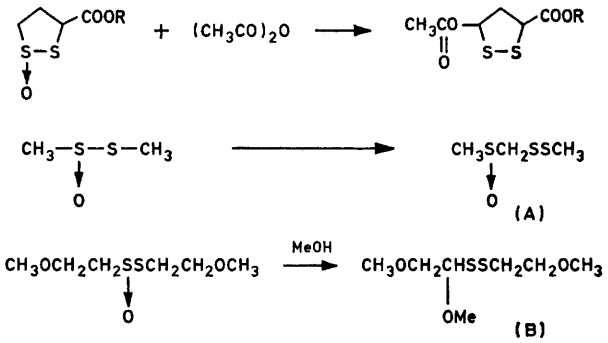
A New Acid-catalysed Rearrangement of Thiosulphinates to α-Acetylthio-sulphoxides in Acetic Anhydride

By **Naomichi Furukawa, Tsuyoshi Morishita, Takeshi Akasaka,** and **Shigeru Oae,*** Department of Chemistry, University of Tsukuba, Sakura-mura, Niihari-gun, Ibaraki 305, Japan

Some thiosulphinates with at least one proton on the carbon adjacent to the sulphenyl sulphur react with acetic anhydride containing acetic acid to afford the corresponding α-acetylthio-sulphoxides. The mechanism of this reaction was studied using thiosulphinates labelled with ^{2}H, ^{13}C, and ^{18}O. These tracer experiments demonstrated that the reaction proceeds *via* an initial E_i reaction to form the corresponding sulphenic acid and thioaldehyde followed by recombination in which the sulphur atom of the sulphenic acid adds to the carbon atom of the thioaldehyde, eventually affording the rearranged α-acetylthio-sulphoxide. The formation of the sulphenic acid was confirmed by trapping it with methyl acrylate. The mechanism of the reaction is discussed.

ALTHOUGH the Pummerer reaction of sulphoxides with acetic anhydride has been investigated extensively,[1] the analogous reaction of thiosulphinates with acetic anhydride has received very little attention. Recently, Fukui and his co-workers reported that the reaction of α-lipoic acid monoxide with acetic anhydride in acetonitrile gives the normal Pummerer type product but only in 6% yield.[2] Block and his co-workers reported, however, that t-butyl methanethiosulphinate did not react with acetic anhydride, unlike lipoic acid monoxide.[3] Kondo *et al.* and Block *et al* found that when a few thiosulphinates were pyrolysed in benzene saturated with water [4] or in methanol,[5] the Pummerer-like products, (A) and (B) are obtained as shown in Scheme 1.



SCHEME 1

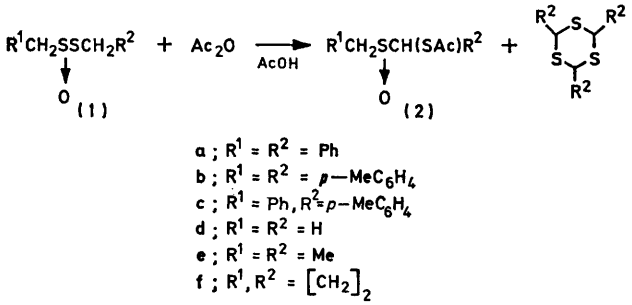
In the course of our studies on α-oxo-sulphoxides,[6] we found that *SO*-dibenzyl thiocarbonate *S*-oxide reacted with acetic anhydride to afford a new rearranged product, α-acetylthiobenzyl benzyl sulphoxide together with a trace of benzyl phenylmethanethiosulphinate [6a] which was found later to be the key intermediate in the formation of the α-acetylthio-sulphoxide.[6] When thiosulphinates (1) were allowed to react with acetic anhydride, the rearranged products (2) were obtained in moderate yields.

In this paper we report on this new rearrangement of thiosulphinates with acetic anhydride, and discuss the mechanism on the basis of ^{2}H, ^{13}C, and ^{18}O tracer experiments and product analyses.

RESULTS AND DISCUSSION

Product Analysis.—Generally the reaction was carried out by heating the thiosulphinates (1a—e) in a large excess of acetic anhydride containing an equimolar amount of acetic acid at 60—90 °C for 2 h. After 60—70% of the starting thiosulphinate (1) was consumed, the reaction was stopped since the rearranged product (2) decomposed when the reaction was allowed to continue for >2 h. The products were separated by preparative t.l.c. or column chromatography while their structures were determined by both spectroscopic and elemental analyses. The products and yields thus obtained are summarized in Table 1.

Inspection of Table 1 revealed that under the reaction conditions employed the thiosulphinates (1a—c) did not give Pummerer products but instead the α-acetylthio-sulphoxides (2a—c) in moderate yield together with a complex mixture of other products, *i.e.*, oligomers of thiobenzaldehyde; in the case of (1a) especially, 2,4,6-triphenyl-1,3,5-trithiacyclohexane [7] was obtained in 2%



SCHEME 2

yield. Similarly, (1d) afforded the corresponding α-acetylthio-sulphoxide (2d) in 20—30% yield together with unidentified products. In the case of (1e), the major products were methyl methanethiosulphonate and dimethyl disulphide which were formed by disproportionation of (1e), while (2e) and 2,3,5-trithiahexane 5-oxide were also obtained in 7 and 4% yields, respectively. 1,2-Dithiacyclohexane *S*-oxide (1f) did not react with acetic anhydride under the same conditions, resulting in

recovery of the starting material. Methyl 1,1-dimethylethanethiosulphinate, which decomposed rapidly in acetic anhydride containing acetic acid at 40 °C, did not give the corresponding α-acetylthio-sulphoxide. Compounds (2a—c) were *ca.* 1 : 1 mixtures of both *erythro*- and *threo*-isomers. In the case of (2a), two isomers (C) and (D) can be separated by preparative t.l.c. on silica gel. The absolute configurations of the two isomers have not yet been determined but one, (C), has m.p. 85—86 °C, and the other, (D), 110.5—111.5 °C. Spectroscopic and analytical data are given in the Experimental section.

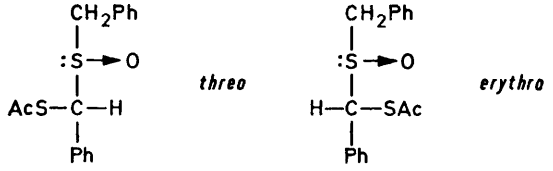
TABLE 1

Reaction of thiosulphinates (1) [a] with acetic anhydride [b]

Compound	Time (h)	Temp. (°C)	(2) (%)	Recovery (%)
(1a)	2	60	50—60	30—40
(1a)	1	60	24	56
(1b)	2	60	75	15
(1c)	2	60	46 [c]	19 [c]
(1d)	2	90	26	40
(1e)	2	90	5—7 [d]	30

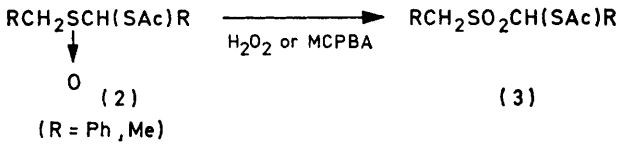
[a] Thiosulphinate 2.0×10^{-1}M. [b] In the presence of acetic acid in amounts equimolar with thiosulphinate. [c] Symmetric sulphoxide (2a) and thiosulphinate (1a) are obtained in 18 and 7%, respectively. [d] Methyl methanethiosulphonate (17%), dimethyl disulphide, and 2,3,5-trithiahexane 5-oxide (4%) were obtained together with (2e).

