

**302.** *The Optically Active Diphenylhydroxyethylamines and isoHydrobenzoins. Part VII. The 1 : 2-cycloHexanediols and Related Compounds.*

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THIS paper deals chiefly with the 1 : 2-cyclohexanediols (I) and 2-aminocyclohexanol (II). A summary of the current knowledge of the 1 : 2-cyclohexanediols has been given by Rothstein (*Ann. Chim.*, 1930, **14**, 461); the preparation, properties and characterisation



of these crystalline alicyclic analogues of the hydrobenzoins have now been studied in greater detail. The optical resolution by Derx (*Rec. trav. chim.*, 1922, **41**, 312) of the diol having the higher melting point (103—104°) showed it to possess the *trans*-configuration. The *d*-form,  $[\alpha]_D + 41^\circ 16'$ , obtained by Derx was apparently somewhat impure : by means of *l*-menthoxyacetyl chloride, we have obtained both *d*- and *l-trans*-1 : 2-cyclohexanediol, m. p. 113—114°,  $[\alpha]_D \pm 46.5^\circ$ .

An examination of the absorption spectra of the optically inactive diols by Mr. R. E. Lishmund, B.Sc., showed that both isomerides give an absorption edge in the ultra-violet region, and that the *cis*- is less transparent than the *trans*-isomeride. This result is of interest, since few spectroscopic investigations of racemic and *meso*-compounds have been carried out : Stewart (*J.*, 1907, **91**, 1540) and Byk (*Z. physikal. Chem.*, 1907, **61**, 1)

obtained curves for *dl*- and *meso*-tartaric acids similar to those now observed for the above *cis*- and *trans*-diol; and Ramart-Lucas and Biquard (*Compt. rend.*, 1932, **94**, 187) have investigated several pairs of *dl*- and *meso*-compounds whose relative configurations are not yet known.

A qualitative determination of the comparative rates of reaction of the monobenzoates of *cis*- and *trans*-1 : 2-cyclohexanediol with *m*-nitro-, *p*-nitro-, and 3 : 5-dinitro-benzoyl chloride has shown that in each instance the *trans*-compound (III) reacts more rapidly than the *cis*-compound (IV). These observations have been adduced as evidence in favour



of the *cis*-disposition of H(3) and H(4) in the two series of *neomenthols* (J., 1934, 1780). The monobenzoates may readily be oxidised to 1 : 2-cyclohexanolone benzoate, thus furnishing a new approach to 1 : 2-cyclohexanolone (cf. Kötze, *Annalen*, 1913, **400**, 62).

It was proposed to investigate similarly the general relationships and relative velocities of esterification of the 1 : 2-dimethyl-1 : 2-cyclohexanediols: the reaction of methylmagnesium iodide with 1 : 2-cyclohexanedione yielded, however, *dl*-1-methylcyclohexan-1-ol-2-one only, and this upon reduction gave *dl*-1-methylcyclohexane-1 : 2-diol.

2-Aminocyclohexanol (II), prepared by shaking 2-chlorohexanol with concentrated aqueous ammonia, has been studied in the manner adopted in these investigations for amino-alcohols of the type Ar·CH(OH)·CH(NH<sub>2</sub>)·Ar; but neither deamination nor exhaustive methylation indicates whether the known compound has the *cis*- or the *trans*-configuration, and attempts to prepare the stereoisomeride have been unsuccessful. Deamination at 0° in presence of oxalic acid results in a regression of the ring system, the sole product of the reaction being cyclopentylformaldehyde (Godchot and Mousseron, *Compt. rend.*, 1934, **198**, 2006); under the different conditions outlined below, some cyclohexene oxide is also formed. When boiled with water in presence of silver oxide, *dl*-cyclohexan-1-ol-2-trimethylammonium iodide gave a mixture which appeared to consist of *dl-trans*-1 : 2-cyclohexanediol and 2-dimethylaminocyclohexanol; and when heated, the latter constituent decomposed, forming cyclohexene oxide and dimethylamine. The *l*-form of the quaternary ammonium iodide behaved similarly, the *trans*-1 : 2-cyclohexanediol being again optically inactive.

