Effect of Diazirine Concentration on the Reaction of 3-Benzyl-3-chlorodiazirine with Methanol

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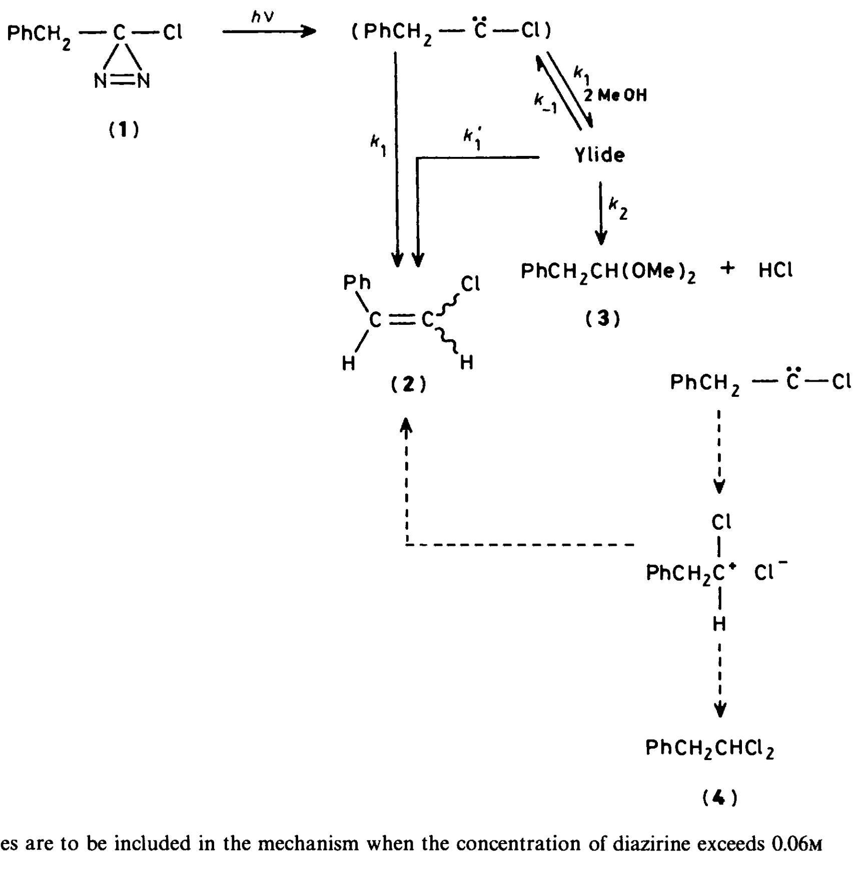
In the reaction of 3-chloro-3-benzyldiazirine with methanol, the concentration of diazirine has pronounced effects on the acetal/chlorostyrene product ratio. A mechanism is proposed to account for these results.

The photolysis of 3-halogeno-3-benzyldiazirine in a variety of alkenes[1–4] and the alcohols[5–7] has been the subject of extensive investigation. For the alkene reactions, the formation of an immediate carbene/alkene adduct has been suggested prior to cyclopropane formation. Additionally, the concentration of diazirine has no effect on product ratio (cyclopropane/chlorostyrene) when alkenes were used as substrates.[3] Photolysis of 3-benzyl-3-chlorodiazirine (**1**) in the presence of an excess of methanol in benzene gave *E*- and *Z*-β-chlorostyrenes (**2**), phenylacetaldehyde dimethyl acetal (**3**), and HCl. However, when the diazirine concentration is increased, a fourth product, 1,1-dichloro-2-phenylethane (**4**), is formed in significant amount. The reaction of chlorobenzylcarbene with methanol shows a second-order dependence in methanol and the results have been interpreted in terms of a kinetic model in which a reversibly formed carbene/methanol ylide is an intermediate (see Scheme).[6] Unlike the reactions involving alkenes, the concentrations of diazirine play a significant role in determining the product ratio (acetal/chlorostyrene) when methanol was the substrate. This report explains this effect and clarifies the mechanism for the reaction of electrophilic carbenes with alcohols.

Results and Discussion

The results on the photolysis of 3-benzyl-3-chlorodiazirine with various diazirine concentrations (0.005—0.08M) in an excess of methanol are given in the Table. These results may be explained by a mechanism which was originally proposed by Liu and Subramanian[6] (see Scheme) to account for the kinetic behaviour for the reaction of benzylchlorocarbene with methanol. The carbene, generated from the photolysis of diazirine (**1**), undergoes 1,2-H migration to give chlorostyrene or reacts with two methanol molecules to give a reversibly formed ylide. Protonation of this ylide followed by elimination gives chlorostyrene. Subsequent reaction of the ylide gives the required acetal (**3**) and HCl.



