Tetrahedron. Vol. 28, pp. 2759 to 2765. Pergamon Press 1972. Printed in Great Britain

THE PUMMERER REARRANGEMENT OF PHENYL METHYL SULPHONIUM BIS(METHOXYCARBONYL)-METHYLIDE

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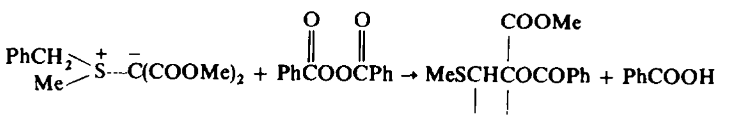
(*Received in Japan* 19 *November* 1971; *Received in the UK for publication* 18 *January* 1972)

Abstract—The reaction between phenyl methyl sulphonium bis(methoxycarbonyl)methylide and either acetic anhydride or benzoyl peroxide proceeds *via* "Pummerer" type rearrangement to afford phenyl α-acyloxymethyl sulphide. The kinetic data suggest that the rate-determining step involves S—C bond cleavage after initial acylation or acyloxylation and subsequent proton removal by acyloxy anion unlike the corresponding reaction of the analogous sulphoxide with acetic anhydride in which the rate determining step is proton removal.

SULPHONIUM YLIDES are trivalent sulphur compounds bearing a semi-polar $>\overset{+}{S}-\overset{-}{X}$ linkage like sulphoxides and sulphilimines and are expected to display similar chemical behaviour, such as the Pummerer reaction which is known to take place readily with sulphoxides bearing a methyl or methylene group. Although the nucleophilic centre of sulphonium bis(methoxycarbonyl)methylide is very poorly nucleophilic, it attacks the peroxy bond of acyl peroxides, giving a rearranged product.[1] For example, the reaction of benzyl methyl sulphonium bis(methoxycarbonyl)-methylide with B.P.O. gives the corresponding methyl-1-phenyl-2,2-(dimethoxycarbonyl)-2-benzoyloxyethyl sulphide (I), *via* a Stevens type rearrangement, (eq. 1).



(eq. 1)

Meanwhile phenyl methyl sulphonium bis(methoxycarbonyl)methylide and B.P.O. was found to give phenyl benzoyloxymethyl sulphide (II) and methyl benzoyloxy malonate (III), apparently *via* a Pummerer reaction (eq. 2).

This imples that, even with a poorly nucleophilic ylide, a Pummerer type reaction would take place and indeed with acetic anhydride, this ylide was found to undergo the Pummerer reaction (eq. 3).

While the Pummerer reaction of sulphoxides has been investigated extensively,[2] practically no work has been done on a possible Pummerer type reaction of any

$$\mathrm{Ph(Me)\overset{+}{S}{-}\overset{-}{C}(COOMe)_2 + B.P.O. \rightarrow \underset{(II)}{PhSCH_2OCOPh} + \underset{(III)}{PhCOOCH(COOMe)_2}} \quad \text{(eq. 2)}$$

$$\mathrm{Ph(Me)\overset{+}{S}{-}\overset{-}{C}(COOMe)_2 + Ac_2O \rightarrow \underset{(IV)}{PhSCH_2OCOMe} + \underset{(V)}{MeCOCH(COOMe)_2}} \quad \text{(eq. 3)}$$

sulphonium ylide. Therefore, we initiated a detailed kinetic study on the Pummerer type reaction of this particular sulphonium ylide especially in comparison with that of the corresponding sulphoxide and possibly with that of another trivalent sulphur compound, the sulphilimine.

We have carried out a detailed kinetic study on the reaction of aryl methyl sulphonium ylides with both acetic anhydride and B.P.O., using substituted-phenyl methyl sulphonium ylides and the trideuterated compound. Here we report the kinetic data and their mechanistic implications.

