Cytotoxic Compounds. Part XX.[1] Reactions of the Methanesulphonates of 2-Aryl-2-(arylthio)ethanols and of 1-Aryl-2-(arylthio)ethanols with Nucleophiles

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The products formed in the reactions of 2-phenyl-, 2-(*p*-methoxyphenyl)-, 2-(*p*-nitrophenyl)-, and 1-(*p*-nitrophenyl)-2-(phenylthio)ethyl methanesulphonate, 1-phenyl-2-(phenylthio)ethyl chloride, and 2-(2,4-dinitrophenylthio)-2-phenylethyl and -1-phenylethyl methanesulphonate with various nucleophiles have been identified, mainly by n.m.r. spectroscopy. Solvolysis in acetic acid or in methanol proceeds under kinetic control, *via* episulphonium ions, to give entirely the secondary acetate or secondary methyl ether. Reactions with potassium acetate, tetramethylammonium acetate, or sodium methoxide give vinyl sulphides from some of the substrates, particularly when an electron-attracting group is present at the β-position; with the acetate reagents, elimination occurs more readily in acetone than in acetic anhydride. Episulphonium intermediates are also involved in most of the reactions with lithium bromide, sodium azide, and arenethiols, to give substitution products, though with sodium azide the primary methanesulphonates carrying nitro-substituents give vinyl sulphides exclusively.

α-(Phenylthio)styrene and α-(phenylthio)-*p*-nitrostyrene are rapidly oxidised, with rearrangement, on exposure to air, to give phenacyl and *p*-nitrophenacyl phenyl sulphide, respectively.

It was shown earlier [2] that the products formed by reaction of methanesulphonates of types (1) and (2) with nucleophiles are determined by the nature both of the aryl group and of the nucleophile. Many of these reactions led to mixtures of isomeric substitution products, indicative of a pathway through an intermediate episulphonium ion, the formation of which is favoured by electron donation from the aryl group. When the intervention of such an intermediate is inhibited (Ar = 2,4-dinitrophenyl), basic reagents, such as sodium methoxide, promoted elimination and gave vinyl sulphides.

The effects of introducing an additional variable, by replacing the *C*-methyl group in compounds (1) and (2) by a second aryl function, have now been examined. Syntheses of some suitable parent alcohols, and their reactions with methanesulphonyl chloride, were described earlier,[3] and as a result of that work the chloride (14) and the six methanesulphonates (3)—(6), (15), and (16) were

[1] Part XIX, A. Behzadi and L. N. Owen, *J.C.S. Perkin I*, 1974, 25.

[2] M. S. Khan and L. N. Owen, *J.C.S. Perkin I*, 1972, 2067.

[3] A. Behzadi and L. N. Owen, *J.C.S. Perkin I*, 1973, 2733.

available; the alcohols had also been converted into the corresponding acetates and methyl ethers to serve as reference compounds. The results of the reactions of the chloride and of the methanesulphonates with a variety of nucleophiles are broadly summarised in the Table.

Solvent effects were also important in the reactions with tetramethylammonium acetate. In acetic anhydride, of the four substrates examined only the primary methanesulphonate (5) gave any major quantity of a vinyl sulphide, (36). In acetone, however, elimination

Products [a] from reactions of the methanesulphonates $Ar^1S{\cdot}CHAr^2{\cdot}CH_2{\cdot}O{\cdot}SO_2Me$ and $Ar^1S{\cdot}CH_2{\cdot}CHAr^2{\cdot}O{\cdot}SO_2Me$ with nucleophiles

			Reagents									
Ar^1	Ar^2		AcOH	KOAc (Ac_2O)	KOAc (Me_2CO)	NMe_4OAc (Ac_2O)	NMe_4OAc (Me_2CO)	MeOH	NaOMe	LiBr	NaN_3	PhSNa
Ph	p-MeO·C_6H_4	(prim.)	S	S			S	S	S	S	S	
Ph	Ph	(prim.)	S	S	SV	S	SV	S	S	S	S	X
Ph	Ph	(sec.) [b]	S	S			S	S	S	S	S	X
Ph	p-NO_2·C_6H_4	(prim.)	S		V	V	V	S	PV	PS	V	P=S
Ph	p-NO_2·C_6H_4	(sec.)	S	S	S	S	S	S	S	PS	S	P=S
2,4-$(NO_2)_2$-C_6H_3	Ph	(prim.)	S	V			V	S	VY	P(V) [c]	V	PY
2,4-$(NO_2)_2$-C_6H_3	Ph	(sec.)	S	S	SV	SV	SV	S	SVY	S	S	Y

[a] P, primary substitution product; S, secondary substitution product; V, vinyl sulphide; X, substitution product of uncertain constitution (sodium toluene-α-thiolate used); Y, by-product (*e.g.* 2,4-dinitroanisole). [b] Chloride. [c] Parentheses indicate trace only.

Solvolysis in acetic acid gave only the secondary acetates (17)—(20), the n.m.r. spectra of the products being devoid of those resonances characteristic [3] of the primary acetates. These reactions were shown to be under kinetic control by the observation that the primary acetates were not isomerised under the experimental conditions. Fission of the intermediate episulphonium ions (34) therefore occurs exclusively by nucleophilic attack at the secondary position,* stabilisation of an incipient carbonium ion [2,5,6] being greater there than at the primary position.

