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FRAGMENTATION OF CYCLOPROPYLMETHOXYCHLOROCARBENE: FORMATION OF CYCLOPROPYLCARBINYL/CHLORIDE ION PAIRS

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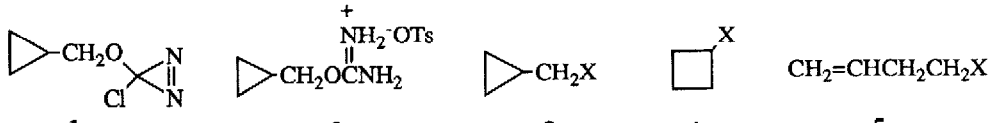
Summary. The decomposition of cyclopropylmethyloxychlorodiazirine in MeCN proceeds via N_2 and CO loss, mainly to tight cyclopropylcarbinyl cation-chloride anion pairs that collapse to C_4 chlorides with substantial skeletal and label retention; the ion pairs can be intercepted by ethanol with less skeletal retention.

The thermolysis of benzyloxychlorodiazirine (25°C, MeCN) affords benzyloxychlorocarbene that undergoes clean fragmentation with the evolution of CO and quantitative formation of benzyl chloride.[1] In methanol, $PhCH_2OMe$ and $PhCH_2Cl$ are formed in a ratio of 1.3. Despite the spectroscopic detection of benzyl radical (λ_{max} 303, 313 nm) upon laser flash photolysis of the diazirine, suggestive evidence indicates that the thermolysis products largely arise from benzyl cation, and not from the corresponding radical; e.g., thermolysis of the diazirine in $BrCCl_3$ gives >95% $PhCH_2Cl$ and only traces of $PhCH_2Br$.[1]

Nevertheless, it would be instructive to examine a system in which alkyl cation participation is "self-indicating". An apposite choice is the cyclopropylcarbinyl system, where cation involvement invariably leads to cyclopropylcarbinyl, cyclobutyl, and allylcarbinyl products,[2] whereas participation of the corresponding radical is signaled by facile ring opening to the allylcarbinyl radical and associated products.[3] Accordingly, we have prepared 3-cyclopropylmethoxy-3-chlorodiazirine, 1, and describe here its decomposition in acetonitrile, ethanol, and mixtures thereof. Product and labeling studies both indicate the intermediacy of "tight" cyclopropylcarbinyl cation-chloride anion pairs.

Cyclopropylmethylisourea tosylate, 2, was prepared by stirring excess cyclopropylcarbinol with cyanamide and anhydrous p-toluenesulfonic acid in dry $CHCl_3$ (48 h, 25°C). Ethereal precipitation and recrystallization from butanone afforded analytically pure 2, mp 117-119 °C, in 35% yield. Diazirine 1 was generated from 2 by Graham's method: rapid oxidation of a cold (0-5°C) DMSO-LiCl-isopentane solution of 2 with a commercial, aqueous (12%) NaOCl solution, saturated with NaCl.[4] The diazirine was extracted into isopentane, washed with brine, and dried over $MgSO_4$. For use in MeCN or EtOH solvents, isopentane was replaced by addition of the new solvent, followed by rotary evaporation at 0°C.

Diazirine 1 had λ_{max} 352, 368 nm (pentane), and 356 nm (MeCN). Its 200 MHz nmr spectrum (α,α-d_2 modification, see below) exhibited two γ ring CH_2 multiplets and a β



1 2 3 4 5

CH resonance at δ 0.29, 0.58, and 1.08, respectively, in CD_3CN. Thermal decomposition of 1, followed by uv spectroscopy at 25°C, gave $k = 5.7 \times 10^{-5}$ s^{-1} (pentane) or 9.0×10^{-5} s^{-1} (MeCN); an Arrhenius study (hexane, 25-50°C) gave E_a = 22 kcal/mol. The kinetic data obtained for benzyloxychlorodiazirine were very similar.[1]

