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free energy" relationship.[51,52] The extent and strength of solvation of the transition state for the β-scission of an alkoxyl radical clearly requires a solvent parameter which probes the cybotactic region of the solvent, i.e., probes the volume around an alkoxyl radical in which the order of the solvent molecules has been affected by the radical.[51–55] The cybotactic solvent parameter most commonly employed is the Dimroth–Reichardt $E_T(30)$ value,[51,56] and indeed, this does correlate reasonably well ($\langle r \rangle = 0.965$) with log ($k_\beta^{CumO}/s^{-1}$), see Figure 1a. As we have found previously for a quite different reaction[52,57] there is a slightly better correlation ($\langle r \rangle = 0.983$) between log ($k_\beta^{CumO}/s^{-1}$) and the nitrogen hyperfine splittings, a^N, for the 4-amino-2,2,6,6-tetramethylpiperdinyl-*N*-oxyl radical,[54] see Figure 1b. We suggest that, as a cybotactic probe, the nitroxide moiety is a not unreasonable model for an incipient carbonyl group, i.e.

While the correlation of log (k_β^{CumO}/s^{-1}) with a^N could possibly be improved by using the hyperfine splittings for a sterically nonprotected nitroxide or by adding an "appropriate" second parameter (such as the solvent's cohesive pressure)[51,52] such "cosmetic" changes appear unnecessary. That is, both correlations shown in Figure 1 imply that solvent effects on k_β^{CumO} are due to a localized interaction between the transition state for β-scission and the adjacent solvent molecules. In particular, it would seem very probable that there is nothing "special" about the high value of k_β^{CumO} in acetic acid;[58] i.e., there is nothing that is unique to β-scission.

Experimental Section

Materials. All solvents were of high purity and commercially available: acetonitrile (OmniSolve), carbon tetrachloride (OmniSolve), chlorobenzene (BDH), benzene (Aldrich), 2-methyl-2-propanol (Fisher Scientific), and acetic acid (Anachemica). They were used as received since experiments demonstrated that further purification had no measurable effects upon the kinetics. Di-α-cumyl peroxide (Aldrich) was recrystallized three times from methanol. Acetophenone (Aldrich) and 2-phenyl-2-propanol (Aldrich) were used as received.

Di-α-cumyl hyponitrite was prepared by the method of Dulog and Klein,[61] mp 75.5–76.5 °C (lit.[61] mp 75 °C); δ_H (200 MHz; $CDCl_3$) 1.58 (12 H, s), 7.06–7.90 (10 H, m).

Yields of acetophenone and 2-phenyl-2-propanol from the decomposition of dicumyl hyponitrite were determined by gas chromatography using a Hewlett-Packard 5890 with a 12-m × 0.02-mm (i.d.) OV-101 column.

The time-resolved infrared spectrometer has been described in detail elsewhere.[62,63]

Acknowledgment. We thank Dr. L. J. Johnston for her friendly advice on the TRVis experiments.

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(55) The dielectric constant, for example, is not a probe of the cybotactic region because it is a macroscopic property of the bulk solvent.
(56) Dimroth, K.; Reichardt, C.; Siepmann, T.; Bohlmann, F. *Liebigs Ann. Chem.* **1963**, *661*, 1–37.
(57) The reactions investigated[52] were the trapping of carbon-centered radicals by nitroxides.
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Experimental Evidence for Ethylidene-d_4

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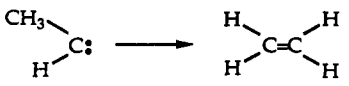
Contribution from the Department of Chemistry, The Ohio State University, 120 West 18th Avenue, Columbus, Ohio 43210. *Received July 20, 1992*

Abstract: Laser flash photolysis (LFP, 351 nm, XeF excimer) of 3-methyldiazirine in the presence and absence of pyridine fails to produce a UV–vis active transient intermediate. However, LFP of 3-methyldiazirine-d_4 in pentane containing pyridine produces a transient absorption attributed to the ethylidene-d_4–pyridine ylide. A double-reciprocal plot of the optical yield of ylide (A_y^{-1}) versus (pyridine concentration)$^{-1}$ is linear and indicates that the lifetime of ethylidene-d_4 is 500 ps in pentane, assuming that the second-order rate constant of reaction of ethylidene-d_4 with pyridine is 1×10^9 M^{-1} s^{-1}. Laser induced fluorescence spectra of methyldiazirine and methyldiazirine-d_4 are reported and discussed.

I. Introduction

The rearrangement of ethylidene to ethylene is a prototypical carbene process.[1] The simplicity of this reaction has invited numerous theoretical studies, which have recently been tabulated by Houk and Evanseck.[2] Schaefer and Gallo[3] have calculated that ethylidene, like methylene, has a triplet ground state, but that singlet ethylidene is only 5 ± 1 kcal/mol above the ground state.



