

hydride in 500 ml. of ether. After refluxing overnight, the excess hydride was destroyed by adding 15.9 g. (166 mmoles) of dried trimethylammonium chloride. Then about 300 ml. of dry benzene was added. Distillation until the b.p. reached about 76°, filtration of the residue, and evaporation of the solvent under reduced pressure gave 2.8 g. (36%) of IV, b.p. 74–75° at 2.35 mm.

*Anal.* Calcd. for  $C_{10}H_{14}NB$ : C, 75.52; H, 8.87; N, 8.81; B, 6.80. Found: C, 74.72; H, 8.94; N, 9.46; B, 7.16.

**1-Methyl-2-phenyl-1,2-azaborolidine (IV) from V and N-Methylallylamine.**—A solution of 5.1 g. (34 mmoles) of V in 150 ml. of diglyme was stirred and gradually heated while 2.4 g. (34 mmoles) of N-methylallylamine in 50 ml. of diglyme was slowly added. The approximate temperature of the diglyme solution was measured by means of a thermocouple in contact with the outer wall of the flask. The gases emitted from the top of the reflux condenser were led through a mercury seal. Trimethylamine evolution was first observed at about 70°, but even at 130–135° the evolution of hydrogen and trimethylamine was slow. The diglyme solution was held at about this temperature as the remainder of the amine solution was added over a period of several hours. Then a small quantity of trimethylammonium chloride was introduced, and the diglyme solution was heated to reflux. Little, if any, additional hydrogen was evolved. Removal of the diglyme at reduced pressure left a liquid from which the crude product was stripped at 2.4 mm. About an equal volume of a solid remained as a residue. Redistillation of the volatile material gave 2.1 g. (39%) of IV, b.p. 78.5–81.5° at 2.55 mm., with an infrared spectrum identical with that of the product from the alternative synthesis.

**2-Phenyl-1,2-azaboracyclohexane (IIa).**—3-Butenylamine (3.65 g., 51.3 mmoles) in 250 ml. of diglyme was added over a period of about 5 hr. to a stirred solution of 7.65 g. (51.3 mmoles) of V in 350 ml. of diglyme at 120–133°. The gases which bubbled through the mercury seal were collected by displacement of hy-

drochloric acid, so that the approximate rate of hydrogen evolution could be observed. Hydrogen formation was evident only at about 120° and above. A work-up similar to the previous preparation, except that the trimethylammonium chloride was omitted, yielded 4.7 g. (58%) of crude product. Redistillation gave relatively pure IIa, b.p. 64–68° at 0.4 mm. The infrared spectrum of IIa included peaks at 3405 (N—H) and 1512  $cm^{-1}$  (B=N).

*Anal.* Calcd. for  $C_{10}H_{14}NB$ : C, 75.52; H, 8.87; N, 8.81; B, 6.80. Found: C, 75.67; H, 8.95; N, 8.87; B, 7.17.

**2-Phenyl-2,1-borazarene (Ib).**—Compound IIa (0.55 g., 3.5 mmoles) was gently refluxed for 8 hr. with about an equal amount of 30% palladium-on-charcoal catalyst<sup>18</sup> in an apparatus similar to that described by Fieser.<sup>19</sup> A very slow stream of nitrogen served to sweep hydrogen from the system. Crystals began to deposit on the cold finger after about 5 hr. The resulting material was taken up in ether, filtered, and the filtrate was treated with wet ether to hydrolyze unreacted IIa. Evaporation of the ether and crystallization from petroleum ether (in which the hydrolyzed IIa was not appreciably soluble) gave 0.14 g. of crude product, m.p. 112–115°. Recrystallization from petroleum ether gave 0.085 g. (16%) of white crystals, m.p. 117–118°. A sample sublimed at 60° (0.5 mm.) and melted at 117–118.5°. The infrared spectrum of Ib (potassium bromide disk) showed maxima (above 1500  $cm^{-1}$ ) at 1546, 1601, 1615, 3010–3075, and 3375  $cm^{-1}$ . The N—H stretching frequency was shifted to 3419  $cm^{-1}$  in carbon tetrachloride solution.

*Anal.* Calcd. for  $C_{10}H_{10}NB$ : C, 77.49; H, 6.50; N, 9.04; B, 6.97; mol. wt., 155. Found: C, 77.35; H, 6.76; N, 8.84; B, 7.25; mol. wt. (Rast), 169

(18) L. F. Fieser, "Experiments in Organic Chemistry," 2nd Ed., D. C. Heath and Co., Boston, Mass., 1941, p. 459.

(19) Reference 18, pp. 461–462.

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

## Conformational Studies. V.<sup>1</sup> Predominance of Intramolecularly Hydrogen Bonded Nonchair Conformations of *cis,cis,cis*-2,5-Di-*t*-alkyl-1,4-cyclohexanediols<sup>2</sup>

By ROBERT D. STOLOW AND MARIA M. BONAVENTURA

RECEIVED AUGUST 7, 1963

*cis,cis,cis*-2,5-Di-*t*-butyl-1,4-cyclohexanediol (1), its monomethyl ether (2), and *cis,cis,cis*-2,5-di-*t*-pentyl-1,4-cyclohexanediol (3) have been prepared. Their infrared spectra, which show intense absorption attributable to transannular intramolecular hydrogen bonding in nonchair conformations, are interpreted in support of the assigned configurations and in terms of negligible populations of *chair* conformations for 1–3 in dilute solution in carbon tetrachloride at 25°.

By suitable choice of substituents, the usual position of equilibrium between chair and nonchair conformations of cyclohexane<sup>3</sup> may be reversed. We wish to report the first example of a monocyclic, saturated cyclohexane derivative for which it has been demonstrated unequivocally that the population of *chair* conformations is negligible.<sup>4</sup>

A *trans*-1,3- or *cis*-1,4-disubstituted cyclohexane in a chair conformation must have one axial substituent. However, in a nonchair conformation, both substituents simultaneously may occupy equatorial-like positions. Therefore, in general, since substituents encounter

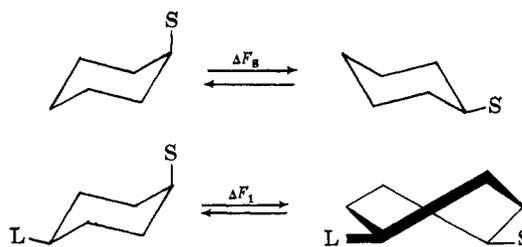
greater repulsive interactions when in axial positions than when in equatorial (or equatorial-like) positions, the population of nonchair conformations should be greater for a *trans*-1,3- or *cis*-1,4-disubstituted cyclohexane than the 0.1% nonchair population (at 25°) estimated for cyclohexane itself.<sup>3,5</sup> For example, it has been pointed out that the nonchair population of a *cis*-4-alkylcyclohexanecarboxylic acid in water solution at 25° should be *ca.* 20) times that of cyclohexane, or *ca.* 2%.<sup>6</sup> For many other *trans*-1,3- and *cis*-1,4-disubstituted cyclohexanes, an estimate of the nonchair population can be made by subtracting an experimental value,<sup>5</sup>  $-\Delta F_S$ , for the "smaller" substituent (S) from 4

(1) (a) Paper I: R. D. Stolor, *J. Am. Chem. Soc.*, **81**, 5806 (1959); (b) Paper II: R. D. Stolor, *ibid.*, **83**, 2592 (1961); (c) Paper III: R. D. Stolor and C. B. Boyce, *ibid.*, **83**, 3722 (1961); (d) Paper IV: R. D. Stolor, *ibid.*, **84**, 686 (1962).

