# Conformational Study of Acyclic Alcohols by NMR Spectroscopic Analysis, Molecular Force Field and Ab Initio Calculations

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(Received April 3, 1986)

Conformations of a series of acyclic alcohols ($CH_3CH(R)CH(OH)CH_3$, $CH_3CH(R)CH(OH)CH(R')CH_3$, and $CH_3CH(R)CH(OH)Bu^t$) were studied (1) by measuring vicinal H-H coupling constants ($^3J_{H\text{-}H}$), (2) by lanthanoid-induced shift (LIS) analysis, (3) by molecular mechanics calculations (MM2), and (4) by ab initio (STO-3G, 4-31G geometry optimization) calculations. In the case of conformationally flexible alcohol as exemplified by 2-butanol and 3-pentanol, population of conformers determined by the LIS method do not agree with those determined by the $^3J_{H\text{-}H}$, MM2, and ab initio methods. The discrepancy comes from the fact that the LIS measurement gives the most stable conformation of the alcohol in the LSR-alcohol complex and not of the free alcohol. In some flexible molecules, the most stable conformer in the complex can be different from that of the free molecule. In general, the conformational equilibrium is shifted by coordination of the shift reagent to the conformer whose alkyl chain stretches opposite to the direction of the coordination site of the shift reagent.

Lanthanoid-induced shift (LIS) analysis[1,2] by NMR is a convenient method to investigate the conformation of organic compounds. The authors have reported the usefulness of the LIS simulation to the conformational studies of rather rigid molecules.[3-6] But a question about the effectiveness of LIS analysis arises when it is applied to conformationally flexible molecules because the shift reagent is bulky and the enthalpies ($\Delta H$) of the complex formation between shift reagents and some substrates are fairly large (8—10 kcal mol$^{-1}$ (1 cal=4.184 J)).[7,8] The conformational equilibria for the flexible molecules can be shifted significantly by the coordination of the shift reagent to the substrates because the free energy differences among the conformers of flexible molecules are considerably less than the $\Delta H$ of the complex formation. Conformational changes by the coordination of the lanthanoid shift reagents (LSR) were evidenced by the LIS measurement on dioxaphosphorinane derivatives[9] and *t*-butoxycarbonyl α-amino acids esters.[10] Therefore, conformations of flexible secondary alcohols were studied both experimentally [(1) the $^3J_{H\text{-}H}$ method and (2) the LIS analysis] and theoretically [(3) MM2 and (4) ab initio calculations]. Populations of the stable conformers obtained by these methods were compared with each other, and the reliability and the limitation of each method was discussed.

## Experimental

**Methods for Conformational Analyses.** Conformations of acyclic secondary alcohols were determined by the following four methods. $^1$H NMR spectra at an ambient temperature were recorded on a JEOL FX-90Q or a GX-400 spectrometer.

**(1) $^3J_{H\text{-}H}$ Method:** $^3J_{H\text{-}H}$ was measured with a GX-400 spectrometer on a homo decoupling mode. As the observed $^3J_{H\text{-}H}$ values reflect the populations of stable conformers, they were determined from the observed $^3J_{H\text{-}H}$ by assuming that the observed coupling constant ($^3J_{obsd}$) is the averaged value of $^3J_g$ and $^3J_t$ in proportion to their populations and in reference to the reported vicinal H-H coupling constants[11] for which conformation of vicinal protons are gauche ($J_g$=1.9 Hz) and trans ($J_t$=11.1 Hz).

