# CCCX.—*The Optically Active Diphenylhydroxyethylamines and* iso*Hydrobenzoins. Part III. Optically Active Diphenylethylene Oxides.*

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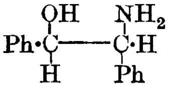
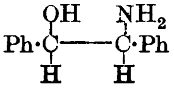
In the preceding papers of this series (J., 1927, 910; 1929, 2305), attention has been drawn to the difficulty of deciding between configurations (I) and (II) for diphenylhydroxyethylamine or *iso*diphenylhydroxyethylamine :

(I.)



$$\mathrm{Ph{\cdot}\overset{OH}{\underset{H}{C}}\text{———}\overset{NH_2}{\underset{Ph}{C}}{\cdot}H}$$



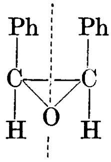
$$\mathrm{Ph{\cdot}\overset{OH}{\underset{H}{C}}\text{———}\overset{NH_2}{\underset{H}{C}}{\cdot}Ph}$$

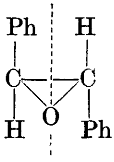
(II.)

The formation of *d-iso*hydrobenzoin and internally compensated hydrobenzoin from both *d-iso*diphenylhydroxyethylamine and *l*-diphenylhydroxyethylamine by the action of nitrous acid proves that in each case one of the products is the result of a configurational change (compare J., 1927, 911) : treatment with nitrous acid thus affords no evidence at all concerning the molecular configurations of the stereoisomeric bases.

It occurred to us that a more definite result might perhaps be achieved by preparing 2 : 3-diphenylethylene oxide from an optically active base of each type, through the corresponding quaternary ammonium hydroxide, $Ph{\cdot}CH(OH){\cdot}CH(NMe_3{\cdot}OH){\cdot}Ph$. Rabe and Hallensleben (*Ber.*, 1910, **43**, 884; compare Emde and Runne, *Ber.*, 1910, **43**, 1727) found that *dl*-diphenylhydroxyethylamine when treated in this way gave an oxide melting at 69°, while the *dl-iso*-base yielded a stereoisomeric oxide melting at 42°. An inspection of configurations (III) and (IV) shows that one of these products (III) should be internally compensated *cis*-2 : 3-diphenylethylene oxide and that the other (IV) should be the externally compensated *trans*-form :

(III.)





(IV.)

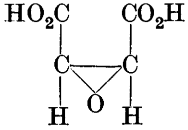
The quaternary ammonium iodides derived from *dl*- and *l-iso*diphenylhydroxyethylamine were readily prepared by a modification of the method of Rabe and Hallensleben, and when steam distilled with silver oxide each of them furnished the same optically inactive 2 : 3-diphenylethylene oxide, m. p. 42°. *d*-Diphenylhydroxyethylamine, however, when treated similarly yielded an optically active oxide, with m. p. 69—70° and $[\alpha]_D$ —306° in ethyl alcohol; the antimeric oxide was obtained from *l*-diphenylhydroxyethylamine, and an equimolecular mixture of the *d*- and *l*-forms of this oxide melted at 69—70°. It is thus evident that *iso*diphenylhydroxyethylamine yields internally compensated *cis*-2 : 3-diphenylethylene oxide, with configuration (III), and that diphenylhydroxyethylamine gives *trans*-2 : 3-diphenylethylene oxide (IV).

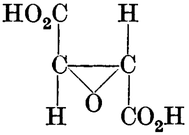
From this investigation it is therefore seen that *d*-diphenylhydroxyethylamine, m. p. 143°, $[\alpha]_D$ + 10·7° (alcohol), yields *l-iso*hydrobenzoin, m. p. 146°, $[\alpha]_D$ —92·0°, when treated with nitrous acid, and gives *l-trans*-2 : 3-diphenylethylene oxide, m. p. 69—70°, $[\alpha]_D$ —306°, by the reaction just mentioned; whereas *l-iso*diphenylhydroxyethylamine, m. p. 115°, $[\alpha]_D$ —133°, gives rise similarly to *l*-*iso*hydrobenzoin and *cis*-2 : 3-diphenylethylene oxide, m. p. 42°.

In every instance the yield of oxide approached the calculated amount, and the product was homogeneous. This fact renders it very unlikely that configurational changes have taken place during the formation of the oxides, since the changes must then be assumed to proceed quantitatively in opposite directions under the same experimental conditions. It appears, therefore, that configurations (I) and (II) must be assigned to diphenylhydroxyethylamine and *iso*diphenylhydroxyethylamine, respectively, the more symmetrical base (II) thus possessing the lower melting point and the higher rotatory power.

