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The Isomers of the Hydrogenation Products of Bisphenol A.
The Separations and Configurations of Three Isomers of 2, 2-Bis-(4-hydroxycyclohexyl)propane and Two of 2-(4-Hydroxycyclohexyl)-2-(*p*-hydroxyphenyl)propane¹⁾

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Hydrogenations of bisphenol A (I) over Raney nickel (W-1) and Urushibara nickel A and B have been carried out, and three stereoisomers of 2,2-bis(4-hydroxycyclohexyl)propane (II) and two of 2-(4-hydroxycyclohexyl)-2-(*p*-hydroxyphenyl)propane (III) have been isolated from the products. The configurations and the preferred conformations of the II isomers, *cis-cis* (m. p. 174—175°C), *cis-trans* (164—165.5°C) and *trans-trans* (188—189°C), and of the III isomers, *cis* (159—161°C) and *trans* (150.5—151.5°C), have been determined by means of the infrared and nuclear magnetic resonance spectra, inversions over sodium to the stable isomers, and other methods. When heated with purified methanol, 2, 2-bis(4-ketocyclohexyl)propane prepared from the chromium trioxide oxidation of an isomeric mixture of II afforded 2, 2-bis(4, 4-dimethoxycyclohexyl)propane, m. p. 140.5—141.5°C. The recrystallization of III_t from benzene yielded III_t·C₆H₆. Treating III_c with acetic anhydride gave 2-(3-cyclohexenyl)-2-(*p*-hydroxyphenyl)propane (where *c*: *cis* and *t*: *trans*).

The catalytic hydrogenation of 2, 2-bis(*p*-hydroxyphenyl)propane, bisphenol A (I), under high pressure gives an isomeric mixture of 2, 2-bis(4-hydroxycyclohexyl)propane (II) and 2-(4-hydroxycyclohexyl)-2-(*p*-hydroxyphenyl)propane (III). This reaction was discussed by Jordan in 1925, who mentioned that, under 10—15 atm. of hydrogen pressure using a less active nickel catalyst, the compound III was mainly obtained as a glassy solid, besides the recovered starting

material, while none of the saturated compound II was observed.³⁾ However, he also observed that the use of a colloidal palladium catalyst gave an oily mixture with an aromatic odor and containing the II isomers. Braun also used a less active nickel catalyst at the temperature of 260°C and under 50 atm. of hydrogen pressure for this reaction; he obtained only hydrogenolysis products, which were presumably cyclohexanol, 4-isopropylcyclohexanols, phenol and *p*-isopropylphenol. However, using decalin as a solvent and using a more active nickel catalyst, he succeeded

1) Presented at the Hokkaido Meeting of the Chemical Society of Japan, Hakodate, July, 1962.

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3) H. Jordan, *Chem. Zentr.*, II, 1587 (1926); Brit. Pat. 252594 (1925).

in preparing III in a good yield, besides a small amount of II.⁴⁾

After these investigations it seems that there have been no other reports concerning the preparation of II,⁵⁾ and that no investigator has isolated the isomers of II and III, or discussed the configurations.⁷⁾ The present study was undertaken in order to isolate these isomers and in order to determine the configuration of the hydroxyl groups, preferred conformations and chemical behavior. These compounds are particularly useful in the production of polyester resins as polyalcohol components.⁸⁾

The above-quoted reports and reports of other analogous hydrogenations have suggested that the use of a more active catalyst⁹⁾ and a higher hydrogen pressure would be necessary, and that this would increase the yield of II rather than that of III and prevent the formation of the hydrogenolysis products. Accordingly, the experiments herein are carried out under about 100 kg./cm² of initial hydrogen pressure over each of three kinds of nickel catalyst, Raney nickel (W-1), and Urushibara nickel A and B,¹²⁾ all of which can easily be prepared and all of which possess considerably high activities.

With regard to the aspects of the hydrogenation, the reaction temperatures and the pressure changes

were measured to elucidate the mechanism of the hydrogen absorption. By hydrogenation up to 210°C using a large amount of Urushibara nickel A or B, only products containing III as a major component were obtained, and even at temperatures as high as 260°C the hydrogenations were not completed, whereas over Raney nickel at 260°C, the hydrogen absorption was completed, giving II in an almost theoretical yield. These observations led us to conclude that the hydrogenation takes place step-by-step on each of the phenolic benzene rings, as has generally been recognized hitherto in the usual hydrogenations of biphenyl compounds,^{10,13)} we also concluded that Urushibara nickel A and B were unsuitable for the hydrogenation of a benzene nucleus of this kind.

Usually a glassy solid was obtained as the hydrogenation product after the resulting solution had been filtered to remove the catalyst and then concentrated to dryness. The residue was separated into the components either by fractional crystallization or by extraction with aqueous alkali, as is summarized in Fig. 1 and as is described in the Experimental section.

Since analogous compounds, like the II diols, often produce the molecular compound among their stereoisomers, for instance, in the cases of bis(4-hydroxycyclohexyl)¹⁴⁾ and 4-cyclohexylcyclohexanol,¹⁵⁾ each of the products, II_i, II_{ii} and II_{iii}, obtained here was confirmed to be a single compound through the regenerative hydrolysis of the diacyl compound to the original diol.

The assignment of the configurations of the hydroxyl groups in II_i, II_{ii} and II_{iii} was initially given from their infrared spectra. The band positions of the secondary alcohol groups in many cyclohexane rings of such compounds as steroids,^{17,18)} 2-decalols¹⁷⁾ and alkylcyclohexanols¹⁹⁾ generally differ according as it is axial or equatorial. The equatorial hydroxyl groups in such alicyclic ring systems absorb in the 1040—1050 cm⁻¹ region, and the axial, at 1000—1010 and 950—960 cm⁻¹. Also, the axial and equatorial acetates both show absorption peaks in the region of about 1230 cm⁻¹, but the axial one shows more complex bands than the equatorial.^{17,18)} II_i had bands at 1072 and 1048; II_{ii}, at 1062, 1020 and 952; and II_{iii}, at 1011 and 958 cm⁻¹. The

4) J. v. Braun, *Ann.*, **472**, 65 (1929).