(2) The authors are grateful to the National Science Foundation for grants in support of this research. Presented at the XIXth International Congress of Pure and Applied Chemistry, London, July 15, 1963.

(3) E. L. Eliel, "Stereochemistry of Carbon Compounds," McGraw-Hill Book Co., Inc., New York, N. Y., 1962, Chapter 8.

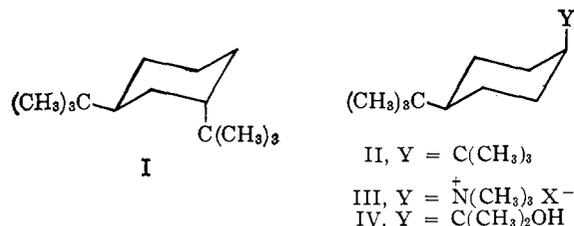
(4) Although considerable attention has been given the subject of nonchair conformations recently, few population studies have been reported for saturated, monocyclic cyclohexane derivatives. In this paper, attention is focused exclusively on such compounds. Nonchair conformations have been detected for numerous polycyclic and unsaturated cyclohexane derivatives, and for some heterocyclic six-membered ring compounds (substituted piperidines, tetrahydropyrans, etc.). Nonchair transition states have also been discussed for numerous reactions. See ref. 3, and references cited therein, and M. Tichý, J. Šipos, and J. Sicher, *Collection Czech. Chem. Commun.*, **27**, 2907 (1962).



(5) Free energy differences between equatorial and axial substituents are tabulated in ref. 3, p. 236. Also see subsequent publications of Prof. E. L. Eliel.

(6) Reference 1a, and footnote 15 therein.

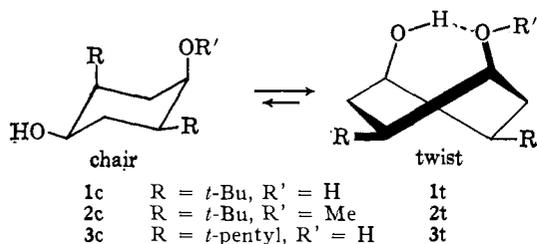
kcal./mole,<sup>3</sup> to give an estimated free energy difference,  $\Delta F_1$ , between a chair and a nonchair conformation.<sup>7</sup> Therefore, for compounds of this type, where  $-\Delta F_S > 4$  kcal./mole, one might expect nonchair conformations to predominate in solution at 25°. Examples include *trans*-1,3-di-*t*-butylcyclohexane (I), *cis*-1,4-di-*t*-butylcyclohexane (II), *cis*-4-*t*-butylcyclohexyltrimethylammonium salts<sup>8</sup> (III) and, probably, *cis*-4-*t*-butyl- $\alpha,\alpha$ -dimethylcyclohexanemethanol<sup>9</sup> (IV).



The entropy of equilibration of I with its *cis* isomer has been interpreted in terms of predominance of nonchair conformations of I.<sup>10</sup> However, the *chair* population is uncertain<sup>11</sup> for I and for II-IV as well. One reason for this uncertainty is that I-IV all lack an easily measurable property characteristic of the chair conformations. Furthermore, for bulky substituents, such as those in compounds I-IV, experimental values of  $\Delta F_S$  are not available. However, if  $-\Delta F_S$  were  $< 6$  kcal./mole for I-IV, as one might expect,<sup>8,10</sup> the chair population would be at least several per cent.

### Discussion and Results

A monocyclic, saturated cyclohexane derivative was desired for which the chair population is negligible. Because of the uncertainties expressed above, disubstituted cyclohexanes (such as II) were rejected as candidates for synthesis. Instead, it was postulated that *cis,cis,cis*-2,5-di-*t*-butyl-1,4-cyclohexanediol (1) might fulfill the requirement, since the chair  $\rightleftharpoons$  nonchair equilibrium (*1c*  $\rightleftharpoons$  *1t*) should be shifted far to the right, relative to II.



The chair conformation *1c* is severely destabilized by the crowding together of the axial *t*-butyl group, the abutting axial hydrogen, and the axial hydroxyl group, whereas in twist conformation *1t*, both *t*-butyl groups may occupy equatorial-like positions, while the hydroxyl groups may form an intramolecular hydrogen bond. Clear evidence of strong intramolecular hydrogen bonding detected by infrared spectroscopy for a 2,5-di-*t*-butyl-1,4-cyclohexanediol, m.p. 157.5-158.5°, assigned structure I, was described in a preliminary communication; the presence of nonchair conformations was demonstrated.<sup>1b</sup> The question of the *chair* population, however, remained unanswered.<sup>1b</sup> There-

(7) Here, negligible attractive interaction between L and S is assumed. Other assumptions have been noted<sup>6</sup>; S "smaller" than L means  $(-\Delta F_S) \ll (-\Delta F_L)$ .

(8) D. Y. Curtin, R. D. Stolow, and W. Maya, *J. Am. Chem. Soc.*, **81**, 3330 (1959).

(9) R. D. Stolow and C. B. Boyce, *J. Org. Chem.*, **26**, 4726 (1961).

(10) N. L. Allinger and L. A. Freiberg, *J. Am. Chem. Soc.*, **82**, 2393 (1960).

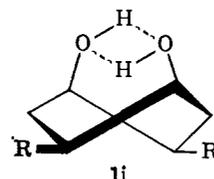
(11) Reference 10, footnote 16, states that "an appreciable amount of the chair form" may be present.

fore, the further work described below was undertaken.

