from laser flash photolysis (LFP) of phenyldiazomethane in CF₂ClCFCl₂, Platz and co-workers have deduced that singlet **1a** lies 2.3 kcal/mol higher in energy than the triplet.¹⁶

One of the central problems in the chemistry of the singlet state of **1a** was the mechanism of the ring expansion reaction that it undergoes.^{1h} In particular, chemists sought to determine whether the ring expansion takes place in a single step, or in two steps via a bicyclic cyclopropene intermediate (Scheme 5).¹⁷



Scheme 5.



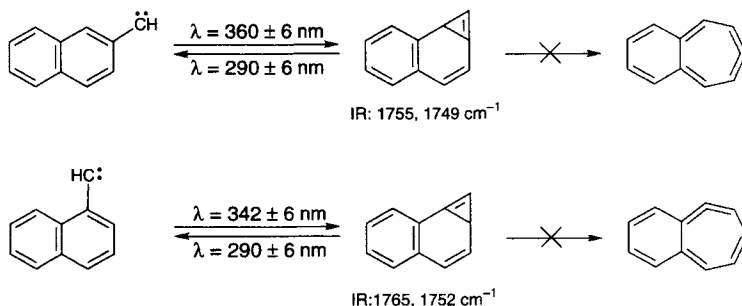
Scheme 6.

The one-step mechanism, depicted in path *a*, consists simply of a 1,2-shift of an *ortho* carbon. While this process is an all-carbon version of the Wolff rearrangement, the bond order of the migrating bond is substantially greater than 1.0. Hence this would represent an unprecedented reaction of carbenes.

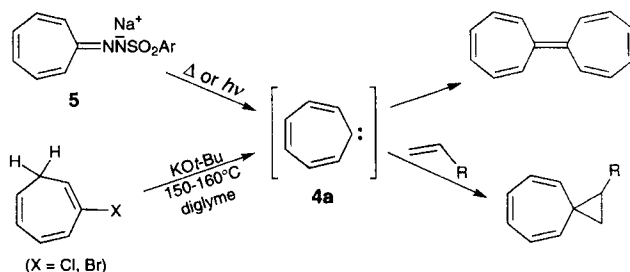
The two-step process, depicted by path *b*, involves initial addition of the carbene carbon to an adjacent π bond to form bicyclo[4.1.0]hepta-2,4,6-triene (**2a**). This process has precedent in the analogous rearrangement of vinylcarbene to cyclopropene (Scheme 6),^{1c,18} and is supported by Gaspar's work on 1-cyclohexenylcarbene.¹⁷ In the second step of the mechanism in Scheme 5, subsequent six-electron electrocyclic ring opening of **2a** yields the cyclic allene **3a**.

The proposed^{5b,6,8a} intermediacy of bicyclo[4.1.0]hepta-2,4,6-triene (**2a**) is consistent with all of the available experimental data, but **2a** has so far eluded detection. However, benzannelated derivatives of **2a** have been both chemically trapped¹⁹ and spectroscopically characterized at low temperatures.²⁰ For example, McMahon and co-workers have demonstrated the photochemical interconversion of 2-naphthylcarbene with 2,3-benzobicyclo[4.1.0]hepta-2,4,6-triene and of 1-naphthylcarbene with 4,5-benzobicyclo[4.1.0]hepta-2,4,6-triene (Scheme 7).^{20b,c} In these two cases, the cyclopropene intermediates are stabilized against undergoing electrocyclic ring opening because, as shown in Scheme 7, this reaction would result in the loss of aromaticity in the remaining benzene ring.

The observation of bicyclic intermediates in the chemistry of the naphthylcarbenes suggests that **2a** may also lie along the reaction coordinate for ring expansion of phenylcarbene. Nevertheless, if **2a** is an energy minimum, the



Scheme 7.

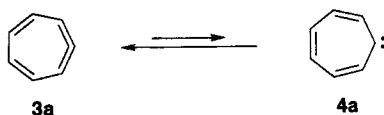
**Scheme 8.**

inability to detect it indicates that the potential energy well in which it lies must be very shallow indeed.

Another longtime subject of debate in C_7H_6 chemistry is the role of cycloheptatrienylidene (**4a**). As already mentioned, **4a** was initially viewed as the product of ring expansion of **1a**. Attempts were also made to generate **4a** directly. Upon pyrolysis or photolysis of the sodium salt of tropone tosylhydrazone (**5**), W.M. Jones and co-workers isolated heptafulvalene, the formal product of dimerization of **4a** (Scheme 8).²¹ In the presence of alkenes, decomposition of **5** or dehydrohalogenation of halocycloheptatrienes afforded mainly spirocyclopropane products, presumably formed by addition of **4a** to the alkene (Scheme 8).²²

Although the observed products are consistent with initial formation of **4a**, Untch proposed that they might arise via the intermediacy of cyclic allene **3a**.²³ Subsequent experiments by W.M. Jones and co-workers supported the initial formation of **3a** in the dehydrohalogenation reactions, but left open the possibility of a rapid equilibrium between cycloheptatetraene (**3a**) and cycloheptatrienylidene (**4a**, Scheme 9).^{22,24} It was also found that fusion of benzene or naphthalene rings to different positions on the seven-membered ring strongly influenced whether a carbenic or allenic structure predominates.²⁵

In the mid 1980s, both Wentrup^{11a} and Chapman²⁶ reported the characterization of triplet **4a** by low-temperature ESR spectroscopy. The spectra reported by the two groups differed substantially from each other, and Chapman's data was later found to be in error.²⁷ The triplet species observed by Wentrup's group did not obey the Curie law, and they suggested the possibility that warming the matrix containing **3a** results in its conversion to allene **3a**.

**Scheme 9.**

Semiempirical and Early Ab Initio Calculations. Until recently, almost all the theoretical studies on phenylcarbene (**1a**) and its ring expansion to **3a** employed semiempirical calculations²⁸ or *ab initio* calculations²⁹ performed at relatively low levels of theory, at least by current standards. Attempts to compute the singlet–triplet gap in phenylcarbene (**1a**) included Dewar and Landman's MINDO/3 result of $\Delta E_{\text{ST}} = 22.3$ kcal/mol (triplet ground state),^{28b} and Dannenberg's AM1 result of $\Delta E_{\text{ST}} = 11.5$ kcal/mol (triplet ground state).^{28f} These values are much higher than the current experimental estimates of $\Delta E_{\text{ST}} = 2\text{--}5$ kcal/mol.^{1i,2e,14–16}

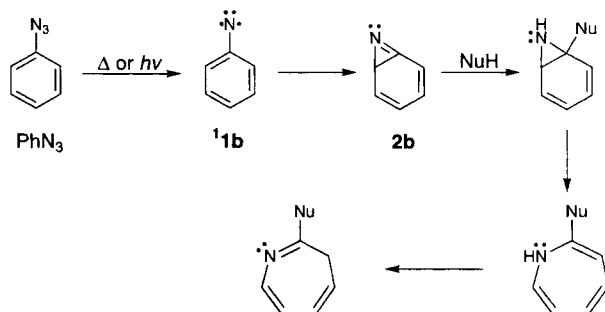
A few of these computational studies computed the energies of other species on the reaction path for ring expansion of **1a**.^{28a,b,c,d,e,29a} Combined force field-SCF calculations by Wentrup and co-workers supported the intermediacy of **2a**.^{28d} The most extensive of the early theoretical studies was the 1977 MINDO/3 study by Dewar and Landman.^{28b} They predicted a barrier for ring expansion of **1a** of about 6 kcal/mol, and a reaction exothermicity of 27 kcal/mol. In addition, their calculations suggested that the product of the ring expansion should be regarded as the cyclic allene **3a** rather than the cyclic carbene **4a**. Significantly, Dewar and Landman predicted the bicyclic structure **2a** to be the intermediate in a two-step mechanism for ring expansion. However, the tendency of the MINDO/3 method to underestimate strain in three-membered rings led the authors to qualify their conclusion regarding the intermediacy of **2a**.

The early calculations on cycloheptatrienylidene (**4a**) uniformly found it to be higher in energy than allene **3a**. INDO calculations by W.M. Jones and co-workers predicted carbene **4a** to be 14 kcal/mol less stable than allene **3a**.^{28a} Waali's MNDO calculations predicted that singlet **4a** is 23 kcal/mol less stable than **3a**, and that **4a** serves as a transition state for the enantiomerization of **3a**.^{28c,e} The HF/4-31G *ab initio* calculations of Radom et al. also found both singlet and triplet states of **4a** to be less stable than allene **3a**.^{29a}

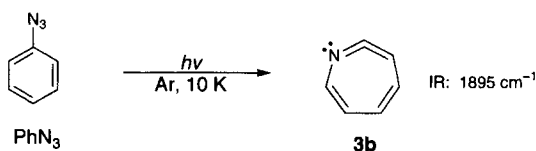
Radom and co-workers investigated two different triplet states of carbene **4a**, $^3\text{B}_1$ and $^3\text{A}_2$, and found the $^3\text{B}_1$ state to lie 1.1 kcal/mol below the $^3\text{A}_2$ state in energy.^{29a} Moreover, the $^3\text{B}_1$ state was predicted to be the ground state of **4a**, with the aromatic, closed-shell, singlet ($^1\text{A}_1$) state 11 kcal/mol higher in energy. However, SCF and two-configuration (TC) SCF/DZ+d calculations by Janssen and Schaefer predicted this singlet to be the ground state of **4a**, with $^3\text{B}_1$ lying ca. 5 kcal/mol higher in energy.³⁰

B. Ring Expansion of Phenylnitrene

Experiments. There are many parallels between the investigations — both experimental and theoretical — of the ring expansion of phenylnitrene and that of phenylcarbene. Huisgen and co-workers demonstrated in the late 1950s



Scheme 10.

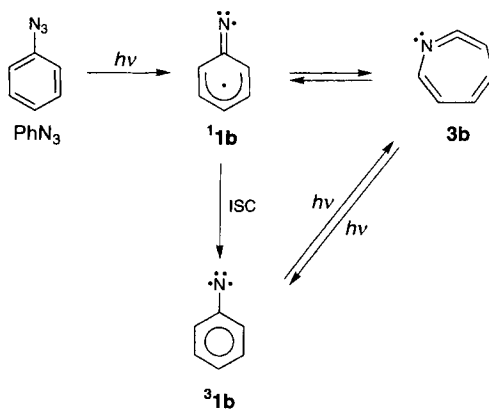


Scheme 11.

that thermolysis of phenyl azide (PhN_3) in the presence of nucleophiles affords ring-expanded products (Scheme 10).³¹ The photochemical version of the ring expansion, first reported by Doering and Odum,³² has been exploited for applications in synthesis, photoaffinity labeling, and photoresist technology.³³

As in the case of phenylcarbene, the details of the mechanism of ring expansion of phenylnitrene have been debated. The products of nucleophilic trapping following decomposition of phenyl azide were initially rationalized as arising from 7-azabicyclo[4.1.0]hepta-2,4,6-triene (**2b**, Scheme 10).³¹ This explanation was generally accepted in subsequent studies³⁴ and supported by calculations,³⁵ but in 1978, Chapman and LeRoux characterized 1-aza-1,2,4,6-cycloheptatetraene (**3b**) using matrix-isolation IR spectroscopy (Scheme 11).³⁶ The existence of the cyclic ketenimine⁴ **3b** was confirmed by later matrix³⁷ and solution³⁸ spectroscopic studies, which also established that **3b** is the species trapped by nucleophiles in solution.^{38c} Chapman's experiments found no evidence for the intermediacy of **2b**.³⁶

Other aspects of the mechanism have been clarified by various groups. The ring expansion has been shown to be a singlet process,³⁹ involving initial loss of nitrogen from PhN_3 to form singlet phenylnitrene (**1b**).⁴⁰ Intersystem crossing of singlet **1b** to the triplet ground state (**3b**) competes with thermal isomerization of singlet **1b** to **3b**.⁴¹ The electronic spectrum of singlet **1b** has recently been obtained using laser flash photolysis (LFP),⁴² and Gritsan and Platz have determined the barrier to rearrangement of **1b** to be 5.6 ± 0.3 kcal/mol, with an Arrhenius pre-exponential factor of $10^{13.1 \pm 0.3} \text{ s}^{-1}$.^{42c} They also were able to extract a value for the rate constant for intersystem crossing,



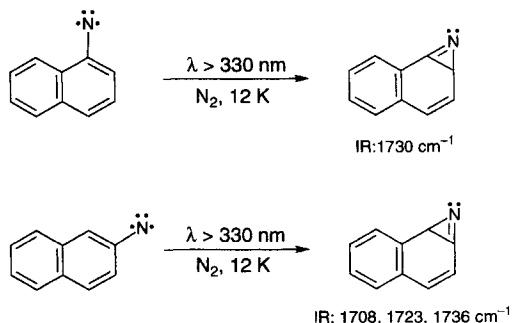
Scheme 12.

$k_{\text{ISC}} = 3.2 \pm 0.3 \times 10^6 \text{ s}^{-1}$, which is nearly four orders of magnitude smaller than k_{ISC} for phenylcarbene.

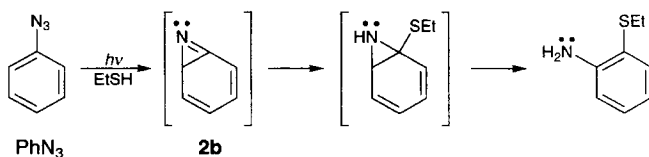
Ketenimine $\mathbf{3b}$ undergoes thermal reversion to triplet $\mathbf{1b}$ over time in solution at ambient temperature.³⁸ In addition, triplet $\mathbf{1b}$ and $\mathbf{3b}$ can be photochemically interconverted in a cryogenic matrix.⁴³ These results are summarized in Scheme 12.

The triplet ground state of phenyl nitrene ($^3\mathbf{1b}$) has been characterized by ESR⁴⁴, UV-Vis⁴⁵, and IR⁴³ spectroscopy. Photoelectron spectroscopy^{46a} and electron photodetachment^{46b} of the anion of $\mathbf{1b}$ have yielded a value of 18 kcal/mol for the singlet-triplet splitting (ΔE_{ST}) of $\mathbf{1b}$.

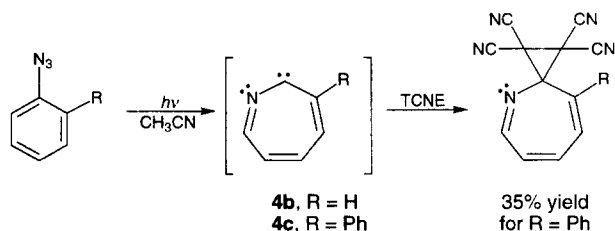
Similar to the case of bicyclo[4.1.0]heptatriene ($\mathbf{2a}$), the proposed³¹ bicyclic intermediate ($\mathbf{2b}$) in the ring expansion of $\mathbf{1b}$ has never been directly observed. However, the analogous azirines, formed by photolysis of 1- and 2-naphthyl azides, have been characterized by IR (Scheme 13),⁴⁷ and both trapping^{48a,b,c} and IR spectroscopic characterization^{48d} of substituted derivatives



Scheme 13.



Scheme 14.



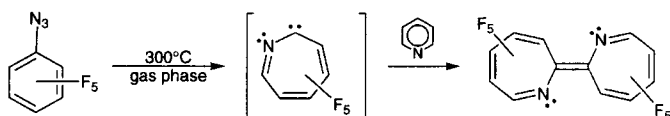
Scheme 15.

of **2b** have been reported.⁴⁸ The strongest evidence to date for the intermediacy of **2b** is the observation that photolysis of phenyl azide in ethanethiol affords *o*-thioethoxyaniline in 39% yield, presumably from nucleophilic trapping of **2b** (Scheme 14).^{48a}

Azacycloheptatrienylidene (**4b**), the aza analogue of cycloheptatrienylidene (**4a**), has on occasion been postulated to be the product of the ring expansion of **1b**.^{1a} In contrast to the case with ³**4a**,^{11a} ³**4b** has never been directly detected. However, Iwamura and co-workers have reported chemical trapping of **4b** and its *o*-phenyl derivative (**4c**) by tetracyanoethylene (TCNE), as shown in Scheme 15.⁴⁹ While the product in Scheme 15 is formally the product of reaction of **4b** with TCNE, the authors noted that it could also arise from reaction of TCNE with ketenimine **3b**.

Banks and co-workers found that gas-phase pyrolysis of pentafluorophenyl azide yields a diazaheptafulvalene (Scheme 16).⁵⁰ The formation of the product was viewed as dimerization of the perfluoro analogue of **4b**, although it is possible that it could, instead, have been formed by dimerization of the corresponding cyclic ketenimine.

Semiempirical Calculations. The C₆H₅N potential energy surface has received less attention from theoreticians than from experimentalists. Until recently, species on the reaction pathway for ring expansion of **1b** had been stud-



Scheme 16.

ied using only semiempirical methods.^{35,38c,51} MNDO calculations by Schuster and co-workers predicted the intermediacy of azabicycloheptatriene **2b** and placed azacycloheptatetraene **3b** below **2b** in energy.^{38c} Schuster's calculations found barriers of 12.4 and 3.6 kcal/mol for, respectively, the first and second steps of the ring expansion. The much lower barrier computed for the ring opening of **2b** to **3b** is consistent with the experimental finding that **3b**, not **2b**, is the species that is trapped in solution.^{38c}

Schuster and co-workers also performed calculations on azacycloheptatrienylidene (**4b**), the planar carbene 'isomer' of ketenimine **3b**. Based on their MNDO results, they proposed that the experimentally observed thermal reversion of **3b** to triplet phenylnitrene (³**1b**) occurs not via singlet **1b**, but rather via a triplet state of **4b**.^{38c} The theoretical work on cycloheptatrienylidene (**4a**)^{28a,c,29a,30} suggests that **4b** too may have several different low-lying spin states. The ground-state multiplicity of **4b** and the role, if any, of its low-lying electronic states in the transformations observed on the C₆H₅N energy surface represent intriguing questions.

C. Experimental Differences Between Phenylcarbene and Phenylnitrene

Although there are some similarities between phenylcarbene (**1a**) and phenylnitrene (**1b**), there are many more differences.³ For example, although both have triplet ground states, $\Delta E_{\text{ST}} = 2\text{--}5$ kcal/mol in **1a**^{15,16} is much smaller than $\Delta E_{\text{ST}} = 18$ kcal/mol in **1b**.⁴⁶ Perhaps more significant, the phenyl group in **1a** has a relatively small effect on reducing ΔE_{ST} from 9 kcal/mol in CH₂,⁵² compared to the effect of this substituent in **1b** on reducing ΔE_{ST} from 36 kcal/mol in NH.⁵³

As already noted, the rate of intersystem crossing to form the triplet from the lowest singlet is nearly four orders of magnitude larger for **1a**⁵⁴ than for **1b**.^{42c} Once formed, triplet **1a** abstracts hydrogen atoms;¹ triplet **1b** does not. Singlet **1a** adds to alkenes and to pyridine¹⁶ to form an ylide; intermolecular reactions of singlet **1b** have not been observed.

Despite the greater intermolecular reactivity of singlet and triplet **1a**, singlet **1b** undergoes ring expansion much faster than does singlet **1a**. For example, thermal ring expansion of singlet **1a** has been observed only in gas-phase pyrolyses;⁵ whereas, thermal ring expansion of singlet **1b** occurs rapidly at low temperatures.⁴¹ Given this large difference in the barriers to ring expansion, it is surprising that this reaction of **1a** is apparently only reversible at temperatures above 300°C; whereas, reversion of **3b** to singlet **1b**, followed by intersystem crossing to the triplet ground state, provides the most reasonable pathway for the observed formation of ³**1b** from **3b** in solution.

III. COMPUTATIONAL RESULTS ON THE MECHANISMS OF RING EXPANSION

In 1995, at the request of Professor Matthew Platz, we carried out calculations on the ring expansion of phenylnitrene (**1b**). For comparison, we decided to perform calculations on the ring expansion of phenylcarbene (**1a**) at the same levels of theory that we were using to explore the analogous reaction of **1b**. Late that summer, we learned that calculations on the rearrangement of phenylcarbene were also being performed by several other research groups, including those of Professors Bob McMahon, Thomas Bally, Curt Wentrup, Paul Schleyer, and Henry Schaefer. A spirited — and mutually supportive — exchange of data and ideas between these six groups ensued. Professors McMahon and Bally were the first to submit a manuscript; we pooled our results with those of Professors Schaefer and Schleyer; and Professor Wentrup published his separately. Thus, three papers on the ring expansion of phenylcarbene appeared in 1996.^{55–57} Happily, for the most part, all three reached the same conclusions.

A. Electronic Structures of the Lowest Singlet States of Phenylcarbene and Phenylnitrene

Phenylcarbene (1a). Just as in triplet methylene (CH_2), in triplet phenylcarbene ($^3\text{A}''\text{-1a}$) one electron occupies the $\text{p}-\pi$ atomic orbital on the carbene carbon and one electron occupies the in-plane σ hybrid orbital. However, in the lowest singlet state of CH_2 and of phenylcarbene ($^1\text{A}'\text{-1a}$), both electrons occupy the hybrid σ orbital, because this orbital is substantially lower in energy than the $\text{p}-\pi$ AO.

The difference in orbital occupancies makes the calculated geometries of $^3\text{1a}$ and $^1\text{1a}$ rather different from each other. The optimized geometries do not change significantly at different levels of theory; and the CASSCF(8,8)/6-31G* structures⁵⁷ are provided in Fig. 1.

While $^3\text{1a}$ has a large bond angle at the carbene carbon (130°) and a relatively short C–C bond to it ($1.416 \text{ \AA}$), $^1\text{1a}$ has a smaller bond angle at this carbon (106.8°) and a longer C–C bond to it ($1.462 \text{ \AA}$). The smaller carbene bond angle in $^1\text{1a}$ is the result of the greater 2s character in the hybrid σ orbital, caused by its occupancy by a pair of electrons, rather than just one, as in $^3\text{1a}$. The shorter exocyclic C–C bond in $^3\text{1a}$ is presumably due to delocalization of the electron in the $\text{p}-\pi$ carbene orbital into the benzene ring being greater than delocalization of benzene π electrons into the empty p orbital in $^1\text{1a}$. In both singlet and triplet **1a**, the geometry of the benzene ring is only slightly affected by the adjacent carbene substituent (Fig. 1).

Singlet–triplet splittings (ΔE_{ST}) for carbenes are notoriously difficult to

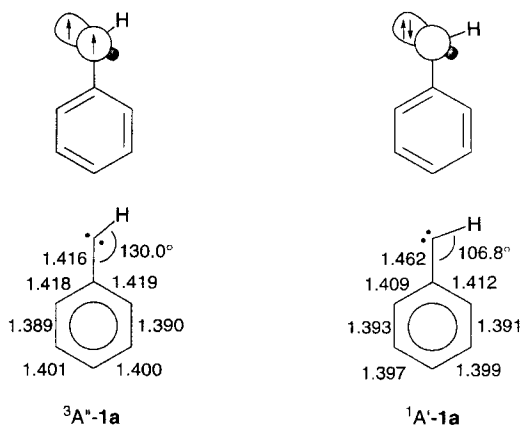


Figure 1. Orbital occupancies for the nonbonding electrons and CASSCF(8,8)/6-31G* optimized geometries of the lowest triplet and singlet states of phenylcarbene (**1a**).⁵⁷ Bond lengths in angstroms, and bond angles in degrees.

Table 1. Calculated Singlet–Triplet Energy Gap (ΔE_{ST} , kcal/mol) in Phenylcarbene (**1a**)^a

Method	ΔE_{ST}	Ref.
BLYP/6-31G*	5.4	55
BLYP/6-311+G(3df,2p)//BLYP/6-31G*	3.8	56
B3LYP/6-311+G*//B3LYP/6-31G*	5.0	57
BVWN5/cc-pVTZ//BVWN5/cc-pVDZ	4.3	59
CASSCF(8,8)/6-311G(2d,p)//CASSCF(8,8)/6-31G*	8.5	57
CASPT2(8,8)/6-311G(2d,p)//CASSCF(8,8)/6-31G*	12.5	57
G2(MP2,SVP)	1.4	56
corrected for $\Delta E_{ST}(\text{CH}_2)$ ^b	3.8	56
CCSD(T)/DZd//CISD/DZd	6.2	57
corrected for $\Delta E_{ST}(\text{CH}_2)$ ^b	2.4	57
CCSD(T)/cc-pVDZ//BLYP/6-31G*	4.5	55
CCSD(T)/cc-pVTZ(est.)//BLYP/6-31G* ^c	2.5	55
Experiment	2.3	16

Notes: ^a A positive value for ΔE_{ST} indicates a triplet ground state.

^b Obtained by subtracting the error in ΔE_{ST} for methylene (CH_2) calculated at the same level of theory.

^c Effects of extending the basis set from cc-pVDZ to cc-pVTZ were estimated based on CCSD/cc-pVTZ calculations.

compute accurately,⁵⁸ and phenylcarbene is no exception. Table 1 shows the results from a variety of computational methods that have been recently applied to the prediction of ΔE_{ST} for **1a**.^{55–57,59}

Especially with large basis sets, density functional theory (DFT) methods give reasonable agreement with the experimental ΔE_{ST} . On the other hand, CASPT2 does a poor job of reproducing the experimental singlet–triplet gap in **1a**. The known tendency of the CASPT2 method to overestimate the stability of open-shell states relative to closed-shell species⁶⁰ causes $^3A''$ -**1a** to be computed by CASPT2 to be unrealistically low in energy, relative to $^1A'$ -**1a**. The best agreement with experiment (without any empirical corrections) is obtained at the CCSD(T)/cc-pVTZ(est.)/BLYP/6-31G* level of theory, in which the effects of extending the basis set from cc-pVDZ to cc-pVTZ were estimated using the results of CCSD calculations.⁵⁵

Phenylnitrene (1b). In phenylnitrene, a lone pair occupies a hybrid orbital, rich in 2s character. Unlike the case in **1a**, the two nonbonding electrons in **1b** both occupy pure 2p orbitals. One of these is a p- π orbital, and the other a p orbital on nitrogen that lies in the plane of the benzene ring. The near-degeneracy of the two 2p orbitals gives rise to three low-lying spin states in **1b** — a triplet ($^3A_2$), an open-shell singlet ($^1A_2$), and a closed-shell singlet ($^1A_1$). The orbital occupancies and CASSCF(8,8)/6-31G* geometries of these states are shown in Fig. 2.⁶¹ In the $^3A_2$ and $^1A_2$ states, the p- π orbital and the in-plane p orbital on N are both singly occupied. The $^1A_1$ state of **1b** is a mixture of two dominant configurations — one in which the in-plane p orbital on N is doubly occupied and the p- π orbital is empty, which is slightly lower in energy than the other configuration in which these orbital occupancies are reversed. In both the $^3A_2$ and $^1A_1$ states the C–N bond is relatively long, and the phenyl ring shows little bond-length alternation. In the $^1A_2$ state, however,

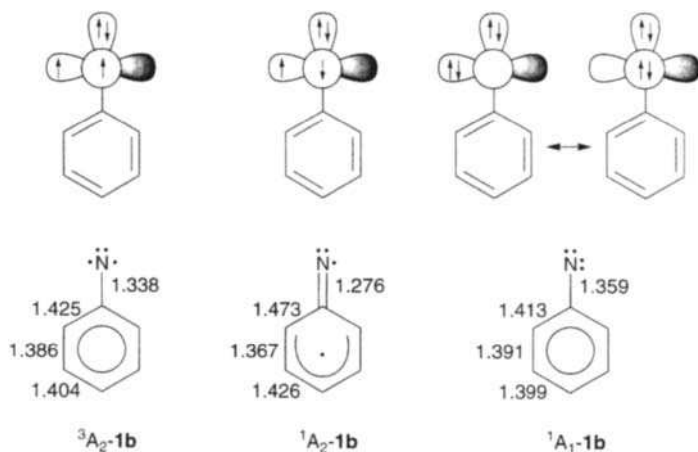


Figure 2. Orbital occupancies for the nonbonding electrons and CASSCF(8,8)/6-31G* optimized geometries of the lowest triplet and singlet states of phenylnitrene (**1b**).⁶¹ Bond lengths in angstroms, and bond angles in degrees.

Table 2. Relative Energies (kcal/mol) of the Lowest Spin States of Phenylnitrene (**1b**)

Method	Electronic state			Ref.
	$^3A_2$	$^1A_2$	$^1A_1$	
CISD+Q/DZ+d	0	18.3	32.4	62a
σ -S, π -SDCI/6-31G [*] //CASSCF(8,8)/3-21G	0	18.3	38.7	62b
DDCI/6-31G [*] //CASSCF(8,8)/3-21G	0	18.3	30.6	64
CASSCF(8,8)/6-31G [*]	0	17.5	42.2	61
CASPT2(8,8)/6-311G(2d,p)//CASSCF(8,8)/6-31G [*]	0	18.5	36.9	61
BLYP/cc-pVTZ//BLYP/cc-pVDZ	0	–	29.5	65
CCSD(T)/cc-pVDZ//CASSCF(8,8)/cc-pVDZ	0	–	35.2	65
Experiment	0	18 $\pm$ 2	30 $\pm$ 5	46a
	0	18.3 $\pm$ 0.7	–	46b

a very short C–N bond (1.276 Å) and benzene ring bond lengths that resemble those of a cyclohexadienyl radical, indicate almost complete delocalization of the electron in the nitrogen p- π orbital into the ring.^{62b}

In NH, $^1A_1$ and $^1A_2$ are degenerate and form the two components of a $^1\Delta$ state, but in phenylnitrene $^1A_2$ lies well below $^1A_1$. In $^1A_2$, delocalization into the benzene ring of the electron in the singly occupied p orbital confines this electron and the opposite-spin electron on nitrogen to different regions of space, thus minimizing their mutual Coulomb repulsion energy.⁶³ This strong delocalization in $^1A_2$ accounts for the difference between the bond lengths in it and $^3A_2$.⁶²

The calculated^{61,62,64,65} and experimentally determined⁴⁶ relative energies of the spin states of phenylnitrene are shown in Table 2. All levels of theory shown predict the lowest singlet state ($^1A_2$) to lie about 18 kcal/mol higher in energy than the triplet ground state ($^3A_2$), in excellent agreement with the results of photoelectron spectroscopy.⁴⁶ Predictions for the relative energy of the $^1A_1$ state vary substantially, with the DFT result of 29.5 kcal/mol⁶⁵ (relative to the $^3A_2$ state) apparently giving the best agreement with the experimental estimate of Ellison and co-workers.^{46a}

Differences Between the Electronic Structures of 1a and 1b. Although both phenylcarbene (**1a**) and the isoelectronic phenylnitrene (**1b**) have triplet ground states, the lowest singlet is the closed-shell $^1A'$ state in **1a**, but the open-shell $^1A_2$ state in **1b**. This difference between the carbene and the nitrene can be ascribed to the fact that in singlet **1a** the two non-bonding electrons can occupy a hybrid AO; whereas, in **1b** the two nonbonding electrons occupy pure p orbitals. Therefore, the near degeneracy of the nonbonding MOs in **1b** is strongly lifted in **1a**, and both nonbonding electrons in **1a** preferentially occupy the σ orbital, which is lower in energy than the p- π orbital.³ As a result of the lifting of

the orbital degeneracy in **1a**, the energy difference between the lowest singlet and the triplet state is much smaller in **1a** ($\Delta E_{\text{ST}} \approx 2 \text{ kcal/mol}^{16}$) than in **1b** ($\Delta E_{\text{ST}} \approx 18 \text{ kcal/mol}^{46}$).

The smaller value of ΔE_{ST} in **1a** than in **1b** contributes to the much faster rate of intersystem crossing in phenylcarbene⁵⁴ than in phenylnitrene.^{42c} However, another contributor is the difference between the nature of the lowest singlet states in **1a** and **1b**. The transition of an electron from a σ orbital in the $^1A'$ state of **1a** to a π orbital in the $^3A''$ state creates orbital angular momentum, which facilitates the change in spin angular momentum by spin-orbit coupling.⁶⁶ In contrast, the $^1A_2$ and $^3A_2$ states of **1b** have the same orbital occupancy; so there is no change in orbital angular momentum to facilitate intersystem crossing.

