Proton Magnetic Resonance of Thiophenes. X. On the Mechanism of Side-chain Couplings in Methylthiophenes *

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It has earlier been shown that a methyl group in the 2-position of thiophene couples with the hydrogen in the 3-position with a coupling constant of 1.00—1.15 c/s and to the 4-hydrogen with 0.2—0.5 c/s [1], these two couplings being of opposite sign [2]. Likewise a methyl group in the 3-position couples with hydrogen 2 with 0.9—1.25 c/s and to the 4- and 5-hydrogens with 0.4—0.5 c/s [1]. These side-chains couplings have been ascribed to hyperconjugation [1,3,4] and on this assumption one would expect [5] a coupling between the methyl groups of 2,3-dimethylthiophene of about 1 c/s as it has been demonstrated that the attenuation factor of the π-electron contribution to the couplings in going from an aromatic proton to a methyl group proton is approximately minus one.

Corio and Weinberg [4] studied the spectrum of 2,3-dimethylthiophene at 60 Mc/s and found no coupling between the α-hydrogen and either of the two methyl groups. The greater broadening of the β-hydrogen as compared to that of the α-hydrogen was ascribed to coupling of the former with the 3-methyl group [4]. The present authors have reinvestigated the spectrum of 2,3-dimethylthiophene and found in addition that the methyl group bands were appreciably broadened due to unresolved fine-structure, which was ascribed to a coupling $J_{CH_3-CH_3}$ [1].

As the magnitude of this latter coupling is a measure of the π-electron contribution to the side-chain couplings in methylthiophenes we have investigated the spectra of 2,3-dimethylthiophenes, substituted in the 4- and 5-positions with non-coupling substituents in order to avoid the additional broadening of the methyl group peaks caused by coupling to the ring hydrogens.

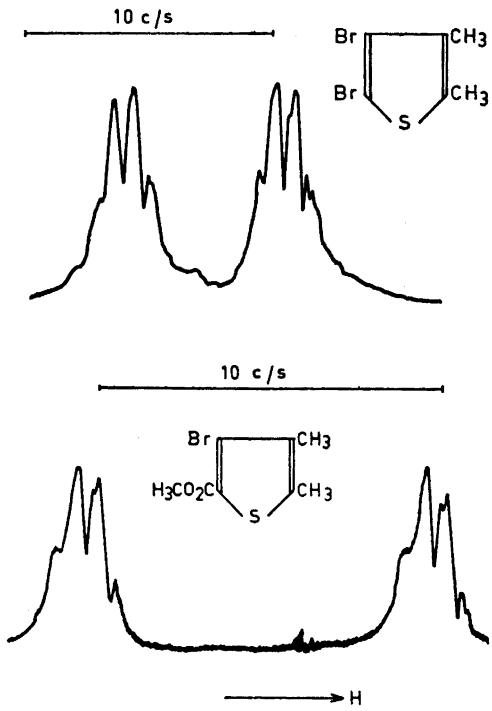

Fig. 1. Methyl group resonance in the 40 Mc/s NMR-spectrum a) of liquid 2,3-dimethyl-4,5-dibromothiophene; b) of methyl 2,3-dimethyl-4-bromo-5-thiophenecarboxylate in *cyclo*-hexane (27 wt%).

2,3-Dimethyl-4,5-dibromothiophene was prepared through bromination of 2,3-dimethylthiophene [7] in CS_2 solution. Through halogen-metal interconversion with *n*-butyllithium followed by carbonation the 2,3-dimethyl-4,5-dibromothiophene was converted to 2,3-dimethyl-4-bromo-5-thiophenecarboxylic acid, the methyl ester of which was obtained through reaction with diazomethane.