All conformations of 1, including *1c* and *1t*, would have one or two "free" hydroxyl groups (with one exception: structure *1i*).<sup>12</sup> *cis,cis,cis*-2,5-Di-*t*-butyl-4-methoxycyclohexanol (2), however, when in any intramolecularly hydrogen bonded conformation such as *2t*, cannot have a "free" hydroxyl group. Only nonhydrogen bonded conformations, such as chair *2c*, the alternate chair, or any of a series of nonhydrogen bonded nonchair conformations of 2 could have a "free" hydroxyl group.<sup>14</sup> Therefore, the observation of negligible "free" hydroxyl for 2 would provide compelling evidence for the presence of a negligible population of *chair* conformations. We wish to present such evidence, obtained by infrared spectroscopy, for a 2,5-di-*t*-butyl-4-methoxycyclohexanol, m.p. 43-44°, assigned structure 2.

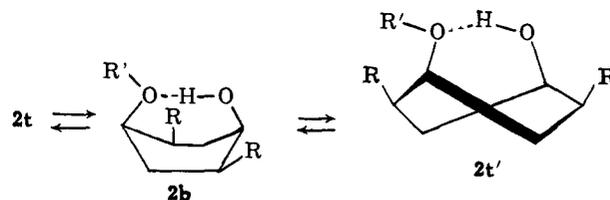
A 0.0020 *M* solution of 2 in carbon tetrachloride exhibited a single detectable absorption band in the region 3900-3200 cm.<sup>-1</sup>, at 3463  $\pm$  5 cm.<sup>-1</sup> (path, 1.0 cm.;  $\nu_{1/2}$ , 67 cm.<sup>-1</sup>; absorbance, 0.25). The absorbance of this band varied linearly with the concentration in the range 0.0002 to 0.004 *M*. A 0.0040 *M* solution of 2 in carbon tetrachloride, when observed in a cell of 5.0-cm. path length, showed an extremely weak absorption band at 3620  $\pm$  3 cm.<sup>-1</sup> (absorbance, 0.023), and no detectable absorbance (0.000) at 3640 cm.<sup>-1</sup>. In a 1.0-cm. cell, the absorbance of this solution at 3463 cm.<sup>-1</sup> was 0.50. By combining the data, one finds the ratio of the absorbance at 3620 cm.<sup>-1</sup> to that at 3463 cm.<sup>-1</sup> for 2 to be less than 0.01. The strong broad band at 3463 cm.<sup>-1</sup> may be assigned to O-H stretching vibrations of hydroxyl groups, the hydrogen atoms of which take part in transannular intramolecular hydrogen bonding to the oxygen of the methoxyl group, forming a seven-membered ring.<sup>16</sup> The extremely weak band at 3620 cm.<sup>-1</sup>

(12) Hydroxyl groups, the hydrogen atoms of which are not hydrogen bonded to oxygen, are called "free." Only monomers are considered. The exception referred to, structure *1i*, has a four-membered ring.<sup>13</sup>



(13) For a discussion of related "cyclic dimers," see L. P. Kuhn and R. E. Bowman, *Spectrochim. Acta*, **17**, 650 (1961).

(14) Appreciation of this point would be aided by the use of models. Intramolecular hydrogen bonding can occur only in the small range of nonchair conformations in which the O...H distance is  $< 2.7$  Å.<sup>15</sup> (In the undeformed chair conformations, this distance is ca. 3.7 Å.) At closest approach without angular strain, O...H distance ca. 0.8 Å, 2 would be in boat conformation *2b*. At that distance, one would expect the net interaction between the hydroxyl and methoxyl groups of *2b* to be strongly repulsive. Let *2t* represent the conformation at an energy minimum expected at some O...H distance intermediate between 0.8 and 2.7 Å, near 1.6 Å.<sup>15</sup> By rotation from *2b* in one direction, *2t* may be reached whereas rotation from *2b* in the opposite direction would give a second intramolecularly hydrogen bonded twist conformation, *2t'*, which would appear to be less stable than *2t* because of a less favorable orientation of the *t*-butyl groups. Further study of models



revealed no conformation of 2 which appeared more stable than *2t*.

(15) L. P. Kuhn, *J. Am. Chem. Soc.*, **74**, 2492 (1952), and subsequent papers; G. C. Pimentel and A. L. McClellan, "The Hydrogen Bond," W. H. Freeman and Co., San Francisco, Calif., 1960.

(16) F. T. Wall and W. F. Clausen, *J. Am. Chem. Soc.*, **61**, 2679 (1939), reported for 4-ethoxy-1-butanol, 0.004 *M* in carbon tetrachloride, bands at ca. 3640 and 3460 cm.<sup>-1</sup> (peak intensity ratio, 0.3). Also see ref. 13, 15, and 1b.

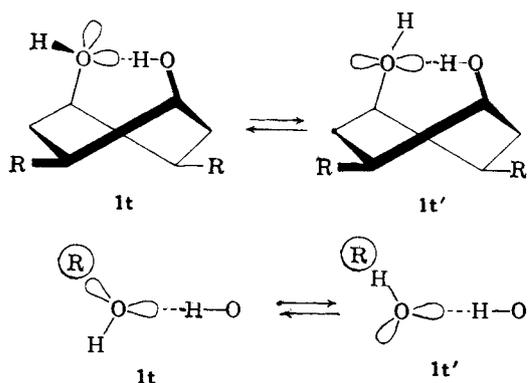
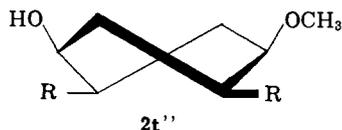


Fig. 1.—The proximity to the neighboring *t*-butyl group (R) of the "free" hydroxyl group's "free" electron pair in 1*t*, and of the "free" hydroxyl group's hydrogen in 1*t*'.

may be attributed to O—H stretching vibrations of the hydroxyl group of 2 in nonhydrogen bonded conformations, including both possible chair conformations. Assuming a normal extinction coefficient for the "free" hydroxyl group, an upper limit of 2% may be set on the population of the nonhydrogen bonded conformations of 2<sup>17</sup>. Of the possible nonhydrogen bonded conformations of 2, the chair conformations are not necessarily the most stable. For example, nonhydrogen bonded twist conformation 2*t*' may be more stable than either chair conformation of 2. Therefore, the chair population might be a small fraction of the total population of nonhydrogen bonded conformations of 2. Clearly, for



2 in dilute solution in carbon tetrachloride at 25°, the intramolecularly hydrogen bonded twist conformations predominate (>98%); the population of chair conformations is negligible (some fraction, possibly quite small, of the remaining <2%).

Before comparison of the infrared spectra of 1 and 2, it would be worthwhile to compare 1 with a 2,5-di-*t*-pentyl-1,4-cyclohexanediol, m.p. 97–98°, assigned structure 3. The comparison reveals a remarkable similarity in the infrared spectra of 1<sup>1b</sup> and 3. Indeed, the spectra are *identical* (within experimental error). For example, for 0.0040 *M* solutions in carbon tetrachloride at *ca.* 25°, the frequency (cm.<sup>-1</sup>) and absorbance of each hydroxyl band are: 1, 3640 (0.26), 3619 (0.23), 3480 (0.48); 3, 3640 (0.26), 3618 (0.23), 3480 (0.47). It would seem logical to conclude that 1 and 3 have the same configuration, and also have essentially the same population distribution among the major conformations. The *t*-butyl group and the *t*-pentyl group differ at a position removed from the site of the major repulsive interactions which determine the conformational equilibria. One might expect similar results for *t*-alkyl substituents in general, in diols analogous to 1 and 3. However, the question of the chair population of 1 (or 3) remains to be considered.

