of crude IV, m.p. 87–96°, which after crystallization from ethanol amounted to 0.140 g. (56%), m.p. 101.2–103.6°. A mixed m.p. showed no depression. The ultraviolet spectrum of crude IV showed no evidence of III.

Treatment of *p*-Chlorophenyl Benzhydryl Ketone (III) with Magnesium Bromide.—When a benzene solution of 0.110 g. of III was added to a suspension of magnesium bromide in ether and subjected to the conditions of the isomerization, 0.095 g. (86%) was recovered, m.p. 106–108°, of which the ultraviolet spectrum was identical with the original ketone. A mixed m.p. showed no depression.

Reaction of *erythro*-I with Butyllithium.—*erythro*-I (0.200 g., 0.00052 mole) was added to a solution of *n*-butyllithium in ether and the procedure used above for the Grignard reactions (excess) was followed. A 97% yield of *trans*-II, m.p. 93–99°, was obtained which after one recrystallization from methanol melted at 102.2–104.0° (mixed m.p. showed no depression).

Reaction of *threo*-I with Butyllithium.—*threo*-I treated as above afforded 0.156 g. (98%) of *cis*-oxide, m.p. 72–86°. After one recrystallization from methanol the m.p. was 87–88.4° and a mixed m.p. with *cis*-II prepared above showed no depression.

The ultraviolet spectra were obtained with a Carey recording spectrophotometer at concentration of 20 mg./l. in ethanol.

URBANA, ILLINOIS

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

The Synthesis of *cis*- and *trans*-3-Methylcyclohexanol. Reassignment of Configuration of the 3-Methylcyclohexanols

BY HARLAN L. GOERING AND CARL SERRES, JR.[1]

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Authentic *cis*- and *trans*-3-methylcyclohexanol have been prepared from the diastereoisomeric 3-hydroxycyclohexane carboxylic acids by synthetic schemes designed to avoid ambiguities concerning configurations. Comparison of the solid derivatives of the authentic isomeric 3-methylcyclohexanols with the derivatives recorded in the literature clearly demonstrates the heretofore accepted assignment of configuration to be in error.

The diastereoisomeric 3-methylcyclohexanols have been reported several times in the literature and although discrepancies in the physical properties and melting points of solid derivatives suggest that the isomers were obtained in varying degrees of purity,[2] it appears that there is complete agreement in the assignment of configuration to the isomers. The 3-methylcyclohexanols were first prepared by Knoevenagel[3] who designated the *trans* configuration to the predominating isomer obtained from the sodium and alcohol reduction of 3-methylcyclohexanone. Skita[4] assumed that the isomer obtained from the catalytic (platinum) reduction of *m*-cresol in warm acid medium was the *cis* isomer and that the *trans* isomer was obtained when the reduction was carried out in cold neutral solution. Kenyon and co-workers[5] assigned *cis* and *trans* configurations from a comparison of the relative viscosities of the alcohols with the relative viscosities of the diastereoisomeric 2- and 4-methylcyclohexanols. From a correlation of various physical constants Skita and Faust[6] assigned configurations to the isomers in agreement with the earlier workers. More recently the Knoevenagel–Kenyon–Skita assignment has been taken for granted in several investigations.[7–9]

In connection with another problem we were concerned with the structure of the 3-methylcyclohexanols. Since the assigned structures had not been unequivocally determined and as evidence was available which indicated that the previous assignment might be in error (see conclusion) we reinvestigated the structures of these isomers. In the present work authentic *cis*- and *trans*-3-methylcyclohexanol have been prepared and the assignment of configuration made by the earlier workers has indeed been found to be in error. Authentic *cis*- and *trans*-3-methylcyclohexanols were prepared from the isomeric 3-hydroxycyclohexanecarboxylic acids of the same configuration. The acids were selected as starting materials for an unequivocal synthesis of the isomeric 3-methylcyclohexanols because there can be no ambiguities concerning the configurations of the acids as the *cis*-3-hydroxycyclohexanecarboxylic acid (I) forms the lactone (II),[10,11] whereas the geometry of the *trans* acid (IX) prohibits lactone formation.

