Arylmethyl Radicals from Arylmethoxybromodiazirines

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ABSTRACT



Photolytic decompositions of 3-arylmethoxy-3-bromodiazirines afford arylmethyl radicals by homolyses of the diazirines' excited states.

The fragmentations of alkoxychlorocarbenes generally proceed via ion pairs (**1**, eq 1), providing access to several classic cations of organic chemistry.¹ These include the 2-norbornyl,² cyclopropylmethyl,³ 3-nortricyclyl/5-norbornen-2-yl,⁴ and various bridgehead cations.⁵ In several instances, however, ROCCl fragmentations also reveal radical character.

$$\operatorname{ROCCl} \to [\operatorname{R}^+ \operatorname{OC} \operatorname{Cl}^-] \to \operatorname{RCl} + \operatorname{CO}$$
(1)
1

Thus, benzyloxychlorocarbene (PhCH₂OCCl) fragments (in part) in Ar matrices to the benzyl radical,⁶ and the fragmentations of ring-substituted benzyloxychlorocarbenes in solution afford parabolic Hammett correlations suggestive of radical character in the reactions of ArCH₂OCCl bearing electron-withdrawing substituents.⁷ There is also evidence for radical fragmentation—ring opening of cyclopropylmethoxychlorocarbene at 365 °C in the gas phase.⁸

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Despite these indications of a radical component to the fragmentations of ROCCl, there is no evidence for mutual diffusion of alkyl and chlorine radicals: the photolysis of PhCH₂OCCl in cumene gave only 2% of toluene,^{6b} and analogous reduction products were absent in the fragmentations of the *p*-nitro and *p*-trifluoromethyl derivatives of ArCH₂OCCl in cumene.⁷ A strict cage effect apparently operates in these fragmentations, with ArCH₂Cl the near-exclusive product of either ion pair or radical pair anteced-ents.

Given that the C–Br bond is weaker than the C–Cl bond, we wondered whether the fragmentations of arylmethoxybromocarbenes (ArCH₂OCBr) would more readily yield interceptable arylmethyl radicals. In the event, we encountered novel fragmentation reactions of the arylmethoxybromodiazirine carbene *precursors*, which serve as photochemical sources of arylmethyl radicals. These are the first examples of alkyl radical formation from the photolytic cleavage of halodiazirines.

The synthetic starting points were alcohols 2a-f; 2a-e were commercially available, whereas 2f was prepared by literature methods,⁹⁻¹² as shown in Scheme S1 (see Supporting Information).



Each alcohol was converted to the corresponding isouronium

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methanesulfonate salt (**3**) with cyanamide and MeSO₃H.¹³ (A sample preparation is included in Supporting Information.) The isouronium salts were then oxidized to 3-arylmethoxy-3-bromodiazirines (**4**) with freshly prepared NaOBr in aqueous DMSO containing NaBr and LiBr.^{14,15}



The diazirines were purified by flash chromatography on silica gel with cold pentane (2:1 pentane/CH₂Cl₂ for the 3-nitro-2-naphthyl derivative). Characterization of the diazirines was provided by UV and ¹H and ¹³C NMR spectroscopy; details appear in Supporting Information. In several cases (**4**, Ar = phenyl, 2-naphthyl, 3-nitro-2naphthyl), the *chloro*diazirines corresponding to **4** were also made by the NaOCl oxidation of **3**.¹⁴

Bromodiazirines **4** were less stable than their chlorodiazirine analogues; some aryl bromide (ArCH₂Br), formed by decomposition of **4** during its synthesis, accompanied the diazirines and could not be separated chromatographically. Therefore, mixtures of the diazirine and bromide were employed in the experiments described below. The initial diazirine/bromide composition was determined by ¹H NMR integration (relative to an internal 1,2-dichloroethane standard) immediately prior to decomposition, permitting product mixtures to be corrected for preexisting ArCH₂Br.

