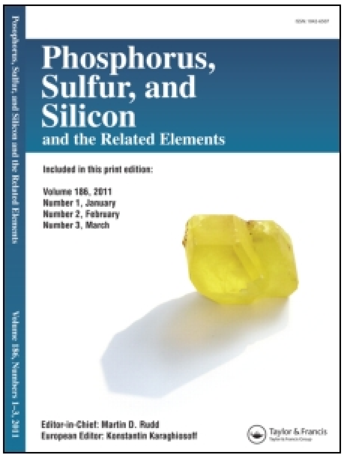

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PUMMERER REARRANGEMENT OF ETHYL METHYLSULFINYLTHIOACETATE

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PUMMERER REARRANGEMENT OF ETHYL METHYLSULFINYLTHIOACETATE

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Ethyl methylsulfinylthioacetate undergoes Pummerer rearrangement with thionyl chloride, trifluoroacetic anhydride or with acetic anhydride-trifluoroacetic anhydride mixture, but not with acetic anhydride alone. These reactivities are compared to those for methyl methylsulfinylacetate and ω-methylsulfinylacetophenone and interpreted in terms of the difference in stability of the intermediate sulfinyl carbonium ions.

Key words: Pummerer; sulfinyl-thioester; sulfinyl-acetophenone; sulfinyl-ester; acetate anion; trifluoroacetate anion.

INTRODUCTION

As a part of more general studies of the properties of α-methylsulfinylthioesters,[1] it became of interest to investigate their reactivity toward Pummerer reagents.

Although a number of functionalized sulfoxides, bearing electron withdrawing groups, such as cyano, ester and carbonyl, have received some attention in the literature,[2–4] no Pummerer reaction with sulfinyl-thioesters has been reported.

RESULTS AND DISCUSSION

This communication presents our results of the reactions of ethyl methylsulfinylthioacetate (**1**) with some Pummerer reagents. Normal Pummerer reaction occurred when (**1**) was allowed to react with thionyl chloride, in CH_2Cl_2. The corresponding α-chloro, α-methylthio derivative (**2**), obtained in 71% yield, was an intermediate for the preparation of the mixed α,α-dialkylthio-thioacetates, as shown by reaction of (**2**) with ethylthiolate, to give ethyl α-methylthio, α-ethylthioacetate (**3**) (Scheme 1).

As for the reaction of (**1**) with acetic anhydride the unaltered reactant was recovered at room temperature and decomposition occurred by heating (Scheme 2). This result resembles that reported for the ω-methylsulfinylacetophenone,[5] which was unreactive toward acetic anhydride at room temperature, but underwent Pummerer rearrangement only by heating.

However, quite different behaviour was shown by methyl methylsulfinylacetate

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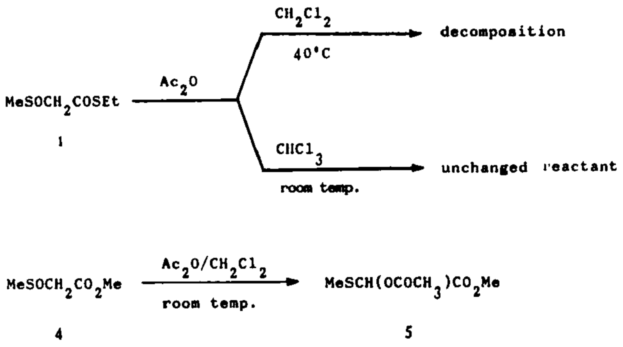
$$\underset{1}{MeSOCH_2COSEt} \xrightarrow{SOCl_2/CH_2Cl_2} \underset{2}{MeSCH(Cl)\text{-}COSEt} \xrightarrow{NaSEt} \underset{3}{MeS\text{-}CH(SEt)\text{-}COSEt}$$

SCHEME 1



SCHEME 2

(**4**), which, when treated with acetic anhydride, at room temperature, afforded the corresponding α-acetoxy, α-methylthio-derivative (**5**) in 58% yield (Scheme 2).

The difference in reactivity between sulfinyl-ester and thioester was confirmed when both compounds were submitted to reaction with acetic anhydride-trifluoroacetic anhydride (TFAA) mixture (Scheme 3). While compound (**4**) afforded, as the only reaction product, α-acetoxy, α-methylthio-derivative (**5**), the ester (**1**) yielded a mixture (1:1) of a α-acetoxy, α-methylthio- (**6**) and α-trifluoroacetoxy, α-methylthio- (**7**) derivatives.