Reaction with potassium acetate in acetic anhydride also led to the secondary acetates, except from the primary 2,4-dinitro-compound (6) which gave α-(2,4-dinitrophenylthio)styrene (37), the electron-withdrawing power of the aryl group attached to sulphur promoting elimination both by diminishing the capacity for forming the episulphonium ring and by increasing the acidity of the hydrogen in the β-position relative to the leaving group. The additional acidity conferred by the phenyl substituent is also essential, because its absence from the β-position in the secondary isomer (16) results in no elimination. An increased tendency to form unsaturated products was observed when some of these reactions with potassium acetate were carried out in acetone. The secondary methanesulphonate (16), although forming some secondary acetate (20), gave mainly β-(2,4-dinitrophenylthio)styrene (38), and the n.m.r. spectrum of the product from the primary methanesulphonate (3) showed that although it was mainly secondary acetate (17) there was present a very small amount of α-(phenylthio)styrene (35). The primary compound (5), which had decomposed when treated in acetic anhydride, gave no substitution product but only α-(phenylthio)-p-nitrostyrene (36).

* Although the carbon atoms in the episulphonium ion are secondary and tertiary, these are designated the primary and the secondary position, respectively, in order to avoid confusion over the nature of the substitution product resulting from attack at a particular position.[2,4–6]

occurred more readily. With the exception of the p-methoxyphenyl-compound (4), which gave only the secondary acetate (18) (reduction of the acidity of the β-hydrogen atom by the electron-donating effect) the primary methanesulphonates all gave vinyl sulphides, (35)—(37); some secondary acetate was also formed from the unsubstituted compound (3), but none from the nitro-compounds (5) and (6). The secondary compounds each gave the corresponding secondary acetate, but the 2,4-dinitro-compound (16) gave also the vinyl sulphide (38), in much greater proportion than had been formed in the corresponding reaction in acetic anhydride.

The seven substrates (3)—(6) and (14)—(16) when solvolysed in methanol gave the corresponding secondary methyl ethers (21)—(24) exclusively. The primary isomers of these ethers [3] were not isomerised under the reaction conditions and the products were therefore the result of kinetically controlled attack on the secondary position of the intermediate episulphonium ions. Sodium methoxide in methanol promoted elimination in the methanesulphonates (5), (6), and (16) to give the vinyl sulphides (36), (37), and (38), respectively; some 2,4-dinitroanisole was present in the products from the dinitro-compounds (6) and (16) as a result of some nucleophilic attack on the Ar–S bond,[7] and, in agreement with the electronic factors already mentioned, some substitution product (24) was given by the secondary methanesulphonate (16) whereas no methyl ether was detected in the product from the primary isomer (6). The substitution product accompanying the vinyl sulphide from the primary compound (5) was the *primary* methyl ether (7) and, although this might be thought to arise from S_N2-type sterically controlled attack [2,5] by methoxide ion at the primary position in the episulphon-

[4] M. V. A. Baig and L. N. Owen, *J. Chem. Soc.* (*C*), 1967, 1400.
[5] M. S. Khan and L. N. Owen, *J.C.S. Perkin I*, 1972, 2060.
[6] G. Durrant, P. D. Edwards, and L. N. Owen, *J.C.S. Perkin I*, 1973, 1271.
[7] *Cf.* N. Kharasch and R. Swidler, *J. Org. Chem.*, 1954, **19**, 1704.

ium ion (34), this seems unlikely in view of the complete absence of primary methyl ether in the product from the secondary methanesulphonate (15). The diminished tendency for episulphonium ion formation caused by the *p*-nitrophenyl group in the primary compound (5) probably allows the production of some primary ether by direct S_N2 attack on the methanesulphonate.

Identification of the acetates and the methyl ethers, obtained in the reactions so far described, was facilitated by the availability of the authentic compounds, but this was not so with regard to the bromides, azides, and sulphides formed in reactions now to be discussed. However, a characteristic feature of the n.m.r. spectra [3] of the authentic alcohols, acetates, methyl ethers, and methanesulphonates was the magnitude of the separation of the

$ArS{\cdot}CHMe{\cdot}CH_2{\cdot}O{\cdot}SO_2Me$
(1)

$Ar^1S{\cdot}CHAr^2{\cdot}CH_2X$

	Ar^1	Ar^2	X
(3)	Ph	Ph	$O{\cdot}SO_2Me$
(4)	Ph	*p*-$MeO{\cdot}C_6H_4$	$O{\cdot}SO_2Me$
(5)	Ph	*p*-$NO_2{\cdot}C_6H_4$	$O{\cdot}SO_2Me$
(6)	2,4-$(NO_2)_2C_6H_3$	Ph	$O{\cdot}SO_2Me$
(7)	Ph	*p*-$NO_2{\cdot}C_6H_4$	OMe
(8)	Ph	Ph	Br
(9)	Ph	*p*-$NO_2{\cdot}C_6H_4$	Br
(10)	2,4-$(NO_2)_2C_6H_3$	Ph	Br
(11)	Ph	*p*-$NO_2{\cdot}C_6H_4$	SPh
(12)	2,4-$(NO_2)_2C_6H_3$	Ph	SPh
(13)	Ph	Ph	$S{\cdot}CH_2Ph$