A mixture of *cis*-(I) and *trans*-(IX) acids was prepared by the hydrolysis of ethyl 3-hydroxycyclohexanecarboxylate, which in turn was prepared from *m*-hydroxybenzoic acid by the method of Clarke and Owen.[12] This proved to be a more convenient method for preparing large amounts of the mixture of isomeric acids than the method of Perkins and Tattersall,[11] which involves the reduction of *m*-hydroxybenzoic acid with sodium and ethanol. The pure isomeric acids were obtained from the mixture as follows. The mixture was dissolved in ethyl acetate from which a crop of the *cis* acid separated. Evaporation of the mother liquor resulted in a mixture of the isomeric acids (as indicated by a neutral equivalent of 145 ± 2 as compared to the calculated value of 144), which

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(1) Taken from the B.S. thesis of Carl Serres, Jr., University of Wisconsin, 1952.

(2) Some discrepancies in the melting points of the solid derivatives are possibly due to polymorphism which appears to be quite common among derivatives of 3-methylcyclohexanol.

(3) E. Knoevenagel, *Ann.*, **297**, 126 (1897).

(4) A. Skita, *ibid.*, **431**, 4 (1923).

(5) G. Gough, H. Hunter and J. Kenyon, *J. Chem. Soc.*, 2052 (1926).

(6) A. Skita and W. Faust, *Ber.*, **64**, 2878 (1931).

(7) (a) A. K. Macbeth and J. A. Mills, *J. Chem. Soc.*, 709 (1945); (b) L. M. Jackman, A. K. Macbeth and J. A. Mills, *ibid.*, 2641 (1949).

(8) W. R. Brode and R. W. van Dolah, *Ind. Eng. Chem.*, **39**, 1157 (1947); Mousseron, Marszak and Bolle, *Bull. soc. chim.*, **9**, 260 (1942); M. Godchot and G. Cauquil, *Compt. rend.*, **198**, 663 (1934).

(9) D. S. Noyce and D. G. Denney, THIS JOURNAL, **72**, 5713 (1950).

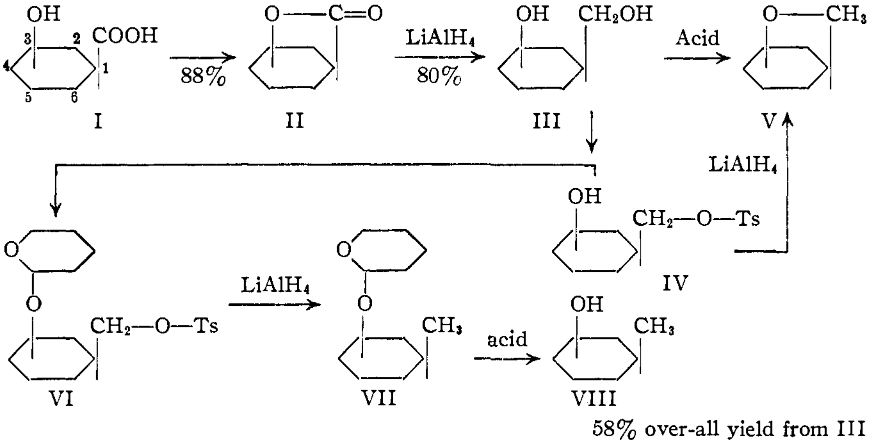
(10) E. J. Boorman and R. P. Linstead, *J. Chem. Soc.*, 258 (1935).

(11) W. Perkins and G. Tattersall, *ibid.*, 486 (1907).

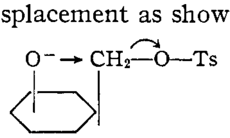
(12) M. F. Clarke and L. N. Owen, *ibid.*, 2108 (1950).

could not be conveniently separated by recrystallization. This mixture was readily separated by taking advantage of the fact that the *cis* acid can be distilled, as the lactone, from the *trans* acid. The lactone was then hydrolyzed to the *cis* acid which was purified by recrystallization. The *trans* acid was obtained from the residue and purified by recrystallization.

The *cis* acid (I) was converted to authentic *dl-cis*-3-methylcyclohexanol (VIII) by a series of reactions, which involves conversion of the carboxyl group to a methyl group without affecting the configuration at C_1 and C_3. Pure I was converted to II and reduced with lithium aluminum hydride to *cis*-3-hydroxymethylcyclohexanol (III). It is clear that these steps should not affect the configuration at C_1 and C_3 as it has been demonstrated that esters of optically active alcohols can be reduced with lithium aluminum hydride without racemizing the alcohol or changing the configuration of the α-carbon atom.[13] The *cis* diol (III) was shown to be the same as the previously reported *cis*-3-hydroxymethylcyclohexanol[12] (obtained from a mixture of the diastereoisomers) by comparison of physical properties and melting points of solid derivatives. Further evidence confirming the *cis* structure was obtained when it was found that the diol is extremely susceptible to intramolecular acid-catalyzed dehydration to 1,3-endomethyleneoxycyclohexane (V).[12]



