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REACTIONS OF DIMETHYLMETHYLTHIOSULFONIUM FLUOROBORATE WITH SOME NUCLEOPHILES

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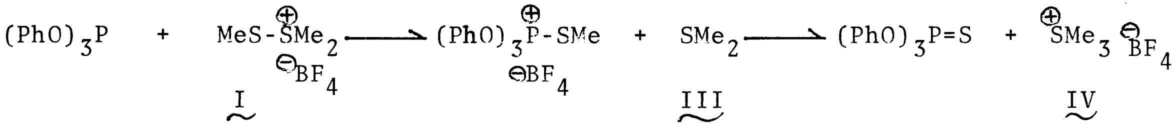
Reactions of dimethylmethylthiosulfonium fluoroborate with phenyl phosphite, pyridine, 4-cyanopyridine, N,N-dimethylaniline, p-nitro-N,N-dimethylaniline, thiophenol or sodium thiophenolate are almost instantaneous at room temperature, while the reactions with phenols and anisole proceed slowly at 60°C. Products are determined, and the mechanisms are discussed.

The S-S bond of dimethylmethylthiosulfonium fluoroborate (I) is cleaved very rapidly by methyl sulfide ($k_1 = 4.5 \times 10^5\ M^{-1}sec^{-1}$ in nitromethane at 40°C).[1,2] The reactions of I with various other nucleophiles appear to be of interest. We have carried out such investigations, and wish to report the results.[3]

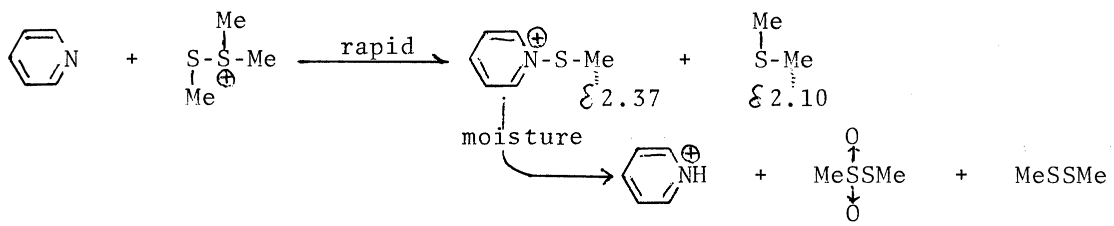
Equimolar amounts of I and phenyl phosphite were dissolved in nitromethane (II), and the NMR spectrum of the mixture was determined, which showed that the following reaction took place rapidly.



$$(PhO)_3P \quad + \quad \underset{\mathbf{I}}{\underset{\ominus BF_4}{MeS\text{-}\overset{\oplus}{S}Me_2}} \longrightarrow \underset{\ominus BF_4}{(PhO)_3\overset{\oplus}{P}\text{-}SMe} \quad + \quad \underset{\mathbf{III}}{SMe_2} \longrightarrow (PhO)_3P{=}S \quad + \quad \underset{\mathbf{IV}}{\overset{\oplus}{S}Me_3\ \overset{\ominus}{B}F_4}$$

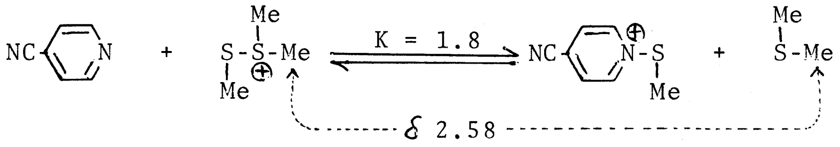
As soon as the reactants were mixed, I disappeared and the NMR singlet absorptions of methyl sulfide (III) and trimethylsulfonium fluoroborate (IV) were observed; the yields of III and IV were 22 and 78% after 5 min, and 14 and 86% after 360 min, respectively. These data show that the first step is very fast and the second step is fairly fast. A weak absorption was observed at δ2.35 ppm, which is probably ascribable to MeS protons of $(PhO)_3\overset{\oplus}{P}\text{-}SMe$. Upon addition of ether, IV precipitated, and the filtrate was concentrated. A column-chromatographic purification of the residue gave phenyl thionophosphate (yield, 86%).