Diazirines 4 were photolyzed in $\sim 2 \text{ mL}$ of CDCl₃ or in CDCl₃ admixed with a hydrogen donor solvent such as cumene or 1,4-cyclohexadiene (1,4-CHD). Photolyses were conducted in small vials or NMR tubes, under a nitrogen atmosphere, using 350 nm lamps in a Rayonet reactor over a period of 1 h at ambient temperature. The reaction products were readily analyzed by NMR because the product mixtures were quite clean, consisting in each case of an arylmethyl bromide (**5**) and an arylmethane (**6**). Table S1 in Supporting Information presents observed and literature NMR data confirming the identities of products **5** and **6** from diazirines **4**. In several instances, GC-MS and NMR spiking experiments with authentic materials further substantiated product structures.

$\begin{array}{cc} ArCH_2Br & ArCH_3 \\ \mathbf{5} & \mathbf{6} \end{array}$

In the absence of cumene or 1,4-CHD, photolyses of diazirines **4** gave only the anticipated fragmentation products,

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Table 1.	Product	Distributions	from	Photoly	vses of	f Diazirines ^a
Lanc Li	Trouuer	Distributions	monn	1 HOLDI		

Ar in diazirine 4	% ArCH ₃ (CDCl ₃) ^b	% ArCH ₃ (cumene) ^c	% ArCH ₃ (1,4-CHD) ^d
phenyl	2.0	8.6 (8.0)	22 (7.0)
phenyl (Cl) ^e	trace	0.1 (2.5)	0.8 (3.0)
<i>p</i> -CF ₃ -phenyl	2.6	5.8 (6.8)	15 (3.0)
<i>p</i> -NO ₂ -phenyl	1.7	12 (10.0)	22 (5.0)
1-naphthyl	3.7	14 (9.0)	30 (6.0)
2-naphthyl	17	34 (6.0)	100 (8.0)
2-naphthyl (Cl) ^e	0.7	0.9 (3.0)	trace (7.0)
3-NO ₂ -2-naphthyl	20	100 (10)	100 (10)
3-NO ₂ -2-naphthyl (Cl) ^e	0.5	1.0 (4.0)	1.1 (20)

^{*a*} See text for photolysis conditions. ^{*b*} CDCl₃ solvent; no added H-donor. The balance of the product is ArCH₂Br. ^{*c*} CDCl₃-cumene solvent. Molar equivalents of cumene (relative to diazirine **4**) are shown in parentheses. The balance of the product is ArCH₂Br. ^{*d*} CDCl₃-1,4-CHD solvent. Molar equivalents of 1,4-CHD are indicated in parentheses. The balance of the product is ArCH₂Br. ^{*e*} CDCl₃-1,4-CHD solvent. Molar equivalents of 1,4-CHD are indicated in parentheses. The balance of the product is ArCH₂Br. ^{*e*} CDCl₃-1,4-CHD solvent.

bromides **5**. However, when the hydrogen donors were present, methylarenes **6** formed as well. The **5**/**6** distribution (corrected for bromide that was initially present; see above) was dependent on the nature of the diazirine's aryl and halo substituents (Br or Cl), as well as the choice and concentration of hydrogen donor. Table 1 summarizes relevant product data. Importantly, control experiments with bromides **5** (Ar = phenyl or 2-naphthyl) demonstrated that photolyses of the bromides in the presence of excess 1,4-CHD led (at most) to traces of hydrocarbons **6**. The latter are therefore primary products of the diazirine photolyses in H-donor solvents; they are not formed by reduction of bromides **5**.