The *cis* diol (III) was converted to *cis*-3-hydroxycyclohexylmethyl *p*-toluenesulfonate (IV)[12] by selective esterification of the primary hydroxyl group with *p*-toluenesulfonyl chloride in pyridine. The monotosylate could not be reduced directly to VIII with lithium aluminum hydride, but instead was converted to V. Presumably this conversion involves formation of the alkoxide ion which undergoes internal displacement as shown



In order to prevent oxide formation IV was converted to the tetrahydropyranyl ether (VI) which was not isolated, but immediately reduced with lithium aluminum hydride. The *cis*-3-methylcyclohexyl tetrahydropyranyl ether (VII) obtained in this way was converted without isolation to *cis*-3-methylcyclohexanol (VIII) by acid hydrolysis.

The melting points of solid derivatives of VIII are summarized in Table I together with the melting points of the corresponding derivatives of the diastereoisomeric 3-methylcyclohexanols recorded in the literature.

TABLE I

COMPARISON OF DERIVATIVES OF VIII WITH DERIVATIVES OF DIASTEREOISOMERIC 3-METHYLCYCLOHEXANOLS

3-Methylcyclohexanol	*p*-Nitrobenzoate, °C.	α-Naphthylurethan, °C.
VIII (authentic *cis*)	56.4–57.2[b]	128–129[b]
"*cis*"[a]	63,[6] 65[5]	118[7a]
"*trans*"[a]	48,[6] 58[5]	130[7a]

[a] These are the previously assigned configurations. [b] Corrected melting points.

These data show that the derivatives of VIII have melting points corresponding to the derivatives of the alleged *dl-trans*-3-methylcyclohexanol. The melting point of the α-naphthylurethan of VIII was not depressed when mixed with the α-naphthylurethan of a pure diastereoisomeric 3-methylcyclohexanol melting at 129.6–130°.[14] The melting point of the *p*-nitrobenzoate of VIII is similar to that reported by Kenyon[5] for the *trans* isomer, but differs from a value reported by Macbeth and Mills.[7a] The latter workers also observed this discrepancy and suggested that Kenyon's sample was impure; however, in the present work we have found this discrepancy to be due to the fact that the compound exists in dimorphic forms. Both modifications were obtained[15] and recrystallized to constant melting points. When the high melting modification, m.p. 56.4–57.2°, was mixed with the low melting modification, m.p. 47.6–48.4°, the mixture melted at 56.4–57.2°. The infrared spectra of carbon disulfide solutions of these modifications were found to be indistinguishable, confirming that the two samples were dimorphic modifications of the same compound.[16]

The foregoing evidence demonstrates that the

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(13) W. G. Brown in R. Adams, "Organic Reactions," Vol. VI, John Wiley and Sons, Inc., New York, N. Y., 1951, p. 469.

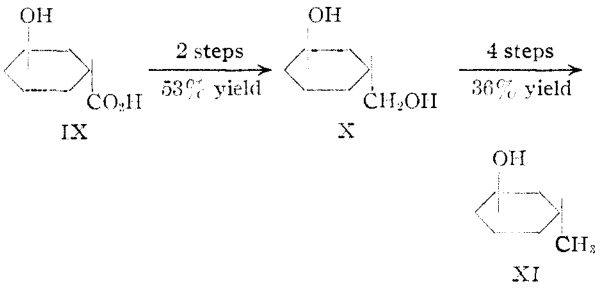
(14) The pure diastereoisomeric 3-methylcyclohexanols, from which derivatives were prepared for comparison with the derivatives obtained in the present work, were prepared by reduction of the isomeric 5-methyl-2-cyclohexenols: J. P. Blanchard and H. L. Goering, unpublished results.

(15) The authors are indebted to Miss Jean Blanchard of this Laboratory for furnishing a sample of the low melting, m.p. 47.6–48.4°, modification. This material was prepared from the 3-methylcyclohexanol resulting from the reduction of a pure diastereoisomeric 5-methyl-2-cyclohexenol. The higher melting modification, m.p. 56.4–57.2°, was obtained in the present work.