Compound (2d) was also identified (n.m.r.) as a *ca.* 3 : 1 mixture of both *erythro*- and *threo*-isomers. The structures of (2a and d) were further confirmed by oxidation to afford the corresponding sulphones. When both the *erythro*- and *threo*-isomers, (2a and d) were



oxidized separately with hydrogen peroxide in acetic acid or *m*-chloroperbenzoic acid (MCPBA) in methylene chloride, both *erythro*- and *threo*-isomers of the two different sulphoxides afforded the identical compound (3a or d) which was assigned as the corresponding sulphone by n.m.r. and i.r. spectroscopy.

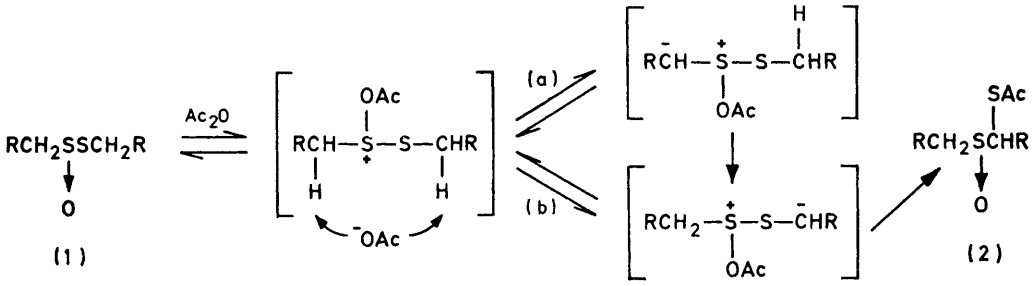
When the reaction of (1a) with acetic anhydride was carried out in the absence of acetic acid, the starting material was completely consumed but the yield of the rearranged product (2a) decreased to only a few percent. Decomposition of (1a) was found to take place by heating even without acetic anhydride. For example, when a solution of (1a) in acetonitrile was kept overnight at 60 °C, the thiosulphinate (1a) decomposed and 2,4,6-triphenyl-1,3,5-trithiacyclohexane was obtained in 42% yield together with other products. These results suggest that acetic acid plays an important role in the



SCHEME 3

reaction. The rearrangement was found to be catalysed similarly with such weak acids as benzoic acid, phenol, and even benzyl alcohol. However, strong acids such as toluene-*p*-sulphonic acid did not promote the rearrangement but disproportionation of the thiosulphinate (1a) to afford benzyl phenylmethanethiosulphonate and dibenzyl disulphide as shown in Table 2.

Mechanism.—Tracer experiments and kinetic isotope effect. If the reaction proceeds *via* initial acylation of the sulphinyl oxygen of thiosulphinate (1) with acetic anhydride, the mechanisms, shown in Scheme 4 can be conceived for the reaction. Route (a) involves initial proton abstraction by acetate ion from the methylene group adjacent to the sulphoxonium group, and subsequent intramolecular proton abstraction from the methylene group adjacent to the sulphenyl sulphur as in



SCHEME 4 Possible mechanism for the reaction

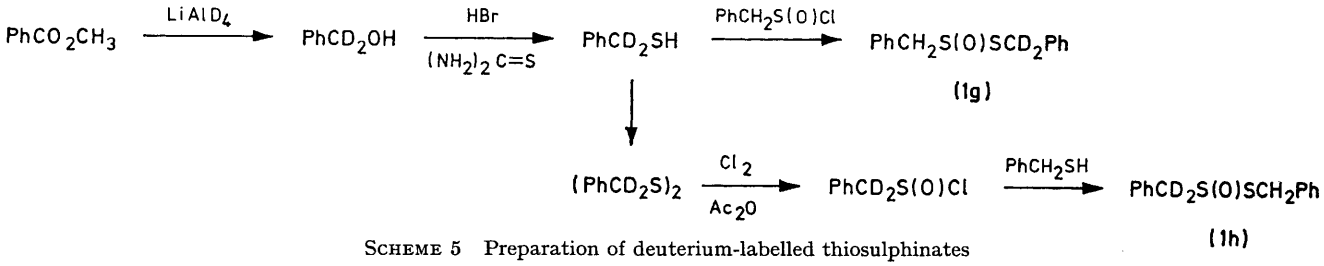
TABLE 2

Influence of various acids on the reaction of benzyl phenylmethanethiosulphinate (1a) with acetic anhydride

Acid [a]	Recovery (2) (%)	Recovery (%)	Others (%)
AcOH	50—60	30—40	
HCO_2H	62	35	
PhOH	58	37	PhOAc (13)
$PhCH_2OH$	42	56	$PhCH_2OAc$ (60)
Bu^tCO_2H	63	36	
$PhCO_2H$	52	30	$(PhCO)_2O$ (36)
p-TsOH	0	0	$(PhCH_2S)_2$ (57)
			$PhCH_2SO_2SCH_2Ph$ (19)
CF_3CO_2H	0	0	$(PhCH_2S)_2$ (65)
			$PhCH_2SO_2SCH_2Ph$ (8)

[a] Equimolar amount with that of (1a).

the E_i reaction of quaternary ammonium or sulphonium salts.[8a] The resulting carbanion once formed attacks the sulphonium sulphur affording the rearranged α-mercapto-sulphoxide which is then acetylated with acetic anhydride to give the α-acetylthio-sulphoxide (2). Route (b) involves initial proton abstraction from the methylene during the reaction. Incorporation of deuterium into the methine group of the rearranged product (2a) and the methylene group attached to the sulphenyl group of recovered (1a) was confirmed when the non-labelled thiosulphinate (1a) was treated with acetic anhydride in the presence of small amounts of deuterium oxide as



SCHEME 5 Preparation of deuterium-labelled thiosulphinates

group adjacent to the sulphenyl sulphur followed by rearrangement similar to that in route (a). A tracer experiment with specifically deuterium-labelled thiosulphinate allows a choice between these two routes. Therefore, we prepared both benzyl phenylmethanethiosulphinates labelled with deuterium at the methylene groups adjacent to either the sulphenyl or the sulphinyl sulphur atom (Scheme 5), and treated them with acetic anhydride. Deuterium-labelled thiosulphinate (1g or h) was recovered and the rearranged product (2g or h) was isolated. Both the position and the amount of deuterium in the recovered thiosulphinate and the product were determined by n.m.r. spectroscopic analysis. The results are shown in Table 3.

