OCH_3); mass spectrum *m/e* (rel intensity) 164 ($M^+ - 30$, 67), 163 (22), 149 (100); mol wt calcd for $C_8H_{10}N_4O_2$ ($M^+ - 30$), 164.06780; found, 164.06882.

Irradiation of II and Benzophenone in Acidified Methanol. A mixture of II, benzophenone, and acidified methanol was irradiated as in the preceding experiment. The neutral fraction yielded benzophenone and methyl benzoate[18] as above. The basic fraction yielded 0.55 g of a gummy solid. Most of this dissolved in 5 ml of methylene chloride, leaving 110 mg of a white solid. The solid was sublimed at 170° (20 mm) to give compound X: ir 3200 cm^{-1} (OH); nmr δ 8.22 (d, 1, $J = 6$ Hz, H_6), 7.88 (s, 1, H_3), 7.62 (s, 1, H_2), 6.98 (d, 1, $J = 5$ Hz, H_7), 5.09 (s, 2, CH_2OH), 3.05 (s, 1, exchanged with D_2O, OH).

Anal. Calcd for $C_7H_7N_3O$: N, 28.17. Found: N, 27.91.

The remaining gummy material, which was soluble in methylene chloride, was chromatographed on 50 g of alumina using increasing amounts of chloroform in petroleum ether (bp 30–60°) as eluent. Fractions 19–22 contained 95 mg of starting II and 10 mg (>1%) of XI (ir and nmr were the same as those of an authentic sample[10]). Fractions 51–60 were further separated on a preparative silica gel tlc plate to yield 60 mg of X. This gave a total yield of 170 mg (22%) of X.

Miscellaneous Irradiations. No reaction was observed when II or tetrazolo[1,5-*a*]pyridazine (XIX) were irradiated in methanol. No reaction was observed when I was irradiated in tetradeuteriomethanol for over 40 hr or in *tert*-butyl alcohol.

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Registry No.—I, 274-83-9; II, 766-55-2; Vb, 50357-91-0; Vc, 50357-92-1; VIb, 50357-93-2; VIc, 50357-94-3; VII, 50357-95-4; IX, 50357-96-5; X, 50357-97-6; 6-chloro-*s*-triazolo[4,3-*b*]pyridazine, 28593-24-0.

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3-Aryl-1,3,5,5-tetramethylcyclohexanols. Preparation and Stereochemical Characterization by Proton Nuclear Magnetic Resonance[1]

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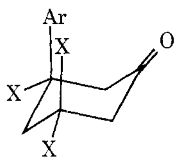
A series of cis and trans isomers of 3-aryl-1,3,5,5-tetramethylcyclohexanols (the 3-aryl substituent being phenyl, *o*-, *m*- or *p*-methoxyphenyl, *p*-chlorophenyl, or α-naththyl) was prepared; the separated isomers were characterized by detailed proton nmr studies. These studies included an extensive characterization of stereochemistry by means of lanthanide-induced shifts (LIS), primarily using $Eu(FOD)_3$, and by temperature variation. The results of these studies are consistent with the existence of biased mobile equilibria between two chair-like conformers. The extent of biasing is much greater in the cis alcohols than in the trans, with the biasing being toward an axial disposition of the hydroxyl group (with the cis aryl substituent also enjoying an axial oientation). LIS data are used to examine the possible mechanisms involved in aryl ring bond rotation processes in these highly hindered systems. The varying steric requirements and resulting LIS variations (including the observation of numerous *upfield* europium-induced LIS) are investigated using ortho, meta, or para substituents; these studies also provide structurally similar cases for probing shift reagent complexation of two sites of greatly differing basicities. An additional conformational biasing, caused by $Eu(FOD)_3$, was observed in the cis *o*-anisyl alcohol derivative.

For some time now, we have studied a number of 3,3,5,5-tetrasubstituted (and other) cyclohexanones,[3] of the type of structure 1, where X is a substituent other than hydrogen and Ar is an aryl moiety. Also, we have studied various alcohols as well as other compounds[4] derived in turn from these ketones. It was found for the cyclohexanones that, when one of the four substituents is an aryl group, this substituent uniformly exhibits a strong tendency to adopt an axial orientation in preference to a methyl group being in the analogous disposition.[3a] Previous reports have dealt with several consequences of this structural preference, the chemistry, the special nmr spectroscopic observations, and the LIS (lanthanide-induced shifts) in these systems.[3b] In addition to findings previously described, we have noted that, in ketones containing an axial phenyl or axial para-substituted phenyl substituent, the two ortho and the two meta hydrogens appear equivalent on the nmr time scale. It is of interest, then, to obtain an understanding of the process(es) that permits the observed equilibration of these energetically



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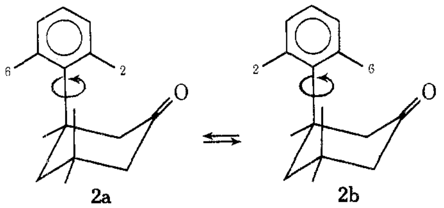
identical conformers, shown for example by structures **2a** and **2b**.



2a **2b**

It is also relevant to see whether a similar time-averaged equivalencing of aryl rotamers such as **2a** and **2b** occurs for the more hindered axial cyclohexan*ols*, and it will be shown that such averaging is indeed the case. For instance, *cis*-3-(*p*-anisyl)-1,3,5,5-tetramethylcyclohexanol (*vide infra*) shows an aryl hydrogen nmr spectrum of the AA′BB′ type (rather than the ABCD type which could arise from an aromatic ring in a fixed orientation), not only at room temperature, but even down to −75°. Even more striking is the observation that the AA′BB′ nature of this spectrum is retained even when the chemical shift difference for these aryl protons is increased by addition of Eu(FOD)$_3$ (*vide infra*) to ten times the undoped-spectrum shift difference; this corresponds to complete rotational averaging of shifts even at an hypothetical 1000-MHz spectrometer frequency, at which processes of one-tenth the rate, *i.e.*, ~1.5 kcal/mol lower energy, would be detectable.

There were, in addition, several other reasons for preparing and studying this series of compounds. The first reason was to investigate any possible aromatic substituent effects on the observed high-field methyl chemical shift of the syn C-5 methyl group of the cis isomers relative to the shift induced by an unsubstituted phenyl. Although ring current induced shifts have been investigated quite extensively for protons lying in or near the aromatic ring plane, few data are available for out-of-plane, diamagnetic shifts (however, see ref 4a). An accurate knowledge of these ring current effects for a wide variety of aromatic substituents is potentially of great use in structural analysis, and such findings have important implications for the spectral studies of biologically interesting systems.[5] The second reason was to make an exploratory study of the LIS observed in cases where there are two binding sites of markedly different basicity in the molecule—a strongly binding alcohol function and a much more weakly binding aryloxy group. The third reason was to study the effects of 3-aryl substituents with different electronic and steric natures on flattened, chair-like cyclohexane rings and on the axial *vs.* equatorial preference of an aromatic substituent. Finally, these methoxyphenyl compounds provide valuable synthetic intermediates for conversion to a variety of benzobicyclic hydrocarbons analogous to previously reported compounds of synthetic and theoretical interest because of their very high-field methyl resonances (δ −0.15 to −0.38).[4a]

This report, then, will be concerned with the detailed analysis of the aromatic and aliphatic parts of the proton nmr spectra of these compounds, with special emphasis placed on the variety of stereochemical information contained therein.