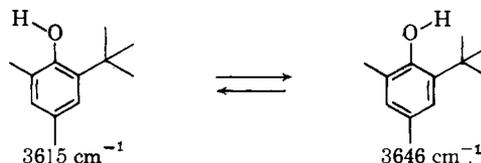
Since the chair population of 2 has been demonstrated to be negligible, one can argue that the chair population of 1 must also be negligible. For 0.0020 *M* solutions in carbon tetrachloride at *ca.* 25°, the following results were obtained for frequency (and absorbance) of hydrogen bonded bands: 1, 3480 (0.25); 2, 3463 (0.25).

(17) The population given is a limiting value, since contributions to absorption at 3620 cm.<sup>-1</sup> due to impurities or other causes may be significant. For example, 2% isomeric impurity would be sufficient to produce the observed absorption at 3620 cm.<sup>-1</sup>.

Assuming that the absolute intensity of the hydrogen bonded band of 1 is equal to that of 2, then since 1 and 2 give the same absorbance (0.25), it follows directly that the nonchair population of 1 and 2 must be nearly the same.

If the hydrogen bonded nonchair population of diol 1 is (like 2) *ca.* >98%, then all O—H bands of 1 must be assigned to *hydrogen bonded* conformations, such as 1*t*. For 0.0040 *M* solutions in carbon tetrachloride at *ca.* 25°, the results obtained for frequency (and absorbance) of the "free" hydroxyl bands are: 1, 3640 (0.26), 3619 (0.23); 2, 3640 (0.000), 3620 (0.005). Specifically, the bands of 1 at 3640 and 3619 cm.<sup>-1</sup> must be assigned to "free" hydroxyl groups, the oxygen atoms of which are involved in intramolecular hydrogen bonding. Note that 2, with no such group, has *no* absorption at 3640. A single conformation, such as 1*t*, would not be expected to show a doublet "free" hydroxyl band.<sup>1b</sup> The doublet is not attributable to Fermi resonance, as shown by the results of deuterium exchange.<sup>1b</sup> The doublet may be interpreted in terms of two hydrogen bonded conformations, present in nearly equal amounts (assuming nearly equal absolute intensities for the two bands of the doublet), one showing its "free" hydroxyl absorption at 3640, the other, at 3619 cm.<sup>-1</sup> (absorbance ratio, 1.15). Such a pair of hydrogen bonded conformations must have nearly equal energies, but must provide significantly different environments for the "free" hydroxyls. For 1, conformations 1*t* and 1*t*', which differ only in the orientation of the free hydroxyl group, might fulfill these requirements. The oxygen of the "free" hydroxyl group is represented as having two equivalent orbitals, either of which may participate in hydrogen bond formation. However, the two possible conformations which result, 1*t* and 1*t*', differ significantly. In 1*t*, the hydrogen of the "free" hydroxyl points away from the neighboring *t*-butyl group. In 1*t*', this hydrogen abuts the *t*-butyl group (Fig. 1). If the "free" unshared pair of electrons of 1*t* and the "free" hydrogen of 1*t*' are about the same steric "size" (*i.e.*, if the repulsion of each with an abutting *t*-butyl group, as shown in Fig. 1, is about the same), then the populations of 1*t* and 1*t*' would be about the same.

A close analogy is provided by the conformational equilibria in unsymmetrically alkylated phenols, for example, 2-*t*-butyl-4,6-dimethylphenol, which shows a similar doublet.<sup>18</sup> The higher frequency band of the doublet is clearly attributable to the hydroxyl group in



the more hindered position.<sup>18</sup> Other examples of doublet "free" hydroxyl absorption attributable to "conformational heterogeneity" have been discussed.<sup>19,20</sup> Therefore, diol 1, in dilute solution in carbon tetrachloride at 25°, might be expected to exist predominantly in nearly equal populations of nonchair intramolecularly hydrogen bonded conformations 1*t* and 1*t*', where 1*t* would contribute to absorption at 3619 and 3480 cm.<sup>-1</sup>, while 1*t*' would contribute to absorption at 3640 and 3480 cm.<sup>-1</sup>. The resultant infrared spectrum predicted for 1, based on the above argument, would be

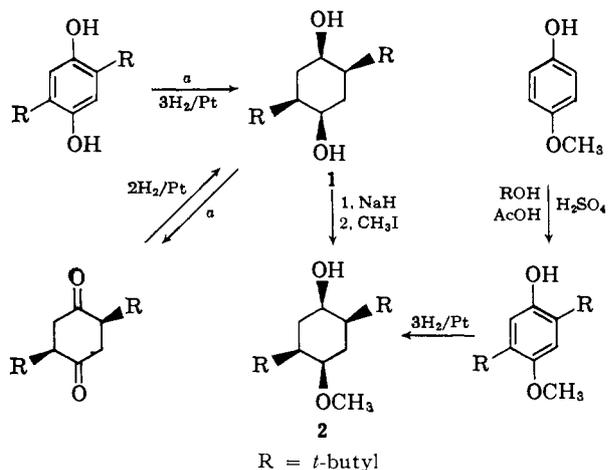
(18) R. F. Goddu, *J. Am. Chem. Soc.*, **82**, 4533 (1960); K. U. Ingold, *Can. J. Chem.*, **40**, 111 (1962). Compare models of 1*t*, 1*t*', and *o*-*t*-butylphenols (Stuart-Briegleb models are suggested).

(19) R. Piccolini and S. Winstein, *Tetrahedron Letters*, No. 13, 4 (1959).

