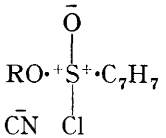
397. *Walden Inversion Reactions of the* p-*Toluenesulphinic and the* p-*Toluenesulphonic Esters of Ethyl* d-*β-Hydroxy-β-phenylpropionate.*

By Joseph Kenyon, Henry Phillips, and Gerald R. Shutt.

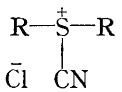
In 1929, Houssa, Kenyon, and Phillips (J., 1700) put forward two chemical methods by which the relative configurations of a secondary alcohol and the corresponding halides could be determined. The relative configurations of β-octanol and its halides were thus determined, but subsequent investigations with phenylmethylcarbinol (Houssa and Phillips, J., 1932, 1332; Kenyon, Phillips, and Taylor, J., 1933, 173) failed, owing to experimental difficulties, to provide equally conclusive evidence concerning the relative configurations of this semi-aromatic alcohol and its (+) halides. Since McKenzie and Humphries (J., 1910, **97**, 121) and McKenzie and Barrow (J., 1911, **99**, 1910) have shown that the stereochemical changes which occur during the formation of the halides from alcohols containing a phenyl group linked to the asymmetric carbon atom may differ from those occurring during the formation of purely aliphatic halides, further experiments have been made, and more complete evidence concerning the relative configurations of ethyl (+) β-hydroxy-β-phenylpropionate and the corresponding (—) halides has now been obtained.

(a) *Replacement of the* p-*Toluenesulphinoxy-group of Ethyl* (+) β-p-*Toluenesulphinoxy-β-phenylpropionate.*—This ester, prepared by the direct interaction of the (+) hydroxy-ester with *p*-toluenesulphinyl chloride in the presence of pyridine, reacted with chlorine and with hypochlorous acid to yield respectively the (—) chloro-ester and the (—) hydroxy-ester. Since from its method of preparation the parent (+) sulphinic ester has the same configuration as the (+) hydroxy-ester, on the assumption previously made (*loc. cit.*), the (—) hydroxy-ester and the (—) chloro-ester arose with inversion and have like configurations. As is usual, more racemisation occurred and smaller yields were obtained than is the case when the sulphinic ester of an aliphatic alcohol, *e.g.*, (+) β-octyl *p*-toluenesulphinate (*loc. cit.*), undergoes similar reactions. The (—) hydroxy-ester was obtained also by the action of nitrous acid on the (+) sulphinoxy-ester, and the (—) bromo-ester was produced from this ester by the action of bromine in either chloroform or aqueous solution. With iodine monochloride, the (+) sulphinoxy-ester gave the (—) chloro-ester and *p*-toluenesulphonyl iodide, but with cyanogen chloride it gave the (—) cyano-ester and *p*-toluenesulphonyl chloride. The last reaction is an example of the tendency of the cyanogen radical to assume the anionic state at the expense of a more negative halogen partner, other examples being the formation of diphenylchloro(bromo)bismuthine and benzonitrile by the action of cyanogen chloride (bromide) on triphenylbismuthine (Wilkinson and Challenger, J., 1924, 854). This variation in the behaviour of the cyanogen radical when linked to halogens can be seen by contrasting the preliminary stages of the interaction of a sulphinic ester (I) and a sulphide (II) with cyanogen chloride, the products of the latter reaction being a thiocyanate and a chloride.

(I.)



$$\begin{array}{lll} & \bar{\mathrm{O}} & \\ & | & \\ \mathrm{RO}\cdot{}^{+} & \mathrm{S}^{+} & \cdot\mathrm{C_7H_7} \\ & | & \\ \bar{\mathrm{C}}\mathrm{N} & \mathrm{Cl} & \end{array}$$