TABLE 3

Change in deuterium content [a] in the reaction of deuterium-labelled benzyl phenylmethanethiosulphinates with acetic anhydride

	Starting (1)			Product (2)		Recovered (1)	
No.	Sulphinyl (%)	Sulphenyl (%)	(1)	Methylene (%)	Methine (%)	Sulphinyl (%)	Sulphenyl (%)
1 [b]	~0 [b]	85	(1g)	~0	64	~0	75
2 [b]	~100 [b]	33	(1h)	~100	24	~100	60—65
3 [c]	~0 [c]	~0	(1g)	~0	16	~0	58

[a] Determined by ^{1}H n.m.r. [b] In the presence of acetic acid. [c] In the presence of deuterium oxide.

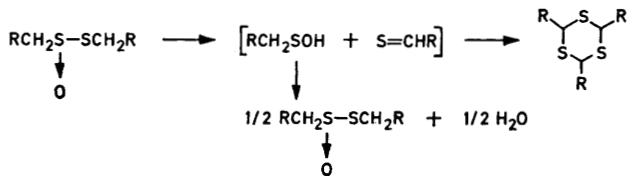
If the reaction proceeds *via* route (a), the deuterium-content of the sulphinyl methylene group of the starting thiosulphinate (1g or h) should be reduced to 50% in the product (2g or h). If the reaction proceeds *via* route (b), the deuterium content of the sulphinyl methylene group in the product (2g or h) should be either 100% if compound (1h) is used or 0% if (1g) is used. Inspection of the results revealed that the deuterium content of the methylene groups of (2g and h) was 100 and 0%, respectively, when the reaction was carried out with either (1h or g) clearly demonstrating that route (a) can be ruled out completely. Therefore, the deuterium-tracer experiment seems to favour route (b) in Scheme 4. However, as shown in run 1 of Table 3 the deuterium content of both the methylene group adjacent to the sulphenyl sulphur of the recovered (1g) and of the methine proton of the rearranged sulphoxide (2g) decreased from that of the starting compound (1g), indicating that substantial H–D exchange took place shown in run 3 of Table 3. However, no H–D exchange was observed at the methylene position adjacent to the sulphinyl sulphur in the starting compound (1a) under the reaction conditions. This H–D exchange observed in recovered (1a) and product (2a) appears to support route (b) in which there is an equilibrium between the acetylated intermediate and the carbanion. However, the deuterium content of the methylene group adjacent to the sulphenyl sulphur of recovered (1) in run 2 of Table 3 increased in contrast to the substantial decrease of deuterium in the case of (1g) in run 1. This indicates that a large portion of deuterium in the recovered thiosulphinate originated from the methylene group attached to the sulphinyl group of the starting compound (1h). Thus, these two results obtained from runs 1 and 2 cannot be rationalized on the basis of the simple mechanistic Scheme 4. Therefore, alternative mechanisms have to be considered.

Pyrolysis of sulphoxides [9] with at least one β-proton has been known to undergo intramolecular *cis*-elimination (E_i) to afford olefins and the corresponding sulphenic acid which condenses bimolecularly to afford the thiosulphinate.[8,10]

Recently, Block and his co-workers demonstrated that the pyrolysis of several alkane thiosulphinates gave the corresponding sulphenic acids and thioaldehydes.[4,11] If we assume the recombination of sulphenic acid and thioaldehyde to be facile after pyrolysis, the mechanism in Scheme 6, which can account for the unusual H–D exchange process, can be drawn, following Block's mechanism for the pyrolysis of thiosulphinates.

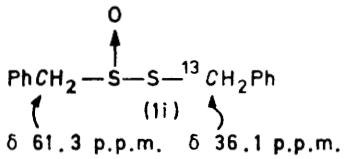
This mechanism involves a carbon skeleton rearrangement which can also account for the results of the

deuterium-tracer experiment, *i.e.*, since the sulphenic acid once formed reverts to the starting thiosulphinate by dimerization, the deuterium content of the methylene



SCHEME 6

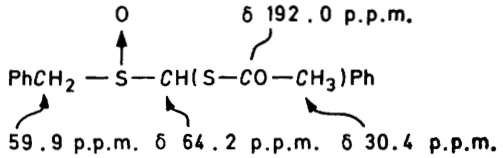
group attached to the sulphenyl group in the recovered thiosulphinate should increase if the thiosulphinate (1h) deuteriated at the methylene attached to the sulphinyl



group is used. In order to examine the validity of this mechanism, we prepared benzyl phenylmethanethiosulphinate (1i) labelled with ^{13}C at the carbon adjacent to the sulphenyl sulphur.

When [α-^{13}C]benzyl phenylmethanethiosulphinate (1i) was treated with acetic anhydride we expected to see a decrease of the ^{13}C content of the rearrangement product (2i) during the reaction, owing to dilution of the starting thiosulphinate by regeneration of non-^{13}C labelled thiosulphinate. The ^{13}C content in both the thiosulphinate (1i) and the sulphoxide (2i) were indeed found to have decreased as shown in Table 4. This result indicates that carbon skeletal scrambling takes place during the reaction and is consistent with the H–D exchange process described above. Thus, the mechanism of this rearrangement does not involve a simple initial acylation as in the Pummerer rearrangement as shown in Scheme 4 but involves initial formation of sulphenic acid *via* β-elimination. Therefore, in order to obtain further evidence in support of the mechanism, we attempted to trap the sulphenic acid formed in our reaction system by treatment with an electrophilic olefin.[11] When the reaction of the thiosulphinate (1a) with acetic anhydride was carried out in the presence of a 10 molar excess of methyl acrylate, benzyl 2-methoxycarbonylethyl sulphoxide (4) was obtained in 83% yield. This result clearly indicates incipient formation of the sulphenic acid.

In the reaction of thiosulphinate (1a) with acetic anhydride containing small amounts of deuterium oxide and acetic acid, the methylene protons adjacent to the sulphenyl sulphur were found to undergo easy H–D exchange. However, this H–D exchange was not limited only to the Pummerer conditions but was found to take place when thiosulphinate (1a) was warmed at 60 °C in aprotic solvents containing small amounts of deuterium oxide (Table 5).



In such a neutral medium this H–D exchange seems to result from initial formation of the sulphenyl carbanion *via* intramolecular proton abstraction from sulphenyl proton by the sulphinyl group. Some of the sulphenic acid and the thioaldehyde thus formed may escape from this solvent cage and self-condensation of the sulphenic acid regenerates the thiosulphinate while the thioaldehyde polymerizes to afford the trimer and higher oligomers.

