CCCI.—*The Optically Active Diphenylhydroxyethylamines and* iso*Hydrobenzoins. Part II.*

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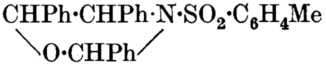
THE introductory paper (J., 1927, 910), dealing with the stereoisomeric bases of the constitution HO·CHPh·CHPh·NH_2, described the optical resolution of *dl*-diphenylhydroxyethylamine, and drew attention to the importance of the optically active forms of *iso*diphenylhydroxyethylamine as sources of *d*- and *l*-*iso*hydrobenzoin. In continuing this work, the pure *l*- and *d*-*iso*-bases have been readily prepared by successively treating the *dl*-*iso*-base with *d*-tartaric acid and *d*-camphor-10-sulphonic acid; the value $[\alpha]_D \pm 133{\cdot}5^\circ$, recorded for the active bases, indicates that Erlenmeyer's preparations, obtained with the aid of helicin or *d*-tartaric acid, and having $[\alpha]_D \pm 109{\cdot}7^\circ$, were optically impure (compare Read and Steele, *loc. cit.*, p. 916, footnote; Ingersoll, *J. Amer. Chem. Soc.*, 1928, **50**, 2264). The *dl*-*iso*-base resembles *dl*-diphenylhydroxyethylamine in forming a partly racemic salt with *d*-α-bromocamphor-π-sulphonic acid.

By treating comparatively large amounts of *d*- and *l*-*iso*diphenylhydroxyethylamine with nitrous acid, *d*- and *l*-*iso*hydrobenzoin have now been prepared in sufficient quantity to permit of accurate characterisation. The optical rotation, $[\alpha]_D \pm 92{\cdot}0^\circ$, observed in alcoholic solution, is slightly higher than the value previously recorded; the sense of the rotation of the original *iso*hydrobenzoin is preserved in the benzylidene and acetone derivatives and reversed in the diacetate, while in all three instances the numerical values are lower than for the parent substance.

Attempts were made to improve the low yields of *iso*hydrobenzoin obtained in the above process by using monoacetyl-*dl*-*iso*diphenylhydroxyethylamine (m. p. 152°) in place of the free base, as it was anticipated that this substance would react smoothly with nitrous acid to give monoacetyl-*dl*-*iso*hydrobenzoin. As a result, it was found that the derivative reacted neither with nitrous acid nor with benzaldehyde. That it had the constitution CHPh(OAc)·CHPh·NH_2, and not CHPh(OH)·CHPh·NHAc, was shown by its capacity to form a well-defined hydrochloride; moreover, acetylated benzylidene-*dl*-*iso*diphenylhydroxyethylamine, CHPh(OAc)·CHPh·N:CHPh, yielded the same substance (m. p. 152°) when decomposed with bromine in alcohol. The inert character of the amino-group in the *O*-acetyl derivative is possibly due to spatial circumstances: the *O*-*p*-toluenesulphonyl derivative of the *dl*-base (m. p. 142—145°) failed even to form a hydrochloride, being insoluble in warm dilute mineral acids.

The benzylidene derivative of the *dl*-base reacted in pyridine solution with *p*-toluenesulphonyl chloride, forming a mixture of two derivatives, each of which gave analytical results corresponding to *O*-*p*-toluenesulphonylbenzylidene-*dl*-*iso*diphenylhydroxyethylamine. The less soluble, colourless substance (m. p. 179°) did not react with bromine in alcohol; but the isomeride, which formed yellow needles (m. p. 173—174°), was hydrolysed by this reagent, with the production of the *O*-*p*-toluenesulphonyl derivative (m. p. 142—145°). Possibly, therefore, the two derivatives correspond, respectively, to the formulæ  $\begin{array}{c}\mathrm{CHPh{\cdot}CHPh{\cdot}N{\cdot}SO_2{\cdot}C_6H_4Me} \\ \diagdown\mathrm{O{\cdot}CHPh}\diagup\end{array}$ and $\mathrm{CHPh(O{\cdot}SO_2{\cdot}C_6H_4Me){\cdot}CHPh{\cdot}N{:}CHPh}$. In the case of the methyleneecamphor derivative of the base, the hydroxyl group is inert, possibly on account of the spatial interference of the substituent attached to the adjacent nitrogen atom.