$Ar^1\overset{+}{S}{\cdot}CH_2{\cdot}CHAr^2$ (34)

$Ar^1S{\cdot}C(Ar^2){:}CH_2$
(35) $Ar^1 = Ar^2 = Ph$
(36) $Ar^1 = Ph$, $Ar^2 = p\text{-}NO_2{\cdot}C_6H_4$
(37) $Ar^1 = 2,4\text{-}(NO_2)_2C_6H_3$, $Ar^2 = Ph$

2,4-$(NO_2)_2C_6H_3{\cdot}S{\cdot}CH{:}CHPh$
(38)

$ArS{\cdot}CH_2{\cdot}CHMe{\cdot}O{\cdot}SO_2Me$
(2)

$Ar^1S{\cdot}CH_2{\cdot}CHAr^2X$

	Ar^1	Ar^2	X
(14)	Ph	Ph	Cl
(15)	Ph	*p*-$NO_2{\cdot}C_6H_4$	$O{\cdot}SO_2Me$
(16)	2,4-$(NO_2)_2C_6H_3$	Ph	$O{\cdot}SO_2Me$
(17)	Ph	Ph	OAc
(18)	Ph	*p*-$MeO{\cdot}C_6H_4$	OAc
(19)	Ph	*p*-$NO_2{\cdot}C_6H_4$	OAc
(20)	2,4-$(NO_2)_2C_6H_3$	Ph	OAc
(21)	Ph	Ph	OMe
(22)	Ph	*p*-$MeO{\cdot}C_6H_4$	OMe
(23)	Ph	*p*-$NO_2{\cdot}C_6H_4$	OMe
(24)	2,4-$(NO_2)_2C_6H_3$	Ph	OMe
(25)	Ph	Ph	Br
(26)	Ph	*p*-$MeO{\cdot}C_6H_4$	Br
(27)	Ph	*p*-$NO_2{\cdot}C_6H_4$	Br
(28)	2,4-$(NO_2)_2C_6H_3$	Ph	Br
(29)	Ph	Ph	N_3
(30)	Ph	*p*-$MeO{\cdot}C_6H_4$	N_3
(31)	Ph	*p*-$NO_2{\cdot}C_6H_4$	N_3
(32)	2,4-$(NO_2)_2C_6H_3$	Ph	N_3
(33)	Ph	Ph	$S{\cdot}CH_2Ph$

$ArCO{\cdot}CH_2{\cdot}SPh$
(39) Ar = Ph
(40) Ar = *p*-$NO_2{\cdot}C_6H_4$

methylene and the methine resonances, $\delta(CH_2 - CH)$, which was significantly smaller in the primary than in the secondary compounds. Treatment of either the primary methanesulphonate (3) or the secondary chloride (14) with lithium bromide in acetone gave a crystalline bromide which showed $\delta(CH_2 - CH)$ 1·2 p.p.m., a value within the range (1·1—2·6) exhibited by the 1-substituted 1-phenyl-2-(phenylthio)ethane series. Consequently the product is considered to be the secondary bromide (25). This conclusion is supported by the observation that when heated the compound partly isomerised, and a new methine resonance appeared corresponding to a value of 0·6 p.p.m. for $\delta(CH_2 - CH)$, indicating the presence of the primary bromide (8) [the range for the 1-substituted 2-phenyl-2-(phenylthio)-ethane series was 0·0—0·6]. The more reactive *p*-methoxyphenyl compound (4) with lithium bromide gave a partly decomposed product which contained a bromide, $\delta(CH_2 - CH)$ 1·3 p.p.m., assigned the secondary structure (26). The isomeric pair of *p*-nitrophenyl compounds (5) and (15) each gave a 1 : 3 mixture of primary (9) and secondary bromide (27), showing $\delta(CH_2 - CH)$ *ca.* 0·7 and *ca.* 1·3 p.p.m., respectively. Clearly all these reactions proceeded through episulphonium ions, but in contrast the 2,4-dinitrophenylthio-compounds (6) and (16) gave, respectively, the primary bromide (10), $\delta(CH_2 - CH)$ 0·97, and the known [8] secondary bromide (28), $\delta(CH_2 - CH)$ 1·27 p.p.m.; with this pair of methanesulphonates the nucleophilicity of the attacking bromide ion competes successfully with the diminished ability of the sulphur atom to form an episulphonium ion.

With sodium azide in dimethylformamide the primary methanesulphonate (3) and the secondary chloride (14) both gave the same azide, which showed $\delta(CH_2 - CH)$ 1·34 p.p.m., indicative of the secondary compound (29). The product from the *p*-methoxyphenyl compound (4) showed $\delta(CH_2 - CH)$ 1·33 p.p.m. and is therefore assigned the secondary structure (30), but the basic character of the azide ion was sufficient to produce only the vinyl sulphide (36) from the primary *p*-nitrophenyl compound (5) (a further illustration of the reluctance of this methanesulphonate to form an episulphonium ion), though, in conformity with its behaviour towards other nucleophiles, the secondary isomer (15) gave only the secondary azide (31), $\delta(CH_2 - CH)$ 1·45 p.p.m. Similarly, the vinyl sulphide was obtained from the primary 2,4-dinitrophenylthio-compound (6) but only secondary azide (32), $\delta(CH_2 - CH)$ 1·46 p.p.m., from the secondary isomer (16).

