

LANTHANIDE INDUCED SHIFTS IN PROTON NMR.

A STATISTICAL COMPARISON

A Thesis

Presented to the

Faculty of the Department of Chemistry

College of Arts and Sciences

University of Houston

In partial fulfillment

of the Requirements for the Degree

Master of Science

by

Einar Helmuth Goerland

May 1973

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To Linda

ACKNOWLEDGMENTS

The author would like to acknowledge Dr. M. Robert Willcott for his personal advice, The Upjohn Company for the use of its equipment and facilities and my supervisor, Dr. Warren J. Rabourn, for his understanding and encouragement.

Personal acknowledgments are too numerous to cover completely, but this paper would not have been submitted without the advice of Dr. Robert Lenkinski, and Jerry L. Decker.

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ABSTRACT

Repetitive lanthanide induced shift, LIS, experiments were performed with $\text{Eu}(\text{fod})_3$ and $\text{Yb}(\text{fod})_3$ on four rigid organic molecules, 1-adamantanol, 1-adamantanamine, 2-adamantanol and 2-adamantanamine, to determine the precision of Demarco-Wenkert and ApSimon data reduction methods. Both methods gave essentially equivalent shift parameters. The Demarco-Wenkert shift parameters, Δ obs plotted against $[\text{L}]/[\text{S}]$, had 2 to 5 per cent precision. This could not be improved by replication. Greater precision, 1 per cent, was realized for ApSimon shift parameters, Δ obs versus $\Sigma \Delta$ obs. $\text{Yb}(\text{fod})_3$ was found to induce downfield shifts approximately 6.4 times as large as $\text{Eu}(\text{fod})_3$ in 2-adamantanamine for the same L/S ratio.

TABLE OF CONTENTS

CHAPTER	PAGE
DEDICATION	i
ACKNOWLEDGMENTS	ii
ABSTRACT	iii
TABLE OF CONTENTS	iv
LIST OF TABLES	vi
LIST OF FIGURES	x
I. INTRODUCTION	1
A. General	1
B. Background	1
C. The Lanthanide Shift Reagent	4
D. The Substrate	7
E. Quantitation of LIS Data	7
F. Application of LIS Data	14
G. Statement of Purpose	17
II. EXPERIMENTAL	19
III. RESULTS AND DISCUSSION	22
A. General	22
B. Data Reduction with the Demarco-Wenkert Method	26
C. Data Reduction with the ApSimon Method	70
D. Comparison to Other Data Reduction Methods	78
E. Results Compared to Scaled Literature LIS Parameters	79
F. Comparison of Eu to Yb LIS Data	79

TABLE OF CONTENTS CONTINUED

CHAPTER	PAGE
IV. CONCLUSION	84
BIBLIOGRAPHY	
APPENDIX	
A. List of Abbreviations	
B. Computer Program	

LIST OF TABLES

TABLE	PAGE
1. Isotropic Shift Data for 4-Vinylpyridine and Line-width Data for 2-Picoline Adducts of Ln(dpm)_3	5
2. Index of Observed and Calculated Data Tables	23
3. Run No. 1, Eu(fod)_3 Induced Proton Shifts in 1-Adamantanol, in CDCl_3 at 60 MHz	27
4. Run No. 2, Eu(fod)_3 Induced Proton Shifts in 1-Adamantanol, in CDCl_3 at 60 MHz	28
5. Run No. 3, Eu(fod)_3 Induced Proton Shifts in 1-Adamantanol, in CDCl_3 at 60 MHz	29
6. Run No. 4, Eu(fod)_3 Induced Proton Shifts in 1-Adamantanol, in CDCl_3 at 60 MHz	30
7. Run Nos. 1-4 Combined, Eu(fod)_3 Induced Proton Shifts in 1-Adamantanol, in CDCl_3 at 60 MHz	31
8. Run No. 1, Yb(fod)_3 Induced Proton Shifts in 1-Adamantanol, in CDCl_3 at 60 MHz	32
9. Run No. 2, Yb(fod)_3 Induced Proton Shifts in 1-Adamantanol, in CDCl_3 at 60 MHz	33
10. Run No. 3, Yb(fod)_3 Induced Proton Shifts in 1-Adamantanol, in CDCl_3 at 60 MHz	34
11. Run No. 4, Yb(fod)_3 Induced Proton Shifts in 1-Adamantanol, in CDCl_3 at 60 MHz	35
12. Run Nos. 1-4 Combined, Yb(fod)_3 Induced Proton Shifts in 1-Adamantanol, in CDCl_3 at 60 MHz	36
13. Run No. 1, Eu(fod)_3 Induced Proton Shifts in 1-Adamantanamine, in CCl_4 at 60 MHz	37
14. Run No. 2, Eu(fod)_3 Induced Proton Shifts in 1-Adamantanamine, in CCl_4 at 60 MHz	38

