Ring-Opening Reactions of Fluorocyclopropanes with Halogens: A General and Useful Route to 1,3-Dihalofluoropropane Derivatives[†,‡]

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Fluorine substituents significantly affect both the structure and the reactivity of cyclopropanes.[1] Hexafluorocyclopropane (**1**) is much less stable thermally than its hydrocarbon counterpart,[2] and its strain energy is about twice that of cyclopropane.[1b,3] At 170−190 °C, **1** extrudes difluorocarbene (E_a = 38.6 kcal/mol),[2b] which can be trapped by alkenes to give difluorocyclopropane derivatives.[2a,4] The :CF$_2$ extrusion process is considered to be concerted, and in general there is no direct evidence for biradical intermediates from homolytic cleavage of carbon−carbon bonds in cyclopropanes.[5] We report here that highly fluorinated cyclopropanes thermally undergo ring-opening reactions with halogens, which may involve the trapping of trimethylene biradical intermediates, to give 1,3-dihalofluoropropanes in good yields.

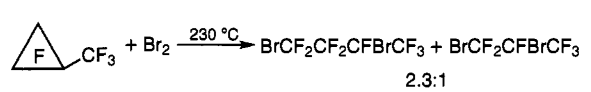
When **1**[11] was heated with halogens at 155 °C in a shaker tube, the corresponding 1,3-dihalohexafluoropropanes were

$$\begin{array}{ll} c\text{-}C_3F_6 + X_2 \rightarrow & X(CF_2)_3X \\ \quad\textbf{(1)} & X = Cl, Br, I, 50-80\% \end{array}$$

obtained in 50−80% isolated yields.[13] The ring-opening reaction also can be carried out with interhalogens such as I−X (X = Br, Cl). With I−Br and **1** at 240 °C, a 4.6:1:1.3 mixture of I(CF$_2$)$_3$Br:Br(CF$_2$)$_3$Br:I(CF$_2$)$_3$I was isolated in 70% yield. Similarly, the major product with ICl was Cl(CF$_2$)$_3$I, along with Cl(CF$_2$)$_3$Cl and I(CF$_2$)$_3$I (83% total yield).

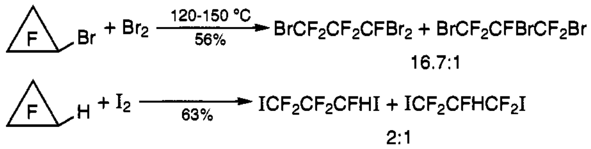
$$\begin{array}{lll} c\text{-}C_3F_6 + X{-}I \xrightarrow{240\,°C} & X(CF_2)_3I + X(CF_2)_3X + I(CF_2)_3I & \\ \quad\textbf{(1)} & X = Cl, 83\% & 1.7:1:1.5 \\ & X = Br, 70\% & 4.6:1:1.3 \end{array}$$

Substituted cyclopropanes readily undergo the ring-opening reactions. With pentafluorocyclopropanes bearing chlorine, bromine, and perfluoroalkoxy substituents, the ring-opening occurred under milder conditions. With bromine, for example, the reactions started at 120−130 °C and were complete within 3 h. Perfluoromethylcyclopropane, however, required higher temperatures (230 °C) for reaction, which may reflect kinetic stabilization of strained rings by the trifluoromethyl substituent,[14] and the products indicate a competition between ring-opening and extrusion of difluorocarbene.



The regiochemistry of the ring-opening reactions depends on the substituents. Chlorine- and perfluoroalkoxy-substituted pentafluorocyclopropanes gave only XCF$_2$CF$_2$CFXY (X = Br and I, Y = Cl and R$_F$O) in 50−86% yields with Br$_2$ and I$_2$ at 150−160 °C, which indicates that the ring-opening occurred exclusively at the substituted carbons.

With bromopentafluorocyclopropane and Br$_2$, a 16:1 mixture of BrCF$_2$CF$_2$CFBr$_2$:BrCF$_2$CFBrCF$_2$Br resulted, whereas pentafluorocyclopropane reacted unselectively with I$_2$ to give a 2:1 mixture of ICF$_2$CF$_2$CFHI:ICF$_2$CFHCF$_2$I.