High-level theory finds that the enthalpy barrier to the exceedingly exothermic rearrangement of ethylidene in its lowest singlet state is either small or 0.[2] The most recent ab initio

(1) For reviews, see: Baron, W. J.; DeCamp, M. R.; Hendrick, M. E.; Jones, M., Jr.; Levin, R. H.; Sohn, M. B. In *Carbenes*; Jones, M., Jr., Moss, R. A., Eds.; Wiley: New York, 1973; Vol. I, pp 2–19.
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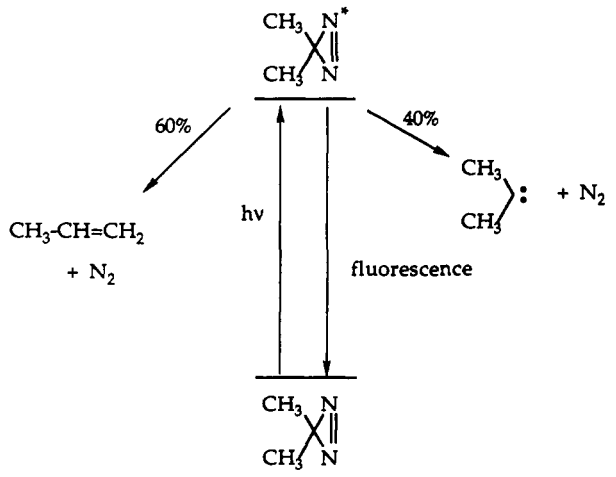
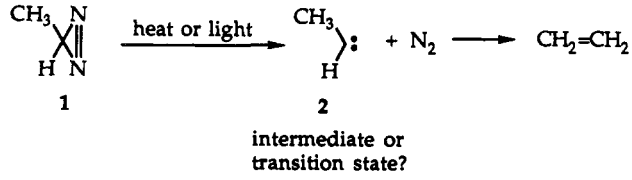
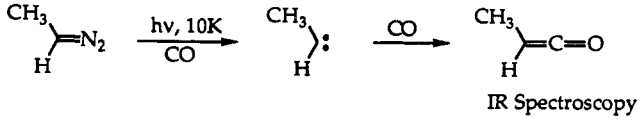
Scheme I



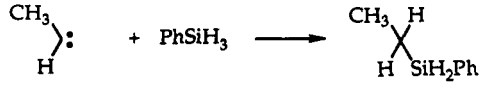
calculations predict that the enthalpic barrier to rearrangement of singlet ethylidene is only 0.6 kcal/mol.[2] Thus the key question concerning ethylidene is whether this species is a true intermediate which exists in a potential energy minimum and has a finite lifetime, or whether it is a transition structure or a nonstationary point on the surface connecting precursor (e.g., methyldiazirine **1**) with ethylene, the ultimate reaction product.



It has been difficult to demonstrate experimentally that ethylidene (**2**) is a reactive intermediate. Attempts to stabilize this species in a rigid cryogenic matrix have not been successful, but this failure only demonstrates that triplet ethylidene either is not formed or is not stable under the conditions of the experiment.[4] Recently, however, McMahon has been able to trap ethylidene in carbon monoxide containing matrices at 10 K.[5] It is also



possible to intercept ethylidene with phenylsilane in solution in 5% yield and with alkenes in low yield.[6] Thus chemical trapping experiments indicate that ethylidene is a true reactive intermediate,



albeit one with a very short lifetime. Frey[7] has estimated that the lifetime of ethylidene in the gas phase is as long as 700 ps, assuming that every collision between ethylidene and alkene trap leads to product formation. Frey recognized that a more realistic collision factor is 0.1; thus, 700 ps was the estimated lower limit to the ethylidene lifetime in the gas phase. Our deductions (vide infra) are in good agreement with this claim.

Fluorescence Spectroscopy. It has been known for decades that photochemical decomposition of alkyldiazirines yields a more complex mixture of stable products than does pyrolysis.[8] These observations led various authors to speculate that photolysis of diazirines can produce diazirine excited states[7] or carbene excited states[8,9] as product-forming species, in addition to the anticipated alkylcarbene. In our recent study of dimethylcarbene we determined that the fluorescence intensity of dimethyldiazirine-d_6 is 50% greater than that of dimethyldiazirine.[10] This was taken as evidence for hydrogen (deuterium) migration in the diazirine excited state. On the basis of methanol trapping studies we deduced that upon decomposition the excited state of dimethyldiazirine yields roughly a 40/60 mixture of dimethylcarbene and propylene, respectively[10] (Scheme I). Thus the failure to chemically trap alkylcarbenes (produced photochemically from alkyldiazirines) in good yield stems in large part from their low yields from diazirine precursors.

