Studies in the Nature of the α,ω-Rearrangement

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The conditions under which two groups X and Y, attached to carbon atoms α and ω in an organic structure, may exchange places have been investigated. The pyrolyses of halogeno-O-thiobenzoates, of bis-O-thiobenzoates, and of bis-imidates have been shown to furnish rearrangement products which can be classified under this principle. In a number of examples the mechanism of rearrangement has been shown to be intermolecular in nature and ionic in character. The ring size of the intermediate ion (5, 6, but not, in general, 7) appears to provide a practical limit to the extent of these α,ω-rearrangements. The familiar diaxial–diequatorial rearrangements can be classified as the first (αβ) examples of the αω-family of rearrangements.

The potential synthetic value of the bis-imidate rearrangements is mentioned.

THE reversible rearrangement (A; $X = Y = Br$, $n = 0$) $\rightleftharpoons$ (B; $X' = Y' = Br$, $n = 0$) is well known.[1] This phenomenon was later generalised in the expression ' diaxial–diequatorial ' rearrangement [2] and includes cases where the groups X and Y are acyloxy and halogen respectively ($n = 0$). The driving force for the diaxial–diequatorial rearrangement is mainly steric in origin. However, it is clear that merely entropy factors would give a 1 : 1 equilibrium mixture. This effect is seen in the thermal equilibration of aliphatic 1,2-halogeno-hydrin esters (A; $X = $ halogen, $Y = $ acyloxy, $n = 0$).[3]

[1] D. H. R. Barton and E. Miller, *J. Amer. Chem. Soc.*, 1950, **72**, 1066; G. H. Alt and D. H. R. Barton, *J. Chem. Soc.*, 1954, 4284; D. H. R. Barton and A. J. Head, *ibid.*, 1956, 932; G. Bellucci, C. Giordano, A. Marsili, and G. Berti, *Tetrahedron*, 1969, **25**, 4515; D. H. R. Barton, H. MacGrillen, P. D. Magnus, C. H. Carlisle, and P. A. Timmins, *J.C.S. Perkin I*, 1972, 1584.

[2] D. H. R. Barton and J. F. King, *J. Chem. Soc.*, 1958, 4398.
[3] D. H. R. Barton, J. P. Poyser, P. G. Sammes, M. B. Hurst-house, and S. Neidle, *Chem. Comm.*, 1971, 715; D. H. R. Barton, J. P. Poyster, and P. G. Sammes, *J.C.S. Perkin I*, 1972, 53; R. G. Pews and R. A. Davis, *J.C.S. Chem. Comm.*, 1973, 269.

Further examples of diaxial–diequatorial rearrangements have been provided by King and his colleagues.[4] It is convenient to classify all these rearrangements as

(A)   (B)
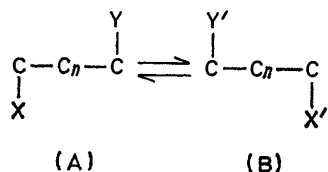
$\alpha,\beta \rightleftharpoons \beta,\alpha$ changes where the two carbon atoms (A; $n = 0$) are designated α and β.

It seemed to us that α,β-rearrangements might represent the first member of a family of rearrangements. Thus, in (A) if $n = 1$, we would consider this an α,γ-rearrangement, if $n = 2$, an α,δ-rearrangement and so on (α,ω being the general term). Furthermore, whilst the α,β-rearrangements previously described depend upon the relief of steric compression, there is no reason in principle why an electronic driving force should not be utilised. Thus, in the change (A) ⟶ (B) the groups X and Y could also change into the more stable bond arrangements of X' and Y' and thus make the rearrangement virtually irreversible. The experiments in the sequel are relevant to these considerations.[5]

α,α'-Dibromo-4-nitro-o-xylene (1e), treated with 1 equiv. of sodium benzoate, afforded a mixture of the two bromo-benzoates (1a and b) as well as the dibenzoate (1c). The two bromo-benzoates correspond to the case (A; X = Br, Y = O·COPh, $n = 2$) (α,δ-rearrangement)
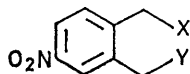
(1)

a; X = O·CO·Ph, Y = Br
b; X = Br, Y = O·CO·Ph
c; X = Y = O·CO·Ph
d; X = H, Y = OH
e; X = Y = Br
f; X = O·CS·Ph, Y = Cl
g; X = Y = OH
h; X = OH, Y = Br
i; X = Br, Y = OH
j; X = Cl, Y = S·CO·Ph
k; X = O·CS·Ph, Y = I
l; X = I, Y = S·CO·Ph
m; X = OH, Y = S·CO·Ph

and for reasons of entropy we expected them to equilibrate. However, heating (1a) in a sealed tube at 200—210° for 3 h gave in small amounts (1b, c, and e) and most of the bromo-benzoate (1a) was recovered unchanged. The constitution of (1b), and hence of (1a), was determined by reducing the bromo-benzoate (1b) with sodium borohydride[6] under solvolytic conditions to give 2-methyl-5-nitrobenzyl alcohol (1d), identical with an authentic specimen.[7]

[4] J. F. King and R. G. Pews, Canad. J. Chem., 1965, **43**, 847; J. F. King, K. Abikar, D. M. Deaken, and R. G. Pews, ibid., 1968, **46**, 1; J. F. King and K. Abikar, ibid., p. 9; see also G. Bellucci, M. Ferretti, G. Ingrosso, F. Marioni, A. Marsili, and I. Morelli, Tetrahedron Letters, 1972, 3527.

[5] See also E. J. Hedgley and N. H. Leon, J. Chem. Soc. (C), 1970, 467.

Hydrolysis of the dibromide (1e) gave the diol (1g) and the phthalan (2). Controlled treatment of the diol (1g) with hydrogen bromide gave the separable bromo-alcohols (1h and i). Benzoylation of (1i) afforded the bromo-benzoate (1b) and thus established the constitutions of (1h and i). Treatment of (1h) with thiobenzoyl chloride–pyridine (1 equiv.) furnished the chloro-O-thiobenzoate (1f), an S_N2 displacement of the benzylic bromide accompanying the thioacylation. We had now constructed a compound where an electronic driving force (O-thiobenzoate ⟶ S-thiobenzoate) had been provided to facilitate an α,δ-rearrangement. The chloro-O-thiobenzoate (1f) rearranged smoothly on
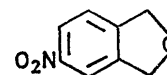
(2)

heating at 160° for 3 h to give the chloro-S-thioester (1j). An authentic specimen of this compound was prepared by treating the bromo-alcohol (1h) with potassium thiobenzoate to furnish the corresponding S-thiobenzoate (1m). This was treated with thionyl chloride to give the ester (1j).

Treatment of the chloro-O-thiobenzoate (1f) with sodium iodide furnished the corresponding iodo-O-thiobenzoate (1k). Whereas the rearrangement of the chloro-compound (1f) to give the chloro-S-thioester (1j) was relatively slow in refluxing chlorobenzene, the iodo-analogue (1k) rearranged smoothly to the S-thiobenzoate (1l) in the same solvent in 2·5 h. This reflects the greater capacity of iodine for neighbouring group participation. An authentic specimen of the rearranged iodo-compound (1l) was prepared from the chloro-S-thiobenzoate (1j) by treatment with iodide ion. These experiments demonstrate that the α,δ-rearrangement can be observed when an adequate electronic driving force is provided.

We used this type of driving force (O-thioester ⟶ S-thioester) to determine the limitation on the number n in the expressions (A) and (B). Ethylene bis-O-thiobenzoate (3a), prepared either by treatment of ethylene glycol with pyridine–thiobenzoyl chloride or by the use of (thiobenzoylthio)acetic acid (' thiobenzoylthioglycolic acid '),[8] rearranged smoothly when heated neat at 140° (1 h) or in solution at 132° (4 h) to give ethylene bis-S-thiobenzoate (3b).[9] None of the mixed ether (3c) could be detected in the product. An authentic specimen of (3c) was synthesised by O-thiobenzoylation of 2-hydroxyethyl S-thiobenzoate[10] and shown to be completely stable at 140°. However, prolonged heating of the

[6] H. C. Brown and H. M. Bell, J. Amer. Chem. Soc., 1966, **88**, 1473.

[7] R. A. Barnes and J. C. Godfrey, J. Org. Chem., 1957, **22**, 1038.

[8] A. Kjaer, Acta Chem. Scand., 1950, **4**, 1347; 1952, **6**, 1374.

[9] S. Mathias, Bol. Fac. Filosofia Cienc. Letras, Univ. São Paulo 14, Quim., 1942, No. 1, 75 (Chem. Abs., 1946, **40**, 2793).

[10] P. Nylen and A. Olsen, Svensk kem. Tidskr., 1941, **53**, 274.

mixed ester (3c) at 195—200° for 13 h did give complete conversion into the bis-S-thiobenzoate (3b).

$$[CH_2]_n \diagdown \genfrac{}{}{0pt}{}{X}{Y}$$

(3)
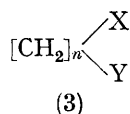
a; $n = 2$, X = Y = O·CS·Ph
b; $n = 2$, X = Y = S·CO·Ph
c; $n = 2$, X = O·CS·Ph, Y = S·CO·Ph
d; $n = 3$, X = Y = O·CS·Ph
e; $n = 3$, X = Y = S·CO·Ph
f; $n = 3$, X = O·CS·Ph, Y = S·CO·Ph
g; $n = 4$, X = Y = O·CS·Ph
h; $n = 2$, X = Y = O·CS·C$_6$D$_5$
i; $n = 2$, X = Y = S·CO·C$_6$D$_5$
j; $n = 2$, X = S·CO·Ph, Y = S·CO·C$_6$D$_5$

Similarly propane-1,3-diyl bis-O-thiobenzoate (3d) was prepared and shown to rearrange (α,γ-rearrangement) on pyrolysis at 175—180° (6 h) to give a mixture of propane-1,3-diyl bis-S-thiobenzoate (3e), identical with an authentic specimen,[9] and the half-rearranged ester (3f). An authentic specimen of the latter was prepared by treating 3-chloropropan-1-ol with potassium S-thiobenzoate and then benzoylating the product. The half-rearranged ester (3f) was not an intermediate in the formation of the diester (3e), because it did not rearrange further on heating at 180—188° for 6 h.

