washed with acetone, and recrystallized from ethanol to yield 7.5 g (0.29 mol): mp 112–120° dec after drying under vacuum at 80°; nmr (TFA) δ 1.64 (s, 3), 2.12 (d, 2, J = 3.5 Hz), 6.96 (s, br, 3), 7.27 (m, 10).

Anal. Calcd for $C_{16}H_{18}NCl$: C, 73.82; H, 6.93; N, 5.41. Found: C, 73.62; H, 6.98; N, 5.26.

4,4-Diphenyl-2-butanone.—To a solution of 231 mg (0.84 mmol) of 1-methyl-2,2-diphenylcyclopropyl amine hydrochloride dissolved in 150 ml of water was added 100 ml of saturated sodium bicarbonate and the reaction mixture was allowed to stir for 24 hr at ambient temperatures. The mixture was extracted with ether and the ether extracted was washed with 5% hydrochloric acid [36 mg (0.13 mmol, 16%) of starting material was recovered]. The residue from the ether extract gave ir ($CHCl_3$) 1715 cm^{-1}; nmr ($CDCl_3$) δ 2.02 (s, 3, CH_3), 3.15 (d, 2, J = 7.5 Hz), 4.60 (t, 1, J = 7.0 Hz), 7.23 (s, 10). The residue was treated with 2,4-dinitrophenylhydrazine and 256 mg (0.64 mmol, 76%) of the hydrazone was isolated, mp 172–175° (lit.[8] mp 173–175°).

Using aqueous sodium hydroxide as the base instead of sodium bicarbonate yielded 63% of ketone and alcoholic sodium hydroxide gave a 69% yield.

Registry No.—1-Methyl-2,2-diphenylcyclopropylamine hydrochloride, 42253-75-8; 1-methyl-2,2-diphenylcyclopropyl isocyanate, 42253-76-9; 4,4-diphenyl-2-butanone, 5409-60-9.

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Conformational Analysis of Hydroxyl by the Nuclear Magnetic Resonance Chemical Shift Method. Equivalence of Cyclohexanol and 4,4-Dimethylcyclohexanol as Mobile Systems

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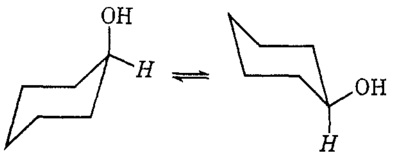
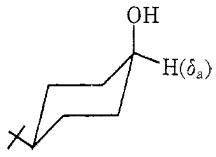
With a view to determining the change of conformational energy with solvent, we had in an earlier study[2] subjected the hydroxyl group to nmr chemical shift analysis[3,4] in a variety of solvents using 2,2,6,6-tetradeuterated cyclohexanol (**1** ⇌ **2**) as substrate and similarly deuterated *cis*- (**3**) and *trans*-4-*tert*-butylcyclohexanol (**4**) as conformationally rigid models.

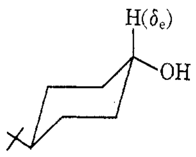
The lack of correlation of free energy with solvent that was found at the time was attributed to possible ring distortion and anisotropy effects introduced by the *tert*-butyl holding group in the model systems.[5] It has recently been suggested, however, that substitution of 4,4-dimethylcyclohexyl systems in place of cyclohexyl would largely compensate for any disturbing factors imposed by the *tert*-butyl holding group and thus allow for accurate free-energy determinations by nmr.[6] From this viewpoint, it seemed worthwhile to repeat our earlier work using tetradeuterated 4,4-dimethylcyclohexanol (**5** ⇌ **6**) as a hopefully more appropriate mobile system.



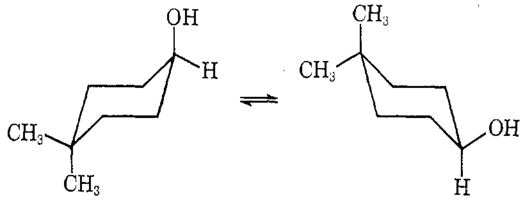
1 **2**



3 (cis)



4 (trans)



5 **6**

Use of the low-temperature nmr method is not practical for a solvent study of this type owing to potential solubility problems, complications from solute–solute association through hydrogen bonding (which would be very serious under these conditions especially in nonpolar solvents), and a lack of choice of a suitable solvent series due to freezing point problems.[7]

The results obtained in the course of this work are presented in Table I along with those of earlier work with deuterated cyclohexanols.[2] Some of the cyclohexanol data are revised values,[8] and, while the shifts in benzene, cyclohexane, and chloroform-*d* are in excellent

TABLE I

FREE ENERGY VALUES FOR THE HYDROXYL GROUP BY THE CHEMICAL SHIFT METHOD OF ELIEL

Solvent	Free energy values at 30°[a] Cyclohexyl	4,4-DMC[b]
Cyclohexane	0.61 ± 0.03[c]	0.60 ± 0.03
Acetone-d_6	0.76 ± 0.06[d]	0.72 ± 0.04
Chloroform-*d*	0.82 ± 0.05	0.88 ± 0.04
Benzene	0.89 ± 0.05[d]	0.85 ± 0.06
tert-Butyl alcohol	0.91 ± 0.07[e]	0.97 ± 0.06

[a] Total concentrations in all cases were 0.03 M or less in order to minimize complications from solute–solute hydrogen bonding. Error limits are standard deviations from the mean. [b] 4,4-Dimethylcyclohexyl. [c] Compared with value of 0.60 ± 0.02 obtained from Raney nickel equilibration of 4-*tert*-butyl cyclohexanones, ref 2b. [d] Revised value. [e] Compared with value of 0.95 ± 0.04 obtained from Raney nickel equilibration of 4-*tert*-butylcyclohexanones, ref 2b.