When equimolar amounts of pyridine and I were mixed in II, I was instantaneously and quantitatively converted to III. A new methyl singlet was observed at δ2.37 ppm, which is most reasonably ascribable to $C_5H_5\overset{\oplus}{N}\text{-}SMe$. This methylthiopyridinium ion is a much weaker methylating agent than $(PhO)_3\overset{\oplus}{P}\text{-}SMe$, since the former does not methylate III in the mixture. When dry ether was added to the mixture and the precipitates were separated, they did not have the MeS- group, and were identified as pyridinium fluoroborate. The filtrate contained MeSSMe (δ2.33) and $MeSO_2SMe$ (two singlets at δ2.67 and 3.29). Apparently the N-methylthiopyridinium ion reacted with trace amount of moisture.



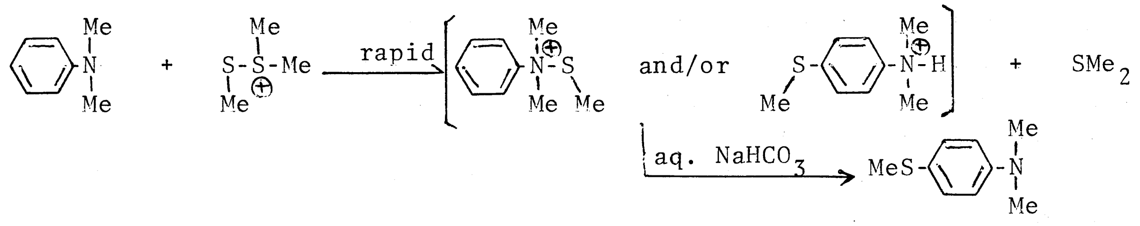
The formation of $MeSO_2SMe$ and MeSSMe can be explained by a mechanistic sequence involving the formation of MeS-OH, its bimolecular condensation to MeS(=O)SMe, and disproportionation of the thiolsulfinate to $MeSO_2SMe$ and MeSSMe.[4]

The above results show that the nucleophilic attack of pyridine toward I was much faster than that of methyl sulfide toward $C_5H_5\overset{\oplus}{N}$-SMe. Therefore, the reaction of an equimolar mixture of 4-cyanopyridine and I was examined in II.



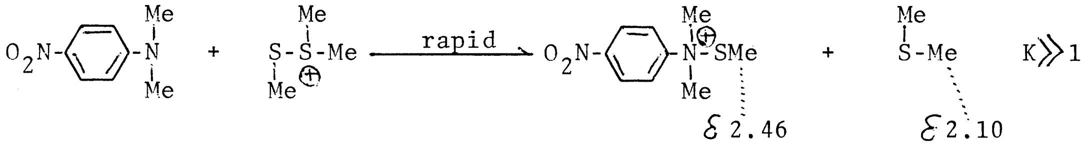
In this case, the nucleophilicity of the pyridine was much smaller due to the electron-withdrawing cyano group, and the equilibrium constant was calculated from the chemical shifts of the Me_2S- group of the mixture (δ2.58),that of pure I (3.22), and that of pure III (2.10); K = 1.8. When the isolation of 4-cyano-N-methylthiopyridinium fluoroborate was attempted, the solids obtained did not possess the S-Me absorption and were identified as $4\text{-CN-}C_5H_5\overset{\oplus}{N}H\ \overset{\ominus}{B}F_4$. The filtrate contained $MeSO_2SMe$ and MeSSMe.

When equimolar amounts of N,N-dimethylaniline and I were mixed in II, again the MeS- group of I disappeared instantaneously and completely, and methyl singlets were observed at δ2.10 (MeSMe), 2.47 and 2.53 (S-Me)(the absorption at 2.47 ppm was slightly stronger than that at 2.53) and 3.31 ($-\overset{\oplus}{N}Me_2$). Absorptions of aromatic protons were observed as multiplets at 7.40-7.45 ppm. These absorptions did not change when the mixture was allowed to stand for 5 hr. After the methyl sulfide was collected by vacuum distillation (85% yield), the mixture was washed with an aqueous $NaHCO_3$ solution and extracted with ether. From the ethereal extracts, p-methylthio-N,N-dimethylaniline was obtained (60% yield: NMR; SMe, δ2.34; NMe_2, 2.88; aromatic H, 6.57(doublet) and 7.67(doublet)). As for the intermediates showing the NMR absorptions at 2.47 and 2.53 ppm, the following two structures are possible.



