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Benzylfluorocarbene: Reactions and Kinetics

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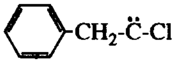
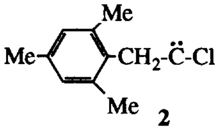
Summary. Benzylfluorocarbene, generated from the corresponding diazirine, is accompanied by considerable azine formation. Its rearrangement to β-fluorostyrene isomers in tetrachloroethane is characterized by $E_a = 3.2$ kcal/mol and log $A = 9.5$ s^{-1}

Among the problems connected with the 1,2-H shift of benzylchlorocarbene (**1**, BCC) to *cis*- and *trans*-β-chlorostyrene is the nonlinear Arrhenius correlation associated with this rearrangement in isooctane.[1] Curvature is apparent below -15 °C, followed by leveling of the correlation at -40 °C.[1a] These phenomena have been attributed to competitive reactions of BCC with the solvent or to quantum mechanical tunneling.[1a] The latter explanation is particularly intriguing because tunneling is strongly implicated in the 1,2-H rearrangement of BCC at cryogenic temperatures,[2] and could be important in the analogous reaction of methylchlorocarbene at near-ambient temperatures.[3,4]


1 (BCC)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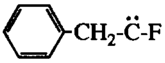
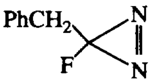

3 (BFC)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Our recent examination of the 1,2-H rearrangement of mesitylmethylchlorocarbene (**2**), a close relative of BCC, revealed similar Arrhenius curvature commencing at -40 °C in isooctane.[5] We found, however, that increasingly competitive azine-forming reactions of **2** with its diazirine precursor at temperatures below ~ -35 °C sufficed to explain the nonlinearity. Indeed, dilution of the diazirine (to ~ 10 mM) afforded a linear Arrhenius correlation for **2** down to -70 °C.[5] Subsequent reinvestigation of the BCC reactions also revealed significant azine formation at temperatures where Arrhenius leveling was apparent, suggesting that tunneling may not be required to rationalize this phenomenon.[5]

If competitive intermolecular carbene/diazirine reactions that afford azine are important with carbenes **1** and **2**, then we might expect them to be even more contributory with benzylfluorocarbene, BFC (**3**). Replacement of Cl in BCC by F in BFC should stabilize the carbene,[6] retard the intramolecular 1,2-H shift,[6] and provide greater opportunity for competitive intermolecular azine formation. Here, we describe initial studies of the generation, reactions, absolute kinetics, and Arrhenius behavior of BFC that conform to these predictions.

Benzylfluorodiazirine, **4**, was made by a "modified" Graham oxidation[7] of 20 mmol of benzylamidine hydrochloride in 200 ml of pentane/175 ml of DMSO, containing 15 g each of LiF and KF, with 150 ml of 12% aqueous NaOCl solution (saturated with 25 g of KF) at 0 °C.[8] Diazirine **4** was isolated from the (washed and dried) pentane product extract by repetitive silica gel chromatography (pentane eluent); benzylchlorodiazirine was the unwanted byproduct. The yield of purified **4** was only 18%, but it was readily characterized by UV (λ_{max} 342, 358 nm, $\varepsilon = 86\ M^{-1}\ cm^{-1}$); ^{1}H NMR ($\delta$, $CDCl_3$): 3.30 (*d*, $J_{HF} = 11.2$ Hz, 2H, CH_2), 7.29 (*m*, 5H, Ph); ^{19}F NMR (δ, $CDCl_3/CFCl_3$): -137.27 (*t*, $J_{HF} = 11.6$ Hz).

Photolysis of **4** ($A_{358} = 1$, 11.6 mM) in pentane, isooctane, or decane (Rayonet reactor, 350 nm, 5 min, 25 °C) destroyed the diazirine and afforded *cis*- and *trans*-β-fluorostyrenes, **5**, and azine **6**.[9] Over several reactions, the olefin yield ranged from 62-80%, with the balance (20 - 38%) comprised of azine. At -55 °C in pentane, the yield of **6** increased to an astonishing 77%! Azine formation from BFC and **4** is thus more

$PhCH{=}CHF$

5

$PhCH_2CF{=}N{-}N{=}CFCH_2Ph$

6

pronounced than the comparable reaction of BCC and benzylchlorodiazirine, where the azine yield was ~ 30% at -70 °C in isooctane.[5] Our expectation that azine formation would be more important with BFC than BCC is thus confirmed.

Determinations of BFC rearrangement kinetics and Arrhenius parameters in isooctane would be untrustworthy due to excessive azine formation. Mindful of Liu's demonstration that $CHCl_3$ is a solvent that minimizes Arrhenius curvature for BCC,[1a] we find 1,1,2,2-tetrachloro-ethane (TCE) to be an appropriate solvent for BFC kinetics. Not only is azine formation mitigated (see below), but the high boiling point of TCE (146 °C), coupled with the thermal stability of diazirine **4**,[10] permits kinetic studies over a wide temperature range.

Although azine **6** forms in 50% yield upon photolysis of **4** ($A_{358} = 1$) in TCE at -50 °C,[11] the yield decreases to 14% at -5 °C, 6% at 25 °C, and 2% at 60 °C. Accordingly, kinetics experiments were carried out at temperatures above -8 °C. Absolute rate constants for the rearrangement of BFC were determined by laser flash photolysis (LFP) at 351 nm using a xenon fluoride excimer laser and pyridine ylide methodology to visualize the carbene.[12] In this procedure, LFP of **4** ($A_{358} = 0.45$ or 1.0) in TCE containing mM concentrations of pyridine gives BFC, and thence its pyridine ylide (λ_{max} 372 nm). From the slope of the observed linear dependence of the apparent rate constants for ylide formation vs. [pyridine], we obtain $k_{ylide} = 4.3 - 6.5 \times 10^9$ $M^{-1}s^{-1}$ (3 experiments) for the second order reaction between BFC and pyridine. Extrapolation of the correlation to [pyridine] = 0 affords an intercept that is taken as the rate constant for the rearrangement of BFC to alkenes **5** (neglecting residual azine formation). At 26 °C in TCE, for example, $k_{re} = 9.2 \times 10^6\ s^{-1}$.

