Tetrahedron. Vol. 31, pp. 2125 to 2133. Pergamon Press 1975. Printed in Great Britain

LANTHANIDE INDUCED ^1H AND ^{13}C NMR SHIFTS AND THEIR USE FOR GEOMETRY ANALYSIS WITH ALICYCLIC COMPOUNDS[1]

H.-J. SCHNEIDER* and E. F. WEIGAND
Universität des Saarlandes, Fachrichtung Organische Chemie D66 Saarbrücken 11, Germany

(*Received in UK 2 April 1975; Accepted for publication 25 April 1975*)

Abstract—Based on computations with conformationally rigid substrates the ambiguities involved in the geometrical analysis of pseudocontact shifts are demonstrated. The minimal agreement factors R and the corresponding lanthanide positions (usually *more* than one) are extremely dependent upon the chosen structural data for the model substrate and on the errors of the experimental shift values. It is observed, that a difference or improvement of R factors of less than 3% is not significant in most cases. This is so, even on the basis of Ytterbium induced ^{13}C shifts, which are found to be more accurate than ^1H shifts and free from contact contributions within the experimental error. Using lanthanide induced shifts some ^{13}C signal assignment problems are discussed. The computed minima for five substituted norbornanols indicate a lanthanide position with an L...O distance of d = 2·5 Å for the secondary alcohols and an orientation avoiding gauche interactions with the two neighbouring C–C bonds. Similar computed results are obtained with five bicyclic ketones, except for an L...O distance from 3 to 4 Å increasing with steric hindrance. The particular problems with the analysis of symmetrical compounds like cyclohexyl derivatives are pointed out.

Numerous publications have been concerned with the application of lanthanide induced NMR shifts[2]† to the evaluation of molecular geometries in solution.[3] Comparatively little attention has been paid to the important question: which factors in this method could lead to an underdetermination of the analysis?[2d,4] Besides focusing on these points we wanted to explore the use of lanthanide induced ^{13}CMR shifts,[5] including some ^{13}C signal assignment problems.

Bicyclo(2.2.1)heptanes provide suitable models for testing the reliability of structural predictions based on LIS values.[6] Their geometry is well defined and the only conformational problem to be solved is the localisation of the lanthanide ion and its principal magnetic axis. Using mainly naturally occuring monoterpenoids bearing methyl groups in different positions, which drastically alter the steric environment of the OH-donor group,[7] we hoped to find well defined lanthanide positions which could then be applied to the analysis of substrates with flexible geometries.

Methods. Relative LIS values were obtained by incremental addition of weighed shift reagent (LSR) to substrates dissolved in $CCl_4/CDCl_3$ containing TMS and subsequent shift measurements by either PFT (^{13}CMR) or CW (^1HMR) technique. The slope (LIS) of shifts versus LSR concentration and its standard deviation were calculated using regression analysis programs. In a few cases, where small amounts of scavengers (e.g. stereoisomers) were detectable, LIS values were normalized to one particular observed nucleus X ($LIS_X \equiv 1{\cdot}00$). Extensive investigations[8] have shown that the standard procedure for evaluation of LIS is justified within certain experimental limits,[8b] referring mainly to concentrations, where only the LS_2 complex in equilibrium with free substrate S is observed. It is a particular advantage of ^{13}CMR measurements, that owing to the sharp lines in the ^1H-decoupled spectra accurate LIS can be obtained with molar LSR:S ratios of less than 0·10. In all cases straight lines were observed with correlation coefficients $r \geqq 0{\cdot}99$.

One of the major problems in LIS analysis that dictates the choice of the proper shift reagents are the contributions of contact shifts and, eventually, complex formation shifts.[2] We have used mainly $Eu(dpm)_3$ for ^1H and exclusively $Yb(fod)_3$ for ^{13}C measurements; for these reagents the predominance of dipolar pseudocontact shifts has aptly been demonstrated.[3a,9-11] A positive test for a pseudocontact shift mechanism is illustrated in Fig. 1, where for isoborneol ^{13}C shifts induced by $Pr(fod)_3$ (literature values[6b]) are plotted versus those induced by $Yb(fod)_3$. A linear correlation (r = 0·9898) is obtained although the contact shift power of Pr as compared to Yb is known to be 11:1·8.[9,11c] This ratio combined with the corresponding pseudocontact shift power ratio (=0·665) which is obtained from the slope of our plot allows the calculation of the contact contributions to observed LIS values. Even for the C1 in isoborneol, which is known to be particularly susceptible to contact shifts,[12] this

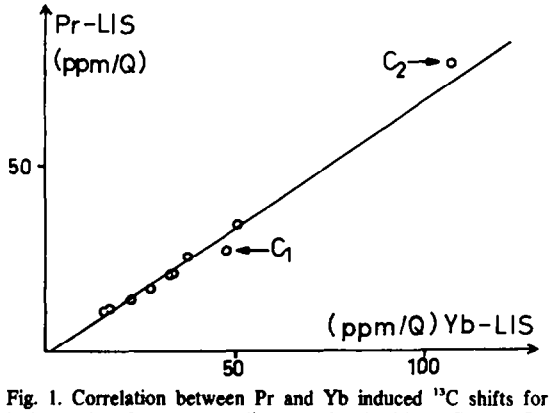


Fig. 1. Correlation between Pr and Yb induced ^{13}C shifts for isoborneol 1. Least square line calculated without C1 and C2. Similar results were obtained with norcamphor 6.