Compound Identification and Nomenclature. To facilitate a clear and simple discussion of these compounds we have adopted the use of abbreviations for compound names[6] rather than constant referral to Roman numerals. The cis or trans naming of these compounds refers to whether the *aryl* group at C-3 is cis or trans to the hydroxyl group at C-1. As shown in Figure 1, the designation of the protons in both the cis and trans isomers is as follows: (1) in the *major* conformer, protons a, c, and e are equatorial and cis to the hydroxyl group whereas protons b, d, and f are axial and trans to the hydroxyl; (2) methyl groups are labeled with respect to their disposition relative to the aromatic ring, such that Me$_{5c}$ is always cis and Me$_{5t}$ is always trans to the aryl moiety. This is consistent with our previous reports on these compounds and is a useful designation, since Me$_{5c}$ is always the group most influenced by the anisotropy of the aromatic ring.

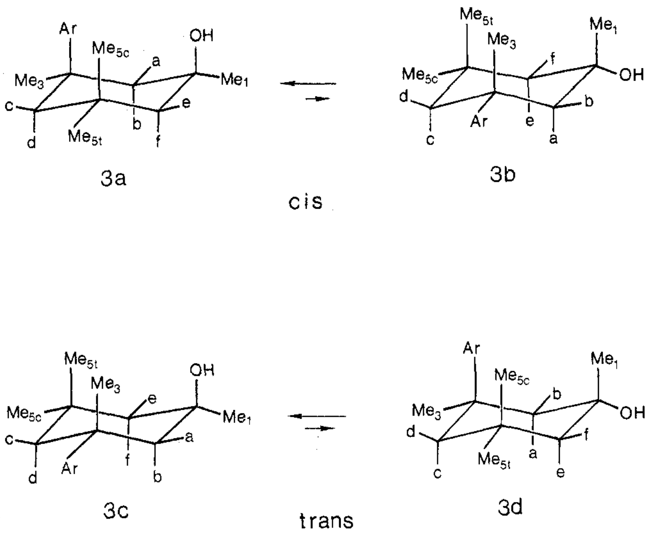


Figure 1. Proton designations for the cis (**3a** and **3b**) and trans (**3c** and **3d**) alcohol isomers where the aryl moiety (Ar) is C_6H_5, p-ClC_6H_4, p-$OMeC_6H_4$, m-$OMeC_6H_4$, o-$OMeC_6H_4$, or α-$C_{10}H_7$.

Preparation and Characterization of Compounds. In all cases, the individual cis and trans isomers were readily separated by chromatography from the mixture of alcohols obtained by the addition of methylmagnesium bromide to the corresponding cyclohexanone.[3b] The expected tertiary alcohol nature of these compounds was confirmed in the usual fashion, as well as by the extensive proton nmr studies to be described. The cis and trans identification of the isomeric tertiary alcohols so obtained was readily accomplished by means of proton nmr spectroscopy. In the cis alcohols, the most immediate evidence of an axially disposed aromatic ring (as the sole or highly predominant conformer) is the observation of a methyl chemical shift (Me$_{5c}$) at markedly high field,[3a] resulting from the perpendicular ring current shielding effect suffered by the methyl in a conformation like **3a.** Although these methyl (Me$_{5c}$) shifts occur at sufficiently high field to permit ready identification of isomers, they are in fact at significantly lower fields than those in their precursor ketones. This fact is readily consistent only with the axial disposition of the hydroxyl function, such that the electric field effect deshielding caused by the oxygen is felt at a syn-axial methyl group, Me$_{5c}$. The axial-hydroxyl, equatorial-aryl nature of the trans isomers was deduced in an analogous fashion. These structural assignments are consistent with expectations based on the principles of conformational analysis.

LIS Methodology. A considerable amount of work has appeared on the mechanism involved in lanthanide shift reagent (LSR)–substrate binding.[7,8] As in most cases of chemical interest, it is clear that we are dealing here with time-averaged spectra of the "fast-exchange" type, where the observed shift, δ_{obsd}, of a given proton is a concentration-weighted average of the shifts of the individual species in solution (S, LS, LS$_2$, *vide infra*).

It has been shown that the observed concentration dependence of the LIS for compounds of these types requires at least a two-step equilibrium model[8] with four parame-

Table I

δ_0 Values Observed and Slope Values[a] Derived for Methyl Protons, from LIS Data Using Eu(FOD)$_3$ at 30°, CCl$_4$ Solution

		Cis alcohols (3a ⇄ 3b)						Trans alcohols (3c ⇄ 3d)					
		PhOH (50361-38-1)[b]	PCOH (50361-40-5)	PAOH (50361-42-7)	MAOH (50361-44-9)	OAOH (50361-46-1)	αNOH (33875-98-8)	PhOH (50361-39-2)	PCOH (50361-41-6)	PAOH (50361-43-8)	MAOH (50361-45-0)	OAOH (50361-47-2)	αNOH (33875-97-7)
δ_0	Me$_{5c}$	0.66	0.66	0.67	0.70	0.67	0.48	1.29	1.29	1.25	1.27	1.24	1.38
	Me$_3$	1.08	1.06	1.04	1.08	1.16	1.59	1.51	1.49	1.44	1.48	1.54	1.91
	Me$_{5t}$	0.90	0.90	0.88	0.90	0.87	0.90	0.90	0.90	0.88	0.90	0.87	0.92
	Me$_1$	1.18	1.21	1.16	1.18	1.16	1.24	1.25	1.22	1.19	1.22	1.17	1.24
λ	Me$_{5c}$	6.56	6.36	5.78	5.70	5.74	5.79	4.40	4.54	4.48	4.42	5.13	6.16
	Me$_3$	3.62	3.38	3.20	3.64	4.66	3.47	4.32	4.42	4.40	4.38	5.25	6.60
	Me$_{5t}$	3.99	3.98	3.44	3.54	3.42	3.84	4.01	3.96	4.22	4.02	3.99	4.12
	Me$_1$	16.68	16.28	14.92	15.40	10.10	16.28	12.59	12.06	13.18	12.44	13.14	13.29

[a] In parts per million. [b] Registry no.

