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REACTIVE INTERMEDIATES IN THE PHOTOLYSIS AND THERMOLYSIS OF 3-CHLORO-3-BENZYLDIAZIRINE

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Abstract—The photochemical and thermal decomposition of 3-chloro-3-benzyldiazirine have been studied in different reaction conditions. The decomposition gives rise to benzylchlorocarbene which can rearrange to E and Z chlorostyrene and/or react with the environment. In the presence of acetic acid the main product is 1-chloro-2-phenylethyl acetate. Experiments with acetic acid-d_4 showed that some of the chlorostyrene is formed from the carbocation; other experiments conducted with tetramethylethylene as a carbene trapping agent show that the carbene is formed even in the presence of acetic acid.

Since the discovery of diazirines in the early nineteen sixties, there has been an increasing interest in the thermolysis and photolysis of these compounds because they provide convenient sources of carbenes.[1-3]

The mechanisms reported in the literature for the decompositions of the diazirines encompass essentially all of the possible modes of fragmentation. These are cleavage of a single C–N bond to give a diazo compound,[4] simultaneous cleavage of two bonds to give the carbene and nitrogen[5] or combination of these two modes.[6]

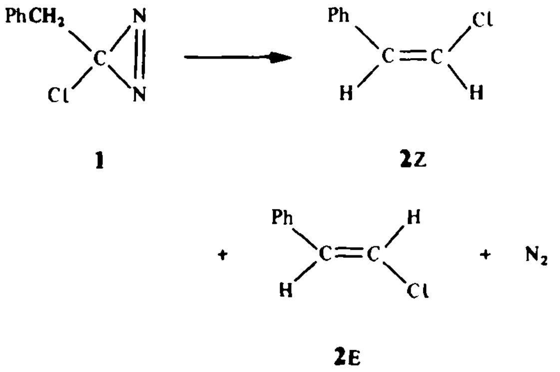
The objective of the study was the clarification of mechanisms of formation and decay of the reactive intermediates in the decomposition of chlorodiazirines. While the involvement of diazocompounds in the decomposition of 3-aryl-3-alkyl and 3,3-dialkyl diazirines has been proved beyond doubt,[4,6] the situation remains unclear with 3-chlorodiazirines, where the isomeric 1-chlorodiazo compounds are very elusive species. We have previously established that the change of the reaction environment such as by the addition of acetic acid, has virtually no influence on the ring opening process itself[7] and that the variation in the final products can be accounted for by secondary reactions of the primary products of decomposition.

In this paper we wish to report the product analysis and kinetics for the thermolysis and photolysis of 3-chloro-3-benzyl diazirine in an inert solvent and in the presence of acetic acid, acetic acid-d_4, tetramethylethylene and their combinations.

RESULTS AND DISCUSSION

3-chloro-3-benzyldiazirine, **1**, undergoes a first-order decomposition in carbon tetrachloride within the temperature range of 80–112°.

The first-order behaviour is maintained through several half-lives. The products are nitrogen and a mixture of Z and E β-chlorostyrenes in the ratio 1:8. The decomposition in benzene gives the same product distribution.



The first-order rate constants for the decomposition of **1** were determined at five temperatures. The data in Table 1 gave an excellent Arrhenius plot from which the following equation was obtained by least-squares analysis:

$$k = 10^{13.82 \pm 0.35} \exp[-(123.85 \pm 2.47)/RT] s^{-1}$$

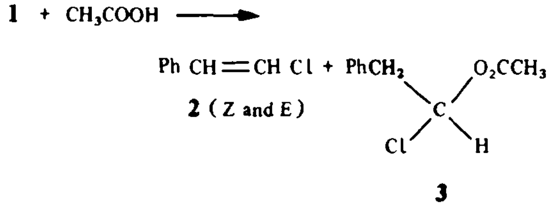
where R is taken as 0.00831 kJ mol^{-1} K^{-1}.

The results indicate that the thermal decomposition of **1** is similar to that of 3-chloro-3-aryldiazirines,[7] i.e. the entropy of activation is close to zero.

The photolysis of **1** in carbon tetrachloride gave the same products as in thermolysis but the distribution of Z and E isomers was different (1:3).

