

Cytotoxic Compounds. Part XVIII.¹ Some 2-Aryl-2-(arylthio)ethanols, 1-Aryl-2-(arylthio)ethanols, and their Methanesulphonates

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The reactions of sodium benzenethiolate with styrene oxide, with *p*-methoxystyrene oxide, and with *p*-nitrostyrene oxide each gave a mixture of the corresponding 2-aryl-2-(phenylthio)ethanol and 1-aryl-2-(phenylthio)ethanol, in the proportions 1:1, 4:1, and 1:2, respectively, illustrating the effect of the substituent on the stability of the benzylic carbonium ion responsible for the formation of the primary alcohols.

Methanesulphonates were prepared from all the primary alcohols, and from 1-(*p*-nitrophenyl)-2-(phenylthio)-ethanol and 2-(2,4-dinitrophenylthio)-1-phenylethanol, but only chlorides could be obtained from 1-phenyl-2-(phenylthio)ethanol and 1-(*p*-methoxyphenyl)-2-(phenylthio)ethanol in their reactions with methanesulphonyl chloride. ¹H N.m.r. spectra of all these compounds, and of the acetates and methyl ethers, show characteristic differences between the primary and the secondary series.

SYNTHESES of some (arylthio)propanols² and the reactions of their methanesulphonates with nucleophiles³ were described earlier. To introduce a further variable substituent effect, by means of a second aryl group, some 1-aryl- and 2-aryl-2-(arylthio)ethanols have now been prepared.

Ring fission of styrene oxide with nucleophiles under basic conditions has been claimed to occur exclusively,⁴ or at least predominantly,⁵ by sterically controlled attack at the terminal carbon atom to produce a secondary alcohol, though with phenoxide ion both the solvent⁶ and the nature of any ring-substituent in the styrene oxide^{7,8} have important effects, and some of the earlier claims would probably require revision if the products

were re-examined with modern analytical techniques. The situation with sulphur nucleophiles is confusing. Benzenethiol,⁹ *p*-aminobenzenethiol,¹⁰ and toluene- α -thiol¹¹ are said to give entirely the secondary alcohol, whereas *o*-aminobenzenethiol¹² apparently forms only the primary alcohol. Naphthalene-2-thiol in aqueous sodium hydroxide also gives the primary alcohol,¹³ but is said (without supporting evidence) to give secondary alcohol when the reaction is carried out with the sodium salt in dioxan.

We find that styrene oxide reacts with sodium benzenethiolate in methanol to give a mixture composed of almost equal proportions of the primary alcohol (1) and the secondary isomer (19), readily separable by chromatography. The constitutions were confirmed by an

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² M. S. Khan and L. N. Owen, *J. Chem. Soc. (C)*, 1971, 1448.

³ M. S. Khan and L. N. Owen, *J.C.S. Perkin I*, 1972, 2067.

⁴ W. S. Emerson, *J. Amer. Chem. Soc.*, 1945, **67**, 516; R. R. Russell and C. A. VanderWerf, *ibid.*, 1947, **69**, 11; R. M. Adams and C. A. VanderWerf, *ibid.*, 1950, **72**, 4368.

⁵ 'Heterocyclic Compounds,' ed. R. C. Elderfield, Chapman and Hall, London, 1950, vol. 1, p. 34; 'The Chemistry of Heterocyclic Compounds,' ed. A. Weissberger, Interscience, London, 1964, vol. 19 (part I), pp. 296 *et seq.*

⁶ C. O. Guss, *J. Amer. Chem. Soc.*, 1949, **71**, 3460; C. O. Guss and H. R. Williams, *J. Org. Chem.*, 1951, **16**, 1809.

⁷ C. O. Guss and H. G. Mautner, *J. Org. Chem.*, 1951, **16**, 887.

⁸ C. O. Guss, *J. Amer. Chem. Soc. (a)*, 1952, **74**, 2561; (b) 1953, **75**, 3177; (c) *J. Org. Chem.*, 1952, **17**, 678.

⁹ H. P. Kaufmann and R. Schickel, *Fette, Seifen, Anstrichm.*, 1963, **65**, 851.

¹⁰ H. Gilman and L. Fullhart, *J. Amer. Chem. Soc.*, 1949, **71**, 1478.

¹¹ C. S. Rondstedt, *J. Org. Chem.*, 1956, **21**, 911.

¹² O. Hromatka, J. Augl, A. Brazda, and W. Grünsteidl, *Monatsh.*, 1959, **90**, 544.

