

$2.3\pi A\nu_{1/2}/cl$, where A is the absorbance at ν_{\max} , $\nu_{1/2}$ is the half band width, c is concentration of bonded OH in moles per liter, and l is the cell length in centimeters. Correction was made for the thermal expansion of CCl_4 .

For the determination of the equilibrium constant of the intermolecular hydrogen bond between butanol and butyl ether, the alcohol and ether in CCl_4 were put in the sample cell and ether in CCl_4 at the same concentration were put in the reference cell.

[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY, TUFTS UNIVERSITY, MEDFORD 55, MASS.]

Conformational Studies. VI.¹ Intramolecular Hydrogen Bonding in Nonchair Conformations of *cis,cis,cis*-2,5-Dialkyl-1,4-cyclohexanediols²

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cis,cis,cis-2,5-Dialkyl-1,4-cyclohexanediols, in dilute solution in carbon tetrachloride at 25°, give infrared spectra which show absorption at $3490 \pm 10 \text{ cm}^{-1}$ attributable to transannular intramolecular hydrogen bonding in nonchair conformations. For each diol, the relative absorbance near 3490 cm^{-1} is interpreted in terms of its nonchair population. The nonchair population increases with the sizes of the alkyl groups from about 5% for *cis,cis,cis*-2,5-dimethyl-1,4-cyclohexanediol (6) to >98% for *cis,cis,cis*-2,5-di-*t*-alkyl-1,4-cyclohexanediols (2 and 3). Intermediate nonchair populations are reported for *cis,cis,cis*-*p*-menthane-2,5-diol (7), *cis,cis,cis*-2-*t*-butyl-5-methyl-1,4-cyclohexanediol (8), both ca. 14%, and for *cis,cis,cis*-2,5-di-*sec*-alkyl-1,4-cyclohexanediols (4 and 5), ca. 80%. Preparations and configurations of the diols are discussed in addition to their conformational equilibria.

Examination of models of 1,4-cyclohexanediols suggests that intramolecular hydrogen bonding can occur only when the hydroxyl groups have the *cis* configuration, and then only in certain *nonchair* conformations.³ Infrared spectroscopic studies have shown that the population of intramolecularly hydrogen bonded nonchair conformations, while negligible for *cis*-1,4-cyclohexanediol (1) itself,⁴ is very large (probably >98%) for *cis,cis,cis*-2,5-di-*t*-alkyl-1,4-cyclohexanediols (2 and 3).^{1,3} Between these extremes, intermediate nonchair populations would be expected for diols like 2 and 3 in which one or both of the *t*-alkyl groups is replaced by a primary or secondary alkyl group. That is, a relationship would be expected between the nonchair population and the relative "sizes" of the alkyl substituents in *cis,cis,cis*-2,5-dialkyl-1,4-cyclohexanediols. We wish to report results of a study of such diols of intermediate nonchair population (4–8).

The frequencies and intensities of all resolved infrared absorption bands in the region $3100\text{--}3900 \text{ cm}^{-1}$ are reported in Table I for 0.0040 *M* solutions of *cis,cis,cis*-2,5-dialkyl-1,4-cyclohexanediols (2–8) in carbon tetrachloride at ca. 25°. Each of the diols 2–8 exhibits a single, broad absorption band at $3490 \pm 10 \text{ cm}^{-1}$, plus absorption in the region $3618\text{--}3640 \text{ cm}^{-1}$, the latter ranging from a resolved doublet for 2 and 3,

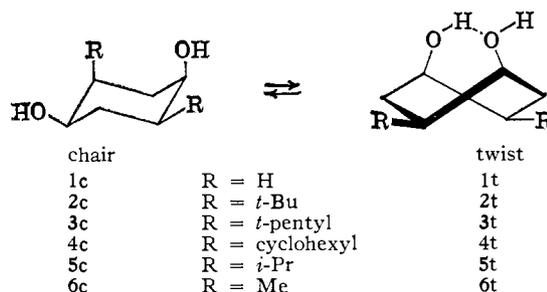


TABLE I

O–H BANDS OF THE 2,5-DIALKYL-1,4-CYCLOHEXANEDIOLS^a

Diol	Free O–H ν, cm^{-1} (absorbance)	Bonded O–H ν, cm^{-1} (absorbance)	Bonded/ bonded-2 absorbance ratio
1 ^b	3626	...	<0.01
2 ^c	3640 (0.26)	3480 (0.48)	1.00
	3619 (.23)		
3 ^c	3640 (.26)	3480 (.47)	1.0
	3618 (.23)		
4	3621 (.32)	3491 (.36)	0.8
5	3622 (.34)	3492 (.40)	.8
6	3628 (.38)	3497 (.026)	.05
7	3626 (.41)	3492 (.062)	.13
8	3625 (.43)	3490 (.067)	.14
9 ^d	3623 (.48)	3500 (<0.01)	<.02

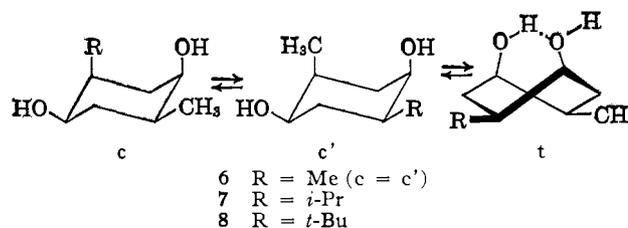
^a In 0.0040 *M* carbon tetrachloride solutions at 25°. ^b See ref. 4. ^c See ref. 1. ^d See ref. 8.

(1) Paper V: R. D. Stolow and M. M. Bonaventura, *J. Am. Chem. Soc.*, **85**, 3636 (1963).

(2) This work was presented at the 145th National Meeting of the American Chemical Society, New York, N. Y., Sept. 13, 1963, and was supported in part by National Science Foundation Grants NSF G12310 and GP-435 and in part by Public Health Service Research Grant GM-08813 from the National Institutes of Health. The authors gratefully acknowledge this assistance.

(3) R. D. Stolow, *J. Am. Chem. Soc.*, **83**, 2592 (1961).

