Organic Fluoronitrogens. X. Reductive Defluorination–Cyclization

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The reaction of fluorocarbons containing geminal NF–groups with reducing agents, such as dicyclopentadienyliron or dicumenechromium, results in the formation of three-membered ring heterocycles. Bis(difluoramino) and trifluoroformamidino derivatives are converted into fluorodiazirines, whereas a compound containing the $R_fNF-\overset{|}{C}-NF_2$ grouping yields a perfluorodiaziridine. The mechanism of the reaction is discussed in terms of nitrogen anion intermediates and internal ion-pair rearrangements.

The reductive defluorination of fluorocarbon difluoramines and secondary fluoramines to the corresponding fluorimines or azomethines has been the subject of a previous publication.[1] In addition, the preparation of difluorodiazirine by the action of dicyclopentadienyliron[2a] or tetrabutylammonium iodide[2b] on bis(difluoramino)difluoromethane, $CF_2(NF_2)_2$, has been reported.

The present paper describes, in general terms, the dicyclopentadienyliron and dicumenechromium reduction of tetrafluoroformamidine,[3a] pentafluoroguanidine,[3] tris(difluoramino)fluoromethane,[3a] and 1,1-bis(difluoramino)perfluoro-2-azapropane[3a] in which three-membered-ring heterocycles containing two nitrogen atoms are the principle isolable products. Since this reaction involves not only reduction, but also loss of fluoride ions and cyclization of the reduced intermediates, it may be conveniently termed "reductive defluorination–cyclization."

Results and Discussion

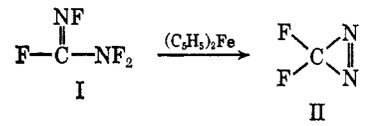
The reaction of fluorocarbons containing either the $>C(NF_2)_2$ or $FN{=}\overset{|}{C}NF_2$ group with organometallic reducing agents, such as dicyclopentadienyliron or dicumenechromium, results in an oxidation–reduction reaction, elimination of fluoride ions, and cyclization to fluorodiazirines. Although the yields are generally low, this technique for the preparation of fluorodiazirines is thought to be a general reaction. The relatively low yields of purified heterocyclic compounds obtained in the present work are probably due in part to the small quantities of starting material employed and to the number of NF– sites available for further reaction.

Like the reduction of simple NF– compounds,[1] the extent of reaction of geminal NF– derivatives is conveniently followed colorimetrically.

Oxidation of the soluble, neutral organometallic reagents to the insoluble cationic species by the NF groups is accompanied by a color change. With dicyclopentadienyliron this is from orange to blue-green and with dicumenechromium from red-brown to yellow.

Reaction of tetrafluoroformamidine, I, with either dicyclopentadienyliron or dicumenechromium in xylene hexafluoride caused a rapid change of color, indicating complete oxidation of the organometallic reducing agent. The volatile products were separated by conventional methods, such as fractional distillation–condensation and vapor phase chromatography.

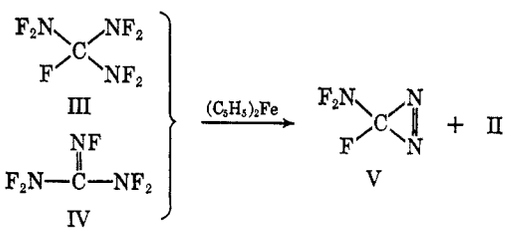
With dicylcopentadienyliron, difluorodiazirine was obtained in 23% yield and identified by comparison of its spectral properties with those of an authentic sample.[2a,4]



I II

In contrast to the very slow formation of CF_2N_2 from $CF_2(NF_2)_2$ and dicyclopentadienyliron,[2a] difluorodiazirine is generated very rapidly from tetrafluoroformamidine. It is difficult to account for the very rapid reaction of tetrafluoroformamidine compared with that of bis(difluoramino)difluoromethane. It can be speculated, however, that the lability of the $FN{=}\overset{|}{C}NF_2$ compounds may be a result of a tendency for the α,β-unsaturated systems of this type to undergo 1,3-fluoride isomerization even though no thermodynamic benefits can be identified.