5) Kalina and Brůthans have reported on this hydrogenation after this investigation was completed. They used various cyclohexanol derivatives as solvents and obtained a white, transparent mass as the product.⁶⁾

6) M. Kalina and V. Brůthans, Czech. Pat. 103572 (1962); *Chem. Abstr.*, **58**, 13846 (1963).

7) The *trans-trans* (II_{t-t}), *cis-trans* (II_{c-t}) and *cis-cis* (II_{c-c}) forms of II, and the *trans* (III_t) and *cis* (III_c) of III are considered to be their configurations of the hydroxyl and isopropylidene groups.⁸⁾

8) Brit. Pat. 464762 (1937); 792485 (1958); 808485 (1958); German Pat. 1011148 (1957); Belgian Pat. 546375 (1959); U. S. Pat. 2828278 (1958).

9) Many examples of the hydrogenation procedure for hydroxybiphenyl compounds and many studies of the activities of various nickel catalysts in analogous reactions have been reported. For instance, Yoshitake¹⁰⁾ examined in detail the activities of several kinds of nickel catalysts in the case of the hydrogenation of *o*-phenylphenol; he reported that the activity sequence was in the following order: Raney nickel > stabilized nickel > flaked nickel > reduced nickel. Morita¹¹⁾ used Urushibara nickel B and nickel Kieselguhr for the hydrogenation of *o*- and *p*-phenylphenols and observed that only the phenolic nuclei were saturated when the former catalyst was used, and that the latter catalyst was not suitable for his purpose because of its low activity.

10) H. Yoshitake, "The Hydrogenation of 2-Phenylphenol, and Chemical Studies of the Products", the Thesis of the Doctor of Pharmacy to Kyoto University, (1961), p. 37; *J. Pharm. Soc. Japan*, **83**, 532, 542 (1963).

11) E. Morita, *The Reports of the Asahigarasu Kogyo Gijitsu Shoreikai*, **6**, 253 (1960).

12) Y. Urushibara and S. Nishimura, "Synthetic Methods of Organic Compounds (Yuuki Kagobutsu Goseiho)," Vol. XI, The Society of Organic Synthetic Chemistry, ed., Gihodo Co., Tokyo (1959), p. 124.

13) S. Kimura, *J. Soc. Org. Synth. Chem. Japan*, **22**, 132 (1964).

14) A. L. Wilds, C. H. Shunk and C. H. Hoffman, *J. Am. Chem. Soc.*, **76**, 1737 (1954).

15) H. E. Ungnade and A. Ludutsky, *J. Org. Chem.*, **10**, 307 (1945).

16) H. E. Ungnade, *ibid.*, **13**, 361 (1948).

17) E. A. Braude and E. S. Waight, "Progress in Stereochemistry," Vol. I, W. Klyne, ed., Butterworths, London (1954), p. 167.

18) M. Ohashi and K. Nakanishi, "Infrared Spectra," Vol. VI, T. Shimanouchi, Y. Mashiko and K. Nakanishi, ed., Nankodo, Tokyo (1958), p. 15.

19) W. Hüchel and Y. Riao, *Ann.*, **637**, 33 (1960).

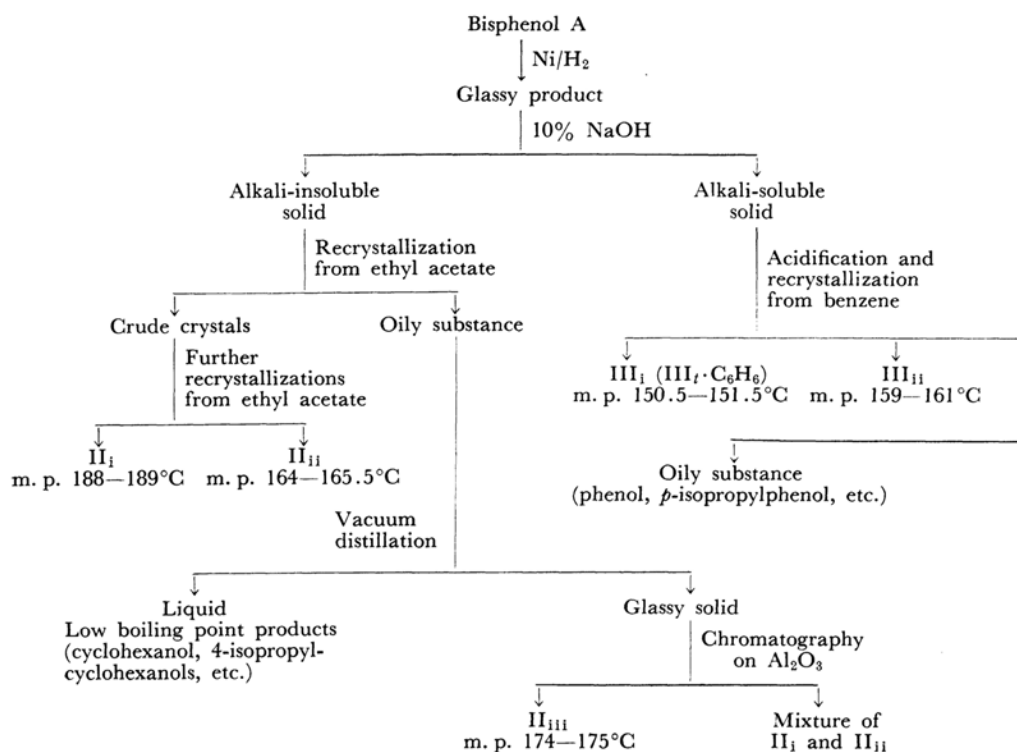


Fig. 1. Separation procedure.

