Nucleophilic Substitution at Bivalent Sulphur. Part II.[1] Trans-sulphenylation Reactions of γ-Hydroxyalkyl 2-Nitrobenzenesulphenates

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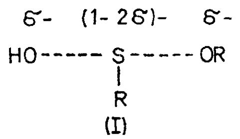
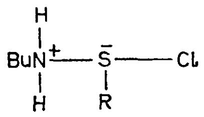
Treatment of 3-hydroxy-1-methylpropyl 2-nitrobenzenesulphenate with sodium hydride in dioxan gives a mixture of 3-hydroxybutyl 2-nitrobenzenesulphenate, starting material, butane-1,3-diyl bis-(2-nitrobenzenesulphenate), and decomposition products. Under similar conditions 3-hydroxybutyl 2-nitrobenzenesulphenate gives only decomposition products. The trans-sulphenylation reactions are best interpreted in terms of a series of intermolecular substitution reactions at the sulphenyl sulphur atom rather than in terms of an intramolecular reaction, which would involve a non-linear transition state for the reaction at the sulphenyl sulphur atom.

Evidence has been advanced[2] that nucleophilic substitution reactions at bivalent sulphur proceed through a linear S_N2-type transition state (I) in which the electron density on the sulphur atom is not substantially increased. The formation of this transition state presumably involves hybrids of only the *s* and *p* orbitals on the sulphur atom. It has recently been suggested[3] that the possibility of formation of an intermediate complex (II) in which the sulphur atom carries a formal negative charge cannot be disregarded, at least for neutral nucleophiles. The formation of this intermediate complex must involve *d* orbital participation and consequently the transition state need not be linear.

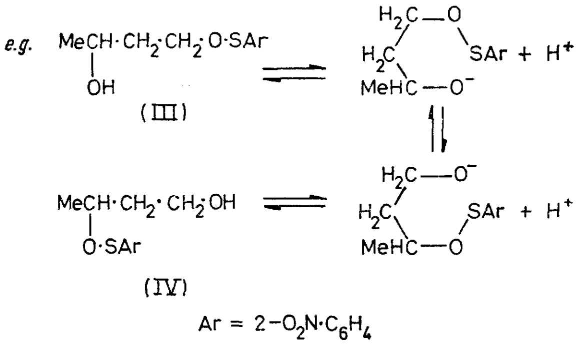


(I)



(II)

The reactions of 3-hydroxybutyl 2-nitrobenzenesulphenate (III) and 3-hydroxy-1-methylpropyl 2-nitrobenzenesulphenate (IV) with sodium hydride in dioxan have been studied in an attempt to obtain evidence for a non-linear transition state for nucleophilic substitution at sulphenyl sulphur. If a non-linear transition state of suitable energy exists then an intramolecular trans-sulphenylation reaction can occur, whereas if the reaction proceeds through a linear transition state the trans-sulphenylation reaction must be intermolecular.

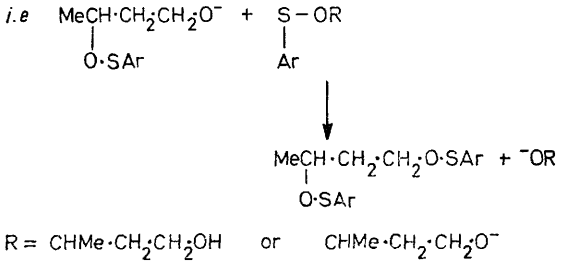


The 2-nitrobenzenesulphenate esters were used because the strong interaction[4] between the sulphur atom and one of the oxygen atoms of the 2-nitro-group is held[5] to reduce the reactivity of the sulphur by the S_N2-type mechanism. If however the interaction persists in the transition state then the sulphur will be associated with 12 electrons and the configuration should be approximately octahedral. In this configuration the three atoms involved in the reaction cannot be linear.

3-Hydroxybutyl and 3-hydroxy-1-methylpropyl 2-nitrobenzenesulphenates were obtained together with butane-1,3-diyl bis-(2-nitrobenzenesulphenate) (V) by treating the sulphenyl chloride with butane-1,3-diol in the presence of pyridine. Separation and estimation of the isomeric hydroxysulphenates showed that they were formed in the ratio 65 : 35, the isomer with the secondary hydroxy-group (III) being the major component.

3-Hydroxy-1-methylpropyl 2-nitrobenzenesulphenate (IV) on treatment with sodium hydride in dioxan gave both isomeric hydroxysulphenates together with butane-1,3-diyl bis-(2-nitrobenzenesulphenate) (V) and decomposition products, whereas the isomer (III) gave only starting material and decomposition products. The isolation of the disulphenate (V) indicated than an intermolecular reaction was occurring, and this conclusion was supported by the observation that no rearrangement could be detected when the reaction mixture was diluted.