¹³ C. O. Guss and H. S. Wilgus, *J. Org. Chem.*, 1959, **24**, 1011.

independent synthesis of the primary compound from methyl mandelate, the toluene-*p*-sulphonate of which, on reaction with sodium benzenethiolate, gave methyl phenyl(phenylthio)acetate (37), which was then reduced with lithium aluminium hydride. It seems improbable that Kaufmann and Schickel's product,⁹ for which no proof of constitution or homogeneity was offered, could have been a pure isomer.

With *p*-methoxystyrene oxide, sodium benzenethiolate again gave a separable mixture (4 : 1) of the two alcohols

greater nucleophilicity and consequent ability to effect some direct S_N2 attack at the terminal position. This is also apparent from the proportion of secondary alcohol (19) formed from the unsubstituted styrene oxide, which is greater than that reported⁶ for the ring fission with phenoxide ion.

Reaction of *p*-nitrostyrene oxide with sodium benzenethiolate gave a separable mixture (1 : 2) of the alcohols (3) and (21). The effect of the nitro-group, opposite to that of the methoxy-substituent, is evident in the

Chemical shifts (τ values) for solutions in CDCl₃ [compounds (13), (14), and (36) in (CD₃)₂CO]

Compound	Ar ¹ S·CHAr ²					
	Ar ¹	Ar ²	R	CH	CH ₂	CH ₃ in R
(1)	Ph	Ph	OH	5.72(q)	6.1(m)	
(2)	Ph	<i>p</i> -MeO·C ₆ H ₄	OH	5.69(q)	6.2(m)	
(3)	Ph	<i>p</i> -O ₂ N·C ₆ H ₄	OH	5.60(q)	6.04(d)	
(4)	2,4-(NO ₂) ₂ C ₆ H ₃	Ph	OH	5.33(t)	5.97(d)	
(5)	Ph	Ph	OAc		5.52(s)	8.07(s)
(6)	Ph	<i>p</i> -MeO·C ₆ H ₄	OAc		5.54(s)	8.07(s)
(7)	Ph	<i>p</i> -O ₂ N·C ₆ H ₄	OAc		5.48(s)	8.06(s)
(8)	2,4-(NO ₂) ₂ C ₆ H ₃	Ph	OAc	5.08(q)	5.5(m)	7.93(s)
(9)	Ph	Ph	OMe	5.58(t)	6.21(d)	6.65(s)
(10)	Ph	<i>p</i> -MeO·C ₆ H ₄	OMe	5.61(t)	6.2(m)	6.68(s)
(11)	Ph	<i>p</i> -O ₂ N·C ₆ H ₄	OMe	5.51(t)	6.16(d)	6.67(s)
(12)	2,4-(NO ₂) ₂ C ₆ H ₃	Ph	OMe	5.26(t)	6.1(m)	6.53(s)
(13)	Ph	Ph	O·SO ₂ Me		5.5(m)	7.12(s)
(14)	Ph	<i>p</i> -MeO·C ₆ H ₄	O·SO ₂ Me		5.5(m)	7.07(s)
(15)	Ph	<i>p</i> -O ₂ N·C ₆ H ₄	O·SO ₂ Me		5.41(s)	7.10(s)
(16)	2,4-(NO ₂) ₂ C ₆ H ₃	Ph	O·SO ₂ Me	5.04(q)	5.3(m)	7.06(s)
(17)	Ph	Ph	Cl	5.61(q)	6.1(m)	
(18)	Ph	<i>p</i> -MeO·C ₆ H ₄	Cl	5.63(q)	6.2(m)	

