

**Structure Elucidation with Lanthanide-Induced Shifts 5.
Evaluation of the Binding Ability
of Various Functional Groups¹**

**Douglas J. Raber*, Milton D. Johnston, jr.*, Catherine M. Campbell,
Anne Guida, George F. Jackson, III², Christopher M. Janks, Joseph W.
Perry, Gary J. Propeck, Nancy K. Raber, Michael A. Schwalke, and
Pamela M. Sutton**

Department of Chemistry, University of South Florida,
Tampa, FL 33620, U.S.A.

(Received 17 May 1979. Accepted 31 May 1979)

The equilibrium binding constants have been evaluated for the association in CCl_4 of the lanthanide shift reagent: $\text{Eu}(\text{fod})_3$, with a series of adamantane derivatives containing a variety of different functional groups. It is shown that if steric effects are held constant the binding abilities of the adamantane derivatives exhibit a good correlation with the proton affinities of the methyl analogs containing the same functional groups. The results permit the prediction of binding strength of other functional groups with $\text{Eu}(\text{dpm})_3$ as well as with $\text{Eu}(\text{fod})_3$ and thus can be of great assistance in planning and interpreting the results of experiments with lanthanide shift reagents.

(Keywords: Adamantane derivatives; Binding constants; Lanthanide induced shifts; Proton affinities)

Strukturermittlung mit LIS 5. Die Koordinationsfähigkeit verschiedener funktioneller Gruppen

Es wurden die Gleichgewichts-Komplexbildungskonstanten für eine Reihe von Adamantanderivaten mit verschiedenen funktionellen Gruppen mit $\text{Eu}(\text{fod})_3$ in CCl_4 bestimmt. Es wird gezeigt, daß bei Konstanthaltung sterischer Effekte die Komplex-Bindungsenergien eine gute Korrelation mit den Protonenaktivitäten der entsprechenden Methylhomologen ergibt. Die gewonnenen Resultate geben (auch für andere funktionelle Gruppen als die unmittelbar untersuchten) eine gute Möglichkeit zur Abschätzung zu erwartender Komplexbildungsstärken.

Introduction

Lanthanide shift reagents (LSRs) have become a valuable tool for the study of molecular structure, both as a qualitative means of simplifying nmr spectra and for carrying out rigorous structure analysis

by mathematical evaluation of the lanthanide induced shifts (LIS)^{3,4}. The effective use of shift reagents demands at least some predictive ability regarding the magnitude of the LIS to be obtained in a particular experiment. In this paper we discuss our studies with a series of substrates containing a variety of functional groups, and demonstrate that these results can be used obtain qualitative predictions of the outcome of LSR experiments.

The results of an nmr experiment can be conveniently discussed by considering only the first step of the multiple equilibria⁵⁻⁷ between lanthanide shift reagent (*L*) and substrate (*S*):



The observed spectrum is a time-average of the free and complexed forms, where each is weighted according to the mole fraction present in solution. The magnitude of the observed LIS for any nucleus will depend on *both* the *bound shift* (i.e., the change in chemical shift corresponding to complete conversion from free substrate to the *LS* complex) and, as is readily apparent from eq. (1), the equilibrium binding constant, K_1 . However, this was not always adequately appreciated in some of the early discussions regarding the "strength" of the interaction between LSR and substrate. For example, the different values for these two parameters in several model compounds was presumably responsible for the conflicting reports⁸ regarding the binding abilities of sulfur and oxygen ligands. Although the slopes of plots of induced shifts *vs* lanthanide: substrate ratios (under the conditions of excess substrate concentration) have generally been considered to reflect the magnitudes of the bound shifts⁴, an early report by *Ernst* and *Mannschreck*⁹ clearly demonstrates the importance of the binding constant. These authors noted the correlation of Eu(*dpm*)₃ induced shifts of the ring protons for a series of *p*-substituted anilines with the *pKa* values of the conjugated acids⁹. Since the *bound shifts* of the ring hydrogens should be nearly independent of the identity of the *p*-substituent, the variation in induced shift must be a consequence of changes in the binding strength of the various substrates. This view is substantiated by the work of *Rackham* and *Cockerill*¹⁰ who measured the binding constants of a series of substituted anilines with Yb(*dpm*)₃ by infrared spectroscopy. The magnitude of the binding constant as a function of the *p*-substituent¹⁰ follows precisely the same sequence as observed for the lanthanide induced shifts⁹.