The isomerisation of the secondary sulphenate (IV) is considered to occur through the intermediate disulphenate (V), which is formed by an intermolecular nucleophilic substitution on sulphenyl sulphur by the primary alkoxide ion.



A similar reaction involving the disulphenate and another

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[1] Part I, D. R. Hogg and P. W. Vipond, *J. Chem. Soc.* (*B*), 1970, 1242.

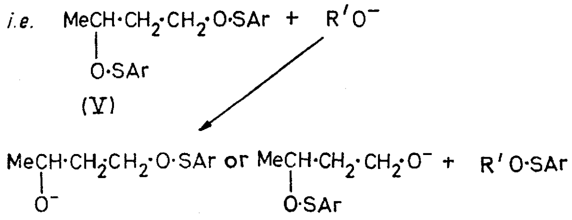
[2] E. Cuiffarin and A. Fava, *Progr. Phys. Org. Chem.*, 1968, **6**, 81, and references therein.

[3] E. Cuiffarin and G. Guaraldi, *J. Amer. Chem. Soc.*, 1969, **91**, 1745.

[4] W. C. Hamilton and S. J. La Placa, *J. Amer. Chem. Soc.*, 1964, **86**, 2289.

[5] E. N. Givens and H. Kwart, *J. Amer. Chem. Soc.*, 1968, **90**, 378.

alkoxide ion would give either the anion derived from the starting material or its isomer.



The disulphenate (V) reacts with sodium ethoxide under similar conditions to give a mixture of the isomeric hydroxysulphenates (III) and (IV) in which the secondary sulphenate (IV) is in a slight excess. This observation is in accord with the slightly greater rate of reaction of primary sulphenates than secondary sulphenates with hydroxide ion.[6] The failure of the reaction with the primary sulphenate (III) is attributed to the decreased reactivity of its secondary alkoxide ion, presumably due to steric effects, which are considered to be of considerable importance in determining the relative rate of this type of reaction.[6] These conclusions are supported by the observations that under similar conditions no reaction was observed between sodium isopropoxide and ethyl 2-nitrobenzenesulphenate, although sodium ethoxide reacted readily with isopropyl 2-nitrobenzenesulphenate to give the ethyl ester.

The trans-sulphenylation reaction observed under these conditions with 3-hydroxy-1-methylpropyl 2-nitrobenzenesulphenate (IV) is best interpreted on the basis of an intermolecular mechanism. Although no general conclusions can be drawn as to whether the *d* orbitals on the sulphur are involved in the formation of the transition state, the strong interaction between the sulphur and one of the oxygens of the nitro-group apparently does not persist in the transition state.

EXPERIMENTAL

Reaction of 2-*Nitrobenzenesulphenyl Chloride with Butane*-1,3-*diol*.—The diol (2 ml.) was added to a solution of the sulphenyl chloride (2·0 g., 0·01 mole) in methylene chloride (30 ml.), then pyridine (*ca.* 1 ml.) was added. The solution was set aside for 16 hr., then evaporated to give an orange oil, which was chromatographed on silica gel. Elution with benzene gave *butane*-1,3-*diyl bis*-2-*nitrobenzenesulphenate* (V) (0·33 g., 13%), an orange oil yielding a yellow solid, m.p. 71·5—72·5°, $\lambda_{max.}$ 241, 276sh, and 401 nm. (log ε 4·48, 4·03, and 3·91); $\nu_{max.}$ 1595, 1569, and 730 cm.$^{-1}$; τ 8·54 (3H, d), 8·02—7·57 (2H, m), 6·05—5·60 (3H, m), 2·90—2·00 (6H, m), and 1·88—1·55 (2H, d) (Found: C, 48·4; H, 4·0; N, 7·1. $C_{16}H_{16}N_2O_6S_2$ requires C, 48·5; H, 4·1; N, 7·1%), together with a trace of bis-2-nitrophenyl disulphide.

Elution with 50% v/v benzene–ethyl acetate gave a mixture of the mono-2-nitrobenzenesulphenates (1·73 g., 56%) as an orange oil. Preparative t.l.c. on silica gel (50% v/v benzene–ethyl acetate containing 5% of triethylamine as irrigant) gave 3-*hydroxybutyl* 2-*nitrobenzenesulphenate* (III), m.p. 54—56°, yellow crystals from benzene, $\lambda_{max.}$ 240, 282sh, and 401 nm. (log ε 4·03, 3·57, and 3·51); $\nu_{max.}$ 3360br (OH), 1594, 1565, and 730 cm.$^{-1}$; τ 8·84—8·59 (3H, d), 8·27—7·82 (3H, m, 1H exchangeable), 6·11—5·77 (3H, m), 2·93—2·10 (3H, m), and 1·92—1·63 (1H, m) [Found: *M*, 243·0568 (mass spectrum). $C_{10}H_{13}NO_4S$ requires *M*, 243·0566], and 3-*hydroxy*-1-*methylpropyl* 2-*nitrobenzenesulphenate* (IV), an orange oil, $\lambda_{max.}$ 243, 278sh, and 401 nm. (log ε 4·08, 3·57, and 3·42); $\nu_{max.}$ 3330br (OH), 1600, 1520, and 735 cm.$^{-1}$; τ 8·71—8·46 (3H, d), 8·21—7·78 (3H, m, 1H exchangeable), 6·28—5·74 (3H, m), 2·93—2·02 (3H, m), and 1·83—1·57 (1H, m) [Found: *M*, 243·0563 (mass spectrum). $C_{10}H_{13}NO_4S$ requires *M*, 243·0566].

