

dielectric relaxation<sup>42</sup> studies clearly demonstrate that both salts exist predominantly (>95%) in the solvent-separated form in the solvents studied. On the basis of the rates of ion-pair exchange presented above, these salts will undergo preferential exchange with the solvent-separated ion pair benzophenone radical anion–diethylaniline radical cation. Thus for all of the reactions examined, we can assume that  $k_3 \gg k_2$  (Scheme II). The change in dynamics observed for the two salts must be due to changes in the rates  $k_1$ ,  $k_{-1}$ , and  $k_3$ .

For the acetonitrile studies, the observed bimolecular rate of exchange with  $\text{Na}^+$  (<1 M) indicates that  $k_3[\text{NaClO}_4] < k_{-1}$ .<sup>40a</sup> Furthermore, the rate of exchange is slower in the case of  $\text{Li}^+$ . The difference in rate observed for the two salts can be accounted for by the difference in solvation energy. Raman studies indicate that lithium interacts more strongly than sodium with acetonitrile solvent molecules.<sup>40a</sup> For ion-pair exchange to occur these ion-dipole forces must be overcome. Therefore, in acetonitrile, the rate-limiting step for ion-pair exchange is not the separation of the amine–ketone ion pair,  $k_{-1}$ , but the desolvation of the alkali cation.

Comparing exchange rates of  $\text{Li}^+$  and  $\text{Na}^+$  in dimethoxyethane, the rate of exchange is independent of the concentration of  $\text{Na}^+$  but dependent on  $\text{Li}^+$  concentration.<sup>40a</sup> The change in relative ordering of the exchange rate in dimethoxyethane and acetonitrile is due to one or both of the following:  $k_{-1}(\text{dimethoxyethane}) < k_{-1}(\text{acetonitrile})$  or the rate of sodium desolvation is faster in dimethoxyethane than in acetonitrile,  $k_3[\text{NaClO}_4](\text{dimethoxyethane}) > k_3[\text{NaClO}_4](\text{acetonitrile})$ .

In dimethyl sulfoxide, no exchange is observed between  $\text{NaClO}_4$  and the amine–ketone ion pair. Al-

(41) (a) Detellier, C.; Lazlo, P. *Helv. Chim. Acta* 1976, 59, 1333. (b) Detellier, C.; Lazlo, P. *Ibid.* 1976, 59, 1346. (c) Greenberg, M. S.; Bodner, R. L.; Popov, A. I. *J. Phys. Chem.* 1973, 77, 2449.

(42) Cachet, H.; Fekir, M.; Lestrade, J. C. *Can. J. Chem.* 1981, 59, 1051.

though dimethyl sulfoxide is similar in donor number to dimethoxyethane, the above results indicate that the exchange process is also sensitive to the polarity of the solvating media.<sup>40a</sup>

The importance of ion-pair reactions in organic chemistry necessitates an understanding of these processes on the molecular level. The above studies have enabled us to begin examining the effect of solvation on ion-pair dynamics. However, we still cannot accurately relate the measured kinetic data to specific solvent interactions. All of the data discussed in this Account clearly demonstrate that *molecular interactions* between solvent and reacting molecules influence the energetics and kinetics of molecular transformations. Further picosecond studies are required in order to more fully understand the “microdynamics” of chemical processes.

### Concluding Remarks

The experimental studies described above demonstrate that picosecond spectroscopic techniques can result in a better understanding of the molecular details associated with organic photoreactions. However, a complete understanding of chemical transformations on the microscopic level rests on advances in both picosecond kinetic techniques as well as in the theory of reaction processes. While, in principle, theoretical approaches are capable of providing a complete picture of the molecular motions in reaction dynamics, only experiment can sufficiently test and give us confidence in these theoretical predictions. Accompanying further improvements in picosecond technology and spectroscopies, a better understanding of the molecular details of chemical reactions is sure to emerge.

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## Flash Photolysis Studies of Carbenes and Their Reaction Kinetics<sup>1</sup>

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The basic principles of carbene chemistry were established in the 1950s by ingenious studies of their reaction products.<sup>2</sup> However, measurements of abso-

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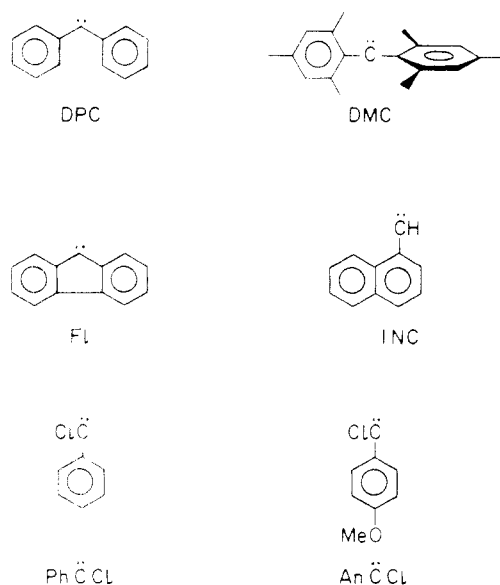
lute rate constants for carbene reactions followed very much later. In 1976, Closs and Rabinow<sup>3</sup> measured the first absolute rate constants for the reaction of a carbene in solution by using conventional flash photolysis. With this technique, the measurements were restricted to microsecond time resolution. However, with the advent of the laser flash photolysis technique, nanosecond time resolution became widely available and caused a resurgence of interest in the kinetics of carbene reactions.

(1) Issued as NRCC publication no. 23389.

(2) Kirmse, W. “Carbene Chemistry”; Academic Press: New York, 1964. Moss, R. A.; Jones, M., Jr. “Carbenes”; Wiley: New York, 1973.

(3) Closs, G. L.; Rabinow, B. E. *J. Am. Chem. Soc.* 1976, 98, 8190.