**(2) LIS Analysis:** Yb(fod)$_3$ was used as an LSR in $CDCl_3$ because the contribution of the contact shift to LIS is negligibly small.[12] $LIS_i^{obsd}$ of a nucleus $i$ was determined experimentally from the induced chemical shift vs. [LSR]/[substrate] plots in the range of [LSR]/[substrate] to be 0—0.3. $LIS_i^{calcd}$ was calculated from the sterical factor ($3\cos^2\theta-1/r^3$) of the McConnel-Robertson equation.[13,14] From these LIS data ($LIS_i^{obsd}$ and $LIS_i^{calcd}$), the agreement factor (R)[15] was calculated by Eq. 1 and the geometry in which R showed minimal value was assigned to the most stable conformation.

$$R = [\sum_i (LIS_i^{obsd} - LIS_i^{calcd})^2 / \sum_i (LIS_i^{obsd})^2]^{1/2} \quad (1)$$

In non-rigid molecules, effective chemical shifts are evaluated by averaging the intrinsic chemical shift weighted by the populations of each conformer. Therefore, we had better take into account the differences of coordination ability of LSR towards each stable conformer and the relative accessibility of LSR to each coordination site of conformers (vide infra). By this LIS simulation we can correctly evaluate the $LIS_i^{calcd}$ and R in Eq. 1.

The coordination ability[16] of each conformer was estimated by the competitive LIS experiment between conformationally rigid model compounds in which Yb(fod)$_3$ competitively coordinated to two model compounds. The coordination ability index of conformer **A** and **B** ($C_A$ and $C_B$) was defined by Eq. 2.

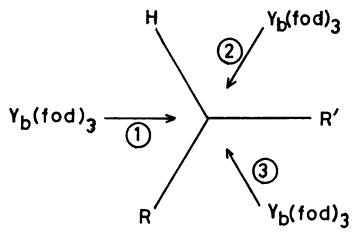
$$C_A/C_B = [S_A^m/S_A^s(1-S_B^m/S_B^s)]/[S_B^m/S_B^s(1-S_A^m/S_A^s)] \quad (2)$$

$S_A^m$ or $S_B^m$: LIS value induced by the competitive coordination of Yb(fod)$_3$ towards conformer **A** and **B**.

$S_A^s$ or $S_B^s$ are LIS values of conformer **A** and **B** induced by Yb(fod)$_3$.

The relative accessibility of Yb(fod)$_3$ to each coordination site of conformers is not thought to be equally favorable.

At the coordination sites 1, 2, and 3 of conformer $k$ of the secondary alcohol illustrated below, the calculated LIS of nucleus $i$ for conformer $k$ is given by Eq. 3.




$$S_{k,i} = A_1S_{k,i}(1) + A_2S_{k,i}(2) + A_3S_{k,i}(3) \quad (3)$$

Here, $A_1$, $A_2$, and $A_3$ are relative accessibility of LSR at the coordination sites 1, 2, and 3, respectively.

$S_{k,i}(1)$, $S_{k,i}(2)$, and $S_{k,i}(3)$ are the calculated LIS's for nucleus $i$ of conformer $k$ in case LSR coordinated to the coordination site 1, 2, and 3, respectively.

By use of coordination ability index, $C$, and $S_{k,i}$ determined by Eqs. 2 and 3, the calculated LIS corresponding to the observed LIS for nucleus $i$ on NMR spectra is derived by Eq. 4, if a secondary alcohol molecule is assumed to have three stable conformers **I**, **II**, and **III**.

$$S_i^{calcd} = C_IX_IS_{I,i} + C_{II}X_{II}S_{II,i} + C_{III}X_{III}S_{III,i} \quad (4)$$

Where $X_I$, $X_{II}$, $X_{III}$ are population of the stable conformer **I**, **II**, **III**, respectively.

**(3) MM2 Calculation:**[17] The calculations were performed on a HITAC M-280H using the MM2 program modified by E. Osawa[18]. The geometry optimization was carried out for the expected stable conformers and the steric energy was calculated. From the relative steric energies of stable conformers, the population of each conformer was calculated tentatively by applying Boltzmann's theorem.

**(4) Ab Initio Calculation:** The ab initio calculations were performed on a HITAC M-200H by use of the Gaussian 80 (QCPE 13) program at the Computer Center of the Institute for Molecular Science. This program allows 127 Contracted Gaussian Type Orbitals (CGTO) for the purpose of the Hartree-Fock SCF calculation. However, geometry optimization can be carried out on the molecules with CGTO≦70. Geometries of conformers were optimized with the Hartree-Fock methods with the STO-3G or 4-31G basis set within the limit for the number of CGTO's. As the optimized geometries and relative energies between stable conformers obtained by MM2 geometry optimization calculations were nearly identical with those obtained by ab initio geometry optimization calculations with the STO-3G or 4-31G basis set (CGTO<70), optimized geometries obtained by MM2 were used as the input geometries for ab initio calculations and the energies were calculated with the STO-3G basis set in the case when the optimization by ab initio calculation is limited (CGTO>70).