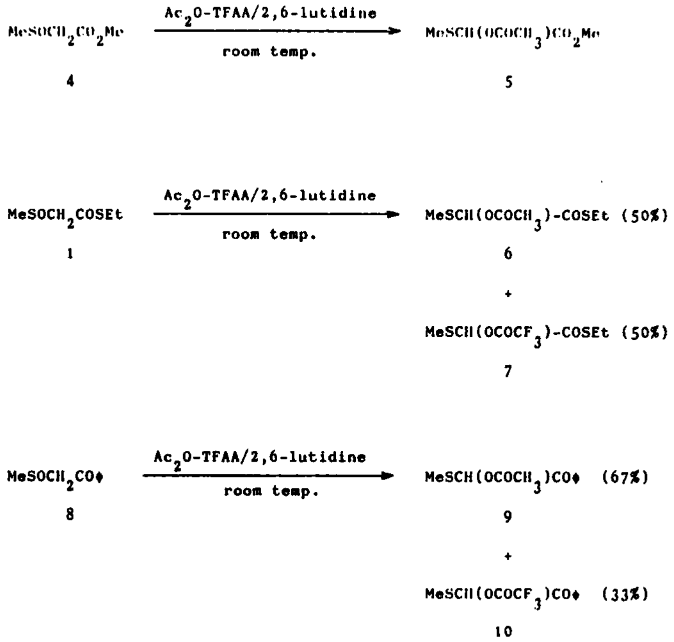
It should be emphasized that the behaviour of methylsulfinyl-ester (**4**) is in line with that observed[6] for a large number of sulfoxides.

However, when ω-methylsulfinylacetophenone (**8**) was submitted to reaction with the same mixture of anhydrides, although α-acetoxy-derivative (**9**) was the major product (67%), the presence of α-trifluoroacetoxy-derivative (**10**) (33%) was also observed (Scheme 3).

It is noteworthy that no difference in reactivity was shown when all three sulfinyl derivatives (**1**), (**4**) and (**8**) were allowed to react with trifluoroacetic anhydride alone, as in all cases the corresponding α-trifluoroacetoxy-derivatives (**7**), (**11**) and (**10**) were obtained (Scheme 4).

The mechanism of the Pummerer rearrangement has been extensively studied.[2,3] It has been suggested[3] that the rate determining step of the reaction between sulfoxides bearing electron withdrawing groups and acetic anhydride is the heterolysis of the S–O linkage of the sulfonium ylide, formed by the reversible deprotonation of the acetyl sulfonium ion, with formation of the sulfenyl carbonium ion.

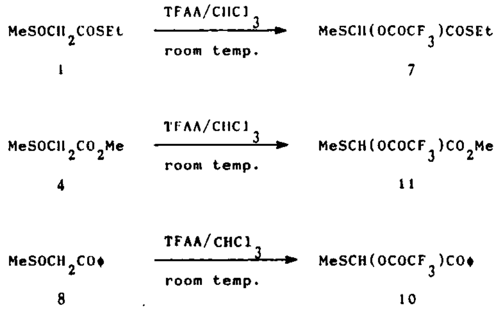
It seems reasonable to admit that the decrease in reactivity in the sulfinylthioacetate toward acetic anhydride may be due to a decrease of the stability of the corresponding sulfenyl carbonium ion caused by withdrawing effect of the neighbouring thioester group. Thus, the heterolysis of the S–O linkage in the sulfonium ylide would become more difficult and no Pummerer rearrangement



SCHEME 3

could occur. However, when, instead of acetic anhydride, trifluoroacetic anhydride or thionyl chloride are employed, the corresponding F_3CCOO^- or ^-SOCl anions are much better leaving groups and, therefore, the heterolysis of the S–O linkage will be favoured.

