CHEMISTRY LETTERS, pp. 609-614, 1977. Published by the Chemical Society of Japan

REACTIONS OF S-METHYL THIOBENZOATE WITH METHYL TRIFLATE AND MAGIC METHYL. FORMATION OF BENZOIC TRIFLUOROMETHANESULFONIC ANHYDRIDE AND BENZOYLDIMETHYLSULFONIUM ION

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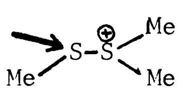
The reactions of S-methyl thiobenzoate with methyl triflate and methyl fluorosulfate yielded benzoic trifluoromethanesulfonic anhydride and benzoyldimethylsulfonium ion, respectively. Both of these reactive intermediates were found to function as powerful benzoylating agents for an arene, amine, alcohol, and phenol.

Caserio et al. reported that dimethylmethylthiosulfonium ion(1) is attacked by methyl sulfide much more rapidly than trimethylsulfonium ion(2) (k = 4.5 x 10^5 $M^{-1}sec^{-1}$ in $MeNO_2$ at 40°; faster than the reaction with 2 by a factor greater than 10^9).[1,2] Satisfactory rationalization has not been proposed for such enormous difference between the rates of reactions of 1 and 2 with nucleophiles,[3-5] but one possible explanation is that the transition state for the reaction of 1 is stabilized by the electron-accepting properties of the sulfenyl S atom of 1. When a nucleophile approaches 1, the sulfenyl S atom can accept a part of the electron pair of the nucleophile by use of its 3d orbital, and the bond-forming between the sulfenyl S atom and the nucleophile can precede the breaking of the S-S bond.[1] In the case of 2, the reaction is a typical S_N2 process on an sp^3 carbon atom, and the bond-breaking and bond-forming must take place simultaneously. In this connection, acylsulfonium ion(3) appears to be of interest, since in the reactions of 3 with nucleophiles the bond-forming may precede the bond-breaking, and 3 may be a powerful acylating agent. Oishi and his co-workers methylated thiolbenzoate with triethyloxonium tetrafluoroborate at 85-100°, or with diethoxycarbonium hexachloroantimonate at 0°, and suggested the intermediacy of acylsulfonium ions, but did not characterize them.[6,7] Because of the interest in 3, methylation of S-methyl thiobenzoate(4) was investigated in detail.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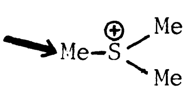
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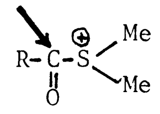
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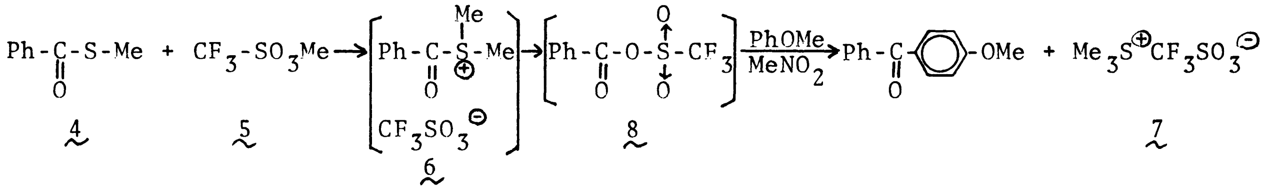
After a mixture of 4(2.90 mmol) and methyl triflate(5)(6.04 mmol) was degassed and sealed in an ampoule, it was allowed to react at room temperature for 3 days. Its PMR spectrum showed that 4 had completely reacted, but no methyl signal assignable to benzoyldimethylsulfonium triflate(6) was found. The PMR spectrum showed the presence of trimethylsulfonium triflate(7)(δ 2.90) and the ^{19}F-NMR spectrum indicated the presence of benzoic trifluoromethanesulfonic anhydride(8)(ϕ 78.2; identical with an authentic sample[8] prepared from benzoyl chloride and silver triflate). Then anisole(5.56 mmol) was added to the mixture, and the solution was again degassed and sealed in the ampoule. After 4 hrs, ether was added to the mixture, and the precipitates formed were found to be 7 (56 mol% based on 4; PMR(CD_3NO_2), δ2.90). The filtrate was concentrated and the residue was subjected to column chromatography (Florisil); 4-methoxybenzophenone was the main product identified (67 mol%; PMR ($CDCl_3$), δ3.87(s, 3H), 6.94(d, 2H), 7.80(d, 2H), 7.50(m, 5H)).[9]

