NOTES.

The Preparation of Some Di-(2 : 3-*epoxy*-n-*propyl*)*amines.*   By R. F. HOMER.

ROSE, HENDRY, and WALPOLE (*Nature*, 1950, **165**, 993) record the cytotoxic action of a selection of the diepoxides prepared in these laboratories as potential tumour inhibitors; this communication describes the preparation of a number of di-(2 : 3-epoxy-*n*-propyl)amines investigated in the course of these researches.   The synthesis of these compounds was carried out by a modification of Strukov's method (*Khim. Farm. Prom.*, 1934, No. 2, 11; *Chem. Abstr.*, 1934, **28**, 5421) by setting aside an aqueous solution of the amine hydrochloride (1 mole) and epichlorohydrin (2 moles) for several days at room temperature whereupon a thick oil or oily solid of the crude di-(3-chloro-2-hydroxypropyl)amine separated.   This was not further purified but the aqueous layer was decanted, the oil taken up in ether, and the ethereal solution dried (Na_2SO_4) and treated with the theoretical amount of powdered potassium hydroxide under reflux for six hours.   Filtration of the reaction mixture and evaporation of the filtrate gave the crude di-(2 : 3-epoxypropyl)amine which was distilled in high vacuum to yield the pure product as a pale-yellow oil, stable at room temperature over long periods.

In a few instances difficulty was experienced in obtaining analytically pure products by distillation, and the compound was then characterised as the di-(3-chloro-2-hydroxypropyl)amine hydrochloride, obtained in quantitative yield by leaving the epoxide overnight with dry ethereal hydrogen chloride. The reaction product from *p*-chloroaniline and epichlorohydrin on distillation gave two fractions, of which the lower-boiling one was *p*-chloro-*N*-(2 : 3-epoxypropyl)aniline and the higher-boiling one the expected *p*-chloro-*NN*-di-(2 : 3-epoxypropyl)aniline.   *p*-Chloro-*N*-(2 : 3-epoxypropyl)aniline polymerised to a hard transparent glass after a few days.   The product obtained from β-naphthylamine and epichlorohydrin could not be distilled, complete polymerisation taking place when it was heated even under pressure as low as 3×10^{-5} mm.

By this method there have been obtained, in addition to *NN*-(2 : 3-epoxypropyl)-*p*-anisidine recently described by Davis, Everett, and Ross (*J.*, 1950, 1333), and the *p*-phenetyl derivative described by Strukov (*loc. cit.*), the following compounds :

NN-Di-(2 : 3-*epoxypropyl*)*aniline* (36% yield), a pale-yellow oil, b. p. 130—133°/0·4 mm. (Found : C, 70·0; H, 7·05; N, 7·1. $C_{12}H_{15}O_2N$ requires C, 70·2; H, 7·3; N, 6·8%); NN-*di*-(2 : 3-*epoxypropyl*)- p-*toluidine* (42·5% yield), a pale-yellow oil, b. p. 146—150°/0·4 mm. (Found : C, 70·7; H, 7·45. $C_{13}H_{17}O_2N$ requires C, 71·2; H 7·76%); treatment of this compound with dry ethereal hydrogen chloride yielded NN-*di*-(3-chloro-2-hydroxypropyl)-p-*toluidine* hydrochloride, m. p. 143—145°, which was recrystallised from methanol (Found : C, 47·3; H, 6·15; Cl, 32·8. $C_{13}H_{19}O_2NCl_2,HCl$ requires C, 47·5; H, 6·1; Cl, 32·4%); NN-*di*-(3-chloro-2-hydroxypropyl)-p-*anisidine* hydrochloride, m. p. 145— 146°, obtained similarly from NN-di-(2 : 3-epoxypropyl)-*p*-anisidine (Found : C, 45·75; H, 5·65; N, 3·5; Cl, 31·0. $C_{13}H_{19}O_3NCl_2,HCl$ requires C, 45·3; H, 5·8; N, 4·05; Cl, 30·9%); p-*chloro*-N-(2 : 3- *epoxypropyl*)*aniline* (23% yield), a pale-yellow oil, b. p. 135—142°/0·4 mm. (Found : C, 59·3; H, 5·4; N, 8·15%; oxiran-O, 0·94. $C_9H_{10}ONCl$ requires C, 58·9; H, 5·45; N, 7·8%; oxiran-O, 1·0 atom/mol.), together with p-chloro-NN-di-(2 : 3-epoxypropyl)aniline (10% yield), a pale-yellow oil, b. p. 178— 180°/0·4 mm., for which a satisfactory analysis could not be obtained; treatment of this with dry ethereal hydrogen chloride gave p-*chloro*-NN-*di*-(3-chloro-2-hydroxypropyl)*aniline* hydrochloride, m. p. 169—171° after recrystallisation from methanol (Found : C, 41·15; H, 4·9; N, 4·65; Cl, 40·7. $C_{12}H_{16}O_2NCl_3,HCl$ requires C, 41·2; H, 4·85; N, 4·0; Cl, 40·7%).