The stereoisomeric 2 : 3-diphenylethylene oxides are proved to be unimolecular. The plane of symmetry of the *cis*-form (shown by the broken line) becomes an axis of symmetry in the *trans*-form (IV). Another example of the same fundamental type of a simple cyclic structure displaying optical activity is evident in fumarylglycidic acid, m. p. 215° (VI), which has recently been resolved into antimeric forms, having $[\alpha]_D$ ±100° (water), by Kuhn and Ebel (*Ber.*, 1925, **58**, 919; 1926, **59**, 2514). The stereoisomeric maleinylglycidic acid (V) has a lower melting point (144—145°) than the *trans*-form, and is optically inactive by internal compensation :

(V.)



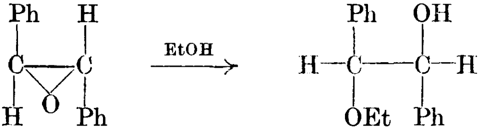


(VI.)

The passage from the open structure of *l*-*iso*hydrobenzoin to the three-membered ring of the *trans*-oxide is attended by a change in the value of $[\alpha]_D$ from —92·0° to —306° (alcohol), the effect of the small ring on the optical rotatory power being very marked; the corresponding values in benzene solution are —128° and —374°. The symmetric *cis*-oxide, like the acid (V) above, has the lower melting point; the *d*-, *l*-, and *dl*-forms of the *trans*-oxide all melt at one temperature, and the melting points of mixtures of the *d*- and *l*-forms give rise to a characteristic racemate curve.

The marked stability of the 2 : 3-diphenylethylene oxides towards such reagents as Fehling's solution, potassium permanganate and chromic acid (compare Rabe and Hallensleben, *loc. cit.*) may be correlated with the views of Thorpe and Ingold on the effect of substituents in relieving the strain inherent in small ring-systems. It is therefore all the more remarkable that when kept in ethyl-alcoholic solution for about a fortnight *l*-*trans*-2 : 3-diphenylethylene oxide was transformed completely into *l*-*iso*hydrobenzoin monoethyl ether (VII), the rotatory power changing meanwhile from —307° to —34·6°. The three-membered ring (IV) thus undergoes fission with addition of a molecule of ethyl alcohol :

(IV.)



(VII.)

No similar effect has been noticed with methyl or propyl alcohol, but it appears that an analogous change is brought about by hydrogen chloride in chloroform solution.

It is of interest that the *dl*-2 : 3-diphenylethylene oxide which is formed in the oxidation of stilbene with perbenzoic acid is now shown to be the *trans*-compound, since its melting point has been recorded as 69—70° by Tiffeneau and Lévy (*Bull. Soc. chim.*, 1926, **39**, 763) and 69·5—70·3° by Böeseken and Elsen (*Rec. trav. chim.*, 1928, **47**, 694). In stereochemical agreement with these observations, stilbene and *allo*-stilbene yield predominately *iso*hydrobenzoin and hydrobenzoin, respectively, when oxidised with peracetic acid (Böeseken and Elsen, *loc. cit.*).

The viscid oil which forms the main product of the action of nitrous acid on the diphenylhydroxyethylamines (J., 1929, 2313) was originally supposed to contain diphenylacetaldehyde or deoxybenzoin (J., 1927, 911), formed as a result of semihydrobenzoin transformation, since from the work of McKenzie and his collaborators on semipinacolinic deamination it is well established that migration of hydrocarbon radicals occurs almost invariably in interactions between nitrous acid and amino-alcohols of the type $R_2C(OH){\cdot}CH(NH_2)R'$ (see, *e.g.*, J., 1924, **125**, 844; *Ber.*, 1929, **62**, 289). Beyond a small amount of benzophenone, however, no aldehydic or ketonic constituent could be diagnosed in the oil. Acetylation indicated that at least one-third of it consisted of hydrobenzoins; and since the material was richer than hydrobenzoin in carbon it appeared that diphenylethylene oxides might also be present, particularly as we have obtained 2 : 3-di-*p*-methoxyphenylethylene oxide by the direct interaction of nitrous acid and di-*p*-methoxyphenylhydroxyethylamine. Meerwein's method of disruption with sulphuric acid (*Annalen*, 1913, **396**, 200) failed to yield an aldehyde or ketone when applied to the oil, and in this respect the material behaved similarly to the *trans*-oxide (Böeseken and Elsen, *loc. cit.*); but a strong indication that no unimolecular ethylene oxide occurs in the product was obtained during an examination of the action of nitrous acid on *d*-diphenylhydroxyethylamine. The oily material had $[\alpha]_D$ −20·0° in benzene, while the corresponding value for the ethylene oxide derived from this base is −374°: this value, even in the absence of any *l*-*iso*hydrobenzoin (which, however, is known to be formed in the reaction) would call for the presence of only 5% of the optically active oxide.