(16) The infrared spectra of the *cis* and *trans* isomers of 3-methylcyclohexyl *p*-nitrobenzoate show considerable differences and thus the two samples cannot be the diastereoisomers of different degrees of purity.

isomeric 3-methylcyclohexanol formerly assigned the *trans* configuration is actually the *cis* isomer.

dl-trans-3-Methylcyclohexanol (XI) was prepared from *trans*-3-hydroxycyclohexanecarboxylic acid (IX) by the series of reactions summarized below. The *trans* acid was converted to methyl 3-hydroxycyclohexanecarboxylate, which in turn was converted to *trans*-3-hydroxymethylcyclohexanol (X) by reduction with lithium aluminum hydride. The di-*p*-nitrobenzoate of X was prepared in nearly quantitative yields and found to be the same as the *trans* diol derivative reported by Clarke and Owen.[12] The *trans* diol was converted to *trans*-3-methylcyclohexanol (XI) by the same series of reactions used in the preparation of the authentic *cis* isomer. Although oxide formation is not possible in the *trans* series the monotosylate of X was converted to the tetrahydropyranyl ether prior to reduction with lithium aluminum hydride in order to prevent intermolecular ether formation and to have conditions corresponding to those used in preparing VIII.



Solid derivatives of authentic *trans*-3-methylcyclohexanol (XI) are compared with the reported melting points of these derivatives of the alleged *cis* isomer in Table II. The infrared spectrum of the *p*-nitrobenzoate of XI was indistinguishable from that of a *p*-nitrobenzoate, m.p. 62.8–63°, prepared from a pure *dl* isomer of 3-methylcyclohexanol.[14]

TABLE II

COMPARISON OF DERIVATIVES OF XI WITH DERIVATIVES OF ALLEGED *cis*-3-METHYLCYCLOHEXANOL

3-Methylcyclohexanol	*p*-Nitrobenzoate, °C.	α-Naphthylurethan, °C.
"*cis*"[a]	63,[7a] 65[8]	118[7a]
XI (authentic *trans*)	62–62.5[b]	114.5–115[b]

[a] This is the previously assigned configuration. [b] These melting points are corrected. The melting points of these derivatives were not depressed when mixed with derivatives of similar melting point derived from a pure diastereoisomeric 3-methylcyclohexanol.[14]

The evidence presented and summarized in Tables I and II demonstrates unequivocally that the diastereoisomeric 3-methylcyclohexanols have previously been assigned the wrong configuration.

Conclusion.—The new assignment of configuration to the 3-methylcyclohexanols is in agreement with the evidence used by the earlier workers to arrive at or support the erroneous assignment. For example, from heats of combustion Skita and Faust[6] found one epimer to be measurably more stable than the other for the 1,2-, 1,3- and 1,4-methylcyclohexanols.[17] They assumed that the *trans* isomer was the more stable one; an assumption that is in agreement with present day theories for the 1,2- and 1,4-disubstituted cyclohexanes, but not for the 1,3-isomers.[18,19] The present work shows that the more stable isomer of 3-methylhexanol, which Skita called *trans*, is actually the *cis* isomer.

The preponderant formation of the *cis* isomer (formerly called *trans*) from the sodium and alcohol reduction of 3-methylcyclohexanone[3,5] is in accord with the general rule (emphasized by Barton[19,20]) that reductions of this type yield preponderant amounts of the more stable isomer.

Similarly Barton[21] has recently called attention to the fact that lithium aluminum hydride reduction of an unhindered keto group apparently results in the preponderant formation of an equatorial hydroxyl group (most stable isomer). Nace and O'Connor[22] have recently provided a similar example by showing that cholestanone is converted primarily to β-cholestanol by lithium aluminum hydride reduction. With the new assignment of configuration to the 3-methylcyclohexanols the stereochemical studies of Noyce and Denney[9] can be reinterpreted and provide what is perhaps some of the best evidence that lithium aluminum hydride reduction of an unhindered ketone results in preponderant formation of the more stable isomer. These workers observed that the *trans*-carbinols predominate from the reduction of the 2- and 4-methylcyclohexanones and that the *cis*-epimer (formerly called *trans*) predominates from 3-methylcyclohexanone.