The most immediate explanation of our results is that photolyses of diazirines **4** produce carbenes **7**, which fragment to radical pairs **8** (eq 2). The arylmethyl radicals of **8** then either collapse with bromine radicals to yield products **5** or are diverted in the presence of good H-donors to give methylarenes **6** by H-abstraction reactions.

$$\begin{array}{cccc} & \text{ArCH}_2\text{O} & \overset{\text{N}}{\underset{\text{Br}}{\overset{\text{I}}{\xrightarrow{}}}} & \overset{\text{hv}}{\underset{\text{N}}{\overset{\text{I}}{\xrightarrow{}}}} & \text{ArOCH}_2\text{OCBr} & \longrightarrow & [\text{ArCH}_2^{\cdot} & \text{OC} & \text{Br}^{\cdot}] & (2) \\ & & 4 & 7 & 8 \end{array}$$

This simple scheme, however, is incorrect: *thermal* decomposition of diazirines 4 (25 °C, 24 h, dark) affords *only* bromides 5, even in the presence of 1,4-CHD. These controls were repeated twice with 4 (Ar = phenyl or 2-naphthyl). Thus, carbenes 7, when thermally generated from diazirines 4, give only "normal" fragmentation reactions yielding bromides 5, presumably via ion pairs;¹ no radical products are formed.

The formation of radical products $ArCH_3$ (Table 1) requires *photolysis* of the diazirines, and we suggest that the diazirines' excited states (4*) are the key intermediates. Recently, we reported that photolyses of diaryloxydiazirines **9** produced aryloxy radicals **10** via α -scission of the diazirines' excited states **9***; thermolyses of **9**, however, gave only products expected from diaryloxycarbenes **11** (dimers,

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O-H insertion products).¹⁶ We suggest that a related scenario accounts for the present findings; cf. Scheme 1. Here, diazirine excited state **4***, represented as a ring-opened diradical,¹⁷ partitions between carbene **7** (which yields bromide **5** by fragmentation) and radical pair **8**, which can either recombine, leading to **5**, or abstract a hydrogen atom from suitable H-donors to give methylarene **6**. Details of the breakdown of **4*** to **8** are unclear, but additional intermediates can be imagined, including an excited carbene and/or a carbyne (ArCH₂OC[•]). Alternatively, the conversion of **4*** to **8** could be concerted.



A reviewer suggested that a diazoalkane or a triplet carbene might intervene between excited diazirine 4* and radical pair 8. Although the photoisomerization of alkyldiazirines to diazoalkanes is well-known,18 the process is of minor importance for *chlorodiazirines*¹⁹ and should be even less important for alkoxyhalodiazirines such as 4. Moreover, any photolytically formed alkoxybromodiazoalkane would be very unstable and rapidly thermally decompose to carbene 7, and, as we have seen, thermally generated 7 does not afford radical pair 8. It is conceivable that excited diazirine 4* might undergo spin inversion to triplet 4* from which triplet carbene 7 could arise by loss of nitrogen, subsequently affording radical pair 8. However, computations²⁰ place the enthalpy of triplet 7 (Ar = phenyl) 33.6 kcal/mol above (cis) singlet carbene 7 and 32.95 kcal/mol above (trans) singlet 7, so that we consider the triplet carbene an unlikely intermediate.

From Table 1, we see that increasing quantities of ArCH₃ are formed in the sequence Ar = 3-nitro-2-naphthyl > 2-naphthyl > 1-naphthyl > p-nitrophenyl > p-trifluoromethylphenyl > phenyl. This trend roughly parallels the anticipated stabilities of ArCH₂ as reflected in the bond

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Figure 1. Percent yield of 2-methylnaphthalene vs molar equivalents of added 1,4-cyclohexadiene (relative to 4) for the photolysis of 4 (Ar = 2-naphthyl) in CDCl₃.

dissociation energies (BDE in kcal/mol) of ArCH₃: Ar = 2-naphthyl (85.6), 1-naphthyl (87.3), *p*-nitrophenyl (86.5), phenyl (89.6).²¹ Further, the *p*-NO₂ substituent more strongly stabilizes a benzylic radical than the *p*-CF₃ substituent,⁷ and the 3-nitro-2-naphthylmethyl radical should be more stable than the 2-naphthyl radical due to the former's conjugated nitro group.

