Kinetics of the Thermal Decomposition of Diazirines: 3-Chloro-3-methoxydiazirine

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The thermal decomposition of 3-chloro-3-methoxydiazirine has been investigated. It decomposes unimolecularly both in solution and in the gas phase with $k = 10^{13.52} \exp(-101.1/RT)$ s^{-1} in methanol and $k = 10^{13.06}$ exp (-101.5) s^{-1} in the gas phase. A direct two-bond cleavage to nitrogen and methoxychlorocarbene is proposed. The influence of substituents on the partition between one-bond and two-bond rupture of the diazirine ring is discussed.

IN our continuing interest in the thermal decomposition reactions of diazirines,[1,2] we here report our investigations on the kinetics of the thermal decomposition of 3-chloro-3-methoxydiazirine (1a). By placing an oxygen substituent on the diazirine ring we hoped to gain some further insight into the nature of the process of ring rupture, which has been the subject of considerable interest.[3-5]

EXPERIMENTAL

3-Chloro-3-methoxydiazirine (1a) was prepared by a modification of the method of Graham,[6] starting from *O*-methylisourea toluene-*p*-sulphonate.[7]

CAUTION. As a neat liquid, this diazirine is unpredictably explosive at ambient temperatures, but in solution it can be handled safely. The details below should be adhered to closely to avoid accidents. It is most important that all traps should contain some solvent. Handled as described, we have had no accidents in over forty preparations of the diazirine.

3-Chloro-3-methoxydiazirine (1a).—*O*-Methylisourea toluene-*p*-sulphonate (21 mmol), anhydrous lithium chloride (196 mmol), and dimethyl sulphoxide (100 ml) were placed in a 2-l, 3-necked flask, equipped with a pressure equalising dropping funnel, magnetic stirrer, and exit tube fitted with a stopcock. The exit tube is connected to a train of three all glass traps containing 1, 2, and 1 ml respectively of redistilled di-n-butyl phthalate. A large glass U-tube fitted with potassium hydroxide pellets was interposed between the first and second traps, and the traps were cooled to −35, −78, and −78 °C respectively. When the salts had dissolved, sodium hypochlorite solution (250 ml, 10—14% w/v available chlorine) containing sodium chloride (50 g) was placed in the dropping funnel, the flask cooled to 0 °C, and the whole apparatus evacuated to 1—2 Torr. The stirring rate was increased to maximum and the hypochlorite solution added dropwise to the flask over *ca.* 4 min. Considerable frothing occurs, which is controlled by adjusting the rate of addition and the stopcock on the exit tube. Evacuation was continued for 5 min after the addition was complete. The traps were then isolated from the flask and the pump, and filled with dry nitrogen. The central trap, which contained most of the diazirine, was isolated, warmed to −35 °C, and cautiously agitated to form a homogeneous solution. The solution is stable and may be stored at −78 °C for several weeks. Yield 60—68%; $\nu_{max.}$ 1 550, 1 470, 1 250, 1 050, and 970 cm^{-1}; $\lambda_{max.}$ (gas) 340—358 nm (ε 45), (hexane) 342 and 362 (ε 50, 50); ^1H n.m.r. (CCl_4) τ 6.38 (s).

Kinetics.—A standard vacuum line equipped with Viton A diaphragm valves was used for transferring the diazirine and for preparing solutions for kinetic runs. These were carried out in stoppered 2-mm Suprasil u.v. cuvettes. The rate of disappearance of diazirine was followed using the absorption near 360 nm, by means of the automatic repeat scan facility of a Perkin-Elmer model 402, u.v. spectrometer. The cell block was thermostatted using a Churchill thermocirculator and the temperature monitored with a thermocouple placed in a cuvette in the cell block adjacent to the sample. At each scan interval the time was noted on a stopcock, the temperature measured, and the peak intensity recorded. Plots of log (peak intensity) *versus* time, gave excellent straight lines to greater than 90% decomposition, showing the first-order nature of the reaction. A least-squares treatment of the data using the normal integrated first-order equation gave the rate constants reported in Table 1. The gas-phase kinetics were determined in a similar manner using 40-mm Suprasil cuvettes. Some difficulty was encountered with deposition of decomposition product (methyl chloroformate azine) on the optical faces of the cell which thereby caused a decrease in its transmittance. This was overcome by monitoring the optical density both at 358 nm [$\lambda_{max.}$ of (1a)] and at 390 nm, where (1a) does not absorb. Good first-order kinetics were obtained by this technique, and the results are also included in Table 1.