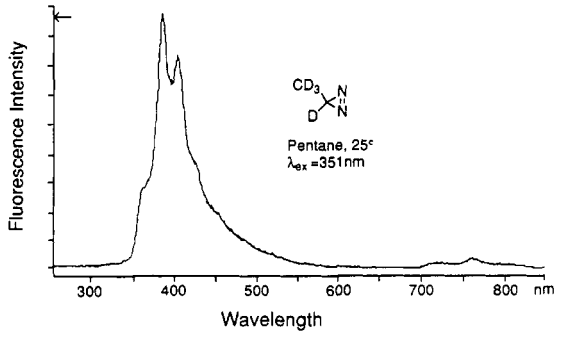


Figure 1. LIF spectrum of methyldiazirine in pentane at 25 °C (λ_{ex} = 351 nm).

The Pyridine Ylide Probe Method. In 1986 this laboratory introduced pyridine ylides as probes of the dynamics of carbenes which lack suitable UV–vis chromophores for laser flash photolysis (LFP).[11] The method is derived from Scaiano's use of benzhydryl ketyl as a probe of free radical dynamics.[12] In the probe experiment a diazirine is decomposed by a pulse of UV radiation in the presence of pyridine. The photogenerated carbene is captured by pyridine to from an ylide which is easily detected by virtue of its intense absorptivity between 360 and 420 nm and its relatively long lifetime ($\tau \gg 10\ \mu s$). Pyridine traps typical singlet carbenes at nearly a diffusion-controlled rate; a typical value of the trapping rate constant, k_{PYR}, is $10^9\ M^{-1}\ s^{-1}$.[11] Since its inception, the pyridine ylide probe technique has been used to study simple alkylchlorocarbenes,[11] dichlorocarbene,[13] adamantylidene,[14]

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(12) The probe method is based on kinetic models developed by Scaiano; see: (a) Small, R. D., Jr.; Scaiano, J. C. *J. Phys. Chem.* **1977**, *81*, 828. (b) Small, R. D., Jr.; Scaiano, J. C. *Chem. Phys. Lett.* **1977**, *50*, 431; (c) **1978**, *59*, 246.

(13) Chateauneuf, J. E.; Johnson, R. P.; Kirchoff, M. M. *J. Am. Chem. Soc.* **1990**, *112*, 3217.

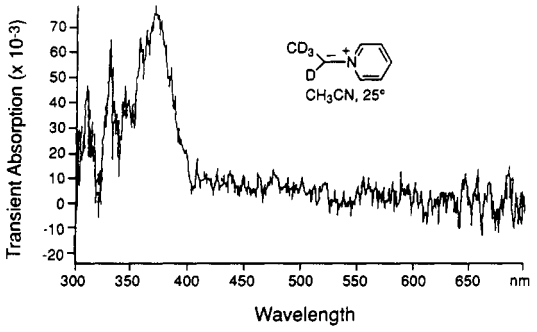


Figure 2. The transient absorption spectrum produced by LFP of methyldiazirine-d_4 in acetonitrile containing pyridine.

homocubanylidene,[15] and dimethylcarbene,[10,16] thereby prompting this study of ethylidene.

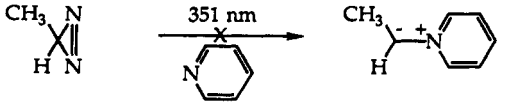
II. Results

1. Fluorescence Spectroscopy. Alkyl- and dialkyldiazirines are known to exhibit a weak fluorescence.[17] Indeed, the laser induced fluorescence (LIF) spectrum of methyldiazirine-d_4 in pentane at ambient temperature is shown in Figure 1. The fluorescence is not measurably quenched by the presence of pyridine (1/4, v/v, pyridine/pentane), demonstrating that the fluorescent excited state of the diazirine does not react with the heterocycle. The fluorescence spectrum of methyldiazirine is greatly reduced in the presence of molecular oxygen, indicating that there is an interaction between the excited state of the diazirine and oxygen. This type of effect has been observed previously with aromatic compounds and ketones and is attributed to the formation of an exciplex.[18]

The relative fluorescence intensities of methyldiazirine and methyldiazirine-d_4 were determined in pentane at ambient temperature at identical optical densities. Significantly, the deuterated diazirine fluorescence intensity is 30% *greater* than the fluorescence intensity of methyldiazirine.

$$\frac{\phi_F(D)}{\phi_F(H)} = 1.3$$

2. Transient Absorption Spectroscopy. Laser flash photolysis (XeF, 351 nm, 12 ns) of methyldiazirine in pentane at ambient temperature in the presence and absence of pyridine fails to produce significant transient absorption. Lowering the temperature to −40 °C again fails to produce a pyridine ylide upon LFP of methyldiazirine in pyridine/pentane.