**Preparation of Materials.** Commercially available secondary alcohols were purified by distillation. As commercially available 2,6-dimethylcyclohexanol is a mixture of three stereoisomers, each isomer was separated by column chromatography on silica gel (eluant; benzene-ether (v/v 6 : 1)) and by gas chromatography (column; SE-30, column Temp; 90 °C).

$Yb(fod)_3$ was prepared by reacting 1,1,1,2,2,3,3-heptafluoro-2,2-dimethyl-3,5-octanedione ($H(fod)_3$) with ytterbium nitrate in aqueous methanol solution at pH 4—6[19-21] and purified by sublimation in vacuo.

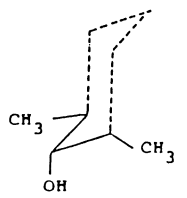
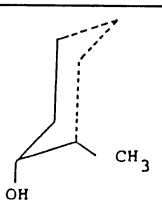
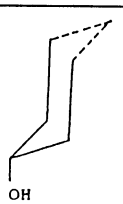
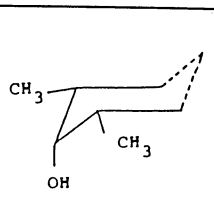
## Results and Discussion

**Coordination Ability of $Yb(fod)_3$ to the Conformers.** Coordination ability of $Yb(fod)_3$ to each stable conformer of a secondary alcohol was estimated from the LIS for conformationally rigid model compounds. *t*-2-Methyl-*t*-6-methyl-*r*-1-cyclohexanol (a), *trans*-2-methylcyclohexanol (b), cyclohexanol (c), and *t*(or *c*)-2-methyl-*c*(or *t*)-6-methyl-*r*-1-cyclohexanol (d) were chosen as rigid model compounds. From the LIS by sole ($S^s$) or competitive ($S^m$) coordination of $Yb(fod)_3$ to the model compounds, coordination ability index (C) in reference to cyclohexanol of each model compound was evaluated (Table 1) by using Eq. 2.

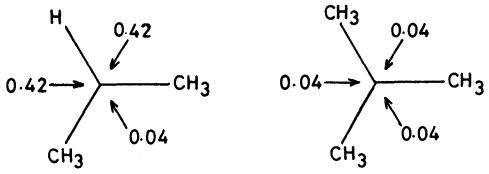
**Relative Accessibility of $Yb(fod)_3$.** Relative accessibility (A) of $Yb(fod)_3$ at each coordination site of some secondary alcohols was estimated from the competitive experiment where the LIS's for two different alcohols were induced by competitive coordination of $Yb(fod)_3$. In the case of isopropyl alcohol R, R'=$CH_3$, for example, relative accessibilities $A_1$, $A_2$ ($A_1$=$A_2$), and $A_3$ were estimated from the competitive LIS experiment using a mixture (1 : 1 mol/mol) of isopropyl alcohol and *t*-butyl alcohol. From the LIS of each alcohol we can determine the ratio of coordination ability indexes of isopropyl alcohol ($C_{iso}$) and *t*-butyl alcohol ($C_{tert}$) by Eq. 2.

$$S_{iso}/C_{tert} = 0.70 \times (1-0.25)/0.25 \times (1-0.70) = 7$$
$$(S_{iso}^m/S_{iso}^s = 0.70 \qquad S_{tert}^m/S_{tert}^s = 0.25)$$
$$C_{iso} : C_{tert} = 0.88 : 0.12$$