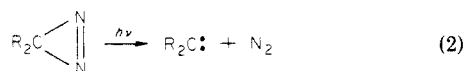
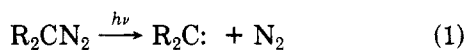
Chart I



In this Account we argue that these kinetic investigations have provided mechanistic insights into carbene chemistry which could not have been discovered from product studies alone. The carbenes discussed and their abbreviations are summarized in Chart I.

### The Experimental Technique

In laser flash photolysis, a solution of a photolabile substrate such as a diazo compound or diazine is photolyzed with a pulse from a nitrogen (337 nm) or excimer (308 or 249 nm) laser to give the transient of interest (eq 1 and 2). Once formed, the transient is



monitored by an optical detection system consisting of a xenon lamp, monochromator, and photomultiplier tube. The output of the photomultiplier tube is fed to a transient digitizer, and the signal is finally fed to a computer for storage and kinetic analysis. It is the laser pulse width of 5–10 ns that normally defines the time resolution of the instrument. Reaction kinetics are investigated at a fixed wavelength by monitoring changes in the optical absorption of a transient with time. The spectrum of a transient is reconstructed from measurements of these time profiles at a series of wavelengths. The technique has been described in much greater detail elsewhere.<sup>4,5</sup>

### Assignment of Optical Spectra

For laser flash photolysis to be a useful technique, it is vital that the absorption spectra of the chemical intermediates be correctly assigned. Trozzolo and Gibbons<sup>6</sup> devised a method for assigning the optical spectra of carbenes which makes use of the fact that many of them have triplet ground states and can therefore be detected by electron paramagnetic resonance, EPR, spectroscopy.<sup>7</sup> In this approach, a glass at  $-196^\circ\text{C}$  that

contains a photolabile precursor of the carbene is subjected to successive periods of irradiation. After each period both the UV-visible and EPR spectra of the sample are recorded. If a new optical absorption is detected whose amplitude increases in direct proportion to growth in the EPR signal, then there is a high probability that the absorption is due to the carbene. The same optical spectrum should be detected as a transient absorption by laser flash photolysis in solutions. This approach has been successfully applied to diphenylcarbene,<sup>6</sup> where the fluorescence rather than optical absorption spectrum was monitored, and dimethylcarbene.<sup>8</sup>

The Trozzolo-Gibbons method cannot easily be applied to carbenes such as fluorenylidene that are not very persistent at 77 K in matrices nor, of course, can they be applied to carbenes with ground-state singlets that do not give EPR signals. In such cases, product studies carried out under the conditions of the laser flash photolysis experiment provide the best evidence for the assignment of the transient absorptions.

Product studies are also vital in view of the low concentrations of carbene precursors, ca.  $10^{-3}$ – $10^{-4}$  M normally used in flash photolysis experiments. This is because labile impurities in solvent or quenching reagent, even if present at levels of 0.01–1% by volume, may well be capable of scavenging all of the carbene produced.

### Carbenes with Triplet Ground States

**Fluorenylidene.** The assignment of transients observed in the chemistry of fluorenylidene (FI) was the subject of considerable controversy and prompted numerous experiments.<sup>9</sup> As a result, the system has now been thoroughly investigated and appears to be well understood.<sup>10–12</sup>

Photolysis of diazofluorene in acetonitrile solvent leads to the formation of the singlet carbene that undergoes intersystem crossing to the triplet with a rate constant of  $3.6 \times 10^9 \text{ s}^{-1}$  at room temperature.<sup>10</sup> The triplet carbene has an absorption spectrum with a maximum at 470 nm and is a particularly reactive species. For example, in an isopentane-diethyl ether glass at 77 K it has a lifetime of  $\sim 80 \mu\text{s}$ .<sup>13</sup> Moreover, no solvent has yet been found that is unreactive toward the carbene at room temperature.<sup>11,12</sup> Even hexafluorobenzene, which is often used as an inert diluent, reacts with the carbene to form a 1:1 adduct.

Triplet fluorenylidene reacts rapidly with hydrogen and chlorine atom donors, respectively, to form the 9-fluorenyl (II) and 9-chlorofluorenyl radicals. To

(7) Trozzolo, A. M. *Acc. Chem. Res.* **1968**, *1*, 329. Trozzolo, A. M.; Wasserman, E. In "Carbenes"; Moss, R. A., Jones, M., Jr., Eds.; Wiley: New York, 1973; Vol. II, p 185.

(8) Nazran, A. S.; Griller, D. *J. Chem. Soc., Chem. Commun.* **1983**, 850; *J. Am. Chem. Soc.* **1984**, *106*, 543.

(9) Zupancic, J. J.; Schuster, G. B. *J. Am. Chem. Soc.* **1980**, *102*, 5958; **1981**, *103*, 944. Zupancic, J. J.; Grasse, P. B.; Schuster, G. B. *Ibid.* **1981**, *103*, 2423. Wong, P. C.; Griller, D.; Scaiano, J. C. *Ibid.* **1981**, *103*, 5934; *Chem. Phys. Lett.* **1981**, *83*, 69.

(10) Grasse, P. B.; Brauer, B.-E.; Zupancic, J. J.; Kaufmann, K. J.; Schuster, G. B. *J. Am. Chem. Soc.* **1983**, *105*, 6833.

(11) Griller, D.; Montgomery, C. R.; Scaiano, J. C.; Platz, M. S.; Hadel, L. *J. Am. Chem. Soc.* **1982**, *104*, 6813.