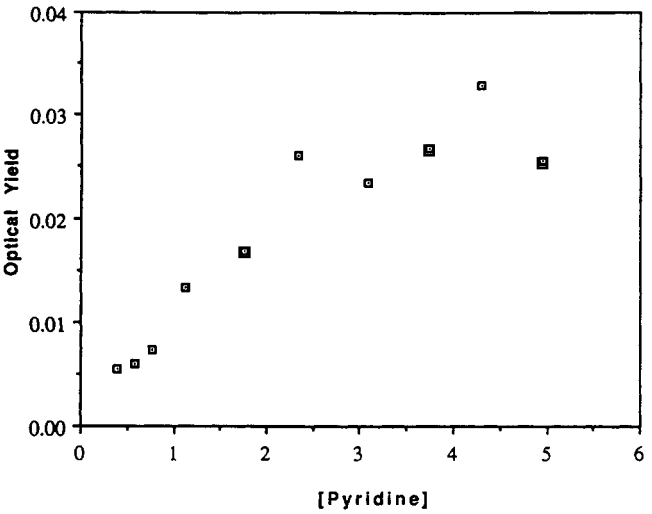
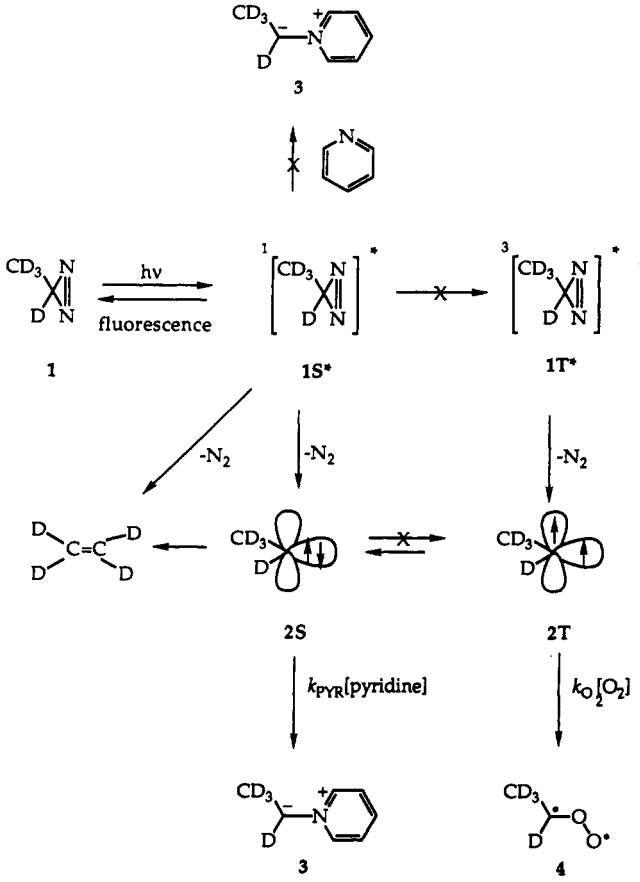


Figure 3. A plot of the yield of ylide produced by LFP of methyldiazirine, ϕ_y, as a function of pyridine concentration in pentane at 20 °C.

Scheme II



In our earlier study of dimethyldiazirine we determined that perdeuteration leads to a 50% increase in the yield of carbene, and that the lifetime of dimethylcarbene-d_6 is 3.2 times longer than that of dimethylcarbene in pentane solution at ambient temperature.[10] Accordingly, LFP of methyldiazirine-d_4 was studied. LFP of methyldiazirine-d_4 in pentane again fails to produce measurable transient absorption. However, LFP of methyldiazirine-d_4 in pentane/pyridine produces the transient absorption spectrum shown in Figure 2. This transient is attributed to pyridine ylide **3** due to its similarity to the ylide spectra of the dimethylcarbene–,[10] methylchlorocarbene–,[11] adamantylidene–,[14] and homocubylidene–pyridine ylides.[15]

The intensity of the transient absorption increases, as expected, with increasing concentration of pyridine (Figure 3). The optical yield of ylide (A_y) is not saturated even at very high pyridine

(14) (a) Morgan, S. C.; Jackson, J. E.; Platz, M. S. *J. Am. Chem. Soc.* **1991**, *113*, 2783. (b) Moss, R. A.; Chang, M. J. *Tetrahedron Lett.* **1981**, *38*, 349. (c) Adding, A. C.; Strating, J.; Wynberg, H.; Schlatmann, J. L. M. A. *Chem. Commun.* **1966**, 657. (d) Isaeu, S. D.; Yuchenko, A. G.; Stepanov, F. N.; Kolyada, G. G.; Novikov, S.; Karpentko, N. F. *J. Org. Chem. USSR (Engl. Transl.)* **1973**, *9*, 724. (e) Bayley, H.; Knowles, J. R. *Biochemistry* **1978**, *17*, 2420; **1980**, *19*, 3883.

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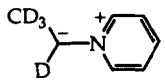
(18) McLean, A. J.; Rodgers, M. A. J. *J. Am. Chem. Soc.* **1992**, *114*, 3145.



