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PARTIALLY FLUORINATED HETEROCYCLIC COMPOUNDS.
PART V.[1] NUCLEOPHILIC AND ELECTROPHILIC SUBSTITUTION REACTIONS OF 4,5,6,7-TETRAFLUOROBENZO[b]THIOPHEN.

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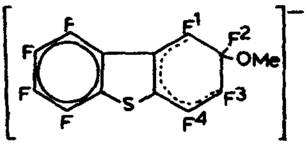
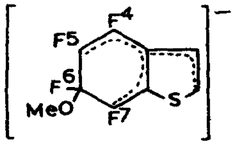
We have reported the preparation of 4,5,6,7-tetrafluorobenzo[b]thiophen (I)[2] and it was of interest to determine the behaviour of this compound towards nucleophilic replacement of fluorine and electrophilic replacement of hydrogen.

(I), when treated with sodium methoxide in methanol gave 6-methoxy-4,5,7-tetrafluorobenzo[b]thiophen (m.p. 40-41° from light petroleum b.p. [40-60°]) and two unidentified isomers in the ratio of 86:7:7 respectively. The structure of the major product and the isomer ratio was based on the analysis of the ^1H and ^{19}F n.m.r. spectra of the mixture of methoxytrifluoroethylbenzenes (b.p. 145°) which was obtained by treatment of the mixture of methoxytrifluorobenzo[b]thiophen compounds with Raney nickel in boiling ethanol. The major product, 4-methoxy-2,3,5-trifluoroethylbenzene had coupling constants which were only consistent with this structure. Thus from the proton spectrum J^{ortho}_{H-F} was 11·4 c/sec; J^{meta}_{H-F}, 6·5 c/sec; and J^{para}_{H-F}, 2·5 c/sec. From the fluorine spectrum J^{ortho}_{H-F} was 11·2 c/sec; J^{meta}_{H-F}, 6·6 c/sec; and J^{para}_{H-F}, 2·7 c/sec; and J^{ortho}_{F-F} was 20·0 c/sec; J^{meta}_{F-F}, 4·0 c/sec; and J^{para}_{F-F}, 13·3 c/sec. The methoxyl proton was a triplet due to the two fluorine atoms ortho to it coupling equally to the extent of 1·0 c/sec.[3] All these coupling constants are of the magnitude to be expected for this type of system.[4]

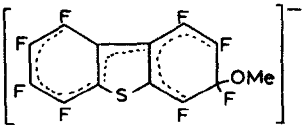
The reaction of sodium methoxide with octafluorodibenzothiophen (II) has been shown to effect replacement of the 2-fluorine atom[5] and was explained on the basis of an intermediate (III) in which the negative charge is stabilised by the sulphur atom.



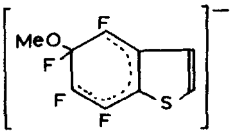
(III)



(IV)



(VI)



(V)

The reaction of (I) with methoxide mainly at position 6, reported here, can be explained on the basis of an intermediate (IV) in which the negative charge can again be stabilised by the sulphur. (IV) is energetically more favourable than the second most likely intermediate (V) which would proceed by replacement of the fluorine atom at position 5. Replacement of the 3-fluorine atom in (II), however, would have required an intermediate (VI) in which the aromatic system of the second benzene ring would have been disrupted and this could explain, in part, the difference between the two systems.

We have also investigated the behaviour of 4,5,6,7-tetrafluorobenzo[b]thiophen (I) towards electrophilic replacement of hydrogen by the treatment of (I) with acetyl chloride and anhydrous aluminium trichloride in carbon disulphide at room temperature. The crude reaction product was shown to contain at least 85% of one isomer on the basis of a strong singlet at τ 1·15 (in acetone); a weak doublet at τ 1·5 could have been due to the other isomer. The major product was shown to be 3-acetyl-4,5,6,7-tetrafluorobenzo[b]thiophen (m.p. 132-134° from benzene-light petroleum [b.p. 60-80°]) by treatment with Raney nickel to give an alcohol which was shown to be 3-(2',3',4',5'-tetrafluorophenyl)-butan-2-ol (b.p. 128-130°) from its ^{1}H n.m.r. There were four regions of absorption: a multiplet at τ 3·0 due to the aromatic proton coupling with the ring fluorine atoms; a multiplet at τ 6·1 due to the 2-proton; a multiplet at τ 7·o due to the 3-proton which was overlapped by a singlet from the hydrogen of the hydroxyl group; and two overlapping doublets centred at τ 8·8 due to two methyl groups. The proton at position 3 in 4,5,6,7-tetrafluorobenzo-[b]thiophen is clearly most susceptible to replacement by the acetylium ion. The reaction of benzo[b]thiophen itself under similar conditions with the same reagents gave 88% of the 3-acetyl compound and 12% of the 2-acetyl compound.[6]

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