night. Nothing was eluted by petroleum ether, but 1:1 petroleum ether–benzene eluted a solid that on crystallization from methanol gave a mat of fine, flat needles (70 mg.), m.p. 120–121°, α_{D} −74.5° Chf (*c* 1.33), λ^{EtOH} 240 mμ (6,350), λ^{Chf} 5.74, 5.86, 6.10, 8.0 μ.

Anal. Calcd. for $C_{29}H_{46}O_3$ (442.66): C, 78.68; H, 10.48. Found: C, 78.83; H, 10.69.

A comparison sample of Δ^5-cholestene-3β-ol-4-one acetate prepared by Miguel A. Romero according to Petrow and Starling[14] melted at 118–119°, α_{D} −77.4° Chf (P. and S. give m.p. 123–124°, α_{D} −76° Chf, λ^{EtOH} 240 mμ[33]). A mixture with the above sample was undepressed in m.p.

Cholestane-3,6-dione Bis-ethylenethioketal (XIV).[28]—A mixture of 300 mg. of Δ^5-cholestene-4α-ol-3-one acetate, 1 cc. of ethanedithiol and 1 cc. of boron fluoride etherate was stirred in a test-tube, when a stiff orange paste soon resulted. After 5–10 min. methanol was added to produce a thin paste of suspended white solid. The collected and dried product (290 mg., m.p. about 190°) was dissolved in dioxane and the solution diluted with ethanol and then water. A crystal powder separated and was crystallized more satisfactorily from hexane, in which it is moderately soluble; the solution slowly deposited rosettes of fine needles, m.p. 219–220°. Recrystallization from hexane gave silken needles, m.p. 219–220°, α_{D} +30.4° Chf (*c* 1.09); no depression in m.p. on admixture with an authentic sample.

Anal. Calcd. for $C_{31}H_{52}S_4$ (552.73): C, 67.36; H, 9.48. Found: C, 67.78; H, 9.57.

Δ^4-Cholestene-4-ol-3-one (XV).[26]—A solution of 455 mg. of Δ^5-cholestene-4α-ol-3-one acetate (VI) in 25 cc. of 95% ethanol was treated with 0.5 cc. of 36% hydrochloric acid, refluxed for 3 hr., diluted with 4 cc. of water and let cool, when 313 mg. of needles separated, m.p. 148–149°. Recrystallization from methanol or methanol–water gave needles, m.p. 150–151°, α_{D} +80.2° Chf (*c* 1.10), λ^{EtOH} 278 mμ (13,000), $\lambda^{\mathrm{Hexane}}$ 275 mμ (14,570), λ^{Chf} 2.92, 5.98, 6.10 μ.

Anal. Calcd. for $C_{27}H_{44}O_2$ (400.62): C, 80.94; H, 11.07. Found: C, 81.18; H, 11.06.

Similar acid hydrolysis of 221 mg. of Δ^5-cholestene-4α-ol-3-one ethylene ketal acetate (Ib) afforded 131 mg. of XV, m.p. 146–148°. The enol XV was also obtained by adding 0.5 cc. of Claisen's alkali to a suspension of 150 mg. of Δ^5-cholestene-4α-ol-3-one acetate (VI) in 5 cc. of methanol at 25°. In a few minutes the substance dissolved to a slightly yellowish solution and then an enolate separated. This was collected, suspended in methanol and acidified with acetic acid and the solution diluted to saturation at the boiling point; needles of XV separated, m.p. 148–149°, mixed m.p. 149–150°.

The enol XV gives a strong ferric chloride test but does not react with diazomethane. When a petroleum ether solution is shaken with Claisen's alkali no yellow color develops but a gelatinous enolate separates at the interface. An attempt to condense XV with ethylene glycol in acetic acid with boron fluoride etherate led only to recovery of XV. Δ^4-Cholestene-4-ol-3-one is readily eluted from acid-washed alumina by 4:1 petroleum ether–benzene.