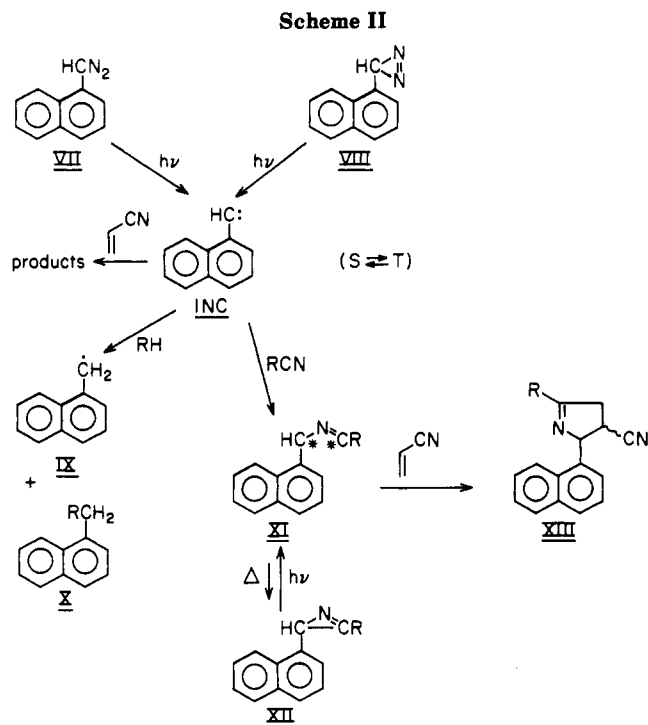
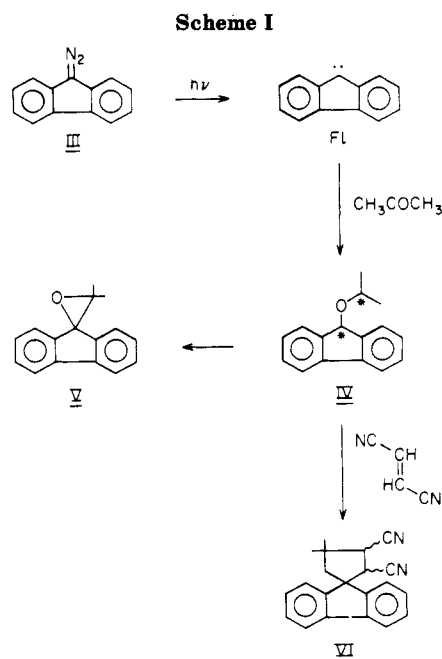
(12) Bauer, B. E.; Grasse, P. B.; Kaufmann, K. J.; Schuster, G. B. *J. Am. Chem. Soc.* **1982**, *104*, 6814.

(13) The EPR spectrum is only detected at high diazofluorene concentrations where microcrystallites of the diazo compound are presumably formed.

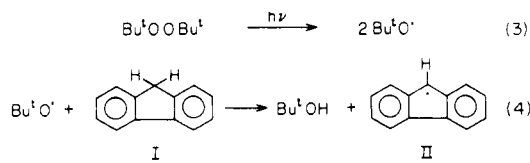
(4) Scaiano, J. C. *J. Am. Chem. Soc.* **1980**, *102*, 7747.

(5) Scaiano, J. C. *Acc. Chem. Res.* **1982**, *15*, 252; **1983**, *16*, 234.

(6) Trozzolo, A. M.; Gibbons, W. A. *J. Am. Chem. Soc.* **1967**, *89*, 239.



confirm the assignment, the 9-fluorenyl radical was generated independently via reactions 3 and 4 and was



detected by laser flash photolysis and by modulation spectroscopy. The spectrum of the radical consists of two main bands ( $\lambda_{\text{max}} = 500 \text{ nm}$ ) whose form and separation are almost identical with those of the triplet carbene.<sup>11</sup> Trozzolo and Gibbons<sup>6</sup> correctly predicted that this situation would apply since the electronic structures of the two species are quite similar.

The spectrum due to triplet fluorenylidene was also quenched by substrates such as alcohols, nitriles, and ketones that are normally thought of as singlet quenchers. These reactions may take place by a mechanism which involves an efficient equilibrium between the singlet and triplet states so that the disappearance of the triplet spectrum is merely a probe of the reactions of the singlet. Such processes are often observed for triplet carbenes, and examples of those for alcohols and nitriles are discussed in subsequent sections.

Triplet fluorenylidene is quenched more efficiently by ketones than by nitriles to give ylides. Thus, rate constant for its reaction with acetone was  $1 \times 10^7 \text{ M}^{-1} \text{ s}^{-1}$  in acetonitrile solvent at 298 K and led to the formation of a carbonyl ylide that had a strong absorption maximum at 640 nm.<sup>14</sup> Product studies showed that the ylide underwent ring closure to form an oxirane (Scheme I), and the Arrhenius parameters that described this process were  $\log(A/\text{s}^{-1}) = 13.26 \pm 0.11$  and  $E_a = 10.96 \pm 0.12 \text{ kcal mol}^{-1}$ .<sup>14</sup>

Carbonyl ylides with similar absorption maxima were also formed by the reaction of fluorenylidene with a series of cycloalkanones and with 2-butanone. As ex-

pected the absorption spectra due to the ylides were quenched by electron-deficient olefins. For example, the ylide derived from acetone was quenched with a rate constant of  $1.45 \times 10^7 \text{ M}^{-1} \text{ s}^{-1}$  by fumaronitrile.<sup>14</sup>

**1-Naphthylcarbene.** The chemistry and reaction kinetics of 1-naphthylcarbene, INC, are very similar to those of fluorenylidene. The optical absorption spectrum of triplet INC has not been detected presumably because like most carbenes, it is blue shifted with respect to that of the radical (IX) that has  $\lambda_{\text{max}} = 363 \text{ nm}$  and would therefore overlap with the absorption band of its diazo precursor. The behavior of the triplet carbene has therefore been inferred by monitoring the growth of its reaction products.<sup>15</sup>