†*Abbreviations*: L, lanthanide ion; LSR, lanthanide shift reagent; S, substrate; dpm, dipivalomethanato; fod, heptafluordimethyloctanedionato; LIS, lanthanide induced shift (normalized for LSR:S = 1:1); r, linear correlation coefficient; n, number of experimental values; for other explanations see text and Fig. 2.

contribution is less than −1 ppm = 2% of the total LIS, whereas for C2 −6·2 ppm (6%) is calculated. Because of the ambiguity involved in an exact geometrical analysis (see below) we have not applied methods for the evaluation of contact contributions, which are based on deviations observed in the geometry analysis[5a,13] or comparison of L positions obtained by ^{1}H- and ^{13}C-measurements.[14] Although recent data[10] indicate more than 95% pseudocontact mechanism in the shifts induced by Yb(fod)$_3$ on functional carbons in saturated alcohols, we have *not* included these shifts in the following geometrical analysis.

Any complete description of the geometric factors involved with pseudocontact shifts should include a special term accounting for anisotropic magnetic fields, except for cases, where dynamic averaging generates axially symmetric fields.[15] Furthermore, it was pointed out, that a realistic procedure should allow for the presence of several lanthanide positions in the time averaged picture.[5a,16] The criterion and hence justification for considering both factors could lie in an improvement between observed and calculated shifts. We have omitted these factors, since in most cases acceptable solutions within the error limits (see below) were obtained based on the single term of the McConnell-Robertson equation with the geometry factor $G = (3\cos^2\theta - 1)\cdot r^{-3}$.

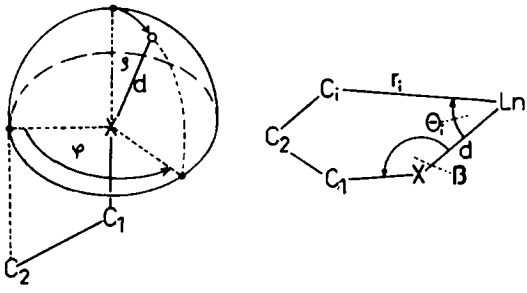


Fig. 2. Coordinates for variation of the L position and the geometry calculation ($\rho = 180° - \beta$; β, C1-X-L angle; X, donor atom; φ, torsional angle C2-C1-X-L; d, distance L...X; θ, C1-L-X angle).

We have written a program, similar to those used by other workers,[6a,17] that varies the lanthanide position around the donor atom in given limits and steps, generates and compares the G factors for each L-position with observed shifts in a least squares treatment and calculates statistical error quantities as standard deviation of shifts, correlation coefficient or Hamilton agreement factor R. These error quantities were parallel in most cases; for the sake of comparison with literature values the agreement factor R[6a] is always given. We found it necessary to introduce as an additional measure of reliability a value $\psi(\psi^2 = (1-r^2)n/(n-2)$, introduced into correlational chemistry by Exner[18]) since R tends to overestimate correlations based on few points (such as for highly symmetrical molecules). The program furnishes best R values for each L...O distance d and the corresponding $\rho(=180° - \beta)$ and φ angles (for one example see Table 1, other tables are available upon request). In one additional set of tables (not shown) all values with $R < (R_{Minimum} + 3\%)$ are printed in a ρ/φ matrix, which gives a semi-three-dimensional picture of "best" L-positions. It was necessary to vary d, ρ and φ first in steps of 0·2 Å and 5°, respectively, and then around the isolated minima in 1° steps.

Errors. Some of the possible pitfalls in the geometric analysis based on "fixed" substrate conformations will be demonstrated with the ^{13}C-LIS values of norcamphor (**6**). As different input for the basic geometry of the bicyclo(2.2.1)heptane skeleton we chose electron diffraction data of the hydrocarbon[19] (geometry **B**), an X-ray structure for 6 - endo - bromo - 5.5 - dimethyl - norbornanone - (2)[20] (geometry **A**, showing a slight "synchro-twist"[21] deformation) and X-ray data of 3-endo-bromocamphor[22] (geometry **C** with a "contra-twist"[21] deformation). The computed "best" lanthanide position in terms of the smallest agreement factor R, is found to depend drastically upon the arbitrarily chosen basic geometries A, B or C (Table 2). The numbers illustrate a frequently observed tendency to find "best" solutions with relatively small β angles by elongation of

Table 1. Dependence of agreement factor (R) on L position (d, β, φ); example: ^{1}H and ^{13}C-LIS analysis with exo-isofenchol **3**

	(^{1}H-LIS)			(^{13}C-LIS)		
d(Å)	β(°)	φ(°)	R(%)	β(°)	φ(°)	R(%)
2.0	135	262	8.2	134	270	5.2
2.2	130	261	7.5	130	271	3.9
2.4	127	261	7.7	127	273	3.1
2.6	129	265	8.7	123	273	3.3
2.8	131	273	9.6	120	266	4.1
3.0	131	276	10.4	116	251	4.5
3.2	132	272	11.4	112	241	4.3
3.4	135	263	12.2	108	235	3.7
3.6	141	238	12.6	104	232	3.3
3.8	139	198	12.6	101	232	3.4
4.0	130	178	12.4	97	233	3.8
4.2	137	198	13.3	93	234	4.4
4.4	141	217	14.0	90	235	5.2
4.6	142	226	14.7	87	236	6.0
4.8	142	230	15.3	84	236	7.0
5.0	141	233	15.9	81	237	8.1

Table 2. Dependence of agreement factor (R) and L position on model geometry (explanation see text)

	R (%)			L position		
	A	B	C	d(Å)	β(°)	φ(°)
1)	1.7	3.0	4.4	2.8	144	348
2)	~3.2	1.6	~3.8	3.6	129	276
3)	4.5	3.1	1.6	4.6	104	90
4)	-	1.7	-	3.0	142	300
5)	-	-	2.2	2.8	144	298

the L . . . O distance. If one does *not* rely upon the absolute smallest agreement factors R one finds solutions (≙ rel. minima in R) with similar L-Positions based on all three substrate geometries (see Table 2, line 4 and 5). The occurence of geometrically entirely different minima is, on our experience, a quite common feature in an LIS analysis.

