

nation of the flexibility introduced into the inhibitor by conversion from a fused bicyclic ring system to an acyclic one in the enamine form of the acyl-enzyme as well as the inherent mobility of the enzyme¹⁷ leads to a significant conformational change on formation of the enamine acyl-enzyme. On the basis of the behavior of enzyme inactivated by **2**, which lacks a side chain on C6 and shows neither the change in secondary structure nor stability at alkaline pH, we believe it is the conformational change, rather than the slow hydrolysis of the β -aminoacrylate, which leads to the irreversible inactivation at alkaline pH by the sulfones of Type A substrates. This conformational change results in displacement of the catalytic groups with respect to the acyl-enzyme bond such that catalysis of deacylation is prevented.

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Methylchlorocarbene: Measurement of Rate Constants for 1,2-Hydrogen Migration and Addition to Alkenes

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There have been no reports so far of the intermolecular capture of dialkylcarbenes, probably because of the ease of intramolecular 1,2-H shift. Moss and Mamantov¹ demonstrated that the presence of the chlorine atom stabilizes methylchlorocarbene (**2**) generated from photolysis of 3-chloro-3-methyldiazirine (**1**) enabling the intermolecular addition to alkenes to compete with the intramolecular 1,2-H shift of the carbene to form vinyl chloride. Absolute rate constants for the addition of a variety of substrates to a number of carbenes generated from arylhalodiazirines have been measured² by laser flash photolysis (LFP). For alkylchlorocarbene, similar measurements have not been reported until recently,³ mainly because the alkylchlorocarbenes do not absorb in a region where they can be monitored. However, the "pyridine probe technique"³ renders the methylchlorocarbene visible. We now report the rate constant for 1,2-H migration in **2**, as well as the rate constants for the reaction of **2** with various olefins. These results indicate an usually slow H migration and the ambiphilic character of this carbene.

3-Chloro-3-methyldiazirine was prepared by Graham's method⁴ and the LFP setup has been described previously.⁵ LFP of **1** (≈ 5 mM in isooctane at 25 °C) in the presence of pyridine produces a transient absorption ($\lambda_{\max} = 360$ nm) that is not observed in the absence of pyridine and is attributed to the pyridinium ylide, **3**. The rate constants for 1,2-H migration, k_i , and for ylide formation, k_y , are determined by measuring, at 360 nm, the rate of growth of the ylide absorption, $k_{\text{growth}} = k_i + k_y[\text{pyridine}]$, as a function of [pyridine]. Least-squares analysis of ten measurements for [pyridine] ranging from 0.2 to 6 mM gives

$$k_y = 8.86 \pm 0.10 \times 10^9 \text{ M}^{-1} \text{ s}^{-1} \text{ and}$$

$$k_i = 3.04 \pm 0.05 \times 10^6 \text{ s}^{-1}$$

When a constant amount of pyridine (0.45 mM) is used, the addition of alkene substrates such as tetramethylethylene (TME)

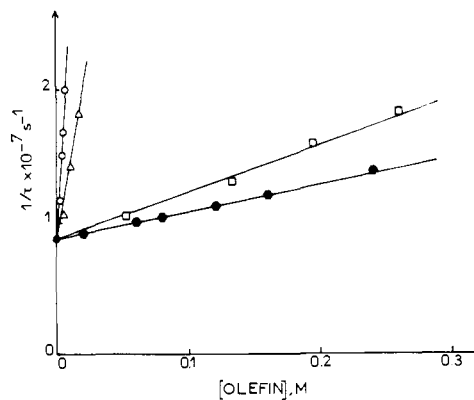


Figure 1. Plot of the pseudo-first-order rate constants for the growth of the ylide ($1/\tau$) vs [olefin], at 25 °C in isooctane with [pyridine] = 0.45 mM: TME (O); HEX (●); ACN (□); CIACN (Δ).