(20) F. Dalton, G. D. Meakins, J. H. Robinson, and W. Zaharia, *J. Chem. Soc.*, 1566 (1962). Pertinent examples are those in which the O—H bond may be directed toward an abutting alkyl group, as in 5 $\alpha$ -cholestan-7 $\beta$ -ol.

exactly like that recorded. Therefore, the infrared spectrum is consistent with interpretation in terms of a negligible chair population for diol 1.<sup>21</sup> Although the chair populations of 1 and 2 would not be expected to differ greatly, evidence for a negligible chair population is considered conclusive only for 2. The evidence seems sufficient, however, to warrant the tentative conclusion that *cis,cis,cis*-2,5-di-*t*-alkyl-1,4-cyclohexanediols, in general, have negligible chair populations.<sup>22</sup>

**Preparation and Configuration.**—Hydrogenation in acetic acid with platinum oxide catalyst at 25° under 2–3 atm. hydrogen pressure of 2,5-di-*t*-butylhydroquinone, 2,5-di-*t*-pentylhydroquinone, and 2,5-di-*t*-butyl-4-methoxyphenol gave product mixtures which, after crystallization and chromatography on alumina, gave a 2,5-di-*t*-butyl-1,4-cyclohexanediol, m.p. 157.5–158.5° (1),<sup>1b</sup> a 2,5-di-*t*-pentyl-1,4-cyclohexanediol, m.p. 97–98° (3), and a 2,5-di-*t*-butyl-4-methoxycyclohexanol, m.p. 43–44° (2), respectively. The fractionation procedure in each case, monitored by infrared analysis, was directed toward isolation of a pure substance exhibiting maximum intramolecular hydrogen bonding. Diol 1



<sup>a</sup> An analogous reaction was obtained for R = *t*-pentyl.

was also prepared in 85% yield by hydrogenation of *cis*-2,5-di-*t*-butyl-1,4-cyclohexanedione<sup>1c</sup> with platinum dioxide catalyst in acetic acid solution at 25°. Jones oxidation of diol 3 gave *cis*-2,5-di-*t*-pentyl-1,4-cyclohexanedione. Diol 1 was converted into its monomethyl ether by taking advantage of the rapid displacement reaction by the alkoxide anion of 1 (formed from 1 with sodium hydride in dimethyl sulfoxide) upon methyl

(21) We recognize that this interpretation of the diol spectra is not unique. We encourage consideration of other interpretations.

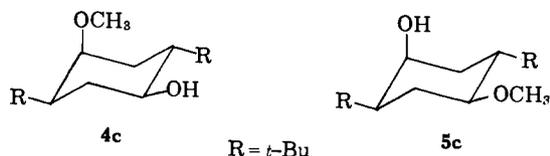
(22) One approach to the estimation of the expected chair population of diol 1 would be calculation of  $\Delta\Delta F = \Delta F_2 - \Delta F_1$ , the difference in free energy change for the chair  $\rightleftharpoons$  nonchair equilibria of 1 and 2, by qualitative evaluation of  $\Delta\Delta H$  and  $\Delta\Delta S$ , as follows:

The relationship between the strength and length of a hydrogen bond of type O-H...O, and the O-H stretching frequency has been discussed.<sup>15</sup> The frequencies reported for 1 and 2, 3480 and 3463 cm.<sup>-1</sup>, suggest the conclusion that the optimum hydrogen bond in 2 is slightly shorter (*ca.* 0.1 Å) and slightly stronger (perhaps 200 cal./mole) than in 1.<sup>15</sup> This result reflects the slightly greater basicity of the methoxyl oxygen relative to the hydroxyl oxygen.<sup>15</sup> The repulsive interactions of the methoxyl group of 2 should not differ significantly from those of a corresponding hydroxyl group of 1; methoxyl and hydroxyl groups on cyclohexane have about the same steric "size."<sup>15</sup> While factors such as these, which influence mainly the enthalpy of conformational equilibria, suggest that diol 1 may have a slightly larger chair population than 2, the entropy term, probably larger in magnitude than the enthalpy term, favors the opposite conclusion. The two non-equivalent chair conformations of 2, if they have nearly equal populations, would give an entropy of mixing term of nearly 1.38 cal./mole deg. For 1, the two chair conformations are equivalent; the corresponding entropy term is zero.<sup>3</sup> Thus, a chair conformation might be a significantly less probable state for 1 than for 2. Similar considerations suggest that the hydrogen bonded conformations may be more probable for 1 than for 2. Therefore, the conclusion that the chair population expected for 1 is not significantly greater than that found for 2 seems a reasonable one.

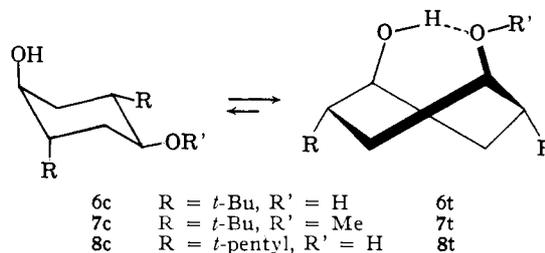
iodide in dimethyl sulfoxide solution at 25–40°. The resulting monomethyl ether of 1 was identical with the 2,5-di-*t*-butyl-4-methoxycyclohexanol (2), m.p. 43–44°, isolated from the hydrogenation product of 2,5-di-*t*-butyl-4-methoxyphenol.

Configurations 1, 2, and 3 were assigned on the basis of the method of synthesis and infrared spectra. Although no rigorous proof of configuration has been carried out, these assignments are consistent with the data available at present, as shown below.

The ten configurational possibilities for 2,5-di-*t*-butyl-1,4-cyclohexanediols have been discussed.<sup>1b</sup> For 2,5-di-*t*-butyl-4-methoxycyclohexanols, 16 configurations (eight racemates) are theoretically possible. Of these, the four racemates with the hydroxyl and methoxyl groups *trans* to one another have no accessible conformation in which the hydroxyl hydrogen may approach the methoxyl oxygen closely enough to form an intramolecular hydrogen bond.<sup>14</sup> For the two racemates in which the hydroxyl and methoxyl groups are *cis* to one another but the *t*-butyl groups are *trans* to one another, 4 and 5, intramolecular hydrogen bonding is possible in certain nonchair conformations, but these would be expected to have much higher free energies (and therefore very much smaller populations) than the chair conformations 4c and 5c in which both *t*-butyl groups occupy equatorial positions.



Therefore, since the chair conformations 4c and 5c are *not* destabilized relative to the nonchair conformations by the *t*-butyl groups, one would expect to find negligible intramolecular hydrogen bonding for 4 and 5, just as for *cis*-1,4-cyclohexanediol.<sup>15</sup> In order to shift the position of chair  $\rightleftharpoons$  nonchair equilibrium significantly to the right by placing alkyl groups at the 2- and 5-positions of *cis*-1,4-cyclohexanediol (the parent compound), it is essential that the alkyl groups be *cis* to one another so that *each* chair conformation will be destabilized by one axial alkyl group. Of all possible 2,5-di-*t*-butyl-4-methoxycyclohexanols, only racemates 2 and 7 have such a structure; only 2 and 7 would be expected to exhibit detectable intramolecular hydrogen bonding. The strong destabilization of chair conformations of 2 relative to nonchair conformations, such as 2t, has been discussed in detail above. Similarly, but to a lesser degree, the chair conformations of 7, 7c, and 7c', are each destabilized by an axial *t*-butyl group, while in nonchair conformations, such as 7t, both *t*-butyl groups



may assume positions with repulsive interactions slightly greater than equatorial positions. The non-chair population of 7 would be expected to be less than that of 2, but would probably be no less than that of *cis*-1,4-di-*t*-butylcyclohexane (II). It is therefore conceivable that nonchair conformations could predominate for 6, 7, and 8 as well as for 1, 2, and 3. Clearly 6, 7, and 8 must be considered as possible structures for the

compounds reported herein as 1, 2, and 3, each of which exhibits intense infrared absorption attributable to intramolecular hydrogen bonding in nonchair conformations (see above).