The acetate[28] (XVI), prepared with acetic anhydride in pyridine at 25°, crystallized very slowly from methanol–water, m.p. 100.5–101.5°. It was recrystallized by dissolving it in cold methanol and adding water until a turbid emulsion separated. After standing for some time at 5° this changes to a paste of fairly well formed crystals, m.p. 100–101°, α_{D} +95.3° Chf (*c* 1.035), λ^{EtOH} 247 (15,100); λ^{Chf} 5.71, 5.93, 6.12 μ.

Anal. Calcd. for $C_{29}H_{46}O_3$ (442.66): C, 78.68; H, 10.48. Found: C, 78.81; H, 10.51.

The phenylhydrazone of XV[28] separated in a crystal crust, m.p. 188–189°. Recrystallization from ethanol gave lemon yellow micro crystals, m.p. 190–191°.

Anal. Calcd. for $C_{33}H_{50}ON_2$ (490.75): C, 80.76; H, 10.27. Found: C, 80.91; H, 10.20.

The quinoxaline derivative[28] of XV was prepared most successfully by heating 200 mg. of the enol and 200 mg. of sublimed, colorless *o*-phenylenediamine at 141° for 15 min. The solidified melt on crystallization from a solution in dioxane diluted with ethanol and then water gave 80 mg. of the quinoxaline, m.p. 188–190°. Recrystallization from dioxane–methanol afforded pale buff-colored plates, m.p. 200–201°, λ^{EtOH} 239, 321 mμ (27,400; 8,870); lit.[2] m.p. 207–208°.

Anal. Calcd. for $C_{33}H_{48}N_2$ (472.72): C, 83.84; H, 10.24. Found: C, 83.52; H, 10.10.

Oxidation of XV.[28]—Oxidation of 0.5 g. of Δ^4-cholestene-4-ol-3-one with hydrogen peroxide in ethanol–sodium hydroxide and crystallization from acetic acid according to Butenandt[25] gave spars of dihydro-Diels acid, m.p. 257–259°; diester (diazomethane, two crystallizations from methanol), m.p. 123–124°, no depression on admixture with a comparison sample[34] made by esterifying Diels acid with diazomethane and hydrogenating the diester in acetic acid in the presence of platinum catalyst and a trace of perchloric acid.

---

(33) See V. A. Petrow, O. Rosenheim and W. W. Starling (footnote), *J. Chem. Soc.*, 135 (1943).

(34) Experiment by Dr. Wei-Yuan Huang.

CAMBRIDGE, MASS.

[CONTRIBUTION FROM THE LABORATORY OF ORGANIC CHEMISTRY OF THE UNIVERSITY OF WISCONSIN]

Steroid Analogs Lacking Ring C. III. Synthesis of 4-(*trans*-4'-Hydroxycyclohexyl)-cyclohexanone[1]

BY A. L. WILDS, CLIFFORD H. SHUNK[2b] AND CARL H. HOFFMAN[2b,3]

RECEIVED SEPTEMBER 17, 1953

Reduction of 4,4'-dihydroxybiphenyl (III) has given the *trans,trans*-, *cis,trans*- and a small amount of *cis,cis*-bicyclohexyl-4,4'-diols (IV), separated as the dibenzoates. Oxidation of the pure isomers or the mixture gave the diketone VI which could be partially reduced to the *trans*-keto alcohol I. Better methods for synthesizing this compound involved partial oxidation of *trans,trans*-diol IV directly or as the monobenzoate.

In extending our synthesis of analogs of the steroidal hormones lacking ring C[1] to the analogs (II) of testosterone, it was necessary to develop a synthesis of the bicyclic keto alcohol I as the key intermediate. The present paper describes the *trans* isomer of this structure. An accompanying paper reports work leading to the *cis* isomer and the evidence on which is based the assignment of configuration of these geometrical isomers and related bicyclohexyl derivatives.

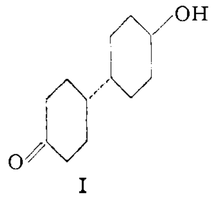
Although 4,4'-dihydroxybiphenyl (III), the starting material for our synthesis, has been prepared for many years by tetrazotization and hydrolysis of benzidine, the procedures available have not

---

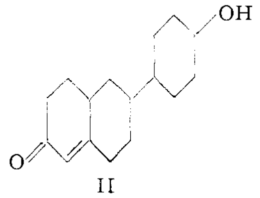
(1) Preliminary report, A. L. Wilds, C. H. Shunk and C. H. Hoffman, THIS JOURNAL, **71**, 3266 (1949). Paper II, A. L. Wilds and C. H. Shunk, *ibid.*, **72**, 2388 (1950).