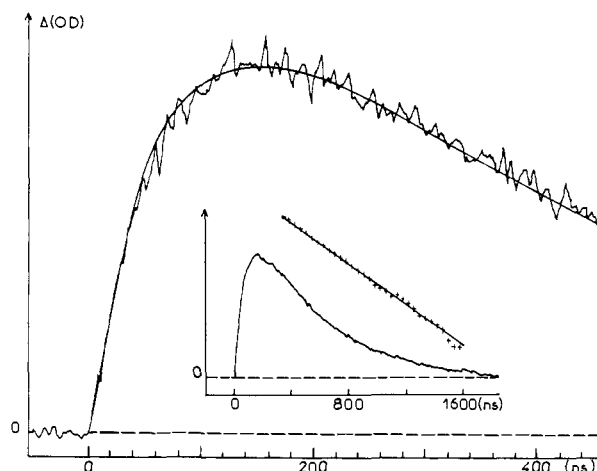
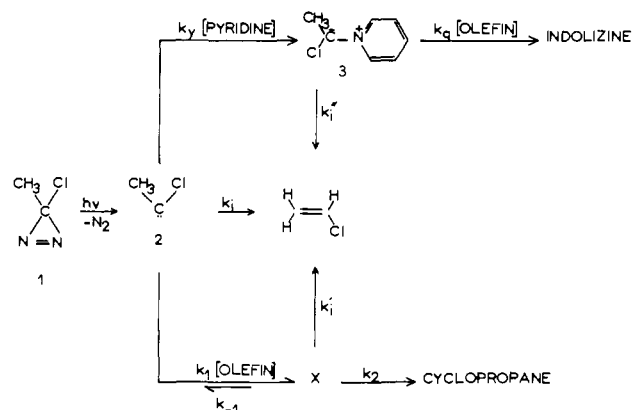


Figure 2. Growth and decay of the ylide absorption with [pyridine] = 0.45 mM and [CIACN] = 12.4 mM at 50 ns/div sweep rate. The solid line is the theoretical curve calculated with eq 1 with $\tau_1 = 70$ ns and $\tau_2 = 400$ ns. Insert: same conditions, at 200 ns/div sweep rate, for determining τ_2 .

and 1-hexene (HEX) decreases the yield of ylide formation because the cycloaddition of **2** to the alkene competes with ylide formation and increases the rate of growth of **3** which becomes $k_{\text{growth}} = k_i + k_y[\text{pyridine}] + k_c[\text{olefin}]$. Excellent linearity was obtained for k_{growth} vs [TME] and [HEX]. The slopes of the plots shown in Figure 1 give the following values for the rate constant, k_c , for addition of **2** to TME and HEX respectively

$$1.32 \pm 0.06 \times 10^9 \text{ and } 2.10 \pm 0.05 \times 10^7 \text{ M}^{-1} \text{ s}^{-1}$$

With α -chloroacrylonitrile (CIACN) and acrylonitrile (ACN), the determination of k_c is not simple because the ylide **3** is also quenched by the nitriles, most probably to give the corresponding indolizines as it has been demonstrated in the case of phenylchlorocarbene.⁶ Then, the relevant mechanistic scheme is



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and the kinetic behavior of the ylide, **3**, is given by

$$[3]_t = Y_m[\exp(-t/\tau_2) - \exp(-t/\tau_1)] \quad (1)$$

where $1/\tau_2 = k_q[\text{olefin}]$, $1/\tau_1 = k_i + k_y[\text{pyridine}] + k_c[\text{olefin}]$, and Y_m is the amount of ylide which would be formed if k_q were zero. As long as the concentration of acrylonitriles is low enough such that $\tau_2 \gg \tau_1$, τ_2 can be accurately measured from the decay of the ylide absorption (see insert in Figure 2). Then the value of τ_1 is calculated from the time for the maximum absorption of **3**, $t_{\text{max}} = \ln(\tau_2/\tau_1) \cdot (\tau_2\tau_1)/(\tau_2 - \tau_1)$ and/or by adjustment of the values of τ_1 and Y_m to get the best fit between the curves $[3]_t$ and OD_t vs time as shown in Figure 2. Measurements of $1/\tau_1$ and $1/\tau_2$ vs [olefin] are linear and give

$$k_c = 3.63 \pm 0.20 \times 10^7 \text{ M}^{-1} \text{ s}^{-1} \text{ and} \\ k_q = 2.06 \pm 0.02 \times 10^7 \text{ M}^{-1} \text{ s}^{-1} \text{ for ACN}$$

$$k_c = 5.21 \pm 0.57 \times 10^8 \text{ M}^{-1} \text{ s}^{-1} \text{ and} \\ k_q = 1.60 \pm 0.15 \times 10^8 \text{ M}^{-1} \text{ s}^{-1} \text{ for CIACN}$$

The rate of addition of **2** to alkenes with increasing π molecular electronegativity (TME, 3.0; HEX, 3.84; ACN, 5.36; CIACN, 5.46) exhibits a parabolic dependence, i.e., high reactivity toward both electron-rich and electron-poor alkenes. This behavior is similar to that of Ph-C-Cl in the presence of the same series of alkenes.^{2d}

It is worth noting that independent measurements with time-resolved photoacoustic calorimetry⁷ yielded the same slow rate ($k_i = 1.4 \times 10^6 \text{ s}^{-1}$ at 295 K in heptane) for the 1,2-H migration in methylchlorocarbene.