Relatively few studies of the binding constants for shift reagent-substrate equilibria have been reported⁴, and many of these are at best approximate. Using data derived exclusively from nmr spectra, only the methods of *Shapiro* and *Johnston*^{4,11}, *Reuben*⁶, and *Bouquant* and *Chuche*¹² afford rigorous solutions to the problem of LSR-substrate equilibria. In any event the available data are difficult to compare since they are derived from studies employing diverse experimental conditions. For this reason we undertook the study of a series of structurally related compounds using the shift reagent Eu(*fod*)₃.

Table 1. *Binding constants and bound shifts for the interaction of l-substituted adamantanes with Eu(fod)₃ in CCl₄*

Substituent	K_1^a	$\Delta_1^{(Ad)^b}$	$\Delta_1^{(\text{Substituent})^c}$
1 OH	700	17.76	—
2 O—CO— CH₃	6,900	9.48	13.81
3 O—CO— CF₃	0.2 ^d	—	—
4 O—CH ₂ — CH₃	6	12.60	12.39
5 O—CH ₂ — CF₃	0.02 ^d	—	—
6 NH—CO— CH₃	1,300	6.04	4.85
7 NH—CO— CF₃	140	6.78	—
8 CN	550	8.25	—
9 CO— CH₃	5,400	10.16	13.88
10 CO— CH₂ Br	56	9.32	14.42
11 CO—O— CH₂ —CH ₃	3,600	9.06	12.99
12 CO—O— CH₂ —CF ₃	74	10.50	14.09
13 CH₂ —OH	6,500	7.96	—
14 CH ₂ —O—CO— CH₃	23,000	3.92	13.05
15 CH ₂ —O—CO— CF₃	0.3 ^d	—	—
16 CH ₂ —CN	290	6.84	—
17 CH ₂ —CO—O— CH₂ —CH ₃	440	6.68	14.54
18 CH ₂ —CO—O— CH₂ —CF ₃	52	7.32	15.14

^a Equilibrium constants are reported to two significant figures; units are M^{-1} .

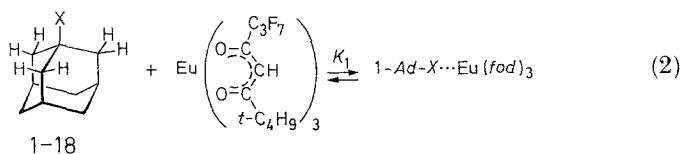
^b Bound shifts for the hydrogens of the three equivalent methylene groups of the adamantane skeleton (see eq. 2).

^c Bound shifts for the hydrogens of the substituent indicated by boldface type in the Table.

^d Only small induced shifts were observed, and the binding constant was estimated with the assumption that the bound shifts are the same as those of the non-fluorinated analog.

Results and Discussion

The equilibrium constants for 1:1 complex formation (eq. 2) for a series of 1-substituted adamantanes with $\text{Eu}(\text{fod})_3$ in CCl_4 are reported in Table 1. Also shown are the bound shifts of the six equivalent methylene hydrogens of the adamantane skeleton as well as of the



protons of the side chain which are indicated in boldface print in the first column of the table.

Several conclusions may be reached from a careful study of Table 1. The data demonstrate that small structural changes in the substituent do not greatly affect the bound shifts as would be expected since the bound shift of a complex is determined by the geometric relationship between the europium and the nucleus in question^{3, 4, 13}. For example, the series of compounds (9-12) for which the binding site is a carbonyl group attached directly to the adamantane nucleus exhibits bound shifts in the regions of 9-10 and 13-14 ppm, respectively, for the two types of hydrogens listed. This narrow range is entirely consistent with the small structural perturbations of the substrate-Eu(*fod*)₃ complexes which would be expected as the other substituent on the carbonyl group is varied along the series: —CH₃ (9), —CH₂Br (10), —OCH₂CH₃ (11), —OCH₂CF₃ (12).