Compound	Ar ¹ S·CH ₂ ·CHR·Ar ²					
	Ar ¹	Ar ²	R	CH	CH ₂	CH ₃ in R
(19)	Ph	Ph	OH	5.30(q)	6.9(m)	
(20)	Ph	<i>p</i> -MeO·C ₆ H ₄	OH	5.30(q)	6.8(m)	
(21)	Ph	<i>p</i> -O ₂ N·C ₆ H ₄	OH	5.18(q)	6.9(m)	
(22)	2,4-(NO ₂) ₂ C ₆ H ₃	Ph	OH	4.88(t)	6.55(d)	
(23)	Ph	Ph	OAc	4.10(q)	6.7(m)	8.00(s)
(24)	Ph	<i>p</i> -MeO·C ₆ H ₄	OAc	4.13(q)	6.7(m)	8.07(s)
(25)	Ph	<i>p</i> -O ₂ N·C ₆ H ₄	OAc	4.07(t)	6.7(m)	7.98(s)
(26)	2,4-(NO ₂) ₂ C ₆ H ₃	Ph	OAc	3.98(t)	6.5(m)	7.85(s)
(27)	Ph	Ph	OMe	5.68(q)	6.8(m)	6.75(s)
(28)	Ph	<i>p</i> -MeO·C ₆ H ₄	OMe	5.74(q)	6.8(m)	6.78(s)
(29)	Ph	<i>p</i> -O ₂ N·C ₆ H ₄	OMe	5.58(t)	6.8(m)	6.71(s)
(30)	2,4-(NO ₂) ₂ C ₆ H ₃	Ph	OMe	5.49(q)	6.7(m)	6.70(s)
(31)	Ph	Ph	O·SO ₂ Me	5.98(q)	{ 7.36(q) 7.63(q)	7.06(s)
(32)	Ph	<i>p</i> -O ₂ N·C ₆ H ₄	O·SO ₂ Me	4.31(t)	6.6(m)	7.07(s)
(33)	2,4-(NO ₂) ₂ C ₆ H ₃	Ph	O·SO ₂ Me	4.18(t)	6.4(m)	7.17(s)
(34)	Ph	Ph	Cl	5.07(q)	6.5(m)	
(35)	Ph	<i>p</i> -MeO·C ₆ H ₄	Cl	5.09(q)	6.5(m)	
(36)	2,4-(NO ₂) ₂ C ₆ H ₃	Ph	Cl	4.50(t)	5.88(d)	

PhCH(SPh)·CO ₂ Me (37)	(PhS·CH ₂ ·CHPh) ₂ O (38)
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(2) and (20); the latter was identical with the product obtained by reduction of *p*-methoxyphenacyl phenyl sulphide with sodium borohydride. The greatly increased proportion of primary alcohol is compatible with stabilisation, by the *p*-methoxy-group, of the benzylic carbonium ion which would be formed in the competing S_N1-type fission of the epoxide. Reaction of the same epoxide with phenoxide ion gives exclusively primary alcohol^{8a} and the fact that benzenethiolate ion gives some secondary alcohol is a reflection of its

relatively small proportion of primary alcohol formed in this case.

Treatment of styrene oxide with sodium 2,4-dinitrobenzenethiolate resulted only in decomposition, but the same sulphide reacted with 2-bromo-2-phenylethanol to give the primary alcohol (4). Because this reaction might have involved the transitory formation of styrene oxide, the constitution of the alcohol was not self-evident, but was confirmed by protection of the hydroxy-function in the bromohydrin as the tetrahydropyranyl

ether, reaction with the sulphide, and final acidic hydrolysis to give the same product. The secondary isomer (22) was prepared by hydrolysis of the secondary chloride (36), obtained¹⁴ by addition of 2,4-dinitrobenzenesulphenyl chloride to styrene. The constitution of this alcohol also is not self-evident from the method of preparation, because of the possible intervention of an episulphonium ion during the hydrolysis, but any such doubt is dispersed by the clear differences between the properties of the two alcohols.

Considerable variations were encountered in the relative stabilities of the methanesulphonates of the various alcohols. The unsubstituted primary compound (1), with methanesulphonyl chloride and triethylamine in dichloromethane at 0°, gave a crystalline derivative (13) which decomposed rapidly at ambient temperature. Under the same conditions the secondary isomer (19) gave only the secondary chloride (34), and in attempts to avoid this displacement the preparation was carried out with (i) sodium hydride, and (ii) silver oxide, instead of triethylamine; and (iii) methanesulphonic anhydride instead of the acid chloride. These experiments gave 15–20% of the ether (38), most of the alcohol being recovered. The secondary methanesulphonate (31) must therefore be extremely reactive; not only does it attack the alcohol itself but it is completely hydrolysed during work-up. Its existence was demonstrated by repeating the reaction involving silver oxide, but in deuteriochloroform; the ¹H n.m.r. spectrum of the filtered solution showed virtual absence of the original alcohol and the presence of the methanesulphonate. The secondary chloride (34), when heated, partly isomerised to the primary isomer (17).

The *p*-methoxy-compounds behaved in a similar way, the primary alcohol (2) giving the unstable crystalline methanesulphonate (14) whereas the secondary isomer (20) gave only chloride, this time as a 1 : 3 mixture of the primary (18) and the secondary compound (35).