LIST OF TABLES CONTINUED

TABLE	PAGE
15. Run No. 3, $\text{Eu}(\text{fod})_3$ Induced Proton Shifts in 1-Adamantanamine, in CCl_4 at 60 MHz	39
16. Run No. 4, $\text{Eu}(\text{fod})_3$ Induced Proton Shifts in 1-Adamantanamine, in CCl_4 at 60 MHz	40
17. Run Nos. 1-4 Combined, $\text{Eu}(\text{fod})_3$ Induced Proton Shifts in 1-Adamantanamine, in CCl_4 at 60 MHz	41
18. Run No. 1, $\text{Yb}(\text{fod})_3$ Induced Proton Shifts in 1-Adamantanamine, in CCl_4 at 60 MHz	42
19. Run No. 2, $\text{Yb}(\text{fod})_3$ Induced Proton Shifts in 1-Adamantanamine, in CCl_4 at 60 MHz	43
20. Run No. 3, $\text{Yb}(\text{fod})_3$ Induced Proton Shifts in 1-Adamantanamine, in CCl_4 at 60 MHz	44
21. Run No. 4, $\text{Yb}(\text{fod})_3$ Induced Proton Shifts in 1-Adamantanamine, in CCl_4 at 60 MHz	45
22. Run Nos. 1-4 Combined, $\text{Yb}(\text{fod})_3$ Induced Proton Shifts in 1-Adamantanamine, in CCl_4 at 60 MHz	46
23. Run No. 1, $\text{Eu}(\text{fod})_3$ Induced Proton Shifts in 2-Adamantanol, in CDCl_3 at 60 MHz	47
24. Run No. 2, $\text{Eu}(\text{fod})_3$ Induced Proton Shifts in 2-Adamantanol, in CDCl_3 at 60 MHz	48
25. Run No. 3, $\text{Eu}(\text{fod})_3$ Induced Proton Shifts in 2-Adamantanol, in CDCl_3 at 60 MHz	49
26. Run No. 4, $\text{Eu}(\text{fod})_3$ Induced Proton Shifts in 2-Adamantanol, in CDCl_3 at 60 MHz	50
27. Run Nos. 1-4 Combined, $\text{Eu}(\text{fod})_3$ Induced Proton Shifts in 2-Adamantanol, in CDCl_3 at 60 MHz	51
28. Run No. 1, $\text{Yb}(\text{fod})_3$ Induced Proton Shifts in 2-Adamantanol, in CDCl_3 at 60 MHz	52

LIST OF TABLES CONTINUED

TABLE	PAGE
29. Run No. 2, Yb(fod) ₃ Induced Proton Shifts in 2-Adamantanol, in CDCl ₃ at 60 MHz	53
30. Run No. 3, Yb(fod) ₃ Induced Proton Shifts in 2-Adamantanol, in CDCl ₃ at 60 MHz	54
31. Run No. 4, Yb(fod) ₃ Induced Proton Shifts in 2-Adamantanol, in CDCl ₃ at 60 MHz	55
32. Run Nos. 1-4 Combined, Yb(fod) ₃ Induced Proton Shifts in 2-Adamantanol, in CDCl ₃ at 60 MHz	56
33. Run No. 1, Eu(fod) ₃ Induced Proton Shifts in 2-Adamantanamine, in CCl ₄ at 60 MHz	57
34. Run No. 2, Eu(fod) ₃ Induced Proton Shifts in 2-Adamantanamine, in CCl ₄ at 60 MHz	58
35. Run No. 3, Eu(fod) ₃ Induced Proton Shifts in 2-Adamantanamine, in CCl ₄ at 60 MHz	59
36. Run No. 4, Eu(fod) ₃ Induced Proton Shifts in 2-Adamantanamine, in CCl ₄ at 60 MHz	60
37. Run Nos. 1-4 Combined, Eu(fod) ₃ Induced Proton Shifts in 2-Adamantanamine, in CCl ₄ at 60 MHz	61
38. Run No. 1, Yb(fod) ₃ Induced Proton Shifts in 2-Adamantanamine, in CCl ₄ at 60 MHz	62
39. Run No. 2, Yb(fod) ₃ Induced Proton Shifts in 2-Adamantanamine, in CCl ₄ at 60 MHz	63
40. Run No. 3, Yb(fod) ₃ Induced Proton Shifts in 2-Adamantanamine, in CCl ₄ at 60 MHz	64
41. Run No. 4, Yb(fod) ₃ Induced Proton Shifts in 2-Adamantanamine, in CCl ₄ at 60 MHz	65
42. Run Nos. 1-4 Combined, Yb(fod) ₃ Induced Proton Shifts in 2-Adamantanamine, in CCl ₄ at 60 MHz	66