In contrast to the bound shifts, the equilibrium constants listed in Table 1 exhibit variations even for small structural changes. As an example the binding constant for 1-adamantylmethylketone (9) decreases by two orders of magnitude upon introduction of a bromine in the α -position (i.e., 10). Since the compounds in Table 1 were selected with the intent of minimizing changes in steric effects, much of the variation of the equilibrium constants can be ascribed to electronic effects. Certainly for those cases in which the only changes are replacement of hydrogen by fluorine (i.e., 2 \rightarrow 3, 4 \rightarrow 5, 6 \rightarrow 7, 11 \rightarrow 12, 14 \rightarrow 15, and 17 \rightarrow 18) the similar conformational energies of these two nuclei¹⁴ require that the change in binding constant be ascribed almost entirely to inductive effects.

On the other hand, steric effects certainly can be important as indicated by the work of *Johnston* and *Shapiro* and their coworkers¹¹ who found consistently smaller equilibrium constants for tertiary alcohols relative to their secondary analogs. Similarly, *Grosse*, *Roth* and *Rewicki*¹⁵ demonstrated that introduction of bulky substituents in the vicinity of a hydroxyl group can cause a substantial reduction in the magnitude of the binding constant. The comparatively small value of K_1 found for 1-adamantyl-ethylether (4) is probably the result of such steric interactions since coordination with an ether requires the relatively close approach of the LSR to at least one of the two alkyl groups. The comparatively weak binding ability of ether groups (and particularly in relation to the binding ability of ketones) has previously been reported by *Hofer*¹⁶.

In any comparison of equilibrium constants it is necessary to consider the experimental error associated with the data. Indeed, the errors associated with equilibrium constants obtained by the method developed by *Shapiro* and *Johnston*^{5, 11} are significant (a standard deviation of $\pm 20\%$ was suggested by them¹¹). In order to assess the importance of experimental errors we report in

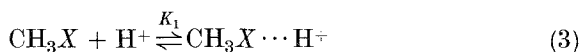
Table 2 the results of a series of experiments in which multiple, independent determinations have been made for several compounds. While there is some variation, these results indicate the $\pm 30\%$ would be more representative of the uncertainty in the equilibrium constants reported in this work¹⁷. While this might at first glance appear to be an unacceptably large margin of error, it should be recalled that this corresponds to an uncertainty on the order of only about ± 0.3 kcal in the free energy of the complexation reaction.

Table 2. *Binding constants and standard errors for the interaction of organic derivatives with $\text{Eu}(\text{fod})_3$ in CCl_4 ^a*

Substrate	Mean K_1	Standard Error	n
1-Adamantyl-CN (8)	480	130	7
3-Alkyl-1-adamantyl-CN	440	120	8
2-Adamantanone	2300	1400	4
Acetone	980	130	3
<i>t</i> -Butyl-CN	130	34	5
4-Methyl-2-pentanone	570	190	3
Methyl-CN	52	4	3
Ethyl-CN	150	57	3
<i>cis</i> -4- <i>t</i> -Butylcyclohexyl-CN	120	29	3
Benzonitrile	22	2	3

^a Standard Error = $\{[\sum (x_i - \bar{x})^2] / [n(n-1)]\}^{1/2}$ where n is the number of independent determinations, x_i is the value for a particular determination and \bar{x} is the mean for all determinations.

The strong qualitative dependency of the association constants upon electronic effects prompted us to investigate the possibility of finding a more quantitative relationship. Equation (1) may be considered as a simple acid—base reaction in which the shift reagent acts as a *Lewis* acid, and it has previously been suggested^{8a} that lanthanide shift reagents fall in the class of hard¹⁸ acids. Consequently, we selected H^+ as the appropriate acid for comparison, and in Table 3 are reported the gas phase proton affinities¹⁹ (eq. 3) of a series of substrates in which the basic site is carbonyl oxygen.