The difference in orbital occupancies between the lowest singlet states of **1a** and **1b** is also responsible for the much greater intermolecular reactivity of the former compared to the latter.³ The empty π non-bonding molecular orbital (NBMO) in the $^1A'$ state of **1a** makes it highly electrophilic, like most singlet carbenes. In contrast, in the $^1A_2$ state of **1b**, one electron occupies each NBMO, thus making the lowest singlet state of phenylnitrene much less electrophilic and more radical-like than the lowest singlet state of phenylcarbene. The reason for the unreactivity of both ^1b and ^3b toward hydrogen abstraction is discussed in Section IV.

Surprisingly, as noted in Section II.C, the intramolecular reactivity toward ring expansion in the lowest singlet state is much larger in **1b** than in **1a**. This difference is also a consequence of the difference between the electronic structures of the lowest singlet states of **1a** and **1b**, and the effect of this difference on the rate-determining step of the ring expansion reaction that each undergoes.⁶¹

B. Calculations on the Ring Expansion of Phenylcarbene

As noted in the introduction to this section, in 1996 three groups published computational results on the ring expansion of phenylcarbene.^{55–57} Matzinger et al. performed calculations at the CCSD(T)/cc-pVTZ(est.)/BLYP/6-31G* level,⁵⁵ Wong and Wentrup employed the G2(MP2,SVP) method,⁵⁶ and Schreiner et al. used CASPT2(8,8)/cc-pVDZ//CASSCF(8,8)/6-31G* as their highest level of theory.⁵⁷ Although the three groups used different computational methods, the results that they obtained were very similar, as shown in Fig. 3.

All three levels of theory predict the ring expansion of singlet phenylcarbene ($^1A'$ -**1a**) to cycloheptatetraene (**3a**) to occur in two steps, via bicyclo[4.1.0]hepta-2,4,6-triene (**2a**) as an intermediate. The first step is addition of the carbene carbon to an adjacent π bond of the ring. The second step involves a six-electron, disrotatory, electrocyclic ring opening, which is allowed by orbital symmetry⁶⁷ and thus proceeds by a highly delocalized transition state. Fig. 4

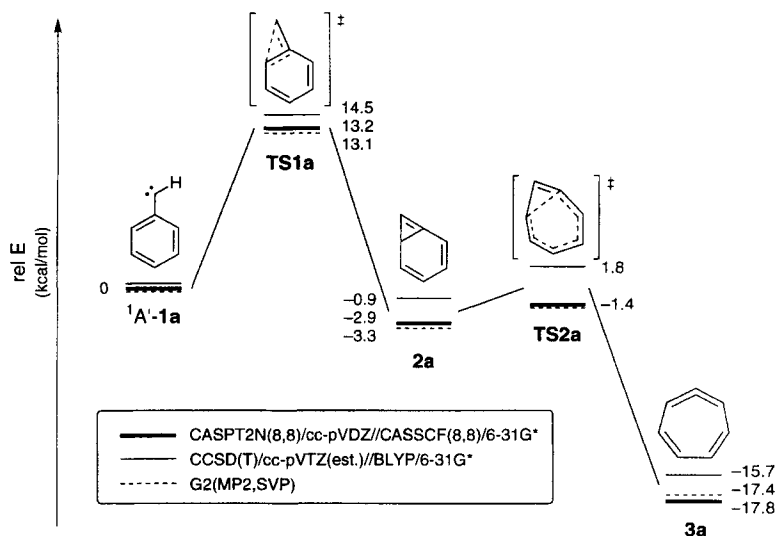


Figure 3. Energetics of the ring expansion of singlet phenylcarbene ($^1A'-1a$), calculated at different levels of theory.^{55–57}

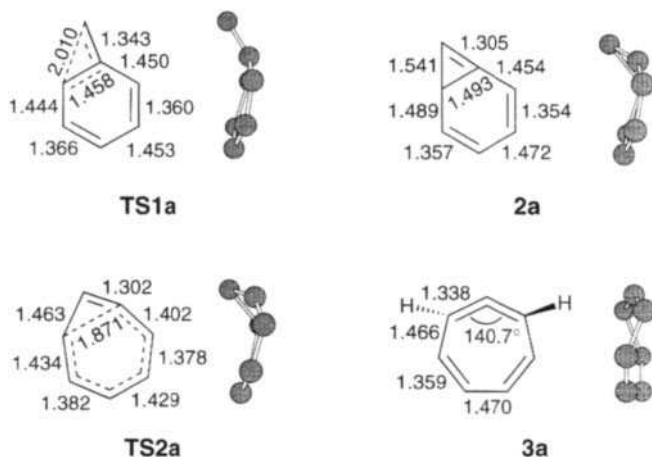


Figure 4. CASSCF(8,8)/6-31G* optimized geometries of stationary points in the ring expansion of singlet phenylcarbene ($^1A'-1a$).⁵⁷ Bond lengths in angstroms, and bond angles in degrees. The ball-and-stick pictures are profiles that indicate the nonplanar nature of these species.

depicts the CASSCF geometries of the stationary points along the reaction path.

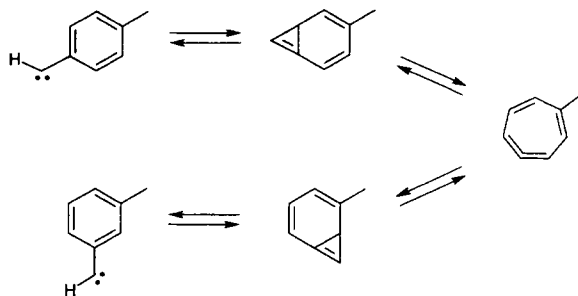
As shown in Fig. 3, all three methods predict a moderate barrier of 13–15 kcal/mol for the first step, followed by a small barrier of 1.5–3 kcal/mol for the

second step, and a substantial overall reaction exothermicity of 16–18 kcal/mol. These results suggest that, after its formation via **TS1a**, the bicyclic intermediate **2a** would have more than enough energy to surmount the barrier, corresponding to **TS2a**, and form cycloheptatetraene (**3a**). Combined with the prediction that **3a** is 14–15 kcal/mol more stable than **2a**, this explains why **2a** has not yet been detected and suggests that its future observation as an intermediate in the ring expansion of **1a** is unlikely. The large exothermicity computed for the ring expansion of **1a** to **3a** provides the explanation for why the thermal reversion of **3a** to **1a** has not been observed, except at very high temperatures.^{6,8,9}

In support of Chapman's assignment⁷ of the matrix infrared spectrum of the product formed from **1a**, the calculations of Matzinger et al. found that the experimental IR spectrum agrees well with the spectrum calculated for **3a**, but not with that computed for **2a**.⁵⁵ The calculations for **3a** reproduced the weak allene stretching band that Chapman et al. observed at 1823 cm⁻¹.

The experimental work of Chapman and co-workers,^{7,9} the recent computational support for the intermediacy of bicyclo[4.1.0]heptatriene,^{55–57} and the energetics in Fig. 3 allow us to write a more detailed mechanism for the interconversion of the isomeric tolylcarbenes and the formation of benzocyclobutene and styrene than the one shown in Scheme 3. The steps involved in the interconversion of the *para*- and *meta*-tolylcarbenes according to this more detailed mechanism are shown in Scheme 17.

The calculations of Xie et al. on the rearrangements of 1- and 2-naphthylcarbene⁶⁸ explain the reluctance of these species to undergo ring expansion.^{7,20} As shown in Scheme 7, the second step in these ring expansions destroys the aromaticity of the remaining benzene ring, and this step is therefore calculated to be endothermic.⁶⁸ This endothermicity is in marked contrast to the low barrier and high exothermicity for the rearrangement of **2a** to **3a** in the ring expansion of **1a**.



Scheme 17.

C. Calculations on the Ring Expansion of Phenylnitrene

Our calculations on the ring expansion of the lowest singlet state of phenylnitrene ($^1A_2$ -**1b**) to azacycloheptatetraene (**3b**) predict a two-step mechanism that is analogous to that for the rearrangement of **1a** to **3a** and which involves the bicyclic azirine intermediate **2b**.⁶¹ The CASPT2 energetics are depicted in Fig. 5, and the CASSCF optimized geometries of the stationary points are shown in Fig. 6.

The first step — cyclization of **1b** to the azirine **2b** — is predicted to be the rate-determining step. The CASPT2 calculated barrier of 9.2 kcal/mol is

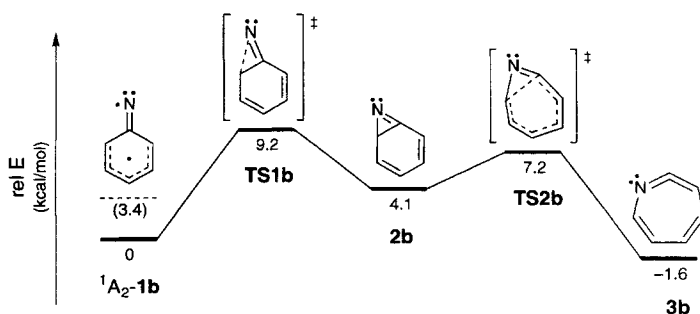


Figure 5. Energetics of the ring expansion of singlet phenylnitrene ($^1A_2$ -**1b**), calculated at the CASPT2(8,8)/6-311G(2d,p)//CASSCF(8,8)/6-31G* level.⁶¹

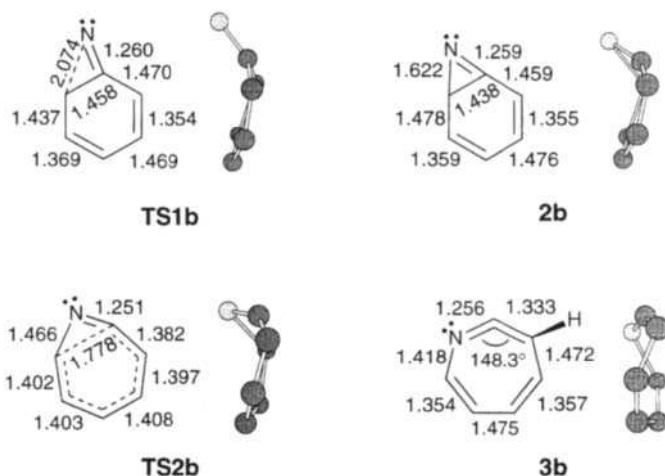


Figure 6. CASSCF(8,8)/6-31G* optimized geometries of stationary points in the ring expansion of singlet phenylnitrene ($^1A_2$ -**1b**).⁶¹ Bond lengths in angstroms, and bond angles in degrees. The ball-and-stick pictures are profiles that indicate the nonplanar nature of these species.

somewhat higher than the experimental barrier of 5.6 ± 0.3 kcal/mol measured by Gritsan and Platz.^{42c} The discrepancy between the calculated and experimental barrier heights is due to the general tendency of the CASPT2 method to overstabilize open-shell species (in this case, $^1\text{A}_2\text{-1b}$) relative to closed-shell species (in this case, all the other stationary points on the reaction path).⁶⁰

This was confirmed by comparing the CASPT2 and multi-reference (MR)-CISD+Q⁶⁹ energy differences between open-shell singlet ($^1\text{A}''$) vinylnitrene and 2*H*-azirine.⁶¹ The nitrene and azirine serve as models for $^1\text{A}_2\text{-1b}$ and **2b**, respectively. This comparison with MR-CISD+Q showed that CASPT2 underestimates the energy of the open-shell nitrene reactant relative to the closed-shell 2*H*-azirine product by 3.4 kcal/mol. If the relative energy of $^1\text{A}_2\text{-1b}$ is also too low by a comparable amount, then a better computational estimate of the barrier for the first step in the ring expansion of **1b** would be ca. 5.8 kcal/mol, in excellent agreement with the experimental value of 5.6 ± 0.3 kcal/mol.

The CASPT2/6-311G(2d,p) barrier for the process **2b** $\rightarrow$ **3b** is only ca. 3 kcal/mol, and this reaction is calculated to be exothermic by about 6 kcal/mol. These computational results are consistent with the failure of Schuster's time-resolved IR experiments to detect **2b**.^{38b,c} A barrier of 3 kcal/mol implies rapid conversion of **2b** to **3b** at room temperature, and a 6 kcal/mol difference in energy between **2b** and **3b** means that at 25°C the equilibrium would overwhelmingly favor **3b**. In addition, azirine **2b** probably absorbs less strongly than cyclic ketenimine **3b** in the infrared, thus rendering detection of the azirine even more difficult.

As shown in Fig. 5, even if the MRCI-derived upward correction of 3.4 kcal/mol to the energy of $^1\text{A}_2\text{-1b}$ is included, the energy difference between $^1\text{A}_2\text{-1b}$ and **3b** is estimated to be only 5 kcal/mol. Therefore, at equilibrium, a small amount of singlet **1b** should be present at ambient temperatures. Intersystem crossing of singlet **1b** to triplet **1b** should then lead to the irreversible conversion of **3b** to the triplet ground state of **1b**. As already mentioned, the reversion of **3b** to triplet **1b** has, in fact, been observed in inert solvents.³⁸

D. Comparison of the Calculated Energetics of the Two Ring Expansion Reactions

While the ring expansions of phenylcarbene and phenylnitrene proceed by similar mechanisms, there are significant differences between the relative energies of the species involved in these reactions. Fig. 7 displays the energetics for both systems calculated at the CASPT2 level of theory,^{57,61} with corrections shown for the known deficiencies of CASPT2 in computing the energies of singlet phenylnitrene⁶¹ and singlet phenylcarbene.⁵⁵

The corrected CASPT2 energies in Fig. 7 show that the ring expansion of **1b** to **3b** is calculated to be 11 kcal/mol less exothermic than that of **1a** to **3a**.

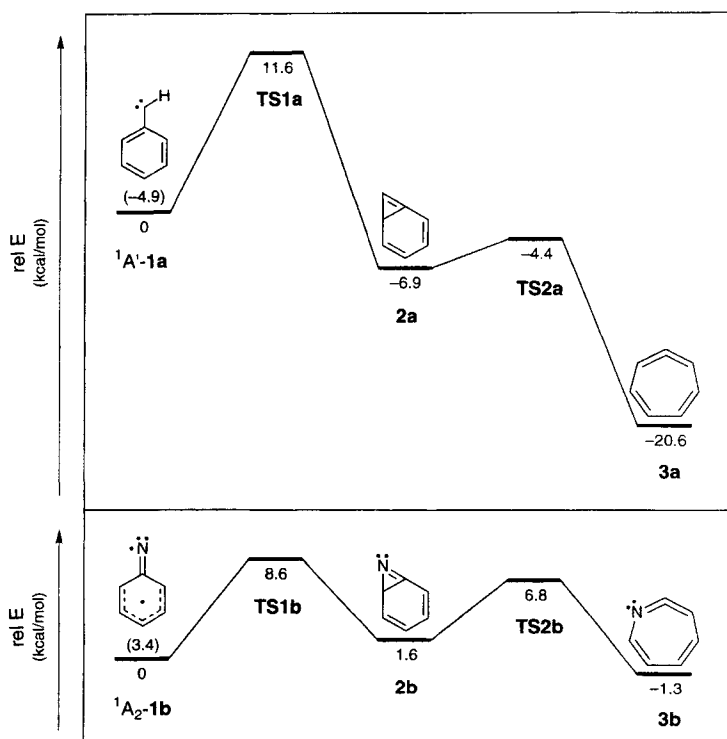
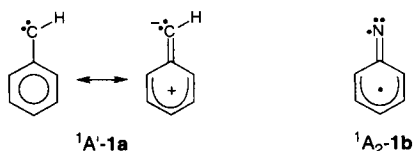


Figure 7. Comparison of the energetics of the ring expansions of phenylcarbene ($^1A'-1a$) and phenylnitrene ($^1A_2-1b$), calculated at the CASPT2(8,8)/6-31G^{*}//CASSCF(8,8)/6-31G^{*} level.^{57,61} The numbers in parentheses represent corrections for the known deficiencies of CASPT2/6-31G^{*} in computing the energies of singlet phenylnitrene⁶¹ and singlet phenylcarbene.⁵⁵ The small differences in the energies in Fig. 5 are a consequence of the difference between the basis sets used in the two sets of calculations.

In addition, the ring opening of **2b** to **3b** is computed to be ca. 10 kcal/mol less exothermic than that of **2a** to **3a**. In order to understand the reasons for these differences, we calculated a number of isodesmic reactions. The results of these calculations suggested that (i) the cyclic cumulenes **3a** and **3b** have similar amounts of strain; and (ii) the bicyclic azirine **2b** is about 10 kcal/mol more thermodynamically stable than the bicyclic cyclopropene **2a**, due to bond angles at imine nitrogens generally being smaller than bond angles at alkene carbons. The implication of these comparisons is that (iii) singlet **1b** is 11 kcal/mol 'more stable' than singlet **1a**. This conclusion is discussed in Section IV.

In the ring expansions of both **1a** and **1b**, the first step is predicted to be rate-determining. If one accounts for the deficiencies of the CASPT2 method, the best estimate is that phenylcarbene (**1a**) has a barrier to intramolecular

reaction that is ca. 10 kcal/mol higher than that in phenylnitrene (**1b**, Fig. 7).⁶¹ This is consistent with the much faster rate of ring expansion of **1b** compared to **1a**.³ The reason for this is that, as discussed in Section III.A, **1a** reacts from a closed-shell singlet state ($^1A'$), whereas the singlet state from which **1b** reacts is open-shell ($^1A_2$). Since **1a** reacts from the $^1A'$ electronic state, closure of the three-membered ring requires that the contribution of the higher energy ionic resonance structure for $^1A'-\mathbf{1a}$ (shown below) increases along the reaction coordinate. In contrast, the resemblance of $^1A_2-\mathbf{1b}$ to a cyclohexadienyliminyl diradical (Fig. 1 and below) means that formation of the three-membered ring in this case requires only closure of an N–C–C bond angle.



E. Calculations on Cycloheptatrienylidene (**4a**)

The nature and role of cycloheptatrienylidene (**4a**) has been a tantalizing puzzle to chemists since the 1960s. An appreciation for the reasons why begins with a consideration of the π, π^* , and carbenic nonbonding molecular orbitals of **4a**, depicted in Fig. 8.

After filling of the $1b_1$, $2b_1$, and $1a_2$ bonding π MOs, the last two electrons must be distributed between the a_1 , $3b_1$, and $2a_2$ orbitals. As depicted in Fig. 8, the carbene hybrid orbital (a_1) is lower than but close in energy to the $3b_1$ and $2a_2$ π^* MOs. Five electronic states are thus worthy of consideration: $^1A_1$, $^1A_2$, $^1B_1$, $^3A_2$, and $^3B_1$. The electron configurations of these states and the CASSCF optimized geometry of each are shown in Fig. 9.⁵⁷

The questions regarding these states that need to be addressed include:

(i) What are the relative energies of the three singlet states? Is each a minimum, or a transition state; and, if the latter, for what process is it a transition state?

(ii) Which of the two triplets, $^3B_1$ or $^3A_2$, is the metastable state that was detected by Wentrup's EPR experiments?

(iii) Which of the five states shown in Fig. 9 is the ground state of **4a**?

Since the five spin states for cycloheptatrienylidene include both singlet and triplet species, and since two of the states are open-shell singlets, this carbene poses a formidable challenge for calculations. There are, as yet, no methods available that can be applied to systems as large as **4a** and that are capable of treating triplets, closed-shell singlets, and open-shell singlets in a sufficiently balanced way, so as to give quantitatively accurate predictions of

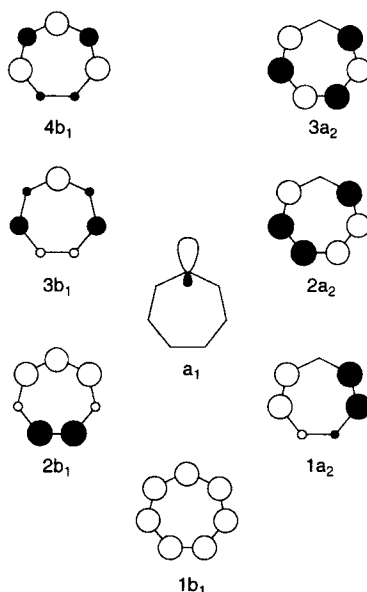


Figure 8. Schematic drawings of the π , π^* , and carbenic molecular orbitals of planar C_{2v} cycloheptatrienyldene (**4a**). The b_1 and a_2 orbitals in each horizontal pair are not strictly degenerate, as they are in D_{7h} cycloheptatrienyl cation. In **4a** a pair of electrons must be distributed between the a_1 , $3b_1$, and $2a_2$ MOs.

relative energies.⁷⁰ Nevertheless, by comparing the results from methods that use different techniques to account for both dynamic⁷¹ and non-dynamic electron correlation, it is possible to draw some reasonable conclusions regarding the above questions. For reference in the following discussion, the energies of the spin states of **4a**, as computed by three different types of methods, are shown in Fig. 10, relative to cycloheptatetraene (**3a**).^{55–57}

The Singlet States. The electronic configurations and CASSCF optimized geometries of the three singlet states of **4a** ($^1A_1$, $^1A_2$, and $^1B_1$) are shown in Fig. 9.⁵⁷ The $^1A_1$ state, with a pair of electrons in the carbene hybrid orbital, has a highly delocalized π system, as indicated by the C–C bond lengths, which show the smallest amount of alternation. This state has the advantage of an aromatic six-electron π system, but the disadvantage of substantial Coulomb repulsion between the two electrons in the hybrid orbital. The $^1A_2$ state resembles a heptatrienyl radical with a relatively long bond between C-3 and C-4. This state, despite its seven-electron π system, has the advantage that the two singly occupied MOs (SOMOs) are disjoint; i.e. as shown in Fig. 8, a_1 and $2a_2$ have no atoms in common. This results in minimal Coulomb repulsion between the two nonbonding electrons.⁶³ In contrast, the $^1B_1$ state suffers from a large amount of Coulomb repulsion, since the a_1 and $3b_1$ SOMOs both have

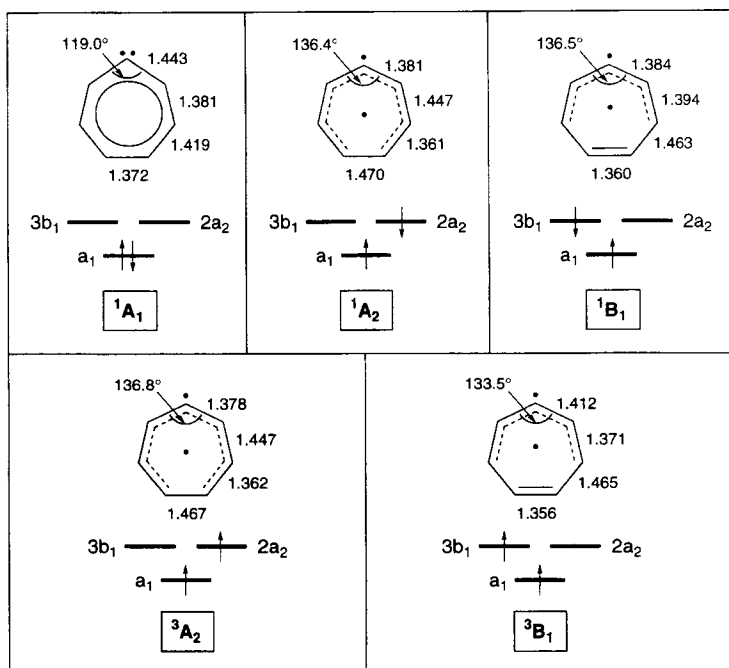


Figure 9. CASSCF(8,8)/6-31G* optimized geometries for the different spin states of cycloheptatrienylidene (**4a**).⁵⁷ Bond distances in angstroms, and bond angles in degrees.

large coefficients on the carbene carbon, and the electrons in these orbitals have opposite spins.

As shown in Fig. 10, the $^1A_2$ state is predicted to be the lowest singlet state of **4a**.^{55,57} The CASSCF vibrational analysis reveals one imaginary frequency for this state, corresponding to an out-of-plane a_2 vibration, which leads to the cyclic allene **3a**.⁵⁷ Thus, $^1A_2$ -**4a** is a transition state for the enantiomerization of **3a**. The analogous process of internal rotation about the C–C bonds in allene is also predicted to occur via an open-shell $^1A_2$ transition state.⁷²

At both the two-configuration (TC)-CCSD⁵⁵ and CASPT2⁵⁷ levels, $^1A_2$ -**4a** is computed to be ca. 21 kcal/mol higher than **3a** (Fig. 10). This is approximately half of the barrier to internal rotation in allene.⁷³ This barrier height in **3a** is reasonable if one considers that the dihedral angle of 48.7° between the bonds from the terminal allenic carbons to C-3 and C-6 in **3a** is approximately halfway to coplanarity, from the analogous dihedral angle of 90° in acyclic allenes.

The closed-shell $^1A_1$ state of **4a** is computed to be less stable than the open-shell $^1A_2$ state by ca. 9 kcal/mol at the CASPT2 level,⁵⁷ and by 5 kcal/mol at the TC-CCSD level.⁵⁵ The latter value is likely to be the more accurate energy difference, since CASPT2 probably overestimates the stability of open-shell

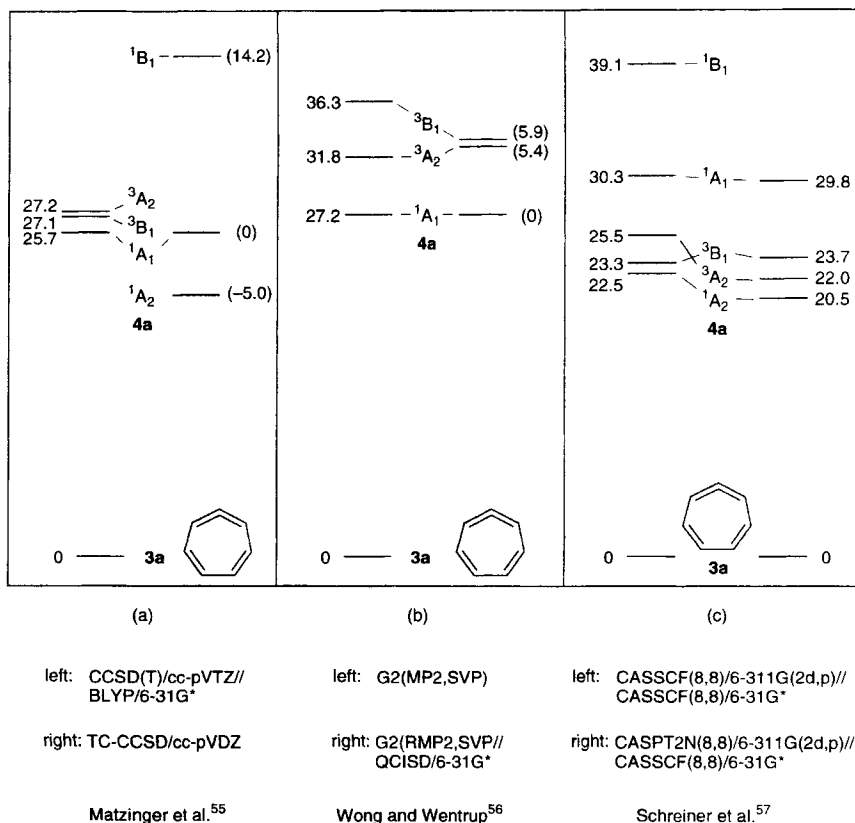


Figure 10. Calculated relative energies (in kcal/mol) of cycloheptatrienylidene spin states (**4a**), relative to cycloheptatetraene (**3a**).^{55–57}

$^1A_2$ relative to closed-shell $^1A_1$.⁶⁰ The finding that $^1A_1$ -**4a** is computed to be higher in energy than $^1A_2$ -**4a** suggests that the aromatic π system of the former does not provide enough of an advantage to outweigh the destabilization due to Coulomb repulsion between the lone pair of electrons in the a_1 NBMO.

However, Matzinger et al. identified another reason for the lower energy of $^1A_2$ relative to $^1A_1$.⁵⁵ They performed model calculations on methylene which suggest that almost all of the energy difference between $^1A_1$ -**4a** and $^1A_2$ -**4a** can be attributed to the fact that the seven-membered ring imposes a much wider carbenic angle in $^1A_1$ (119°) than that which is optimum for closed-shell singlet carbenes (ca. 102°). They state, “It may be the effect of the geometric distortion which pushes the open-shell below the closed-shell singlet in [cycloheptatrienylidene] whereas the aromatic stabilization and the difference in electron repulsion nearly cancel.”⁵⁵

At the MP2, BLYP, and B3LYP levels, $^1A_1$ -**4a** is predicted to be a transition

state for the enantiomerization of **3a**,^{55,57} in accord with the earlier MNDO calculations of Waali.^{28c,e} With CASSCF, $^1A_1$ -**4a** is predicted to be a minimum, although the a_2 vibrational mode leading toward **3a** has a calculated frequency of only 59 cm^{-1} .⁵⁷ Since $^1A_1$ and $^1A_2$ both lie on the ground-state potential surface for planarization of **3a**, they represent two possible transition structures for its enantiomerization.⁵⁷ As already noted, $^1A_2$ is computed to be the lower of the two in energy, but it seems likely that $^1A_1$ would be selectively stabilized by a hydroxylic solvent that could hydrogen bond to the lone pair in the a_1 NBMO.

The $^1B_1$ state of **4a** is predicted to lie 16–19 kcal/mol above the $^1A_2$ state in energy.^{55,57} $^1B_1$ -**4a** is destabilized by the strong Coulomb repulsion that results from both of the SOMOs (a_1 and $3b_1$ in Fig. 8) having large coefficients on the carbene carbon atom. The nondisjoint nature of these two MOs results in the electrons of opposite spin which occupy them simultaneously appearing in the regions of space where both of these orbitals have electron density; and this creates high-energy ionic terms in the wavefunction for the $^1B_1$ state.⁶³

Which Triplet State Has Been Observed? As first noted by Radom et al.^{29a} **4a** can exist in two geometrically distinct triplet states, $^3A_2$ and $^3B_1$, depending on whether the $3b_1$ or $2a_2$ MO is singly occupied. The calculated geometries of these two states are shown in Fig. 9.⁵⁷ The bond lengths indicate that $^3A_2$ -**4a** resembles a heptatrienyl radical whose terminal carbons have been connected by a bond, whereas $^3B_1$ -**4a** resembles a pentadienyl radical whose terminal carbons have been joined by an etheno bridge. At the BLYP/6-31G* level, $^3B_1$ -**4a** is a transition state for pseudorotation of the $^3A_2$ state,⁵⁵ while at the CASSCF(8,8)/6-31G* level the opposite is the case.⁵⁷ At higher levels of theory, these two states are very close in energy, and their ordering depends on the computational method used (Fig. 10).^{55–57}

Although the calculations do not permit a definitive conclusion regarding which triplet state is lower in energy, it is possible to deduce which of them is the more likely to have been observed by EPR.^{11a} The very similar geometries of $^3A_2$ -**4a** and $^1A_2$ -**4a** and the lower energy predicted for the singlet should result in rapid intersystem crossing from the former to the latter. Since $^1A_2$ -**4a** is predicted to be the transition state for enantiomerization of **3a**, the detection of $^3A_2$ -**4a** is unlikely. In contrast, the $^3B_1$ state lies well below the $^1B_1$ state, and at its equilibrium geometry $^3B_1$ also lies substantially below the $^3A_2$ state. Therefore, it seems likely that $^3B_1$ is the metastable state observed in the EPR experiments of Wentrup and co-workers.^{11a}

This assignment of Wentrup's EPR spectrum to the $^3B_1$ state of **4a** is supported by the fact that the D and E values they report for **4a** ($D/hc = 0.425\text{ cm}^{-1}$, $E/hc = 0.0222\text{ cm}^{-1}$)^{11a} are very similar to those they reported for the naphthalene-fused derivative **6** ($D/hc = 0.453\text{ cm}^{-1}$, $E/hc = 0.0193\text{ cm}^{-1}$).^{11a} The naphthalene π system should cause the seven-membered ring to prefer a bond-length pattern more like that in $^3B_1$ -**4a** than like that in $^3A_2$ -**4a**

(see Fig. 9). In addition, the large value of D in **4a** and **6** is consistent with the unpaired electrons both appearing on the carbene carbon, which they do in the $^3B_1$ but not in the $^3A_2$ states.