Butane-1,4-diyl bis-O-thiobenzoate (3g) did not rearrange on heating at 187° for 7 h, thus showing a limit at ($n = 2$) in expression (A) for (X = Y = Ph·CS·O). n-Propyl O-thiobenzoate (4) and 2-phenoxyethyl O-thio-

Pr^{n}O·CS·Ph   PhO·CH$_2$CH$_2$·O·CS·Ph
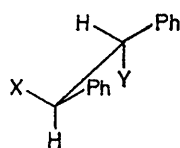(4)   (5)
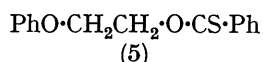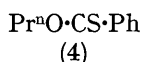
benzoate (5) were stable at 180—182° for 6·5 h and at 180° for 6 h, respectively. Prolonged heating of ester (5) at 240—250° for 26 h gave extensive decomposition, but no rearrangement.

The stereochemistry of these bis-O-thioester rearrangements was established in the following examples. meso-1,2-Diphenylethylene bis-O-thiobenzoate (6a) rearranged smoothly on pyrolysis at 206—210° (neat, 40 min) or at 132° in solution (10 h) to give meso-1,2-diphenylethylene

(6)   (7)
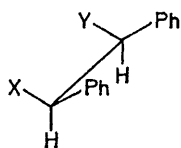
a; X = Y = O·CS·Ph   a; X = Y = O·CS·Ph
b; X = Y = S·CO·Ph   b; X = Y = S·CO·Ph

bis-S-thiobenzoate (6b). An authentic sample was prepared by benzoylation of meso-1,2-diphenylethane-1,2-

[11] C. G. Overberger and A. Ducker, J. Org. Chem., 1964, 29, 360.
[12] A. Lawson and D. H. Mills, J. Chem. Soc., 1959, 2865.
[13] J. H. Billman and L. R. Caswell, J. Org. Chem., 1951, 14, 1041.

dithiol.[11] Similarly, (±)-1,2-diphenylethylene bis-O-thiobenzoate (7a), where the conformational features are less helpful for rearrangement, gave (±)-1,2-diphenylethylene bis-S-thiobenzoate (7b) in modest yield on pyrolysis at 195° (neat, 1 h). An authentic specimen of dibenzoate (7b) was prepared by benzoylation of (±)-1,2-diphenylethane-1,2-dithiol.[11]
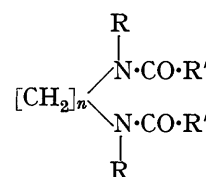
Of other functional groups which possess, in principle, adequate electronic reorganisation energy to participate in α,ω-type rearrangements, we considered the suitability of the imidate function. During rearrangement this would change to the more stable amide group. We anticipated that bis-imidates as in [A; X = Y = O·C(Ph)=N·Ph] would rearrange to bis-amides as in (B; X' = Y' = N(Ph)·CO·Ph].

Treatment of N-phenylbenzimidoyl chloride [12] with ethylene glycol and sodium hydride gave the bis-imidate (8a) of undefined (and irrelevant) geometry. Pyrolysis of this compound at 132° for 9 h gave the bis-amide (9a) [13] and the half-rearranged isomer (10a) (ca. 30%). This latter compound could not be crystallised; its constitution was established by mild acid hydrolysis to O,N-dibenzoyl-N-phenyl-2-aminoethanol.[14]
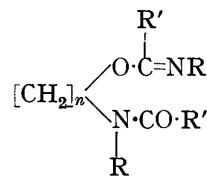

(8)   (9)
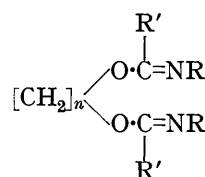
a; $n = 2$, R = R' = Ph   a; $n = 2$, R = R' = Ph
b; $n = 3$, R = R' = Ph   b; $n = 3$, R = R' = Ph
c; $n = 2$, R = Me, R' = Ph   c; $n = 2$, R = Me, R' =Ph
d; $n = 2$, R = C$_6$H$_2$D$_3$, R' = Ph

(10)

a; $n = 2$, R = R' = Ph
b; $n = 3$, R = R' = Ph

The half-rearranged isomer was not an intermediate, for it did not rearrange further when heated at 132° for 9 h. The bis-amide (9a) was, of course, also stable at this temperature.

Similarly the bis-1,3-imidate (8b) was prepared from propane-1,3-diol and shown to rearrange at 154° (83 h) in a slow reaction to give a poor yield of bis-amide (9b).[15] Also produced was the half-rearranged isomer (10b) characterised by mild acid hydrolysis to O,N-dibenzoyl-N-phenyl-3-aminopropanol.[16]
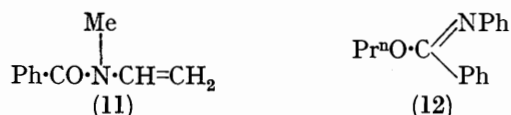
We also investigated the behaviour on pyrolysis of the

[14] P. Schorigin and W. Below, Ber., 1935, 68, 833.
[15] W. C. L. Veer, Rec. Trav. chim., 1938, 57, 989.
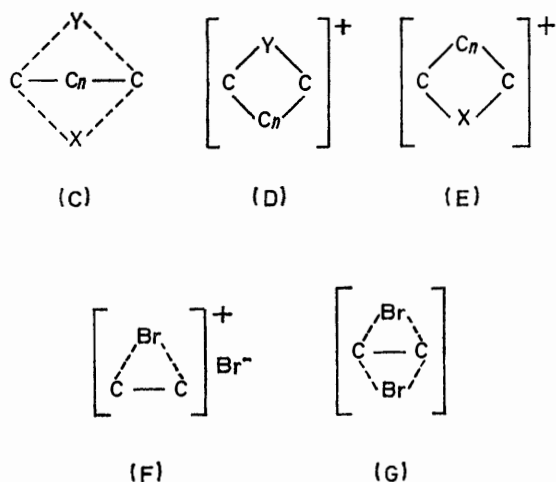[16] S. Searles and V. P. Gregory, J. Amer. Chem. Soc., 1954, 76, 2789.

N-methyl-bis-imidate (8c), prepared from *N*-methyl-benzimidoyl chloride [17] and ethylene glycol dianion. Pyrolysis at 145—150° for 4 h in the absence of solvent gave, as principal product, the bis-amide (9c), identical with an authentic specimen.[18] In contrast pyrolysis at 132° in chlorobenzene afforded the bis-amide (9c) in poor yield and the major products were *N*-methyl-benzamide and the unsaturated amide (11). The constitution of the latter was confirmed by hydrogenation to *N*-ethyl-*N*-methylbenzamide, identical with an authentic specimen.[19] Heating *N*-methylbenzamide and the vinylamide (11) together at 145° did not furnish the bis-amide (9c), nor did the latter fragment into

$$\underset{(11)}{\overset{\overset{\displaystyle Me}{|}}{Ph \cdot CO \cdot N \cdot CH = CH_2}} \qquad \underset{(12)}{Pr^n O \cdot C \overset{\nearrow NPh}{\underset{\searrow Ph}{}}}$$

N-methylbenzamide and the vinylamide at this temperature.

It is noteworthy that the simple benzimidate (12) was thermally stable at the temperatures needed for the rearrangement of the bis-imidates (8a—c).

We attempt now to place all the reactions discussed so far upon a common mechanistic basis. Excluding free radical routes (evidence is presented below) there are two extreme mechanisms: (*a*) a fully concerted process from (A) to (B) with a transition state as in (C); (*b*) an ion-pair route with intimate or solvent separated ion-pairs. In the latter case the intermediate ion could be represented by either (D) or (E).

(C)   (D)   (E)

(F)   (G)

We consider first the α,β-dibromide rearrangement. Before the concept of intimate ion-pairs had been developed it had been suggested [20] that this rearrangement proceeded through discrete bromonium ions (F)

and bromine anions. Later a merged mechanism was proposed [21] in which the transition state can be represented as in (G). Later workers [2,4] have tended to accept this merged mechanism. Orbital symmetry considerations [22] permit all the rearrangements mentioned in this paper as concerted. The general names dyotropic [22] or diplotropic [23] have been suggested for this class of rearrangement. It is clear, however, that orbital symmetry arguments do not contribute in this case to the elucidation of mechanism. In the α,β-dibromide rearrangement external anions, even azide ions in high concentration,[24] do not capture an intermediate bromonium ion. These experiments possibly support a concerted mechanism.

We decided to apply the stringent test of isotopic labelling for the intramolecularity of some of the rearrangements described in this paper. The bis-*O*-thiobenzoate (3a) was rearranged to the bis-*S*-thiobenzoate (3b) in a melt in admixture with an equal amount of the bis-[$^2H_5$]phenyl analogue (3h). A fully concerted mechanism would furnish equal amounts of non-deuteriated (3b) and its fully deuteriated analogue (3i). A fully ionic intermediate would afford (3b), the pentadeuterio-analogue (3j), and (3i) in the ratio of 1 : 2 : 1. The product showed molecular ions at *m/e* 302, 307, and 312 in the relative abundance 4 : 6 : 5. Clearly the major pathway is intermolecular and *not* concerted. When the rearrangement was carried out in refluxing chlorobenzene the product showed molecular ions at *m/e* 302, 307, and 312 in the ratio of 5 : 9 : 5. In chlorobenzene as solvent the ion-pairs are, therefore, solvent separated and the concerted mechanism definitely does not operate.

