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

Steroid Analogs Lacking Ring C. IV. 4-(*cis*-4'-Hydroxycyclohexyl)-cyclohexanone. Configuration of the Bicyclohexyl-4,4'-diols[1]

BY A. L. WILDS, TILLMON H. PEARSON[2,3] AND CARL H. HOFFMAN[4,5]

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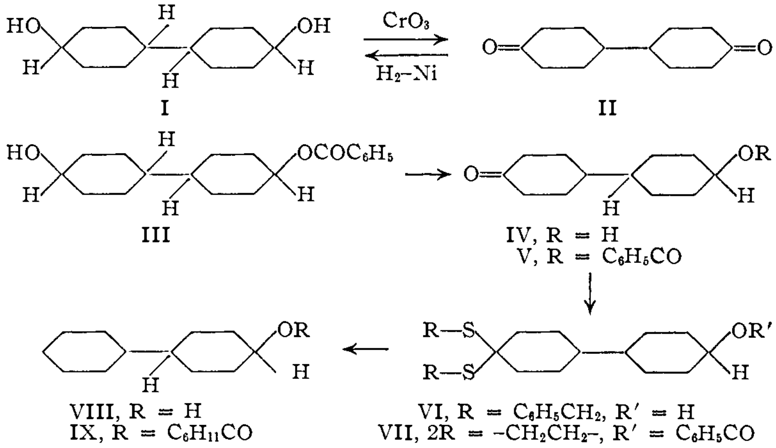
cis,cis-Bicyclohexyl-4,4'-diol (I), formed in only 1–3% yield by hydrogenation of 4,4'-dihydroxybiphenyl, has been obtained in 29–31% yield from bicyclohexyl-4,4'-dione using aged W-2 Raney nickel. Oxidation of the diol as the monobenzoate afforded a good route to the *cis*-hydroxy ketone (IV). A similar sequence of reactions with the *cis,trans*-diol gave the *trans*-hydroxy ketone as did partial oxidation of this diol. Selective hydrolysis of the *cis,trans*-dibenzoate and oxidation gave the *cis* derivative of IV. These transformations established the configuration of the *cis,trans*-diol. The *cis*- and *trans*-hydroxy ketones IV were each converted to the ethylene mercaptole benzoate and desulfurized to the derivative of *cis*- and *trans*-4-cyclohexylcyclohexanol, respectively. On the basis of configurations assigned to the latter by Ungnade, the above assignments are made to the diols and hydroxy ketones. These configurations are in accord with other considerations including polar-equatorial conformational analysis.

In the preceding paper of this series[1] was described the synthesis of the *trans* isomer of the hydroxy ketone IV, needed as the key intermediate for preparing analogs of testosterone lacking ring C. In configuration of the hydroxylated ring, however, this *trans* isomer corresponds to the physiologically less active 17α-hydroxy isomer of testosterone, rather than the natural 17β-compound. Preparation of the *cis* isomer of IV, therefore became essential for adequate evaluation of these analogs for possible androgenic activity.

In theory the *cis* isomer of IV could be prepared either from *cis,cis*-bicyclohexyl-4,4'-diol (I) or from the *cis,trans* isomer by oxidation at the *trans*-hydroxylated ring. Preliminary efforts were turned toward the latter approach, since the *cis,trans* isomer is readily available together with the *trans,-trans* isomer from hydrogenation of 4,4'-dihydroxybiphenyl. Monoöxidation of the *cis,trans*-diol gave the *trans*-hydroxy ketone IV. Monobenzoylation of the same diol followed by oxidation gave the benzoate of the *trans*-hydroxy ketone. These results, involving in each case reaction of the group *trans* to the ring junction (hydrogen in the direct oxidation[6] and hydroxyl in monobenzoylation) are in line with predictions from simpler series.[7] Since in each case the more reactive group lies in an equatorial position (see Fig. 1), the smaller hindrance to approach of the reagent, compared with the corresponding group in a polar position of the opposite ring, can account for its higher reactivity.[8]



I; II; III; IV, R = H; V, R = C_6H_5CO; VI, R = $C_6H_5CH_2$, R' = H; VII, 2R = $-CH_2CH_2-$, R' = C_6H_5CO; VIII, R = H; IX, R = $C_6H_{11}CO$

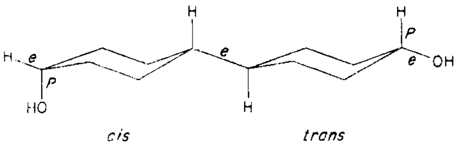


Fig. 1.