Since 1 would result from 2,5-di-*t*-butylhydroquinone if a stereospecific addition of all six hydrogen atoms occurred from the same side of the plane of the ring to give an all-*cis* configuration, structure 1 appears more probable than 6 for the diol obtained.<sup>1b</sup> The hydrogenation conditions used, when applied to other aromatic compounds, yield mostly *cis*-substituted cyclohexane derivatives.<sup>23</sup> Furthermore, hydrogenation of *cis*-2,5-di-*t*-butyl-1,4-cyclohexanedione, which gave the same diol in >85% yield, would be expected to give 1 in preference to 6, since 1 would be formed by addition of hydrogen from the less hindered side of the ring. In addition, the doublet observed in the infrared spectrum of the diol is consistent with structures 1t  $\rightleftharpoons$  1t', as shown above, but cannot be interpreted in terms of an analogous pair of structures, 6t  $\rightleftharpoons$  6t', since the "free" hydroxyl groups in both 6t and 6t' would have nearly equivalent, unhindered environments. Examination of a model of 6 revealed no intramolecularly hydrogen bonded conformation in which the free hydroxyl group would be expected to give an absorption band at 3640 cm.<sup>-1</sup>. Assignment of structure 1 to the 2,5-di-*t*-butyl-1,4-cyclohexanediol, m.p. 157.5–158.5°, compels analogous assignment of structure 2 to its monomethyl ether (2,5-di-*t*-butyl-4-methoxycyclohexanol, m.p. 43–44°), and requires assignment of structure 3 to the 2,5-di-*t*-pentyl-1,4-cyclohexanediol, m.p. 97–98°, since both diols were prepared in the same manner and gave essentially identical infrared absorption in the O–H stretching region.<sup>24</sup>

### Experimental<sup>25</sup>

**2,5-Di-*t*-butyl-1,4-cyclohexanediol (1), M.p. 158°.**—2,5-Di-*t*-butylhydroquinone (Eastman practical grade, recrystallized several times from glacial acetic acid, colorless crystals, m.p. 222–223° uncor.) was hydrogenated by use of a Parr apparatus<sup>26</sup> equipped with a neoprene stopper. Twenty runs were carried out under the following conditions.

To 5.0 g. (0.023 mole) of 2,5-di-*t*-butylhydroquinone was added 120 ml. of boiling glacial acetic acid (du Pont, reagent grade). The solid dissolved rapidly to give a colorless solution (negligible air oxidation) which was immediately cooled to room temperature. The solution was rinsed into a 500-ml. hydrogenation bottle with 30 ml. of additional acetic acid. The catalyst, platinum dioxide (Engelhard Industries, Inc.), 1.0 g., was added. At 25° and 2–3 atm. hydrogen pressure, hydrogenation generally stopped in 6–8 hr. after 85  $\pm$  10% of the calculated amount of hydrogen had reacted. The acetic acid solution was separated from the catalyst by filtration. The catalyst and bottle were washed with 3  $\times$  20 ml. of acetic acid. The filtrate plus washings were concentrated to ca. 15 ml. at 20 mm. The concentrate was added slowly to 150 ml. of water cooled to 0–5°. The precipitate was collected and dried, to give ca. 4.7 g. of white powder, m.p. ca. 110–130°. The product from three runs, 14 g., was recrystallized from acetonitrile to give 5.5 g. of white crystals, m.p. 137–144°. Recrystallization from 1–2 l. of pentane at 20° gave 1.4 g. (9%) of white needle-like crystals, m.p. 155.5–157°. Further recrystallizations brought the yield to 20%. Improved yields were obtained by chromatography of the solid recovered from the pentane filtrates (or by direct chromatography of the crystals obtained from acetonitrile) on alumina (Fisher Scientific Co., No. A-540), 100 g. per g. of product. Elution first with

(23) Reference 1a, and ref. 29–31 therein.

(24) Even if one were to reject the evidence and argue that the compounds reported as 1, 2, and 3 actually had structures 6, 7, and 8, one would still be likely to conclude that the chair populations of 1, 2, and 3 (which undoubtedly should be less than those of 6, 7, and 8) would be negligible.

(25) Routine infrared spectra were recorded by use of a Perkin-Elmer Model 21 spectrophotometer and solutions in dried "Spectranalyzed" carbon tetrachloride. Gas chromatography was carried out by use of a flame ionization detector and 0.25-in. o.d. copper columns packed with 2% "Versamid on Chromosorb W, Acid Washed, Silanized," 60/80 mesh (F and M Scientific Corp.). Microanalyses were determined by Dr. S. M. Nagy.

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

benzene gave a fraction, m.p. ca. 120°. When no further material was eluted by benzene, elution with anhydrous ether yielded a solid, m.p. 156–157°. Recrystallization from pentane gave a 2,5-di-*t*-butyl-1,4-cyclohexanediol, m.p. 157.5–158.5°.

*Anal.* Calcd. for C<sub>14</sub>H<sub>22</sub>O<sub>2</sub>: C, 73.63; H, 12.36. Found: C, 73.63; H, 12.11.

The diol exhibited intense absorption at 3480 cm.<sup>-1</sup>. The maximum amount of the diol present in the total hydrogenation products was about 40% (infrared analysis of 0.005 *M* solutions in carbon tetrachloride at 3480 cm.<sup>-1</sup>). Gas chromatography of the diol on a 60-cm. column<sup>26</sup> at 140° gave a single symmetrical peak of retention time 10.6 min.