Scheme 1. The dotted lines are to be included in the mechanism when the concentration of diazirine exceeds 0.06M

Table. Product composition in 3-chloro-3-benzyldiazirine–methanol reaction as a function of diazirine concentrations at 20 °C.

[Diazirine]/M	0.005			0.02			0.04			0.06			0.08		
[MeOH]/M	(2)	(3)	(4)	(2)	(3)	(4)	(2)	(3)	(4)	(2)	(3)	(4)	(2)	(3)	(4)
0.10	82.7	13.0	4.3	83.1	11.4	5.5	80.9	11.1	7.9	—	—	—	—	—	—
0.15	69.3	24.1	6.6	69.6	21.4	9.0	67.9	20.5	11.6	70.0	17.4	12.6	—	—	—
0.20	61.1	31.3	7.5	60.0	30.9	9.1	60.6	27.5	11.8	63.4	22.4	14.2	62.6	21.7	15.7
0.30	51.0	41.8	7.2	53.4	37.6	9.0	51.8	36.0	11.4	56.6	30.0	13.4	58.3	26.7	15.0
0.40	45.2	47.8	7.0	48.3	43.3	8.4	48.7	41.3	10.0	54.5	33.0	12.4	54.3	32.3	13.4
0.60	39.8	53.7	6.4	—	—	—	44.7	46.0	9.3	—	—	—	51.7	36.5	11.8
0.80	—	—	—	39.0	53.6	7.4	—	—	—	45.5	44.8	9.7	48.9	40.5	10.6
1.20	34.5	59.1	6.4	35.5	57.7	6.8	37.2	55.6	7.2	39.8	51.7	8.5	43.9	46.9	9.3
k_i/k_t	0.058 ± 0.001			0.066 ± 0.002			0.065 ± 0.001			0.071 ± 0.005			0.075 ± 0.008		
Correlation coefficient	0.99			0.99			0.99			0.98			0.97		

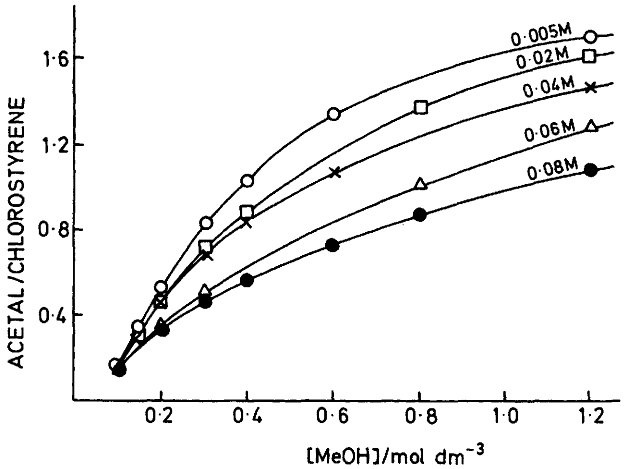


Figure 1. Plot of acetal/chlorostyrene *vs.* [MeOH] at 20 °C with various diazirine concentrations

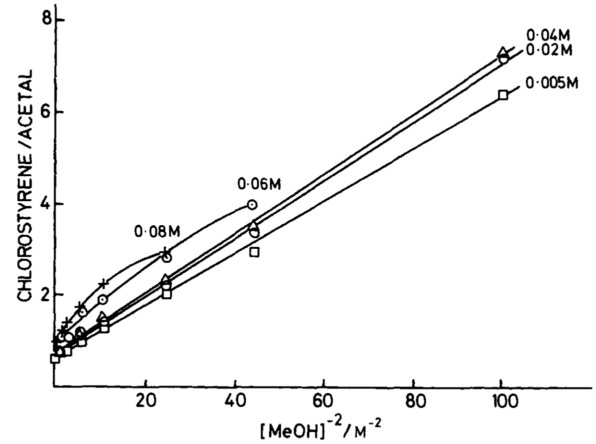


Figure 2. Plot of chlorostyrene/acetal *vs.* 1/[MeOH]^2 at 20 °C with various diazirine concentrations

Application of steady-state treatment to the Scheme leads to:

$$\frac{(2)}{(3)} = \frac{k_i}{k_t}\frac{1}{[\text{MeOH}]^2} + \frac{k_i'}{k_2} \qquad (1)$$

where $k_t = k_i k_2/(k_{-1} + k_i' + k_2)$.

Equation (1) predicts an inverse second-order dependence of the chlorostyrene (**2**)/acetal (**3**) product ratio on the methanol concentration.

Plots of (**3**)/(**2**) *vs.* [MeOH] are displayed in Figure 1. The product ratio (**3**)/(**2**) decreases when the diazirine concentration is increased. This relationship cannot be explained satisfactorily by the mechanism presented in the Scheme because the ratio (**3**)/(**2**) should be independent of diazirine concentrations. Further modification to the Scheme is therefore necessary. As the diazirine concentration is increased, the amount of HCl in the reaction mixture builds up. The HCl reacts with the carbene to form an ion-pair,[8] which partitions into (**2**) and (**4**). Thus, the ratio (**3**)/(**2**) depends upon the concentration of diazirine.