Experimental[23]

***cis*-(I) and *trans*-(IX)-3-Hydroxycyclohexanecarboxylic Acids.**—A solution of 495 g. (3.0 moles) of ethyl 3-hydroxycyclohexanecarboxylate,[12] in two liters of 20% potassium hydroxide was refluxed for one-half hour. The alcohol formed in the hydrolysis was removed by distillation until the vapor temperature reached 100°. During this azeotropic distillation water was added as required to keep the volume essentially constant. After acidification to congo red with concentrated hydrochloric acid the solution was extracted with ether for five hours with an efficient continuous extractor. Removal of the ether yielded an isomeric mixture of the acids which sometimes crystallized but usually was obtained as a viscous oil. This residue was taken up in hot ethyl acetate (3 ml. of solvent per gram of solute) from which 43 g. of crude *cis* acid, m.p. 120–124°, crystallized as the solution cooled. After two additional recrystallizations from ethyl acetate 33 g. of I, m.p. 130–132°,

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(17) It has been suggested that Skita had impure epimers of the 1,3-[7a] and 1,4-methylcyclohexanols (Macbeth, *et al.*, *J. Chem. Soc.*, 1717 (1949)), however, it seems likely that the epimers were probably pure as they were obtained from solid derivatives recrystallized to constant melting point and reformed the derivatives with the same melting point. The discrepancies in the melting points of the solid derivatives reported by Skita and Macbeth are probably due to polymorphism. It is clear that Macbeth's suggestion that Skita's *cis*-4-methylcyclohexanol was actually an impure sample of the *trans* isomer is invalid as the melting points of the solid derivatives of *cis*-4-methylcyclohexanol recorded by Skita are higher than those reported by Macbeth and are depressed by the epimer.

(18) C. W. Beckett, K. S. Pitzer and R. Spitzer, THIS JOURNAL, **69**, 2488 (1947).

(19) D. H. R. Barton, *Experientia*, **6**, 316 (1950).

(20) D. H. R. Barton and W. J. Rosenfelder, *J. Chem. Soc.*, 1048 (1951).

(21) D. H. R. Barton and N. J. Holness, *ibid.*, 78 (1952).

(22) H. R. Nace and G. L. O'Connor, THIS JOURNAL, **73**, 5824 (1951).

(23) All melting points are corrected.

was obtained. The solvent was removed from the combined mother liquors and the residual mixture, which could not be conveniently separated by fractional crystallization, was placed in a preheated oil-bath at 170° for three-quarters of an hour in order to convert the *cis* acid (I) to the lactone (II). The pressure was then reduced and the lactone removed by distillation, b.p. 115–140° (15 mm.). The crude lactone[24] obtained in this way could not be conveniently purified by recrystallization or redistillation and was saponified to the *cis*-hydroxy acid (IV) as previously described.[10] The *cis* acid was isolated from the hydrolysis solution by ether extraction with a continuous extractor and after removal of the ether the solid residue of *cis* acid was recrystallized from ethyl acetate (yield 74 g., m.p. 130–132°). A total of 107 g. (25% yield) of pure *cis*-3-hydroxycyclohexanecarboxylic acid, m.p. 130–132°, was obtained (lit.[10] 130–132°).

trans-3-Hydroxycyclohexanecarboxylic acid (IX) was isolated from the residue remaining from the distillation of the lactone as follows: High neutral equivalents of the residue (522 to 1062) suggested that the *trans* acid had undergone condensation polymerization, consequently the residue was submitted to hydrolysis with refluxing methanolic potassium hydroxide for one-half hour. After dilution with water the methanol was removed by distillation until the vapor temperature reached 100°. The colored alkaline solution was extracted with ether to remove neutral impurities and then acidified to congo red and continuously extracted with ether for five hours. The residue (oil) resulting from the evaporation of ether was dissolved in ethyl acetate from which 76 g. of crude *trans* acid, m.p. < 100°, crystallized. After two recrystallizations from acetonitrile 50.4 g. (12% yield) of IX, m.p. 117–118°,[25] (lit.[11] m.p. 119–120°) was obtained. The melting point of the *trans*-hydroxy acid (IX) obtained in this way was depressed on admixture with the *cis*-isomer.

Conversion of *cis*-3-Hydroxycyclohexanecarboxylic Acid (I) to *cis*-3-Hydroxymethylcyclohexanol (III).—Pure *cis* acid (I), 107 g. (0.743 mole) m.p. 130–132°, was placed in a preheated oil-bath at 170° for one-half hour. The pressure was then reduced and the material distilled yielding 83 g. (88.5%) of the **lactone of *cis*-3-hydroxycyclohexanecarboxylic acid** (II), b.p. 125–127° (15 mm,). After recrystallization of the sticky white solid from petroleum ether, the lactone melted at 118° (lit.[10] 119°).