Table II

δ_0 Values Observed and Slope Values[a] Derived for Methylene Protons, from LIS Data Using Eu(FOD)$_3$ at 30°, CCl$_4$ Solution

		Cis alcohols (3a ⇄ 3b)						Trans alcohols (3c ⇄ 3d)					
		PhOH	PCOH	PAOH	MAOH	OAOH	αNOH	PhOH	PCOH	PAOH	MAOH	OAOH	αNOH
δ_0	a	2.62	2.62	2.62	2.64	2.90	2.92	1.95	1.90	1.89	1.92	2.05	2.25
	e	1.37	1.38	1.42	1.45	1.43	1.42	1.54	1.52	1.55	1.53	1.50	1.62
	b	1.21	1.22	1.28	1.27	1.17	1.48	1.72	1.64	1.66	1.68	1.80	1.92
	f	1.25	1.25	1.19	1.19	1.19	1.24	1.21	1.21	1.21	1.19	1.21	1.32
	c	2.39	2.33	2.34	2.39	2.90	2.80	1.78	1.78	1.74	1.79	1.89	2.16
	d	1.18	1.27	1.20	1.22	1.03	1.36	1.57	1.49	1.52	1.52	1.64	1.80
λ	a	14.43	14.40	12.86	13.98	15.80	13.45	15.63	15.68	16.70	15.62	15.73	16.73
	e	15.81	15.78	14.24	14.90	13.06	15.85	16.02	15.48	16.76	15.90	16.90	17.25
	b	9.24	8.76	8.00	8.52	8.44	9.17	12.83	12.56	13.66	12.64	12.61	11.62
	f	9.10	9.02	8.06	8.70	7.06	9.25	12.25	11.60	12.96	11.96	12.24	11.07
	c	5.18	4.98	4.66	4.92	5.90	5.14	5.14	5.06	5.40	5.04	5.38	6.28
	d	6.37	6.10	5.56	5.92	6.18	5.94	5.05	5.14	5.36	5.14	5.88	6.28

[a] In parts per million.

ters being necessary to describe fully the observed shifts, as shown in eq 1, where K_1 and K_2 are the equilibrium

$$\begin{aligned} \mathrm{L} + \mathrm{S} &\rightleftarrows \mathrm{LS} \qquad (K_1, \Delta_1) \\ \mathrm{LS} + \mathrm{S} &\rightleftarrows \mathrm{LS_2} \qquad (K_2, \Delta_2) \end{aligned} \tag{1}$$

constants for association and Δ_1 and Δ_2 are the incremental shifts of the pure LS and LS$_2$ species, respectively. Both Δ_1 and Δ_2 are intrinsic functions of the LS and LS$_2$ species, and have been shown[8] to be related directly to the observed initial slope (λ) of a δ_{obsd} *vs.* ρ ($= L_0/S_0$ where L_0 = the total molar LSR concentration and S_0 = the total substrate molarity) plot, by

$$\lambda = \frac{\partial(\Delta\delta)}{\partial\rho} \approx \frac{\Delta_1}{S_0K_2} + 2\Delta_2 \tag{2}$$

In the incremental dilution, constant S_0 method employed in this work, the slope observed up to $\rho \leq$ *ca.* 0.4 is a linear combination of Δ_1 and Δ_2. If K_2 be very small, both terms in the equation are required. However, when K_2 is large, λ is simply $2\Delta_2$ to an excellent degree of approximation. We have found that the term containing Δ_1 is dominant for tertiary alcohols; these findings will be presented elsewhere. Although sufficient "contamination" of the slope by Δ_2 enters in so as to preclude the slopes as being suitable numbers for a rigorous structure calculation, the λ values are more than adequate for the present purposes. Even though two binding sites are available in each molecule, the two-step mechanism is still valid owing to LSR binding at the hydroxyl being much greater than the binding to (aryl) methoxy. The LSR interaction with the methoxy group will be discussed later.

Thus in the discussion which follows, we will be using λ values for incorporation into the pseudo-contact shift equation,[9] which may then be conveniently expressed as

$$\lambda_i = k(3\cos^2\theta_i - 1)(R_i^{-3}) \tag{3}$$

where k is a collection of constants, θ_i is the angle describing the position of the proton i relative to the principle magnetic axis of the LSR, and R_i is taken as a proton-lanthanide ion distance. Parenthetically, one should note that the constant, k, has different values depending upon which parameter is being fitted [*i.e.*, λ_i, observed shifts, $(\Delta_1)_i$, $(\Delta_2)_i$, etc.]. The λ_i values, then, may be used for assessments of molecular geometry, *viz.*, to distinguish between the relative importance of two or more specific geometric possibilities. Rather than attempting to fit the structures in a fully rigorous parametric fit to eq 3, we shall simply compare the magnitudes of λ for protons symmetrically disposed to the alcohol oxygen, and therefore to the metal of the LSR.

It may be pointed out that, by the incremental dilution, constant-S_0 method employed here, the λ_i values are determined experimentally to very high precision: for doping levels expressed by $\rho \leq$ *ca.* 0.4, a linear least-squares regression analysis yields a correlation coefficient always greater than 0.99 for any acceptable set of data (usually >0.999) and it is useful in obtaining δ_0 values (the chemical shifts in the absence of LSR) of partially obscured or strongly coupled protons.[3b,10] Values of this coefficient less than *ca.* 0.98 are most often caused by "scavenging" (*i.e.*, binding by strongly basic impurities),[10] and are cause for rejection of the data of a particular experiment.

Results and Discussion

In Tables I–III are presented the δ_0 values (either observed or obtained by extrapolation) and λ values for the methyl, methylene, and aromatic protons, respectively, for the alcohol isomers. The λ values refer to 0.15 *M* sub-

Table III
δ_0 Values Observed and Slope Values[a] Derived for Aromatic Protons, from LIS Data Using Eu(FOD)$_3$ at 30°, CCl$_4$ Solution

		Cis alcohols (3a ⇄ 3b)						Trans alcohols (3c ⇄ 3d)					
		PhOH	PCOH	PAOH	MAOH	OAOH	αNOH	PhOH	PCOH	PAOH	MAOH	OAOH	αNOH
δ_0	2	7.45	7.42	7.35	7.09	7.59	7.88	7.32	7.18	7.22	6.88	7.18	b
	3	7.22	7.14	6.70	7.10	6.80	7.27	7.21	7.21	6.72	7.11	7.05	b
	4	7.05			6.58	7.07	7.56	7.05			6.57	b	b
	5	7.22	7.14			6.80	7.72	7.21	7.21	6.72		b	b
	6	7.45	7.42		7.16			7.32	7.18	7.22	6.83		
	OMe			3.71	3.74	3.84				3.72	3.75	3.82	
λ	2	3.99	3.28	3.50	4.14	5.74	6.69	3.59	3.51	3.82	3.68	4.19	4.45
	3	−3.52	−4.30	−3.10	−3.94	−3.46	−7.76	1.20	1.36	1.72	1.42	1.48	
	4	−2.56			−1.26	−1.14	−1.98	1.40			1.22		
	5	−3.52	−4.30	−3.10		0.76	−0.45	1.20	1.36	1.72			
	6	3.93	3.28	3.50	5.30			3.59	3.51	3.82	3.76		
	OMe			−1.70	−1.54	1.40				1.02	0.96	1.50	

[a] In parts per million. [b] Resonances obscured owing to complex multiplets.

strate solutions in CCl$_4$, at 30° and, except where noted, doped with Eu(FOD)$_3$. Coupling constants ($^2J_{HH}$ and $^4J_{HH}$) were typical in magnitude for a cyclohexane chair structure, but were not measured precisely, for they are of little utility for the present purposes. It should be noted that the specific assignments given do not rest on any interpretation of the relative LIS *magnitudes,* but are of course consistent with these. Rather, the assignments follow unambiguously from the undoped shifts (*cf.* ref 3b) and the multiplicity and relative widths of the individual signals seen in the LIS-dispersed spectra. The methylene assignments were confirmed by the appropriate spin-decoupling experiments.