Thermolysis and photolysis of **1** in acetic acid, in addition to giving **2Z** and **2E** also results in the formation of 1-chloro-2-phenyl ethyl acetate. The identity of the acetate was established from spectral data and comparison with an authentic sample prepared independently.[8]

The relative distributions of the products are given in Table 2. The data in Table 2 show that an



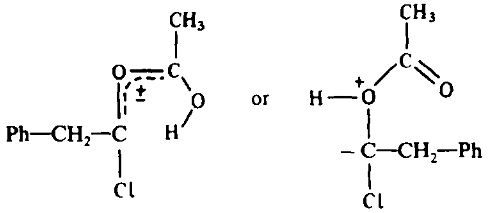
increased amount of acetic acid relative to the diazirine **1** brings about an increase in the amount of the acetate **3**. Our previous studies concerning decomposition of 3-phenyl-3-n-butyldiazirine in acetic acid[4b] showed that no such dependence is to be expected in this system where a diazocompound (formed as an intermediate) is protonated to give a carbocation which, in turn, gives rise to an acetate and an olefin.

The data presented here suggest that there are two competitive pathways for olefin formation: firstly, by proton abstraction from a carbocation formed by protonation of the carbene (path C, D) and, secondly, by a rearrangement through a 1,2-hydrogen shift of the carbene itself (path B). It is worth noting that no products derived from rearrangement of the carbocation were observed. Apparently, the carbocation is stabilized by the chlorine atom at the cationic centre.[9]

Table 1. First-order rate constants for the decomposition of 1 in carbon tetrachloride

T(°C)	k x 10^4 (s^{-1})
80.9	0.344
95.4	2.00
99.0	2.81
105.8	5.70
112.0	10.2

The acetate **3** can arise either from the direct carbene insertion into the O–H bond of HOAc (path F) or from the protonation of the carbene by HOAc followed by the collapse of the ion pair (path C, E). Possible reaction paths are shown in Scheme 1. Yet another possible mechanism involves the addition of the carbene to an oxygen lone pair to form an ylide, which then gives the product by O⇒C proton transfer.



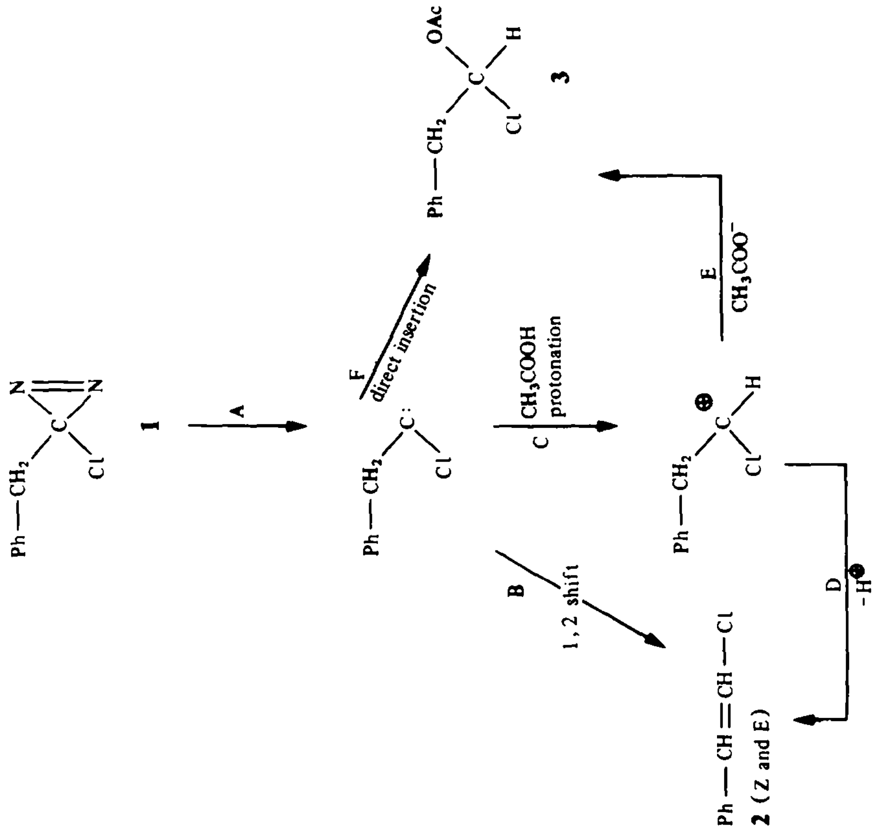
However, this mechanism is not in keeping with the results of laser flash photolysis experiments, since the quenching rate constant for chlorophenylcarbene with ethyl acetate is less than $10^5\,M^{-1}\,s^{-1}$ whereas the chlorophenylcarbene reacts with acetic acid[10] with a rate constant $k_q \sim 2 \times 10^9\,M^{-1}\,s^{-1}$.