The variation in the magnitude of $\delta(CH_2 - CH)$, according to the primary or the secondary nature of the functional group in the authentic compounds, stems from the combination of two factors: (i) the deshielding effects are larger on the methine than on the methylene protons, and (ii) the deshielding effects of hydroxy-,

[8] F. Kaluza and G. W. Perold, *J. S. African Chem. Inst.*, 1957, **10**, 54.

acetoxy-, methoxy-, and methylsulphonyloxy-groups are significantly greater than those of arylthio-groups. The justification for using this method for the bromides and azides is that those functional groups, also, conform to the second factor, but clearly this is not the case when the displacing group is itself a thiol, and the magnitude of $\delta(CH_2 - CH)$ for the product of such a reaction is indecisive. Both the primary methanesulphonate (3) and the secondary chloride (14) reacted with sodium toluene-α-thiolate to give the same single product, but no convincing choice can be made between the constitutions (13) and (33). Each of the *p*-nitrophenyl compounds (5) and (15) reacted with sodium benzenethiolate to give the only possible substitution product (11), and with the same reagent the primary 2,4-dinitrophenylthio-compound (6) gave mainly 2,4-dinitrophenyl phenyl sulphide (nucleophilic attack on the aryl group) with a small amount of a substitution product which, if non-intervention of an episulphonium ion is assumed from analogy with the reaction with lithium bromide, is probably the unrearranged compound (12). No substitution product could be detected in the product (mainly 2,4-dinitrophenyl phenyl sulphide) obtained from the reaction of the secondary 2,4-dinitrophenylthio-compound (16) with sodium benzenethiolate.

Inspection of the Table as a whole shows that elimination is favoured, for reasons already discussed, by an electron-withdrawing arylthio-group; additionally, in the primary compounds this tendency is increased by an electron-withdrawing β-aryl group. In the compounds (1) and (2), studied earlier, the second factor is reversed because in the primary methanesulphonate the β-methyl group reduces the acidity of the β-hydrogen atom; thus, in contrast to the present results, with potassium acetate in acetic anhydride the secondary methanesulphonate (2; Ar = 2,4-dinitrophenyl) underwent elimination whereas the primary isomer did not. The different electronic effects of a methyl and an aryl substituent are also evident from the fact that the substitution products obtained (under kinetic control) in the reactions of the methanesulphonates (1) and (2) were mixtures of primary and secondary products, indicating that the nucleophile attacked both positions in the intermediate episulphonium ion, whereas in the present work the attack was exclusively at the secondary position because an incipient carbonium ion at that position is stabilised better by aryl than by methyl. Another difference between the two series is that (except for the 2,4-dinitrophenylthio-compound) the primary acetates and primary methyl ethers corresponding to the methanesulphonate (1) were wholly or partly converted in acetic acid or methanol, containing methanesulphonic acid, into the secondary isomers, whereas the primary acetates and methyl ethers so treated in the present work were unaffected; this illustrates how the capacity for sulphur to form the episulphonium ion is sensitive to the nature of the neighbouring substituent, and is completely destroyed by the presence of an aryl function when only a poor leaving group (acetoxy or methoxy) is present.

The mixture of α-(phenylthio)styrene (35) and secondary acetate (17) obtained from the reaction of the methanesulphonate (3) with tetramethylammonium acetate was separated by t.l.c. to give a fairly pure specimen of the vinyl sulphide (n.m.r. spectrum), the constitution of which was confirmed by reaction with acidic 2,4-dinitrophenylhydrazine to give acetophenone 2,4-dinitrophenylhydrazone. The vinyl sulphide was unstable: a very minor singlet at τ 5·75 in its n.m.r. spectrum gradually increased in intensity while the vinyl resonances diminished; after several days, phenacyl phenyl sulphide (39) was isolated by t.l.c. Similar behaviour was shown, in an enhanced degree, by α-(phenylthio)-*p*-nitrostyrene (36), which on exposure to air was very rapidly converted into *p*-nitrophenacyl phenyl sulphide (40). A solution of the freshly prepared vinyl sulphide (36) in deuteriochloroform was distributed among three n.m.r. tubes; one was left open, one was sealed, and to the third (left open) was added a trace of 2,6-di-t-butyl-*p*-cresol. Daily recordings of the n.m.r. spectra established that conversion into the ketone occurred most readily in the first tube, presumably by a free-radical mechanism involving atmospheric oxygen, though there seems to be no precedent for the formation of such a product by autoxidation of a vinyl sulphide.[9] α-(2,4-Dinitrophenylthio)styrene (37) was stable, and showed no trace of ketonic impurity after storage in air for a year; formation of the phenacyl compounds presumably involves migration of the arylthio-group, which could well be inhibited in the dinitro-compound.