In the preliminary communication, reference was made to the apparently incomplete resolution of *dl*-*iso*hydrobenzoin achieved by the mechanical separation of *d*- and *l*-crystals which had been deposited from solutions in ether (Erlenmeyer, *Ber.*, 1897, **30**, 1531). In carrying out the necessary reinvestigation of the subject, we show below that crystals of pure *d*- and *l*-*iso*hydrobenzoin, when deposited from ethyl acetate, exhibit characteristic hemihedral facets; when chloroform is used as solvent, however, the distinctive facets are not developed. In agreement with these observations, pure *dl*-*iso*hydrobenzoin, when crystallised from ethyl acetate, separates as a conglomerate of enantiomorphously related crystals, composed of *d*- and *l*-*iso*hydrobenzoin, respectively; but the crystals deposited from chloroform are morphologically indistinguishable from one another so far as plane faces are concerned. The latter crystals, however, have been shown by polarimetric examination to be also of two kinds, consisting again of the pure *d*- and *l*-forms; moreover, despite the absence of plane hemihedral facets, segregation is here rendered possible through the circumstance that either the right or the left side of each crystal displays a marked tendency to degenerate into curved boundaries. This tendency is not evident in crystallising the separate *d*- and *l*-forms from chloroform. In brief, therefore, the cleavage of *dl*-*iso*hydrobenzoin into *d*- and *l*-forms, separating in distinct crystals, is definite and complete in both solvents, but is more obvious from ethyl acetate, since the hemihedry is here formally declared by the development of distinctive plane facets.

It was shown in the preceding paper that the specimens of optically active *iso*hydrobenzoin obtained by Erlenmeyer in a similar manner were mixtures, containing at the most 54% of one component. The fission, hitherto accepted as complete, was thus demonstrated to be incomplete. Upon the evidence then available, the explanation of this circumstance was sought in the possible formation of mixed crystals possessing hemihedral facets, particularly as formyl-*dl*-*neo*menthylamine appears to offer an example of this kind. It is now evident, however, that from the solvents which we have studied, *dl*-*iso*hydrobenzoin crystallises as a conglomerate, a conclusion which is not incompatible with the form of the melting-point curve observed for mixtures of *d*- and *l*-*iso*hydrobenzoin (J., 1927, 912), when the difficulty of securing entirely satisfactory experimental values is taken into account. Thus, although Erlenmeyer's original fission of *dl*-*iso*hydrobenzoin by the method of " spontaneous separation of enantiomerides " was only partly accomplished, the present investigation shows that this substance may be accepted as providing a striking example of Pasteur's first method of optical resolution.

The low rotatory powers shown by Erlenmeyer's material, which was deposited from ether, may possibly be associated with the tendency of the enantiomorphous crystals of *d*- and *l*-*iso*hydrobenzoin to form twins. This behaviour was originally observed by Bodewig (*Annalen*, 1876, **182**, 279), and it appears to be favoured by the use of ether as solvent. Our observations indicate that such crystals cannot be dissevered so as to yield optically pure material. In a recent paper by Reis and Schneider (*Z. Krist.*, 1928, **69**, 62), a further reference is made to the crystallisation of *dl*-*iso*hydrobenzoin from ether. The crystals, like those obtained by us from chloroform, displayed no hemihedral facets, but they were shown to be pyroelectric : this behaviour, in the case of a monoclinic crystal, proves the class to be enantiomorphous. The melting point of a single powdered crystal was 146—147°. It appears, therefore, that from ether, as well as from ethyl acetate and chloroform, *dl*-*iso*hydrobenzoin separates as a conglomerate.

The detailed observations given below on the forms of *d*- and *l*-*iso*hydrobenzoin deposited from various solvents have some bearing on the frequently argued question whether molecularly enantiomorphous substances necessarily crystallise in enantiomorphous forms (see, *e.g.*, Werner, " Lehrbuch der Stereochemie," 1904, p. 36; Stewart, " Stereochemistry," 1919, p. 38). The enantiomorphism of crystal structure in such instances is presumably not in doubt, since it is impossible to arrange wholly dextro- or wholly lævo-particles in such a way as to confer on the assemblage the property of identity with its mirror-image. Fine details of crystal structure are, however, still largely a matter for speculation except in very simple molecules.* What is really of practical interest in organic chemistry is to know whether it is possible to establish molecular enantiomorphism from a study of crystal form.

If this question be posed as a matter of principle (the so-called Pasteur principle), the answer must take the form of a negative. There is nothing in the undoubted enantiomorphism of structure of *d*- and *l-iso*hydrobenzoin crystals which categorically demands plane-faced boundaries, still less facets indicating right- or left-handedness. The nature of the forces controlling crystal forms, it must be admitted, are still so obscure that it remains a matter for surprise that a crystal has a definite shape at all.

Thus, at the present time, the only question which can be raised is that of the frequency with which enantiomorphism of structure unfolds itself on the surface. The student of minerals is familiar with the very rare occurrence of quartz crystals which happen to show enantiomorphous " hemihedrism." Similarly, in the province of complex carbon compounds, this much-prized type of declared hemihedrism is a good deal rarer than is generally supposed, since in many cases it stands revealed only after repeated attempts at crystallisation, possibly with changes of solvent: such laboratory experiments are analogous to the untiring efforts of the mineralogist to study finds from new localities.