The NMR data showed that what reacted with anisole was not 6 but 8. The formation of 7 and 8 from 4 and 5 can be explained by assuming initial formation of 6, which decomposed by the nucleophilic attack of triflate on the benzoyl carbon atom; the methyl sulfide produced was further methylated by 5. The reactions which took place among 4, 5, and anisole may be expressed as follows.



$$\underset{\mathbf{4}}{Ph\text{-}\overset{\displaystyle}{\underset{O}{\underset{\|}{C}}}\text{-}S\text{-}Me} + \underset{\mathbf{5}}{CF_3\text{-}SO_3Me} \longrightarrow \underset{\mathbf{6}}{\left[\begin{array}{c} Ph\text{-}\underset{O}{\underset{\|}{C}}\text{-}\overset{Me}{\overset{|}{\underset{\oplus}{S}}}\text{-}Me \\ CF_3SO_3^{\ominus} \end{array}\right]} \rightarrow \underset{\mathbf{8}}{\left[Ph\text{-}\underset{O}{\underset{\|}{C}}\text{-}O\text{-}\overset{O}{\overset{\uparrow}{\underset{O}{\underset{\downarrow}{S}}}}\text{-}CF_3\right]} \xrightarrow[MeNO_2]{PhOMe} Ph\text{-}\underset{O}{\underset{\|}{C}}\text{-}C_6H_4\text{-}OMe + \underset{\mathbf{7}}{Me_3S^{\oplus}CF_3SO_3^{\ominus}}$$

The fact that 6 is not stable and is converted to 8 shows that benzoyldimethylsulfonium ion is very susceptible to attack of very weak nucleophiles and that even triflate anion can attack it.

In a similar manner, after mixtures of various thiolesters and 5 were allowed to react, nucleophiles were added, and the products were determined. The results are summarized in Table 1.

Table 1.

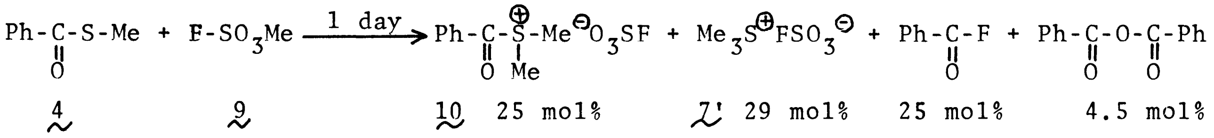
Products of the Reactions between Nucleophiles and Mixtures of Thiolester-$CF_3SO_3CH_3$

Initial Reactants (mmol)	Nucleophile Added(mmol)	Products (mol% based on Thiolester used)
4(2.96), 5(6.90)	PhH(5.13)	PhCOPh(62), 7(43)
4(1.77), 5(4.10)	Et_2NH(4.85)	$PhCONEt_2$(44), 7(63)
p-$O_2NC_6H_4COSEt$(0.84), 5(3.70)	PhOMe(1.38)	p-$O_2NC_6H_4COC_6H_4$-OMe-p(41), p-$O_2NC_6H_4CO_2Me$(13), p-$O_2NC_6H_4COSEt$(28)
p-$MeC_6H_4SO_2SMe$(0.87), 5(3.22)	PhOMe(3.48)	p-$MeC_6H_4SO_2C_6H_4OMe$-p(51)
p-$MeC_6H_4SO_2SMe$(1.06), 5(4.01)	PhOH(2.15)	p-$MeC_6H_4SO_3Ph$(45)
$PhCH_2COSMe$(1.86), 5(2.98), PhOMe(2.78)	a	$PhCH_2COC_6H_4OMe$-p(38), $PhCH_2COSMe$(34)
2,4,6-$Me_3C_6H_2COSMe$(1.01), 5(2.70)	PhOMe(1.21)	2,4,6-$Me_3C_6H_2COC_6H_4OMe$-p(24), 2,4,6-$Me_3C_6H_2CO_2Me$(22)[b]

[a] When thiolesters possessing hydrogen atoms on their α carbon atoms ($PhCH_2COSMe$, CH_3COSMe, $CH_3CH_2CH_2COSMe$) were treated with 5, no methylene NMR absorptions were observable after 2 days. Probably the acylsulfonium ions or acyl trifluoromethanesulfonic anhydrides lost their α-hydrogens, forming ketenes, which further reacted. However, when anisole was mixed with $PhCH_2COSMe$ and 5 from the beginning, the anisole was successfully phenylacetylated.

[b] The formation of methyl mesitoate is probably ascribable to methylation of mesitoic acid(formed by the reaction between the mesitoic sulfonic anhydride and moisture) with excess 5.