EXPERIMENTAL

^{1}H N.m.r. spectra were recorded for solutions in deuteriochloroform on a Varian A-60 or HA-100 instrument; resonances are reported only for products not described in the earlier paper,[3] and all aromatic proton resonances are omitted. I.r. spectra were measured for solutions in chloroform. Petroleum refers to the fraction of b.p. 40—60°. Organic extracts were dried over magnesium sulphate, and solvents were removed under reduced pressure below 50°. Kieselgel GF_{254} (Merck) was used for t.l.c.

The methanesulphonates and the chloride were freshly prepared, by the methods previously described,[3] and were used immediately. Products were identified, when possible, by comparison of n.m.r. spectra with those of authentic compounds.

Reactions with Acetic Acid.—A solution of 2-phenyl-2-(phenylthio)ethyl methanesulphonate (3) (0·50 g) in acetic acid (20 ml) and acetic anhydride (1 ml) was kept at 60° for 5 h, then cooled, diluted with water, and extracted with benzene. The extract was washed with 2N-sodium hydroxide and with water, then dried and evaporated to give 1-phenyl-2-(phenylthio)ethyl acetate (17) (0·40 g).

Similar yields of secondary acetates were obtained from the other substrates, under the following conditions: compound (4) (ambient temperature, 170 h); (5) (ambient temperature, 100 h); (6) (70°, 12 h); (14) (60°, 24 h); (15) (50°, 5 h); (16) (70°, 12 h).

[9] *Cf.* L. Bateman and J. I. Cunneen, *J. Chem. Soc.*, 1955, 1596; D. Barnard, L. Bateman, and J. I. Cunneen, 'Organic Sulfur Compounds,' ed. N. Kharasch, Pergamon, Oxford, 1961, vol. 1, p. 229.

Reactions with Potassium Acetate in Acetic Anhydride.—A solution of the methanesulphonate (3) (0·30 g) and potassium acetate (0·3 g) in acetic anhydride (25 ml) was stirred at 60° for 5 h, then worked up as described above to give the secondary acetate (17) (0·25 g).

Secondary acetates were likewise obtained from substrates (4) (5°, 170 h); (14) (60°, 7 h); (15) (55°, 4 h or 10°, 72 h); and (16) (70°, 12 h).

Similar treatment of 2-phenyl-2-(2,4-dinitrophenylthio)-ethyl methanesulphonate (6) (0·25 g), at 70° for 12 h, gave α-(2,4-*dinitrophenylthio*)*styrene* (37) (0·15 g), m.p. 95—97° (from carbon tetrachloride), τ 3·66 (1H, s) and 3·83 (1H, s) (:CH_2) (Found: C, 55·6; H, 3·3; N, 9·15; S, 10·6. $C_{14}H_{10}N_2O_4S$ requires C, 55·6; H, 3·3; N, 9·3; S, 10·6%).

Reactions with Potassium Acetate in Acetone.—(i) A solution of the methanesulphonate (3) (0·30 g) in dry acetone (25 ml) was gently boiled under reflux for 5 h, then worked up as described above. The product (0·25 g) was the secondary acetate (17), containing a trace of α-(phenylthio)-styrene (35) (τ 4·31 and 4·66), described more fully below.

(ii) The methanesulphonate (5) (0·30 g), treated at 0° for 100 h, gave a mixture (0·18 g) of α-(phenylthio)-*p*-nitrostyrene (36) and its autoxidation product, *p*-nitrophenacyl phenyl sulphide (40). The mixture showed τ 4·21 (s) and 4·44 (s) (:CH_2) and 5·74 (s, $\cdot CH_2 \cdot CO$).

(iii) The methanesulphonate (15) (0·26 g), treated at ambient temperature for 70 h, gave the secondary acetate (19) (0·22 g).

(iv) The methanesulphonate (16) (100 mg), treated at reflux temperature for 12 h, gave a 1 : 2 mixture (65 mg) of secondary acetate (20) and β-(2,4-dinitrophenylthio)-styrene (38), τ 2·67 (d) and 3·16 (d) (·CH:CH·).

Reactions with Tetramethylammonium Acetate in Acetic Anhydride.—(i) A mixture of the methanesulphonate (3) (0·50 g) and tetramethylammonium acetate [5] (0·4 g) in acetic anhydride (20 ml) was stirred at 40° for 5 h, then worked up as described above to give the secondary acetate (17) (0·40 g).

(ii) The methanesulphonate (5) (0·25 g), treated at 0° for 70 h, gave a 4 : 1 mixture (0·18 g) of the vinyl sulphide (36), τ 4·21 (s) and 4·44 (s), and the ketone (40), τ 5·74 (s).

(iii) The isomer (15) (0·10 g) reacted at 0° for 40 h to give the secondary acetate (19) (0·92 g).

(iv) The 2,4-dinitro-compound (16) (0·20 g) after reaction at 70° for 12 h, gave a 3 : 1 mixture (0·13 g) of secondary acetate (20) and the vinyl sulphide (38), τ 2·65 (d) and 3·15 (d).