In analogous experiments the imidate (8a) and its di-[$^2H_3$]phenyl analogue (8d), prepared from 2,4,6-trideuterioaniline,[25] were pyrolysed in equal amounts in chlorobenzene. The bis-amide thus obtained did not show the molecular ion in its mass spectrum. It was reduced with lithium aluminium hydride to give, instead of the expected tertiary amine, 1,2-dianilinoethane. The latter showed peaks at *m/e* 212, 215, and 218 in the relative abundance of 1 : 2 : 1. Rebenzoylation gave the starting amide. Again, it is clear that the rearrangements are not concerted. It is also clear that the twofold rearrangements of bis-*O*-thiobenzoates and of bis-imidates do not involve $S_N i$ reactions, either simultaneous or consecutive.

We believe that all the rearrangements which we discuss in the present paper are best interpreted as ion-pair processes. The α,β-dibromide rearrangement and related diaxial rearrangements will not be considered further here as they have recently been examined in some detail.[4]

[17] H. H. Bosshard and H. Zollinger, *Helv. Chim. Acta*, 1959, **42**, 1659.
[18] L. Bauer, *J. Amer. Chem. Soc.*, 1956, **78**, 1945.
[19] J. von Braun and J. Weismantel, *Ber.*, 1922, **55**, 3165.
[20] D. H. R. Barton and E. Miller, ref. 1.
[21] C. A. Grob and S. Winstein, *Helv. Chim. Acta*, 1952, **35**, 782.

[22] M. T. Reetz, *Angew. Chem. Internat. Edn.*, 1972, **11**, 129, 130; *Tetrahedron*, 1973, **29**, 2189.
[23] C. W. Jefford, A. Sweeney, and F. Delay, *Helv. Chim. Acta*, 1972, **55**, 2214.
[24] D. H. R. Barton, H. MacGrillen, and P. D. Magnus, unpublished observations.
[25] A. P. Best and C. L. Wilson, *J. Chem. Soc.*, 1946, 239.

The α,δ-rearrangement of (1f) to (1j) and of (1k) to (1l) proves that the two groups change places as in the α,β-rearrangement. The halogenonium ion (13; X = Cl or I) would seem a more likely intermediate than the seven-membered ring ion (14), but the latter would explain better the regiospecificity of the reaction. The rearrangement of the bis-O-thiobenzoates (3a) and (3d)


(13)   (14)

(15)
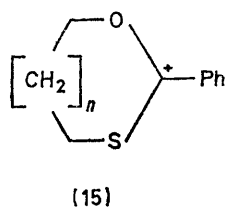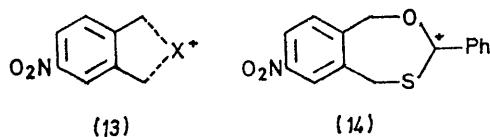
is, at least in the case of (3a), intermolecular. The ion (15; $n = 0$ or 1) must be an intermediate. Attack of the Ph·COS⁻ anion through sulphur at the carbon attached to oxygen affords the products (3b) and (3e). Attack by the Ph·COS⁻ anion through oxygen at the carbon attached to oxygen, or attack through sulphur at the carbon attached to sulphur, affords ($n = 1$) the half-rearranged ester (3f). The alternative mechanism for the formation of ester (3f) would be by an S_Ni rearrangement without migration. Such a mechanism certainly exists.[5] The half-rearranged esters (3c) and (3f) were, as already discussed, not intermediates in the two-fold rearrangements. This point is also emphasised by the relative stability of O-thioesters (4) and (5). The fact that butane-1,4-diyl bis-O-thiobenzoate (3g) is thermally stable is also relevant and shows that if a five- or six-membered cyclic ion cannot be formed the rearrangement does not take place. The ester (3g) would require the seven-membered cyclic ion (15; $n = 2$).

The mechanism of two-fold O-thioester rearrangement discussed above required inversion of configuration at both carbon atoms to which O-thiobenzoate functions are attacked. The pyrolytic behaviour of the esters (6a) and (7a) shows that configuration is either not inverted at either centre or is indeed inverted at both centres.

Similar considerations apply to our work on the pyrolysis of bis-imidates. The intermediate ion can be represented as in (16). For the bis-imidate (8a) attack of benzanilide anion upon the carbon attached to oxygen of ion (16; $n = 1$) through nitrogen would afford the observed bis-amide (9a), and attack through oxygen would give the other observed product (10a). The same argument applies for the pyrolysis of the bis-

imidate (8b). The thermal stability of the monoimidate (12) and of the half-rearranged products (10a and b) again shows that an S_Ni type of rearrangement is not


(16)   (17)
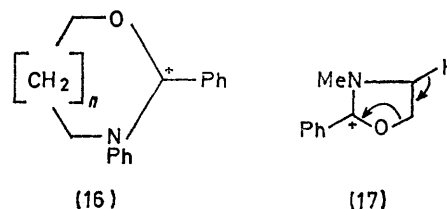
taking place in the double rearrangement of the bis-imidates (8a and b). In the pyrolysis of the bis-imidate (8c) the formation of the bis-amide (9c) proceeds through attack of the N-methylbenzamide anion on the intermediate ion (17). The pyrolysis in chlorobenzene reveals another logical fate for the ion (17). Elimination of a proton (17; see arrows) gives N-methyl-N-vinylbenzamide (11) and N-methylbenzamide.

These bis-imidate rearrangements are of potential value in the synthesis of 1,2- and 1,3-diamino-compounds.

The possibility that the rearrangements described in this paper might proceed by free radical intermediates has already been mentioned, and discounted, above. In order to put the matter beyond question some typical rearrangements were carried out in the presence of free radical traps.

The bis-O-thioester (3a) rearranged smoothly to the bis-S-thiobenzoate (3b) in the presence of small or massive amounts of 2,6-di-t-butyl-4-methylphenol and at the normal rate. If thiobenzoyl and CH₂CH₂O·CS·Ph radicals had been involved then the former would have afforded dibenzoyl disulphide and the latter would have attacked the phenol.

Rearrangement of the bis-O-thioester (3a) in thiophenol as solvent still gave substantial amounts of the bis-S-thiobenzoate (3b), as well as a new compound identified by synthesis as 2-phenylthioethyl S-thiobenzoate (18). This is the expected product from anionic trapping by thiophenoxide ion of the intermediate cation (15; $n = 0$).

Ph·CO·S·CH₂CH₂·SPh

(18)
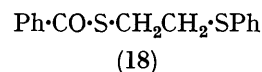
When the bis-imidate (8a) was rearranged in chlorobenzene under reflux to the bis-imide (9a) in the presence of small amounts of 2,6-di-t-butyl-4-methylphenol, the reaction proceeded normally. However, in the presence


(19)
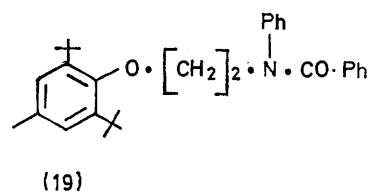
of a massive amount of the phenol the reaction products were phenolic derivative (19) and benzanilide. The

formation of the derivative (19) is readily explained by anionic trapping of the intermediate cation (16; $n = 0$). The rate of disappearance of the bis-imidate (8a) in this experiment was normal. Radical trapping involving the phenol would not have given [26] a reaction on phenolic oxygen.

Ionic reactions involving bridged cations are characterised by a high degree of stereospecificity. Analogous radical reactions usually involve racemisation or loss of stereospecificity. The rearrangements of *meso*- (6a) and ($\pm$)- (7a) 1,2-diphenylethylene bis-*O*-thiobenzoates cited above show a high degree of stereospecificity, as do diaxial–diequatorial rearrangements in general.[2,4] Radical mechanisms are therefore unlikely. We have made one additional study which shows a high degree of stereospecificity in an α,β-bis-*O*-thiobenzoate rearrangement.

(*S*)-(+)-1-Phenylethane-1,2-diol (20a), $[\alpha]_D +57°$ was prepared by the reduction of methyl (*S*)-(+)-mandelate with lithium aluminium hydride. A rotation of $[\alpha]_D$ $-58°$ has been recorded for the optically pure (*R*)-(−)- enantiomer.[27] Treatment of the diol (20a) with thiobenzoyl chloride in pyridine gave the bis-*O*-thiobenzoate

Ph—X | —Y
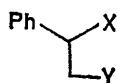
(20)

a; X = (*S*) — OH, Y = OH
b; X = (*S*) — O·CS·Ph, Y = O·CS·Ph
c; X = (*R*) — S·CO·Ph, Y = S·CO·Ph
d; X = (*R*) — SH, Y = OH
e; X = (*R*) — S·CO·Ph, Y = O·CO·Ph
f; X = (*R*) — S·CS·Ph, Y = OH
g; X = (*R*) — S·CS·Ph, Y = 3,5-$(NO_2)_2C_6H_3$·CO·O

Ph—X | CO_2Me
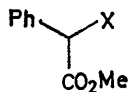
(21)

a; X = (*S*) — OTs
b; X = (*R*) — S·CO·Me

(20b). This rearranged smoothly on heating in chlorobenzene to furnish the (*R*)-(−)-1-phenylethylene bis-*S*-thiobenzoate (20c), $[\alpha]_D$ $-142°$. The critical question is the configuration and optical purity of this bis-*S*-thiobenzoate.