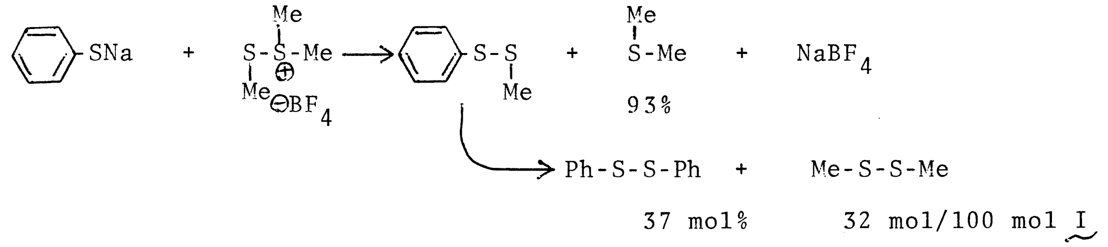
As a less nucleophilic aniline which has a para substituent for prevention of the attack of SMe on the para position, p-nitro-N,N-dimethylaniline was allowed to react with I in II. The methyl absorption of methyl sulfide appeared at δ2.10 ppm.

This shows that the nucleophilicity of p-nitro-N,N-dimethylaniline is very large in spite of the presence of the electron-withdrawing p-nitro group.

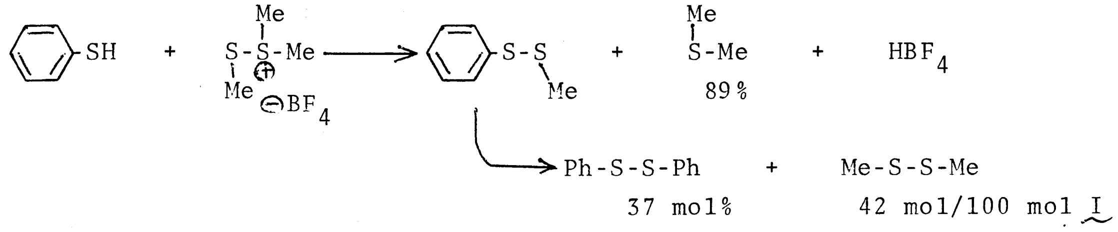


When the isolation of the methylthioanilinium salt was attempted by precipitation-filtration, the solids obtained were p-nitro-N,N-dimethylanilinium fluoroborate.

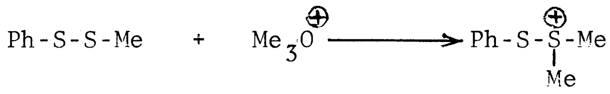
When sodium thiophenolate and I were mixed in II, the mixture reacted instantaneously, and its NMR spectrum showed the presence of methyl sulfide and methyl phenyl disulfide. When the methyl sulfide was removed by vacuum distillation and the mixture was allowed to stand, the disulfide disproportionated to phenyl disulfide and methyl disulfide. Their amounts were determined by NMR absorptions, and two disulfides were separated by column chromatography and identified.



The reaction between thiophenol and I in II was equally fast, and the products were essentially the same.



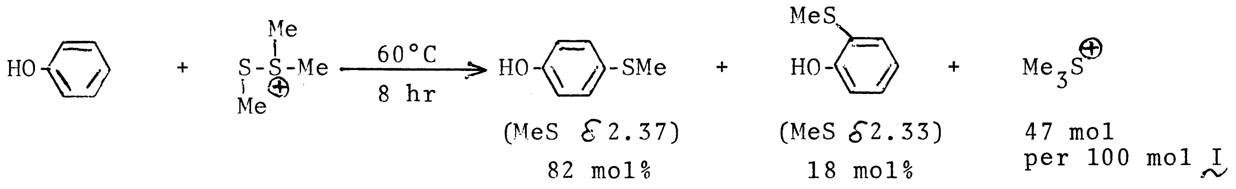
The intermediacy of methyl phenyl disulfide was ascertained by converting it to dimethylphenylthiosulfonium ion by the reaction with trimethyloxonium fluoroborate.