A solution of 75 g. (0.595 mole) of II in dry ether was reduced with lithium aluminum hydride according to the general procedure of Nystrom and Brown[26] for the reduction of esters. The *cis* diol III was isolated by ether extraction of the aqueous layer for 30 hours with a continuous extractor. In order to avoid acid-catalyzed intramolecular dehydration to the oxide, V, potassium carbonate was placed in the ether pot to prevent the ether extract from becoming acidic. After removal of the ether, 62 g. (80%) of ***cis*-3-hydroxymethylcyclohexanol** (III) was obtained as a colorless viscous oil, b.p. 119–120° (1 mm.), $n^{25}\text{D}$ 1.4900 (lit.[12] b.p. 115–117° (0.2 mm.) $n^{25}\text{D}$ 1.4902). In one large run 1,3-endomethyleneoxycyclohexane (V), identified by its characteristic odor and m.p. 95–97° (lit.[12] m.p. 96–97°) was obtained in 50% yield, instead of III. This result was apparently due to the fact that the diol was distilled from a flask containing traces of acid and illustrates the ease with which III is converted to V by acid-catalyzed intramolecular dehydration.

The *cis* diol was converted to the di-*p*-nitrobenzoate m.p. 140–141° (lit.[12] m.p. 140–141°), in 93% yield by reaction with a 10% excess of *p*-nitrobenzoyl chloride in dry pyridine. No evidence was obtained for the presence of the epimer.

The dimethanesulfonate of III was prepared from the diol and methanesulfonyl chloride as previously described.[12] After recrystallization from absolute ethanol the derivative, m.p. 102.5–103.5° (lit.[12] 102.5–103.5°), was obtained in 89% yield.

Conversion of *cis*-3-Hydroxymethylcyclohexanol to *cis*-3-Methylcyclohexanol (VIII).—Ten grams of (III) was converted to the *p*-toluenesulfonate (IV) in 70% yield by the method of Clarke and Owen.[12] This material, 14.5 g., was obtained as an oil and without purification was converted to the tetrahydropyranyl ether, VI, according to the method of Dauben and Bradlow.[27] After removal of most of the excess dihydropyran, the residual oil was dissolved in absolute ether and reduced with 5.5 g. of lithium aluminum hydride according to the method described by Karrer[28] for the reduction of *p*-toluenesulfonates. After hydrolysis of the resulting tetrahydropyranyl ether, VII, with hydrochloric acid,[29] the product was extracted from the aqueous solution with five 50-ml. portions of ether. The combined ether layers were dried with saturated brine and potassium carbonate. On removal of the ether by distillation through a Vigreux column a residue of approximately 12 ml. was obtained. Distillation of this residue at reduced pressure yielded 5.1 g. (58% over-all yield from III) of ***cis*-3-methylcyclohexanol** (VIII), b.p. 80–84° (15 mm.), $n^{25}\text{D}$ 1.4555 (lit. b.p. 60° (2 mm.),[7a] 78° (20 mm.),[5] $n^{25}\text{D}$ 1.4573,[7a] $n^{25}\text{D}$ 1.4554[5]).[30]

The alcohol was converted to *cis*-3-methylcyclohexyl *p*-nitrobenzoate in 78% yield by reaction with *p*-nitrobenzoyl chloride in dry pyridine. The crude material melted at 53–55° and after three recrystallizations from aqueous methanol a constant melting point of 56.4–57.2° was obtained (lit. m.p. 48°,[7a] m.p. 58°[5]).[30]

Anal. Calcd. for $C_{14}H_{17}O_4N$: C, 63.86; H, 6.51. Found: C, 63.94; H, 6.29.

The infrared spectrum of the above *cis*-*p*-nitrobenzoate was indistinguishable from that of a *p*-nitrobenzoate, m.p. 47.6–48.4°, prepared from a pure isomer of 3-methylcyclohexanol.[14] This confirmed that the two samples are dimorphic modifications of the same compound.

The α-naphthylurethan of VIII was prepared in the usual way.[7a] After recrystallization from petroleum ether the material melted at 128–129° (lit. m.p. 130°[7a]).[30] On admixture with an α-naphthylurethan derivative, m.p. 129.6–130°, obtained from a pure isomer of 3-methylcyclohexanol[14] the melting point was not depressed.

Conversion of *trans*-3-Hydroxycyclohexanecarboxylic Acid (IX) to *trans*-3-Hydroxymethylcyclohexanol (X).—The methyl ester of IX was prepared in 83% yield according to the general method of Clinton and Laskowski[31] and obtained as a colorless liquid, b.p. 129–130° (12 mm.), $n^{25}\text{D}$ 1.4660.

Anal. Calcd. for $C_8H_{14}O_3$: C, 60.74; H, 8.92. Found: C, 60.74; H, 8.98.