On the other hand, selective hydrolysis of the dibenzoate of the *cis,trans*-diol I should result in faster reaction of the *trans*-ester. Such a hydrolysis led to a mixture which on oxidation did in fact give the benzoate of the new *cis*-hydroxy ketone IV. The low yield, however, made it necessary to find a better approach.

The stereochemical aspects of selective oxidation are not present with the *cis,cis*-diol I, to which attention was next directed. Since this isomer is formed in but 1–3% under the drastic conditions necessary for nickel hydrogenation of 4,4'-dihydroxybiphenyl, platinum hydrogenation of the diphenol and its diacetate were tried at room temperature.[9] The extensive hydrogenolysis accompanying hydrogenation made this approach unpromising, and we turned to the milder reductions possible with the diketone II. Hydrogenation of II with platinum or palladium under acidic conditions again led to appreciable hydrogenolysis. Hydrogenation of the bis-enol acetate of II deserves mention. The hydrogenolysis[10] which accompanies hydrogenation with platinum was minimized using

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[1] Paper III, A. L. Wilds, C. H. Shunk and C. H. Hoffman, THIS JOURNAL, **76**, 1733 (1954).

[2] Wisconsin Alumni Research Foundation Research Assistant, 1949–1951.

[3] Hampden-Sidney College, Hampden-Sidney, Va.

[4] Wisconsin Alumni Research Foundation Research Assistant, 1946–1947; Ciba Pharmaceutical Products Fellow, 1948–1949.

[5] Merck and Co., Inc., Rahway, N. J.

[6] F. H. Westheimer and N. Nicolaides, THIS JOURNAL, **71**, 25 (1949).

[7] H. E. Ungnade, *J. Org. Chem.*, **13**, 361 (1948).

[8] *Cf.* D. H. R. Barton, *Experientia*, **6**, 316 (1950); *J. Chem. Soc.*, 1027 (1953).

[9] *Cf.* R. P. Linstead, W. E. Doering, S. B. Davis, P. Levine and R. R. Whetstone, THIS JOURNAL, **64**, 1985 (1942).

[10] L. J. Roll and R. Adams, *ibid.*, **53**, 3469 (1931); see also H. H. Inhoffen, G. Stoeck, G. Kölling and U. Stoeck, *Ann.*, **568**, 52 (1950).

Raney nickel at atmospheric pressure. The product contained considerable *trans,trans*-diacetate, however, making it unsuitable for our present purpose.

The best approach to the *cis,cis*-diol found was hydrogenation of the dione II at low pressure with W-2 Raney nickel catalyst.[7] The mixture of isomers which resulted was subjected to an extensive separation procedure involving fractional crystallization and selective dissolution of the dibenzoate mixture. In this way it was possible to obtain 29–31% of the *cis,cis* isomer and only 7–9% of the *trans,trans* compound, the remainder being largely *cis,trans* isomer. It is interesting to note that a greater proportion of *cis* reduction was obtained with aged and less active catalyst preparations. This may reflect a reduced activity of the catalyst for *dehydrogenation* (followed by rehydrogenation) of the resulting diol, which seems to us the most attractive explanation for *trans* hydrogenation of this, as well as other types.[11]

Having developed an adequate, though not easy, route to the *cis,cis*-diol I, it was obviously preferable to use that method for conversion to the hydroxy ketone IV which best conserved the *cis* configuration in the by-products as well as in IV. The diol was converted into the *cis,cis*-monobenzoate III in 41% yield, the remainder being diol or dibenzoate readily saponified to *cis,cis*-diol suitable for reuse. Oxidation of the monobenzoate III gave the *cis*-hydroxy ketone derivative V in 79% yield. This was suitable for use as such in the subsequent synthesis of the testosterone analog, or could be saponified to the free hydroxy ketone IV.

Now it is necessary to consider the evidence upon which is based the assignment of configuration for these geometrical isomers. Of the three bicyclohexyl-4,4′-diols (I), m.p. 216°, 197° and 178°, corresponding to the three possible stereoisomers, the *cis,trans*-configuration can be assigned unequivocally to the 178° diol. This diol has been partially oxidized to both *cis*- and *trans*-hydroxy ketones IV as outlined above. Since the remaining diols are symmetrical, their configurations can be established by using the two hydroxy ketones.

