S-Alkylthiophenium Salts

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Summary The n.m.r. spectra of *S*-alkylthiophenium salts, obtained from thiophens with silver tetrafluoroborate and alkyl halides and which are powerful alkylating agents, are consistent with a pyramidal arrangement for the sulphur–carbon bonds.

A VIOLENT explosion took place on one occasion during the *S*-alkylation of thiophen by methyl iodide in the presence of silver perchlorate when the large excess of thiophen previously employed[1] was reduced. We therefore replaced the silver perchlorate by the tetrafluoroborate[2] and using 1,2-dichloroethane as solvent obtained *S*-methyl and *S*-ethyl derivatives from a number of alkylthiophens, alkyl-, bromo-, and chloro-benzo[*b*]thiophens, and dibenzo[*bd*]thiophen. The thiophenium salts were isolated as the tetrafluoroborates, or occasionally as the hexafluorophosphates or perchlorates. A carbonyl substituent at position 2 of the thiophen prevented alkylation. Benzo[*b*]thiophen with silver tetrafluoroborate and di-iodomethane, 1,2-dibromoethane, isopropyl iodide, and phenethyl bromide gave the corresponding 1-iodomethyl-, 1-(2-bromoethyl)-, 1-isopropyl-, and 1-phenethyl-benzo[*b*]thiophenium tetrafluoroborates. Increasing the number of electron-donating substituents, and particularly the addition of each fused benzene ring, increased the yield and stability of the thiophenium salts.

The n.m.r. spectra of the salts showed the *S*-methyl groups as singlets (τ 6·63—6·80) and the aromatic protons appeared at lower field than those of the parent heterocycles. The main features of the aromatic region of the 1-alkylbenzo[*b*]thiophenium salts was the presence of the 7-proton at τ 1·6—1·8 and the greater downfield shift, relative to the parent benzo[*b*]thiophen, of the 3- than of the 2-proton.

Although a normal A_2X_3 resonance was observed for the ethyl group of 1-ethylbenzo[*b*]thiophenium tetrafluoroborate and its 3-methyl derivative, nonequivalence of the methylene protons of the ethyl group was observed in the 3-bromo-compound and in all the 2-substituted (Me, Br, $PhCH_2CH_2$, PhCH : CH·) derivatives. The ABX_3 system gave rise to an apparent 10- or 12-line multiplet from the AB part of the spectrum. The observed spectra were simulated accurately using a 7-spin computer programme.[3] The chemical-shift difference for protons A and B at 100 MHz. varied from 10 Hz. for the 3-bromo-compound to 36·2 Hz. for the 2-phenethyl derivative, and the spectra of 1-ethyl-2,3,5-trimethylbenzo[*b*]thiophenium tetrafluoroborate in deuteriochloroform and methyl cyanide were essentially the same. The nonequivalence of the methylene protons is explained if the bonds from the sulphur atom are not coplanar, as is the case for sulphoxides.

The u.v. spectra of the thiophenium salts differed from those of the corresponding thiophen but resembled those of thiophen 1-oxide[4] and 1,1-dioxide[5] by possessing maxima at 267—285 nm. The fine structure of the u.v. spectra of the benzo[*b*]thiophens was lost on *S*-alkylation and longer-wavelength maxima appeared at 267—280 and 299—315 nm.

In the mass spectrometer the *S*-substituent was lost so readily that the molecular ion was detected only in one instance, the base peak always being due to the parent heterocycle. The most significant fragment observed above the base peak was at *m/e* ($M^+ - 1$) but in only one instance did this have a relative intensity of greater than 8%. The thiophen ring probably expands when the hydrogen atom is lost.

The *S*-alkylthiophenium salts all decomposed to the parent heterocycle in hydroxylic solvents, decomposition being much faster in methanol than in water. Kinetic measurements of the solvolysis of the benzo[*b*]thiophenium salts showed that (a) the 1-ethyl salts were solvolysed faster than their 1-methyl analogues, (b) the rates of hydrolysis of both were accelerated by hydroxyl ion but the 1-ethyl salts reacted more slowly than the 1-methyl compounds under these conditions, (c) the rates of solvolysis of both 1-methyl and 1-ethyl salts increased with a reduction in the dielectric constant of the solvent, *i.e.* in the order EtOH > MeOH > H_2O, and (d) electron-releasing substituents in the benzo[*b*]thiophen ring decreased the rate of solvolysis while electron-attracting substituents caused an increase. These results suggest that solvolysis of the 1-ethyl salts proceeds largely by an S_N1 mechanism but S_N2 kinetics are followed in the presence of hydroxyl ion.

1-Methylbenzo[*b*]thiophenium tetrafluoroborate at room temperature methylated pyridine, acridine, and 2-methylbenzotriazole, and dimethyl sulphoxide on the oxygen atom. As some methylating agents have anti-tumour properties Dr. C. Chester Stock kindly arranged for a number of the *S*-alkylthiophenium salts to be screened at the Sloan–Kettering Institute for Cancer Research, but no activity was observed.

Bromination of 1-methylbenzo[*b*]thiophenium tetrafluoroborate gave either 2,3-dibromo-2,3-dihydro-1-methylbenzo[*b*]thiophenium tetrafluoroborate or 2,3-dibromobenzo[*b*]thiophen, while bromination of 5-methyldibenzo[*bd*]thiophenium tetrafluoroborate yielded 2,8-dibromodibenzo[*bd*]thiophen.

These results suggest a difference in the bonding used by the sulphur atom in the *S*-alkylthiophenium salts from that of the parent thiophen. Less interaction between the lone-pair on the sulphur atom of these salts with the π-electrons of the 5-membered ring would be expected and a consequent reduction in aromaticity as occurs in the formal conversion of thiophen into the 1-oxide and 1,1-dioxide.

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