The methyl ester was converted to ***trans*-3-hydroxymethylcyclohexanol** (X) by reduction with lithium aluminum hydride.[26] The *trans* diol was isolated by the procedure described above for the *cis* isomer in 64% yield as a semi-solid slush, b.p. 120–121° (0.3 mm.), $n^{25}\text{D}$ 1.4852.

The di-*p*-nitrobenzoate was prepared in excellent yields by the method described for the *cis* isomer and melted at 161.8–162.6° (lit.[12] 162°). A mixture of equal parts of this derivative and the di-*p*-nitrobenzoate of III, m.p. 140–141°, melted at 126–130°.

Conversion of *trans*-3-Hydroxymethylcyclohexanol (X) to *trans*-3-Methylcyclohexanol (XI).—The *trans* diol (X) was converted to authentic *trans*-3-methylcyclohexanol by the same procedure described above for the epimer. A total of 7.0 g. of XI, b.p. 71–73° (10 mm.), $n^{25}\text{D}$ 1.4565 (lit. b.p. 72–73° (20 mm.),[7a] b.p. 77–78° (20 mm.),[5] $n^{20}\text{D}$ 1.4583,[7a] $n^{25}\text{D}$ 1.4530[5])[32] corresponding to a 36% yield, was obtained from 22 g. of X.

The *p*-nitrobenzoate of XI, m.p. 62–62.5° (lit. 63°,[7a] 65°[5])[32] was obtained in 70% yield. The melting point of

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[24] The lactone was accompanied by approximately an equal amount of oil, which was not identified, but which is probably a cyclohexenecarboxylic acid. The pure lactone was obtained when pure *cis* acid was lactonized.

[25] The *trans* acid (IX) appears to exist in dimorphic modifications as recrystallizing to constant melting point from acetonitrile yields material melting at 117–118.4°, whereas recrystallization from ethyl acetate gives a product melting 120–121°.

[26] N. F. Nystrom and W. G. Brown, THIS JOURNAL, **69**, 1197 (1947).

[27] W. G. Dauben and H. L. Bradlow, *ibid.*, **74**, 559 (1952).

[28] P. Karrer, H. Asmis, K. N. Sareen and R. Schwyzer, *Helv. Chim. Acta*, **34**, 1022 (1951).

[29] A. C. Ott, M. F. Murray and R. L. Pederson, THIS JOURNAL, **74**, 1239 (1952).

[30] Comparison is being made with the isomer heretofore assigned and reported as having the *trans* configuration.

[31] R. O. Clinton and S. C. Laskowski, THIS JOURNAL, **70**, 3135 (1948).

[32] Comparison is being made with the isomer formerly called the *cis* isomer.

the epimeric p-nitrobenzoate, m.p. 56.4–57.2°, was depressed when mixed with this material. The infrared spectrum of this derivative was indistinguishable from the spectrum of a p-nitrobenzoate, m.p. 62.8–63°, prepared from a pure isomer of 3-methylcyclohexanol.[14]

The α-naphthylurethan of XI was prepared in the usual way. After recrystallization from petroleum ether this material melted at 114.5–115° (lit.[7a] 118°).[32] The melting point of this derivative was depressed when mixed with the epimer, m.p. 128–130°. The melting point was not depressed when mixed with an α-naphthyl urethan, m.p. 116.8–117°, obtained from a pure isomer of 3-methylcyclohexanol.

MADISON, WISCONSIN

[CONTRIBUTION FROM THE CHEMICAL LABORATORY OF THE UNIVERSITY OF CALIFORNIA]

Studies of Configuration. I. The Configurations of the 3-Methylcyclohexanols*

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Lithium aluminum hydride reduction of *cis*-3-hydroxycyclohexanecarboxylic acid to *cis*-3-hydroxycyclohexanemethanol, followed by conversion to the ω-monotosylate and reduction to *cis*-3-methylcyclohexanol has given the more stable isomer, previously assigned the "*trans*" configuration on the basis of the von Auwers–Skita rule. Similar reduction of *trans*-3-hydroxycyclohexanecarboxylic acid has afforded *trans*-3-methylcyclohexanol, confirming the stereospecificity of the reaction sequence. The isomeric 3-methylcyclohexanols thus show the same reversal of properties as the 1,3-dimethylcyclohexanes, and are in full accord with Pitzer's equatorial-polar concept with regard to relative stability.