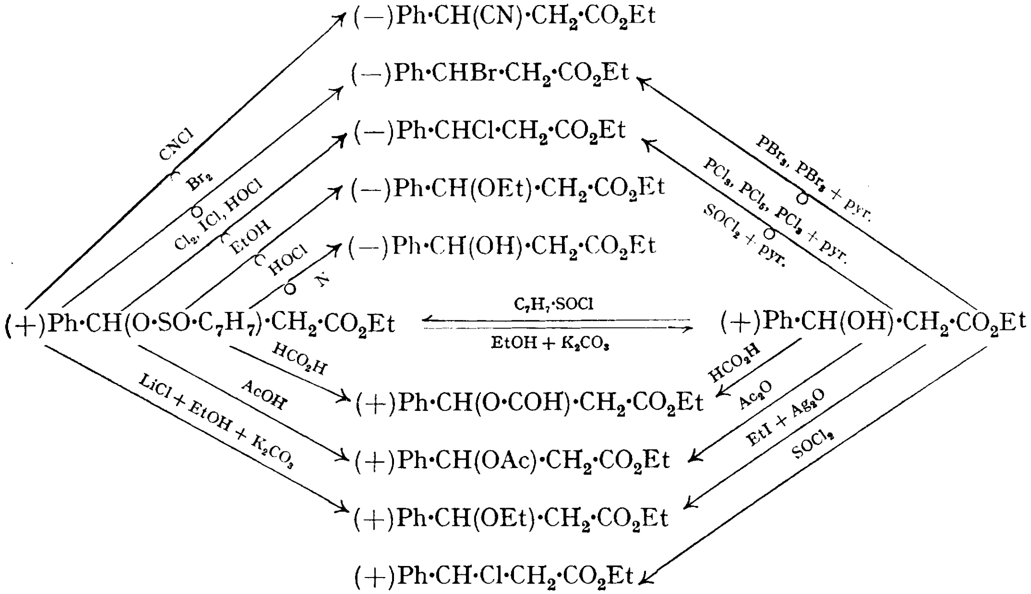


$$\begin{array}{ccc} \mathrm{R} - & \overset{+}{\mathrm{S}} & - \mathrm{R} \\ & | & \\ \bar{\mathrm{C}}\mathrm{l} & \mathrm{CN} & \end{array}$$

(II.)

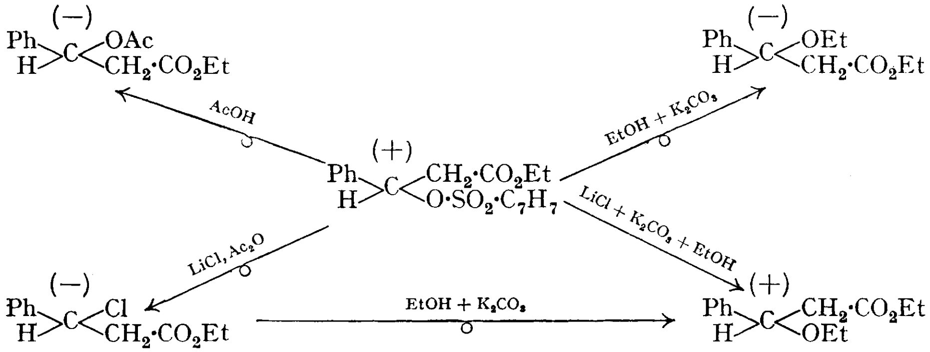
In common with (+) phenylmethylcarbinyl *p*-toluenesulphinate, but in contrast to the *p*-toluenesulphinates of purely aliphatic alcohols, the *p*-toluenesulphinoxy-group of ethyl (+) β-*p*-toluenesulphinoxy-β-phenylpropionate was replaced by the ethoxy-group with inversion and some racemisation when this ester was heated with ethyl alcohol. On the other hand, when the sulphinoxy-ester was heated with ethyl alcohol containing potassium carbonate, the (+) hydroxy-ester was formed by alcoholysis without loss of rotatory power. Although the avoidance of acid conditions in this reaction prevented the occurrence of an inversion, the (+) sulphinoxy-ester was converted into the (+) formoxy- and the (+) acetoxy-ester without inversion by formic and acetic acid respectively.

The following scheme summarises the reactions of the (+) sulphinoxy-ester and illustrates the stereochemical relationships of the products.



(b) *Replacement of the Hydroxy-group of Ethyl* (+) β-*Hydroxy*-β-*phenylpropionate.*—By the action of the chlorides and bromides of phosphorus, the (+) hydroxy-ester was converted into the (—) chloro- and the (—) bromo-ester, the observed inversion and the rather large amount of racemisation being similar to that occurring during the same reaction with other semi-aromatic hydroxy-compounds. Under the action of thionyl chloride in the presence of pyridine, the (+) hydroxy-ester also yielded the (—) chloro-ester, although, in the absence of pyridine, thionyl chloride yields the (+) chloro-ester (McKenzie and Barrow, J., 1910, **97**, 2564). Further support is thus afforded for the view, previously based on similar results obtained with ethyl (+) mandelate (Kenyon, Lipscomb, and Phillips, J., 1930, 415) and with (+) phenylmethylcarbinol (Kenyon, Phillips, and Taylor, J., 1931, 382), that, whereas a tertiary base has no obvious influence on the course of the reaction between thionyl chloride and a purely aliphatic alcohol, when a phenyl group is linked to the asymmetric carbon atom the presence of a tertiary base modifies the reaction so profoundly that a chloro-derivative of opposite sign is produced and a Walden inversion occurs.

