Oxidative Properties of Triflic Anhydride. Oxidation of Alcohols and Sulfides

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The reaction of dimethyl sulfide with triflic anhydride leads to the formation of the corresponding dimethyl(trifluoromethanesulfonyl)sulfonium salt. The latter can be used in the mild oxidation of primary and secondary alcohols including unsaturated and natural ones to the corresponding carbonyl compounds in 34−75% yield. The reaction of various sulfides with triflic anhydride was studied. It was found that the reactions give rise to the corresponding dialkyl(trifluoromethanesulfonyl)sulfonium salts. Succeeding treatment with water leads to the formation of sulfoxides in 25−73% yield. Formation of sulfones does not proceed.

Introduction

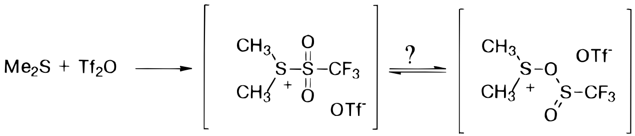
Recently, we have found that dimethyl sulfide reacts with acylium salts to form dimethylacylsulfonium salts.[1] These sulfonium salts are mild acylating reagents for different unsaturated hydrocarbons—alkenes, acetylenes, and conjugated dienes. This method of acylation was found to be particularly important for labile dienes having the propensity to cationic polymerization. Furthermore, using this approach, we have proposed a novel method of direct electrophilic perfluoroacylation of unsaturated hydrocarbons that is based on utilization of trifluoroacetic anhydride in the presence of the dimethyl sulfide−boron trifluoride complex.[2−4]

Some properties of anhydrides of carboxylic acids are similar to those of anhydrides of sulfonic acids. In this research, we have studied interaction of trifluoromethanesulfonic acid anhydride (triflic anhydride) with different sulfides. Triflic anhydride has found wide application in organic synthesis.[5] However, little is known about oxidative properties of this reagent.[6,7] Reactions of triflic anhydride with sulfides have not yet been described.

Results and Discussion

We have found that dimethyl sulfide reacts with triflic anhydride in methylene chloride at −60 °C to form a white solid. It is worthy of note that the reaction of dimethyl sulfide with less electrophilic methanesulfonic anhydride does not take place during 1 week under room temperature. It would be reasonable to assume that the formation of dimethyl(trifluoromethanesulfonyl)sulfonium salt (**1a**) takes place. The other possible structure having an S−O instead of an S−S bond could be sulfonium salt **1b** formed via isomerization of **1a** (Scheme 1).

Scheme 1



1a **1b**

We have attempted to establish the structure of the dimethyl sulfide/triflic anhydride complex on the basis of NMR spectra. The ^{1}H and ^{13}C NMR spectra show singlets at 3.13 and 24.24 ppm correspondingly (−20 °C, in CD_2Cl_2/CH_3NO_2 2/1), both of which are shifted to low field in comparison to the signals of dimethyl sulfide (2.08 and 19.5 ppm). The downfield shift indicates a considerable positive charge at the sulfonium sulfur atom and is characteristic for sulfonium methyls.

Chemistry of similar sulfonium salts can be considered as nearly unexplored. Only one example of dimethylsulfonylsulfonium salt was previously described.[8] Dimethyltosylsulfonium triflate (obtained by reaction of methyl (toluenethio)sulfonate with methyl triflate) displays in the ^{1}H NMR spectrum a singlet of sulfonium methyls at 3.12 ppm. Our spectral data are very close (3.13 ppm), *i.e.*, the structure of triflic anhydride/dimethyl sulfide complex is very likely to be dimethyl(trifluoromethanesulfonyl)sulfonium salt (**1a**). It should be mentioned that compounds **1a** and **1c** have two electrophilic centers, sulfonium sulfur (path A) and sulfonate sulfur (path B) (Figure 1), and a nucleophile can attack both of them. Previously reported dimethyltosylsulfonium triflate (**1c**) (Scheme 2) was found to undergo nucleophilic attack by anisole and diethylamine on the S(VI) atom (path B).[8]

In contrast, we have found that the reaction of the dimethyl sulfide/triflic anhydride complex with primary and secondary alcohols proceeded exclusively at sulfonium sulfur (path A) with formation of the corresponding alkoxysulfonium salts. Treatment of the alkoxysulfonium salts with triethylamine leads to effective formation of the corresponding carbonyl compounds in 34−75% yield (Scheme 3).

