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A Duality of Mechanisms for the Fragmentation of Substituted Benzyloxychlorocarbenes

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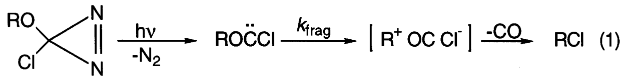
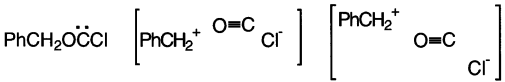
The fragmentations of alkoxychlorocarbenes to alkyl chlorides have been rationalized with ion pair intermediates, eq 1.[1] Examples



include reactions of benzyloxychlorocarbene,[2a] *sec*-butoxychlorocarbene,[2b] cyclobutoxychlorocarbene and cyclopropylmethoxychlorocarbene,[2c] 2-norbornyloxychlorocarbene,[2d] and various bridgehead ROCCl.[2e] Carbene fragmentation not only offers novel entry to several classic carbocations of organic chemistry, but laser flash photolysis (LFP)[3,4] and time-resolved infrared spectroscopy (TRIR)[4] permit measurements of rate constants and activation parameters for these very fast processes.

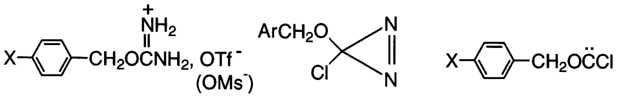
The fragmentation of benzyloxychlorocarbene (**1**) is illustrative. It is taken to proceed via ion pairs *cis*-**2** and *trans*-**2**,[1,2a] which derive from alternative geometries of carbene **1**.[5] In dichloroethane (DCE),



1 *cis*-**2** *trans*-**2**

k_{frag} lies between 6.2×10^4 (LFP) and 2.9×10^5 s^{-1} (TRIR).[4] $PhCH_2Cl$ is the only product in DCE, whereas, in MeOH, $PhCH_2Cl$ (43%) and $PhCH_2OMe$ (57%) are produced by ion pair collapse and cation capture, respectively.[2a] The B3LYP/6-31G* computed E_a for the fragmentation of (cis) **1** is 6.7 kcal/mol in the gas phase and 1.4 kcal/mol in MeOH.[6] Ion pair formation imposes positive charge on the benzylic carbon as carbene **1** fragments to **2**. We therefore undertook a Hammett study of the fragmentation kinetics of several substituted benzyloxychlorocarbenes.

O-Benzyl isouronium mesylates (**3a**, **c**) or triflates (**3b**, **d**−**g**) were prepared from $ArCH_2OH$, cyanamide, and methane or trifluoromethane sulfonic acids.[7] Graham oxidation[8] converted **3a**−**g** to



3 **4a-g** **5a-g**

a, X=*p*-Me; **b**, X=*p*-Ph;
c, X=H, **d**, X=*p*-Cl; **e**, X=*m*-Cl;
f, X=*p*-CF$_3$; **g**, X=*p*-O$_2$N

(note, **5c** = **1**)

the benzyloxychlorodiazirines, **4a**−**g**, which were purified by chromatography over silica gel (eluents: pentane, or 1:1 CH_2Cl_2-pentane for **4g**). The diazirines displayed λ_{max} 344−347 nm in pentane. Photolysis of **4a**−**4g** in DCE ($A = 1.0$ at λ_{max}, $\lambda > 320$ nm) gave only $ArCH_2Cl$, via carbenes **5a**−**g**, with product identities confirmed by GC−MS and GC spiking experiments with authentic samples.

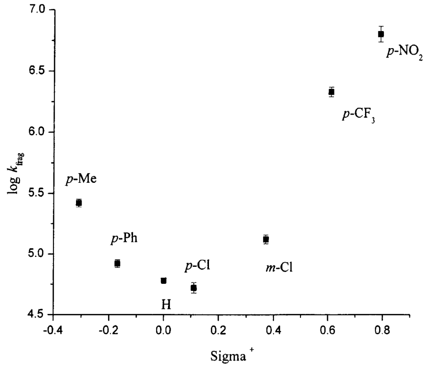


Figure 1. Hammett treatment of log k_{frag} for carbenes **5a**−**g** vs σ^+.