An even more severe obstacle to unambiguous structural predictions can be seen in the errors of the experimental LIS values. Computation of minimal R factors for norcamphor, based (a) on the experimental LIS values, then on LIS values which are equally (b) enhanced or (c) diminished by the threefold LIS-standard deviation s_a ($+3s_a$ or $-3s_a$, respectively) show substantial differences in the "best" L position (Table 3). These differences are nearly prohibitive for any safe predictions if one allows for a systematic LIS deviation by (d) enhancing the higher LIS-values by $3s_a$ while lowering the smaller LIS-values by $3s_a$ or (e) the reverse of procedure (d). It should be noted that this example, which would render differences of R below 3% meaningless, is based on quite accurate ^{13}C-LIS measurements ($s_a = \pm 1\%$ to $\pm 3\%$). Literature data on experimental LIS errors are sparse, but some recent HMR data indicate LIS deviations of $\sim \pm 10\%$.[23]

An additional difficulty involved in the LIS analysis of flexible geometries lies in conformational changes following complexation.[24] The rejection of poor solutions on the basis of Hamilton R factor tests[25,26] requires for example for norcamphor a ratio of $R_x/R_{min} \geqq 2{\cdot}29$ or $R_x \geqq 3{\cdot}45\%$, if one wants to have a confidence level of at least 90%. Moreover, the proposed procedure with a dimension of only b = 1 is probably too liberal and the systematic errors discussed in this paper have to be taken into account.[25]

Bicyclo(2.2.1)*heptanols*-2. Five isomeric alcohols (1 to 5) were investigated using both Yb(fod)$_3$ induced ^{13}C shifts and Eu(fod)$_3$ induced ^1H shifts (Tables 4 and 5). ^1H signal assignments for 2–5[27] were obtained by decoupling experiments, and confirmed by comparison of coupling constants; isoborneol (1) ^{1}HMR data were taken from the literature.[6b] The original ^{13}C signal assignments for C1 and C7 in isoborneol (1)[28] have been debated,[14] but the criticism was based upon Eu induced shifts contaminated by contact contributions. The analysis with Yb induced shifts furnished agreement factors of 17·2% for the reversed[14] assignment, whereas R = 2% (ψ = 6·8%) was obtained for the original assignment,[28] which was supported by T1 measurements.[29] The 1-Me and the 7-*syn*-Me signals in 1 on the other hand can only be distinguished on the basis of T1 data,[29] since LIS analysis based on either assignment leads only to the too small R difference of between 2·0% and 3·95%, respectively. For similar reasons, the 5-*exo*/*endo*-Me ^{1}H-signals in exo-isofenchol (2) are not distinguishable by the LIS method (which in view of their similar LIS values has little influence on the subsequent geometry analysis). Further examples, where interchange of signal assignments does not alter either R values nor L positions significantly enough, are included in Tables 4 and 5.

The cartesian coordinates needed for the geometry computation were taken from electron diffraction data[19] for the skeleton; Me and OH groups were attached using standard geometries; Me proton coordinates were obtained as the center of the circle described by rotation around the C–Me bond.[6b,16b] The LIS geometry analysis with isoborneol (1) furnished the rather unique result of a single minimum for the L position, which is quite similar for both ^{1}H literature values[6b] and ^{13}C shifts (Table 6).

Table 3. Agreement factor R and L position as function of error in LIS (explanation see text)

	R (%)					L position*)		
	(d)	(b)	(a)	(c)	(e)	d(Å)	β(°)	φ(°)
	$+3s_a$ $-3s_a$	$+3s_a$	± 0	$-3s_a$	$-3s_a$ $+3s_a$			
1)	4.4	5.7	4.5	3.8	8.7	4.2	94	90
2)	7.3	1.3	2.3	4.0	3.1	4.6	100	90
3)	6.2	2.2	1.6	2.5	4.3	4.6	94	90
4)	5.7	3.4	2.2	1.9	5.5	4.6	90	90
5)	9.8	3.8	4.8	6.3	1.6	5.0	98	90

*) L-positions are chosen as similar as possible for the sake of comparison of R factors. A smaller R factor (3.7%) is observed in case (d) for another L position (d=2.8 Å, β=128°, φ=334°)

