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SHORT COMMUNICATION

BENZYLOXYFLUOROCARBENE: RESISTANCE TO FRAGMENTATION

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Benzyloxyfluorocarbene resists fragmentation to benzyl fluoride, and can be intercepted by water, fluoride ion, methanol or acrylonitrile. In contrast, benzyloxybromocarbene and benzyloxychlorocarbene fragment to the corresponding benzyl halides, and are not efficiently trapped

INTRODUCTION

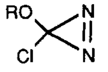
Alkoxychlorocarbenes, **1**, undergo intramolecular fragmentation with the formation of carbon monoxide and alkyl cation–chloride ion pairs, **2**, whose ultimate fate depends on the reaction conditions.[1] When **1** is generated by the thermolysis of diazirine **3**,[1a,b,d] or by the reaction of phase transfer-generated CCl_2 with ROH,[1c,e] good yields of alkyl chlorides result, often without rearrangements.[1c] In particular, decomposition of **3** ($R = PhCH_2$) in acetonitrile at 25 °C afforded a quantitative yield of benzyl chloride, presumably via benzyloxychlorocarbene and ion pair **2**.[1b] The reaction of CCl_2 and benzyl alcohol gave benzyl chloride in 90% yield, together with a small amount of benzyl formate (from the capture of **1** by water; see below).[1e]

$RO\ddot{C}Cl$

1

$[R^+ \; O{\equiv}C \; Cl^-]$

2



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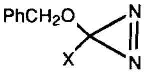

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$PhCH_2O\ddot{C}X$

5

(**a**, X=F; **b**, X=Cl; **c**, X=Br)

We now report that benzyloxyfluorocarbene resists fragmentation, participating instead in intermolecular reactions, where it can be efficiently trapped by addition to acrylonitrile, or intercepted by water, methanol or fluoride ion. Benzyloxybromocarbene, on the other hand, behaves analogously to the chlorocarbene, efficiently fragmenting to benzyl bromide.

RESULTS

Preparation of diazirines

O-Benzylisourea *p*-toluenesulfonate[1b] in 50 : 50 (v/v) dimethyl sulfoxide–pentane was oxidized[2] to bromodiazirine **4c** by the action of freshly prepared aqueous NaOBr solution at 0 °C for 10 min. The dried ($MgSO_4$) pentane extract of **4c**, after rapid filtration through a short silica gel column, contained *ca* 35% of **4c** (λ_{max} 246, 350, 366 nm; δ_{CH_2} 4·93) and an equivalent amount of benzyl bromide (δ_{CH_2} 4·58) unavoidably formed by decomposition of **4c** during its preparation.

Benzyloxychlorodiazirine (**4b**) was obtained in *ca* 60% yield, accompanied by < 10% of benzyl chloride, by the previously reported,[1b] analogous hypochlorite oxidation[2] of *O*-benzylisourea tosylate. The dried ($CaCl_2$), chromatographed (silica gel) pentane solution of **4b** was used directly, either for generation of carbene **5b** or conversion into benzyloxyfluorodiazirine (**4a**).

In the latter case, diazirine **4b** [in dimethylformamide (DMF) solution, after evaporative replacement of pentane] was stirred with 'anhydrous' $n\text{-}Bu_4N^+F^-$ [prepared from the trihydrate by threefold azeotropic removal of water with 2 : 1 (v/v) acetonitrile–benzene under reduced pressure at 25 °C, followed by reduced pressure replacement of the solvents with dry DMF], at

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25 °C for 12 h in the dark. The reactants were initially mixed at 0°C. [*Note*: the conversion of **4b** to **4a** by F^- is essentially complete within 2 h. The extended reaction time is needed to convert the benzyl chloride side product (from fragmentation of **4b**) to benzyl fluoride, which is readily separable from the desired **4a**. Benzyl chloride is not easily separated from **4a**.] After an aqueous workup and pentane extraction, benzyloxyfluorodiazirine (**4a**) was purified from the accompanying benzyl fluoride by silica gel chromatography (pentane). We obtained 35–40% of pure **4a** (SE-30 capillary gas chromatography (GC) at 50 °C); IR, 1546 cm^{-1} (N=N); UV (λ_{max}, pentane), 248, 350, 368 nm; ^1H NMR (δ, CD_3CN), 5·05, s, 2H, CH_2; 7·40 's,' C_6H_5; ^{19}F NMR (CD_3CN), 35·41 ppm upfield from external CF_3COOH.