TABLE 1

Rates of decomposition of 3-methoxy-3-chlorodiazirine

Solvent		Results				
Hexane	$t/°C$	22.83	26.44	30.22	37.10	43.64
	$10^5k/s^{-1}$	3.55	6.01	10.6	23.0	51.3
Ether	$t/°C$	22.83	26.44	30.22		
	$10^5k/s^{-1}$	4.02	6.70	11.6		
Acetonitrile	$t/°C$	25.30	26.70	30.27		
	$10^5k/s^{-1}$	6,91	8.24	13.4		
Methanol	$t/°C$	25.30	26.70	30.27	37.10	43.64
	$10^5k/s^{-1}$	5.87	7.99	12.6	29.9	65.2
Gas phase	$t/°C$	31.85	35.45	40.77	45.53	49.43
	$10^5k/s^{-1}$	4.42	7.35	13.0	23.5	41.5

Rate constants were evaluated over as wide a range of temperature as was possible, and the results subjected to a standard Arrhenius treatment, using a least-squares fitting procedure. The Arrhenius parameters, and the enthalpy and entropy of activation at 30 °C are recorded in Table 2.

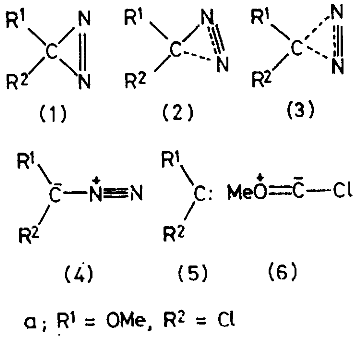
TABLE 2

Thermodynamic parameters for 3-chloro-3-methoxydiazirine thermolysis

Solvent	E_a / kJ mol^{-1}	log A	$\Delta H^{\ddagger}$ / kJ mol^{-1}	$\Delta S^{\ddagger}$ / JK^{-1} mol^{-1}
Hexane	100.0 ± 2.7	13.22	97.4	−0.2
Methanol	101.1 ± 2.6	13.52	98.6	5.5
Gas phase	101.5 ± 3.3	13.06	99.1	−3.2

Products.—The diazirine (1a) (13 mmol) was allowed to decompose in dry diethyl ether (10 ml), and the volatile products evolved collected by means of a pneumatic trough, after passage through a trap at −78 °C. After 48 h, 385 ml (corrected) of gas (17.2 mmol; 66% of two equivalents) had been collected. Gas chromatographic analysis (1 m, 5A molecular sieve) showed it to consist of nitrogen and carbon monoxide. The cold trap contents were analysed by gas chromatography–mass spectrometry and shown to consist of diethyl ether (*m/e* 74), methyl formate (*m/e* 60), and methyl chloride (*m/e* 52, 50). Removal of ether from the flask gave a liquid residue (280 mg, 11.6%) identified as 1,4-dichloro-1,4-dimethoxy-2,3-diazabuta-1,3-diene (methyl chloroformate azine) (Found: C, 26.5; H, 3.3; N, 15.6%. $C_4H_6Cl_2N_2O_2$ requires C, 26.6; H, 3.3; N, 15.2%). The mass spectrum had *m/e* 188, 186, and 184 in the ratio 1 : 6 : 9.5 showing two Cl atoms per molecule; $\nu_{max.}$ 2 930, 2 820, 1 625, 1 220, 1 170, and 810 cm^{-1}; ^{1}H n.m.r. (CCl_4) τ 6.03 (s) and 6.35 (s), OMe, in a ratio of 1 : 2, two isomeric forms. After 2 years, colourless needles, m.p. 51—51.5 °C, crystallised out.

Decomposition in carbon tetrachloride solution gave results which were virtually identical. In the gas phase, substantially the same products were also formed; but in addition HCl was identified by its i.r. absorption. Addition of water vapour before decomposition resulted in an increase in the amount of methyl formate produced at the expense of the other organic products.