(c) *Replacement of the* p-*Toluenesulphonoxy-group of Ethyl* (+) β-*p-Toluenesulphonoxy*-β-*phenylpropionate.*—This ester could not be prepared by the direct interaction of the (+) hydroxy-ester and *p*-toluenesulphonyl chloride, but the *p*-toluenesulphinoxy-ester was oxidised rapidly by hyperol (urea–hydrogen peroxide) and the *p*-toluenesulphonoxy-ester was isolated as a pale yellow oil too unstable to distil at low pressures. Accordingly, for each reaction studied, the (+) sulphinoxy-ester was oxidised with hyperol in a solution of the reagent, reaction of which with the resulting (+) sulphonoxy-ester was to be examined. The experimental results can be summarised as follows :



The conversion of the (+) sulphinate into the (+) sulphonate involves merely the addition of an oxygen atom to the sulphur atom of the *p*-toluenesulphinoxy-group, a reaction unlikely to involve configurative change. The (+) sulphonate therefore has the same configuration as the (+) sulphinate. The interaction of the (+) sulphonate with acetic acid and with ethyl alcohol gave respectively the (—) acetate and the (—) ethyl ether. Both reactions were therefore attended by inversion of configuration, accompanied by somewhat more racemisation than occurred during similar reactions of the *p*-toluenesulphonates of purely aliphatic alcohols, but less than that which accompanied similar reactions of (—) phenylmethylcarbinyl *p*-toluenesulphonate (*loc. cit.*).

When heated, in the presence of potassium carbonate, with ethyl alcohol and with an ethyl-alcoholic solution of lithium chloride, the (+) sulphonate gave respectively the (—) and the (+) ethoxy-ester. It is probable that during the second reaction the (+) sulphonate interacted with the lithium chloride to give rise to the (—) chloro-ester, which, in the presence of potassium carbonate, was converted into the (+) ethoxy-ester by interaction with the solvent. This interpretation of the reaction is made more probable by the conversion of the (+) sulphonate into the (—) chloro-ester by heating it with a solution of lithium chloride in acetic anhydride. During this reaction some (—) acetoxy-ester was formed, owing presumably to the formation of lithium acetate. The (—) acetoxy-ester was also produced by the interaction of the (+) sulphonate with acetic acid. Since the (+) acetoxy-ester can be prepared by the action of acetic anhydride on the (+) hydroxy-ester, a reaction unlikely to occur with inversion, the formation of the (—) acetoxy-ester from the (+) sulphonate in the reactions described above was accompanied by a Walden inversion. These reactions involve the replacement of the *p*-toluenesulphonoxy-anion by the acetate anion and are similar in type to the reactions of the (+) sulphonate with lithium chloride in which the *p*-toluenesulphonoxy-anion is replaced by the chloride anion. It is therefore probable that, since the (—) acetoxy-ester was produced with inversion, so also was the (—) chloro-ester and hence that these two esters have the same configuration.

Ethyl (—) β-hydroxy-β-phenylpropionate thus has the same configuration as ethyl (—) β-chloro-β-phenylpropionate, a conclusion in agreement with that reached from a consideration of the reactions of the *p*-toluenesulphinoxy-ester.

EXPERIMENTAL.

Resolution of β-*Hydroxy*-β-*phenylpropionic Acid*.—McKenzie and Humphries (J., 1910, **97**, 121) resolved this acid by means of morphine: the less expensive brucine can be used. Brucine (238 g.) was dissolved in a hot solution of *dl*-β-hydroxy-β-phenylpropionic acid (100 g.) in ethyl acetate (1200 c.c.). The crystals (246 g.) which separated on cooling had m. p. 128° and after six crystallisations from ethyl acetate were obtained (79 g.) optically pure, m. p. 145°, $[\alpha]_{5893}$ + 37·85° $[\alpha]_{5461}$ + 45·8° (*c*, 5·00; *l*, 2) in ethyl-alcoholic solution. A further quantity of pure salt was obtained from the mother-liquors.

By decomposition of the brucine salt in aqueous solution with hydrochloric acid, followed by extraction with ether, *d*-β-hydroxy-β-phenylpropionic acid, m. p. 115°, was obtained. It had $[\alpha]^{17°}_{5893}$ + 18·9°, $[\alpha]^{17°}_{5461}$ + 23·4°, and $[\alpha]_{4358}$ + 33·4° (*c*, 5·000; *l*, 2) in ethyl-alcoholic solution.

When the *l* + *dl*-acid, obtained by decomposition of more soluble fractions of the brucine salt, was fractionally crystallised from water, optically pure *l*-β-hydroxy-β-phenylpropionic acid (25 g.), m. p. 115—116°, $[\alpha]_{5893}$ — 19·0° (*c*, 5·130; *l*, 2) in ethyl alcohol, was obtained.

Ethyl *d*-(+)-β-hydroxy-β-phenylpropionate was prepared by slowly passing hydrogen chloride for 10 hours into a solution of the *d*-acid (25 g.) in ethyl alcohol (250 c.c. of 99%) heated on the steam-bath and was obtained (23 g.) with b. p. 90—91°/< 0·1 mm., $d^{17°}_{4°}$ 1·058, $n^{17°}_{D}$ 1·5125, $\alpha^{17°}_{5893}$ + 19·17°, $\alpha^{17°}_{5461}$ + 23·39°, $\alpha^{17°}_{4358}$ + 31·52° (*l*, 1·0).

