Nucleophilic Substitution Reactions of Heterocyclic Amines and Acyclic Diamines with Chlorofluoroolefins and Hexafluoropropylene Oxide

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Received May 21, 1993•

The reactions of $CH_3N(H)CH_2CH_2N(H)CH_3$, $CH_3N(H)CH_2CH_2CH_2N(H)CH_3$, and the cyclic amines piperazine, *N*-phenylpiperazine, and *N*-methylpiperazine with both cyclic and acyclic 1,2-dichloroperfluoroolefins are reported. Nucleophilic attack occurs at olefinic carbon, followed, in some cases, by cyclization and β-elimination. A variety of unusual polyfluorinated tertiary amines and heterocycles are synthesized.

Introduction

Per- and polyfluorinated heterocycles find application in areas ranging from blood substitutes[2,3] and valuable precursors to other biologically active compounds,[4-6] to use as extractants specific for a single metal[7,8] and as unusual ligands capable of forming complexes with anions[9] as well as exhibiting the potential to form stable complexes with neutral molecules.[10] Such wide potential for useful applications and the uncommon chemistry exhibited by this class of polyfluorinated compounds has provided the impetus for intense study of these materials over the last 30–40 years and for the ongoing interest in their synthesis and characterization today.

As a part of our continuing study of these highly interesting compounds,[11-15] we now report the preparation of a variety of N-substituted heterocyclic amines that contain 2-chlorohexafluorobutenyl-2 ($CF_3CCl{=}CCF_3$) or 1-chloroperfluorocycloalkenyl [$\overline{C{=}C(Cl)(CF_2)_n}CF_2$ (n = 1, 2, 3)] groups and heterocyclic amides that contain the pentafluoroethyl moiety. In order to compare the effect of the structure of the reactant amines on the products obtained, reactions with chlorofluoroolefins and hexafluoropropylene oxide are also carried out with some selected acyclic diamines.

Our study indicates that in reactions of various secondary amines with chlorofluoroolefins, 1,2-dichloro(hexafluoro)cyclopentene-1 reacts more smoothly and gives better yields than *trans*-2,3-dichlorohexafluorobutene-2. In both cases, even in the presence of a large excess of the amine, only singly substituted olefins are obtained. When piperazine is reacted with 1,2-dichloro(hexafluoro)cyclopentene-1, both mono and di-N-substituted products are formed. When a stronger electrophile, such as hexafluoropropylene oxide, is used, replacement of all of the amine hydrogen atoms in piperazine, *N,N'*-dimethylethylenediamine, and 1,4,8,11-tetraazacyclotetradecane is observed.

Results and Discussion

Much of the older literature dealing with nucleophilic attack on poly- and perfluorinated acyclic and cyclic alkenes has been well reviewed.[16] More recently an excellent series of papers on the chemistry of polyfluorinated cycloalkenes has been published,[17] and nucleophilic reactions with a wide variety of fluorocarbons are subjects of wide interest.[12,18] The reactions of polyfluorinated alkenes are generally considered to proceed by addition followed by β-elimination.

The products we have obtained from the reactions of 1,2-dichloro(hexafluoro)cyclopentene-1, *trans*-2,3-dichloro(hexafluoro)butene-2, and hexafluoropropylene oxide with various amines are illustrated below. It is well-known that fluorinated cyclic or vinylic olefins undergo nucleophilic substitution reactions, for example, the reaction of 1,2-dichloro(hexafluoro)cyclopentene-1 with secondary aliphatic amines or pyrrolidine and 3,3,4,4-tetrafluoropyrrolidine[19] to give singly substituted (C-1) products.[20] Displacement of both chlorine atoms is possible only when a strong nucleophilic reagent, such as mercaptide anion,[21] trialkyl phosphite,[22] or polyfluorinated sulfonamide,[12] is employed in the metathesis reaction. The results of this study of the reactions of heterocyclic secondary amines, i.e., *N*-methylpiperazine, *N*-phenylpiperazine, and pip-

• Abstract published in *Advance ACS Abstracts,* December 1, 1993.

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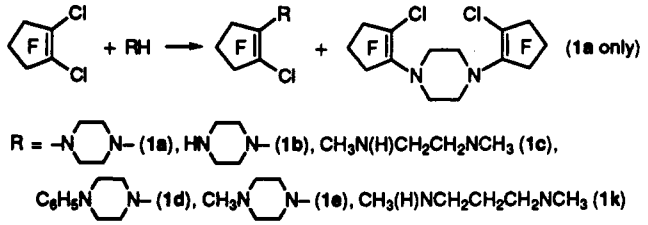
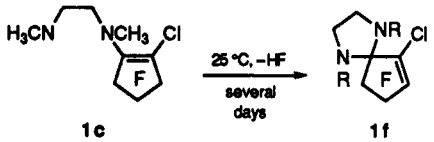
erazine with 1,2-dichloro(hexafluoro)cyclopentene-1 are consistent with this general observation. In the case of