Like fluorenylidene, 1-naphthylcarbene has a short lifetime in most common solvents, e.g., cyclohexane, 144 ns, and benzene,  $\sim 300 \text{ ns}$ .<sup>15</sup> It has been generated from diazo and diazine precursors (i.e., eq 1 and 2) and readily forms nitrile ylides that have  $\lambda_{\text{max}} \approx 390 \text{ nm}$  and that in nitriles as solvent are formed in 100–200 ns. The ylides are quenched by a variety of unsaturated compounds. For example, acrylonitrile reacted with the acetonitrile ylide of INC with a rate constant of  $5.4 \times 10^6 \text{ M}^{-1} \text{ s}^{-1}$ , and, as the reaction products showed, it also functioned as a scavenger of the carbene itself.<sup>15</sup> The same ylide (XI) can also be generated from the corresponding azirene (XII), and its kinetic behaviour is identical with the carbene-derived ylide (see Scheme II).<sup>16</sup>

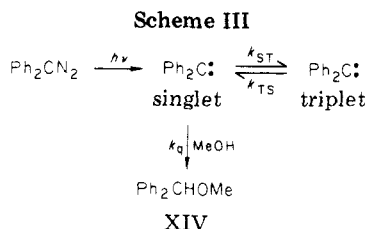
It was assumed that the singlet and triplet states of INC are in equilibrium under the reaction conditions and that the triplet, in part, gives rise to the cyclopropane products while the nitrile ylide and heterocyclic products are formed from the singlet carbene.

**Diphenylcarbene.** The absolute reactivity of triplet diphenylcarbene (DPC) toward standard substrates was

(15) Hadel, L. M.; Platz, M. S.; Scaiano, J. C. *Chem. Phys. Lett.* 1983, 97, 446.

(16) Barcus, R. L.; Wright, B. B.; Platz, M. S.; Scaiano, J. C. *Tetrahedron Lett.* 1983, 24, 3955.

(14) Wong, P. C.; Griller, D.; Scaiano, J. C. *J. Am. Chem. Soc.* 1982, 104, 6631.



far less than those of fluorenylidene or 1-naphthylcarbene.<sup>17,18</sup> For example, in cyclohexane solvent at 300 K the lifetime of the carbene was 5  $\mu\text{s}$  and was therefore ca. 2–3 orders of magnitude greater than that of fluorenylidene under the same conditions.<sup>18</sup> It also showed relatively low reactivity toward olefin addition. Even when the substrate was a diene (isoprene), the rate constant for carbene scavenging was only  $3.5 \times 10^5 \text{ M}^{-1} \text{ s}^{-1}$  whereas triplet fluorenylidene<sup>11</sup> reacted with a normal olefin (e.g., *cis*-4-methyl-2-pentene) with a rate constant of  $2.1 \times 10^8 \text{ M}^{-1} \text{ s}^{-1}$ .

The relatively low reactivity of triplet diphenylcarbene may reflect the ability of the phenyl rings to rotate so that the unpaired electrons that are in orthogonal orbitals may be more effectively delocalized. The notion that the orientation of the aryl groups can affect the stabilization of the triplet state was recognized by Skell, Etter, and Skovronec.<sup>19</sup> It has been supported by theoretical calculations on diphenylcarbene, which show that the singlet–triplet energy separation shows a strong dependence on the orientation of the phenyl groups.<sup>20,21</sup> This concept probably accounts for the substantial difference in reactivity between diphenylcarbene and fluorenylidene.

Perhaps the most perplexing aspect of the chemistry of triplet diphenylcarbene is its reaction with methanol.<sup>22</sup> The optical absorption spectrum of the carbene is quenched by methanol and follows the concentration dependence required by eq 5. Product studies show

$$k_{\text{exptl}} = k_0 + k_{\text{q}}[\text{quencher}] \quad (5)$$

that the reaction involves insertion of the carbene into the O–H bond, where  $k_{\text{exptl}}$  is the pseudo-first-order rate constant for carbene decay,  $k_0$  the rate constant in the absence of quencher, and  $k_{\text{q}}$  the rate of quenching.

At first sight, the very fact that the reaction takes place appears to conflict with the Skell–Woodworth rules<sup>23</sup> which are based on the principle of spin conservation and dictate that it is only the singlet carbene which ought to react with substrates like methanol which have singlet ground states. The observation was explained<sup>24a</sup> by proposing that the singlet and triplet

states of the carbene were in equilibrium under the reaction conditions (Scheme III). Now the Skell–Woodworth rules are satisfied because the reaction can take place via the singlet manifold.

Experiments of varying complexity have been used to measure rate constants for the elementary reactions shown in Scheme III and have led to estimates of the free energy difference between the singlet and triplet states.<sup>3,17,24,25</sup>

The rate constant for singlet–triplet intersystem crossing was measured<sup>17</sup> in acetonitrile solvent by monitoring the growth of the signal due to triplet diphenylcarbene in the picosecond time domain and was found to be  $(9.1 \pm 1) \times 10^9 \text{ s}^{-1}$ . This value was used in a competition experiment to measure the rate constant,  $k_{\text{S}}$  for reaction of the singlet carbene with methanol.<sup>22</sup> In this approach the quantum yield for the formation of the triplet carbene,  $\Phi$ , was measured ca. 50 ns after the laser pulse. This time was sufficiently long that singlet to triplet intersystem crossing was complete and was sufficiently short that no significant quenching of the triplet had taken place. The relationship between the rate constants is defined in eq 6, where  $\Phi_0$  is the

$$\Phi_0/\Phi - 1 = k_{\text{S}}/k_{\text{ST}} [\text{MeOH}] \quad (6)$$

quantum yield for triplet formation in the absence of methanol. With this approach we find<sup>22</sup>  $k_{\text{S}} = 5 \times 10^{10} \text{ M}^{-1} \text{ s}^{-1}$  in acetonitrile at 293 K, a result which is in agreement with the value of  $(3.5 \pm 0.5) \times 10^{10} \text{ M}^{-1} \text{ s}^{-1}$  obtained by a more circuitous route.<sup>17</sup>