Absolute rate constants for the fragmentation of **5a**−**g** were determined by LFP[3,4,9] of the diazinines at 351 nm using UV detection and pyridine ylide visualization.[10] k_{frag} ranged from 6.3×10^6 s^{-1} (**5g**) to 5.2×10^4 s^{-1} (**5d**). The results are summarized in Table 1 (see Supporting Information). A Hammett correlation of log k_{frag} vs σ^+ appears in Figure 1.[11]

If the ion pair mechanism of eq 1 held for all seven substituted benzyloxychlorocarbenes, we would expect a linear correlation of log k_{frag} versus σ^+ with $r < 0$, corresponding to increasing activation energies and decreasing fragmentation rates as the positive charge imposed on the benzylic carbons in the fragmentation transition states unfavorably interacts with the electron-withdrawing substituents. Indeed, B3LYP/6-31G* computed[12] activation energies for the fragmentations of (cis) carbenes **5a**, **5c**, **5f**, and **5g** in DCE are 1.82, 2.30, 4.17, and 6.25 kcal/mol, respectively, in keeping with the anticipated Hammett trend, where carbene **5g** ($X = NO_2$) should exhibit the lowest k_{frag}. (See Supporting Information).

Figure 1 clearly diverges from these expectations. Rather than the least rapid, carbene **5g** is the *most rapid* to fragment, with $k_{frag} = 6.3 \times 10^6$ s^{-1}. Not only is this inconsistent with the simple ion pair mechanism, but solvolytic studies of $ArCH_2Y$ in partially aqueous solvents suggest that the lifetime of *p*-$O_2NPhCH_2^+$ is $\sim 3 \times 10^{-14}$ s,[13] implying that ion pair *cis*-**2** with this cation would be too short-lived for independent existence.

The "curved" Hammett plot of Figure 1 may be ascribed to "a constant change of position of the transition state, " where "increasing the electron-withdrawing nature of the substituents [...] not only decelerates the reaction, but also may destabilize the transition state to such an extent that the mechanism changes to one in which there is less or no separation of charge."[14] We associate the decreasing k_{frag} values of carbenes **5a**−**5d** with the ion pair mechanism, but what alternative is responsible for the increasing k_{frag} values of carbenes **5e**−**5g**?

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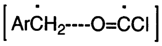
(1) S_N2 reactions are known for (e.g.) *n*-BuOCCl and (to a lesser extent) $PhCH_2OCCl$ in MeCN.[9] However, the dependence of k_{frag} on 0.25−1.75 M added $Bu_4N^+Cl^-$ in DCE for carbenes **5c** and **5e** afforded $k_2 = 3.2 \pm 0.2 \times 10^5$ and $8.0 \pm 0.9 \times 10^4$ M^{-1} s^{-1}, respectively, for the chloride-carbene reactions.[15] Given that the bimolecular fragmentation is less pronounced with *m*-Cl-substituted **5** than with the parent carbene, it seems unlikely that such reactions can account for the observed higher fragmentation rates of the electron-withdrawing group-substituted carbenes, **5e**−**g**.[16]

(2) Heterolytic fragmentation of **5c** via an ion pair is appropriate in polar solvents, but in apolar solvents (pentane) or in a vacuum, computational studies conclude that fragmentation of *cis*-**5c** will occur by a concerted mechanism.[17] One might suggest that substitution of carbenes **5** with electron-withdrawing substituents would similarly favor concerted fragmentation over ionic fragmentation, even in polar solvents. However, this would not explain why the fragmentations of (e.g.) **5f** and **5g** are *faster* than the fragmentation of **5c**. Indeed, the computed activation energies for the fragmentations of (cis) **5f** (4.17 kcal/mol) and **5g** (6.25 kcal/mol) in DCE are greater than that of **5c** (2.30 kcal/mol), so that fragmentations of **5f** and **5g** are predicated to be *slower* than that of **5c**, whether the mechanism is ionic or concerted.