The *p*-nitro-compounds (3) and (21) each gave the corresponding methanesulphonate [(15) and (32)], which when freshly prepared were pure individuals. When stored at ambient temperature, however, isomerisation slowly occurred (n.m.r. spectra), presumably through an episulphonium ion-pair. Nevertheless, the fact that the secondary derivative could actually be isolated illustrates the deactivating effect of the *p*-nitro-substituent. All the methanesulphonates, whether primary or secondary, are activated by anchimeric assistance by sulphur, but the secondary compounds, unlike the primary, are benzylic methanesulphonates, and therefore their even greater reactivity (and instability) is understandable.

The 2,4-dinitro-compounds (4) and (22) also gave individual crystalline methanesulphonates (16) and (33). Here the deactivation diminishes the ability of the sulphur to participate in expulsion of a methylsulphonyloxy-group, so that even the secondary (benzylic) compound is relatively stable.

To serve as reference compounds for the analysis, by n.m.r. spectroscopy, of reaction products from nucleophilic displacements on the methanesulphonates (to be described subsequently), the various alcohols were converted into the acetates [(5)–(8) and (23)–(26)] and the methyl ethers [(9)–(12) and (27)–(30)]. Some of the nitro-compounds could not be methylated with dimethyl sulphate-sodium hydroxide, probably because of fission of the phenyl-sulphur bond,¹⁵ and it was necessary to use diazomethane and fluoroboric acid. Those n.m.r. parameters of diagnostic value are recorded in the Table, and an important feature is that, for all the compounds of unquestionable constitution, the separation of the CH and CH₂ resonances is significantly smaller for the primary type than for the secondary type. The constitutions of the chlorides (for which there is no chemical proof) are assigned on this basis, and this difference between the primary and the secondary compounds has proved to be particularly useful in more recent investigations on the reactions of the methanesulphonates with nucleophiles.

EXPERIMENTAL

¹H N.m.r. spectra were recorded for solutions in deuteriochloroform on Varian A-60 or HA-100 instruments. Kieselgel GF₂₅₄ (Merck) was used for t.l.c., and silica M.F.C. (Hopkin and Williams) for column chromatography. Petroleum refers to the fraction of b.p. 40–60°. Organic solvents were removed under reduced pressure below 50°.

2-Phenyl-2-(phenylthio)ethanol and 1-Phenyl-2-(phenylthio)ethanol.—Benzenethiol (12.8 g) was added to a solution prepared from sodium (2.5 g) and methanol (150 ml), followed by styrene oxide (14.0 g). After 2 h the mixture was diluted with water, then stirred overnight, and extracted with chloroform. The organic layer was washed successively with 2N-sodium hydroxide and water, and was then dried and concentrated to an oil, which by column chromatography (benzene) was separated into *2-phenyl-2-(phenylthio)ethanol* (11.5 g), *R_F* 0.15 (t.l.c. in benzene), m.p. 35–36° (from ether-petroleum) (Found: C, 72.9; H, 6.1; S, 13.8. C₁₄H₁₄OS requires C, 73.0; H, 6.1; S, 13.9%), and *1-phenyl-2-(phenylthio)ethanol* (13.0 g), *R_F* 0.3 (t.l.c. in benzene), b.p. 135° at 10⁻³ mmHg, *n_D*²⁴ 1.6216 (Found: C, 72.9; H, 6.1; S, 13.9%).

Reaction of methyl mandelate (1.0 g) with toluene-*p*-sulphonyl chloride (1.3 g) in pyridine (10 ml) gave the toluene-*p*-sulphonate (0.94 g), m.p. 90–91° (from methanol) (lit.,¹⁶ m.p. 89–90°) (Found: C, 59.9; H, 5.0; S, 9.8. Calc. for C₁₆H₁₆O₅S: C, 60.0; H, 5.0; S, 10.0%). This derivative (2.5 g) and sodium benzenethiolate (1.5 g) were heated together in dry dimethylformamide for 24 h at 100° under nitrogen. The cooled mixture was then diluted with water and extracted with benzene. The extract was washed with 2N-sodium hydroxide and with water, then evaporated to give an oil, which contained some diphenyl disulphide (t.l.c.). Column chromatography (benzene) gave *methyl phenyl(phenylthio)acetate* (1.6 g) (previously described as a crude oil¹⁶), m.p. 39–41° (from methanol) (Found: C, 69.8; H, 5.65; S, 12.3. C₁₅H₁₄O₂S requires C, 69.7; H, 5.5; S, 12.4%).

¹⁴ F. Kaluza and G. W. Perold, *J. S. African Chem. Inst.*, 1957, **10**, 54.

¹⁵ N. Kharasch and K. Swidler, *J. Org. Chem.*, 1954, **19**, 1704.

¹⁶ W. A. Bonner, *J. Org. Chem.*, 1967, **32**, 2496.