Cis Alcohols. Aliphatic Protons. Inspection of the δ_0 values of Table I immediately permits the conclusion that the structures of the various cis alcohols do not vary appreciably, at least for the substituted phenyl alcohols, from one to the other. For example, one may note the constancy of the chemical shift of a given type of methyl. The exceptions of Me$_3$ and Me$_{5c}$ in *cis*-αNOH clearly arise from the additional ring-current and anisotropy effects associated with ring B of the α-naphthyl system. A similar trend is observed on a qualitative examination of the *methylene* δ_0 values (Table II). It is also of some theoretical interest here that the Me$_{5c}$ chemical shift cannot be used to distinguish between the various substituted phenyl groups on C-3. The correlations observed for the aryl anisotropy and alterations in it caused by various substituent groups have also been of interest in other types of compounds studied in our work. For instance, in a closely related system where all the aromatic hydrogen atoms are replaced by chlorine, no substantial difference in the upfield shifts experienced by Me$_{5c}$ was observed.[11]

This similarity of structure is also evident from the observed λ values. An important aspect of these values is the consistent pairing of proton types equivalently disposed about a pseudo-symmetry plane (*i.e.*, a plane passing through the hydroxyl group, C-1, and C-4), *viz.*, a and e, b and f, as well as Me$_3$ and Me$_{5t}$. This complementary pairing of the methylene protons and equatorial methyl protons is consistent with the results obtained on the ketone precursors of these alcohols and is most readily rationalized in terms of a flattened cyclohexanoid ring system which possesses chair-like symmetry and shape. (The complementary pairing of the LIS would be unlikely for otherwise plausible twist-boat conformations, without numerous fortuitous shift averagings.)

This view is supported both by the similarity of the slopes obtained for proton d and for Me$_{5c}$, and by four-bond couplings of proton a (and proton e) to proton c without analogous proton b–d and proton f–d couplings.

The observed flattening distortion to this ring is caused by a syn-axial compression ("reflex effect") between the two large axial substituents at C-3 and C-5. This deformation appears to have only lateral, rather than longitudinal, twisting components; that is, the axial C-3 and C-5 substituents move away from each other along the normal of the O-C$_1$-C$_4$ plane. In the case of 3-(*p*-chlorophenyl)-3,5,5-trimethylcyclohexanone (PCK), LIS-based conclusions about such a structural feature in the liquid state are found precisely mirrored in the carefully determined solid-state structure.[12] The present LIS data suggest strongly that similar considerations should apply to the cyclohexanols.

We turn now to a more detailed examination of the λ values obtained for the cis alcohols. Looking first at the methyls at the C-3 and C-5 cyclohexyl ring positions, it is clear that Me$_{5c}$ consistently has larger λ values than do the equatorial Me$_3$ and Me$_{5t}$. The reverse behavior is noticed for the methylene protons at C-2 and C-6 (Table II), with the equatorial protons havig the larger LIS. In addition, as previously observed for the ketones,[3b] proton d has a similar λ value to Me$_{5c}$. This presumably results from the flattening of the chair due to the reflex effect.

In *cis*-OAOH there is somewhat of a departure from the similarity of the LIS experienced for complementary proton pairs. An example of this deviation can be observed on examination of the λ values for Me$_3$ and Me$_{5t}$. A reasonable explanation of this difference involves the orientation of the aryl substituent. From the δ_0 values in Table II, it is readily observed that the proton c resonance for *cis*-OAOH is abnormally downfield in comparison with the other phenyl-type compounds, but displays a similar shift to the analogous proton of *cis*-αNOH. For *cis*-αNOH this downfield shift has been explained[3a] by ring B of the α-naphthyl system spending a considerable amount of time near proton c, its edge effect (and associated paramagnetic anisotropy) causing the observed downfield displacement. A similar orientation of the *o*-anisyl ring would place the oxygen of the methoxy group near proton c, causing deshielding resulting from the electric field effect of the oxygen.[13] Proton d is probably placed in the shielding region of the oxygen anisotropy and/or the aromatic ring, and the resonance shifted upfield. The LIS results for *cis*-OAOH can then most readily be accommodated by a biased rotation of the aromatic ring, upon addition of Eu(FOD)$_3$, to a conformer in which the methoxy group is oriented toward the hydroxy group. In such an orientation, a bidentate chelate species could be formed with the LSR, as depicted in Figure 2.

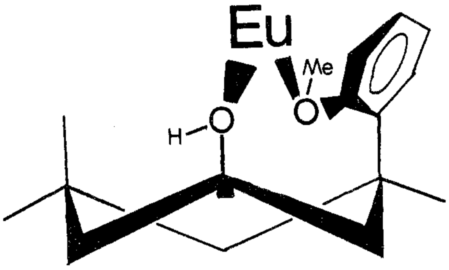
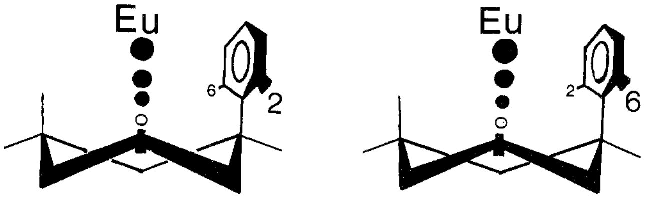


Figure 2. Bidentate chelate complex for *cis*-OAOH.

Inspection of molecular models serves to confirm the steric reasonableness of this proposal. Such binding probably causes the LSR to move slightly away from the O–C_1–C_4 pseudo-symmetry plane closer to protons a and b than to protons e and f, and similarly closer to Me_3 than to Me_{5t}. The observed λ values are consistent with this notion, as is the absence of this effect in the other cis alcohols. (These arguments require only a reasonable similarity in the O–Eu–H angles, so that the observed differences are sensitive primarily only to the R_i^{-3} distance term of eq 3.) Although this effect of bidentate chelation appears to be small, it becomes more important to the observed LIS of *cis*-OAOH at lower temperatures, as discussed later.