The Ground State of Cycloheptatrienylidene. In addition to being the lowest singlet state of **4a**, $^1A_2\text{-4a}$ is also predicted by CASSCF and CASPT2 to be slightly lower than both of the triplets (Fig. 10c), making $^1A_2$ the ground state of **4a**.⁵⁷ The prediction that $^1A_2\text{-4a}$ is more stable than $^3A_2\text{-4a}$ constitutes a formal violation of Hund's rule, which states that a triplet state should be lower in energy than the singlet that has the same configuration.⁷⁴ The violation predicted for **4a**⁷⁵ has the same origin as that predicted for planar allene.⁷² Both violations can be understood qualitatively on the basis of π spin polarization, which results in negative spin in the p- π AO at the carbenic carbon in both the $^1A_2$ and $^3A_2$ states. In the singlet state this negative spin is the same as that of the electron that occupies the a_1 hybrid orbital at this carbon. The Pauli principle thus acts to minimize the Coulombic repulsion between these electrons of the same spin in the singlet but not in the triplet, where the σ and π spins at the carbenic carbon are opposite.⁶¹

F. Calculations on Azacycloheptatrienylidene (**4b**)

Enforcing planarity on azacycloheptatetraene (**3b**) gives azacycloheptatrienylidene (**4b**). In performing calculations on **4b**,⁶¹ we considered the four lowest-energy spin states of the planar (C_s symmetric) carbene — the closed-shell singlet ($^1A'$), an open-shell singlet ($^1A''$), and two triplets ($1^3A''$ and $2^3A''$) that differ in which of the two nearly degenerate π^* MOs is occupied. The π^* SOMO in each A'' state and the π bonding in both the A' and A'' states are depicted in Fig. 11.⁶¹ Also shown are the CASSCF(8,8)/6-31G* optimized geometries of the $^1A'$, $^1A''$, $1^3A''$, and $2^3A''$ states of **4b**.⁶¹

In addition to the large difference between the bond angles at the carbene carbon in the open-shell (135–138°) and closed-shell (120.3°) states, there are substantial differences between the C–C bond lengths in the four states. The latter can be understood on the basis of the π^* MO that is occupied in each state and the π bonding that results.

The closed-shell singlet ($^1A'$) has no electrons in the π^* orbitals, and the bond lengths indicate only a small amount of delocalization of the six π electrons into the empty p- π orbital at the carbenic carbon. In both $^1A''$, $1^3A''$, and $2^3A''$ the π^* SOMO has the nodal pattern expected for a pentadienyl NBMO mixed

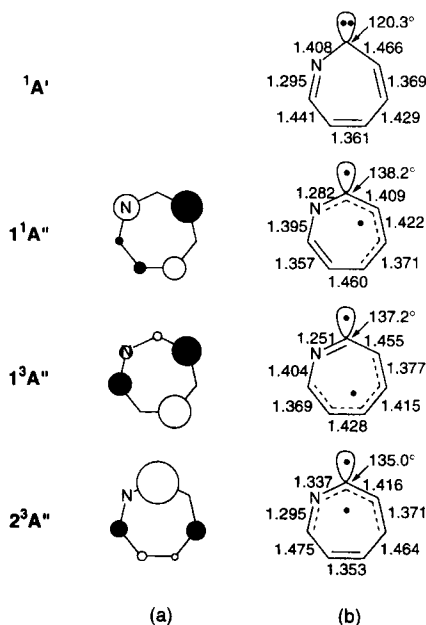


Figure 11. (a) Schematic drawings of the singly occupied π^* molecular orbital in the three A'' states of planar azacycloheptatrienyldiene (**4b**). (b) CASSCF(8,8)/6-31G* optimized geometries of the four spin states of **4b**, showing approximate π bonding patterns.⁶¹

in an out-of-phase fashion with the bonding π MO of a double bond (Fig. 11a). However, the high Coulombic repulsion that would be engendered in the $1A''$ state, if the electron in the π^* SOMO were to appear at the carbenic carbon (where the unpaired electron of opposite spin is localized in a σ orbital), causes the positions of the nodes in the π^* SOMO to be somewhat different in $1A''$ than in $1^3A''$ and $2^3A''$. The π^* SOMO in $2^3A''$ is similar in form to those in $1A''$ and $1^3A''$ but is largely localized on the carbenic carbon. Consequently, the bond-length pattern is different in all three of these electronic states.

The CASPT2 energies for the four spin states of planar **4b**, relative to the ketenimine **3b**, are shown in Fig. 12.⁶¹ The $1^3A''$ and $1A''$ states are predicted to be 6–7 kcal/mol more stable than the $2^3A''$ state, presumably because, as shown by the C–N bond lengths, the latter has the least amount of C–N π bonding. The $1^3A''$ state of **4b** lies below the $1A''$ state by 1.4 kcal/mol. This is the opposite ordering of the two analogous spin states ($^3A_2$ and $^1A_2$) in **4a**, for which the ground state is predicted to be the open-shell singlet ($^1A_2$).⁵⁷

This difference between these two carbenes can be attributed to the presence of the lone pair of electrons on nitrogen in **4b**. Two-center, three-electron bonding in the molecular plane of **4b**, involving the lone pair, produces some unpaired σ spin density on nitrogen. Coulombic repulsion between the σ and π electrons of

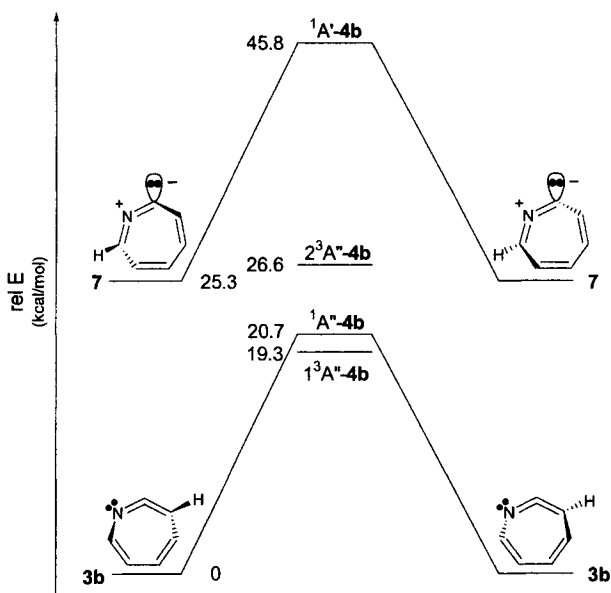


Figure 12. Energies of four different spin states of planar azacycloheptatrienyliene (**4b**), relative to azacycloheptatetraene (**3b**), calculated at the CASPT2(8,8)/6-311G(2d,p)//CASSCF(8,8)/6-31G* level.⁶¹

opposite spin on nitrogen in $1A''$ causes this state to lie slightly above $1^3A''$ in energy.

At the CASSCF(8,8)/6-31G* level, $1A''-4b$ is predicted to be a transition state for the enantiomerization of **3b**. The CASPT2 calculated barrier for this process is ca. 21 kcal/mol (Fig. 12). This predicted value for the barrier to enantiomerization of **3b** is essentially the same as that calculated for the racemization of **3a**,^{55,57} which, as already noted, is approximately half of the experimental value of ca. 42 kcal/mol for racemization of allene.⁷³

The closed-shell singlet state ($1A'$) of **4b** is predicted to be much higher in energy than the open-shell $1A''$ state. The energy difference between them is computed to be 25 kcal/mol at the CASPT2 level. In contrast, as shown in Fig. 10, in **4a** the energy difference between these two states ($1A_1$ and $1A_2$) is computed to be only 5–10 kcal/mol.^{55,57} The dramatic destabilization of $1A'-4b$ is due to the four-electron, repulsive interaction between the σ lone pair of electrons at the carbenic center in this state and the nonbonding lone pair on the adjacent nitrogen.

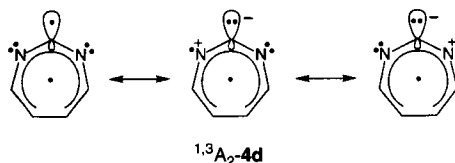
The $1A'$ state of **4b** is predicted to be a transition state for interconversion of the enantiomers of a cyclic cumulene (**7** in Fig. 12) that is an isomer of **3b**. In **7** the roles of the lone pairs on nitrogen and carbon are reversed, so that the nitrogen is the central atom of a 2-aza-allene unit, formed by overlap of the

nitrogen lone pair with the empty p orbital on the carbene carbon. This zwitterionic structure was proposed as a resonance structure for **3b** by Chapman and LeRoux,³⁶ but our calculations predict very different geometries for **3b** and **7**.⁶¹

The CASPT2 barrier to enantiomerization of **7** via $^1A'-4b$ is 20.5 kcal/mol (Fig. 12), which is almost the same as that calculated for the enantiomerization of **3b** via $^1A''-4b$. Although the out-of-plane distortion of $^1A'-4b$ to one of the enantiomers of **7** provides dramatic energy lowering, the zwitterionic character of **7** still results in its being calculated to be ca. 25 kcal/mol higher in energy than its isomer **3b**.

Both $^1A''-4b$ and $^2A''-4b$ are predicted to be minima on the potential surface at the CASSCF level.⁶¹ This is in contrast with the situation for **4a**, where one triplet state is calculated to be a transition state for pseudorotation of the other.⁵⁵⁻⁵⁷ A derivative of triplet **4b** has been implicated in solution trapping experiments,⁴⁹ but there have been no reports of the direct observation of **4b**. Facile intersystem crossing from the triplet ground state ($^1A''$) to the open-shell singlet state ($^1A''$), followed by vibrational relaxation to one of the enantiomers of **3b** (Fig. 12), would be expected to rapidly depopulate the $^1A''$ state of **4b**. Thus, direct detection of triplet **4b** may prove to be much more difficult than detection of **4a** was.^{11a}

As discussed above, the presence of a nitrogen adjacent to the carbenic center stabilizes the $^1A''$ state of **4b**, relative to the $^1A''$ state, and results in the triplet being the predicted ground state by ca. 1 kcal/mol. If nitrogen atoms were incorporated on *both* sides of the carbenic center, as in 1,6-diaza-1,3,5-cycloheptatrien-7-ylidene (**4d**), both nitrogen lone pairs would be delocalized into the singly occupied σ orbital on this carbon; so one might expect the triplet to fall substantially below the singlet. CASPT2/6-31G* calculations on **4d** do, indeed, find that the $^3A_2$ state of **4d** lies 2.6 kcal/mol below the open-shell $^1A_2$ state;⁶¹ and Wentrup and co-workers have, in fact, observed the ESR spectrum of triplet **4d**.^{11a}



IV. WHY ARE NITRENES MORE STABLE THAN CARBENES?

As discussed in Section III, calculations on the ring expansions of phenylcarbene (**1a**) and phenylnitrene (**1b**) suggest that singlet **1b** is thermodynamically

more stable than singlet **1a** by ca. 11 kcal/mol. Of course, **1a** and **1b** are not isomers, so there is no direct way of testing this conclusion. However, as already noted, Wentrup has found that all three pyridylcarbenes rearrange to phenylnitrene (Scheme 4).^{10,11} This finding is certainly consistent with the inference that singlet **1b** is considerably more stable than singlet **1a**.

If singlet **1b** is 11 kcal/mol more stable than singlet **1a**, then the 16 kcal/mol larger singlet–triplet splitting in **1b** than in **1a** means that triplet **1b** must be 27 kcal/mol more stable than triplet **1a**. Wentrup^{1a,f} and Platz³ have, in fact, each suggested that a large difference between the thermodynamic stabilities of triplet **1a** and triplet **1b** is the origin of the much lower reactivity of ³**1b** compared to ³**1a**. Wentrup and Platz also each proposed that the greater thermodynamic stability of ³**1b**, relative to ³**1a**, parallels the relative thermodynamic stabilities of triplet NH versus triplet CH₂, as exemplified, for instance, by the 19 kcal/mol⁷⁶ lower bond dissociation energy (BDE) in forming triplet NH from •NH₂ than in forming triplet CH₂ from •CH₃.

A. Calculations on Phenylnitrene versus Pyridylcarbene

Wentrup's experimental work on carbene-to-nitrene rearrangements¹⁰ suggested that calculations on phenylnitrene (**1b**) and the isomeric pyridylcarbenes might provide some useful relative energies. Kemnitz et al. carried out calculations on **1b** and 3-pyridylcarbene (**1c**).⁷⁷ The latter molecule was used to provide a link between the energies of not only phenylcarbene (**1a**) and phenylnitrene (**1b**), but also between CH₂ and NH.

As discussed in Section III, the lowest singlet states of **1a** and **1b** have different orbital occupancies. In contrast, ³**1a** and ³**1b** have the same orbital occupancies. This makes comparison of the triplet ground states of **1a** and **1b** much easier, both conceptually and computationally, than comparison of their singlet states. Therefore, Kemnitz et al. performed calculations on the triplet ground states of **1b** and **1c**.

As shown in Table 3, triplet **1b** is computed to be 25–26 kcal/mol lower in enthalpy than triplet **1c**.⁷⁷ Table 3 also shows that radicals **8b** and **8c**, formed by adding a hydrogen atom to **1b** and **1c**, respectively, differ in enthalpy by only 1–3 kcal/mol. Therefore, the large enthalpy difference between ³**1b** and ³**1c** is not due to a difference between the abilities of the phenyl and pyridyl groups to stabilize an unpaired π electron. Instead it must reflect an intrinsic enthalpy difference between arylnitrenes and arylcarbenes. Table 3 also shows that aniline (**9b**) and β -picoline (**9c**) are also predicted to have very similar enthalpies, thus providing further evidence that the large enthalpy difference between **1b** and **1c** is, indeed, due to the fact that **1b** is a nitrene, while **1c** is a carbene.

Table 3. Relative Enthalpies (298 K, in kcal/mol) of Triplet Phenylnitrene ($^3\mathbf{1b}$), Triplet 3-Pyridylcarbene ($^3\mathbf{1c}$), ^a and Pairs of Molecules Formed from them by Addition of Hydrogen Atoms ^b

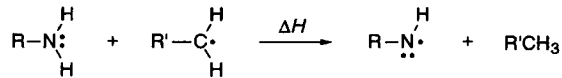
Method	 $^3\mathbf{1b}$	 $^3\mathbf{1c}$	 $\mathbf{8b}$	 $\mathbf{8c}$	 $\mathbf{9b}$	 $\mathbf{9c}$
CASPT2/6-31G [*]	0	26.4	0	1.5	0	-1.9
BVWN5/AUG-ccpVTZ	0	25.3	0	3.3	0	3.2

Notes: ^a Relative enthalpies for $^3\mathbf{1c}$ are for the *syn* conformer.^b Data from Ref. 77, at CASSCF(8,8)/6-31G^{*} optimized geometries. Relative energies have been converted to enthalpy differences by correcting for ΔZPE and $\Delta C_v \times 298$ K.

B. N–H versus C–H Bond Dissociation Energies

The data in Table 3 also show that the N–H BDE of aniline ($\mathbf{9b}$) and the C–H BDE of β -picoline ($\mathbf{9c}$) are quite similar and are calculated to differ by only 0.1 kcal/mol at the BVWN5/AUG-cc-pVTZ level of theory. This is also true for cases other than $\mathbf{9b}$ versus $\mathbf{9c}$ as shown by the calculated enthalpies in Table 4.⁷⁷ The isodesmic reaction in Table 4 gives the difference between the N–H BDEs of RNH_2 and the C–H BDEs of comparable $\text{R}'\text{CH}_3$ species. For $\text{R}=\text{R}'=\text{Ph}$, the calculated difference in BDEs between aniline ($\mathbf{9b}$) and toluene is only 0.3 kcal/mol; and for $\text{R}=\text{R}'=\text{H}$, the N–H BDE in NH_3 is computed to be only 1.4 kcal/mol larger than the C–H BDE in CH_4 . The latter energy difference is close to the experimental value of 3.7 kcal/mol.⁷⁶ Thus, the results in Table 4 show that *the N–H BDEs of primary amines are, in general, nearly*

Table 4. BVWN5/AUG-cc-pVTZ Calculated BDEs (DH_{298} in kcal/mol) of RNH_2 Relative to $\text{R}'\text{CH}_3$ ^a

	
Substituents	ΔH (expt) ^b
$\text{R}=\text{R}'=\text{H}$	1.4 (3.7)
$\text{R}=\text{R}'=\text{Ph}$	0.3
$\text{R}=\text{Ph}, \text{R}'=3\text{-pyridyl}$	-0.1

Notes: ^a Data from Ref. 77, at CASSCF(8,8)/6-31G^{*} optimized geometries. Data for $^3\mathbf{1c}$ are for the *syn* conformer.^b Experimental ΔDH_{298} (kcal/mol) in parentheses, determined using averaged values from Ref. 76.

Table 5. BVWN5/AUG-cc-pVTZ calculated BDEs (DH_{298} in kcal/mol) of RNH Relative to $R'CH_2^a$

$R-\overset{\cdot}{\underset{\cdot\cdot}{N}}-H + R'-\overset{\cdot}{\underset{H}{\overset{ }{C}}} \xrightarrow{\Delta H} R-\overset{ }{N} + R'-\overset{\cdot}{\underset{H}{\overset{H}{C}}}$	
Substituents	ΔH (expt) ^b
R=R'=H	-17.5 (-18.7)
R=R'=Ph	-22.5
R=Ph, R'=3-pyridyl	-21.9

Notes: ^a Data from Ref. 77, at CASSCF(8,8)/6-31G* optimized geometries.

^b Experimental ΔDH_{298} (kcal/mol) in parentheses, determined using averaged values from Ref. 76.

the same as the C–H BDEs of the analogous primary alkanes, despite the greater electronegativity of nitrogen compared to carbon.

In contrast, the much lower enthalpy computed for **31b**, compared to **31c**, means that the N–H BDE of the aniliny radical **8b** is much lower than the C–H BDE of the 3-pyridylmethyl radical **8c**. The results in Table 5 show that this is indeed the case, not only for R=Ph and R'=3-pyridyl, but also for R=R'=Ph and R=R'=H.⁷⁷ The data in Table 5 indicate that, not just for **1b** and **1c** but in general, triplet nitrenes are ca. 20 kcal/mol more thermodynamically stable than comparably substituted triplet carbenes.

These computational results confirm the suggestions of Wentrup^{1a,f} and Platz³ that: (i) The relative lack of reactivity and the greater selectivity found for triplet **1b**, compared to triplet **1a**, has a thermodynamic origin. (ii) This difference between the thermodynamic stabilities of **1a** and **1b** is but one example of a more general difference between the thermodynamic stabilities of carbenes and nitrenes. (iii) A manifestation of this general difference is the large difference between the C–H BDE in $\bullet CH_3$ and the N–H BDE in $\bullet NH_2$.

Despite the 13–16 kcal/mol larger value of ΔE_{ST} in **1b** than in **1a**,^{16,46} the much larger difference between the thermodynamic stabilities of triplet **1b** and triplet **1a** results in the computational finding, described in Section III, that singlet **1b** is ca. 11 kcal/mol more thermodynamically stable than singlet **1a**. The greater thermodynamic stability of singlet **1b** accounts for the computational result that, as shown schematically in Fig. 5, the ring expansion of singlet **1a** to **3a** is very exothermic; whereas, ring expansion of singlet **1b** to **3b** is nearly thermoneutral.

C. Effects of Hybridization on BDEs

The results in Table 3 show that the explanation of why nitrenes are thermodynamically more stable than carbenes must be the same as the reason why the N–H

BDEs in $\text{RNH}\bullet$ radicals are much smaller than the C–H BDEs in $\text{RCH}_2\bullet$ radicals. Two factors which contribute to this difference are (i) the difference between the hybridization of the X–H bonds that are broken in the two radicals, and (ii) the difference between the *changes* in hybridization that accompany formation of triplet NH and triplet CH_2 from the corresponding radicals.

Regarding the first of these factors, comparison of CISD-calculated bond angles in $\bullet\text{NH}_2$ (102.6°) and $\bullet\text{CH}_3$ (120.0°) indicates that the N–H bonds in $\bullet\text{NH}_2$ have less 2s character than the C–H bonds in $\bullet\text{CH}_3$.⁷⁷ Such a difference, however, was found to account for no more than a quarter of the ca. 18 kcal/mol difference between the BDEs in Table 5 for $\text{R}=\text{R}'=\text{H}$.⁷⁷

The major contribution to the difference in BDEs comes rather from the second factor, i.e. the difference between the *changes* in hybridization that occur upon removing a hydrogen atom from $\bullet\text{NH}_2$ and $\bullet\text{CH}_3$.⁷⁷ Loss of $\text{H}\bullet$ from both $\bullet\text{NH}_2$ and $\bullet\text{CH}_3$ allows the 2s character in the remaining doubly occupied σ orbitals to increase. However, the electrons in the lone pair orbital of triplet NH benefit from rehybridization more than those in the C–H bonding orbitals of triplet CH_2 or, for that matter, more than the electrons in the N–H bonding orbital of triplet NH. The reason is that the lone pair of electrons in NH is localized almost entirely on N; whereas, the pair of electrons in a C–H or N–H bond is shared between hydrogen and the atom to which it is bonded.

The $\text{R}(\text{O})\text{HF}/6\text{-}311\text{G}(2\text{d},\text{p})$ orbital energies for NH_3 , $\bullet\text{NH}_2$, and triplet NH are depicted in Fig. 13,⁷⁷ which shows graphically the 38 kcal/mol decrease in the energy of the lone pair orbital on going from $\bullet\text{NH}_2$ to triplet NH. Fig. 13 also shows that an increase in 2s character, due to rehybridization, also stabilizes the

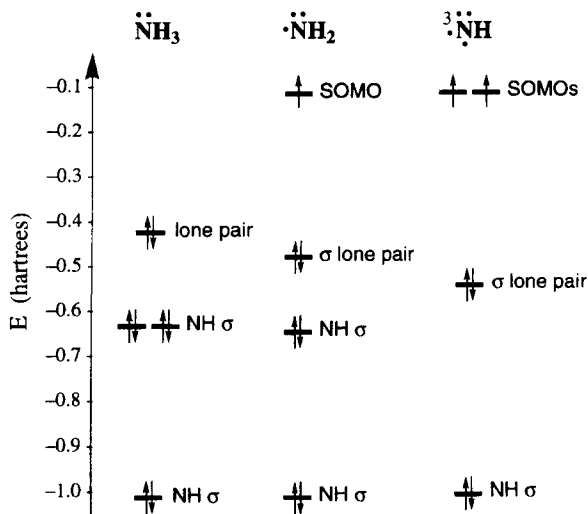


Figure 13. $\text{R}(\text{O})\text{HF}/6\text{-}311\text{G}(2\text{d},\text{p})$ MO energies (hartrees) for NH_3 , $\bullet\text{NH}_2$, and triplet NH.⁷⁷

orbital occupied by the lone pair of electrons on formation of $\bullet\text{NH}_2$ from NH_3 . The lowering of the energy of this MO acts to stabilize $\bullet\text{NH}_2$, relative to $\bullet\text{CH}_3$, since $\bullet\text{CH}_3$ lacks a lone pair of electrons. The greater stabilization provided by rehybridization in $\bullet\text{NH}_2$, compared to $\bullet\text{CH}_3$, provides an explanation for why the measured BDEs⁷⁶ of CH_4 (105 kcal/mol) and NH_3 (109 kcal/mol) are very similar, despite the greater electronegativity of nitrogen compared to carbon.

V. SUBSTITUENT EFFECTS ON THE RATES AND REGIOCHEMISTRY OF THE RING EXPANSION OF PHENYLNITRENE

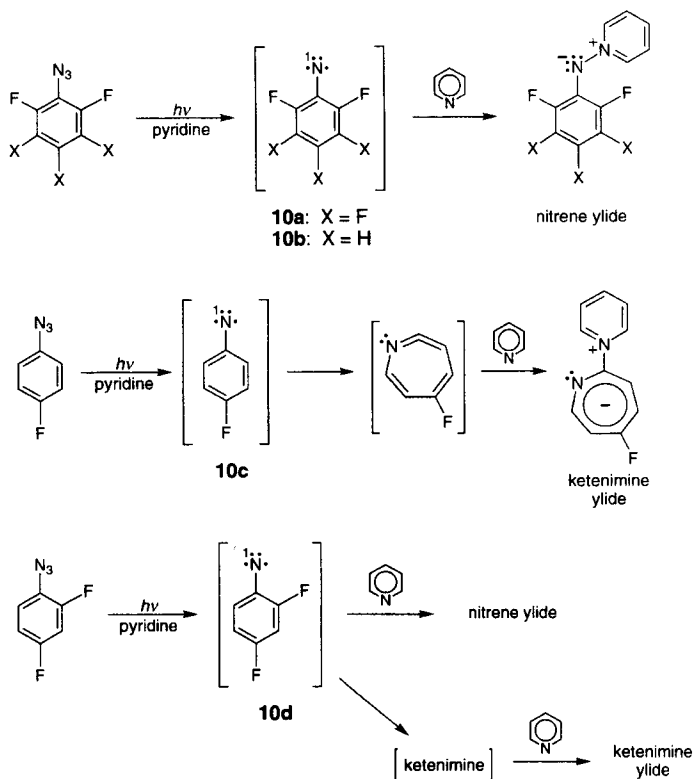
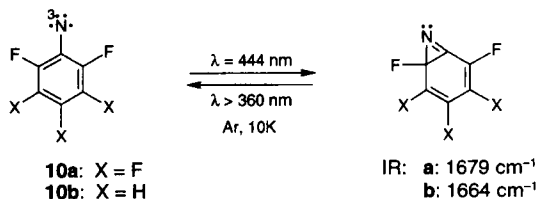
Arylnitrenes have found practical application in the areas of polymer cross-linking (photoresists) and photoaffinity labeling.⁷⁸ The latter technique relies primarily on intermolecular insertion reactions of the nitrenes, and thus is most efficient when ring expansion to the ketenimine is slow in comparison with insertion. Since the early demonstration by Banks and co-workers that polyfluorinated aryl nitrenes give increased yields of insertion products,⁷⁹ fluorinated aryl azides have become popular photoaffinity labeling reagents,⁸⁰ and the study of substituent effects on the rate of ring expansion of phenyl nitrene has grown into an active area of research.

A. Fluorine and Methyl Substituents

The effects of the number and positions of fluorine substituents on the rate of ring expansion of phenyl nitrene (**1b**) have been extensively investigated by Platz and co-workers.⁸¹ Using the pyridine-ylide probe method⁸² they found that, whereas both pentafluorophenyl nitrene (**10a**) and 2,6-difluorophenyl nitrene (**10b**) give nitrene ylides, 4-fluorophenyl nitrene (**10c**) yields only the ketenimine ylide, and 2,4-difluorophenyl nitrene (**10d**) affords a mixture of nitrene ylide and ketenimine ylide (Scheme 18).^{81c,d} They concluded that fluorine substitution at both *ortho* positions is necessary in order to inhibit ring expansion effectively. Subsequent laser flash photolysis (LFP) studies by Platz and co-workers indicated that the barrier to ring expansion for **10a** and **10b** is ca. 3 kcal/mol higher than that for **1b**.^{81e,g}

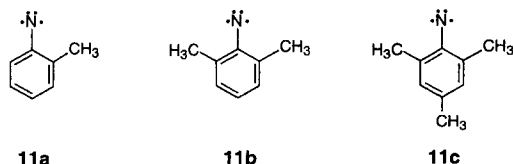
Earlier, Dunkin and Thomson had observed that matrix-isolated triplet **10a** did not undergo photochemical ring expansion.⁸³ However, Morawietz and Sander have recently provided evidence for photochemical conversion of $^3\text{10a}$ and $^3\text{10b}$ to the corresponding fluorinated azirines (Scheme 19).^{48d} This represents a rare instance where an azabicyclo[4.1.0]heptatriene, the putative intermediate in the ring expansion of a phenyl nitrene, has actually been observed.

Ring expansion of alkyl-substituted aryl nitrenes has also been studied. Sundberg and co-workers found that generation of several 2-alkyl-substituted aryl nitre-

**Scheme 18.****Scheme 19.**

nes (e.g. 2-methylphenylnitrene, **11a**) in diethylamine affords nucleophilic trapping products that are consistent with initial cyclization to only the unsubstituted *ortho* carbon.⁸⁴ Dunkin reported that matrix-isolated 2,6-dimethylphenylnitrene (**11b**) undergoes inefficient ring expansion,⁸⁵ and Tomioka and co-workers have observed the trapping of singlet mesitylnitrene (**11c**), and of its ring-expansion product, by TCNE.⁸⁶

The results for methyl derivatives **11a-c** suggest that steric effects play a role in determining the barrier to ring expansion, as suggested by Dunkin.⁸⁵ Other



explanations have been proposed for the substituent effects observed in the ring expansion reactions of fluorinated phenylnitrenes,^{65,81b} but the results of our *ab initio* calculations on the effects of fluoro, chloro, and methyl substituents strongly indicate the importance of steric effects in these reactions.⁸⁷

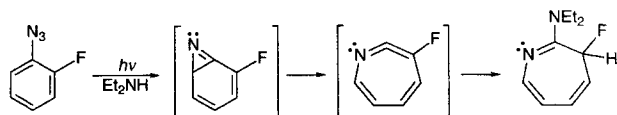
Our calculations showed that the first step, cyclization of the nitrene to an azabicyclo[4.1.0]heptatriene, is rate-determining. Our calculated barriers for cyclization of four fluorinated derivatives of **1b** are given in Table 6.⁸⁷ The CASPT2/cc-pVDZ barrier of 13.4 kcal/mol for cyclization of 2,6-difluorophenylnitrene (**10b**) is 4.1 kcal/mol higher than the barrier computed for **1b** → **2b**. In contrast, the calculated barriers to rearrangement of 3,5-difluorophenylnitrene (**10e**) and 4-fluorophenylnitrene (**10c**) are very similar to that computed for unsubstituted phenylnitrene (**1b**). These computational results are consistent with the observed reluctance of pentafluorophenylnitrene (**10a**) and 2,6-difluorophenylnitrene (**10b**) to rearrange,^{48d,81,83} and with the relative ease

Table 6. CASPT2/cc-pVDZ Barrier Heights (kcal/mol) for Ring Expansions of Fluorinated Singlet Phenylnitrenes ^a

Nitrene	Mode of cyclization	E_a	ΔE_a ^b
1b 	—	9.3	0
10b 	—	13.4	+4.1
10e 	—	8.6	-0.7
10c 	—	9.1	-0.2
10f 	Away from F	9.9	+0.6
	Toward F	13.0	+3.7

Notes: ^a Data for **1b** from Ref. 61, all other data from Ref. 87. At CASSCF(8,8)/6-31G* optimized geometries. Barriers are for the first step of ring expansion, and include corrections for ΔZPE .

^b Relative barrier height compared to that for **1b**.



Scheme 20.

of ring expansion in 4-fluorophenylnitrene (**10c**).^{81c} Moreover, our results are in good quantitative agreement with the LFP studies of Platz and co-workers, who found the barriers for ring expansion of **10a** and **10b** both to be ca. 3 kcal/mol higher than that for ring expansion of **1b**.^{81e,g}

For 2-fluorophenylnitrene (**10f**), the barrier for cyclization at the fluorinated *ortho* carbon is computed to be ca. 3 kcal/mol higher than that for cyclization at the unfluorinated *ortho* carbon (Table 6).⁸⁷ These results are in agreement with experimental observations that nitrene **10f** rearranges rapidly to a ketenimine in solution^{81c} and that 2,4-difluorophenylnitrene (**10d**) undergoes ring expansion some 15 times faster than 2,6-difluorophenylnitrene (**10b**).^{81c,d} Both **10f** and 2,4-difluorophenylnitrene (**10d**) can cyclize at an unfluorinated *ortho* carbon; but this is not possible for 2,6-difluorophenylnitrene (**10b**).