(4) L. P. Kuhn, *ibid.*, **74**, 2492 (1952).



to a fairly symmetrical singlet for 6. The absorbance of these bands varies linearly with the concentration at concentrations below 0.0040 *M*. Upon replacement of the hydroxyl hydrogens by deuterium, these absorption bands are replaced by new bands having similar relative intensities and appearing near 2580 and 2680 cm^{-1} . Therefore the results are consistent with interpretation of the absorption bands in the region $3100\text{--}3900 \text{ cm}^{-1}$ in terms of O–H stretching vibrations of hydroxyl groups of the monomeric diol.⁵

The band near 3490 cm^{-1} may be assigned to hydroxyl groups, the hydrogen atoms of which form a transannular intramolecular hydrogen bond to oxygen

(5) See R. N. Jones and C. Sandorfy in "Chemical Applications of Spectroscopy," Vol. IX of A. Weissberger, "Technique of Organic Chemistry," Interscience Publishers, Inc., New York, N. Y., 1956, pp. 417–424.

in nonchair conformations such as *t*.^{1,3} Absorption in the region 3618–3640 cm^{-1} may be attributed to "free" hydroxyl groups; that is, to hydroxyl groups the hydrogen atoms of which are not engaged in hydrogen bonding.^{1,3,6}

A detailed interpretation of the infrared data for diols **2** and **3** has been reported.¹ The near identity of the infrared results for **2** and **3** has encouraged us to propose a simple interpretation of the infrared data for diols **4–8** in terms of conformational equilibria.

If one assumes the validity of the conclusion¹ that the population of nonchair conformation *t* is >98% for *cis,cis,cis*-2,5-di-*t*-alkyl-1,4-cyclohexanediols **2** and **3**, and if one also assumes that the absolute intensity of the band near 3490 cm^{-1} is a constant over the series of *cis,cis,cis*-2,5-dialkyl-1,4-cyclohexanediols, then the absorbance/mole at 3480 cm^{-1} for **2** and **3** may be taken as an estimate of the absorbance/mole of conformation *t* for diols **4–8** and for related diols. If this approach is valid, then the estimated nonchair population for each diol is simply the ratio of the absorbance of its band near 3490 cm^{-1} to the absorbance of the 3480 cm^{-1} band of diol **2**, as recorded in Table I.

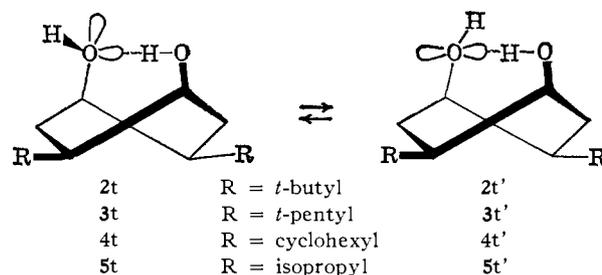
For the *cis,cis,cis*-2,5-di-*sec*-alkyl-1,4-cyclohexanediols **4** and **5**, the absorbance of the band near 3490 cm^{-1} attributable to intramolecular hydrogen bonding is about 0.8 times the absorbance of the corresponding band for the di-*t*-alkyl diols **2** and **3**. Therefore, the population of hydrogen bonded nonchair conformations appears to be *ca.* 80% for the dicyclohexyl diol **4** and the diisopropyl diol **5**. The cyclohexyl and isopropyl groups appear to have nearly the same "size." One may rationalize this fact if one notes that the two groups differ beyond the sites of the major repulsive interactions which determine the conformational equilibria. These results suggest the generalization that in dilute solution in carbon tetrachloride at 25° for *cis,cis,cis*-2,5-dialkyl-1,4-cyclohexanediols in which each alkyl group is either secondary or tertiary, *nonchair conformations predominate*.

When one or two methyl groups are present, the results are markedly different. For each *cis,cis,cis*-2-alkyl-5-methyl-1,4-cyclohexanediol (**6–8**, Table I), the population of intramolecularly hydrogen bonded nonchair conformations, such as *t*, is less than *ca.* 15%. Yet even for the dimethyl diol **6**, which has the smallest possible alkyl substituents, the hydrogen bonded nonchair population is clearly significant, *ca.* 5%. We conclude that *cis,cis,cis*-2,5-dialkyl-1,4-cyclohexanediols, in general, exhibit detectable intramolecular hydrogen bonding. This generalization has obvious applications to the problem of the assignment of configuration to such diols, as shown below.

The [doublet "free" hydroxyl absorption of the *cis,cis,cis*-2,5-di-*t*-alkyl-1,4-cyclohexanediols **2** and **3** was interpreted previously in terms of two nonequivalent intramolecularly hydrogen bonded nonchair conformations *t* and *t'*, present in nearly equal populations.¹ A similar pair of conformations can be written

(6) Conformations which have no hydrogen bond (such as *c*) would have two "free" hydroxyl groups. Hydrogen bonded conformations (such as *t*) would have one "free" hydroxyl group. Possible intramolecularly hydrogen bonded conformations have been discussed for a related compound, *cis,cis,cis*-2,5-di-*t*-butyl-4-methoxycyclohexanol, in ref. 1, footnote 14. The special case of a diol conformation with no "free" hydroxyl group is pictured in ref. 1, footnote 12.

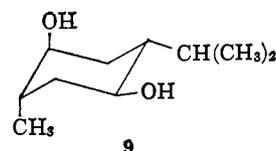
for each of the *cis,cis,cis*-2,5-di-*sec*-alkyl-1,4-cyclohexanediols **4** and **5**.



Whereas in conformations *2t'* or *3t'* the hydrogen of the "free" hydroxyl group abuts the neighboring *t*-alkyl group,¹ in *4t'* or *5t'* the neighboring *sec*-alkyl group, when in its most favorable rotational conformation, would *not* abut the hydrogen of the "free" hydroxyl group. The 3640 cm^{-1} band of **2** (and **3**) was attributed to the special environment of the "free" hydroxyl group in conformation *2t'* (and *3t'*).¹ Since this special environment (the abutting alkyl group) is not present for *4t'* or *5t'*, one would not expect an absorption band at 3640 cm^{-1} for **4** and **5**. Indeed, no absorption band at 3640 cm^{-1} is observed for **4** or **5**; each gives a somewhat unsymmetrical singlet with the peak at 3621–3622 cm^{-1} . Therefore, the results for diols **4** and **5** not only are consistent with the earlier interpretation of the spectra of diols **2** and **3**, but provide further evidence in support of that interpretation.¹