In order to test the above scheme, thermal and photochemical decomposition of **1** was repeated in the presence of deuterated acetic acid-d_4, as in this case one should be able to distinguish clearly the chlorostyrenes derived directly from the carbene intermediate (which should not be deuterated) from the deuterated ones derived from the carbocation (Scheme 2). It has been established that β-chlorostyrene does not exchange hydrogen for deuterium under the reaction conditions used. Indeed, besides the acetate which was necessarily deuterated, a mixture of deuterated and non-deuterated styrenes was obtained. The relative distribution of the products is given in Table 2.

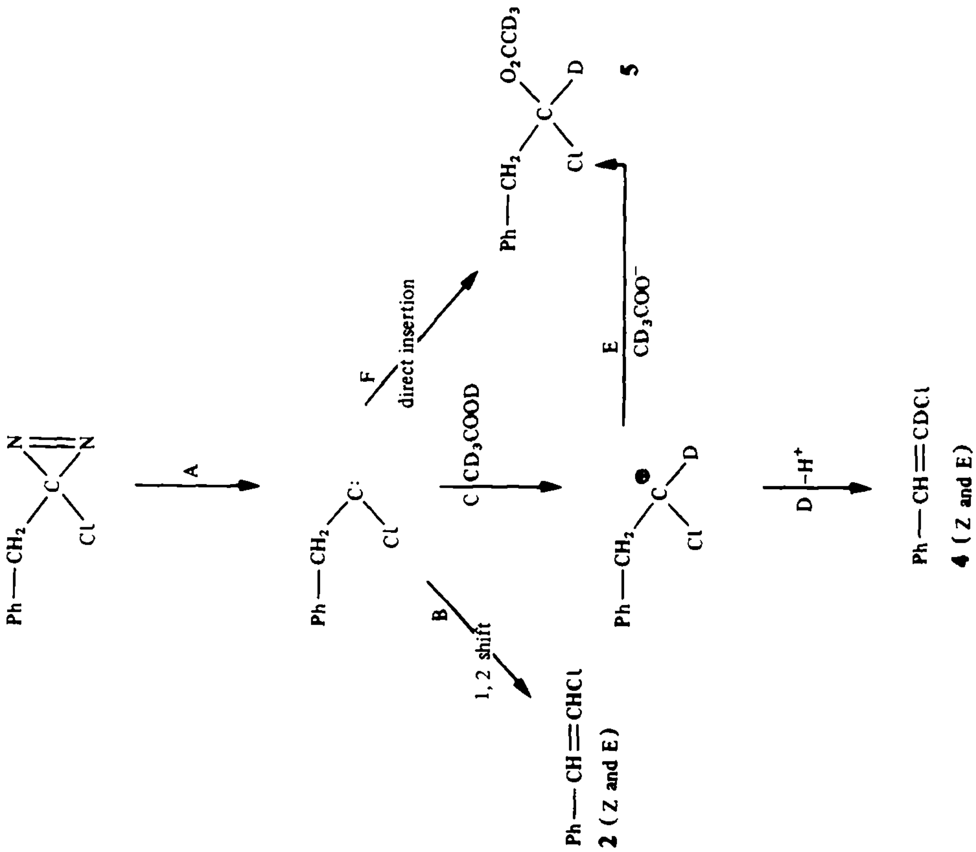
Table 2. Product distribution in mole% in the thermolysis and photolysis of 1