(1) (2) (3)

(4) (5) (6)

a; R¹ = OMe, R² = Cl

TABLE 3

Activation parameters for thermal gas-phase decomposition of diazirines (1)

R¹	R²	$\log_{10}A$	E_a kJ mol^{-1}	$\Delta S^‡$ JK^{-1} mol^{-1}	Ref.
Me	Me	14.02	138.6	15.1	9, 11
Me	Cl	14.13	129.9	9.6	12
Et	Et	13.73	133.3	17.2	13
Et	Cl	13.99	127.3	13.5	14
MeO	Cl	13.06	101.5	−3.2	This work

DISCUSSION

The mechanism of the ring opening of diazirines has been the subject of a fair amount of discussion, and transition states involving either one-bond (2) [3,8-10] or two-bond rupture (3) [1,2,11-14] have been proposed. Recently it has been shown that 3-phenyl-3-n-propyldiazirine (1; R¹ = Ph, R² = Prⁿ) thermolyses to the extent of at least 90% by initial one-bond cleavage to afford the corresponding diazomethane.[3] Although it was originally suggested that some two-bond cleavage might occur,[15] it is now argued that this does not happen. We have already proposed that thermolysis of cycloalkanespirodiazirines proceeds by concurrent one- and two-bond cleavage pathways.[1]

The decomposition of 3-chloro-3-methoxydiazirine (1a) proceeds with good first-order kinetics and in view of the absence of any u.v. irregularities, clean isosbestic points being observed under all the conditions studied, we would favour a single path only for its thermolysis. One-bond cleavage would lead to the diazo-compound (4a), which does not accumulate in the system (no u.v. absorption in the range 390—460 nm, nor i.r. absorption in the 2 100 cm^{-1} region) and, therefore, either decomposes or is not formed. The absence of any detectable u.v. irregularities suggests the latter; it is possible though that the stationary concentration of (4a) is always below our detectability limit.

Like all the other diazirines studied, (1a) would appear to decompose by a unimolecular route. It is evident from Table 2 that the thermodynamic parameters are very insensitive to phase and also to the polarity of the solvent. The observed *A* factors of $10^{13.5 \pm 0.5}$ are entirely consistent with a unimolecular process. The consistently small value of the $\Delta S^‡$ shows that no new free rotations have developed at the transition state and that, therefore, the transition complex must strongly resemble the diazirine in structure, regardless of whether a one-bond (2) or a two-bond rupture (3) is involved. In seeking models for these two possibilities, it is clear that any diradical-like transition state with one bond extensively cleaved, as in the pyrolysis of cyclopropanes and oxirans, is ruled out by the magnitude of the *A* factor, *e.g.* 1,1-dimethylcyclopropane has $A = 10^{15.05}$,[16a] and *trans*-2,3-dimethyloxiran has $A = 10^{14.59}$.[17] We would argue that the best model for the properties of (2) would be the linear diazo-compound (4). The conversion of (1) into (4) is a thermally allowed electrocyclic ring-opening [16b] the two molecules correlating in the ground-state and representing different minima on the same energy hypersurface.[5] Therefore, the transition state for their interconversion should have some of the characteristics of (4). Such a transition state will involve some degree of charge separation, and might be expected to show some sensitivity to change of phase and of solvent. Diazomethane has been the subject of a recent MO study using configuration interaction. The results of these calculations suggest that the ground-state is diradical-like with strong coupling of radicals.[18] However, this is totally at variance both with the physical evidence from ^{13}C n.m.r. shielding,[19] which shows that (4) is the principal contributor to the ground-state hybrid, and also with the chemical reactivity of diazo-compounds, which behave consistently as nucleophiles at carbon,[20] and as highly polar molecules. Indeed on the basis of substituent effects, Liu and Chien [8a] have argued for a polarised radical-like transition state comparable to (2) in the thermolysis of the 3-aryl-3-chlorodiazirines (1; R¹ = Ar, R² = Cl). This, despite the fact that the maximum effect of solvent on rate they observed was only a factor of 1.6 (cyclohexane to dimethyl sulphoxide), in close concordance with the change we observe of 1.4 between hexane and acetonitrile (see Table 1). For 3-chloro-3-methoxydiazirine the change from the gas phase to solution in methanol causes a rate acceleration of a factor of 3.4 only. Examination of Table 2 shows that this is due almost entirely to a small change in $\Delta S^{\ddagger}$, the E_a being virtually identical in the two phases. Such behaviour has been observed previously in the thermal unimolecular isomerisation of 1,2-dimethylcyclobutene, where the relative rates in the gas phase, in dodec-1-ene and in dimethyl phthalate are 1 : 1.4 : 1.6; this again arises almost entirely from a change in the A factor.[21] Cyclobutenes are known to isomerise by a concerted electrocyclic process, which is allowed in the ground state, and in which no charge is developed.[16]