Our prediction, that 2-fluorophenylnitrene (**10f**) should preferentially cyclize away from the fluorine, was subsequently verified experimentally by Leyva and Sagredo.⁸⁹ They photolyzed 2-fluorophenyl azide in diethylamine and isolated the trapping product expected from cyclization of the nitrene away from the fluoro substituent (Scheme 20).⁸⁹

Fig. 14 shows graphically the computed barriers for both the first⁸⁷ and the second⁸⁸ steps of the ring expansion reactions of mono- and difluorophenyl nitrenes, in a way that permits energetic comparisons of isomeric species. Fig. 14a shows that singlet 2,6-difluorophenylnitrene (**10b**) is calculated to be 3.8 kcal/mol less stable than the 3,5-difluoro isomer (**10e**), and Fig. 14b shows that 2-fluorophenylnitrene (**10f**) is computed to be 2.5 kcal/mol less stable than 4-fluorophenylnitrene (**10c**). The relative energies of the isomeric nitrenes shown in Fig. 14a (**10b** versus **10e**) and Fig. 14b (**10f** versus **10c**) indicate that *ortho* fluorine substituents actually destabilize the open-shell singlet nitrenes. Thus, the relative barrier heights cannot be explained on the basis of stabilization of the nitrenes by *ortho* fluorines.^{81b} In addition, the calculations predict that, of the two possible cyclization modes of 2-fluorophenylnitrene (**10f**), the higher barrier actually leads to the lower-energy azirine product (Fig. 14b), in which there is a favorable interaction between the filled C=N π MO and the unfilled C-F σ^* MO.^{87,90} Therefore, the relative energies of azirine products cannot be responsible for the relative energies of the transition states leading to them.

Inspection of the optimized geometries of the transition states for cyclization suggested that steric hindrance is important in cases where N cyclizes toward F.⁸⁷ This steric explanation of the rates and regiochemistry of cyclization was

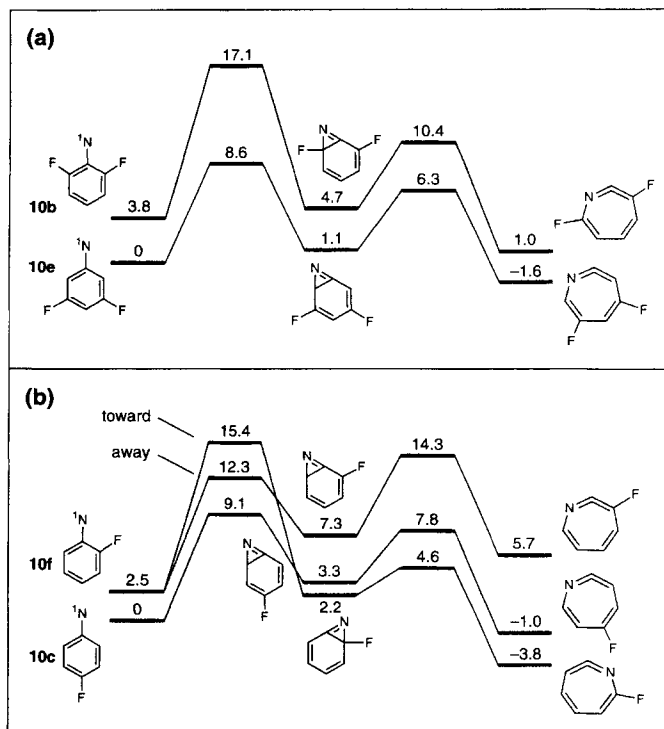


Figure 14. Energetics (in kcal/mol) of the ring expansions of fluoro-substituted phenylnitrenes, calculated at the CASPT2(8,8)/cc-pVDZ//CASSCF(8,8)/6-31G* level.^{87,88} (a) Difluorinated nitrenes. (b) Monofluorinated nitrenes.

supported by calculations on the cyclization reactions of 2-chlorophenylnitrene and 2-methylphenylnitrene (**11a**).⁸⁷ The barrier to cyclization toward the substituent was calculated to be higher than that for cyclization away from the substituent, by 3.7 kcal/mol for chlorine, and by 2.0 kcal/mol for methyl. The results for 2-methylphenylnitrene are consistent with the solution trapping experiments of Sundberg⁸⁴ and the matrix photolysis results of Dunkin.⁸⁵

The CASPT2 results for the second step of the ring expansion⁸⁸, shown in Fig. 14, are at least partially understood, and similar computational results have been obtained using the B3LYP method.⁸⁸ The prediction, that the least stable ketenimine in each isomeric set is the one with fluorine attached to the cumulene moiety (Fig. 14), is consistent with a recent computational study showing that a fluorine substituent destabilizes a ketenimine by ca. 8 kcal/mol relative to hydrogen.⁹¹ On the other hand, a fluorine adjacent to the nitrogen in a ketenimine is stabilizing, presumably due to partial delocalization of the nitrogen lone pair into the C–F σ^* orbital. The barrier heights for ring opening of the azabicyclo[4.1.0]heptatrienes parallel the exothermicities of this step.

Table 7. Experimental Activation Parameters for Ring Expansion of Fluoro- and Methyl-Substituted Phenylnitrenes

Nitrene	Substituents	E_a (kcal/mol)	ΔE_a^a (kcal/mol)	log A	Ref.
1b	–	5.6 ± 0.3	0	13.1	42c
Fluorine derivatives					
10a	pentafluoro	8.8 ± 0.4	+3.2	13.8	81g
		7.8 ± 0.6	+2.2	12.8	88
10b	2,6-difluoro	7.3 ± 0.7	+1.7	11.5	88
		8.0 ± 1.5	+2.4	12.0	88
10c	4-fluoro	5.3 ± 0.3	–0.3	13.2	93
10e	3,5-difluoro	5.5 ± 0.3	–0.1	12.8	88
10f	2-fluoro	6.7 ± 0.3	+1.1	13.0	88
10g	2,4,6-trifluoro	8.4^b	+2.8	13 ^b	81e
Methyl derivatives					
11a	2-methyl	5.3 ± 0.4	–0.3	12.8	93
11b	2,6-dimethyl	7.0–7.5	+2.4–2.9	13.0	93
11c	2,4,6-trimethyl	7.3 ± 0.4	+2.7	13.4	93
11d	4-methyl	5.8 ± 0.4	+0.2	13.2	93

Notes: ^a Relative E_a , compared to that for **1b**.

^b Determination of E_a employed an assumed value of 13 for log A .

Gritsan, Platz, and co-workers tested the computational predictions in Table 6 by performing LFP studies to measure the activation parameters for the ring expansions of several fluoro- and methyl-substituted phenylnitrenes.^{81g,88,92,93} Their data, along with some of their earlier results, are shown in Table 7. Comparison of the experimental results for fluorinated nitrenes **10** in Table 7 with the computational predictions in Table 6 reveals that, although the calculated barriers are systematically too high for the reason discussed in Section III.C, there is good agreement between the predicted and measured barrier heights, relative to phenylnitrene (**1b**) (ΔE_a in Tables 6 and 7).

The results in Table 7 for methyl-substituted phenylnitrenes show that 2-methyl (**11a**) and 4-methyl (**11d**), which can both cyclize toward an unsubstituted *ortho* carbon, have barriers that are ca. 1.5–2 kcal/mol smaller than 2,6-dimethyl (**11b**) and 2,4,6-trimethyl (**11c**), both of which can only cyclize toward a substituted carbon.⁹² This agrees well with the predicted 2.0 kcal/mol difference in barrier heights for the two cyclization modes of 2-methylphenylnitrene (**11a**).⁸⁷

B. Cyano Substituents

The apparent absence of large electronic effects on the cyclization reactions of derivatives of phenylnitrene has been attributed to the nature of the wave function for the lowest singlet state, which, as discussed earlier, resembles a

cyclohexadienyl radical, with a σ iminyl radical center doubly bonded to the remaining ring carbon. One might expect, therefore, that a radical-stabilizing substituent, such as a cyano group, at an *ortho* or *para* ring carbon would tend to localize the unpaired π electron at the carbon to which the substituent is attached. This localization should make attack of nitrogen at a substituted *ortho* carbon more favorable when the substituent is cyano, rather than fluoro or methyl, which are less radical-stabilizing.

Consistent with this hypothesis, Smalley and coworkers have found that singlet 2-cyanophenylnitrene (**12a**) undergoes ring expansion to afford the product formed via cyclization toward the cyano substituent, as well as the product formed via cyclization away from the cyano group.⁹⁴ Similar results have been found in the ring expansion of singlet *o*-acetylphenylnitrene.⁹⁵

Because no unpaired spin appears at the *meta* carbons of **1b**, a cyano substituent at one of these carbons should have only a small effect on the barrier to cyclization at either of the two, non-equivalent *ortho* carbons. However, if a *para* cyano substituent tends to localize spin at the carbon to which it is attached, the concomitant decrease in unpaired spin density at the *ortho* carbons might raise the barrier to cyclization.

In order to test the validity of these qualitative expectations, CASPT2/6-31G* calculations on the ring expansion reactions of *ortho*, *meta*, and *para*-cyano-phenylnitrene (**12a-c**) were performed.⁹⁶ Fig. 15 summarizes the results. In all three cases, the ring expansions were computed to be nearly thermoneutral, with the first step rate-determining.

Of particular interest in Fig. 15 are the results for cyclization of *ortho*-cyanophenylnitrene (**12a**). Cyclization toward the cyano substituent is predicted to have a slightly lower barrier height than cyclization away from the cyano group, which is calculated to have the same barrier height as cyclization of **1b** at the CASPT2 level of theory. This prediction is very different from the computational⁸⁷ and experimental results for cyclization of *ortho*-methylphenylnitrene (**11a**)^{84,92} and *ortho*-fluorophenylnitrene (**10f**),⁸⁹ where cyclization away from the *ortho* substituent is strongly preferred over cyclization toward the substituent. As already noted, this predicted difference between the cyclization of **10f** and **11a** on one hand and **12a** on the other has already been confirmed experimentally.⁹⁴

In the cyclization of *m*-cyanophenylnitrene (**12b**), since the cyano group is on a carbon at which the π NBMO in the reactant has a node, it seems unlikely that radical stabilization is likely to influence the direction in which **12b** cyclizes. In fact, the barrier heights connecting **12b** to either of the two possible azirines are computed to be quite comparable; and the small kinetic preference predicted for cyclization toward the cyano group may well be a consequence of the slightly lower energy calculated for the linearly conjugated product, relative to the cross-conjugated product.

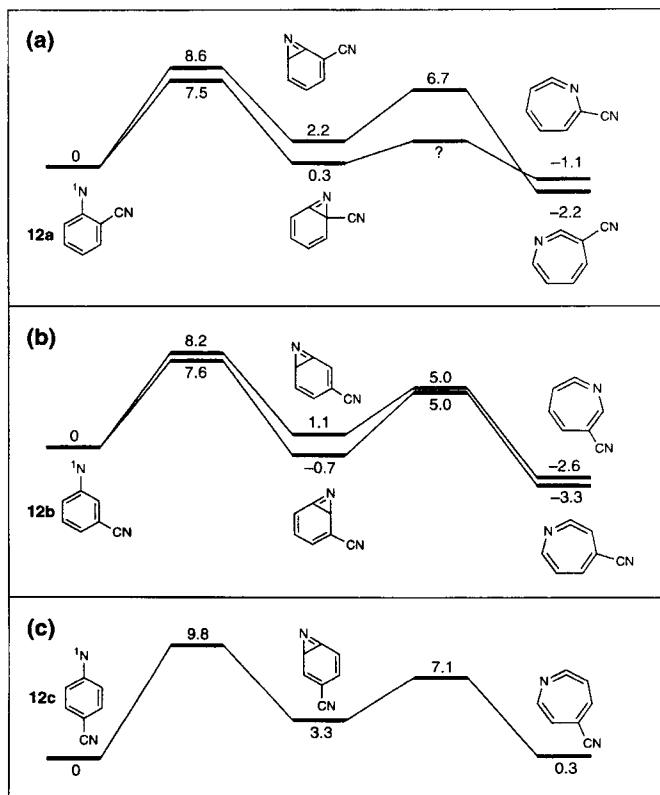


Figure 15. Energetics (in kcal/mol) of the ring expansions of cyano-substituted phenylnitrenes, calculated at the CASPT2(8,8)/cc-pVDZ//CASSCF(8,8)/6-31G* level.⁹⁶

Fig. 15 shows that the barrier computed for cyclization of *para*-cyanophenylnitrene (**12c**) is more than 1 kcal/mol higher than that for either of the other two cyanophenylnitrenes. In addition, the cyclization of **12c** is calculated to be more endothermic than any of the other cyclizations shown. Both facts are attributable to the ca. 3 kcal/mol lower energy computed for **12c**, relative to both **12a** and **12b**.

These predictions regarding relative barrier heights in the ring expansions of the isomeric cyanophenylnitrenes have recently been confirmed experimentally.⁹⁶

VI. CONCLUSIONS

Despite the superficial similarities between phenylcarbene (**1a**) and phenylnitrene (**1b**), there are significant differences between these reactive intermediates. Phenylcarbene undergoes intersystem crossing and intermolecular reactions

much faster than phenylnitrene, but the latter (**1b**) undergoes ring expansion much faster than the former (**1a**). These differences can be understood in terms of the difference between the electronic structures of the lowest singlet states of **1a** and **1b** and the much greater thermodynamic stability of triplet **1b**, relative to triplet **1a**.

Calculations have proven invaluable in understanding the many differences between **1a** and **1b**. In addition, calculations have provided insight into the substituent effects on the ring expansion reactions of derivatives of **1b**. Finally, calculations have made predictions about the barriers to and regiochemistries of these reactions. Some of these predictions have been verified; others await experimental test.

By furnishing both explanations and predictions, calculations have not only led to an understanding of experiments that have already been performed on **1a** and **1b**, but also have motivated new ones. The study of the chemistry of phenylcarbene (**1a**) and phenylnitrene (**1b**), particularly the ring expansion reaction that each undergoes, thus provides an excellent example of the synergy between calculations and experiments.

ACKNOWLEDGEMENTS

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PHOTOACOUSTIC CALORIMETRY OF CARBENES

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I. INTRODUCTION

The chemistry of carbenes in solution has been extensively studied over the past few decades.¹⁻⁵ Although our understanding of their chemistry is often derived from product analyses, mechanistic details are often dependent on thermodynamic and kinetic data. Kinetic data can often be obtained either directly or indirectly from time-resolved spectroscopic methods however, thermochemical data is much less readily obtained. Reaction enthalpies are most commonly estimated from calculations, Benson group additivities,⁶ or other indirect methods.

In this chapter, we describe how time-resolved photoacoustic calorimetry (PAC) can be used to obtain both the energetics and kinetics of carbenes in solution.⁷⁻⁹ PAC measures the magnitude and temporal profile of volume changes in solution following deposition of energy. These time-resolved volume changes can be directly related to carbene reaction enthalpies. We will first discuss the principles of this photoacoustic technique and then how it has been

applied to the study of carbenes formed in photoreactions. Although this chapter concerns the use of PAC to study carbenes, this technique has also been used to investigate other reactive intermediates and has been reviewed elsewhere.^{7,10-12}

II. BACKGROUND

Although the photoacoustic (PA) effect was initially discovered by Alexander Graham Bell in 1880, its application has dramatically increased in the past thirty years with the advent of modern instrumentation.¹³ The PA effect has been greatly utilized in chemistry as a calorimetric and spectroscopic tool. The principles of the PA effect have been well established and reviewed by Tam and Patel.^{14,15} Briefly, upon the absorption of a photon by a molecule, the energy may be converted into thermal energy, E_{th} , which will result in an increase in temperature along a cylinder defined by the path of the excitation beam through the sample. This rise in temperature, ΔT , increases the volume of the solution, ΔV_{th} , along the irradiated cylinder, generating an outwardly propagating pressure wave. If all of the photon energy is converted into thermal energy, the increase in E_{th} along the laser beam is expressed as

$$E_{th} = E_o(1 - 10^{-A}) \quad (1)$$

where A is the absorbance of the sample and E_o is the energy of the laser pulse. The increase in temperature is given by

$$\Delta T = E_{th}/\rho C_p V_o \quad (2)$$

where ρ is the density of the solution, C_p is its heat capacity, and V_o is the initial volume.

This temperature rise can be detected directly (laser calorimetry and optical calorimetry), or indirectly by measuring the change in either the refractive index (thermal lensing, beam deflection or refraction and thermal grating) or the volume (photo- or optoacoustic methods). This review will focus primarily on photoacoustic methods because they have been the most widely used to obtain thermodynamic and kinetic information about reactive intermediates. Other calorimetric methods are discussed in more detail in a recent review.⁷

The volume change of the medium induced by the heat deposition is related to the temperature change by the thermal coefficient of expansion of the solution, β .

$$\Delta V_{th} = \beta V_o \Delta T \quad (3)$$

Consequently, the magnitude of the volume change can vary greatly depending on β . For example, the volume change in organic solvents is typically orders of magnitude greater than in water, which has a small and temperature dependent β .

An acoustic wave detector, typically a piezoelectric transducer, measures the volume change (see Section III). This detector is sensitive to the magnitude and the temporal profile of the acoustic wave. As we will see, the amplitude of the wave provides valuable enthalpic information about reactive intermediates, and the temporal profile can reveal the dynamics of these intermediates.

For chemical systems of interest, photolysis produces intermediates, such as radicals or biradicals, whose energetics relative to the reactants are unknown. The energetics of the intermediate can be established by comparison of the acoustic wave generated by the non-radiative decay to create the intermediate, producing thermal energy E_{th} , with that of a reference or calibration compound whose excited-state decay converts the entire photon energy into heat, $E_{th}(\text{ref})$. The ratio of acoustic wave amplitudes, α_{th} , represents the fraction of the photon energy that is converted into heat.

$$\alpha_{th} = E_{th}/E_{th}(\text{ref}) \quad (4)$$

The enthalpy of the intermediate relative to the reactant, ΔH , is given by

$$\Delta H = E_{hv}(1 - \alpha_{th}) \quad (5)$$

where E_{hv} is the photon energy.

The above discussion assumes unit quantum efficiency for the photochemical reaction. Consider the more general case where the excited state either undergoes a photochemical reaction with quantum yield Φ , or decays back to its ground state non-radiatively with quantum yield $(1 - \Phi)$. The enthalpy of reaction is expressed as

$$\Delta H = E_{hv}(1 - \alpha_{th})/\Phi \quad (5')$$

Consequently, if the reaction enthalpy is unknown for a given process, the quantum yield must be determined from other measurements. Conversely, if the reaction enthalpy is known, then the quantum yield for the photochemical reaction can be measured. PAC has been used to obtain quantum yields for excited state processes, such as fluorescence, triplet state formation, and ion pair formation and separation. In systems in which competitive reactions occur, care must be taken to accurately account for the partitioning. For example, if a reactive intermediate yields two products, then the measured heat of reaction is the sum of the two individual heats of reaction multiplied by their respective yields. Consequently, there are three unknowns, the partitioning and the individual heats of reaction. Two of them must be known to properly evaluate the third.

In most photoacoustic experiments, it has been generally assumed that the experimental volume change resulted only from the thermal deposition of energy to the solvent. In such cases, the ratio of the volume change of the sample to that of the reference compound, α_{th} , could be related to the enthalpy of reaction

using Eqs. 4 and 5. However, many reactions also undergo a reaction volume change, which will also contribute to the observed acoustic wave. Complexation, ionization, covalent bond formation or breakage, and conformational changes can all contribute to the photochemical reaction volume change.¹⁶ The total acoustic wave, ΔV , produced by two different types of volume changes is given by

$$\Delta V = \Delta V_{\text{th}} + \Delta V_{\text{rx}} \quad (6)$$

where ΔV_{th} and ΔV_{rx} are the thermal and reaction volume changes, respectively. If the reaction volume change is positive due to volume expansion, the acoustic wave will be larger than anticipated if only thermal expansion for the system is considered. This would result in an erroneous value for ΔH .

Several methods have been developed to resolve these two volume contributions under suitable experimental conditions.^{7,17-21} This allows both the enthalpy of reaction and the photochemical reaction volume to be determined simultaneously. These methods all involve changing the solvent properties, β , ρ , and C_p , and thereby effectively varying the thermal contribution in a systematic manner. PAC has been employed to investigate several chemical²¹⁻²³ and biological^{19,20,24-26} reactions in both aqueous and non-aqueous media to determine reaction volumes. In organic solvents, however, the thermal volume change usually dominates due to the large expansion coefficient β , and so the reaction volume contribution is often ignored. For example, a reaction volume change of 20 ml/mol will introduce an error of about 2 kcal/mol in the calculated heat of reaction in organic solvents, but an error of 20 kcal/mol in water because of the significantly smaller expansion coefficient in water.

Time resolution of the enthalpy changes is often possible and depends on a number of experimental parameters, such as the characteristics of the transducer (oscillation frequency and relaxation time) and the acoustic transit time of the system, τ_a , which can be defined by $\tau_a = r_o/v_a$ where r_o is the radius of the irradiated sample, and v_a is the speed of sound in the liquid. The observed voltage response of the transducer, $V(t)$ is given by the convolution of the time-dependent heat source, $H(t)$ and the instrument response function, $T(t)$.^{1,11}

$$V(t) = H(t) \cdot T(t)$$

Under conditions of short laser pulses and where τ_a is less than the transducer response time, τ_o , three transducer voltage responses can be described depending on the time scale of the heat deposition, τ_h .

When $\tau_h \ll \tau_o$, $H(t)$ is effectively a delta function, an "instantaneous" heat deposition, and the resultant voltage response of the transducer is simply the instrument response function, $T(t)$. Although heat depositions cannot be time resolved in this regime, their magnitude and consequently the enthalpy

of reaction can be evaluated relative to the calibration compound. Calibration compounds are employed under these experimental conditions because they deposit a known amount of heat rapidly, and effectively yield the instrument response function. When $\tau_h \gg \tau_o$, no detector response is observed, i.e. long-time events are transparent to the transducer and ignored. When $\tau_h \cong \tau_o$, the voltage response can be analyzed to obtain both enthalpic and kinetic information about the heat deposition. Several deconvolution methods have been described for this purpose.²⁷⁻³¹ In many chemical systems, several heat depositions can contribute to $H(t)$ and each can be separately evaluated.

To date, most PAC experiments have measured kinetic processes on a time scale of 10 μ s–10 ns. Although PAC could indeed be utilized for slower kinetic events, other techniques such as thermal lensing and thermal beam deflection have typically been used.⁷ Although in theory, the time resolution of PAC can be increased, it will be difficult to do experimentally because of the inherent transit acoustic time limitations. Although sample cell designs may alleviate this problem to some extent,³² other technical considerations limit this technique to >10 ns. However, the limitations of the transit acoustic time can be fully overcome by using the transient grating technique,³³⁻³⁶ in which the volume changes are effectively detected by changes in the refractive index of the system. This technique has been used to monitor kinetic events on the picosecond time scale.

We can illustrate the application of PAC to a simple photochemical reaction. Acetone is readily excited to its singlet excited state which rapidly undergoes efficient intersystem crossing to its triplet state. The triplet state decays in solution primarily by radiationless decay. The PAC experimental waveforms obtained from the photoexcitation of acetone in air and argon-saturated cyclohexane are shown in Fig. 1. In addition, the waveform obtained from the calibration compound 2-hydroxybenzophenone is also shown.

The calibration compound undergoes no photochemistry. It deposits all of the photon energy rapidly, <10 ns, as heat. Its waveform, T-Wave, serves as the instrument response function and is used to deconvolute the experimental waves. As is readily apparent, the experimental waves E-Wave(1) and E-Wave(2) are phase shifted relative to the T-Wave. This indicates that energy is deposited to solution within the time resolution of the transducer. Deconvolution of the E-Waves indicates two heat depositions. The first, defined as <10 ns, corresponds to the rapid formation of the triplet state of acetone. The amplitude of the heat deposition can be used to calculate the triplet state energy. The experimental value of 76 ± 2 kcal/mol is in good agreement with the spectroscopic value of 78 kcal/mol.³⁷ The second decay corresponds to the decay of the triplet state in air-saturated, 75 ns, or argon-saturated, 450 ns, cyclohexane. The shorter lifetime for the triplet state in air-saturated solvent suggests that it is effectively quenched by oxygen.

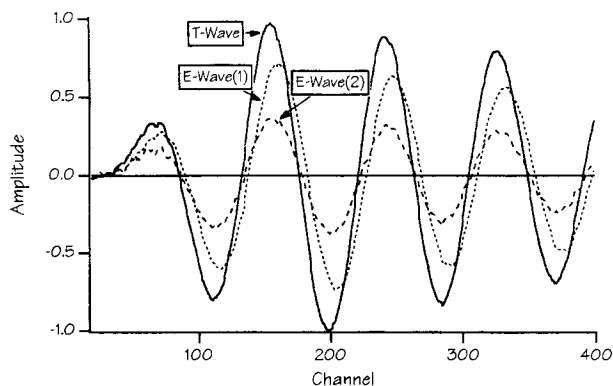


Figure 1. Experimental waveforms from excitation (266 nm) of 2-hydroxybenzophenone (T-Wave, and acetone in air-saturated (E-Wave(1)) and argon-saturated (E-Wave(2)) cyclohexane. (With permission from Joshua L. Goodman.)

There are several unique features about PAC. First, PAC and the related methods are the only experimental techniques currently available, which can measure the heats of reaction of carbenes on the microsecond and faster time scale. This usually allows for an accurate determination of the heats of formation of these reactive intermediates. Second, PAC can monitor the reactions of transients which are optically transparent, i.e. do not have an UV-VIS optical absorbance. Hence, in addition to thermodynamics, PAC can also provide important kinetic information about these “invisible” species.

III. INSTRUMENTATION

The experimental design for the photoacoustic experiment is relatively simple. The apparatus is quite similar to that employed for nanosecond absorption spectroscopy with the major difference being that a piezoelectric transducer is used to monitor the acoustic waves rather than a photomultiplier tube to analyze the incident light. A representative schematic for PAC is shown in Fig. 2.

Nanosecond Nd : YAG, excimer, or nitrogen pulsed lasers are typically used as the light source. A fraction of the light beam is reflected to a photodiode, which triggers the experimental data collection. The beam then impinges on the sample within the cell. The generated acoustic signal is detected by the piezoelectric transducer, amplified, digitized and stored in the computer. The acoustic waves are normalized for absorbance, which is determined *in situ* using the two energy meters, and fluctuations in laser power. The computer analyzes the waveforms using a deconvolution program to obtain the requisite kinetic and thermodynamic information.

Several different cell designs have been used for PAC. In the cell design

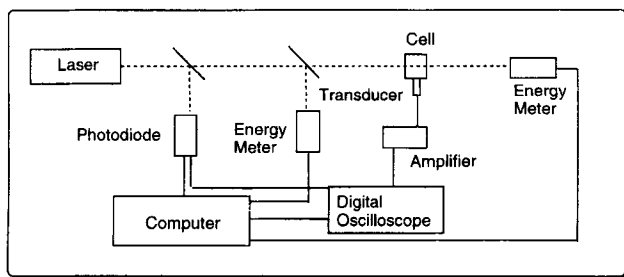


Figure 2. Schematic representation for photoacoustic calorimeter.

above, the beam passes through the cell wall at a right angle to that to which the transducer is attached. The time resolution in this cell design is given by the beam diameter and the velocity of sound in the solvent, i.e. τ_a . An alternate front face design has been developed by Melton in which the beam passes through the cell wall parallel to that affixed to the transducer.³² The time resolution in this cell is given simply by the cell thickness. Each design has certain advantages (and disadvantages) with regard to sensitivity, time resolution, sample preparation and ease of operation.

A variety of piezoelectric transducers have been employed for PAC. Ceramic transducers, usually lead zirconate titanate, are most commonly employed because of their sensitivity, time resolution and commercial availability. However, their acoustic response is often dominated by their own resonance, and so polymeric film detectors, such as polyvinylidenedifluoride, are often used. These piezoelectric materials are non-resonant, but not as sensitive as the ceramic detectors. Again, each detector has its own advantages (and disadvantages).^{14,15}

The accuracy of the thermochemical data obtained by this technique has been examined in numerous systems. In general, the data compares well, ± 1 kcal/mol, with that obtained by other spectroscopic and calorimetric methods. The accuracy and reproducibility of the data is dependent on the magnitude and time scale of the heat deposition detected by PAC that is associated with a given chemical process. Highly exothermic reactions are easy to detect, whereas ones that are not are difficult to detect. A thermoneutral reaction is invisible to PAC. Reactions that occur significantly slower than the response time of the transducer are not detected. Reactions that occur either slightly slower or faster than the response time are difficult to resolve accurately. Clearly, the proper choice of the transducer is extremely important in order to resolve accurately a given chemical event.

Thermochemical data obtained from experiments in which only a fast heat deposition is detected is more reliable than those in which two or more heat depositions are observed. This is due in part to the necessity for deconvolution of the experimental data. With conventional transducers and low pulses energies,

$<10 \mu\text{J}$, the signal to noise ratio is typically >10 , and so signal averaging is usually not necessary. Fluctuations in the measured heat depositions are usually small, $<2\%$ from experiment to experiment.

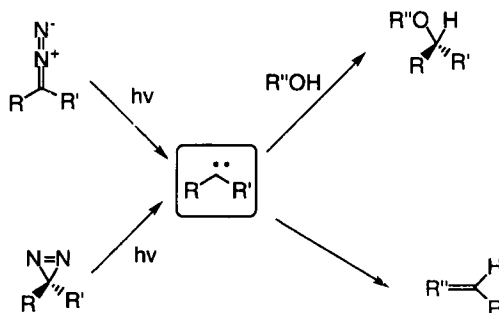
Picosecond optical grating calorimetry, a technique similar to PAC, has also been used to study carbene reactions.^{38,39} In this method, a thermal grating or interference pattern is established using two crossed, time-coincident pulses (355 nm, 25 ps). A probe pulse that detects changes in the refractive index of the medium measures the subsequent volume changes that destroy the thermal grating. Although the time resolution can be significantly shorter than that of PAC, the experimental setup and data analyses are somewhat more difficult.

IV. EXPERIMENTAL RESULTS

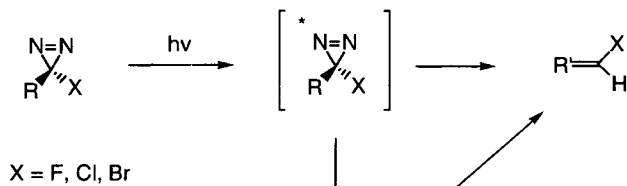
A. Heats of Formation

In principle, the heat of formation of carbenes can be determined from PAC heats of reaction and either the carbene precursor or the carbene products' heats of formation (Scheme 1).

In fact, the first application of PAC to carbenes was by Peters who investigated the photolysis of diphenyldiazomethane to yield triplet diphenylcarbene.^{10,40} The heat of reaction was found to be almost thermoneutral, which suggests that the heats of formation of diphenyldiazomethane and diphenylcarbene are similar. In addition, the rate and energetics of the reaction of the carbene with oxygen to form the carbonyl oxide were determined. Alternatively, carbene heats of formation can be determined from the heats of carbene reactions. The bimolecular reaction of carbenes with alcohols can be measured by PAC and then used to determine the heats of formation for the singlet carbenes.^{41,42} For example, the heat of reaction of dimethoxycarbene, $\text{C}(\text{OCH}_3)_2$, with CH_3OH is -24.8 kcal/mol .⁴² Using the heats of formation of CH_3OH and the product, $\text{CH}(\text{OCH}_3)_3$, the calculated heat of formation of $\text{C}(\text{OCH}_3)_2$ is -54.7 kcal/mol .