LIST OF TABLES CONTINUED

TABLE		PAGE
43.	Comparison of Shift Parameters Generated by the Demarco-Wenkert Method for 1-Adamantanol (V) and 1-Adamantanamine (VI)	67
44.	Comparison of Shift Parameters Generated by the Demarco-Wenkert Method for 2-Adamantanol (VII) and 2-Adamantanamine (VIII)	68
45.	Comparison of Shift Parameters Generated by the ApSimon Method for 1-Adamantanol (V) and 1-Adamantanamine (VI)	71
46.	Comparison of Shift Parameters Generated by the ApSimon Method for 2-Adamantanol (VII) and 2-Adamantanamine (VIII)	72
47.	Comparison of Demarco-Wenkert and Scaled ApSimon LIS Parameters for 1-Adamantanol	74
48.	Comparison of Demarco-Wenkert and Scaled ApSimon LIS Parameters for 1-Adamantanamine	75
49.	Comparison of Demarco-Wenkert and Scaled ApSimon LIS Parameters for 2-Adamantanol	76
50.	Comparison of Demarco-Wenkert and Scaled ApSimon LIS Parameters for 2-Adamantanamine	77
51.	Comparison of Shift Parameters to Scaled Literature LIS Parameters	81
52.	Least-Squares Correlation of Demarco $Eu(fod)_3$ Shift Indexes versus $Yb(fod)_3$ Shift Indexes	82
53.	Least-Squares Correlation of ApSimon $Eu(fod)_3$ Shift Indexes versus $Yb(fod)_3$ Shift Indexes	83

LIST OF FIGURES

FIGURE	PAGE
1. The Coordinate System	15
2. Proton Assignments for 1-Adamantanol and 1-Adamantanamine	24
3. Proton Assignments for 2-Adamantanol and 2-Adamantanamine	25

I.

INTRODUCTION

INTRODUCTION

A. General

Hinckley reported in 1969 that addition of the dipyridine adduct of tris-dipivaloylmethano-europium III, $\text{Eu(dpm)}_3 \cdot 2\text{py}$, to a carbon tetrachloride solution of cholesterol induced downfield proton chemical shifts in the NMR experiment⁽¹⁾. The induced chemical shifts separated some overlapping resonances and reduced parts of the spectrum to first order. These results are rationalized as contact, (spin delocalization) or pseudocontact (anisotropic) shift, or a combination of these two effects^(2,3).

Hinckley's first report⁽¹⁾ prompted intense activity in the field of paramagnetic shift reagents. In the intervening three years over 300 papers dealing with methodology and explanations of principles have appeared. Many points are still controversial and require careful study before elucidation.

B. Background

Hinckley was not the first to observe paramagnetically induced shifts in proton resonance spectra. Phillips, Looney and Ikeda found that Co^{2+} affected the proton spectra of n-propanol and n-hexanol⁽⁴⁾. Several years later, Eton, Josey, Phillips and Benson simplified proton spectra of organic molecules by using paramagnetic complexes⁽⁵⁾. Other papers

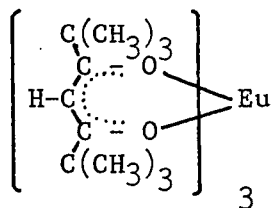
have reported proton shifts, ascribed to dipolar pseudocontact, in rare-earth acetylacetonates⁽⁶⁾, tropolonates⁽⁷⁾ and acetates⁽⁸⁾.