Following model experiments with 2-mercaptoethanol and with (+)-methyl mandelate the following procedure was adopted. (*S*)-(+)-methyl mandelate toluene-*p*-sulphonate (21a) was treated with sodium thioacetate in ethanol–benzene at $-2°$ for 48 h to give, with inversion of configuration, methyl (*R*)-(−)-acetylthio(phenyl)-acetate (21b). Reduction of this diester with lithium hydride afforded (*R*)-(−)-2-mercapto-2-phenylethanol (20d), which was characterised as its crystalline di-

benzoate (20e). The mercaptoethanol was then selectively thiobenzoylated on sulphur using thiobenzoylthioglycollic acid [8] in aqueous ethanolic sodium hydroxide [28] to give the dithiobenzoate (20f), characterised as its crystalline 3,5-dinitrobenzoate (20g). The dithiobenzoate (20f) was converted into its toluene-*p*-sulphonate in the usual way. This was solvolysed in aqueous bis-(2-methoxyethyl) ether and the product benzoylated to give the bis-*S*-thiobenzoate (20c) with a rotation of $-142°$. The only step in this synthesis of configurational importance is the S_N2 displacement, of the toluene-*p*-sulphonate (21a) derived from (*S*)-(+)-methyl mandelate by thioacetate anion. On the normally made assumption that this process is one of 100% inversion, the rearrangement of the bis-*O*-thiobenzoate (20b) to the bis-*S*-thiobenzoate (20c) must also be 100% inversion. Such a clear cut stereochemical result again indicates that radical reactions are not involved.

EXPERIMENTAL

M.p.s were taken with a Kofler hot stage apparatus. Unless otherwise stated i.r. spectra were measured for Nujol mulls. N.m.r. spectra were taken for solutions in deuteriochloroform at 20° with tetramethylsilane as internal standard unless stated otherwise. N.m.r. spectra were in accord with the constitutions assigned and are not listed. Light petroleum refers to the fraction of b.p. 40—60°. All thermal rearrangements were conducted either by heating sealed samples (neat) under an inert atmosphere in a tube or in solution in a kinetic flask under oxygen-free nitrogen or argon. Sodium hydride refers to a 58% dispersion in mineral oil and unless otherwise stated was used as such without removing the oil. Mass measurements were run by the Nier–Johnson technique.

2-*Bromomethyl-4-nitrobenzyl Benzoate* (1a), 2-*Bromo-methyl-5-nitrobenzyl Benzoate* (1b), *and* 4-*Nitro-o-xylene-*α,α'-*diyl Dibenzoate* (1c).—α,α'-Dibromo-4-nitro-*o*-xylene [29] (2 g) in acetone (15 ml) and water (5 ml) was treated in portions with sodium benzoate (700 mg) during 4 h. The homogeneous solution obtained after addition of more acetone was left at room temperature for 48 h. After concentrating the solution under reduced pressure, the product was isolated with ether and partially purified by p.l.c. to give unchanged starting material (770 mg) and the *dibenzoate* (1c) (380 mg), m.p. 153—154° (from acetone-light petroleum and from ethyl acetate), ν_{max} 1710, 1540, and 1280 cm^{-1} (Found: C, 67·45; H, 4·45; N, 3·55. $C_{22}H_{17}NO_5$ requires C, 67·5; H, 4·4; N, 3·6%). The crystalline residual mixture of bromobenzoates (1a and b) was separated by triangular crystallisation and p.l.c. to yield (1a) (412 mg, m.p. 108—112°) and (1b) 289 mg, m.p. 110—117°). Two crystallisations of the *bromo-benzoate* (1a) provided the analytically pure specimen, m.p. 115—116° (cubes from ether–dichloromethane), ν_{max} 1720, 1540, and 1280 cm^{-1} (Found: C, 51·3; H, 3·5; N, 4·05; Br, 22·75. $C_{15}H_{12}BrNO_4$ requires C, 51·4; H, 3·4; N, 4·0; Br, 22·9%). After chromatographic purification the *bromo-benzoate* (1b) was obtained as feathery needles, m.p.

[26] A. R. Forrester, J. M. Hay, and R. H. Thomson, ' Organic Chemistry of Stable Free Radicals,' Academic Press, London, 1968, p. 281 *et seq.*

[27] M. H. Delton and G. U. Yuen, *J. Org. Chem.*, 1968, **33**, 2473.
[28] N. H. Leon and R. S. Asquith, *Tetrahedron*, 1970, **26**, 1719.
[29] M. Kerfanto, *Bull. Soc. chim. France*, 1965, **12**, 3537.

116—117° (from ether–dichloromethane), $v_{max.}$ 1720, 1540, and 1280 cm⁻¹ (Found: C, 51·7, 51·75; H, 3·55, 3·5; N, 3·9, 3·85; Br, 22·3, 22·65. $C_{15}H_{12}BrNO_4$ requires C, 51·4; H, 3·4; N, 4·0; Br, 22·85%), mixed m.p. with (1a) 95—115°.

2-*Methyl-5-nitrobenzyl Alcohol* (1d).—A mixture of sodium borohydride (64 mg), sodium hydroxide (20 mg), bis-(2-methoxyethyl) ether (0·25 ml), water (0·14 ml), and finely-powdered (1b) (50 mg) was stirred at 55—60° (3 h). The dried product, after evaporation of the solvents *in vacuo*, was purified by t.l.c. to yield (1d) (32%, 8·5 mg), m.p. 77—78° (from benzene–light petroleum), undepressed on admixture with an authentic sample,[7] m.p. 77—78°. Identical t.l.c. behaviour and i.r. spectra further confirmed identity.

4-*Nitro-o-xylene-*α,α′-*diol* (1g) *and* 5-*Nitrophthalan* (2).— α,α′-Dibromo-4-nitro-*o*-xylene (6·4 g) in acetone (128 ml) and water (64 ml) was refluxed for 47 h. The solution, after concentrating to *ca.* 1/4 its original volume, was poured onto ice and extracted with ethyl acetate, the extract dried (Na_2SO_4), and evaporated to give the *diol* (1g) (2·19 g, 58%), m.p. 87—89° (from methanol–ether), $v_{max.}$ 3250, 1540, and 1350 cm⁻¹ (Found: C, 52·4; H, 4·95; N, 7·45. $C_8H_9NO_4$ requires C, 52·45; H, 4·95; N, 7·65%). The residue obtained after evaporation of the mother-liquor was chromatographed on alumina (neutral, activity III). The *nitrophthalan* (2) was eluted with dichloromethane and crystallised from benzene as yellow needles, m.p. 92—93° (Found: C, 58·2; H, 4·5; N, 8·55. $C_8H_7NO_3$ requires C, 58·2; H, 4·25; N, 8·5%).

2-*Bromomethyl-4-nitrobenzyl Alcohol* (1h) *and* 2-*Bromo-methyl-5-nitrobenzyl Alcohol* (1i).—Hydrogen bromide was passed intermittently through a vigorously stirred solution of the diol (1g) (4·578 g) in chloroform (180 ml) and methanol (7 ml) at room temperature until the reaction was almost complete (t.l.c. control). The solution was poured into ice, extracted with dichloromethane, and the extract washed with water. Evaporation of the dried (Na_2SO_4) extract gave a mixture of bromo-alcohols which was separated into (1h) (1·920 g) and (1i) (0·015 g) by a combination of column and preparative layer chromatography. Crystallisation of (1h) from benzene–light petroleum afforded long needles of the *benzyl alcohol*, m.p. 88—90°, $v_{max.}$ 3350, 3200, and 1580 cm⁻¹ (Found: C, 39·1; H, 3·3; N, 5·6. $C_8H_8BrNO_3$ requires C, 39·05; H, 3·25; N, 5·7%). Heating a mixture of the above compound (30 mg), benzoic anhydride (25 mg), and toluene-*p*-sulphonic acid monohydrate (10 mg) at 100° for 4 h and the usual work-up yielded a benzoate identical with (1a) (m.p., mixed m.p., i.r., t.l.c.). Crystallisation of (1i) from benzene–light petroleum yielded needles of the *alcohol*, m.p. 76—78°, $v_{max.}$ 3490, 3400, 1540, and 1350 cm⁻¹ (Found: C, 39·25; H, 3·45; N, 5·75. $C_8H_8BrNO_3$ requires C, 39·05; H, 3·25; N, 5·7%). Benzoylation of (1i) as above, yielded (1b) (m.p., mixed m.p., i.r., t.l.c.).

2-*Chloromethyl-4-nitrobenzyl* O-*Thiobenzoate* (1f).—Dry pyridine (0·8 ml) was added with stirring to thiobenzoyl chloride (1·555 g) in dry tetrahydrofuran (5 ml) at 0° and the mixture stirred at 0° for 5 min. The bromo-alcohol (1h) (530 mg) was added in one lot, and the mixture was kept at 0° for 3 min and then at room temperature for 20·5 h. It was then poured into water, extracted with dichloromethane, and the extract washed with water. After evaporation of the dried (Na_2SO_4) extract, the residue in ether was seeded with a crystal of the O-thiobenzoate (from a previous experiment) and refrigerated. The crystals that had

separated overnight were collected. Chromatographic purification of the mother-liquor provided an additional amount of the O-thioester which was combined with the original material. Further purification by p.l.c. followed by crystallisation from dichloromethane–light petroleum gave bright yellow cubes of the *chloro*-O-*thiobenzoate* (312 mg, 44%), m.p. 104—105°. A slightly improved yield (52%) was obtained using benzene as the solvent, $v_{max.}$ 1630 and 1360 cm⁻¹ (Found: C, 56·05; H, 3·9; N, 4·2; Cl, 10·65; S, 9·95. $C_{15}H_{12}ClNO_3S$ requires C, 56·05; H, 3·7; N, 4·35; Cl, 11·05; S, 9·95%), *m/e* 321 (M^+).