We interpret this trend to reflect either (a) enhanced partition of **4*** toward radical pair **8** (rather than carbene **7**) as radical stability increases or/and (b) enhanced diffusion and capture of ArCH₂• from the radical pair (rather than recombination to **5**) as radical stability increases. The data of Table 1 also suggest that the trapping of ArCH₂• is more efficient with the better H-donor 1,4-CHD (BDE = 75 kcal/mol) than with cumene (BDE = 84.8 kcal/mol).^{21,22}

Strikingly, virtually no ArCH₂• is produced, and very little ArCH₃ is formed, with either cumene or 1,4-CHD H-donors, when **4*** is generated from a *chlorodiazirine* rather than a bromodiazirine (see Table 1, Ar = phenyl, 2-naphthyl, and 3-nitro-2-naphthyl). Homolysis of a C-Cl bond in **4*** must be minimal compared to that of a C-Br bond,²³ so that **4***(**Cl**) almost exclusively gives the carbene (ArCH₂OCCl) and then ArCH₂Cl by fragmentation.

We examined the radical cleavage of $4^{*}(Br)$ (Ar = 2-naphthyl) more closely. Figure 1 shows that the yield of radical product (ArCH₃) increases linearly with increasing quantities of 1,4-CHD in the CDCl₃ solvent. With 8 molar equiv of 1,4-CHD, the yield of ArCH₃ reaches 100%, suggesting that the fate of 4^{*} with Ar = 2-naphthyl is complete homolysis to radical pair 8 and that the 2-naphthyl

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Figure 2. UV spectrum of the 2-naphthylmethyl radical obtained by LFP of 4 (Ar = 2-naphthyl) in pentane.

radical can be quantitatively intercepted by a sufficient quantity of a good H-donor. Moreover, the linear relationship evident in Figure 1 argues against the incursion of chain processes in the $ArCH_2^{-1}/1$,4-CHD reaction.

The 2-naphthylmethyl radicals generated from bromodiazirine **4** (Ar = 2-naphthyl) can be observed by laser flash photolysis (LFP).²⁴ LFP of **4** at 351 nm in pentane at 25 °C produced the 2-naphthylmethyl radical with λ_{max} 369 nm; cf. Figure 2. Published spectra of this radical, generated by ps LFP of 2-(halomethyl)naphthalenes in hexane, feature maxima at ~378 nm.²⁵ The 2-naphthyl radicals were readily quenched by added 1,4-CHD or cumene. Plots of the observed rate constants for quenching versus the quencher concentrations were linear, with slopes of $2.8 \times 10^5 \text{ M}^{-1} \text{ s}^{-1}$ for 1,4-CHD and $3.1 \times 10^5 \text{ M}^{-1} \text{ s}^{-1}$ for cumene (see Figures S1 and S2 in Supporting Information). We do not understand why the rate constants for quenching by cumene and 1,4-CHD are comparable, given that 1,4-CHD is the more efficient trapping agent (see Table 1) and possesses both statistical and thermodynamic²¹ advantages as a H-donor. Nevertheless, the LFP evidence clearly supports the formation of arylmethyl radicals (cf. Scheme 1).

In conclusion, photolyses of 3-arylmethoxy-3-bromodiazirines afford arylmethyl radicals by homolyses of the diazirines' excited states. The arylmethyl radicals can be trapped by appropriate hydrogen donors. In contrast, the analogous 3-arylmethoxy-3-chlorodiazirines afford arylmethoxychlorocarbenes upon photolysis; radical formation is suppressed.

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Supporting Information Available: Sample preparations of isouronium salts (**3**) and diazirines (**4**), spectral data for **4**, Table S1 (product NMR data), Figures S1 and S2 (kinetics of quenching of the 2-naphthyl radical), and Scheme S1 (preparation of 3-nitro-2-naphthylmethanol). This material is available free of charge via the Internet at http://pubs.acs.org.

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