There is general agreement that observed lanthanide induced shift, LIS, proton data can be reasonably explained by a simplified* form of the McConnell-Robertson⁽⁹⁾ pseudocontact equation,

$$\Delta = \frac{K (3 \cos^2 \theta - 1)}{r^3} \quad , \quad (1)$$

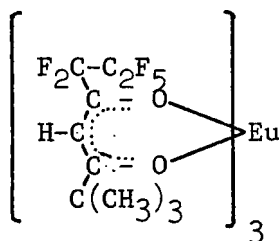
where r is the length of the radius vector from the metal atom to the resonating nucleus and θ is the angle of this vector with the principal magnetic axis of the lanthanide shift reagent, LSR. It is obvious for many cases that the principal factor influencing the magnitude of induced shift, for a particular proton, is the distance between it and the paramagnetic Ln ion. Thus protons closer to the Ln ion are shifted farther than those farther away.

Shortly after Hinckley's 1969 communication⁽¹⁾, Sanders and Williams reported that pyridine-free $\text{Eu}(\text{dpm})_3$, I, was a more efficient LSR than the bipyridine adduct⁽¹⁰⁾.



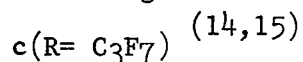
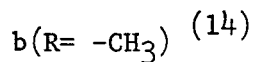
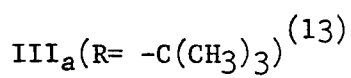
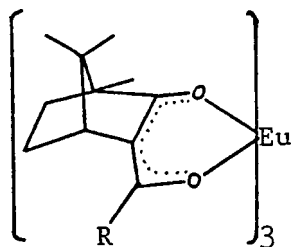
* Axial symmetry is assumed in the simplified form.

Other workers explored the use of different lanthanide and β -diketone combinations. $\text{Pr}(\text{dpm})_3$ was reported to induce upfield proton shifts in substrate molecules⁽¹¹⁾. Rondeau and Sievers reported the europium chelate of 1,1,1,2,2,3,3,-heptafluoro-7,7-dimethyl-4,6-octanedione, $\text{Eu}(\text{fod})_3$, II, to be more attractive due to its greater solubility⁽¹²⁾.



II

Chiral shift reagents, formed from chiral β -diketones such as 3-(tertbutylhydroxymethylene)- α -camphor, III_a ⁽¹³⁾ or others^(14,15) are capable of resolving the spectra of enantiomeric mixtures and even the prochiral methylene protons of ethanol.



C. The Lanthanide Shift Reagent

Lanthanide shift reagents are chelates of paramagnetic lanthanide (III) ions and β -diketone anions. Until now the most effective β -diketones seem to be H(dpm)⁽¹⁾, dipivaloylmethane, and H(fod)⁽¹²⁾, 1,1,1,2,2,3,3-heptafluoro-7,7-dimethyl-4,6-octanedione.

H(dpm) can readily be prepared in yields of 60 to 70 per cent by the method of Kopecky et. al.⁽¹⁶⁾. The procedure involves formation of the sodium enolate of pinacolone in dimethoxyethane by the action of sodium hydride. The enolate is then acylated in situ with methyl pivalate. Springer et.al. prepared H(fod) in 55 per cent yield by adding pinacolone to a sodium methoxide/ethylheptafluorobutyrate/ether slurry⁽¹⁷⁾.

The lanthanide ion is chosen by several criteria, (a) the direction of induced shift, (b) line broadening, and (c) relative shifting ability. Eu(III)⁽¹⁾ and Pr(III)⁽¹¹⁾ are most commonly used because they induce minimal line broadening. Yb(III) has also been used. In some cases, it induces down-field shifts approximately four times as large as Eu(III) for the same L/S ratio⁽¹⁸⁾. Horrocks and Sipe have investigated the action of eleven Ln(dpm)₃ complexes on the spectra of 4-vinylpyridine, 4-picoline N-oxide, and n-hexyl alcohol⁽¹⁹⁾. Some of their findings are summarized in Table 1.

Table 1. Isotropic Shift Data for 4-Vinylpyridine and Line-width Data for 2-Picoline Adducts of $\text{Ln}(\text{dpm})_3$

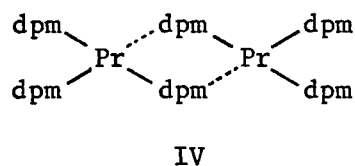
<u>Ln</u>	<u>Observed Vinyl Proton Shift</u> ^(a)	<u>Peak Width at Half Height for Methyl of 2-Picoline</u> ^(a)
Pr	+ 6.6	5.6
Nd	+ 3.2	4.0
Sm	+ 0.8	4.4
Eu	- 3.5	5.0
Tb	+30.7	96
Dy	+33.8	200
Ho	+24.0	50
Er	- 9.0	50
Tm	-23.6	65
Yb	-11.0	12

(a) Measured at 30°C for a lanthanide to substrate ratio of 0.125.