It is interesting that the above-described rotation of *cis*-OAOH and subsequent chelation is not observable when $Eu(DPM)_3$ is used as the LSR, as indicated by the λ values of the complementary proton pairs (Table IV). A possible explanation lies in the fact that $Eu(DPM)_3$ is a weaker Lewis acid than $Eu(FOD)_3$ with, therefore, far smaller binding to the weakly basic methoxy oxygen. The larger magnitude for the LIS produced by $Eu(DPM)_3$ is consistent with our previous findings.[14]

Aromatic Protons. The aromatic resonances show LIS behavior much different from that observed for the other protons discussed above. The observation of *upfield* shifts is noteworthy owing to the important stereochemical implications associated with them.[4b,15] Such shifts are predicted by the pseudo-contact equation, the direction of the shift change being a consequence of the molecular geometry of the system studied, as required by the angle-dependent term of eq 3. These LIS to high field were first observed in *cis*-αNOH[4b] and serve to further confirm the axial disposition and the rotational preference of such an aromatic moiety. The similar structures of *cis*-αNOH and the other cis alcohols here suggest that upfield LIS might be observed. In fact, it was found that the λ values for protons at the phenyl ring positions 3 and 4 have negative (upfield) shifts (see Table III). (Analogous *downfield* shifts induced by *Pr*(DPM)$_3$ for protons 3 and 4 in *cis*-PAOH were observed.) As previously mentioned, protons 2 and 6 are nmr equivalent, as are protons 3 and 5. Examination of Dreiding models and the precise X-ray crystallographic structure of PCK indicate that it may be difficult for the aryl protons, such as 2 and 6, in the phenyl or para-substituted aromatic rings to become equivalent simply by rotation of the aromatic ring in a single aryl-axial conformer such as indicated in **2a**.



4a 4b

Figure 3. Orientations of the two low-energy rotamers in the case of phenyl or para- or meta-substituted phenyl aryl substituents.

A method for estimating the rotational orientation of the aryl substituent was developed for the analogous ketones and is also applicable here. The model assumes that the energy minima for aryl rotation occur when the aromatic ring is parallel (or nearly so) to the C_2–C_3 cyclohexane ring bond, and that, if this be so, one may be able to neglect other orientations to a fair degree of approximation. Thus for phenyl or para-substituted phenyl, there is an equal population of rotamers **2a** and **2b**. Now in ortho- or meta-substituted compounds, if protons 2 and 3 have LIS similar to those of protons 6 and 5, respectively, it is assumed that the aromatic moiety does not show substantial biasing toward one rotamer or another as indicated by structures **2a** and **2b**. Since, for steric reasons, *cis*-αNOH is capable of only one low-energy orientation (that which places ring B of the naphthyl system near proton c), it serves as a good model. In a system in which there is no single preferred aryl orientation, the LIS experienced by protons 2 and 3 should be about one-half those observed for the *cis*-αNOH, since they are in an analogous position, for one-half the time. Actually, considering protons 2 and 6, this is due to an averaging of a large downfield LIS occurring from an orientation of the aromatic ring such as in **4a** with a small downfield shift occurring in **4b** (see Figure 3).

Thus these LIS's for protons 2 and 6 are mainly due to the R_i^{-3} term of eq 3, since the variation in $\cos^2 \theta$ is not substantial between these two rotamers. Similarly, for proton 3 and 5, a large *upfield* shift is averaged with a small downfield shift; hence the observed results. Previously it was shown that *cis*-OAOH is capable of existing in two descrete orientations with the minor one facilitated by the methoxy interaction with the LSR. Judging from the LIS of proton 2, the aryl group behaves so as to be hindered in rotation more like the α-naphthyl group in *cis*-αNOH.

The molecular dynamics by which protons 2 and 6 (as well as 3 and 5) are made equivalent is worthy of comment. For reasons previously mentioned the simple rotation of an unsubstituted (or para-substituted) phenyl ring might be energetically prohibitive even for the reflex effect flattened cyclohexanone or cyclohexane rings. Such a view would seem to require that aryl rotation occur in the cyclohexane ring inverted conformer **3b** which, of course, need not be present to a major extent if the aryl rotation barrier in **3b** be markedly less than that for the **3a** ⇄ **3b** interconversion, as is reasonable.

Table IV
λ Values[a] Observed for *cis*-OAOH Using Eu(DPM)$_3$ [Eu(FOD)$_3$ Values in Parentheses for Comparison]

Me_1	Me_3	Me_{5c}	Me_{5t}	a	e	b	f	c	d	H_2	H_3	H_4	H_6	OMe
20.20 (10.10)	5.66 (4.66)	8.66 (5.74)	5.48 (3.42)	21.34 (15.80)	21.85 (13.06)	13.94 (8.44)	14.28 (7.06)	8.24 (5.90)	8.74 (6.18)	13.14 (5.74)	−8.04 (−3.46)	−2.26 (−1.14)	~0 (0.76)	0.39 (1.40)

[a] In parts per million.

An alternative mechanism involving a "gearing" of aryl rotation with some cyclohexane ring flexing process remains to be considered, for such a process seems consistent with both the experimental evidence now available and with the known lowered ring inversion barriers in 1,1,3,3-polysubstituted cyclohexane rings.[16]

LSR-Methoxy Interaction. Although a relatively minor effect overall, methoxy binding is important in order to understand more completely the LIS observed for the aromatic proton types. Since an excellent comparison exists between *cis*-PAOH and *cis*-PCOH, the only difference in these being chlorine *vs.* methoxy, any interactions resulting from methoxy binding should be directly observable. It was found that the LIS of protons 3 and 5 in *cis*-PAOH is of significantly smaller magnitude than that for the 3,5 pair in *cis*-PCOH. This observation is in accord with the methoxy group acting as a secondary binding site in competition with complexation at the hydroxyl group. (The probability of complexation occurring at both sites simultaneously is, of course, negligible.) Even a small interaction by the methoxy should cause the LIS of the cyclohexyl proton shifts to be reduced, as observed on comparing the λ values for *cis*-PCOH *vs.* *cis*-PAOH. Additionally, when the LSR is bound to the methoxy group, only the closer ring protons 3 and 5 are afforded a substantially enhanced downfield shift. It is the above interaction which probably causes the large differences in the LIS of protons 2 and 6 in *cis*-MAOH and the downfield shift of proton 5 in *cis*-OAOH. Finally, it is noticed at high doping levels ($\rho \approx 3$) that, when a limiting shift is approached for even greatly shifted resonances ($\lambda > 12$ ppm), the methoxy resonance continues to be altered in value (now with a *downfield* LIS for *cis*-PAOH and *cis*-MAOH). The resonances of the protons adjacent to the methoxy also continue to be shifted downfield. The *direct* effect of the LSR-methoxy interaction on the cyclohexane ring proton shifts is negligible.

Trans Alcohols. All of the LIS observed for the trans alcohols are to lower field and, like their cis isomers, show similar λ values for the symmetry-paired proton types. Except for *trans*-αNOH and *trans*-OAOH, the difference between the LIS magnitude for equatorial and axial proton types is markedly smaller than was obtained for the cis isomers. Considering first only the methylene protons at C-2 and C-6, the average differences were found to be 3.28, 3.50, 3.42, and 3.54 ppm for *trans*-PhOH, -PCOH, -PAOH, and -MAOH, respectively, 4.39 ppm for the *trans*-OAOH, and 6.14 ppm for *trans*-αNOH. In comparison, the average difference observed in the cis isomers was 5.85 ppm, clearly indicating that, at least for the first four trans isomers, some additional interaction must be occurring so as to tend to equalize the λ values of the C-2 and C-6 protons.