The hydroxy ketones were converted into the 4-cyclohexylcyclohexanols, to which Ungnade has assigned configurations.[7] While none of the methods used by him can be considered rigorous in itself, the fact that all gave the same conclusion supports the view that the assignment is correct.[12]

The 130° hydroxy ketone (IV) gave a crystalline dibenzyl mercaptole (VI) which was desulfurized by heating with Raney nickel. The only product isolated as the alcohol or the phenylurethan was *trans*-4-cyclohexylcyclohexanol. While this constituted strong evidence favoring the *trans*-configuration for the 130° hydroxy ketone, the possibility of an inversion was not completely excluded. In this Laboratory Dr. Zeitschel[12a] has observed dehydrogenation of an alcohol to a ketone during the course of a desulfuration; this finding and the well known fact that a ketone can be hydrogenated under these conditions[13] indicate that a pathway for inversion is available in the present case.

To exclude this possibility, the benzoate V of the hydroxy ketone was used. This was converted to the ethylene mercaptole VII which on desulfuration led, *via* the crystalline hexahydrobenzoate, again to *trans*-4-cyclohexylcyclohexanol. In a similar way the benzoate of the 93° hydroxy ketone was converted to the mercaptole VII, desulfurized and saponified to afford *cis*-4-cyclohexylcyclohexanol (VIII). Thus, we may assign the *cis* configuration to the 93° hydroxy ketone IV and *cis,cis* to the related 197° diol (I), the *trans*-configuration to the 130° hydroxy ketone IV and *trans,trans* to the related 216° diol.

These assignments are in accord with other considerations including deductions based on conformational analysis given above for the selective reactions of the *cis,trans*-diol and dibenzoate. In addition, the *trans,trans*-diol, having both hydroxyls equatorial was the most strongly adsorbed isomer (on alumina) while the *cis,cis*-diol (both hydroxyls polar) was the least strongly adsorbed of the three diols. The highest melting point of the series for the *trans,trans*-diol and particularly for its dibenzoate also is in accord with the greatest degree of symmetry in this stereoisomer. Finally, the formation of larger amounts of the thermodynamically more stable *trans,trans*-diol under the more drastic conditions of hydrogenation is consistent.

The assignment of configurations to the three diols in the present bicyclohexyl series also lends support to the views of Ungnade and Ludutsky on the configuration of the perhydro-*meso*-hexestrols.[14] As in the present case, the two preponderant isomers from high temperature Raney nickel hydrogenation were the *trans,trans* and *cis,trans* isomers. the former being the highest melting isomer.

Experimental[15]

Hydrogenation of Diacetate of 4,4′-Dihydroxybiphenyl.—A mixture of 17.6 g. of diacetate (m.p. 162.5–164.5°),[1] 120 ml. of dioxane and 4 g. of copper–chromium oxide catalyst[16] was heated and shaken with hydrogen at 5200 p.s.i. and 250° for a total of 24 hours (4 g. of fresh catalyst being added after 2 hours). The total hydrogen uptake was 121% of theory for 6 moles. Crystallization of the product from alcohol gave 2.71 g. (21%) of *trans,trans*-bicyclohexyl-4,4′-diol, m.p. 200–207° (sint. 185°). Separation of the remaining material as the dibenzoates indicated the total *trans,trans*-isomer to be 45%, with only 5% of *cis,cis*-diol. the remainder being mainly *cis,trans*-diol.

Bis-enol Acetate of Bicyclohexyl-4,4′-dione.—A mixture of 5 g. of the diketone II,[1] 21 g. of isopropenyl acetate[17] and

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(11) Compare also A. L. Wilds and W. B. McCormack, THIS JOURNAL, **70**, 4127 (1948), who obtained the same mixture of perhydro isomers from high temperature hydrogenation of the two hexahydro-*meso*-hexestrols.

(12) W. G. Dauben, V. M. Alhadeff and M. Tanabe, THIS JOURNAL, **75**, 4580 (1953), have now confirmed these configurations by relating the 4-cyclohexylcyclohexanols to the 4-cyclohexylcyclohexylcarboxylic acids and the hexahydroterephthalic acids.