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[7] C. H. Bushweller, J. A. Beach, J. W. O'Neil, and G. U. Rao, *J. Org. Chem.*, **35**, 2086 (1970).

[8] The present data were obtained by single scans on a Varian XL-100 instrument. The earlier results[2b] were derived from data obtained on a Varian A-60A instrument by repeated scanning and computer averaging with a CAT. Such scanning of dilute solutions may be affected by drift and by false triggering caused by impurity peaks.

agreement with the results previously obtained, the same is not true for acetone-d_6 and *tert*-butyl alcohol; for these solvents the new results are in much better agreement with those obtained by equilibration studies[2b,9] or expected on *a priori* considerations.

From the data in Table I, it is seen that both systems yield the same results within the experimental error of the method; substitution of 4,4-dimethylcyclohexanol for cyclohexanol has very little effect on $\Delta G°_{OH}$ obtained by the chemical shift method of Eliel. These data, moreover, point out again the difficulty involved when one makes a solvent study of a potentially interacting X group using the *tert*-butyl systems as standards. While the results in cyclohexane, acetone-d_6, and *tert*-butyl alcohol are in accord with the expected values (based on other techniques for measuring conformational equilibria using the *tert*-butyl substituted models), the free energies obtained in chloroform-*d* and especially benzene are not.[2,9,10] It is generally accepted that chloroform is a significantly weaker hydrogen donor and benzene a much weaker hydrogen acceptor than the data indicate.

An inequality in shielding of the axial and equatorial carbinyl protons in the mobile cyclohexanols compared with the *tert*-butyl analogs probably accounts for the anomalously high apparent free-energy values observed in these solvents. The 4-*tert*-butyl compounds fail as even approximate models when differential solvent–solute interactions of this type come into play. This inequality may be ascribed to differential dipole[11] and/or buttressing effects[12] in the *tert*-butyl models (as compared with the mobile systems), both of which could affect the relative shielding of the carbinyl protons and hence the free energy.

Based on the data obtained from this work, we conclude that the 4,4-dimethylcyclohexyl system is generally not a better model than cyclohexyl for use in the Eliel nmr equation, but is in fact essentially equal to it. This conclusion agrees with that earlier reached by Reisse[7,8] with respect to halocyclohexanes. We further conclude, as have others before us,[6,13,14] that the chemical-shift method of Eliel generally yields reasonable *approximate* values of $\Delta G°$ in inert solvents, and may still be useful as a semiquantitative tool for conformational studies when the low-temperature method is inapplicable because of potential complications (strong solute–solute interactions, solubility problems, freezing of solvent, etc.).

Experimental Section

Cyclohexanol-*2,2,6,6-d*$_4$ as well as *cis*- and ***trans*-4-*tert*-butylcyclohexanol-*2,2,6,6-d*$_4$** were all available from our previous study.[2b]

4,4-Dimethylcyclohex-2-enone was prepared *via* the method of Bordwell and Wellman.[15]

4,4-Dimethylcyclohexanone was prepared by hydrogenation of 4,4-dimethylcyclohex-2-enone over 10% palladium in acetic acid.[15]

4,4-Dimethylcyclohexanone-*2,2,6,6-d*$_4$ was synthesized by deuteration of 4,4-dimethylcyclohexanone using the method of Streitwieser, *et al.*[16] The procedure is entirely analogous to that used for preparation of the deuterated ketone intermediate leading to cyclohexanol-*2,2,6,6-d*$_4$.[2b] Nmr showed the ketone (mp 38–40°, >99% pure by glpc analysis) to be over 95% deuterated in the α positions.

4,4-Dimethylcyclohexanol-*2,2,6,6-d*$_4$ was obtained by mixed hydride ($LiAlH_4$–$AlCl_3$) reduction of 4,4-dimethylcyclohexanone-*2,2,6,6-d*$_4$.[2b,17] From 8 g (0.062 mol) of the ketone was obtained 7 g (0.053 mol) of product which was distilled (76–77°, 10 mm) to give 4.5 g of pure alcohol (99.9% by glpc analysis). Integration of the nmr spectrum showed the material to be >96% deuterated in the α positions.

Nmr Determination of Equilibrium Constants.—The instrument used was a Varian XL-100 spectrometer. The probe temperature was 30° in all cases. In order to avoid having to measure absolute shifts, a modification of the Eliel equation was used for analysis (eq 1).

$$K_{eq} = \frac{(\delta_a - \delta)/(\delta_a - \delta_e)}{1 - [(\delta_a - \delta)/(\delta_a - \delta_e)]} \qquad (1)$$

Two alcohol mixtures were prepared for each solvent studied, one containing deuterated 4,4-dimethylcyclohexanol and deuterated *cis*-4-*tert*-butylcyclohexanol which yielded $\delta_a - \delta$, the other containing both deuterated *cis*- and *trans*-4-*tert*-butylcyclohexanol which yielded $\delta_a - \delta_e$. In order to minimize solute–solute hydrogen bonding, each alcohol of the pair was present in a concentration of 0.015 *M* or less. Shift differences were measured between the centers of the carbinyl hydrogen peaks. Analyses using deuterated cyclohexanol were carried out in analogous fashion.

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Registry No.—Cyclohexanol, 108-93-0; 4,4-dimethylcyclohexanol, 932-01-4.

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[9] See E. L. Eliel and S. H. Schroeter, *J. Amer. Chem. Soc.*, **87**, 5031 (1965), for a comprehensive study of the dependence of the free energy of the hydroxyl group on solvent.

[10] As one proceeds from inert to polar solvents, $-\Delta G°_{OH}$ (ax $\rightleftharpoons$ eq) becomes larger, because the polar solvent associates more strongly with the equatorial than with the axial group, thus stabilizing the former.

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