RESULTS AND DISCUSSION

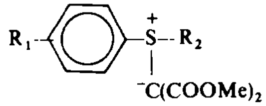
The rate of the Pummerer reaction between the ylide and acetic anhydride can be readily followed spectrophotometrically, taking an advantage of the difference of UV spectra of the starting ylide and that of the final compounds, *i.e.*, arylmercaptan obtained by quenching the reaction mixture with water, and the reaction was found to have a pseudo-first order kinetic relationship. Meanwhile, in the case of benzoyl peroxide, iodometric titration developed by Bartlett and Altschul[3] was used for the kinetic measurement and the reaction was found to be second order. The rate constants obtained for both reactions are listed in Table 1 and 2, respectively, while Hammett's ρ value and activation parameters are tabulated in Table 3 in comparison with those of the corresponding sulphoxide and sulphilimine.

Like the Pummerer reaction of sulphoxide[2] the overall reaction may be depicted as shown below. The reaction involves the initial formation of a sulphonium salt (A) by the nucleophilic attack of ylide carbanion (step 1), the subsequent proton removal by the corresponding anion from (A) (step 2), the cleavage of the S—C bond and the final recombination of the reaction intermediate (B) with an anion (step 3) (Scheme 1).

In order to examine the possibility of proton removal as rate-determining (step 2), the kinetic isotope effect was measured using trideuterated-methyl phenyl sulphonium ylide and the values of $k_H/k_D = 1{\cdot}57$ for Ac_2O, 1·10 for B.P.O., respectively, were obtained. The relatively small size of the isotope effect as compared to that of sulphoxide ($k_H/k_D = 2{\cdot}86$) suggests that proton removal is not rate-determining.

In order to examine a possible proton excnange, a quenching experiment of the reaction mixture of trideuterated methyl phenyl sulphonium ylide with Ac_2O in the presence of AcOH at about 20% completion was carried out. The ylide thus recovered

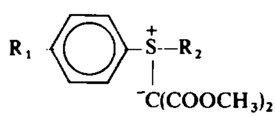
TABLE 1. KINETIC DATA ON THE PUMMERER REACTION IN ACETIC ANHYDRIDE[a]



R_1	R_2	Temp (°C)	$k \times 10^5$ (sec^{-1})
H	Me	120	8·35
H	CD_3	120	5·42
Me	Me	120	9·66
OMe	Me	120	13·1
Cl	Me	120	6·90
H	Me	130	14·6
H	Me	140	34·6
H	Me	120	11·3[b]

[a] Ylide, 4×10^{-5} mole, was treated with acetic anhydride without solvent.
[b] 0·1 gram AcOH was added.

TABLE 2. THE RATE CONSTANT OF THE PUMMERER REACTION OF



WITH B.P.O.

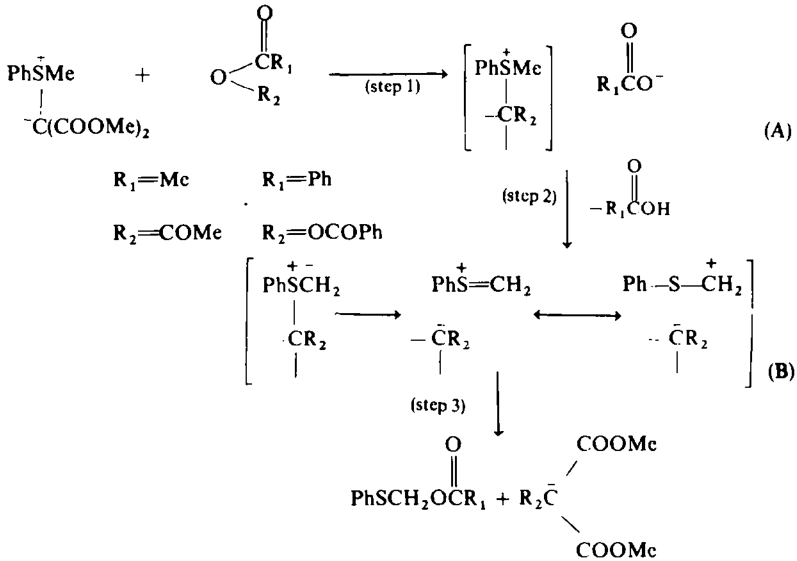
R_1	R_2	Temp (°C)	$k \times 10$ ($l . mol^{-1} . min^{-1}$)
MeO	Me	70	6·86
Me	Me	70	5·78
H	Me	60	2·39
		70	4·10
		80	10·12
H	CD_3	70	3·62
Cl	Me	70	2·61

The concentration of the ylide and B.P.O. used were both $0·9 \times 10^{-2}$ M.