If $3 \cos^2\theta - 1$ is a positive number, upfield shifts are observed for Pr, Nd, Sm, Tb, Dy, and Ho, while Eu, Er, Tm and Yb cause downfield shifts.

The actual structure of (dpm) and (fod) LSR's is not clear⁽¹²⁾. The availability of empty 5d, 6s and 6p orbitals in lanthanides allows them to accommodate electron pairs donated by Lewis bases and exhibit eightfold or greater coordination⁽²⁰⁾. The neutral LSR is thought to be a chelate in which the three bidentate ligands surround the hexacoordinated lanthanide⁽¹²⁾.

In the crystalline state, $\text{Pr}(\text{dpm})_3$ has been found to exist as a dimer, IV,



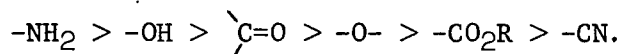
in which each Pr atom is surrounded by seven oxygens⁽¹²⁾. A single crystal x-ray has shown that one oxygen atom from each of the two bridging chelate rings is shared equally between the Pr atoms⁽¹²⁾. Sievers and coworkers, who first synthesized $\text{Ln}(\text{fod})_3$ complexes, observed that these preferred a monohydrated state⁽¹⁷⁾. It is thought that the water is hydrogen bonded to two perfluoropropyl side chains in the ligands and is not bonded to the metal ion⁽¹²⁾.

The structure of two LSR-substrate molecules has been determined. Horrocks reported the crystal and molecular

structure of the bis(4-picoline) adduct of Ho(dpm)_3 via x-ray crystallography⁽²²⁾. The coordination sphere can be described as a square antiprism in which the picoline occupies apices of opposite square faces. Axial symmetry is not present in the solid state. Cramer and Seff have reported similar data for the solid dipyridine adduct of Eu(dpm)_3 ⁽²³⁾.

D. The Substrate

Lanthanide shift reagents have been used successfully with a variety of substrate functional groups. The main criterion for effective LIS seems to be the Lewis basicity of the substrate. Sanders and Williams comment that strong Lewis bases have large LIS's while moderate Lewis bases are shifted less⁽²⁴⁾, and report the following order of functional group effectiveness,

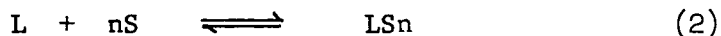


Lanthanide induced shifts have also been observed for other functional groups: e.g. nitro groups⁽²⁴⁾, phosphines⁽²⁴⁾, thioethers⁽²⁵⁾, oximes⁽²⁶⁾, and amides⁽²⁷⁾, sulfoxides⁽²⁸⁾ and epoxides⁽²⁹⁾.

E. Quantitation of LIS Data

Several graphical and analytical methods have been used to describe the behavior of lanthanide induced shifts, LIS's, in terms of shift indexes or parameters. Hinckley was quick to note that the LIS is dependent on the LSR concentration relative to the substrate⁽¹⁾. This implies a fast exchange,

on the NMR time scale between the complexed, and free substrate.



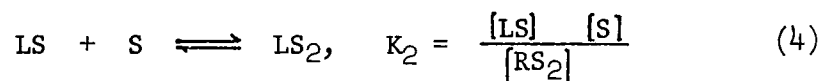
L represents the free LSR, S the unbound substrate and LS the bound substrate.

It is obvious that this equilibrium is temperature dependent, but the form of the dependence is not yet certain. Several reports have shown that the magnitude of LIS varies inversely with temperature^(18,30) (i.e. greater LIS is observed at lower temperatures) and this qualitative feature is secure.

The equilibrium expression for a 1:1 LSR-substrate adduct (complex) is

$$K_1 = \frac{[S][L]}{[LS]} \quad (3)$$

When a 2:1 LSR-substrate adduct is formed, the following equilibrium expression is applicable.



Reuben has shown the $K_2 = 4 K_1$ for an LSR with two equivalent and independent coordinating positions⁽³¹⁾.