One contributory cause to this simulation of higher symmetry is no doubt the circumstance that the solubility (or surface tension, or a close texture of atoms, or whatever it is that produces a plane boundary) has almost equal values for right- and left-handed facets; so that it is the rule rather than the exception for such facets to accompany each other. Crystals of *d*- and *l-iso*hydrobenzoin show this tendency in a high degree. The set of planes *a*, *m*, *M*, *c*, *R* are evidently highly favoured, since they appear on all crystals from all solvents used. It is important to note that even at this low stage of development the crystals have, as it were, taken the necessary steps to disguise their hemihedral nature; for there is nothing in the structure that demands the appearance of *m* in presence of *M*, or

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* There does not appear to be on record in the *X*-ray literature a single case in which an optically active substance is proved to possess an enantiomorphous configuration. When critically examined, the conclusions drawn from researches which have been made in this direction are seen to rest not on the *X*-ray experiments but on postulates which can only be accepted in so far as they are based on the evidence of physico-chemical methods. In the domain of enantiomorphism especially, the *X*-ray method labours under such heavy disabilities that the property and all its chemical consequences would still remain unknown if progress had depended on this method of investigating crystal structure.

vice versâ. Only with the appearance of the planes q and Q is there a marked tendency to reveal the latent enantiomorphism, the conditions becoming even more helpful with the appearance of O, which is never observed with its enantiomorph o. It is further to be noted that both in the case under discussion and in that of formyl-*dl*-*neo*menthylamine, previously studied (J., 1926, 2219, 2228), the differentiation of *d*- and *l*-forms seems to be facilitated by the presence in solution of the opposite kind of molecule. Whether this is, indeed, a general property might be explored further by crystallising sodium ammonium *d*-tartrate and *dl*-tartrate under identical conditions.

The main conclusion concerning the crystal form of enantiomorphous molecules would therefore seem to be that the success attending any attempt to separate two forms from a crystallising conglomerate depends mainly on the amount of time the observer is prepared to expend in varying the conditions of crystallisation. It is of course presupposed that he has the power to see what is there: it will presumably forever remain unknown whether Mitscherlich's historic failure to distinguish between the two kinds of sodium ammonium tartrate, three years before Pasteur's memorable discovery, was due to an absence of hemihedral facets, or to the simultaneous development on each crystal of *d*- and *l*-facets, or to incomplete observation.

EXPERIMENTAL.

Preparation of d- *and* l-iso*Diphenylhydroxyethylamine.*—1. The first fraction obtained in the resolution of *dl*-*iso*diphenylhydroxyethylamine with *d*-tartaric acid (*Annalen*, 1904, **337**, 321; J., 1927, 916), when recrystallised several times from boiling water, gave pure *l*-*iso*diphenylhydroxyethylamine hydrogen *d*-tartrate, m. p. 177°, $[\alpha]_D - 42{\cdot}6°$, $[M]_D - 155°$, $[\alpha]_{5461} - 52{\cdot}6°$, $[M]_{5461} - 191°$ (c 1·0, water). The pure *l*-base liberated from this salt had m. p. 115°, $[\alpha]_D - 133°$ (c 1·25, absolute alcohol); it yielded a hydrochloride with m. p. 204°, $[\alpha]_D - 83{\cdot}7°$, $[M]_D - 209°$ (c 1·0, water). The crude *d*-base furnished by the original mother-liquor from this resolution had $[\alpha]_D + 109°$. The first separation of salt obtained on crystallising from boiling water a mixture of this base with an equivalent quantity of *d*-camphor-10-sulphonic acid had, after drying at 100°, $[\alpha]_D + 60{\cdot}4°$, $[M]_D + 269°$, $[\alpha]_{5461} + 69{\cdot}0°$, $[M]_{5461} + 307°$ (c 1·0, water); it thus consisted of pure *d*-*iso*diphenylhydroxyethylamine *d*-camphor-10-sulphonate (compare Ingersoll, *J. Amer. Chem. Soc.*, 1928, **50**, 2264). The pure *d*-base obtained by decomposing this salt with aqueous ammonia had m. p. 115°, $[\alpha]_D + 134°$ (c 1·25, absolute alcohol). The immediate yields of pure *d*- and *l*-base prepared according to this method were, respectively, about 55% and 70% of the amounts theoretically possible.

2. Upon mixing equivalent weights of *dl-iso*diphenylhydroxyethylamine and *d*-camphor-10-sulphonic acid in hot water, the first fraction of salt which separated on cooling had $[\alpha]_D + 55{\cdot}0°$ (*c* 1·0, water); a second fraction, obtained on concentrating the solution, had $[\alpha]_D - 25{\cdot}0°$. The first fraction yielded pure *d-iso*diphenylhydroxyethylamine *d*-camphor-10-sulphonate after one recrystallisation from hot water; three similar recrystallisations of the second fraction gave pure *l-iso*diphenylhydroxyethylamine *d*-camphor-10-sulphonate (compare Ingersoll, *loc. cit.*, p. 2266), having m. p. 205°, $[\alpha]_D - 35{\cdot}7°$, $[M]_D - 159°$ (*c* 1·0, water; salt dried at 100°). The yields of the pure *d*- and *l*-base were much less than those afforded by the first process of resolution; the respective values of $[\alpha]_D$ observed for the preparations made by the second process were + 130° and − 129° (*c* 1·25, absolute alcohol).