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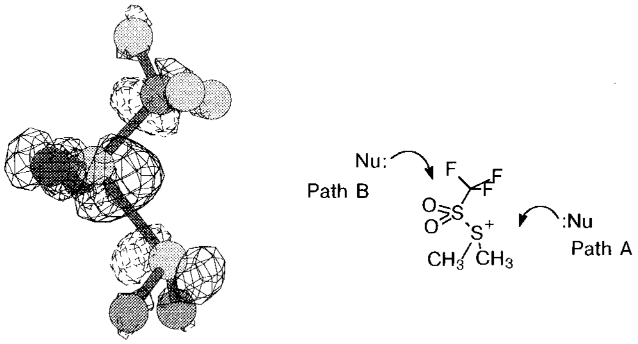
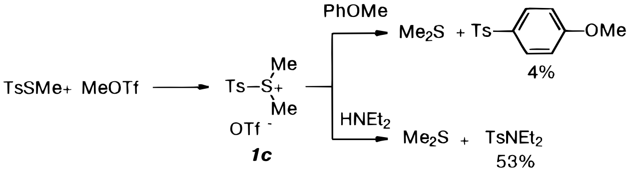


Figure 1. LUMO of **1a (**dashed and solid lines correspond to different signs of wave function) and two possible paths of reaction of **1a** with nucleophiles.

Scheme 2



Scheme 3

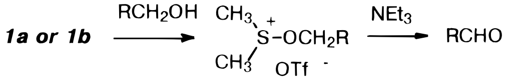


Table 1. Oxidation of Alcohols with Dimethyl Sulfide/ Triflic Anhydride Complex

entry	alcohol	product	isolated yields (%)
1	2-phenylethanol (**2a**)	phenylacetaldehyde (**3a**)	45[a]
2	benzyl alcohol (**2b**)	benzaldehyde (**3b**)	60[a]
3	2-(2-thienyl)ethanol (**2c**)	(2-thienyl)acetaldehyde (**3c**)	34[b]
4	cinnamyl alcohol (**2d**)	cinnamaldehyde (**3d**)	55[a]
5	cyclohexanol (**2e**)	cyclohexanone (**3e**)	75[a]
6	menthol (**2f**)	menthone (**3f**)	75
7	cholesterol (**2g**)	5-cholesten-3-one (**3g**)	50

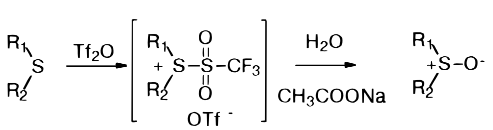
[a] Isolated as the semicarbazone. [b] Isolated as the diethyl acetal.

Thus, the overall result of this one-pot procedure is mild oxidation of alcohols to carbonyl compounds (Table 1). Although this method is similar to other methods based on dimethyl sulfoxide-derived reagents,[9] it proceeds under mild conditions and is suitable for unsaturated and natural substrates. Thus, in some cases, it could constitute a useful addition to known methods.

In order to rationalize the observed difference between our data and the data in the literature[8] and get insight into the electronic structure of the new electrophilic reagent, we have performed molecular orbital calculations on compound **1a**. For this purpose, we have applied a recently developed semiempirical PM3[10] method that had been reported to give satisfactory results for sulfur organic compounds including hypervalent ones.[11]

In accord with molecular orbital perturbation theory,[12] the selectivity of the reaction appears to arise from the interplay between charge and orbital interactions. Both sulfur atoms bear high positive charge.[13] At the same time, it can be seen from Figure 1, representing the LUMO of the new reagent, that orbital factors favor S_N2-like nucleophilic attack on the S(II) atom, followed by S(II)−S(VI) bond cleavage. It should be mentioned that the frontier orbital interactions are expected to be important in this case because the LUMO has very low energy (−8.0 eV). Thus, consideration of both charge and orbital factors leads one to expect nucleophilic attack on the S(II) atom in full accord with the experiment. We believe that the dramatic distinction in the reaction path for **1c** and **1a** is connected with the electron-withdrawing influence of the CF_3 group.