If Scheme III adequately describes the reaction of diphenylcarbene with methanol so that the singlet and triplet states are in equilibrium under the reaction conditions, then the observed rate constant for the reaction will be defined by eq 7. In acetonitrile as solvent

$$k_{\text{q}} = k_{\text{S}}/K_{\text{eq}} \quad (7)$$

at 298 K the observed value<sup>22</sup> was  $2.6 \times 10^7 \text{ M}^{-1} \text{ s}^{-1}$  which when combined with the data described above gives  $K_{\text{eq}} = 1.4 \times 10^3$ . If the difference in entropy between the singlet and triplet carbenes reflects only the triple degeneracy of the latter's electronic state, it follows that  $\Delta H = -4.3 \text{ kcal mol}^{-1}$ .

This thermochemical estimate is based on the assumption that Scheme III accurately describes the reaction mechanism. If correct, it follows that the activation energy for the observed quenching of the triplet carbene by methanol will be equal to  $-\Delta H$  plus ca. 2 kcal  $\text{mol}^{-1}$  for the essentially diffusion-controlled reaction of the singlet with methanol. The observed activation energies were  $1.66 \pm 0.20$  (acetonitrile),  $3.61 \pm 0.36$  (isooctane), and  $1.17 \pm 0.36 \text{ kcal mol}^{-1}$  (benzene) and immediately imply that there are deficiencies in the proposed mechanism or in the measurements themselves.<sup>22</sup>

Several explanations are possible. First, all of the results are consistent with a reaction of the triplet carbene with methanol during which intersystem crossing to the singlet manifold takes place. This substrate-catalyzed intersystem crossing is quite distinct from thermal equilibration through the uncomplexed singlet carbene (Scheme III). We note that an equilibrium mechanism (such as Scheme III) predicts that the experimental activation energy ( $E_{\text{a}}$ ) should be an

(25) Turro, N. J. *Tetrahedron* 1982, 38, 809.

(17) Eisenthal, K. B.; Turro, N. J.; Aikawa, M.; Butcher, J. A., Jr.; DuPuy, C.; Hefferson, G.; Hetherington, W.; Korenowski, G. M.; McAuliffe, M. J. *J. Am. Chem. Soc.* 1980, 102, 6563.

(18) Hadel, L. M.; Platz, M. S.; Scaiano, J. C. *J. Am. Chem. Soc.* 1984, 106, 283.

(19) Etter, R. M.; Skovronek, H. J.; Skell, P. S. *J. Am. Chem. Soc.* 1959, 81, 1008.

(20) Metcalfe, J.; Halevi, E. A. *J. Chem. Soc., Perkin Trans. 2* 1977, 364.

(21) Hoffman, R.; Zeiss, G. D.; Van Dine, G. W. *J. Am. Chem. Soc.* 1968, 90, 1485.

(22) Griller, D.; Nazran, A. S.; Scaiano, J. C. *J. Am. Chem. Soc.* 1984, 106, 198.

(23) Woodworth, R. C.; Skell, P. S. *J. Am. Chem. Soc.* 1959, 81, 3383.

(24) (a) Bethell, D.; Stevens, G.; Tickle, P. *J. Chem. Soc. D* 1970, 792. (b) Bethell, D.; Hayes, J.; Newall, A. R. *J. Chem. Soc., Perkin Trans. 2* 1974, 1307.

upper limit to  $-\Delta H_{TS}$ , while in a surface crossing type of mechanism one would generally expect  $E_a$  to be a lower limit for  $-\Delta H_{TS}$ . Other likely possibilities are that the measured value of  $k_{ST}$  is incorrect or, since some of the early experiments were carried out in different solvents, that there is a solvent effect on the triplet-singlet energy gap.<sup>26</sup> However, which of these possibilities actually applies as yet remains a mystery.<sup>35</sup>

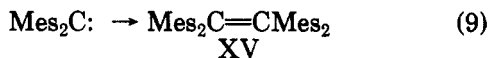
Unfortunately, product studies on the methanol reaction have little bearing on details of the mechanism since they can be interpreted in terms of an equilibrium scheme or in terms of a mechanism in which all of the products are derived from a single precursor, namely, the triplet carbene.<sup>24a</sup> However, this is not the case for the reaction of diphenylcarbene with butylamines.<sup>24b</sup> The effects of tritium and deuterium labeling on the product distribution led to the conclusion that there is no significant triplet to singlet intersystem crossing as required by the equilibration mechanism. This result supports our conclusion about the possible role of the triplet carbene in the methanol reaction. That is, the triplet may not function simply as a reservoir of the singlet carbene through an equilibrium mechanism but may be an active participant in the reaction with the alcohol.

**Dimesitylcarbene.** While all of the above carbenes have triplet ground states, they are quenched by singlet substrates to yield molecular products in apparent contravention of the Skell-Woodworth rules. Thus, alcohols, nitriles, and parent diazo compound (eq 8) all quench the optical absorption spectra of the triplet carbenes.



These examples have traditionally been rationalized in terms of a singlet-triplet equilibrium of the type described in Scheme III. However, such schemes would be credible if diarylcarbenes could be discovered whose singlet and triplet states carried out the distinct chemistries required by the principles of spin selection.

In 1964 Zimmerman and Pascovich<sup>27</sup> discovered such a case. During their investigations of steric effects in carbene chemistry, they found that dimesitylcarbene (DMC) did not react with its parent diazo compound to form azine (reaction 8) even though samples of the latter were perfectly stable under the reaction conditions. Instead, the carbene dimerized at room temperature in either benzene or cyclopentane solutions to give the sterically congested olefin XV (eq 9).



