(7) Using different samples of $[Rh(CO)_2Cl]_2$ the yields of isolated products in the stoichiometric experiments varied from 65 to 90% in the case of **5** and from 30 to 87% in the case of **10**. The reason for this difference is unknown to us. The catalytic processes using CO pressure, however, always afforded almost quantitative yields of **5** and **10**.

(8) The evolution of some free CO was also observed (ir 2270 cm^{-1}). The presence of an absorption at 1850 cm^{-1} remains unexplained.

(9) (a) H. C. Volger, H. Hogeveen, and M. M. P. Gaasbeek, *J. Am. Chem. Soc.*, **91**, 218 (1969); (b) P. G. Gassman and J. A. Nikora, *J. Organomet. Chem.*, **92**, 81 (1975).

(10) R. F. Heldeweg and H. Hogeveen, *J. Am. Chem. Soc.*, **98**, 2341 (1976).

(11) Isolation and purification by column chromatography (Al_2O_3/hexane). ^1H NMR ($CDCl_3$; 35 °C) δ 2.16 (s, 6 H), 2.18 (s, 6 H), 3.60 (s, 2 H); ^{13}C NMR ($CDCl_3$ 35 °C; δ relative to internal Me_4Si; noise decoupled) δ 15.6, 16.0, 16.5, 17.0, 33.3, 116.7, 119.0, 120.5, 129.6, 130.3, 135.9, and 174.7; ir (Nujol mull): 1800 cm^{-1}; MS: M^+ peak at *m/e* 190. Anal. Calcd for $C_{12}H_{14}O_2$: C, 75.76; H, 7.42. Found: C, 75.82; H, 7.50. Mp 143.5–144.5 °C.

(12) G. R. Sprengling, *J. Am. Chem. Soc.*, **74**, 2937 (1952).

(13) H. E. Holmquist, *J. Org. Chem.*, **34**, 4164 (1969).

(14) When **3** was heated in *o*-dichlorobenzene in the presence of $[Rh(CO)_2Cl]_2$ to 150 °C a reaction did take place. The obtained mixture was not examined further, however, because of its complexity.

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Received March 29, 1976

Structure Elucidation with Lanthanide-Induced Shifts. The Use of Bound Shifts and High-Symmetry Substrates

Sir:

Nuclear magnetic resonance spectroscopy has become a basic and essential structural tool during the past 20 years. Hinckley's discovery[1] of lanthanide-induced shifts (LIS), which are a function[1,2] of molecular geometry, suggested the possibility that the NMR technique might develop into a liquid state structure elucidation method as powerful as solid-state crystallographic techniques. Unfortunately, this possibility has not yet been realized.[3,4] We report here an experimental and computational approach which we believe represents a major advance in the use of LIS as a rigorous method for structure determination. Not only do we obtain experimental NMR data which are in excellent agreement with molecular structure, but we can now for the first time accurately predict the LIS behavior of a substrate independently of the experimental data for a particular compound. Since no adjustable parameters are involved, the comparison between calculated and experimental LIS provides a far more accurate and reliable assessment of a proposed structure than has been available previously.

The problems involved in structural interpretations of LIS are most easily discussed in terms of a simplified form of the pseudocontact equation[1-4] such as given below:

$$\Delta\delta_i = k(3\cos^2\theta_i - 1)/r_i^3 \qquad (1)$$

This is for a hypothetical lanthanide shift reagent (LSR) substrate complex such as illustrated in Figure 1. Thus, the induced shift, $\Delta\delta_i$, depends on: (1) r_i, the distance between the metal ion and the nucleus of interest, (2) θ_i, the angle subtended by the line connecting the metal ion and the observed nucleus and the line representing the LSR magnetic axis (assumed here to be equivalent to the bond between the lanthanide ion and the heteroatom X), and (3) a constant, k, which should be a characteristic property of the particular LSR.

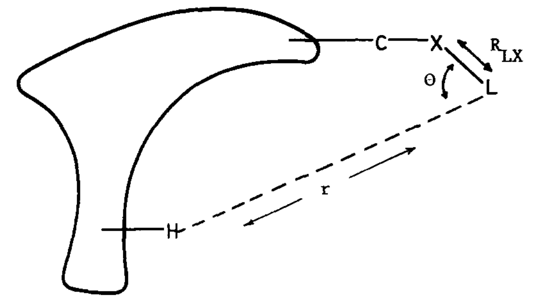


Figure 1. Representation of the geometric relationship between the lanthanide ion L and a hydrogen atom in terms of distance and angle from the magnetic axis for a complex of an organic substrate where X is the binding site.