Ethyl d-(+)-β-*ethoxy*-β-*phenylpropionate* (18 g.), b. p. 85—86°/< 0·1 mm., $n^{18°}_{D}$ 1·4983, $d^{17°}_{4°}$ 1·067, $\alpha^{17°}_{5461}$ + 7·59° (*l*, 0·25) (Found: C, 70·4; H, 8·25. $C_{13}H_{18}O_3$ requires C, 70·5; H, 8·2%), was obtained when a mixture of ethyl *d*-β-hydroxy-β-phenylpropionate (10 g.), ethyl iodide (7·8 g.), dry silver oxide (6 g.), and anhydrous ether (30 c.c.), after standing for 2 hours, was heated under reflux for 4 hours. When ethyl *d*-β-hydroxy-β-phenylpropionate (10 g.) in anhydrous ether (40 c.c.) was allowed to react with potassium (2·1 g.), the principal product was ethyl cinnamate (5 g.), b. p. 270° (Found: C, 75·1; H, 6·8. Calc.: C, 75·0; H, 6·8%).

Ethyl *d*-(+)-β-acetoxy-β-phenylpropionate (9 g.), prepared by heating ethyl *d*-(+)-β-hydroxy-β-phenylpropionate (10 g.) and acetic anhydride (8 g.) for 2 hours on the steam-bath, had b. p. 102—103°/< 0·1 mm., $d_{4^\circ}^{17^\circ}$ 1·088, $n_D^{17^\circ}$ 1·5168, $\alpha_{5893}^{17^\circ}$ + 1·32°, $\alpha_{5461}^{17^\circ}$ + 1·66°, $\alpha_{4358}^{17^\circ}$ + 2·79° (*l*, 0·25) (Found: C, 66·5; H, 6·3. Calc.: C, 66·4; H, 6·4%).

Ethyl *d*-(+)-β-formoxy-β-phenylpropionate (8 g.), prepared by heating ethyl *d*-(+)-β-hydroxy-β-phenylpropionate (10 g.) and anhydrous formic acid (5 g.) for 6 hours on the steam-bath, had b. p. 95—97°/< 0·1 mm., $d_{4^\circ}^{17^\circ}$ 1·1293, $n_D^{20^\circ}$ 1·5333, $\alpha_{5893}^{17^\circ}$ + 2·47°, $\alpha_{5461}^{17^\circ}$ + 2·98°, $\alpha_{4359}^{17^\circ}$ + 4·39° (*l*, 0·25) (Found: C, 64·9; H, 6·4. Calc.: C, 64·9; H, 6·4%).

Ethyl d-(+)-β-p-*Toluenesulphinoxy-β-phenylpropionate*.—Ice-cold *p*-toluenesulphinyl chloride (12 g.) was slowly added to a mixture of ethyl *d*-β-hydroxy-β-phenylpropionate (10 g.) and pyridine (6 g.) cooled in ice and salt. After 12 hours, *ethyl* d-β-p-*toluenesulphinoxy-β-phenylpropionate* was isolated from the reaction mixture as a yellow oil which could not be distilled (Found: C, 65·3; H, 6·3; S, 9·6. $C_{18}H_{20}O_4S$ requires C, 65·1; H, 6·1; S, 9·7%. 0·5362 G. required for complete hydrolysis 0·1286 g. NaOH. Calc., 0·1292 g.). It had $\alpha_{5461}^{17^\circ}$ + 3·77° (*l*, 0·25); $n_D^{18^\circ}$ 1·15286, $d_{4^\circ}^{17^\circ}$ 1·178.

As is shown later, this sulphinate, when heated with ethyl alcohol in the presence of potassium carbonate, yields the original hydroxy-ester of unchanged rotatory power.

Conversion of Ethyl d-(+)-β-p-*Toluenesulphinoxy-β-phenylpropionate into Ethyl* d-(+)-β-*Acetoxy-β-phenylpropionate by Means of Acetic Acid*.—A mixture of acetic acid (4 g.), acetic anhydride (2 g.), and the *d*-sulphinate (10 g.) was heated for 6 hours on the steam-bath, and the cooled product poured into water. The ethyl *d*-β-acetoxy-β-phenylpropionate (5·5 g.) which separated had b. p. 102—104°/< 0·1 mm., $n_D^{17.5^\circ}$ 1·5168, α_{5461} + 1·48° (*l*, 0·25).

