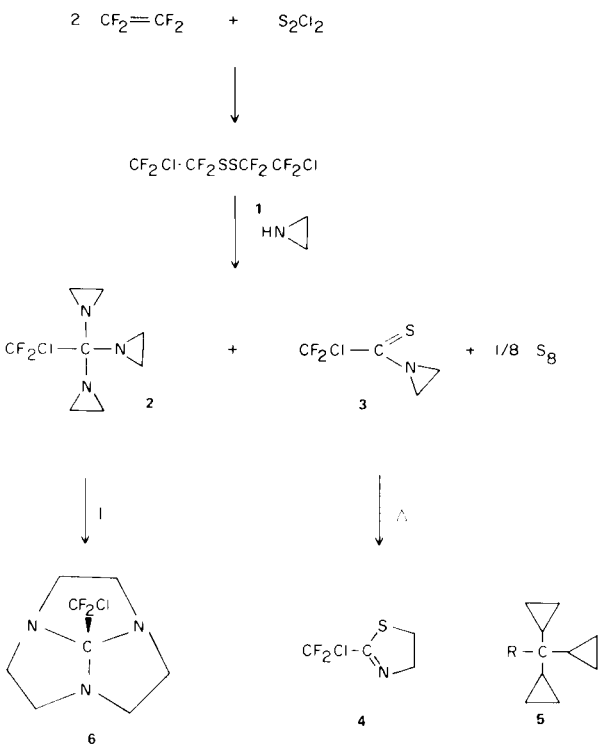
The Reaction of bis-(2-Chlorotetrafluoroethyl) Disulfide with Aziridine

F. Lautenschlaeger

Dunlop Research Centre

The most characteristic behaviour of α-fluorinated ethers is their strong tendency to undergo substitution reactions in the α-position (1). A demonstrative example of this reactivity is the elimination of hydrogen fluoride from perfluorothiols in reactions with nucleophilic reagents (2). For example, complete hydrolysis to inorganic products occurred when trifluoromethylmercaptan was treated with dilute sodium hydroxide (2,3). It has also been shown (4) that in case of aliphatic disulfides, containing strongly electron withdrawing α-substituents, carbon-sulfur cleavage may occur as a result of an initial α-substitution. More recently, such a mode of cleavage was observed on α,β-unsaturated disulfides with primary amines (5). With perfluoroalkyl disulfides, secondary amines lead to sulfur-sulfur bond cleavage (6). We would like to report the reaction of aziridine and several other secondary amines with bis-(2-chlorotetrafluoroethyl) disulfide (**1**), prepared from sulfur monochloride and tetrafluoroethylene (7,8).

The reaction of **1** with amines was observed to occur spontaneously at temperatures of −20 to −60°. With aziridine, exothermic secondary reactions were observed before the crude reaction products reached ambient temperature. The predominant product, 1,1,1-chlorodifluorotriaziridinylethane (**2**), was obtained in a yield of 40%. In addition, the isolation of 1-chlorodifluoromethylthiazoline (**4**) suggests the initial formation of the aziridinyl thioamide **3**. Thermal rearrangement of **3** is not unexpected. Similar thermally or chemically initiated rearrangements of β-substituted aziridines are well known (9). More recent examples are the rearrangements of 2-aroylaziridines or oxazolines (10,11) and 1-thioacylaziridines to 2-arylthiazolines (12) as well as the related rearrangement of 1-thioacylazetidines to 2-substituted dihydrothiazines (13).



The structure of **2** is evident from its spectroscopic characteristics and its chemical behaviour. The nuclear magnetic resonance spectrum (deuteriochloroform) recorded on a JEOL HR-100 spectrophotometer at 33° shows the equivalence of all protons, evidenced by a single signal (δ 1.86 ppm). On decreasing the temperature of the probe to −60°, a separation of the signal into two peaks of equivalent size at δ 2.03 and δ 1.62 ppm occurs. Coalescence of these signals occurs below ambient temperature which may be compared with the coalescence at 41° for aziridinyl adamantane and 25° for 1-*t*-butylaziridine (14), in which cases steric repulsion with the ring hydrogen atoms were assumed to contribute to this relatively low temperature of coalescence. A molecular model of **2** indicates that random flipping and random free rotation of the three aziridinyl groups should be impossible because of steric interactions, and the low temperature of coalescence may be the result of the relative stability of the intermediate planar transition state of the aziridinyl ring.

The isolation of **2** represents the first example of the formation of a substituted triaziridinylmethyl group. The corresponding unsubstituted triaziridinylmethane was reported prior to the publication of these results (15). The formation of a carbon skeleton such as **5** where three three-membered aliphatic rings are attached to one carbon atom has not yet been reported.