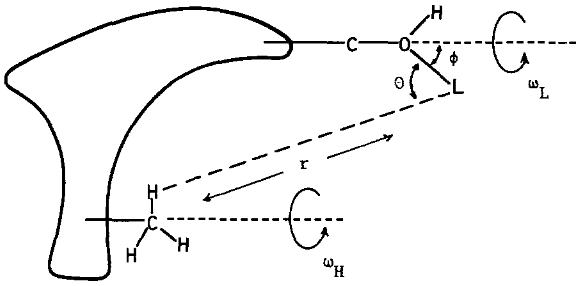
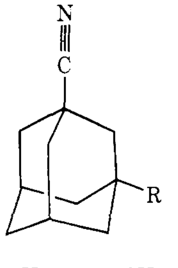


Figure 2. Representation of the geometric relationships in a complex of an alcohol in which conformational flexibility is available for both the lanthanide ion (ω_L) and for a hydrogen of interest on the organic substrate (ω_H).

The difficulty in applying eq 1 lies in the fact that, of the four parameters, only $\Delta\delta_i$ is measured directly; even here most workers have utilized relative shifts for LIS.[4-9] The problems associated with estimating values for r_i and θ_i can be seen in Figure 2, which illustrates the case of a complex with an alcohol. In order to obtain values of θ_i and r_i it is necessary to specify the geometric coordinates of both the metal ion and the observed nucleus relative to the oxygen atom. However, the bond length R_{LX} and the C–X–L bond angle are both unknown as is ω_L, the angle of rotation about the carbon-oxygen bond. Similarly, it may be difficult to specify the exact location of the observed proton. While bond angles and bond lengths for organic molecules can be estimated with reasonable accuracy,[10] one cannot ignore the different available conformations (i.e., the appropriate value or values of ω_H). Earlier workers have used a variety of unjustified simplifications and most commonly have treated these "constants" as variable parameters in their shift optimizations.[4]

We have attempted to overcome these difficulties by careful selection of substrates, observed shifts, and experimental and computational methods. In order to reduce uncertainty in the location of the lanthanide ion, we have turned to substrates in which the metal ion should lie on the line defined by the C–X bond: it is therefore possible to specify that $\phi = 0$; ω_L no longer has any relevance. Thus, three parameters have been reduced to one, and only the L–X bond distance (R_{LX}) need be considered. We have also attempted to reduce the other problem shown in Figure 2 (i.e., conformational mobility of the organic moiety as illustrated by ω_H) by turning to conformationally restricted molecules. We further decided to utilize substrates with a high degree of symmetry in order to simplify analyses of spectra and structural computations. The compounds which



1, R = H; **2**, R = CH_3
3, R = C_2H_5; **4**, R = *i*-C_3H_7

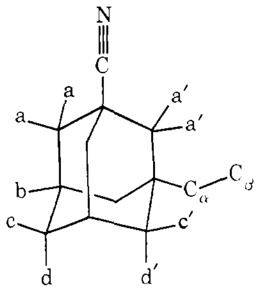


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Table I. Calculated and Observed Values of Bound Shifts (Δ_1) for 3-Alkyl-1-adamantanecarbonitriles Complexed with Eu(fod)$_3$[a,b]

H	Calcd[c]	**1** (R = H)[d]	**2**(R = CH$_3$)[d]	**3**(R = C$_2$H$_5$)[d]	**4**(R = *i*-C$_3$H$_7$)[d]
a	8.25	8.20	8.23	8.17	8.46
a′	8.25	—	8.25	8.16	8.45
b	3.17	3.18	3.23	3.20	3.34
c	3.40	3.33	3.41	3.38	3.49
c′	3.40	—	3.39	3.35	3.46
d	2.54	2.46	2.48	2.48	2.55
d′	2.54	—	2.50	2.47	2.55
α	2.21[e] (2.21)[f]	—	2.20	2.19	2.28
β	1.55[e] (1.81)[f]	—	—	1.56	1.60

[a] All studies were conducted with 0.2 M substrate in CCl$_4$ containing 1% Me$_4$Si. Spectra were obtained on a Varian A-60 NMR spectrometer operating at 60 MHz. The chart paper was carefully calibrated, and accuracies in shifts were assured by use of audio sidebands. Samples were prepared by the incremental dilution technique described in ref 12a. [b] Shifts are in parts per million. [c] From eq 1 using $k = 7.60 \times 10^2$, $R_{LN} = 1.89$ Å, and SGM coordinates (ref 10). [d] Observed values of Δ_1 were obtained independently for each compound using the LISA2 computer program (ref 12b). [e] Calculated using coordinates based on 2,2,3,3-tetramethylbutane (ref 16). [f] Calculated using SGM coordinates (ref 10).