Full details of biological tests on these compounds will be published elsewhere in due course.— IMPERIAL CHEMICAL INDUSTRIES LIMITED, RESEARCH LABORATORIES, BLACKLEY, MANCHESTER, 9. [*Received, September* 16*th*, 1950.]

Experiments with Optically Active Diphenyls. By F. BELL and G. A. DINSMORE.

THE following observations were made during unsuccessful attempts to realise a cycle of the following type with optically active diphenyls (cf. Bell and Waring, *J.*, 1949, 1579).
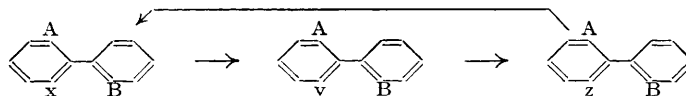
6 : 6′-*Dibromo*-2 : 2′-*ditolyl* (Me = 2).—(−)-6 : 6′-Diamino-2 : 2′-ditolyl (Me = 2) (4·5 g.) in 10% hydrochloric acid (120 c.c.) was diazotised at 5° with sodium nitrite (2·0 g.). Excess of nitrous acid was destroyed with sulphamic acid, and the filtered diazo-solution was added to a cold solution of cuprous bromide (1 g.) in 48% hydrobromic acid (10 c.c.). Nitrogen was evolved vigorously and after 30 minutes the reaction was completed by heating the mixture on the steam-bath for 1 hour. A black tar separated which hardened on cooling. This was taken up in alcohol and repeatedly treated with charcoal until the solution was a clear reddish-brown. On concentration and cooling, crystals accompanied by tar separated. The crystals were recrystallised twice from alcohol giving 6 : 6′-dibromo-2 : 2′-ditolyl as needles, m. p. 108—110° (0·1 g.), devoid of optical activity (*c*, 4 in ethanol, *l* = 1). Angeletti and Migliardi (*Gazzetta*, 1935, **65**, 819) give m. p. 109—110°, $[\alpha]_D$ −6·2°, for 6 : 6′-dibromo-2 : 2′-ditolyl obtained from (−)-6- amino-6′-bromo-2 : 2′-ditolyl.

Attempts to prepare 6-cyano-6′-nitro-2 : 2′-ditolyl from 6-amino-6′-nitro-2 : 2′-ditolyl by diazotisation or from 6-iodo-6′-nitro-2 : 2′-ditolyl by heating it with cuprous cyanide in pyridine resulted in resinous or tarry products.

Attempts to prepare 6 : 6′-dinitro-2 : 2′-ditolyl from 6-amino-6′-nitro-2 : 2′-ditolyl by Starkey's method (*Org. Synth.*, **19**, 40) or Hodgson's method (*J.*, 1947, 325, 1392) were unsuccessful.