Structures of the type **5** with or without heteroatoms in the cyclic groups should lend themselves to an internal cyclization in preference to polymerization, since the probability of reactions between adjacent ring structures

should be higher than intermolecular polymerization. Treatment of **2** with sodium iodide in acetone led to the rearranged tricyclic system 1,4,7-triaza-10-chlorodifluoromethyltricyclo[5.2.1.$0^{4,10}$]decane (**6**) in a yield of 75%. The trivial name azasterane is suggested for the ring skeleton **7** and consequently, 10-chlorodifluoromethylazasterane is suggested for **6**.

The structure of **6** is evident from its nuclear magnetic resonance spectrum (JEOL HR-100). The spectrum shows a multiplet at δ 3.13 ppm (deuteriochloroform), representing the H_A and H_B protons in *endo*- and *exo*-position. A chemical shift difference of approximately 10 cps is observed between H_A and H_B (J_{AB} = 16 cps). Couplings $J_{AA'}$ and $J_{BB'}$ are approximately 6 cps. Molecular models show **6** to be a relatively rigid structure (Fig. 1).

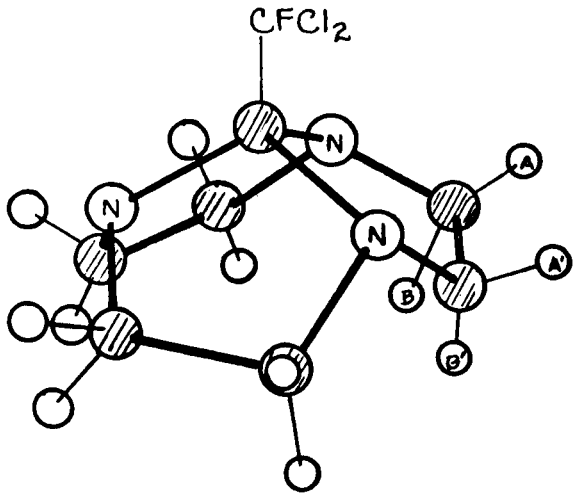
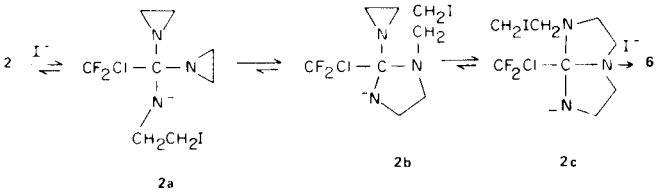


Fig. 1

Significant physical differences were observed between the two isomeric structures **2** and **6**. A melting point increase from 47° to 161° was observed on conversion of **2** to **6**, gas chromatographic retention time increased by a factor of three on an Apiezon chromatography column; also, **6** is water soluble in contrast to **2**. These factors reflect the increased basicity of the nitrogen atoms on conversion from **2** to **6**.

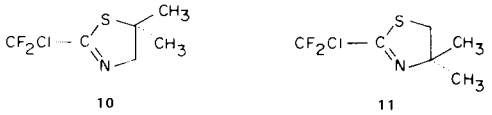
It is of interest to compare the mass spectroscopic fragmentation of both **2** and **6**. In case of **2**, a very weak molecular ion is observed but a fragment ion at m/e 181 and 183 results from the loss of C_2H_4N. In contrast, very few ions of appreciable intensity other than the molecular ion are observed in the case of the more compact structure **6**. The major fragment ion results from the loss of CF_2Cl.

The intramolecular cyclization of **2** to **6** is assumed to involve attack by iodide ion and formation of the intermediate anion **2a**. Displacement of iodide by an adjacent aziridinyl group would lead to **2b**. After a second



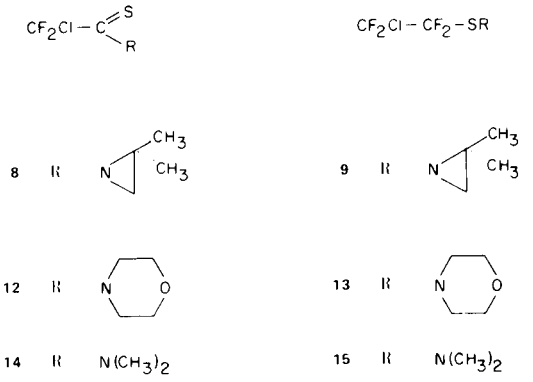
cyclization and formation of **2c**, anionic displacement of iodide ion would give the isomerized product **6**.