meet these criteria and which we have used to initiate our studies are the 3-alkyl-1-adamantanecarbonitriles (**1–4**).[11]

A key feature of our approach has been to use *absolute*, rather than *relative*, values for the induced shifts; this, in turn, allows us to obtain specific and reproducible values for both k and R_{LN}. The magnitudes of the LIS were obtained by nonlinear regression analysis[12] of the NMR data which allows isolation of the shift components arising from the various species present in solution.[12,13] The observed shifts are the weighted averages (eq 4) of the shifts for the species indicated in the equilibria of eq 2 and 3 (where L = LSR and S = substrate; [S$_0$] is the total concentration of substrate in all forms).

$$L + S \overset{K_1}{\rightleftharpoons} LS \tag{2}$$

$$LS + S \overset{K_2}{\rightleftharpoons} LS_2 \tag{3}$$

$$\delta = \delta_0 + \frac{[LS]}{[S_0]}\Delta_1 + \frac{2[LS_2]}{[S_0]}\Delta_2 \tag{4}$$

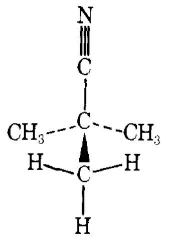
We have restricted our analyses to the LS species (thus using the bound shift, Δ_1)[12] because it is only this complex which can reasonably be expected to possess (or at least closely approximate[9]) the axial symmetry assumed in eq 1. The actual approach used involves the separate analysis of the Eu(fod)$_3$-induced shift of each proton in a substrate (cf. structure **5**) to obtain the corresponding values of Δ_1, Δ_2, K_1, and K_2. Parameterization of eq 1 was then accomplished by independent analysis of the adamantane skeletal protons of **1–4** to afford values of k and R_{LN} for each compound. The mean values of these parameters ($k = 7.60 \times 10^2$; $R_{LN} = 1.89$ Å) were then used in the subsequent predictions for Δ_1 values of *all* protons for a given substrate. These results are summarized in Table I together with the Δ_1's determined independently for each compound. Clearly the agreement between calculated and experimental values is very good.

We next turned our attention to the side chains of **2–4**. Since no single conformation of the side chain should be preferred, the predicted LIS for a particular proton was calculated as the arithmetic mean of the LIS for each available (*stable*) orientation.[14] While we were able to accurately predict the LIS for the α-protons, the errors incurred for the β-protons were substantial. Careful consideration of structures **3** and **4** indicates that the β-methyl groups have no conformations available which alleviate the gauche interactions with the methylene groups of the adamantane moiety; relief of these steric interactions should be manifested as deformations in bond angles and bond lengths.[15] Based on the structure calculated by Allinger for 2,2,3,3-tetramethylbutane,[16] we revised the geometric coordinates for the side chains of **3** and **4** accordingly. With this correction the agreement between predicted and observed shifts is excellent.

Table II. Statistical Analysis of Deviations between Calculated and Observed Values of Bound Shifts (Δ_1)[a]

	1 (R = H)	**2** (R = CH$_3$)	**3** (R = C$_2$H$_5$)	**4** (R = *i*-C$_3$H$_7$)
Table I, R[b]	0.0101	0.0057	0.0114	0.0260
Table I, % error[b]	1.44	0.76	1.32	2.63
Free float, R[c]	0.0052	0.0054	0.0055	0.0069
Free float, % error[c]	0.92	0.68	0.78	0.69

[a] Where R is the agreement factor as defined in ref 7; % error refers to the weighted average of the absolute values of the individual percent errors. [b] Raw error is the difference between the calculated and observed values in Table I. [c] Errors obtained when each compound is analyzed independently according to eq 1 with k and R_{LN} both treated as variable parameters.



6

As a final test in the preliminary work we predicted the LIS for pivalonitrile (**6**), which is not conformationally restricted, but has "free" rotation about each of the single bonds in the molecule. Using the parameters determined above the calculated value of Δ_1 for **6** is 7.38 ppm (the weighted average of the LIS for each stable conformation); the experimentally observed value is 7.56 ppm.