In an attempt to prepare a benzoyldimethylsulfonium salt containing an anion less nucleophilic than triflate anion, reactions of thiolesters with magic methyl (methyl fluorosulfate)(9) were investigated. When a mixture of 4(4.01 mmol) and 9 (10.7 mmol)(^{19}F-NMR ϕ-31.2) was degassed and sealed in an ampoule, white crystals were formed in 1 hr at room temperature. After 1 day the ampoule was opened, and the following compounds were found as products.

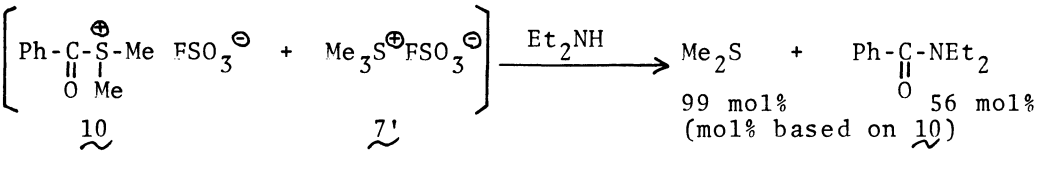


$$\underset{\mathbf{4}}{\mathrm{Ph{-}\underset{\underset{O}{\|}}{C}{-}S{-}Me}} + \underset{\mathbf{9}}{\mathrm{F{-}SO_3Me}} \xrightarrow{\text{1 day}} \underset{\mathbf{10}\ \ \text{25 mol\%}}{\mathrm{Ph{-}\underset{\underset{O}{\|}}{C}{-}\underset{\underset{Me}{|}}{\overset{\oplus}{S}}{-}Me\ {}^{\ominus}O_3SF}} + \underset{\mathbf{7'}\ \ \text{29 mol\%}}{\mathrm{Me_3S^{\oplus}FSO_3^{\ominus}}} + \underset{\text{25 mol\%}}{\mathrm{Ph{-}\underset{\underset{O}{\|}}{C}{-}F}} + \underset{\text{4.5 mol\%}}{\mathrm{Ph{-}\underset{\underset{O}{\|}}{C}{-}O{-}\underset{\underset{O}{\|}}{C}{-}Ph}}$$

(mol% based on 4)

The NMR spectrum in CD_3NO_2 showed the presence of 7'(trimethylsulfonium fluorosulfate) and benzoyldimethylsulfonium fluorosulfate(10)(PMR,δ3.21; ^{19}F,ϕ-39.2). By adding CH_2Cl_2(1 ml) to the mixture, benzoyl fluoride(IR, 1820 cm^{-1}) was determined by use of the ^{19}F chemical shift at ϕ-16.9 with p-Br-C_6H_4-CF_3 as the internal standard, and the amount of benzoic anhydride (IR, 1790, 1725 cm^{-1}) was determined from the amount of benzoic acid formed by hydrolysis.

It was possible to isolate 10 as a mixture with 7'. After a mixture of 4(3.28 mmol) and 9(7.76 mmol) was allowed to stand in a degassed and sealed ampoule at room temperature for 1 day, liquid products and excess 9 were extracted off by CH_2Cl_2(1 ml). The PMR and ^{19}FMR spectra(CD_3NO_2) of the white precipitates showed that the mixture consists of 10(20 mol% based on 4) and 7'(26 mol%). When diethylamine(2.05 mmol) was added to this CD_3NO_2 solution, an exothermic reaction took place, and the NMR spectrum showed the formation of methyl sulfide. The solution was concentrated, and the column-chromatographic separation of the residue yielded N,N-diethylbenzamide.

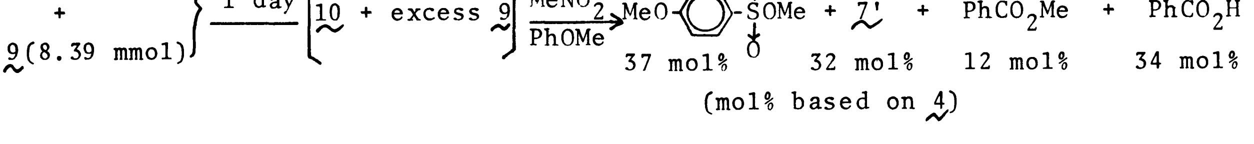


$$\left[\underset{\mathbf{10}}{\mathrm{Ph{-}\underset{\underset{O}{\|}}{C}{-}\underset{\underset{Me}{|}}{\overset{\oplus}{S}}{-}Me\ \ FSO_3^{\ominus}}} + \underset{\mathbf{7'}}{\mathrm{Me_3S^{\oplus}FSO_3^{\ominus}}}\right] \xrightarrow{Et_2NH} \underset{\text{99 mol\%}}{\mathrm{Me_2S}} + \underset{\text{56 mol\%}}{\mathrm{Ph{-}\underset{\underset{O}{\|}}{C}{-}NEt_2}}$$

(mol% based on 10)

Crystals of 10 were unstable toward moisture, and could not be separated from 7'. However, its identity appears to be certain from its NMR spectra(^{1}H,δ3.20; ^{19}F,ϕ-39.2) and its reaction with diethylamine liberating methyl sulfide.