3. When the hydrochloride of *dl-iso*diphenylhydroxyethylamine was treated in aqueous solution with half an equivalent proportion of ammonium *d*-camphor-10-sulphonate, the first separation consisted of optically pure *d-iso*diphenylhydroxyethylamine *d*-camphor-10-sulphonate, but the resulting yield of the pure *d*-base was inferior to that obtained by the first process.

Crystallisation of d-, l-, *and* dl-iso*Diphenylhydroxyethylamine with* d-α-*Bromocamphor*-π-*sulphonic Acid.*—Pure d-iso*diphenylhydroxyethylamine* d-α-*bromocamphor*-π-*sulphonate* was prepared from the component acid and base; it crystallised from water in hard, glistening, inch-long needles, having m. p. 220° (decomp.), $[\alpha]_D + 94{\cdot}0°$, $[M]_D + 493°$ (*c* 0·5, water). The salt was anhydrous (Found: *M*, by titration, 523·5. $C_{24}H_{30}O_5NBrS$ requires *M*, 524). l-iso*Diphenylhydroxyethylamine* d-α-*bromocamphor*-π-*sulphonate* was prepared analogously; it was more soluble in water than the foregoing salt, and formed small soft needles, m. p. 210° (decomp.), $[\alpha]_D + 15{\cdot}9°$, $[M]_D + 83{\cdot}3°$ (*c* 0·5, water). It was anhydrous (Found: *M*, by titration, 527·7).

Upon attempting to resolve the *dl*-base by means of the above *d*-acid, the first fraction of the salt, consisting of hard glistening needles, had $[\alpha]_D + 51{\cdot}7°$, $[M]_D + 271°$. This value remained practically unaltered after repeated fractional crystallisation from hot water, and the regenerated specimens of the base were optically inactive: the product was therefore regarded as the partly racemic salt, dl-iso*diphenylhydroxyethylamine* d-α-*bromocamphor*-π-*sulphonate* (Found: *M*, by titration, 524·0).

Derivatives of d-, l-, *and* dl-iso*Diphenylhydroxyethylamine.*—According to Erlenmeyer (*Annalen*, 1904, **337**, 348), the *dl*-base when warmed with an excess of acetyl chloride in benzene yields the hydrochloride of the *O*-monoacetyl derivative. A better result was obtained by using somewhat more than the calculated quantity of acetic anhydride in place of acetyl chloride. *O*-Acetyl-*dl*-*iso*diphenylhydroxyethylamine separated from benzene in fine silky needles, m. p. 152°. It gave no reaction with nitrous acid. It failed also to react with benzaldehyde in hot alcoholic solution, or when heated with the aldehyde at 140° under diminished pressure in an atmosphere of carbon dioxide. The mixed derivative was obtained, however, by boiling benzylidene-*dl*-*iso*diphenylhydroxyethylamine (*Annalen*, 1899, **307**, 121) with an excess of acetic anhydride; the resulting *acetylbenzylidene*-dl-iso*diphenylhydroxyethylamine* crystallised from alcohol in lustrous prisms, m. p. 114° (Found: C, 80·4; H, 6·1. $C_{23}H_{21}O_2N$ requires C, 80·5; H, 6·1%). Upon treatment in warm rectified spirit with bromine, this derivative gave *O*-monoacetyl-*dl*-*iso*diphenylhydroxyethylamine, m. p. 152°, described above. O-*Acetyl*-l-iso*diphenylhydroxyethylamine* had m. p. 158°, $[\alpha]_D$ − 6·3° (*c* 1·25, absolute alcohol) (Found: C, 75·1; H, 6·8. $C_{16}H_{17}O_2N$ requires C, 75·2; H, 6·7%). O-*Acetyl*-l-iso*diphenylhydroxyethylamine hydrochloride*, prepared by dissolving the derivative (2 g.) in boiling 3*N*-hydrochloric acid (25 c.c.), formed small needles, m. p. 190°, $[\alpha]_D$ − 32·8° (*c* 1·1, water). The aqueous solution yielded *O*-acetyl-*l*-*iso*diphenylhydroxyethylamine upon treatment with ammonia (Found: Cl, by titration, 12·8. $C_{16}H_{18}ONCl$ requires Cl, 12·2%).