Thermolysis of 0.1 M diazirine 1 (20 h, 23°C) in MeCN, EtOH, or binary mixtures of these solvents, afforded mixtures of cyclopropylcarbinyl (3), cyclobutyl (4), and allycarbinyl (5) chlorides (**a** series) and ethyl ethers (**b** series), in distributions that depended on the concentration of ethanol; see Table 1. Products were identified by nmr and gc comparisons (12 m x 0.22 mm bonded-phase vitreous silica SE-30 capillary column operated at 20°C) with authentic materials. Chlorides **3a** and **4a** were commercial samples (Chemical Dynamics Co.) whereas **5a** was prepared from allylcarbinol and $SOCl_2$.[5] Ethers **3a** - **5a** were prepared by reactions of diethyl sulfate with the Na salts of the corresponding alcohols in dibutyl ether.[6,7]

The paucity of allylcarbinyl products suggests that the cyclopropylcarbinyl cation,[2] not the corresponding radical,[3] is a key intermediate in these decompositions. (The bicyclobutonium ion is apparently of similar energy and readily interconvertible with the cyclopropylcarbinyl cation,[8] but our data cannot distinguish these ions.)

The high degree of skeletal retention in the RCl products is striking, with the cyclopropylcarbinyl/cyclobutyl ratio (3a/4a) at 5.2 in pure MeCN, remaining nearly constant through 50% EtOH/MeCN, and increasing to 8.4 in pure EtOH. This is consonant with the intermediacy of <u>tight</u> cyclopropylcarbinyl cation/chloride ion pairs, where Cl^- collapses mainly at the initial CH_2 reaction center. In eq. (1), diazirine 1 affords cyclopropylmethoxychlorocarbene, **6**, by loss of nitrogen; the carbene fragments to ion pair **7** with loss of CO; and products **3a** - **5a** arise from collapse of **7**. The product distribution in MeCN is very similar to those obtained from reactions of cyclopropyldiazomethane with ethereal benzoic acid (3:4:5 = 79:14:7, as benzoates), or of cyclopropylmethane diazotate with benzoyl chloride (78:13:9), where first cyclopropylmethyldiazonium-benzoate, and then cyclopropylcarbinyl cation-benzoate ion pairs, are putative intermediates.[9] In contrast, the distributions of <u>ethers</u> **3b** - **5b** from decompositions of 1 in EtOH/MeCN mixtures are all ~1-1.3, very similar to the product distributions obtained from the "free" cyclopropylcarbinyl cations of the nitrous acid deamination of cyclopropylcarbinylamine,[2] or the hydrolysis of cyclopropylmethane diazotate.[10]

The high **3a/4a** product ratios obtained from **1** in MeCN do not reflect the incursion of S_N2 displacements by liberated Cl^- on **6** or **7**. Thus decomposition of **1** in the presence of added 0.7 M dodecyltrimethylammonium chloride actually leads to <u>less</u> **3a** (**3a**:**4a**:**5a** = 67:25:7) than in pure MeCN. This is most likely due to a salt effect on the behavior of **7**, because a similarly altered product distribution (64:27:9) is observed upon the addition of 0.7 M $Bu_4N^+BF_4^-$.

In Figure 1 (closed points), we plot mol-% of total C_4-OEt product vs. [EtOH] from decompositions of **1** in EtOH/MeCN. We also superimpose (open points) the mol-% of $PhCH_2OMe$ vs. [MeOH] observed in decompositions of the benzyl analogue of **1** in MeOH/MeCN.[1] The 2 data sets are remarkably similar, indicative of the intermediacy of analogous ionic intermediates. The

$$1 \xrightarrow{-N_2} \left[\triangleright CH_2O\ddot{C}Cl\right] \xrightarrow{-CO} \left[\triangleright CH_2^+\ Cl^-\right] \longrightarrow \mathbf{3-5} \qquad (1)$$