As indicated above, in *trans*-αNOH two methyls (Me$_3$ and Me$_{5t}$) have similar λ values of considerably larger magnitude than that of Me$_{5c}$. This observation is in accord only with an axially disposed hydroxyl group and an equatorial aromatic ring and is similar to the results obtained in the cis isomers. In *trans*-OAOH the difference in the λ values for these methyl protons is not as large as in *trans*-αNOH. However, in the other trans alcohols, despite the similar LIS for the symmetry-paired cyclohexyl protons, all three methyls have nearly identical LIS. It is our present view that this unexpected result probably originates from the presence of a less biased equilibrium mixture of the two possible chair conformers which now both contribute significantly to the time-averaged structure.

These equilibria can be illustrated schematically by eq 4, where A is the axial-OH conformer, E is the equatorial-OH conformer (the structures of A and E are given in Figure 1, **3c** and **3d**, respectively), and AL and EL are the respective complexed species. It appears from our data that A and E *each* form their own complex with the LSR. The results cannot be explained by an alteration of the above equilibria where the formation of EL must arise from the prior formation of AL (*i.e.*, equilibration between AL and EL is much less important than equilibration between A and E). Conversely, AL and EL may not be long lived enough to undergo interconversion. It should be noted that any equatorial conformer present would bind more readily to the LSR then would the axial (OH) conformer.[17]

$$\begin{tikzcd} A + L \arrow[r, shift left] \arrow[d, shift left] & AL \arrow[l, shift left] \arrow[d, shift left] \\ E + L \arrow[r, shift left] \arrow[u, shift left] & EL \arrow[l, shift left] \arrow[u, shift left] \end{tikzcd} \qquad (4)$$

An alternative possibility (ref 18) which should be considered involves the *a priori* reasonable contribution from twist-boat and/or boat forms in the trans isomer. We feel that such involvements may be neglected as less probable than the above explanation, for the following reasons. The first reason is that, as with the cis isomers, there is marked symmetry pairing of the slopes observed for protons a-f. Any reasonable twist-boat or boat form would destroy the possibility of the observed symmetry pairing of the λ values, in the absence of several coincidences of shift averaging, plus the requirement that this coincidental averaging be uniform for the several cases where symmetry pairing is observed. The second reason is that, again as in the case of the cis isomers, the observation of line-width variations or actually observed long-range couplings for protons a, c, and e, but not for b, d, and f, suggest strongly that any time-averaged structure partakes very little of the nonchair conformation.

The data, then, serve to indicate that the $A \rightleftarrows E$ and subsequently the $E + L \rightleftarrows EL$ equilibria are not important for *trans*-αNOH, moderately important for *trans*-OAOH, and quite significant for *trans*-PhOH, -PCOH, -PAOH, and -MAOH. For instance, considering Me$_3$, Me$_{5c}$, and Me$_{5t}$, it was found that the Me$_3$ (or Me$_{5c}$) to Me$_{5t}$ λ ratio (Table I) averaged to 1.61 for *trans*-αNOH, to 1.30 for -OAOH, and to only 1.09 for the other trans alcohols, *trans*-PhOH, -PCOH, -PAOH, and -MAOH. (Additionally, it may be noted that a qualitative experiment where the aryl substituent was *p*-tolyl yielded results similar to those of the latter group of compounds.) Since the normal trends still predominate in these latter compounds [LIS of equatorial protons (of **3c**) are greater than axial protons at C-2 and C-6], it is necessary that the AL complex always be predominant.

When the conformer with an equatorial hydroxyl is present to a significant amount as part of an equilibrium mixture, such as in *trans*-PAOH, its effects on the behavior of the LIS can be predicted. In a recent study of 4-*tert*-butylcyclohexanol[19] it was found that the difference between the LIS for the axial and equatorial protons on C-2 and C-6 in the trans isomer (equatorial OH) is less than for the cis isomer (axial OH). A similar result was noticed for protons in the C-3 and C-5 positions but with the axial protons of the trans isomer having a larger LIS. The relationsip of these results to our system is instructive. If an equatorially disposed hydroxyl conformer were present to any significant extent, the LIS differences in protons a, b, e, and f would become less than the LIS differences observed for the same protons in the cis alcohols, which appear to be much more conformationally pure. Similarly, the differences in Me$_{5c}$, Me$_{5t}$, and Me$_3$ should become smaller. Also, in the *trans*-*tert*-butylcyclohexanol, H$_1$ has a LIS less than the LIS of H$_1$ of the cis isomer.

Table V
Variable-Temperature LIS Data Slope Values[a] Derived for Methyl Groups [Eu(FOD)$_3$, CS$_2$ Solution]

	Ketones and cis alcohols							Trans alcohols			
	PAK[b]	MAK[c]	OAK[d]	PAOH	MAOH	OAOH	PCOH	PAOH	MAOH	OAOH	PCOH
Me$_1$				3.00	3.63	−0.51	3.60	2.78	3.07	2.45	2.76
Me$_{5c}$	1.33	1.12	1.30	1.07	1.00	0.91	1.53	0.44	0.38	0.42	0.49
Me$_3$	0.37	0.21	0.45	0.53	0.64	0.92	0.55	0.41	0.44	0.51	0.45
Me$_{5t}$	0.54	0.46	0.64	0.65	0.68	0.39	0.81	0.69	0.74	0.49	0.70

[a] In parts per million. [b] 3-(*p*-Anisyl)-3,5,5-trimethylcyclohexanone. [c] 3-(*m*-Anisyl)-3,5,5-trimethylcyclohexanone. [d] 3-(*o*-Anisyl)-3,5,5-trimethylcyclohexanone.

Table VI[a]
Variable-Temperature LIS Data Slope Values[b] Derived for Methylene Protons [Eu(FOD)$_3$, CS$_2$ Solution]

	Ketones and cis alcohols							Trans alcohols			
	PAK	MAK	OAK	PAOH	MAOH	OAOH	PCOH	PAOH	MAOH	OAOH	PCOH
a	2.60	1.93	2.79	2.45	2.45	2.77	2.74	2.26	2.52	1.98	2.48
e	2.80	2.12	3.39	2.49	2.75	0.60	3.27	2.79	3.16	2.06	2.70
b	1.60	1.20	1.85	1.63	1.86	1.21	1.75	2.35	2.56	1.78	2.34
f	1.69	1.44	1.98	1.66	1.86	0.40	1.97	2.46	2.69	2.00	2.46
c	0.81	0.78	0.94	0.84	0.90	0.90	1.02	0.65	0.72	0.57	0.72
d	0.94	0.79	1.08	1.04	1.07	1.08	1.20	0.73	0.83	0.62	0.72

[a] See footnotes to Table V. [b] In parts per million.