MOLES OF 1[a]	MOLES HOAc	METHOD	2Z	2E	3	4(Z + E)	5
1.0×10^{-3}	0.6×10^{-3}	Δ	6.1	27.2	66.6	-	-
1.0×10^{-3}	1.0×10^{-3}	Δ	4.6	16.8	78.5	-	
1.0×10^{-3}	1.3×10^{-3}	Δ	2.6	9.9	87.4	-	
1.2×10^{-3}	1.6×10^{-2}	Δ	2.9	5.5	91.5	-	
1.7×10^{-3}	4.6×10^{-2}[b]	Δ	6.0		-	5.0	89.0
1.0×10^{-3}	0.6×10^{-3}	hν	24.7	33.0	42.3	-	-
1.0×10^{-3}	1.3×10^{-3}	hν	20.7	24.0	55.3	-	-
0.6×10^{-3}	1.6×10^{-2}	hν	17.5	19.7	62.7	-	-
1.6×10^{-3}	4.2×10^{-2}[b]	hν	24.2		-	6.2	69.6

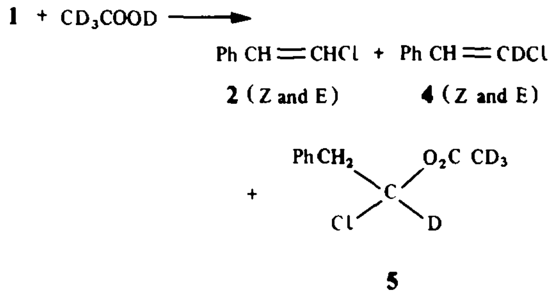
[a] In 10 ml CCl_4 [b] Moles of CD_3COOD



Scheme 1.



Scheme 2.



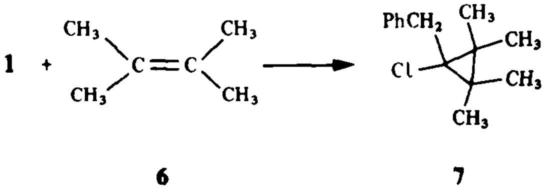
Analysis of the data in Table 2 shows that there is a significant difference between the results of photochemical and thermal decomposition of **1**. First, with the photochemical decomposition there is a much higher Z:E isomer ratio for chlorostyrene than with thermolysis. We attributed this to photochemical isomerization because of the following: experiments on thermolysis of **1** gave the *β*-chlorostyrene mixture; upon photolysis of this mixture, the Z:E ratio was increased. However, this does not exclude completely the possibility of the involvement of an excited carbene in the photo chemical process.

The second important feature is the fact that the total yield of styrenes compared with the acetate is markedly higher in the photochemical experiments. It is known that the 1,2-hydrogen shift in carbenes is a process with very small energy of activation[11] and so the temperature has little or no influence on the reaction rate. In addition, the carbene reaction with acetic acid approaches the diffusion- controlled region[10] and should show a normal temperature dependence. The photochemical experiments were carried out at much lower temperatures than the thermolysis reactions and therefore we expect a lower yield of acetate in the former case.

The same explanation can account for the fact that in the photochemical experiment there is a less percentage of deuterated styrene than in thermolysis since the deuterated styrene is formed via the carbene reaction with acetate acid.

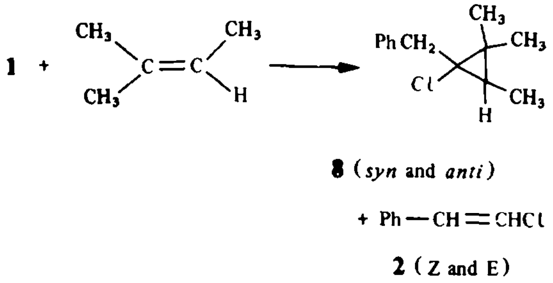
Further evidence of our proposed scheme follows our trapping experiments.

When **1** was photolyzed in tetramethylethylene, **6**, as a solvent, the major product was 1 - benzyl - 1 - chloro - 2,2,3,3 - tetramethyl cyclopropane (**7**); only traces of *β*-chlorostyrene were observed.