TABLE 4

Arrhenius parameters for thermolysis of substituted diazirines

Entry	R^1	R^2	Solvent	log A	E_a / kJ mol^{-1}	Ref.	% *via* Diazo	Ref.
1	$-[CH_2]_5-$		Gas phase	13.34	129.0	14	25	1
2	Et	Cl	Cyclohexane	13.82	123.7	*a*	?	
3	MeO	Cl	Hexane	13.22	100.0	This work	0	This work
4	MeO	Cl	Methanol	13.52	101.1	This work	0	This work
5	F	F	Gas phase	13.1	134.5	10	?	
6	Ph	Cl	Cyclohexane	13.87	117.0	*b*	?	
7	Ph	Br	Cyclohexane	13.75	114.4	*b*	?	
8	$CH_2{=}CH$	Me	CCl_4	13.70	107.0	*a*	95	*d*
9	Ph	Bu^n	Me_2SO	13.26	117.4	3	>90	3, 15
10	$-(C_6H_4\text{-}o)-NMe-CO-$		C_6D_6	15.3	113.3	5	100	5
11	$-[CH_2]_4CO-$		Methanol	13.7	*ca.* 97	*c*	?	
				15.0	*ca.* 104	*c*	?	

[a] M. T. H. Liu and K. Toriyama, *Canad. J. Chem.*, 1973, **51**, 2393. [b] M. T. H. Liu and K. Toriyama, *J. Phys. Chem.*, 1972, **76**, 797. [c] These two values for E_a are calculated on the basis of the $t_{\frac{1}{2}}$ of 1 h at room temperature given by E. Schmitz, A. Stark, and C. Hörig (*Chem. Ber.*, 1965, **98**, 2509; E. Scmitz, XXIII IUPAC Congress Reports, Butterworths, London, 1971, Vol. 2, p. 283) and assuming a value for log A of either 13.7 (most diazirines) or 15.0 (as entry 10). [d] E. Schmitz, C. Hörig, and C. Grundemann, *Chem. Ber.*, 1967, **100**, 2093.

A comparison of the gas-phase activation parameters for thermolysis of diazirines with change of substituent, Table 3, reveals that although the change from alkyl to chloro produces a small diminution in E_a, the further change from alkyl to methoxy produces an additional reduction in E_a which is between three and four times as large. The effect of a chloro-substituent is to render chlorodiazomethane much less stable than diazomethane,[22] entirely in line with expectation based on (4); a methoxy-substituent would be expected to exhibit a similar but more pronounced effect. Thus to the extent that a transition-state like (2), in which only one bond is broken, resembles a diazo-compound, we would expect that it would be raised in energy by substitution with either chlorine or methoxy, and to show significant sensitivity to changes of state and solvent polarity, contrary to what is observed.

On the other hand, the direct two-bond cleavage represented by (3) which is also a thermally allowed chelotropic process,[16b] would give rise to carbene (5) and nitrogen directly. Using the carbene as a model for this transition state, one observes that both chloro- and methoxy-groups stabilise a carbene centre, as evidenced by the greatly reduced reactivity and enhanced selectivity of chlorocarbene, dichlorocarbene, and dimethoxycarbene as compared to methylene itself.[23] Hence, we would expect that both chlorine and methoxy would lower the energy of (3), with the latter being more effective than the former, exactly as is found. Taken together with the solvent effects, we suggest that this evidence points strongly in favour of a direct two-bond rupture in the transition state for the thermolysis of 3-chloro-3-methoxydiazirine.