#### EXPERIMENTAL.

##### *cis*- and *trans*-1 : 2-cycloHexanediol.

*Separation of cis- and trans-1 : 2-cycloHexanediol.*—The crude cyclohexanediol, m. p. 72—83°, used in this work was prepared by Messrs. Howards and Sons, Ltd., Ilford, by the catalytic hydrogenation of catechol. When the mixture (40 g.) was recrystallised three times from benzene, the least soluble fraction (15 g.) consisted of orthorhombic leaflets (*Ann. Chim.*, 1905, **6**, 248) of the pure *trans*-diol, m. p. 103—104° (cf. Rothstein, *loc. cit.*). The residues (50 g.) from the first mother-liquors of several such operations, when recrystallised seven times from benzene, gave orthorhombic leaflets (*Ann. Chim.*, 1905, **6**, 283) of the pure *cis*-diol, m. p. 98—99°. The derived mixtures of the 3 : 5-dinitrobenzoates and the *p*-nitrobenzoates crystallised analogously, furnishing a large yield of pure *trans*- and a small yield of pure *cis*-ester in each case.

The *cis*-diol, unlike the *trans*-isomeride, undergoes condensation with dry acetone containing 1% of hydrogen chloride, in presence of sodium sulphate (cf. Derx, *Rec. trav. chim.*, 1922, **41**, 312; Rothstein, *loc. cit.*). The acetone derivative, an oil smelling of peppermint, b. p. 80—81°/25 mm., 179—182°/760 mm., yields the pure *cis*-diol when boiled for 2 hrs. with a mixture of *N*-hydrochloric acid (1 c.c.) and acetone (10 c.c.). *Benzylidene-cis-1 : 2-cyclohexanediol*, b. p. 151—152.5°/14 mm.,  $n_D^{17}$  1.5332, is formed when the mixture of diols (20 g.) is heated at 140—150° for 1 hr. with benzaldehyde (120 g.) in a current of carbon dioxide (Found: C, 76.0; H, 7.8. C<sub>13</sub>H<sub>16</sub>O<sub>2</sub> requires C, 76.5; H, 7.8%). It may be hydrolysed like the acetone derivative, yielding the pure *cis*-diol.

*Derivatives of dl-trans-1 : 2-cycloHexanediol.*—The derivatives described were made by dissolving the diol in dry pyridine and adding slightly more than the calculated amount of the appropriate acid chloride. The mono- and di-acetate were liquids. The *monobenzoate*,

b. p. 200—205°/35 mm., distilled as a viscid syrup, which crystallised from light petroleum in colourless needles, m. p. 92—93° (Found: C, 70.1; H, 7.2.  $C_{13}H_{16}O_3$  requires C, 70.1; H, 7.3%). The *dibenzoate*, m. p. 93°, was very soluble in light petroleum, but crystallised from aqueous alcohol (Found: C, 74.2; H, 6.1.  $C_{20}H_{20}O_4$  requires C, 74.1; H, 6.2%). The *di-m-nitrobenzoate* separated in prisms, m. p. 141—142°, from benzene-light petroleum (Found: C, 58.2; H, 4.5.  $C_{20}H_{18}O_8N_2$  requires C, 58.0; H, 4.4%). The *di-p-nitrobenzoate* crystallised from benzene in large, pale yellow, doubly terminated prisms, m. p. 149—150° (Found: C, 58.0; H, 4.3%). The *bis-3:5-dinitrobenzoate* crystallised from benzene in fine, pale yellow prisms, m. p. 179° (Found: C, 47.7; H, 3.3.  $C_{20}H_{16}O_{12}N_4$  requires C, 47.6; H, 3.2%). In the last three cases it was not possible to prepare the mono-ester, either by half-esterification of the diol or by half-saponification of the di-ester.