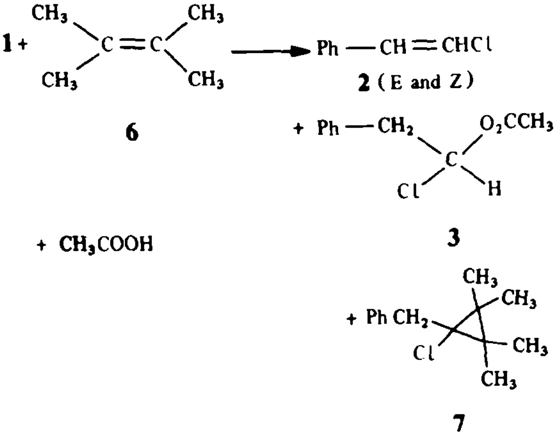
Apparently, with the large excess of **6** the cheletropic reactions of the carbene with **6** compete very successfully with the 1,2-hydrogen shift. However, when **1** was photolysed in trimethyletylene,[12] the yields for *β*-chlorostyrene and 1 - benzyl - 1 - chloro - 2,2,3 - trimethyl cyclopropane (**8**) were approx. 1:5.

Addition of benzylchlorocarbene to Z-4-methyl-2-pentene was stereospecific[12] which shows that the carbene is in the singlet state. The rate constants for addition of phenylchlorocarbene to tetramethylethylene and trimethylethylene have been reported as $1.3 \times 10^8\,M^{-1}s^{-1}$ and $7.7 \times 10^7\,M^{-1}s^{-1}$ respectively.[13]



Our relative rates for $PhCH_2\text{–}\ddot{C}\text{–}Cl$ addition to tetramethylene and to trimethylethylene follow the trend already established in the case of phenylchlorocarbene. However, if the addition to alkenes or the reaction with HOAc are similar for $PhCH_2\text{–}\ddot{C}\text{–}Cl$ and $Ph\text{–}\ddot{C}\text{–}Cl$, then the product concentrations indicate a rate constant of the order $10^7 \sim 10^8\,s^{-1}$ for the 1,2-hydrogen migration in benzylchlorocarbene. We believe this to be the first estimate of the magnitude of this rate constant.

When **1** was irradiated in **6** in the presence of a two fold excess of acetic acid, we observed the formation of all three possible products, viz **2**, **3** and **7** in the relative amount of 5.9, 44.8 and 49.3%.



It is apparent that the carbene intermediate is formed in the reaction mixture even in the presence of acetic acid. It has previously been believed that the reaction with HOAc was so rapid that other trapping reactions were not competitive. It is worth noting that whereas practically no *β*-chlorostyrene (**2**) was formed in **6** without acetic acid, it did form in the latter case. Within the experimented error the ratio of **2** to **3** in this case is similar to the deuterated chlorostyrene:acetate ratio in the labelling experiment (see Table 2); this suggests that all the olefin comes from the carbocation.

The present results do not explain the origin of the carbocation as to whether it is formed by protonation of carbenes as shown on the scheme or by protonation of the intermediate diazo compound. However, it is known that the protonation of a diazo compound is a process slow enough to be measured by classical kinetics methods.[14] Therefore this latter reaction is a rather unlikely process in our case.

EXPERIMENTAL

The IR, NMR and UV spectra were recorded with a Beckman model 4230 spectrophotometer, a Varian T-60 spectrometer (samples dissolved in $CDCl_3$), and a Varian Carey 210 spectrophotometer. GLC analyses were performed on a Perkin–Elmer model F-11 chromatograph equipped with a hydrogen flame ionization detector and fitted with a 6 ft column of 6% SE 30 on Chromosorb W.

Irradiation was done with a Hanovia 450 W medium pressure mercury lamp in a water-cooled quartz immersion well, equipped with a Corning # 5840 glass filter to allow transmission to the reaction mixture of wave lengths between 330 and 400 nm. All the yields reported are isolated yields. Anhydrous magnesium sulphate was employed as a drying agent. The solvents were dried and distilled before use.

Synthesis

Benzylamidine hydrochloride. Anhydrous hydrogen chloride gas was bubbled through a solution of freshly distilled phenylacetonitrile (60 g, 0.51 mole) in dry ethanol (24 g, 0.52 mole) at 0° until the solution became saturated with the gas (3 h). The reaction flask was stoppered and left in the freezer for 4 days. Anhydrous ether (150 ml) was added. The mixture became milky and the iminoether hydrochloride precipitated. The solvent was removed under reduced pressure and the residue was dried in a desiccator over silica gel to yield a white solid (101 g, 99%, m.p. 78–79°).