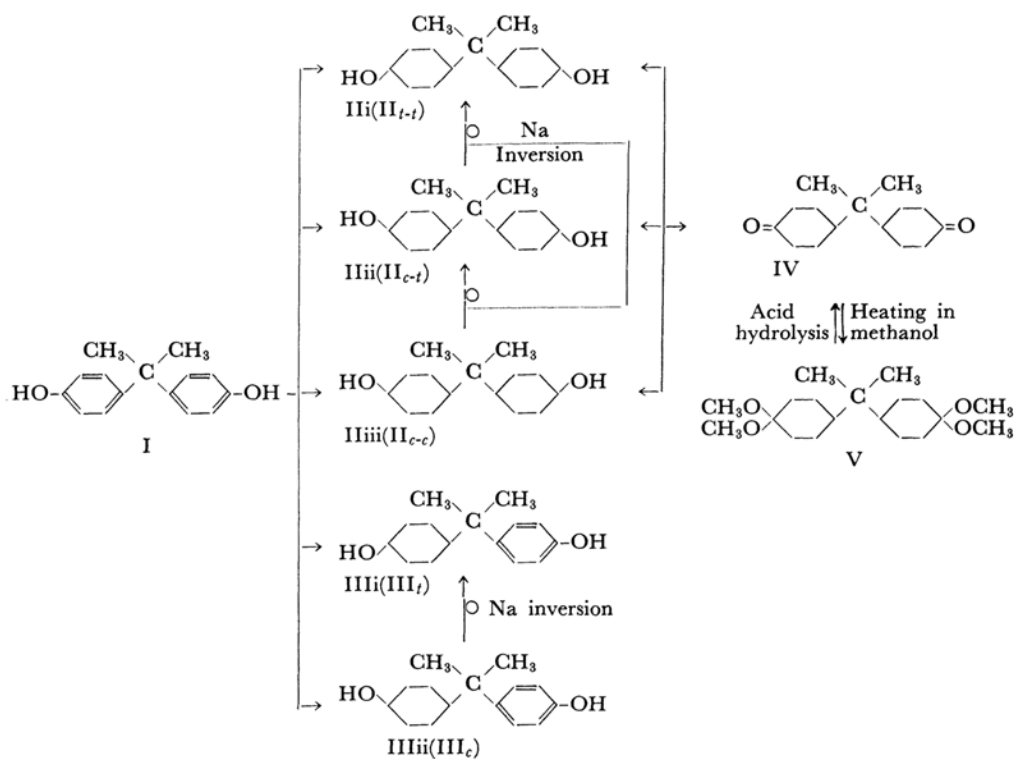


Fig. 2

diacetate of II_{III} showed the most complex absorption bands among the three isomers, that of II_{II} was next, and that of II_I was the simplest. Therefore, the two hydroxyl groups at C_4 and C_4' of II_I were concluded to be both equatorial; one of those of II_{II} was equatorial and another axial, and all of those of II_{III} were axial.

Generally, the cyclohexanes having equatorial hydroxyl groups are more stable than the corresponding axial isomers; therefore, when a polycyclic secondary alcohol is equilibrated with alkali metal, the isomer which is preponderant in the reaction product will be that which has equatorial hydroxyl.^{10,15,20} When II_{II} and II_{III} were each heated with sodium, II_I was preferentially obtained. Since it is most probable that the isopropylidene groups attached to both C_1 and C_1' of the two cyclohexane rings of II isomers are arranged equatorially, the configurations of the hydroxyl groups in II_I with respect to the isopropylidene should be both *trans* (II_{t-t}), *cis* and *trans* (II_{e-t}) in II_{II} , and all *cis* (II_{e-e}) in II_{III} . The adsorption of these isomers on activated aluminum oxide also indicated the same conclusion, that to be expected from the above results. The *cis, cis* isomer was least strongly adsorbed, followed by the *cis, trans*, and *trans, trans* isomers in that order.²¹ Thus, the above-mentioned conclusions from the infrared spectrum studies were also supported by these other results, as well as by the nuclear magnetic resonance spectra of the diacetates, as will be shown in the Experimental section.

The oxidation of the isomeric mixture of II with chromium trioxide gave the diketone compound IV in a good yield. The recrystallization of this diketone from purified methanol afforded the tetramethyl diketal, 2,2-bis(4,4-dimethoxycyclohexyl)propane, while when other carbinols, such as absolute ethanol or propanol, were used, no formation of ketal was observed.

The diketone IV promptly absorbed two moles of hydrogen on hydrogenation over a platinum catalyst and gave a mixture of the diol containing II_{e-t} mainly, plus II_{e-e} and II_{t-t} in minor amounts in that order.

On the acidification of the alkali extract of the hydrogenation product with mineral acid, a mixture of phenolic compounds was deposited as a glassy solid mass. Crystallization from benzene yielded a phenolic material, III_I , m. p. 150.5–151.5°C. The infrared spectrum of III_I showed the absorption peaks of phenolic groups, *p*-disubstituted benzene and equatorial ring alcohol, while its ultraviolet spectrum showed a peak of the phenolic compound at 278 μ , the intensity

of which was approximately half that of bisphenol A. These results led us to the conclusion that III_I still possessed a phenolic benzene ring, besides a cyclohexanol ring. Drying III_I in vacuo at the boiling point of xylene quantitatively removed one mole of the benzene, but the melting point was unchanged. It was, therefore, concluded that the benzene was the solvent of crystallization and that the molecular formula of III_I was $\text{C}_{15}\text{H}_{22}\text{O}_2 \cdot \text{C}_6\text{H}_6$, while III_I was concluded to be the *trans* isomer, III_t , by the above spectral analysis. The diacetate was also prepared in order to confirm that the III_t was a single compound.