The 1-(3':5'-*dinitrobenzoate*)-2-*benzoate* was prepared by the general method from the mono-*benzoate*. It crystallised in two forms: (i) pale yellow, rectangular leaflets, m. p. 105°, from alcohol; (ii) pale yellow, doubly terminated prisms, m. p. 132.5°, from alcohol-acetone. When an alcoholic solution of the first form was seeded with the second form, it deposited prisms, m. p. 132.5°, identical with the second form (Found: C, 57.7; H, 4.2.  $C_{20}H_{18}O_8N_2$  requires C, 58.0; H, 4.3%). The 1-*p-nitrobenzoate*-2-*benzoate* crystallised from aqueous alcohol in pale yellow prisms, m. p. 131° (Found: C, 65.2; H, 5.1.  $C_{20}H_{18}O_6N$  requires C, 65.0; H, 5.2%). The 1-*m-nitrobenzoate*-2-*benzoate* melted at 102° (Found: C, 64.9; H, 5.1%). The mono- and the di-*d*-camphor-10-sulphonate were solids of a buttery consistency which could not be recrystallised.

*Derivatives of cis-1:2-cycloHexanediol.*—When treated with benzoyl chloride (1 equiv.) in pyridine, the *cis*-diol gave a mixture of the mono- and di-*benzoate* and an unsaturated hydrocarbon. The *monobenzoate*, separated by fractional distillation, was a colourless viscid syrup, b. p. 139—140°/0.5 mm. (Found: C, 70.6; H, 7.3%). The *dibenzoate* crystallised from light petroleum (b. p. 40—60°) in fine, long, colourless needles, m. p. 63—64° (Found: C, 73.9; H, 6.1%). The *di-p-nitrobenzoate* crystallised from alcohol-acetone in fine, pale yellow prisms, m. p. 128—128.5° (Found: C, 58.2; H, 4.3%). The *bis-3:5-dinitrobenzoate* separated from alcohol-acetone in fine prisms, m. p. 169° (Found: C, 47.7; H, 3.1%). It was not possible to prepare mono-esters in the last two cases.

The 1-(3':5'-*dinitrobenzoate*)-2-*benzoate* crystallised from alcohol-acetone in pale yellow prisms, m. p. 102° (Found: C, 58.1; H, 4.3%). The 1-*p-nitrobenzoate*-2-*benzoate* separated from alcohol in prisms, m. p. 82° (Found: C, 64.9; H, 5.2%). The 1-*m-nitrobenzoate*-2-*benzoate* crystallised from aqueous alcohol in small prisms, m. p. 96—97° (Found: C, 64.8; H, 5.2%).

The above *cis*- and *trans*-monobenzoates were completely hydrolysed when boiled for 1 hr. with the calculated amount of 2.5% methyl-alcoholic potassium hydroxide. Most of the alcohol was distilled off, the residue acidified, the benzoic acid separated by filtration, and the filtrate evaporated to dryness and extracted with boiling benzene. The pure diol was thus recovered in 85% yield. The di-*p*-nitrobenzoates gave a yield of 70%, and the bis-3:5-dinitrobenzoates 45%, after 6 hrs' boiling with the alcoholic alkali.

*Optical Resolution of dl-trans-1:2-cycloHexanediol.*—*dl-trans-1:2-cycloHexanediol* (10 g.) was mixed in dry pyridine (35 c.c.) with *l*-menthoxyacetyl chloride (20 g.) and left over-night. Only the mono-ester was formed when the proportion of acid chloride was increased to 2 equivalents. Dilution with water yielded a semi-solid ester, which when extracted, washed, and dried in the usual way (*J. Soc. Chem. Ind.*, 1932, 51, 329r), had  $[\alpha]_D - 62.5^\circ$  (*c* 1.0, alcohol). Recrystallisation from light petroleum, and later from aqueous alcohol, yielded long transparent prisms (5.2 g.) of *d-trans-1:2-cyclohexanediol l-menthoxyacetate*, m. p. 126—127°,  $[\alpha]_D - 32.7^\circ$  (*c* 0.8, alcohol) (Found: C, 69.1; H, 10.2.  $C_{18}H_{32}O_4$  requires C, 69.2; H, 10.3%).