Resolution of 3 : 5-*Dinitro*-6-α-*naphthylbenzoic Acid*.—Lesslie and Turner (*J.*, 1931, 1189) and Wallis and Moyer (*J. Amer. Chem. Soc.*, 1933, **55**, 2598) have described the resolution using brucine and, owing to the low solubility of the salt, relatively large volumes of solvent are required. It was decided to examine other alkaloidal salts. Morphine in alcohol gave as crop a salt, $[\alpha]_{5461}$ −37° (*c*, 0·59 in chloro- form), which on decomposition gave an acid, $[\alpha]_{5461}$ +33·3° (*c*, 0·60 in chloroform). The (−)-acid obtained from the original mother-liquor had $[\alpha]_{5461}$ −39·0° (*c*, 0·54 in chloroform). A trial experiment with quinidine again furnished as the first crop a salt of the (+)-acid and the result appeared more favourable than that with morphine. A larger-scale experiment led to an altogether less advantageous result. The acid (30 g.) was dissolved in boiling ethanol (475 c.c.), and quinidine (29·5 g.) added. The slightly cloudy solution was filtered and left overnight. The crop consisted of two types of crystal—pale yellow feathery needles (18 g.) and deep yellow clusters of square prisms (20 g.) of relatively high specific gravity. The crystals were separated roughly by hand picking, and a further mechanical separation was effected by shaking them with a small bulk of mother-liquor and decanting, to carry away the feathery needles, leaving the heavy crystal clusters. The pale yellow needles were recrystallised until of constant rotatory power, $[\alpha]_{5461}$ −25·1° (*c*, 0·64 in chloroform), and this salt on decomposition gave 6·9 g. of acid of $[\alpha]_{5791}$ −57·7° (*c*, 0·61 in acetone). This on recrystallisation from alcohol gave 5·6 g. of acid, m. p. 177—179°, $[\alpha]_{5791}$ −60° (*c*, 0·60 in acetone). The other quinidine salt on recrystallisation from alcohol gave 7·5 g. of salt of $[\alpha]_{5461}$ +295°, which on decomposition gave 3·5 g. of acid, $[\alpha]_{5791}$ +50° (*c*, 0·54 in acetone). This could be purified by further recrystallisation, for it was strikingly evident that the optically active forms were less soluble and crystallised more readily and in much more compact crystals than the inactive acid.

(−)-α-(6-*Amino*-2 : 4-*dinitrophenyl*)*naphthalene*.—(−)-6-α-Naphthyl-3 : 5-dinitrobenzoic acid (5 g.) was dissolved in thionyl chloride, and the excess of thionyl chloride removed under vacuum. The acid chloride formed was taken up in dry benzene (60 c.c.), and finely ground sodium azide (7·5 g.) added. The solution was boiled for 11 hours. Sodium hydroxide (60 c.c.; 3N.) was added and the solution refluxed for a further 4 hours. The benzene was removed in steam, and the crude product triturated with sodium

hydroxide solution (5%), filtered off, and washed with water. The crude amine was dissolved in dry ether, and the clear solution treated with hydrogen bromide. The hydrobromide was filtered off and decomposed with dilute aqueous ammonia, and the recovered amine crystallised from aqueous alcohol. The product (1·2 g.) had m. p. 155—157° and $[\alpha]_D$ —279° (*c*, 0·43 in alcohol). Wallis and Moyer (*loc. cit.*) give $[\alpha]_D$ —292·4° for this amine prepared from the acid by the Hofmann reaction.

Attempts to convert this optically active amine into 6-α-naphthyl-3 : 5-dinitrobenzonitrile by the Sandmeyer reaction resulted in unpurifiable products.—COLLEGE OF TECHNOLOGY, BELFAST, N. IRELAND. [*Received, August 1st,* 1950.]

Carbohydrate Primers in the Synthesis of Starch. By J. M. BAILEY, W. J. WHELAN, and S. PEAT.