It appears to us that the main constituent of the oil is a chemically inert and optically inactive product of polymerisation containing carbon, hydrogen and oxygen only. A mixture of hydrobenzoins and polymerised diphenylethylene oxides would seem to be capable of displaying all the characteristics of the material in question. Thus, no migration of hydrocarbon radicals appears to take place during the deamination of the diphenylhydroxyethylamines with nitrous acid, and a similar state of affairs holds for di-*p*-methoxyphenylhydroxyethylamine, another amino-alcohol of the general type $Ar{\cdot}CH(OH){\cdot}CH(NH_2){\cdot}Ar$, which we have recently examined.

## EXPERIMENTAL.

cis-2 : 3-*Diphenylethylene Oxide.*—(1) *dl*-*iso*Diphenylhydroxyethylamine (25 g.), dissolved in three times its weight of dry methyl alcohol, was heated under reflux for an hour with methyl iodide (2 mols.), and again for 10 minutes after the addition of sodium methoxide (1 mol.) dissolved in a little methyl alcohol. The whole treatment was then repeated. The residue obtained upon evaporation yielded glistening needles of *dl*-*iso*diphenylhydroxyethyltrimethylammonium iodide, m. p. 219°, (40 g.) when recrystallised from absolute alcohol (compare *Ber.*, 1910, **43**, 885). The iodide was shaken with freshly precipitated silver oxide (40 g.) and water (170 c.c.), and when the mixture was steam-distilled, *cis*-2 : 3-diphenylethylene oxide was obtained as an oil which quickly crystallised (17·5 g.). It separated from 70% alcohol in fine needles, m. p. 42°.

(2) *l*-*iso*Diphenylhydroxyethyltrimethylammonium iodide, prepared similarly from *l*-*iso*diphenylhydroxyethylamine, separated from absolute alcohol in glistening needles, m. p. 214°, $\alpha_D$ −0·20°, $[\alpha]_D$ −4·0° (*c* 2·5010, methyl alcohol).* When treated with silver oxide, as above, it gave a homogeneous product identical with the foregoing *cis*-2 : 3-diphenylethylene oxide (m. p. 42°; an absolute alcoholic solution containing 0·5 g. in 20 c.c. was optically inactive in a 2-dcm. tube in mercury-green light).

l-trans-2 : 3-*Diphenylethylene Oxide.*—*d*-Diphenylhydroxyethyl-

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* All the values of α quoted in this paper were observed in a 2-dcm. tube at the ordinary temperature (about 15°); the weight (*c* gram) of the substance contained in 100 c.c. of the solution is given in each instance.

amine* was prepared as described previously (Read and Steele, J., 1927, 913). *d*-Diphenylhydroxyethyltrimethylammonium iodide, prepared therefrom in the usual way, crystallised from absolute alcohol in glistening leaflets, m. p. 145°, $\alpha_D$ + 3·01°, $[\alpha]_D$ + 92·4° (*c* 1·6290, methyl alcohol); the yield was 95% of the calculated amount. Upon treatment with silver oxide, in the way mentioned above, the iodide furnished l-trans-2 : 3-*diphenylethylene oxide* in almost quantitative yield. The oxide crystallised from 70% alcohol in feathery needles attaining 1·5 cm. in length, m. p. 69—70°, $\alpha_D$ —8·35°, $[\alpha]_D$ —306° (*c* 1·3660, absolute alcohol) (Found: C, 85·8; H, 6·1; *M*, in camphor, 186, 185. $C_{14}H_{12}O$ requires C, 85·7; H, 6·1%; *M*, 196).