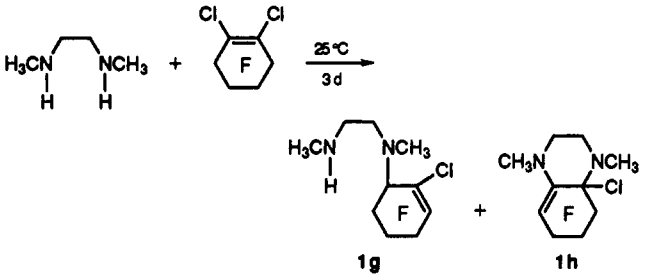


piperazine, both mono- and di-N-substituted products **1a** and **1b** are obtained. The relative amounts of the two products can be controlled by varying the stoichiometric ratio of the piperazine and the olefin. It is interesting to note that with acyclic diamines, such as *N,N'*-dimethylethylenediamine and *N,N'*-dimethyl-1,3-propylenediamine, nucleophilic substitution occurs at only one of the two functional hydrogens. While standing at 25 °C, compound **1c** gradually reacts intramolecularly to form **1f** with concomitant elimination of HF. The driving force

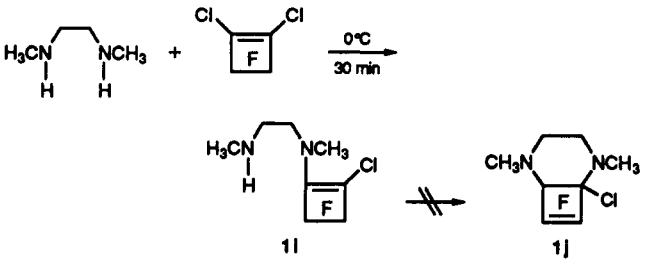


for this spontaneous cyclization is thought to be the formation of a five-membered ring since such processes do not take place with compound **1k** where, if cyclization occurs, a six-membered ring is formed.

To explore this possibility, 1,2-dichloro(tetrafluoro)-cyclobutene-1 and 1,2-dichloro(octafluoro)cyclohexene-1 are each reacted with *N,N'*-dimethylethylenediamine. Owing to the longer reaction time required for 1,2-dichloro-(octafluoro)cyclohexene-1, compounds **1g** and **1h** are found

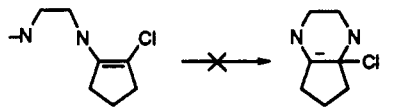


as a mixture when the reaction is terminated. However, as in the case of **1c** cyclizing to **1f**, **1g** reacts slowly to give **1h** while standing at 25 °C. When triethylamine is added, **1h** is the only product observed. In the reaction with 1,2-dichloro(tetrafluoro)cyclobutene-1, formation of compound **1i** is essentially complete after 30 min at 0 °C. Rather



than undergoing internal cyclization, compound **1i** polymerizes slowly at 25 °C. While this is surprising, it may be rationalized in terms of increased bond angle strain at the C-1 position.[23] The cyclic compounds **1g** and **1h** are identified by comparison with ^{19}F NMR data for similar compounds.[24]

It is interesting to note the direction of cyclization. Neither 1,2-dichloro(perfluoro)cyclopentene nor 1,2-dichloro(perfluoro)cyclohexene gives a product which results from intramolecular nucleophilic attack at the carbon bonded to the second chlorine atom, even though the intermediate anion found would be expected to be a stable species.[16,25] This is consistent with the mixture of products obtained when ethylene glycol is reacted with decafluorocyclohexene.[26] The absence of an intermediate structure as below is demonstrated when Tatlow and his co-workers obtain only a spiro product from the cyclization of 1-chloro-2-(2-hydroxyethoxy)nonafluorocyclohexane.[27]



Steric interactions may influence the direction of cyclization. For example, the reactivity of 1-alkoxy-2-chloro-(hexafluoro)cyclopentene with a secondary amine is found to decrease in the order $MeO^- > EtO^- \gg i\text{-}PrO^-$.[28] Bidirectional attack by a variety of nucleophiles is observed only when fluorine and/or chlorine are α to the double bond.[29] Park's reactivity rule implies that attack by a nucleophile will result in the most stable carbanion formation and does work well for attack on olefins that lead to α-chloro as compared to α-fluoro carbanions.[16]

The two new spiro diamines **1f** and **1h** have a distinct peppermint odor and are hydrolytically stable as determined by extended contact with water at 25 °C. Compared to their parent molecules **1c** and **1g**, the peaks observed in the ^{19}F NMR spectra of **1f** and **1h** are shifted upfield. In the infrared spectra, the carbon–carbon double bond stretching band appears at higher frequencies. This indicates that the nitrogen bonded to C-1 is not sp^2 hybridized and that the two rings are not coplanar.