When boiled for a few minutes with acetic anhydride, the bases yielded diacetyl derivatives; these substances, which were insoluble in hot water, separated from aqueous alcohol in small needles, and had the following constants: diacetyl-*dl*-*iso*diphenylhydroxyethylamine, m. p. 118°; *diacetyl*-l-iso*diphenylhydroxyethylamine*, m. p. 127°, $[\alpha]_D$ + 27·7° (*c* 1·25, absolute alcohol) (Found: C, 71·6; H, 6·5. $C_{18}H_{19}O_3N$ requires C, 72·7; H, 6·4%). When allowed to separate slowly from cold alcoholic solutions, diacetyl-*dl*-*iso*diphenylhydroxyethylamine formed well-developed elongated prisms; no optical activity was observed upon dissolving individual crystals in absolute alcohol and examining the solution in sodium light (0·01 g. in 30 c.c.; 4-dcm. tube). When warmed in aqueous acetone with one equivalent of *N*-sulphuric acid, diacetyl-*l*-*iso*diphenylhydroxyethylamine readily yielded *O*-acetyl-*l*-*iso*diphenylhydroxyethylamine, identical with the substance described above; the last-named compound, when boiled with concentrated hydrochloric acid, was hydrolysed further with regeneration of the *l*-base. According to Erlenmeyer (*loc. cit.*, p. 349), the optically active monoacetyl derivatives undergo racemisation in boiling alcoholic solution; no change in rotatory power was observed, however, upon treating the mono- or di-acetyl derivatives of the *l*-base in this way for several hours. Moreover, the free base, recovered by hydrolysis, exhibited the full rotatory power.

O-p-*Toluenesulphonyl*-dl-iso*diphenylhydroxyethylamine*, prepared by the interaction of the free base and *p*-toluenesulphonyl chloride in pyridine at the ordinary temperature, crystallised from alcohol in fine colourless needles, m. p. 142—145° (Found: C, 68·5; H, 5·7. $C_{21}H_{21}O_3NS$ requires C, 68·7; H, 5·7%). This substance was insoluble in warm dilute hydrochloric acid, and it failed to react with benzaldehyde. On the other hand, when benzylidene-*dl-iso*-diphenylhydroxyethylamine was mixed with *p*-toluenesulphonyl chloride in pyridine, reaction occurred slowly at the ordinary temperature. The crude yellow product (20·5 g.) when crystallised from acetone yielded colourless needles (12·3 g.), m. p. 179°, consisting of O-p-*toluenesulphonylbenzylidene*-dl-iso*diphenylhydroxyethylamine* (Found: C, 73·5; H, 5·6. $C_{28}H_{25}O_3NS$ requires C, 73·8; H, 5·5%). This substance remained unaffected when treated with bromine in warm rectified spirit. From the above acetone mother-liquors an isomeric O-p-*toluenesulphonylbenzylidene*-dl-iso*diphenylhydroxyethylamine* was isolated (3·5 g.); this formed fine yellow needles, m. p. 173—174° (Found: C, 73·5; H, 5·7%). When treated with bromine in warm rectified spirit, it was hydrolysed with the formation of *O-p*-toluenesulphonyl-*dl-iso*diphenylhydroxyethylamine, m. p. 142—145°. The latter derivative readily underwent acetylation when boiled with acetic anhydride; N-*acetyl*-O-p-*toluenesulphonyl*-dl-iso*diphenylhydroxyethylamine* crystallised from alcohol in small colourless plates, m. p. 161—162° (Found: C, 67·3; H, 5·8. $C_{23}H_{23}O_4NS$ requires C, 67·5; H, 5·6%).

d-iso*Diphenylhydroxyethylamino*-d-*methylenecamphor*, when prepared and purified in the usual way (J., 1913, **103**, 444), separated from ether–light petroleum in colourless glistening prisms, m. p. 168°, $[\alpha]_D + 144°$ (*c* 1·25, alcohol), rising after 48 hours to + 179° (Found: C, 79·6; H, 8·0. $C_{25}H_{29}O_2N$ requires C, 80·0; H, 7·8%). When titrated with bromine in warm rectified spirit, this substance reacted normally, with the formation of *d*-bromo-oxymethylenecamphor and *d-iso*diphenylhydroxyethylamine hydrobromide (Found: Br, 27·8. Calc.: Br, 27·2%). It was sought, without definite result, to acetylate the methylenecamphor derivative, and also to cause it to react with *p*-nitrobenzoyl chloride, 3 : 5-dinitrobenzoyl chloride, hydrobromic acid, and hydriodic acid.