Perfluoroalkoxycyclopropanes reacted with I$_2$ at 240 °C to form ICF$_2$CF$_2$COF and R$_F$I in quantitative yields via decomposition of the primary product R$_F$OCFICF$_2$CF$_2$I. This reaction pathway is supported by the observation that authentic R$_F$OCFICF$_2$CF$_2$I cleanly decomposed to ICF$_2$CF$_2$COF and R$_F$I

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[‡] Dedicated to Professor Donald J. Burton on the occasion of his 60th birthday.

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(2) (a) Birchall, M. J.; Fields, R.; Haszeldine, R. N.; McClean, R. J. *J. Fluorine Chem.* **1980**, *15*, 487. (b) Atkinson, B.; McKeagan, D. *J. Chem. Soc., Chem. Commun.* **1966**, 1890.

(3) (a) Liebmann, J. F.; Dolbier, W. R., Jr.; Greenberg, A. *J. Phys. Chem.* **1986**, *90*, 394. (b) Inagaki, S.; Ishitani, Y.; Kakefu, T. *J. Am. Chem. Soc.* **1994**, *116*, 5954.

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(5) Recent theoretical calculations indicate that the singlet trimethylene biradicals $^•CH_2CH_2CH_2^•$, $^•CH_2CF_2CH_2^•$, and $^•CH_2CH_2CF_2^•$ can be transition states but not energy minimum species,[6] and thermochemical data likewise show $^•CH_2CH_2CH_2^•$ to be either a transition state or a very shallow energy intermediate with a barrier to ring closure of <1 kcal/mol.[7] Just after this paper was submitted, it was reported that the trimethylene biradical, generated by photolysis of cyclobutanone, could be observed by femtosecond transition-state spectroscopy as a transient species with a lifetime of about 120 fs.[8] To our knowledge, the properties of $^•CF_2CF_2CF_2^•$ have not been similarly investigated, although related biradicals have been postulated in thermal reactions. For example, 1,1,2,2-tetrafluoro- and hexafluorospiropentane thermally extrude :CF$_2$ and competitively rearrange to methylenecyclobutanes.[9] (Octafluorospiropentane, however, exclusively extrudes :CF$_2$.)[9] The rearrangement products were explained by a ring-opening biradical mechanism, but the results do not distinguish between biradical transition states and intermediates. The strong preference for nonplanarity in α-fluororadicals[10] implies that *both* radical sites in $^•CF_2CF_2CF_2^•$ will be pyramidal. The properties of such a biradical may therefore be quite different from those of the previously studied trimethylene biradicals. A direct femtosecond laser study of the hexafluorotrimethylene biradical produced by photolysis of hexafluorocyclobutanone is planned.

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(11) All fluorocyclopropanes in this paper were prepared by heating the appropriate fluoroalkene with hexafluoropropylene oxide (HFPO).[12] The trifluoroacetyl fluoride byproduct produced does not interfere with the ring-opening reactions with halogens, and it is therefore unnecessary to purify the fluorocyclopropane. The X(CF$_2$)$_3$X dihalides can thus be prepared by first heating HFPO at 180−190 °C, adding the halogen X$_2$, and then heating to 150−240 °C.

(12) (a) Sargeant, P. B.; Krespan, C. G. *J. Am. Chem. Soc.* **1969**, *91*, 415. (b) Sargeant, P. B. *J. Org. Chem.* **1970**, *35*, 678. (c) Chepik, S. D.; Petrov, V. A.; Galakhov, M. V.; Belen'kii, G. G.; Mysov, E. I.; German, L. S. *Izv. Akad. Nauk SSSR, Ser. Khim.* **1990**, *8*, 1844.

(13) For **1** and bromine, the reaction pressure increased with increasing temperatures and reached a maximum pressure at 155 °C. It then decreased, and after 340 min it remained constant.

(14) Greenberg, A.; Liebman, J. F.; Van Vechten, D. *Tetrahedron* **1980**, *36*, 1161.

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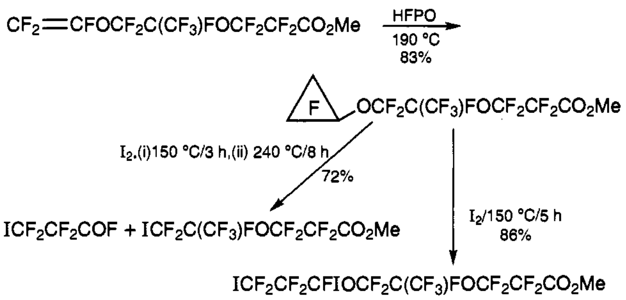
when heated at 240 °C. This chemistry was used to synthesize other more complex, functionalized iodides, as illustrated below.