1m-18m

Since the proton affinities of the adamantane derivatives themselves (1-18) have not been reported in the literature, we have used the methyl analogs (designated as **1m-18m**) for which proton affinity data either had been explicitly reported or could be easily estimated from closely

Table 3. Proton affinities of substituted methanes and $\text{Eu}(\text{fod})_3$ binding energies for the corresponding substituted adamantanes^a

Substituent X	Proton Affinity (CH_3X)	$\log K$ (1-Adamantyl-X)	ΔG (1-Adamantyl-X)
$\text{CH}_2\text{—CO—O—CH}_2\text{—CH}_3$	201.4 ^b	2.64	—3.71
$\text{CO—O—CH}_2\text{—CH}_3$	198.1	3.56	—5.00
$\text{CH}_2\text{—O—CO—CH}_3$	198.1	4.36	—6.13
O—CO—CH_3	195.4	3.84	—5.39
CO—CH_3	193.9	3.73	—5.24
$\text{CO—CH}_2\text{Br}$	192.1 ^c	1.75	—2.46
$\text{CH}_2\text{—CO—O—CH}_2\text{—CF}_3$	191.4 ^d	1.72	—2.41
$\text{CO—O—CH}_2\text{—CF}_3$	187.7 ^e	1.87	—2.63
$\text{CH}_2\text{—O—CO—CF}_3$	183.2	—0.52	0.73
O—CO—CF_3	180.3	—0.70	0.98

^a Proton affinities are in kcal/mol and were obtained from ref.¹⁹; binding energies for 35 °C in kcal/mol.

^b Calculated by assuming that the difference between the proton affinities of $\text{CH}_3\text{CH}_2\text{CO}_2\text{Et}$ and $\text{CH}_3\text{CO}_2\text{Et}$ is the same as the difference of 3.2 kcal/mol for $\text{CH}_3\text{CH}_2\text{CN}$ and CH_3CN .

^c Calculated from the proton affinity of acetone and the decrease in proton affinity of 3.3 kcal/mol observed upon introduction of an α -bromine in $\text{CH}_3\text{CO}_2\text{Et}$; *S. R. Smith and T. D. Thomas, J. Amer. Chem. Soc.* **100**, 5459 (1978).

^d Estimated from the $\beta\text{-CF}_3$ effect of 10.4 kcal/mol (footnote e) and the proton affinity of $\text{CH}_3\text{CH}_2\text{CO}_2\text{CH}_2\text{CH}_3$ (footnote b).

^e Calculated from the proton affinity of $\text{CH}_3\text{CO}_2\text{CH}_2\text{CH}_3$ and the decrease in proton affinity of 10.4 kcal/mol between $\text{HCO}_2\text{CH}_2\text{CH}_3$ and $\text{HCO}_2\text{CH}_2\text{CF}_3$.

related compounds¹⁹. Table 3 also reports the free energies of complexation for the adamantane derivatives with $\text{Eu}(\text{fod})_3$.

While the data in Table 3 indicate a qualitative correlation between proton affinity and LSR binding constant, a more quantitative assessment of the relationship is available from Fig. 1, which shows a plot of these for a restricted group of compounds (ketones and esters). These derivatives were selected since they all coordinate with the shift reagent at carbonyl oxygen and thus provide a series of compounds for which changes in steric environments are minimized. Fig. 1 demonstrates a very clear correlation between proton affinity and shift reagent binding ability; the mean deviation of the ΔG values from the least squares line is 0.8 kcal/mol. This is somewhat larger than the ± 0.4 kcal/mol suggested for the uncertainty in our equilibrium measurements and indicates that the correlation is only approximate. Nevertheless, useful information about the binding ability of other functional groups can be obtained from this plot.

For example, the nitrile derivatives **8** and **16** would be predicted to have equilibrium constants in the range of $10\text{--}50 M^{-1}$ based on the proton affinities of **8m** and **16m**. The observed values are somewhat larger, even when experimental error for **8** (Table 2) is considered; this discrepancy may reflect a difference in steric environment of the nitriles relative to the esters as well as a basic difference in the coordination at nitrogen *vs* oxygen. On the other hand the proton affinities of a variety of simple aliphatic nitriles²⁰ fall in the range of 188–194 kcal/mol,