Conversion of Ethyl d-(+)-β-p-*Toluenesulphinoxy-β-phenylpropionate into Ethyl* d-(+)-β-*Formoxy-β-phenylpropionate by Means of Formic Acid*.—When a mixture of anhydrous formic acid (4 g.) and the *d*-sulphinate (10 g.) was heated for 5 hours on the steam-bath, ethyl *d*-β-formoxy-β-phenylpropionate (6 g.), b. p. 95°/< 0·1 mm., $n_D^{20^\circ}$ 1·5334, $\alpha_{5461}^{17^\circ}$ + 1·46° (*l*, 0·25), was produced.

Walden Inversion Reactions.

Conversion of Ethyl d-(+)-β-p-*Toluenesulphinoxy-β-phenylpropionate into Ethyl* l-(−)-β-*Chloro-β-phenylpropionate*.—(a) *By means of chlorine in chloroform solution.* A slow stream of dry chlorine was passed during 2 hours into a solution of the *d*-sulphinate (10 g.) in dry chloroform (75 c.c.). The solvent was then removed at room temperature, and the residual oil diluted with cold light petroleum and filtered: the white crystalline material precipitated had m. p. 69°, alone and when mixed with *p*-toluenesulphonyl chloride. The light petroleum was removed from the filtrate; the residual ethyl *l*-(−)-β-chloro-β-phenylpropionate (3 g.) had b. p. 70—72°/< 0·1 mm., $n_D^{17^\circ}$ 1·5344, $\alpha_{5461}^{18^\circ}$ − 1·57° (*l*, 0·25) (Found: Cl, 17·6. Calc., 17·8%).

(b) *By means of chlorine water.* The *d*-sulphinate (10 g.) was shaken with a freshly prepared solution of chlorine (2·2 g.) in water (100 c.c.): the chlorine was rapidly absorbed and crystals soon appeared. The liquid was filtered, and the solid residue separated by means of cold light petroleum into *p*-toluenesulphonyl chloride (m. p. and mixed m. p. 69°) and ethyl *l*-β-chloro-β-phenylpropionate (4 g.), b. p. 71—72°/< 0·1 mm., $n_D^{18^\circ}$ 1·5344, α_{5461} − 1·30° (*l*, 0·25).

(c) *By means of hypochlorous acid.* The *d*-sulphinate (10 g.) was shaken for 12 hours with a freshly prepared solution of hypochlorous acid (1·75 g.; 1·2 mols.) in water (85 c.c.). The cooled liquid was filtered, and the residue separated by means of cold light petroleum into *p*-toluenesulphonyl chloride (m. p. 68°) and an oil. The latter was separated by fractional distillation into (i) ethyl *l*-β-chloro-β-phenylpropionate, b. p. 72—73°/< 0·1 mm., $n_D^{17^\circ}$ 1·5345, $\alpha_{5461}^{17^\circ}$ − 0·72° (*l*, 0·25), and (ii) ethyl *l*-β-hydroxy-β-phenylpropionate (3·5 g.), b. p. 90—91°/< 0·1 mm., $n_D^{17^\circ}$ 1·5129, $\alpha_{5461}^{17^\circ}$ −3·53° (*l*, 0·25).

(d) *By means of iodine monochloride.* The *d*-sulphinate (10 g.) was shaken with an aqueous solution (150 c.c. of approx. 0·3*N*) of iodine monochloride (Orton, J., 1900, **77**, 830) and then left at 0° for 12 hours. The liquid was filtered, and the residue separated by means of cold light petroleum into *p*-toluenesulphonyl iodide (m. p. 86°, alone and mixed with an authentic specimen) and ethyl *l*-β-chloro-β-phenylpropionate (2·5 g.), b. p. 73°/< 0·1 mm., $n_D^{17^\circ}$ 1·5344, $\alpha_{5461}^{17.5^\circ}$ − 2·27° (*l*, 0·25).

Conversion of Ethyl d-(+)-β-p-*Toluenesulphinoxy-β-phenylpropionate into Ethyl* l-(−)-β-*Bromo-β-phenylpropionate*.—(a) *By means of bromine in chloroform solution.* A solution of the *d*-sulphinate (10 g.) in chloroform (50 c.c.), cooled in a freezing mixture, was slowly mixed with a solution of bromine (5 g.) in chloroform (75 c.c.) and shaken at frequent intervals during 6 hours, by which time most of the bromine had reacted. After removal of the solvent at room temperature, the residue was separated by means of cold light petroleum into *p*-toluenesulphonyl bromide (m. p. 97°, alone and mixed with an authentic specimen) and *ethyl* l-β-*bromo-β-phenyl-*

propionate (4·0 g.), b. p. 82—84°/< 0·1 mm., $n_D^{17°}$ 1·5424, $\alpha_{5461}^{17.5°}$ − 1·43° (*l*, 0·25) (Found: Br, 30·8. $C_{11}H_{13}O_2Br$ requires Br, 31·1%).