Scheme 4



The behavior of **1a** in the reaction with alcohols permitted us to suggest the possibility of selective oxidation of sulfides to sulfoxides by reaction of triflic anhydride with sulfides followed by hydrolysis.

In spite of the fact that there are numerous reagents for oxidation of sulfides to the corresponding sulfoxides,[14] some of the methods give rise to competitive formation of sulfones. Therefore, elaboration of new selective methods for oxidation of sulfides is a desirable goal.

We have found that reaction of triflic anhydride with various sulfides leads to formation of the complexes, which are possibly dialkyl(trifluoromethanesulfonyl)sulfonium salts. Succeeding treatment of the reaction mixture with aqueous sodium acetate results in the corresponding sulfoxides without sulfone formation (Scheme 4).

In order to determine the scope and limitations of this method, we have applied it to a number of sulfides (Table 2) and found that the reaction is sensitive to electronic and steric factors. The yields of the sulfoxides are better in the case of aliphatic sulfides. The presence of functional groups in the original sulfide does not prevent the oxidation, but the reaction requires higher temperature and yields of the corresponding sulfoxides are lower. Oxidation of diphenyl sulfide, methyl 4-nitrophenyl sulfide, (cyclohexylthio)methyl cyanide, and 1-adamantyl ethyl sulfide does not take place even at room temperature; the formation of complexes with triflic anhydride does not proceed, and sulfides are recovered.

In the case of thioanisole (**4f**), the corresponding sulfoxide was isolated in low yield (25%). We have found that a competing electrophilic substitution reaction takes place to form diarylmethylsulfonium salt **5g**. We believe that the sulfonylsulfonium salt reacts as a sulfonium electrophile toward the electron-rich aromatic nucleus of thioanisole. Raising the reaction temperature changes the reaction selectivity. In this case, only sulfonium salt **5g** was isolated in 67% yield. For 4-methylthioanisole (**4h**), similar to the reaction with **4f**, the corresponding sulfonium salt **5h** was isolated in 73% yield. In this case, electrophilic substitution at the ortho position to the methylthio group takes place.

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(9) *Houben-Weyl. Methoden der Organishen Chemie*; Klamann, D., Ed.; Verlag: Stuttgart, 1985; B. E11, p 365.

(10) Stewart, J. P. *J. Comput. Chem.* **1989**, *10*, 221.

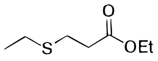
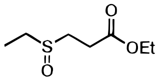
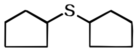
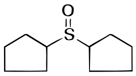
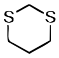
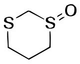
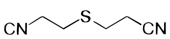
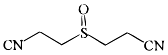
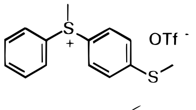
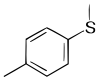
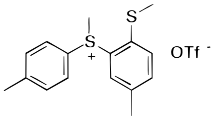
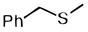
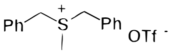
(11) Stewart, J. P. *J. Comput. Chem.* **1990**, *11*, 543.

(12) *Chemical reactivity and reactions paths*; Klopman, G., Ed.; Wiley: New York, 1974.

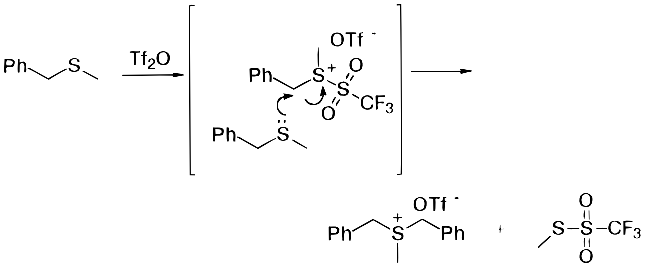
(13) Unfortunately, it is impossible to judge on the basis of PM3 data which sulfur atom (S(II) or S(VI)) is more positive because the PM3 method is known to overestimate Mulliken net charges on sulfur(VI) atoms. Nevertheless, it is obvious that both of the sulfur atoms are positively charged.