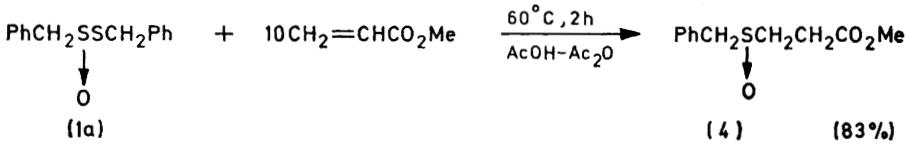
TABLE 4

Change in ^{13}C content in the reaction of [α-^{13}C]benzyl phenylmethanethiosulphinate (1i) with acetic anhydride

	Starting (1i)		Product (2i)		Recovered (1i)	
Time (h)	Sulphinyl (%)	Sulphenyl (%)	Methylene (%)	Methine (%)	Sulphinyl (%)	Sulphenyl (%)
2 [a]	0.0	32.0 (100)	0.0	24.5 (76)	0.3	19.8 (62)
2 [b]	0.0	55.0 (100)	0.0	43.0 (78)	0.0	27.0 (50)
1 [b]	0.0	55.0 (100)	0.0	53.0 (98)	0.0	45.0 (82)

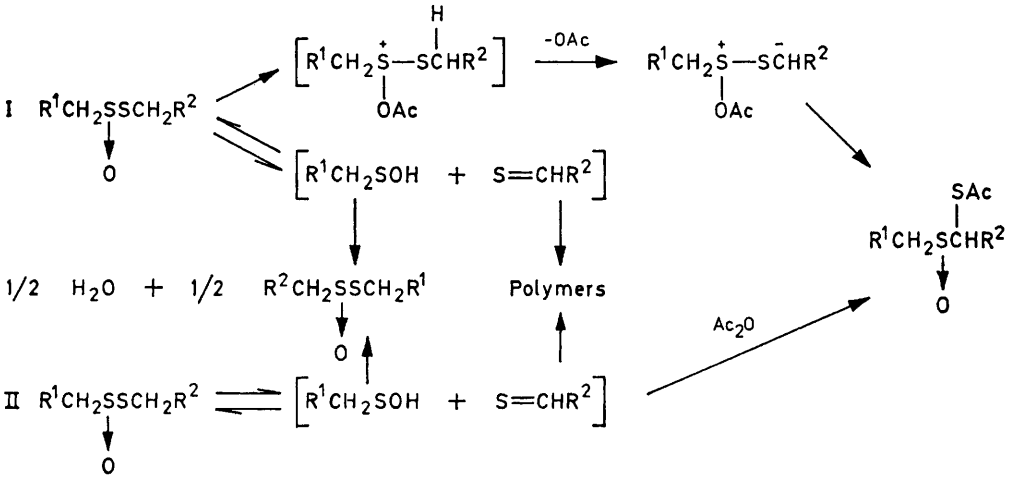
[a] ^{13}C Content was determined by ^{13}C n.m.r. [b] Determined by ^{1}H n.m.r. by ^{13}C satellite method.

One remaining question is why acetic anhydride and a small amount of acetic acid are necessary. Thus, a Pummerer-type process involving initial acetylation of



sulphinyl oxygen cannot be ruled out completely. In the Pummerer reaction of sulphoxides or sulphinates, the sulphinyl oxygen of the sulphoxide [12] or sulphinate [13] is known to undergo ^{18}O exchange with that of the acyl anhydride through a sulphurane intermediate. We found that the sulphinyl oxygen of benzyl phenylmethanethiosulphinate (1a) was also exchanged with that of trifluoroacetic anhydride during reaction at −70 °C, though the products were benzyl phenylmethanethiosulphonate (18—37%) and dibenzyl disulphide (41—49%) as shown in Table 6.

Such an ^{18}O exchange should be observed if the Pummerer-type mechanism operates in the reaction of the thiosulphinate. Therefore, a tracer experiment was carried out with ^{18}O labelled thiosulphinate (1j). The deuterium kinetic isotope effect should be observed. Thus, both the rate of decrease of the starting material (1a) and of [α,α-$^2H_2$]benzyl phenylmethanethiosulphinate (1g) were determined for comparison. The reactions



SCHEME 7 Reaction mechanism

results of the reaction shown in Table 7 [14] indicate clearly that the ^{18}O content in both the starting and recovered (1j) and also the sulphoxide (2j) is identical

TABLE 5

H–D Exchange at the methylene protons adjacent to the sulphenyl sulphur of (1a) in various solvents containing a small amount of deuterium oxide

Temp. (°C)	Time (min)	Solvent	Deuterium content (%)
60	20	Acetone	19 [a]
Room	20	Acetone	<5 [a]
60	20	THF	15
60	20	[$^2H_4$]Methanol	*ca.* 0 [b]
60	30	Acetonitrile	31
60	120	Acetonitrile	26
60	20	Acetic anhydride	20 [a]

[a] Samples purified by chromatographic method were used for the measurement of n.m.r. spectra. [b] Most of the starting material had been decomposed by the solvent.

TABLE 6

Change in ^{18}O content [a] in the reaction of ^{18}O-labelled thiosulphinate (1j) with trifluoroacetic anhydride in methylene chloride at −70 °C

Run	Starting (1j) (%)	Thiosulphonate (%)	Recovered (1j) (%)
1	100.0 [b]	37.7	
	100.0	46.6	53.1
2	100.0	47.4	38.7
	100.0		37.1
3	100.0	46.0	33.8
	100.0	52.9	

[a] Measured twice for each sample. [b] Percentages were measured on the basis of the ^{18}O content of starting material (1j); 0.833 ± 0.032 excess atom % for run 1, 0.843 ± 0.015 for runs 2 and 3.

within experimental errors, and hence a Pummerer-type mechanism involving the initial acetylation can be ruled out.

If the initial E_i process is rate determining, a sizeable were found to follow the first-order kinetic equation and the rate constants were calculated to be k_H 1.12 ± 0.08 × 10^{-4} and k_D 0.84 ± 0.10 × 10^{-4} s^{-1}, respectively. Thus, the value of k_H/k_D was *ca.* 1.3 as shown in Table 8 and the Figure. This small isotope effect suggests

TABLE 7

Change in ^{18}O content [a] in the reaction of ^{18}O-labelled thiosulphinate (1j) with acetic anhydride

Run	Starting (1j) (%)	Product (2j) (%)	Recovered (1j) (%)
1	100.0 [b]	102.8	102.6
	100.0	105.6	99.5
2	100.0	105.8	96.6ω
	100.0		87.0

[a] Measured twice for each sample. [b] Percentages were measured on the basis of the ^{18}O content of starting thiosulphinate (1j); 0.833 ± 0.032 excess atom % for run 1, 0.843 ± 0.015 for run 2.

that the initial hydrogen abstraction is not rate determining but is a part of the ready reversible E_i and recombination process.