IT is now generally recognised that phosphorylase cannot initiate the synthesis of amylose from glucose-1 phosphate unless a pre-formed chain of glucose units is also present. The length of such a " priming " chain is of importance in respect of the mechanism of phosphorylase action, and hitherto a clear-cut definition of function has not been possible because of the difficulty experienced in preparing homogeneous primers of known chain length. Weibull and Tiselius (*Arkiv Kemi, Min., Geol.,* 1945, **19,** *A,* No. 1) separated a mixture of " normal " dextrins, by adsorption analysis, into fractions corresponding to tri-, tetra-, penta-, and hexa-saccharides. Each of these fractions showed priming activity, from which it was concluded that the minimum length for a priming chain is 3 glucose units (cf. Bourne, Sitch, and Peat, *J.,* 1949, 1448).

We now report that by an application of the elegant method, devised by Whistler and Durso (*J, Amer. Chem. Soc.,* 1950, **72,** 677) for the chromatographic separation of mono-, di-, and tri-saccharides, we have been able to separate a mixture of dextrins derived from amylose by acid hydrolysis, and so have obtained pure specimens of glucose, maltose, maltotriose, maltotetraose, maltopentaose, and maltohexaose. The mixture is adsorbed on a charcoal–Celite column and the individual members are eluted with increasing concentrations of ethanol in water. The ethanol concentrations used were, respectively, 0, 7·5, 15, 20, 20—23, and 25%. An absolute separation of the first three members and an almost complete separation of the other three members was achieved by a single application of this fractionation procedure.

The higher saccharides are slightly hygroscopic, amorphous solids containing small amounts (1—3%) of inorganic matter. Further properties of the saccharides are listed in the Table, concentrations being calculated from the amounts of glucose liberated by acid hydrolysis.

	$[\alpha]_D^{20}$ (equilibrium value in H_2O).	Chain length :		Primer activity.[c]
		by hypoiodite oxidation.[a]	by R_{Cu}.[b]	
Glucose	52·0°	0·98	1·0	0
Maltose monohydrate	131	2·04	2·0	0
Maltotriose	167	3·01	3·03	+
Maltotetraose	180	—	3·89	+ + + +
Maltopentaose	183	—	5·10	+ + + +
Maltohexaose	204	—	5·90	+ + + +

[a] The hypoiodite method (Hirst *et al., J.,* 1949, 928) gave erratic results with the higher saccharides. [b] These values (measured with Somogyi's reagent, *J. Biol. Chem.,* 1945, **160,** 61) were obtained, in the cases of glucose and maltose, by comparison with the pure substances, and in the other cases by a correction calculated from the extent by which maltose departs from a stoicheiometrical relationship with glucose. [c] For polysaccharide synthesis by potato phosphorylase from glucose-1 phosphate.

It will be seen that maltotriose is the first member of the series which will act as a primer for polysaccharide synthesis, thus confirming the results of Weibull and Tiselius. We are satisfied that this activity is not due to maltotetraose impurity in the maltotriose by virtue of the fact that the action of crystalline β-amylase for a short period (see below) does not affect the priming activity of the maltotriose but causes a substantial diminution in the activity of the tetraose.

The action of β-amylase on these pure saccharides is of interest in this connection. The glucose and maltose fractions were entirely unaffected by this enzyme; maltotriose was attacked very slowly, the reducing power becoming constant at a value which was 102% of that calculated for an equimolecular mixture of glucose and maltose. Maltotetraose was attacked extremely rapidly, yielding 2 moles of maltose (100%). The pentaose was rapidly converted into maltose and maltotriose and thereafter more slowly to give finally a mixture of 2 moles of maltose and one of glucose (93%). The hexaose was smoothly and rapidly converted into maltose (3 moles).