This resolution was repeated three times, and in each instance the original value,  $[\alpha]_D - 62.5^\circ$  to  $- 63.6^\circ$ , for the crude ester, rose upon fractional crystallisation to  $- 91.7^\circ$ , instead of falling to  $- 32.7^\circ$  as before. The product was pure *l-trans-1:2-cyclohexanediol l-menthoxyacetate*, m. p. 64°,  $[\alpha]_D - 91.7^\circ$  (*c* 1.4, alcohol) (Found: C, 69.6; H, 10.1%). This ester was the more soluble of the two and the yield was smaller than that of the diastereoisomeride. Recrystallisation of residues from the mother-liquors of the later resolutions failed to yield the less soluble ester in a pure condition.

When boiled for 1½ hrs. with 2.5% methyl-alcoholic potassium hydroxide (1.2 mols.), and treated as described above for the monobenzoates, the ester of m. p. 64° yielded *l-trans-1:2-cyclohexanediol*, which crystallised from benzene in glistening leaflets, m. p. 113—114°,  $[\alpha]_D - 46.5^\circ$  (*c* 1.6, water). The ester of m. p. 126—127° similarly yielded the *d-trans*-diol.

The following derivatives of *l-trans-1:2-cyclohexanediol* were made: the *dibenzoate* was

a semicrystalline mass, too soluble to permit of recrystallisation; the di-*p*-nitrobenzoate crystallised from alcohol-acetone in pale yellow, silky needles, m. p. 126.5°,  $[\alpha]_D - 25.5^\circ$  (*c* 1.1, chloroform); the bis-3:5-dinitrobenzoate crystallised from alcohol-chloroform in similar needles, m. p. 160°,  $[\alpha]_D - 83.0^\circ$  (*c* 1.8, chloroform) (Found: C, 47.7; H, 3.3.  $C_{20}H_{16}O_{12}N_4$  requires C, 47.6; H, 3.3%).

The bis-3:5-dinitrobenzoate of *d-trans*-1:2-cyclohexanediol crystallised from alcohol-chloroform in pale yellow, silky needles, m. p. 160°,  $[\alpha]_D + 83.9^\circ$  (*c* 1.5, chloroform).

*Relative Velocities of Esterification of cis- and trans-1:2-cycloHexanediol Monobenzoate.*—Accurately weighed amounts (*ca.* 2 g.) of each monobenzoate were mechanically stirred in separate flasks (100 c.c.), immersed in a thermostat at 17.0°, with 25 c.c. of a standard benzene-pyridine solution (18 c.c. of dry pyridine and 500 c.c. of dry benzene). A weighed amount (1.1 mols.) of the finely powdered acid chloride was added to each flask simultaneously. After a measured time (5–25 mins.), the reaction was stopped by adding 25 c.c. of a standard dilute solution of sodium hydroxide to each flask. Each product was extracted with chloroform (25 c.c.) and washed with measured volumes of dilute sodium hydroxide solution (twice), dilute hydrochloric acid (three times), and water (four times); the extract was then dried over sodium sulphate and distilled under diminished pressure. The residual semicrystalline mixture of mono- and di-benzoate was weighed, and in each case the product furnished by the *trans*-monobenzoate was the heavier. From the percentage of nitrogen in the product, the percentage of mono-ester which had been converted into di-ester was calculated in each experiment. The results show that in each case the *trans*-reacted more rapidly than the *cis*-monobenzoate. In two experiments with 3:5-dinitrobenzoyl chloride the average percentages of the monobenzoate undergoing esterification were 34 (*cis*) and 45 (*trans*); in three experiments with *p*-nitrobenzoyl chloride the corresponding values were 38 and 46; and one experiment with *m*-nitrobenzoyl chloride gave 44 and 49.

*dl-1-Methylcyclohexan-1-ol-2-one.*—1:2-cycloHexanedione, prepared by oxidising cyclohexanone with selenium dioxide (Riley, Morley, and Friend, J., 1928, 1878), crystallised from light petroleum in colourless needles, m. p. 36–38°: its absorption spectrum, as recorded by Mr. R. E. Lishmund, B.Sc., showed an absorption band with head at about 2650 Å.; the molecular extinction coefficient was about 2700, corresponding to the presence of a marked proportion of the enol form (cf. J., 1934, 240).