(b) *By means of bromine water.* The *d*-sulphinate (10 g.), vigorously shaken with a solution of bromine (1·0 g.) in water (200 c.c.) until the bromine had almost completely reacted, furnished, by the procedure described above, (i) *p*-toluenesulphonyl bromide (m. p. and mixed m. p. 98°), ethyl *l*-β-bromo-β-phenylpropionate (3 g.), b. p. 82—84°/< 0·1 mm., $n_D^{20°}$ 1·5425, $\alpha_{5461}^{17°}$ − 0·86° (*l*, 0·25), and (iii) ethyl *l*-β-hydroxy-β-phenylpropionate (0·4 g.), b. p. 90—91°/< 0·1 mm., $n_D^{15°}$, 1·5126, $\alpha_{5461}^{17°}$ − 1·34° (*l*, 0·25).

Conversion of Ethyl d-(+)-β-p-*Toluenesulphinoxy*-β-*phenylpropionate into Ethyl* l-(−)-β-*Cyano*-β-*phenylpropionate by Means of Cyanogen Chloride.*—Dry cyanogen chloride was slowly passed for 30 minutes into an ice-cold solution of the *d*-sulphinate (10 g.) in light petroleum, which was then kept over-night. By filtration there were obtained *p*-toluenesulphonyl chloride (2 g.) (m. p. and mixed m. p. 68°) and, after removal of light petroleum from the filtrate, *ethyl* l-(−)-β-*cyano*-β-*phenylpropionate* (2·5 g.), b. p. 78—79°/< 0·1 mm., $n_D^{18°}$ 1·5243, $d_{4°}^{17°}$ 1·1811, $\alpha_{5893}^{17°}$ − 0·38°, $\alpha_{5461}^{17°}$ − 0·53°, $\alpha_{4359}^{17°}$ − 0·92° (*l*, 0·25) (Found: N, 6·2. $C_{12}H_{13}O_2N$ requires N, 6·9%).

Conversion of Ethyl d-(+)-β-p-*Toluenesulphinoxy*-β-*phenylpropionate into Ethyl* l-(−)-β-*Hydroxy*-β-*phenylpropionate* [see also under (b) and (c) above].—*By means of nitrous acid.* A well-stirred suspension of the *d*-sulphinate (8 g.) in a solution of sodium nitrite (5 g.; 3 mols.) in water (75 c.c.) immersed in a freezing mixture was mixed slowly with hydrochloric acid (50 c.c. conc. + 25 c.c. water). After 4 hours, the mixture was shaken with ether, which extracted ethyl *l*-(−)-β-hydroxy-β-phenylpropionate (4 g.), b. p. 90—91°/< 0·1 mm., $n_D^{17°}$ 1·5124, $\alpha_{5461}^{17°}$ −2·57° (*l*, 0·25).

Conversion of Ethyl d-(+)-β-p-*Toluenesulphinoxy*-β-*phenylpropionate into Ethyl* l-(−)-β-*Ethoxy*-β-*phenylpropionate by Means of Ethyl Alcohol.*—A solution of the *d*-sulphinate (10 g.) in ethyl alcohol (75 c.c. of 99%) was heated under reflux in an atmosphere of nitrogen for 48 hours. Removal of the excess of alcohol and some *p*-toluenesulphinic acid left ethyl *l*-β-ethoxy-β-phenylpropionate (5 g.), b. p. 85°/< 0·1 mm., $n_D^{18°}$ 1·4984, $\alpha_{5461}^{17°}$ − 3·73° (*l*, 0·25). When this experiment was repeated in the presence of anhydrous potassium carbonate, no trace of the ethoxy-derivative was obtained; the main product was optically pure ethyl *d*-(+)-β-hydroxy-β-phenylpropionate.

Conversion of Ethyl d-(+)-β-p-*Toluenesulphinoxy*-β-*phenylpropionate into Ethyl* d-(+)-β-*Ethoxy*-β-*phenylpropionate by Means of an Ethyl-alcoholic Solution of Lithium Chloride.*—A solution of the *d*-sulphinate (10 g.) and lithium chloride (7 g.) in ethyl alcohol (75 c.c.), mixed with anhydrous potassium carbonate (12 g.), was heated under reflux in an atmosphere of nitrogen for 48 hours. The excess of alcohol was removed by distillation, and from the residue was isolated ethyl *d*-β-ethoxy-β-phenylpropionate (2·5 g.), b. p. 84—85°/< 0·1 mm., $n_D^{17°}$ 1·4983, $\alpha_{5461}^{17°}$ + 4·91° (*l*, 0·25).