Table 4. ^{13}C shifts[a] and ^{13}C LIS values[b] for 1-5

		C-1	C-2	C-3	C-4	C-5	C-6	C-7			
									Me-1[#]	Me-7-syn[#]	Me-7-anti
Isoborneol	δ	48.96	79.39	40.57	45.12	27.44	34.07	46.36	20.22	11.44	20.61
1	LIS	48.02	107.78	50.74	28.52	17.20	22.48	33.63	33.48	37.46	15.92
	s_a[c]	2.6	1.1	3.0	1.2	6.9	4.0	1.6	6.6	1.4	4.0
									Me-1	Me-5-endo	Me-5-exo
exo-	δ	49.54	75.94	38.17	47.20	37.39	50.58	39.86	16.77	26.66	31.01
Isofenchol	LIS	71.05	156.44	69.78	40.77	24.81	31.58	50.44	55.64	12.40	14.23
2	s_a[c]	1.3	0.3	2.8	2.0	2.7	4.6	3.0	1.2	2.6	5.3
									Me-1	Me-5-endo	Me-5-exo
endo-	δ	49.61	76.20	35.31	48.18	37.65	43.71	44.02	19.38	26.14	31.79
Isofenchol	LIS	45.38	95.66	41.73	23.94	24.63	36.16	21.90	29.27	20.75	12.16
3	s_a[c]	1.8	2.1	2.5	2.8	3.0	1.9	1.5	1.9	1.9	3.6
									Me-2	Me-5-endo	Me-5-exo
endo-β-Fen-	δ	54.10	79.13	44.73	52.54	38.88	41.42	41.74	34.59	29.45	35.31
chenhydrate	LIS	47.66	110.90	48.27	26.60	23.49	28.96	30.03	59.59	17.36	9.98
4	s_a[c]	1.3	1.1	2.1	1.7	2.8	0.5	6.0	0.9	0.1	2.1
									Me-1[#]	Me-3-endo[#]	Me-3-exo
endo-	δ	49.33	84.81	39.32	48.23	26.32	25.28	41.27	19.63	20.47	30.87
Fenchol	LIS	46.98	96.05	41.48	24.00	23.00	34.11	23.00	27.92	34.11	18.06
5	s_a[c]	1.0	1.2	1.6	3.3	1.9	2.0	2.0	2.6	2.0	1.6

a) δ_{TMS} in (ppm). b) LIS in (ppm/Q), where Q=(Yb(fod)$_3$)/(Substrate); substrate concentration: ~1M, Yb(fod)$_3$ concentration from 0 to ~0.09M; solvent: CCl_4 + 10% TMS (standard) + 10% C_6F_6 (lock); 30°C. c) Standard deviation in LIS(%). [#]) Signals have possibly to be interchanged.

Table 5. ^1H shifts[a] and ^1H LIS values[b] for 2-5

	exo-Isofenchol 2		endo-Isofenchol 3		endo-β-Fen-chenhydrate 4		endo-Fenchol 5	
	δ	LIS	δ	LIS	δ	LIS	δ	LIS
H-1					-	-		
Me-1	1.15	16.0	1.05 [#]	9.2			1.1 [#]	10.4
H-2-exo			3.75	21.7			3.2	24.4
Me-2-exo					1.28	15.6		
H-2-endo	3.33	29.4						
H-3-exo	1.65	21.2	~1.6	7.9	~1.4[c]	9.2		
Me-3-exo							1.0 [#]	5.1
H-3-endo	~2.80[c]	~11.3	~1.4[c]	15.4	~1.7[c]	15.3		
Me-3-endo							0.8 [#]	11.0
H-4	1.65	8.0	~1.45[c]	5.2	~1.35[c]	5.5	~1.25[c]	4.9
H-5-exo							-	-
Me-5-exo	1.0 [#]	4.0	1.0	3.7	1.0[d]	3.2		
H-5-endo							-	-
Me-5-endo	1.0 [#]	3.2	1.03 [#]	6.6	1.08[d]	6.1		
H-6-exo	~1.2[c]	6.95	-	-	~1.1[c]	6.6	-	-
H-6-endo	~1.2[c]	5.8	~1.6[c]	15.7	~2.0[c]	14.7	~1.67[c]	14.8
H-7-syn	~1.35[c]	18.5	-	-	-	-	-	-
H-7-anti	~1.7[c]	9.0	-	-	-	-	-	-

a) δ_{TMS} in (ppm). b) LIS in (ppm/Q), where Q=(Eu(fod)$_3$)/(Substrate); substrate concentration 0.4M, Eu(fod)$_3$ concentrations from 0 to 0.14M; solvent: CCl_4 + 1% TMS, 40°C. c) From extrapolation of LIS to (LSR)=0. [#]) Signals have possibly to be interchanged. Missing signals were not unambiguously detectable at low LSR concentrations.

Table 6. Minimal agreement factors R and corresponding L positions for Bicyclo(2.2.1)heptanols 1-5 (Torsional angle φ: C3-C2-O-L)

		HMR[6b]	CMR		
1	d	2.5	2.6		(Å)
	β	130	132		(°)
	φ	277	246		(°)
	n	11	9		
	R	4.5	2.1		(%)
	ϕ	-	6.8		(%)
		HMR	CMR		
			a	b	
2	d	2.2	2.4	3.6	(Å)
	β	130	127	105	(°)
	φ	261	273	232	(°)
	n	11	9	9	
	R	7.5	3.2	3.4	(%)
	ϕ	15.2	7.9	8.4	(%)
		HMR	CMR		
			a	b	
3	d	3.0	2.6	4.4	(Å)
	β	130	123	95	(°)
	φ	76	70	138	(°)
	n	8	9	9	
	R	6.3	5.5	4.5	(%)
	ϕ	14.4	17.7	16.1	(%)
		HMR	CMR		
			a	b	
4	d	3.8	3.4	2.4	(Å)
	β	122	115	154	(°)
	φ	101	83	212	(°)
	n	8	9	9	
	R	7.2	14.5	10.3	(%)
	ϕ	20.3	41.5	25.8	(%)
		HMR	CMR		
			a	b	
5	d	2.4	2.6	4.2	(Å)
	β	168	155	91	(°)
	φ	287	60	140	(°)
	n	6	9	9	
	R	14.2	6.6	6.7	(%)
	ϕ	35.1	26.4	27.7	(%)

However, inspection of extensive tabulations of R as a function of d, φ and ρ (not shown) discloses a very flat minimum[6a]; e.g. R < 5% is observed for 2·0 Å < d < 3·8 Å with φ and β angles between 235°...256° and 140°...104°, respectively. Analysis with *exo*-(2) and *endo*-isofenchol (3) yields one distinct minimum only on the basis of ^1H shifts, whereas the more accurate ^{13}C shifts show the presence of two minima (Tables 1 and 6). The second minimum can only be excluded, if one assumes similar steric requirements[3a,30] for Eu(fod)$_3$ and Yb(fod)$_3$.