When treated with somewhat more than 2 mols. of methylmagnesium iodide in dry ether, 1:2-cyclohexanedione yielded *dl*-1-methylcyclohexan-1-ol-2-one as a pale yellow syrup, b. p. 91–95°/30 mm. The *semicarbazone* crystallised from boiling water in stout transparent prisms, m. p. 202° (Found: C, 51.5; H, 8.1.  $C_8H_{15}O_2N_3$  requires C, 51.9; H, 8.1%). The *p*-nitrobenzoate separated from acetone-alcohol in pale yellow needles, m. p. 125–126° (Found: C, 60.5; H, 5.3.  $C_{14}H_{15}O_5N$  requires C, 60.7; H, 5.4%), and the 3:5-dinitrobenzoate in pale yellow, nacreous plates, m. p. 158° (Found: C, 52.1; H, 4.5.  $C_{14}H_{14}O_7N_2$  requires C, 52.2; H, 4.4%). The *l*-menthoxyacetate and *d*-camphor-10-sulphonate were syrups.

*dl-1-Methylcyclohexane-1:2-diol.*—When reduced with sodium (8 equivs.) and alcohol, the above ketol yielded a brown viscid syrup, non-volatile in steam. Upon distillation this gave a fraction, b. p. 129–131°/27 mm., which after several recrystallisations from benzene-light petroleum furnished *dl*-1-methylcyclohexane-1:2-diol in small colourless prisms, m. p. 84°. The bis-3:5-dinitrobenzoate crystallised from alcohol-chloroform in small, pale yellow needles, m. p. 189° (Found: C, 48.3; H, 3.6.  $C_{21}H_{18}O_{12}N_4$  requires C, 48.6; H, 3.6%). An acetone compound, isolated as a colourless peppermint-smelling oil, b. p. 72–73°/20 mm., was presumably derived from the *cis*-diol, but the amount available was too small to permit of hydrolysis.

#### 2-Aminocyclohexanol.

*Preparation.*—The following method is preferable to heating cyclohexene oxide with alcoholic ammonia under pressure (Brunel, *Compt. rend.*, 1903, 137, 1999; Godchot and Mousseron, *Bull. Soc. chim.*, 1932, 51, 1277). 2-Chlorocyclohexanol (100 g.), obtained by the action of hypochlorous acid on cyclohexene (“Organic Syntheses,” Coll. Vol. I, 1932, 151), is shaken for 24 hrs. with excess of concentrated aqueous ammonia. The aqueous liquid is separated from the small quantity of oil and concentrated on the water-bath (350 c.c.). The base is liberated by adding solid sodium hydroxide, extracted with a mixture of chloroform and ether, and distilled under diminished pressure (61 g.): b. p. 110°/24 mm., m. p. 65°. The *d*-camphor-10-sulphonate forms a crystalline partial racemate,  $[\alpha]_D + 64.7^\circ$  (*c* 1.2, water) (cf. Godchot and Mousseron, *loc. cit.*).

*Methylation.*—The *dl*-base was methylated by treatment with sodium methoxide and excess of methyl iodide in methyl alcohol (J., 1930, 2381). The methyl alcohol was distilled away, and the quaternary ammonium iodide extracted from the residue with chloroform. *dl*-cyclo-Hexan-1-ol-2-trimethylammonium iodide (71% yield) crystallised from alcohol-ethyl acetate in fine long prisms, m. p. 214° (Found, by Volhard's method: I, 44.1, 44.2. C<sub>9</sub>H<sub>20</sub>ONI requires I, 44.5%). When treated similarly, the *d*-amino-alcohol (Godchot and Mousseron, *loc. cit.*) yielded the *d*-iodide, crystallising in prisms, m. p. 217°,  $[\alpha]_D + 25.8^\circ$  (*c* 3.5, water).