3

concentration, demonstrating that the lifetime of ethylidene-d_4 in pentane at ambient temperature is so short that only a portion of the carbene can be successfully trapped (Scheme II) under these conditions.

The yield of pyridine ylide 3 is not affected by the presence of 2.5 M isoprene. These results demonstrate first that ethylidene is probably not generated by decomposition of the triplet state of methyldiazirine-d_4 to form ethylidene-d_4 in its (presumably) ground triplet state (Scheme I). The yield of ylide is noticeably reduced (51%) by the presence of oxygen (saturated solution). It is unlikely that triplet ethylidene-d_4 reacts with oxygen in pentane to form a carbonyl oxide because this species was not detected and because nascent singlet ethylidene-d_4 probably isomerizes more rapidly than it undergoes intersystem crossing (vide infra). The oxygen effect on the ylide yield is most likely due to the previously mentioned quenching of the fluorescent excited state of the diazirine.

A double-reciprocal treatment of the data of Figure 3 is shown in Figure 4. Scheme I predicts eqs 1–3. Thus from a plot (Figure 4) of $1/A_y$ versus $1/[\mathrm{PYR}]$ one can deduce the ratio of k_0/k_{PYR} by dividing the slope by the intercept. In eqs 1–3, A_y is the optical

$$\phi_y = \phi_c\left(\frac{k_{\mathrm{PYR}}[\mathrm{PYR}]}{k_0 + k_{\mathrm{PYR}}[\mathrm{PYR}]}\right) \quad (1)$$

$$A_y = \phi_y A_y^{\mathrm{SAT}} \quad (2)$$

$$\frac{1}{A_y} = \frac{1}{\phi_c A_y^{\mathrm{SAT}}} + \frac{1}{\phi_c A_y^{\mathrm{SAT}}}\frac{k_0}{k_{\mathrm{PYR}}}\frac{1}{[\mathrm{PYR}]} \quad (3)$$

yield of ylide, A_y^{SAT} is the optical yield of ylide that would be obtained at infinite pyridine concentration, ϕ_c is the quantum yield of carbene formation, ϕ_y is the quantum yield of ylide formation, k_{PYR} is the absolute rate constant of the reaction of ethylidene with pyridine, and k_0 is the sum of all rate constants of all first-order and pseudo-first-order processes which consume ethylidene in the *absence* of pyridine. These processes are limited to intramolecular rearrangement of the carbene to ethylene-d_4 and reaction of ethylidene-d_4 with solvent. The lifetime of ethylidene-d_4 is so short (vide infra) that it does not have time to react with impurities or even with the dilute diazirine precursor.

The lifetime of ethylidene-d_4 ($\tau = 1/k_0$) in pentane at ambient temperature is calculated to be 500 ps, assuming that k_{PYR} is 1×10^9 $\mathrm{M^{-1}\,s^{-1}}$. The lifetime of ethylidene-d_4 is deduced to be 42 times shorter than that of dimethylcarbene, and 134 times shorter than that of dimethylcarbene-d_6 in pentane at ambient temperature. Of course, if k_{PYR} of ethylidene-d_4 is larger than that of dimethylcarbene for steric reasons, then ethylidene-d_4 has that much shorter a lifetime than dimethylcarbene.

Intersystem crossing (ISC) in diphenylcarbene and fluorenylidene requires 100 and 250 ps, respectively.[19] We expect that ISC of ethylidene-d_4 will be a slower process than that observed with arylcarbenes because of a larger singlet–triplet gap in ethylidene.[3] Thus our analysis indicates that singlet ethylidene-d_4 isomerizes to ethylene more rapidly than it undergoes ISC to the lower energy triplet state.

The lifetime of dimethylcarbene is extended by deuteration of the solvent (Table I).[10] The lifetime of ethylidene-d_4 does not exhibit solvent isotope effects, demonstrating that dimethylcarbene is sufficiently long lived to react with solvent (CH_3CN, $CHCl_3$) but that ethylidene-d_4 is not. The lifetime of ethylidene-d_4 is shorter in acetonitrile and chloroform than in pentane because solvent polarity is known to influence the rate of 1,2 hydrogen

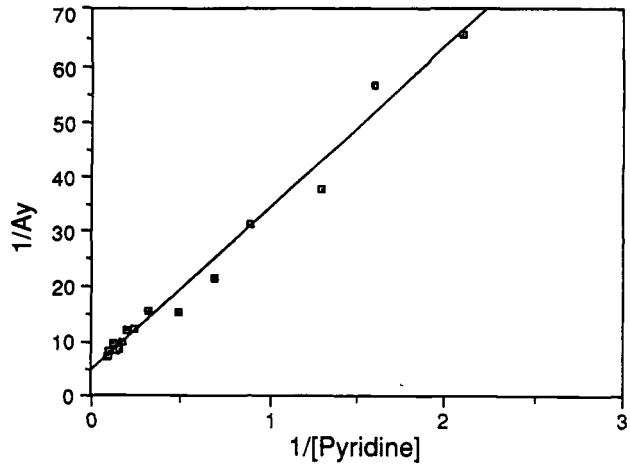


Figure 4. A double-reciprocal treatment of the data of Figure 3.