By the use of maltotetraose as a primer in phosphorylase synthesis it has been possible to determine with precision the relation between the blue value and the chain length of a polymer-homologous series of unbranched chains of the amylose type. It appears that the shortest chain which gives a finite blue value contains at least ten glucose members. Within the series containing between 10 and 80 glucose units per chain there is a strict proportionality between chain length and blue value. With chains of more than 80 members this proportionality no longer holds and a maximum and constant blue value is given by chains of *ca.* 140 or more glucose units.—UNIVERSITY COLLEGE OF NORTH WALES, BANGOR. [*Received, August 8th,* 1950.]

*The Hydrogenolysis of Dithioesters and Thioamides.* By J. BADDILEY.

A RECENT report on the hydrogenolysis of primary aromatic thioamides (Brovet, *Arhiv Kem.*, 1948, **20**, 70) has prompted the publication of some related experiments on the hydrogenolysis of dithioesters and of thioamides derived from primary and secondary amines.

The hydrogenolysis of monothioesters with Raney nickel and hydrogen is known to give rise to either aldehydes (Wolfrom and Karabinos, *J. Amer. Chem. Soc.*, 1946, **68**, 1455) or alcohols (Prelog, Norymberski, and Jeger, *Helv. Chim. Acta*, 1946, **29**, 360) according to the experimental conditions employed, whereas in the absence of hydrogen aromatic thioesters give mainly sulphides (Hauptmann and Wladislaw, *J. Amer. Chem. Soc.*, 1950, **72**, 710). By analogy, it was considered that dithioesters should give hydrocarbons according as follows :

$$\text{R·CS}_2\text{Me} \longrightarrow \text{R·CH}_3 + \text{CH}_4$$

The correctness of this view was established by the very ready conversion of methyl phenyldithio-acetate into ethylbenzene when its alcoholic solution was treated with excess of Raney nickel. The inaccessible nature of dithioesters in general, however, limits the application of this reaction as a general method for the introduction of alkyl groups into aromatic compounds.

The hydrogenolysis of thioamides appears to be more complex. Primary aromatic thioamides are stated by Brovet (*loc. cit.*) to give aldehydes and ammonia. It is shown here that when *N-cyclo*hexylphenylthioacetamide is refluxed with Raney nickel in 80% alcohol ethylbenzene is the main product. The nitrogenous fragment was isolated as a picrate, m. p. 168°, which from its analysis was probably a mixture of the picrates of *cyclo*hexylamine and *N*-ethyl*cyclo*hexylamine. Phenylthio-acetomorpholide behaved similarly but in this case an excellent yield of 4-ethylmorpholine was obtained and isolated as its picrate.

$$\text{Ph·CH}_2\text{·CS·N}\langle\text{--}\rangle\text{O} \longrightarrow \text{Ph·CH}_2\text{·CH}_3 + \text{EtN}\langle\text{--}\rangle\text{O}$$
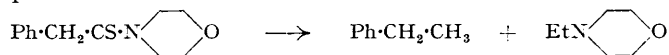
The mechanism of the reaction has not been investigated in detail but apparently involves the fission of the C–N bond followed by ethylation of the resulting amine by ethyl alcohol; alkylation of amines under similar conditions has been observed previously by Mozingo, Spencer, and Folkers (*J. Amer. Chem. Soc.*, 1944, **66**, 1859). In support of this mechanism it was shown that morpholine readily gave 4-ethylmorpholine when heated in aqueous alcohol with Raney nickel.

When the reactions were carried out in dioxan a more complex change gave mixtures of bases. From phenylthioacetomorpholide a small amount of 4-2'-phenylethylmorpholine was isolated as its picrate, and *N-cyclo*hexylphenylthioacetamide gave a low yield of *N-cyclo*hexyl-2-phenylethylamine, also isolated as its picrate.