The decrease of selectivity shown by sulfinyl-thioester and, partly, by sulfinyl-acetophenone, in comparison with sulfinyl-ester, when allowed to react with acetic anhydride-TFAA mixture, may be also rationalized in terms of the decrease of stability of the intermediate sulfenyl carbonium ion. Thus, although both, acetate and trifluoroacetate anions are present,[6] in the case of the sulfinyl ester, the corresponding sulfenyl carbonium ion would undergo reaction exclusively with the acetate anion which is a stronger nucleophile. On the contrary, in the case of sulfinyl-thioester and sulfinyl-acetophenone, the cor-



SCHEME 4

TABLE I

^{13}C ($CDCl_3$) and ^1H-NMR (CCl_4/TMS) chemical shifts (ppm)

Comp.	C=O	CH_2	
		^{13}C	^1H
1	191.7	65.1	3.82
4	165.7	57.5	3.60
8	193.4	62.2	4.43

responding carbonium ions, destabilized respectively by neighbouring thioester and phenacyl groups, would react with both anions.

It was of interest to compare the results of the reactivities with ^{13}C and ^1H-NMR measurements (Table I). It may be seen that the chemical shifts of the carbonyl and methylene carbons in the sulfinyl-thioester (**1**) undergo a downfield change by about 26 ppm and 7.6 ppm, respectively, in comparison with those corresponding to the sulfinyl-ester (**4**). It is noteworthy that the corresponding values for the sulfinyl-acetophenone (**8**) approach those for the sulfinyl-thioester (**1**). These relationships are confirmed by the ^1H-NMR values.

Thus, it may be concluded that the chemical shifts of the carbonyl and methylene carbons for the sulfinyl-thioester and acetophenone, in comparison with the sulfinyl-ester, are in line with their decrease of reactivity in the Pummerer rearrangement. The similarity between the withdrawing effect on the methylene group by the thioester and phenacyl group is of interest and may be explored in further reactivity studies.

EXPERIMENTAL

All melting points are uncorrected. The IR spectra were run on a Perkin-Elmer 283 spectrometer (Grating) in KBr or in CCl_4. The ^1H and ^{13}C-NMR spectra were recorded, respectively, on a Varian T-60 or on a Bruker AC-200 spectrometer. The carbon and hydrogen analyses were carried out on a Perkin–Elmer elemental analyser 240-B. ω-Methylsulfinylacetophenone (**8**) was prepared from dimethylsulfoxide and ethylbenzoate according to literature procedure.[7] Methyl methylthioacetate[8] was prepared from methylthioacetyl chloride and methanol. Methyl methylsulfinylacetate was prepared by oxidation of the corresponding sulfide with H_2O_2 according to literature procedure.[9]

Ethyl methysulfinylthioacetate (**1**). To a solution of 3.2 g (21.3 mmol) of ethyl methylthiothioacetate (b.p. 67–9°C/4 mmHg) in 40 ml of methanol, was added dropwise, at 0–5°C, a mixture of selenium dioxide (2.37 g; 21.4 mmol), hydrogen peroxide (50%; 1.20 ml; 21.3 mmol) and 10.6 ml of water. When the addition was completed the reaction mixture was further stirred for 2 minutes, then poured into 100 ml of water and saturated with sodium chloride. The aqueous layer was extracted with dichloromethane (3 × 50 ml), the combined organic extracts dried over anhydrous $MgSO_4$ and the solvent evaporated in vacuum. Distillation of the crude product under reduced pressure yielded 2.90 g (82%) of (**1**), as a pale yellow liquid. b.p. 108–9°C/0.18 mmHg. $C_5H_{10}O_2S_2$ (166.26) Calc. %: C, 36.12; H, 6.06. Found %: C, 36.51; H, 5.95. ^1H-NMR (CCl_4/TMS): δ 1.30 (t, $J = 7$ Hz, 3H), 2.67 (s, 3H), 2.92 (q, $J = 7$ Hz, 2H), 3.82 (s, 2H). IR ν_{max} 1670 (C=O), 1065 (S=O) cm^{-1}.

Reaction of ethyl methylsulfinylthioacetate (**1**) *with thionyl chloride*. To a solution of 3.86 g (32.4 mmol) of thionyl chloride in 6.0 ml of dichloromethane, heated at 40°C, was added a solution of 4.75 g (28.6 mmol) of (**1**) in 6.0 ml of dichloromethane. The resulting stirred mixture was refluxed 2 hours. After removal of solvent, benzene (10 ml) was added, and evaporated in vacuum. Distillation of the crude product under reduced pressure yielded 3.75 g (71%) of (**2**). b.p. 106–8°C/3 mmHg.