Recent investigations of the stereochemistry of substituted cyclohexane derivatives have shown the usefulness and validity of the concept of equatorial and polar bonds in the cyclohexane ring system as developed by Pitzer[1] and Hassel.[2] Barton[3] has shown these concepts to be successful in the interpretation of the reactions of fused ring systems, including steroids and triterpenes. The structures of the hexachlorocyclohexanes[4] have also been correlated with these considerations.

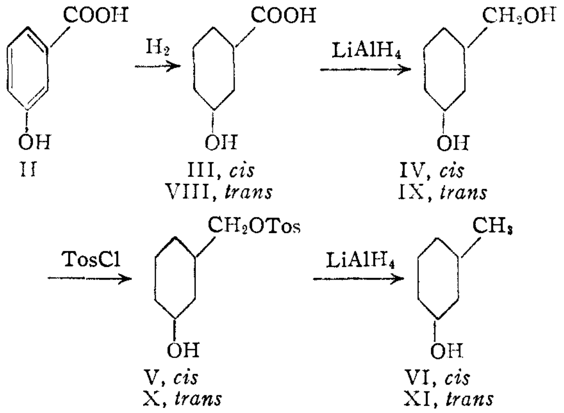
In a substituted cyclohexane the equatorial position tends to be preferred by a substituent,[5] and Pitzer and co-workers[1] have considered that the equatorial chair conformation is 1.8 kcal./mole more stable than the polar chair conformation for methylcyclohexane. In the case of the isomeric 1,3-dimethylcyclohexanes (I) it has been shown[1,6] that *cis*-I in which both methyl groups may be allocated to equatorial positions is more stable than *trans*-I. This is the reverse of the assignment on the basis of the von Auwers–Skita rule, in which it is proposed that the stereoisomer with the lower density and lower index of refraction is the *trans* isomer.

The reversal of the von Auwers–Skita rule for other 1,3-dialkylcyclohexane derivatives has most recently been shown for 1,3,5-trimethylcyclohexane[7] and 1,3,5-triethylcyclohexane. Further, Plattner[8] has pointed out that in 1,3-dimethylcyclohexan-2-one similar considerations apply.

It would appear that such reversal should be common to all 1,3-disubstituted cyclohexanes, irrespective of whether or not the two substituent groups are the same. We wish to report evidence at the present time obtained in the course of other work to show that in the case of the isomeric 3-methylcyclohexanols a similar reversal occurs.

The sequence of reactions used is outlined in Chart I. Reduction of m-hydroxybenzoic acid (II) as its sodium salt with Raney nickel and hydrogen afforded good yields of the mixed *cis*- and *trans*-3-hydroxycyclohexanecarboxylic acid, from which, however, *cis*-3-hydroxycyclohexanecarboxylic acid (III) was isolated in rather poor yield by extended fractional crystallization from ethyl acetate. Reduction of II with platinum oxide and hydrogen in ethanol afforded a mixture containing appreciable amounts of cyclohexanecarboxylic acid, from which III could be isolated readily in satisfactory yield. That III has the *cis* configuration is shown by the formation of the lactone.[9]

CHART I



Reduction of III with lithium aluminum hydride afforded *cis*-3-hydroxycyclohexanemethanol (IV) in good yield. The derivatives of IV agreed with those reported by Clarke and Owen[10] thereby

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[1] C. W. Beckett, K. S. Pitzer and R. Spitzer, THIS JOURNAL, **69**, 2488 (1947).

[2] O. Hassel, *Tids. Kjemi Bergvesen*, **3**, 32 (1943).

[3] D. H. R. Barton, *Experientia*, **6**, 316 (1950).

[4] J. M. Bijvoet, *Rec. trav. chim.*, **67**, 777 (1948); A. J. Kolka, H. D. Orloff and M. E. Griffing, Abstracts, 121st Meeting A.C.S., March, 1952, p. 5K.

[5] Other specific interactions may change this situation. See L. P. Kuhn, THIS JOURNAL, **74**, 2492 (1952).

[6] M. Mousseron and R. Granger, *Bull. soc. chim.*, **5**, 1618 (1938).

[7] G. Chiurdoglu, *Bull. soc. chim. Belg.*, **60**, 39 (1951).

[8] Pl. A. Plattner, A. Furst and J. Hellerbach, *Helv. Chim. Acta*, **30**, 100 (1947).

[9] W. H. Perkin, Jr., and G. Tattersall, *J. Chem. Soc.*, **91**, 480 (1907); E. J. Boorman and R. P. Linstead, *ibid.*, 262 (1935).

[10] M. F. Clarke and L. N. Owen, *ibid.*, 2208 (1950).