Attempts to synthesize homologues of **2** with other secondary amines failed. No evidence for the formation of the trisubstituted product analogous to **2** was obtained with 2,2-dimethylaziridine. In analogy to the reaction of **1** with aziridine, the dimethylaziridinyl derivative **8** was not obtained. Instead, the sulfenamide **9** was isolated in addition to the thiazoline **11**. The formation of **11** presumably results from the intermediate thioamide **8**. The structure **11** in preference to **10** was evident from the

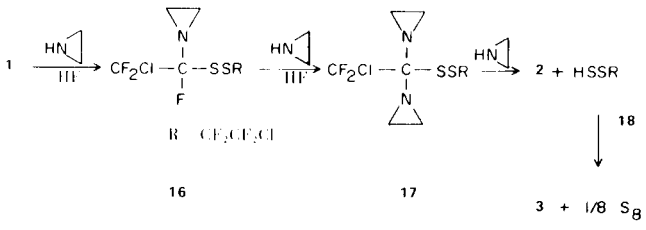


nuclear magnetic resonance spectrum, which shows a single peak for the methyl groups at δ 1.44 ppm (deuteriochloroform) and a singlet for the methylenic protons at δ 3.29 ppm. These chemical shift values are comparable with the signal for the methylene group adjacent to sulfur in structure **4** which is observed at δ 3.50 ppm in contrast to the value of δ 4.42 ppm for the methylene group adjacent to nitrogen.

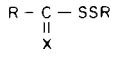
The reactions with morpholine or dimethylamine lead exclusively to a cleavage of the sulfur-sulfur bond and the thioamides **12** and **14** as well as the sulfenamides **13** and **15** were obtained. This result is anticipated in view of earlier reports on the cleavage of perfluoroalkyl disulfides (6). The reaction of **1** with dimethylamine follows a similar path. The thioamide **14** as well as the sulfenamide **15** were isolated as the predominant products.



The scission of the carbon-sulfur bond of **1** with aziridine in contrast to the apparently exclusive scission of the sulfur-sulfur bond of **1** in the reaction with morpholine or dimethylamine represents a difference of carbon- *versus* sulfur-nucleophilicity in these secondary amines. The different behavior of these secondary amines cannot be rationalized as a function of their basicity which was reported to be nearly identical for morpholine (pK_a = 8.45) and aziridine (pK_a = 8.15) (16). It is obvious that of the two alternative initial reactions of **1** with a secondary amine, heterolytic cleavage of the sulfur-sulfur bond or the replacement of an α-fluoride ion, cleavage of the disulfide linkage would account for the reaction products obtained from morpholine and aliphatic secondary amines but not for the formation of **2**. Therefore, in the case of the reaction with aziridine, initial replacement of an α-fluoride ion is assumed, which leads to the intermediate monosubstituted product **16**, where the remaining fluorine atom would become more susceptible to nucleophilic replacement and would lead to the intermediate product **17** in a second replacement step. Subsequent scission of the carbon-sulfur bond to give **2** and **18** would be in analogy to the reaction of disulfides of the structure **19**



where strongly electron withdrawing groups in α-position render the α-carbon atom more susceptible to nucleophilic



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attack than the disulfide linkage (4).

The difference in the reaction of **1** with aziridine and 2,2-dimethylaziridine emphasizes the exceptional behaviour of the unsubstituted aziridine and suggests a steric effect in the two alternative approaches, the substitution of an α-fluoride ion *versus* sulfur-sulfur bond cleavage. However, such conslusions are necessarily of limited value considering the low yield of isolated and identified products in several of the reported reactions.

EXPERIMENTAL

Tetrafluoroethylene was obtained from Pierce Chemical Co., Rockford, Illinois, U.S.A. and was applied as received. Sulfur monochloride was otained from Hooker Chemical Co. Niagara Falls, U.S.A. and was distilled at a reduced pressure of 12 mm prior to use. Amines were purified by distillation prior to use.

Nuclear magnetic resonance spectra were recorded in deuteriochloroform on an JEOL HR-100 instrument (tetramethylsilane as internal standard) and infrared spectra were recorded on a Perkin-Elmer 521 instrument, either in potassium bromide (solids) or neat (liquids). Preparative scale chromatography was carried out on a 776 Hewlett-Packard instrument.

The Reaction of Sulfur Monochloride with Tetrafluoroethylene.