It has been demonstrated that nucleophilic substitution reactions with vinylic halogens activated by electron-withdrawing groups proceed stereospecifically and retain the original *cis* or *trans* configuration.[30] Displacement of chlorine by alkoxide ion from the *trans* isomer of *cis*- and *trans*-2,3-dichloro(hexafluoro)butene-2 is approximately 70% stereospecific, while with the *cis* isomer the stereospecificity is greater than 90%.[31] It is concluded that the reaction proceeds by elimination of chlorine with the formation of a planar carbanion intermediate. Internal rotation is inhibited by the bulky CF_3 group; that is, the stereospecificity of the reaction is kinetically controlled. These investigators carried out a similar study with the same olefins by using $NaBH_4$ in diglyme and $LiAlH_4$ in

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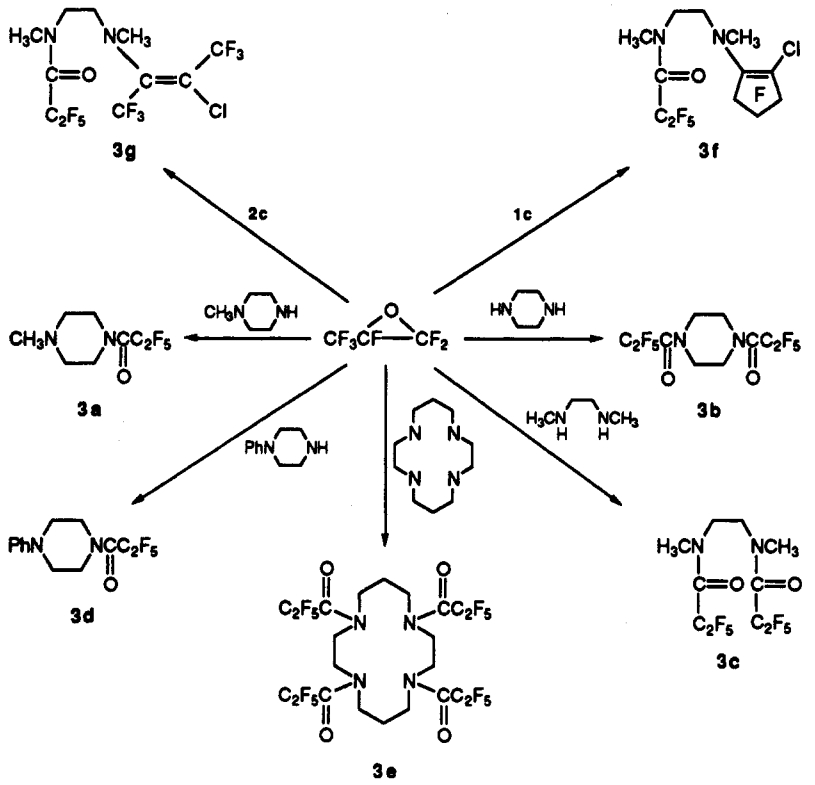
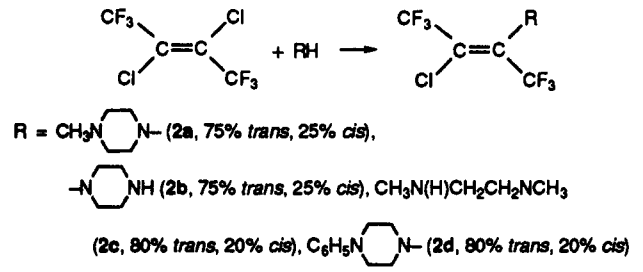
Scheme 1



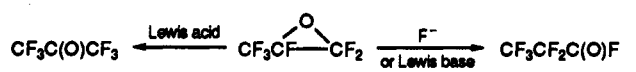
ether as nucleophiles.[32] The less bulky BH_4^- reacts more stereospecifically with the *cis* isomer while the bulkier AlH_4^- reacts more stereospecifically with the *trans* isomer. It is important to note that in our study of the reactions of *trans*-$CF_3C(Cl)=C(Cl)CF_3$ with smaller, rigid heterocyclic amines, such as piperazine and *N*-methyl- and *N*-phenylpiperazines, the reactions are 70–80% stereospecific which is consistent with the alkoxide reactions reported.[20] With the larger, more flexible acyclic *N,N'*-



dimethylethylenediamine, substitution is completely stereospecific as in the case of reaction with $LiAlH_4$.

It is worth noting that no di-N-substituted products are obtained even when the dilithium salt of the acyclic amine is used as the nucleophilic reagent. We find that lithiation of the amine followed by displacement of chlorine from $CF_3C(Cl)=C(Cl)CF_3$ in general requires much longer reaction time than with the cyclic amine and gives rise to lower yields. In addition, purification of the product(s) is also very difficult using this route.

As indicated in Scheme 1, when hexafluoropropylene oxide (HFPO) is reacted with the same diamines, all of the amine hydrogens are displaced resulting in the formation of diamides. Evidently HFPO is a much more potent electrophile than the chlorofluoroolefins. This is perhaps best exemplified by the reaction of 1,4,8,11-tetraazacyclotetradecane with HFPO which results in the formation of the polyamide **3e**. The same product is obtained when $CF_3CF_2C(O)F$ is the electrophile used. Furthermore, when HFPO is reacted with **1c** and **2c**, the amino hydrogens are readily displaced to form the doubly substituted species **3f** and **3g**. One of the most frequently observed reactions of HFPO with nucleophiles is its initial isomerization to perfluoropropionic acid fluoride, $CF_3CF_2C(O)F$, often catalyzed by Lewis bases or fluoride ion. On the other hand, catalytic rearrangement of HFPO in the presence of Lewis acids results in the formation of hexafluoroacetone.[33] Although it is not entirely clear



whether the reaction of HFPO with secondary amines involves the formation of $CF_3CF_2C(O)F$ as an intermediate,[33] in our study of the reactions of HFPO with various heterocyclic/acyclic amines, either with or without KF, only amides are formed.