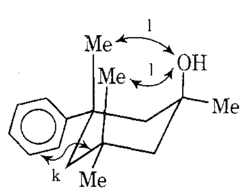
Table VII[a]
Variable-Temperature LIS Data Slope Values[b] Derived for Aromatic Protons [Eu(FOD)$_3$, CS$_2$ Solution]

	Ketones and cis alcohols							Trans alcohols			
	PAK	MAK	OAK	PAOH	MAOH	OAOH	PCOH	PAOH	MAOH	OAOH	PCOH
2	1.75	1.34	3.26	0.32	0.36	1.00	0.27	0.53	0.24	0.53	0.52
3	0.31	0.36	*c*	−0.98	−1.31	−0.05	−1.08	0.22	0.26	*c*	0.20
4		0.43	*c*		−0.53	0.01			0.00	*c*	
5	0.31		*c*	−0.98		0.35	−1.08	0.22	*c*	*c*	0.20
6	1.75	2.51		0.32	1.15		0.27	0.53		*c*	0.52
OMe	0.00	0.37	0.40	−0.41	−0.59	0.59		0.16	0.16	0.24	

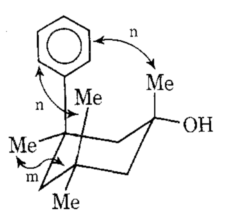
[a] See footnotes tc Tables IV. [b] In parts per million. [c] Resonance obscured owing to complex multiplets.

Therefore, the LIS of Me$_1$ in the trans alcohols should be less than that obtained for the cis isomers. The LIS magnitudes for protons a, e, b, and f in the trans alcohols are seen to be similar to those observed in the corresponding ketones (where the average λ values for protons a, e, b, and f are 16.54, 16.18, 14.18, and 14.46 ppm, respectively). This is not surprising, since if an equilibrium mixture of A and E existed the LSR would behave, on the average, as if it were near the plane bisecting the Me$_1$-C-1-OH angle and in a position similar to where the LSR is believed to be for the ketones.[3b]

Substantial involvement of the equatorial-OH conformer in the trans alcohols may be rationalized by an examination of the relative energies in each conformer, as indicated in the diagram below. The major factors involved in comparing the two conformers are as follows: in **5a** there are two 1,3-diaxial methyl–hydroxyl (l) interactions and one aromatic–cyclohexane ring (k) while in **5b** there are two 1,3-diaxial aromatic–methyl interactions (n) and one methyl–cyclohexane ring (m). It can be assumed that the other steric interactions in these two compounds are approximately the same. Allinger[20] recently calculated that, in 1-(phenyl)-1,3,3-trimethylcyclohexane, the conformer with an axial phenyl group is favored by 3.3 kcal/mol. It can then be calculated that the difference in energy between these two systems is approximately 1.15 kcal/mol or about 85% in favor of the conformer with the axial hydroxyl.[21] Qualitative estimates of the relative amount of each conformer present by LIS data are made difficult by the LIS not only depending on the ratio of components in solution, but on the respective association equilibrium constants of each conformer. Although **5b** may be present to a lesser degree, it would be a proportionally larger contributor to the observed LIS because of the stronger LSR binding of equatorial *vs.* axial hydroxyl groups.[17]



5a



5b

A possible reason for *trans*-αNOH and -OAOH preferring **5a** to a greater extent than do the other trans alcohols involves the steric nature of each of these aromatic substituents. In **5b**, the aromatic ring is axial, and, as seen from the data on the cis isomers of αNOH and OAOH, is capable of only one low-energy orientation of the aryl substituent, resulting in a loss of entropy. Owing to the similar energies of **5a** and **5b** this relatively small factor now becomes important and results in the observed trends.

Temperature Effects. To obtain a further understanding of rotational behavior of the aromatic substituent and the conformational mobility of these compounds, the nmr spectra of the LSR-doped and undoped ketones and alcohols were studied as a function of temperature. Virtually no change was observed in any of the undoped trans alcohols over the temperature range studied (43 to −75°). The ketones and cis alcohols did exhibit some relatively minor changes in their spectra on decreasing temperature; the only significant change was in the chemical shift of Me$_{5c}$, where on the average an *upfield* shift change of 0.1 ppm was observed. This upfield shift in the ketones and cis alcohols is consistent with an even greater biasing of the chair-to-chair equilibrium (shown in Figure 1) such that the population of the conformer having the axially substituted aryl moiety is enhanced. The overall effect, then, would be to keep Me_{5c} in the face of the aromatic ring for a greater fraction of the time.

Although studies involving LSR have been very numerous,[22] the temperature dependence of these solutions has received comparatively little attention.[23] Investigations have shown that the magnitude of the LIS increases with decreasing temperature, and behavior opposite to this probably arises from changes in the steric requirement of the lanthanide,[23c] hence its binding position. In this study the concentrations of the substrate solutions were prepared as close as possible to the concentrations used in the incremental dilution method. The ρ value of 0.3 was chosen so that it was in the linear portion of the LIS curve, ensuring that the shifts induced by varying the temperature would be of the largest magnitude. The slopes obtained $[(\delta_{ds} - \delta_0)/\rho$ where δ_{ds} is the chemical shift of proton in the LSR doped solution] in CS_2 solutions at ambient temperature were found to be very similar to those obtained from the incremental dilution method, indicating that both the lanthanide complexation equilibria and the binding position are similar for both solvents. This finding is consistent with other recently published results.[24]

In the LSR-doped solutions (see Tables V–VII), the ketones and cis alcohols, as expected, showed trends similar in the temperature dependence of their LIS to those exhibited in the incremental dilution data. For instance, the average Me_{5c} to Me_3 λ values in *cis*-MAOH is 1.55 ppm for the incremental dilution method *vs.* 1.50 ppm for the temperature-dependence data, suggesting that the average binding position in these alcohols (except for *cis*-OAOH) is not affected very much by the variation of temperature. If any change in this binding position does occur, it is probably along the symmetry plane previously described, since symmetry-paired protons still show similar LIS (see Tables V–VII).

An interesting result was obtained from the variable-temperature study of *cis*-OAOH. Except for Me_1, all of the proton types show the usual downfield shifts with decreasing temperature. Surprisingly, Me_1 showed an *upfield* shift (Me_1 in all the other alcohols shows the *largest downfield* shifts). Again one must consider the orientation of the aromatic ring to understand this anomaly. As the temperature is lowered, the rotamer where the methoxy group points toward the hydroxy group becomes very important. This orientation and subsequent chelation could well change the binding position of the LSR, causing the Eu–O–Me_1 angle to be greater than $\sim 55°$, the angle at which the angle term in eq 3 requires an upfield LIS. Additionally, this new LSR position is responsible for the now very large differences between the LIS of protons a and e as well as b and f (see Table VI).