(12a) A. L. Wilds, R. H. Zeitschel, R. E. Sutton and J. A. Johnson, *J. Org. Chem.*, in press.

(13) *Cf.* G. Rosenkranz, St. Kaufmann and J. Romo, THIS JOURNAL, **71**, 3689 (1949).

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

(15) All melting points are corrected. Some of the microanalyses were carried out by John Belew, Ernest Blades, Bennett Buell, Gerald Gilbert and Edward Shiner.

(16) Homer Adkins, "Reactions of Hydrogen," University of Wisconsin Press, Madison, Wis., 1937, p. 13.

(17) Tennessee Eastman Co.; see H. J. Hagemeyer and D. C. Hull *Ind. Eng. Chem.*, **41**, 2920 (1949).

0.15 g. of *p*-toluenesulfonic acid was distilled slowly through a 7.5-cm. Vigreux column, the temperature of the distillate rising from 58 to 90° during the one-hour period of heating. The residue, which solidified on cooling, was washed in chloroform solution with bicarbonate solution and crystallized from ethyl acetate, 4.64 g., m.p. 146–154.5° and 1.58 g., m.p. 144–150°, totalling 87% yield of the mixture of diastereoisomers. Efforts to obtain one of the isomers pure by further recrystallizations from ethyl acetate alone or mixed with petroleum ether were unsuccessful, although the m.p. was raised to 151.5–158°. Material melting at 145–150°, diamond-shaped plates, was analyzed.

Anal. Calcd. for $C_{16}H_{22}O_4$: C, 69.0; H, 7.97. Found: C, 69.2; H, 8.14.

The enol acetate (399 mg.) was easily hydrolyzed to the diketone with 25 ml. of 1.2 *N* hydrochloric acid and 10 ml. of alcohol, heating 1 hour. The diketone was crystallized from ethyl acetate–petroleum ether, yielding 125 mg., m.p. 115–116°, and 106 mg., m.p. 113–115.5°, for 83% recovery.

Hydrogenation of the Bis-enol Acetate.—A solution of 1.84 g. of the bis-enol acetate (m.p. 145–153.5°) in 50 ml. of purified dioxane was hydrogenated at 35 p.s.i., adding 3 one-teaspoonful portions of W-2 Raney nickel catalyst[18] (one week old) over an 18-hour period; total hydrogen uptake 103% of theory for two moles. The product crystallized partially from ethyl acetate–petroleum ether, to give 0.265 g. (14%) of material essentially all the diacetate of the *trans,trans*-diol, m.p. 128–138° (sint. from 80°). Alkaline hydrolysis of this material gave 100% of *trans,trans*-diol, m.p. 211–215°; saponification of the material in the filtrate and conversion to the dibenzoate gave 0.12 g. (5%) of crude *trans,trans*-dibenzoate, m.p. 185–208°, as well as a mixture of isomers, m.p. 120–195°.

Hydrogenation of Bicyclohexyl-4,4′-dione (II). *cis,cis* **Bicyclohexyl-4,4′-diol (I).**—The most favorable ratio of *cis* reduction resulted from using old W-2 Raney nickel catalyst preparations. With freshly prepared catalyst or with W-6 Raney nickel a higher proportion of *trans,trans* isomer resulted.

A solution of 14.2 g. of the diketone II in 180 ml. of methanol was shaken with 6 teaspoonsfuls of W-2 Raney nickel catalyst[18] (seven weeks old) and hydrogen at 40 p.s.i. at room temperature. The theoretical amount of hydrogen was absorbed in 20 hours. After filtration and evaporation, 15.8 g. of the crude diol mixture resulted.