Scheme 1.

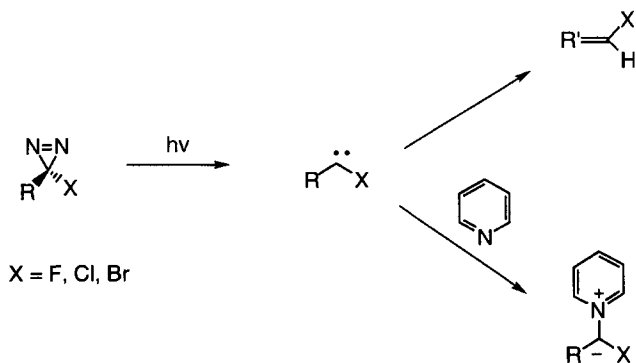
**Scheme 2.**

This is in good agreement with the AM1 value of -53 kcal/mol. Unimolecular carbene reactions, such as rearrangements, can be also used to determine heats of formation.^{43,44}

In the determination of carbene heats of reaction, the quantum yield for formation of the *carbene* must be accurately known, as described earlier. Errors in the yield can lead to inaccurate heats of reaction. The following example will illustrate this concern (Scheme 2). The photolysis of alkylhalodiazirines results in the formation of vinyl halides presumably via the alkylhalocarbenes, which undergo a 1,2-hydrogen rearrangement. PAC and competition product studies indicate *two* pathways for the formation of vinyl halides: (i) a 1,2 intramolecular hydrogen shift of the carbene, and (ii) an excited state pathway which circumvents the carbene.^{44,45} So although the quantum yield for vinyl halide formation approaches unity, the quantum yield for *carbene* formation is significantly less than unity. Using a quantum yield of unity for carbene formation would yield carbene heats of formation different than those predicted from calculations. In fact, the partitioning between these two pathways for vinyl halide formation can be determined using the calculated heats of formation.

B. Unimolecular Reactions

Both PAC and transient grating spectroscopy have been used to investigate unimolecular rearrangements of carbenes.^{39,43} Depending on the time scale of the reaction and the time resolution of the apparatus, both the reaction enthalpies and rates can be determined. Many carbenes are spectroscopically “invisible”, in that they have no easily identifiable chromophore. PAC and transient grating spectroscopy can measure the dynamics of these species by measuring their heat depositions. Unfortunately, any deposition of given magnitude and rate will appear identical and so does not provide any structural information. Care must be taken to corroborate the reaction detected by these methods with chemical studies or some indirect method. Fortunately, many of the rearrangement rates measured can be indirectly confirmed by the “pyridine ylide” method developed

**Scheme 3.**

by Platz⁴⁶ (Scheme 3). In most cases, good agreement has been obtained between the various methods.

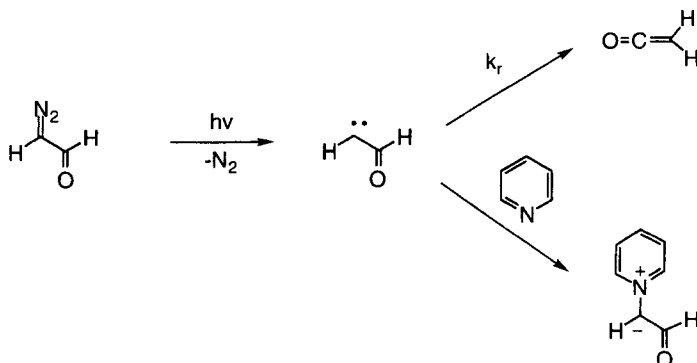
The rearrangement rates for several halocarbenes have been determined as a function of temperature, and in many cases, the obtained Arrhenius plots are curved.^{47–49} At high temperatures, the slopes yield activation parameters in good agreement with theoretical calculations.^{50,51} However, the parameters deviate significantly at lower temperatures. These deviations have been attributed to quantum mechanical tunneling, solvent effects and secondary reactions. Currently, the most reasonable explanation is that bimolecular reactions of the carbenes with solvent and/or their diazine precursors occur at low temperatures.⁵² Although these reactions are entropically disfavored, they have very low enthalpic barriers and so predominate at low temperature over the 1,2-hydrogen rearrangement.

The lifetime of formylcarbene was determined by transient absorption and grating spectroscopies.³⁹ Photolysis of formyldiazomethane produces formylcarbene which can isomerize, k_r , to ketene or react with pyridine (Scheme 4). Using the “pyridine ylide” method, the lifetime of singlet formylcarbene was estimated to be 150–730 ps in CH_2Cl_2 . This is in reasonable agreement with the lifetime of 900 ps determined by transient grating spectroscopy.

C. Bimolecular Reactions

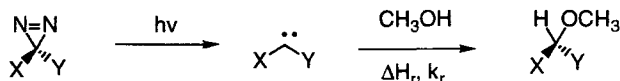
The reaction of singlet carbenes with alcohols has been studied by PAC and the results have led to some interesting mechanistic implications.^{41,42} The rates, k_r , and heats of reaction, ΔH_r , of the singlet carbenes with methanol vary with substitution (Fig. 3).⁵³

With increasing π electron-donating ability of the substituents, ΔH_r decreases. This reflects primarily the increased stability of the carbene, and is

**Scheme 4.**

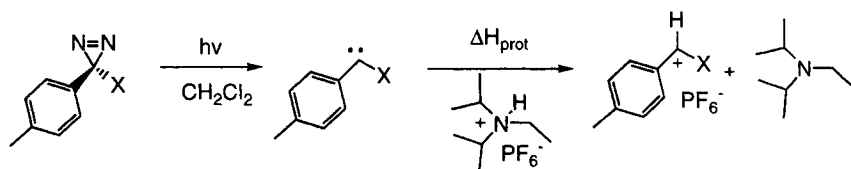
reflected in the decreasing k_r . However, the most stable carbene, $X=Y=\text{OCH}_3$, reacts more rapidly than expected and most likely indicates a change in mechanism. The electrophilic carbenes, $X=\text{CH}_3$, Ph, $Y=\text{Cl}$, react rapidly with CH_3OH potentially via an ylide intermediate. In contrast, dimethoxycarbene reacts rapidly as a nucleophile by initial deprotonation of CH_3OH to form an ion pair that subsequently collapses to product. The reaction rates with ambiphilic carbenes, $X=\text{OCH}_3$, $Y=\text{Cl}, \text{F}$, are quite slow and probably occur by a combination of these two pathways.

The heats and rates of reaction of carbenes with substituted pyridines to form ylides have been measured and used to calculate the ylides' heats of formation.⁵⁴ The heats of reaction of methylchloro- and phenylchlorocarbene with were found to correlate well with the pK_a 's and proton affinities of the pyridines. However, the correlation is not good for sterically demanding



X	Y	ΔH_r (kcal/mol)	k_r ($\text{M}^{-1}\text{s}^{-1}$)
CH_3	Cl	-63	10^8
Ph	Cl	-51	10^8
OCH_3	Cl	-31	10^4
OCH_3	OCH_3	-25	10^6

Figure 3. The reaction of substituted carbenes with CH_3OH .



X	ΔH_{prot} (kcal/mol)	ΔpK_a	pK_a
Cl	-20.3	14.9	33.0
F	-28.1	20.6	38.7

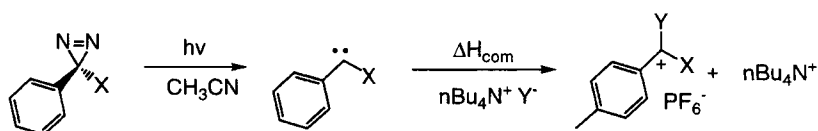
Figure 4. The protonation of tolylhalocarbenes with ammonium salt in CH_2Cl_2 .

pyridines, presumably because of the large size of the carbene relative to a proton. In fact, some pyridines do not readily form ylides with the carbenes. The rates of ylide formation with the carbenes were also found to increase with the basicity of the pyridines.⁵³ In addition, the reaction of methylene with acetone and acetonitrile to form carbonyl and nitrile ylides, respectively, has also been examined by PAC and used to calculate the ylides' heats of formation.⁵⁵

The protonation of carbenes by acids has been studied by PAC. Using sterically hindered acids to prevent collapse of the ion pair, the heat of reaction can be obtained and used to determine the pK_a s of the resultant carbocations (Fig. 4).⁵⁶ The results indicate that deprotonation of the carbocations to generate carbenes should be possible with strong hindered bases. This method has only rarely been used in the literature.^{1,57}

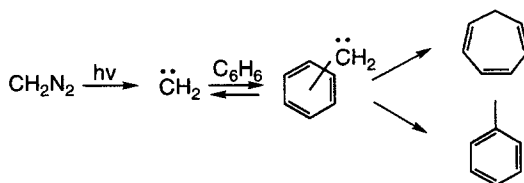
A more general method for preparing carbenes often involves the α elimination of halides from carbanions.^{1,57} PAC can be used to examine the rates and energetics of the reverse reactions, the complexation of halides with carbenes (Fig. 5).⁵⁸ Plots of ΔH_{com} versus the proton affinities (PA) of the halides are linear for the two carbenes studied. Although the slopes of the plots are similar, complexation of the halides with phenylchlorocarbene is more exothermic than phenylfluorocarbene. This indicates that fluoro substitution stabilizes the carbene relative to the carbanion more than chloro substitution. The rate of complexation of carbenes with salts has also been examined by nanosecond absorption spectroscopy.⁵⁹

Many chemical reactions involving carbenes are believed to involve the initial formation of weak, highly reactive complexes. For example, several reactions of electrophilic carbenes with various nucleophiles are thought to involve π complexes.^{49,60–64} However, while kinetic and product studies often suggest their existence, their direct detection is often quite difficult. Recently,



Y (PA)	ΔH_{com} (kcal/mol)	
	X=Cl	X=F
Cl^- (333)	-24.8	-15.2
Br^- (324)	-21.7	-11.8
I^- (315)	-14.4	-4.9

Figure 5. The complexation of phenylhalocarbenes with tetrabutylammonium halides in CH_3CN . The numbers in parentheses are gas phase proton affinities.



Scheme 5.

picosecond optical grating calorimetry was used to detect a highly reactive transient in the photochemical decomposition of diazomethane in benzene.³⁸

Photochemical decomposition of diazomethane yields methylene, which reacts with benzene to form toluene and cycloheptatriene (via norcaradiene) (Scheme 5).^{65,66}

Although concerted C=C and C-H insertion into benzene by methylene is possible, several experiments on the effect of various solvents on the product ratio suggest the intermediacy of a complex between methylene and benzene.⁶⁷⁻⁶⁹ Based on the obtained kinetic and thermodynamic data, the transient is believed to be a complex formed between singlet methylene and benzene.

V. CONCLUSIONS

In this chapter, we have described the application of photoacoustic calorimetry to determine the heats and rates of reaction of carbenes. It can also be readily

applied to study other reactive intermediates such as singlet and triplet states, strained rings, antiaromatics, ion pairs, metal and organometallic complexes, and odd electron species.⁷ The technique is simple both in the experimental design and data analysis. It is an extremely versatile, highly sensitive analytical method, which requires only that the reactive intermediate be generated rapidly (<10 ns) under photochemical conditions and that it causes a volume change in solution. PAC can detect "invisible" transients in that it does not require any given structural feature. Furthermore, PAC can serve as an excellent complementary technique to others such as absorption and emission spectroscopies.

ACKNOWLEDGEMENTS

I would like to thank the National Science Foundation and the Alfred P. Sloan Foundation who have generously supported the work on the application of PAC to carbenes. I am deeply indebted to the numerous researchers who have contributed to the use of PAC to study carbene reactions.

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SOME ASPECTS OF THE CARBENE BRIDGEHEAD–OLEFIN CARBENE REARRANGEMENT

Günter Szeimies

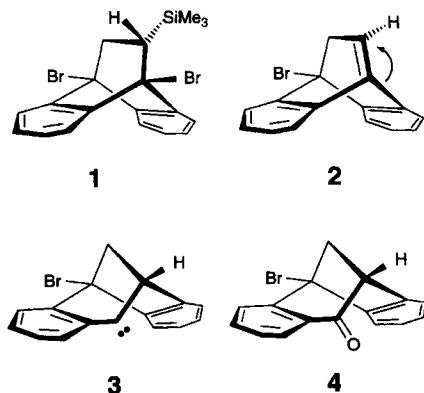
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I. INTRODUCTION

The carbene route to bridgehead olefins is a well established reaction and has been developed to a major method for the generation of bridgehead alkenes. The field has been recently reviewed by one of the main contributors to this area.¹ The reversed reaction, the formation of carbenes from distorted olefins, has also been known for a long time. Distortion of the π bond in alkenes is easily affected by photoexcitation. In connection with those reactions, carbene chemistry has been observed and the field has also been reviewed some years ago.²

Only little information is available on carbene formation by rearrangement of bridgehead olefins, generated in thermal reactions. A prominent example is the rearrangement of bridgehead olefin **2**, obtained as short-lived intermediate from bromosilane **1** by reaction with potassium fluoride in DMSO at 110°C. Carbene

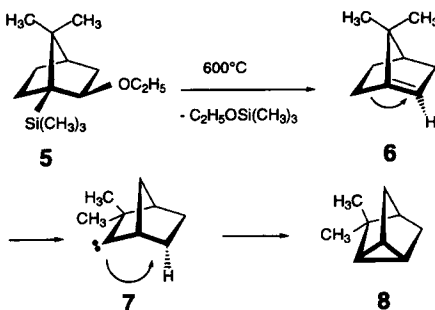
3, generated from alkene **2** by a 1,2-shift of the aryl group reacted either with the solvent DMSO to give ketone **4** or, if THF was present, inserted into the CH bond of the α -carbon atom of THF.³



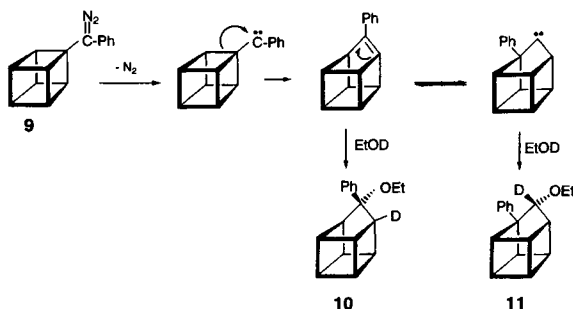
A second example has been reported by Barton and Yeh. They found that silane **5** gave rise to the formation of dimethylnortricyclane **8** when heated to about 600°C in the gas phase.⁴ A probable reaction route for this process is depicted in Scheme 1.

After elimination of ethoxytrimethylsilane, 7,7-dimethyl-1-norbornene (**6**) rearranges to 3,3-dimethyl-2-norbornylidene (**7**), which undergoes a 1,3-CH insertion reaction into the *endo*-6-H to give tricyclane **8**. Nortricyclane formation has been shown to be the fastest intramolecular mode of stabilization of 2-norbornylidene.^{5,6}

The first example of a carbene bridgehead–olefin carbene rearrangement comes from the laboratory of Eaton.⁷ Cubylphenyldiazomethane (**9**), when photolyzed or heated in ethanol, afforded a mixture of ethers **10** and **11**. The reaction follows the route shown in Scheme 2. It has been reviewed,¹ and the exiting chemistry of the parent system **12** → **13** → **14**, elucidated by Jones and

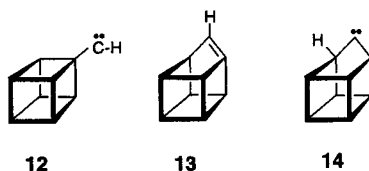


Scheme 1.



Scheme 2.

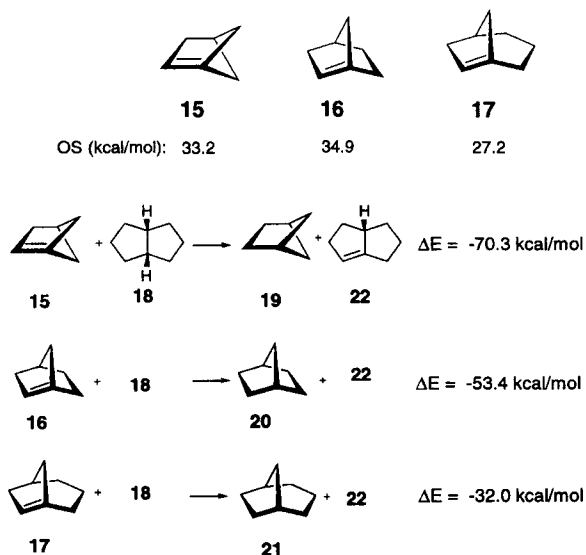
Platz and their groups,⁸ has also been discussed.¹ Experiment and theory agree that **13** and **14** are close in energy, but whereas experiments seem to indicate that the barrier between these two molecules should be low (<5 kcal/mol),⁸ Holthausen and Koch obtained a value as high as 23.5 kcal/mol by the (2/2) CASSCF procedure.⁹ Hrovat and Borden revisited the problem and, using a higher level of theory for their calculations, computed a barrier of 12.9 kcal/mol for this rearrangement,¹⁰ which is still in contradiction with experiment. At the reliability of the results of high-level MO calculation to problems of organic chemistry, it would be desirable to have these discrepancies solved.



II. RECENT COMPUTATIONAL CONTRIBUTIONS TO THE FIELD

Before we present recent results, it is probably helpful to obtain some quantitative aspects of the energetics of the bridgehead olefin, which is necessary for the rearrangement to occur. Maier and Schleyer have defined *olefinic strain energy* (OS) as the difference of the total strain energy of the parent hydrocarbon in its most stable conformation and the total strain energy of the corresponding olefin in its most stable conformation.¹¹ For bridgehead olefins **15**, **16**, and **17** OS values as obtained from MM1 force field calculations are given under the structural formulas.¹¹

The energy differences seem to be somewhat unrealistic, specifically if one considers that **15**, **16**, and **17** can be regarded as analogues of *trans*-cyclopentene, *trans*-cyclohexene, and respectively, as *trans*-cycloheptene.¹² As has

**Scheme 3.**

been shown earlier for pyramidalized alkenes, high-level ab initio calculations give more reliable OS values for transient species.¹³ We have carried out DFT calculations using Becke's 3 parameter functional¹⁴ and the gradient-corrected correlation functional of Perdue, Burke and Wang.¹⁵ This method (B3PW91) is implemented in the Gaussian 98 program package¹⁶ which was used throughout. The results of the isodesmic reactions of the corresponding olefins with bicyclo[3.3.0]octane (**18**) to give the corresponding alkanes **19**, **20**, and **21**, and the tri-substituted alkene **22** are shown in Scheme 3. The energy values were obtained from B3PW91/6-311G(d,p)//B3PW91/6-311G(d,p) calculations, including zero-point energy corrections, computed at the same level of theory.

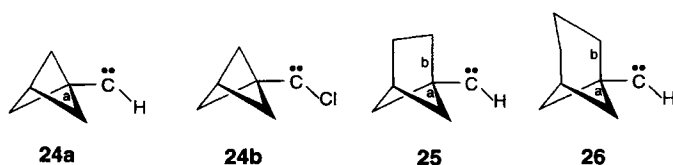
The absolute energy values shown in Scheme 3 could be regarded as 'olefinic strain energy' (OSE) of the bridgehead olefins **15**, **16**, and **17**. As the standard in our calculations was bicyclo[3.3.0]oct-1-ene (**22**), the energies of Scheme 3 are not directly related to those of Borden,¹³ who used bicyclo[3.3.0]oct-1(5)-ene (**23**) as the standard. We computed **23** to be more stable by 2.9 kcal/mol than **22** (B3PW91/6-311D(d,p)//B3PW91/6-311D(d,p), including ZPE correction). In addition, the theoretical model was different in both approaches.

**23**

The OSE of Scheme 3 indicate the varying degree of olefinic distortion, which should be reflected in the differing propensity of the olefins to undergo

the rearrangement to the corresponding carbene. Unfortunately, the OSE cannot be used as a quantitative measure for the ability of the olefins to rearrange, because the activation barriers will also be influenced by the structure of the developing carbenes. Therefore, it is necessary to obtain the stationary points of the rearrangement process to judge on the feasibility of the reaction under appropriate reaction conditions. We have recently carried out such calculations for the rearrangements of **15**, **16**, and **17**.^{17,18}

As our experimental investigations started by generating carbenes of type **24**, **25**, and **26**, we will as well include results of calculations of these carbenes and their conversion to the corresponding bridgehead olefins.



For carbenes **25** and **26** 1,2-shifts of bonds *a* and *b* will lead to different bridgehead olefins, **17** and **27** for **26**, and 1-norbornene **16** and bicyclo[3.1.1]hept-1-ene (**30**) for **25**, whereas carbene **24a** will only give alkene **15**. In accordance with experimental observations,¹⁹ calculations show that the more strained bond will migrate preferentially.

Details on the structures of the intermediates and transition states of Fig. 1 are found in Ref. 18. We note that at 0.7 kcal/mol the barrier of migration along *a* is very small, whereas at 7.9 kcal/mol the barrier for the competitive rearrangement via *b* is considerably higher and will not be followed at low temperature to any visible extent. Both reorganizations are strongly exothermic and they are certainly not reversible under normal reaction conditions.

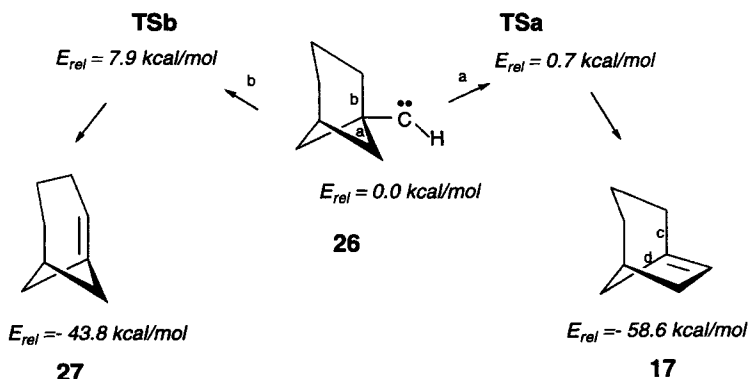


Figure 1. Energy profile for the rearrangement of carbene **26**, based on calculations at the B3LYP/6-311G(d,p)//B3LYP/6-31G(d) level of theory.¹⁸

Could bridgehead alkene **17** rearrange further? Not according to the results of the B3LYP calculations. Carbene **28**, generated from **17** by a 1,2-shift of bond *c* is computed to be higher in energy by 32.2 kcal/mol than **17**, and carbene **29**, formed by migration of bond *d*, by 53.5 kcal/mol. These numbers made it unnecessary to determine the activation barriers of these reactions, as these will be at least as high as the energy differences of the intermediates.



The situation is somewhat more favorable for the rearrangement of olefin **27** to give carbene **28**. Here, the energy difference of $E(\mathbf{28}) - E(\mathbf{27})$ is computed as only 17.3 kcal/mol, indicating the relief of strain energy of **27**.

The energy profile of the rearrangement of carbene **25** is given in Fig. 2.

As for the higher homologue **26**, the barrier of rearrangement of carbene **25** to give 1-norbornene **16** by migration of the four-membered ring carbon atom is, at 2.3 kcal/mol, rather small; the barrier of the 1,2-shift of bond *b* of **25** needs 7.3 kcal/mol of activation and is higher by 4.9 kcal/mol. At -39.3 and -34.2 kcal/mol, respectively, both reactions are strongly exothermic. An answer to the question, if 1-norbornene could further rearrange to carbene **31** or **32**, is given in Fig. 3.

At a barrier of 42.5 kcal/mol, the least probable rearrangement will be the reaction of 1-norbornene **16** going to carbene **31**. The rearrangement of **30** to **32** needs 26.8 kcal of activation. At an energy difference of only 4.2 kcal/mol between **30** and **32**, an interconversion under strongly forcing reaction conditions might be possible. This also holds for the conversion of **16** $\rightarrow$ **32**,

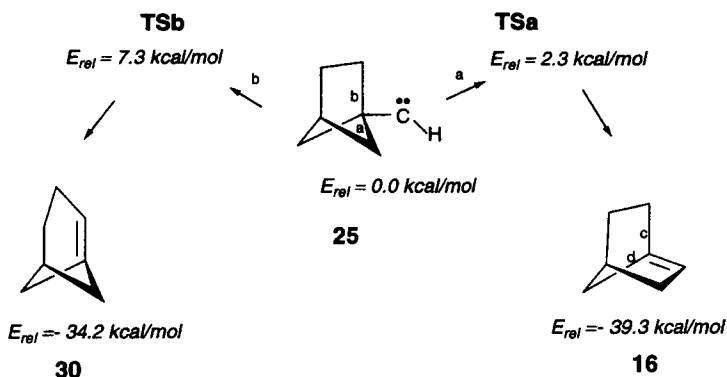


Figure 2. Energy profile for the rearrangement of carbene **25**, based on calculations on the B3LYP/6-311G(d,p)//B3LYP/6-31G(d) level of theory.¹⁸

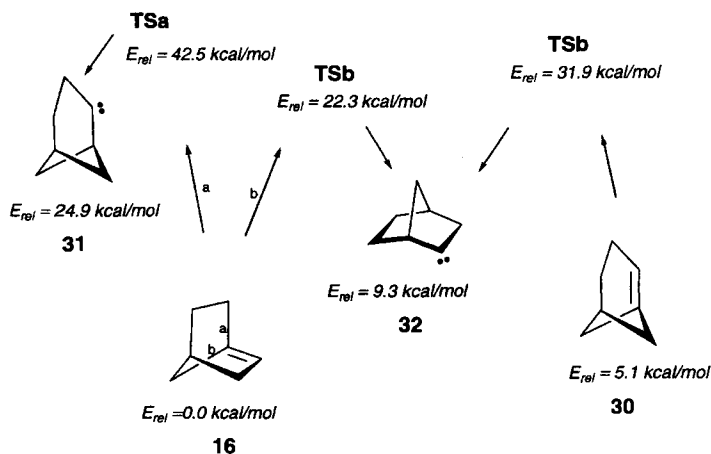


Figure 3. Energy profile for the rearrangement of bridgehead olefins **16** and **30** to carbenes **31** and **32**, based on calculations at the B3LYP/6-311G(d,p)//B3LYP/6-31G(d) level of theory.¹⁸

specifically if there exists an efficient reaction path for the carbene **32** to be stabilized, as found in the facile CH insertion to afford the nortricyclane skeleton (see above for the reaction of **7** → **8**).

Carbene **24a** was not a local minimum on the C_6H_7 energy hypersurface at the B3LYP/6-31G(d) level of theory. Chlorocarbene **24b** was found to be a local minimum; its isomerization to give **15b** was separated by a computed barrier of 7.1 kcal/mol.¹⁷ Both, **15a** and **15b**, are converted in exothermic reactions of 8.4 kcal/mol and 5.4 kcal/mol into carbenes **33a** and **33b** crossing barriers of 9.8 kcal/mol and 9.0 kcal/mol. An important aspect from the experimental point of view is the ability of carbenes of type **33** to stabilize by 1,2-hydrogen shift affording bicyclo[2.1.1]hex-2-enes (**34**). Our computed barriers of **33a** → **34a** were 12.6 kcal/mol, and for **33b** → **34b** 12.4 kcal/mol. These values are slightly lower than the calculated barrier of 16.2 kcal/mol for **33a** → **34a** reported recently.⁵ In any case, hydrogen migration of carbene **33** seems to need a somewhat higher activation than the rearrangements of carbene **24b** → **15b**, and **15** → **33b**. This might open a chance to trap carbenes of type **33** in bimolecular reactions. In Fig. 4 the energy profile for the conversion of **24b** into **34b** is given.

Two results of our calculations deserve specific mention: The barrier of inversion of **15b-1** → **15b-2** was calculated as 7.6 kcal/mol (MCQDPT/6-31G(d)//MCQDPT/6-31G(d)).¹⁷ In the transition state of this inversion process, the orbitals at C1 at C2 are orthogonal. The low inversion barrier could be regarded as a measure of the olefinic bond energy of **15b**, which seems to be reduced to a value slightly higher than 10% of the π -part of the CC double bond energy

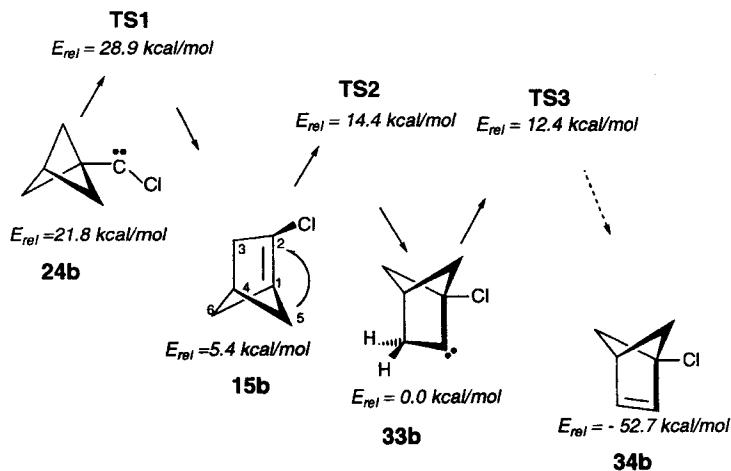
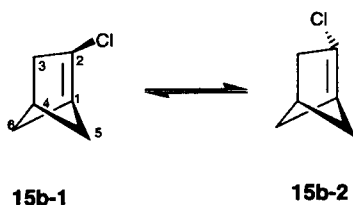


Figure 4. Energy profile for the rearrangement cascade **24b** $\rightarrow$ **15b** $\rightarrow$ **33b** $\rightarrow$ **34b**, based on calculations at the B3LYP/6-311G(d,p)//B3LYP/6-31G(d) level of theory.¹⁷

of unstrained alkenes. The second point is concerned with the question which of the two C atoms of alkene **15b**, C5 or C6, will migrate to C-2. Calculations show that C5, the C-atom at the same side of the molecule as the substituent at C-2, migrates preferentially.



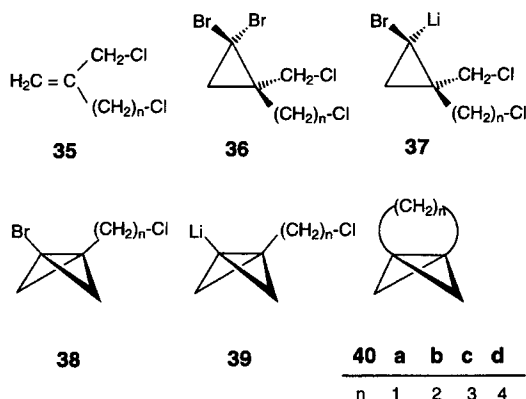
The calculations indicate that only the most highly strained bridgehead olefins, specifically of the *trans*-cyclopentene type, are candidates for a rearrangement to carbenes. Only at high temperature is there a chance for *trans*-cyclohexene analogues to undergo such a conversion.

III. EXPERIMENTAL RESULTS

A. Starting Materials

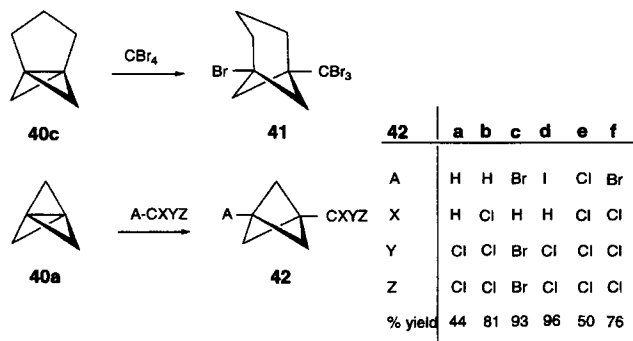
Our approach to the synthesis of model compounds, suited for the generation of carbenes, which are bound to the bridgehead of a strained bicyclic system, used the facile synthesis of [*n*.1.1]propellanes, which we developed some years ago. Starting from substituted allyl chlorides **35**, dibromocarbene addi-

tion leads to cyclopropanes **36**. Reaction of **36** with 2 equiv. of methyllithium or butyllithium affords after Li–Br-exchange by cyclization of the intermediate **37** the bicyclo[1.1.0]butane derivative **38**; after a second Li–Br-exchange of **38**, the bridgehead lithiated bicyclo[1.1.0]butane **39** is able to cyclize to the final propellane **40**.