Crystals of III_{II} were deposited from the mother liquor, from which III_t had completely been removed. Recrystallization from benzene gave the other isomer, III_{II} , melting at 159–160°C; this was concluded to be the *cis* isomer, III_e . The configuration of the hydroxyl group was also recognized as axial by means of a study of the infrared spectrum and by the sodium inversion to III_t . The acetylation of III_e using acetic anhydride in the presence of potassium acetate gave an oily mixture whose infrared spectrum showed strong bands of hydroxyl, and weak bands of acetyl groups and also of the carbon-carbon double bond. After the phenyl urethane formation, it was found that the main product in the acetylation was 2-(3-cyclohexenyl)-2-(*p*-hydroxyphenyl)propane. The following explanation was proposed for the formation of this dehydrated compound. Since the hydroxyl group in the cyclohexane ring of III_e was axial, it was easily dehydrated and gave the cyclohexene derivative rather than the diacetoxyl compound.²²

As to the preferred conformations of both the cyclohexane rings to the isopropylidene group in II isomers, the following remarks may be made. If it can be assumed that all of the energy barriers of internal rotation among the methyl, methylene and methyldene groups are equivalent by neglecting the detailed stereochemical factors, the conformations $\text{II}: \text{A}$ (*gauche*)²³ and $\text{II}: \text{B}$ (*anti*)²³ (Fig. 3) each of which has four *gauche* interactions like *n*-butane, are less strained than the other possible conformations. However, if one of the cyclohexane rings is placed as $\text{II}: \text{A}$ with respect to the isopropylidene group, and another ring, as $\text{II}: \text{B}$ (i. e., $\text{II}: \text{A} + \text{II}: \text{B} = \text{II}: \text{D}$), the internuclear distance between the two carbon atoms, C-2 and C-6', will approach about 2.5 Å, and the axial hydrogen atom attached to C-2 and the equatorial atom attached to C-6' must face each other at about 0.73 Å.²⁴ On the other hand, when both the

22) Some analogous examples can be found in the case of *cis, cis*-perhydrodiethylstilbestrol.¹⁵⁾

23) Correlations between isopropylidene methyls and the two bonds of the cyclohexane ring (C-1–C-2, and C-1–C-6).

24) Measured by Dreiding molecular models.

20) W. Klyne, Ref. 17, p. 57.

21) Analogous facts were observed by Ungnarde¹⁶⁾ and Wilds et al.¹⁴⁾ in the cases of hydrodiethylstilbestrols and bis(4-hydroxycyclohexane).

cyclohexane rings are "anti" configurations with respect to the isopropylidene group (II:C), each of the two pairs of the methylene carbon atoms, C-2:C-6' and C-6:C-2', will also approach each other at a distance of about 2.5 Å, and the four axial hydrogen atoms attached to these four carbon atoms must face each other in each pair. Therefore, these two steric arrangements, II:C and II:D, are actually impossible and the other conformation, II:E, is the most probable. The II:E conformation is a combination of two II:A conformations, where the two chair cyclohexane rings are contrarily twisted 60° (the projected valency angles about the carbon-carbon bonds between the isopropylidene and each of the rings) from the completely-eclipsed situations with the isopropylidene methyls. The two bonds, C-1-C-6 and C-1'-C-6', and the bisector of the bond angle of CH₃-C-CH₃ should, therefore, be coplanar.

Regarding the preferred conformation of III, if it can also be assumed that all the steric strains among the methyl, methylene, and the carbon atoms at the junction of the benzene ring are equivalent, as in II isomers, the conformations of III:A and III:B shown in Fig. 3 should have equal relative stabilities and be more probable than the other possible conformations. However, while only one methylene group (C-2) in III-C is near to the hydrogen atom attached to an ortho position of the benzene ring, two of the methylene groups in III:D (C:2 and C:6) will approach two of the ortho hydrogens. Hence, a whole-molecular conformation such as III:C is energetically more probable.

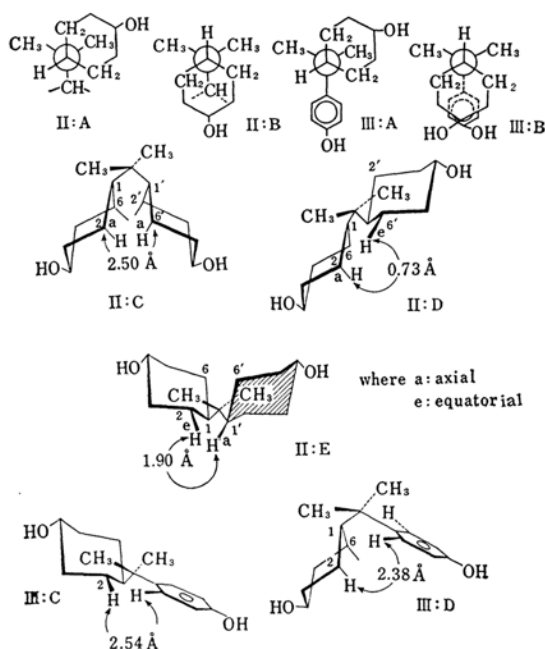


Fig. 3

Experimental

The Hydrogenation of Bisphenol A over Raney Nickel Catalyst (W-1).—Fifty grams of bisphenol A dissolved in 120 ml. of absolute ethanol and 20 ml.²⁵⁾ of Raney nickel (W-1) were charged in a one-liter stainless-steel autoclave and shaken under 94 kg./cm² of initial hydrogen pressure. The temperature was allowed to rise up to 260°C during a period of 120 min. in order to complete the hydrogen absorption. The resulting solution was filtered, and the solvent was removed under diminished pressure. The obtained glassy solid was refluxed and stirred in 400 ml. of 10% sodium hydroxide for 5 hr. in order to remove any phenolic component; then the remaining crystalline solid was repeatedly washed with large amounts of hot water. This yielded 51.0 g. (96%) of an isomeric mixture of II, m. p. 133–153°C.