Table I. Calculated Lifetimes (±10%) of Alkylcarbenes

compound	solvent	lifetime (ns)[a]
dimethylcarbene[b]	pentane	21
	α,α,α-trifluorotoluene	24
	acetonitrile	4
	acetonitrile-d_3	6
	chloroform	6
	chloroform-d	7
dimethylcarbene-d_6[b]	pentane	67 (τ_D/τ_H = 3.2)
ethylmethylcarbene	pentane	2
methylcarbene-d_4[c]	pentane	0.5
(ethylidene-d_4)	acetonitrile	0.3
	acetonitrile-d_3	0.4
	chloroform	0.1
	chloroform-d	0.1

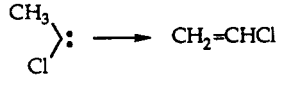
[a] Assuming $k_{\mathrm{PYR}} = 1 \times 10^9$ $\mathrm{M^{-1}\,s^{-1}}$. [b] Reference 10. [c] This work.

migration in carbenes.[20] If the Arrhenius A factor for the rearrangement of ethylidene-d_4 to ethylene-d_4 is 10^{11} $\mathrm{s^{-1}}$ (as with $CH_3CCl \rightarrow CH_2{=}CHCl$),[21] then the activation energy barrier of 1,2 deuterium migration of ethylidene-d_4 is calculated to be 2.3 kcal/mol in pentane, in good agreement with the calculations of Houk and Evanseck.[2]

However, the ratio of k_0/k_{PYR} was determined between −28 °C and 30 °C, and it varies only slightly (0.032–0.035) over this temperature interval. This demonstrates that the activation energies to isomerization and pyridine capture of ethylidene-d_4 are comparable and are both probably close to 0. The ratio of preexponential factors is startling:

$$\log\left(\frac{A_0}{A_{\mathrm{PYR}}}\right) = -1.35 \pm 0.08$$

As typical values of $A_{\mathrm{pyr}} \approx 10^9$–$10^{10}$ $\mathrm{M^{-1}\,s^{-1}}$,[11] we can deduce that the preexponential factor to isomerization is quite small, much smaller in fact than the previously cited preexponential factor measured by Goodman and LaViila[21] for the isomerization of chloromethylcarbene. Thus the entropy change for isomerization



of ethylidene is quite unfavorable. The A factor for pyridine capture (A_{PYR}) is probably 10^9–10^{10} $\mathrm{M^{-1}\,s^{-1}}$, which requires that the A factor of isomerization of ethylidene to 10^8–10^9 $\mathrm{s^{-1}}$. This in turn requires that $\Delta S^{\ddagger} \approx -17$ eu and that there be an activation energy barrier that is 0 or slightly negative for hydrogen migration. Negative activation energies are well-known in carbene chemistry[22]

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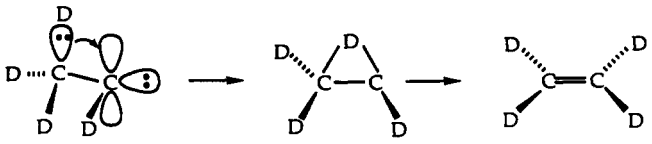
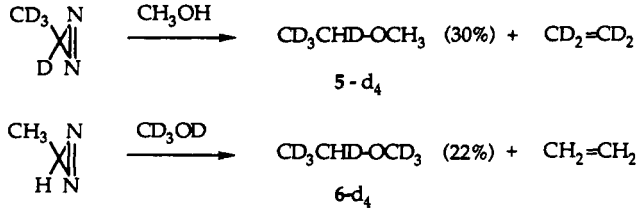
and are a consequence of free energy barriers which are dominated by entropic factors.[23] The unfavorable entropy change associated with 1,2 migrations in alkylcarbenes has been noted by Moss.[24] It is surely associated with the fact that the migrating atom must make a 90° turn away from the original trajectory, *after* reaching the transition state. This leads to an inefficient passage through the transition state to the product of reaction, or in other words a small transmission coefficient or steric factor in the preexponential term of the rate equation.[25] The low Arrhenius A factor and negative $\Delta S^{\ddagger}$ may also be a consequence of a contribution of quantum mechanical tunneling to the H(D) migration. As the position of the transition state on the free energy surface is dominated by the $T\Delta S$ term, the position of the transition state is a function of temperature.



Transition State

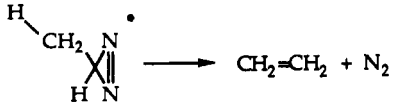
3. Product Analysis. Photolysis of methyldiazirine-d_4 in methanol gives ether **5** in 30% yield, whereas photolysis of methyldiazirine in methanol gives adduct **6** in only 22% yield.