$C_5H_9ClOS_2$ (184.71) Calc. %: C, 32.51; H, 4.91. Found %: C, 32.36; H, 4.77. ^{1}H-NMR (CCl_4/TMS): δ 1.33 (t, $J = 7$ Hz, 3H), 2.28 (s, 3H), 2.93 (q, $J = 7$ Hz, 2H), 5.33 (s, 1H). IR ν_{max}1680 (C=O) cm^{-1}.

Reaction of ethyl α-chloro, α-methylthiothioacetate (**2**) *with sodium ethylthiolate.* To a solution of ethanethiol (2.0 ml; 26.7 mmol) in dry benzene (25 ml) sodium (0.615 g; 26.7 mmol) was added in small pieces. After stirring overnight a solution of ethyl α-chloro, α-methylthiothioacetate (**2**) (2.50 g; 13.5 mmol) in dry benzene (10 ml) was added dropwise. The reaction mixture was further stirred for 3 hours and poured into an aqueous 5% solution of ammonium chloride. The aqueous layer was extracted with benzene (3 × 20 ml) and the combined organic extracts were washed with water (20 ml) and dried over anhydrous $MgSO_4$. Removal of solvent yielded 1.96 g (69%) of (**3**). b.p. 144–6°C/2 mmHg. $C_7H_{14}OS_3$ (210.38). Calc. %: C, 39.96; H, 6.71. Found %: C, 39.76; H, 6.59. ^{1}H-NMR (CCl_4/TMS): δ 1.30 (t, 6H), 2.15 (s, 3H), 2.45–3.10 (m, 4H), 4.30 (s, 1H). IR ν_{max} 1672 (C=O) cm^{-1}.

Reaction of sulfinyl derivatives with acetic anhydride.
General Procedure. A mixture of (1) (1.10 g; 6.63 mmol), acetic anhydride (1.25 ml; 13.2 mmol) and chloroform (10 ml) was stirred at room temperature for 2 hours. After removal of solvent in vacuum, the residue was disolved in benzene (10 ml) and washed with aqueous 5% sodium bicarbonate (3 × 10 ml). Removal of solvent yielded 0.985 g of unreacted starting material.

Under similar conditions, methyl α-acetoxy, α-methylthioacetate ((**5**); 58%) was obtained by the reaction of (**4**) with acetic anhydride. $C_6H_{10}O_4S$ (178.21). Calc. %: C, 40.44; H, 5.66. Found %: C, 40.33; H, 5.78. ^{1}H-NMR (CCl_4/TMS): δ 2.13 (s, 3H), 2.16 (s, 3H), 3.80 (s, 3H), 5.75 (s, 1H). IR ν_{max} 1745 (C=O) cm^{-1}.

Reaction of the sulfinyl derivatives with acetic anhydride—Trifluoroacetic anhydride.
General Procedure. A mixture of trifluoroacetic anhydride (1.48 ml; 10.5 mmol) and acetic anhydride (7.0 ml; 74.1 mmol) was stirred for 5 hours at room temperature. After this time, methyl methylsulfinylacetate (**4**) (0.950 g, 6.99 mmol) was added dropwise, followed by 2,6-lutidine (1.63 ml, 14.0 mmol). The reaction mixture was further stirred for 2 hours, the excess of acetic anhydride evaporated in vacuum, and the residue was dissolved in 10 ml of benzene. This solution was washed with 10% hydrochloric acid (20 ml) followed by saturated aqueous sodium bicarbonate (20 ml). Removal of benzene in vacuum yielded 0.570 g (46%) of (**5**). ^{1}H-NMR (CCl_4/TMS): δ 2.13 (s, 3H); 2.16 (s, 3H), 3.80 (s, 3H), 5.75 (s, 1H). IR ν_{max} 1745 (C=O) cm^{-1}.

Under similar conditions, by reaction of (1) (0.850 g; 5.12 mmol) with an acetic anhydride-trifluoroacetic anhydride mixture, 0.810 g of crude product was obtained. ^{1}H-NMR (CCl_4/TMS): δ 1.30 (t), 1.33 (t), 2.15 (s), 2.26–3.13 (m), 6.20 (s), 6.26 (s). IR ν_{max} 1790 (C=O), 1752 (C=O), 1685 (C=O) cm^{-1}. The relative proportions of methyl α-acetoxy, α-methylthiothioacetate (**6**) and methyl α-trifluoroacetoxy, α-methylthiothioacetate (**7**) was estimated from the ^{1}H-NMR spectra of the crude product. On the basis of the integration of the methine protons signals, assigned to each compound, the ratio (**7**):(**8**) was 1:1.