Experimental.—Hydrogenolysis of methyl phenyldithioacetate. The ester (2·5 g.) was added to a suspension of Raney nickel (25 g.) in 80% alcohol (80 c.c.). Heat was evolved and the reaction was completed by heating for 1 hour under reflux. Water (150 c.c.) was added and the mixture distilled until most of the alcohol had been removed. From the distillate ethylbenzene (1·0 g.) separated, b. p. 136°, which gave styrene dibromide, m. p. 73°, with bromine (2 mols.) at 130°.

N-cycloHexylphenylthioacetamide. To a solution of *cyclo*hexylamine (5 g.) in alcohol (10 c.c.) was added methyl phenyldithioacetate (9·2 g.). A vigorous evolution of methanethiol took place and the reaction was completed under reflux for 10 minutes. On storage the *thioamide* crystallised as needles. Recrystallised from aqueous alcohol, it had m. p. 73—74° (10·5 g.) (Found : C, 71·6; H, 7·6; N, 6·1. $\text{C}_{14}\text{H}_{19}\text{NS}$ requires C, 72·0; H, 8·1; N, 6·0%).

Hydrogenolysis of N-cyclo*hexylphenylthioacetamide.* (a) *In alcohol.* The thioamide (3·0 g.) was added to a suspension of Raney nickel (30 g.) in 80% alcohol (100 c.c.), and the mixture refluxed for 2 hours. Nickel was filtered off and washed with a little hot alcohol. The combined filtrate and washings were acidified with hydrochloric acid, diluted with water (100 c.c.), and distilled to half volume. On dilution of the distillate with water ethylbenzene separated (0·6 g.), b. p. 136°, giving styrene di-bromide, m. p. 73°. The solution remaining in the distillation flask was evaporated to dryness under reduced pressure, and the residue dissolved in a little water, neutralised with sodium hydrogen carbonate, and picric acid (2 g.) in alcohol added. When the solution was kept at room temperature a picrate, m. p. 168—169°, crystallised out (Found : C, 45·6; H, 5·2; N, 16·2. Calc. for $\text{C}_6\text{H}_{13}\text{N,C}_6\text{H}_3\text{O}_7\text{N}_3$: C, 44·0; H, 4·9; N, 17·1. Calc. for $\text{C}_8\text{H}_{17}\text{N,C}_6\text{H}_3\text{O}_7\text{N}_3$: C, 47·2; H, 5·6; N, 15·7%).

(b) *In dioxan.* The reaction was carried out in 80% dioxan and the product worked up by the method described above. *N-cycloHexyl-2'-phenylethylamine picrate*, m. p. 140—150°, was isolated (Found : C, 54·5; H, 5·2; N, 12·4. $\text{C}_{14}\text{H}_{21}\text{N,C}_6\text{H}_3\text{O}_7\text{N}_3$ requires C, 55·2; H, 5·5; N, 12·7%).

Hydrogenolysis of phenylthioacetomorpholide. (a) *In alcohol.* Phenylthioacetomorpholide (1·5 g.) was refluxed in 80% alcohol (150 c.c.) with Raney nickel (15 g.) for 2 hours and the mixture worked up as above. A picrate, m. p. 190° (1·6 g.), was obtained as long needles (Found : C, 42·2; H, 4·8; N, 16·2. Calc. for $\text{C}_{12}\text{H}_{17}\text{ON,C}_6\text{H}_3\text{O}_7\text{N}_3$: C, 42·0; H, 4·7; N, 16·3%). Its m. p. was undepressed on admixture with 4-ethylmorpholine picrate, m. p. 190°, prepared by the method described below.

(b) *In dioxan.* This was performed as above. *4-2'-Phenylethylmorpholine picrate*, m. p. 166°, was isolated (Found : C, 51·2; H, 4·8; N, 12·9. $\text{C}_{12}\text{H}_{17}\text{ON,C}_6\text{H}_3\text{O}_7\text{N}_3$ requires C, 51·4; H, 4·8; N, 13·3%).