O-Benzoyl-*l-iso*diphenylhydroxyethylamine, prepared as indicated by Erlenmeyer, had m. p. 215°, $[\alpha]_D - 38·5°$ (*c* 1·25, methyl alcohol) and − 24·6° (*c* 1·25, acetone): Erlenmeyer's preparation, having $[\alpha]_D$ −29·0° in methyl alcohol, was therefore optically impure, a result which may be correlated with the preparation of a series of optically active derivatives (*loc. cit.*) from an optically impure base, having $[\alpha]_D$ about − 110° instead of about − 130°. The following derivatives of the *l*-base were also prepared, the corresponding externally compensated substances having been described by Erlenmeyer (*loc. cit.*, p. 344 *et seq.*). *O-p*-Nitrobenzoyl-*l-iso*diphenylhydroxyethylamine separated from alcohol in yellow needles, m. p. 132°, $[\alpha]_D$ − 48·3° (*c* 1·25, absolute alcohol), and − 28·6° (*c* 1·25, acetone). The salicylidene derivative crystallised from alcohol in pale yellow plates, m. p. 132—134°, $[\alpha]_D$ − 91·5° (*c* 1·25, absolute alcohol) and − 74·8° (*c* 1·25, acetone). The anisylidene derivative crystallised from alcohol in colourless glistening needles, m. p. 152°, $[\alpha]_D$ − 72·4° (alcohol) and − 51·1° (acetone). The similar piperonylidene derivative had m. p. 144°, $[\alpha]_D$ − 83·3° (alcohol) and − 175° (acetone). The 4-hydroxy-3-methoxybenzylidene derivative formed pale yellow needles, m. p. 155°, $[\alpha]_D$ − 84·4° (alcohol) and −53·0° (acetone). The *l*-base condensed with acetoacetic ester, yielding a syrupy liquid, having $[\alpha]_D$ − 135° (alcohol) and − 74·1° (acetone).

l-iso*Hydrobenzoin and Derivatives.*—Among many modifications of the original treatment of the above bases with nitrous acid (J., 1927, 916), the following was found to give the best yields of *iso*hydrobenzoin. An ice-cooled solution of *l-iso*diphenylhydroxyethylamine (5 g.) in somewhat more (25 c.c.) than the calculated quantity of *N*-sulphuric acid was diluted with about twice its volume of water. After careful titration with a slight excess of aqueous sodium nitrite (1·8 g. in 50 c.c.), the mixture was kept cold for ½ hour; about two equivalents (50 c.c.) of *N*-sulphuric acid were then added, and the mixture was heated on the water-bath for several hours. After cooling over-night, the aqueous liquid contained a suspension of small colourless needles, together with a larger quantity of a thick oil. The crystals (0·5 g.), which were readily separated, melted at 130—136°; and by extracting the oil with ether a further quantity (0·15 g.) of identical crystalline material was obtained. Altogether, 7·5 g. of crude *l-iso*hydrobenzoin were prepared in this way, only 5 g. of base being used in each operation. After decolorisation with charcoal in benzene, it crystallised from this solvent in small transparent leaflets, m. p. 146°, $[\alpha]_D$ −92·0°, $[\alpha]_{5461}$ − 111° (*c* 1·25, absolute alcohol). *l-iso*Hydrobenzoin is very soluble in methyl or ethyl alcohol, acetone, or ethyl acetate; readily soluble in warm chloroform; and moderately easily soluble in warm benzene or ether. It is deposited from ether in opaque prisms attaining an inch in length, but the best crystals are formed when it separates slowly from chloroform or ethyl acetate at the ordinary temperature (*vide infra*).

Diacetyl-l-iso*hydrobenzoin*, prepared by boiling *l-iso*hydrobenzoin for 5 minutes with a large excess of acetic anhydride, crystallised from alcohol in long colourless prisms, m. p. 109—110°, $[\alpha]_D + 26{\cdot}9°$ (*c* 0·6, alcohol) (Found : C, 72·5; H, 6·2. $C_{18}H_{18}O_4$ requires C, 72·5; H, 6·1%). *Benzylidene*-l-iso*hydrobenzoin* was made by keeping a solution of *l-iso*hydrobenzoin (1 g.) in freshly distilled benzaldehyde (10 c.c.) in an atmosphere of carbon dioxide at 140° for ½ hour; the excess of benzaldehyde was distilled off under diminished pressure, and the residual product was poured into light petroleum and recrystallised from absolute alcohol. It formed fine, colourless needles, m. p. 70·5°, $[\alpha]_D - 27{\cdot}6°$ (*c* 1·25, alcohol) (Found : C, 83·5; H, 6·1. $C_{21}H_{18}O_2$ requires C, 83·4; H, 6·0%). *Benzylidene*-dl-iso*hydrobenzoin*, prepared similarly, melted at 84° (Found : C, 83·5; H, 6·0%).