2-*Iodomethyl-4-nitrobenzyl* O-*Thiobenzoate* (1k).—Anhydrous sodium iodide (564 mg), the chloro-O-thioester (1f) (96 mg), and dry acetone (6 ml) were stirred at room temperature for 45 min. The mixture after concentration under reduced pressure at room temperature was poured into water and extracted with dichloromethane. Evaporation of the water-washed and dried (Na_2SO_4) extract yielded the *iodo-compound* (1k) (90 mg, 73%), m.p. 117—119° (from dichloromethane–light petroleum), $v_{max.}$ 1630 and 1360 cm⁻¹ (Found: C, 43·4; H, 3·0; I, 30·65; N, 3·15; S, 8·1. $C_{15}H_{12}INO_3S$ requires C, 43·6; H, 2·9; I, 31·0; N, 3·4; S, 7·75%), *m/e* 413 (M^+).

2-*Chloromethyl-5-nitrobenzyl* S-*Thiobenzoate* (1j).—(*a*) The chloroester (1f) (150 mg) was heated in a nitrogen filled sealed tube at 150—163° for 3 h. The mixture, on purification by p.l.c., yielded changed starting material (11 mg) and 2-chloromethyl-5-nitrobenzyl S-thiobenzoate (102 mg), m.p. 60—62° (from benzene–light petroleum), $v_{max.}$ 1670 cm⁻¹, *m/e* 321 (M^+) (analysis, see below).

(*b*) The O-thiobenzoate (1f) (50 mg) in chlorobenzene (5 ml) was refluxed under an atmosphere of nitrogen for 8 h. Work-up in the usual manner yielded unchanged starting material (36 mg).

(*c*) The O-thiobenzoate (1f) (5 mg) in chlorobenzene (4 ml) was refluxed as above for 48 h. T.l.c. examination indicated *ca.* 70% conversion into the S-thiobenzoate.

2-*Hydroxymethyl-5-nitrobenzyl* S-*Thiobenzoate* (1m).—The bromide (1h) (246 mg) in acetone (10 ml) and water (2 ml) was treated with potassium thiobenzoate (228 mg) in water (1 ml). After stirring at room temperature for 51 h the product was isolated in the usual manner to give the S-*thiobenzoate* (1m) (276 mg), m.p. 91—93° (from benzene–light petroleum), $v_{max.}$ 3500 and 1660 cm⁻¹ (Found: C, 59·55; H, 4·4; N, 4·6; S, 10·7. $C_{15}H_{13}NO_4S$ requires C, 59·4; H, 4·3; N, 4·6; S, 10·55%).

The foregoing benzyl alcohol (130 mg) and freshly distilled thionyl chloride (*ca.* 15 drops) in benzene (9 ml) was heated under reflux for 2 h. After removing the excess of thionyl chloride by repeatedly co-distilling it with benzene, the product was isolated by p.l.c. The *chloro*-S-*thioester* (1j) (93 mg), m.p. 61—63° (from benzene–light petroleum), was identical with the compound described above (i.r., ¹H n.m.r., t.l.c., and mixed m.p.) (Found: C, 55·9; H, 3·65; N, 4·15. $C_{15}H_{12}ClNO_3S$ requires C, 56·0; H, 3·7; N, 4·35%).

2-*Iodomethyl-5-nitrobenzyl* S-*Thiobenzoate* (1l).—The iodo-O-thioester (1k) (68 mg) in chlorobenzene (1 ml) was refluxed for 2·5 h. After evaporating the solvent *in vacuo* at room temperature the product was isolated and purified by p.l.c. to give needles of the S-*thioester* (1l) (47 mg), m.p. 100—101° (from dichloromethane–light petroleum), $v_{max.}$ 1660 cm⁻¹ (Found: C, 43·6; H, 3·0; N, 3·9. $C_{15}H_{12}INO_3S$ requires C, 43·6; H, 2·9; N, 4·0%). An authentic sample, m.p. 99—100°, prepared from the chloro-S-thioester (1j)

and sodium iodide in acetone, was identical (mixed m.p., i.r., t.l.c.) with the rearrangement product.

Ethylene Bis-O-thiobenzoate (3a).—(*a*) Thiobenzoyl chloride (1·76 g) in dry pyridine (3 ml) and dry chloroform (4 ml) was treated with ethylene glycol (0·25 ml) at 0°. After 20 h at room temperature, the mixture was poured into ice–water and the product extracted with ether, and the extract was washed with water and dried (Na_2SO_4). Evaporation of the solvent yielded a red oil from which the *diester* (3a) (200 mg) was isolated by p.l.c. as yellow cubes, m.p. 112—113° (from ether–light petroleum), $\nu_{max.}$ 1220 cm^{-1} (Found: C, 63·5; H, 4·8; S, 21·15. $C_{16}H_{14}O_2S_2$ requires C, 63·55; H, 4·65; S, 21·15%).

(*b*) A mixture of sodium hydride (4·663 g), ethylene glycol (0·9 ml), and dry glyme (40 ml) was refluxed and stirred under argon for 15 min. It was then cooled and treated with (thiobenzoylthio)acetic acid [8] (8 g) in glyme (20 ml) during 30 min. After stirring at room temperature for 45 min, the mixture was poured into ice–water and the product extracted with ether. The extract was washed with water and dried (Na_2SO_4), and evaporation of solvent yielded the bis-O-thioester (m.p. 102—114°) which after p.l.c. crystallised as bright yellow cubes (1·002 g), m.p. 112·5° (from dichloromethane–methanol).

Ethylene Bis-S-thiobenzoate (3b).—The foregoing diester (70 mg) was heated at 180° for 10 min (no yellow colour). The product (52 mg), isolated by t.l.c. and purified by crystallisation (dichloromethane–light petroleum), had m.p. 93—94° (45 mg) and was identified as the bis-S-thiobenzoate (3b) by comparison (i.r., ^{1}H n.m.r., t.l.c., and mixed m.p.) with a reference sample [9] prepared by benzoylation of ethane-1,2-dithiol.

(*b*) The bis-O-thioester (520 mg) in chlorobenzene was refluxed for 3·5 h. Aliquot portions were taken at 30 min intervals, evaporated (room temperature, high vacuum), and the residue examined (^{1}H n.m.r.). Signals due to the presence of the mixed ester could at no time be observed. The half-life of the rearrangement was ca. 30 min.

(*c*) The rearrangement was virtually complete (t.l.c.) at 135—141° in 1 h.

(*d*) The diester (3b) (50 mg) in chlorobenzene (1·5 ml) was refluxed for 4 h. T.l.c. examination of the residue obtained after the evaporation of the solvent showed no product other than the starting material.

(*e*) The diester (3a) (240 mg) and 2,6-di-t-butyl-4-methylphenol (2·4 mg) in chlorobenzene (5 ml) were heated under reflux for 6 h. Removal of the solvent *in vacuo* and p.l.c. gave the bis-S-thiobenzoate (3b) (132 mg).

The bis-O-thioester (3a) (50 mg) and 2,6-di-t-butyl-4-methylphenol (50 mg) in chlorobenzene (2·4 ml) were treated exactly as above to give the bis-S-thiobenzoate (3b) (24 mg).

(*f*) The bis-O-thioester (3a) (100 mg) in thiophenol (20 ml) was heated at 132° for 5 h. The thiophenol was removed *in vacuo* and the products isolated by p.l.c. to give the bis-S-thiobenzoate (3b) (38·2 mg) and 2-phenylthioethyl S-thiobenzoate (18) (32·4 mg). An authentic specimen of this latter compound was prepared as follows. Toluene-*p*-sulphonyl chloride (470 mg) and 2-hydroxylethyl S-thiobenzoate [10] (450 mg) in dry pyridine (5 ml) were kept at 0° for 48 h. Isolation of the product in the usual way gave the *toluene-p-sulphonate* (780 mg), m.p. 98—99° (from dichloromethane–light petroleum) (Found: C, 57·35; H, 4·7; S, 18·85. $C_{16}H_{16}O_4S_2$ requires C, 57·15; H, 4·8; S, 19·05%).

This toluene-*p*-sulphonate (120 mg), thiophenol (0·03 ml), anhydrous K_2CO_3, and acetone (5 ml) were heated under reflux for 14 h under argon. Filtration, removal of solvent *in vacuo*, and p.l.c. gave 2-*phenylthioethyl* S-*thiobenzoate* (18) as an oil, $\nu_{max.}$ (CHCl$_3$) 1660 cm^{-1}, identical with the material described above (Found: C, 65·75; H, 5·15; S, 23·0. $C_{15}H_{14}OS_2$ requires C, 65·7; H, 5·15; S, 23·35%).

2-*Benzoylthioethyl* O-*Thiobenzoate* (3c).—A mixture of potassium thiobenzoate (1·77 g), ethylene chlorohydrin (0·7 ml), acetone (2·5 ml), and water (2·5 ml) was stirred at room temperature. More water and acetone were added to dissolve the solid that had separated and stirring was continued for 40 h. The solution was concentrated, the residue mixed with water, and the product isolated in the usual manner. Chromatographic purification (silica) yielded the alcohol (542 mg) as a viscous oil, $\nu_{max.}$ (neat) 1660 and 3500 cm^{-1}. 2-*Benzoylthioethyl* O-*thiobenzoate* (3c) (12%), prepared by treating the foregoing alcohol with thiobenzoyl chloride in benzene–pyridine, crystallised as bright yellow needles, m.p. 58—59·5° (from methanol), $\nu_{max.}$ 1670 cm^{-1} (Found: C, 63·35; H, 4·6. $C_{16}H_{14}O_2S_2$ requires C, 63·55; H, 4·65%). The mixed ester was stable (t.l.c.) at 147° (1 h). Continued heating at 195—200 (13 h) resulted in conversion into (3b) (t.l.c.).