Both tris(difluoramino)fluoromethane, III, and pentafluoroguanidine, IV, were used for the preparation of NF_2CFN_2 and were found to undergo facile "reductive defluorination–cyclization" to afford mixtures of the desired diazirine, V, and difluorodiazirine, II. The ratio of V to II was generally from 4:1 to 7:1. As above, the fluorimino derivative, IV, was more reactive to dicyclopentadienyliron than the saturated compound, III. Elemental and spectral analyses as reported[5] were employed to establish the structure of V.



III IV V

As noted previously,[5] extreme caution should be used when manipulating difluoraminofluorodiazirine since it can explode violently and is sensitive to phase changes. Whenever possible, the purified material was not cooled below −119° (the freezing point of

(1) R. A. Mitsch, *J. Amer. Chem. Soc.*, **87**, 328 (1965).

(2) (a) R. A. Mitsch, *J. Heterocycl. Chem.*, **3**, 245 (1966); (b) R. L. Rebertus, J. J. McBrady, and J. G. Gagnon, *J. Org. Chem.*, **32**, 1944 (1967).

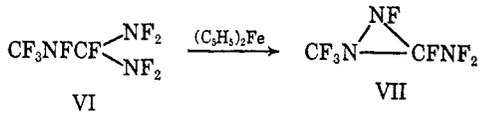
(3) (a) R. J. Koshar, C. D. Wright, and D. R. Husted, *ibid.*, **32**, 3589 (1967); (b) R. A. Davis, J. L. Kroon, and D. A. Rausch, *ibid.*, **32**, 1662 (1967).

(4) R. A. Mitsch, *J. Heterocycl. Chem.*, **1**, 59 (1964).

(5) R. A. Mitsch, E. W. Neuvar, R. J. Koshar, and D. H. Dybvig, *ibid.*, **2**, 271 (1965).

ethyl bromide, at which temperature the diazirine is still a liquid). On occasions when the material was cooled to −145° explosions occurred.

The generality of the "reductive defluorination–cyclization" reaction in the classes of nitrogen–fluorine compounds described herein is further illustrated by the isolation of 1-trifluoromethyl-2,3-difluoro-3-difluoraminodiaziridine, VII, in 33% yield from the reaction of dicyclopentadienyliron with 1,1-bis(difluoramino)perfluoro-2-azapropane, VI, at room temperature. The formation of the fluorodiaziridine, VII, from VI is consistent with the previous observation



VI VII

that the secondary fluoramino group, —NF—, is more susceptible to reaction with reducing agents than the difluoramino moiety.[1]

The fluorodiaziridine, VII, was identified primarily on the basis of its infrared and F^{19} nuclear magnetic resonance spectral properties. Its infrared spectrum exhibits the expected absorptions in the normal CF and NF regions, as well as an absorption of medium–strong intensity at 7.13 μ, assigned to the three-membered-ring vibration. The 6.7–7.2-μ region has been shown to be particularly diagnostic for the presence of three-membered-ring fluoro heterocycles of oxygen, sulfur, and nitrogen containing one or two heteroatoms.[6]

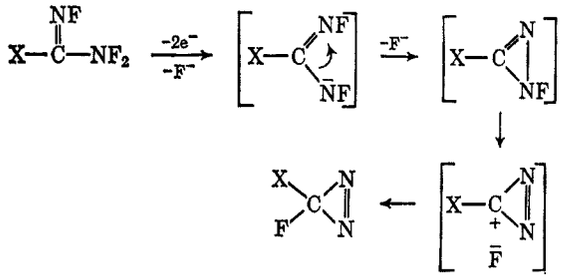
The F^{19} nuclear magnetic resonance spectrum of VII shows the following absorptions in area ratios of approximately 2:1:3:1: ϕ^* −30.2[7] (—NF_2), 8.3 (>NF), 61.7 (CF_3, doublet, J = 9.8 cps), and 154.2 (>CF).

Since several different techniques for the preparation of halodiazirines have now been reported, a comparison of the probable mechanisms and the role of the nitrogen anion in each is worthy of attention.