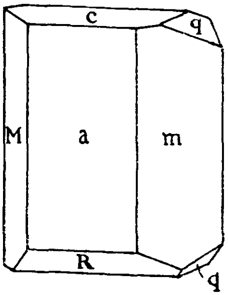
d-iso*Hydrobenzoin and Derivatives.*—About 6 g. of *d-iso*hydrobenzoin were prepared by the action of nitrous acid on *d-iso*diphenylhydroxyethylamine, in the way described above; it had m. p. 146°, $[\alpha]_D + 92{\cdot}0°$ (*c* 1·25, absolute alcohol); $[\alpha]_D + 101°$, $[\alpha]_{5461} + 121°$ (*c* 1·2, acetone); $[\alpha]_D + 111°$, $[\alpha]_{5461} + 133°$ (*c* 1·4, ethyl acetate); $[\alpha]_D + 99{\cdot}1°$, $[\alpha]_{5461} + 121°$ (*c* 0·8, chloroform); $[\alpha]_D + 128°$, $[\alpha]_{5461} + 166°$ (*c* 0·3, benzene). *d-iso*Hydrobenzoin is sparingly soluble in boiling water, less than 0·04 g. being dissolved by 20 c.c.; long, fine needles separate from the solution on cooling. The substance (1 g.) yielded an *acetone* derivative when kept for 48 hours in acetone (20 c.c.) containing 1% of acid. Upon distilling away the solvent in presence of an excess of barium carbonate and extracting the derivative with dry ether, it was obtained in small colourless prisms, m. p. 48°, $[\alpha]_D + 65{\cdot}2°$ (*c* 0·75, alcohol) (Found : C, 80·2; H, 7·1. $C_{17}H_{18}O_2$ requires C, 80·3; H, 7·1%).

The Crystallisation of d- *and* l-iso*Hydrobenzoin.*—Well-developed crystals suitable for goniometric examination were readily obtained by allowing *d-* or *l-iso*hydrobenzoin to separate slowly at the ordinary temperature from solutions in ethyl acetate or chloroform; with the latter solvent, the crystals are specifically lighter than their mother-liquor. The main observations are summarised below.

d-iso*Hydrobenzoin*. Crystals of this optical modification from an ethyl acetate solution are somewhat elongated, as shown in Fig. 1, and generally reveal the symmetry of the enantiomorphous class of the monoclinic system by the presence at the right side (*i.e.*, the crystal's left side) only of a pair of *q*-facets, the full combination being *a*(100), *m*(110), *M*($1\bar{1}0$), *c*(001), *R*($\bar{1}01$) and *q*(011). Two crystals measured on the two-circle goniometer gave angular values within a few minutes of those cited by Bodewig (*loc. cit.*).

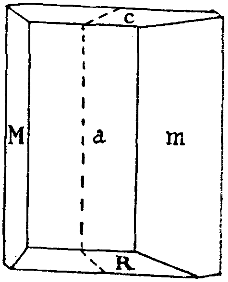
Although the above combination may be regarded as normal, other styles of development are occasionally favoured. Out of a crop of twenty crystals examined in detail, no fewer than thirteen had the normal development; five showed no q-facets, thus appearing to exhibit the plane of symmetry indicated by broken lines in Fig. 2; and two, in addition to right-handed q-faces, exhibited left-handed facets, $Q(0\bar{1}1)$, whereby the crystals again appeared to have the symmetry plane previously mentioned.

FIG. 1.



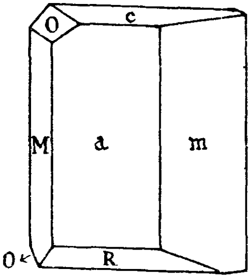
d-iso*Hydrobenzoin.*

FIG. 2.



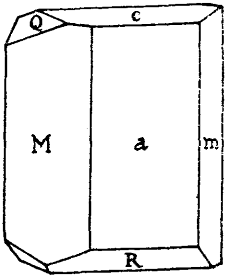
d-iso*Hydrobenzoin.*

FIG. 3.



d-iso*Hydrobenzoin.*

FIG. 4.



l-iso*Hydrobenzoin.*

From a solution in chloroform, the crystallisation is somewhat different. Of twenty-nine crystals belonging to a crop examined in detail, twenty-three exhibited the simple combination a, m, M, c, R, while the remaining six exhibited a new form $O(1\bar{1}1)$ on the left side, as shown in Fig. 3.

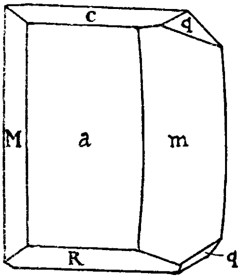
l-iso*Hydrobenzoin.* Crystals from ethyl acetate generally behaved in the opposite sense to the foregoing enantiomeride. Of a crop of twenty crystals, fifteen exhibited the combination a, m, M, c, R, Q, as shown in Fig. 4; four exhibited the simple combination *a*, *m*, *M*, *c*, *R* of Fig. 2; and one developed in addition *q* and *Q* simultaneously.

From a solution in chloroform, the whole of a crop of about twenty crystals exhibited the simple combination *a*, *m*, *M*, *c*, *R*, a right-handed form *o*(111) in no case being observed, although its appearance was to be occasionally expected from the previous study of the *d*-enantiomeride.

The Crystallisation of dl-iso*Hydrobenzoin*.—Externally compensated *iso*hydrobenzoin was prepared by evaporating to dryness an alcoholic solution of equal weights of the *d*- and *l*-components; the resulting material melted at 119° and was optically inactive (*c* 3·0, absolute alcohol).