A solution of this ester (0.8 g) in dry tetrahydrofuran (10 ml) was added to a stirred slurry of lithium aluminium hydride (0.3 g) in the same solvent (25 ml) at 0°. After 30 min, the mixture was boiled under reflux for 3 h, cooled and treated with a little ethyl acetate, then acidified and extracted with benzene. Evaporation of the washed and dried extract gave an oil which contained some benzenethiol. Column chromatography gave 2-phenyl-2-(phenylthio)ethanol (0.5 g), m.p. and mixed m.p. 35–36°.

Acetates.—Treatment of the two alcohols with acetic anhydride in pyridine at ambient temperature overnight gave 2-phenyl-2-(phenylthio)ethyl acetate, b.p. 118° at 10⁻⁴ mmHg, n_D^{22} 1.5880 (Found: C, 70.5; H, 6.1; S, 11.7. C₁₆H₁₆O₂S requires C, 70.55; H, 5.9; S, 11.8%), and 1-phenyl-2-(phenylthio)ethyl acetate, b.p. 126° at 10⁻⁴ mmHg, n_D^{22} 1.5860 (Found: C, 70.7; H, 5.8; S, 11.5%).

Methyl Ethers.—Dimethyl sulphate (2 ml) in tetrahydrofuran (10 ml) was slowly added to a stirred mixture of 2-phenyl-2-(phenylthio)ethanol (1.0 g) and powdered sodium hydroxide (2 g) in tetrahydrofuran (30 ml) at 45°. After 16 h, the solution was evaporated and the residue was extracted with benzene. The washed and dried extract afforded 1-methoxy-2-phenyl-2-(phenylthio)ethane (1.0 g), b.p. 90° at 10⁻⁴ mmHg, n_D^{19} 1.6034 (Found: C, 74.1; H, 6.6; S, 12.9. C₁₅H₁₆OS requires C, 73.7; H, 6.6; S, 13.1%).

In a similar way, 1-phenyl-2-(phenylthio)ethanol (0.65 g) gave 1-methoxy-1-phenyl-2-(phenylthio)ethane (0.65 g), b.p. 90° at 10⁻⁴ mmHg, n_D^{22} 1.5954 (Found: C, 73.7; H, 6.4; S, 12.9%).

2-Phenyl-2-(phenylthio)ethyl Methanesulphonate.—Methanesulphonyl chloride (0.27 g) in dichloromethane (10 ml) was added dropwise to a stirred solution of 2-phenyl-2-(phenylthio)ethanol (0.5 g) and triethylamine (0.33 g) in dichloromethane (25 ml) at 0°. After a further 30 min the mixture was washed with cooled solutions of 2N-hydrochloric acid and sodium hydrogen carbonate, then with water, and was dried and concentrated at 0° to give the *methanesulphonate* (0.68 g), m.p. 57° (from ether-petroleum), ν_{\max} (CHCl₃) 1340 and 1200 cm⁻¹ (Found: C, 59.2; H, 5.4; S, 21.4. C₁₅H₁₆O₃S₂ requires C, 58.4; H, 5.2; S, 20.8%). The compound rapidly decomposed at ambient temperature, and better analytical figures could not be obtained.

1-Phenyl-2-(phenylthio)ethyl Chloride.—Treatment of 1-phenyl-2-(phenylthio)ethanol (0.67 g) with methanesulphonyl chloride under the same conditions as in the preceding experiment gave the chloride (0.68 g), which partly isomerised into the primary chloride when distilled; the mixture had b.p. 104° at 10⁻⁴ mmHg, n_D^{23} 1.6168 (Found: C, 67.6; H, 5.3; Cl, 13.85. Calc. for C₁₄H₁₃ClS: C, 67.6; H, 5.3; Cl, 14.25%).

Bis-[1-phenyl-2-(phenylthio)ethyl] Ether (38).—A solution of 1-phenyl-2-(phenylthio)ethanol (0.5 g) in dichloromethane (10 ml) was added dropwise to methanesulphonic anhydride¹⁷ (0.8 g) and triethylamine (0.42 g) in dichloromethane (30 ml) at 0°. The mixture was kept at 0° overnight, then treated as described for the above methanesulphonate to give a mixture of the original alcohol and the ether (0.1 g). The latter, isolated by column chromatography (benzene) had b.p. 190° at 10⁻⁵ mmHg, τ 2.5–2.9 (20H, m, aromatic), 5.3–5.8 (2H, m, CH), and 6.5–6.9 (4H, m, CH₂) (Found: C, 75.9; H, 5.9; S, 14.3. C₂₈H₂₆OS₂ requires C, 76.0; H, 5.9; S, 14.5%).