II_{1-t}.—One recrystallization of the above-obtained crystalline mixture from ethyl acetate gave 35.1 g. of the first crop, which had a melting point of 147–183°C. From the mother liquor 10.0 g. of other crystals, the second crop, m. p. 133–153°C, were recovered. The further recrystallization of the first crop from the same solvent gave an analytical sample of II₁ (II_{1-t}), m. p. 188–189°C.

Found: C, 74.94; H, 11.75. Calcd. for C₁₅H₂₈O₂: C, 74.95; H, 11.74%.

$\nu_{\text{max}}^{\text{Nujol}}$ 3310 (OH); 1072, 1048 cm⁻¹ (equatorial alcohol).

II_{c-t}.—Repeated recrystallizations of the second crop, obtained above, from ethyl acetate gave an analytical sample of II_c (II_{c-t}), m. p. 164–165.5°C. The melting point was depressed when it was mixed with II_{1-t}.

Found: C, 74.75, 74.91; H, 11.68, 11.58. Calcd. for C₁₅H₂₈O₂: C, 74.95; H, 11.74%.

$\nu_{\text{max}}^{\text{Nujol}}$ 3360 (OH); 1062 (equatorial alcohol); 1020, 952 cm⁻¹ (axial alcohol).

All the mother liquors from the above recrystallization procedures were combined separately with the corresponding fractions of the other experimental runs described later, and stored for used in the detection of II_{c-c}.

III_t.—Upon acidification with dilute hydrochloric acid of the alkaline extract obtained above, a viscous oil was isolated. After sufficient washings with hot water, 2.0 g. of powder were obtained. Crystallization from benzene gave 0.15 g. of III₁ (III₁-C₆H₆), m. p. 150.5–151.5°C.

Found: C, 80.18, 80.35; H, 9.27, 9.15; C₆H₆; 26.42;²⁶⁾ mol. wt. (Rast), 170. Calcd. for C₁₅H₂₂O₂·C₆H₆: C, 80.74; H, 9.02; C₆H₆, 26.28%; mol. wt., 312.46.

$\nu_{\text{max}}^{\text{KBr}}$ 3454, 3130 (OH, broad); 1961, 1813 (benzene); 1612, 1595, 1518 (phenyl); 1242 (phenol); 1046 (equatorial alcohol); 832 cm⁻¹ (*p*-disubstituted benzene).

$\lambda_{\text{max}}^{\text{EtOH}}$ 224.1, 255, 278 mμ (ε, 10600, 1080, 2300).

The drying course using a thermobalance under

25) Measured in the volume as a precipitate in absolute ethanol.

26) Weight loss upon drying at the boiling point of xylene under a vacuum until a constant weight was obtained.

atmospheric pressure showed that the dissociation temperature of the benzene was as low as below 80°C.

$\nu_{\text{max}}^{\text{KBr}}$ of benzene-free III_t : 3410, 3240 (OH, broad); 1878, 1613, 1596, 1517 (phenyl); 1250 (phenol); 1060 (equatorial alcohol); 831 cm^{-1} (*p*-disubstituted benzene).

The mother liquor collected and gathered from the above recrystallization procedures of $\text{III}_t\text{-C}_6\text{H}_6$ was combined with similar fractions of the later experimental runs, and they stored for use in the detection of III_c .

The Hydrogenation of Bisphenol A with Urushibara Nickel-A.—Reduction up to 220°C.—The hydrogenation of 50.0 g. of I in 100 ml. of absolute ethanol over 10 ml.²⁵ of a U-Ni-A catalyst was carried out under 100 kg./cm² of initial hydrogen pressure, with the temperature rising up to 220°C over a period of 225 min. After working-up as usual, a sirupy product was obtained; this was, as usual, separated into alkali-insoluble and soluble portions. The crystallization of the insoluble part from ethyl acetate gave the following crops: (a) m. p. 141—170°C; 15.0 g. (28.5%); (b) m. p. 140.5—149°C; 7.45 g. (14.1%), and (c) m. p. 130—140°C; 2.07 g. (3.9%); the total of 24.5 g. (46.5%). These crops were identified as follows; the fraction a consisted mainly of II_{t-t} , and the b, of II_{c-t} , as was confirmed by mixed-melting-point tests.

The acidification of the alkali-soluble portion with hydrochloric acid gave 6.5 g. of crude crystals of III_t , which were mostly III_t .

Reduction up to 260°C.—This was carried out under 100 kg./cm² of initial hydrogen pressure, using 30 ml. of a U-Ni-A. The reaction temperature was raised up to 260°C over a period of 195 min. After working up as usual, 18.5 g. (35%) of crystals insoluble in alkali were obtained, m. p. 142—150°C, 17.9 g., these crystals contained mainly II_{c-t} , with II_{t-t} the remainder.

From the alkaline solution, a solid mass (phenolic material) was recovered on acidification. Crystallization from benzene-acetone gave 30 g. of a crude crystalline mixture with a melting point of 97°C. Another recrystallization from benzene yielded 19.1 g. (27.9%) of a pure sample of $\text{III}_t\text{-C}_6\text{H}_6$.

The Hydrogenation of Bisphenol A over Urushibara Nickel-B.—Reduction up to 220°C.—This was carried out as usual, using 70 ml. of a U-Ni-B¹² under 92 kg./cm² of initial hydrogen pressure. The temperature was allowed to rise up to 220°C over a period of 135 min. After working-up as usual and subsequent crystallization from benzene, 33.5 g. of crystals were obtained, m. p. 97—137°C. This product was easily soluble in ethyl acetate and in alkali, and gave no crystals from the ethyl acetate solution on cooling. Therefore, this fraction consisted of phenolic compounds and no saturated ones. Recrystallization from benzene-acetone gave 21.1 g. (32%) of $\text{III}_t\text{-C}_6\text{H}_6$.