By analogy with the di-*t*-alkyl diols **2** and **3**, one might suggest that the di-*sec*-alkyl diols **4** and **5**, in dilute solution in carbon tetrachloride at 25°, each exist predominantly (*ca.* 80%) in nearly equal populations of intramolecularly hydrogen bonded nonchair conformations *t* (*ca.* 40%) and *t'* (*ca.* 40%), with a minority (*ca.* 20%) of nonhydrogen-bonded conformations, including the chair conformation. The nonhydrogen-bonded nonchair populations of diols **2** and **3** appear to be <2%.¹ By analogy, and by examination of models, there appears to be no reason to expect substantially larger populations of nonhydrogen-bonded nonchair conformations for diols **4–8**. Therefore, it is tentatively suggested for diol **4** or **5** that the chair population *c* is *ca.* 20%.⁷ Similarly, it is tentatively suggested that the chair population is *ca.* 95% for the dimethyl diol **6** and *ca.* 86% for both the 2-isopropyl-5-methyl diol **7** and the 2-*t*-butyl-5-methyl diol **8**.

Diol Configuration.—We consider the significant intramolecular hydrogen bonding exhibited by diol **7** to provide conclusive proof of its configuration.⁸ Since diol **9** exhibits negligible intramolecular hydrogen bonding (Table I),⁸ the related 2,5-dimethyl-1,4-cyclohexanediol (**9**, but with Me in place of *i*-Pr) and all of its stereoisomers, except **6**, would certainly be expected to exhibit negligible intramolecular hydrogen bonding. There-

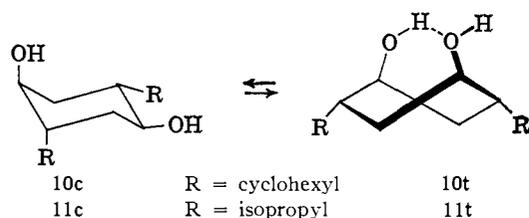


(7) Since three conformations, *t*, *t'*, and *c*, would be expected to contribute significantly to the "free" hydroxyl band for diol **4** (or **5**), it is not surprising that the band at 3621 cm^{-1} lacks symmetry. See ref. 1, and footnotes 18–20 therein.

(8) R. D. Stolow, *J. Am. Chem. Soc.*, **86**, 2170 (1964).

fore the 2,5-dimethyl-1,4-cyclohexanediol, m.p. 81° , which exhibits significant intramolecular hydrogen bonding (Table I) is assigned the all-*cis* configuration, structure 6. The 2-*t*-butyl-5-methyl-1,4-cyclohexanediol, m.p. 100° , which shows significant intramolecular hydrogen bonding analogous to that of diol 7 (Table I), and which was prepared by the same route as diol 7, is also assigned the all-*cis* configuration, structure 8, by analogy with diol 7.

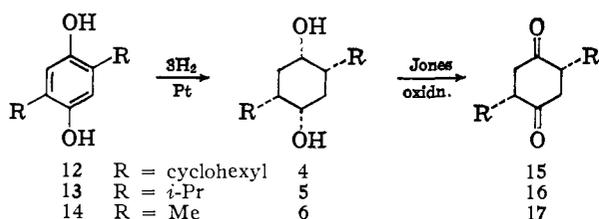
In order to assign structures 4 and 5 to the 2,5-di-*sec*-alkyl-1,4-cyclohexanediols reported in Table I, it is first necessary to rule out structures 10 and 11 for these diols, as pointed out for the analogous 2,5-di-*t*-alkyl-1,4-cyclohexanediols.^{1,3}



Compare diols 10 and 11 with diol 9. Replacement of the methyl group in diol 9 by an isopropyl group would give diol 11. It would seem unlikely that the intramolecularly hydrogen bonded nonchair population of diol 11 could be *ca.* 80% while that of diol 9 is negligible, especially if one were to consider the isopropyl group and the methyl group to have nearly the same "size."⁹ Therefore it would seem more reasonable to assign the all-*cis* configuration 5 to the 2,5-diisopropyl-1,4-cyclohexanediol, m.p. $111.5\text{--}112^\circ$, which shows intense absorption attributable to intramolecular hydrogen bonding (Table I). Assignment of structure 5 to the 2,5-diisopropyl-1,4-cyclohexanediol, m.p. $111.5\text{--}112^\circ$, requires analogous assignment of structure 4 to the 2,5-dicyclohexyl-1,4-cyclohexanediol, m.p. $170.5\text{--}171.5^\circ$, since both diols were prepared in the same manner and gave similar infrared absorption in the O-H stretching region (Table I).

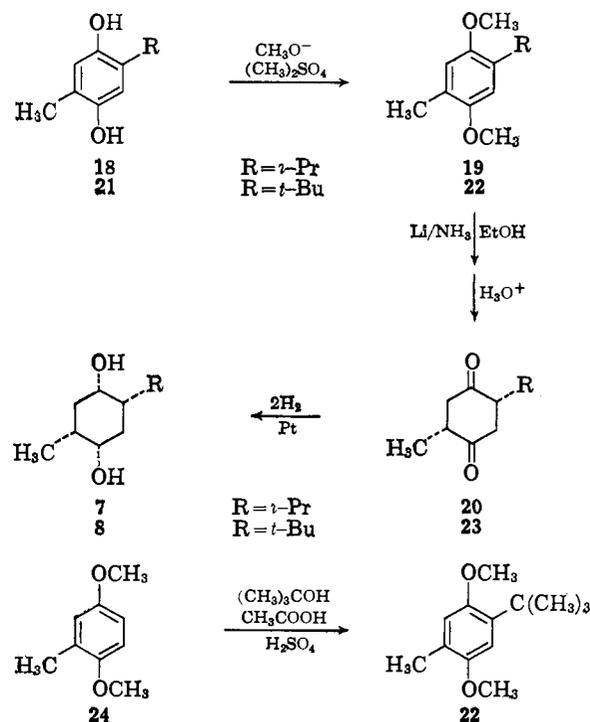
Preparation.—Hydrogenation of the appropriate 2,5-dialkylhydroquinone or *cis*-2,5-dialkyl-1,4-cyclohexanediol gave product mixtures which, after chromatography on alumina and recrystallization, gave *cis,cis,cis*-2,5-dialkyl-1,4-cyclohexanediols 4-8. As noted previously for 2 and 3,¹ in each case the fractionation procedure was guided by infrared analysis toward isolation of a substance exhibiting maximum intramolecular hydrogen bonding.