1-Phenyl-2-(phenylthio)ethyl Methanesulphonate.—Meth-

anesulphonyl chloride (36 mg) in deuteriochloroform (2 ml) was slowly added to a suspension of silver oxide (45 mg) in a stirred solution of 1-phenyl-2-(phenylthio)ethanol (69 mg) in deuteriochloroform at 0°. After a further 30 min, the mixture was dried, filtered, and concentrated at 0° to ca. 0.5 ml. The n.m.r. spectrum was recorded on this solution of the methanesulphonate.

2-(p-Methoxyphenyl)-2-(phenylthio)ethanol and 1-(p-Methoxyphenyl)-2-(phenylthio)ethanol.—Under the conditions described for the reaction with styrene oxide, *p*-methoxystyrene oxide¹⁸ (20.5 g), benzenethiol (15 g), sodium (3 g), and methanol (150 ml) gave an oil, which by column chromatography (ether-petroleum, 1 : 3) was separated into 2-(*p*-methoxyphenyl)-2-(phenylthio)ethanol (22.5 g), m.p. 44–45° (from ether-petroleum) (Found: C, 69.0; H, 6.2; S, 12.4. C₁₅H₁₆O₂S requires C, 69.2; H, 6.2; S, 12.3%), and 1-(*p*-methoxyphenyl)-2-(phenylthio)ethanol (5.2 g), n_D^{22} 1.6111 (Found: C, 68.9; H, 6.05; S, 12.2%). An attempt to distil the latter alcohol resulted in dehydration, to give trans-1-(*p*-methoxyphenyl)-2-(phenylthio)ethylene, m.p. 50–53° (from petroleum), ν_{\max} (CHCl₃) 960 cm⁻¹, τ 2.4–2.8 (7H, m, aromatic), 3.13 (2H, d, aromatic), 3.23 (2H, s, CH:CH), and 6.20 (3H, s, OCH₃) (Found: C, 74.6; H, 5.7; S, 13.3. C₁₅H₁₄OS requires C, 74.3; H, 5.8; S, 13.2%).

A solution of sodium borohydride (0.38 g) in methanol (5 ml) was added to a stirred mixture of α -(phenylthio)-*p*-methoxyacetophenone¹⁹ (2.58 g), methanol (54 ml), and water (5 ml). Stirring was continued overnight, and then the solvent was removed by distillation and the residue was diluted with water and extracted with ether to give 1-(*p*-methoxyphenyl)-2-(phenylthio)ethanol (2.5 g), identical (n.m.r. spectrum) with that described above.

Acetates.—Acetylation of the alcohols, as described above, gave 2-(*p*-methoxyphenyl)-2-(phenylthio)ethyl acetate b.p. 140° at 10⁻⁴ mmHg, n_D^{22} 1.5841 (Found: C, 67.45; H, 6.3; S, 10.7. C₁₇H₁₈O₃S requires C, 67.5; H, 6.0; S, 10.6%), and 1-(*p*-methoxyphenyl)-2-(phenylthio)ethyl acetate, b.p. 150° at 10⁻⁴ mmHg, n_D^{22} 1.5811 (Found: C, 67.9; H, 5.8; S, 10.6%).

Methyl Ethers.—Prepared as described for the unsubstituted analogues, 1-methoxy-2-(*p*-methoxyphenyl)-2-(phenylthio)ethane had b.p. 130° at 10⁻⁴ mmHg, n_D^{25} 1.5925 (Found: C, 69.9; H, 6.6; S, 11.9. C₁₆H₁₈O₂S requires C, 70.0; H, 6.6; S, 11.7%), and 1-methoxy-1-(*p*-methoxyphenyl)-2-(phenylthio)ethane had b.p. 124° at 10⁻⁴ mmHg, n_D^{18} 1.5903 (Found: C, 70.0; H, 6.5; S, 11.7%).

2-(p-Methoxyphenyl)-2-(phenylthio)ethyl Methanesulphonate.—2-(*p*-Methoxyphenyl)-2-(phenylthio)ethanol (0.30 g), under the conditions used for the unsubstituted compound, gave the *methanesulphonate* (0.34 g), m.p. 55–56° (from chloroform-petroleum) (Found: C, 57.0; H, 5.2; S, 18.7. C₁₆H₁₈O₄S₂ requires C, 56.8; H, 5.4; S, 18.9%), which was unstable at ambient temperature.