Experimental Section

All reagents from commercial sources are used as received. They are: piperazine, *N*-methylpiperazine, *N*-phenylpiperazine, *N,N'*-dimethylethylenediamine, *N,N'*-dimethyl-1,3-propanediamine (Aldrich); 1,2-dichlorohexafluorocyclopentene-1, *trans*-2,3-dichlorohexafluorobutene-2, 1,2-dichlorotetrafluorocyclobutene-1, 1,2-dichloro(octafluoro)cyclohexene-1, hexafluoropropylene oxide (PCR).

General Procedure. Gases and volatile liquids are handled in a conventional Pyrex glass vacuum system equipped with a Heise–Bourdon tube gauge and a Televac thermocouple gauge.

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Volatile compounds are measured quantitatively by using PVT techniques. Infrared spectra are recorded with a Perkin-Elmer Model 1710 FT spectrometer and liquid/solid film between NaCl disks. ^{19}F and ^{1}H NMR spectra are obtained on a Bruker AC 200 NMR spectrometer operating at 188.31 and 200.13 MHz, respectively. $CDCl_3$ is used as the solvent. Mass spectra are recorded with a VG 7070 HS mass spectrometer. Melting points are obtained with a Thomas-Hoover apparatus. Elemental analyses are performed by Beller Mikroanalytisches Laboratorium, Göttingen, Germany.

General Method of Preparation. The starting amine (typically 3–7 mmol) is first dissolved in 5–10 mL of dry benzene or tetrahydrofuran (THF) in a 50–100 mL round-bottomed flask equipped with a 14/20 ground glass joint, a rubber septum, and a magnetic stirring bar. Stoichiometric amounts of triethylamine or KF and $ClC{=}C(Cl)(CF_2)_nCF_2$ (n = 1, 2, 3), or CF_3CFCF_2O are added to the reaction flask, and the mixture is stirred at 25 °C. After the reaction, any undissolved solid is removed, and the remaining liquid is washed with approximately 2 mL of water. The organic oil layer is separated and concentrated under vacuum to approximately 1 mL, and the product is purified by Kugelrohr distillation.

Preparation of 1a. Piperazine is first dissolved in benzene, and 2 equiv each of triethylamine and 1,2-dichloro(hexafluoro)-cyclopentene-1 are added. The mixture is stirred at 25 °C for 2 d. The product, a white solid (mp = 186 °C), is obtained in 60% yield following purification by sublimation under vacuum and recrystallization from benzene. Spectral data obtained are as follows: IR (solid film/NaCl) 2938 m, 1637 vs, 1254 vs, 1126 vs, 978 vs cm^{-1}; ^{19}F NMR δ −108.8 (s), −109.5 (s), −129.4 (s); ^{1}H NMR δ 3.68 (s); MS (CI^+) [m/e (species) intensity] (observed isotope ratios are correct) 467 (M^+ − Cl) 19.6, 259 (*N*-(3,3,4,4-tetrafluorobut-1-enyl)piperazyl + 1) 100. Anal. Calcd for $C_{14}H_8F_{12}Cl_2N_2$: C, 33.4; H, 1.60. Found: C, 34.2; H, 1.83.

Preparation of 1b. This compound is obtained as a colorless oil in 30% yield following removal of benzene. Spectral data are as follows: IR (liquid film/NaCl) 3285 w, 2998 m, 2919 m, 2880 m, 2804 m, 1642 s, 1285 s, 1120 s, 981 s, 861 s cm^{-1}; ^{19}F NMR δ −107.9 (s), −109.7 (s), −129.3 (s); ^{1}H δ 1.74 (s, 1H), 2.78 (m, 4H), 3.42 (m, 4H); MS (CI^+) [m/e (species) intensity] (observed isotope ratios are correct) 294 (M^+) 31.8, 275 (M^+ − F) 86.3, 259 (M^+ − Cl) 100. Anal. Calcd for $C_9H_9F_6ClN_2$: C, 36.7; H, 3.06; F, 38.7. Found: C, 37.1; H, 3.20; F, 38.0.

Preparation of $CH_3(H)NCH_2CH_2N(CH_3)C{=}C(Cl)(CF_2)CF_2$ (1c). The reaction mixture is stirred at 25 °C for 4–5 h. The crude product is distilled at 45–47 °C/0.4 Torr to give a colorless oil (30% yield). Spectral data obtained are as follows: IR (liquid film/NaCl) 3310 w, 2946 m, 2854 m, 2805 m, 1641 s, 1476 s, 1412 s, 1334 s, 1273 vs, 1231 vs, 1191 vs, 1120 vs, 1087 vs, 1062 vs, 982 vs, 869 s cm^{-1}; ^{19}F NMR δ −107.3 (d, 2 F), −109.3 (d, 2 F), −128.7 (s, 2 F); ^{1}H NMR δ 1.23 (s, 1H), 2.42 (s, 3H), 2.75 (t, 2H, J_{H-H} = 6.8 Hz), 3.13 (s, 3H), 3.50 (t, 2H); MS (CI^+) [m/e (species) intensity] (observed isotope ratios are correct) 296 (M^+) 0.8, 277 (M^+ − F) 23.3.