The concentration of the above-obtained mother liquor gave 2.4 g. (4.6%) of other crystals, m. p. 173—185°C, a crude II_{t-t} .

The finally-remaining oily substance (29 g.) was stored for use in the detection of the other isomers of II and III.

Reduction up to 260°C.—This was carried out as usual under a 103 kg./cm² initial hydrogen pressure, using 82 ml. of a U-Ni-B. The temperature was allowed to rise up to 263°C over a period of 195 min. Working-up as usual yielded 43 g. (81%) of an alkali-insoluble

product, m. p. 122—148°C. Recrystallization from ethyl acetate gave the following crops: (a) m. p. 167—182°C, 15 g. (28%), which mainly consisted of II_{t-t} ; (b) m. p. 156—159°C, 13 g. (24%), almost all II_{c-t} ; and (c) m. p. 132—150°C, 4.4 g. (8%).

The Diacetate of II_{t-t} .—A mixture of 1.0 g. of II_{t-t} , 0.2 g. of anhydrous sodium acetate, and 1.67 g. of acetic anhydride was heated in a boiling-water bath for 5 hr. After cooling, the solution was poured into ice-water and neutralized with sodium bicarbonate powder. The white precipitate was then collected on a filter, washed with water, and dried to give the crude crystals, 1.30 g. (96%). Recrystallization from methanol gave the analytical sample, m. p. 136—138°C.

Found: C, 70.32; H, 9.92. Calcd. for $\text{C}_{19}\text{H}_{32}\text{O}_4$: C, 70.33; H, 9.94%.

$\nu_{\text{max}}^{\text{Nujol}}$ 1736, 1730 (C=O, acetate); 1259, 1244 (acetate); 1038, 1019 cm^{-1} (C—O).

NMR²⁷, (70 mg./0.45 ml. of CCl_4): 5.58 τ (axial hydrogens at C-4 and C-4').

The Dibenzoate of II_{t-t} .—One gram of II_{t-t} , 3 g. of pyridine, 5 ml. of dioxane, and 3 g. of benzoyl chloride were mixed and heated under reflux for 2 hr. This mixture, after the usual work-up, gave 1.45 g. (78%) of the dibenzoate of II_{t-t} as white needles, m. p. 192—193°C, these needles were insoluble in both ethanol and methanol.

Found: C, 77.61; H, 7.99. Calcd. for $\text{C}_{29}\text{H}_{36}\text{O}_4$: C, 77.64; H, 8.09%.

$\nu_{\text{max}}^{\text{Nujol}}$ 1708 (C=O, benzoate); 1274 cm^{-1} (benzoate).

The Hydrolysis of the Diacetate of II_{t-t} .—A mixture of 0.15 g. of the diacetate in 3 ml. of methanol with 0.3 g. of sodium hydroxide in 2 ml. of water was refluxed for 3.5 hr. After concentration and then dilution with water, white crystals (0.10 g., 90%) separated out; these crystals melted at 188—189°C and did not depress the melting point of an authentic sample of II_{t-t} .

The Diacetate of II_{c-t} .—This was prepared as has been described in the case of II_{t-t} . After working-up, 1.35 g. of the crude diacetate melting at 70—74°C were obtained. Recrystallization from ethanol gave 1.05 g. (77%) of the analytical sample, m. p. 75.5—76.5°C.

Found: C, 70.44; H, 9.83. Calcd. for $\text{C}_{19}\text{H}_{32}\text{O}_4$: C, 70.33; H, 9.94%.

$\nu_{\text{max}}^{\text{Nujol}}$ 1742, 1730 (C=O, acetate); 1266, 1243, 1221 (acetate); 1039, 1019 cm^{-1} (C—O).

NMR, 70 mg./0.45 ml. of CCl_4 : 5.10 τ (equatorial hydrogen at C-4); 5.58 τ (axial hydrogen at C-4').

The Dibenzoate of II_{c-t} .—One gram of the diol was benzoylated in the same manner as II_{t-t} . After working-up as usual the resulting oil was crystallized from methanol to give a crude dibenzoate of II_{c-t} . Another recrystallization from methanol gave 1.4 g. (76%) of the analytical sample, melting at 105—105.5°C.

Found: C, 77.51; H, 8.08. Calcd. for $\text{C}_{29}\text{H}_{36}\text{O}_4$: C, 77.64; H, 8.09%.

$\nu_{\text{max}}^{\text{Nujol}}$ 1710 (C=O, benzoate); 1276 cm^{-1} (benzoate).

The Hydrolysis of Diacetate of II_{c-t} .—A sample

27) The nuclear magnetic resonance spectra were obtained by Dr. Keishi Kotera, the Osaka Research Laboratory of Tanabe Seiyaku Co., on a Japan Electron Optics Laboratory 60 MC spectrometer, using dilute solutions in carbon tetrachloride, with tetramethylsilane as an internal standard.

of 0.30 g. of the diacetate of II_{c-t} was hydrolyzed as in the case of that of II_{t-t} ; this gave 0.21 g. (94%) of II_{c-t} , m. p. 163–164°C. This sample showed no melting-point depression on admixture with the original sample of II_{c-t} .

The Isolation of II_{c-c} .—A mother liquor obtained from all the separation procedures for II_{t-t} and II_{c-t} was concentrated under reduced pressure, and then heated in methanol with an excess of sodium ethoxide in order to remove the still-remaining phenolic compounds as water-soluble sodium salts.

After the removal of the solvent and sufficient washings with hot water, the remaining glassy solid was dissolved in benzene and passed through an activated-aluminum oxide column; this gave crystals from an elute using ethyl acetate. Recrystallization from ethyl acetate gave a sample melting at 167–170°C. The melting point was depressed on admixture with II_{t-t} or II_{c-t} . Therefore, this was confirmed to be the last isomer of II , II_{c-c} .