The recombination of the two fragments *via* combination of the sulphenyl sulphur and the thiocarbonyl

TABLE 8

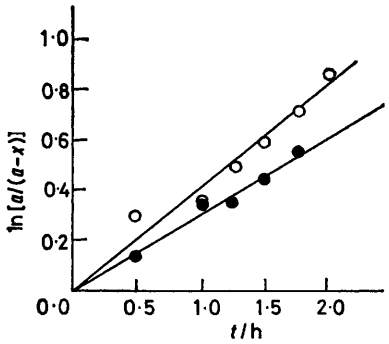
Kinetic data on the reaction of benzyl phenylmethanethiosulphinate (1a and g) in acetic anhydride at 60 ± 1 °C

Thiosulphinate	$10^4k/s^{-1}$
(1a) [a] (H)	1.12 ± 0.08
(1g) [b] (D)	0.84 ± 0.10

[a] (1a) 2.00 × 10^{-1} M; acetic acid 2.03 × 10^{-1} M. [b] (1g) 2.00 × 10^{-1} M; acetic acid 2.03 × 10^{-1} M.

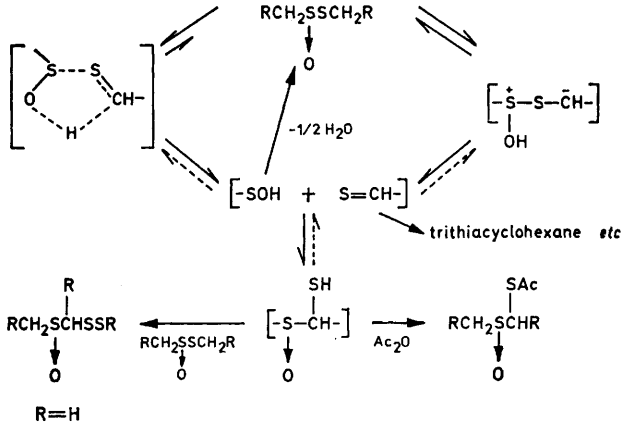
carbon atom in the cage gives an α-mercapto-sulphoxide, an unstable intermediate which is immediately acetylated in an irreversible reaction. Some thioaldehyde which escapes from the cage gives oligomers while some sulphenic acid reverts to the original thiosulphinate. In

some cases, the α-mercapto-sulphoxide apparently reacted with starting material to give an α-sulphinyldisulphide (Scheme 8; R = H). Once the α-mercapto-sulphoxides are acetylated, reverse deacylation or acyl



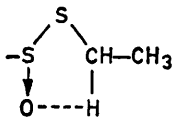
Plot of log[a/(a — x)] *versus* time for the reaction of benzyl phenylmethanethiosulphinate (1a) (○) and [α,α-$^2H_2$]benzyl phenylmethanethiosulphinate (1g) (●) with acetic anhydride

exchange does not seem to take place since neither exchange of the acetyl group nor H–D exchange of the methine proton of the product (2) was observed even when a solution of (2a) in [$^2H_6$]acetic anhydride containing [$^2H_4$]acetic acid was kept standing for 2 h in a thermostatted bath at 60 °C. The weak acid probably activates the acetic anhydride at the acylation stage of



SCHEME 8

the intermediate α-mercapto-sulphoxide.* Recently, the ^1H n.m.r. spectra of the methylene protons attached to the sulphenyl group in a thiosulphinate were found to show an abnormal downfield shift while the ^{13}C n.m.r. of the sulphenyl methylene group shows an upfield shift compared with that of disulphide, sulphinate, or even thiosulphonate.[15] This indicates that in thiosulphinates the protons of the methylene group attached to the sulphenyl group should be highly acidic and thus can



(E)

assume the favoured five-membered ring conformation (E) through hydrogen bonding with sulphinyl oxygen even in the ground state. This seems to be responsible

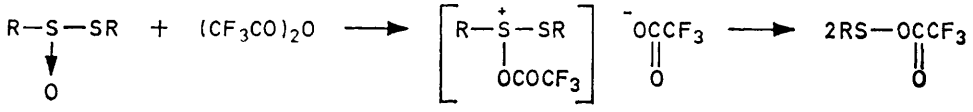
	Ph–SO_2–S–CH_2–CH_3	Ph–SO–S–CH_2–CH_3	Ph–S–S–CH_2–CH_3
δ_C (p.p.m.)	30.5 14.1	27.6 15.9	32.6 14.1
δ_H	3.00 1.28	3.13 1.43	2.71 1.29

for the initial facile E_i process in this rearrangement. Therefore, the overall reaction to form the α-acetylthiosulphoxide (2) *via* an initial E_i process and subsequent recombination can be depicted as in Scheme 8.

EXPERIMENTAL

M.p.s are uncorrected. I.r. spectra were taken as thin films on a Hitachi 215 grating spectrophotometer. ^1H N.m.r. spectra were obtained with either a Hitachi R-24A or a Hitachi–Perkin-Elmer R-20 high resolution spectrometer. ^{13}C N.m.r. spectra were measured by Fourier transform spectrometer (JEOL JNM FX-100). Mass spectra were determined on a Hitachi RMU-6MG mass spectrometer. Liquid phase chromatography was carried out with a Yanaco L-1030 liquid chromatograph. A 50 cm × 3 mm column of Yanapak Gel 5510 (MeOH as eluant) was used for analytical purposes. Preparative t.l.c. was performed on 2 mm thick Merck PF_{254} silica gel plates.

Syntheses of Symmetrical Thiosulphinates.—Methyl methanethiosulphinate (1e). To a solution of dimethyl disulphide (4.72 g, 50 mmol) in methylene chloride (10 ml) at 0 °C was added 80% *m*-chloroperbenzoic acid (10.9 g, 50 mmol) during 10 min. After the solution was stirred for an additional 5 h at 0 °C, the resulting precipitates were filtered off. The organic phase was treated with powdered sodium carbonate in order to remove the remaining *m*-chlorobenzoic acid and the solution was concentrated *in vacuo*. Vacuum distillation afforded compound (1e) (4.74 g, 86%), b.p. 53—56 °C at 15 mmHg. The other symmetrical thiosulphinates were prepared by the same procedure except the solid thiosulphinates which were purified by recrystallization from ether: ethyl ethanethiosulphinate



(4) (5)

* The roles of acetic anhydride and acetic acid are still not established. However, when the reaction was carried out with trifluoroacetic anhydride, the mixed anhydride (5) was formed and trapped with olefins. The results will be published in due course. This indicates clearly that a strong acylating agent such as trifluoroacetic anhydride gives rise to the Pummerer reaction. However, acetic anhydride is too weak an acylating agent toward sulphinyl oxygen to give rise to a Pummerer-type intermediate. Therefore, under the present reaction conditions, E_i-type thermolysis is predominant and acetic acid may play a role in activating acetic anhydride to acylate the intermediate thiol.