Similarly, the reaction of ω-methylsulfinylacetophenone (**8**) (1.00 g; 5.49 mmol) with a mixture of acetic anhydride-trifluoroacetic anhydride yielded 0.860 g of crude product. ^{1}H-NMR (CCl_4/TMS): δ 2.03 (s), 2.08 (s), 2.15 (s), 6.60 (s), 6.78 (s), 7.26–7.55 (m), 7.76–8.03 (m). IR ν_{max} 1790 (C=O), 1750 (C=O), 1692 (C=O), 1680 (C=O). The relative proportion of α-acetoxy, ω-methylsulfinylacetophenone (**9**) and α-trifluoroacetoxy, ω-methylsulfinylacetophenone (**10**) was estimated as above and was 2:1.

Reaction of sulfinyl derivatives with trifluoroacetic anhydride. General Procedure. To a solution of (**1**) (0.850 g; 5.12 mmol) in 8.0 ml of chloroform, kept at 0°C, trifluoroacetic anhydride (1.45 ml; 10.2 mmol) was added dropwise. The reaction mixture was allowed to warm to room temperature and further stirred for 2 hours. The solvent was removed in vacuum, benzene (10 ml) was added and the resulting solution was washed with 20 ml aqueous saturated sodium bicarbonate. Removal of benzene in vacuum yielded 0.680 g of crude (**7**) (51%). ^{1}H-NMR (CCl_4/TMS): δ 1.33 (t, $J = 7$ Hz, 3H), 2.22 (s, 3H), 2.97 (q, $J = 7$ Hz, 2H), 6.17 (s, 1H). IR ν_{max} 1792 (C=O), 1687 (C=O) cm^{-1}.

Under similar conditions, methyl α-trifluoroacetoxy, methylthioacetate (**11**) (57%) was obtained by reaction of (**4**) with trifluoroacetic anhydride. ^{1}H-NMR (CCl_4/TMS): δ 2.27 (s, 3H), 3.88 (s, 3H), 6.00 (s, 1H). IR ν_{max} 1790 (C=O), 1755 (C=O) cm^{-1}.

Similarly, the reaction of (**8**) with trifluoroacetic anhydride yielded α-trifluoroacetoxy, ω-methylsulfinylacetofenone (**10**) (80%). ^{1}H-NMR (CCl_4/TMS): δ 2.13 (s, 3H), 6.83 (s, 1H), 7.37–7.60 (m, 3H), 7.87–8.10 (m, 2H). IR ν_{max} 1692 (C=O), 1788 (C=O) cm^{-1}.

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REFERENCES

1. B. Wladislaw, L. Marzorati and J. Gruber, *XIII International Symposium on Organic Chemistry of Sulfur,* Odense, Denmark, 1988, Abstract Book p. 119.
2. S. Oae, The Pummerer Rearrangements, *In Topics in Organic Sulfur Chemistry.* M. Tisler, Ed. University Press, Ljubljana, Jugoslavia, **1978,** 289–336.
3. T. Numata, O. Itoh, T. Yoshimura and S. Oae, *Bull. Chem. Soc. Jpn.*, **56,** 257 (1983).
4. J. K. Stamos, *Tetrahedron Letters,* **1985,** 477.
5. T. Matsumoto, H. Shirakama, F. Sakan and K. Takigawa, *Bull. Chem. Soc. Jpn.*, **50,** 325 (1977).
6. R. Tanikaga, Y. Yabuki, N. Ono and A. Kaji, *Tetrahedron Letters,* **1976,** 2257.
7. E. J. Corey and M. Chaykovsky, *J. Am. Chem. Soc.*, **87,** 1345 (1965).
8. J. M. Carpenter and G. Shaw, *J. Chem. Soc.* (*C*), **1970,** 2016.
9. T. Minami, Y. Tsumori, K. Yoshida and T. Agawa, *J. Org. Chem.*, **39,** 3412 (1974).