Activation of Weak Organic Bases: the Alkylation of *NN*-Disubstituted Sulphonamides

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Summary Methylation of the *NN*-disubstituted sulphonamides (IIIa,b) by dimethoxycarbonium hexachloroantimonate (II) gave the crystalline *N*-methylated salts (IVa,b), which afforded methyl amine derivatives on acid hydrolysis.

THE behaviour of weak organic bases in highly acidic media has been studied extensively and valuable information concerning the protonation site and carbonium ion species have been obtained.[1] However, alkylation could be superior to protonation in some cases for activating these weak bases.[2] We report the first isolation of the sulphonamidium salts (IVa,b) by alkylation of the sulphonamides (IIIa,b) and the hydrolysis of these activated species leading to N–S bond cleavage.

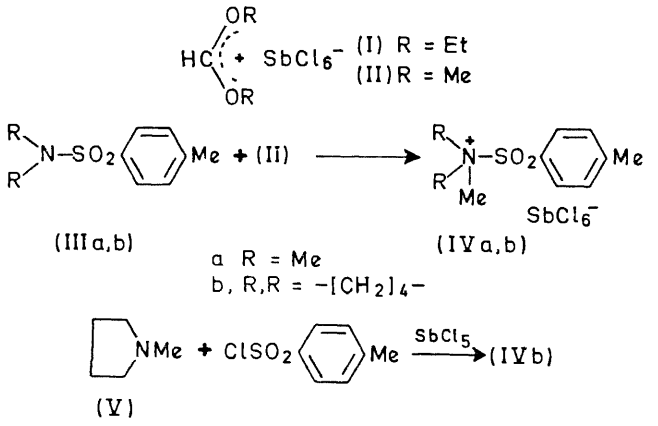
We reported previously that sulphonamides are inert towards triethyloxonium tetrafluoroborate;[3] the more reactive diethoxycarbonium hexachloroantimonate (I)[4] has been used for the present work. The crystalline salt which was obtained from (I) and *p*-toluenesulphonpiperidide, however, was exclusively the protonated species, in which the proton could be coming from the ethyl groups in the reagent (I). Recently, it has been reported that the protonation of sulphonamides takes place on nitrogen.[5] This assignment would hold in the present case, as well.

This difficulty was overcome by using the dimethoxycarbonium ion (II)† which could not provide a proton. An equimolar mixture of the *NN*-dimethylsulphonamide (IIIa) and (II) in CH_2Cl_2 was allowed to stand overnight, giving the crystalline product (IVa)‡ in 60% yield (crude), m.p. 111—112° (after recrystallization from a mixture of CH_2Cl_2 and CCl_4). Similarly, the salt (IVb),‡ m.p. 111—112° (after recrystallization from the same solvent system), was prepared from the sulphonpyrrolidide (IIIb) and (II) in 80% yield (crude).

† The compound (II) was prepared from trimethyl orthoformate by the same procedure as that for (I) and subjected to the reaction without isolation because there was practically no difference in solubility between (II) and the by-product ($MeOSbCl_4$) in the solvent (CH_2Cl_2).

‡ Satisfactory elemental analyses were obtained for (IVa) and (IVb).

The n m r spectrum of the salt (IVa) in CD_3NO_2 exhibits a sharp singlet at τ 6 64 (9H), which strongly suggests that the alkylation occurs on nitrogen rather than on oxygen

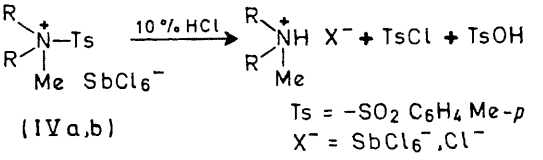


SCHEME 1

In the i r spectra of both (IVa) and (IVb), intense bands due to the SO_2 stretching vibrations appear at 1395 and 1178 cm^{-1} (Nujol) The remarkable hypsochromic shifts of these bands as compared with those of (IIIa) (1335 and 1164 cm^{-1}) and (IIIb) (1333 and 1155 cm^{-1}) indicate that an electron-attracting group is attached directly to the SO_2 group,[6] supporting the above assumption

Finally, the sulphonamidium salt (IVb) was identified by comparing its i r and n m r spectra and m p with those of a sample[7] authenticated by its preparation through tosylation of *N*-methylpyrrolidine (V) These facts clearly demonstrate that nitrogen is the alkylation site

Treatment of the crude salts (IVa,b) thus obtained with 10% hydrochloric acid at room temperature afforded in high yields products resulting from the cleavage of ^+N–S bonds, which is also compatible with the above results



SCHEME 2

This finding offers a useful method for the cleavage of *NN*-disubstituted sulphonamides

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[1] R J Gillespie *Accounts Chem Res* 1968, **1**, 202 and references therein
[2] T. Oishi M Ochiai K Kamata U Sendo H Nakakimura, T Nakayama, T Onuma, M Nagai and Y Ban Abstracts of Papers First Symposium on Heterocyclic Chemistry Osaka, Japan 1968 p 87
[3] T Oishi, M Nagai T Onuma, H Moriyama K Tsutae M Ochiai, and Y Ban, *Chem and Pharm Bull (Japan)*, 1969 **17**, 2306
[4] S Kabuss *Angew Chem Internat Edn* 1966 **5**, 675
[5] F M Menger and L Mandell, *J Amer Chem Soc*, 1967, **89**, **4424**, and references therein.
[6] L J Bellamy The Infra red Spectra of Complex Molecules " Methuen London, 1958, p 363
[7] Klages *et al* (F Klages and K Hoheisel *Chem Ber* 1963 **96**, 2057, F Klages and F E Malecki *Annalen*, 1966, **691** 15) have claimed that the corresponding sulphonamidium salt was prepared from triethylamine and toluene *p* sulphonium perchlorate but failed to isolate it as a crystalline salt They have also noted that the counteranion should be a perchlorate anion However we were able to isolate the salt (IVb) by adding antimony pentachloride to a cooled solution of (V) and toluene *p* sulphonyl chloride in CH_2Cl_2 which had been heated under reflux for 20 min beforehand See also W Loop and E Lukers *Annalen* 1953 **580** 235, G M Atkins jun and E M Burgess *J Amer Chem Soc* 1968, **90**, 4744