This mixture was benzoylated in 70 ml. of purified dioxane with 37 ml. of benzoyl chloride and 50 ml. of dry pyridine, refluxing 4.5 hours, and washed in chloroform solution with dilute acid, sodium bicarbonate and water. Successive crystallization from chloroform and from ethyl acetate–petroleum ether gave the following fractions: A, 9.51 g., m.p. 150–175°; B, 1.68 g., m.p. 156–162.5° (sint. 140°); C, 4.88 g., m.p. 93–135° (trace of solid to 165°); D, 3.78 g., m.p. 90–120° (solid to 169°); and E, 2.26 g., m.p. 45–115°. Saponification of the residual material gave 1.42 g. (10%) of *cis,trans*-diol, m.p. 165–172°. Fraction A was extracted in a Soxhlet extractor five times with petroleum ether (b.p. 30–60°), each time for 1.5 hours. Recrystallization of the residue from chloroform–ethyl acetate gave 2.20 g. (7%) of *trans,trans*-dibenzoate, m.p. 200–213°, followed by two crops of crude *cis,cis*-dibenzoate totaling 2.61 g., m.p. 156–165°. The latter were combined with fraction B and the solids obtained by cooling the 3rd and 4th extracts from fraction A (0.50 g., m.p. 156–162°), and recrystallized from methanol–chloroform, giving 4.21 g. of *cis,cis*-dibenzoate, m.p. 157–164°. Another recrystallization gave 3.62 g. (12%) of the *cis,cis*-isomer, m.p. 161.5–165.5°.

The other fractions were subjected to repeated fractional crystallization to afford material melting in the range 150–160° with some solid remaining to 180°, which was a mixture of *cis,cis* and *trans,trans* isomers, and material melting in the range 90–96° with some solid to 150°, which was the *cis,trans* containing some *cis,cis* isomer. Mixtures of the first type were triturated with benzene at room temperature, filtered to remove *trans,trans* isomer, evaporated and the residue then recrystallized from methanol–chloroform. Mixtures of the second type were extracted for 1 hour with petroleum ether (b.p. 30–60°) in a Soxhlet extractor to remove most of the *cis,trans* isomer and the residue (m.p. 95–145°) recrystallized again. In this way an additional 2.25 g. (melting in the range 160–164.5° and 2.87 g.) melting between 145–161° was obtained for a total of 9.33 g. (31%) of *cis,cis*-dibenzoate. An additional 0.39 g. of *trans,trans*-dibenzoate, m.p. 201–206°, brought the total of this isomer to 9%, and 4.08 g., m.p. 94–98°, and 2.58 g., m.p. 92–96°, made the total of *cis,trans* isomer isolated 32%.

The effect of the catalyst activity on the ratio of *cis,cis* to *trans,trans* isomer is indicated by the following results: using seven weeks old W-6 Raney nickel[19] (stored under absolute alcohol at 10°) 18% of *trans,trans*-dibenzoate and 17% of *cis,cis*-dibenzoate were isolated; using three year old W-6 Raney nickel (stored at 10°), 7% of *trans,trans* and 21% of *cis,cis*-dibenzoate were separated. In each case the remaining material was mainly the *cis,trans* isomer. W-2 Raney nickel used at 1800 p.s.i. and room temperature, resulted in 15% of *trans,trans* isomer and 11% *cis,cis* isomer in addition to the *cis,trans* isomer.

Mixtures of the dibenzoates also could be separated partially by adsorption on and fractional elution from alumina. The *cis,cis* isomer was least strongly adsorbed, followed by the *cis,trans* and *trans,trans* isomers in that order.

Monobenzoate of *cis,cis*-**Bicyclohexyl-4,4′-diol (III).**—A solution of 5.18 g. of the *cis,cis*-diol in 50 ml. of dry dioxane and 50 ml. of dry pyridine was treated with 4.79 g. of benzoyl chloride in 30 ml. of dioxane as described for the *trans,-trans*-diol. After heating for 2 hours and removing most of the solvents, the residue was treated with water and chloroform; filtration gave 1.51 g. (29%) of unreacted diol, m.p. 185–196°. The chloroform layer was washed with dilute acid, evaporated and the oil triturated with 25 ml. of methanol, afforded 1.90 g. (18%) of the *cis,cis*-dibenzoate, m.p. 156–160°. Evaporation of the filtrate and crystallization of the oil from petroleum ether–ethyl acetate gave 2.87 g., m.p. 84–88°, and 0.36 g., m.p. 75–85°, for a total of 41% of crude monobenzoate. Further recrystallization from the same solvent pair gave platelets melting at 88.5–89.5°.

Anal. Calcd. for $C_{19}H_{26}O_3$: C, 75.5; H, 8.67. Found: C, 75.5; H, 8.80.