Reactions with Tetramethylammonium Acetate in Acetone.—(i) Treatment of the methanesulphonate (3) (0·50 g) in a similar way for 24 h at 40° in acetone gave a 3 : 1 mixture (0·35 g) of the secondary acetate (17) and α-(phenylthio)-styrene (35). The latter, τ 4·32 (s) and 4·69 (s), was separated by preparative t.l.c. (benzene), and a portion (70 mg) was added to a solution of 2,4-dinitrophenylhydrazine (150 mg) and conc. sulphuric acid (0·5 ml) in ethanol (5 ml); the mixture was stirred at 35—40° for 3 h and the yellow precipitate of acetophenone 2,4-dinitrophenylhydrazone (110 mg), after being washed with hot ethanol and recrystallised from ethyl acetate–petroleum, had m.p. 235—239° (lit.,[10] 237°). When the vinyl sulphide (35) was stored in air, after 5 days it was completely converted into phenyl phenacyl sulphide, which after crystallisation from petroleum had m.p. 50—52°, $\nu_{max.}$ 1685 cm^{-1}, τ 5·75 (2H, s, CH_2) (lit.,[11] m.p. 53—54°).

(ii) The chloride (14) (0·52 g), treated under reflux for 110 h, gave the secondary acetate (17) (0·42 g).

(iii) The methanesulphonate (4) (0·40 g) after 170 h at 5° gave the secondary acetate (18) (0·32 g).

(iv) The *p*-nitro-compound (5) (0·25 g), treated at 0° for 70 h, gave a mixture (0·16 g) of α-(phenylthio)-*p*-nitrostyrene (36), τ 4·21 (s) and 4·44 (s), with *ca.* 15% of *p*-nitrophenacyl phenyl sulphide. After storage in air for 2—3 days oxidation was complete, and purification by t.l.c. (benzene), followed by crystallisation, gave the phenacyl compound, m.p. 101—103°, $\nu_{max.}$ 1680 cm^{-1}, τ 5·74 (2H, s, CH_2) (Found: C, 61·4; H, 4·0; N, 5·2. Calc. for $C_{14}H_{11}N_3O_3S$: C, 61·5; H, 4·1; N, 5·1%) (lit.,[11] m.p. 100—101°). It was not possible to purify the vinyl sulphide by t.l.c. because of its extreme susceptibility to oxidation.

(v) The isomer (15) (100 mg), on reaction for 40 h at ambient temperature, gave the secondary acetate (19) (90 mg).

(vi) The 2,4-dinitro-compound (6) (90 mg), after 70 h at ambient temperature, gave α-(2,4-dinitrophenylthio)styrene (37) (60 mg), τ 3·65 (s) and 3·81 (s).

(vii) The isomer (16) (0·20 g), after 12 h under reflux, gave a 1 : 3 mixture (0·17 g) of secondary acetate (20) and β-(2,4-dinitrophenylthio)styrene (38), τ 2·65 (d) and 3·14 (d).

Reactions with Methanol.—A solution of the methanesulphonate (3) (0·60 g) in dry methanol was kept at 60° for 5 h, then concentrated, diluted with benzene, washed with water, dried, and evaporated to give 1-methoxy-1-phenyl-2-(phenylthio)ethane (21) (0·45 g).

Similarly, secondary methyl ethers were obtained from compounds (4) (5°, 170 h); (5) (0°, 100 h or 55°, 7 h); (6) (60°, 12 h); (14) (60°, 24 h); (15) (50°, 5 h); and (16) (60°, 12 h).

Reactions with Sodium Methoxide.—(i) When the reaction of sodium (0·1 g) with dry methanol (30 ml) was complete, the methanesulphonate (3) (0·60 g) was added, and the solution was kept at 60° for 5 h, then worked up as for the reaction with methanol to give the secondary ether (21) (0·46 g).

Secondary methyl ethers were likewise obtained from compounds (4) (5°, 170 h); (14) (60°, 8 h); and (15) (0°, 70 h).

(ii) The *p*-nitro-compound (5) (0·50 g), after reaction at 0° for 70 h, gave a mixture (0·32 g) of 1-methoxy-2-(*p*-nitrophenyl)-2-(phenylthio)ethane (7) (65%), α-(phenylthio)-*p*-nitrostyrene (36) (25%), τ 4·21 (s) and 44·4 (s), and *p*-nitrophenacyl phenyl sulphide (40) (10%), τ 5·74 (s).

(iii) The 2,4-dinitro-compound (6) (0·30 g), treated at 0° for 90 h gave α-(2,4-dinitrophenylthio)styrene (37) (0·18 g), τ 3·64 (s) and 3·81 (s), with *ca.* 10% of 2,4-dinitroanisole, τ 5·85 (s). When the reaction was carried out at ambient temperature the product was mainly 2,4-dinitroanisole, m.p. 83—85° (from ethanol) (lit.,[10] m.p.s 86, 89, and 95°).

(iv) The isomer (16) (0·20 g), on reaction at ambient temperature for 24 h, gave a mixture (0·12 g) of secondary methyl ether (24) (30%), β-(2,4-dinitrophenylthio)styrene (38) (55%), and 2,4-dinitroanisole (15%). The vinyl sulphide was isolated by t.l.c. (chloroform) and after crystallisation from chloroform–petroleum had m.p. 176—178°, τ 2·65 (d) and 3·14 (d) (Found: C, 55·5; H, 3·45; N, 9·1; S, 10·7. Calc. for $C_{14}H_{10}N_2O_4S$: C, 55·6; H, 3·3; N, 9·3; S, 10·6%) (lit.,[8] m.p. 174°).