Determinations of rotatory power were made in various other solvents, as follows: methyl alcohol, $\alpha_D$ —3·31°, $[\alpha]_D$ —311° (*c* 0·5320); *n*-propyl alcohol, $\alpha_D$ —2·97°, $[\alpha]_D$ —287° (*c* 0·5180); *iso*propyl alcohol, $\alpha_D$ —2·85°, $[\alpha]_D$ —279° (*c* 0·5110); chloroform, $\alpha_D$ —2·59°, $[\alpha]_D$ —249°, $\alpha_{5461}$ —3·33°, $[\alpha]_{5461}$ —320° (*c* 0·5205); acetone, $\alpha_D$ —3·29°, $[\alpha]_D$ —291°, $\alpha_{5461}$ —4·01°, $[\alpha]_{5461}$ —355° (*c* 0·5655); ethyl acetate, $\alpha_D$ —3·14°, $[\alpha]_D$ —313°, $\alpha_{5461}$ —3·85° $[\alpha]_{5461}$ —384° (*c* 0·5020); benzene, $\alpha_D$ —3·73°, $[\alpha]_D$ —374°, $\alpha_{5461}$ —4·55°, $[\alpha]_{5461}$ —456° (*c* 0·4985). The methyl alcohol was dried with magnesium before use, but the specimens of *n*- and *iso*-propyl alcohol were not specially purified. Since the *n*-propyl alcohol used for this purpose gave $\alpha_D$ —1·62° in a 2-dcm. tube, a corresponding correction was made in the observed reading. Purified specimens of chloroform, acetone,† ethyl acetate and benzene were used.

No alterations were manifest upon keeping any of the above solutions at the ordinary temperature for several days. Specially purified ethyl alcohol was not used as a solvent; when, however, ordinary "absolute" alcohol was employed, the original rotatory power, $\alpha_D$ —8·35°, $[\alpha]_D$ —306°, underwent a gradual change to a practically constant value, $\alpha_D$ —1·29°, $[\alpha]_D$ —47·1°, after 15 days; among the intermediate readings were $\alpha_D$ —6·69° (24 hours), $\alpha_D$ —2·73° (72 hours), $\alpha_D$ —2·50° (5 days), and $\alpha_D$ —1·51° (10 days).

* The value of $[\alpha]_D$ for this base in acetone changed from + 15·1° to — 120·8° in 6 hours (Read and Steele, *loc. cit.*). On repeating this observation, we found that the residue recovered by allowing the acetone to evaporate at the ordinary temperature melted at 107—109° and contained C, 83·0 and H, 5·8%. Since the original base, $C_{14}H_{15}ON$, has m. p. 143° and requires C, 78·9 and H, 7·1%, the change in rotatory power appears to be due to chemical interaction between the base and acetone and not to mutarotation as was previously suggested.

† Certain specimens of acetone which we have examined recently have exhibited a distinct lævorotation, *e.g.*, $\alpha_D$ — 0·61° in a 4-dcm. tube, and a much more pronounced effect has been observed with specimens of *n*-propyl alcohol, as indicated above (compare McKenzie and Mitchell, *Biochem. Z.*, 1929, **208**, 467).

Upon allowing the solvent to evaporate at the ordinary temperature, fine needles were deposited having m. p. 45—50°, $\alpha_D$ —0·39°, $[\alpha]_D$ —34·6° (*c* 0·5640, absolute alcohol). The weight of this product, which appeared to be l-iso*hydrobenzoin monoethyl ether*, was greater than that of the original *l*-oxide (Found : C, 79·1 ; H, 7·4 ; OEt, 18·1. $C_{14}H_{13}O{\cdot}OEt$ requires C, 79·3 ; H, 7·5 ; OEt, 18·6%).

A chloroform solution containing 0·2008 g. of the *l*-oxide, together with one equivalent of hydrogen chloride, in 20 c.c., gave $\alpha_D$ —4·67°, $[\alpha]_D$ —233°, and this value remained unaltered after the solution had been kept for several days at the ordinary temperature. With 5 equivalents of hydrogen chloride in a similar solution containing 0·2032 g. of the *l*-oxide, the appended readings were noted : 5 mins., $\alpha_D$ —3·03°, $[\alpha]_D$ —149° ; 15 hours, $\alpha_D$ —2·72°, $[\alpha]_D$ —134° (constant). When a solution containing 10 equivalents of hydrogen chloride and 0·2007 g. of *l*-oxide in 20 c.c. was used, the polarimetric readings were as follows : 5 mins., $\alpha_D$ —1·29°, $[\alpha]_D$ —64·3° ; 4 hours, $\alpha_D$ —0·52°, $[\alpha]_D$ —25·9° (constant). It proved possible to recover the unchanged substance only from the first solution ; the others yielded syrupy material when the solvent was allowed to evaporate at the ordinary temperature.