Benzoate of 4-(*cis***-4′-Hydroxycyclohexyl)-cyclohexanone (V).**—Oxidation of a solution of 1.57 g. of *cis,cis*-monobenzoate (m.p. 80–88°) with 400 mg. of chromium trioxide in a total of 190 ml. of acetic acid and 3 ml. of water for 12 hours at 25°, gave the *cis*-ketobenzoate (V) in 79% yield, most melting at 74–76°. Further recrystallization from petroleum ether–ethyl acetate gave needles, m.p. 76.5–77.5°.

Anal. Calcd. for $C_{19}H_{24}O_3$: C, 76.0; H, 8.05. Found: C, 76.0; H, 7.97.

4-(*cis***-4′-Hydroxycyclohexyl)-cyclohexanone (IV).**—A mixture of 554 mg. of the *cis*-ketobenzoate and 25 ml. of 5% methanolic potassium hydroxide was heated at reflux for 1 hour, then just acidified with hydrochloric acid and treated with sodium bicarbonate solution. Extraction with chloroform and crystallization from ethyl acetate–petroleum ether gave 336 mg., m.p. 92–93°, and 9 mg., m.p. 81–87° (95% yield). Further recrystallization from ethyl acetate afforded fluffy plates of m.p. 92.5–93.5°.

Anal. Calcd. for $C_{12}H_{20}O_2$: C, 73.4; H, 10.27. Found: C, 73.4; H, 10.33.

The above procedure was arrived at after experiments with the *trans*-ketobenzoate and the diketone demonstrated that self-condensation of the ketone under these conditions was negligible (*cf.* Wilds and McCormack[11]); the yield of *trans*-keto alcohol was 94%, m.p. 127.5–129.5°.[1]

Partial Oxidation of *cis,trans*-**Bicyclohexyl-4,4′-diol (I).**—A solution of 1.00 g. of the *cis,trans*-diol (m.p. 175–177°) was oxidized with 0.37 g. of chromium trioxide in a total of 50 ml. of acetic acid and 4 ml. of water (oxidizing agent added during 1 hour, total time 19 hours, temperature 10°). After isolation, the crude product was crystallized from benzene to give 116 mg. of the starting diol, m.p. 170–173° (mixed m.p. 173–176°). The residue was chromatographed on 30 g. of acid-washed alumina and eluted with benzene. After 10 mg. of oil in fractions 1–3, nearly pure bicyclohexyl-4,4′-dione was eluted (fractions 4–13, 172 mg. (18%), m.p. 113–115° with previous softening). The next eluates (fractions 14–44) ranging from benzene and benzene–ether mixtures to ether alone afforded less pure material which, on recrystallization from carbon tetrachloride alone or

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(18) R. Mozingo, *Org. Syntheses*, **21**, 15 (1941).

(19) H. Adkins and H. R. Billica, THIS JOURNAL, **70**, 695 (1948).

mixed with ethyl acetate, gave 252 mg. of the *trans*-hydroxy ketone,[1] m.p. 129–130°, and 77 mg., m.p. 123–129°, for a total yield of 33%. From later eluates an additional 20 mg. (total recovery 14%) of the *cis,trans*-diol, m.p. 173–175° (previous softening) was recovered.

***trans*-Monobenzoate of *cis,trans*-Bicyclohexyl-4,4'-diol.**—A solution of 1.00 g. of the *cis,trans*-diol (m.p. 175–177°) in 10 ml. of dry pyridine was heated with 0.6 ml. of benzoyl chloride at reflux for 2.5 hours. After isolating the product with chloroform, washing and drying the extracts and then evaporating the solvent, the crude product was digested with 10 ml. of hot carbon tetrachloride and filtered to give 0.28 g. (28%) of recovered diol, m.p. 174–177°. Crystallization of the remaining oil from petroleum ether (b.p. 60–68°) gave 0.33 g., m.p. 109–111°, of crude monobenzoate. Further crystallization from the same solvent containing a small amount of ethyl acetate gave 0.23 g. (15%) of *trans*-monobenzoate of the *cis,trans*-diol, m.p. 121–122°. Additional recrystallizations from petroleum ether or cyclohexane gave rosettes of colorless needles, m.p. 121.5–122.5°.

Anal. Calcd. for $C_{19}H_{26}O_3$: C, 75.5; H, 8.67. Found: C, 75.5; H, 8.60.

Attempts to obtain the other monobenzoate from the filtrates were unsuccessful.