Table 1. Coordination Ability Indexes of $Yb(fod)_3$ to the Model Compounds for LIS Simulation of Acyclic Secondary Alcohols

|  |  |  |  |
|---|---|---|---|
| (a) *t*-2-Methyl-t-6-methyl-*r*-1-cyclohexanol | (b) *trans*-2-Methyl-cyclohexanol | (c) Cyclohexanol | (d) *t*(or *c*)-2-Methyl-*c*(or *t*)-6-methyl-*r*-1-cyclohexanol |
| 0.18 | 0.57 | 1.0 | 0.22 |

From this ratio, the relative accessibility for each coordination site of isopropyl and *t*-butyl alcohols can be estimated as shown below by assuming that the coordination is solely dependent on the steric effect and that the coordination from the direction between the two methyl groups is equally favored in isopropyl and *t*-butyl alcohols.




The relative accessibility at each coordination site of several secondary alcohols was determined in the same

Table 2. Relative Accessibility of Yb(fod)$_3$ to Each Coordination Site of RR'CHOH-Type Alcohols

| R | R' | $P_1$ | $P_2$ | $P_3$ |
|---|---|---|---|---|
| $CH_3$ | $CH_3$ | 0.42 | 0.42 | 0.04 |
| $C_2H_5$ | $CH_3$ | 0.29 | 0.66 | 0.05 |
| $C_2H_5$ | $t$-$C_4H_9$ | 0.66 | 0.34 | 0.0 |
| $i$-$C_3H_7$ | $CH_3$ | 0.13 | 0.79 | 0.08 |
| $i$-$C_3H_7$ | $C_2H_5$ | 0.31 | 0.69 | 0.0 |
| $i$-$C_3H_7$ | $t$-$C_4H_9$ | 0.46 | 0.54 | 0.0 |

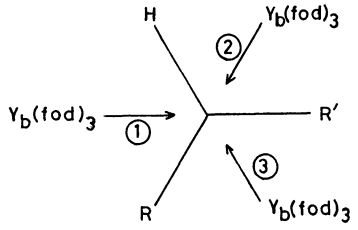


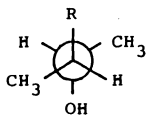
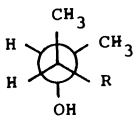
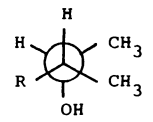

Table 3. Lanthanoid-Induced Shift (LIS) for $CH_3CH(R)CH(OH)CH_3$-, $CH_3CH(R)CH(OH)CH(R')CH_3$-, and $CH_3CH(R)CH(OH)C(CH_3)_3$- Type Acyclic Secondary Alcohols

| | Proton ($^1$H) | | | | | | | | Carbon ($^{13}$C) | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | 1-H[a)] | 2-H | 3-H | 4-H | 5-H | 2-$CH_3$ | 3-$CH_3$ | 4-$CH_3$ | 1 | 2 | 3 | 4 | 5 | 2-$CH_3$ | 3-$CH_3$ | 4-$CH_3$ |
| (**1**) R=H | 0.36 | 0.64 | 0.35<br>0.38 | 0.21 | — | — | — | — | 0.49 | 1.0 | 0.48 | 0.25 | — | — | — | — |
| (**2**) R=$CH_3$ | 0.36 | 0.65 | 0.38 | 0.22 | — | — | 0.22 | — | 0.49 | 1.0 | 0.47 | 0.26 | — | — | 0.27 | — |
| (**3**) R=H | 0.21 | 0.34<br>0.39 | 0.64 | 0.34<br>0.39 | 0.21 | — | — | — | 0.26 | 0.48 | 1.0 | 0.48 | 0.26 | — | — | — |
| (**4**) R=H, R'=$CH_3$ | 0.21 | 0.32 | 0.67 | 0.37<br>0.39 | 0.23 | 0.22 | — | — | 0.27 | 0.48 | 1.0 | 0.49 | 0.27 | 0.29 | — | — |
| (**5**) R=R'=$CH_3$ | 0.20 | 0.36 | 0.67 | 0.36 | 0.20 | 0.25 | — | 0.25 | 0.26 | 0.50 | 1.0 | 0.50 | 0.26 | 0.31 | — | 0.31 |
| (**6**) R=$CH_3$ | 0.22 | — | 0.67 | 0.30 | 0.21 | 0.22 | — | 0.30 | 0.27 | 0.48 | 1.0 | 0.49 | 0.25 | 0.27 | — | 0.35 |
| (**7**) R=H | 0.23 | — | 0.65 | 0.28<br>0.42 | 0.19 | 0.23 | — | — | 0.35 | 0.49 | 1.0 | 0.44 | 0.26 | 0.35 | — | — |