Preparation of 1d. The reaction mixture is stirred at 25 °C for 48 h. After the usual workup, the resulting white solid is recrystallized from chloroform to give a 20–40% yield of the product (mp = 68–72 °C). Higher yields are obtained when triethylamine is not used as a base. Spectral data obtained are as follows: IR (solid film/NaCl) 2920 m, 2835 m, 1640 s, 1599 s, 1255 vs, 1236 vs cm^{-1}; ^{19}F NMR δ −108.0 (s), −109.5 (s), −129.2 (s); ^{1}H NMR δ 3.21 (m, 4H), 3.75 (m, 4H), 6.92–7.21 (m, 5H); MS (CI^+) [m/e (species) intensity] (observed isotope ratios are correct) 370 (M^+) 63.1, 351 (M^+ − F) 33.8.

Preparation of 1e. The reaction mixture is stirred at 25 °C for 4 h. Following concentration of the benzene solvent, the product is distilled at 50 °C (0.6 Torr) to give the product as a pale yellow liquid (90% yield). Spectral data obtained are as follows: IR (liquid film/NaCl) 2946 s, 2852 m, 2801 s, 1638 vs, 1459 s, 1430 m, 1381 m, 1363 m, 1299 vs, 1278 vs, 1227 vs, 1191 vs, 1177 vs, 976 vs, 837 vs cm^{-1}; ^{19}F NMR δ −107.9 (s), −109.9 (s), −129.4 (s); ^{1}H NMR δ 2.27 (s, 3H), 2.44 (m, 4H), 3.57 (m, 4H); MS (CI^+) [m/e (species) intensity] (observed isotope ratios are correct) 308 (M^+) 76.9, 289 (M^+ − F) 100. Anal. Calcd for $C_{10}H_{11}F_6ClN_2$: C, 38.9; H, 3.58; F, 37.0; N, 9.08. Found: C, 39.0; H, 3.69; F, 36.9; N, 9.17.

Preparation of $H_3CNCH_2CH_2N(CH_3)CC(Cl){=}CFCF_2CF_2$ (1f). After standing at 25 °C for several days, the mixture containing $CH_3(H)NCH_2CH_2N(CH_3)C{=}C(Cl)(CF_2)_2CF_2$ is distilled at 30 °C (1 Torr) to give this cyclic product, as a colorless oil having a distinct peppermint odor. This compound can also be synthesized from the reaction between $ClC{=}C(Cl)(CF_2)_2CF_2$ and $CH_3N(H)CH_2CH_2N(H)CH_3$ in C_6H_6 in the presence of $(C_2H_5)_3N$ at 25 °C over a period of 3 d. Spectral data are as follows: IR (liquid film/NaCl) 2890 m, 2875 m, 2860 m, 1694 s, 1362 s, 1350 s, 1141 s, 1111 s, 938 s, 838 s cm^{-1}; ^{19}F NMR δ −118.2 (s, 2F), −128.1 (s, 2F), −138.5 (s, 1F); ^{1}H NMR δ 2.25 (s, 6H), 3.03 (m, 2H), 3.15 (m, 2H); MS (CI^+) [m/e (species) intensity] (observed isotope ratios are correct) 276 (M^+) 17.5, 257 (M^+ − F) 25.4, 175 (M^+ − C_2HF_4) 100. Anal. Calcd for $C_9H_{10}F_5ClN_2$: C, 39.06; F, 34.36; H, 3.62. Found: C, 39.27; F, 34.1; H, 3.81.

Preparation of $H_3C(H)NCH_2CH_2N(CH_3)C{=}C(Cl)(CF_2)_3CF_2$ (1g) and $H_3CNCH_2CH_2N(CH_3)CC(Cl){=}CF(CF_2)_2CF_2$ (1h). After stirring the reaction mixture at 25 °C for 3 d, a mixture of **1g** and **1h** is obtained by distillation of the product at 40 °C (1.2 Torr). After standing for an additional 3 d at 25 °C, followed by Kugelrohr distillation (30 °C, 0.8 Torr), or after addition of $(C_2H_5)_3N$, only compound **1h**, which exhibits a characteristic peppermint odor, is obtained in 55–60% yield. Spectral data obtained for **1g** are as follows: IR (liquid film/NaCl) 1605 s, cm^{-1} (C=C); NMR ^{19}F δ −106.1 (s), −109.2 (s), −132.4 (s), −133.9 (s); ^{1}H δ 1.40 (s, 1H), 2.40 (s, 6H), 2.71 (t, 2H, J_{H-H} = 6 Hz), 3.34 (t, 2H). Spectral data obtained for **1h** are as follows: IR (liquid film/NaCl) 2937 m, 2850 m, 1677 m, 1476 m, 1453 m, 1336 s, 1307 s, 1285 s, 1214 s, 1187 s, 1143 s cm^{-1}; ^{19}F NMR δ −117.8 (s, 2F), −123.9 (s, 2F), −124.9 (m, 1F), −132.1 (s, 2F); ^{1}H NMR δ 2.52 (s, 6H), 2.93 (m, 2H), 3.22 (m, 2H); MS (CI^+) [m/e (species) intensity] (observed isotope ratios are correct) 326 (M^+) 7.7, 175 (M^+ − $3CF_2$ − H) 100.