Oxidation of Ethyl d-(+)-β-p-*Toluenesulphinoxy*-β-*phenylpropionate to Ethyl* d-(+)-β-*p*-*Toluenesulphonoxy*-β-*phenylpropionate.*—Hyperol (0·1807 g.) was added to a solution of the *dl*-sulphinate (0·6382 g.) in pure ether (25 c.c.): after 4 hours, the mixture did not produce a blue colour with acidified starch–iodide paper. On titration, 0·3 c.c. of perbenzoic acid solution (1% in chloroform) was required to produce a blue coloration (0·6382 g. of sulphinate would require 26·5 c.c. for complete oxidation to sulphonate). In a separate experiment 0·5296 g. of the sulphinic ester required 0·207 g. of perbenzoic acid for complete oxidation (calc., 0·220 g.).

As it was not possible to distil the sulphonate, solutions of the sulphinate were oxidised separately for each of the following reactions.

Conversion of Ethyl d-(+)-β-p-*Toluenesulphonoxy*-β-*phenylpropionate into Ethyl* l-(−)-β-*Ethoxy*-β-*phenylpropionate.*—A mixture of the *d*-sulphinate (10 g.), hyperol (8 g.), potassium carbonate (15 g.), and ethyl alcohol (50 c.c.), after standing for 12 hours, was heated under reflux for 12 hours, cooled, and poured into water. Extraction with ether yielded ethyl *l*-(−)-β-ethoxy-β-phenylpropionate (3·5 g.), b. p. 84—86°/< 0·1 mm., $n_D^{17°}$ 1·4984, $\alpha_{5461}^{17°}$ − 5·12° (*l*, 0·25).

Conversion of Ethyl d-(+)-β-p-*Toluenesulphonoxy*-β-*phenylpropionate into Ethyl* d-(+)-β-*Ethoxy*-β-*phenylpropionate.*—A mixture of the *d*-sulphinate (10 g.), hyperol (10 g.), potassium carbonate (15 g.), lithium chloride (8 g.), and ethyl alcohol (75 c.c.), similarly treated and extracted, yielded ethyl *d*-(+)-β-ethoxy-β-phenylpropionate (4·5 g.), b. p. 84—85°/< 0·1 mm., $n_D^{18°}$ 1·4983, $\alpha_{5461}^{17°}$ + 4·36° (*l*, 0·25).

Conversion of Ethyl l-(−)-β-*Chloro*-β-*phenylpropionate into Ethyl* d-(+)-β-*Ethoxy*-β-*phenylpropionate.*—The chloro-ester (α_{5461} − 2·37°; *l*, 0·25), heated under reflux with ethyl alcohol containing potassium carbonate, readily gave the (+)-ethoxy-ester, $\alpha_{5461}^{26°}$ + 0·23° (*l*, 0·25).

Conversion of Ethyl d-(+)-β-p-*Toluenesulphonoxy*-β-*phenylpropionate into Ethyl* l-(−)-β-

Acetoxy-β-phenylpropionate.—A solution of the *d*-sulphinate (10 g.) and hyperol (10 g.) in anhydrous acetic acid (50 c.c.) was kept for 12 hours, heated on the steam-bath for 12 hours, and worked up in the usual manner. The resulting ethyl *l*-(−)-β-acetoxy-β-phenylpropionate (6 g.) had b. p. 103°/< 0·1 mm., $n_{\mathrm{D}}^{17^\circ}$ 1·5168, $\alpha_{5461}^{17^\circ}$ − 0·85° (*l*, 0·25).

Conversion of Ethyl d-(+)-β-p-*Toluenesulphonoxy-β-phenylpropionate into Ethyl* (−)-β-*Chloro-β-phenylpropionate and Ethyl* l-(−)-β-*Acetoxy-β-phenylpropionate.*—A mixture of the *d*-sulphinate (9 g.), hyperol (8 g.), lithium chloride (10 g.), and acetic anhydride (50 c.c.) was kept for 12 hours, heated on the steam-bath for 4 hours, cooled, and poured into dilute sodium carbonate solution. Extraction with ether yielded (a) ethyl (−)-β-chloro-β-phenylpropionate (1·5 g.), b. p. 72—73°/< 0·1 mm., $n_{\mathrm{D}}^{17^\circ}$ 1·5343, $\alpha_{5461}^{17^\circ}$ − 1·3° (*l*, 0·5), and (b) ethyl *l*-(−)-β-acetoxy-β-phenylpropionate (4 g.), b. p. 103—104°/< 0·1 mm., $n_{\mathrm{D}}^{17\cdot5^\circ}$ 1·5166, $\alpha_{5461}^{17^\circ}$ − 1·23° (*l*, 0·25).

The Replacement of the Hydroxy-group in Ethyl d-(+)-β-*Hydroxy-β-phenylpropionate by Halogen.*—(a) *By means of phosphorus pentachloride.* The *d*-hydroxy-ester (10 g.), dissolved in ether (25 c.c.), was added slowly to a well-cooled solution of phosphorus pentachloride (14 g.) in ether (25 c.c.). After the initial vigorous reaction had ceased, the mixture was gently warmed for 1½ hours, cooled, and poured into water. The ethyl (−) β-chloro-β-phenylpropionate (5 g.) isolated had b. p. 72—74°/< 0·1 mm., $n_{\mathrm{D}}^{17^\circ}$ 1·5345, $d_{4^\circ}^{17^\circ}$ 1·2180, $\alpha_{5461}^{17^\circ}$ − 1·59° (*l*, 0·25) (Found : Cl, 17·7. Calc. : Cl, 17·8%).