The spectrum of 2,3-dimethyl-4,5-dibromothiophene (Fig. 1a) displays two 1:3:3:1 quartets due to the coupling $J_{CH_3-CH_3}$ equal to 0.75 ± 0.10 c/s. The splitting of the two largest peaks in each quartet has the value of 0.73 ± 0.10 c/s, and one-third of the separation between the two outermost components equals to 0.68 ± 0.04 c/s. The difference between these two values can be ascribed to the

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partial overlapping of the quartet components, which reduces the separation of the overlapping lines, thereby introducing a systematic error of the order of 0.05 c/s. Similarly in methyl 2,3-dimethyl-4-bromo-5-thiophenecarboxylate (Fig. 1b) a coupling $J_{CH_3-CH_3} = 0.60 \pm 0.10$ c/s is observed. Due to the low solubility of 2,3-dimethyl-4-bromo-5-thiophenecarboxylic acid in non-polar solvents the spectrum was recorded in dimethyl sulphoxide solution (37 wt %). The methyl group spectrum so obtained consists of two bands in which the splitting only of the central lines of the quartets were resolved. The lower resolution obtained in this case might be due to strong intermolecular association. From the resolved splitting we obtain $J_{CH_3-CH_3} = = 0.55 \pm 0.10$ c/s.

We have earlier used the method of methyl substitution to demonstrate that the coupling between the thiol and ring protons in thiophenethiols is dominated by a π-electron contact mechanism [1] and that this mechanism does not account for the sidechain couplings of 2-thiophenealdehydes [1,6]. The fact that the coupling $J_{CH_3-CH_3}$ in substituted 2,3-dimethylthiophenes is only slightly smaller than J_{CH_3-2} in 3-methylthiophene or J_{CH_3-3} in 2-methylthiophene proves that the largest contribution to the side-chain couplings in the methylthiophenes is also due to π-electron interactions.

Experimental. *2,3-Dimethyl-4,5-dibromothiophene.* To an ice-cold solution of 22.4 g (0.20 mole) of 2,3-dimethylthiophene [7] in 120 ml of dry carbon disulphide was added dropwise 64 g (0.20 mole) of bromine in 40 ml of carbon disulphide. After standing over-night the solvent was distilled off, the residue refluxed for 4 h with 12 g of potassium hydroxide in 15 ml of methanol and then steam-distilled. The organic layer of the distillate was taken up in ether, dried and fractionated, yielding 30.3 g (56 %) of 2,3-dimethyl-4,5-dibromothiophene, b.p. 129–130°/15 mm Hg, $n^{20}D = 1.6030$. (Found: C 26.50; H 2.15; Br 58.94. Calc. for $C_6H_6Br_2S$ (270.0): C 26.69; H 2.24; Br 59.23). Though this preparation analysed correctly, the NMR-spectrum revealed the presence of small amounts of impurity which, however, did not cause any complication in the interpretation.

2,3-Dimethyl-4-bromo-5-thiophenecarboxylic acid. 37 ml of 1.35 N *n*-butyllithium was added to 12.0 g (0.044 mole) of 2,3-dimethyl 4,5-dibromo-thiophene in 50 ml of dry ether at −70° in the usual nitrogen-swept four-necked flask. After 10 min, the mixture was poured onto solid carbon dioxide covered with ether. The reaction mixture was hydrolyzed with water and the ether phase extracted with 2 N sodium hydroxide. On acidification with 2 N hydrochloric acid, the combined aqueous phase yielded 8.2 g (79 %) of crude acid which was recrystallized from aqueous methanol. M.p. 222–224°. (Found: C 35.90; H 3.00; Br 33.67. Calc. for $C_7H_7BrO_2S$ (235.1): C 35.76; H 3.00; Br 33.99;)

Methyl 2,3-dimethyl-4-bromo-5-thiophenecarboxylate. An ethereal solution of diazomethane was added drop-wise to an ice-cooled solution of 1.09 g (0.0046 mole) of 2,3-dimethyl-4-bromo-5-thiophenecarboxylic acid in 40 ml of ether until the yellow diazomethane colour persisted. Removal of the ether gave 0.9 g (78 %) of the methyl ester which crystallized from petrol-ether in needles, m.p. 64–65°. (Found: C 38.37; H 3.79; Br 31.84. Calc. for $C_8H_9Br_2S$ (249.1): C 38.57; H 3.64; Br 32.07.)

The NMR-spectra were obtained with a Varian Associates model V 4300B high resolution spectrometer operating at 40.00 Mc/s and a flux-stabilized 12 in magnet equipped with shim-coils from the same company. The magnet sweep was calibrated with the modulation sideband technique.

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