$$\text{Ph-S-S-Me} + \text{Me}_3\overset{\oplus}{\text{O}} \longrightarrow \text{Ph-S-}\underset{\text{Me}}{\overset{\oplus}{\text{S}}}\text{-Me}$$

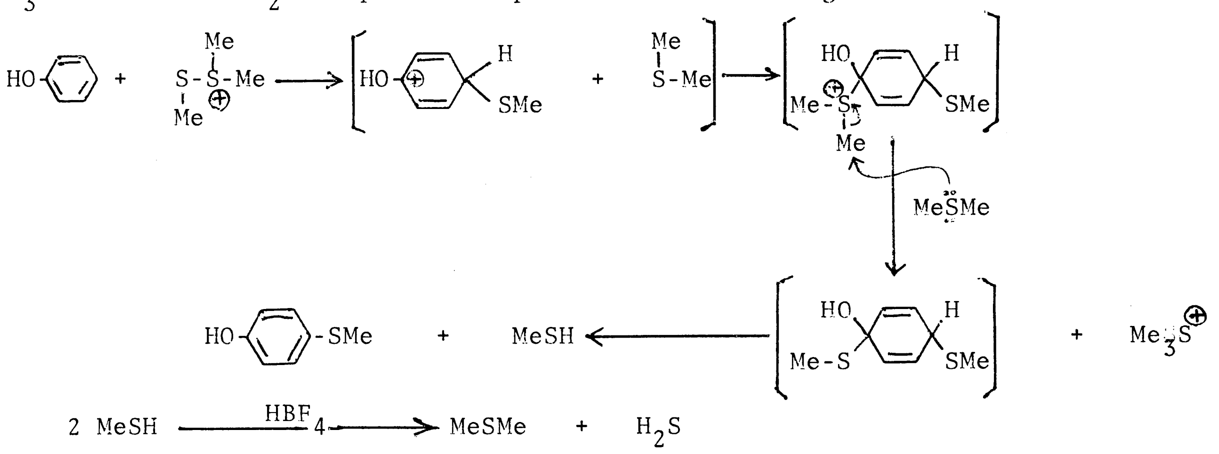
The reaction described so far are fast reactions, which appear to take place instantaneously at room temperature by the nucleophilic attack of a hetero atom (P, N, S) on the sulfur atom adjacent to the sulfonium atom of I. However, such nucleophiles as phenol, anisole and 2,6-di-t-butylphenol did not react at all with I at room temperature. Therefore, the reactions with these nucleophiles were carried out at 60°C.

An equimolar mixture of phenol and I in II was heated in a sealed ampoule at 60°C for 8 hr. Its NMR spectrum showed the following results.