Direct hydrogenation of hydroquinones by procedures similar to those reported for the preparation of diols 2 and 3¹ was used to prepare the *cis,cis,cis*-2,5-dialkyl-1,4-cyclohexanediols 4, 5, and 6.



(9) N. L. Allinger, L. A. Freiberg, and S.-H. Hu, *J. Am. Chem. Soc.*, **84**, 2836 (1962).

(\pm)-*cis,cis,cis*-*p*-Menthane-2,5-diol (7) was prepared indirectly from thymohydroquinone (18) via its dimethyl ether (19) and (\pm)-*cis*-*p*-menthane-2,5-dione (20). (\pm)-*cis,cis,cis*-2-*t*-Butyl-5-methyl-1,4-cyclohexanediol (8) was prepared analogously, from 21 via 22 and 23. A second route for preparation of 2-*t*-butyl-5-methyl-1,4-dimethoxybenzene (22), alkylation of 2,5-dimethoxytoluene (24), was faster and simpler than formation of the dimethyl ether 22 from 2-*t*-butyl-5-methylhydroquinone (21).



The reduction of the *p*-dimethoxybenzenes 19 and 22, by use of lithium metal in liquid ammonia plus ethanol, followed the procedure reported for the analogous preparation of 2,5-dimethyl-1,4-cyclohexanediones.^{10,11} Without isolation, the reduction product, presumably the 3,6-dihydro derivative of 19 or 22, was converted to dione by acid-catalyzed hydrolysis of the enol-ether functions. Under these conditions, one would expect the stereochemistry of the product diones to be equilibrium controlled. This was the case. Fractional recrystallization of the product mixture from hexane gave the *cis*-dione 20 or 23. From the more soluble fractions, *trans*-rich dione mixtures were isolated. Acid-catalyzed equilibration of the diones, approached from each side, showed that the *cis* isomers 20 and 23 are more stable than their respective *trans* isomers. A similar result, found for other 2,5-dialkyl-1,4-cyclohexanediones, has been interpreted in terms of the predominance of nonchair conformations.^{11,12}

Preparation of (\pm)-*p*-menthane-2,5-diones was reported 70 years ago by Baeyer.¹³ Although no details were given, it is likely from the method of preparation that the reported solid, m.p. $64\text{--}65^\circ$, labeled the "trans" dione, was actually a *cis*-rich mixture, close in composi-

(10) J. Fishman, E. R. H. Jones, G. Lowe, and M. C. Whiting, with J. S. Stephenson, *J. Chem. Soc.*, 3984 (1960).

(11) R. D. Stolow and M. M. Bonaventura, *Tetrahedron Letters*, No. 2, 95 (1964).

(12) R. D. Stolow and C. B. Boyce, *J. Am. Chem. Soc.*, **83**, 3722 (1961).

(13) A. Baeyer, *Ber.*, **26**, 232 (1893).

tion to the equilibrium mixture, m.p. 60.5–63°. A detailed study of the equilibration of the *cis*- and *trans*-diones and proof of their assigned configurations will be presented in a subsequent publication. At present, it is sufficient to note that upon Jones oxidation, diol 7 gave dione 20, and diol 8 gave dione 23.¹⁴ Also, diols 5 and 6 gave the corresponding diones 16 and 17.¹⁴ One example of the use of the Jones oxidation is given herein—the preparation of *cis*-2,5-dicyclohexyl-1,4-cyclohexanedione (15) from diol 4.

Experimental¹⁵

2,5-Dimethylhydroquinone¹⁶ (14) was recrystallized from water and methanol (in a nitrogen atmosphere) to give white crystals, m.p. 216.5–218.5°. **Thymoquinone**¹⁶ (18) was recrystallized from aqueous ethanol to give fluffy white needles, m.p. 141–143°. Further samples of 14 and 18 were prepared by reduction of 2,5-dimethyl-*p*-benzoquinone (25, Eastman) and thymoquinone (26, K and K Laboratories) by the procedure used below in the preparation of 21.

2,5-Dicyclohexylhydroquinone (12).—Crude 12,¹⁶ m.p. 212–225°, was recrystallized from acetone to give white crystals, m.p. 231.5–233°; reported¹⁷ m.p. 225–227°, 228–229°.

(±)-*cis,cis,cis*-2,5-Dicyclohexyl-1,4-cyclohexanediol (*cis,cis,cis*-1,1':4',1''-Tercyclohexane-2',5'-diol) (4).—To a solution of 5.02 g. (0.0183 mole) of 12 in 150 ml. of 1-propanol was added 1.1 g. of platinum dioxide catalyst and 1 drop of concentrated hydrochloric acid. Hydrogenation in the manner described below for 6 required 21 hr. Removal of catalyst and solvent gave 5 g. of white solid, m.p. 150–180°, which contained 30% of 4 (infrared analysis at 3490 cm.⁻¹). Chromatography on a 20 mm. i.d. column containing 230 g. of alumina, eluting first with dry benzene, benzene-ether mixtures, and anhydrous ether, gave with 1:9 methanol-ether, after evaporation of solvent, 0.90 g. (17%) of white solid. Recrystallization from aqueous ethanol gave an analytical sample of 4, m.p. 170.5–171.5°, which showed intense absorption at 3491 cm.⁻¹ (Table I).

Anal. Calcd. for C₁₈H₃₂O₂: C, 77.09; H, 11.49. Found: C, 77.22; H, 11.73.

(±)-*cis*-2,5-Dicyclohexyl-1,4-cyclohexanedione (*cis*-1,1':4',1''-Tercyclohexane-2',5'-dione) (15).—The procedure reported for analogous Jones oxidation of diols 2 and 3 to the corresponding diones was employed.¹ To 0.300 g. (1.07 mmoles) of diol 4 dissolved in 75 ml. of acetone (reagent grade, redistilled) and cooled to 3° was added dropwise during 5 min. 1.0 ml. (50% excess) of 2.67 *M* chromium trioxide solution while the mixture, cooled in an ice-water bath, was stirred vigorously. Isolation of the total crude product as reported¹ gave 0.27 g. (91%) of white solid, m.p. 198–200°. Several recrystallizations from methanol gave the analytical sample of the dione, m.p. 200–201°. The infrared spectrum showed no evidence for the presence of hydroxyl groups.