Mes = 2,4,6-trimethylphenyl

The observations were explained by proposing that the singlet and triplet states of this carbene had a relatively large energy separation. Thus, the triplet ground state once formed could not access the singlet manifold either by direct methods or by state mixing to form ether or azine. Olefin was formed through the reaction between two triplet carbenes for which there

is a 1/9 probability of forming a singlet product.

Laser flash photolysis experiments were used to monitor the behavior of triplet dimesitylcarbene. Its first lifetime is cyclopentane solutions was typically ca. 200  $\mu\text{s}$  and must reflect the bimolecular decay of the carbene since olefin was the major isolated product. This result contrasts sharply with the behavior of triplet fluorenylidene, 1-naphthylcarbene, and diphenylcarbene all of which readily attack hydrogen donor solvents and implies that the reactivity of the carbene is moderated by the steric influence of the ortho-methyl groups.

Triplet dimesitylcarbene reacted readily with oxygen with a rate constant of  $1.9 \times 10^8 \text{ M}^{-1} \text{ s}^{-1}$  to give ketone as final product. Of course, this triplet-triplet reaction is consistent with the Skell-Woodworth rules. However, unlike the other diarylcarbenes mentioned above, the lifetime of triplet dimesitylcarbene was essentially unaffected by the addition of methanol, implying a consistency with the rules of spin selection that has not been found for any of the other diarylcarbenes.<sup>8</sup>

The singlet state of dimesitylcarbene was quenched both by methanol and 1-propanol as evidenced by reductions in the quantum yields for triplet formation when the alcohols were added to the samples. Rate constants for these reactions were investigated by using a Stern-Volmer type of approach based on the yield of triplet carbene (see eq 6). However, since the rate constant for singlet triplet intersystem crossing is not yet known for this carbene, they can only be reported as lower limits, viz.,  $k \geq 1.8 \times 10^7 \text{ M}^{-1} \text{ s}^{-1}$  (methanol) and  $k > 2.2 \times 10^7 \text{ M}^{-1} \text{ s}^{-1}$  (1-propanol).

There was no detectable quenching of either singlet or triplet dimesitylcarbene with *cis*-2-pentene as substrate. However, a preparative photolysis experiment carried out at low light intensities gave dimer XV (ca. 50%) as well as *cis*- and *trans*-cyclopropanes XVI and XVII (ca. 25% each). The yield of dimer increased at



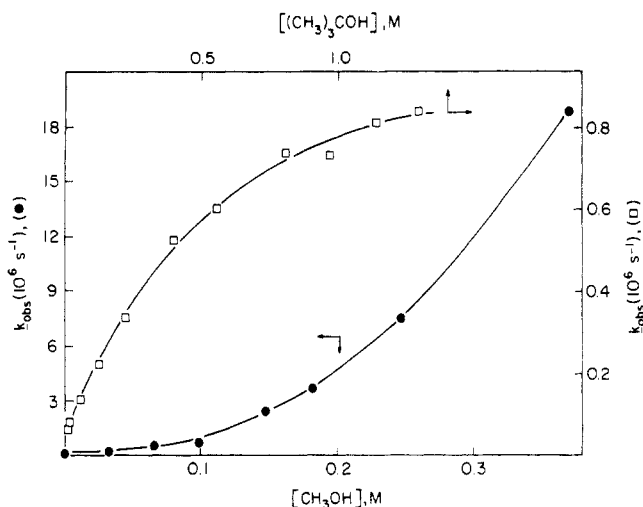
the expense of the cyclopropanes in experiments carried out at higher light intensities and hence at higher carbene concentrations. This result indicates that dimerization and cyclopropanation are competitive processes and that all of the products were derived from the triplet carbene. Again, nonstereospecific cyclopropanation by the triplet carbene is in accord with the dictates of the Skell-Woodworth rules.

EPR studies of triplet dimesitylcarbene<sup>28</sup> show that its central C-C-C angle is much larger than that in diphenylcarbene and that its aromatic rings are orthogonal. Theory indicates that this distortion enhances the energy gap between the triplet and the singlet state in which the two electrons occupy the same orbital. However, the trend toward linearity will tend to stabilize the singlet state that is electronically identical with the triplet with the exception that the unpaired electrons have antiparallel spins. Whichever of these states is lower lying in dimesitylcarbene, its chemistry clearly shows that no singlet state is readily

(26) This is now known to be true, though it is not clear if the magnitude of the solvent effect is in itself sufficient to explain the unusual observations for methanol quenching. We are grateful to Professor N. J. Turro (Columbia) for communicating these unpublished results.

(27) Zimmerman, H. E.; Pascovich, D. H. *J. Am. Chem. Soc.* 1964, 86, 2149.

(28) Nazran, A. S.; Gabe, E. J.; LePage, Y.; Northcott, D. J.; Park, J. M.; Griller, D. *J. Am. Chem. Soc.* 1983, 105, 2912 and unpublished results.

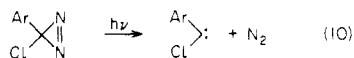


**Figure 1.** Quenching of *p*-anisylchlorocarbene by alcohols at 300 K: methanol in acetonitrile (●, left and bottom scales) and *tert*-butyl alcohol in isooctane (□, top and right scales). The continuous trace is an arbitrary fit to the data.

accessible from the triplet that gives rise to typical singlet chemistry such as insertion into alcohols.

### Carbenes with Singlet Ground States

Arylchlorocarbenes are the only carbenes with singlet ground-states that have been investigated in detail by laser flash photolysis. These carbenes are easily generated by photolysis of their corresponding diazirines (reaction 10).<sup>29</sup> Their transient absorption spectra in solution are substantially more difficult to characterize than those of triplet carbenes, (vide supra).