Thermal stabilities of benzyloxyhalodiazirines

The thermolyses of diazirines **4a–c** (presumably to carbenes **5a–c**) were followed spectrophotometrically in hydrocarbon solvents. The decompositions were first order, affording kinetic results and activation parameters that are summarized in Table 1. The order of kinetic stability is **4a** ≫ **4b** > **4c**. Benzyloxyfluorodiazirine (**4a**) is much more stable than its Br and Cl analogues, owing to its 3–4 kcal mol^{-1} higher activation energy for decomposition. Indeed $\tau_{1/2}$ at 66 °C is 7430 s, indicating why **4a** can be successfully gas chromatographed at 50 °C (30-m SE-30 capillary column; retention time 2·8 min). The extrapolated $\tau_{1/2}$ for **4a** at 25 °C is 460 h, so that **4a** is easily manipulated in solution. Comparison of the Arrhenius parameters in Table 1 with those for other diazirine thermolyses[3] shows that **4b** and **4c** are 'unusually' labile (low E_a), whereas **4a** has 'normal' thermal stability.[3] Alkoxy substituents (MeO, $PhCH_2O$) tend to lower E_a for diazirine decomposition (e.g. E_a for the thermolysis of methoxychlorodiazirine in hexane is 23·9 kcal mol^{-1}, similar to that of **4b**[4]), whereas a fluorine substituent raises E_a. It is clear from these results that the thermal stabilities of the diazirines are not governed by the expected stabilities of the carbenes formed on nitrogen loss (**5a** most stable). However, in the absence of detailed calculations on the diazirines, carbenes and appropriate transition states, the origin of the diazirine stability sequence remains unknown.

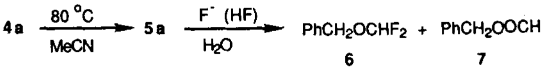
Table 1. Thermal decompositions of benzyloxyhalodiazirines **4a–c**

Diazirine	$\tau_{1/2}$ (s)	k (s^{-1})	E_a (kcal mol^{-1})	Log A (s^{-1})
4a	7430[a]	$9{\cdot}33 \times 10^{-5}$ [a]	26·4 ± 0·3[c]	13·0 ± 0·4
4b	11 600[b]	$5{\cdot}98 \times 10^{-5}$ [b]	23·3 ± 0.35[d]	12·9 ± 0·2
4c	2810[b]	$2{\cdot}47 \times 10^{-4}$ [b]	22·7 ± 0.2[e]	13.0 ± 0.2

[a] At 66 °C, in decane, monitored at 368 nm.
[b] At 25 °C, in isooctane, monitored at 366 nm.
[c] Over 66–86 °C; 5 points.
[d] Over 25–49 °C; 6 points.
[e] Over 20–49 °C; 7 points.

Product studies

On thermolysis (25–40 °C) or photolysis (λ > 300 nm) in acetonitrile, the chloro- and bromo-diazirines **4b** and **4c** afford only the corresponding benzyl halides in near quantitative yields, with simultaneous loss of CO and N_2. In contrast, thermolysis (80 °C, 5 h, sealed tube) or photolysis (λ > 300 nm) of benzyloxyfluorodiazirine (**4a**) give complicated product mixtures (SE-30 capillary GC, 50–220 °C) containing < 10% of benzyl fluoride. The major identified products in 18% and 16% (GC) yields are benzyloxydifluoromethane (**6**) and benzyl formate (**7**). These are most easily rationalized as fluoride ion (HF) and water trapping products of carbene **5a**:



$$\mathbf{4a} \xrightarrow[MeCN]{80\,^\circ C} \mathbf{5a} \xrightarrow[H_2O]{F^-\ (HF)} \underset{\mathbf{6}}{PhCH_2OCHF_2} + \underset{\mathbf{7}}{PhCH_2OOCH} \quad (1)$$

Formate **7** is the expected product from addition of (adventitious) H_2O to $PhCH_2OCX$, followed by the loss of HX.[1b,e,g] In the case of **5a**, loss of HF provides the fluoride for converting **5a** to **6**, the identity of which was established by ^1H and ^{19}F NMR and mass spectrometry.