Oxidation of 154 mg. of the above monobenzoate with chromium trioxide gave the benzoate of 4-(*trans*-4'-hydroxycyclohexyl)-cyclohexanone in 87% yield; most melted at 150–152° (mixed m.p. 150–152.5°).

***cis*-Monobenzoate of *cis,trans*-Bicyclohexyl-4,4'-diol (I).**—A mixture of 205 mg. of the *cis,trans*-dibenzoate (m.p. 95–97.5°) and 10 ml. of 0.05 *N* methanolic potassium hydroxide was heated at reflux for 1 hour, then concentrated, just acidified and treated with bicarbonate solution. Extraction with chloroform afforded an oil which partially crystallized when triturated with petroleum ether, giving 74 mg. of solid, m.p. 60–65°. Treatment of the solid with hot cyclohexane gave a trace of the *cis,trans*-diol, m.p. 165–176°, in the insoluble fraction, but still gave impure material on crystallization, m.p. 59–70°. Adsorption on alumina gave some dibenzoate in the first fractions (benzene eluates). From the last fractions (15–18, eluted with 1% methanol in ether) was obtained about 30% of material which on crystallization from cyclohexane melted at 64–73° and gave a melting point depression (51–74°) when mixed with the *cis, trans*-dibenzoate.

Since further attempts to obtain this *cis*-monobenzoate pure were not encouraging, 109 mg. was oxidized in acetic acid with chromium trioxide. Crystallization of the product from petroleum ether alone and mixed with ethyl acetate gave a few milligrams of the diketone, m.p. 110–114°, and 59% of the benzoate (V) of *cis*-hydroxy ketone, m.p. 72–75° (mixed m.p. 73–75°).

Conversion of 4-(*trans*-4'-Hydroxycyclohexyl)-cyclohexanone (IV) to *trans*-4-Cyclohexylcyclohexanol (VIII). (a) Dibenzyl Mercaptole of (IV).—Benzyl mercaptan (2 ml.) was added slowly to an intimate mixture of 410 mg. of the *trans*-hydroxy ketone (m.p. 129–130°), 1 g. of anhydrous sodium sulfate and 1 g. of freshly fused and powdered zinc chloride, while the mixture was shaken and cooled in an ice-bath. After three days at room temperature the mixture was thoroughly triturated with portions of benzene and of ether, the combined solutions were washed with dilute sodium hydroxide and dried. The product was crystallized from benzene giving in two crops 404 mg. (45%) of fluffy white needles, m.p. 143–146°, and 622 mg. of residual oil. Further recrystallization of the solid gave the pure dibenzyl **mercaptole of 4-(*trans*-4'-hydroxycyclohexyl)-cyclohexanone** melting at 149–151.5°.

Anal. Calcd. for $C_{26}H_{34}OS_2$: C, 73.2; H, 8.03. Found: C, 73.2; H, 7.89.

(b) **Desulfuration of the Mercaptole to (VIII).**—A solution of 368 mg. of the above mercaptole (m.p. 143–146°) in 20 ml. of absolute alcohol and 20 ml. of benzene was heated at reflux for 6 hours with 1.5 teaspoonfuls (*ca.* 5 g.) of W-2 Raney nickel.[18] After cooling, filtering and concentrating, 153 mg. (97%) of material was obtained, micro m.p. 93–98°. Recrystallization of the material from petroleum ether gave fractions melting as high as 98–100°. A small amount (11 mg., 6%) of *trans,trans*-diol I was obtained from the petroleum ether-insoluble portion after recrystallization from ethyl acetate, m.p. 209–212°. The residue from this and the petroleum ether-soluble fraction were sublimed at 100–120° (0.2 mm.) and crystallized from petroleum ether. After a small fraction (7 mg.), m.p. 150–160°, not further investigated, 68 mg. of *trans*-4-cyclohexylcyclohexanol, micro m.p. 102–103°, was obtained as thin white needles (reported[7] for *trans* isomer, m.p. 103–104°; for *cis*, m.p. 92–93°). An additional 16 mg., m.p. 100–102.5°, brought the total yield of *trans* isomer to 53%.

The remaining oil (12 mg.) was converted to the phenylurethan, yielding 5 mg. from petroleum ether, micro m.p. 155–157° (reported m.p. 156–156 8°[7]).