Earlier work on nitriles in which the LIS-structure fits were analyzed using *relative* shifts and allowing R_{LN} and k to be freely floating parameters with each substrate has afforded "agreement factors" [7,17] in the range 0.04–0.06 for europium LSR's.[6] In the present work we have used *fixed* values of these parameters in conjunction with *bound* shifts. Even using fixed parameters, our agreement factors are considerably smaller than those obtained in earlier work, as is shown in the first two rows of Table II. The last two rows of this table show that independent analyses of each substrate with R_{LN} and k allowed to vary afford an additional reduction in the magnitudes of the errors. While this further demonstrates the superiority of using bound shifts (rather than relative LIS values), we believe that the parameterization method (Table I) is more powerful since it allows the a priori prediction of LIS.

Clearly LSR studies have now advanced to the point where rigorous, reliable, and accurate assessment of proposed structures can be made. Consideration of the side-chain data for compounds **3** and **4** indicates that this method is even capable of detecting relatively small and subtle structural deviations such as arise from nonbonded interactions. This approach is now being extended to molecules of increasing complexity.

Acknowledgments. This work was supported by a grant from the Research Corporation (to M.D.J.) and in part by the donors of the Petroleum Research Fund, administered by the American Chemical Society. We thank Professor N. L. Allinger for helpful discussions.

References and Notes

(1) C. C. Hinckley, *J. Am. Chem. Soc.*, **91**, 5160 (1969).
(2) H. M. McConnell and R. E. Robertson, *J. Chem. Phys.*, **29**, 1361 (1958).
(3) R. E. Sievers, Ed., "Nuclear Magnetic Resonance Shift Reagents", Academic Press, New York, N.Y., 1973.
(4) A. F. Cockerill, G. L. O. Davies, R. C. Harden, and D. M. Rackham, *Chem. Rev.*, **73**, 553 (1973).
(5) P. V. Demarco, B. J. Cerimele, R. W. Crane, and A. L. Thakkar, *Tetrahedron Lett.*, 3539 (1972).
(6) R. E. Davis, M. R. Willcott III, R. E. Lenkinski, W. von E. Doering, and L. Birladeanu, *J. Am. Chem. Soc.*, **95**, 6846 (1973).
(7) M. R. Willcott III, R. E. Lenkinski, and R. E. Davis, *J. Am. Chem. Soc.*, **94**, 1742 (1972).
(8) A. F. Cockerill and D. M. Rackham, *Tetrahedron Lett.*, 5149, 5153 (1970).
(9) R. M. Wing, J. J. Uebel, and K. K. Andersen, *J. Am. Chem. Soc.*, **95**, 6046 (1973).
(10) J. A. Pople and D. L. Beveridge, "Approximate Molecular Orbital Theory", McGraw-Hill, New York, N.Y., 1970, pp 111–112.
(11) The possible advantages of nitriles as substrates in LSR studies have been recognized previously (ref 6). The compounds utilized in this study were either commercially available (**1** and **6**) or were prepared by successive conversion of the appropriate carboxylic acid to the acid chloride, amide, and nitrile. The preparations of the carboxylic acids corresponding to **2**, **3**, and **4** have been reported: J. R. Alford, B. D. Cuddy, D. Grant, and M. A. McKervey, *J. Chem. Soc., Perkin Trans. 1*, 2707 (1972); D. J. Raber, R. C. Fort, E. Wiskott, C. W. Woodworth, P. V. R. Schleyer, J. Weber, and H. Stetter, *Tetrahedron*, **27**, 3 (1971).
(12) (a) B. L. Shapiro and M. D. Johnston, Jr., *J. Am. Chem. Soc.*, **94**, 8185 (1972); (b) M. D. Johnston, Jr., B. L. Shapiro, M. J. Shapiro, T. W. Proulx, A. D. Godwin, and H. L. Pearce, *ibid.*, **97**, 542 (1975).
(13) For additional evidence pertaining to the stoichiometry of complex formation, see (a) J. Reuben, *J. Am. Chem. Soc.*, **95**, 3534 (1973); (b) J. W. ApSimon, H. Beierbeck, and A. Fruchier, *ibid.*, **95**, 939 (1973).
(14) The use of a single average location for a set of hydrogen atoms which are conformationally interconverting is incorrect although that approach has sometimes been utilized (cf. ref 9). We find that this assumption yields highly unsatisfactory results.
(15) N. L. Allinger, M. T. Tribble, M. A. Miller, and D. H. Wertz, *J. Am. Chem. Soc.*, **93**, 1637 (1971).
(16) N. L. Allinger, private communication. We thank Professor Allinger for providing us with unpublished structural data.
(17) R. E. Davis and M. R. Willcott III, *J. Am. Chem. Soc.*, **94**, 1744 (1972).