When 9 was used as a methylating agent, excess 9 must be removed before the addition of nucleophiles, since nucleophiles were found to be methoxysulfonylated by 9 rather than benzoylated by 10.



(mol% based on 4)

Reactions of acylsulfonium ions with some other nucleophiles were also examined without isolating acylsulfonium ions. The results are summarized in Table 2.

Table 2.

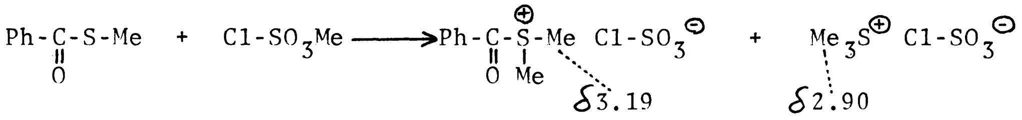
Products of the Reactions between Acylsulfonium Ions and Nucleophiles[a]

Initial Reactants (mmol)	Intermediates Formed (mol% based on RCOSR)	Nucleophile (mmol)	Products Found (mol% based on RCOSR)
4(3.95), 9(10.7)	10(31), 7'(45)	Et_2NH(3.89)	Me_2S(31), $BzNEt_2$(33), BzOMe(4), BzOH(4)
4(3.83), 9(8.42)	10(31), 7'(35)	PhOH(4.11)	Me_2S(25), BzOPh(27), BzOH(12) p-MeS-C_6H_4-OH(12)
11(1.47), 9(5.67)	2,4,6-$Me_3C_6H_2COSMe_2$ (36), 7'(37)	MeOH(4.88)	2,4,6-$Me_3C_6H_2CO_2Me$(79), 7'(61)

[a] After a mixture of thiolester-FSO_3Me was allowed to react for 1-2 days, excess 9 was removed, and then a nucleophile was added. The amounts of acylsulfonium ions, 7', and methyl sulfide were determined from NMR spectra, and those of other products were determined by column chromatography.

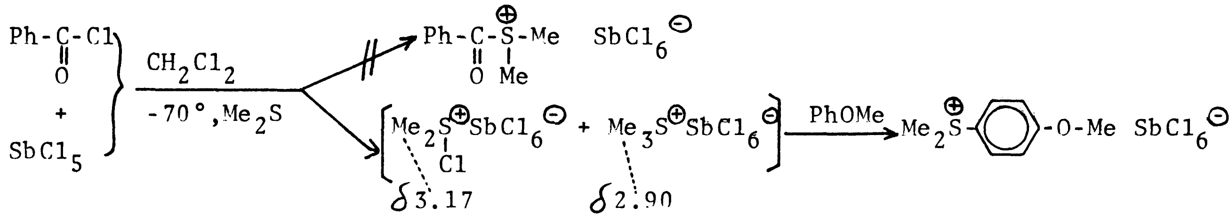
A part of the N,N-diethylbenzamide and phenyl benzoate is ascribable to the reaction of benzoyl fluoride with the nucleophiles, but all the amount of methyl sulfide and most of the amide and ester must be ascribed to the reaction of 10 with the nucleophiles.[10] The identity of p-(methylthio)phenol was established by comparison with an authentic sample, but it is difficult to formulate a reasonable mechanism for its formation.

It was possible to prepare benzoyldimethylsulfonium ion from methyl chlorosulfate in place of 9. A degassed mixture of 4 (3.47 mmol) and methyl chlorosulfate(9.31 mmol) was allowed to react in a sealed ampoule at room temperature for 2 days. No formation of crystals was observed. Its PMR spectrum showed the presence of benzoyldimethylsulfonium chlorosulfate(34 mol% based on 4) and trimethylsulfonium chlorosulfate(23 mol%).



$$Ph\text{-}\underset{\underset{O}{\|}}{C}\text{-}S\text{-}Me + Cl\text{-}SO_3Me \longrightarrow Ph\text{-}\underset{\underset{O}{\|}}{C}\text{-}\overset{\oplus}{\underset{\underset{Me}{|}}{S}}\text{-}\underset{\delta 3.19}{Me}\ Cl\text{-}SO_3^{\ominus} + \underset{\delta 2.90}{Me_3S^{\oplus}}\ Cl\text{-}SO_3^{\ominus}$$