In keeping with previous mechanistic speculations concerning the role of the nitrogen anion in reductions of NF– bonds,[1,2a] the formation of difluorodiazirine from tetrafluoroformamidine and difluoraminofluorodiazirine from pentafluoroguanidine can both be rationalized as involving a primary two-electron reduction of a nitrogen–fluorine bond.

Inasmuch as the nitrogen atom of the NF_2 group in trifluoroformamidino compounds is in a higher relative oxidation state than the imino nitrogen (=NF), it is probable that in the general reaction of this class of compounds with a reducing agent, initial reduction occurs at the NF_2 group (Scheme I). Reduction accompanied by loss of fluoride ion would lead to the N-fluoro anion which could ring close to the proposed N-fluorodiazirine by direct displacement of fluoride from the fluorimino nitrogen. Since these reactions were carried out in a poorly ion-solvating media, it seems reasonable to assume that the final isomerization of the N-fluorodiazirine involves a tight ion-pair intermediate. The resulting isomerization is favored thermodynamically and represents additional evidence for the tendency of α,β-unsaturated NF systems of the

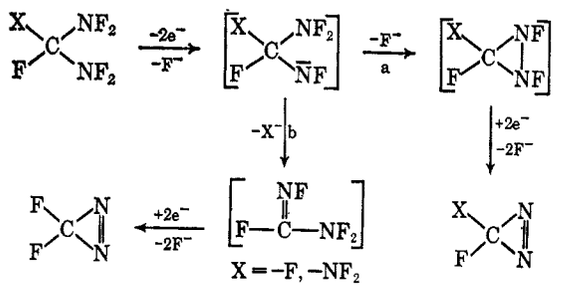
SCHEME I



types —C=C—NF and —C=N—NF to undergo 1,3-fluoride shifts from nitrogen to carbon.[8]

In the case of the geminal —NF_2 derivatives $CF_2(NF_2)_2$ and $CF(NF_2)_3$, reaction with a reducing agent and loss of fluoride leads presumably to the nitrogen anion shown below. However, in order to account for the formation of both CF_2N_2 and F_2NCFN_2 from $CF(NF_2)_3$ and CF_2N_2 from $CCl_2(NF_2)_2$,[2b] the nitrogen anion must undergo further reaction by at least two routes (Scheme II). Route a, which involves cyclization by direct displacement of fluoride, leads to the transient existence of the perfluorodiaziridine which undergoes further reduction to the diazirine. With $CF_3NFCF(NF_2)_2$, where initial reduction probably occurs at the secondary —NF— group, the perfluorodiaziridine, VII, is the isolated product.

SCHEME II



Route b is rationalized as involving the elimination of fluoride ion in the $CF_2(NF_2)_2$ reaction or difluoramino anion in the $CF(NF_2)_3$ reaction and in both cases leads to the intermediacy of tetrafluoroformamidine which undergoes further "reductive defluorination–cyclization" to difluorodiazirine.

While tetrafluoroformamidine is shown as one of the possible two-electron reduction products of bis(difluoramino)difluoromethane and tris(difluoramino)fluoromethane, no experiments to date have given any evidence that the trifluorformamidino compound is an isolable intermediate. In the preparation of fluorodiazirines, attempts to incorporate anions other than fluoride into the diazirine have not been successful. Thus, reaction of bis(difluoramino)difluoromethane with iodide in the presence of a 10 M excess of chloride in acetonitrile afforded a nearly quantitative yield of difluorodiazirine and no evidence for chlorofluorodiazirine.

The mechanism described above for the cyclization of FN=C—NF_2 compounds with reducing agents is simi-

(6) C. S. Cleaver and C. G. Krespan, *J. Amer. Chem. Soc.*, **87**, 3719 (1965); R. A. Mitsch, E. W. Neuvar, and P. H. Ogden, *J. Heterocycl. Chem.*, **4**, 389 (1967).

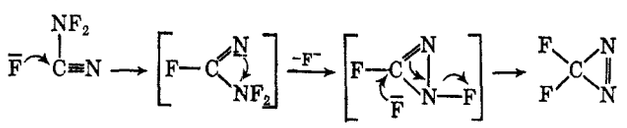
(7) Trichlorofluoromethane was used as an internal reference; see G. Filipovich and G. V. D. Tiers, *J. Phys. Chem.*, **63**, 761 (1959).