(2) (a) Wisconsin Alumni Research Foundation Research Assistant, 1941–1942; (b) Merck and Co., Inc., Rahway, N. J.

(3) Wisconsin Alumni Research Foundation Research Assistant, 1946–1947; Ciba Pharmaceutical Products Fellow, 1948–1949.



I

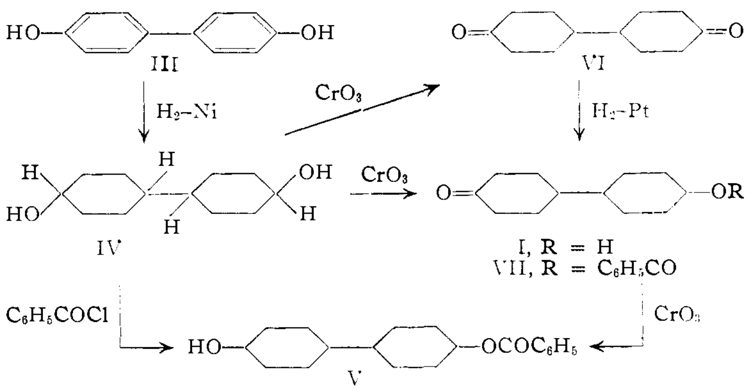


II

given material of high purity in satisfactory yield. An improved procedure was developed in the course of our work leading to the biphenol (III) in 60–65% yields from technical benzidine.

Hydrogenation of the biphenol with Raney nickel proceeded smoothly to the perhydro derivative IV and by crystallization readily afforded one geometrical isomer of this diol (m.p. 216°, *trans, trans*). Further crystallization gave material melting at 182.5–183.5°, which, however, proved not to be a single isomer but a molecular compound of the 216° isomer with a second isomer (*cis,trans*) melting at 178°. The most satisfactory method of separation was found to be fractional crystallization of the dibenzoates, which did not form molecular compounds, and with which the solubility differences among the isomers were accentuated. Saponification of the pure dibenzoates readily led to the pure diols. In this way the hydrogenation mixture gave the *trans,trans*-diol in 37–43% yield together with 12–23% of the *cis,trans*-diol. Only a trace (1–3%) of the *cis,cis*-diol (m.p. 197°) was formed.

Oxidation of the pure diols or the stereoisomeric mixture with chromium trioxide readily gave the diketone VI in 62% over-all yield from III. This method is superior to that reported by Schaefgen and Flory[4,5] involving dehydrogenation of IV over copper–chromium oxide (17% yield from III).



Three methods for preparing the *trans*-keto alcohol I were studied. With a limited amount of chromium trioxide and using a two-phase system, partial oxidation of *trans,trans*-diol IV led directly to I in 36% yield, the remainder being diol and diketone. This was the simplest method for preparing the *trans*-keto alcohol I. Less satisfactory was partial reduction of the diketone VI over platinum, although some of the same *trans* isomer of I could be isolated from the resulting mixture. The third procedure depended upon monobenzoylation and oxidation of the diol. This *trans,trans*-monobenzoate V could be prepared in 43% yield, the remainder consisting of diol and some dibenzoate readily hydrolyzed for reuse. Oxidation of the monobenzoate gave the benzoate of the *trans*-keto alcohol (VII) in 94% yield.