Into a 1 l. Monel-lined steel autoclave containing stainless steel pressure inlet tubing and a thermocouple well was placed 300 g. (2.23 moles) of sulfur monochloride. The system was then thoroughly rinsed with nitrogen and the autoclave heated to 120°. Over a period of 5 hours the autoclave was periodically pressurized with tetrafluoroethylene, not exceeding a pressure of 150 psi. After cooling and flushing the autoclave with nitrogen prior to opening, 697 g. of product was obtained which was distilled as described earlier (8). The yellow product contained small amounts of sulfenyl chlorides which were removed by adding cyclohexene and redistillation after a negative test had been obtained with potassium iodide. The fraction of b.p. 62-64°/60 mm, 410 g. n_D^{20} = 1.3919, was applied in subsequent reactions.

A 5% solution of **1** in acetone containing excess sodium iodide oxidizes iodide spontaneously at ambient temperatures.

The Reaction of **1** with Aziridine, 1,1,1-Triaziridinylchlorodifluoroethane (**2**), and 1-Chlorodifluoromethylthiazoline (**4**).

To a solution of 129 g. (3 moles) of aziridine in 300 ml. of dry methylene chloride, maintained at -40° by external cooling, was added with vigorous stirring over a period of 20 minutes, 100 g. (0.28 mole) of **1**. The solution was allowed to stand at -50° for 48 hours and was then evaporated to dryness on a rotary evaporator at an internal temperature of -10°. During the evaporation, an exothermic reaction proceeded, causing darkening of the product. A brown syrupy residue was obtained. Distillation of the residue yielded **4** in varying amounts (b.p. 37-38°/3 mm Hg; n_D^{20} = 1.4721) up to 16% yield, and **2** (b.p. 64°/0.02 mm Hg) 25 g. (40%), m.p. 47°.

Anal. Calcd. for **2**; $C_8H_{12}ClF_2N_3$: C, 42.96; H, 5.39; N, 18.83; Cl, 15.88. Found: C, 42.81; H, 5.63; N, 18.76; Cl, 16.12; S, 0.

Anal. Calcd. for **4**; $C_4H_4ClF_2NS$: C, 37.98; H, 2.33; N, 8.16; S, 18.65. Found: C, 28.35; H, 2.52; N, 8.36; S, 18.93.

The infrared spectrum of **2** showed major absorptions at 3080, 3000, 1435, 1270, 1225, 1133, 1060, 998, 995 and 810 cm^{-1}. The nmr spectrum showed a single peak at δ 1.86 cps at 30° (deuteriochloroform).

The infrared spectrum of **4** showed major absorption bands at 1622, 1317, 1265, 1235, 1130, 1030, 1000, 880 and 845 cm^{-1}. The nuclear magnetic resonance spectrum (deuteriochloroform) showed the center of the NCH_2 signals at δ 4.42 ppm and the center of the CH_2S signals at δ 3.50 ppm.

1,4,7-Triaza-10-difluoromethyltricyclo[5.2.1.$0^{4,10}$]decane (**6**).

A solution of 2.0 g. of **2** in 30 ml. of acetone and 0.7 g. of sodium iodide was heated for 65 hours under reflux. Gas chromatographic analysis indicated the disappearance of **2** and formation of a new component of longer retention time on an Apiezon column. The solution was decanted, the solvent evaporated and the crystalline residue extracted with pentane. The pentane was evaporated and the crystalline residue sublimed at 60°/1 mm Hg to give 1.5 g. of **6** (75%), m.p. 161.5-163°. The product was well

soluble in common organic solvents and water.

The infrared spectrum showed intense absorption peaks at 2950, 2830, 1490, 1453, 1265, 1250, 1163, 1100, 1050, 1000 and 873 cm^{-1}. The nmr spectrum (deuteriochloroform) showed an ABA'B' pattern centered at δ 3.13 ppm.

Anal. Calcd. for $C_8H_{12}ClF_2N_3$: C, 42.96; H, 5.39; N, 18.81; Cl, 15.88. Found: C, 43.42; H, 5.61; N, 18.78; Cl, 15.81.

The Reaction of **1** with 2,2-Dimethylaziridine. *N*-(2,2-Dimethylaziridinyl)-2-chlorotetrafluoroethanesulfenamide (**9**) and 2-Chlorotrifluoromethyl-4,4-dimethyl-2-thiazoline (**11**).

