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SYNTHESIS AND SOME PROPERTIES OF S-ALKYLTHIOPHENIUM IONS

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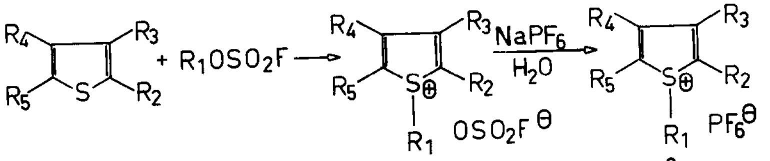
A method that has been described for the preparation of S-alkylthiophenium salts involves alkylation of thiophenes with silver tetrafluoroborate (or perchlorate) and methyl or ethyl iodide.[1,2] Yields are low however (3-12%). We have examined alternative syntheses of these species with the objective of raising the yields to a point where examination of the chemistry can be carried out. We report here positive results in this area.

Method A: Alkylation on sulphur by methyl and ethyl esters of fluorosulphonic acid.[3] The results are shown below. In the case of 1b salt 3b was a component of a complex reaction mixture.



1 2 3

a) $R_1=CH_3$; $R_2=R_3=R_4=R_5=H$ Yield 2a : nihil
b) $R_1=R_2=R_5=CH_3$; $R_3=R_4=H$ Yield 2b : 15%
c) $R_1=R_2=R_3=R_4=R_5=CH_3$ Yield 2c : > 95%
d) $R_1=R_2=R_5=CH_3$; $R_3=R_4=CH_2D$ Yield 2d : > 95%
e) $R_1=C_2H_5$; $R_2=R_3=R_4=R_5=CH_3$ Yield 2e : > 95%

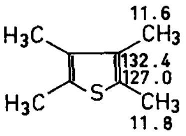
The following procedure is representative. Thiophene 1c, 2.80 g (20.0 mmoles), and 2.80 (24.6 mmoles) CH_3OSO_2F were allowed to react at 80°C for three hours under exclusion of moisture On addition of the cooled reaction mixture to a saturated solution of $NaPF_6$ in ice-water 5.70 g

1,2,3,4,5-pentamethylthiophenium hexafluorophosphate 3c precipitated (95% yield), m.p. 94.0-94.5°C The structural assignment is based on the correct elemental analysis (found: C, 35.8; H, 5.1; S,10.8%; calculated: C,36.0; H, 5.0; S, 10.6%) and on the PMR data (δ 2.08 (s, 6H, 3,4-diMe), 2.31 (s, 6H, 2,5-diMe), 3.07 (s, 3H, 1-Me)); unambiguous peak assignment was done using dideuterocompound 3d. In the case of $C_2H_5OSO_2F$ it is important to keep the reaction temperature below 30°C in order to prevent the formation of significant amounts of byproducts. Under otherwise identical conditions, the reaction time is about 48 hours at room temperature. 1-Ethyl-2,3,4,5-tetramethylthiophenium hexafluorophosphate 3e could be purified only after repeated dissolution in methylene chloride and precipitation with n-pentane (PMR data: δ 1.08 (t, J=7.0 Hz, 3H, 1-$CH_2\underline{CH_3}$), 2.16 (s, 6H, 3,4-diMe), 2.32 (s, 6H, 2,5-diMe), 3.77 (q, J=7.0 Hz, 2H, 1-$\underline{CH_2}CH_3$)).

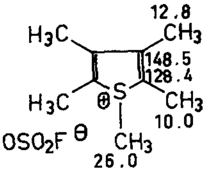
Method B: Since method A does not constitute a satisfying synthesis for compounds 3a and 3b, the method of Acheson and Harrison[2] was modified in the following manner in order to increase the yield. Methyl iodide (4.0 ml) was introduced with stirring to a suspension of 2.30 g (11.8 mmoles) $AgBF_4$ in 25 ml of thiophene compound 1a (or 1b) at 0°C over at least half an hour. When all the iodide had been added, the stirring was continued for two hours, the last hour at room temperature. Filtration and extraction of the precipitate with ice-water and addition of 2.00 g (12.0 mmoles) $NaPF_6$ to the combined filtrate and extracts gave 1.70 g (7.0 mmoles) 3a (or 1.90 g (7.0 mmoles) 3b) (60 % yield based on the intake of $AgBF_4$). The higher yields compared to those obtained by Acheson and Harrison are probably due to the fact that the thiophenes themselves are used as the solvent.

The reaction mixture obtained by method A is dark purple; this colour arises from an impurity. Since no ESR signal could be detected in this mixture it is unlikely that the colour is due to radicals or radical cations. In order to investigate whether the S-alkylation is a normal bimolecular process, a kinetic study was made of the reaction between 1c and CH_3OSO_2F. The reactions were carried out under pseudo first - order conditions, the molar ratio of 1c: CH_3OSO_2F being 1:20, and they were followed by PMR spectroscopy till at least 75% completion. Good first-order rate constants were obtained from which the enthalpy of activation $\Delta H^{\neq}$ was calculated to be 17.3 kcal.mole^{-1} and the entropy of activation $\Delta S^{\neq}$ to be -20 e.u..