Found: C, 75.10, 75.14; H, 11.85, 11.78. Calcd. for $\text{C}_{15}\text{H}_{28}\text{O}_2$: C, 74.95, H, 11.74%.

The Diacetate of II_{c-c} .—This was prepared as that of II_{t-t} , using 0.5 g. of II_{c-c} ; 0.68 g. (theoretical yield) of white crystals, m. p. 113.5–115°C, was thus obtained. Another recrystallization from methanol gave the analytical sample, m. p. 117–117.5°C.

Found: C, 70.33, H, 9.97. Calcd. for $\text{C}_{19}\text{H}_{32}\text{O}_4$: C, 70.33, H, 9.94%.

$\nu_{\text{max}}^{\text{Nujol}}$ 1735 (broad, C=O, acetate); 1260, 1251, 1220, 1217, 1209 (acetate); 1009 cm^{-1} (C–O).

NMR, (75 mg./0.45 ml. of CCl_4): 5.15 τ (equatorial hydrogens at C-4 and C-4').

The Dibenzoate of II_{c-c} .—A sample of 0.5 g. of II_{c-c} was benzoated as usual. The recrystallization of the product from methanol gave white needles (0.66 g., 71%), m. p. 152–153°C.

Found: C, 77.61; H, 8.07. Calcd. for $\text{C}_{29}\text{H}_{36}\text{O}_4$: C, 77.64; H, 8.09%.

$\nu_{\text{max}}^{\text{Nujol}}$ 1710 (C=O, benzoate); 1608, 1589 (phenyl); 1280, 1272 cm^{-1} (benzoate).

The Hydrolysis of the Dibenzoate of II_{c-c} .—A solution of 0.24 g. of the dibenzoate in 4 ml. of acetone, and 2 ml. of water containing 0.10 g. of sodium hydroxide were mixed and refluxed for 6 hr. After the solvent had been removed, the resulting crystals were gathered on a glass filter, washed with water, and dried. Recrystallization from benzene–petroleum benzene gave 0.10 g. (77%) of II_{c-c} , m. p. 174–175°C.

Found: C, 74.86, 75.04; H, 11.71, 11.62. Calcd. for $\text{C}_{15}\text{H}_{28}\text{O}_2$: C, 74.95; H, 11.74%.

$\nu_{\text{max}}^{\text{Nujol}}$ 3380 (OH); 1012, 959 cm^{-1} (axial alcohol).

The Sodium Inversion of II_{c-t} to II_{t-t} .—One gram of II_{c-t} was dissolved in 1 ml. of xylene. To this solution at 160°C, 0.4 g. of sodium was added in small portions. The reaction system evolved hydrogen gas, and after a while it precipitated some solids. After reaction at 180°C for 12 hr., the reaction mixture was decomposed by the drop-by-drop addition of ethanol and water. The precipitate was gathered on a glass filter, washed with water, dried, and weighed (0.96 g. (96%)), m. p. 175–184°C. Recrystallization from ethyl acetate gave an analytical sample, m. p. 188–189°C, which was identical with an authentic sample of II_{t-t} .

The Sodium Inversion of II_{c-c} to II_{t-t} .—This was carried out as above, using 0.50 g. of II_{c-c} ; it gave 0.35 g. (70%) of a pure sample of II_{t-t} .

2, 2-Bis(4-ketocyclohexyl)propane (IV)²³.—An isomeric mixture of II (54.0 g., m. p. 150–178°C) was dissolved in 250 ml. of glacial acetic acid. To this solution, under stirring and cooling at 17–18°C, there was added, drop by drop over a period of about 2 hr., 55.0 g. of chromium trioxide in a dilute acetic acid (250 ml. of glacial acetic acid and 40 ml. of water). After another one hour's reaction, 275 ml. of isopropyl alcohol was added under water-cooling; the solution was then allowed to stand overnight. Concentration under reduced pressure and the pouring of the remaining product into water precipitated powdery white crystals. After filtration and drying, 41.0 g. (78%) of the crude diketone, m. p. 159–163°C, was obtained. Recrystallization from benzene raised the melting point to 162.5–163°C (lit.,⁴) m. p. 158–160°C).

Found: C, 76.36; H, 10.18. Calcd. for $\text{C}_{15}\text{H}_{24}\text{O}_2$: C, 76.23; H, 10.24%.

$\nu_{\text{max}}^{\text{Nujol}}$ 1718 cm^{-1} (six-membered-ring ketone).

Disemicarbazone.—This was prepared as usual, m. p. 220–223°C (decomp.) (lit.,⁴) 220–223°C). Another melting point, 238–239°C (decomp.), was observed when the disemicarbazone was measured with a rapid temperature rise.

The Formation of 2, 2-Bis(4, 4-dimethoxycyclohexyl)propane (V) and the Regeneration of the Original Diketone IV by Acid Hydrolysis.—When the diketone IV was heated in purified methanol and the solution was concentrated, fair white plates of the tetramethyl diketal, m. p. 140.5–141.5°C, were obtained in a theoretical yield.

Found: C, 69.11; H, 10.80. Calcd. for $\text{C}_{19}\text{H}_{36}\text{O}_4$: C, 69.47; H, 11.05%.

$\nu_{\text{max}}^{\text{Nujol}}$ no peak in the region of six-membered-ring ketone; 1161, 1100, 1040 cm^{-1} (tetramethyl diketal).

Similar procedures using other alcohols, such as ethanol or propanol, gave no reaction, and only the original diketone was recovered.

The tetramethyl diketal (1.00 g.) in a mixed solution of 15 ml. of acetone and 5 ml. of water containing 2.0 ml. of concentrated hydrochloric acid was refluxed for 2 hr. After the addition of 15 ml. of water to the reaction system and the removal of the acetone by distillation, crystals of IV were recovered.