Experimental[6,7]

4,4′-Dihydroxybiphenyl (III).—The procedure of Hirsch[8] has been improved as follows.[9]

A solution of 200 g. of technical benzidine (Eastman Kodak Co.) in a hot mixture of 210 ml. of concentrated hydrochloric acid and 2150 ml. of water was cooled to 25°, an additional 235 ml. of hydrochloric acid added, and the suspension cooled and stirred below 10°. A solution of 151 g. of sodium nitrite in 450 ml. of water was added slowly, stirred 20 minutes after complete addition and 1 g. of urea added. The diazonium solution was added slowly to a hot (85–90°) solution of 215 ml. of sulfuric acid in 4300 ml. of water, heated 10 minutes longer, cooled, filtered and dried. This solid was added[10] to 400 ml. of acetic anhydride, the mixture was heated for 3 hours at reflux, cooled and filtered, giving 295 g. of crude diacetate; this material was distilled at 0.1–0.5 mm. from a two-bulb flask[11] and crystallized from benzene, giving 159 g. of nearly colorless 4,4′-diacetoxybiphenyl, m.p. 161–162.5°, and 12.6 g., m.p. 160–162°. Distillation and recrystallization of the material from the acetic anhydride filtrate gave an additional 40–50 g., m.p. 158–160°, bringing the total yield of the 4,4′-diacetate to 62–65%. The purest sample melted at 163–164° (reported 162.5–163.5°).[12] From the filtrates was obtained 3–4% of the 2,4′-diacetoxybiphenyl, m.p. 99.5–101° (reported 94.5–96.5°[13]), arising from the corresponding isomer of benzidine as an impurity.

To a suspension of 75 g. of the diacetate in 200 ml. of alcohol was added over a five-minute period 22 g. of sodium hydroxide in 50 ml. of water. After heating the suspension for 30 minutes, 750 ml. of water was added followed by sufficient 1:1 hydrochloric acid to make the solution strongly acid. The mixture was digested on the steam-bath for 1 hour, cooled and filtered. The washed and dried (at 80°) material amounted to 50–51 g. (97–99%), m.p. 279–282°, and generally was suitable for hydrogenation without further purification. In other runs the 4,4′-dihydroxybiphenyl was recrystallized from alcohol as shiny white leaflets (95–99% yield), with crops melting from 279.5–281.5° to 282–284° (nitrogen-filled, sealed capillary).

The monobenzoate of 4,4′-dihydroxybiphenyl was prepared by shaking a solution of 1.86 g. of the dihydroxy compound in 15 ml. of water, 15 ml. of dioxane and 10 ml. of 1.13 *N* sodium hydroxide with 1.25 g. (0.9 equivalent) of benzoyl chloride for 5 minutes at 5°. Dilution gave 2.36 g. (90%) of monobenzoate, m.p. 228–230° (softening at 220°). Successive recrystallizations from acetone, benzene and ethanol gave the analytical sample melting at 234.5–236° (Pyrex m.p. tube); in a soft glass capillary the m.p. was lower (m.p. 223–226°).

Anal. Calcd. for $C_{19}H_{14}O_3$: C, 78.6; H, 4.85. Found: C, 78.5; H, 4.66.

The dibenzoate, prepared in hot dioxane and pyridine using excess benzoyl chloride, crystallized from dioxane as colorless, wedge-shaped platelets, m.p. 250.5–251.5°, yield 88% (reported m.p. 241°).[14]

---

[4] J. R. Schaefgen and P. J. Flory, This Journal, **70**, 2823 (1948).

[5] See also J. R. Schaefgen, U. S. Patent 2,496,960 (Feb. 7, 1950).

[6] All melting points are corrected.

[7] Much of the preliminary work was carried out in 1941-1942 (by C.H.S.).

[8] R. Hirsch, *Ber.*, **22**, 335 (1889); *cf.* however, W. H. Hunter and G. H. Woollett, This Journal, **43**, 149 (1921), who obtained 20% yield by this procedure.

[9] This reaction was studied by Herman L. Becker, B. S. Thesis, University of Wisconsin, 1942.

[10] The reverse addition led to a tarry mass and incomplete acetylation (Tillmon H. Pearson).

[11] L. F. Fieser, "Experiments in Organic Chemistry," 2nd ed., D. C. Heath and Co., New York, N. Y., 1941, p. 250.

[12] A. Weissberger and J. W. Williams, *Z. physik. Chem.*, **B3**, 369 (1929).

[13] A. H. Popkin, This Journal, **65**, 2045 (1943).

[14] J. Moir, *J. Chem. Soc.*, **91**, 1305 (1907).