With ^1H shifts of β-fenchene hydrate (4) only one good minimum is obtained, whereas the ^{13}C values indicate a second minimum at a sterically less favourable position (Table 6). Although ^1H analysis suffers in this case from less accurate LIS and signal assignments, which on the basis of significance tests of the R-factors[25,26] are not conclusive, the results suggest a substantially longer

Table 7. ^{13}C shifts[a] and ^{13}C LIS values[b] for 6–10

		C-1	C-2	C-3	C-4	C-5	C-6	C-7			
Norcamphor	δ	49.73	216.94	45.12	35.37	27.24	24.18	37.64			
6	LIS	59.2	151.5	60.9	30.0	23.0	23.7	32.2			
	s_a[c]	1.7	0.7	1.2	1.5	3.5	2.1	2.9			
									Me-5-exo	Me-5-endo	
8-Fencho-	δ	52.09	216.76	41.37	46.47	36.10	37.27	41.21	31.13	26.58	
Camphorone	LIS	2.008	5.102	1.986	1.023	0.776	1.000	1.102	0.359	0.556	
7	s_a[c]	0.9	0.6	0.3	0.7	2.0	--	1.3	2.0	1.8	
									Me-3-exo	Me-3-endo	
Camphenilone	δ	50.08	221.80	46.89	46.21	23.24	24.57	35.06	23.33	21.51	
8	LIS	1.572	3.840	1.474	0.782	0.592	0.810	0.755	0.934	1.000	
	s_a[c]	0.9	0.5	0.3	0.3	1.4	1.1	1.2[d]	1.7	--	
									Me-7-syn	Me-7-anto	Me-1
Camphor	δ	57.39	218.06	43.09	43.16	27.10	29.93	46.63	19.72	19.14	9.26
9	LIS	58.4	154.8	64.3	30.5	21.8	33.3	32.1	24.2	14.4	40.0
	s_a[c]	0.8	0.9	1.0	1.6	1.1	1.3	1.2	2.0	1.7	0.7
		C-1	C-2	C-3	C-4	C-5	C-6	C-7			
									Me-3-exo	Me-3-endo	Me-1
Fenchone	δ	53.95	222.00	47.22	45.33	25.00	31.82	41.62	23.33	21.68	14.62
10	LIS	1.585	3.694	1.585	0.815	0.627	0.858	0.814	0.936	1.000	0.934
	s_a[c]	1.4	0.7	0.8	0.2	0.5	1.3	0.3	1.0	--	0.8

Explanations see footnotes to table 4

L...O distance d for this *tertiary* alcohol. The very limited ^1H shifts of *endo*-fenchol **5** (Table 4) yields values of R < 10% only for L...O distances d > 4·4 Å. ^{13}C shifts (Table 5) lead to more realistic L positions (Table 6), although application of the basic symmetric coordinates[19] might not be justified in this case.

In summary, the most probable L-positions indicate, that in the secondary alcohols the L ion approaches the O donor atom to ~2·5 Å.[31] The L ion is found to be as close as 2 Å to the van der Waals radii of neighbouring groups. The effects of Me groups, particularly in the 1 and the 7-*syn* positions on φ and β seem to follow the principle of least steric hindrance,[6a,6b,6c,30] and the LSR complex consistently avoids positions which are gauche to both the C2–C1 and C2–C3 bonds.

Bicyclo(2.2.1)*heptanones*-(2). Yb(fod)$_3$ induced ^{13}C shifts (Table 7) were analyzed for five bicyclic substrates (**6–10**, Table 8) with a varying steric environment around the CO group. The basic geometry of the norbornyl substrate was obtained in the same way as described for the alcohols, since available structural data[20,22,33] indicate only minor geometry distortions upon introduction of carbonyl groups into an sp^3 carbon framework.

With the least hindered norcamphor (**6**, Table 7) one minimum is found for an L position with d = 3 Å, and two other minima with longer distances, the latter essentially coexisting, as inspection of the detailed R = f(d, ρ, φ) tables reveals. The last two minima were not reported in an ^1H-LIS literature analysis[6c] and, in view of the results with compound **7** are probably computational artifacts. The ^{13}C spectrum of β-fenchocamphorone (**7**) poses some interesting assignment problems. The analysis for C1 to C5 was straightforward using off resonance decoupling, specific deuteration at C3 and shift rules. Literature shift increments[28a] predict C7 to resonate at substantially higher field than C6; the R significance test[26] with the observed LIS values gave only a probability for rejection of this assignment of 90–95%, but the corresponding distance d = 2·0 Å is unrealistically small. The geometry computation with the revised C6/C7 values (Table 8) gives, as with structure **6**, a minimum at long distance (as usual at the expense of a small C-O-L β angle, see p. 2126 with an *exo* orientation to the bicycloheptane; but the more realistic minimum lies at 2·8Å distance (Table 7).