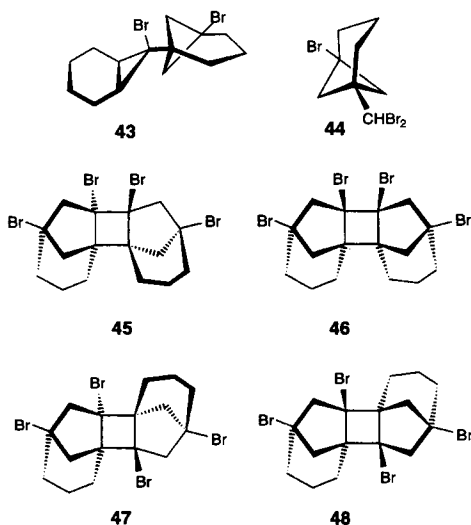
For $n = 1$, this is the standard synthesis of [1.1.1]propellane **40a**.^{20,21} Also for $n = 3$, this method makes [3.1.1]propellane **40c** accessible with reasonable effort.²² Although [2.1.1]propellane **40b** was detected by its IR spectrum at liquid nitrogen temperature,²³ it could not be obtained as a stable compound via this route.²² The addition of halomethanes across the central bond by a radical chain mechanism is common to **40a** and **40c**. The addition of carbon tetrabromide to **40c** afforded a 45% yield of **41**.¹⁸ Likewise, a number of bicyclo[1.1.1]pentane derivatives **42** were obtained by reaction of the corresponding halomethanes with **40a**.^{17,24}

Starting from **41** or **42**, organometallic methodology will lead to carbenoids, which are expected to eliminate metal halides and generate the corresponding carbenes; these can be detected by appropriate trapping reactions.



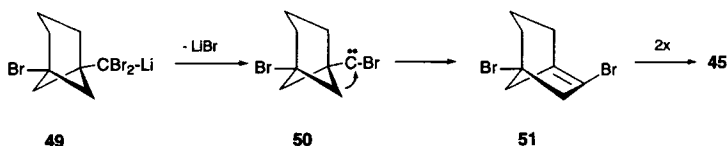
B. Bromo-(5-bromobicyclo[3.1.1]hept-1-yl)carbene

When tetrabromide **41** was treated with an excess of MeLi/LiBr in cyclohexene as a trap for carbenoids and carbenes, adduct **43** was obtained in 4% yield. In addition, **44** was isolated in 3% yield. The main product, however, was tetrabromide **45**, whose yield amounted to 32%. The structure of **45** was established by single crystal X-ray crystallography.¹⁸



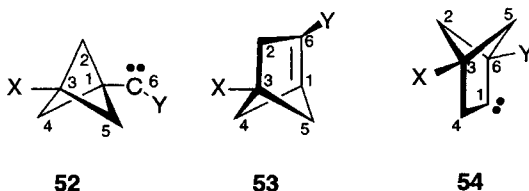
Besides **45**, a 5% yield of a stereoisomer was obtained, whose structure is presumably **46**, but **47** and **48** cannot be excluded with certainty.¹⁸

The formation of the first two compounds seems to originate from carbenoid **49**, which in addition to protonation leading to **44** reacts with cyclohexene to give the adduct **43**. **45** is best interpreted as the head-to-head dimerization product of bridgehead olefin **51**. **51** could only be formed by rearrangement of carbene **50**. This then is another example of the preference for ring-enlargement of the smaller ring in stabilizing a carbene center, bound to the bridgehead position of a bicyclic system. This result is in accordance with our calculations and with earlier experimental observations.¹⁹

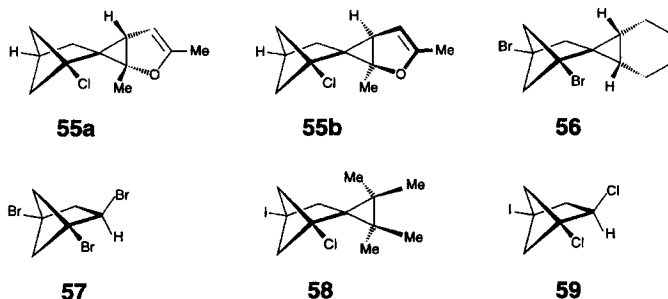


C. Halo-(3-halobicyclo[1.1.1]pent-1-yl)carbene

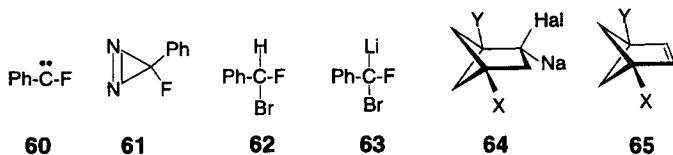
According to the results of our calculations, carbenes of type **52** are ideal models for the carbene **52**–bridgehead olefin **53**–carbene **54** rearrangement. The numbers of the C-atoms of formula **52** have been retained in formulas **53** and **54** to show, which bonds are broken and which C atoms migrate.



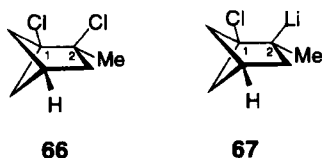
Several experiments, in which **52** was generated led to the isolation of trapping products of **54**²⁴. Thus, **42a** and MeLi in the presence of an excess of 2,5-dimethylfuran afforded a 29% yield of a 1 : 1 mixture of **55a** and **b**. The crystalline carbene adduct **56** was obtained in 10% yield when **42c** was treated with sodium bis(trimethylsilyl)amide [NaN(SiMe₃)₂] in the presence of cyclohexene. In addition, solid 1,2,4-tribromobicyclo[2.1.1]hexane (**57**) was isolated in 16% yield. The reaction of **42d** with NaN(SiMe₃)₂ in the presence of tetramethylethylene led to the formation of the crystalline adduct **58** in 10% yield, together with **59** in a yield of 25%. The structures of **56**, **57**, and **58** have been determined by single crystal X-ray spectroscopy. Whereas the formation of the adducts **55**, **56**, and **58** can be attributed to the cycloaddition of a carbene of type **54** to the corresponding traps, the generation of the trihalides **57** and **59** is less obvious. We refer to a paper of Moss and coworkers, who observed that phenylfluorocarbene (**60**), generated by irradiation of phenylfluorodiazirine (**61**) in the presence of lithium bromide in acetonitrile afforded a 55% yield of α -bromo- α -fluorotoluene **62**.²⁵ This result was interpreted by reaction of **60** with lithium bromide to give carbenoid **63**, which is protonated by the solvent. Likewise, the formation of **57** and **59** could be rationalized by addition of



sodium bromide or chloride to the corresponding carbenes **54** to give carbenoids **64**, which then are protonated by protic sources in the reaction medium. It should be remembered that the intramolecular stabilization of **54** to give alkene **65** obviously needs too much activation, which is not available at low temperature.



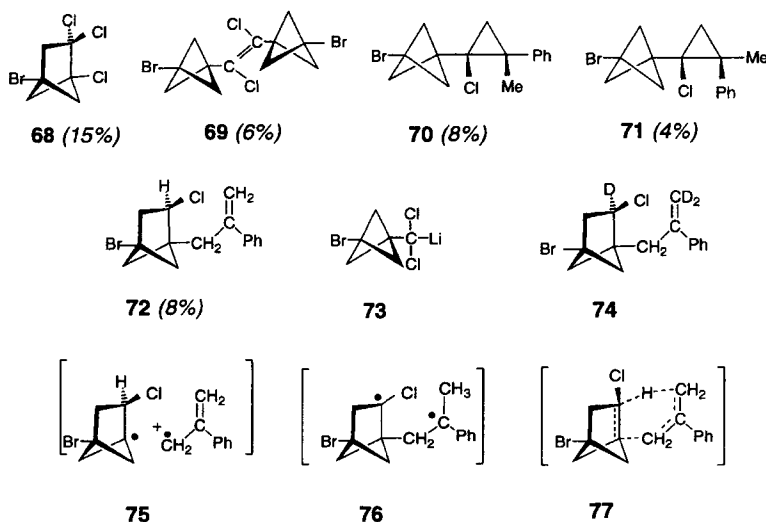
At 62% yield, the main product of the reaction of **42b** with MeLi (molar ratio 1:5.5) was 1,2-dichloro-2-methylbicyclo[2.1.1]hexane (**66**). Again, the most probable mechanism leading to **66** is addition of MeLi to carbene **54** (X=H, X=Cl), followed by lithium chlorine exchange of the intermediate tertiary alkyl lithium base **67** with the trichloride **42b**. An alternative mechanism, addition of LiCl to carbene **54** and methylation of the intermediate carbenoid by MeLi, formed during the reaction from MeLi and **42b**, is less probable.²⁴



Whereas the intermediacy of carbene **54** seems definite the results presented so far leave two ways for its formation: (a) **54** could be generated by cleavage of the bond C1–C5 of **53** and formation of the new bond between C5 and C6. (b) Alternatively, the carbon framework of **53** could be retained and the halide Y could migrate from C6 to C1 in alkene **53**. Labeling of the exocyclic carbon atom C6 of **42b** with ¹²C and reaction with MeLi afforded [1-¹²C]**66**, having all the label at C1.²⁴ This excludes chloride migration, which would have placed the carbon label at C2. The same result was obtained, when [6-¹²C]**42d** was reacted with NaN(SiMe₃)₂ in pentane, which gave rise to a 20% yield of [1-¹²C]-1,2-dichloro-4-iodobicyclo[2.1.1]hexane ([1-¹²C]**59**).²⁴

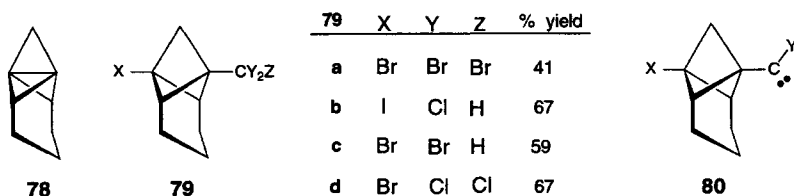
The low barrier of the rearrangement of **53** → **54** made the trapping of bridgehead alkene **53** a demanding task. The reaction of 1.04 equiv. of MeLi with **42f** in the presence of α-methylstyrene afforded products **68–72** in yields given below the formulas. Whereas **70** and **71** are the result of the addition of carbenoid **73** to α-methylstyrene, and **69** is the product of carbenoid dimerization, a consistent route to **68** might lead via carbene **54** (X=Bf, Y=Cl), which adds LiCl, and the corresponding carbenoid then undergoes a lithium chlorine

exchange with the starting material **42f**.¹⁷ **72** is the product of an ene reaction of **53** (X=Bf, Y=Cl). According to the biradical nature of this olefin, several intermediates or transition states could be involved in this reaction. To gain some insight into this process, [CD₃] α -methylstyrene was used as a trap and afforded **74**, again in 8% yield.¹⁷ This result seems consistent with intermediate **76** or transition state **77**, whereas the intermediacy of the radical pair **75** is less probable, because it should show at least some label scrambling.

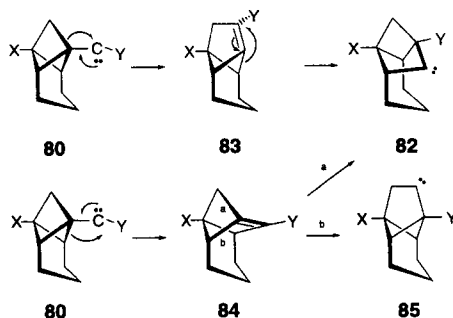


D. Internal Trapping of the 'Second' Carbene

The addition of halomethanes across the central bond of [1.1.1]propellane **78** leads to 1-halo-7-(*n*-halomethyl)tricyclo[4.2.0.0^{2,7}]octanes **79**, which are suitable precursors for the generation of type **80** carbenes.²⁶

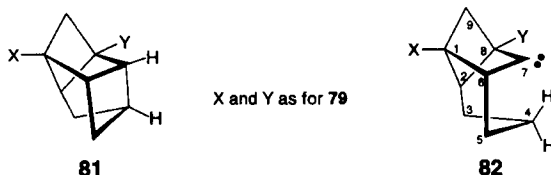


The reaction of **79a** with MeLi (salt-free) or of **79b** and **79c** with NaH (SiMe₃)₂ afforded the tetracyclic compound **81a**, or respectively, **81b** and **81c** in yields of 54%, 73%, and 88%.²⁶ The structure of **81** leads one to assume that carbene **82** is the precursor of **81**, which is formed by CH insertion of the carbenic center C7 into the axial hydrogen of C4 of **82**. Looking somewhat closer



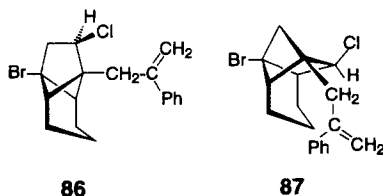
Scheme 4.

into the reaction sequence, the remarkable selectivity of the overall process is unexpected, because **81** was the only product obtained in yields as high as 88%. In Scheme 4 it can be seen that carbene **80** has two routes of stabilization, migration of the methylene group to give alkene **83**, and migration of one of the methine carbon atoms to afford olefin **84**.



Whereas the subsequent rearrangement of bridgehead olefin **83** can lead only to **82**, the isomeric olefin **84** could afford either carbene **82** (route a) or carbene **85**. Obviously, further experiments were necessary to find out the reason for the selectivity of product formation.

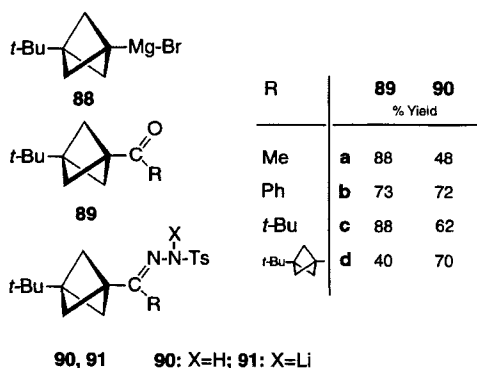
The reaction **79d** with salt-free MeLi in the presence of α -methylstyrene gave rise to the formation of 1 : 1 mixture of ene adducts **86** and **87** in a total yield of 6%.²⁶ This result indicates that both bridgehead olefins **83** and **84** are formed. Furthermore, this finding suggests that the energy barrier of path *b* should be considerably higher than that of path *a* to account for the observed selectivity of product formation. This assumption could be confirmed by DFT calculations [B3LYP/6-311G(d,p)//B3LYP/6-31G(d)] which showed that the barrier of path *a* was lower by 4.9 kcal/mol than that of path *b*.²⁶



E. Diazoalkane Pyrolysis

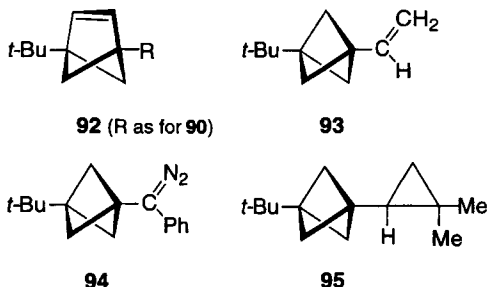
The interpretation of the reaction cascade starting with carbenoids of type **73** and subsequently proceeding with carbenes **52** and bridgehead olefins **53** and ending with carbenes **54** would gain substantial support, if we could generate the carbene of type **52** by a different method and then show that similar products were obtained as via the organometallic route.

Precursors for this task were obtained by addition of *t*-butylmagnesium bromide to the central bond of [1.1.1]propellane **40a** followed by conversion of the 3-*t*-butylbicyclo[1.1.1]pentyl-magnesium bromide (**88**) into the ketones **89** by standard methods.²⁷ Reaction of ketones **89** with tosyl hydrazide afforded the hydrazones **90**, which gave the corresponding lithium salts **91** by reaction with MeLi in ether. These salts were dried under high vacuum and then pyrolyzed at 4×10^{-5} torr in the temperature range of 100–130°C and the volatile products condensed in a liquid nitrogen-cooled trap.



The thermal decomposition of **91a** gave rise to a 2 : 1 mixture of **92a** and **93** in a total yield of 33%. **91b** afforded diazoalkane **94** in 76% yield, which was a crystalline compound, whose structure could be determined by X-ray analysis. Besides **94**, **92b** was produced in trace quantities. However, when the pyrolysis reaction of **91b** was carried out at 9 torr, **92b** was isolated in 48% yield. Decomposition of **91c** resulted also in a 1.4 : 1 mixture of **92c** and **95** in 34% yield, whereas **92d** was the sole product (37% yield) of **91d**.²⁷

Most significant is the formation of **92** in all thermalolysis reactions of **91**. This result is consistent with the sequence **91** → diazoalkane of type **94** → carbene **52** → bridgehead olefin **53** → carbene **54** → H shift to afford **92**. Formation of olefin **93** is best interpreted by H shift from the methyl group of carbene **52** (X=*t*-Bu, Y=Me) to the carbenic carbon, whereas **95** is formed by insertion of the carbenic center of **52** (X=Y=*t*-Bu) into the C–H bond of the *t*-Bu group.



Summing up these results, it has been shown that the carbene bridgehead olefin-carbene rearrangement is also observed when diazoalkanes are the precursors for the generation of the bicyclo[1.1.1]pent-1-ylcarbenes of type **52**.

ACKNOWLEDGEMENTS

The author is indebted to the co-workers cited in the references for their hard work in this field of chemistry. Financial support by the *Deutsche Forschungsgemeinschaft* and by the *Fonds der Chemischen Industrie* is gratefully acknowledged.

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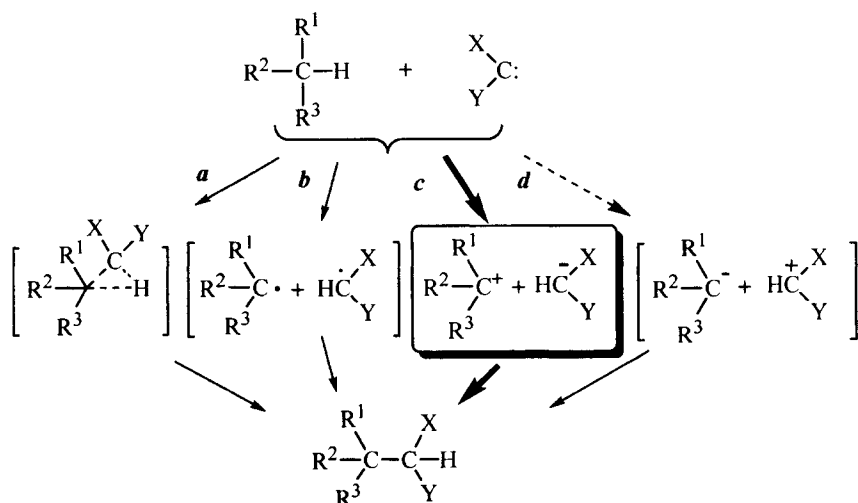
INSERTION OF CARBENES INTO C-H BONDS OF ALKOXIDES

Akira Oku and Toshiro Harada

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I. INTRODUCTION

Carbenes as divalent carbon species and their analogue carbenoids can form two bonds on a single carbon atom center introducing two different groups at one time or consecutively.¹ This is due to the ambiphilic character of singlet carbenes or triplet biradical character, which can be controlled by changing the



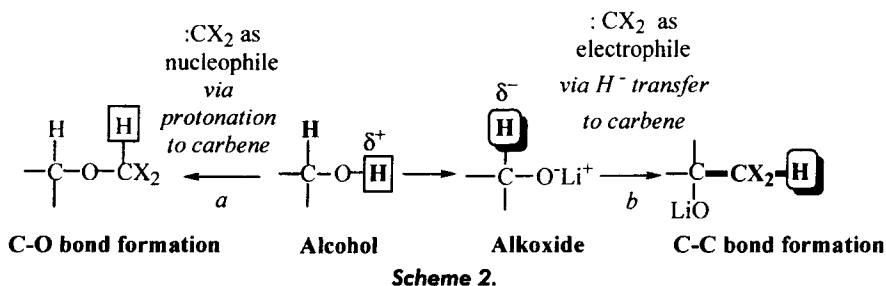
Scheme 1.

structure and substituent. If this varying nature of carbenes is combined with properly controlled polar character of reaction partners, such as by *umpolung* or protection, a number of selective carbene reactions can be realized.²

Among typical carbon-carbon bond (C-C) formation reactions with carbenes, the cyclopropanation reaction with olefins has been well studied including its application to industrial processes. The second typical reaction of carbenes is the insertion reaction into the carbon-hydrogen bond (C-H) which seems to be a direct and efficient C-C bond forming reaction. However, its use for synthetic purpose has often been limited due to low selectivity of the reactions.³

As a tool to improve the regio- and stereoselectivity of C-H insertion, activation of a specific C-H bond of substrates to be inserted seems to be appropriate in conjunction with the manipulation of carbene character. These two tools for the improvement of insertion selectivity will provide us with useful tools of the C-C bond formation by carbenes and carbenoids.

The four hitherto known routes of the C-H insertion are shown in Scheme 1. In general, the insertion by singlet carbenes proceeds via route *a* in one step, whereas the reaction by triplet carbenes proceeds sequentially via route *b*, i.e., hydrogen abstraction followed by recombination of the radical pairs.⁴ Other stepwise mechanisms are hydride abstraction (route *c*) and proton abstraction (route *d*), both being followed by the recombination of ion pairs. However, extended study on routes *c* and *d* for synthetic purposes had not been done before we started, except for a few earlier studies on carbanion-promoted β C-H insertion reactions.^{5,6} Recent advances in transition metal-catalyzed



carbenoid-like reactions of diazoalkanes can add a new route to this scheme,⁷⁻⁹ but it will not be described in this chapter.

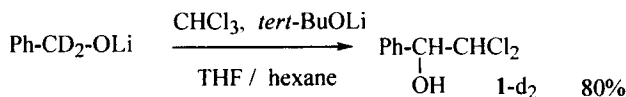
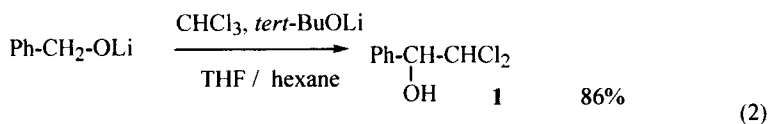
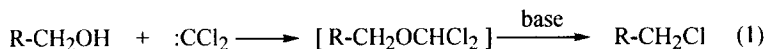
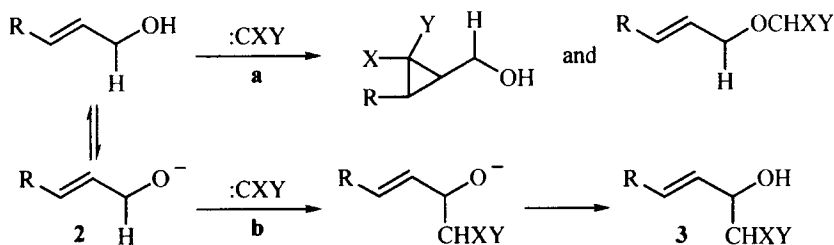
The oxyanion-promoted activation of the C-C and C-H bond in their cleavage reaction were known.¹⁰ For example, significant rate-acceleration effects in the oxy-Cope rearrangement and homolytic C-H bond fission were known.¹¹ The $S_{\text{RN}}2$ type reactions, recently proposed as a new concept,¹² also seem to be accountable by the oxyanionic effect. We noticed that this effect can be utilized for selective C-H insertion by carbenes (route *c*, Scheme 1). In Scheme 2, the basic concept of the present insertion reaction is shown in terms of switching both the polarity and the reaction site. It had been reported in preceding studies that a carbene reacts with alcohols to give O-H insertion products, in that a singlet carbene is protonated by an alcohol to generate an ion pair, which finally produces an ether.¹³ In contrast, our strategy for converting primary and secondary alcohols into alkoxides leads to the C-C bond forming reaction, in that the α C-H bond of alkoxides is activated as a hydride ion, rather than as a hydrogen atom, toward the attack by carbenes. Thus, a simple conversion of an alcohol to the corresponding alkoxide can change its reacting site with carbenes. This is the theoretical basis of the present study.²

In this chapter, the term 'carbene' includes the species called 'carbenoid' which is often considered as an α -metal-substituted carbocation or its equivalent. In some cases the term 'carbenoid' also includes encumbered carbenes complexed with metal halides.

II. REGIOSELECTIVITY OF THE CARBENE INSERTION INTO α C-H BONDS OF ALKOXIDES

A. C-H Insertion Reaction with Dichlorocarbene

Tabushi reported that dichlorocarbene :CCl_2 reacts with benzyl alcohol to form an O-H insertion product, i.e., benzyl dichloromethyl ether as the primary product, which undergoes a further base-catalyzed elimination reaction to give benzyl chloride as the final product (Scheme 3, Eq. 1).¹⁴ In contrast to this

**Scheme 3.**

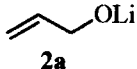
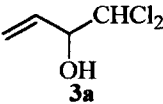
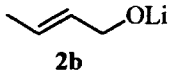
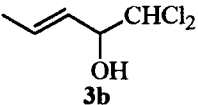
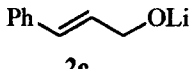
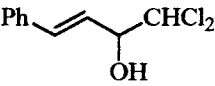
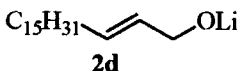
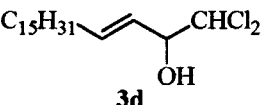
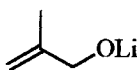
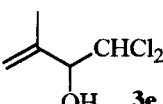
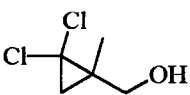
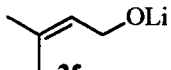
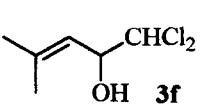
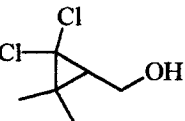
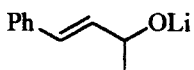
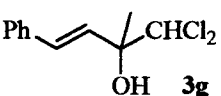
report, we found that the use of benzyl alkoxides in place of alcohol exclusively afforded the α C-H insertion product **1**, namely, 2,2-dichloro-1-phenylethanol, instead of benzyl chloride (Eq. 2).^{15,19} This finding enabled us to discover a series of C-C bond formation reactions with carbenes and carbenoids thereafter.

Not only benzylic alkoxides but also allylic alkoxides **2** undergo the C-H insertion reaction by :CCl_2 into the α C-H bond effectively (Table 1),¹⁵ indicating that the reaction can be synthetically used for the preparation of dichloromethylcarbinols **3** from the corresponding carbinols. The high regioselectivity of the C-H insertion over cyclopropanation¹⁶ and ether formation indicates that the α C-H bond of alkoxides, in general, is largely activated, although the latter two carbene reactions are typical with allylic alcohols (Scheme 4).

Nevertheless, another possibility remained for the formation of insertion products, that they might be formed from the O-H insertion product, e.g., dichloromethyl benzyl ether **5**, by the Wittig rearrangement of dichloromethoxycarbanion **4**, (Scheme 5, Eq. 1).¹⁷ However, treatment of independently prepared benzyl dichloromethyl ether **5** with the same base solely gave benzyl chloride, but the insertion product was not obtained (Eq. 2). Hence, a Wittig-type rearrangement process was excluded.

With regard to the C-H insertion process, two mechanisms are possible: the first one is a concerted one-step process (a) and the second one is a stepwise process (b). Due to the finding that the reaction of a mixture of α, α - d_2 -benzyloxide **6**

Table 1. Reaction of Dichlorocarbene with Alkoxides ^a

Entry	Alkoxides	Product(s)	Yield ^b , % (ratio) ^c
1	PhCH ₂ OLi	PhCH(OH)CHCl ₂ ^d (1a)	87
2	(<i>p</i> -anisyl)CH ₂ OLi	(<i>p</i> -anisyl)CH(OH)CHCl ₂ (1b)	81
3 ^f	PhCH ₂ CH ₂ OLi	PhCH ₂ CH(OH)CHCl ₂ (1c)	32 ^e
4	 2a	 3a	55 ^e
5	 2b	 3b	76 ^e
6	Ph-  2c	Ph-  3c	83
7	C ₁₅ H ₃₁ -  2d	C ₁₅ H ₃₁ -  3d	91
8	 2e	 3e 	78 (2.0 : 1)
9	 2f	 3f 	74 (1 : 1.8)
10 ^g	Ph-  2g	Ph-  3g	38

Notes: ^a Unless otherwise noted, lithium alkoxide (1 equiv) and *t*-BuOLi (3 equiv) were prepared in one pot from the corresponding alcohol with BuLi-hexane in THF and the mixture was allowed to react with CHCl₃ (3 equiv) under reflux for 0.5 h.

^b Yields refer to the isolated yield based on starting alcohols unless otherwise noted.

^c Ratios were determined by ¹H NMR.

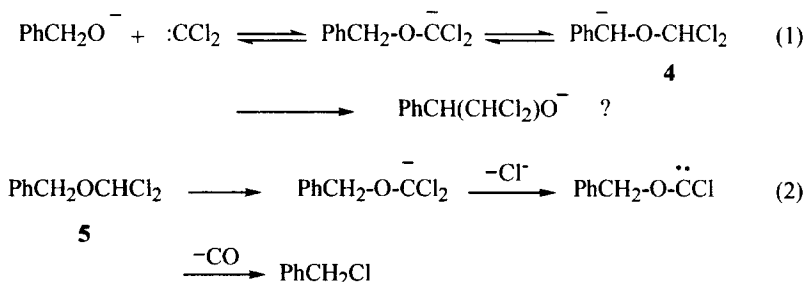
^d Köbrich, G.; Grosser, J.; Werner, W. *Chem. Ber.* **1973**, *106*, 2610.

^e Yields were determined by VPC.

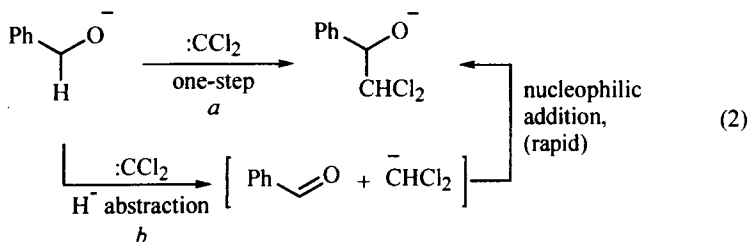
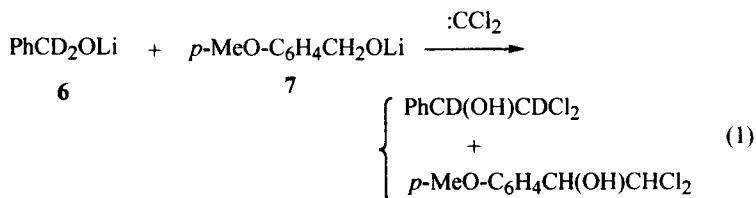
^f Six equiv of *t*-BuOLi and CHCl₃ were used.

^g The reaction was performed at an ambient temperature for 10 h.

and unlabelled *p*-methoxybenzyloxide **7** with :CCl₂ did not give any cross-over insertion product (Scheme 6, Eq. 1),¹⁵ the stepwise process in which dichloromethyl anion and benzaldehyde are formed as intermediates by the hydride ab-



Scheme 5.