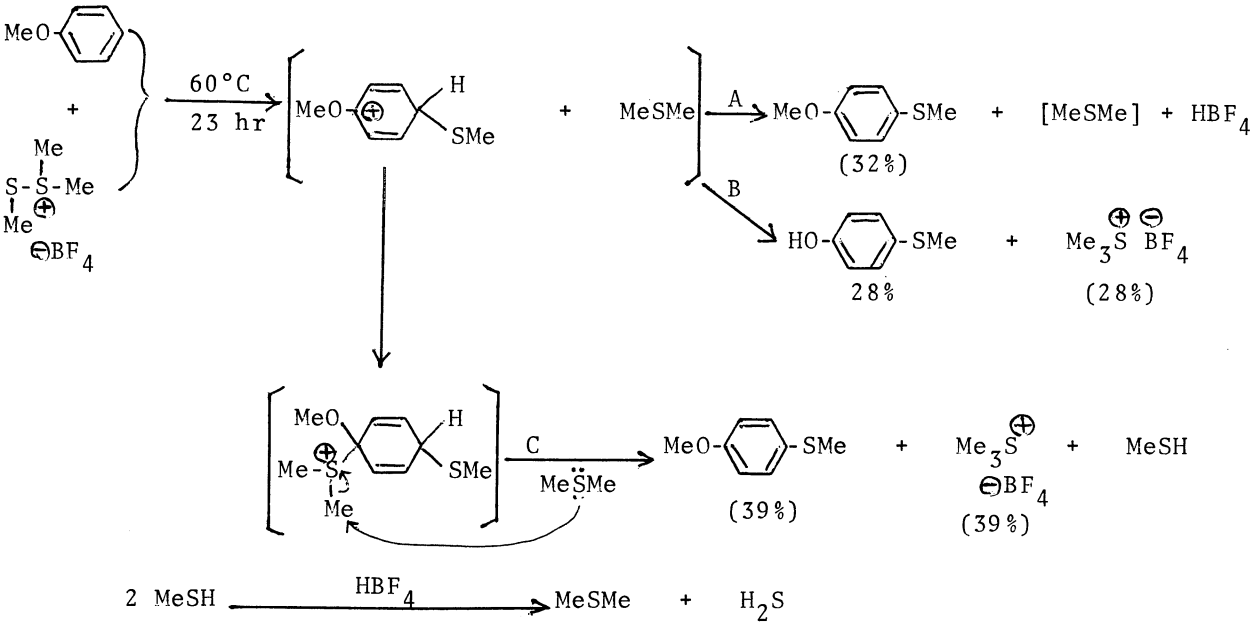
After their amounts were determined by their NMR absorptions, IV was precipitated by the addition of ether. The filtrate was concentrated, and the two methylthiophenols were separated by column chromatography.

In contrast with the results of the fast reactions described above, no III was found, but IV was found. Since all the MeS- group in I are accounted for by the o- and p-methylthiophenols, all the three methyl groups of IV must come from the Me_2S- group of I. This means that Me_2S or $Me_2\overset{\oplus}{S}$- must be disproportionated to $Me_3\overset{\oplus}{S}$ and MeSH or H_2S. A plausible path is the following.



Formation of methyl sulfide from methanethiol and hydrogen fluoroborate was checked by a separate experiment.^{5}

In a similar manner, anisole and I were allowed to react in II in a sealed tube at 60°C for 23 hr. Its NMR spectrum showed that III (δ 2.10 ppm) was absent and IV was present in a 67% yield. The NMR spectrum showed the presence of p-methylthioanisole (71% yield) and p-methylthiophenol (28 % yield). Ether was added to the mixture, and IV precipitated. The filtrate was concentrated, and the residue was subjected to column chromatography. p-Methylthioanisole and p-methylthiophenol were separated and identified. These results are explained by the following sequence.

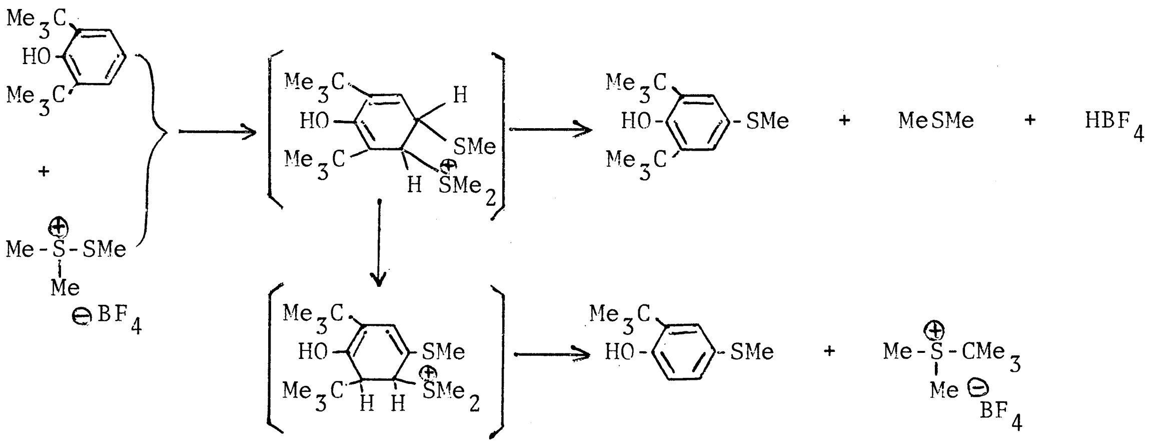


The yield of p-methylthiophenol (28%) suggests that 28% of IV is formed by path B (demethylation by the attack of III). Then 39% (67 - 28%) of IV may be assigned to path C, and 39% of p-methylthioanisole is accounted for by path C. Thus, 32% (71 - 39%) of p-methylthioanisole is probably assignable to path A.