Anal. Calcd. for C₁₈H₂₈O₂: C, 78.21; H, 10.21. Found: C, 78.10; H, 10.43.

2,5-Diisopropylhydroquinone (13).—The water-insoluble fraction of crude 13¹⁶ was recrystallized from toluene in the dark to give white crystals, m.p. 143–145°. Purification was effected, as reported,¹⁸ by conversion to the diacetate, m.p. 126.5–128° (reported m.p. 127–128°) and regeneration of 13, fine white crystals from benzene, m.p. 167–168°; reported m.p. 168–169°.

(±)-*cis,cis,cis*-2,5-Diisopropyl-1,4-cyclohexanediol (5).—To a solution of 10.0 g. (0.0515 mole) of 13 in 125 ml. of absolute ethanol was added 1.2 g. of platinum dioxide catalyst and 1 drop of con-

centrated hydrochloric acid. Hydrogenation, in the manner described below for 6, required 30 hr. Removal of catalyst and solvent gave 9.2 g. of white semisolid which contained 30% of 5 (infrared analysis at 3490 cm.⁻¹). The solid, 9.15 g., was slurried with 7 ml. of benzene at room temperature. The benzene-insoluble fraction, separated by filtration, was slurried with two more portions of benzene (10 ml. each). The final benzene-insoluble fraction, 2.75 g., m.p. 115–130°, contained 30% of 13 (ultraviolet analysis) and 50% of 5 (infrared analysis).

The benzene-soluble fractions were combined and chromatographed on a 20 mm. i.d. column containing 200 g. of alumina. Elution with benzene, 1:1 ether-benzene, ether, and methanol-ether mixtures gave, with 2–5% methanol in anhydrous ether after evaporation of solvent, 1.25 g. (12%) of a white fibrous solid, m.p. 106–108°. Recrystallization from hexane, aqueous methanol, and, finally, aqueous ethanol, gave the analytical sample, m.p. 111.5–112°, which showed intense absorption at 3492 cm.⁻¹ (Table I).

Anal. Calcd. for C₁₂H₂₄O₂: C, 71.95; H, 12.08. Found: C, 72.03, 71.98; H, 11.92, 11.91.

(±)-*cis,cis,cis*-2,5-Dimethyl-1,4-cyclohexanediol (6).—Hydrogenation of 2,5-dimethylhydroquinone (14)¹⁶ was carried out in a Parr apparatus (Model 3911)¹⁹ equipped with a 500-ml. pressure bottle and a neoprene stopper at room temperature and 2–3 atm. hydrogen pressure. To 9.85 g. (0.0713 mole) of 14 in 150 ml. of absolute ethanol was added 1.6 g. of platinum dioxide catalyst and 1 drop of concentrated hydrochloric acid. The reaction was stopped, after agitation for 40 min., when the calculated drop in pressure had occurred. The catalyst was separated by filtration and the solvent was removed at 20 mm. pressure to give 7.2 g. of off-white semisolid residue. The reduction product contained 39% of reactant 14 (ultraviolet analysis). The infrared spectrum of a dilute solution in carbon tetrachloride did not show significant intramolecular hydrogen bonding. The 7.2 g. of residue was extracted with several 10-ml. portions of benzene. The benzene-insoluble fraction, 2.35 g., was 90% 14 (ultraviolet analysis). The benzene-soluble fraction was chromatographed on a column of 200 g. of alumina. Elution with redistilled benzene, 1:1 ether-benzene, and anhydrous ether was followed by elution with 1:19 methanol-ether. The latter fractions, upon evaporation, gave a pale yellow residue which crystallized at 3°. Six recrystallizations from benzene gave 0.50 g. (5%) of white crystals, m.p. 80.5–81.5°, which showed weak absorption at 3497 cm.⁻¹ (Table I).

Anal. Calcd. for C₈H₁₆O₂: C, 66.62; H, 11.19. Found: C, 66.47; H, 10.91.

Gas chromatography¹⁵ at 140° gave a single peak, retention time 10.0 min.

2-*t*-Butyl-5-methyl-*p*-benzoquinone (27).—6-*t*-Butyl-*m*-cresol (Eastman technical grade, redistilled) was converted to 27 by D. J. Henry in 75% yield by modification of a reported procedure.^{20,21} Recrystallization from 95% ethanol gave bright yellow crystals, m.p. 98–99° (reported²¹ m.p. 97–98°).

2-*t*-Butyl-5-methylhydroquinone (21).—To 70.0 g. (0.394 mole) of 27 in 360 ml. of acetic acid and 270 ml. of water was added 90 g. of zinc (20 mesh). The mixture was heated under reflux until colorless (*ca.* 1 hr.). Then 360 ml. of boiling water was added and the solution was decanted from the zinc. The zinc and reaction flask were rinsed with an additional 360 ml. of boiling water. The solution was cooled to 0°. A quantitative yield of pink-tinted crystals was obtained. Recrystallization from benzene gave pink-tinted crystals, m.p. 122–125° (reported²² m.p. 122–123°).

2-*t*-Butyl-5-methyl-1,4-dimethoxybenzene (22). (A) **Preparation of 22 from 21.**—In a nitrogen atmosphere, 15.8 g. (0.087 mole) of 21, 58 ml. of methanol, and 29 ml. of dimethyl sulfate were stirred vigorously and heated under reflux. Then 75

(14) R. D. Stolow, R. R. Krikorian, P. M. McDonagh, and M. M. Bonaventura, unpublished work.

(15) Routine spectral data were recorded by use of Perkin-Elmer Model 21 and Beckman DK-2 spectrophotometers. Ultraviolet spectra were recorded in 95% ethanol solutions; infrared spectra in dried Spectranalyzed carbon tetrachloride solutions. The diols were analyzed by gas chromatography by use of a flame ionization detector and a 165-cm., 0.25-in. o.d. column packed with 2% Versamid on acid-washed silanized Chromosorb W (F and M Scientific Co.). Microanalyses were determined by Dr. S. M. Nagy.

(16) We are indebted to P. Morison and J. K. Rosser, Chemicals Division, Eastman Chemical Products, Inc., for kindly supplying small samples of hydroquinones 14 and 18, and generous samples of hydroquinones 12 and 13, in crude form.