Propane-1,3-diyl Bis-O-thiobenzoate (3d).—Sodium hydride (2·197 g; washed free of the mineral oil with light petroleum), propane-1,3-diol (0·98 ml), and glyme (50 ml) were stirred and heated at reflux for 2·5 h. The cooled mixture was treated with (thiobenzoylthio)acetic acid (6·1 g) in glyme (20 ml) during 30 min. After stirring overnight at room temperature, the product was isolated in the usual manner. Two crystallisations yielded the *diester* (3d) (1·652 g), m.p. 59—60° (from light petroleum), $\nu_{max.}$ 1220 cm^{-1} (Found: C, 64·35; H, 5·0; S, 19·95. $C_{17}H_{16}O_2S_2$ requires C, 64·55; H, 5·1; S, 20·2%).

Propane-1,3-diyl Bis-S-*thiobenzoate* (3e).—The O-thioester (3d) (662 mg) was heated at 175—180° for 6 h. T.l.c. revealed the pyrolysate to be a mixture of three compounds, two of which were yellow. P.l.c. yielded the starting material (39 mg), the title compound (471 mg) (m.p. 55—56°), identical with an authentic specimen [9] (mixed m.p., t.l.c., ^{1}H n.m.r., and i.r.), and the mixed ester (3f) (47 mg), the structure of which was confirmed by comparison (t.l.c., i.r., ^{1}H n.m.r.) with a reference sample synthesised as described below.

A mixture of 3-chloropropanol (1·4 ml), potassium thiobenzoate (3·45 g), sodium iodide (5—10 mg), water (10 ml), and acetone (10 ml) was stirred at room temperature for 50 h. The usual work-up followed by chromatographic purification of the alcohol (silica; 8% ethyl acetate–dichloromethane) yielded an oil (2·08 g). The crude alcohol (600 mg) in dichloromethane (10 ml) and dry pyridine (4 ml) was treated with thiobenzoyl chloride (0·92 ml) at 0° and the mixture kept at room temperature for 36 h. The usual work-up followed by p.l.c. of the products yielded 3-*benzoylthiopropyl* O-*thiobenzoate* (3f) (680 mg) as a bright yellow oil, $\nu_{max.}$ (neat) 1660 cm^{-1} (Found: C, 64·4; H, 5·0; S, 20·0. $C_{17}H_{16}O_2S_2$ requires C, 64·55; H, 5·1; S, 20·2%).

A chromatographically homogeneous sample of (3f) was heated at 180—188° for 6 h. T.l.c. examination of the pyrolysate revealed that it was mainly the unchanged starting material with traces of four other contaminants.

Butane-1,4-diyl Bis-O-*thiobenzoate* (3g).—The bis-O-thioester was prepared in the usual manner from the dianion

of butane-1,4-diol (0·9 ml) and (thiobenzoylthio)acetic acid (4·8 g) in glyme. Chromatography on silica followed by crystallisation (light petroleum–benzene or dichloromethane–methanol), yielded the bis-O-thiobenzoate 3g) (700 mg), m.p. 100—101°, $v_{max.}$ 1240 cm^{-1} (Found: C, 65·55; H, 5·6; S, 19·35. $C_{18}H_{18}O_2S_2$ requires C, 65·45; H, 5·5; S, 19·44%). The foregoing ester (192 mg) was heated at 187° for 7 h. T.l.c. examination of the pyrolysate showed virtually no change in the starting material.

2-Phenoxyethyl O-Thiobenzoate (5).—Ethyl phenoxyacetate [30] was reduced with an excess of lithium aluminium hydride to give 2-phenoxyethanol.[31] This alcohol (1·0 g) was O-thiobenzoylated with thiobenzoylthioglycolic acid (1·5 g) in glyme (40 ml). Chromatographic purification of the O-thioester on silica yielded the O-thiobenzoate (5) (120 mg), m.p. 100° (from methanol), $v_{max.}$ 1220 cm^{-1} (Found: C, 69·75; H, 5·65; S, 12·35. $C_{15}H_{14}O_2S$ requires C, 69·75; H, 5·45; S, 12·4%). This O-thioester was heated at 240—245° for 26·5 h. T.l.c. examination of the pyrolysate showed a number of products with unchanged starting material predominating.

meso-1,2-Diphenylethylene Bis-S-thiobenzoate (6b).—(a) A suspension of the diester [32] (6a) (40 mg) in chlorobenzene (4 ml) was refluxed for 10 h. The needles which had separated overnight were collected, washed with light petroleum, and dried to give chromatographically homogeneous meso-bis-S-thiobenzoate (6b) (27 mg), m.p. 270° (Found: C, 73·9; H, 4·85; S, 13·8. Calc. for $C_{28}H_{22}O_2S_2$: C, 74·0; H, 4·9; S, 14·1%). The n.m.r., i.r., and t.l.c. behaviour were identical with those of an authentic sample prepared from meso-1,2-diphenylethane-1,2-dithiol,[11] benzoyl chloride, and pyridine (100°; 1 h).

(b) The diester (6a) (100 mg) was pyrolysed at 206—220° (40 min). The solid was washed with ether and dried to give pure (t.l.c.) bis-S-thioester (6b) (55 mg).

(±)-1,2-Diphenylethylene Bis-O-thiobenzoate (7a).—(±)-Hydrobenzoin (300 mg), pyridine (3 ml), and chloroform (3 ml) were treated with thiobenzoyl chloride (0·8 ml) in chloroform (4 ml). After standing at room temperature for 36 h, the mixture was worked up in the usual manner to give a brown-red oil which was extracted with hot light petroleum. Chromatography of the extract on alumina (activity III) and elution with benzene–light petroleum (1 : 4) yielded a red-yellow solid (160 mg). Further purification by p.l.c. (silica) gave the bis-O-thioester (7a) (60 mg), m.p. 168—170° (from acetone–light petroleum) (Found: C, 74·05; H, 4·95. $C_{28}H_{22}O_2S_2$ requires C, 74·0; H, 4·9%).

(±)-1,2-Diphenylethylene Bis-S-thiobenzoate (7b).—The bis-O-thioester (7a) (40 mg) was pyrolysed at 195° for 1 h. The title compound (7b) (12·5 mg), isolated from the pyrolysate by p.l.c., and purified by several crystallisations, had m.p. 183—185°, $v_{max.}$ 1650 cm^{-1}. An authentic sample of the bis-S-thioester [11] had m.p. 187—188° (from benzene–light petroleum), mixed m.p. undepressed. The i.r. spectra and t.l.c. behaviour of the two samples were identical (Found: C, 73·9; H, 5·1. Calc. for $C_{28}H_{22}O_2S_2$: C, 74·0; H, 4·9%).

n-Propyl O-Thiobenzoate (4).—Sodium n-propoxide [prepared from propan-1-ol (0·41 ml) and sodium hydride (230 mg; freed from mineral oil)] in glyme (5 ml) was treated dropwise with (thiobenzoylthio)acetic acid (1·06 g) in glyme (10 ml). The mixture after stirring overnight at

room temperature, was poured onto ice and the propyl ester extracted with water and dried (Na$_2$SO$_4$). Evaporation of the solvent yielded a red oil which was distilled in vacuo to give the O-thiobenzoate (4) as a bright yellow liquid (460 mg, 51%), $v_{max.}$ (neat) 1240 cm^{-1} (Found: C, 66·4; H, 6·65; S, 17·7. $C_{10}H_{12}OS$ requires C, 66·65; H, 6·7; S, 17·75%). This O-thiobenzoate was stable (t.l.c. and i.r.) at 170—180° (1 h) and at 180—182° (6·5 h).

n-Propyl N-Phenylbenzimidate (12).—Sodium n-propoxide [prepared from sodium hydride (320 mg) and propan-1-ol (0·4 ml) in glyme (7 ml)] was treated with N-phenylbenzimidoyl chloride [12] (1 g) in glyme (10 ml). After stirring overnight, the mixture was poured into ice–water and the product extracted with ether (2 × 50 ml), and the extract was washed with water and dried (Na$_2$SO$_4$). The yellow oil obtained on evaporation of the solvent was chromatographed on silica and eluted with benzene to give the imidate (12) (481 mg), as an oil, $v_{max.}$ 1660 and 1120 cm^{-1}, m/e 239·1299 (M^+) ($C_{16}H_{17}NO$ requires 239·1310) (Found: C, 80·25; H, 7·15; N, 5·65. $C_{16}H_{17}ON$ requires C, 80·3; H, 7·15; N, 5·85%). This imidate was virtually unaffected (i.r. and t.l.c.) when heated either at 169° (4 h), or at 188° (47 h).

Ethylene Bis-N-phenylbenzimidate (8a).—N-Phenylbenzimidoyl chloride (2·905 g) in glyme (20 ml) was added dropwise with stirring at room temperature to the dianion of ethylene glycol [prepared from sodium hydride (660 mg) and ethylene glycol (0·38 ml)] under argon. After stirring at room temperature for 15 min, the mixture was heated to reflux for 1 h and then stirred at room temperature overnight. The product, isolated in the usual manner, crystallised from ether–light petroleum to give needles of the bis-imidate (1·415 g), m.p. 89—92°. The analytically pure specimen had m.p. 96—98°, $v_{max.}$ 1660 and 1120 cm^{-1} (Found: C, 79·75; H, 5·8; N, 6·55. $C_{28}H_{24}N_2O_2$ requires C, 78·0; H, 5·75; N, 6·65%).

Pyrolysis of (8a).—(a) The above imidate (8a) (12 mg) was pyrolysed at 140° (2 h). The product, a mixture of four compounds (t.l.c.), was separated by preparative t.l.c. (alumina) to give NN'-dibenzoyl-NN'-diphenylethylene-diamine [13] (7 mg) as the major product, m.p. 190—192° (from dichloromethane–light petroleum).

