Synthesis of Polyfluorinated Heterocycles by Indirect Fluorination with Silver Fluorides. V. Fluorothiophene[1,2]

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Reaction of tetrachlorothiophene with silver difluoride gave 2,2,5,5-tetrafluoro-3,4-dichlorothiolene. Experiments were carried out to exchange halogen atoms of chlorinated and brominated 2,5-dimethylthiophenes with fluorine by means of silver fluoride. Only these halogen atoms were substituted by fluorine which were attached to methyl groups. An attempt to force the replacement of the β-bonded chlorine atoms of 2,5-bis(trifluoromethyl)-3,4-dichlorothiophene by means of silver difluoride resulted in opening and desulfurization of the thiophene ring, thereby forming 1,1,1,2,5,6,6,6-octafluoro-3,4-dichlorohexadiene-3,4.

The direct fluorination of thiophene gave only cleavage products instead of fluorinated thiophene.[3,4] The only reported preparation of a compound with fluorine attached to the thiophene nucleus is the synthesis of 2-fluorothiophene from 2-iodothiophene by means of arsenic trifluoride in nitromethane. The yield in this case, however, was very low.[5]

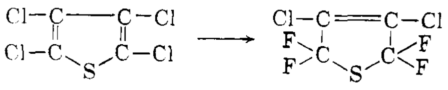
As part of a comprehensive study of the preparation of fluorinated heterocyclic compounds.[2,6–9] our investigations were extended to thiophenes. In our first experiments we attempted the fluorination of ring halogenated thiophenes. For this purpose, the reaction of tetrabromothiophene (I)[10] and tetrachlorothiophene (II)[11] with metal fluorides such as silver fluoride, silver difluoride, or mercuric difluoride was investigated.

Surprisingly, I and II did not react with excess silver fluoride or mercuric difluoride. This is in contrast to our observations on other heterocyclic compounds[2,6–8] in which under the same conditions replacement of chlorine atoms by fluorine could be easily accomplished. Reaction of the tetrahalothiophenes could not be achieved even on heating with silver fluoride to 220°.

In an attempt to use silver difluoride for the fluorination of the tetrabromo compound I, the reaction was so violent that complete decomposition of I occurred. Although also the reaction of silver difluoride with the corresponding tetrachloro compound II could not be controlled, even when carried out in an ice bath, a considerable amount of a fluorine-containing product was isolated. Analytical data and molecular weight determination indicated the composition $C_4Cl_2F_4S$. Based on the evaluation of the NMR spectrum, this compound is believed to be 2,2,5,5-tetrafluoro-3,4-dichlorothiolene-3 (III). The spectrum consists of a single line with no fine structure indicating that the fluorines are equivalent. The chemical shift using the classical side band technique was found to be $\tau = 73.76$ p.p.m., relative to trichlorofluoromethane. The observed value is consistent with NMR data reported for perfluoroalkylsulfur fluorides.[12]

There are other possible chemical isomers having the empirical formula $C_4Cl_2F_4S$, but in all cases the fluorine atoms would not be equivalent.

Apparently, III is formed by 1,4-addition of fluorine to the conjugated system besides substitution of the more reactive α-chlorine atoms by fluorine. Hexachlorothiolene-3 from which III may have been derived by partial fluorination was not present in the starting material (II). Analogous to our findings in other heterocyclic systems,[7,8] replacement of the β-chlorine atoms by fluorine could not be achieved.



II III

This observation was also confirmed when our investigations were extended to thiophene derivatives with halogenated methyl groups in the 2- and 5-positions.