It is interesting to see what changes occur in the chemical and spectroscopic behaviour of the thiophene skeleton on alkylation of sulphur. The U.V. spectra of thiophenium salts are known to resemble those of the corresponding sulphoxides and sulphones rather than those of the parent thiophenes.[2,4,5] Another sensitive physical method for detecting changes in the thiophene skeleton on S-alkylation is CMR spectroscopy. By taking the CMR spectra of 1c, 1d, 2c and 2d in CH_3OSO_2F solution using Fourier transform and by considering also the proton noise decoupled spectra, all absorptions could be assigned.[6] The proton noise decoupled spectra of 1d and its salt 2d show in the aliphatic region a singlet due to methyl carbon atoms at positions 2 and 5 and a triplet due to methyl carbon atoms 3 and 4, the latter splitting being due to coupling with deuterium. The CMR spectra show furthermore that each ring carbon atom couples most strongly with its nearest hydrogens as judged from the width of the absorption signals. The CMR chemical shifts of 1c and 2c (expressed in ppm from external TMS) are given below[7]:

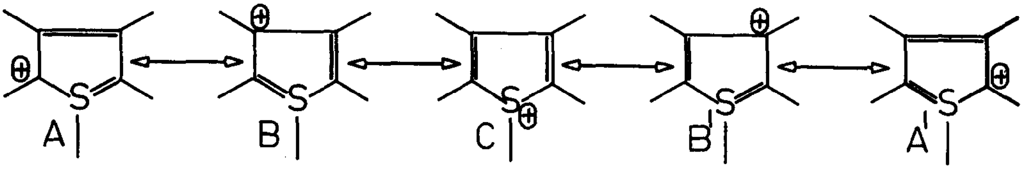


1c



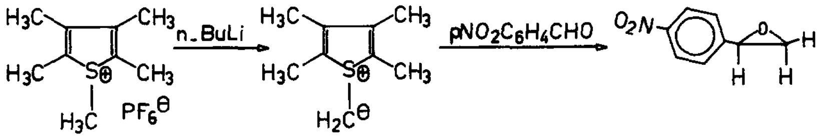
2c

Although the difference in CMR chemical shifts of ring carbon atoms 2 and 5 in the compounds 1c and 2c is negligible (Δ= 1.4 ppm), there is a remarkable difference in chemical shifts of ring carbon atoms 3 and 4 (Δ=16.1 ppm). This probably indicates that the amount of positive charge on these atoms increases considerably when going from the neutral compound 1c to the positively charged ion 2c. In a simple valence-bond picture one might visualize this by assuming structures B and B' to be relatively important.



Our interest in the chemistry of the thiophenium salts[8,9] brought us to study the reactivity of these salts in Diels-Alder reactions. Attempted reactions involve 3c and perfluorobutyne-2 (90°C; 60 hrs), dicyanoacetylene (80°C, 8 hrs) or perfluorobenzyne (35° C, 2 hrs). Lack of reactivity in these cases indicates that the thiophenium salts are less reactive than the corresponding thiophenes[10,11] and sulphones.[12] Therefore it may be concluded that methylation on sulphur in thiophenes gives an overall decrease in reactivity towards Diels-Alder reactions: the effect of some loss of aromaticity is apparently smaller than the effect of the positive charge of the thiophenium ion.

We have looked for a base capable of proton abstraction affording the corresponding thiophenium methylide. With NaOMe (in CD_3OD) and $KOBu^{tert}$ (in CD_3CN) both at room temperature only demethylation was observed. However, on treating a solution of 60 mg 3c in CD_3CN at -45° C with 0.2 ml 1.5 N n-BuLi in ether a new compound was observed by PMR spectroscopy (δ 1.97 (s, 6H, 3,4-diMe) 2.25 (s, 6H, 2,5-diMe), 2.68 (s, 2H, 1-CH_2)), to which we assign structure 4.[13] Trapping of the ylide 4 generated by 4.0 ml 1.5 N n-BuLi (6.0 mmoles) in a THF solution of 1.20 g (4.0 mmoles) 3c by 1.00 g (6.6 mmoles) p-nitrobenzaldehyde gave 0.10 g (0.6 mmoles) of epoxide 5[14] (yield 15%):



3c 4 5

The formation of epoxide 5, albeit obtained in low yield in the preliminary experiments, constitutes additional evidence for the existence of 2,3,4,5-tetramethylthiophenium methylide in solution

Footnotes and references:

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