Conversion of the *trans*-Ketobenzoate V to *trans*-4-Cyclohexylcyclohexanol. (a) The Benzoate of *trans*-4-Hydroxy-4'-ethylenemercaptobicyclohexyl (VII).—A procedure similar to that of Ralls, Dodson and Riegel[20] for 3-cholestanone was used. To a solution of 1.22 g. of the *trans*-keto-benzoate V (m.p. 151–153°) in 75 ml. of glacial acetic acid and 15 ml of concentrated hydrochloric acid was added in one portion 0.42 g. of 1,2-ethanedithiol. Almost immediately, white crystals began to form and after standing overnight the mixture had a creamy consistency. The mixture was chilled in ice, filtered and the white precipitate washed with cold methanol, yielding 1.43 g., m.p. 143.5–145° (94%). Recrystallization from ethyl acetate–petroleum ether and methanol–chloroform gave thin plates of m.p. 144.6–145.4°.

Anal. Calcd. for $C_{21}H_{28}O_2S_2$: C, 67.0; H, 7.50. Found: C, 67.3; H, 7.51.

(b) **Desulfuration of the Ethylene Mercaptole VII to the Hexahydrobenzoate of *trans*-4-Cyclohexylcyclohexanol (IX).**—A mixture of 1.04 g. of the mercaptole VII (m.p. 144.5–145.5°), 4 teaspoonfuls of W-6 Raney nickel[19] and 50 ml. of pure dioxane was refluxed for 5 hours. Removal of the catalyst and evaporation of the solvent under reduced pressure yielded an oil. Crystallizations from ethanol–water gave 714 mg. (88%), m.p. 61–66°. Further recrystallizations gave pure hexahydrobenzoate of *trans*-4-cyclohexylcyclohexanol (IX), as fluffy needles, m.p. 74.1–74.7°.

Anal. Calcd. for $C_{19}H_{32}O_2$: C, 78.0; H, 11.03. Found: C, 77.7; H, 10.82.

(c) **Saponification of the Hexahydrobenzoate IX to *trans*-4-Cyclohexylcyclohexanol (VIII).**—All the filtrates and material from the desulfuration (preceding paragraph) were combined (except 83 mg. of the analytical sample) and crystallized from dilute ethanol to give 326 mg. of hexahydrobenzoate, m.p. 65–70.5°. This solid was saponified with 25 ml. of methanolic potassium hydroxide and the product recrystallized from petroleum ether to give 117 mg. of *trans*-4-cyclohexylcyclohexanol, m.p. 102.5–104°. Saponification of the filtrates gave an additional 154 mg. of the *trans* isomer, m.p. 103–104.5°,[7] bringing the yield to 60%.

The phenylurethan was prepared from the residue (74 mg.) and recrystallized from petroleum ether giving 87 mg. (11%), m.p. 154–156°,[7] corresponding to a total of 71% of *trans*-4-cyclohexylcyclohexanol.

Conversion of the *cis*-Ketobenzoate V to *cis*-4-Cyclohexylcyclohexanol. (a) The Benzoate of *cis*-4-Hydroxy-4'-ethylenemercaptobicyclohexyl (VII).—Treatment of 964 mg. of the *cis*-ketobenzoate with ethanedithiol as described for the *trans* isomer gave 802 mg. from petroleum ether, m.p. 75.5–77°, and 74 mg., m.p. 74–76°, totaling 72%. Further recrystallization from the same solvent gave plates, m.p. 76–77°.

Anal. Calcd. for $C_{21}H_{28}O_2S_2$: C, 67.0; H, 7.50. Found: C, 66.7; H, 7.33.

(b) **Desulfuration and Saponification of *cis*-4-Cyclohexylcyclohexanol (VIII).**—A solution of 345 mg. of the above *cis*-mercaptole in 10 ml. of purified dioxane was heated with 1.5 teaspoonsful of W-6 Raney nickel[19] for 7 hours. The resulting oily product was saponified and the neutral portion (191 mg.) triturated with petroleum ether, giving 67 mg. of impure *cis*-alcohol, m.p. 82–88°. The solid and remaining oil were converted to the phenylurethan, giving 158 mg. (57%) of the *cis* derivative, m.p. 109–111° (reported 107–108° and 111–112°).[7]

Madison 6, Wis.

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(20) J. W. Ralls, R. M. Dodson and B. Riegel, This Journal, **71**, 3322 (1949).