d-trans-2 : 3-*Diphenylethylene Oxide*.—Crude *l*-diphenylhydroxyethylamine, obtained by decomposing impure *l*-diphenylhydroxyethylamino-*d*-methylenecamphor (Read and Steele, J., 1927, 914) with bromine in rectified spirit, was condensed with *l*-oxymethylenecamphor. Two recrystallisations of the product from ether–light petroleum yielded pure *l*-diphenylhydroxyethylamino-*l*-methylenecamphor, m. p. 146°, $\alpha_D$ —4·51°, $[\alpha]_D$ —235° (*c* 0·9600, absolute alcohol). The *l*-base, isolated in the usual way, had m. p. 143°, $\alpha_D$ —0·23°, $[\alpha]_D$ —10·7° (*c* 1·0750, absolute alcohol) ; the derived *l*-diphenylhydroxyethyltrimethylammonium iodide had m. p. 145°, $\alpha_D$ —1·10°, $[\alpha]_D$ —102° (*c* 0·5385, methyl alcohol) ; and d-trans-2 : 3-*diphenylethylene oxide*, prepared by steam-distilling the last-named compound with silver oxide, had m. p. 69—70°, $\alpha_D$ + 3·21°, $[\alpha]_D$ + 310° (*c* 0·5170, absolute alcohol) (Found : C, 85·6 ; H, 6·2%).

*Melting-point Curve of Mixtures of* d- *and* l-trans-2 : 3-*Diphenylethylene Oxide*.—*dl-trans*-2 : 3-Diphenylethylene oxide, prepared by Rabe and Hallensleben (*Ber.*, 1910, **43**, 884), melted at the same temperature (69—70°) as its optically active components, described above. Solid mixtures of known composition were made by mixing and evaporating measured volumes of standard methyl-alcoholic solutions of the two antimeric forms. The equimolecular mixture melted sharply at 69—70° ; the other mixtures melted less definitely, and the appended temperatures are the points of complete fusion : 100% of *l*-form, m. p. 69—70° ; 95%, 69° ; 90%, 65·5° ; 85%, 61·5° ;

80%, 60·5°; 75%, 62°; 66·7%, 63°; 60%, 67°; 45%, 69°. The melting point was taken a second time in each case, when the substance had resolidified, without any appreciable difference being noticed.

*Further Observations upon the Action of Nitrous Acid on* l- *and* dl-iso*Diphenylhydroxyethylamine.*—When treated with nitrous acid in the way described in the preceding paper (J., 1929, 2313), 5 g. of *l-iso*diphenylhydroxyethylamine yielded about 0·65 g. of crystalline *l-iso*hydrobenzoin and 3·5 g. of a thick, dark brown oil. The crude oil, when separated and dried, had $\alpha_D$ −1·63°, $[\alpha]_D$ −30·7° (*c* 2·6580, absolute alcohol). When boiled with an excess of acetic anhydride, the oil failed to yield any crystalline acetate of hydrobenzoin, but the carefully washed product upon hydrolysis with standard alkali was found to contain 10·3% of acetyl, corresponding to about 36% of hydrobenzoins in the original oily residue.

Upon distillation under greatly diminished pressure, 11·9 g. of the oil yielded a first fraction consisting of 4·2 g. of a pale yellow oil, b. p. 147°/3 mm., $n_D^{17°}$ 1·5972; the residue showed signs of decomposition. A very similar oil slowly passed over when the crude oil was steam-distilled. This product was optically inactive; 3·5 g., when treated with hydroxylamine acetate, gave 2·8 g. of crystalline material, melting indefinitely at about 120°, and two recrystallisations from aqueous alcohol furnished 1·4 g. of colourless needles, m. p. 141—143°. This substance was shown to be benzophenoneoxime ("Organic Syntheses," 1930, **10**, 10).

Upon bringing *dl-iso*diphenylhydroxyethylamine into reaction with nitrous acid in the manner indicated above, the product obtained consisted solely of a dark brown oil. This material after extraction with a hot solution of sodium bisulphite contained more carbon than the amount calculated for *iso*hydrobenzoin (Found: C, 80·1; H, 6·2. Calc. for $C_{14}H_{14}O_2$: C, 78·5; H, 6·5%); it crystallised partially when kept in a desiccator. Subsequent treatment with ether and light petroleum furnished pure *dl-iso*hydrobenzoin, m. p. 119° (2·0 g.). No definite product could be isolated from the sodium bisulphite solution.

The oily by-product obtained by the action of nitrous acid on *d*-diphenylhydroxyethylamine had $\alpha_D$ −0·24°, $[\alpha]_D$ −20·0° (*c* 0·6000, benzene).

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