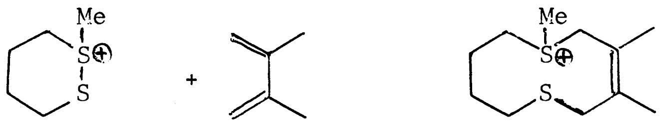
Then, the reaction between I and 2,6-di-t-butylphenol in II was examined. If the reaction between I and phenol involves initial attack of the oxygen lone pair on the MeS- group of I, the presence of the 2,6-di-t-butyl groups should prevent the reaction. Since this phenol has a high boiling point, the mixture can be heated in an open tube so that III (bp 40°C) can be removed as formed. When an equimolar mixture of I and 2,6-di-t-butylphenol in II was heated in an open tube at 60°C for 6 hr, its NMR spectrum showed that I completely disappeared. Addition of dry ether yielded solid precipitates, which were identified as t-butyldimethylsulfonium fluoroborate (63% yield). The filtrate was evaporated and the residue was chromatographed; 2,6-di-t-butyl-4-methylthiophenol (24%) and 2-t-butyl-4-methylthiophenol (29%) were isolated.

These results suggest that the reactions between I and phenols (and probably anisole too)do not involve the initial attack of the oxygen lone pair on the MeS-group of I. The attack of P, N and S on the MeS- group of I is extremely fast, whereas the reactivity of phenols and anisole with I is quite different.

It is of interest that t-butyl cation was fairly efficiently trapped by III even though the reaction was carried out in an open tube at 60°C. The low-boiling III must have been removed as it was liberated. Since no free III was observable in the reaction mixtures between the phenols and I, the intermediate formed from the reaction between the phenols and I must capture III and prevent it from evaporation. The reaction path is perhaps expressed by the following scheme involving a 1,2- or 1,4-addition of I to phenols.



A similar 1,4-addition of a thiosulfonium ion to a diene was reported in the literature.[7]



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1) S. H. Smallcombe and M. C. Caserio, J. Amer. Chem. Soc., 93, 5826 (1971).

2) J. K. Kim and M. C. Caserio, ibid., 96, 1930 (1974).

3) All the reactions were carried out in nitromethane which can dissolve **I** and other onium ions produced. The amounts of the products were determined by the intensities of their NMR absorptions unless otherwise stated. Then sulfonium salts and non-ionic products were separated by precipitating the former with the addition of ether. The filtrate was concentrated, and the non-ionic products were separated by column chromatography and identified.

4) E. Brock and S. W. Weidman, ibid., 95, 5046 (1973).

5) Formation of methyl sulfide from methanethiol and hydrogen fluoroborate was checked as follows. When a 29% aqueous CH_3SNa solution (2.0g) was added drop by drop to a 42% aqueous HBF_4 solution (2.0 g), a gas was evolved which possessed the odor of hydrogen sulfide. After the gas evolution ceased, the solution was extracted with chloroform. The NMR spectrum of the chloroform extracts showed two absorptions of about equal intensity at $\delta 2.07$ ppm (MeSMe) and 1.95 (MeSH). Olah et al. showed the formation of $R\overset{\oplus}{S}H_2$ and $R^{\oplus}$ from RSH in acidic media.[6]

6) G. A. Olah, D. H. O'Brien, and C. U. Pittman, Jr., J. Amer. Chem. Soc., 89, 2996 (1967).

7) N. E. Hester, G. K. Helmkamp, and G. L. Alford, Int. J. Sulfur Chem., Part A, 1, 65 (1971).

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