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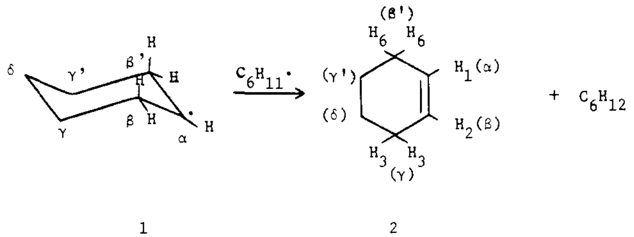
CIDNP Evidence for Stereoselectivity in the Disproportionation of Two Cyclohexyl Radicals

Sir:

The ESR spectrum of the cyclohexyl radical, **1** (Scheme I), observed under a variety of conditions,[1] reveals that the two β-protons adjacent to the carbon containing the unpaired electron are nonequivalent. The proton hyperfine splittings of 41 and 5 G are presumed to be due to the pseudoaxial and pseudoequatorial protons, respectively, in a chair-like conformation of the radical.[1i] The possibility thus exists for preferential reactivity of the two stereochemically different β-hydrogens in a reaction involving removal of a hydrogen atom from the cyclohexyl radical. We wish to report the observation of an NMR spectrum exhibiting CIDNP in a manner which implies that the disproportionation reaction between two cyclohexyl radicals to give cyclohexene, **2**, does indeed display preferential reactivity of one of the two types of β-hydrogen.

Scheme I



1 **2**

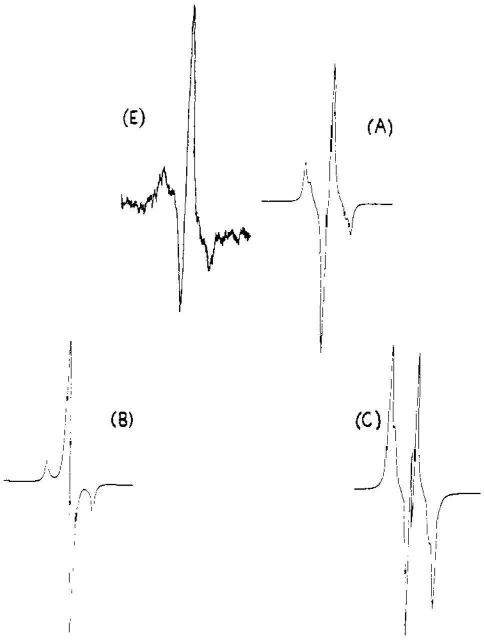


Figure 1. NMR spectra of the olefinic protons of cyclohexene formed by the disproportionation of two cyclohexyl radicals: (E) experimentally observed spectrum obtained during the reaction of cyclohexyl bromide with metallic magnesium in THF at room temperature; simulated spectra calculated assuming (A) removal of pseudoequatorial hydrogen, (B) removal of pseudoaxial hydrogen, and (C) conformational equilibration of radicals before hydrogen removal.

While observing the NMR spectrum of a tetrahydrofuran solution of cyclohexyl bromide reacting with magnesium metal we have obtained the CIDNP spectrum of the olefinic protons of **2** reproduced in Figure 1E. In other studies of the reaction between alkyl halides and magnesium,[2] alkenes have been observed to exhibit CIDNP consistent with their formation via encounters between freely diffusing alkyl radicals. We thus interpret Figure 1E as a record of the disproportionation reaction between two free cyclohexyl radicals.

Using published values for the hyperfine splittings in cyclohexyl radical[1g] and the spin–spin coupling constants in **2**,[3] we have carried out a calculation of the CIDNP intensity pattern for the olefinic protons of **2** using three difference models for the disproportionation process: (A) removal of a pseudoequatorial β-hydrogen (a = 5 G); (B) removal of a pseudo-axial β-hydrogen (a = 41 G); (C) removal of a β-hydrogen whose hyperfine splitting is the mean of models A and B. Model C serves as an approximation to the case where ring flipping in **1** is fast compared to the radical pair lifetime. The computation of NMR spin state populations in the radical pair included the α- and β-protons on both radicals ($a_\alpha = -21$ G[1g]) and was carried out using a modified NMR simulation program[4] to incorporate the radical pair model for CIDNP proposed by Adrian.[5] A calculation based on the CKO model[6] gave nearly identical spectra in this case. The simulations for the models A–C are shown in Figures 1A–1C, respectively.

The nearly perfect agreement between simulation A and the