When the *dl*-quaternary ammonium iodide was boiled in water with twice its weight of fresh silver oxide, trimethylamine was slowly evolved, but the reaction was incomplete after 84 hrs. The strongly basic product dissolved completely in water but only partly in benzene. It gave no derivative with semicarbazide acetate, but reacted (2 g.) with 3 : 5-dinitrobenzoyl chloride to yield *dl-trans*-1 : 2-cyclohexanediol 3 : 5-dinitrobenzoate, m. p. 179° (0.6 g. purified). When dry-distilled, the crude product yielded some cyclohexene oxide and dimethylamine.

The *l*-quaternary ammonium iodide,  $[\alpha]_D - 25.2^\circ$ , when treated similarly with silver oxide, gave a crude product with  $[\alpha]_D - 30.5^\circ$  (*c* 2.3, water). This behaved like the product obtained from the *dl*-iodide, except that the yield of *dl*-diol 3 : 5-dinitrobenzoate (m. p. 179°; optically inactive) was smaller.

*Deamination.*—Upon deamination in the usual way (this vol., p. 1121), in presence of dilute sulphuric acid, 2-aminocyclohexanol furnished some nitrogen when the mixture was boiled. The main product was cyclopentylformaldehyde (Godchot and Mousseron, *loc. cit.*), but cyclohexene oxide was also formed.

*Attempts to prepare a Stereoisomeric 2-Aminocyclohexanol.*—(i) cycloHexanone was treated below 5° with amyl nitrite in presence of concentrated hydrochloric acid (cf. Vanino, "Handbuch der präparativen Chemie," 1923, ii, 678). The resulting pale yellow needles (decomp. 190°) were soluble in water and unstable; the substance was apparently isonitrosocyclohexanone nitrite (Found: C, 38.1; H, 5.9. C<sub>6</sub>H<sub>9</sub>O<sub>2</sub>N.HNO<sub>2</sub>.H<sub>2</sub>O requires C, 37.5; H, 6.2%). Attempts to reduce it with sodium and alcohol, or by catalytic hydrogenation, led to decomposition.

(ii) Crude 1 : 2-cyclohexanediol monobenzoate (45 g.) was added to a solution of potassium dichromate (60 g.) in a mixture of water (300 c.c.) and concentrated sulphuric acid (27 c.c.). The mixture was slowly warmed, and kept at 80° for  $\frac{1}{4}$  hr. The thick brown sludge deposited by the cooled solution was collected, and extracted twice with ether; when washed with alkali, acid, and water, the extract became colourless, and upon evaporation gave a syrupy residue which crystallised when rubbed with light petroleum. The microscopic prisms (17.4 g.), m. p. 85–86°, deposited from benzene-light petroleum appeared to consist of 1 : 2-cyclohexanolone benzoate (Found: C, 71.8; H, 6.4. C<sub>13</sub>H<sub>14</sub>O<sub>3</sub> requires C, 71.6; H, 6.4%). Kötze and his collaborators (*Annalen*, 1913, 400, 62) record m. p. 122–123° for this substance. The oxime crystallised from benzene-light petroleum in needles, m. p. 120° (Found: C, 67.1; H, 6.5. C<sub>13</sub>H<sub>15</sub>O<sub>3</sub>N requires C, 67.0; H, 6.4%). 1 : 2-cycloHexanolone, obtained by boiling the benzoate for 2 hrs. with the calculated amount of 2.5% methyl-alcoholic potassium hydroxide, melted at 129–130° (Found: C, 63.1; H, 8.9. Calc.: C, 63.2; H, 8.8%). 1 : 2-cycloHexanolone oxime, m. p. 109°, when reduced with sodium and alcohol yielded only the 2-aminocyclohexanol, m. p. 65°, described above.

We thank the Carnegie Trust for the Universities of Scotland for the award of a Scholarship to one of us (N. A. B. W.), and Messrs. Howards and Sons, Ltd., Ilford, for a gift of 1 : 2-cyclohexanediol.

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[Received, July 12th, 1935.]