(b) The imidate (8a) (520 mg) in chlorobenzene (6 ml) was refluxed under argon at 132° for 9 h. After evaporation of the solvent in vacuo at room temperature, the residue was purified by p.l.c. to give (i) recovered starting material (49 mg) (t.l.c. and m.p.), (ii) benzanilide (14 mg) (m.p., t.l.c., i.r.), (iii) the half rearranged product (10a) (126 mg), $v_{max.}$ 1660, 1640, and 1120 cm^{-1}, and (iv) the bis-amide (9a) (246 mg), m.p. 189—193°, identical (^{1}H n.m.r., mixed m.p., t.l.c.) with an authentic sample [13] of NN'-dibenzoyl-NN'-diphenylethylenediamine. The foregoing half rearranged oily product (60 mg) was heated under reflux in chlorobenzene (4 ml) for 5·5 h. T.l.c. examination of the residue after evaporation of the solvent showed the absence of the bis-amide.

(c) The imidate (8a) (400 mg) in chlorobenzene (5 ml) was refluxed for 22·5 h. The residue obtained on evaporating the solvent under reduced pressure at room temperature was triturated with ether and filtered to give the bis-amide (9a) (260 mg). The filtrate was taken to dryness, the residue dissolved in tetrahydrofuran (5 ml) containing dilute sulphuric acid (6N; 1 ml), and the solution left at

[30] R. Fusco and F. Mazzucchi, Gazzetta, 1941, 71, 406.
[31] A. Halasz, Bull. Soc. chim. France, 1941. 8, 170.

[32] D. H. R. Barton, M. Bolton, P. D. Magnus, K. G. Marathe, G. A. Poulton, and P. J. West, J.C.S. Perkin I, 1973, 1574.

room temperature for 2 days. After evaporating the bulk of the solvent under reduced pressure, the residue was mixed with water, extracted with dichloromethane, and the extract was washed with water and dried (Na_2SO_4). P.l.c. of the residue, obtained after removal of the solvent, yielded ON-dibenzoyl-N-phenyl-2-aminoethanol [14] (75 mg) as needles, m.p. (from ether–light petroleum) 93—94°, identical with an authentic specimen (i.r., m.p., mixed m.p., t.l.c., and ^{1}H n.m.r.).

(d) The bis-amide (9a) (92 mg) in chlorobenzene (5 ml) was refluxed for 8 h. Crystallisation of the residue obtained on evaporation of the solvent yielded the unchanged starting material (83 mg) (i.r., t.l.c., and m.p.). T.l.c. examination of the mother-liquor showed no half re-arranged product (10a).

(e) The bis-imidate (8a) (41 mg) and 2,6-di-t-butyl-4-methylphenol (2 mg) in chlorobenzene (3 ml) were heated under reflux for 18 h. Removal of the solvent in vacuo and p.l.c. gave, after crystallisation from dichloromethane–light petroleum, the bis-amide (9a) (18·5 mg).

In a second experiment the bis-imidate (8a) (500 mg) and 2,6-di-t-butyl-4-methylphenol (500 mg) in chlorobenzene (5 ml) were heated under reflux for 22 h. The residue obtained on removal of the solvent in vacuo was triturated with ether and the benzanilide remaining (110 mg) was filtered off. The filtrate was purified by p.l.c. to give N-[2-(2,6-di-t-butyl-4-methylphenoxy)ethyl]-N-phenylbenz-anilide (19) (300 mg), m.p. 110—112°, $\nu_{max.}$ 1650 cm^{-1} (Found: C, 81·1; H, 8·15; N, 3·15. $C_{27}H_{37}NO_2$ requires C, 81·2; H, 8·4; N, 3·15%). Also isolated were benzanilide (62 mg) and recovered phenol (152 mg).

The rate of disappearance of bis-imidate (8a) was the same irrespective of the amount of 2,6-di-t-butyl-4-methyl-phenol added.

Ethylene Bis-N-methylbenzimidate (8c).—N-Methylbenz-imidoyl chloride [17] (12·1 g) in glyme (20 ml) was added with stirring to the dianion of ethylene glycol [prepared from sodium hydride (4 g) and ethylene glycol (1·9 ml)] and the mixture was stirred overnight at room temperature. The usual work-up, followed by two crystallisations of the product, yielded needles of the *bis-imidate* (8c) (3·5 g), m.p. (from benzene–light petroleum) 84—85° (an additional 3·5 g of slightly less pure product was obtained from the mother-liquor), $\nu_{max.}$ 1665 and 1120 cm^{-1} (Found: C, 72·9; H, 6·75; N, 9·25. $C_{18}H_{20}N_2O_2$ requires C, 72·95; H, 6·8; N, 9·45%).

Pyrolysis of the Bis-imidate (8c).—(a) The imidate (8c) (500 mg) was heated at 145—150° for 3 h. Direct crystal-lisation of the pyrolysate from ether yielded NN'-di-benzoyl-NN'-dimethylethylenediamine (9c) (240 mg), m.p. 175—179°. Recrystallised from acetone–dichloromethane, this had m.p. 177—180°, and was identical (i.r., ^{1}H n.m.r., t.l.c., and mixed m.p.) with an authentic sample.[18] P.l.c. of the residue obtained from the mother-liquor (silica, solvent ethyl acetate–dichloromethane 2 : 5) yielded N-methyl-N-vinylbenzamide (11) as an oil (108 mg), $\nu_{max.}$ (neat) 1660 and 1620 cm^{-1}, m/e 161·0838 ($C_{10}H_{11}NO$ requires M, 161·0841). The compound (11) in ethyl acetate (10 ml) was hydrogenated at atmospheric pressure in the presence of platinum oxide (7 mg) for 2 h to give N-ethyl-N-methyl-benzamide. An authentic specimen was prepared by the methylation of N-ethylbenzamide with sodium hydride and methyl iodide in glyme.

(b) The imidate (8c) (500 mg) was refluxed in chloro-benzene (12 ml) for 15·5 h. The products were isolated as

above to give (i) the amide (11) (192 mg), (ii) the bis-amide (9c) (84 mg), and (iii) N-methylbenzamide (151 mg).

(c) N-Methyl-N-vinylbenzamide (56·9 mg) and N-methyl-benzamide (49 mg) were heated at 145—152° for 3 h 55 min. T.l.c. examination of the pyrolysate indicated the presence only of the starting materials.

(d) The bis-amide (9c) (83·5 mg) was pyrolysed at 148—155° for 16 h. T.l.c. confirmed the absence of the amide (11) and of N-methylbenzamide.

Propane-1,3-diyl Bis-N-phenylbenzimidate (8b).—N-Phenylbenzimidoyl chloride (8·37 g) in glyme (50 ml) was added with stirring to a suspension of the dianion prepared from sodium hydride (2·1 g), propane-1,3-diol (1·1 ml), and glyme (50 ml) under nitrogen. The mixture was heated to reflux for 2 h and then stirred at room temperature over-night. The product, isolated in the usual manner, was dissolved in ether and filtered to remove a small amount of benzanilide. The residue from evaporation of the filtrate was chromatographed on alumina (neutral, activity III). Elution with benzene (t.l.c. control) yielded pale yellow cubes of the *bis-imidate* (8b) (3·83 g), m.p. (from light petroleum) 88—89°, $\nu_{max.}$ 1660 and 1120 cm^{-1} (Found: C, 80·05; H, 5·95; N, 6·35. $C_{29}H_{26}N_2O_2$ requires C, 80·15; H, 6·05; N, 6·45%).

Pyrolysis of the Bis-imidate (8b).—The imidate (707 mg) in anisole (12 ml) was refluxed for 83·25 h. The residue obtained on evaporation of the solvent, in a minimum amount of ether, was left overnight at room temperature. The crystals of the bis-amide (9b) (48 mg) that had separ-ated were collected. The filtrate was evaporated and the residue purified by p.l.c. to give (i) starting material (336 mg), (ii) benzanilide, (iii) the half rearranged oily product (10b) (123 mg), which could not be isolated pure, $\nu_{max.}$ (neat) 1725, 1650, 1280, and 1120 cm^{-1}, and (iv) the bis-amide (9b). Two crystallisations of the combined amide fractions yielded NN'-diphenyl-NN'-dibenzoylpropane-1,3-diamine (9b), m.p. (from ether–light petroleum) 136—138°, identical with an authentic sample [15] (i.r., t.l.c., m.p., mixed m.p., ^{1}H n.m.r.).

The oily half rearranged imidate (10b) in tetrahydrofuran containing sulphuric acid (4N; 10 drops) was left at room temperature for 48 h. The product, isolated in the usual manner, was purified by p.l.c. and crystallised to give needles of ON-dibenzoyl-N-phenyl-3-aminopropan-1-ol,[16] m.p. (from ether–light petroleum) 83—84°, identical with an authentic specimen (i.r., m.p., mixed m.p., t.l.c., ^{1}H n.m.r.).

[2',4',6'-^{2}H$_3$]Benzanilide.— 2,4,6-Trideuterioaniline [25] (1·315 g) in benzene (10 ml) was treated with benzoic anhydride (3·206 g) in one lot and the mixture was left at room temperature overnight. The crystals were collected, washed successively with benzene–light petroleum mixture and light petroleum, and dried to give the title compound (2·533 g, 92%), m.p. 165—167°.

N-([2,4,6-^{2}H$_3$]phenyl)benzimidoyl Chloride.—The foregoing anilide (1 g) and freshly distilled thionyl chloride (1·1 ml) were refluxed for 2·25 h. The solution was evaporated under reduced pressure, the residue dissolved in dry light petroleum (60—80°), and the solution again taken to dryness. The low melting solid thus obtained was used directly in the next reaction.