Deuteration of ethylidene leads to an increased yield of *trappable* carbene. This is due to three kinetic isotope effects (KIEs): (a) the partitioning of the diazirine excited state (Scheme I), (b) the KIE to hydrogen (deuterium) migration in ethylidene, and (c) the KIE to insertion of the carbene into the OH(D) bond of the alcohol.

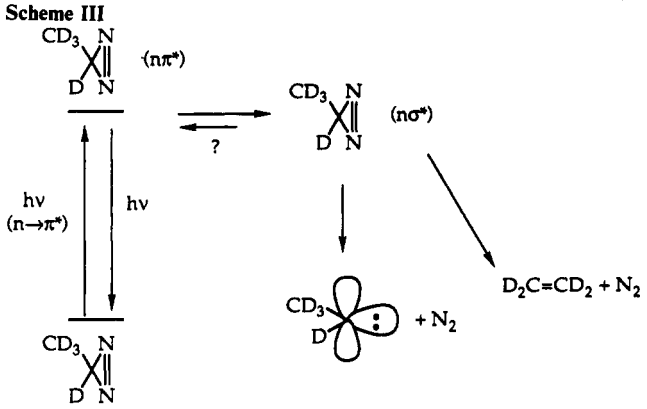
III. Discussion

Photolysis of an alkyl- or dialkyldiazirine at 351 nm produces an n–π^* excited singlet state.[17] This state can decay in part by fluorescence. It is unlikely that deuteration of the diazirine carbon will increase the fluorescence rate constant of the excited state of the diazirine; thus, the isotope effect on the fluorescence yield must be due to retardation of other decay processes of the diazirine excited state. The most likely competitive process which would display such an isotope effect is 1,2 hydrogen (deuterium) migration (to carbon or nitrogen[10]) in competition with nitrogen extrusion. Thus it is possible to capture ethylidene-d_4 with

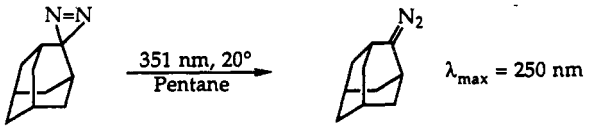


pyridine, but it is not possible to trap ethylidene itself because of two isotope effects. Deuteration leads to a greater *yield* of carbene per diazirine decomposition and to a longer lifetime of the photogenerated carbene and a more favorable ratio of k_0/k_{PYR}.

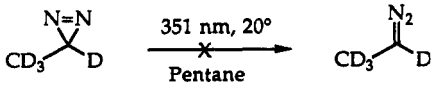
Scheme III



Diazirine excited states can also in general isomerize to diazo compounds.[26] We can easily detect the formation of diazoadamantane from adamantyldiazirine by LFP methods at ambient temperature, but we do not observe the formation of diazo-



ethane-d_4 at ambient temperature by this technique.[27] Thus diazo formation is a minor process in the photochemistry of methyldiazirine-d_4 in solution at ambient temperature.



Theory suggests that diazirines have two important singlet excited states: an n–π^* state and an n–σ^* state.[28] It is the n–π^* state which is populated upon absorption of light and which fluoresces, but it is the n–σ^* state which theory[28] suggests leads to isomerization to the diazo isomer and, we predict, to nitrogen extrusion. Turro[29] and Morgan[27] have both presented evidence for two excited singlet states of cyclic azo compounds and of adamantyldiazirine, respectively. The isotope effect on the yield of diazirine fluorescence (ϕ_F) demonstrates that hydrogen (deuterium) migration likely proceeds in the fluorescent n–π^* state. If 1,2 migration occurs from the nonfluorescent n–σ^* state of the diazirine, then the data *require* that the n–π^* and n–σ^* singlets *must be interconvertable* (Scheme III).

Pyridine does not quench the n–π^* fluorescence of methyldiazirine-d_4, which proves that this state does not react with pyridine to form ylide **3**. The data is permissive of the possibility that the nonfluorescent n–σ^* state reacts with pyridine to form ylide **3** but only if the n–π^* and n–σ^* states are *not* interconvertible. There is ample precedent for the reaction of singlet carbenes with pyridine to form ylides,[11] but there is no precedent or evidence for the reaction of the n–σ^* excited state of the diazirine with pyridine to form an ylide. Thus the most economical interpretation of the data is that it is ethylidene-d_4 and not the n–σ^* state of the diazirine that has been captured by pyridine.

The data analysis presented herein deduces that the lifetime of ethylidene-d_4 in pentane at ambient temperature is 500 ps. Because the singlet carbene lifetime is extremely short, the standard diffusional kinetic model used to derive this lifetime is surely inadequate. Neither static nor time dependent quenching has been considered. The decay of singlet ethylidene-d_4 is unlikely to be described as a simple exponential decay and should be modeled in a more sophisticated fashion as discussed by Scaiano

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and Siebrand[30] in their treatment of the second excited singlet state of anthracene. However, due to the necessary assumption of the magnitude of k_{PYR} in our analysis, we believe that a more complex analysis of our data is not warranted at this time.