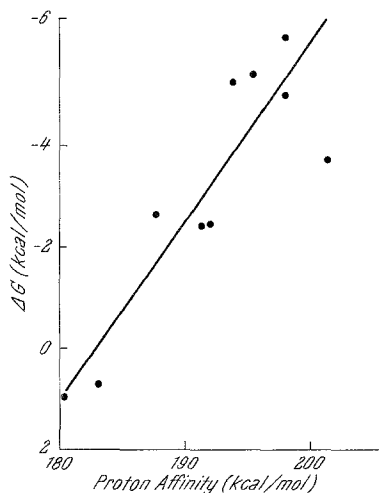



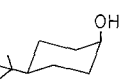
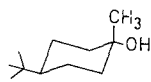
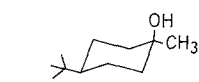
Fig. 1. Correlation of proton affinities of methyl substituted derivatives with the free energies of binding between the corresponding 1-adamantyl derivatives and $\text{Eu}(\text{fod})_3$. The line is that obtained by linear regression analysis of all points

corresponding to a range of equilibrium constants of $10\text{--}200 M^{-1}$ which agrees well with the other data for nitriles reported in Table 2.

Despite its approximate nature the correlation shown in Fig. 1 permits the prediction of whether a particular functional group will bind "weakly" or "strongly" to $\text{Eu}(\text{fod})_3$. Thus the high proton affinity of amides²¹ allows the prediction that this functional group will also bind strongly with a shift reagent, in agreement with the data for **6** in Table 1. Similarly, the substantially decreased equilibrium constants in Table 1 which are observed for fluorine substitution is in accord with a large decrease in the analogous proton affinities¹⁹. The Figure also suggests that functional groups with proton affinities of less than approximately 180 kcal/mol should fail to interact with $\text{Eu}(\text{fod})_3$, as is indeed the case with simple organic halides. An important exception to

this correlation arises in the case of sulfur derivatives, which bind far more weakly to LSRs than do their oxygen analogs^{8, 22}; the correlation shown in the Figure would have led to the opposite prediction. This anomaly appears to result from the fact that proton affinities are gas phase measurements. In aqueous solutions the oxygen analogs are considerably more basic²³.

The equilibrium constants we have obtained for the interaction of $\text{Eu}(\text{fod})_3$ in CCl_4 with a variety of substrates permits the comparison with the results obtained by others. Although few groups have measured equilibrium constants accurately, and frequently both shift reagent and solvent have been changed, *Bouquant* and *Chuche*^{12, 24} have studied several substrates with $\text{Eu}(\text{dpm})_3$ which have also been investigated with $\text{Eu}(\text{fod})_3$. For 3 α ,4,4-trimethylcholestan-3 β -ol in CCl_4 they reported an equilibrium constant of 63 ± 4 with $\text{Eu}(\text{dpm})_3$ ^{24a} and a value which was larger by an order of magnitude with $\text{Eu}(\text{fod})_3$ ^{23, 24}. They also studied two substrates in both CDCl_3 and CCl_4 finding equilibrium constants which were about fivefold larger in CCl_4 in both cases; we have observed comparable solvent dependencies in our work²². On this basis we can consider the different binding abilities of $\text{Eu}(\text{dpm})_3$ and $\text{Eu}(\text{fod})_3$ for substrates **19-22**. Assuming the solvent effect (CDCl_3 is more polar than CCl_4) to cause a fivefold change in the binding constant, data for the two secondary alcohols **19** and **20** suggest that $\text{Eu}(\text{fod})_3$ has binding constants which are larger by a factor of 4-6.

				
	19	20	21	22
K_1 $\text{Eu}(\text{fod})_3$, CCl_4 [Ref. 4]	5,345	10,061	614	209
K_1 $\text{Eu}(\text{dpm})_3$, CDCl_3 [Ref. 24c]	252	324	127	72

However, the values for the tertiary alcohols are quite similar, and it is not clear whether it is the solvent effect or difference between $\text{Eu}(\text{dpm})_3$ and $\text{Eu}(\text{fod})_3$ which has been compressed. Nevertheless it would appear that a decrease in binding constant of up to a factor of 10 can generally be expected upon substituting $\text{Eu}(\text{dpm})_3$ for $\text{Eu}(\text{fod})_3$.

Conclusions

The correlation of lanthanide shift reagent binding ability and gas phase basicity of various functional groups permits a qualitative prediction of the LSR-substrate interaction to be expected in a shift reagent experiment. The association constants observed for $\text{Eu}(\text{dpm})_3$ are approximately a factor of ten smaller than those observed for the

fluorinated shift reagent, $\text{Eu}(\text{fod})_3$; knowledge of this change in Lewis acidity will facilitate the choice of the most appropriate shift reagent in any particular experiment.