(8) R. A. Mitsch, submitted for publication; W. H. Graham, private communication.

lar to that proposed by Graham[9] for the formation of halodiazirines by halogenation of amidines. In the hypohalite reaction of amidines, the N-halo anion is generated in a classical manner through the removal of a proton from nitrogen by base with subsequent formation of an N-halodiazirine intermediate.[9]

The fact that acetate was incorporated into the diazirine when chlorination of acetamidine was carried out in the presence of added acetate in dimethyl sulfoxide suggests that in this highly ionizing solvent, the ion pair is probably less tightly bound, although exchange of acetate for chloride could also occur prior to the final diazirine formation.[9]

Still another technique for the synthesis of difluorodiazirine which is worthy of mechanistic consideration is the vapor phase isomerization of difluorocyanamide over CsF.[10] Although the authors[10] did not propose a mechanism for this isomerization, it probably proceeds *via* initial fluoride attack at the nitrile carbon atom and appears to reinforce the role of nitrogen anions in cyclization reactions leading to N-halodiazirine intermediates and the strong tendency for α,β-unsaturated NF— systems to undergo 1,3-fluoride shifts.



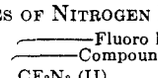
Thus, it appears that regardless of the initiation step, reduction of an NF— bond, removal of a proton by base or fluoride catalysis, all of these techniques for the synthesis of halodiazirines involve a nitrogen anion, an N-halodiazirine, and 1,3-halide shifts.

Experimental Section

Chromatographic analyses were performed with a Model 154D Perkin-Elmer vapor fractometer, utilizing fluorocarbon-type stationary phases. The relative retention times recorded in Table I were obtained at 25° using 0.5-in.-o.d. tube 2 m long and packed with FX-45[11] or KF-8126[11] on Celite. For the most part, the preparative-scale separations were done on a large unit employing 0.5-in.-o.d. tubes, 6 m long and packed with similar FC-45 on acid-washed Celite.

TABLE I

RELATIVE RETENTION TIMES OF NITROGEN FLUOROCARBONS

Nitrogen–fluorine compound		Fluoro heterocycle	
Compound	T_r[a]	Compound	T_r[a]
$NF_2CF{=}NF$ (I)	29.8	CF_2N_2 (II)	6.17
$FC(NF_2)_3$ (III)	134.6	NF_2CFN_2 (V)	24.8
$(NF_2)_2C{=}NF$ (IV)	95.0		
$CF_3NFCF(NF_2)_2$ (VI)	315.0	CF_3N——$CFNF_2$ (VII)	33.2[b]

[a] T_r = relative retention time = $100[(T_{compd} - T_{air})/(T_{CFCl_3} - T_{air})]$. [b] Vapor phase chromatography obtained on KF-8126 on Celite column. All others were run on the FX-45 on Celite unit.

Procedure.—Resublimed dicyclopentadienyliron was weighed out into a heavy-wall Pyrex ampoule and xylene hexafluoride solvent added. After degassing, a calculated amount of difluoramino reactant was condensed into the ampoule at liquid nitrogen temperature by appropriate vacuum transfer techniques. The sealed ampoule was shaken periodically while at room temperature. Preliminary separation of the products from the solvent was accomplished by fractional distillation–condensation techniques using −23, −78, and −196° receivers. Vapor phase chromatography was used to effect the final separation, employing the usual trapping techniques. The components were condensed from the effluent gas in a beaded trap, cooled to −196°, except where otherwise noted.

Difluorodiazirine (II).—Into a degassed sample of 0.186 g (1.0×10^{-3} mol) of dicyclopentadienyliron in 1.5 ml of xylene hexafluoride was condensed 0.116 g (1.0×10^{-3} mol) of tetrafluoroformamidine at −196°. After the reaction mixture had been shaken for 3 hr at room temperature, it was fractionated and afforded 2.96×10^{-4} mol of volatile product in the −196° trap. Infrared and chromatographic analyses of the crude mixture indicated 78.9% conversion (23% yield) to II.