IV. Conclusion

Laser flash photolysis of methyldiazirine-d_4 generates ethylidene-d_4, which can be intercepted with pyridine to form an ylide (λ_{max} = 365 nm). A double-reciprocal plot of the yield of ylide versus the concentration of pyridine is linear. Assuming that k_{PYR} is 1×10^9 M^{-1}, the lifetime (τ) of singlet ethylidene-d_4 is calculated to be 500 ps in pentane at ambient temperature and the activation barrier to its isomerization is less than 2.3 kcal/mol. Photolysis of methyldiazirine also leads to ethylene formation concerted with nitrogen extrusion in competition with carbene formation.

V. Experimental Section

Product Analysis. Methyldiazirine and methyldiazirine-d_4 were prepared by the method of Schmitz.[31] The fluorescence[10] and LFP[32] techniques used in this work have been described previously.

The yields of methylcarbene-d_4 and methylcarbene have been measured by analyzing methanolic solutions of the parent diazirines by NMR. The deuterio and protio diazirines were prepared in methanol and methanol-d_4, respectively; a small amount of benzene-d_6 (or benzene) was added as an internal standard. Three peaks were found in the initial ^{2}H NMR spectrum of methyldiazirine-d_4: benzene-d_6 (δ 7.15) and methyldiazirine-d_4 (CD_3, δ 0.6899; D, δ 0.6531). Several additional peaks were observed for 12-h photolysis with 350-nm light (Rayonet reactor) at 4 °C. These were assigned to the insertion product (CD_3, δ 0.9175, doublet; D, δ 3.1869, doublet) and ethylene-d_4 (δ 5.1664). When these peaks are integrated against the benzene standard, we find ~30% yield of carbene insertion product (ethyl-d_4 methyl ether) and 28% ethylene-d_4. The spectra for methyldiazirine can be analyzed in the same manner, showing 22% yield of carbene insertion product (ethyl methyl-d_3 ether) and 18% ethylene. The ratio (yield of **5**-d_4/yield of **6**-d_4 = 1.36) obtained from this experiment is consistent within experimental error with our earlier findings concerning the yield of carbene obtained from photolysis of dimethyldiazirine-d_6 and dimethyldiazirine.[10]

Acknowledgment. Support of this work by the National Science Foundation (CHE-8814950) is gratefully acknowledged.

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Thermodynamics of Molecular Recognition by Cyclodextrins. 1. Calorimetric Titration of Inclusion Complexation of Naphthalenesulfonates with α-, β-, and γ-Cyclodextrins: Enthalpy–Entropy Compensation

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Abstract: Calorimetric titrations have been performed at 25 °C in buffered aqueous solution (pH 7.20) to give the complex stability constants and the thermodynamic parameters for the inclusion complexation of naphthalenesulfonates **1–6** and naphthaleneacetate **7** with α-, β-, and γ-cyclodextrins (CDs). Data analyses assuming 1:1 stoichiometry were successfully applied to all of the host–guest combinations employed, except for the inclusion of 2-naphthalenesulfonate **2** with γ-CD, where both 1:1 and 1:2 host–guest complex formations were observed. The thermodynamic parameters obtained are critical functions of the position, number, and type of the anionic substituent(s) introduced to the guest molecule. The inclusion complexation is mostly enthalpy-driven with a minor or major positive entropic contribution, but in some cases a substantial positive entropic contribution determines the complex stability. Furthermore, the general validity of the enthalpy–entropy compensation effect, originally proposed for the cation binding by acyclic and macro(bi)cyclic ligands, was tested for the inclusion complexation by CD. Using all the thermodynamic data obtained here and reported elsewhere, the ΔH–$T\Delta S$ plot for CD gave a good straight line. On the basis of our explanation proposed previously, the slope very close to unity (α 0.90) indicates that, despite the apparently rigid skeleton of CD, the inclusion complexation causes substantial conformational changes involving the reorganization of the original hydrogen bond network, while the intermediate intercept ($T\Delta S_0$ 3.1) means fairly extensive dehydration occurring upon inclusion. It is thus demonstrated that, beyond the major driving forces operating in both types of complexation, i.e., ion–dipole and van der Waals interaction, the host–guest complexation phenomena involving the weak interactions may be understood in the general context of the enthalpy–entropy compensation effect.

Natural and chemically modified cyclodextrins (CDs) are known to recognize a wide variety of organic, as well as inorganic, guest molecules, forming host–guest inclusion complexes in aqueous solution.[1] They also provide an excellent model system mimicking the substrate-specific interaction of enzymes; some of them are successful enzyme models,[2–9] while the others are applied

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