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Measurement of the Absolute Rate of 1,2-Hydrogen Migration in Benzylchlorocarbene

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A very common reaction of an alkylcarbene is the 1,2-migration of a hydrogen atom to produce an alkene.⁵ Calculations⁶⁻¹⁰ have deduced barriers to the rearrangement of singlet ethylidene ranging from 0 to 27 kcal mol⁻¹ with the more recent ab initio methods favoring the smaller value. The intramolecular rearrangement

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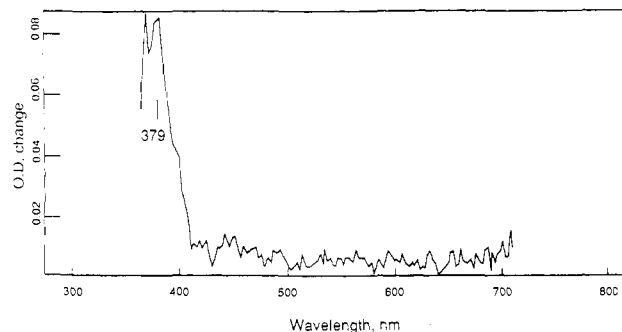
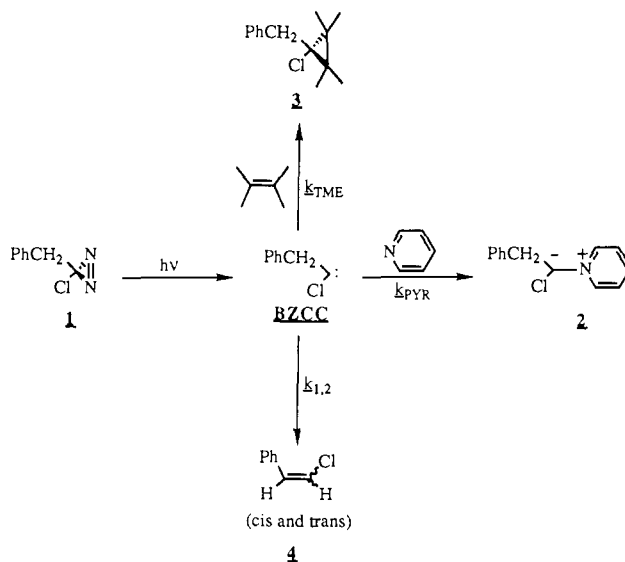


Figure 1. The transient spectrum of ylide **2** produced by laser flash photolysis of diazine **1** in toluene containing pyridine solution.

Scheme I



has proven to be so rapid in simple singlet alkyl carbenes that it is impossible to intercept these species intermolecularly.

Experimental work on 1-aryl-2-diazopropanes has produced evidence in favor of a barrier to 1,2-H-migration in dialkylcarbenes, but the barrier height was not estimated.¹¹ Recently, the products obtained from the thermolysis of 4-diazirinopentanoic acid¹² produced an estimate of $1.1 \pm 1 \text{ kcal mol}^{-1}$ for the barrier height (ΔH^\ddagger) of the 1,2-H-shift in the corresponding dialkylcarbene.

The pioneering work of Moss and co-workers¹³ has demonstrated that the presence of a halogen atom at a carbene center greatly stabilizes the singlet electronic state. This stabilization is sufficient to render the halo carbenes ground-state singlet species in contrast to methylene in which the triplet is the ground state.¹⁴ The stabilization due to the chlorine substituent apparently retards the rate of the hydrogen shift reaction thereby enabling intermolecular reactions of the carbene to successfully compete with the intramolecular rearrangement.

Liu and Subramanian¹⁵ have recently estimated the values of the barrier to rearrangement in benzylchlorocarbene by measuring

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