

# ELECTROPHILIC TRICHLOROMETHYLATION OF SOME HALOGENATED THIOPHENES

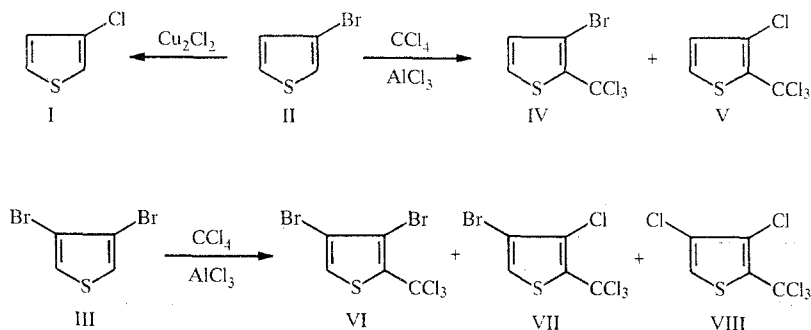
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*The electrophilic trichloromethylation of 3-chloro-, 3-bromo-, and 3,4-dibromothiophene was studied. It is shown that reaction is directed towards position 2, accompanied by frequent formation of the corresponding substituted di-(2-thienyl)dichloromethane. Trichloromethylation of  $\beta$ -bromothiophenes is complicated by exchange of chlorine for bromine under the reaction conditions.*

Earlier [1] we showed the possibility of trichloromethylation of 2,4- and 2,5-dichlorothiophene by carbon tetrachloride in the presence of aluminum chloride, using methylene chloride or excess carbon tetrachloride as solvents. Reaction with 2,4-dichlorothiophene proceeds smoothly, leading in high yield to 3,5-dichloro-2-trichloromethylthiophene, and in the case of the 2,5-dichloride which is complicated by isomerization, to a mixture of isomeric 2,5-dichloro-3-trichloromethyl- and 3,5-dichloro-2-trichloromethylthiophene. In both cases, the steric shielding of the trichloromethyl group by the chlorine atom holds to a minimum the undesirable 'coupling' reaction with the formation of the corresponding substituted dithienyldichloromethane.

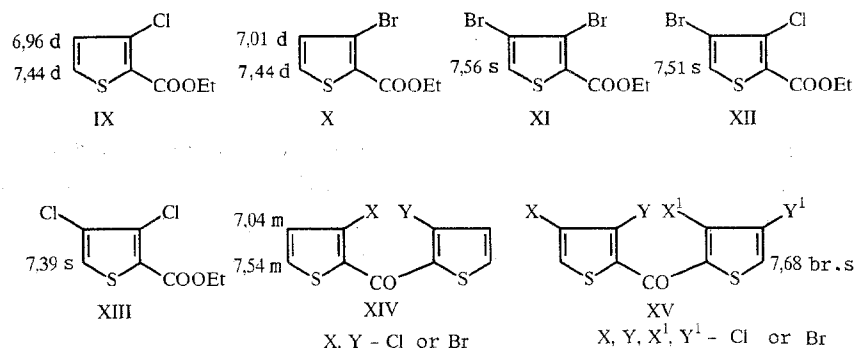
In view of these results, halogenated thiophenes having two free  $\alpha$ -positions were selected as objects for further study: 3-chlorothiophene (I), 3-bromothiophene (II), and 3,4-dibromothiophene (III). These compounds rather easily undergo trichloromethylation, although in the cases of the bromides II and III the reaction was complicated by partial halogen exchange.

According to GLC-MS and  $^1\text{H}$  NMR spectroscopy, the bromides II and III gave trichloromethylation products as well as the substituted dithienyldichloromethanes (in ratios of nearly 1:0.7 and 1:1.7, respectively). Thus, from 3-bromothiophene was obtained a mixture containing 3-bromo-2-trichloromethylthiophene (IV) and 3-chloro-2-trichloromethylthiophene (V) in a ratio of 2:1, and from the dibromide III an analogous mixture of 3,4-dibromo (VI) and 4-bromo-3-chloro-2-(trichloromethyl)thiophene (VII) in a ratio of VI:VII = 11:1, containing a trace of 3,4-dichloro-2-trichloromethylthiophene (VIII).



Since our preparation of 3-chlorothiophene I from the bromide II by the method of [2] is known to contain significant admixture of the starting bromide (according to [2], 3-chlorothiophene has a purity of 85 to 98%), the trichloromethylation products contained significant quantities of 3-bromo-2-trichloromethylthiophene IV in addition to the 3-chloro-2-trichloromethylthiophene V (ratio of V:IV  $\sim$  2:1). The ratio of trichloromethylation products to 'coupled' materials was near 1:0.5.

The composition of the mixtures presented above was established from the integral curves in the  $^1\text{H}$  NMR spectra of samples obtained after treatment of the reaction product with ethanol in the presence of sulfuric acid (see [1]), the result of which is the transformation of the trichloromethyl group into the corresponding ethyl esters (IX-XII), and the dithienyldichloromethanes into the substituted-2-thienyl ketones (XIV, XV). The latter were determined only as total ketones. The value of the chemical shift and the characteristic multiplets of the protons of the thiophene ring used for analysis are presented in the formulas below.