Anhydrous ammonia was bubbled into dry ethanol (400 ml) for 1.5 h at 0° and the iminoether hydrochloride (100 g, 0.50 mole), suspended in dry ethanol (80 ml) was slowly added to the stirred ammonia/ethanol) solution at 0°. The reaction mixture was allowed to stir at room temperature overnight. The mixture was concentrated under reduced pressure until crystals of ammonium chloride precipitated. These were removed by filtration. Removal of the solvent from the filtrate under reduced pressure yielded benzylamidine hydrochloride, a gummy solid (75 g, 88%).

3-*chloro*-3-*benzyldiazirine* 1

benzylamidine hydrochloride (6.64 g, 0.04 mole), lithium chloride (20 g, 0.47 mole) in dimethylsulfoxide (150 ml), and carbon tetrachloride (100 ml) was stirred at 0°. Sodium hypochlorite solution (7%, 300 ml) containing sodium chloride (60 g, 1.02 mole) was added to the mixture in 10–15 min with vigorous stirring. The reaction mixture was further stirred for 1 h at the same temperature. The mixture was diluted with water (200 ml), the organic layer was separated, and the aqueous layer was extracted with carbon tetrachloride (2 × 100 ml). The combined extracts were washed with water (100 ml) and dried. The solvent was removed under reduced pressure leaving a light coloured liquid. This crude product was purified by column chromatography on silica gel (40 g), eluting with petroleum ether–ether (95:5) to give 3-chloro-3-benzyl diazirine (1.42 g). The spectral data of this product are as follows: ν_{max} 1565, 1500 cm^{-1}; λ_{max} (ethanol) 358 (ϵ600), 344 (ϵ660); NMR δ7.37 (s, 5H), 3.26 (s, 2H).

1-*Chloro*-2-*phenylethylacetate* 3

Obtained by the method of Naidan and Naidan[8] by chloroarylation of vinyl acetate with benzyldiazonium chloride. However, the given procedure gave phenol as the main product. The desired product was obtained when the acetone: water ratio was increased. The reaction residue was extracted with pentane and passed through a short column of silica-gel. Removal of the solvent afforded 3, IR: ν_{max} 1765 cm^{-1}, NMR: δ7.37 (s, 5H), 6.57 (t, 1H, J = 6 Hz), 3.25 (d, 2H, J = 6 Hz), 2.01 (s, 3H).

Thermolysis of 1

3-Chloro-3-benzyldiazirine (100 mg) in CCl_4 (15 ml) was heated at 72° for 62 h. The mixture was cooled and solvent was removed under reduced pressure. Analysis of this product by GLC at 70° and by NMR showed two components: Z and E-β-chlorostyrene in a ratio of 1:8; ν_{max} 1625, 1600, 1495 cm^{-1}; *m/e* 140 (34) 138 (100%, M$^+$ C_8H_7Cl), 103 (94, M–Cl), 91 (86, C_7H_7), 77 (37, M–Cl–C_2H_2); NMR; δ (ppm), 7.38 (phenyl); AB quartet with the outer pairs centered at δ 6.63 and 6.78 (E-olefinic H) and AB quartet with the outer pairs centered δ at 6.08 and 6.63 (Z-olefinic H).[15]

Thermolysis of 1 *in acetic acid*

A mixture of 1 (200 mg, 1.2×10^{-3} mol) and acetic acid (2 ml, 3.3×10^{-2} mol) in 5 ml of CCl_4 was refluxed for 65 h. After cooling, the reaction mixture was diluted with water and extracted repeatedly with carbon tetrachloride. The combined extracts were washed with saturated solution of $NaHCO_3$ and with water and dried. Removal of the solvent yielded 170 mg of a mixture which was chromatographed on silica gel (35 mg) with petroleum ether–ether (95:5). Two fractions were collected. The first was a mixture of the isomeric β-chlorostyrenes (29 mg); the other was 1-chloro-2-phenylethylacetate which was identical with the authentic sample.

The procedure was then repeated several times using the amounts given in Table 2 and the products were analyzed by gas chromatography.