The temperature dependence of the LIS of the trans alcohols exhibits the normal downfield shifts for all proton types. Additionally, the observed values for the temperature-dependent LIS follow the same trends as did the LIS obtained for the incremental dilution data. Since *trans*-αNOH behaves very differently from the other trans alcohols, it will be discussed first. As previously found, Me_3 and Me_{5t} have λ values larger (by an average ratio of 1.79) than that of Me_{5c}. This is indicative of a compound having an axial OH as pictured in **3c**, and compares well with the axial to equatorial methyl λ ratios in the cis isomers.

In the incremental dilution data, *trans*-OAOH was an intermediate example of the biasing of the equilibria shown. It is seen that now Me_3, Me_{5t}, and Me_{5c} have nearly identical LIS. Finally, for *trans*-PCOH, -PAOH, and -MAOH, the LIS of Me_{5c} is 1.60 times larger than for Me_3 and Me_{5t}, and "axial" methyls of **3c**. Similar trends are observed for the methylene protons for all of the trans alcohols.

Experimental Section

***cis*- and *trans*-3-(Aryl)-1,3,5,5-tetramethylcyclohexan-1-ols.** A mixture of approximately 60:40 cis (**3a**) to trans (**3c**) cyclohexanols was obtained in quantitative yield from the reaction (at reflux, for *ca.* 2 days) of the corresponding 3-(aryl)-3,5,5-trimethylcyclohexanone[3b] with excess ethereal methylmagnesium bromide. These isomers were cleanly separated by column chromatography on silica by elution with a 5% hexane–acetone mixture, the cis isomer eluting much more rapidly. Satisfactory combustion analyses were obtained for the alcohols.

All nmr spectra were run on a Varian HA-100 nuclear magnetic resonance spectrometer in the frequency sweep mode. Shifts were measured on carefully precalibrated chart paper and are estimated to be accurate to ±0.01 ppm or better. Temperature was varied using a standard Varian Associates variable-temperature probe and controller; the temperature was determined using methanol in the standard fashion.

The LSR used (unless otherwise noted) was europium(III) tris-1,1,1,2,2,3,3-heptafluoro-7,7-dimethyl-4,6-octanedione, denoted as $Eu(FOD)_3$. For comparison of LIS values from one compound to another, it is essential to use carefully purified LSR and to start with a very pure substrate (especially one dry and solvent free). In our experience, $Eu(FOD)_3$ supplied by Merck Sharp and Dohme is suitable. For each run, the LSR was sublimed *in vacuo* and stored for at least 24 hr over P_4O_{10} *in vacuo*. The solvent employed for all samples was molecular sieve dried CCl_4 or CS_2; the latter was used for the variable-temperature data (owing to the insolubility of the solutes in CCl_4 at lower temperatures). All substrates were stored over $CaSO_4$ or P_4O_{10} in a vacuum desiccator prior to use.

The method used in the LSR runs was the incremental dilution, constant S_0 technique described in detail by Shapiro and Johnston.[8] All regression analyses were performed on a Hewlett-Packard Model 9100B programmable calculator with ten significant figure precision. The fits were optimized in terms of maximizing the correlation coefficient, *R*.

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References and Notes

(1) Lanthanide-Induced Shifts in Proton Nuclear Magnetic Resonance Spectra. X. For Part IX, see ref 17.

(2) (a) Postdoctoral Fellow of The Robert A. Welch Foundation; (b) Predoctoral Fellow of The Robert A. Welch Foundation.

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Carbon-13 Nuclear Magnetic Resonance. Conformation in Some 1,3-Dioxacycloheptanes

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The carbon-13 nuclear magnetic resonance chemical shifts for some 1,3-dioxacycloheptanes are reported. The chemical shifts for the ring carbons are affected by the positions and conformations of the substituents. Substituent shift parameters can be transferred from 1,3-dioxanes and cycloheptanes to 1,3-dioxacycloheptanes. Bulky substituents in the 2, 4, and 7 positions of the 1,3-dioxacycloheptanes do little to reduce the number of available low-energy conformations.

Carbon-13 nuclear magnetic resonance is a potent tool for conformational analysis because carbon-13 chemical shift substituent parameters reflect both substituent and conformational effects. Appropriate substituent parameters can be obtained not only in cyclohexanes,[3] but also in cycloheptanes[4] and 1,3-dioxanes,[5] provided that the effects of oxygen substitution in the six-membered ring and of pseudo-rotation of the seven-membered ring are taken into account.

Encouraged by previous work,[3-5] we undertook a study of carbon-13 substituent effects in some 1,3-dioxacycloheptanes in an effort to extend the correlations to this ring system and to provide a basis for conformational assignment therein.

Conformational analysis of cyclohexane[6] and 1,3-dioxane[5] is facilitated by the absence of a low-energy pseudorotational barrier and the availability of only one low-energy conformation. The interpretation of conformational data for cyclopentanes,[7] 1,3-dioxolanes,[8] cycloheptanes,[4] and 1,3-dioxacycloheptane[1b] is made more difficult by the availability of numerous low-energy conformations and by the low-energy pseudo-rotational barriers for each of these compounds, with the result that in these systems one must think in terms of conformational arrays.

The geometry of 1,3-dioxacycloheptane has been discussed previously and comparisons were made with cyclohexanes, cycloheptanes, and 1,3-dioxanes:[1b] there are four distinct chair conformations for 1,3-dioxacycloheptane compared to one for each of the other compounds; the 1,3-COC distance is small owing to the shorter carbon–oxygen bond (compared to the CCC distance); 1,3-diaxial Me–H interactions are more severe (as in the 1,3-dioxanes)[9,10] than in cyclohexane and cycloheptane;[10] and the 4,7-diaxial Me–H interaction is more severe than that in cycloheptane. Accordingly, an additional objective of these studies was to test whether these more severe interactions could be used to advantage to produce compounds with only one or two low-energy conformations in the conformational array. Therefore the synthesis of 1,3-dioxacycloheptanes with a number of bulky substituents properly located to take advantage of the decreased 1,3-diaxial and 4,7-diaxial distances was undertaken.

The carbon-13 spectra were recorded at ambient temperatures at which the rates of interconversions of the conformations were fast. Therefore the chemical shifts are average values to which each of the conformations contributes according to its population.

The carbon-13 chemical shifts for a series of 1,3-dioxacycloheptanes are summarized in Table I. The assignments of the carbon-13 resonances were made on the basis of relative intensities, comparisons with chemical shifts for 1,3-dioxanes,[5,11] and comparison with values for 1,3-dioxacyclohept-5-ene.[1]

The chemical shift assignments are reasonably straightforward. The *tert*-butyl methyl carbons were readily distinguished from methyl groups substituted directly on the ring by signal intensity. The signal of the quaternary carbon of the *tert*-butyl group was distinguished from those for C_5 and C_6 by its reduced intensity.[12] The chemical shifts for C_5 and C_6 were readily assigned, since they were the only ones without parallel in the spectrum of 1,3-dioxacyclohept-5-ene. The signals assigned to C_2, C_4, and C_7 correspond to the chemical shifts for C_2, C_4, and C_6 in 1,3-dioxanes.

Some important generalizations may be drawn from Table I. The difference in geometry between a seven- and