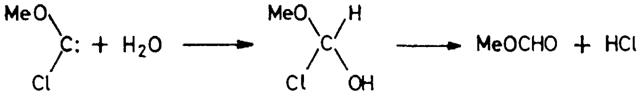
We ascribe this preference for a direct two-bond cleavage to the great increase in stability of the carbene being generated in this case. The result forms a direct parallel to that found in the base-catalysed generation of dihalogenocarbenes. Thus the hydrolysis of chloroform occurs with pre-equilibrium proton exchange, that of bromodifluoromethane shows an isotope effect $k_H/k_D = 2.02$, and that for the hydrolysis of dichloromethyl methyl ether (to give methoxychlorocarbene) a $k_H/k_D = 5.4$, showing that a changeover in mechanism from two-step to one-step has occurred.[24] Hine and his co-workers suggested that this was a result of the destabilisation of the intermediate carbanion and of an increase in stabilisation of the carbene formed, both for CF_2 and MeOCCl.

Indeed, in our opinion, the data on the thermolysis of the arylchlorodiazirines is also better interpreted in terms of a concerted two-bond cleavage. The very low ρ value (we calculate $\rho = -0.13$ from the reported data [8]) for the *meta*-substituted compounds shows that inductive effects are negligibly small and, together with the near absence of solvent effects referred to above, argues against any development of polarity in the transition state. The marked accelerating effect of *p*-MeO and to a lesser extent of *p*-Cl are exactly to be expected from a carbene-like contribution to the transition state, and further the slight increase in rate of the *p*-NO_2 compound, relative to the unsubstituted case, fits well with predictions based on the 1,1-dipolar character of a singlet carbene, which is known to be stabilised both by electron-donating and electron-withdrawing groups. In addition, the near identity of the rates of decomposition in cyclohexene and in acetic acid, together with the absence of any irregularities in the u.v. absorption spectra during decomposition [4] also point in the direction of a transition state like (3) for these compounds.

A survey of those diazirines for which kinetic or activation energy data have been reported, Table 4, shows that thermolysis is accelerated both by electron-donating substituents (entries 2—4, 6—9) and also by electron-withdrawing ones (entries 10, 11). Within the confines of a single mechanism this would be difficult to accommodate, unless the mechanism involved a 1,1-dipolar species like a carbene. However, it is clear that some diazirines thermolyse exclusively to diazo-compounds, while others do so to a limited extent or not at all (Table 4). The extent to which isomerisation occurs would appear to depend on the stability of the diazo-compound formed (*e.g.* diazoamide > aryldiazomethane > dialkyldiazomethane > halogenodiazomethane) as well as on that of the carbene which would be produced. We therefore propose that the two routes *viz.* one-bond rupture to give diazo-compounds and two-bond cleavage to carbene, are competitive processes, the ratio being controlled by the nature of the substituents present on the diazirine ring. Clearly, such a competition does not rule out the possibility of consecutive reactions as well, and should these lead to the same intermediate, then the distinction may be only a semantic one.

Product Studies.—The formation of methyl chloride, carbon monoxide, and nitrogen are entirely consistent with the intermediate formation of methoxychlorocarbene (5a), and in complete accord with its mode of breakdown when formed by the alkaline methanolysis of chloroform [equation (1)].[24] Azine would be expected from the attack of (5a) on starting material (1a) and methyl formate and HCl from the reaction of (5a) with water [equation (2)]. The near identity of the products in ether, carbon tetrachloride, and the gas phase would confirm that the decomposition of MeOCCl goes by the ion-pair route proposed by Skell,[25] and not by way of a radical process. Somewhat surprising is the fact that no products were formed which would have resulted from an intramolecular insertion or migration in (5a) [equation (3)], despite reports of this type of reaction in other cases where alkoxyhalogenocarbenes have been proposed as intermediates.[26] However, it is in accord with the product studies reported on methoxy- and dimethoxy-carbene.[27] We ascribe this to the increased stabilisation of (5a) due to the mesomeric effect of the oxygen lone-pair (6), which extensively diminishes the tendency for intramolecular reaction.

$$\mathrm{CHCl_3 \xrightarrow{MeONa} CCl_2 \xrightarrow{MeONa} MeOCCl \longrightarrow Me^{+} + CO + Cl^{-}} \quad (1)$$



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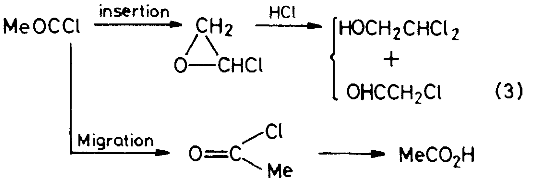

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