In conclusion, we have discovered an unprecedented ring-opening reaction of highly fluorinated cyclopropanes with halogens at elevated temperatures. These reactions provide the first useful synthesis of 1,3-dihalofluoropropane intermediates, which are important building blocks for making various fluorinated materials but heretofore have been difficult and costly to make.[15] Although the mechanism of this reaction is unclear, a working hypothesis is that the primary step involves the homolytic cleavage of a strained carbon–carbon bond to afford a 1,3-diradical intermediate which is trapped by rapid reaction with halogen.[16,18–20] Mechanistic studies and further applications of this novel chemistry will be reported in the future.

Supplementary Material Available: Experimental details and characterization of all products (7 pages). This material is contained in many libraries on microfiche, immediately follows this article in the microfilm version of the journal, can be ordered from the ACS, and can be downloaded from the Internet; see any current masthead page for ordering information and Internet access instructions.

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[15] For prior syntheses of $XCF_2CF_2CF_2X$ (X = Cl, Br, and I), see: (a) Hauptschein, M.; Saggiomo, A. J.; Stokes, C. S. *J. Am. Chem. Soc.* **1952**, *74*, 848. (b) Brel, V. K.; Uvarov, V. I.; Zefirov, N. S.; Stang, P. J.; Caple, R. *J. Org. Chem.* **1993**, *58*, 6922.

[16] An electrophilic ring-opening mechanism is very unlikely given the relative unreactivity of perfluoroalkanes and -alkenes toward electrophiles.[17] A control experiment shows that c-C_3F_6 is inert to HCl at 160 °C, which argues against an electrophilic process with halogens under similar conditions.

[17] (a) Smart, B. E. *Organofluorine Chemistry: Principles and Commercial Applications*; Plenum Press: New York, 1994; Chapter 3, pp 70–76. (b) Belen'kii, G. G.; German, L. S. In *Soviet Scientific Reviews, Section B, Chemistry Reviews*; Ellis Horwood: London, 1984; pp 183–218. (c) Chambers, R. D. *Fluorine in Organic Chemistry*; Wiley: New York, 1973.

[18] Tonelli, C.; Tortelli, V. *J. Fluorine Chem.* **1994**, *67*, 125.

[19] An alternative S_H2 radical process involving initial halogen atom attack on the cyclopropane has considerable precedent in the photochemical halogenations of nonfluorinated cyclopropanes, see: (a) Upton, C. J.; Incremona, J. H. *J. Org. Chem.* **1976**, *41*, 523 and references therein. (b) Shea, K. J.; Skell, P. S. *J. Am. Chem. Soc.* **1973**, *95*, 6728. (c) Wiberg, K. B.; Waddell, S. T.; Laidig, K. E. *Tetrahedron Lett.* **1986**, *27*, 1553. The fluorinated cyclopropanes in this study, however, did not undergo similar photochemical (254 nm) halogenations at 25–50 °C. The observation that the reaction between c-C_3F_6 and Br_2 appears to be complete after about 6 h at 155 °C,[13] whereas c-C_3F_6 has a thermal half-life of 566 h at this temperature,[2b] would seem to refute the 1,3-biradical mechanism. However, this assumes that the biradical immediately fragments and excludes reclosing to cyclopropane. Free radical additions to c-C_3F_6 ordinarily do not give significant amounts of 1,3-hexafluoropropane products. For example, c-C_3F_6 and PhSSPh at 200 °C give mainly $PhSCF_2CF_2SPh$ with <5% $PhSCF_2CF_2CF_2SPh$, whereas c-C_3F_6 and *t*-BuN=N*t*-Bu at 190 °C produce a complex mixture of over a dozen products.

[20] The only other example of clean addition to c-C_3F_6 discovered so far seems more consistent with a 1,3-biradical mechanism. Fullerene C_{60} reacts with either c-C_3F_6 at 150 °C or $ICF_2CF_2CF_2I$ at 200 °C to give in good yields the same five-membered ring adduct of the $CF_2CF_2CF_2$ unit across a C_{60} double bond (to be published).