Ethylene Bis-N-([2,4,6-^{2}H$_3$]phenyl)benzimidate.—The di-anion of ethylene glycol, prepared from ethylene glycol (0·275 ml) in glyme (2 ml) and sodium hydride (580 mg), was treated with the above imidoyl chloride and the

mixture stirred at room temperature overnight. The product isolated in the usual manner was crystallised twice (300 mg) from ether–light petroleum, m.p. 97—99°.

Pyrolysis of a Mixture of the Deuterio- and the Non-deuteriated Imidates.—The foregoing bis-imidate (25 mg) and the non-deuterio-analogue (35 mg) in chlorobenzene (5 ml) was refluxed for 17·25 h. The amide (49 mg) isolated by p.l.c. (silica) was crystallised from ether–light petroleum, m.p. 193—195°. As the molecular ions could not be detected in the mass spectrum of the sample, it (40 mg) was reduced with excess of lithium aluminium hydride in tetrahydrofuran (10 ml) (reflux 1 h; overnight stirring at room temperature) to give a mixture of products. The 1,2-dianilinoethane (6 mg), isolated by p.l.c., exhibited molecular ions at m/e 212, 215, and 218 (relative abundance 1 : 2 : 1). Rebenzoylation of this diamine (benzoyl chloride–pyridine) afforded an amide, m.p. 193—194° (from ether–dichloromethane–light petroleum) identical with the starting amide (m.p., i.r., mixed m.p.).

([²H₅]Thiobenzoylthio)acetic Acid.—To a Grignard solution prepared from magnesium (0·82 g) and pentadeuterio-bromobenzene (CIBA) (5·08 g) in ether under nitrogen was added carbon disulphide (4 ml) in ether (5 ml) at −5°. After the addition was complete, the mixture was stirred at 0—5° for 2 h and then allowed to warm to room temperature overnight. The complex was decomposed with ice and the mixture filtered through Celite, the filtrate washed twice with ether, and the aqueous solution treated with chloroacetic acid (3·2 g) in aqueous sodium carbonate (1·98 g in 12·5 ml water). The red solution was kept at 0° for 46 h and then at room temperature for 12 h. The (thiobenzoylthio)acetic acid was isolated in the usual manner and crystallised (1·22 g), m.p. 125—127° (from benzene).

Ethylene Bis-O-thio[²H₅]benzoate.—To the dianion of ethylene glycol, prepared from sodium hydride (1·2 g), ethylene glycol (0·225 ml), and glyme (10 ml), was added under nitrogen with stirring, the foregoing (thiobenzoylthio)acetic acid (2·02 g) in glyme (15 ml), and the mixture was refluxed for 1 h. The bis-O-thioester, isolated in the usual manner and purified by p.l.c., had m.p. 110—112° (from dichloromethane–light petroleum), m/e 312 (M^+).

Pyrolysis of a Mixture of Deuterio- and Non-deuterio-ethylene Bis-O-thiobenzoates.—(a) The foregoing O-thio-benzoate (20 mg) and the non-deuterio-analogue (20 mg) were heated at 186° for 50 min. The pyrolysate was purified by p.l.c. (silica) and the bis-S-thioesters (29·5 mg) were crystallised from dichloromethane–light petroleum. The mass spectrum of the sample showed molecular ions at m/e 302, 307, and 312 (relative abundance 4 : 6 : 5).

(b) Equal amounts of the deuterio- and non-deuterio-bis-O-thioesters in chlorobenzene (4 ml) were heated under reflux for 4 h. The bis-S-thioester was isolated by p.l.c. and purified by crystallisation (from dichloromethane–light petroleum). The presence of molecular ions at m/e 302, 307, and 312 (relative abundance 5 : 9 : 5) in the mass spectrum confirmed that an almost complete crossover has occurred.

(S)-(+)-Phenylethylene Bis-O-thiobenzoate (20b).—*(S)-*(+)-1-Phenylethane-1,2-diol (20a) (350 mg), $[\alpha]_D^{20}$ +56·9° (c, 3·2 in ether) in dry dichloromethane (3 ml) and pyridine (3 ml) was treated with thiobenzoyl chloride (1·3 g) in dichloromethane (3 ml) at 0°. The mixture was kept at 0° (48 h) and the product worked up in the usual manner. The *bis-O-thiobenzoate* (20b) (712 mg) was purified by

chromatography, m.p. (yellow needles from methanol–ether) 61—62°, $[\alpha]_D^{23}$ −174° (c, 1·57 in CHCl₃) (Found: C, 69·75; H, 5·0; S, 16·65. $C_{22}H_{18}O_2S_2$ requires C, 69·85; H, 4·8; S, 16·9%).

(R)-(−)-Phenylethylene Bis-S-thiobenzoate (20c).—The bis-O-thioester (20b) (200 mg) in chlorobenzene (2 ml) was heated under reflux (155 min). Removal of the solvent *in vacuo* gave (from dichloromethane–light petroleum) the title compound (170 mg). Further purification (p.l.c.) gave the *bis-S-thiodibenzoate* (20c) as needles, m.p. 112°, $[\alpha]_D^{20}$ −142° (c, 0·35 in CHCl₃), $\nu_{max.}$ 1660 cm⁻¹ (Found: C, 70·05; H, 4·55; S, 17·1. $C_{22}H_{18}O_2S_2$ requires C, 69·85; H, 4·8; S, 16·9%).

Methyl (R)-(−)-Acetylthio(phenyl)acetate (21b).—Sodium thioacetate (0·45 ml) in ethanol (2 ml) was added to sodium ethoxide (3·6 ml) [from sodium (0·5 g) and ethanol (25 ml)]. The mixture was added slowly to methyl (S)-(+)-mandelate toluene-p-sulphonate (21a) (1 g) in ethanol (2 ml) and benzene (3 ml) at 0°. After stirring at −2° (48 h), the mixture was poured into ice and extracted with ether. The extract was washed with water then with cold dilute sodium hydrogen carbonate, again with water, and dried (Na_2SO_4). Evaporation of the solvent and purification of the residue (680 mg) by p.l.c. yielded the *acetylthio-derivative* (21b) (616 mg) as an oil, $\nu_{max.}$ 1740 and 1690 cm⁻¹, $[\alpha]_D^{21}$ −236·5° (c, 3·37 in CHCl₃) (Found: C, 58·6; H, 5·4; S, 14·0. $C_{11}H_{12}O_3S$ requires C, 58·95; H, 5·4; S, 14·25%).

(R)-(−)-2-Mercapto-2-phenylethanol (20d).—The foregoing ester (21b) (583 mg) in ether (5 ml) was added dropwise with stirring to lithium aluminium hydride (580 mg) in ether (10 ml) at 0°. The mixture was stirred at 5—10° (2 h) and then at room temperature (2·5 h). The usual work-up (cold dilute sulphuric acid) yielded the mercapto-ethanol (20d) (410 mg) (i.r., no carbonyl group). The *OS-dibenzoyl derivative* (20e), obtained in the usual manner (benzoyl chloride–pyridine at room temperature overnight), was purified by p.l.c., as needles, m.p. (from n-hexane) 85—87°, $[\alpha]_D^{21}$ −125° (c, 0·2 in CHCl₃), $\nu_{max.}$ 1710, 1660, and 1280 cm⁻¹ (Found: C, 72·75; H, 4·95; S, 9·0. $C_{22}H_{18}SO_3$ requires C, 72·9; H, 5·0; S, 8·85%).

(R)-(−)-2-Hydroxy-1-phenylethyl Dithiobenzoate (20f).—The mercaptoethanol (20d) (390 mg) in ethanol (5 ml) was added to (thiobenzoylthio)acetic acid (550 mg) in dilute sodium hydroxide solution [28] (0·1N; 27 ml) during 5 min with stirring. The mixture, after having been stirred at room temperature (3·5 h), was refrigerated overnight. The dithiobenzoate was extracted into dichloromethane, washed with water, and dried (Na_2SO_4). Evaporation of the solvent, followed by purification of the residue by p.l.c. yielded the starting material (242·8 mg) and the oily dithiobenzoate (20f) (38 mg). The derived 3,5-*dinitro-benzoate* (20 g), prepared in the usual manner (pyridine–3,5-dinitrobenzoyl chloride, 48 h at 0°) had m.p. (from ethyl acetate–n-hexane–ether) 128—130°, $\nu_{max.}$ 1720 cm⁻¹, $[\alpha]_D^{23}$ −362·4° (c, 0·42 in CHCl₃) (Found: C, 56·35; H, 3·35; N, 5·85; S, 13·6. $C_{22}H_{16}N_2O_6S_2$ requires C, 56·4; H, 3·4; N, 5·9; S, 13·65%).

(R)-(−)-Phenylethylene Bis-S-thiobenzoate.—The foregoing hydroxy-dithiobenzoate (20f) (12 mg) in pyridine (1 ml) was treated with toluene-p-sulphonyl chloride (10 mg) at 0° and the mixture refrigerated (−2°) for 36 h. It was then poured into ice and the toluene-p-sulphonate extracted quickly with a large volume of ether, washed with ice-cold dilute hydrochloric acid (1N), then with water, and dried (Na_2SO_4). Evaporation of the solvent yielded a pink oil

which was solvolysed at 100° in water and diglyme (1·5 ml each) for 3·5 h. The solvent was removed under high vacuum and the residue benzoylated (benzoyl chloride–pyridine at 100° for 45 min). The bis-S-thiobenzoate was isolated in the usual manner, and purified by p.l.c. (4·8 mg) followed by crystallisation (dichloromethane–light petroleum), m.p. 110—112·5°, undepressed on admixture with the product of thermal rearrangement (20b) (see above), mixed m.p. 110—112·5°, $[\alpha]_D^{19}$ —142·3° (c, 0·253 in CHCl$_3$). The two samples had identical i.r. spectra.