[10] ' Dictionary of Organic Compounds,' 4th edn., Eyre and Spottiswoode, London, 1965.

[11] R. F. Brookes, J. E. Cranham, D. Greenwood, and H. A. Stevenson, *J. Sci. Food Agric.*, 1957, **8**, 561.

Reactions with Lithium Bromide.—(i) A solution of the methanesulphonate (3) (1·0 g) and lithium bromide (1·2 g) in dry acetone (25 ml) was kept at 50° for 5 h, then concentrated, diluted with benzene, washed with water, dried, and evaporated to give 1-*phenyl*-2-(*phenylthio*)*ethyl bromide* (25) (0·8 g), m.p. 65—80° (decomp.), τ 4·99 (1H, q, CH), 6·2 (2H, m, CH_2) (Found: C, 57·5; H, 4·35; Br, 27·3; S, 10·9. $C_{14}H_{13}BrS$ requires C, 57·3; H, 4·5; Br, 27·25; S, 10·9%). An identical product (0·52 g) was obtained under similar conditions from the chloride (14) (0·54 g).

A solution of the bromide in chloroform was boiled under reflux for 3 h and then evaporated to give a mixture of the primary (8) and secondary bromide (25), τ 4·99 (0·5H, q, CHBr), 5·57 (0·5H, q, CH·S), and 6·1—6·4 (2H, m, CH_2).

(ii) Reaction of the *p*-methoxy-compound (4) (0·50 g) for 120 h at 0° gave a crude product (0·28 g) containing the secondary bromide (26), τ 4·97 (q, CH), 6·3 (m, CH_2), and 6·22 (s, OMe). This was very unstable and could not be purified.

(iii) The *p*-nitro-compound (5) (0·25 g) after 100 h at 0° gave a 3 : 1 mixture (0·11 g) of the secondary (27) and the primary bromide (9), τ 4·99 (0·75H, q, CNBr), 5·47 (0·25H, q, CHS), and 6·1—6·4 (2H, m, CH_2).

(iv) The isomer (15) (0·25 g) under the same conditions gave a similar mixture (0·15 g) (identical n.m.r. spectrum).

(v) The 2,4-dinitro-compound (6) (0·3 g) on reaction at 70° for 24 h gave a product (0·25 g) which contained *ca.* 10% of α-(2,4-dinitrophenylthio)styrene (37), τ 3·64 (s) and 3·82 (s). Purification by t.l.c. (benzene) gave 2-(2,4-*dinitrophenylthio*)-2-*phenylethyl bromide* (10) as an unstable oil (0·18 g), τ 5·26 (1H, t, CH) and 6·23 (2H, d, CH_2) (Found: C, 44·6; H, 3·2; Br, 19·9; N, 7·0; S, 8·4. $C_{14}H_{11}BrN_2O_4S$ requires C, 43·9; H, 2·9; Br, 20·8; N, 7·3; S, 8·4%).

(vi) The isomer (16) (0·54 g), treated at 55° for 12 h, gave 2-(2,4-dinitrophenylthio)-1-phenylethyl bromide (28) (0·50 g), m.p. 141—144°, τ 4·84 (1H, q, CH), and 6·11 (2H, d, CH_2) (lit.,[8] m.p. 142—143°).

Reactions with Sodium Azide.—(i) A solution of the methanesulphonate (3) (0·57 g) and sodium azide (1·0 g) in dimethylformamide (40 ml) was kept at 60° for 5 h, then diluted with water, and extracted with benzene. The extract was washed with water, then dried and evaporated to give 1-*phenyl*-2-(*phenylthio*)*ethyl azide* (29) (0·45 g), b.p. 104° at 10^{-4} mmHg, n_D^{23} 1·6136, $\nu_{max.}$ 2100 cm^{-1}, τ 5·40 (1H, t, CH), and 6·74 (2H, d, CH_2) (Found: C, 65·7; H, 5·0; N, 16·2; S,12·6. $C_{14}H_{13}N_3S$ requires C, 65·85; H, 5·1; N, 16·45; S, 12·55%).

The chloride (14) (0·70 g), treated under the same conditions, gave an identical product (0·64 g).

(ii) The *p*-methoxy-compound (4) (0·60 g), after reaction for 100 h at 5°, gave 1-(p-*methoxyphenyl*)-2-(*phenylthio*)*ethyl azide* (30) (0·35 g), b.p. 130° at 10^{-4} mmHg, $\nu_{max.}$ 2150 cm^{-1}, τ 5·44 (1H, t, CH), 6·77 (2H, d, CH_2), and 6·20 (3H, s, OMe) (Found: C, 63·2; H, 5·4; N, 14·6; S, 11·15. $C_{15}H_{15}N_3OS$ requires C, 63·1; H, 5·3; N, 14·7; S, 11·2%).

(iii) The *p*-nitro-compound (5) (0·25 g), on reaction at 0° for 70 h, gave a mixture (0·15 g) of α-(phenylthio)-*p*-nitrostyrene (36) and *p*-nitrophenacyl phenyl sulphide (40), τ 4·21 (0·75H, s), 4·44 (0·75H, s), and 5·74 (0·25H, s).