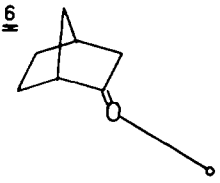
The literature·assignment[33] for C5 and C6 in camphenilone (**8**) has to be reversed in view of an LIS R factor improvement from 9·65% to 4·27%. From the computed three minima (Table 7) the one at 2·2 Å distance can be disregarded as being too short compared with X-ray data;[31] the other two could be interpreted so as to reflect an equilibrium between *exo* and *endo* orientation. These ambiguities, which may have their origin in different populated L orientations, but which cannot be resolved by the LIS method show up even more in the geometry analysis of camphor **9**, which arrives at four different minima (Table 7), one of which resembles the only L position cited in an ^1H LIS literature[6c] analysis. Again, for fenchone (**10**) (Table 7) the minimum at d = 2·4 Å can only be excluded as being too short for this most hindered ketone.

Ketones might be expected to lead to better defined L positions, since the electron donating orbitals are geometrically fixed, as opposed to C–O single bonds in alcohols. In fact, the most acceptable L positions for the ketones are found nearly perpendicular to the C3-C=O plane (mostly on the endo side). The effective L...O distance seems to increase from 2·8 to almost 4 Å with increasing steric hindrance.[6c] In view of the many minima found particularly with the carbonyl compounds these conclusions are considered to be only tentative.

Cyclohexyl derivatives. The geometry analysis with symmetrical compounds like 4-t-butylcyclohexanone (**11**) or the methyl ether (**12**) (LIS values Table 9) can proceed by either (a) counting nuclei, which are identical by

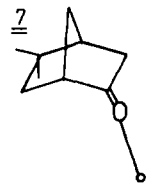
Table 8. Minimal agreement factors R and corresponding L positions for Bicyclo(2.2.1)heptanones **6–10** (Torsional angle φ: C3-C2-O-L)

6



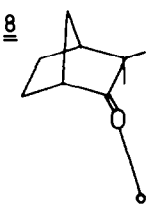
	CMR a	b	c	
d	3.0	3.6	4.4	(Å)
ß	142	129	104	(°)
φ	300	278	88	(°)
n	6	6	6	
R	1.7	1.6	1.7	(%)
ϕ	6.3	5.9	6.2	(%)

7



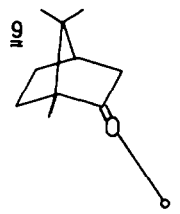
	CMR a	b	
d	2.8	4.8	(Å)
ß	148	91	(°)
φ	234	91	(°)
n	8	8	
R	1.0	3.5	(%)
ϕ	2.4	8.4	(%)

8



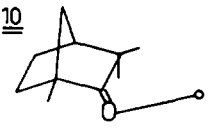
	CMR a	b	c	
d	2.2	3.4	3.6	(Å)
ß	169	124	128	(°)
φ	156	104	244	(°)
n	8	8	8	
R	4.3	4.3	4.3	(%)
ϕ	16.7	16.9	16.1	(%)

9



	CMR a	b	c	d	
d	2.4	3.2	4.0	4.4	(Å)
ß	164	127	114	110	(°)
φ	322	12	283	73	(°)
n	9	9	9	9	
R	6.6	5.0	4.6	4.6	(%)
ϕ	19.5	14.8	13.5	13.7	(%)

10



	CMR a	b	
d	2.4	3.4	(Å)
ß	180	124	(°)
φ	-	92	(°)
n	9	9	
R	3.4	4.5	(%)
ϕ	13.6	17.7	(%)

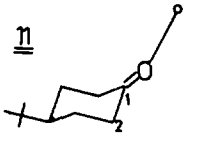
symmetry, independently (e.g. six signals for the ring carbons) or (b) only the effectively measured LIS (e.g. four signals for the ring carbons). Procedure (a) necessarily leads to L positions in a plane dissecting the ring (Table 10), whereas (b) can generate asymmetric positions, as cited in the literature.[11b] Furthermore, (a) and (b) can furnish quite different values for R, d and β. Our computation on **11**, based on structural data from the literature,[34,35] and following procedure (a) indicated R values below 2·1% for distances ranging from 2·0 to 5·0 Å. It is noteworthy, that for the realistic distances d < 3 Å (*cf* ketones **6** to **10**) only one orientation is obtained, which avoids gauche interaction with the C_α–C_β bonds; a similar situation holds for the ether **12** (Table 10).

Table 9. NMR shifts and LIS values for cyclohexyl derivatives 11 and 12

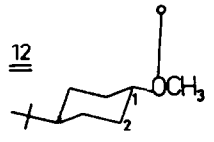
		H-2,6 a	H-2,6 e	H-3,5 a	H-3,5 e	H-4 a	t-Bu	
4-t-Butylcyclohexanone	δ	~2.6	~2.8	~1.6	~2.1		0.9	
11 $^1H_{MR}$[a]	LIS	27.98	38.13	17.51	11.99		4.57	
	$*_a$	1.9	1.8	7.2	5.3		1.4	
		C-1	C-2,6	C-3,5	C-4	C-7	C-8,9,10	
4-t-Butylcyclohexanone	δ	208.19	46.88	32.44	96.23	40.96	27.63	
11 $^{13}C_{MR}$[b]	LIS	141.3	57.02	26.54	20.39	9.46	5.60	
	$*_a$	0.4	1.1	1.8	3.3	4.8	6.1	
		-O-CH_3	C-1	C-2,6	C-3,5	C-4	C-7	C-8,9,10
cis-4-t-Butylcyclo-	δ	55.08	74.13	29.80	21.09	47.93	32.79	27.59
hexylmethylether	LIS	0.509	0.578	0.379	0.375	0.246	0.151	0.111
12 $^{13}C_{MR}$[c]	$*_a$	1.0	2.2	1.3	2.3	1.7	6.4	5.8

a) Concentrations: substrate (S)=0.31M, $(Yb(fod)_3)$=0 to 0.085M; 27°C. b) (S)=3.45M, $(Yb(fod)_3)$=0 to 0.24M; 30°C. c) (S)=1.1M, $(Yb(fod)_3)$=0 to 0.15M; -80°C. Other explanations see footnotes to tables 4 and 5.