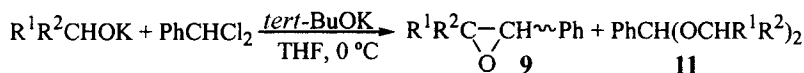


Scheme 6.

straction seemed unlikely, at first. However, the stepwise mechanism cannot necessarily be excluded because, if the hydride abstraction by a carbene is followed by a rapid recombination of the intermediate dichloromethyl anion and benzaldehyde in a cage-like environment (Eq. 2), cross-over exchanging of the coupling partner between different alkoxide systems will be suppressed. According to the analogous mechanism, the rate of recombination of a carbanion with a ketone which is derived from secondary alkoxides must be slower than with primary alkoxides. This discussion will be revisited in Sections III.A, III.B and V.

B. C-H Insertion Reaction with Chloro(phenyl)carbene

Chloro(phenyl)carbene or carbenoid generated from benzal chloride reacts with potassium salts of benzylic, allylic, and other alkoxides to produce phenyl-substituted oxiranes **9** in high yields, as an approximately 1:1 mixture of *cis*

Table 2. Reaction of Chloro(Phenyl)Carbene with Alkoxides ^a

Entry	Alkoxides		Time (min)	Products ^b (yield, %)
	R ¹	R ²		
1	C ₆ H ₅	H	30	9a (79)
2	<i>p</i> -ClC ₆ H ₅	H	30	9b (76)
3	CH ₂ =CH	H	20	9c (66) ^c
4	<i>trans</i> -CH ₃ CH=CH	H	60	9d (56) ^c , 12 (6) ^d
5	CH ₂ =C(CH ₃)	H	60	9e (69)
6	CH ₂ =CH	CH ₃	30	9f (60) ^e
7	C ₆ H ₅ CH ₂	H	30	9g (16) ^f , 11g (9), 13 (33)
8	<i>n</i> -C ₇ H ₁₅	H	60	9h (33) ^f , 11h (6)
9	CH ₃	CH ₃	60	9i (28) ^g
10	CH ₃ CH ₂	H	60	9j (66), 11j (6)

Notes: ^a Potassium alkoxides (2.5 equiv) prepared in situ from the corresponding alcohols with KH in THF were allowed to react with PhCHCl₂ (1 equiv) and *t*-BuOK (equivalent to alkoxide) at 0°C for the period indicated.

^b Except entry 7, yields refer to the isolated one based on PhCHCl₂.

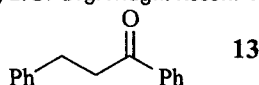
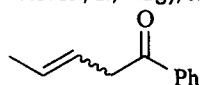
^c Paladini, J.; Chucho, J. *Bull. Chim. Soc. Fr.* **1974**, 192.

^d Manat, P.; Dieter, S. *Angew. Chem.* **1977**, 89, 333.

^e Mauzé, B. J. *Organomet. Chem.* **1979**, 365, 170.

^f Tamura, Y.; Bayomi, S.M.; Sumoto, K.; Ikeda, M. *Synthesis* **1977**, 693.

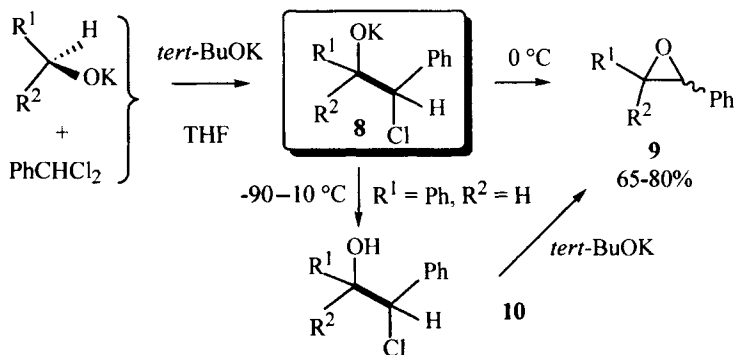
^g Hevesi, L.; Nagy, J.B.; Krief, A.; Derouane, E.G. *Org. Magn. Reson.* **1977**, 10, 14.



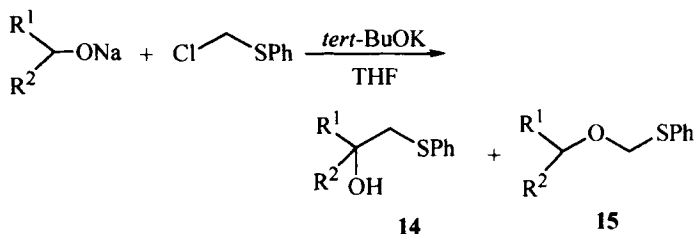
and *trans* isomers (Table 2).¹⁵ The mechanism of the oxirane formation is that the insertion reaction affords chlorohydrin oxide ion **8** as the primary product which further undergoes a ring-closing reaction (Scheme 7). The intervention of chlorohydrin oxide **8** was proven by the isolation of **10** from the reaction of lithium benzyloxide, which was further cyclized to stilbene oxide. With phenethoxide, 2-methoxyethoxide and methallyloxide, the C–H insertion took place exclusively at the α position of alkoxides regardless of the presence of benzylic hydrogen atoms, ethereal α hydrogen atoms, and olefinic double bonds (Table 2). The results indicate that the reactivity of chloro(phenyl)carbene, or its carbenoid, in the insertion is more selective than that of dichlorocarbene.

C. C–H Insertion Reaction with (Phenylthio)carbene

(Phenylthio)carbene,¹⁸ a heteroatom-substituted carbene, reacts similarly with a variety of alkoxides to give α-thiomethyl-substituted alcohols **14** (Scheme 8



Scheme 7.



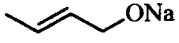
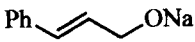
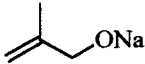
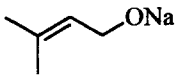
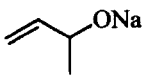
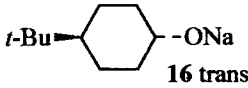
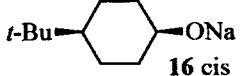
Scheme 8.

and Table 3).¹⁹ The C–H insertion is always accompanied by O–H insertion (product **15**) and, therefore, one might suspect that **14** is formed from **15** via a Wittig rearrangement. However, this possibility can be ruled out because independent treatment of **15a** ($\text{R}^1 = \text{vinyl}$, $\text{R}^2 = \text{H}$) with tert-BuOK caused only the isomerization of the double bond. Besides, **15** was not formed in the absence of tert-BuOK and, therefore, it was formed by the insertion of (phenylthio)carbene into the oxygen–metal bond (O–M), not by the Williamson-type reaction.

The stereochemistry of the insertion by (phenylthio)carbene to the α C–H bond of *trans*- and *cis*-4-*tert*-butylcyclohexyloxides **16** was investigated¹⁹ to find that the reaction proceeds stereospecifically giving *trans* and *cis*-4-*tert*-butyl-1-methylcyclohexanol **19**, respectively, after desulfurization of the primary insertion products **17** (Scheme 9).

The difference in reactivity between isoprenol and isoprenyloxide, methallyl methyl ether and methallyloxide were investigated in the reaction with (phenylthio)carbene generated under phase-transfer conditions. With isoprenol, (phenylthio)methyl ether (41%) was the major product, whereas with methyl ether cyclopropanation (36%) was the sole reaction.^{15,19} With alkoxides, in contrast, the major product was the C–H insertion product (45%) and (phenyl-

Table 3. Reaction of (Phenylthio)Carbene with Alkoxides ^a

Entry	Alkoxides	Alkoxides/ ClCH ₂ SPh (equiv)	Time (h)	Product ^b (yield%) ^c	
				C–H insertion	O–M insertion
1		(2.5)	0.5	14a ^d (29)	15a ^d (64)
2 ^e		(2.5)	0.5	14a (26)	15a (30)
3		(2.5)	0.5	14b ^d (43)	15b ^d (38)
4		(2.5)	0.5	14c ^d (45)	15c ^d (43)
5		(2.5)	0.5	14d (42)	15d (40)
6		(2.5)	0.5	14e (38) ^f (13)	15e (34)
7		(1.25)	0.5	14f (41)	15f (23)
8	CH ₃ C≡CCH ₂ ONa	(2.5)	0.5	14g (22)	15g (22) + ^g (39)
9	PhCH ₂ OLi ^h	(1.25)	1.0	14h ^d (48)	15h ^d (22)
10	<i>n</i> -PrONa	(1.25)	0.5	14i (9)	15i (91)
11	<i>i</i> -PrOLi ^h	(1.25)	1.0	14j (12)	15j (36)
12	 16 trans	(1.25)	0.5	17-trans ^d (6)	18-trans ^d (27)
13	 16 cis	(1.25)	0.5	17-cis ^d (22)	18-cis ^d (18)

Notes: ^a Unless otherwise noted, sodium alkoxides (1.25–2.5 equiv) prepared in situ from the corresponding alcohols with NaH in THF were allowed to react with ClCH₂SPh (1 equiv) and *t*-BuOK (equivalent to alkoxides) for the period indicated.

^b All products showed satisfactory spectral data (IR, ¹H NMR, and mass).

^c Yields refer to the isolated yield based on ClCH₂SPh.

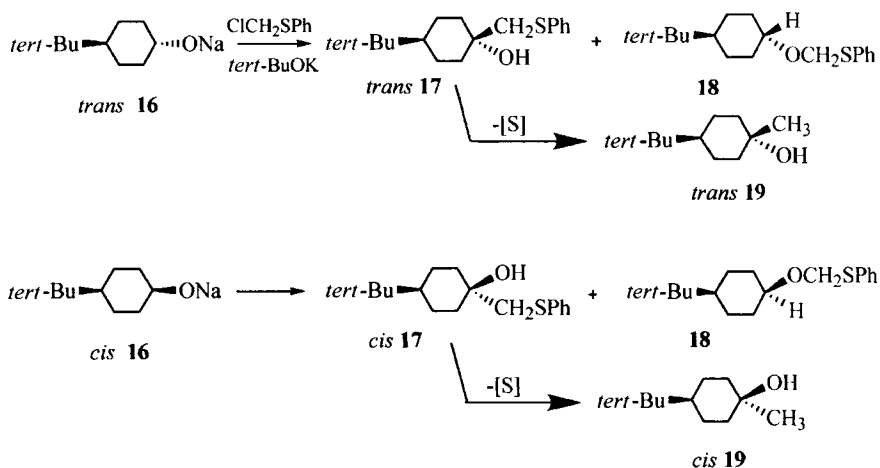
^d Satisfactory analytical results were obtained for these compounds.

^e *t*-BuONa (2.5 equiv) was employed in place of *t*-BuOK.

^f [3,3-dimethyl-2-(phenylthio)cyclopropyl]methanol (mixture of isomers).

^g CH₂=C=CHOCH₂SPh.

^h Lithium alkoxide prepared in situ from the corresponding alcohol with BuLi was used.

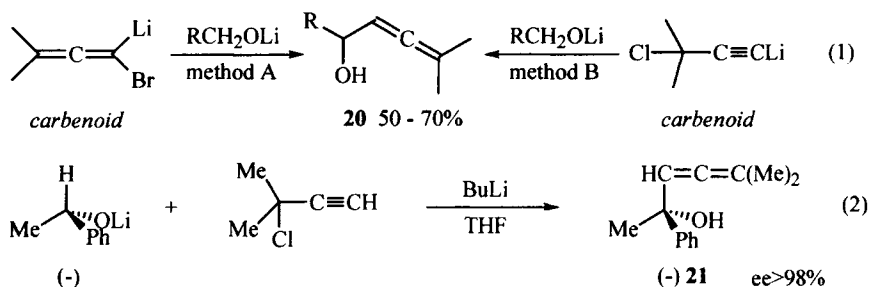


Scheme 9.

thio)methyl ether was a minor product. This finding demonstrates that the essential requisite for the α C–H insertion is the oxide ion.

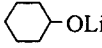
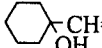
D. C–H Insertion Reaction with Vinylidenecarbene

Vinylidenecarbene or allenylidene^{3a} $(\text{R})_2\text{C}=\text{C}=\text{C}:$ has a lance-shaped, unsubstituted and sp -hybridized carbene center and, therefore, will not be easily subject to steric hindrance in its insertion reactions. On this assumption, (2-methyl)propenylidenecarbene or its carbenoid was chosen as a prototype of typical vinylidenecarbenes and its insertion reaction with several different types of alkoxides was investigated by employing two methods (A and B, Scheme 10) for carbene generation.²⁰ The insertion products **20** were obtained almost exclusively except lithium allyloxide (Table 4, entry 10).²¹ By-products such as propargyl ether and allenyl ether were not formed at all. To be noted here, in



Scheme 10.

Table 4. Reaction of Dimethylvinylidenecarbene with Alkoxides ^a

Entry	Alkoxides	Method	Products	Yield ^b (%)
1	PhCH ₂ OLi	A	20a PhCH(OH)CH=C=C(CH ₃) ₂	65
2	PhCH ₂ OLi	B	20a	68
3	(<i>p</i> -anisyl)CH ₂ OLi	A	20b (<i>p</i> -anisyl)Ph(OH)CH=C=C(CH ₃) ₂	50
4	PhCH(CH ₃)OLi	A	21 PhC(CH ₃)(OH)CH=C=C(CH ₃) ₂	35
5	(–)PhCH(CH ₃)OLi ^c	B	21 (–) ee >98%	52
6	PhCH ₂ CH ₂ OLi	A	20c PhCH ₂ CH(OH)CH=C=C(CH ₃) ₂	50
7	PhCH ₂ CH ₂ OLi	B	20c	51
8	C ₈ H ₁₇ OLi	A	20d C ₇ H ₁₅ CHCH=C=C(CH ₃) ₂	35
9	 OLi	A	20e  CH=C=C(CH ₃) ₂	39
10	CH ₂ =CHCH ₂ OLi	A	20f CH ₂ =CHCH(OH)CH=C=C(CH ₃) ₂	17
			and  CH ₂ (CH ₃) ₂ C=C=C–CHCH ₂ OH	14

Notes: ^a Unless otherwise noted, reactions were performed employing 2.5 equiv and 1.0 equiv of alkoxides in methods A and B, respectively.

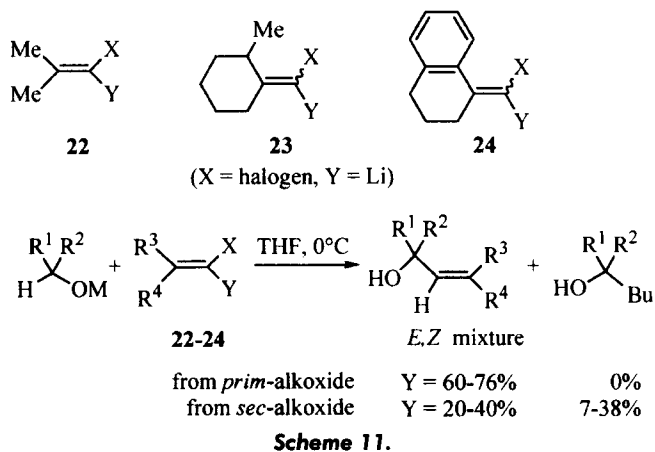
^b Yields refer to the isolated yields. In method B, yields were based on the alcohol consumed. Conversions for entries 2, 5, and 7 were 39, 66, and 31%, respectively.

^c (–)- α -Phenethyl alcohol was used.

contrast to other carbenes, is that not only primary but also secondary alkoxides react smoothly as well, indicating a high reactivity of this least-crowded carbene. This characteristic reactivity of alkenylidenecarbenes can be used for the synthesis of allenylcarbinols **20**, whose conventional preparative method from a carbonyl compound and allenylmetal reagent is often accompanied by the formation of propargylic by-products. Again, the high reactivity was illustrated by the highly stereospecific and retentive insertion to give an optically active tertiary alcohol **21** whose preparation by means of hitherto known methods was difficult (Scheme 10, Eq. 2).

E. C–H Insertion Reaction with Alkylidenecarbene

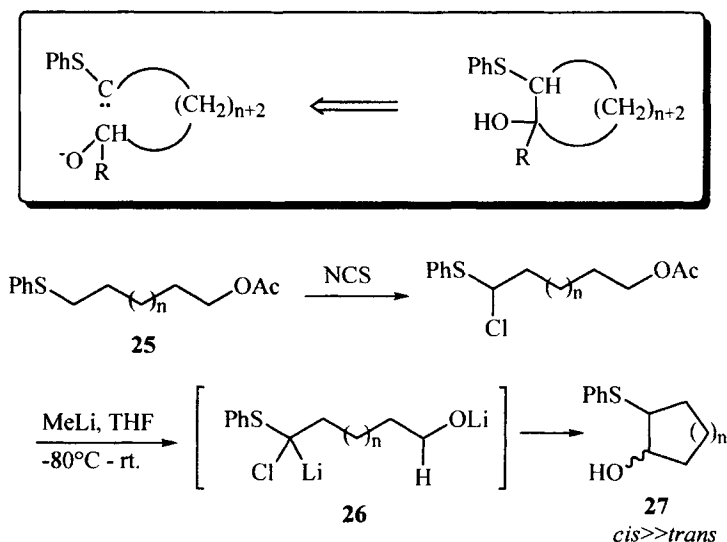
Although alkylidenecarbenes (R)₂C=C: and carbenoids **22–24** have an *sp*-hybridized carbene center similar to that of vinylidenecarbenes, the reactivity will be subject to the steric influence of substituents R³ and R⁴ because its location is closer to the carbene center than vinylidenecarbenes (Scheme 11). The steric effect was exerted in the reactions of 2-methylpropenylidene **22** generated from 2-methyl-1-chloropropene and butyllithium (BuLi) (Scheme 11).^{22,23} The results are summarized in Table 5. A more detailed discussion on the stereoselectivity of this reaction will be revisited in Section III.A.

**Table 5.** Reaction of 2-Methylpropenyldiene **22** with Alkoxides

Alkoxides	Products	Yield (%)
Ph-OK		62
<i>p</i> -Cl-Ph-OK		55
Ph-CH ₂ -OK		67
		50
Ph-CH(CH ₃)-OK	and	15, 15
	and	41, 43
		60

F. Ring-Construction by Intramolecular C–H Insertion of (Phenylthio)carbenes

The intramolecular C–H insertion reaction of carbene species has been used in a number of studies for the synthesis of strained molecules and cage com-



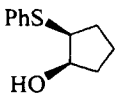
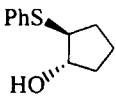
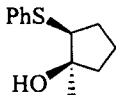
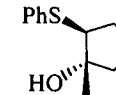
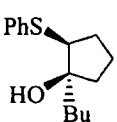
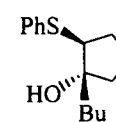
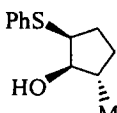
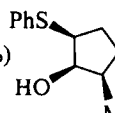
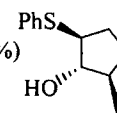
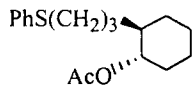
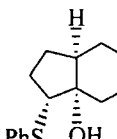
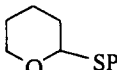
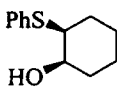
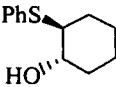
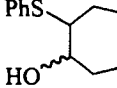
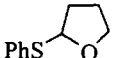
Scheme 12.

pounds,^{1a,24} however its application is limited because of its low regio-selectivity and 1,2-hydride shift that forms olefins. We expected that the oxyanionic effect on the carbene insertion can be effectively utilized for ring-construction. For this purpose, several ω -oxidoalkyl(phenylthio)carbenoids **26** were generated from ω -(phenylthio)alkyl acetate **25** by chlorination followed by the treatment with methyllithium, and cyclized insertion products **27** were obtained (Scheme 12).²⁵ The results are summarized in Table 6.

(Phenylthio)carbenoids **26** possessing different chain lengths (Scheme 12, $n = 1, 2, 3$), namely, 4-, 5-, and 6-oxidoalkyl(phenylthio)carbenes (Table 6, entries 1, 7 and 8), undergo similar regioselective cyclization reactions to give 2-(phenylthio)cycloalkanols **27**.

An interesting stereochemical profile of this cyclization is that in the five-membered product structures, substituents PhS and OH groups are placed *cis* to each other, whereas in six-membered products the placement is *trans* (Table 6, entry 7). The *cis* selectivity in the five-membered ring systems is not affected by α and β -substituents of the alkoxides (entries 2, 3 and 4), indicating that the steric effect is not the dominant factor. Instead, interaction between the oxido and carbene center composes a five- (or seven-) membered transition state **28**, which allows the carbene to abstract the nearest *quasi axial* hydrogen as a hydride to produce a carbonyl intermediate **29**, leading to the cyclization products **27** and **30** (Scheme 13, Eq. 1). Similarly, the stereoselective stepwise cyclization of *cis*- and *trans*-2-(3,3-dithiopropyl)cyclohexanol to 2-phenylthio-

Table 6. Intramolecular Insertion by (Phenylthio)Carbenes into α C-H Bonds of Alkoxides ^a

Entry	Starting material 25	Insertion products 27 (isolated yield) ^b	
1	PhS(CH ₂) ₅ -OAc	 (45%)	 (24%)
2	PhS(CH ₂) ₄ CH(Me)-OAc	 (49%)	 (26%)
3	PhS(CH ₂) ₄ CH(<i>n</i> -Bu)-OAc	 (42%)	 (21%)
4	PhS(CH ₂) ₃ CH(Me)CH ₂ OAc	 (42%)	 (10%)  (16%)
5		 (49%)	
6 ^d	Phs(CH ₂) ₅ -OSi(Me) ₂ <i>t</i> -Bu	 (30%)	
7 ^c	PhS(CH ₂) ₆ -OAc	 (7%) ^e	 (23%)
8	PhS(CH ₂) ₇ -OAc	 (8%) ^f	
9	PhS(CH ₂) ₄ -OAc	 (54%)	

Notes: ^a Unless otherwise noted, reactions were performed by the procedure described in the text.

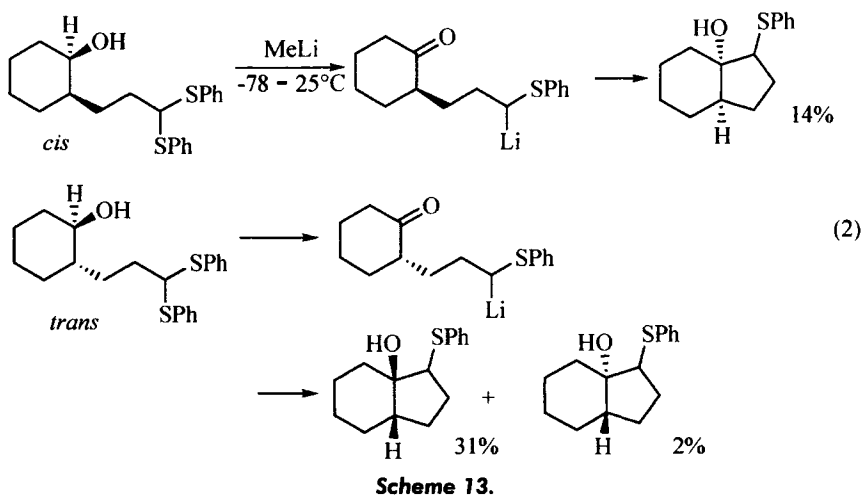
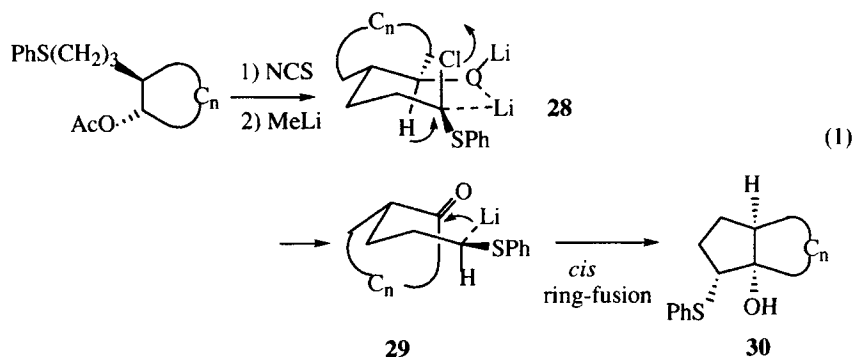
^b Overall yields based on (phenylthio)alkyl acetate **25**.

^c After the addition of MeLi (2 equiv) at -85°C , *n*-BuLi (1.1 equiv) was separately added at -85°C (entry 5) or -40°C (entry 7).

^d 1.3 Equiv of MeLi was used. After the reaction, the crude mixture was treated with *n*-Bu₄NF in THF.

^e Veibel, J.J.; Miasezewski, R.F.; Arlt, R.E. *J. Org. Chem.* **1977**, *42*, 585.

^f The stereochemistry was not determined.



bicyclo[4.3.0]nonan-1-ol, reported by Cohen and coworkers,²⁶ also agrees with this stepwise mechanism (Scheme 13, Eq. 2).

The stereochemistry of products **27** (Table 6, entries 2, 3, and 4) can be explained distinctly on the same basis that alkyl substituents R^1 , R^2 are positioned in *quasi equatorial* positions in the transition structure. Exclusive formation of the all-*cis* isomer in the reaction of cyclohexyl acetate (entry 5) is further evidence to support the oxido-carbene interaction in a double-chaired bicyclic structure **28**, as depicted in Scheme 13, Eq. 1.

III. STEREOCHEMISTRY OF THE OXYANION-PROMOTED C–H INSERTION REACTION

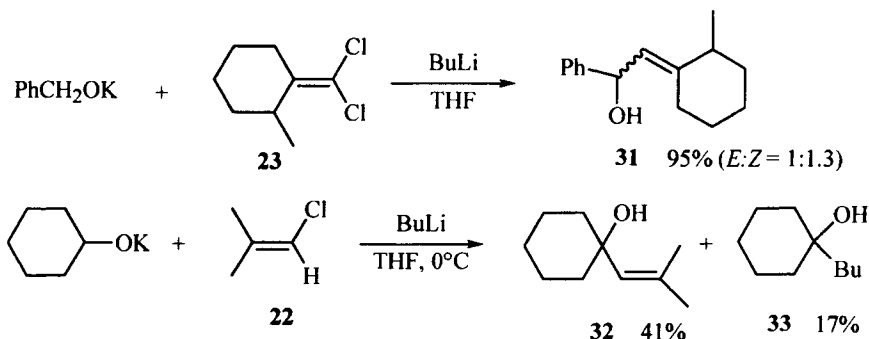
While a number of studies have reported on stereochemical and mechanistic aspects of the carbene addition to unsaturated bonds,¹ C–H insertion reactions

with free carbenes or carbenoids had been scarcely studied from mechanistic points of view, due to the high reactivity and low selectivity of the insertion reaction. As described in the preceding sections, a general mechanism proposed for the insertion of alkylidenecarbenes and vinylidenecarbenes into the α C–H bonds of alkoxides is a sequential one, i.e., a hydride abstraction–recombination process. In this section, the stereochemical aspects of the insertion will be explained in more detail.

A. Mechanistic Study on the C–H Insertion with Alkylidenemethylene Carbenoids

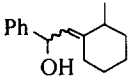
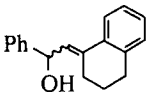
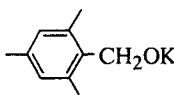
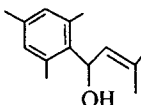
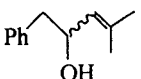
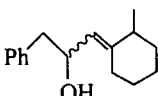
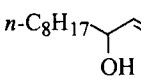
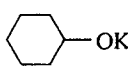
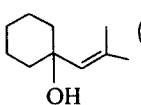
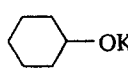
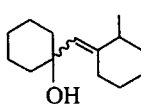
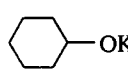
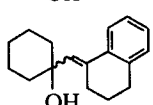
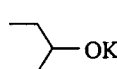
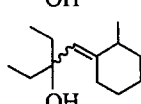
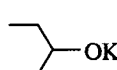
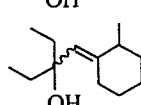
(a) **Stepwise mechanism:** Alkylidenemethylene carbenoids **22**, **23** and **24**,^{3,27} generated in the reaction of the corresponding haloalkenes with BuLi, insert into the α C–H bonds of primary and secondary alkoxides (Scheme 14, Table 7).^{22,23} With primary alkoxides, the insertion took place exclusively (e.g., product **31**), whereas with secondary alkoxides the yield of insertion product **32** decreases with the increase of butylated alcohols **33**. This finding supports a stepwise mechanism of the reaction, at least with secondary alkoxides, which generates a ketone as a common precursor of both insertion product **32** and alkylation product **33** with butyllithium.

(b) **Stereochemical profile of the insertion of carbenoid **22** into menthyl oxide:** In contrast to the stereospecific outcome of the insertion with phenylthiocarbene and vinylidenecarbene (Sections II.C and II.D), the reaction of menthyl oxide **34** with alkylidenemethylene (or its carbenoid) **22**, generated by the treatment of **35** with butyllithium, produced a mixture of *axial* insertion product **36**, *equatorial* insertion product **37** and butylated menthol **38** in the ratio of 24 : 4 : 72 (combined yield 56%) (Scheme 15).²³ The formation of **38** and **37**, where the substrate configuration is inverted, is indicative of the intermediary formation of menthone **40**. In contrast to menthyl oxide, the reaction

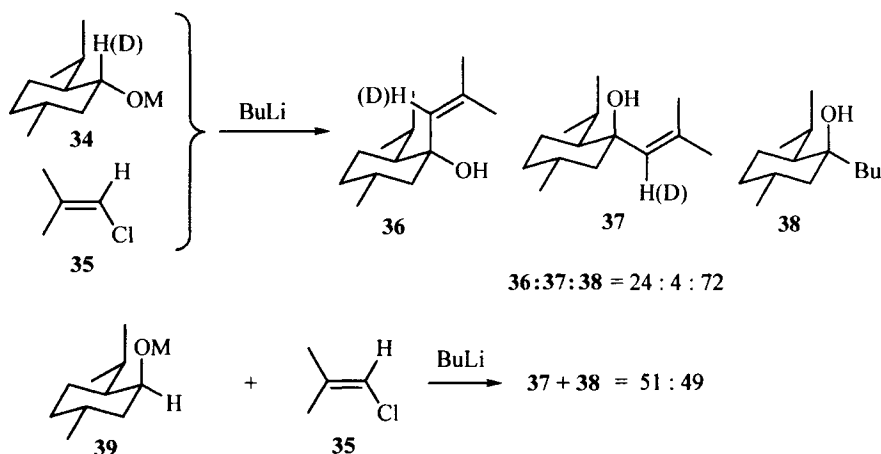


Scheme 14.

Table 7. Reaction of Prim- and Sec-Alkoxides with Alkylidenemethylene Carbenoids at 0°C

Entry	Alkoxide	Carbenoid	Insertion product [E : Z], yield (%)	Bu-adduct
1	PhCH ₂ OK	22	PhCH(OH)CH=C(Me) ₂ (62)	
2	PhCH ₂ OK	22 ^a	PhCH(OH)CH=C(Me) ₂ (65)	
3	PhCH ₂ OK	23	 [1 : 1.1] (82)	
4	PhCH ₂ OK	24	 [2.8 : 1] (76)	
5	 CH ₂ OK	22	 (64)	
6	Ph(CH ₂) ₂ OK	22	 (67)	
7	Ph(CH ₂) ₂ OK	23	 [1 : 1.5] (60)	
8	<i>n</i> -C ₈ H ₁₇ CH ₂ OK	22	 (50)	
9	 OK	23	 (18)	(7)
10	 OK	23 ^b	 [1 : 2.8] (18)	(7)
11	 OK	24	 [2.2 : 1] (38)	(8)
12	 OK	23	 [1 : 1.1] (26)	(23)
13	 OK	23 ^b	 [1 : 1.1] (33)	(12)

Notes: ^a Generated from 1-bromoalkene.^b Generated from dichloroalkene.