(iv) The isomer (15) (0·30 g) under the same conditions gave 1-(p-*nitrophenyl*)-2-(*phenylthio*)*ethyl azide* (31) (0·20 g), $\nu_{max.}$ 2120 cm^{-1}, τ 5·28 (1H, t, CH) and 6·73 (2H, d, CH_2) (Found: C, 56·2; H, 4·0; N, 18·6; S, 10·8. $C_{14}H_{12}N_4O_2S$ requires C, 56·0; H, 4·0; N, 18·65; S, 10·7%).

(v) The 2,4-dinitro-compound (6) (0·30 g) was treated at 0°. After 3 h the mixture had darkened and it was therefore worked up. The product (0·20 g) contained *ca.* 40% of α-(2,4-dinitrophenylthio)styrene (37), τ 3·65 (s) and 3·82 (s), the remainder being starting material.

(vi) The isomer (16) (0·40 g), after treatment at ambient temperature for 12 h, gave 2-(2,4-*dinitrophenylthio*)-1-*phenylethyl azide* (32) (0·24 g), m.p. 115—116° (from chloroform–petroleum), $\nu_{max.}$ 2150 cm^{-1}, τ 5·14 (1H, t, CH) and 6·60 (2H, d, CH_2) (Found: C, 48·6; H, 3·4; N, 20·2; S, 9·1. $C_{14}H_{11}N_5O_4S$ requires C, 48·7; H, 3·2; N, 20·3; S, 9·3%).

Reactions with Sodium Toluene-α-thiolate.—When the reaction of sodium (0·1 g) with dry methanol (30 ml) was complete, toluene-α-thiol (0·7 g) was added, followed by the methanesulphonate (3) (0·50 g). The mixture was heated at 60° under nitrogen for 5 h, then concentrated, diluted with benzene, washed with 2N-sodium hydroxide and with water, then dried and evaporated. The product (0·58 g) was purified by t.l.c. (carbon tetrachloride) to give 1-benzylthio-1-(or 2)phenyl-2-(phenylthio)ethane [(13) or (33)], b.p. 120—130° at 10^{-4} mmHg, τ 6·14 (1H, q, CH), 6·6 (2H, m) CH_2), and 6·45 (2H, s, $PhCH_2$·S) (Found: C, 75·0; H, 5·9. Calc. for $C_{21}H_{20}S_2$: C, 74·95; H, 6·0%).

An identical product (0·64 g) was obtained under the same conditions from the chloride (14) (0·60 g).

Reactions with Sodium Benzenethiolate.—The reagent was prepared from benzenethiol (0·7 g) by the procedure described for toluene-α-thiol.

(i) Reaction with the *p*-nitro-compound (5) (0·25 g) for 70 h at 0° gave 1-(p-*nitrophenyl*)-1, 2-*bis*(*phenylthio*)*ethane* (11) (0·30 g), which, after purification by t.l.c. (benzene) and crystallisation from benzene–petroleum, had m.p. 105—107°, τ 5·68 (1H, q, CH) and 6·5 (2H, m, CH_2) (Found: C, 65·4; H, 4·65; N, 3·7; S, 17·2. $C_{20}H_{17}NO_2S_2$ requires C, 65·4; H, 4·7; N, 3·8; S, 17·45%).

(ii) The secondary isomer (15) (0·25 g) under the same conditions gave the same product (0·32 g), m.p. 105—107°.

(iii) The 2,4-dinitrophenyl-compound (6) (0·30 g) after reaction at ambient temperature for 16 h gave a product (0·39 g) which was separated by t.l.c. (benzene–petroleum, 2 : 1) into 2,4-dinitrophenyl phenyl sulphide, m.p. 119—120° (from ether–petroleum) (lit.,[10] 121°), and 1-(2,4-*dinitrophenylthio*)-1-*phenyl*-2-(*phenylthio*)*ethane* (12) (*ca.* 10%), τ 5·59 (1H, q, CH) and 6·40 (2H, d, CH_2) (Found: C, 58·4; H, 4·1; N, 6·8; S, 15·25. $C_{20}H_{16}N_2O_4S_2$ requires C, 58·2; H, 3·9; N, 6·8; S, 15·55%).

(iv) Similar treatment of the isomer (16) (0·30 g) gave a product (0·23 g) which was essentially 2,4-dinitrophenyl phenyl sulphide, m.p. 119—120°, with a trace of the secondary methyl ether (24).

Control Reactions.—(a) *Acetates.* Typically, a solution of 2-phenyl-2-(phenylthio)ethyl acetate [3] (0·30 g), and methanesulphonic acid (0·10 g) in acetic anhydride (1 ml) and acetic acid (25 ml) was heated at 60° for 5 h and then worked up by the procedure described for the solvolyses in acetic acid. The product (0·27 g) was unchanged.

(b) *Methyl ethers.* Typically, a solution of 1-methoxy-2-phenyl-2-(phenylthio)ethane (0·32 g) and methanesulphonic acid (0·10 g) in dry methanol (30 ml) was heated at 60° for 5 h and worked up as described for the solvolyses in methanol. The product (0·28 g) was unchanged.

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