(17) W. Flaig, T. Ploetz, and H. Biergans, *Ann.*, **597**, 196 (1955); L. F. Fieser, M. T. Ieffler, and co-workers, *J. Am. Chem. Soc.*, **70**, 3186 (1948).

(18) V. A. Bogolyubskii, *Zh. Obshch. Khim.*, **32**, 869 (1962).

(19) K. B. Wiberg, "Laboratory Technique in Organic Chemistry," McGraw-Hill Book Co., Inc., New York, N. Y., 1960, p. 230.

(20) D. J. Henry, B.S. Thesis, Tufts University, 1963. The procedure for the preparation of thymoquinone (26) of E. Kremers, N. Wakeman, and R. M. Hixon, "Organic Syntheses," Coll. Vol. I, John Wiley and Sons, Inc., New York, N. Y., 1941, p. 511, was modified in step A by use of a cylindrical reaction flask and vigorous mechanical stirring, and in step B by substitution of 1600 cc. of 95% ethanol for 1600 cc. of water. The 4-amino-2-*t*-butyl-5-methylphenol (product of step B) was precipitated by dilution with 6 l. of water.

(21) M. S. Carpenter, W. M. Easter, and T. F. Wood, *J. Org. Chem.*, **16**, 586 (1951).

(22) O. A. Zeide and B. M. Dubinin, *J. Gen. Chem. USSR*, **2**, 455 (1932).

ml. of saturated methanolic potassium hydroxide was added dropwise. Four more 29-ml. portions of dimethyl sulfate were added in alternation with four more 75-ml. portions of the base. Then most of the methanol was removed by distillation through a 30-cm. Vigreux column. Water (500 ml.) was added to the reaction mixture which was then extracted with 5 × 300 ml. of ether. The ether extract was washed with 2 × 100 ml. of water. The water washings were extracted with 2 × 100 ml. of ether. The combined ether extracts were dried over anhydrous sodium sulfate. The ether was removed and the brownish oily residue was distilled to give 12.0 g. of a yellowish oil, b.p. 96° (2 mm.), which solidified at room temperature. Recrystallization at -5 to -10° from methanol gave white crystals, 10.1 g. (56%), m.p. 36-37°.

Anal. Calcd. for C₁₃H₂₀O₂: C, 74.96; H, 9.68. Found: C, 74.64; H, 9.91.

(B) Preparation of 22 by Alkylation of 2,5-Dimethoxytoluene (24).—The procedure was adapted from Fieser's modification²³ of a reported²⁴ preparation of 2,5-dimethoxy-1,4-di-*t*-butylbenzene. To a solution of 13.2 g. (0.087 mole) of 2,5-dimethoxytoluene (24, Eastman) in 20 ml. of acetic acid and 10.0 ml. (0.106 mole) of *t*-butyl alcohol cooled in an ice-water bath at 2° was added, dropwise during 5 min., an ice-water-cooled solution of 10 ml. of 20% fuming sulfuric acid in 10 ml. of concentrated sulfuric acid. The reaction mixture, in a 125-ml. erlenmeyer flask, was constantly swirled in the ice-water bath during the addition, and then for another 5 min. Crushed ice was added, then ice-water to fill the flask. The white solid which separated from the mixture was collected and washed thoroughly with 100 ml. of water. The solid was recrystallized from 50 ml. of methanol at -5° to give 22, 13.1 g. (70%), m.p. 37-38°. Further recrystallizations from methanol gave white needles, m.p. 43-44°. The infrared spectra of samples of 22 prepared by routes A and B were essentially identical.

Anal. Calcd. for C₁₃H₂₀O₂: C, 74.96; H, 9.68. Found: C, 74.84; H, 9.60.

2,5-Dimethoxy-*p*-cymene (19).—Procedure A above for 22 was employed to prepare the dimethyl ether 19 from 39.5 g. (0.238 mole) of thymohydroquinone (18) (prepared from thymoquinone (26), as for 21 and recrystallized from toluene to give thick white needles, m.p. 146-148°). Five 72-ml. portions of dimethyl sulfate and proportional portions of base were used as above. Isolation of the product as above gave a pale yellow distillate, 34.0 g. (74%), b.p. 128° (12 mm.) (reported²⁵ b.p. 133-134° (18 mm.)).

(±)-*cis-p*-Menthane-2,5-dione (20).—To a solution of 6.0 g. (0.031 mole) of 2,5-dimethoxy-*p*-cymene (19) in 14 g. of absolute ethanol, 110 ml. of anhydrous ether, and 140 ml. of distilled liquid ammonia in a 3-necked flask equipped with a stirrer, addition funnel, and a Dry Ice-acetone-cooled dewar condenser was added 2.0 g. (0.28 g.-atom) of 1/8 in. lithium wire in 2-cm. lengths. The blue solution was stirred for 5 min. Then absolute ethanol was added dropwise until the solution became colorless. The ammonia was allowed to evaporate. After addition of 300 ml. of water, the solution was extracted with 5 × 100 ml. of ether. The ether was washed with 3 × 100 ml. of water. The washings were extracted with 3 × 100 ml. of ether. The ether solutions were combined, dried over anhydrous sodium sulfate, concentrated to 460 ml., and stirred for 2 hr. at 20° with 1.8 ml. of concentrated hydrochloric acid. The ether solution was neutralized and washed by extraction with 200 ml. of 5% aqueous sodium bicarbonate followed by 3 × 50 ml. of water. The ether solution was dried. Evaporation of the ether gave 5.8 g. of yellowish oil which solidified at 25°. Recrystallization from 30 ml. of hexane gave colorless crystals, 5.0 g. (96%) of a mixture of *cis*- and *trans-p*-menthane-2,5-dione, m.p. 60.5-63°. Seven recrystallizations from hexane gave 0.81 g. (16%) of (±)-*cis-p*-menthane-2,5-dione (20), m.p. 72-73°.

Anal. Calcd. for C₁₀H₁₆O₂: C, 71.39; H, 9.59. Found: C, 71.20; H, 9.80.