Thermolysis of 1 *in acetic acid-d*$_4$

3-Chloro-3-benzyldiazirine (292 mg, 1.7×10^{-3} mole) and CD_3COOD (2.92 ml, 4.6×10^{-2} mole) were refluxed for 65 h in carbon tetrachloride. The standard isolation procedure (see above) was employed. A mixture of the deuterated and undeuterated olefins, 20 mg (MS: *m/e* 141 (22), 140 (29), 139 (67), 138 (84), 104 (72), 103 (100), and 1 - chloro - 1 - deuterio - 2 - phenylethyl acetate-d$_3$ (234 mg) was obtained. λ_{max} 1765 cm^{-1} (CO_2CD_3); NMR, δ 7.37 (s, 5H), 3.30 (s, 2H); *m/e* 167 (8, M–Cl), 141 (33), 140 (14), 139 (100), 121 (15), 105 (6), 104 (16), 91 (78).

Attempted reaction of β-*chlorostyrene with* CD_3COOD

2 (30 mg) was heated at 80° in CCl_4 with CD_3COOD (0.2 ml) for 10 h. After the work-up, only the starting material was recovered. It did not undergo a deuterium exchange as checked by MS.

Photolysis of 1

3-Chloro-3-benzyldiazirine (161 mg) in CCl_4 (10 ml) was degassed and irradiated in a Pyrex tube at room temperature. The reaction was monitored by UV spectroscopy. No change in colour was observed. After 16 h or irradiation, the diazirine absorption (λ_{max}, 358 nm) had disappeared. The solvent was removed under reduced pressure. GLC analysis of this product at 70° showed two components; Z-β-chlorostyrene and E-β-chlorostyrene in a ratio of 1:3.

Photolytical isomerisation of β-*chlorostyrene*

The mixture of Z and E β-chlorostyrene formed by thermal decomposition of 1 in benzene (ratio 1:8) was irradiated in benzene. After 10 h of irradiation the Z/E ratio had changed to (1:4) as checked by GLC.

Photolysis of 1 *with acetic acid*

A solution of 1 (100 mg, 0.6×10^{-3} mole) in carbon tetrachloride (5 ml) and acetic acid (1 ml, 1.6×10^{-2}) was irradiated for 16–18 h. The reaction mixture was worked up as described above. The products were identified by GLC as Z-β-chlorostyrene (17.5%), E-β-chlorostyrene (19.7%) and 1-chloro-2-phenylethylacetate (62.7%). The procedure was repeated several times with the amount given in Table 2 and products were analyzed by GLC.

Photolysis of 1 *with acetic acid-d*$_4$

Photolysis of 1 (276 mg, 1.6×10^{-3} mole) in carbon tetrachloride (10 ml) and CD_3COOD (2.7 ml, 4.2×10^{-2} mole) was carried on as described above. The product obtained was a mixture of deuterated and undeuterated E and Z β-chlorostyrenes (49 mg), MS: 141 (4.3), 140 (21.3), 139 (15.4), 138 (58.8), 104 (22), 103 (100), and 1-d-1-chloro-2-phenylethyl acetate-d$_3$ (165 mg), NMR: δ, (ppm) 7.28 (s, 5H) 3.31 (s, 2H).

Photolysis **1** *in tetramethylethylene*

1 (350 mg) was dissolved in 8 ml of tetramethylethylene **6** and photolyzed at 0°. The solvent was removed. Column chromatography on silica gel with pentane–ether (95:5) afforded 370 mg of 1-phenyl-1-chloro-3,3,4,4-methyl cyclopropane, **7**. NMR δ, (ppm) 7.18 (s, 5H), 3.18 (s, 2H), 1.25 (s, 6H), 1.13 (s, 6H).

Photolysis of **1** *in tetramethylethylene with acetic acid*

1, (300 mg, 1.8×10^{-3} mole) and acetic acid (0.22 g, 3.6×10^{-3} mole) were dissolved in 8 ml of **6** and irradiated at 0°. The reaction mixture was diluted with ether, washed twice with saturated NaHCO$_3$ solution and water and dried. After removal of the solvent, the residue was analyzed by GLC. Analysis indicated the presence of **2**, **3** and **7** in ratio of 0.12:0.91:1.0.

Kinetic measurements

The rates of reaction were determined by following the disappearance of diazirine. Details have been described elsewhere.[7]

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