$CH_3CH(R)CH(OH)CH_3$: **1**—**2**, $CH_3CH(R)CH(OH)CH(R')CH_3$: **3**—**5**, $CH_3CH(R)CH(OH)C(CH_3)_3$: **6**—**7**.

a) The figures indicate the positional number of carbon atoms in IUPAC nomenclature. LIS values of $^1$H and $^{13}$C nuclei are normalized to the maximum LIS value in each compound.

Table 4. Population of Stable Conformers for $CH_3CH(R)CH(OH)CH_3$

| |  |  |  |
|---|---|---|---|
| | 2-Butanol (**1**) (R=H) | | |
| | (I) | (II) | (III) |
| ab initio | | | |
| STO-3G | 0.667 | 0.181 | 0.152 |
| ($\Delta E$) | (0.0) | (+0.782) | (+0.886) |
| 4-31G | 0.674 | 0.187 | 0.139 |
| ($\Delta E$) | (0.0) | (+0.769) | (+0.947) |
| MM2 | 0.597 | 0.250 | 0.153 |
| ($\Delta E$) | (0.0) | (+0.524) | (+0.821) |
| $^3J_{H-H}$ | 0.51 | 0.43 | 0.06 |
| LIS | 0.4 | 0.5 | 0.1 |
| | 3-Methyl-2-butanol (**2**) (R=$CH_3$) | | |
| | (I) | (II) | (III) |
| MM2 | 0.428 | 0.186 | 0.386 |
| ($\Delta E$) | (0.0) | (+0.502) | (+0.062) |
| $^3J_{H-H}$ | 0.46 | 0.54 | |
| LIS | 0.6 | 0.3 | 0.1 |

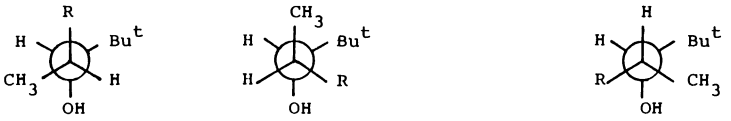
($\Delta E$): Relative energy (kcal mol$^{-1}$).