Three independent Arrhenius studies of k_{re} were conducted for BFC, covering temperature ranges of -7 to 66 °C (6 points, $r = 0.99$), 22 - 68 °C (6 points, $r = 0.98$), and -2.5 - 55 °C (6 points, $r = 0.99$). The first 2 series employed [**4**] ~ 12 mM; the third used [**4**] ~ 5.2 mM. The respective Arrhenius parameters obtained were $E_a = 3.07$, 2.92, or 3.77 kcal/mol, and $\log A = 9.23$, 9.37, or 9.82 s^{-1}, affording mean values of $E_a = 3.25 \pm 0.34$ kcal/mol and $\log A = 9.47 \pm 0.23$ s^{-1}. The latter corresponds to $\Delta S^{\ddagger}$ (298K) = -17.2 e.u. with $\Delta G^{\ddagger}$ ~ 7.8 kcal/mol.

For comparison, we carried out an analogous Arrhenius study of BCC in TCE between -71.4 °C and 3.2 °C; a linear correlation was obtained (11 points, $r = 0.99$).[13] Parallel product studies at -70, -35, and 0 °C revealed only the β-chlorostyrene 1,2-H shift products;[1a] azine was absent. The BCC Arrhenius parameters were $E_a = 3.25$ kcal/mol, $\log A = 10.1$ s^{-1}, $\Delta S^{\ddagger}$ (298 K) = -14.3 e.u., and $\Delta G^{\ddagger}$ ~ 6.9 kcal/mol.[14] What is surprising about the BCC values in TCE is their similarity to those of BFC: the activation energies are identical, while the activation entropies differ by ~ 2.9 e.u. The latter difference generates a larger $\Delta G^{\ddagger}$ for the BFC rearrangement of ~ 0.9 kcal/mol.[15]

In accord with our expectations, azine formation is considerably more pronounced with BFC than with BCC. Even in TCE, where azine is not observed in BCC experiments down to -70 °C, as much as 50% of azine forms from BFC in photolyses of **4** at -30 to -50 °C ($A_{358} = 1$). The difference must, in part, be attributed to a slower 1,2-H rearrangement of BFC relative to BCC, which allows more time for the intermolecular carbene/diazirine reaction that produces azine **6**. Direct comparisons of the apparent rate constants for carbene disappearance (k_d) as a function of temperature are in accord with this contention. Thus, $(10^{-7}k_d) = 1.2$, 3.0, 2.4, and 2.7 s^{-1} at -40, -20, -10, and 0 °C, respectively, for BCC in TCE, while parallel data for BFC are $(10^{-7}k_d) = 0.25$, 0.38, 0.52, and 0.61 s^{-1}. There is a 4.4 - 5.1-fold difference in rate constants that can be associated with less efficient rearrangement and greater azine formation on the part of the "slower" BFC.[16]

Previously,[6a] we observed that the enhanced stabilization afforded by a fluoro, relative to a chloro substituent in alkylhalocarbenes, affects the reactivity only modestly, and considerably less than anticipated on theoretical grounds.[6b] The present benzylhalocarbene results reinforce this point. What remains surprising, however, is that a major difference in azine formation for BFC and BCC arises from such small differences in rearrangement rate constants and activation parameters.

Clearly, rigorous product studies must underlie kinetics before we can hope to clarify the contribution of tunneling to carbenic rearrangements that occur near room temperature.[1]

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(8) This procedure is adapted from that of W. Sander and C. Junker, unpublished; private communication from W. Sander, 22 January, 1996. We thank Professor Sander for this information.

(9) The structures of **5** and **6** were established by ^{1}H NMR and high resolution MS. Control experiments showed that **5** and **6** were stable to the photolysis conditions.

(10) Thermolysis of **4** (A_{358} = 1) at 70 °C in TCE results in only 3.6% decomposition after 18 h.

(11) At A_{358} = 0.45, the photolytic yield of **6** is 23% at -40 °C in TCE. The more commonly employed polar solvent MeCN was not useful: 30% of azine formation was observed at 25 °C.

(12) Jackson, J.E.; Soundararajan, N.; Platz, M.S.; Liu, M.T.H. *J. Am. Chem. Soc.* **1988**, *110*, 5595.

(13) The pyridine ylide methodology[12] was used with the diazirine absorbance A_{346} = 1, [pyridine] = 1.4 - 9.0 mM, and λ_{max} (ylide) = 370 nm.

(14) The Arrhenius parameters are in reasonable agreement with those reported by Liu[1a] for BCC in $CHCl_3$, where the correlation was linear to -60 °C and afforded E_a = 3.6 kcal/mol, log A = 10.3 s^{-1}.

(15) The dominant $\Delta S^{\ddagger}$ parameters are typical of several carbenic rearrangements;[1c] for a related phenomenon, see: Skell, P.S.; Cholod, M.S. *J. Am. Chem. Soc.* **1969**, *91*, 7131.

(16) It is also possible that the efficiencies of the (intermolecular) carbene + diazirine → azine reactions differ for BFC and BCC, with azine formation favored for BFC. The comparative importance of tunneling in the 1,2-H shifts of BCC and BFC remains to be explored.

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