Difluorodiazirine (II).—Into a 30-cc glass ampoule fitted with a polytetrafluoroethylene needle valve and containing a magnetic stirring bar was placed 1 cc of 1 *M* tetrabutylammonium iodide and 10 cc of 1 *M* tetraethylammonium chloride, both in anhydrous acetonitrile. The ampoule was cooled to −196° and degassed and 0.0308 g (2×10^{-4} mol) of bis(difluoramino)difluoromethane was added by condensation. The reaction mixture was warmed to room temperature and stirred overnight. Fractional distillation–condensation afforded a near quantitative yield of difluorodiazirine. Chlorofluorodiazirine could not be detected spectroscopically.

Difluoraminofluorodiazirine (V).—A sample of tris(difluoramino)fluoromethane, weighing 0.500 g (2.67×10^{-3} mol), reacted for 3 hr with 0.995 g (5.34×10^{-3} mol) of dicyclopentadienyliron in 4 ml of xylene hexafluoride. After fractionation in the usual manner, the volatile product contained in the −196° receiver (6.50×10^{-4} mol) had the following composition (determined by vapor phase chromatographic analysis): CF_2N_2 (II, 17.4%), NF_2CFN_2 (V, 69.7%), and $FC(NF_2)_3$ (III, 12.9%). Preparative vapor phase chromatographic trapping techniques, using *receivers* at −119°, afforded a 17% yield pure difluoraminofluorodiazirine having a boiling point of about −36° (isoteniscope) and infrared absorption peaks at 4.45 (w), 6.33 (m), 7.76 (s), 8.86 (m), 9.44 (w), 10.17 (s), 11.08 (s), and 12.03 μ (m).

Anal. Calcd for CF_3N_3: C, 10.8; N, 37.8; F, 51.4; mol wt, 111. Found: C, 11.3; N, 38.8; F, 51.9; mol wt, 111 (gas density).

Extreme caution should be applied when manipulating purified difluoraminofluorodiazirine; the material *should not* be cooled below −119°.

Difluoraminofluorodiazirine (V).—A second procedure for obtaining V is by the reaction of 0.313 g (1.68×10^{-3} mol) of dicyclopentadienyliron dissolved in 5 ml of xylene hexafluoride with 0.250 g (1.68×10^{-3} mol) of pentafluoroguanidine. After 3 hr, the mixture was fractionated to give a −196° sample (4.35×10^{-4} mol) of the following composition: CF_2N_2 (II, 11.5%, 3% yield), NF_2CFN_2 (V, 87.8%, 23% yield), and $FN{=}C(NF_2)_2$ (IV, <1%). Samples of the above composition frequently detonated while cooling the vapor from room temperature to −196°.

1-Trifluoromethyl-3-difluoraminofluorodiaziridine (VII).—A 0.278-g (1.18×10^{-3} mol) sample of VI was condensed into a 15-ml heavy-wall ampoule, cooled to −196°, and containing 0.617 g (3.32×10^{-3} mol) of dicyclopentadienyliron and 7 ml of xylene hexafluoride. The ampoule was sealed, shaken at room temperature for 1.5 hr, and opened for fractionation through −78 and −196° traps. The −196° fraction (0.409×10^{-3} mol) was separated by vapor phase chromatography. The major component of the mixture (81% of the crude product, 33% yield) was identified as 1-trifluoromethyl-3-difluoraminofluorodiaziridine by infrared and F^{19} nmr spectroscopy.

Anal. Calcd for $C_2F_7N_3$: F, 66.8; mol wt, 199. Found: F, 65.7; mol wt, 195 (gas density).

Registry No.—II, 693-85-6; V, 4823-43-2; VII, 16005-32-6.

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(9) (a) W. H. Graham, *J. Amer. Chem. Soc.*, **87**, 4396 (1965); (b) W. H. Graham, private communication.

(10) M. D. Meyers and S. Frank, *Inorg. Chem.*, **5**, 1455 (1966).

(11) Minnesota Mining and Manufacturing Co.