The introduction of electronegative substituents in the vicinity of the binding site causes a large decrease in the equilibrium constant for association with LSR. In the case of alcohols, conversion of a hydroxyl group to the corresponding trifluoroacetate affords a group with binding constant of less than unity. This provides concrete support for the idea that trifluoroacetates and other fluorinated esters may be used as blocking groups for shift reagent studies with polyfunctional compounds^{4c, 25}.

Acknowledgements

This work was supported by the donors of the Petroleum Research Fund, administered by the American Chemical Society, and by grants from the Research Corporation.

Experimental

Nuclear magnetic resonance spectra were obtained using Varian EM-360 and A-60 spectrometers. All spectra were recorded at either 600 Hz (EM-360) or 500 Hz (A-60) sweep widths. Chemical shifts were measured relative to internal *TMS* and sweep widths were calibrated with an external audio oscillator. When the widths of the spectra exceeded the sweep widths, offset spectra were recorded and peak positions were measured relative to a *TMS* audio side band.

Shift reagent runs utilized the incremental dilution method⁴ in which a CCl_4 solution containing both shift reagent (0.6 *M*) and the substrate (0.2 *M*) is successively diluted with a 0.2 *M* CCl_4 solution of the substrate. Thus the concentration of the substrate remains constant at 0.2 *M*, while the concentration of the shift reagent decreases with each dilution. The precise concentrations of shift reagent and substrate were determined gravimetrically for each sample by weighing the sample tube after each dilution, and spectra were recorded for a total of ca. 25 different concentrations of shift reagent.

Bounds shifts and equilibrium constants were calculated *via* nonlinear regression analysis as described by *Shapiro* and *Johnston*⁴.

Compounds **1-18** were either commercially available or were readily prepared by standard reactions (e.g., esterification or solvolysis) of commercially available materials. $\text{Eu}(\text{fod})_3$ was purchased from Aldrich Chemical Co. (EuFOD^{TM} , # 16,093-8) and was sublimed (160-165 °C, 0.05 Torr) and stored in a vacuum desiccator over P_2O_5 for at least 48 h prior to use.

References

- 1 Part 4: *D. J. Raber, M. D. Johnston, jr., C. M. Campbell, C. M. Janks, and P. Sutton*, *Org. Mag. Res.* **11**, 323 (1978).
- 2 Chemistry Department, University of Tampa, Tampa, FL 33606, U.S.A.
- 3 (a) *D. J. Raber, M. D. Johnston, jr., J. W. Perry, and G. F. Jackson III*, *J. Org. Chem.* **43**, 229 (1978). (b) *D. J. Raber, M. D. Johnston, jr., and M. A. Schwalke*, *J. Amer. Chem. Soc.* **99**, 7671 (1977). (c) *M. D. Johnston, jr., D. J. Raber, N. K. DeGennaro, A. D'Angelo, and J. W. Perry*, *J. Amer. Chem. Soc.* **98**, 6042 (1976).