(1d), yield 56%, b.p. 63.0—65.5 °C at 2 mmHg; 1,2-dithiacyclohexane *S*-oxide (1f), 78%, m.p. 60—62 °C; benzyl phenylmethanethiosulphinate (1a), 69%, m.p. 80—82 °C; *p*-methylbenzyl *p*-tolylmethylmethanethiosulphinate (1b), 36%, m.p. 80—81 °C.

Syntheses of Unsymmetrical Thiosulphinates and Benzyl Phenylmethanethiosulphinate (1a).—*Benzyl phenylmethanethiosulphinate* (1a). Phenylmethanesulphinyl chloride [16] was prepared in an excellent yield by chlorinolysis at −10 °C of the mixture of dibenzyl disulphide and acetic anhydride until an equimolar quantity of chlorine was absorbed. Generally, a solution of phenylmethanesulphinyl chloride (2.0 g, 9.2 mmol) prepared as above in anhydrous ether (20 ml) was added for 20 min to a vigorously stirred solution of toluene-α-thiol (1.2 g, 9.7 mmol) and anhydrous triethylamine in anhydrous ether (30 ml), maintained at −20 °C. A heavy precipitate was formed during the addition. After the addition, the solution was stirred until the temperature rose to 0 °C. The solvent was removed *in vacuo* and the residue was dissolved in water and extracted with methylene chloride. The organic layer was separated, washed with ice-cold water, dried ($MgSO_4$), and the solvent was evaporated *in vacuo*. The crude product was washed with hexane and recrystallized from ether to give (1a) (1.54 g, 64%), m.p. 81—83 °C. The other unsymmetrical thiosulphinates were prepared by this procedure: methyl 1,1-dimethyl ethanethiosulphinate; [17] yield 91%, b.p. 75—77 °C at 2 mmHg; *p*-methylbenzyl phenylmethanethiosulphinate (1c), 64%, m.p. 73—74 °C.

1,1-*Dimethylethanesulphinyl chloride*. This sulphinyl chloride was prepared in a two-step process from bis-(1,1-dimethylethyl) disulphide by initial oxidation with 30% H_2O_2 at 0 °C and subsequent dilution with water and extraction into chloroform. Chlorinolysis was performed until an equivalent amount of chlorine was absorbed at 10 °C.

Syntheses of Deuterium-labelled Thiosulphinates.—[α,α-$^2H_2$]Benzyl phenylmethanethiosulphinate (1g) and benzyl phenyl[$^2H_2$]methanethiosulphinate (1h) were prepared from the corresponding α-deuteriated toluene-α-thiol and phenylmethanesulphinyl chloride by the procedure for (1a). Compound (1g) (56%) had m.p. 85—86 °C, (1h) (59%) m.p. 80—81 °C.

[α,α-$^2H_2$]*Benzyl alcohol*. This alcohol was prepared by the reduction of methyl benzoate with lithium aluminium deuteride in anhydrous ether in 81% yield, b.p. 110.0—111.5 °C at 31 mmHg.

[α,α-$^2H_2$]*Toluene-α-thiol*.[18] A mixture of benzyl alcohol (10.6 g, 96 mmol) and thiourea (7.5 g, 99 mmol) was refluxed for 9 h in 47% hydrobromic acid (50 g, 0.29 mol) and cooled to room temperature. After a solution of sodium hydroxide (11.7 g, 0.29 mol) in water (120 ml) was added, the mixture was refluxed for 2 h under nitrogen. The solution was acidified with sulphuric acid, extracted with ether, and dried ($MgSO_4$). Vacuum distillation afforded [α,α-$^2H_2$]-toluene-α-thiol (9.13 g, 75%), b.p. 88—90 °C at 21 mmHg.

Bis([α,α-$^2H_2$]*benzyl*) *disulphide*. The disulphide was prepared by alkaline iodide oxidation of [α,α-$^2H_2$]toluene-α-thiol in 93% yield, m.p. 70.0—71.5 °C.

Phenyl[$^2H_2$]*methanesulphinyl chloride*. To a mixture of dibenzyl disulphide (2.0 g, 8.0 mmol) and acetic anhydride (1.7 g, 16.0 mmol) was added an equivalent amount of chlorine (1.7 g, 24.0 mmol) at −10 °C. After the disulphide was dissolved completely, the resulting acetyl chloride was removed under reduced pressure. The residue was washed with hexane. The decantation of the supernatant solution and complete evaporation of the solvent gave a yellow oil (1.7 g, 85%).

Synthesis of [α-^{13}C]*Benzyl Phenylmethanethiosulphinate* (1i).—The thiosulphinate (1i) was prepared from [α-^{13}C]-toluene-α-thiol and phenylmethanesulphinyl chloride by the same procedure as that of (1a), yield 71%, m.p. 81—83 °C. The ^{13}C content of the methylene carbon adjacent to the sulphenyl sulphur was 55 or 32%, $\delta_C(CDCl_3)$ 35.3 (CH_2S), 61.3 (CH_2SO), 127.1, 128.2, 128.5, 129.5, 129.8, and 136.2 p.p.m. (aromatic); *m/e* 123, 122, 121, 92, and 91 (100%).

Benzoic [^{13}C]*acid*.[19] The acid (86%) was prepared by treating phenylmagnesium bromide with $^{13}CO_2$ generated by adding concentrated H_2SO_4 to $Ba^{13}CO_3$ (^{13}C content 60%) in a vacuum line.

[α-^{13}C]*Benzyl alcohol*. The reduction of benzoic [^{13}C]acid with lithium aluminium hydride afforded the alcohol in 94% yield, b.p. 120 °C at 26 mmHg.

[α-^{13}C]*Toluene-α-thiol*.[18] The thiol was prepared from [α-^{13}C]benzyl alcohol and thiourea in 47% hydrobromic acid in 77% yield, b.p. 90 °C at 18 mmHg; $\delta_C(CDCl_3)$ 28.8 (CH_2S), 126.9, 127.9, 128.5, and 141.0 (aromatic); *m/e* 125 (M^+), 124, 92 (100%), and 91.

Synthesis of Benzyl Phenylmethanethio[^{18}O]*sulphinate* (1j).—The thiosulphinate (1j) was prepared from toluene-α-thiol and phenylmethane[^{18}O]sulphinyl chloride by the same procedure as that of (1a), yield 70%, m.p. 79.5—80.5 °C. The ^{18}O content of the sulphinyl oxygen was 0.833 ± 0.032 or 0.843 ± 0.015 excess atom %.