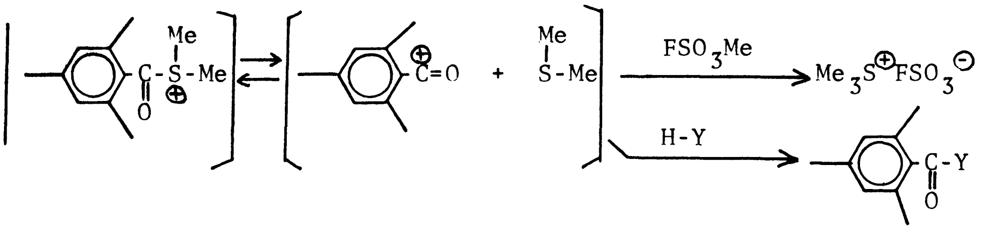
Preparation of benzoyldimethylsulfonium ion was attempted by treating benzoyl chloride with methyl sulfide and $SbCl_5$. When methyl sulfide was added to a CH_2Cl_2 solution of benzoyl chloride and $SbCl_5$ at -70°, chlorodimethylsulfonium ion rather than benzoyldimethylsulfonium ion was formed. When anisole was added to the mixture, p-anisyldimethylsulfonium ion was formed.[11]



It appeared to be of interest to investigate the methylation of S-methyl thiomesitoate. Although esterification of mesitoic acid and hydrolysis of alkyl mesitoates do not proceed under the ordinary mild conditions suitable for sterically-unhindered benzoates, alcoholysis or hydrolysis of mesitoyl chloride proceeds very fast, even faster than p-nitrobenzoyl chloride.[12-15]

After a degassed mixture of S-methyl thiomesitoate(11)(1.91 mmol) and 9(5.92 mmol) had been allowed to react in a sealed ampoule for 2 days, excess 9 was removed under vacuum, and the PMR spectrum of the residue in CD_3NO_2 indicated the presence of mesitoyldimethylsulfonium fluorosulfate (δ 3.20; 32 mol% based on 11) and 7'(39 mol%). In contrast with the case of thiolbenzoates, which yielded benzoyl fluoride, no mesitoyl fluoride was found by ^{19}FMR. When diethylamine (4.76 mmol) was added, an exothermic reaction took place, forming methyl sulfide (29 mol%). When the solution was concentrated and the residue was subjected to column chromatography(Florisil), N,N-diethylmesitamide (δ 1.02(t, 3H), 1.27(t, 3H), 2,18(s, 6H), 2.25(s, 3H), 3.10(q,2H), 3.60(q, 2H), 6.87(s, 2H)) and mesitoic anhydride (δ 2.25 (s, 6H), 2.38(s, 12H), 6.87(s, 4H); IR, 1735, 1710 cm^{-1}) were isolated.[16]

The carbonyl carbon atom of the mesitoylsulfonium ion must be sterically blocked, and the approach of a nucleophile to its π-orbital must be difficult. It is possible that the mesitoylsulfonium ion is in equilibrium with mesitoyl cation and methyl sulfide.



However, this possibility is rejected from the fact that methyl sulfide was produced upon addition of diethylamine. If the mesitoylsulfonium ion did dissociate to mesitoyl cation and methyl sulfide, the methyl sulfide formed must have been converted to trimethylsulfonium ion by 9 and no free methyl sulfide should be formed upon addition of diethylamine. A plausible explanation is that the nucleophile attacks the carbonyl carbon atom in a manner similar to that of an S_N2-type reaction with the transition state, $\mathrm{Nu}\cdots\overset{|}{\underset{\overset{\|}{O}}{C}}\cdots\mathrm{SMe_2}$.

Thus, thiolesters are converted, 1) to acyl trifluoromethanesulfonic anhydrides by 5, and 2) to acyldimethylsulfonium ion by 9, and both of these two reactive intermediates are powerful acylating agents for various nucleophiles.

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9) Trifluoromethanesulfonic acid was one of the products, but its amount was not determined.
10) Benzoic acid is ascribable to the hydrolysis of **10** with moisture, and methyl benzoate is ascribable to the methylation of benzoic acid with **9**.
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16) The formation of mesitoic anhydride is probably ascribable to the reaction between the mesitoylsulfonium ion and the mesitoic acid formed by the reaction between the mesitoylsulfonium ion and moisture. Acylsulfonium salts (and especially mesitoylsulfonium salts) are extremely susceptible to hydrolysis with moisture, and some hydrolysis takes place even when well-dried reactants were used with great care.

(Received March 18, 1977)