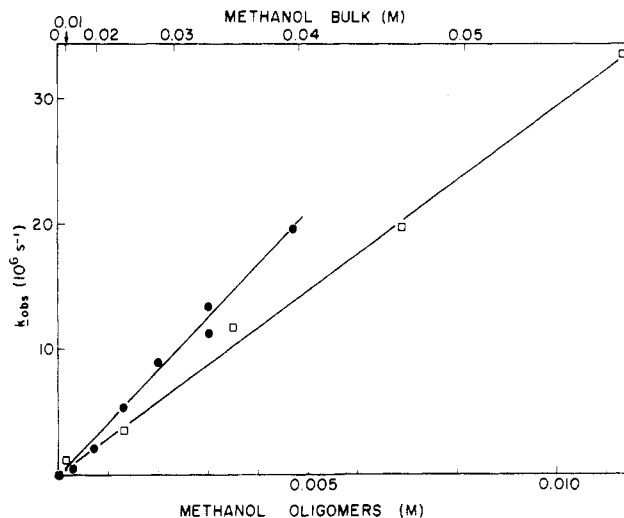
The assignments were made<sup>29</sup> by demonstrating first that the transient lifetimes were insensitive to dissolved oxygen and, secondly, that the transient absorptions were quenched by olefins to give cyclopropanes that were formed stereospecifically. The rate constant for the reaction of phenylchlorocarbene with tetramethylethylene was found to be  $(3.3 \pm 0.2) \times 10^8 \text{ M}^{-1} \text{ s}^{-1}$  at 298 K in isooctane solvent.<sup>29,30</sup> However, the reaction showed a negative activation energy of  $-1.7 \text{ kcal mol}^{-1}$ . The result was explained by invoking the reversible formation of a carbene-olefin complex.

Although the overall reaction had a complex mechanism, an excellent Hammett correlation was obtained<sup>31</sup> for the reactions of a series of para-substituted phenylchlorocarbenes with tetramethylethylene and other olefins. As a result, it was proposed that the dominant substituent effect applied to reaction of the complex to yield the cyclopropane. However, this should not be taken to imply that linear free energy relationships will always function adequately in instances where the reaction mechanism is complex. Indeed the converse is most likely to be true, i.e. that the failure of a linear free energy relationship may well be symptomatic of a complex mechanism.

(29) Turro, N. J.; Butcher, J. A., Jr.; Moss, R. A.; Guo, W.; Munjal, R. C.; Fedorynski, M. *J. Am. Chem. Soc.* 1980, 102, 7576.

(30) Turro, N. J.; Lehr, G. F.; Butcher, J. A., Jr.; Moss, R. A.; Guo, W. *J. Am. Chem. Soc.* 1982, 104, 1756.

(31) Moss, R. A.; Perez, L. A.; Turro, N. J.; Gould, I. R.; Hacker, N. P., *Tetrahedron Lett.* 1983, 24, 685.



**Figure 2.** Quenching of  $\text{Ph}\ddot{\text{C}}\text{Cl}$  (□) and  $\text{An}\ddot{\text{C}}\text{Cl}$  (●) by methanol in isooctane at 300 K, plotted as a function of the oligomer concentration.

### Reaction of Phenylchlorocarbene with Methanol

In a study of the reaction of phenylchlorocarbene,  $\text{Ph}\ddot{\text{C}}\text{Cl}$ , and *p*-anisylchlorocarbene,  $\text{An}\ddot{\text{C}}\text{Cl}$  ( $\text{An} = p\text{-CH}_3\text{OC}_6\text{H}_4$ ) with methanol and *tert*-butyl alcohol we found nonlinear plots when the observed reciprocal lifetimes for carbene decay were plotted by using eq 5; see Figure 1.<sup>32</sup> Analysis of the reaction products showed that they had indeed resulted from the expected insertion process (eq 11 and 12). However, for meth-



anol, the curvature in the kinetic plot implied that this substrate was in some way becoming disproportionately more reactive as its concentration was increased while, for *tert*-butyl alcohol, the converse was true.

We explained these results with the proposal that the hydrogen-bonded oligomers of methanol, which were increasingly formed as its concentration was increased, were more reactive toward the carbene than its monomer. For *tert*-butyl alcohol the converse must have applied and was explained with the suggestion that the *tert*-butyl groups sterically protected the hydrogen-bonded hydroxyl groups in the oligomers from attack.

The distribution of monomers, dimers, and oligomers at a given concentration of alcohol was calculated from data obtained in vapor pressure studies.<sup>32</sup> When  $k_{\text{obs}}$ , for the two carbenes, were plotted vs. the concentration of methanol oligomers, plots of excellent linearity were obtained as was also the case for a plot involving the concentration of *tert*-butyl monomer (Figures 2 and 3).

Rate constants for the reactions of  $\text{Ph}\ddot{\text{C}}\text{Cl}$  and  $\text{An}\ddot{\text{C}}\text{Cl}$  with methanol monomer were respectively  $(2.9 \pm 0.2) \times 10^9$  and  $(4.3 \pm 0.4) \times 10^9 \text{ M}^{-1} \text{ s}^{-1}$  (per methanol unit), implying that in hydrocarbon solvent, the rate constants were close to the diffusion-controlled limit. By contrast, extrapolation of the data to zero methanol concentration gave a rate constant of  $2 \times 10^7 \text{ M}^{-1} \text{ s}^{-1}$  for the reaction of  $\text{An}\ddot{\text{C}}\text{Cl}$  with methanol monomer in isooctane.

(32) Griller, D.; Liu, M. T. H.; Scaiano, J. C. *J. Am. Chem. Soc.* 1982, 104, 5549.