The chemistry of the halogen exchange under trichloromethylation conditions is apparently the same as that in obtaining 3-chlorothiophene I from the bromide II by the method of [2]. The aluminum chloride and the HCl produced in the trichloromethylation reaction may be the source of the chlorine, which can react with excess bromides II or III or with the substitution products IV and VI. Similar processes have been observed earlier by us [3] and other investigators [4-6] upon bromination of carbonyl compounds in the furan series in the presence of aluminum chloride using hydrocarbons as solvent.

## EXPERIMENTAL

The  $^1\text{H}$  NMR spectra were obtained with JEOL FX-90Q (90 MHz) and Bruker WM-250 (250 MHz) instruments in  $\text{CDCl}_3$ .

Chromatographic analyses were carried out on an LKhM-80 ("Khromatograf" Plant) gas chromatograph with flame ionization detection, a  $2 \times 1500$  mm stainless steel column of 5% SE-30 on Chromosorb R in isothermic (150-160°C) and linear programmed (130-200°C, 8 deg/min) temperature regimes.

Mass spectra were obtained with a Varian MAT CH-6 mass spectrometer with direct introduction of the sample into the ionization chamber (ionization energy = 70 eV, emission current = 100  $\mu\text{A}$ ) and a Varian MAT-111A chromatomass spectrometer (ionization energy = 70 eV, emission current = 500  $\mu\text{A}$ ) with a 25 m capillary column, stationary phase = SE-30.

Elemental analysis data for C, H, Br, and S corresponded with the calculated values for compound XI.

**Starting Materials.** 3-Chlorothiophene (I), bp 83-90°C (100 mm Hg) was synthesized from the bromide II by treatment with  $\text{CuCl}$  according to [2] and contained ~20% admixture of starting bromide (by GLC).

3-Bromothiophene II was obtained by debromination of 2,3,5-tribromothiophene by zinc in acetic acid by a known method [7], bp 46°C/12 mm Hg.  $^1\text{H}$  NMR spectrum: 7.26 (2H, bs, 2-H and 5-H); 7.06 (1H, qu, 4-H).

3,4-Dibromothiophene III was obtained analogously from tetrabromothiophene, bp 97-100°C/12 mm Hg.  $^1\text{H}$  NMR spectrum: 7.31 (2H, s).

**Electrophilic Trichloromethylation of Halothiophenes I-III.** To a suspension of 3.5 g (0.026 mole) of anhydrous  $\text{AlCl}_3$  in a boiling (40°C) mixture of 10 ml of  $\text{CCl}_4$  and 40 ml of  $\text{CH}_2\text{Cl}_2$  was added dropwise with energetic stirring a solution of 0.01 mole of the thiophene compound in a mixture of 6 ml  $\text{CCl}_4$  and 7 ml of  $\text{CH}_2\text{Cl}_2$  over 40 min. The boiling was continued for about 1 h more and then the mixture was kept at room temperature for 3 h and poured over ice. The organic layer was separated, the water was extracted with methylene chloride, and the combined extract was washed with water, 1% NaOH, water, and dried over  $\text{CaCl}_2$ . The solvent was removed and the residue (before or after vacuum distillation) was transformed into a mixture of ethyl esters of the corresponding carboxylic acids by boiling in ethanol in the presence of a catalytic amount of concentrated sulfuric acid. The trichloromethylation of 3-chlorothiophene I and 3-bromothiophene II under conditions described above gave mixtures which, after formation of the ethyl esters, were studied by GLC,  $^1\text{H}$  NMR, and MS.

Assignments of signals in the  $^1\text{H}$  NMR spectra were carried out with the help of data from [1] for esters of isomeric dichloro-2-thiophene carboxylic acids, and also the previously known samples of ethyl esters of 3-bromo- (X) and 3,4-dibromo-2-thiophene (XI) carboxylic acids.

Column chromatography on silica gel (eluent: heptane–ether, 10:1) of the mixture of esters IX and X obtained by treatment with ethanol of the products of trichloromethylation of 3-bromothiophene, gave isolated ester X, bp 170-180°C (bath temperature)/8 mm Hg,  $M^+$  234.  $^1\text{H}$  NMR spectrum: 7.41 (1H, d, 5-H); 7.02 (1H, d, 4-H,  $J_{45} = 5.5$  Hz); 4.31 (2H, qu,  $\text{CH}_2$ ); 1.35 (3H, t, Me,  $J = 7$  Hz), which correspond with data from [8]. Yield 26%.

The ester XI was prepared from 3,4-dibromothiophene by the action of  $\text{EtOCHCl}_2$  (from ethyl formate and  $\text{PCl}_5$ ) in the presence of  $\text{TiCl}_4$  to give 3,4-dibromo-2-thiophenealdehyde, mp 107°C (from heptane), see [9], yield 89%. Treatment of the latter under Jones conditions gave the corresponding carboxylic acid, mp 205-207°C (from benzene), see [10], yield 93%. Esterification of this acid (with ethanol in the presence of catalytic  $\text{H}_2\text{SO}_4$ ) gave the ethyl ester of 3,4-dibromo-2-thiophene carboxylic acid XI,  $\text{C}_7\text{H}_6\text{Br}_2\text{O}_2\text{S}$ , mp 62-63°C (from heptane).  $^1\text{H}$  NMR spectrum: 7.57 (1H, s, 5-H); 4.35 (2H, qu,  $\text{CH}_2$ ); 1.45 (3H, t, Me,  $J = 7$  Hz). Yield 70%.

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