Table 5. Population of Stable Conformers for $CH_3CH(R)CH(OH)CH(R)CH_3$

| | 3-Pentanol (**3**) (R=H, R'=H) | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|
| | (I) | (II) | (III) | (IV) | (V) | (VI) | (VII) | (VIII) | (IX) |
| ab initio | | | | | | | | | |
| 4-31G | 0.235 | 0.182 | 0.191 | 0.182 | 0.01 | — | 0.191 | — | — |
| ($\Delta E$) | (0.0) | (+0.258) | (+0.208) | (+0.258) | (+2.490) | — | (+0.208) | — | — |
| MM2 | 0.373 | 0.135 | 0.106 | 0.155 | 0.006 | 0.062 | 0.104 | 0.057 | 0.002 |
| ($\Delta E$) | (0.0) | (+0.610) | (+0.759) | (+0.530) | (+2.500) | (+1.087) | (+0.766) | (+1.144) | (+3.291) |
| $^3J_{H-H}$ | | 0.58 | | | 0.30 | | | 0.12 | |
| LIS | 0.0 | 0.4 | 0.1 | 0.4 | 0.0 | 0.0 | 0.1 | 0.0 | 0.0 |
| | 2-Methyl-3-pentanol (**4**) (R=H, R'=$CH_3$) | | | | | | | | |
| | (I) | (IV) | (VII) | (II) | (V) | (VIII) | (III) | (VI) | (IX) |
| MM2 | 0.230 | 0.137 | 0.319 | 0.011 | 0.004 | 0.165 | 0.128 | 0.002 | 0.004 |
| ($\Delta E$) | (+0.199) | (+0.508) | (0.0) | (+2.209) | (+2.723) | (+0.399) | (+0.550) | (+2.954) | (+2.624) |
| $^3J_{H-H}$ | | 0.71 | | | 0.22 | | | 0.07 | |
| LIS | 0.0 | 0.3 | 0.0 | 0.0 | 0.0 | 0.4 | 0.3 | 0.0 | 0.0 |
| | 2,4-Dimethyl-3-pentyanol (**5**) (R=$CH_3$, R'=$CH_3$) | | | | | | | | |
| | (I) | (II) | (III) | (IV) | (V) | (VI) | (VII) | (VIII) | (IX) |
| MM2 | 0.007 | 0.003 | 0.490 | 0.011 | 0.0 | 0.013 | 0.446 | 0.007 | 0.022 |
| ($\Delta E$) | (+2.518) | (+3.012) | (0.0) | (+2.285) | (+4.272) | (+2.174) | (+0.056) | (+2.573) | (+1.865) |
| $^3J_{H-H}$ | | 0.46 | | | 0.02 | | | 0.52 | |
| LIS | 0.0 | 0.3 | 0.0 | 0.3 | 0.0 | 0.2 | 0.0 | 0.2 | 0.0 |

($\Delta E$): Relative energy (kcal mol$^{-1}$).

Table 6. Population of Stable Conformers for $CH_3CH(R)CH(OH)C(CH_3)_3$




| | 2,2,4-Trimethyl-3-pentanol (**6**) (R=$CH_3$) | | |
|---|---|---|---|
| | (I) | (II) | (III) |
| ab initio | | | |
| STO-3G | 0.034 | 0.0 | 0.966 |
| ($\Delta E$) | (+2.412) | (+5.138) | (0.0) |
| MM2 | 0.121 | 0.007 | 0.872 |
| ($\Delta E$) | (+1.147) | (+2.914) | (0.0) |
| $^3J_{H-H}$ | 0.02 | 0.98 | |
| LIS | 0.2 | 0.0 | 0.8 |
| | 2,2-Dimethyl-3-pentanol (**7**) (R=H) | | |
| | (I) | (II) | (III) |
| MM2 | 0.975 | 0.013 | 0.012 |
| ($\Delta E$) | (0.0) | (+2.599) | (+2.640) |
| $^3J_{H-H}$ | 0.93 | 0.01 | 0.06 |
| LIS | 1.0 | 0.0 | 0.0 |

($\Delta E$): Relative energy (kcal mol$^{-1}$).

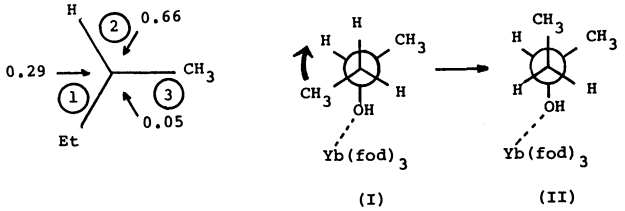
way (Table 2).

**Conformational Equilibrium of Acyclic Secondary Alcohols.** The LIS's for the proton and carbon resonances of acyclic secondary alcohols **1**—**7** are listed in Table 3.

Populations of stable conformers for various types of alcohols (**1**—**7**) were estimated both experimentally and theoretically and given in Tables 4, 5, and 6.