TABLE 3. THE KINETIC DATA FROM EACH PUMMERER REACTION

	Ylide + Ac_2O	Ylide + B.P.O.	Sulphoxide + Ac_2O	Sulphilimine + Ac_2O*
ρ	−0·76	−0·98	−1·60	−0·71
$k_H k_D$	1·57	1·13	2·85	1·57
$\Delta H^{\ddagger}$ (Kcal/mol)	21·4	17·3	21·2	15·2
$\Delta S^{\ddagger}$ (e.u.)	−22·2	−18·7	−20·7	−41·2

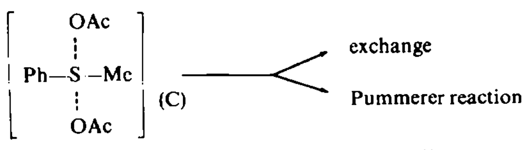
* Unpublished work from our laboratory.



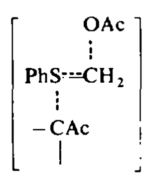
SCHEME I

was found to have lost about 80% of deuterium originally incorporated in the Me group of the ylide. Thus there is substantial proton exchange, and hence step (A) → (B) is not rate-determining.

The relatively small negative ρ-value (−0·76) obtained in the reactions of substituted-phenyl methyl sulphonium ylides with acetic anhydride seems to suggest that the nucleophilic attack of the ylide carbanion on acetic anhydride (acylation) to form the sulphonium salt (or an ion pair intermediate) is not important unlike the reaction of sulphoxide ($\rho = -1{\cdot}60$). The value of the acivation entropy resembles that of the corresponding sulphoxide though the ρ-values are different. This is probably due to the different characters of the intermediates at the rate determining steps of the two reactions. In the case of the sulphoxide, both Pummerer and oxygen exchange reactions could produce a common intermediate (C), however, such a common intermediate is not conceivable in the case of the ylide, since no nucleophilic substitution on the sulphur atom occurs with these ylides.

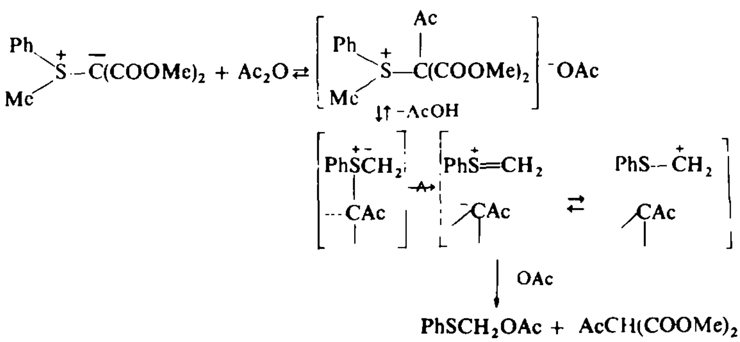


Thus the rate-determining step of this reaction is likely to be after initial fast proton removal from the sulphonium salt. In view of the small hydrogen-deterium kinetic isotope effect a concerted mechanism shown below is also quite unlikely.



The most likely one is that involving initial proton removal, followed by a rate-determining S—C bond cleavage and subsequent recombination with acetate to form final product. Both the ρ-value and facile hydrogen-deuterium exchange support this hypothesis.