2-(p-Nitrophenyl)-2-(phenylthio)ethanol and 1-(p-Nitrophenyl)-2-(phenylthio)ethanol.—By the method described for styrene oxide, *p*-nitrostyrene oxide⁷ (1.0 g) gave, after separation by column chromatography (benzene-chloroform, 1 : 1), 2-(*p*-nitrophenyl)-2-(phenylthio)ethanol (0.53 g), n_D^{23} 1.6306 (Found: C, 60.9; H, 5.0; N, 5.0; S, 11.5. C₁₄H₁₃NO₃S requires C, 61.1; H, 4.75; N, 5.1; S, 11.6%), and 1-(*p*-nitrophenyl)-2-(phenylthio)ethanol (1.08 g), n_D^{20} 1.6338 (Found: C, 60.9; H, 4.9; N, 5.0; S, 11.7%). Both alcohols decomposed when distilled.

¹⁷ L. N. Owen and S. P. Whitelaw, *J. Chem. Soc.*, 1953, 3723.

¹⁸ V. Franzen and H.-E. Driesen, *Chem. Ber.*, 1963, **96**, 1881.

¹⁹ J. E. Banfield, W. Davies, N. W. Gamble, and S. Middleton, *J. Chem. Soc.*, 1956, 4791.

Acetates.—Prepared as described for the unsubstituted compounds, 2-(*p*-nitrophenyl)-2-(phenylthio)ethyl acetate had b.p. 160° at 10⁻⁴ mmHg (Found: C, 60.4; H, 4.9; N, 4.4; S, 10.4. C₁₆H₁₅NO₄S requires C, 60.55; H, 4.8; N, 4.4; S, 10.1%), and 1-(*p*-nitrophenyl)-2-(phenylthio)ethyl acetate had b.p. 177° at 10⁻⁴ mmHg (Found: C, 60.7; H, 4.9; N, 4.4; S, 10.2%).

Methyl Ethers.—A solution of diazomethane (ca. 1.2 g) in ether was added to a solution of 2-(*p*-nitrophenyl)-2-(phenylthio)ethanol (0.5 g) and fluoroboric acid (40%; 2 ml) in dichloromethane (60 ml). After 24 h at ambient temperature, the solution was neutralised with 2*N*-sodium hydroxide, then concentrated, washed with water, dried, and evaporated to an oil, which contained some original alcohol. T.l.c. (chloroform) gave 1-methoxy-2-(*p*-nitrophenyl)-2-(phenylthio)ethane, m.p. 51–54° (Found: C, 62.3; H, 5.3; N, 4.7; S, 10.85. C₁₅H₁₅NO₃S requires C, 62.3; H, 5.2; N, 4.8; S, 11.1%).

Methylation of 1-(*p*-nitrophenyl)-2-(phenylthio)ethanol, with dimethyl sulphate and powdered sodium hydroxide as described for the unsubstituted analogue, gave 1-methoxy-1-(*p*-nitrophenyl)-2-(phenylthio)ethane, which after t.l.c. (benzene) and crystallisation from ether-petroleum had m.p. 41–42° (Found: C, 62.0; H, 5.2; N, 4.8; S, 11.4%).

2-(*p*-Nitrophenyl)-2-(phenylthio)ethyl Methanesulphonate. —Under the conditions described for the unsubstituted analogue, 2-(*p*-nitrophenyl)-2-(phenylthio)ethanol (0.4 g) gave the methanesulphonate (0.35 g), m.p. 78–81° (from dichloromethane-petroleum) (Found: C, 50.9; H, 4.3; N, 3.9; S, 17.95. C₁₅H₁₅NO₅S₂ requires C, 51.0; H, 4.3; N, 4.0; S, 18.1%).

1-(*p*-Nitrophenyl)-2-(phenylthio)ethyl Methanesulphonate. —1-(*p*-Nitrophenyl)-2-(phenylthio)ethanol (0.52 g), similarly treated, gave the methanesulphonate (0.48 g), m.p. 55° (decomp.) (from dichloromethane-petroleum) (Found: C, 50.95; H, 4.3; N, 3.8; S, 18.0%).