The perhalogenation of dimethylthiophene was difficult. Thus, the attempt to prepare 2,5-bis-

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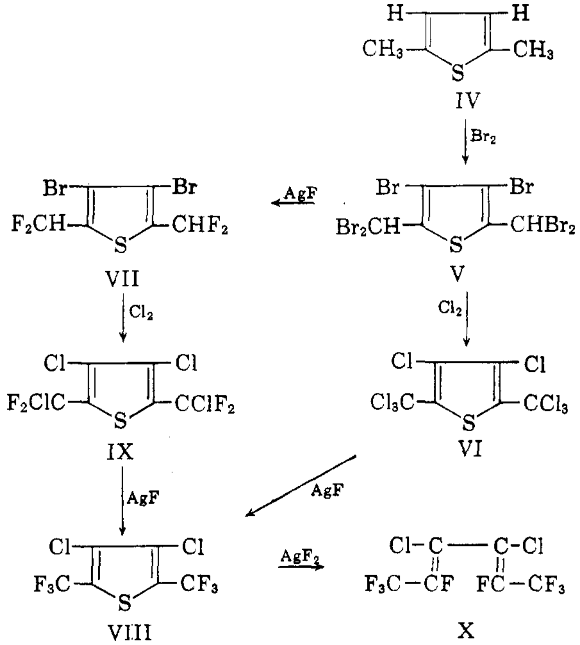
(tribromomethyl)-3,4-dibromothiophene,[13] using a large excess of bromine and ultraviolet irradiation, resulted only in the formation of 2,5-bis(dibromomethyl)-3,4-dibromothiophene(V).[14] However, a perhalogenated 2,5-dimethylthiophene—that is, 2,5-bis(trichloromethyl)-3,4-dichlorothiophene (VI)—was prepared by chlorination of V in refluxing carbon tetrachloride with ultraviolet irradiation.

Treatment of VI and of the partially brominated 2,5-dimethylthiophene (V) with silver fluoride resulted, surprisingly, in the exchange of the halogen atoms on the methyl groups by fluorine to give 2,5-bis(trifluoromethyl)-3,4-dichlorothiophene (VIII) and 2,5-bis(difluoromethyl)-3,4-dibromothiophene (VII), respectively. Compound VII was subsequently chlorinated to yield 2,5-bis(chlorodifluoro)-3,4-dichlorothiophene(IX) which, upon treatment with silver fluoride, gave also 2,5-bis(trifluoromethyl)-3,4-dichlorothiophene (VIII). Attempts to exchange the chlorine atoms in the β-position with fluorine by heating with excess silver difluoride at 130° resulted in a vigorous reaction which gave an oil, the analysis of which is in accord with the compound 1,1,1,2,5,6,6,6-octafluoro-3,4-dichlorohexadiene-3,4 (X). This ring cleavage reaction with elimination of the sulfur atom is the reverse of the synthesis of thiophene derivatives by reaction of butadiene derivatives with sulfur.[15] No reaction occurred when 2,5-dimethyl-3,4-dichlorothiophene (XI) or 2,5-dimethyl-3,4-dibromothiophene (XII)[16] was treated with silver fluoride. These findings and the observation that fluorination of II, V, VIII, and IX with silver fluoride or silver difluoride did not result in the exchange of the β-halogen atoms, support also for the thiophene system the fact that α-halogen atoms of aromatic heterocyclic systems are rather reactive, whereas halogen atoms in β-position are very firmly bonded. Apparently, the electron withdrawing effect even of the α-trihalomethyl groups in VI, VIII, and IX is not sufficient to promote exchange of the halo atoms in β-position.



Experimental[17]

Tetrabromothiophene (I) was prepared in a quantitative yield from commercial 2,5-dibromothiophene and excess bromine. **Tetrachlorothiophene** (II), b.p. 232°, n^{28}_D 1.5904 was obtained from 2,5-dibromothiophene in a 80% yield upon chlorination in boiling carbon tetrachloride. Chlorine addition products were thermally decomposed on distillation at normal pressure.