6 7

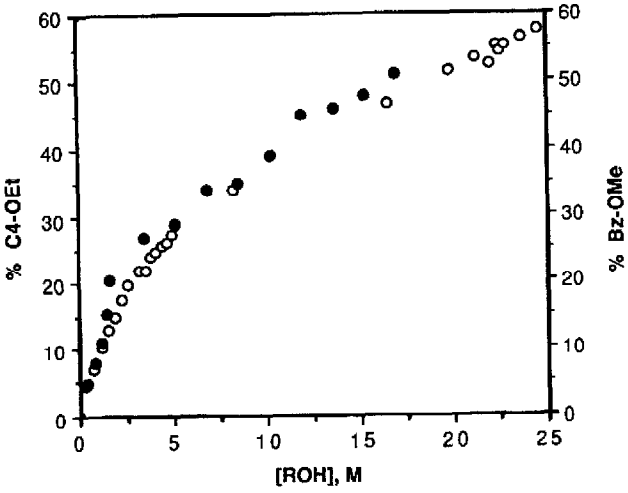


Figure 1. Mol-% ether products vs. [ROH] in MeCN for thermolysis of diazirine 1 (filled circles, left ordinate) or of benzyloxychlorodiazirine (open circles, right ordinate). The balance of the product is RCl in each case.

persistence of RCl products, even in pure alcohol, suggests the participation of cis-7, which should be prone to Cl^- return and less readily scavenged by alcohol. Alternatively, the ether products may largely derive from trans-7, where alcoholysis should dominate Cl^- collapse.[11]

Finally, we examined CH_2 scrambling in the cations derived from 1-α,α-d_2 prepared from cyclopropylcarbinol-α,α-d_2). Nmr (200 MHz, CD_3CN) revealed the absence of α-protons in labeled **1**, but an α doublet did appear in product **3a**. Complete equilibration in 7 (or related ionic species[2,8]) would distribute 0.33 of the available CH_2 weight in the δ 3.46 - 3.50 carbinyl doublet of **3a**, with the residuum divided between the δ 0.65 and 0.35 ring γ methylenes. In the event, **3a** formed from 1-d_2 in CD_3CN had 0.09 - 0.12 (2 experiments) of CH_2 weight at the α position, corresponding to 27-36% of complete scrambling, considerably less than the 72% of scrambling found in Roberts' classic HNO_2 deamination of α-^{14}C-cyclopropylcarbinylamine.[12,13] Again, our observations are consistent with a tight ion pair (e.g., cis-7) as the principal product-forming precursor of **3a**. Similar results are obtained when labeled **1** decomposes in 1:2 or 2:1 CD_3OD/CD_3CN, where **3a** displays 45% or 33% of scrambling, respectively.

A still imperfectly understood finding is that the cyclopropylmethyl methyl(CD_3) ether formed in these latter experiments also displayed 37-39% scrambling. Why should the ether, nominally the solvolysis product, display such incomplete scrambling? Possibly, ion pair cis-7 is "too simple" to adequately represent reality in an alcoholic mixed solvent. Perhaps it should include at least one ROH molecule, H-bonded to the chloride as an integral part of the ion pair, with an opportunity similar to that of chloride to capture the cation at the original CH_2 reaction center, without label scrambling.

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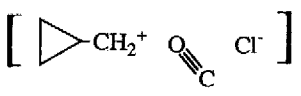
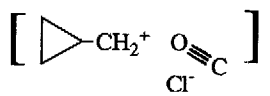


trans-7



cis-7

Table 1. Products from the Decomposition of Diazirine 1 in MeCN/EtOH[a]

[EtOH]	% RCl				% ROEt				
M[b]	3a	4a	5a	total RCl	3b	4b	4c	total ROEt	ROEt/RCl
0.0	78	15	7	100					0.0
0.85	72	15	5.5	92.5	4	4	tr	8	0.086
1.19	70.5	13.5	5	89	5.5	5.5	0.2	11	0.12
1.70	63	12	4.5	79.5	10	10	0.3	20.3	0.26
5.10	56	11	3	70	14.5	14	0.5	29	0.41
8.5	52	10	2.5	64.5	18	16.5	0.5	35	0.54
13.6	45	7.5	1.5	54	24	21	1	46	0.85
17.0[c]	42	5	1.5	48.5	28	22	1	51	1.04

[a]Distributions are from capillary gc analysis using a calibrated flame ionization detector, and are in mol-%. [b] molarity in MeCN. [c]100% ethanol.

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(13) We observed 80% of scrambling in the cyclopropylcarbinol derived from the corresponding deamination of the α,α-d_2 amine.[10]

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