The Rapid Hydrogenation of the Diketone IV over Platinum Black Catalyst.—A solution of 1.00 g. of IV in 35 ml. of glacial acetic acid was shaken with 0.37 g. of a platinum black catalyst and hydrogen under atmospheric pressure at room temperature. After 55 min., 110% of the theoretical amount of hydrogen was absorbed. Working-up as usual gave 1.05 g. of a sirup which was subsequently separated chromatographically, using 120 g. of an activated aluminum oxide, into three main fractions. The first fraction, eluted with ether-methanol, was 200 mg. (19.7%) of crude crystals, containing II_{c-c} mainly. The second was 636 mg. (62.5%) of a sirup consisting mainly of II_{c-t} , plus some II_{t-t} . These two fractions were confirmed

28) This procedure followed the analogous method by Wilds et al. used for the preparation of bicyclohexyl-4, 4'-dione.¹⁴

by a study of their infrared spectra and by mixed-melting-point tests with authentic samples after repeated recrystallizations from benzene. The third fraction consisted of 32 mg. (3.1%) of almost pure crystals of III_t , m. p. 183—185°C.

The Diacetate of III_t .—A solution of 1.33 g. of $\text{III}_t \cdot \text{C}_6\text{H}_6$ in 2.0 g. of acetic anhydride containing two drops of concentrated sulfuric acid was heated in a boiling-water bath for 1.5 hr. After working-up as usual and recrystallization from methanol, 0.67 g. (49%) of crystals melting at 108—109.5°C was obtained.

Found: C, 71.75; H, 8.30. Calcd. for $\text{C}_{19}\text{H}_{26}\text{O}_4$: C, 71.67; H, 8.23%.

$\nu_{\text{max}}^{\text{Nujol}}$ 1760, 1227 (phenyl acetate); 1730, 1249 (acetate of secondary alcohol); 1610, 1511 (phenyl); 1039, 1022 (C—O); 841 cm^{-1} (*p*-disubstituted benzene).

The Isolation of III_c .—The mother liquor collected from the purification of the alkali-soluble product, which was almost free from III_t , was repeatedly extracted with a hot alkali solution in order to separate it from alkali-insoluble materials. On acidification, from the extract there separated a viscous oil which deposited crystals when left standing. Recrystallization from benzene gave an analytical sample melting at 159—161°C, this was concluded to be III_c by a mixed-melting-point test with an authentic sample of III_t and by the following analyses.

Found: C, 76.82; H, 9.51. Calcd. for $\text{C}_{15}\text{H}_{22}\text{O}_2$: C, 76.88; H, 9.46%.

$\nu_{\text{max}}^{\text{Nujol}}$ 3445, 3220 (OH); 1613, 1597, 1509 (phenyl); 1231 (phenol); 1008, 944 (axial alcohol); 825 cm^{-1} (*p*-disubstituted benzene).

The Sodium Inversion of III_c to III_t .—A sample of 0.50 g. of III_c in 0.50 g. of xylene was refluxed with 0.20 g. of sodium at 180°C for 10 hr. After the solution had been treated with ethanol and then water, and acidified with dilute hydrochloric acid, the isolated product was worked-up as usual and recrystallized from benzene-acetone to give 0.21 g. (42%) of crystals melting at 147.5—150°C. Further recrystallization gave an analytical sample which was found to be identical with an authentic sample of III_t by a mixed-melting-point test.

The Reaction of III_c with Acetic Anhydride.—A mixture of 0.20 g. of III_c and 0.1 g. of potassium acetate

in 1.0 ml. of acetic anhydride was heated in a boiling-water bath for 10 hr., and then poured into ice-water and neutralized with sodium bicarbonate. The oily product which separated was taken up in benzene, washed with water, and dried over anhydrous sodium sulfate. After the removal of the solvent, there was obtained 0.34 g. of an oily mixture which did not crystallize upon the usual treatment. This mixture was, therefore, vacuum-distilled in order to purify it; it gave one fraction, boiling in the range of 120—160°C/0.55 mmHg without decomposition. The distillate almost entirely solidified like a wax after it had stood for a while, but it still was not pure enough to analyze. Therefore, a chromatographic separation of this distillate through a silica gel column was carried out. Elution with benzene-ether (2 : 3) gave 240 mg. (76%) of crude crystals melting below 60°C; these crystals were concluded, by the following tests, to be 2-(3-cyclohexenyl)-2-(*p*-hydroxyphenyl)propane formed by the dehydration, not the diacetate of III_c .

Found: C, 82.13, 82.10; H, 9.31, 9.29. Calcd. for $\text{C}_{15}\text{H}_{20}\text{O}$: C, 83.28; H, 9.32%.

$\nu_{\text{max}}^{\text{Liquid}}$ 3330 (OH); 3040, 2990 (=CH); 1230 (phenol); 827 cm^{-1} (*p*-disubstituted benzene).

Phenyl Carbamate.—This was prepared as usual from 200 mg. of the above-obtained crude sample and 0.50 g. of phenyl isocyanate; it was obtained as a waxy crystalline product melting at 100—110°C. By a chromatographic separation using a silica gel column and subsequently repeated recrystallizations from petroleum benzene and then ethanol-water, the melting point was raised to 116—117.5°C, 2-(3-cyclohexenyl)-2-(*p*-phenylaminocarboxyphenyl)propane.

Found: C, 78.53; H, 7.73; N, 4.35. Calcd. for $\text{C}_{22}\text{H}_{25}\text{NO}_2$: C, 78.77; H, 7.51; N, 4.18%.

$\nu_{\text{max}}^{\text{KBr}}$ 3350 (bonded NH); 3057, 3018 (unsaturated CH); 1740—1709 (amide I); 1652 (RHC=CHR', *cis*); 1615, 1600, 1500 (phenyl); 1543 (amide II); 848 cm^{-1} (*p*-disubstituted benzene).

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