When an equivalent of water was deliberately added to the acetonitrile solvent, analogous thermolysis of **4a** gave **6** and **7** in enhanced yields (47% and 39%, respectively), but only 4% of benzyl fluoride was formed. Decomposition of **4a** at 80–85 °C in isooctane containing a sevenfold excess of HF–pyridine complex gave difluoride **6** in 60% yield, together with *ca* 30% of formate **7** and 3% of benzyl fluoride.

In contrast, the thermal decomposition at 30 °C of the bromodiazirine **4c** in acetonitrile containing either 1 or 20 equivalents of water gave only benzyl bromide. Decomposition of the chlorodiazirine **4b** under similar conditions gave benzyl chloride and benzyl formate in a molar ratio of *ca* 5 : 1, with *no* benzyl alcohol. With a 20-fold excess water, benzyl chloride and benzyl alcohol (from hydrolysis of **7**) were again formed in a *ca* 5 : 1 ratio.

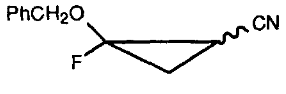
These experiments suggest that bromocarbene **5c** fragments to benzyl bromide faster than it can be intercepted by water; fluorocarbene **5a** does not fragment rapidly, and is easily captured by water or fluoride; and chlorocarbene **5b** undergoes competitive intramolecular fragmentation and intermolecular trapping by water.

The reluctance of benzyloxyfluorocarbene to fragment also follows from methanol trapping experiments.

Decomposition of **4a** in methanol (60 °C, 12 h, sealed tube) gave no benzyl fluoride. Instead, 71% of benzyl alcohol was formed, which we interpret as arising from acid (HF)-catalyzed methanolysis and methanol exchange of the primary methanol carbene trapping product, fluoroacetal **8**. A related sequence occurs in the reaction of methoxyfluorocarbene and methanol.[5]

$PhCH_2OCHFOMe$

8



9

Analogous decompositions of chlorodiazirine **4b** or bromodiazirine **4c** gave mixtures of benzyl halides and benzyl methyl ether, arising from fragmentations of carbenes **5b** or **5c**, via ion pairs resembling **2**. This kind of reaction has been discussed in detail.[1a,b]

Finally, thermolysis (85 °C, 6 h) of fluorodiazirine **4a** in acrylonitrile gave a 1·2 : 1 mixture of isomeric cyclopropanes, **9**, isolated in 81% yield and 97% purity after silica gel chromatography ($CHCl_3$). An analytical sample (C, H, N) was obtained by preparative GC (SE-30, 135 °C). The structure of **9** was supported by ^1H NMR [δ($CDCl_3$) 1·56–1·95, 2·10–2·30, 2 m, 3H, cyclopropyl H; 4·80–4·96 and 4·96–5·06, 2 AB quartets, $J = 11$ Hz in each case, total 2H, $PhC\mathit{H}_2O$; 7·30–7·50, m, 5H, Ph] and ^{19}F NMR [(188·2 MHz in $CDCl_3$) 58·77 and 65·10, 2 m upfield from external CF_3COOH].

In contrast to the efficient trapping of **5a** by acrylonitrile, thermolyses of bromo- or chloro-diazirines **4c** or **4b** in the same olefin led only to the benzyl halide fragmentation products, with no evidence (GC, NMR) for the formation of cyclopropanes.

CONCLUSION

The evidence from water, fluoride, methanol and acrylonitrile trapping experiments is that benzyloxyfluorocarbene is 'slow' to fragment, and therefore offers a rich intermolecular chemistry resembling that of the related ambiphile methoxyfluorocarbene.[5,6] Benzyloxychlorocarbene and benzyloxybromocarbene, on the other hand, fragment more rapidly, and are not easily or efficiently trapped. The origin of these differences presumably resides in the relative strengths of the C—X bonds in $PhCH_2OCX$; the strong C—F bond opposes the efficient fragmentation of carbene **5a**. We note that the naturally strong C—F bond will be stronger in carbene **5a**, where one expects partial C=F character due to F → C lone-pair donation.[7] Further analysis of the relative stabilities of $PhCH_2OCX$ awaits *ab initio* calculations.

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