For solutions with diazirine concentrations below 0.04M, plots of (**2**)/(**3**) *vs.* 1/[MeOH]^2 yield straight lines (Figure 2) with similar slopes, and hence similar k_i/k_t values prevail. However, deviation from linearity occurs for solutions exceeding 0.06M diazirine. This implies that as long as the diazirine concentration is kept low, the kinetics in (1) will be obeyed.

Examination of data in the Table reveals certain trends. As the concentration of diazirine is increased, the chlorostyrene concentration increases at the expense of the acetal. Further, the formation of dichloride (**4**) reaches a maximum at low methanol concentration and becomes significant at high diazirine concentration. The reactions of the carbene toward HCl and methanol are competitive processes. The quenching of the carbene by HCl is linear (*i.e.* first-order in HCl),[8] whereas the quenching by methanol is not.

Laser photolysis has shown that the reactions with the carbene ($\text{Ph-}\ddot{\text{C}}\text{-Cl}$) are not first-order with respect to methanol, and that reaction is dependent on the methanol monomer/dimer concentrations.[9] The reaction of carbene with methanol supersedes the carbene–HCl reaction at high methanol concentrations, hence the formation of dichloride is expected to decrease.

Tomioka and co-workers[7] recently reported the incorporation of deuterium in β-chlorostyrene during the photolysis of 3-benzyl-3-chlorodiazirine in MeOD. This they regarded as evidence for the protonation of chlorobenzylcarbene by MeOD. These results are undoubtedly correct; however, re-examination of data is advisable in view of several existing experimental facts. First, kinetic studies on the reaction of benzylchlorocarbene with methanol show a second-order dependence in methanol and the termolecular trapping rate constant has been estimated[5] to have a frequency factor of 2×10^5 l^2 mol^{-2} s^{-1} and an activation energy of -4.5 kcal mol^{-1}.* Secondly, laser

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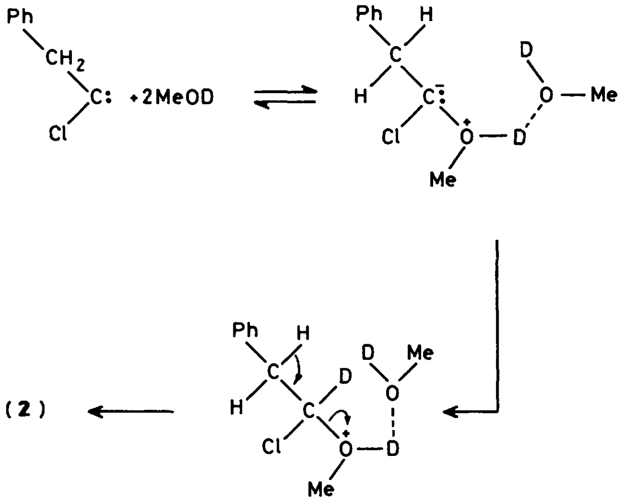
* 1 cal = 4.184 J.

photolysis has demonstrated[9] the activation energy for the reaction of $p\text{-MeOC}_6\text{H}_4\text{–}\ddot{\text{C}}\text{–Cl}$ with MeOH to be -4.7 ± 0.3 kcal mol^{-1}. The observed negative activation energies can only be explained in terms of a kinetic model (such as the Scheme) in which a complex is formed reversibly by the reaction of the carbene with two methanol molecules contained in the oligomer chain. Liu and Subramanian have depicted this complex[6] to be an ylide from the electrophilic attack of carbenes on methanol. Protonation of the ylide by MeOD produces a species which can undergo elimination to yield the required β-chlorostyrene.



Clearly, deuterium incorporation in this system provides no evidence for protonation of the electrophilic carbene by methanol. Furthermore, the HCl generated in the system can also protonate the carbene,[8] although this may only be a very minor route for the incorporation of deuterium.

Experimental

3-Benzyl-3-chlorodiazirine was synthesized by Graham's method.[10] The products were identified by comparing the measured n.m.r. spectra with authentic samples. The spectral data for products have been reported previously.[6,8]

G.l.c. analyses of relative product yields were performed on a Varian Vista 6000 gas chromatograph fitted with a 6 ft × 2 mm (i.d.) glass column packed with CSP 20M and using the flame ionization detector. Peak areas were integrated with a Hewlett-Packard 3390 A recorder.

Irradiation was carried out with a 275 W GE sunlamp until all the diazirine was destroyed. A CS-052 filter allowed transmission of wavelength >350 nm.

Acknowledgements

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