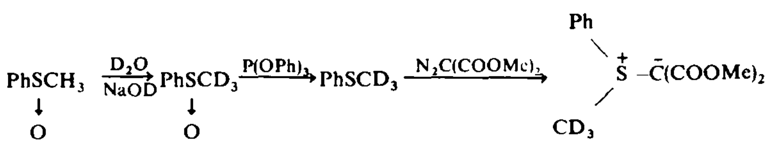
Furthermore addition of AcOH was found to accelerate the overall rate. Probably, AcOH addition not only tends to shift the equilibrium to the right-hand side to increase sulphonium salt concentration, but also facilitates S—C bond heterolysis by protonation, thus increasing the Pummerer reaction rate. From the kinetic observations, the plausible mechanism appears to involve fast proton removal and subsequent rate-determining S—C bond cleavage of the ylide through an EleB type process, then followed by fast recombination with acetate ion to form the final product, as depicted below.



EXPERIMENTAL

Several substituted-phenyl methyl sulphonium ylides were prepared by the reaction of dimethyl diazomalonate with substituted phenyl methyl sulphides in the presence of copper sulphate.[4] Yields (%) and their m.ps are as follows: p-H: 83, 126–127, p-Cl: 80, 166·5–167·5, p-Me: 78, 137–138, p-MeO: 85, 142–142. Benzoyl peroxide was purified by the procedure of C. G. Swain.[5] Phenyl methyl-d_3 sulphonium bis(methoxycarbonyl)-methylide was prepared by first treating phenyl methyl sulphoxide in NaOD/D_2O, then deoxygenated by triphenyl phosphite[6] to phenyl methyl-d_3 sulphide which was treated again with dimethyl diazomalonate.

The NMR spectra indicated no appreciable methyl proton at about 3·2 ppm.



The reaction of phenyl methyl sulphonium bis(methoxycarbonyl)methylide with B.P.O.

An equimolar mixture of the ylide and B.P.O. dissolved in benzene was refluxed overnight. The product was isolated and collected by GLC (SE-30, 5%, 2m, 210°C, H_2 as a carrier gas) and identified by comparing the NMR and IR spectra with authentic samples. Phenyl benzoyloxymethyl sulphide (II) and methyl benzoyloxy malonate (III) were obtained quantitatively. II was prepared by Pummerer reaction of phenyl methyl sulphoxide with benzoic anhydride[7] or more directly, the reaction of phenyl methyl sulphide with B.P.O.[8] III was also prepared by the reaction of sodium methyl malonate with B.P.O.[9]

(II): NMR (ppm, $CDCl_3$, TMS) 5·02 (s, 2H, —CH_2—) 7·42, 8·08 (m, 10H, Ph, —OCOPh) IR (ν_{CO}) 1730 cm^{-1}

(III): NMR (ppm, $CDCl_3$, TMS) 3·86 (s, 6H, —COOMe) 5·67 (s, 1H, —CH—), 7·52, 8·15 (m, 5H, —$OCOC_6H_5$) IR (ν_{CO}) 1732, 1760, 1782 cm^{-1}

The reaction of phenyl methyl sulphonium bis(methoxycarbonyl)methylide with acetic anhydride

An Ac_2O solution of ylide was heated at 130–140° for 6 hr in a sealed tube. After usual work up, the products obtained were phenyl acetoxymethyl sulphide (IV) and methyl acetyl malonate (V). IV was prepared easily from the reaction of phenyl methyl sulphoxide with Ac_2O,[6] and V also from the reaction of sodium methyl malonate with acetyl chloride.[10]

(IV): NMR (ppm, $CDCl_3$, TMS), 2·04 (s, 3H, —COMe) 5·38 (s, 2H, —CH_2—) 7·33 (m, 5H, Ph) IR (ν_{CO}, neat) 1735 cm^{-1}

(V): NMR (ppm, CCl_4, TMS) 2·20, 2·28 (d, 3H, —COMe) 3·72, 3·81 (d,6H, —COOMe) 4·28, 13·5 (s, 1H, —CH or HO—C=C) IR (neat) 1726, 1743, 1618, 1650, 1664 cm^{-1} (>CO) 1603 cm^{-1} (>C=C) 3660–3400 cm^{-1} (—OH).