Fractional recrystallization of the mother liquors from hexane readily gave solid mixtures of *cis*- and *trans-p*-menthane-2,5-dione containing from ca. 1% to ca. 70% of *trans*-dione. The composition of the mixtures was analyzed by gas chromatography by use of a 180 cm., 0.25 in. o.d. column packed with 2% GEHE60 (General Electrical Co., cyanoethylated silicone polymer) on

60-80 mesh "HMDS treated" Chromosorb W (Fisher Scientific Co.) at 115°. The retention time of the *cis*-dione was 2-3 min. greater than that of the *trans*-dione. The original product mixture, m.p. 60.5-63°, was found to have a composition like that of equilibrium mixtures of the *cis*- and *trans*-diones. Acid-catalyzed equilibration, approached from both sides, gave mixtures in which the predominant stereoisomer was the *cis*-dione.

The above preparation of 20 was repeated on a fivefold larger scale.

(±)-*cis,cis,cis-p*-Menthane-2,5-diol (7).—To 2.00 g. (0.0119 mole) of (±)-*cis-p*-menthane-2,5-dione (20) in 100 ml. of acetic acid (reagent grade) in a 500-ml. reaction bottle was added 0.5 g. (0.002 mole) of platinum dioxide catalyst. Hydrogenation at 25° and 2-3 atm. pressure (Parr apparatus)¹⁹ proceeded readily. The catalyst was removed by filtration. The acetic acid was removed by evaporation at ca. 20 mm. pressure. The resulting colorless oil was dissolved in 20 ml. of ether, shaken with 5 ml. of 5% aqueous sodium bicarbonate, followed by 5 ml. of water, then dried and evaporated under reduced pressure to give 1.84 g. of colorless residue. The residue, dissolved in 4 ml. of benzene, was placed on a chromatography column, 25 mm. i.d., packed with 200 g. of alumina (Fisher Scientific Co., A-540). Elution with benzene, 1:1 ether-benzene, ether, and 1:9 methanol-ether gave 36 fractions. Fractions 15-17, eluted with anhydrous ether, gave 660 mg. (32%) of white solid. Seven recrystallizations from benzene and finally three from water gave white crystals of 7, m.p. 105-105.5°.

Anal. Calcd. for C₁₀H₂₀O₂: C, 69.72; H, 11.70. Found: C, 69.67; H, 11.71; O, 11.64.

(±)-*cis-2-t*-Butyl-5-methyl-1,4-cyclohexanedione (23).—To a solution of 9.63 g. (0.0462 mole) of 2-*t*-butyl-5-methyl-1,4-dimethoxybenzene (22, m.p. 36-37°) in 21.6 g. of absolute ethanol, 180 ml. of anhydrous ether, and 225 ml. of liquid ammonia, was added 3.1 g. (0.45 g.-atom) of 1/8 in. lithium wire in 2-cm. lengths. The blue solution was stirred for 15 min. The procedure was analogous to that above for the preparation of 20. Evaporation of the final dried ether extract gave 8.79 g. of yellowish oil which solidified at 0°. Three recrystallizations from hexane gave 3.00 g. (36%) of white needle-like crystals, m.p. 50-57°, a mixture of ca. 86% of the *cis*-dione 23, and ca. 14% of its *trans* stereoisomer. Eleven more recrystallizations from hexane gave 23, 0.46 g. (5.5%), m.p. 69-70°.

Anal. Calcd. for C₁₁H₁₈O₂: C, 72.49; H, 9.95. Found: C, 72.28; H, 9.87.

Fractional recrystallization of the mother liquors from hexane readily gave solid mixtures of 23 with its *trans* stereoisomer containing from ca. 1% to ca. 60% of *trans*-dione. The composition of the mixtures was analyzed as above for 20 by gas chromatography on the same column at 120°. The *cis*-dione gave the greater retention time, as in the case of 20. In the original reaction product (presumably at equilibrium) the predominant stereoisomer was the *cis*-dione 23.

(±)-*cis,cis,cis-2-t*-Butyl-5-methyl-1,4-cyclohexanediol (8).—To a solution of 0.90 g. (4.9 mmoles) of a mixture containing 90% of *cis*-dione 23 and 10% of its *trans* stereoisomer in 30 ml. of acetic acid was added 0.30 g. (1.3 mmoles) of platinum dioxide catalyst. Hydrogenation at atmospheric pressure and 25° readily consumed 98% of 9.8 mmoles of hydrogen. The resulting mixture, treated as for 7 above, gave 0.9 g. of neutral colorless oil which was dissolved in 20 ml. of anhydrous 1:1 ether-benzene and chromatographed on a 16 mm. i.d. column containing 100 g. of alumina. Elution with anhydrous 1:1 benzene-ether, anhydrous ether, and 1:9 methanol-ether gave 38 fractions. Fractions 13-29, eluted with anhydrous ether, were essentially identical according to infrared analysis (2500-4000 cm.⁻¹ region, 1 mg./ml. in dried carbon tetrachloride, 1-cm. cells) and were combined to give 0.54 g. of diol. Recrystallization from hexane, then from water, and again from hexane gave white crystals, 94 mg. (10%), m.p. 99-100°.

Anal. Calcd. for C₁₁H₂₂O₂: C, 70.92; H, 11.91. Found: C, 70.87; H, 11.97.

Gas chromatography¹⁵ of the analytical sample at 160° gave a single sharp peak, retention time 9.3 min. The original total hydrogenation product gave additional minor peaks attributable to the starting diones (retention time 1.4 and 2.0 min.) and, probably, intermediate hydroxy ketones (7.1 min. with a shoulder at 6.6 min.).

Infrared Spectra of Diols 1-9.—A Perkin-Elmer Model 421DG spectrophotometer was used to record infrared spectra in the region 2500-4000 cm.⁻¹ by use of stoppered Beckman near-in-

(23) L. F. Fieser, private communication.

(24) R. D. Stolow and J. W. Larsen, *Chem. Ind. (London)*, 449 (1963); P. F. Oesper, C. P. Smyth, and M. S. Kharasch, *J. Am. Chem. Soc.*, **64**, 937 (1942).

(25) R. Royer, P. Demerseman, A. Cheutin, E. Allégrini, and R. Michelet, *Bull. soc. chim. France*, 1379 (1957).

frared silica cells of path length 1.00 cm. at *ca.* 25°. The frequencies were calibrated by recording atmospheric water vapor absorption with each spectrum. The accuracy of the frequencies reported is believed to be ± 2 cm.⁻¹ near 3620 and ± 4 cm.⁻¹ near 3500 cm.⁻¹. The absorbance reported is a measure of the peak intensity. Data recorded for 0.0040 *M* solutions of the diols in

dried Spectranalyzed carbon tetrachloride are presented in Table I. A small contribution to absorption at 3490 ± 10 cm.⁻¹, attributable to intermolecular hydrogen bonding, is observed in the 0.0040 *M* solutions. This factor, which appears to cancel out when the absorbance ratio is computed, has been neglected in Table I.