2,2,5,5-Tetrafluoro-3,4-dichlorothiolene-3 (III).—Tetrachlorothiophene (10 g.) was added to excess silver difluoride (30 g.) at 0°. Immediately, a vigorous reaction was observed with evolution of white fumes and some gaseous material. Distillation from the silver salts yielded 5.2 g. (51%) of crude reaction product. The combined material from four runs was distilled twice over silver difluoride and rectified by using a Widmer column. Thus, III (18.5 g., 45%), b.p. 117–119°, n^{31}_D 1.4269, was obtained.

Anal. Calcd. for $C_4Cl_2F_4S$: C, 21.25; Cl, 31.37; F, 33.62; S, 14.15; Mol. wt., 226. Found: C, 21.17, 21.24; Cl, 31.07, 30.92; F, 33.60, 33.73; S, 14.10, 14.04; mol. wt., 248, 259.

2,5-Bis(trichloromethyl)-3,4-dichlorothiophene (VI).—Chlorine was passed through a boiling solution of 20 g. of 2,5-bis(dibromomethyl)-3,4-dibromothiophene in 100 ml. of carbon tetrachloride with ultraviolet irradiation for 24 hr. After evaporation of the solvent, a viscous oil remained which, after distillation *in vacuo* (b.p. 144–145° (5 mm.), n^{24}_D 1.6079), deposited some crystals on standing, presumably the 2,5-bis(dichloromethyl)-3,4-dichlorothiophene, m.p. 83–86° (lit.[14]: m.p. 80°). The oil proved to be slightly impure VI.

Anal. Calcd. for C_6Cl_8S: C, 18.58; Cl, 73.14; S, 8.26. Found: C, 17.84, 17.85; Cl, 71.46, 71.76; S, 7.95, 7.76.

2,5-Bis(difluoromethyl)-3,4-dibromothiophene (VII).—2,5-Bis(dibromomethyl)3,4-dibromothiophene (39 g.) was mixed with excess silver fluoride (100 g.) by grinding in a mortar (if the starting materials are not pure, reaction can occur upon mixing the components due to frictional heating) and heated in an oil bath. At 107°, a vigorous reaction occurred and the reaction product partly sublimed into the reflux condenser. The reaction product was distilled from the silver salts *in vacuo* to give VII (18.5 g., 81%), b.p. 113° (18 mm). Upon recrystallization from alcohol–water, leaflets, m.p. 54–56°, were obtained.

Anal. Calcd. for $C_6H_2Br_2F_4S$: Br, 46.74; F, 22.22. Found: Br, 45.58; F, 22.09.

2,5-Bis(difluorochloromethyl)-3,4-dichlorothiophene (IX).—Chlorine was passed through a boiling solution of 44.2 g. of VII in 100 ml. of carbon tetrachloride with ultraviolet irradiation. After 5 hrs., the evolution of bromine ceased. To complete the reaction, the introduction of chlorine was continued for an additional 5 hr. Distillation *in vacuo* afforded IX (36.2 g., 89%); b.p. 76–80° (5 mm.); b.p. 218–219° (760 mm.); n^{25}_D 1.5008.

Anal. Calcd. for $C_6Cl_4F_4S$: C, 22.39; Cl, 44.05; S, 9.94. Found: C, 21.62, 21.62; Cl, 44.95, 44.66; S, 9.83, 9.84.

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2,5-Bis(trifluoromethyl)-3,4-dichlorothiophene (VIII).—IX (27.5 g.) was added to excess silver fluoride (90 g.) and heated in an oil bath. At 115°, a smooth reaction started which was completed at 150°. Distillation *in vacuo* and rectification by using a Widmer column yielded VIII (13.2 g., 54%); b.p. 46–50° (7 mm.); b.p. 173–174° (760 mm.); $n^{27}D$ 1.4402.

Anal. Calcd. for $C_6Cl_2F_6S$: C, 24.93; Cl, 24.53; F, 39.44. Found: C, 24.72, 24.83; Cl, 24.72, 24.44; F, 39.22, 39.00.

The same product VIII (4.2 g., 43%) was obtained from VI (13 g.) and excess silver fluoride (60 g.) upon heating in an oil bath; $n^{15}D$ 1.4438.