2-(2,4-Dinitrophenylthio)-2-phenylethanol. —(i) A solution of 2-bromo-2-phenylethanol²⁰ (2.5 g) in methanol (20 ml) was added to the reagent prepared from sodium (0.35 g), methanol (100 ml), and 2,4-dinitrobenzenethiol (4.0 g), under nitrogen. After stirring at 50° for 4 h, water (10 ml) was added, and the mixture was maintained at 50° overnight, then filtered, concentrated, and extracted with chloroform. The extract was washed with 2*N*-sodium hydroxide and with water, then dried and evaporated to an oil. Column chromatography (chloroform) gave the alcohol (1.7 g), m.p. 129–132° (from chloroform-petroleum) (Found: C, 52.5; H, 4.0; N, 8.5; S, 10.0. C₁₄H₁₂N₂O₅S requires C, 52.5; H, 3.8; N, 8.7; S, 10.0%).

(ii) Dihydropyran (2.2 g) was added dropwise to 2-bromo-2-phenylethanol (5.0 g). Reaction occurred without addition of a catalyst, and was completed by stirring at ambient temperature for 5 h. Excess of dihydropyran was removed under reduced pressure to leave the tetrahydropyranyl ether

as an oil, τ 2.65 (5H, m, aromatic), 4.90 (1H, q, CHBr), 5.2–7.0 (5H, m, O-CH₂ and H-2, H-6, H-6' of tetrahydropyran ring), and 8.35br (6H, s, other protons in ring). The i.r. spectrum (CHCl₃) showed the absence of OH. The crude compound (which decomposed on distillation) (3.5 g) was added to the reagent prepared from 2,4-dinitrobenzenethiol (4.0 g) as described above; the mixture was kept at 70° overnight and worked up in the same way to give a red oil (4.8 g), which was dissolved in methanol (100 ml) and 5*N*-hydrochloric acid (10 ml). The solution was boiled under reflux for 2 h, then concentrated, and the residue was purified by column chromatography (chloroform) and crystallisation from chloroform-petroleum to give the same alcohol (3.2 g), m.p. 129–132°.

2-(2,4-Dinitrophenylthio)-1-phenylethanol. —2-(2,4-Dinitrophenylthio)-1-phenylethyl chloride¹⁴ (5.0 g) was heated under reflux in dioxan (50 ml) and water (10 ml) for 20 h. Evaporation, and column chromatography (chloroform) gave the alcohol (3.0 g), m.p. 132–134° (from chloroform-petroleum) (lit.,¹⁴ 134°).

Acetates.—Prepared from the alcohols, 2-(2,4-dinitrophenylthio)-2-phenylethyl acetate had m.p. 129–130° (from chloroform-petroleum) (Found: C, 52.9; H, 4.0; N, 7.5; S, 8.7. C₁₆H₁₄N₂O₆S requires C, 53.0; H, 3.9; N, 7.7; S, 8.85%), and 2-(2,4-dinitrophenylthio)-1-phenylethyl acetate had m.p. 112–113° (lit.,¹⁴ 113°).

Methyl Ethers.—These were prepared by the diazomethane-fluoroboric acid method, the ethers being separated from unchanged alcohol by column chromatography (chloroform).

2-(2,4-Dinitrophenylthio)-1-methoxy-2-phenylethane (yield 30%) had m.p. 124–126° (from ether-petroleum) (Found: C, 53.9; H, 4.4; N, 8.3; S, 9.7. C₁₅H₁₄N₂O₅S₂ requires C, 53.9; H, 4.2; N, 8.3; S, 9.6%). 2-(2,4-Dinitrophenylthio)-1-methoxy-1-phenylethane (yield 11%) had m.p. 139–143° (from chloroform-petroleum) (Found: C, 53.65; H, 4.3; N, 8.1; S, 9.65%).

2-(2,4-Dinitrophenylthio)-2-phenylethyl Methanesulphonate. —Reaction of 2-(2,4-dinitrophenylthio)-2-phenylethanol (0.6 g) with methanesulphonyl chloride (0.25 g) under the conditions described for the unsubstituted analogue gave the methanesulphonate (0.65 g), m.p. 107° (from dichloromethane-ether) (Found: C, 45.55; H, 3.5; N, 6.7; S, 16.0. C₁₅H₁₄N₂O₇S₂ requires C, 45.2; H, 3.45; N, 7.0; S, 16.1%).

2-(2,4-Dinitrophenylthio)-1-phenylethyl Methanesulphonate. —Similar treatment of 2-(2,4-dinitrophenylthio)-1-phenylethanol (1.0 g) with methanesulphonyl chloride (0.4 g) gave the methanesulphonate (1.0 g), m.p. 75° (decomp.) (from dichloromethane-ether) (Found: C, 45.1; H, 3.5; N, 6.75; S, 16.1%).

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²⁰ S. L. Shapiro, H. Soloway, and L. Freedman, *J. Amer. Chem. Soc.*, 1958, **80**, 6060.