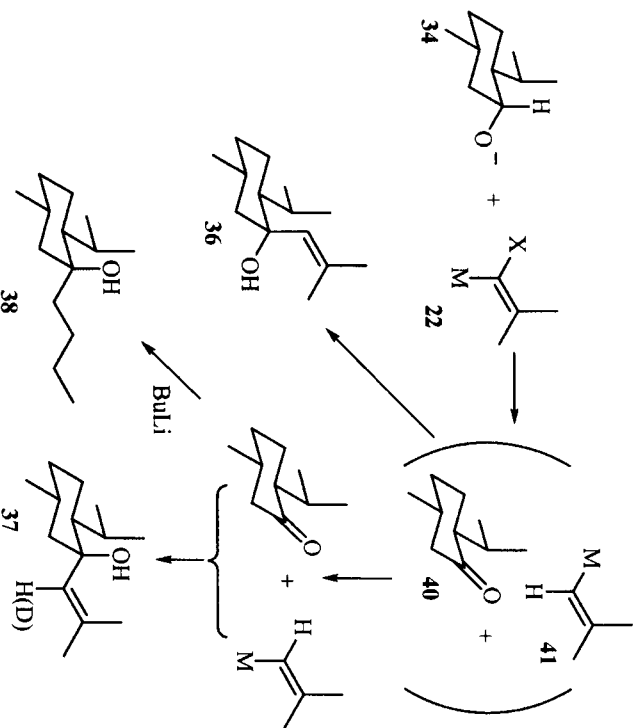


Scheme 15.

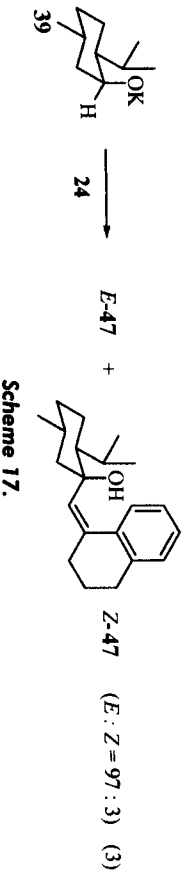
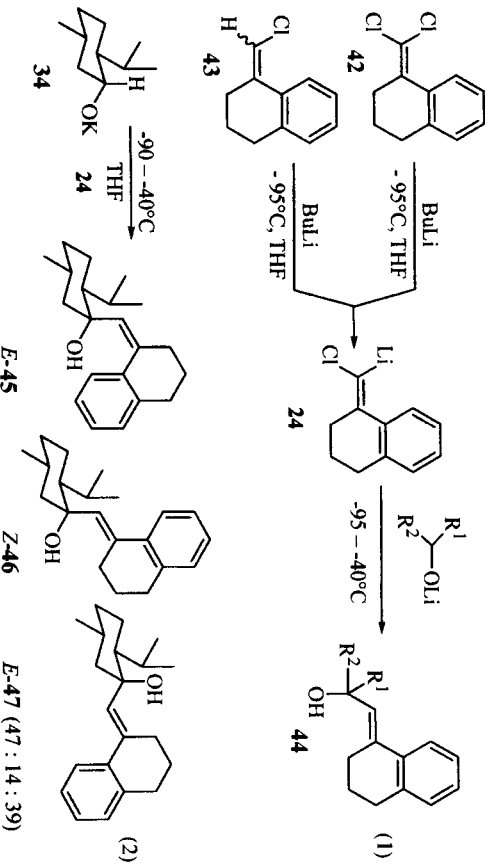
of neomenthyloxide **39** with **22** gave **37** and **38** but not **36**. These results are in accord with the stepwise mechanism of the insertion in which, similarly to the known behavior of parent menthone,²⁹ the nucleophilic attack of transiently formed alkenyl anion **41** to another intermediate menthone takes place in the equatorial position (Scheme 16).

(c) Insertion of (2,3-benzo-2-cyclohexenylidene)methylene carbenoid 24: While the reaction of alkoxides with 2-methylpropylidene carbenoid **22**, which was generated from the corresponding chloroalkene and BuLi at -0°C , was often accompanied by the formation of butylated alkoxides (Table 7), the analogous reaction with carbenoid **24**,²⁹ which was generated at -95°C by the treatment of (2,3-benzo-2-cyclohexenylidene)chloromethane (**43**) or dichloromethane analogue **42** with a stoichiometric amount of BuLi, did not produce the butylated alkoxide due to the stability of **24** during its preparation (Scheme 17, Eq. 1 and Table 8). By warming-up the reaction mixture, insertion product **44** was obtained as a mixture of *E* and *Z* isomers with a higher *E/Z* ratios than those at 0°C (compare Tables 7 and 8).²³ Similar reactions of **24** with menthyloxide **34** also formed a mixture of insertion products *E*-**45**, *Z*-**46** and *E*-**47** (47 : 14 : 39, overall 26%, Eq. 2). With neomenthyloxide **39**, a mixture of *E*-**47** and *Z*-**47** (97 : 3, overall 53%, Eq. 3) was formed. The formation of *E*-**47** from **34** shows that, even at such a low temperature, the insertion takes place in a stepwise manner.

The stepwise mechanism was also illustrated in terms of a temperature-dependent cage effect.²³ Reaction of **24** with a mixture of lithium cyclohexyl-1-*d*-oxide (**48**) and 3-pentyloxide (**49**) at 0°C , produced cross-over products **50** and **51**, both in *E*- and *Z*-forms, and the deuterium was scrambled in both isomers (89% in **50** and 6-12% in **51**). In contrast, at -95 – -40°C , no

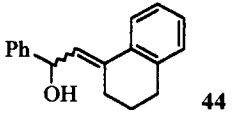
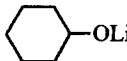
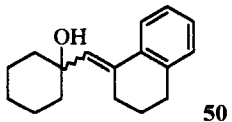
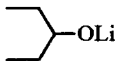
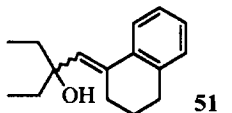


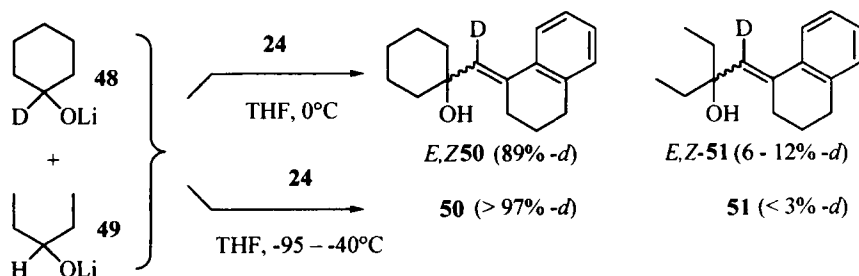
Scheme 16.



Scheme 17.

Table 8. Reaction of Lithium Alkoxides with (2,3-Benzo-2-Cyclohexenylidene)-Chloromethylithium (**24**) at Low Temperatures (-95 — -40°C)

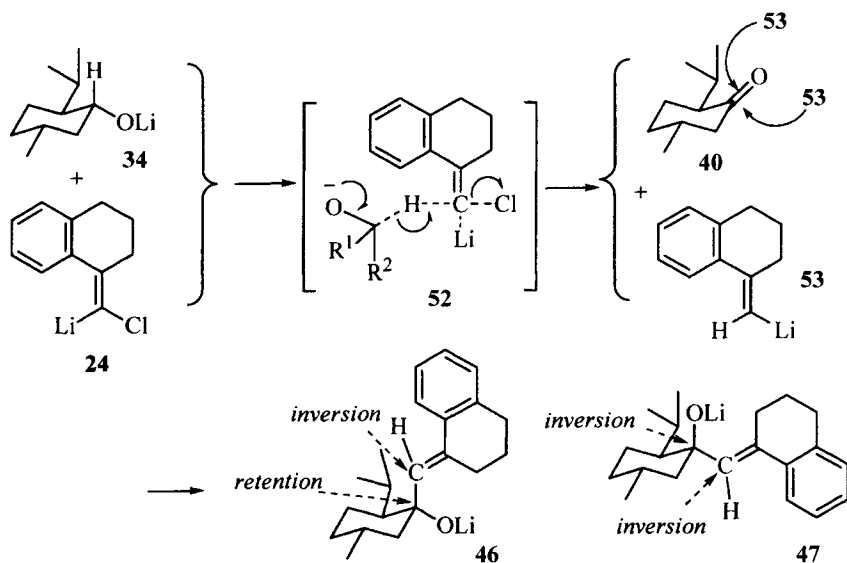
Alkoxide	Product	[E : Z] ratio (yield %)
	 44	[3.6 : 1] (49)
	 50	[2.7 : 1] (40)
	 51	[4.7 : 1] (45)



Scheme 18.

cross-over product was observed (Scheme 18). The results indicate that at low temperatures the recombination between a ketone and an alkenyl anion takes place in the solvent cage, whereas, at higher temperatures, it occurs outside of the cage to some extent.

E,Z-Selectivity in the insertion by unsymmetrical carbenoid **24**, is specifically indicative of the transition state of the stepwise mechanism. Based on the evidence that carbenoid **24**, which is generated from **42** or **43** (*E* : *Z* = 84 : 16), exists nearly exclusively in the *E*-configuration under the equilibrium even at -95°C ,²⁹ the observed stereoselectivity for *E*-isomers in the insertion products verifies that hydride abstraction takes place via an $\text{S}_{\text{N}}2$ -like transition state **52** with inversion of configuration at the carbenoid carbon, followed by the recombination of menthone **40** and carbanion **53** (Scheme 19).

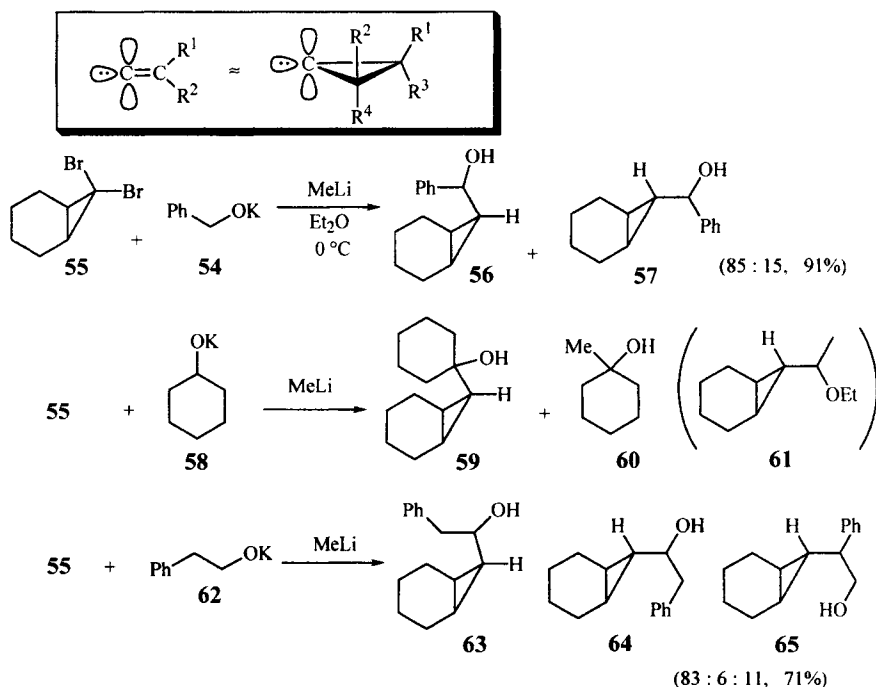


Scheme 19.

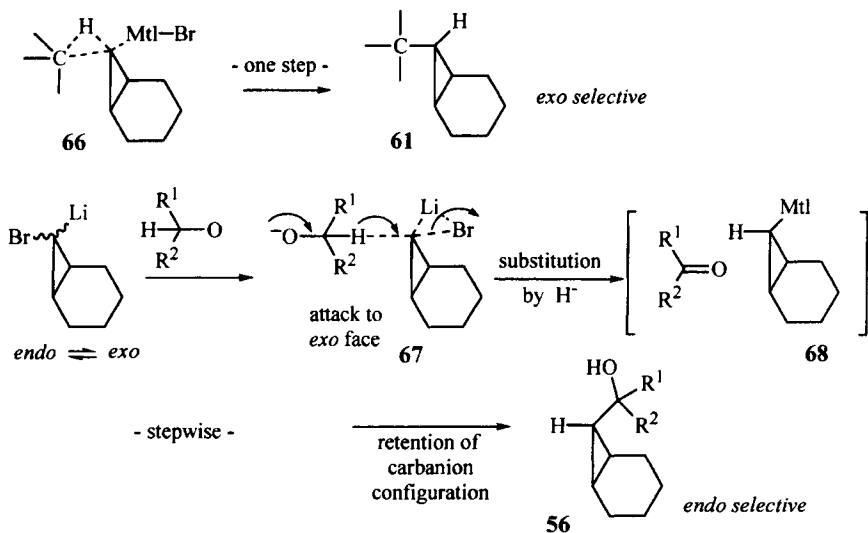
B. *Endo*, *Exo*-Selectivity in the C–H Insertion with Norcaranylidene Carbenoids

As demonstrated in the preceding Section III.A, configurations of not only the C–H bond of the alkoxide to be inserted but also the carbenoid center present is evidence for the insertion mechanism. In this regard, norcaranylidene carbenoid ³⁰ has an unsymmetrical stereochemical environment similar to those of alkylidenemethylene carbenes (Scheme 20) and, therefore, it is expected to be informative of the insertion mechanism.

Treatment of a mixture of potassium benzyloxide **54** and dibromonorcarane **55** with methyllithium in ether at 0°C produced *endo*-insertion product **56** preferentially over *exo*-isomer **57** (Scheme 20).³¹ The analogous insertion reaction with cyclohexyloxide **58** gave only the *endo*-isomer **59**. In both reactions, **61** the insertion product of norcaranylidene carbenoid with diethyl ether was always formed and its configuration was determined *exo*. In addition, the reaction with β-phenethyloxide **62** gave α C–H insertion products as a mixture of *endo* and *exo* isomers **63**, **64**, and β C–H insertion product **65** only with *exo* configuration (Scheme 20). The *endo* stereoselectivity observed here clearly demonstrates that a sequential insertion reaction is taking place. First, the hydride transfer takes place on the *exo*-face of norcarane ring in a S_N2 fashion via **67** to generate *endo* cyclopropyl anion **68**, which is known as one of the configurationally stable carbanion species.³² A second, coupling reaction



Scheme 20.



Scheme 21.

between the anion **68** and the carbonyl molecule derived from the alkoxide, both being present as a transient pair of reactants within a solvent cage, takes place on the *endo* face to give the formal insertion product **56**. The *exo* configuration of the concerted insertion product **61**³³ also supports the *exo* selective hydride abstraction route in the first stage (Scheme 21).

From a synthetic point of view, the formation of sterically crowded *endo*-insertion products **56**, **59**, **63** from dihalonorcarane is of great interest. If one would attempt to generate *endo* 7-norcaranyl carbanion **68** from an appropriate 7-halo-norcaranes for the purpose of C–C bond formation, it is generally difficult to control the stereochemistry.

IV. OTHER CARBENE REACTIONS FOUND IN THE STUDY OF INSERTION REACTIONS

This section diverges from the main subject but, being studied together with the insertion of (phenylthio)carbenes with alkoxides, is worth describing here due to its synthetic versatility as C–C bond forming reactions.

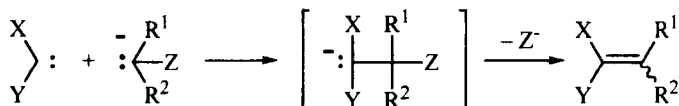
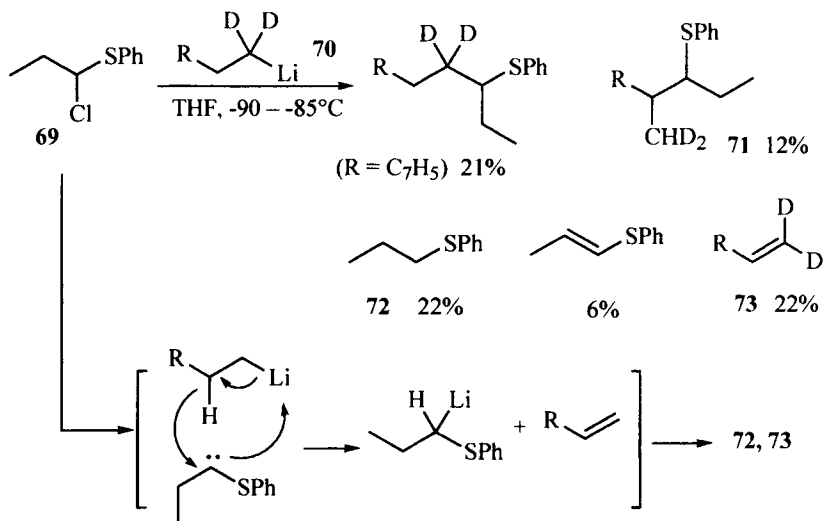
A. Insertion into β C–H Bonds of Alkylolithium Compounds³⁴

Since alkylolithium compounds and their carbanions have an isoelectronic structure with alkoxides, their reaction behavior with carbenes is expected to be similar to that of alkoxides, showing enhanced reactivity in both C–H insertion and hydride abstraction.³⁵ In this reaction, the hydride abstraction cannot be followed by recombination and, therefore, can be differentiated from the insertion. Indeed, the reaction of alkylolithium compounds **70** or nitrile anions (see Section IV.B) with ethyl(phenylthio)carbenoid, which is generated by the reaction of 1-chloropropyl sulfide **69** with BuLi, takes place at the β -position of **70** more or less in a similar manner giving both insertion product **71** and hydride abstraction products **72** and **73**, respectively. This again supports a general rule “C–H bonds at the vicinal position of a negatively charged atom are activated toward carbene insertion reactions” (Scheme 22).

B. Preparation of Vinyl Sulfides by the Reaction of (Phenylthio)carbenes with Nitrile Anions

In general, the reaction of carbanions with carbenes takes place smoothly to form primary product carbanions. However, they react further with electrophiles and this secondary reaction is difficult to control.³⁶ To overcome this disadvantage, carbanions bearing an appropriate leaving group were designed and utilized for olefin synthesis (Scheme 23).

Treatment of a mixture of nitrile anion **74** and 1-chloroalkyl phenyl sulfides



75, prepared by chlorination of alkyl phenyl sulfides, with BuLi produced vinyl sulfides **76** in 34–91% yields (Table 9, Scheme 24).³⁷ Aryl-substituted acetonitriles reacted effectively (entries 1–7) whereas those bearing an alkyl substituent behaved less effectively (entries 8–10) and even much less with a dialkyl-substituted one (entry 11).

An explanatory mechanism for the formation of vinyl sulfides is shown in Scheme 24. In route *a*, (phenylthio)carbene **77** generated from chlorosulfide **75** reacts with the nitrile anion to form (phenylthio)carbanion **79**, which then undergoes elimination of cyanide ion to produce vinyl sulfide **76**. In route *b*, **75** reacts first with the nitrile anion **74** to produce β-(phenylthio)nitrile **78** followed by base-catalyzed β-elimination. However, route *b* is unlikely because **79** cannot be generated from **68** due to a larger *pK_a* value of its α proton than that of the nitrile. In fact, the reaction of chlorosulfide **75a** with lithionitrile **80** gave a different product **81** in 63% yield.

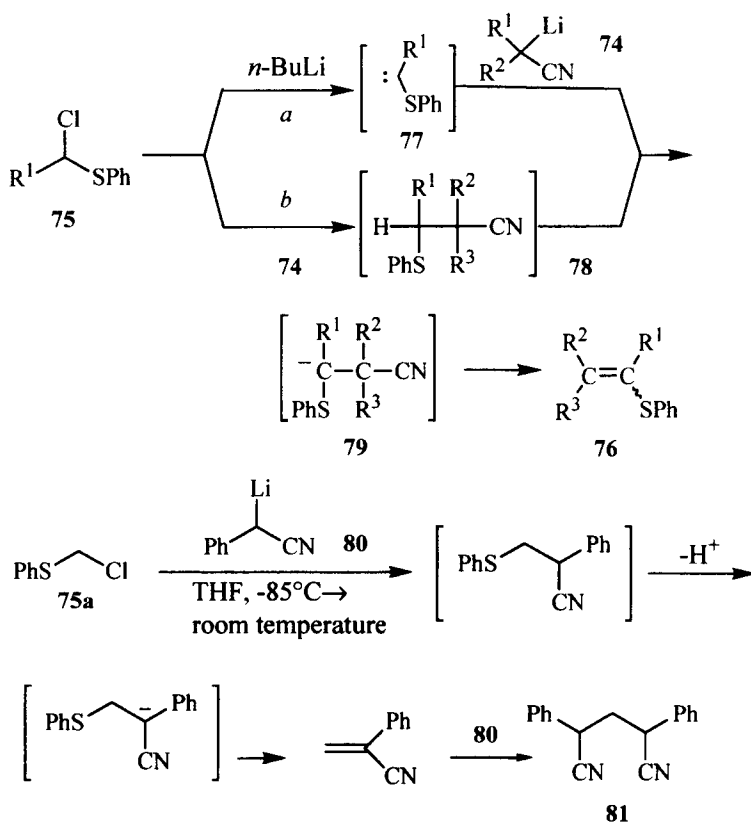
A similar strategy can be applied to intramolecular systems for the synthesis of cyclic alkenyl sulfides³⁷ (Scheme 25). Instead of chloroalkyl sulfides **82**, dithioacetals **83** can be used more effectively as the precursor of thiocarbenes

Table 9. Reaction of (Phenylthio)carbenoids with Nitrile Anions

Entry	Nitrile	Sulfide	Product 76	Yield (%) ^a	Isomer ratio ^b
1	PhCH ₂ CN	PhSCH ₃		52	[1.0:0]
2	PhCH ₂ CN	PhSCH ₂ CH ₃		73	[2.1:1]
3	PhCH ₂ CN	PhS(CH ₂) ₂ CH ₃		91	[1.7:1]
4	PhCH ₂ CN	PhS(CH ₂) ₃ CH ₃		75	[1.3:1]
5	PhCH ₂ CN	PhSCH ₂ Ph		46	°
6	α-NaphCH ₂ CN	PhSCH ₂ CH ₃		77	°
7	α-NaphCH ₂ CN	PhS(CH ₂) ₂ CH ₃		70	°
8	CH ₃ CN	PhSCH ₂ CH ₃		46	
9	CH ₃ CN	PhS(CH ₂) ₂ CH ₃		55, 53	
10	CH ₃ CH ₂ CN	PhS(CH ₂) ₂ CH ₃		60, 70	[2.2:1]
11	(CH ₃) ₂ CHCN	PhS(CH ₂) ₂ CH ₃		34	

Notes: ^a Isolated overall yield from sulfide.^b The identification of E and Z isomers was not performed.^c Oida, T.; Tanimoto, S.; Ikehira, H.; Okano, M. *Bull. Chem. Soc. Jpn.* **1983**, *56*, 959.^d Campaigne, E.; Leal, J.R., *J. Am. Chem. Soc.* **1954**, *76*, 1972.^e The isomer ratio was not determined.^f Grobel, B.-T.; Seebach, D. *Chem. Ber.* **1977**, *110*, 867.

for the purpose. For example, cyclopentenyl sulfides **85** and **86** were produced from **83** and **84** in 87 and 56% yield, respectively. For the synthesis of **86**, this carbene route seems to be superior to the conventional method starting from 3-methylcyclopentanone which is accompanied always by the formation of the 4-methyl-isomer as by-product. Not only five-membered sulfides but also six- (**88**) and seven-membered (**91**) cycloalkenyl sulfides can be prepared from the corresponding ω-cyanoalkanal dithioacetals **87** and **90** bearing a longer chain. However, by-products **89** and **92** with a smaller ring by one carbon are formed. This is due to the carbene insertion into the β C-H bond of the nitrile anion (see also Section IV.A).

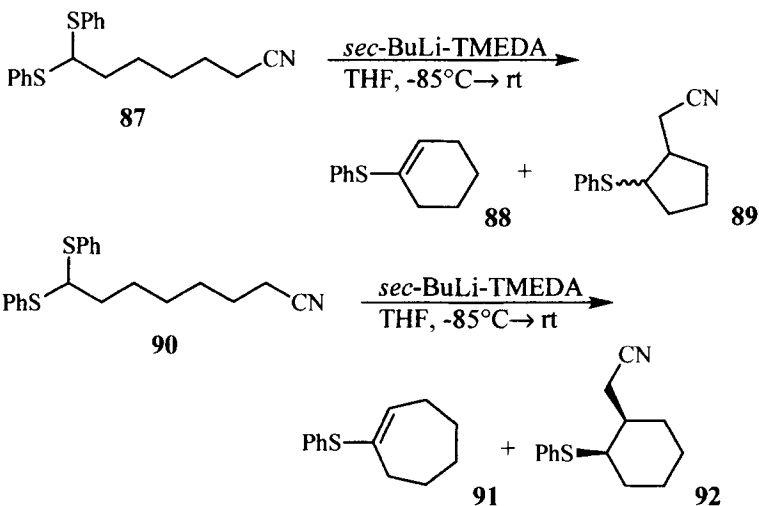


Scheme 24.

Not only the formation of these insertion by-products but also the ring-formation described in Section II.f (see also Table 6) proved that the activation of the α C-H bond by a vicinal negative charge for the carbene insertion is more effective than the non-ionic as well as entropy-controlled formation of five-membered rings.

C. Intramolecular Cyclization of (ω -Oxido)diazoalkanes

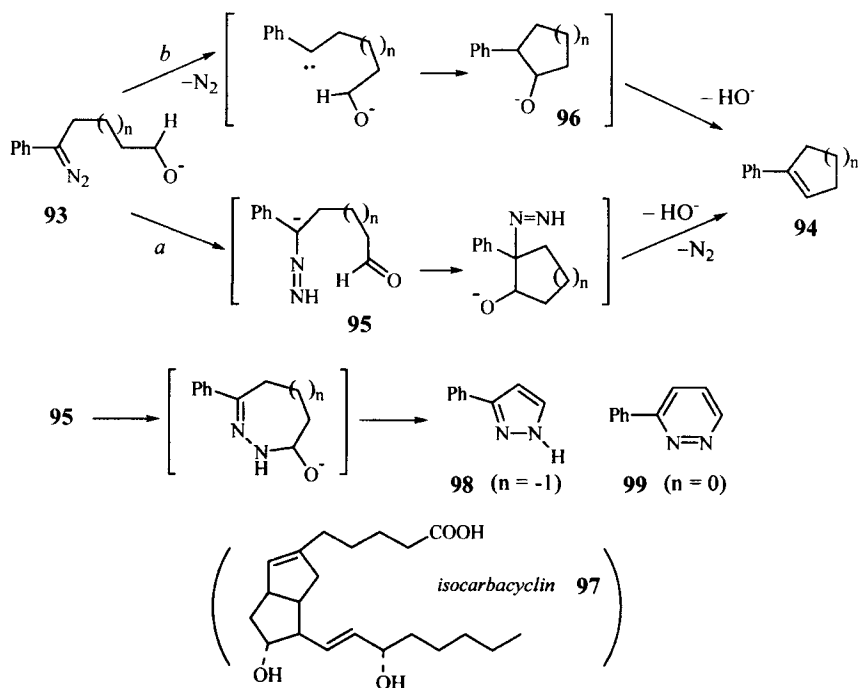
By analogy with the intramolecular insertion of phenylthiocarbenes, the reaction of (ω -oxido)diazoalkanes **93** resulted in the formation of cycloalkenes **94**.³⁸ However, the reaction was proven to proceed not via a carbene route *b* but a nitrene route *a* as shown in Scheme 26. The nitrene route is supported by the formation of heterocyclic products **98** and **99**.³⁹ This insertion reaction was used in the cyclization step to the cyclopentene ring formation of isocarbacycline **97**.⁴⁰



Scheme 25.

V. SUMMARY

The first aim of the present study was based on the working hypothesis that carbenes, in general, can react with primary and secondary alkoxides to give C-H insertion products more selectively than ethers or cyclopropanes. In fact, the activation effect of an alkoxide on the insertion reaction of α C-H bond has been proven significantly large throughout the study as summarized in Scheme 27. A more significant profile of the insertion reaction that was found unexpectedly and proven in the extended study, is the stepwise insertion mechanism. Namely, carbenes, preferably carbenoids or encumbered carbenes, react as strong electrophiles to abstract a hydride ion from alkoxides forming a pair of carbanion and carbonyl compound. Subsequently, this redox product pair rapidly undergoes a coupling reaction to give the α -alkylated alkoxide. In other words, secondary alkoxides are formed from primary alkoxides via aldehydes, whereas tertiary alkoxides derive from secondary alkoxides via ketones. With primary alkoxides, a coupling reaction between the intermediate

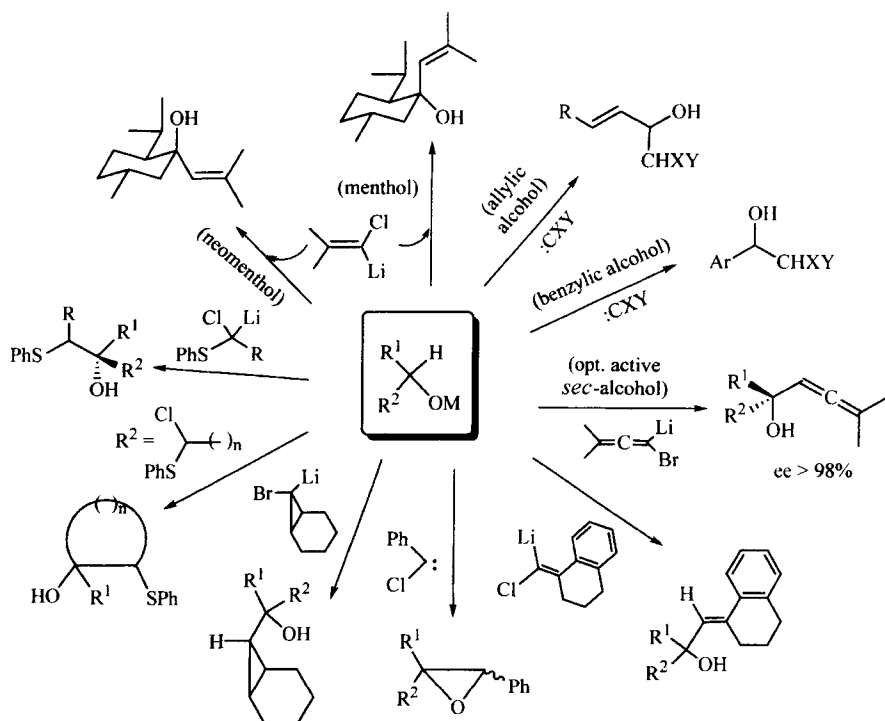


Scheme 26.

aldehyde and carbanion, the latter being originated from a carbene, takes place rapidly, presumably in a solvent cage, on the same face of alkoxides where the abstraction occurs first. This was evidenced by the attempt of a crossover reaction, which eventually failed (Scheme 18). With secondary alkoxides, the coupling reaction between the intermediate ketone and carbanion takes place at a relatively slow rate in comparison with primary alkoxides. Therefore, in some reactions where one or both of the ketone and carbanion intermediate are sterically crowded or have low reactivity, the rate of recombination becomes slow enough to leave time for the carbanion to change its reacting position on the carbonyl face. Or, the carbanion can be replaced by another one, e.g., butyllithium, being present in the reaction system. The latter example was demonstrated by the reactions of alkylidenecarbenes (Scheme 17).

Most of the carbenes examined in this study have more or less a carbenoid nature because they are generated from halogenated precursors and strong base. In this regard, it still remains as an intriguing problem to verify experimentally the higher electrophilicity and selectivity of carbenoids^{41,42} in comparison to those of free carbenes in the insertion reaction.

Another remaining issue is the question about the sequential or concerted nature of the insertion, though most of the reactions described above provide



ample evidence for supporting the stepwise mechanism. At this stage of the study, it seems not easy to exclude the one-step insertion mechanism for the fast reactions, such as stereospecific retentive insertion reactions (Scheme 10).

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