1,1,1,2,5,6,6,6-Octafluoro-3,4-dichlorohexadiene-3,4 (X).—VIII (4.5 g.) was added to silver difluoride (10 g.) and heated in an oil bath. At 93°, the reaction started and became vigorously with evolution of white fumes at 130°. The temperature was maintained for several minutes and, after cooling, the liquid reaction product was distilled from the silver salts. Fractionation yielded X (1.4 g., 33%); b.p. 122–124°; $n^{21}D$ 1.3558.

Anal. Calcd. for $C_6Cl_2F_8$: C, 24.42; F, 51.52. Found: C, 24.13, 24.33; F, 53.00, 53.37; S, traces (qualitative chlorine test was positive).

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The Preparation and Polymerization of *p*-Vinylbenzyl Ethers

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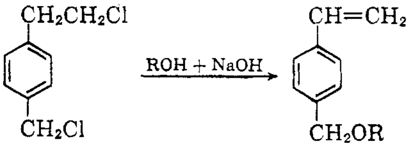
p-Vinylbenzyl ethers were prepared by the action of alcoholic base on *p*-(β-chloroethyl)benzyl chloride. The reaction proceeded successfully for normal and secondary alcohols, but tertiary alcohols and phenols did not give the desired product. These ethers were polymerized to give products which were soft and extensible at room temperature when the ether group was larger than butyl. Normal alkyl or alkoxyethyl ethers gave polymers having a gradual reduction in glass temperature as the length of the substituent group was increased. Polymers from the branched ethers and those containing a terminal hydroxyl on the substituent group gave glass temperatures well above the corresponding *n*-alkyl ethers. By comparison of the glass temperatures of the *p*-vinylbenzyl *n*-alkyl and ethoxyalkyl ethers with those of *p*-*n*-alkylstyrenes it was found that these values depend only on the number of atoms in the substituent group on the benzene ring and not on whether these atoms are carbon or oxygen.

When *p*-(β-chloroethyl)benzyl chloride[2] was allowed to react with an alkali metal hydroxide in an alcohol, the product was the corresponding *p*-vinylbenzyl ether. Nucleophilic replacement of the benzyl chlorine and dehydrohalogenation occurred in a single reaction step:



The reaction proceeded smoothly and in good yield. Polymerization in the final distillation step complicated recovery of the product and precluded careful fractionation of all but the lowest members of the series. Phenylenediamine and diphenylpicrylhydrazine were the best inhibitors found for this distillation. Hydroquinone proved to be too volatile especially in the case of the higher boiling members and sulfur gave contamination of the distilled monomer which interfered with subsequent polymerization steps.

All primary and secondary alcohols gave the desired product. *t*-Butyl alcohol gave a sluggish reaction and no *t*-butyl ether was obtained. Instead some impure *p*-vinylbenzyl alcohol and a small yield of a crystalline compound, m.p. 60°, tentatively identified as 4,4′-divinyldibenzyl ether were the only products isolated. Phenol did not give the expected *p*-vinylbenzyl phenyl ether but led to much more complicated products which were not identified. The only *p*-vinylbenzyl ether previously reported was the optically active *sec*-butyl ether by Marvel and Overberger.[3]

The *p*-vinylbenzyl ethers were polymerized in solution at 120° using di-*t*-butyl peroxide as initiator. Toluene or methanol was used as a solvent. The polymerization conditions used were chosen such that approximately a 60–85% conversion was obtained. These conditions were chosen to minimize gelation of the polymer which results when the polymerization is allowed to proceed to higher conversion or run at lower temperatures. We believe this tendency to cross-linking is due to extensive chain transfer at the benzyl hydrogen sites in the monomer and polymer. Cross-linking by chain transfer to polymer has been reported for other monomers such as methyl acrylate or vinyl acetate.[4]

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(1) Address inquiries concerning this paper to the above at Western New England College, Springfield 9, Massachusetts.

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