4-Ethylmorpholine. Morpholine (3 g.) was added to a suspension of nickel (30 g.) in 80% alcohol (100 c.c.), and the mixture refluxed for 2 hours. Nickel was filtered off and washed with hot alcohol, and the combined filtrate and washings were acidified with hydrochloric acid, then evaporated to dryness under reduced pressure. The residue was dissolved in water and neutralised with sodium

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hydrogen carbonate, and a hot solution of picric acid (3 g.) in water (50 c.c.) added. 4-Ethylmorpholine picrate crystallised, on cooling, as needles, m. p. 190° (5·0 g.).

Part of this work was carried out during the tenure of an I.C.I. Fellowship at the University of Cambridge.—UNIVERSITY CHEMICAL LABORATORY, CAMBRIDGE. THE LISTER INSTITUTE, LONDON, S.W.1. [*Received, September 8th, 1950.*]

A Method of Direct Iodination of Aromatic Compounds. By D. H. DERBYSHIRE and WILLIAM A. WATERS.

WE recently showed (*J.*, 1950, 573) that in the presence of a mineral acid aromatic compounds could readily be brominated by means of bromine and a soluble silver salt, and now report that a similar procedure is effective for direct iodination though a considerably more concentrated acid must be taken to stabilise the iodine cation. Under conditions such as those described below the active iodination cation, I^+, will react with the organic substrate as it is slowly formed and consequently we consider our iodination procedure to be both experimentally simpler and more controllable than that of Masson (*J.*, 1938, 1708) who worked with solutions of " hypoiodous cations " in concentrated sulphuric acid that had been prepared by oxidising free iodine with the requisite proportion of iodine pentoxide and obtained, in consequence, poly-iodo-derivatives.

It may now be suggested that the direct iodination of aromatic hydrocarbons by means of iodine and concentrated nitric acid (Datta and Chatterjee, *J. Amer. Chem. Soc.*, 1917, **39**, 435) or nitrosulphonic acid (Varma and Panickar, *J. Indian Chem. Soc.*, 1926, **3**, 291, 342; 1930, **7**, 503) also depends on the slight ionisation of iodine and the subsequent removal of iodide anions by oxidation, and not upon any action between the acid and the aromatic substrate.

The following preparation of *m*-iodobenzoic acid illustrates the essential details of our procedure.

Benzoic acid (13 g., 0·1 mol.), silver sulphate (16 g., 0·05 mol.), concentrated sulphuric acid (240 ml.), and a little water (30 ml.) were heated, with stirring, on a boiling water-bath. Finely powdered iodine (26 g., 0·11 mol.) was added in portions, and the heating and stirring were maintained for 80 minutes, during which silver iodide was steadily deposited. The resulting mixture was diluted to 2 l. with water, excess of iodine was removed (Na_2SO_3), and the solution was extracted with ether, as also was the solid which had separated. The extracts, after evaporation, were recrystallised from aqueous acetone and gave 20 g. (75%) of *m*-iodobenzoic acid, m. p. 185—186° (Found : C, 33·7; H, 2·1; I, 51·4. Calc. for $C_7H_5O_2I$: C, 33·9; H, 2·0; I, 51·2%).

In the absence of benzoic acid, a mixture of iodine with silver sulphate in concentrated sulphuric acid solution does not deposit silver iodide even after being kept at 100° for 12 hours. If benzene is added to such a mixture, precipitation of silver iodide occurs at room temperature.

It is essential to powder the iodine finely and to stir vigorously in order to minimise the coating of unchanged iodine particles with insoluble silver salt.—THE DYSON PERRINS LABORATORY, OXFORD. [*Received, September 9th, 1950.*]

The Optical Resolution of β-Hydroxy-β-phenylbutyric Acid. By JOAN A. REID and E. E. TURNER.