**Conformational Equilibrium Determined by the LIS Analysis:** The conformational distribution derived from the LIS analysis is different from those of ab initio, MM2, and $^3J_{H-H}$ in the cases of conformationally flexible alcohols shown in Tables 4 and 5. In the case of 2-butanol, ab initio, MM2, and $^3J_{H-H}$ methods lead to the same conclusion on the conformer distribution. The most stable conformer **I** has a stretched alkyl chain, and the population decreases in the order **I**, **II**, and **III**. On the contrary, the LIS method concludes that conformer **II** is the most stable. This can be explained that conformational equilibrium is shifted by the complexation to $Yb(fod)_3$ on 2-butanol. Conformational preferences of alcohol molecules in the

LSR-alcohol complexes can be quite different from those of uncomplexed alcohols since the complexes are apt to lessen the steric strain around the metal ion by the conformational change of the flexible alcohol component. In this aspect, we considered the sterical crowdedness at the coordination sites of 2-butanol. It is unlikely that the conformational equilibrium will be shifted by coordination of $Yb(fod)_3$ at site 2 (the relative accessibility is the highest: 0.66) because the sterical crowdedness is not large. However, the change of the conformational equilibrium by coordination of $Yb(fod)_3$ at site 1 (relative accessibility is 0.29) is probable because the sterical congestion after complexation is estimated to be very large and the ethyl group is flexible. Therefore, a part of conformer **I** is expected to isomerize to conformer **II** by the coordination of $Yb(fod)_3$ at site 1 to avert the sterical congestion.




In the case of 3-methyl-2-butanol (**2**), we also find that the LIS method again predicts a conformational distribution different from those obtained by the three other methods, i.e., the LIS method leads to a larger population of conformer **I** and a less population of conformer **III** than the populations of the corresponding conformers estimated from the $^3J_{H\text{-}H}$ method and MM2. This shift in conformational equlibrium is thought to come from the conformation change from **III** to **I** by the coordination of $Yb(fod)_3$. As the sterical congestion around OH group is large in conformer **III**, it is easily converted to conformer **I** to relax the crowdedness.

Table 5 shows the populations of conformers for $CH_3CH(R)CH(OH)CH(R')CH_3$ (**3**, **4**, and **5**). Alcohols of this type have 9 stable conformations (Fig. 1) arising from the internal rotations about $C_2$-$C_3$ and $C_4$-$C_3$ bonds. In the case of 3-pentanol (**3**) both ab initio and MM2 calculations predict that conformer **I** is the most stable and the predicted conformational distribution from these calculations is similar. But LIS method predicts that **II** and **IV** are the most stable conformers which are favorable for complex formation with $Yb(fod)_3$. The LIS data suggest that a part of the most stable conformer **I** is converted to conformer **II** or **IV** by the coordination of $Yb(fod)_3$ and the conformational equilibrium is shifted. The same trends are also noticed in the cases of 2-methyl-3-pentanol (**4**) and 2,4-dimethyl-3-pentanol (**5**), where the LIS methods again resulted in the dominating conformers with favorable coordination site (s). From the results discussed above, it is certain that the conformational equilibria of flexible acyclic alcohols are shifted by the coordination of the shift reagent towards the conformer whose alkyl chains stretch opposite to the direction of the coordination site of the shift reagent.

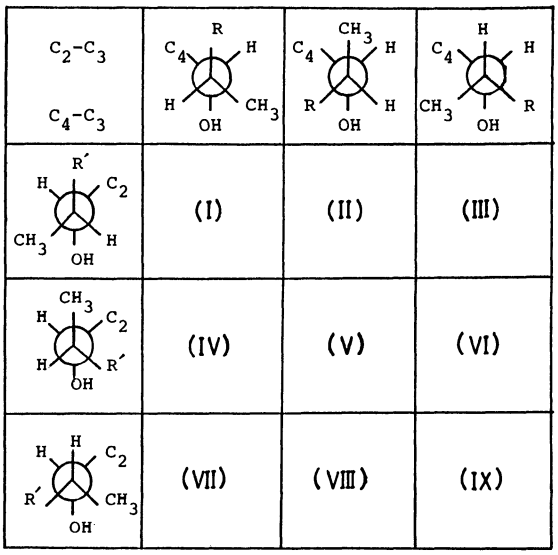



Fig. 1. Stable conformations for $CH_3CH(R)CH(OH)$-$CH(R')CH^3$-type alcohols.