Preparation of $H_3C(H)NCH_2CH_2N(CH_3)C{=}C(Cl)CF_2CF_2$ (1i). The reaction mixture is stirred at 0 °C for 2 h. The product is obtained in 80% yield as a colorless oil by distillation (40 °C, 0.5 Torr). Spectral data obtained are as follows: IR (liquid film/NaCl) 3291 w, 2945 w, 2894 m, 2854 m, 2802 m, 1703 s, 1398 s, 1299 s, 1007 s cm^{-1}; ^{19}F NMR δ −111.2 (s), −114.4 (s); ^{1}H NMR δ 1.13 (s, 1H), 2.41 (s, 3H), 2.77 (t, 2H, J_{H-H} = 6.5 Hz), 3.01 (s, 3H), 3.32 (t, 2H); MS (CI^+) [m/e (species) intensity] (observed isotope ratios are correct) 227 (M^+ − F) 45.3.

Preparation of 1k. The product is a colorless oil which is obtained in 80% yield after stirring the reaction mixture at 25 °C for 2 h. This compound is purified by distillation at 48 °C at a pressure of 0.8 Torr. Spectral data obtained are as follows: IR (liquid film/NaCl) 3292 w, 2945 s, 2800 s, 1638 vs, 1472 s, 1412 s, 1277 vs, 1189 vs, 1122 vs, 1087 vs, 1062 vs, 981 vs cm^{-1}; ^{19}F NMR δ −107.2 (s), −109.4 (s), 128.8 (s); ^{1}H NMR δ 1.0 (s, 1H), 1.77 (m, 2H), 2.39 (s, 3H), 2.57 (t, 2H, J_{H-H} = 6 Hz), 3.09 (s, 3H), 3.47 (t, 3H); MS (CI^+) [m/e (species) intensity] (observed isotope ratios are correct) 289 (M^+ − H_2F) 16.8, 255 (M^+ − Cl − HF) 59.4.

Preparation of 2a. *N*-Methylpiperazine is lithiated with *n*-butyllithium in hexane under nitrogen at −78 °C with stirring. The resulting slurry is warmed to 0 °C and stirred for 10 min. Following cooling to −78 °C, an equimolar amount of 2,3-dichloro-(hexafluoro)-2-butene is added, and the mixture is stirred for 30 min. The reaction mixture is then warmed slowly to 25 °C, the solvent is removed under vacuum, and the products are distilled (65 °C, 0.3 Torr) to give a mixture of *cis* and *trans* (1:3) product as an orange oil in 50% yield. Spectral data obtained are as follows: IR (liquid film/NaCl) 2943 s, 2853 s, 2802 s, 2748 s, 1630 m, 1459 m, 1375 vs, 1290 vs, 1275 vs cm^{-1}; ^{19}F NMR δ −62.23 (s), −62.46 (s), *trans* isomer; −59.69 (q, J_{F-F} = 14 Hz), −60.67 (q), *cis* isomer; ^{1}H NMR δ 2.28, 2.45 (m), 2.99 (br s), 3.11 (m); MS (CI^+) [m/e (species) intensity] (observed isotope ratios are correct)

296 (M^+) 100, 277 ($M^+ - F$) 93.0. Anal. Calcd for $C_9H_{11}F_6ClN_2$: C, 36.4; F, 38.4; N, 9.44; H, 3.71. Found: C, 35.7; F, 39.0; N, 8.96; H, 3.31.

Preparation of 2b. The reaction mixture is stirred in THF for 2–3 d at 25 °C. Any undissolved solid is removed by filtration, and the filtrate is reduced under vacuum to approximately 1 mL. The yellow residue remaining after sublimation (−78 °C) is identified as a *cis/trans* product mixture (1:4). Spectral data obtained are as follows: IR (liquid film/NaCl) 3290 w, 2949 s, 2918 s, 2854 s, 1636 s, 1600 s, 1456 s, 1445 s, 1275 vs, 1242 vs, 1165 vs, 981 vs cm^{-1}; ^{19}F NMR δ −62.53 (s), −62.69 (s), *trans* isomer; −59.73 (q, J_{F-F} = 15 Hz), −60.56 (q), *cis* isomer; ^1H NMR δ 2.77 (s, 1H), 2.90 (s, 8H); MS (CI^+) [*m/e* (species) intensity] (observed isotope ratios are correct) 282 (M^+) 22.8, 263 ($M^+ - F$) 42.1, 247 ($M^+ - Cl$) 100.