IT was shown recently (Reid and Turner, *J.*, 1949, 3365) that when acetophenone, zinc, and (−)-menthyl bromoacetate interact in the presence of benzene, the resulting Reformatsky synthesis leads to (−)-menthyl β-hydroxy-β-phenylbutyrate. Total hydrolysis of the latter gives a (+)-rotatory β-hydroxy-β-phenylbutyric acid with $[a]_{5461}^{25}$ +2·7° (*c*, 7·74) or +3·15° (*c*, 14·35) in absolute ethyl alcohol, the specific rotation of the acid varying only slightly with change in conditions of the Reformatsky reaction.

In order to discover the approximate extent of this asymmetric synthesis it was necessary to resolve the racemic hydroxy-acid. This has now been done through the morphine salts, and it is considered that the (−)-acid has been obtained in a state of optical purity, having $[a]_{5461}^{23}$ −8·9° in absolute ethyl alcohol (*c*, 1·75), that is, approximately three times that of the Reformatsky product. The purest (+)-acid obtained had $[a]_{5461}^{23}$ +7·5°. The partial racemate appears to have solubilities in water and ethyl alcohol very similar to those of the diastereoisomerides and particularly to have a solubility similar to that of the morphine salt of the (+)-acid.

Experimental.—The (±)-acid (9·0 g., 1 mol.) and morphine monohydrate (15·1 g., 1 mol.) were dissolved in 300 c.c. of hot water. After some hours, 15·5 g. of salt separated with $[a]_{5780}^{20}$ −81·3°. Five crystallisations of this salt from water gave a *morphine* salt, in rhombic prisms, $[a]_{5780}^{20}$ −68·2° and $[a]_{5461}^{20}$ −76·9° in water (*c*, 0·9820) (Found : C, 68·3; H, 6·9. $C_{17}H_{19}O_3N,C_{10}H_{12}O_3,0·5H_2O$ requires C, 68·3; H, 6·8%). The salt was shaken with chloroform and dilute alkali. The aqueous solution was extracted three times with chloroform and then once with ether. It was then acidified and extracted five times with ether. The combined ether layers were washed twice with water and evaporated. The residue became crystalline after some time and was recrystallised from light petroleum (b. p. 80—100°). It had m. p. 71—72°, $[a]_{5780}^{20}$ +6·3° and $[a]_{5461}^{20}$ +7·5°, in absolute ethyl alcohol (*c*, 1·660) (Found : C, 66·8; H, 7·0. Calc. for $C_{10}H_{12}O_3$: C, 66·6; H, 6·7%).

Concentration of the original morphine salt mother-liquor, followed by repeated crystallisation from water, gave a morphine salt, in spherical nodules, $[a]_{5780}^{21}$ −87·8° and $[a]_{5461}^{21}$ −99·7° in ethyl alcohol, but material with this approximate rotation was more readily obtained by carrying out a partial resolution in water, as described above, and then recrystallising, from absolute alcohol, crops with a specific

rotation of about $[a]_{5780}$ $-75°$. This led to what is apparently the *morphine* salt of the pure $(-)$-acid, having $[a]_{5780}^{26}$ $-90·3°$ and $[a]_{5461}^{26}$ $-103·4°$ in water (c, 1·000) (Found: C, 69·3; H, 6·8. $C_{17}H_{19}O_3N,C_{10}H_{12}O_3$ requires C, 69·6; H, 6·7%). The rotation of the salt was unchanged by recrystallisation.

Decomposition of the salt in the manner described above gave the $(-)$-acid, which after being crystallised from light petroleum (b. p. 80—100°) had m. p. 79—80°, $[a]_{5780}^{23}$ $-8·0°$, $[a]_{5461}^{23}$ $-8·9°$ in absolute ethyl alcohol (c, 1·7544) (Found: C, 66·8; H, 7·0%). Recrystallisation from light petroleum did not alter the specific rotation.

An attempt to obtain one morphine salt preferentially by using racemic acid and morphine salt in the molecular ratio 3 : 1, in either aqueous or alcoholic solution, was unsuccessful. Brucine formed a well-crystallised salt from aqueous solution, but led to no appreciable resolution.