On the contrary, the LIS method correctly predicts the conformational distribution of sterically congested $CH_3CH(R)CH(OH)Bu^t$-type secondary alcohols as shown in Table 6. In both cases (**6** and **7**) the conformational populations from the LIS method agreed with those from ab initio, MM2, and $^3J_{H\text{-}H}$ methods nearly quantitatively. All methods predict that the most stable conformer is **III** for **6** and **I** for **7**. Sterical congestion is so large in these alcohols that the conformational change during the complex formation with shift reagent becomes very difficult.[22]

**Conformational Equlibrium Determined by MM2 and Ab Initio Calculations:** In general, MM2 and ab initio calculations predict the conformational distribution correctly. From the geometry optimization study by MM2 and ab initio calculation on the every conformer of 2-butanol (**1**) (Table 3), it was shown that the populations and optimized geometries determined by the both calculations were almost the same. As proved by the several comparative studies shown above, the geometries and populations of the conformers can be predicted with enough accuracy by MM2. When we consider about the economical and technical restriction for ab initio calculation (CPU time, the number of CGTO), it is practical to use MM2 calculation for a conformational study of alcohols.

From the MM2 and ab initio studies, we considered the conformational equilibrium from a viewpoint of relative energy ($\Delta E$) of each conformer. As shown in Table 4 and 5, $\Delta E$'s between the most stable and next stable conformers of **1**—**5** are very small (less than 1 kcal $mol^{-1}$). Therefore, we should recognize that the most stable conformers are convertible by the coordination of shift reagents in the cases of these conforma-

tionally flexible alcohols. The sequence of stability of the conformers can be perturbed by the complexation with shift reagents.

On the other hand, $\Delta E$'s between the most and the next stable conformers are pretty large in the cases of sterically congested alcohols. As shown in Table 6, $\Delta E$'s for **6** and **7** are larger (more than 2 kcal mol$^{-1}$) than those $\Delta E$'s for **1**—**5**. Sterical congestion in **6** and **7** is reflected on their optimized geometries determined by MM2. In the case of 2,2,4-trimethyl-3-pentanol (**6**), for example, widening of bond angles and deviation of dihedral angles from the normal values for both trans and gauche conformers were rationalized by the calculations. This fact, as well as their considerably large steric energies, suggests the presence of sterical congestion in these molecules. To avert the steric repulsion between gauche-positioned Bu$^t$, OH and $CH_3$ groups in the most stable conformer **III**, the dihedral angles between these groups Bu$^t$-C-C-$CH_3$, and HO-C-C-$CH_3$) are deviated from the normal value of 60° to ca. 90°.

**Conformational Equilibrium Determined from the $^3J_{H\text{-}H}$:** Application of the Karplus type equation on the observed $^3J_{H\text{-}H}$ predicts reasonable conformational distributions which agree with those obtained by MM2 and ab initio calculations. Though the $^3J_{H\text{-}H}$ method can not predict individual population of each conformer in the cases of **3**—**5** (Table 5), the summed-up populations ($X_1+X_2+X_3 : X_4+X_5+X_6 : X_7+X_8+X_9$) show fairly good agreement with those from the ab initio and MM2 calculations. The populations from the $^3J_{H\text{-}H}$ agreed even in the case of sterically congested alcohols (**6** and **7**). However, there remains a question whether $^3J_{H\text{-}H}$ method is applicable properly to the conformational equilibria of such distorted molecules.

In conclusion, the conformational equilibria for flexible alcohols can often be perturbed significantly by the complexation with LSR. Thus attention must be paid when the conclusions from the LIS analysis are compared with those from other theoretical and experimental methods. MM2 predicts the nearly identical populations of conformers and geometries with those derived from ab initio calculations and is proved to be a powerful tool in this field.

The authors are very grateful to Prof. Keiji Morokuma, the Institute for Molecular Science, for his kind permission to use a HITAC M-200H computer and the Gaussian 80 program and also for his valuable advice.

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22) Alternative explanation that the steric hindrance prevents these alcohols from forming a strong LSR-alcohol complex seems possible. However, the magnitude of their induced shifts are comparable to those of less hindered alcohols, and the contribution of weaker coordinate bond should be at most subsidiary.