Preparation of $H_3C(H)NCH_2CH_2N(CH_3)C(CF_3)=C(Cl)-CF_3$ (2c). Following stirring of the reaction mixture in THF at 25 °C for 24 h, the *trans* isomer is isolated by distillation (50 °C, 1 Torr) as a colorless liquid in 15% yield. Spectral data obtained are as follows: IR (liquid film/NaCl) 3289 w, 2943 s, 2884 s, 1691 s, 1242 vs, 1152 vs cm^{-1}; ^{19}F NMR δ −63.31 (s), −64.08 (s); ^1H NMR δ 1.41 (s, 1H), 2.41 (m, 3H), 2.52 (m, 2H), 2.65 (m, 3H), 3.06 (m, 2H); MS (CI^+) [*m/e* (species) intensity] (observed isotope ratios are correct) 283 ($M^+ - 1$) 19.1, 245 ($M^+ - 2F - H$) 18.1, 167 ($CH_2NCH_3CF_2CCCF_2^+$) 100. Anal. Calcd for $C_8H_{11}F_6N_2Cl$: C, 33.7; H, 3.87; F, 40.1. Found: C, 34.8; H, 3.95; F, 38.9.

Preparation of 2d. The reaction mixture, containing no solvent or base, is stirred for 2–3 d at 25 °C. The products are dissolved in chloroform, and any undissolved solids are removed by filtration. The solvent is removed, and the residue is distilled (Kugelrohr at 50 °C, 1.5 Torr) to give a *cis/trans* (1:4) mixture of isomers as a yellow solid (mp = 40–42 °C). Spectral data obtained are as follows: IR (solid/KBr) 3087 w, 3042 w, 2942 m, 2827 m, 1600 s, 1576 w, 1242 vs, 1142 vs cm^{-1}; ^{19}F NMR −61.93 (s), −62.21 (s), *trans* isomer; −59.70 (q, J_{F-F} = 13 Hz), −60.01 (q), *cis* isomer; ^1H δ 3.07, 3.14 (m, 8H), 6.89, 7.22 (m, C_6H_5); MS (CI^+) [*m/e* (species) intensity] (observed isotope ratios are correct) 358 (M^+) 100.

Preparation of 3a. The appropriate stoichiometric amount of HFPO is condensed into the reaction mixture at −196 °C. The mixture is warmed to 25 °C over a period of 2 h. The product is obtained as a colorless oil by distillation (40 °C, 1.5 Torr). Spectral data obtained are as follows: IR (liquid film/NaCl) 2947 s, 2852 s, 2800 s, 2753 s, 1685 vs, 1330 s, 1298 s, 1230 s cm^{-1}; ^{19}F NMR δ −81.87 (s, 3F), −114.99 (s, 2F); ^1H NMR δ 2.27 (s, 3H), 2.42 (m, 4H), 3.64 (m, br, 4H); MS (CI^+) [*m/e* (species) intensity] 247 ($M^+ + 1$) 88, 119 ($C_2F_5^+$) 42.8. Anal. Calcd for $C_8H_{11}F_5N_2O$: C, 39.0; F, 38.6; N, 11.4. Found: C, 39.2; F, 38.4, N, 11.4.

Preparation of 3b. Piperazine is first dissolved in benzene and the solution is stirred at 25 °C for 10 min. A stoichiometric amount (1:1 with respect to piperazine) of HFPO is added at −196 °C in the absence of triethylamine. After stirring at 25 °C for 24 h, the solids are removed by filtration, dissolved in water, and washed twice with benzene, and the benzene layers are combined. Upon evaporation of the benzene, the product is obtained as a white solid (mp = 78–80 °C) in 90% yield. Spectral data obtained are as follows: IR (solid/KBr) 1710 s, 1251 s, 1246 s, 1147 s, 982 s cm^{-1}; NMR ^{19}F δ −82.38 (s, 3F), −115.07 (s, 2F); ^1H NMR δ 3.70 (s); MS (CI^+) [*m/e* (species) intensity] 379 ($M^+ + 1$) 76.5, 259 ($M^+ - C_2F_5$) 100. Anal. Calcd for $C_{10}H_8F_{10}N_2O_2$: C, 31.75; H, 2.84. Found: C, 31.3; H, 2.12.

Preparation of $CF_3CF_2C(O)N(CH_3)CH_2CH_2N(CH_3)-C(O)CF_2CF_3$ (3c). The amine, *N,N'*-dimethylethylenediamine (7 mmol), is mixed with 1 g of KF in a 50-mL glass vessel equipped with a Teflon stopcock. HFPO (14 mmol) is condensed into the vessel at −196 °C, and the reaction mixture is allowed to warm slowly in a cold Dewar. The product, a colorless oil, is obtained in 30% yield by distillation. Spectral data obtained are as follows: IR (liquid film/NaCl) 2955 w, 1686 s, 1229 s, 1197 s, 1163 s, 1126 s, 1019 s cm^{-1}; ^{19}F NMR δ −82.43 (s, 3F), −116.33 (s, 2F); ^1H NMR δ 3.20 (m, 3H), 3.68 (s, 2H); MS (CI^+) [*m/e* (species) intensity] 381 ($M^+ + 1$) 38.2, 204 ($C_2F_5C(O)N(CH_3)CH_2CH_2^+$) 100. Anal. Calcd for $C_{10}H_{10}F_{10}N_2O_2$: C, 31.58; H, 2.63; F, 50.0. Found: C, 31.75; H, 2.94; F, 49.7.