- ⁴ For reviews see: (a) *O. Hofer* in Topics in Stereochemistry, Vol. 9, pp. 111-197; Ed. by *N. L. Allinger* and *E. L. Eliel*. New York: John Wiley, 1976. (b) *M. R. Willcott III* and *R. E. Davis*, Science **190**, 850 (1975). (c) *A. F. Cockerill*, *C. L. O. Davies*, *R. C. Harden*, and *D. M. Rackham*, Chem. Revs. **73**, 553 (1973). (d) *B. C. Mayo*, Chem. Soc. Revers. **2**, 49 (1973). (e) *J. Reuben*, Prog. Nucl. Mag. Resonance Spectrosc. **9** 1 (1973).
- ⁵ *B. L. Shapiro* and *M. D. Johnston, jr.*, J. Amer. Chem. Soc. **94**, 8185 (1972).
- ⁶ (a) *J. Reuben*, J. Amer. Chem. Soc. **95**, 3534 (1973). (b) *R. E. Lenkinski*, *G. A. Elgavish*, and *J. Reuben*, J. Magnet. Res. **32**, 367 (1978).
- ⁷ (a) *K. Roth*, *M. Grosse* and *D. Rewicki*, Tetrahedron Lett. 1972, 435. (b) *I. Armitage*, *G. Dunsmore*, *L. D. Hall* and *A. G. Marshall*, Chemical Commun. **1971**, 1281. (c) *J. W. ApSimon*, *H. Beiberbeck* and *A. Fruchier*, J. Amer. Chem. Soc. **95**, 939 (1973).
- ⁸ (a) *T. C. Morill*, *R. J. Optiz*, and *R. Mozzer*, Tetrahedron Lett. **1973**, 3715. (b) *A. v. Bruijnsvoort*, *C. Kruk*, *E. R. de Waard*, and *H. O. Huisman*, *ibid.* **1972**, 1737. (c) *H. Hart* and *G. M. Love*, *ibid.* **1971**, 625.
- ⁹ *L. Ernst* and *A. Mannschreck*, *ibid.* **1971**, 3023.
- ¹⁰ *D. M. Rackham* and *A. F. Cockerill*, Spectroscopy Lett. **10**, 305 (1977).
- ¹¹ (a) *M. D. Johnston jr.*, *B. L. Shapiro*, *M. J. Shapiro*, *T. W. Proulx*, *A. D. Godwin*, and *H. L. Pearce*, J. Amer. Chem. Soc. **97**, 542 (1975). (b) *F. Inagaki*, *M. Tasumi* and *T. Miyazawa*, Bull. Chem. Soc. Japan **48**, 1427 (1975).
- ¹² (a) *J. Bouquant* and *J. Chucho*, Tetrahedron Lett. **1972**, 2337. (b) The procedure of *Bouquant* and *Chucho* is rigorous only in the case that a single complex is formed with 1:1 stoichiometry. However, it still affords an approximate value of K_1 even when some LS_2 complex is present. In the case of $Eu(dpm)_3$ where the 1:1 complex predominates⁴, their procedure should afford quite reliable equilibrium constant. (c) *D. M. Rackham* and *J. Binks*, Spectroscopy Lett. **12**, 17 (1979).
- ¹³ *H. M. McConnell* and *R. E. Robertson*, J. Chem. Phys. **29**, 1361 (1958).
- ¹⁴ *J. A. Hirsch* in Topics in Stereochemistry, Vol. 1, pp. 199-222, Ed. by *N. L. Allinger* and *E. L. Eliel*. New York: John Wiley, 1967.
- ¹⁵ *M. Grosse*, *K. Roth* and *D. Rewicki*, Org. Mag. Res. **10**, 115 (1977).
- ¹⁶ *O. Hofer*, Mh. Chem. **109**, 405 (1978).
- ¹⁷ If the standard errors of Table 2 are expressed as relative errors, the average of the ten entries in the table corresponds to an uncertainty in the equilibrium constants of $\pm 27\%$.
- ¹⁸ *R. G. Pearson*, J. Amer. Chem. Soc. **85**, 3533 (1963); J. Chem. Educ. **45**, 581 (1968).
- ¹⁹ *J. F. Wolf*, *R. H. Staley*, *I. Koppel*, *M. Taagepera*, *R. T. McIver, jr.*, *J. L. Beauchamp*, and *R. W. Taft*, J. Amer. Chem. Soc. **99**, 5417 (1977).
- ²⁰ *R. H. Staley*, *J. E. Kleckner*, and *J. L. Beauchamp*, *ibid.* **98**, 2081 (1976).
- ²¹ See Figure 6 of ref.¹⁹.
- ²² Unpublished results from these laboratories.
- ²³ *J. Hine*, Structural Effects on Equilibria in Organic Chemistry, p. 189. New York: John Wiley, 1975.
- ²⁴ (a) *J. Bouquant* and *J. Chucho*, Tetrahedron Lett. **1973**, 493. (b) *J. Bouquant* and *J. Chucho*, Bull. Soc. Chim. France **1977**, 959. (c) *J. Bouquant*, These de Doctorat es Sciences, Universite de Reims, 1978.
- ²⁵ (a) *P. Girard*, *H. Kagan*, and *S. David*, Tetrahedron **27**, 5911 (1971). (b) *D. R. Crump*, *J. K. M. Sanders* and *D. H. Williams*, Tetrahedron Lett. **1970**, 4949. (c) *A. Ius*, *G. Vecchio*, and *G. Carrea*, *ibid.* **1972**, 1543.