[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY, TUFTS UNIVERSITY, MEDFORD 55, MASS.]

Conformational Studies. VII.¹ *p*-Menthane-2,5-diols and the Relative "Size" of the Isopropyl Group²

BY ROBERT D. STOLOW

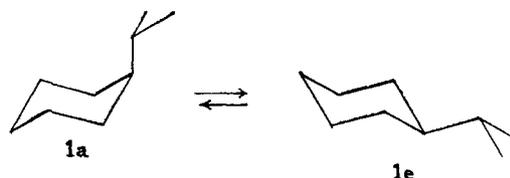
RECEIVED DECEMBER 2, 1963

Unique among the racemic *p*-menthane-*cis*-2,5-diols (4, 8, 9, and 10) is (\pm)-*cis,cis,cis*-*p*-menthane-2,5-diol (4), m.p. 105°, which exhibits significant intramolecular hydrogen bonding. The configurations assigned diols 4, 8, 9, and 10 are discussed, as well as their infrared spectra and their behavior upon gas chromatography. Comparative observations of conformational equilibria of *cis,cis,cis*-2,5-dialkyl-1,4-cyclohexanediols (3-7) suggest that an isopropyl group may have an apparent relative "size" ranging between that of a methyl and a *t*-butyl group, the "size" depending upon the details of the system and the specific observation made upon it.

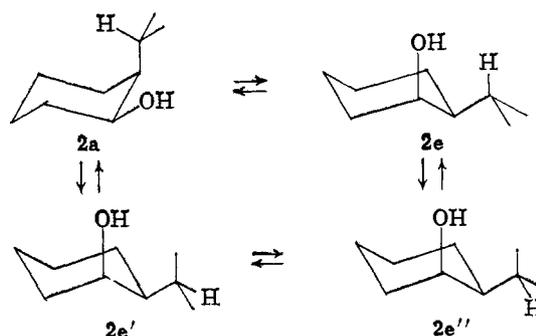
The isopropyl group, when a substituent on a cyclohexane ring, appears almost as "big" as a *t*-butyl group in certain experiments and nearly the same "size" as a methyl group in others.³ A further opportunity to consider the relative "sizes" of the methyl and the isopropyl groups is afforded by the results of a study of the conformational equilibria of (\pm)-*cis,cis,cis*-*p*-menthane-2,5-diol and related compounds.¹ While the actual size of the isopropyl group is obviously constant, its effect upon conformational equilibria depends in part upon its immediate environment, which is far from constant over the range of systems under consideration.^{1,3}

It seems clear that at 25°, the equatorial conformation of isopropylcyclohexane is more stable than the axial conformation by about 2.1 kcal./mole.³⁻⁷ The corresponding value for methylcyclohexane is about 1.7 kcal./mole³⁻⁶; for *t*-butylcyclohexane, >5.5 kcal./mole. The isopropyl group gives nearly the same value as the methyl group.³⁻⁶ In derivatives of isopropylcyclohexane which have the same environment in the immediate vicinity of the isopropyl group as isopropylcyclohexane itself, the isopropyl group would still be expected to appear nearly the same "size" as a methyl group. In derivatives of isopropylcyclohexane which have substituents close enough to produce repulsive interactions with either or both of the isopropyl's methyl groups, these interactions would affect the conformational equilibria. In such an environment the isopropyl group would not necessarily appear nearly the same "size" as a methyl group, as illustrated below.

In isopropylcyclohexane (1) the axial isopropyl group exists predominantly in a single rotational conformation, 1a.³ One of its two methyl groups would be sub-



jected to a substantial repulsive interaction by a *cis* (equatorial) substituent on an adjacent carbon atom. For example, consider *cis*-2-isopropylcyclohexanol (2). One would expect the repulsive interaction between the methyl and hydroxyl groups in 2a to be about the same as the direct interaction between an axial methyl group and an axial hydroxyl group in *cis*-3-methylcyclohexanol, since the distance separating the methyl and the hydroxyl groups is about the same in each case.⁸ On the other hand, in 2e, as distinguished from its



rotational conformers 2e' and 2e'', there is an hydrogen-hydroxyl type repulsive interaction, rather than the stronger methyl-hydroxyl type interaction. Since the repulsive interaction between substituents is greater in 2a than in 2e, the interaction tends to shift the conformational equilibrium toward 2e, thus enhancing the apparent "size" of the isopropyl group. By applying to 2 the method of calculation reported for 1 by Allinger and Hu,⁹ one may calculate $-\Delta G^\circ = 2.2$ kcal./mole, for

(1) Paper VI: R. D. Stollow, P. M. McDonagh, and M. M. Bonaventura, *J. Am. Chem. Soc.*, **86**, 2185 (1964).

(2) Presented, in part, at the 145th National Meeting of the American Chemical Society, New York, N. Y., Sept., 1963. Support of this work by the National Science Foundation is gratefully acknowledged.

(3) N. L. Allinger, L. A. Freiberg, and S.-E. Hu, *J. Am. Chem. Soc.*, **84**, 2836 (1962).

(4) A. H. Lewin and S. Winstein, *ibid.*, **84**, 2464 (1962).

(5) E. L. Eliel and T. J. Brett, Abstracts, 145th National Meeting of the American Chemical Society, New York, N. Y., 1963, p. 19Q.

(6) This value was suggested as an average of the best available experimental values by Prof. E. L. Eliel, during his oral presentation of ref. 5. All values are for 298°K.

(7) It is important to note that the value of 3.3 (or >3.3) referred to in ref. 3 (and ref. 4a and 5 therein) has been retracted in ref. 4.

(8) E. L. Eliel and H. Haubenstock, *J. Org. Chem.*, **26**, 3504 (1961). Some consideration was given this type of interaction by S. Yamana, *Bull. Chem. Soc. Japan*, **34**, 1414 (1961).

(9) N. L. Allinger and S.-E. Hu, *J. Org. Chem.*, **27**, 3417 (1962).