Anal. Calcd. for $C_{26}H_{18}O_4$: C, 79.2; H, 4.60. Found: C, 79.1; H, 4.40.

Hydrogenation of 4,4'-Dihydroxybiphenyl. Bicyclohexyl-4,4'-diol (IV).[15]—Hydrogenation of 34 g. of the dihydroxybiphenyl was carried out in 200 ml. of absolute alcohol using 3 teaspoonsful[16] of W-2 Raney nickel catalyst, heating at 150–200° with hydrogen at 2000–3800 p.s.i. until 100–108% of the theoretical amount was absorbed (2 to 12 hours depending upon the quality and age of the biphenol). After removing the catalyst and the solvent, the residue was digested with 300 ml. of hot 5% sodium hydroxide, cooled, filtered and washed. This crude mixture of isomers amounted to as high as 97% yield, m.p. 170–200°.

Crystallization from a considerable amount of alcohol gave 12–22% of *trans,trans*-**bicyclohexyl-4,4'-diol (IV)**,[17] melting as high as 212–214°. Further recrystallization from alcohol–benzene gave the pure *trans,trans* isomer as shiny plates, m.p. 214–215.5°.[15]

Anal. Calcd. for $C_{12}H_{22}O_2$: C, 72.7; H, 11.2. Found: C, 72.6; H, 11.1.

Attempts to obtain more pure material by direct crystallization usually gave a molecular compound of the *trans,trans* and *cis,trans* isomers, m.p. 182–183° (see below).

In one hydrogenation run with W-6 Raney nickel[18] for which the hydrogen uptake was only 75% of theory, digestion of the crude product with hot 5% potassium hydroxide gave from the aqueous layer after acidification 7% of phenolic material, m.p. 196–208°. After sublimation at 140° (0.1 mm.) and recrystallization from ethyl acetate and alcohol, one of the isomers (presumably *trans*) of **4-(4'-hydroxycyclohexyl)-phenol** was obtained, m.p. 222.5–223.5°. The compound gave a positive Folin–Denis phenol test.[19]

Anal. Calcd. for $C_{12}H_{16}O_2$: C, 75.0; H, 8.39. Found: C, 74.8; H, 8.45.

Separation of the Stereoisomeric Bicyclohexyl-4,4'-diols (IV) as the Dibenzoates.—The remaining mixture of isomers (*ca.* 30 g.) was dissolved in 150 ml. purified dioxane and 90 ml. dry pyridine, treated at reflux with 80 g. benzoyl chloride and heated for 2 hours. After removing most of the solvents under reduced pressure, the residue was dissolved in benzene and chloroform, part of the *trans,trans*-dibenzoate was allowed to crystallize, and the warm filtrate was washed with warm sodium carbonate, dilute acid and water. After concentration and cooling, further crops of dibenzoate crystallized, m.p. ranging from 195–206° to 209–211°, and together with the diol isolated above brought the total yield of the *trans,trans* isomer to 37–43%. The *trans,trans*-**dibenzoate** crystallized from benzene with solvent of crystallization (1.0–1.5 molecules) and changed to white powder on drying at 70°; m.p. unchanged. The purest sample melted at 211–212°.

Anal. Calcd. for $C_{26}H_{30}O_4$: C, 76.8; H, 7.4. Found: C, 76.7; H, 7.4.

Evaporation of the mother liquors and trituration of the residue with 300 ml. of ether resulted in a fraction (*ca.* 5%), m.p. 144–150°, containing crude *cis,cis* isomer. Further concentration (to about 60 ml.) gave fractions containing crude *cis,trans* isomer, m.p. 93–140°.[20] Several recrystallizations from petroleum ether, benzene–petroleum ether or ethyl acetate gave the *cis,trans* isomer in 12–23% yield, m.p. 96–98°. The purest sample of **dibenzoate of** *cis,trans*-**bicyclohexyl-4,4'-diol**[17] melted at 97–98°.

Anal. Calcd. for $C_{26}H_{30}O_4$: C, 76.8; H, 7.4. Found: C, 76.8; H, 7.4.