Preparation of 3d. HFPO (1:1 ratio with piperazine) is condensed into the reaction mixture at −196 °C. The mixture is allowed to warm to 25 °C and stirred at that temperature for 16 h. Following distillation (50 °C, 6 Torr) the product is obtained in 70% yield as a colorless oil which crystallizes slowly at room temperature. Spectral data obtained are as follows: IR (solid/KBr) 3064 w, 3061 w, 2922 m, 2829 m, 1685 s, 1601 s, 1331 s, 1274 s, 1234 s, 1169 s, 1127 s cm^{-1}; ^{19}F NMR δ −82.32 (s, 3F), −119.37 (s, 2F); ^1H NMR δ 3.04 (d, 8H), 6.89–7.25 (m, 5H); MS (CI^+) [*m/e* (species) intensity] 309 ($M^+ - 1$) 43.5, 149 (*N*-C_5H_4-piperazinium + 1) 100. Anal. Calcd for $C_{13}H_{13}F_5N_2O$: C, 50.65; H, 4.31; F, 30.84. Found: C, 50.76; H, 4.22; F, 31.0.

Preparation of $[CH_2N(C(O)C_2F_5)(CH_2)_2N(C(O)C_2F_5)-CH_2]_2$ (3e). Cyclam (0.25 mmol) and triethylamine (1 mmol) are mixed in 1 mL of benzene. HFPO (1.2 mmol) is then condensed into the reaction mixture at −196 °C. After stirring for 3 h at 25 °C, all volatiles are removed under vacuum. The remaining solids are washed with water and recrystallized from chloroform to give the white solid product which decomposes at 220 °C. Spectral data obtained are as follows: IR (solid/KBr) 2974 w, 1683 s, 1666 s, 1209 s, 1183 s, 1132 s, 1050 s cm^{-1}; ^{19}F NMR δ −82.35 (m, 3F), −115.0 (m, 2F); ^1H NMR δ 1.31 (br, 1H), 1.56 (br, 1H), 2.00 (br, 2H), 3.58–3.71 (br, 6H); MS (CI^+) [*m/e* (species) intensity] 785 ($M^+ + 1$) 100, 393 ($M^+/2 + 1$) 50.4. Anal. Calcd for $C_{22}H_{20}F_{20}O_4N_4$: C, 33.67; H, 2.55. Found: C, 33.82; H, 2.97.

Preparation of $C_2F_5C(O)N(CH_3)CH_2CH_2N(CH_3)\overline{C=C(Cl)-(CF_2)_2CF_2}$ (3f). HFPO (5 mmol) is condensed into a flask containing $CH_3N(H)CH_2CH_2N(CH_3)\overline{C=C(Cl)(CF_2)_2CF_2}$ (1.22 g, 4 mmol) and KF (0.4 g). The mixture is allowed to stir at 25 °C overnight. The product, a viscous oil (60% yield) which slowly solidifies at 25 °C, is obtained by distillation (60 °C, 0.6 Torr). Spectral data obtained are as follows: IR (solid/KBr) 2957 s, 1689 vs, 1641 vs, 1334 vs, 1281 vs, 1214 vs, 1120 vs, 1064 vs, 1026 vs cm^{-1}; ^{19}F NMR δ −82.64 (s, 3F), −108.13 (s, 4F), −109.47 (s, 2F), −129.16 (s, 2F); ^1H NMR δ 3.16 (s, 3H), 3.62 (s, 2H); MS (CI^+) [*m/e* (species) intensity] (observed isotope ratios are correct) 443 ($M^+ + 1$) 6.6, 423 ($M^+ - F$) 72.9. Anal. Calcd for $C_{12}H_{10}F_{11}N_2OCl$: C, 32.54; H, 2.26. Found: C, 32.86; H, 2.59.

Preparation of $C_2F_5C(O)N(CH_3)CH_2CH_2N(CH_3)C-(CF_3)=C(Cl)CF_3$ (3g). Following the usual workup of the reaction mixture, a pale yellow impure oil is obtained by distillation (50 °C, 0.6 Torr). The oil is not purified by repetitive distillations. Spectral data obtained are as follows: IR (liquid film/NaCl) 1693 s, 1605 m, 1240 vs, 1192 vs, 1154 vs cm^{-1}; ^{19}F NMR δ −65.87 (s, 3F), −69.04 (s, 3F), −82.49 (s, 3F), −116.34 (s, 2F); ^1H δ 2.5–3.6 (m); MS (CI^+) [*m/e* (species) intensity] (observed isotope ratios are correct) 431 ($M^+ + 1$) 3.1, 240 ($M^+ - CH_2N-(CH_3)C(O)C_2F_5$) 100, 204 ($C_2F_5C(O)N(CH_3)CH_2CH_2^+$) 100.

Acknowledgment. We are grateful for the support of the National Science Foundation (Grant CHE-9003509) and the Air Force Office of Scientific Research (Grant 91-0189) for support of this research. Q.C.M. thanks Yakima Valley College for a sabbatical leave.