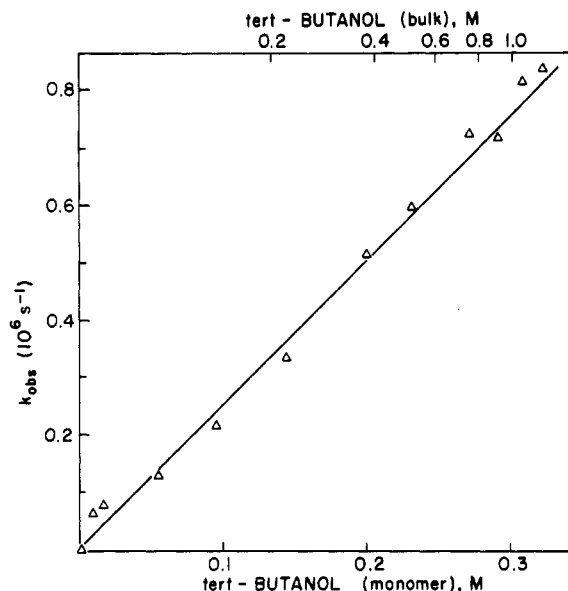


Figure 3. Quenching of  $An\dot{C}Cl$  by *tert*-butyl alcohol in isoctane at 300 K, plotted as a function of the monomer concentration.

The corresponding rate constant for the reaction of *tert*-butyl alcohol monomer was  $(2.5 \pm 0.2) \times 10^6 M^{-1} s^{-1}$ .<sup>32</sup>

The temperature dependence of the reaction of  $An\dot{C}Cl$  with methanol was in accord with this model since the observed rate constant increased as the temperature decreased. This observation is consistent with the increased formation of dimer and higher oligomers at the lower temperatures. Indeed, the observed activation energy of  $-4.7 \pm 0.3 \text{ kcal mol}^{-1}$  is similar to the enthalpy change associated with hydrogen bond formation.<sup>33</sup>

Interestingly, similar effects were not observed in the reactions of the same arylchlorocarbenes with acetic and other acids, e.g., reaction 13. In these cases dimers of  $Ph\dot{C}Cl + MeCO_2H \rightarrow PhCH(OCOMe)Cl \rightarrow PhCHO + MeCOCl$  (13)

the acids are the highest oligomers that form and the rate constants for these reactions were found to be close to the diffusion-controlled limit ( $k_{13} = (3.1 \pm 0.6) \times 10^9 M^{-1} s^{-1}$  in isoctane solvent at 298 K).<sup>34</sup>

### Concluding Remarks

Laser flash photolysis studies of carbene reactions have provided insights into their mechanisms beyond those which could have been gained by product or competitive kinetic studies. Examples are the reversible formation of intermediates in cyclopropanation by phenylchlorocarbenes, discrimination by those carbenes toward alcohol monomers and oligomers. Measurements of absolute rate constants for carbene reactions have shown that electronic and steric factors can have an enormous effect on carbene lability. At one extreme, fluorenylidene reacts rapidly and relatively indiscriminately with almost all substrates while at the other extreme dimesitylcarbene is highly selective in its behavior and is relatively persistent. We expect that the experiments described in this Account are modest forerunners of those yet to come, in which the laser techniques are extensively applied in carbene chemistry.

(33) Joesten, M. D.; Schaad, L. J. "Hydrogen Bonding"; Marcel Dekker: New York, 1974; Chapter 5.

(34) Griller, D.; Liu, M. T. H.; Montgomery, C. R.; Scaiano, J. C.; Wong, P. C. *J. Org. Chem.* 1983, 48, 1359.

(35) Note Added in Proof. A recent report indicates that  $k_{ST}$  in acetonitrile is ca. one-third of the value originally reported<sup>17</sup> and that  $k_{ST}$  is solvent dependent. Sitzmann, E. V.; Langan, J.; Eisenthal, K. B. *J. Am. Chem. Soc.* 1984, 106, 1868.

## Nucleophilic Additions to Tetrahydropyridinium Salts. Applications to Alkaloid Syntheses

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A previous *Account* from these laboratories<sup>1</sup> dealt with the development of two new and quite general methods for the stereospecific total synthesis of structurally diverse alkaloids. In that *Account*, a high premium was placed on efficiency of bond construction and stereochemical control. For example, the acid-catalyzed

rearrangement of various cyclopropylimines to the corresponding 4,5-dihydropyrroles (cf. 1 to 2) provides an illustration wherein two new bonds are produced, as does the subsequent annulation of these and other endocyclic enamines (e.g., 4) to afford exclusively *cis*-fused hydroindolones (3) or hydroquinolones (5) (Scheme I). It is the goal of this *Account* to outline the genesis of a powerful heuristic<sup>2</sup> principle and to retrace the course of events from its inception to the present time.

Professor Robert Velman Stevens was born on March 24, 1941, in Mason City, Iowa, and studied at Iowa State University for his B.S. degree, which he completed in 1963. In 1966, immediately following his graduate studies at Indiana University with Professor Ernest Wenkert, he was appointed to the faculty at Rice University, where he served for 11 years before joining the Department of Chemistry at the University of California, Los Angeles, as Professor of Chemistry. He earned for himself an international reputation as a master in the art of synthesis of complex organic structures and will be well remembered for his impressive synthetic approach to Vitamin B-12. In addition, his research interests focused on the development of new methodologies and strategies for the total synthesis of natural products including vitamins, steroids, terpenoids, and antibiotics, as well as alkaloids.

\* Deceased March 9, 1984. Due to his untimely death, revision of Professor Stevens' original manuscript was conducted by his research group under the supervision of Professor Michael E. Jung. Please address correspondence to Dr. Jung, Department of Chemistry and Biochemistry, UCLA.

(1) Stevens, R. V. *Acc. Chem. Res.* 1977, 10, 193.

(2) Webster defines heuristic as "serving to discover or to stimulate investigation; of methods of demonstration which tend to lead a person to investigate further".