The filtrate from the crude *cis,trans* isomer gave some additional material melting at 93–142° and at 150–180°. The last was combined with the fraction m.p. 144–150° and recrystallized from benzene. After fractions melting at 209–210°, 155–190° and 156–180°, two additional crops, m.p. 159–163° and 156–162°, were obtained, amounting to 3% of nearly pure **dibenzoate of** *cis,cis*-**bicyclohexyl-4,4'-diol**.[17] In other runs less than 0.5% of this isomer could be isolated. Further recrystallization from benzene–petroleum ether gave the analytical sample melting at 164–165°.

Anal. Calcd. for $C_{26}H_{30}O_4$: C, 76.8; H, 7.4. Found: C, 76.3; H, 7.2.

In this manner some 50–66% of reasonably pure isomers was obtained, the remainder being a mixture. Further separation was difficult, and the mixture was usually hydrolyzed and oxidized to bicyclohexyl-4,4'-dione.

The Pure Stereoisomeric Bicyclohexyl-4,4'-diols (IV) by Hydrolysis of the Dibenzoates.—The *trans,trans*-dibenzoate was saponified by refluxing a suspension of 23.2 g. (m.p. 205–211°) in 300 ml. of methanol and 20 ml. of water containing 12 g. of potassium hydroxide. After 5 hours, the now clear solution was diluted with 200 ml. of water, filtered while hot, and concentrated, yielding a total of 10.3 g. (100%) of the *trans-trans*-**diol**, m.p. 212–215°. The purest sample melted at 215–216°.

Similar saponification of 14.8 g. of the *cis,trans*-dibenzoate (m.p. 96–98°) gave a total of 7.20 g. (100%), m.p. 175–177°. Recrystallization from ethyl acetate gave *cis,trans*-**bicyclohexyl-4,4'-diol**, m.p. 176.5–178°.

Anal. Calcd. for $C_{12}H_{22}O_2$: C, 72.7; H, 11.2. Found: C, 72.4; H, 11.0.

Saponification of 1.21 g. of the *cis,cis*-dibenzoate (m.p. 164–165°) with 0.63 g. of potassium hydroxide in 2 ml. of water and 35 ml. of methanol, refluxing 5 hours, gave 0.58 g. (98%) of the diol, m.p. 191–194°. Recrystallization from ethyl acetate gave *cis,cis*-bicyclohexyl-4,4'-diol, melting as high as 196–197°.

Anal. Calcd. for $C_{12}H_{22}O_2$: C, 72.7; H, 11.2. Found: C, 72.6; H, 11.1.

Molecular Compound of the *trans,trans* **and** *cis,trans* **Isomers of Bicyclohexyl-4,4'-diol.**—After the first crops of *trans,trans* isomer of the diol were crystallized from the mixture of isomers obtained by hydrogenation of 4,4'-dihydroxybiphenyl, the next crops usually melted in the range 175–179° to 181–183°. Further recrystallization from ethyl acetate gave the molecular compound, m.p. 182.5–183.5°.

Anal. Calcd. for $C_{12}H_{22}O_2$: C, 72.7; H, 11.2. Found: C, 72.5; H, 11.1.

The molecular compound was shown to contain a 1:2 ratio of *trans,trans*- to *cis,trans*-diol by separation as the benzoates, by the melting points of known mixtures and by recrystallization of such a mixture from methanol–ether (94% recovery with m.p. and mixed m.p. 182.5–183.5°).

Bicyclohexyl-4,4'-dione (VI).—To a suspension of 81 g. of crude diols (m.p. 145–193°) in 500 ml. of acetic acid, stirred and cooled to 10–15°, was added over a two-hour period a solution of 110 g. of chromium trioxide in 500 ml. of acetic acid and 80 ml. of water. After another hour (at 15–20°) 550 ml. of isopropyl alcohol was added and the mixture allowed to stand overnight. Following concentration to a sirup at reduced pressure, chloroform, water and hydrochloric acid were added. After several chloroform extractions, washing the combined extracts with dilute acid, sodium bicarbonate, water, and drying over sodium sulfate, the diketone was crystallized from carbon tetrachloride, affording 51.6 g., m.p. 113.5–115.5°, and 6.3 g., m.p. 109–114°, for a total of 73%. In another run in which the entire product from reduction of 4,4'-dihydroxybiphenyl was oxidized, the over-all yield of diketone was 62%.