H-D exchange reaction

An Ac_2O solution of phenyl methyl-d_3 sulphonium bis(methoxycarbonyl)methylide was heated at 120° with AcOH and the reaction stopped at about 20% completion. The NMR spectra of the recovered ylide, separated by column chromatography (silica gel, 200 mesh, ether-MeOH), indicated about 80% loss of deuterium in the originally deuterated-methyl group of the ylide.

Kinetic measurement

(i) *Reaction of phenyl methyl sulphonium bis(methoxycarbonyl)methylide with B.P.O.*

The reaction was carried out in 5 ml ampoules at 70 ± 0·05°. From time to time ampoules were taken out and the reaction stopped by sudden cooling in ice-water while the rates were measured in the range of 0–60% completion. The sample (generally 3–5 ml) was pipetted into a mixture of 20 ml) glacial AcOH, 1 ml freshly prepared sat KI aq. and a few lumps of dry-ice. After 5 min, 20–30 ml of water was added and the mixture titrated with 0·01N $Na_2S_2O_3$ till the iodine colour disappeared. A typical run is as follows; (70°)

time (min.)	0·01 N $Na_2S_2O_3$ (ml)	$k \times 10$ (l . mol^{-1} . min^{-1})
0	5·98	4·09
30	5·32	4·10
65	4·71	4·02
110	4·13	4·01
140	3·81	4·21
185	3·35	4·14
260	2·86	4·18

B.P.O. = 0·9 × 10^{-2} M Means: 4·10 ± 0·04 × 10^{-1}
Ylide 0·9 × 10^{-2} M

These data were determined from the following equation

$$k_2 t = \frac{x}{a(a-x)}:$$

a; the same initial concentration of phenyl methyl sulphonium ylide and B.P.O.

x; concentration of sulphide produced.

(ii) *The reaction of phenyl methyl sulphonium bis(methoxycarbonyl)methylide with acetic anhydride*

The Pummerer reaction was carried out at 120° ± 0·1° on sealed tubes in which *p*-substituted-phenyl methyl sulphonium ylides (4 × 10^{-5} mole) was dissolved in 10 ml of Ac_2O. From time to time a sealed tube containing 1 ml of mixture was removed and cooled in an ice-bath. The mixture was hydrolyzed with alkali (50 ml 3%). The rate of the Pummerer reaction was readily followed, by the difference in UV spectra of the starting compound (λ_{max}: 227–237 mμ for *p*-substituted-phenyl methyl bis(methoxycarbonyl)-methylides) and the final hydrolyzed compound (λ_{max}: 257–262 mμ for *p*-substituted-phenyl mercaptides[2]).

All the rate constants listed in Table I were determined from the equation for the Pummerer reaction.

$$\log \frac{a_\infty - a_0}{a_\infty a_t} = \frac{kt}{2{\cdot}303}$$

a_∞: the final intensity of resulting mercaptide.
a_0: the initial intensity of resulting mercaptide.
a_t: the intensity of resulting mercaptide after t.

UV spectra of *p*-substituted-phenyl methylsulphonium bis(methoxycarbonyl)methylides are as follows [λ_{max} (mμ) log ε, 95% H_2O-5% MeOH H: 227, 4·15 Me: 229, 4·22 Cl: 229, 4·19 MeO 237, 4·20].

A typical run is shown below (120°)

time (sec.)	a_t	$\log \frac{a_\infty - a_0}{a_\infty a_t}$	$k(\text{sec}^{-1}) \times 10^5$
24×10^2	0·510	0·0832	7·95
42×10^2	0·540	0·1541	8·41
54×10^2	0·560	0·1956	8·30
66×10^2	0·581	0·2431	8·46
81×10^2	0·602	0·2968	8·39
108×10^2	0·638	0·4075	8·64

$a_0 = 0{\cdot}445$ Mean: $8{\cdot}35 \pm 0{\cdot}16 \times 10^{-5}$
$a_\infty = 0{\cdot}762$

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