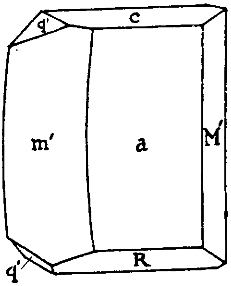
Crystallisation from ethyl acetate. Measurements of the first few crystals examined established their essential identity with the crystals of the foregoing *d*- and *l*-modifications, the main difference being the presence of curved faces. Some of the crystals were joined together in pairs, but generally without any recognisable regularity; in such cases the individuals were cut apart for study and measurement. A single crop of crystals was thus separated into nine right-handed crystals (*i.e.*, crystals carrying a pair of *q*-facets on the right side), four left-handed crystals, and one crystal which was provisionally held to consist of dextro-material, since it exhibited large *q*-facets, small *Q*-facets and the form $O(1\bar{1}1)$ previously observed on *d*-*iso*hydrobenzoin.

FIG. 5.



d-iso*Hydrobenzoin*.

FIG. 6.



l-iso*Hydrobenzoin*.

The above segregation into *d*- and *l*-individuals (subsequently proved correct in every case tested by the polarimeter) was facilitated by the pronounced curvature of the *q*- and *m*-faces, as shown diagrammatically from enantiomorphous standpoints in Figs. 5 and 6. Further, among the pairs grown together, at least one example of the " Siamese twinning " observed by Bodewig was established by measurement. Another pair was found to be a regular union in which *a*(100), instead of *b*(010), is the twin- and composition-plane.

Several individual crystals of each kind, averaging 0·03 g. in weight, were examined polarimetrically in absolute alcoholic solution (30 c.c.) in a 4-dcm. tube, with the following results: dextro-oriented crystals, $[\alpha]_D$ + 92·0°, + 90·1°; lævo-oriented crystal, $[\alpha]_D$ − 89·0°. The largest dextro-oriented crystal examined, weighing 0·0809 g., gave α_D + 1·06°, $[\alpha]_D$ + 98·3°. The crystal with large *d*-facets and small *l*-facets was shown to consist of pure *d*-*iso*hydrobenzoin. The melting point in all these instances was 146°. A crystal having lævo-oriented curved facets gave $[\alpha]_D$ − 75·6°, while another with both lævo plane and lævo curved facets gave $[\alpha]_D$ − 76·6°. The Siamese twin broke up when cut apart, but the portions were segregated as completely as possible: the dextro-oriented portion had $[\alpha]_D$ + 44·5° and the other portion had $[\alpha]_D$ − 59·2°, the respective melting points being about 124—130° and 124—142°.

Crystallisation from chloroform. The crystals deposited from a solution of *dl*-*iso*hydrobenzoin in chloroform were similar to those of pure *d*- or *l*-*iso*hydrobenzoin from the same solvent, in that they exhibited no plane hemihedrism. In every crystal examined, however, either the right or the left side showed a pronounced tendency to degenerate into curved boundaries, and it was found possible to utilise this morphological peculiarity in effecting a segregation. That the individuals were of high optical purity was shown by the polarimetric examination of four crystals selected at random. The first, weighing 0·0700 g., gave α_D − 0·76°, $[\alpha]_D$ − 81·5°, in absolute alcohol (30 c.c., 4-dcm. tube), and the others gave the following results: 0·0097 g., α_D − 0·10°, $[\alpha]_D$ − 80·0°; 0·0142 g., α_D + 0·18°, $[\alpha]_D$ + 93·3°; 0·0206 g., α_D + 0·26°, $[\alpha]_D$ + 94·6°. The respective melting points were 144—146°, 144—146°, 146° and 146°.

Upon segregation being undertaken, each one of the five selected crystals exhibited the predicted sense of optical rotation when examined polarimetrically. Three crystals rounded on the left side displayed the following rotatory powers when dissolved in benzene (30 c.c., 4-dcm. tube): 0·0081 g., α_{5461} − 0·17°, $[\alpha]_{5461}$ − 157°; 0·0058 g., α_{5461} − 0·12°, $[\alpha]_{5461}$ − 155°; 0·0036 g., α_{5461} − 0·09°, $[\alpha]_{5461}$ − 167°. Two other crystals, rounded on the right side, gave the following values: 0·0045 g., α_{5461} + 0·11°, $[\alpha]_{5461}$ + 183°; 0·0052 g., α_{5461} + 0·11°, $[\alpha]_{5461}$ + 159°. The values observed for pure *d*-*iso*hydrobenzoin were $[\alpha]_D$ + 92·0° in alcohol and $[\alpha]_{5461}$ + 166° in benzene.

We express our indebtedness to the Carnegie Trust for a scholarship awarded to one of us (I. G. M. C.). An investigation of homologues of diphenylhydroxyethylamine and hydrobenzoin is in progress.

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