(14) *Houben-Weyl. Methoden der Organishen Chemie*; Klamann, D., Ed.; Verlag: Stuttgart, 1985; B. E11, p 702.

Table 2. Oxidation of Sulfides with Triflic Anhydride[16]

Entry	Sulfide		Conditions	Product		Isolated Yield
1	Bu_2S	**4a**	-40 °C	Bu_2SO	**5a**	73%
2		**4b**	-30 °C		**5b**	62%
3		**4c**	-30 ÷ 0 °C		**5c**	52%
4		**4d**	-30 °C		**5d**	51%
5		**4e**	-30 ÷ 0 °C		**5e**	40%
6	PhSMe	**4f**	-78 ÷-50 °C	PhS(O)Me	**5f**	25%
7	PhSMe	**4f**	20 °C		**5g**	67%
8		**4h**	20 °C		**5h**	73%
9		**4i**	-40 °C		**5i**	65%

Scheme 5



Reaction of methyl benzyl sulfide (**4i**) with triflic anhydride does not result in formation of the corresponding sulfoxide, but gives only dibenzylmethylsulfonium triflate (**5i**). We assume that the anomalous reaction path is due to enhanced propensity of the benzyl group to nucleophilic substitution resulting in transbenzylation (Scheme 5).

Conclusion

Thus, the reaction of dimethyl sulfide with triflic anhydride leads to formation of a complex. This complex was investigated as an oxidant of alcohols, and it was found that formation of the corresponding carbonyl compounds could be achieved in 34–75% yields. The structure of the reagent was studied by NMR spectroscopy and semiempirical quantum chemical PM3 calculations. The computational data were found to be in good accord with the experimental results. Various sulfides can be converted to sulfoxides, without overoxidation to sulfones, under mild conditions using treatment with triflic anhydride followed by hydrolysis. Yields are in the range of 25–73%. The reaction is sensitive to electronic and steric factors.

Experimental Section

Melting points were determined in sealed capillaries and are uncorrected. Column chromatography was performed on silica gel (63–200 mesh, Merck). All solvents were dried and distilled according to the standard procedure. Triflic anhydride was prepared according to literature procedure[5] from trifluoromethanesulfonic acid (Merck).

General Procedure for Alcohol Oxidation. A solution of 1.7 g (6 mmol) of triflic anhydride in 30 mL of anhydrous CH_2Cl_2 was cooled to −70 °C. A solution of 0.31 g (6 mmol) of dimethyl sulfide in 10 mL of CH_2Cl_2 was added dropwise. A white precipitate formed. After 5 min, 5 mmol of the alcohol was added dropwise, the reaction mixture was stirred for 15 min, and 1.3 g (13 mmol) of triethylamine was added. The reaction mixture was allowed to warm to rt, and 20 mL of water was then added. The organic layer was separated and washed with water (2 × 20 mL). The solution was diluted with 30 mL of ether and filtered. The filtrate was dried with Na_2SO_4, and solvents were removed *in vacuo*. The isolated carbonyl derivative gave spectroscopic data and physical constants in accord with the literature.[15,16]

General Procedure for Sulfide Oxidation. A solution of 1.7 g (6 mmol) of triflic anhydride in 30 mL of anhydrous CH_2Cl_2 was cooled to −40 °C. Over a period of 10 min, 5 mmol of the corresponding sulfide in 10 mL of CH_2Cl_2 was added dropwise. The reaction mixture was allowed to warm (Table 2) followed by addition of an aqueous solution of sodium acetate. The resulting mixture was stirred for an additional 15 min. The organic layer was separated, and the aqueous layer was extracted with CH_2Cl_2 (3 × 20 mL). The organic fraction was dried with Na_2SO_4, and solvents were removed *in vacuo*. The product was purified by column chromatography (silica gel, benzene–$CHCl_3$ 10/1). Isolated sulfoxides **5a,d–f** gave spectroscopic data and physical constant in accord with the literature.[15,17,18]