Similar oxidation of 1.0 g. of the *trans,trans*-diol (m.p. 213–214.5°) gave the diketone in 95% yield. The purest sample, obtained as needles from acetone–petroleum ether, melted at 115–116° (reported by Schaefgen and Flory, m.p. 118–119°[5]).

Anal. Calcd. for $C_{12}H_{18}O_2$: C, 74.2; H, 9.3. Found: C, 74.3; H, 9.2.

The disemicarbazone, prepared in 99% yield by heating in ethanol–pyridine for 45 minutes, was too insoluble for satisfactory recrystallization, and was purified for analysis by digesting with hot water and ethanol, m.p. 248–249° (dec., tube inserted in bath at 230°).

---

(15) *Cf.* C. R. Waldeland, W. Zartman and H. Adkins, THIS JOURNAL, **55**, 4236 (1933).

(16) The use of 30–50% more catalyst and a lower temperature of hydrogenation (130–150°) gave less of the *trans,trans* isomer, but is preferable when old samples of diphenol are to be reduced, or the mixture oxidized to the diketone.

(17) Evidence for the assignment of configuration of the diols is presented in an accompanying paper, A. L. Wilds, T. H. Pearson and C. H. Hoffman, THIS JOURNAL, **76**, 1737 (1954).

(18) H. Adkins and H. R. Billica, *ibid.*, **70**, 695 (1948).

(19) O. Folin and W. Denis, *J. Biol. Chem.*, **12**, 240 (1912).

(20) If most of the *trans,trans*-dibenzoate had not been removed previously, this fraction melted over a wider range (90–170°). In this case, the material was digested with hot ether and filtered to remove most of the higher melting isomer before recrystallization.

Anal. Calcd. for $C_{14}H_{24}N_6O_2$: C, 54.5; H, 7.84. Found: C, 54.7; H, 7.66.

4-(*trans*-4′-Hydroxycyclohexyl)-cyclohexanone (I). (a) By Partial Oxidation of the *trans,trans*-Diol (IV).—The following two-phase oxidation gave the best results of several variations tried. A fine suspension of 5.0 g. of the *trans,trans*-diol (m.p. 212–214.5°) was prepared by dissolving in 50 ml. of hot acetic acid, cooling and adding 25 ml. of water with stirring. Chloroform (50 ml.) was added and to the stirred and cooled (13–15°) mixture was then added over 45 minutes a solution of 2.05 g. of chromium trioxide (1.2 equivalents) in 10 ml. water. After stirring overnight at room temperature, water (300 ml.) was added, the layers shaken and then filtered to separate a total of 1.80 g. (36%) of recovered diol (m.p. 212–214°). The filtrate was treated with hydrochloric acid, repeatedly extracted with chloroform and these extracts were washed with acid, bicarbonate, water and dried over sodium sulfate. The solvent was removed, the residue digested with 60 ml. of boiling carbon tetrachloride and filtered to remove an additional 0.22 g. (4%) of crude diol, m.p. 180–190°. Concentration of the filtrate afforded 1.27 g. of hydroxyketone, m.p. 124–126°, and 0.37 g., m.p. 116–120°. Recrystallization of the second crop gave 0.30 g., m.p. 124.5–125.5°, making the total yield of satisfactory material 32% (or 53% net, based on starting material not recovered). The recovered diol gave slightly better yields of hydroxy ketone (36% or 56% net).

Further recrystallization of a sample from ethyl acetate gave the *trans*-hydroxy ketone (I) as needles, m.p. 129–130°.

Anal. Calcd. for $C_{12}H_{20}O_2$: C, 73.4; H, 10.3. Found: C, 73.9, 73.6; H, 10.2, 10.1.