**Preparation of Diol 1 by Hydrogenation of *cis*-2,5-Di-*t*-butyl-1,4-cyclohexanedione** (with R. H. Ragland).—To 0.380 g. (1.69 mmoles) of *cis*-2,5-di-*t*-butyl-1,4-cyclohexanedione<sup>1c</sup> in 27 ml. of acetic acid was added 80 mg. of platinum dioxide catalyst. Hydrogenation at atmospheric pressure and 26° with agitation by a magnetic stirrer required 2–3 hr. for reaction of the calculated volume of hydrogen. The catalyst was separated by filtration. The solvent was evaporated under reduced pressure. The white, solid residue was dried and then dissolved in 42 ml. of dried carbon tetrachloride. A sample for infrared analysis was diluted to 0.004 *M*, and the spectrum recorded. An increase of 10  $\pm$  5% in the intensity of the 3619 cm.<sup>-1</sup> band relative to the intensity of the 3640 and 3480 cm.<sup>-1</sup> bands of pure diol 1 was observed. That is, the infrared spectrum of the total product was consistent with the presence of 90  $\pm$  5% diol 1 plus 10  $\pm$  5% of isomeric diols which contribute to absorption at ca. 3620, but not at 3640 or 3480 cm.<sup>-1</sup>. Two recrystallizations from acetonitrile of the solid recovered from the carbon tetrachloride solution gave a crop of white needle-like crystals, 125 mg. (32%), m.p. 156–158°.

**2,5-Di-*t*-butyl-4-methoxycyclohexanol (2), M.p. 43–44°.**—2,5-Di-*t*-butyl-4-methoxyphenol<sup>27</sup> (10.4 g., 0.043 mole, m.p. 102.5–103°) was hydrogenated as above<sup>26</sup> in two portions, each in 150 ml. of glacial acetic acid with 2 g. of platinum dioxide catalyst. In each case, the reaction stopped in ca. 24 hr. at 25° and 2–3 atm. hydrogen pressure. About 80% of the calculated amount of hydrogen had reacted. The catalyst was separated by filtration and the combined filtrates were concentrated (20 mm.) to give 10 g. of oil. The oil was dissolved in 10 ml. of hexane. The hexane solution was washed with 5% sodium bicarbonate and with water, dried over anhydrous sodium sulfate, and concentrated to ca. 13 ml. The solution was chromatographed on 225 g. of alumina (Brockman activity I, basic). Elution with hexane and hexane–benzene mixtures gave fractions which showed no absorption at ca. 3460 cm.<sup>-1</sup>. Elution with pure benzene gave an oil which showed intense absorption at ca. 3460 cm.<sup>-1</sup>. Four recrystallizations from pentane at –30° of the fractions eluted with benzene gave 0.86 g. (9%) of white crystals, m.p. 43–44°.

*Anal.* Calcd. for C<sub>15</sub>H<sub>20</sub>O<sub>2</sub>: C, 74.32; H, 12.48. Found: C, 74.20; H, 12.60.

**Preparation of 2 by Monomethylation of Diol 1.**—To 457 mg. (2.00 mmoles) of diol 1, m.p. 157–158°, plus 134 mg. (3.00 mmoles, 50% excess) of a 53.7% dispersion of sodium hydride in mineral oil (Metal Hydrides, Inc.) in a 3-necked 25-ml. pear-shaped flask fitted with an oil-sealed stirrer, thermometer, condenser, equilibrated dropping funnel, and drying tube under an atmosphere of dry nitrogen, was added 10.0 ml. of dimethyl sulfoxide (freshly distilled from calcium hydride at 3 mm. pressure). The mixture was heated and stirred at 65–70° for 45 min., during which time the diol dissolved, a gas was evolved, and a white suspension formed. The mixture was cooled to 30° and 2.0 ml. (a large excess) of methyl iodide was added dropwise during 4 min. with continued stirring. The white suspension gradually disappeared, giving a clear colorless solution 2 min. after the addition of methyl iodide was completed. The solution was heated to 41° during 30 min., and then was allowed to cool gradually to room temperature. After 8 hr., the clear yellow solution was poured into 20 ml. of water at 0°. Two liquid phases formed. The product was extracted with benzene (25, 12.5, and 12.5 ml.). The benzene solution was washed with four 10-ml. portions of water. The clear, colorless benzene extract, dried over anhydrous sodium sulfate, was evaporated under reduced pressure. The resulting oil, dissolved in 2 ml. of hexane, was chromatographed on basic alumina, as above. The fractions eluted with benzene were combined and recrystallized from pentane at –30° to give 105 mg. (43% of 1 mmole) of crystals, m.p. 42–44°, which gave an infrared spectrum identical with that of the analytical sample of 2 reported above. The two samples also gave the same retention time, 13.9 min., in gas chromatography with a 165-cm. column<sup>28</sup> at 120°, while the dimethyl ether of 1

(27) Reported<sup>28</sup> m.p. 101.5–103°. The phenol was prepared by John W. Larsen, B.S. Thesis, Tufts University, 1962, by alkylation of *p*-methoxyphenol by a procedure reported for the analogous preparation of 2,5-di-*t*-butyl-1,4-dimethoxybenzene: P. P. Oesper, C. P. Smyth, and M. S. Kharasch, *J. Am. Chem. Soc.*, **64**, 927 (1942).

(28) C. D. Cook, R. G. Inskeep, A. S. Rosenberg, and E. C. Curtis, Jr., *ibid.*, **77**, 1672 (1955).

gave retention time 4.8 min. Analysis of the total methylation product (oil from benzene extract) by gas chromatography suggested that the ratio of monomethyl ether 2 to dimethyl ether of 1 formed in the reaction was 2:1 (by estimation of relative peak areas). No recovered diol 1 was detected.

**2,5-Di-*t*-pentyl-1,4-cyclohexanediol (3), M.p. 97–98°.**—2,5-Di-*t*-pentylhydroquinone (Brothers Chemical Co., practical grade 2,5-di-*t*-amylhydroquinone, recrystallized in a nitrogen atmosphere from 7 ml. of boiling glacial acetic acid plus 2.5 ml. of boiling water per 1.0 g., colorless crystals after four recrystallizations, m.p. 185.5–186.5°; reported<sup>29</sup> m.p. 185°) was hydrogenated as above.<sup>26</sup> To 5.00 g. (0.0200 mole) of 2,5-di-*t*-pentylhydroquinone in 150 ml. of acetic acid (reagent grade) was added 1.23 g. of platinum dioxide catalyst. At 25° and 2–3 atm. hydrogen pressure, hydrogenation stopped within 70 hr. after 60% of the calculated amount of hydrogen had reacted. Isolation of the crude product (as above for 1) by concentration and precipitation gave 4.78 g. of white solid, m.p. 67–83°. The crude products from five hydrogenations were combined and crystallized from 30 ml. of acetonitrile to give 9.45 g. of white crystals, m.p. 118–156°. From this solid, a hexane-soluble fraction was obtained, 4.71 g. of solid, which was dissolved in 10 ml. of benzene and was chromatographed on a 30-mm. i.d. column packed with 400 g. of alumina (Fisher A-540). Elution with anhydrous benzene, ether–benzene mixtures, and methanol–ether mixtures, gave 58 fractions. The solids obtained from selected fractions were analyzed by infrared spectroscopy in 0.004 *M* solutions in carbon tetrachloride. Fractions 28–42, which showed intense absorption at 3480 cm.<sup>-1</sup>, were combined (1.30 g.) and recrystallized twice from acetonitrile to give 1.05 g. (4%) of crystals, m.p. 95–96.5°. Twelve recrystallizations from acetonitrile gave the analytical sample, m.p. 97–98°.