A portion of the monosulphenate mixture was separated by t.l.c. and each component was extracted with dioxan. The dioxan solutions were made up to 50 ml. and the concentrations were determined spectrophotometrically at 400 nm. The ratio of (III) to (IV) was 65 : 35. The mixture of the monosulphenates was completely acetylated with acetic anhydride and pyridine. The crude mixture of acetoxy-monosulphenates had ^{1}H n.m.r. bands at τ 4·7—5·2 (m) and 5·7—6·3 (m). Integration of these bands, which were attributed to the methine proton α to the acetoxy-group and to the other methylene and methine protons α to the functional groups, respectively, gives a ratio of (III) to (IV) of 63 : 37.

Attempted Rearrangement of the Mono-2-*nitrobenzenesulphenates of Butane*-1,3-*diol*.—A sample (1 ml.) of a stock solution (6 × 10^{-3}M) of 3-hydroxy-1-methylpropyl 2-nitrobenzenesulphenate in dioxan was taken, sodium hydride (50% suspension in oil; 0·05 g.) was added, and the solution was boiled for 2—3 min. The mixture was acidified with dilute hydrochloric acid, water was added, and the mixture was extracted with ether. The dried extracts were chromatographed (t.l.c.) with 50% v/v benzene–ethyl acetate containing 5% triethylamine as irrigant. A mixture of compounds (III), (IV), and (V) was used for reference. The bands were scraped off the plate and extracted with dioxan, and the concentrations of product were determined spectrophotometrically. 3-Hydroxy-1-methylpropyl 2-nitrobenzenesulphenate (IV), 3-hydroxybutyl 2-nitrobenzenesulphenate (III), and butane-1,3-diyl bis-(2-nitrobenzenesulphenate) (V) were found in the ratio 1 : 1 : 1·25, together with decomposition products. When the reaction mixture had been set aside for 12 hr. at room temperature the ratio of products was 2 : 3·5 : 1.

Under similar conditions 3-hydroxybutyl 2-nitrobenzenesulphenate gave only starting material together with decomposition products. With either isomer only decomposition products were obtained when the reaction mixture was boiled for 10 min.

Dilution of either stock solution (1 ml.) with dioxan (24 ml.) before reaction gave only starting materials (25—35%, depending upon the conditions) together with decomposition products.

Reactions of 2-*Nitrobenzenesulphenates with Sodium Alkoxides*.—(*a*) Dry sodium ethoxide (0·20 g.) was added to a solution of isopropyl 2-nitrobenzenesulphenate (0·67 g.) in dioxan (15 ml.). The mixture was boiled for 3 min., set aside for 15 min., and acidified with dilute hydrochloric acid. Water (40 ml.) was added, and the solution was extracted with ether. The solvent was removed from the dried extracts to give an orange oil (0·58 g.). T.l.c. showed that two compounds of very similar R_F value were present. The ^{1}H n.m.r. spectrum corresponded to that of a 1 : 3

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[6] C. Brown and D. R. Hogg, *Chem. Comm.*, 1967, 38.

mixture of ethyl and isopropyl 2-nitrobenzenesulphenates.

(*b*) Ethyl 2-nitrobenzenesulphenate (0·60 g.) was similarly treated with dry sodium isopropoxide (0·245 g.) to give, after chromatography, only unchanged ester (0·515 g., 86%), m.p. 30—31° (lit.,[7] 26°), ^1H n.m.r. spectrum identical with that of an authentic specimen.

(*c*) Butan-1,3-diyl bis-2-nitrobenzenesulphenate (0·41 g.) was similarly treated with dry sodium ethoxide (0·09 g.) to give, after chromatography, ethyl 2-nitrobenzenesulphenate (0·07 g., 18%), starting material (0·19 g., 46%), and a mixture (0·045 g., 18%) containing 3-hydroxybutyl 2-nitrobenzenesulphenate (47%) and 3-hydroxy-1-methylpropyl 2-nitrobenzenesulphenate (53%).

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[7] T. Zincke and F. Farr, *Annalen*, 1912, **391**, 55.