(b) By Partial Reduction of the Diketone (VI).—A solution of 8.31 g. of the diketone (m.p. 114.5–116°) in 70 ml. of ethanol and 7.5 ml. of glacial acetic acid was stirred with 205 mg. of platinum oxide and hydrogen at atmospheric pressure, two further portions of catalyst (202 and 203 mg.) being added when the rate diminished. After 64% of the theoretical (for 1 mole) amount of hydrogen was absorbed in 10 hours, the solution was filtered, evaporated and the residue chromatographed on 200 g. of alumina.[21] The first twelve fractions (benzene and 1:1 benzene–ether) gave a total of 37% of recovered diketone, most melting at 114.5–115.5°. The next eight fractions (1:1 benzene–ether to pure ether) contained 2.10 g. of material which was recrystallized from ethyl acetate–ether mixtures, giving 0.486 g., m.p. 127.5–129°, 0.336 g., m.p. 125–127.5° (sint. 111°) and 0.054 g., m.p. 121–127° (sint. 97°) for a total of 0.876 g. (11%) of the *trans*-hydroxy ketone I. Further elution gave mixtures of the diols melting from 95–135° to 165–180°.

Monobenzoate of *trans,trans*-Bicyclohexyl-4,4′-diol.[22]—To a stirred, refluxing solution of 6.84 g. of *trans,trans*-diol (m.p. 215–216°) in 500 ml. of dry dioxane with 47 ml. of dry pyridine was added during 25 minutes a solution of 6.05 g. (1.25 equivalents) of redistilled benzoyl chloride in 50 ml. of dry dioxane. After heating for 2 hours longer, most of the solvent was removed by distillation, water added and the solid removed by filtration. The dried solid was digested with 340 ml. of hot carbon tetrachloride, cooled to room temperature and filtered to remove 1.66 g. (24%) of starting diol, m.p. 202–213°. The filtrate was evaporated to dryness and the residue triturated with 75 ml. of methanol with slight warming. After cooling to room temperature and filtering 3.01 g. (22%) of the dibenzoate was obtained, m.p. 188–207°. Recrystallization of the remaining material from ethyl acetate–petroleum ether (b.p. 60–68°) gave 3.08 g. of the monobenzoate, m.p. 159–160°, and 1.29 g., m.p. 154–157°, for a total yield of 42%. The remaining material could be recovered as diol by saponification. The analytical sample was recrystallized from carbon tetrachloride, m.p. 158.5–159°.

Anal. Calcd. for $C_{19}H_{26}O_3$: C, 75.5; H, 8.7. Found: C, 75.2; H, 8.7.

Benzoate of 4-(*trans*-4′-Hydroxycyclohexyl)-cyclohexanone (VII). (a) By Oxidation of the *trans,trans*-Monobenzoate V.[22]—A solution of 1.11 g. of chromium trioxide in 85 ml. of acetic acid and 5 ml. of water was added to a solution of 4.38 g. of *trans,trans*-monobenzoate (m.p. 159–160°) in 440 ml. of acetic acid. After 42 hours at room temperature 200 ml. of isopropyl alcohol was added, most of the solvent removed under reduced pressure and the product isolated with chloroform. Crystallization from petroleum ether–ethyl acetate gave 3.57 g., m.p. 151–153°, and 0.52 g., m.p. 150–152.5°, for a total yield of 94%. The analytical sample melted at 152–153°.

Anal. Calcd. for $C_{19}H_{24}O_3$: C, 76.0; H, 8.0. Found: C, 76.0, 76.2; H, 7.5, 7.7.

(b) From 4-(*trans*-4′-Hydroxycyclohexyl)-cyclohexanone (I).—The *trans*-hydroxy ketone (50 mg., m.p. 129–130°) was heated in 2 ml. of chloroform and 0.5 ml. of pyridine with 0.1 ml. of benzoyl chloride for 2 hours and let stand overnight. After washing the product in chloroform solution it was crystallized from carbon tetrachloride; yield 59 mg. (77%), m.p. 148–150°. Further recrystallization from ethyl acetate–petroleum ether gave needles melting at 151.5–152.5° and undepressed in m.p. on admixture with the product in (a).

MADISON 6, WIS.

---

[21] Alcoa F-20 (80–200 mesh).

[22] This run was carried out by Tillmon H. Pearson.