Phenylmethane[^{18}O]*sulphinyl chloride*. The sulphinyl chloride was prepared from dibenzyl disulphide, acetic anhydride enriched with ^{18}O (^{18}O content 0.854 excess atom %) and chlorine gas in 81% yield.[13]

Reaction of Thiosulphinates (1) *with Acetic Anhydride Containing Acetic Acid*.—A typical procedure is as follows. Benzyl phenylmethanethiosulphinate (1a) (1.42 g, 5.42 mmol) and acetic acid (0.327 g, 5.45 mmol) were dissolved in acetic anhydride (20 ml). The mixture was allowed to stand for 2 h at 60 °C. After excess of acetic anhydride and acetic acid were removed under reduced pressure, the residue was dissolved in a small amount of chloroform and insoluble 2,4,6-triphenyl-1,3,5-trithiacyclohexane (29 mg, 2.2%) was filtered off. The solution was added dropwise to methanol (50 ml) and cooled to 0 °C in an ice-bath with stirring. After removal of the precipitate, which was presumed to consist of either polymers or oligomers of thiobenzaldehyde, the solvent was evaporated. The residual oil was chromatographed on a silica gel column (Wakogel C-300) using chloroform as eluant. Recovered (1a) (482 mg, 34%) and α-acetylthiobenzyl benzyl sulphoxide (2a) (955 mg, 58%) were collected. The *erythro*- and *threo*-isomers of (2a) were separated by preparative t.l.c. on silica gel using benzene–ethyl acetate (6 : 1) as eluant. The configurations of the two isomers were not determined. 2,4,6-Triphenyl-1,3,5-trithiacyclohexane [7] had m.p. 225—227 °C, δ_H ([$^2H_6$]DMSO) 5.83 (1 H, s) and 7.3—7.5 (5 H, m). Compound (2a), isomer (A) had m.p. 85—86 °C, $\delta_H(CDCl_3)$ 2.35 (3 H, s), 3.60 and 3.76 (2 H, q, *J* 13.2 Hz), 5.50 (1 H, s), and 7.1—7.4 (10 H, m); $\nu_{max.}$ (KBr) 1 702 (C=O) and 1 040 cm^{-1} (S–O); *m/e* 165 $(PhCHS\text{-}COCH_3)^+$, 122 $(PhC{=}S)^+$, and 91 ($C_7H_7^+$, 100%) (Found: C, 63.1; H, 5.3; S, 20.7. Calc. for $C_{16}H_{16}O_2S_2$: C, 63.1; H, 5.3; S, 21.1%). Isomer (B) had m.p. 110.5—111.5 °C, $\delta_H(CDCl_3)$ 2.40 (3 H, s), 3.59 and 3.83 (2 H, q, *J* 12.8 Hz),

5.63 (1 H, s), and 7.2—7.4 (10 H, m); $\nu_{max.}$ (KBr) 1 692 (C=O) and 1 040 cm^{-1} (S–O); *m/e* 165 $(PhCHSCOCH_3)^+$, 122 $(PhCH{=}S)^+$, and 91 ($C_7H_7^+$, 100%) (Found: C, 63.0; H, 5.2; S, 20.6%).

The reactions of the other thiosulphinates (1b—f) and the labelled benzyl phenylmethanethiosulphinates (1g—j) with acetic anhydride containing acetic acid or other acids were carried out as described above. The results are shown in Tables 1—4, 6, and 7.

α-Acetylthio[α-^{13}C]benzyl benzyl sulphoxide (2i), isomer (A) had δ_C ($CDCl_3$) 30.4 (CH_3), 56.9 (CH_2SO), 64.2 (CH), 128.3, 128.8, 129.2, 129.6, 129.9, 130.7 (aromatic), and 192.0 p.p.m. (CO); *m/e* 166, 165, 123, 122 (100%), and 91.

(α-Acetylthio)-*p*-methylbenzyl *p*-methylbenzyl sulphoxide (2b), isomer (A) had m.p. 41.0—42.5 °C, δ_H($CDCl_3$) 2.28, 2.30, and 2.32 (9 H, 3 × s), 3.54 and 3.67 (2 H, q, *J* 13.1 Hz), 5.42 (1 H, s), and 6.9—7.4 (8 H, m); $\nu_{max.}$ (KBr) 1 695 (C=O) and 1 055 cm^{-1} (S–O). Isomer (B) had m.p. 117—118 °C, δ_H($CDCl_3$) 2.31, 2.37, and 2.42 (9 H, 3 × s), 3.63 and 3.84 (2 H, q, *J* 12.4 Hz), 5.56 (1 H, s), and 6.9—7.4 (8 H, m); $\nu_{max.}$ (KBr) 1 685 (C=O) and 1 040 cm^{-1} (S–O).

The *erythro*- and *threo*-isomers of (α-acetylthio)-*p*-methylbenzyl benzyl sulphoxide (2c) were not separated because the product obtained from the reaction of (1c) with acetic anhydride was a mixture of (2c) (73%) and (2a) (27%). Isomer (A) had δ_H($CDCl_3$) 2.33 and 2.38 (6 H, 2 × s), 3.54 and 3.76 (2 H, q, *J* 12.4 Hz), 5.48 (1 H, s), 7.1—7.5 (9 H, m).

1-Acetylthioethyl ethyl sulphoxide (2d) was an oil (mixture of *erythro*- and *threo*-isomers), $\nu_{max.}$ (neat) 1 700 (C=O) and 1 050 cm^{-1} (S–O). Isomer (A) had δ($CDCl_3$) 1.37 (3 H, t, *J* 7.1 Hz), 1.59 (3 H, d, *J* 7.3 Hz), 2.39 (2 H, s), 2.68 (2 H, m), and 4.52 (1 H, q, *J* 7.3 Hz). Isomer (B) had δ($CDCl_3$) 1.34 (3 H, t, *J* 7.4 Hz), 1.71 (3 H, d, *J* 7.5 Hz), 2.42 (3 H, s) 2.68 (2 H, m), and 4.58 (1 H, q, *J* 7.5 Hz).

Acetylthiomethyl methyl sulphoxide (2e) was an oil, δ($CDCl_3$) 2.45 (3 H, s), 2.56 (3 H, s), and 4.13br (2 H, s); $\nu_{max.}$ (neat) 1 700 (C=O) and 1 045 cm^{-1} (S–O).

2,3,5-Trithiahexane 5-oxide was an oil, δ($CDCl_3$) 2.53 (3 H, s), 2.68 (3 H, s), and 3.89, and 4.10 (2 H, q), *J* 13.3 Hz); $\nu_{max.}$ (neat) 1 040 cm^{-1} (S–O).