(3) We are left with the incursion of homolytic fragmentation. We suggest that the fragmentations of X-$PhCH_2OCCl$ change from predominantly heterolytic (eq 1) to predominantly homolytic (cf., transition state **6**) as X is altered from electron-donating (Me, Ph) to electron-withdrawing (*m*-Cl, CF_3, NO_2). A smooth change in transition-state electron distribution between charge-separated heterolytic and “neutral” homolytic character would account for the curved Hammett correlation.



$$\left[Ar\dot{C}H_2\text{----}O{=}\dot{C}Cl\right]$$

6

There is strong precedent for radical character in carbene fragmentation. The heterolytic fragmentation of cyclopropylmethoxychlorocarbene in DCE[2c] assumes radical character in gas-phase flash vacuum pyrolysis at 500 °C.[18] Moreover, a minor (<10%) incursion of benzyl radical was observed during the LFP-induced fragmentation of carbene **5c**,[2a] and the (minor) formation of benzyl and OCCl radicals has been detected during the photolysis of diazirine **4c** in cryogenic Ar matrices.[17]

Most importantly, Merkley and Warkentin found that in the homolytic fragmentations of $PhCH_2OCOCH_2Ar$ at 110 °C, the competitive formation of $ArCH_2\cdot$ vs $PhCH_2\cdot$ was 11.4/1 (Ar = *p*-nitrobenzyl), 3.0/1 (Ar = *p*-trifluoromethylbenzyl), and 0.94/1 (*p*-tolyl).[19] Electron-withdrawing groups dominate homolytic carbene fragmentation. This selectivity pattern matches our kinetics observations for the fragmentations of **5g**, **5f**, and **5c** (or **5a**).

Support for a heterolytic to homolytic shift of the fragmentation mechanism also comes from comparisons of the computed[12] activation energies (E_{act}) for fragmentations of (cis) carbenes **5** with computed energies for the cleavage of **5** into benzyl and chlorocarbonyl radicals (E_{rad}). In vacuo (298.15 K, with zero-point energy corrections), we find ($E_a - E_{rad}$) = −3.2, −1.6, +2.3, and +5.9 kcal/mol, respectively, for **5** with X = Me, H, CF_3 or NO_2.[20] That is, the radical cleavage becomes increasingly competitive, and finally superior to “heterolytic” fragmentation as X becomes more electron withdrawing.[21] In simulated DCE, single-point pcm calculations alter the ($E_a - E_{rad}$) energies to −12.2, −11.5, −7.1, and −2.1 kcal/mol, respectively. The stabilizing influence of the polar solvent is apparent, but the trend toward competitive radical cleavage with electron-withdrawing nitro and trifluoromethyl substituents remains.

The admixture of radical character to the transition states for the fragmentations of (e.g.) **5f** and **5g** does not lead to radical pairs that initiate subsequent radical reactions. Photolysis of **5c** in cumene gave only 2% of toluene (possibly from $PhCH_2\cdot$) and 98% of $PhCH_2Cl$, the normative fragmentation product.[2a] Similarly, we find no substituted toluene products upon the photolytic generation and fragmentation of carbenes **5f** and **5g** in cumene. Freely diffusing $ArCH_2$ and Cl radicals are not formed in the fragmentations of carbenes **5** at ambient temperature; a strict cage effect must operate.[22,23]

In conclusion, we suggest that the heterolytic, ion pair fragmentation of ROCCl in polar solvents admixes significant homolytic character when polar solvent is absent,[17] or when substituents strongly destabilize developing cationic character on R. The Greek sea god Proteus had the power to assume many forms; the fragmentation of alkoxyhalocarbenes appears to be similarly protean.

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Supporting Information Available: Table 1 (kinetics data) and computed enthalpies corrected for zero-point energy and thermal effects at 298.15 K for all structures (PDF). This material is available free of charge via the Internet at http://pubs.acs.org.

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