(29) W. Koenigs and C. Mai, *Ber.*, **25**, 2649 (1892).

*Anal.* Calcd. for C<sub>16</sub>H<sub>32</sub>O<sub>2</sub>: C, 74.94; H, 12.58. Found: C, 75.33; H, 12.75.

***cis*-2,5-Di-*t*-pentyl-1,4-cyclohexanediol.**—The procedure previously reported for the analogous Jones oxidation of diol 1 to *cis*-2,5-di-*t*-butyl-1,4-cyclohexanediol was employed.<sup>16</sup> To 0.400 g. (1.56 mmoles) of diol 3 dissolved in 25 ml. of acetone (reagent grade, redistilled from potassium permanganate) and cooled to 5° in a 50-ml. erlenmeyer flask was added dropwise during 3 min. 1.56 ml. (50% excess) of 2.67 *M* chromium trioxide solution while the mixture, cooled in an ice–water bath, was stirred vigorously. The product mixture was immediately combined with 75 ml. of water containing 0.33 g. of sodium hydrogen sulfite, and was extracted with two 35-ml. portions of ether. The ether extract was washed with two 25-ml. portions of 10% aqueous ammonium chloride followed by two 25-ml. portions of 6% sodium bicarbonate. The ether solution was dried with anhydrous sodium sulfate and was evaporated (at ca. 20 mm.). The resulting white solid, 0.38 g., after three recrystallizations from 95% ethanol, gave the dione, 0.18 g. (46%), m.p. 75–75.5°.

*Anal.* Calcd. for C<sub>16</sub>H<sub>28</sub>O<sub>2</sub>: C, 76.14; H, 11.18. Found: C, 75.99; H, 11.21.

A second crop of crystals, 0.10 g., m.p. 72–73°, was isolated from the combined filtrates.

**Infrared Spectra of 1–3.**—A Perkin–Elmer Model 421 DG spectrophotometer was used to record infrared spectra in the region 2500–4000 cm.<sup>-1</sup> by use of stoppered Beckman near-infrared silica cells of path length 1.00 and 5.00 cm. 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.<sup>-1</sup> near 3620 and ±4 cm.<sup>-1</sup> near 3500 cm.<sup>-1</sup>. The absorbance reported is a measure of the peak intensity. Data recorded for solutions in dried "Spectranalyzed" carbon tetrachloride are presented above (see Discussion and Results).

[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY, UNIVERSITY OF KANSAS, LAWRENCE, KAN.]

## Dialkyl Peroxide-Induced Reductions of Aromatic Ketones<sup>1</sup>

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Decomposing di-*t*-butyl peroxide at 130° in a solution of benzophenone in 2-butanol reduced the ketone to benzhydrol and oxidized the 2-butanol to 2-butanone. In a similar reaction, acetophenone is reduced to a mixture of *meso*- and *rac*-2,3-diphenyl-2,3-butanediol. A mechanism involving reaction of 1-hydroxyalkyl radical with the carbonyl function of the ketone is proposed to account for these reductions. Competition reactions involving *m*- and *p*-substituted acetophenones show that the reactivity of the carbonyl function toward reaction with a 1-hydroxyalkyl radical follows a  $\log k/k_0 = \rho\sigma$  correlation with  $\rho = +1.59$ . The nature of this polar effect is discussed in terms of possible mechanisms for the reaction of the 1-hydroxyalkyl radical with the carbonyl function.

Although numerous examples of reactions involving the interaction of free radicals with a carbon–carbon unsaturated linkage are known, comparatively few radical reactions have been reported that involve the interaction of a free radical with carbonyl functions. The proposed mechanism for the formation of *meso*-dihydrobenzoin dibenzoate by the reaction of di-*t*-butyl peroxide with benzaldehyde requires the addition of a benzoyl radical to the carbonyl function of benzaldehyde.<sup>3</sup> A similar reaction is suggested to explain the formation of 4-(benzoyloxybenzyl)pyridine in the di-*t*-butyl peroxide-induced reaction of benzaldehyde with pyridine.<sup>4</sup> The photochemically-induced reactions of aromatic aldehydes with phenanthraquinone and chloranil yield products which suggest the addition of a radical to a carbonyl function.<sup>5</sup> The action of quinones as free radical vinyl polymerization inhibitors

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(2) National Science Foundation Cooperative Fellow, 1962–1963. Taken in part from the thesis submitted by D. C. N. in partial fulfillment of the requirements for the Ph.D. degree, University of Kansas, 1963.

(3) F. F. Rust, F. H. Seibold, and W. E. Vaughan, *J. Am. Chem. Soc.*, **70**, 5258 (1948).

(4) M. S. Kharasch, D. Schwartz, M. Zimmermann, and W. Nudenberg, *J. Org. Chem.*, **18**, 1051 (1953).

(5) R. F. Moore and W. A. Waters, *J. Chem. Soc.*, 238 (1953); other examples are given by A. Schönberg and A. Mustafa, *Chem. Rev.*, **40**, 181 (1947).

is proposed to involve the addition of polymer radicals to a carbonyl function.<sup>6</sup> The di-*t*-butyl peroxide-induced additions of alkanes to formaldehyde, a reaction leading to the formation of primary alcohols, very likely proceeds by addition of an alkyl radical which attacks the carbon atom of the carbonyl function.<sup>7</sup>

Of particular interest relating to the work reported in this paper is the reaction of a 1-hydroxyalkyl radical with benzophenone producing a benzhydrol radical (reaction 3) suggested by Pitts and co-workers in their mechanism for the photochemical reduction of benzophenone to benzpinacol in 2-propanol.<sup>8</sup> In this mechanism, the 1-hydroxyalkyl radical B· is produced by abstraction of a hydrogen from the alcohol molecule by the benzophenone diradical A, a species which results from the photochemical excitation of benzophenone. The benzpinacol is produced by the radical coupling reaction of two benzhydrol radicals C, half of the C· formed in reaction 2, and half in reaction 3. If the benzhydrol radical C· is indeed produced in a reaction such as 3, it should be possible to reduce benzophenone using 1-hydroxyalkyl radicals such as B·

(6) J. W. Breitenback and A. J. Renner, *Can. J. Research*, **26B**, 509 (1950).

(7) G. Fuller and F. F. Rust, *J. Am. Chem. Soc.*, **80**, 6148 (1958).

(8) J. N. Pitts, R. L. Letsinger, R. P. Taylor, J. M. Patterson, G. Reinkenwald, and R. B. Martin, *ibid.*, **81**, 1068 (1959).