Oxidation of α-Acetylthiosulphoxides (2).—*Oxidation of α-acetylthiobenzyl benzyl sulphoxide* (2a). Sulphoxide (2a) (0.17 g, 0.56 mmol) was oxidized with 30% H_2O_2 (1.06 g, 3.0 mmol) in acetic acid (5 ml). The mixture was stirred for 20 h at room temperature and poured into a separating funnel together with water (30 ml). The aqueous solution was extracted with benzene (5 × 2 ml). The organic phase was washed with aqueous base, dried ($MgSO_4$), and concentrated *in vacuo*. The crude sulphone was obtained in 74% yield and recrystallized from ethanol, m.p. 109.0—109.5 °C, δ($CDCl_3$) 2.40 (3 H, s), 4.22 (2 H, s), 5.76 (1 H, s), and 7.2—7.6 (10 H, m); $\nu_{max.}$ (KBr) 1 710 (C=O), 1 310, 1 307 (SO_2), 1 135, and 1 125 cm^{-1} (SO_2); *m/e* 165 $(PhCHSOCH_3)^+$ and 91 ($C_7H_7^+$, 100%) (Found: C, 60.1; H, 5.0. Elemental analysis. Calc. for $C_{16}H_{16}O_2S_2$: C, 60.0; H, 5.0%).

Oxidation of 1-acetylthioethyl ethyl sulphoxide (2d). This sulphoxide (2d) was oxidized with *m*-chloroperbenzoic acid in methylene chloride at room temperature to give the corresponding sulphone (4d) in 65% yield oil, δ($CDCl_3$) 1.40 (3 H, t, *J* 7.2 Hz), 1.73 (3 H, d, *J* 7.2 Hz), 2.43 (3 H, s), 3.07 (2 H, q, *J* 7.2 Hz), 4.80 (1 H, q, *J* 7.2 Hz); $\nu_{max.}$ (neat) 1 700 (C=O), 1 310 (SO_2), and 1 130 cm^{-1} (SO_2).

Thermal Decomposition of Benzyl Phenylmethanethiosulphinate (1a) *in Acetonitrile*.—A solution of (1a) (32 mg, 1.65 mmol) in acetonitrile (10 ml) was allowed to stand overnight at 60 °C. After the solvent was removed *in vacuo*, 2,4,6-triphenyl-1,3,5-trithiacyclohexane (169 mg, 42%), which was insoluble in benzene, was filtered off and then the filtrate was condensed *in vacuo*. The residue was chromatographed through a column packed with silica gel using benzene as eluant. The eluant gave benzyl phenylmethanethiosulphinate (17 mg, 4%) and an unidentified complex mixture (180 mg) together with dibenzyl disulphide.

Trapping of Phenylmethanesulphenic Acid with Methyl Acrylate in the Reaction of Benzyl Phenylmethanethiosulphinate (1a) *with Acetic Anhydride*.—A solution of (1a) (394 mg, 1.5 mmol) and acetic acid (92 mg, 1.5 mmol) in acetic anhydride (10 ml) was heated for 2 h at 60 °C in the presence of methyl acrylate (1.29 g, 15 mmol). After excess of anhydride and methyl acrylate was removed under reduced pressure, the residue was chromatographed through a column packed with silica gel using chloroform as eluant. The resulting benzyl 2-methoxycarbonylethyl sulphoxide (5) was obtained in 83% yield and recrystallized from benzene–hexane, m.p. 80.0—81.5 °C, δ($CDCl_3$) 2.81 (4 H, m), 3.67 (3 H, s), 3.98 (2 H, s), and 7.31 (5 H, s); $\nu_{max.}$ (KBr) 1 720 (C=O) and 1 035 cm^{-1} (S–O).

Preparation of the Authentic Benzyl 2-Methoxycarbonylethyl Sulphoxide (5).—Benzyl 2-methoxycarbonylethyl sulphide was prepared by stirring a solution of toluene-α-thiol (4.0 g, 32 mmol) and methyl acrylate (15 g, 174 mmol) in methanol (10 ml) in the presence of small amounts of sodium methoxide. The excess of methyl acrylate and the solvent were removed *in vacuo*. Vacuum distillation at 133 °C and 4 mmHg afforded the sulphoxide (5.96 g, 88%). This sulphide (2.10 g, 10 mmol) was oxidized with 90% *m*-chloroperbenzoic acid (1.93 g, 10.1 mmol) in methylene chloride (50 ml). After stirring the mixture for 3 h at 0 °C, the precipitate was removed and the organic phase was washed with aqueous base and water and dried ($MgSO_4$). The solvent was removed *in vacuo*. A solid (5) was obtained in 79% yield and recrystallized from benzene–hexane, m.p. 79—80 °C, δ ($CDCl_3$) 2. 81 (4 H, m), 3.67 (3 H, s), (2 H, s), and 7.31 (5 H, s); $\nu_{max.}$ (KBr) 1 720 (C=O) and 1 035 cm^{-1} (S–O) (Found: C, 58.35; H, 6.1. Calc. for $C_{11}H_{14}O_3S$: C, 58.4; N, 6.2%).

Measurement of the Deuterium Kinetic Isotope Effect in the Reaction of Benzyl Phenylmethanethiosulphinate (1a) *with Acetic Anhydride*.—A solution of [α,α-$^2H_2$]benzyl phenylmethanethiosulphinate (1g) (486 mg, 1.84×10^{-3} mol), acetic acid (112 mg, 1.87×10^{-3} mol), and benzyl phenyl ether (85 mg, 4.63×10^{-4} mol) in acetic anhydride (9.2 ml) was prepared. A solution of (1a) (482 mg, 1.84×10^{-3} mol), acetic acid (112 mg, 1.87×10^{-3} mol), and benzyl phenyl ether (85 mg, 4.63×10^{-4} mol) in acetic anhydride (9.2 ml) was also prepared separately as the standard solution. The reaction of both deuterium-labelled and unlabelled thiosulphinates was carried out at 60 ± 1 °C in a thermostatted bath. A portion (1 ml) of the mixture was taken up at 10 min intervals for 50 min. Each portion of the mixture was condensed *in vacuo* and dissolved in $CDCl_3$. The decrease of starting material (1a) was followed by comparing the n.m.r. spectrum with that of benzyl phenyl ether as internal standard. The reaction was found to obey first-order kinetics for the initial phase of the conversion of (1a). The rate constants obtained are k_H $1.12 \pm 0.08 \times 10^{-4}$ and k_D $0.84 \pm 0.10 \times 10^{-4}$ s^{-1}. The value of

k_H/k_D at 60 °C calculated from these experimental data was *ca.* 1.3.

Determination of Isotope Content.—Both the position and amount of deuterium were determined by ^1H n.m.r. The ^{13}C content was determined by comparing the relative intensities (peak heights or areas) of the respective carbon atoms in natural abundance and ^{13}C enriched compounds [20] or by ^1H n.m.r. using the ^{13}C satellite method which was available for the determination of the ^{13}C content because of the large ^{13}C–^1H coupling constants. ^{18}O Analyses were carried out by converting the ^{18}O containing sample to CO_2 by a modification of the method of Rittenberg and Ponticorvo.[21] The carbon dioxide formed was purified and subjected to mass spectrometric analysis. The ^{18}O content was calculated from the peak heights at *m/e* 44 and 46.

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