Ethyl 3-(ethylsulfinyl)propanoate (5b): yield 62%; oil; IR (neat) 1030, 1050, 1740 cm^{-1}; ^{1}H NMR (CD_2Cl_2) δ 4.12 (q, 2H, $J = 7.0$ Hz), 3.16 −2.63 (m, 6H), 2.52 (q, 2H, $J = 7.0$ Hz),

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1.15 (t, 3H, J = 7.0 Hz), 1.13 (t, 3H, J = 7.0 Hz); ^{13}C NMR (CD_2Cl_2) δ 171.7, 61.7, 48.2, 46.2, 31.4, 14.2, 7.3. Anal. Calcd for $C_7H_{14}O_3S$: C, 47.17; H, 7.92. Found: C, 47.35; H, 7.99.

Dicyclopentyl sulfoxide (5c): yield 52%; oil; IR (Nujol) 1050 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 3.01 (m, 2H), 2.13 (m, 2H), 1.87 (m, 4H), 1.75−1.57 (m, 10H); ^{13}C NMR ($CDCl_3$) δ 55.4, 25.9, 24.2, 23.7, 23.0. Anal. Calcd for $C_{10}H_{18}OS$: C, 64.47; H, 9.74. Found: C, 64.13; H, 9.75.

Sulfonium salts **5g**−**i** were prepared under this procedure, but they were purified by crystallization (chloroform) instead of column cromatography.

Methylphenyl[4-(methylthio)phenyl]sulfonium trifluoromethanesulfonate (5g): yield 67%; oil; IR (Nujol) 1300−1100, 1040, 1000 cm^{-1}; ^{1}H NMR (CD_3COCD_3) δ 8.14 (d, 2H, J = 7.4 Hz), 8.04 (d, 2H, J = 7.4 Hz), 7.81−7.69 (m, 3H), 7.61 (d, 1H, J = 7.9 Hz), 7.52 (d, 2H, J = 8.6 Hz), 3.90 (s, 3H), 2.52 (s, 3H); ^{13}C NMR (CD_3COCD_3) δ 148.9, 134.4, 131.5, 130.9, 130.1, 128.0, 127.4, 121.7, 121.6 (q, J = −320.8 Hz), 27.5, 14.1. Anal. Calcd for $C_{15}H_{15}F_3O_3S_3$: C, 45.44; H, 3.81. Found: C, 45.56; H, 3.83.

Methyl(4-methylphenyl)[2-[4-methyl(methylthio)phenyl]sulfonium trifluoromethanesulfonate (5h): yield 73%; mp 129−130 °C; IR (Nujol) 1300−1100, 1040, 990 cm^{-1}; ^{1}H NMR (CD_3COCD_3) δ 8.12 (s, 1H), 7.92 (d, 2H, J = 8.0 Hz), 7.69 (d, 1H, J = 7.9 Hz), 7.61 (d, 1H, J = 7.9 Hz), 7.52 (d, 2H, J = 8.0 Hz), 3.85 (s, 3H), 2.50 (s, 3H), 2.46 (s, 3H), 2.41 (s, 3H); ^{13}C NMR (CD_3COCD_3) δ 144.3, 139.2, 136.2, 134.3, 131.5, 130.6, 129.5, 127.9, 126.1, 122.9, 121.4 (q, J = −319.9 Hz), 25.9, 19.6, 19.1, 16.9. Anal. Calcd for $C_{17}H_{19}F_3O_3S_3$: C, 48.10; H, 4.51. Found: C, 48.45; H, 4.38.

Dibenzylmethylsulfonium trifluoromethanesulfonate (5i): yield 65%; mp 103−104 °C; IR (Nujol) 1300−1100, 1040, 990 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 7.53−7.21 (m, 10H), 4.82 (m, 4H), 2.70 (s, 3H); ^{13}C NMR ($CDCl_3$) δ 130.2, 129.8, 129.2, 126.7, 122.3 (q, J = −320.0 Hz), 19.8. Anal. Calcd for $C_{16}H_{17}F_3O_3S_2$: C, 50.78; H, 4.53. Found: C, 50.53; H, 4.56.

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