To a solution of 15.3 g. of **1** (0.0455 mole) in 100 ml. of methylene chloride which was cooled to −60° was added 14.5 g. (0.137 mole) of finely powdered anhydrous sodium carbonate. To the rapidly stirred suspension was added a solution of 28 g. (0.394 mole) of 2,2-dimethylaziridine over a period of 30 minutes. After stirring at −50° for 3 hours, the suspension was allowed to warm up, filtered, the solvent was distilled off and 38.7 g. of product was distilled off at 0.005 mm without fractionation. Attempts to identify non-volatile products were unsuccessful. Gas chromatographic analysis of the distilled portion showed two products. Separation of 1 g. by preparative gas chromatography gave 0.32 g. of **9**, n_D^{20} 1.4140 and 0.22 g. of **11**, n_D^{20} 1.4554.

The nuclear magnetic resonance spectrum of **9** (deuteriochloroform) showed two single peaks at δ 1.88 (CH_2) and δ 1.30 ppm (CH_3) in the proportion 1:3. Major infrared absorption bands were observed at 2980, 2965, 1457, 1448, 1375, 1325, 1237, 1160, 1110, 1060, 1030, 935, 905 and 820 cm^{-1}.

Anal. Calcd. for $C_6H_8ClF_4NS$: C, 30.31; H, 3.37; N, 5.89. Found: C, 30.60; H, 3.39; N, 5.90.

The nuclear magnetic resonance spectrum of **11** (deuteriochloroform) showed two single peaks at δ 3.29 (CH_2S) and δ 1.44 ppm (CH_3) in a proportion 1:3. Major infrared absorption bands were observed at 2970, 1625, 1362, 1190, 1174, 1132, 1076, 1023, 900 and 845 cm^{-1}.

Anal. Calcd. for $C_6H_8ClF_2NS$: C, 36.09; H, 4.01; S, 16.04. Found: C, 36.47; H, 4.17; S, 15.68.

The Reaction of **1** with Morpholine. Chlorodifluoromethyl-4-morpholinothioamide (**12**) and *S*-Morpholino-2-chlorotetrafluoroethanesulfenamide (**13**).

To a solution of 2.7 g. (0.008 mole) of **1** with 50 ml. of methylene chloride was added 4.35 g. (0.05 mole) of morpholine at 25°. After a mild exotherm, the solution was allowed to stand at ambient temperature for 24 hours and then evaporated. The semicrystalline residue was extracted with 40 ml. pentane to leave 2.9 g. of crystalline morpholine hydrofluoride, identified by its nuclear magnetic resonance spectrum and comparison of its infrared spectrum with an authentic sample.

On cooling the pentane solution to −20°, 1.2 g. of yellow crystals of **12** separated, m.p. 57-61°. Sublimation at 40°/1 mm Hg produced an analytically pure sample, m.p. 60.5-62°.

Anal. Calcd. for $C_6H_8ClF_2NOS$: C, 33.49; H, 3.75; N, 6.51; Cl, 16.47. Found: C, 33.83; H, 3.93; N, 6.55; Cl, 16.55.

The mother liquor of **12** (1.3 g.) was distilled under reduced pressure to give 0.4 g. of **13**, for which no physical constants are available.

Anal. Calcd. for $C_6H_8ClF_4NOS$: C, 28.8; H, 3.13; Cl, 13.97; N, 5.52; S, 12.62. Found: C, 29.0; H, 3.39; Cl, 13.96; N, 5.85; S, 12.82.

The Reaction of **1** with Dimethylamine. Chlorodifluoromethyl-*N*,*N*-diethylthioamide, (**14**) and *N*,*N*-Dimethyl-2-chlorotetrafluoroethanesulfenamide (**15**).

Into 50 ml. of methylene chloride which was cooled to −55° was condensed 45 g. (1 mole) of dimethylamine. To this solution was added 21 g. (0.059 mole) of **1** and the reaction mixture was maintained at −55° for 2 hours and then allowed to warm up to room temperature, washed with water; the organic layer was dried over magnesium sulfate and distilled to give the following fractions: a) 60°/140 mm; 9.0 g.; and b) 47°/0.05 mm Hg, 6.5 g.; n_D^{20} 1.5181. Fraction a) was identified as **15**.

The compound showed major infrared absorption bands at 1158, 1100, 1012, 900 and 800 cm^{-1}.

Anal. Calcd. for $C_4H_6ClF_4NS$: C, 22.69; H, 2.87; N, 6.61. Found: C, 22.70; H, 2.97; N, 6.30.

Fraction b) was identified as **14**. The compound showed major infrared absorption peaks at 1518, 1387, 1200, 1150, 1125, 1050, 1025, 920 and 840 cm^{-1}.

Anal. Calcd. for $C_4H_6ClF_2NS$: C, 27.67; H, 3.46; N, 8.07; S, 18.44; Cl, 20.46. Found: C, 27.95; H, 3.57; N, 8.24; S, 18.50; Cl, 20.58.

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