(b) *By means of phosphorus pentachloride in the presence of pyridine.* A solution of phosphorus pentachloride (14 g.) in ether (25 c.c.) was added slowly to a solution of the *d*-hydroxy-ester (10 g.) and pyridine (9·6 g.; 2 mols.) in ether (30 c.c.) surrounded by a freezing mixture. The ethyl (−) β-chloro-β-phenylpropionate isolated after the mixture had been warmed for 1 hour had b. p. 72—73°/< 0·1 mm., $n_{\mathrm{D}}^{17^\circ}$ 1·5344, $\alpha_{5461}^{17^\circ}$ − 2·46° (*l*, 0·25).

(c) *By means of phosphorus trichloride.* A solution of the *d*-hydroxy-ester (10 g.) in ether (25 c.c.) was added slowly to an ice-cold solution of phosphorus trichloride (12 g.) in ether (20 c.c.), and the mixture warmed until the evolution of hydrogen chloride ceased. The ethyl (−) β-chloro-β-phenylpropionate (3 g.) obtained had b. p. 72°/< 0·1 mm., $n_{\mathrm{D}}^{17^\circ}$ 1·5344, $\alpha_{5461}^{17^\circ}$ − 1·04° (*l*, 0·25).

(d) *By means of phosphorus trichloride in the presence of pyridine.* A solution of the *d*-hydroxy-ester (10 g.) and pyridine (8 g.; 2 mols.) in ether (40 c.c.) was added slowly to an ice-cold ethereal solution of phosphorus trichloride (12 g.), and the mixture subsequently warmed. The resulting ethyl (−) β-chloro-β-phenylpropionate (7 g.) had b. p. 72—73°/< 0·1 mm., $n_{\mathrm{D}}^{17^\circ}$ 1·5345, $\alpha_{5461}^{17^\circ}$ − 2·69° (*l*, 0·25).

(e) *By means of thionyl chloride.* The *d*-hydroxy-ester (7 g.) was mixed with thionyl chloride (10 g.) and kept cold during the vigorous reaction. The excess of the thionyl chloride was removed at a temperature below 20°; the resulting ethyl (+) β-chloro-β-phenylpropionate (5·2 g.) had b. p. 72—73°/< 0·1 mm., $n_{\mathrm{D}}^{17^\circ}$ 1·5344, $\alpha_{5461}^{17^\circ}$ + 2·87° (*l*, 0·25) (Found : Cl, 17·7%).

(f) *By means of thionyl chloride in the presence of pyridine.* The *d*-hydroxy-ester (11·6 g.) and pyridine (10 g.; 2 mols.), dissolved in ether (40 c.c.), were added slowly to thionyl chloride (13·5 g.), and the mixture heated under reflux for ½ hour. The resulting ethyl (−) β-chloro-β-phenylpropionate (8 g.) had b. p. 72—73°/< 0·1 mm., $n_{\mathrm{D}}^{17^\circ}$ 1·5344, $\alpha_{5461}^{17^\circ}$ − 2·21° (*l*, 0·25).

(g) *By means of phosphorus tribromide.* The *d*-hydroxy-ester (10 g.) in ether (30 c.c.) was added slowly to an ice-cold ethereal solution of phosphorus tribromide (6 g.), and the mixture warmed until the evolution of hydrogen bromide ceased. The *ethyl* (+) β-*bromo*-β-*phenylpropionate* (7 g.) had b. p. 83—84°/< 0·1 mm., $n_{\mathrm{D}}^{17^\circ}$ 1·5424, $d_{4^\circ}^{17^\circ}$ 1·3559, $\alpha_{5461}^{17^\circ}$ − 5·08° (*l*, 0·25) (Found : C, 51·7; H, 5·1; Br, 30·9. $C_{11}H_{13}O_2Br$ requires C, 51·8; H, 5·1; Br, 31·1%).

(h) *By means of phosphorus tribromide in the presence of pyridine.* A solution of the *d*-hydroxy-ester (10 g.) and pyridine (10 g.; 2 mols.) in ether (25 c.c.) was added slowly to an ethereal solution of phosphorus tribromide (6 g.), and the mixture warmed for 1 hour. The resulting ethyl (−) β-bromo-β-phenylpropionate (8 g.) had b. p. 83—84°/< 0·1 mm., $n_{\mathrm{D}}^{17^\circ}$ 1·5424, $\alpha_{5461}^{17^\circ}$ − 7·25° (*l*, 0·25).

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