Table 10. Minimal agreement factors R and corresponding L positions for cyclohexyl compounds 11 and 12 (Torsional angle φ: C2-C1-O-L)



		HMR	CMR a	CMR b	
d		2.8	2.4	5.0	(Å)
s		164	159	91	(°)
e		270	270	90	(°)
n		9	6	6	
R		3.2	0.3	1.4	(%)
Φ		8.9	0.8	3.7	(%)



	CMR a	CMR b	
d	3.8	4.6	(Å)
s	95	118	(°)
e	241	61	(°)
n	6	6	
R	1.6	3.1	(%)
Φ	3.8	7.5	(%)

EXPERIMENTAL

60-MHz HMR spectra were measured on Varian instruments A60 and EM360 (decoupling experiments). 22·63 MHz ^{13}CMR spectra were recorded on a Bruker HX90 spectrometer connected to a Nicolet 1080 computer; digital resolution was 0·06 or 0·03 ppm. Calculations were carried out using a FORTRAN IV program on the Telefunken TR440 of the Rechenzentrum der Universität des Saarlandes.

Solvents were dried prior to use over NaOH or molecular sieve; shift reagents were used as purchased. The bicyclic alcohols and ketones were obtained as described previously[27] or were commercial products: their purity was checked by GLC and improved by recrystallization or sublimation, if necessary. 4-*trans*-t-butyl-cyclohexanol was obtained 99·5% pure from the commercial stereoisomeric mixture by column chromatography on neutral Al_2O_3; the corresponding ether (12) was prepared (97% pure by GLC) by reaction of 1 g alcohol and 0·2 g $BF_3 \cdot OEt_2$ in 20 ml Et_2O with a tenfold excess of CH_2N_2 in 100 ml Et_2O.[36]

Acknowledgements—This investigation was supported by the Deutsche Forschungsgemeinschaft and the Fonds der Chemischen Industrie. We thank Dr. C. J. Liddiard for help with the preparation of the manuscript.

REFERENCES

[1] ^{13}C-NMR spectroscopic and stereochemical investigations, Part IX. Part VIII: H.-J. Schneider, W. Freitag and M. Schommer, *J. Magn. Resonance* in press.

[26a] R. E. Sievers, (Editor), *NMR Shift Reagents*. Academic Press, New York (1973); [b] A. F. Cockerill, G. L. O. Davies, R. C. Harden and D. M. Rackham, *Chem. Rev.* **73**, 553 (1973); [c] B. C. Mayo, *Chem. Soc. Rev.* **2**, 49 (1973); [d] W. DeW. Horrocks, Jr, In *NMR of Paramagnetic Molecules*, (Edited by G. N. La Mar), Academic Press, New York (1973); [e] R. von Ammon and R. D. Fischer, *Angew. Chem.* **84**, 737 (1972); *Int. Ed.* **11**, 675 (1972).

[36a] C. D. Barry, J. A. Glasel, A. C. T. North, R. J. P. Williams and A. V. Xavier, *Nature* **232**, 236 (1971); [b] G. Montaudo, V.

Librando, S. Caccamese and P. Maravigna, *J. Am. Chem. Soc.* **95**, 6365 (1973); [c]K. L. Williamson, D. R. Clutter, R. Emch, M. Alexander, A. E. Burroughs, C. Chua and M. E. Bogel, *J. Am. Chem. Soc.* **96**, 1471 (1974); [e]K. L. Servis and D. J. Bowler, *J. Am. Chem. Soc.* **97**, 80 (1975); [f]C. G. Andrieu, B. Lemarié and D. Paquer, *Org. Magn. Res.* **6**, 479 (1974).

[4]M. R. Willcott and R. E. Davis in Ref. 2[a], p. 159.

[5a]J. D. Roberts, G. E. Hawkes, J. Husar, A. W. Roberts and D. W. Roberts, *Tetrahedron* **30**, 1833 (1974); [b]J. Briggs, F. A. Hart, G. P. Moss and E. W. Randall, *Chem. Comm.* 364 (1971); [c]H. Kessler and M. Molter, *Angew. Chem.* **86**, 553 (1974); [d]W. B. Smith, D. L. Deavenport, J. A. Swanzy and G. A. Pate, *J. Magn. Res.* **12**, 15 (1973).

[6a]M. R. Willcott, R. E. Lenkinski and R. E. Davis, *J. Am. Chem. Soc.* **94**, 1742 (1972); [b]G. E. Hawkes, D. Leibfritz, D. W. Roberts and J. D. Roberts, *J. Am. Chem. Soc.* **95**, 1659 (1973); [c]P. V. Demarco, B. J. Cerimele, R. W. Crane and A. L. Thakkar, *Tetrahedron Letters* 3539 (1972).

[7]H.-J. Schneider, *J. Am. Chem. Soc.* **94**, 3636 (1972); H,-J. Schneider and R. Hornung, *Liebigs Ann. Chem.* 1864 (1974); *R. J.* Ouellette, G. E. Booth and K. Liptak, *J. Am. Chem. Soc.* **87**, 3436 (1965).

[8a]Ref. 2[a], p. 231, 313, 341; [b]B. L. Shapiro and M. D. Johnston, Jr., *J. Am. Chem. Soc.* **94**, 8185 (1972).

[9]H. Kessler and M. Molter, *Angew. Chem.* **86**, 552 (1974).

[10]K. Ajisaka and M. Kainosho, *J. Am. Chem. Soc.* **97**, 330 (1975).

[11a]J. Reuben, *J. Magn. Res.* **11**, 103 (1973); [b]D. J. Chadwick and D. H. Williams, *Chem. Comm.* 128 (1974); [c]C. M. Dobson, R. J. P. Williams and A. V. Xavier, J. C. S. Dalton 2662 (1973); [d]O. A. Gansow, P. A. Loeffler, R. E. Davis, M. R. Willcott and R. E. Lenkinski, *J. Am. Chem. Soc.* **95**, 3389 (1973).

[12]Ref. 2[a], p. 129.

[13]Ref. 2[a], p. 143.

[14]O.A. Gansow, M. R. Willcott and R. E. Lenkinski, *J. Am. Chem. Soc.* **93**, 4295 (1971).

[15a]Ref. 2[a], p. 319; [b]J. M. Briggs, G. P. Moss, E. W. Randall and K. D. Sales, *Chem. Comm.* 1180 (1972); [c]R. E. Cramer, R. Dubois and K. Seff, *J. Am. Chem. Soc.* **96**, 4125 (1971); [d]W. DeW. Horrocks, Jr., *J. Am. Chem. Soc.* **96**, 3022 (1974).

[16a]Ref. 2[a], p. 313; [b]R. M. Wing, J. J. Uebel and K. K. Andersen, *J. Am. Chem. Soc.* **95**, 6046 (1973); [c]G. Montaudo, S. Caccamese, V. Librando and P. Maravigna, *Tetrahedron* **29**, 3915 (1973).

[17]A. J. Rafalski, J. Barciszewski and M. Karonski, *J. Mol. Struct.* **19**, 223 (1973).

[18]O. Exner, In *Advances in Linear Free Energy Relationships* (Edited by N. B. Chapman and J. Shorter), p. 18 Plenum Press, New York (1972).

[19]J. F. Chiang, C. F. Wilcox, Jr. and S. H. Bauer, *J. Am. Chem. Soc.* **90**, 3149 (1968).

[20]P. P. Williams, *Acta Cryst.* **B25**, 409 (1969).

[21]C. Altona, In *Conformational Analysis* (Edited by G. Ghiurdoglu), Academic Press, New York (1971).

[22]F. H. Allen and D. Rogers, *J. Chem. Soc.* (B), 632 (1971).

[23]B. A. Levine, J. M. Thornton and R. J. P. Williams, *Chem. Comm.* 669 (1974).

[24a]H. Kessler and M. Molter, *Angew. Chem.* **85**, 1059 (1973); [b]R. A. Fletton, G. F. H. Green and J. E. Page, *Chem. Comm.* 1134 (1972); [c]A. Tangermann and B. Zwanenburg, *Tetrahedron Letters* 5195 (1973); [d]T. P. Forrest, D. L. Hooper and S. Ray, *J. Am. Chem. Soc.* **96**, 4286 (1974); [e]J. Bouquant, M. Wuilmet, A. Maujean and J. Chuche, *Chem. Comm.* 778 (1974); [f]A. Zschunke, A. Hauser, H. Oehme and J. Tauchnitz, *Org. Magn. Res.* **6**, 568 (1974).

[25]W. C. Hamilton, *Acta Cryst.* **18**, 502 (1965).

[26]R. E. Davis and M. R. Willcott, *J. Am. Chem. Soc.* **94**, 1744 (1972).

[27]For compound **4** compare: H.-J. Schneider, N. C. Franklin and W. Hückel, *Liebigs Ann. Chem.* **745**, 1 (1971).

[28a]E. Lippmaa, T. Pehk, J. Paasivirta, N. Belikova and A. Platé, *Org. Magn. Res.* **2**, 581 (1970); [b]H.-J. Schneider and W. Bremser, *Tetrahedron Letters*, 5197 (1970).

[29]G. C. Levy and R. A. Komoroski, *J. Am. Chem. Soc.* **96**, 678 (1974).

[30]J. Briggs, F. A. Hart and G. P. Moss, *Chem. Comm.* 1506 (1970).

[31]W. F. Wagner *et al.*, *Inorg. Chem.* **6**, 499 (1967); *Ibid.* **7**, 2295 (1968); *Ibid.* **8**, 22 (1969).

[32]R. A. Alden, J. Kraut and T. G. Traylor, *J. Am. Chem. Soc.* **90**, 74 (1968).

[33]J. B. Grutzner, M. Jautelat, J. B. Dence, R. A. Smith and J. D. Roberts, *J. Am. Chem. Soc.* **92**, 7107 (1970).

[34]J. C. Tai and N. L. Allinger, *J. Am. Chem. Soc.* **88**, 2179 (1966).

[35]E. M. Engler, J. D. Andose and P. von R. Schleyer, *J. Am. Chem. Soc.* **95**, 8005 (1973).

[36]W. Hückel and J. Kurz, *Liebigs Ann. Chem.* **645**, 194 (1961).