The observed net chemical shift, Δ , can be represented by

$$\Delta = \Delta m \frac{S_b}{S_t}, \quad (5)$$

where Δm is the maximum shift of a given proton in the complex

relative to its uncomplexed shift. The concentration of bound substrate is S_b and the total concentration of substrate is S_t . Reuben has also shown that the intrinsic dissociation constant for n equivalent binding sites is

$$K = \frac{S_f (nL_t - S_b)}{S_b} \quad (6)$$

where S_f is the concentration of free substrate and L_t the total LSR concentration. Substituting S_b/S_t by σ and rearranging equation (6) yields

$$\sigma = \frac{n\rho}{1 + \frac{K}{(S_t - S_b)}}, \quad (7)$$

where $L_t/S_t = \rho$.

The observed net chemical shift can then be represented by

$$\Delta = \Delta_m \rho \quad (8)$$

From this it follows that at very low LSR concentrations and constant S_t where $S_t \gg S_b$, the plot of σ or Δ versus ρ will be linear. The slope of this line will be $n/[1 + K/S_t]$, where K is the intrinsic dissociation constant of the adduct. Demarco and Wenkert first applied this method of data manipulation⁽³²⁾, and defined an index. They plotted the Δ Eu for each LSR increment, versus the mole ratio of LSR to substrate. Their substrates were rigid alcohols, trans- and cis-4-tert-butyl-cyclohexanols, isoborneol, borneol, cholesterol and friedalanol.

Linear plots were claimed for L/S ratios ranging from 0 to 0.7. Deviations of approximately 2% were observed at low LSR concentrations. Demarco and Wenkert defined a paramagnetic induced shift index, ΔEu as

$$\Delta Eu = \delta_{\text{CDCl}_3} - \delta_{\text{Eu(dpm)}_3}^{n=1} \quad (9)$$

where δ_{CDCl_3} is the substrate proton chemical shift without LSR and $\delta_{\text{Eu(dpm)}_3}^{n=1}$ is the extrapolated proton chemical shift at and L/S ratio = 1.

Sanders and Williams subsequently reported similar results with Eu(dpm)_3 for a variety of substrates using L/S ratios up to 0.8⁽²⁴⁾.

Rondeau and Sievers investigated the effects of Eu(fod)_3 on ethyl propionate and di-n-butyl ether⁽¹²⁾. Since the greater solubility of fod complexes permits L/S ratios of greater than 1, they were able to demonstrate that the LIS leveled-off at L/S ratios of 1 or greater. Inaccurate knowledge of total LSR or substrate concentrations yields misleading values for shift parameters.

Algebraic manipulation of equation (7) can give

$$\frac{nL_t}{\sigma} = S_t + \frac{KS_t}{(S_t - S_b)} \quad (31) \quad (10)$$

Under the conditions $S_t \gg S_b$, equation (10) reduces to

$$S_t = \frac{nL_t}{\sigma} - K. \quad (11)$$

With the substitution of $\frac{1}{\sigma} = \frac{\Delta m}{\Delta}$, equation (11) becomes

$$S_t = \frac{nL_t \Delta m}{\Delta} - K. \quad (12)$$

Kelsey has used equation (12) for evaluating shift data⁽³³⁾.

He plotted S_t versus $1/\Delta$ with the condition that L_t be kept constant and $S_t \gg L_t$. Experimentally, this method requires the incremental addition of substrate to an LSR solution of known concentration. Such a plot for the acetoxy protons of allyl acetate resulted in a straight line and numerical value for K . When n , in equation (9) is known, the slope yields accurate values of Δm .

Solvent interactions and impurity interactions can cause problems⁽³¹⁾. An impurity, such as water, reduces the apparent Δm and appears to raise the value of K . Substrate association with the solvent decreases the slope and value of Δm .

Plots of L_t versus S_t at constant σ can yield similar information. Another rearrangement of equation (7) leads to

$$L_t = \frac{S_t \sigma}{n} + \frac{K \sigma}{n(1-\sigma)}. \quad (13)$$

Sanders et.al. have used this method for the data reduction of methyladamantanol versus $\text{Ln}(\text{dpm})_3$ in CCl_4 solution⁽³⁴⁾. The

experiment involves a series of LSR additions to various concentrations of substrate. Linear plots of L_t versus S_t with a slope of σ/n are obtained. If the value of n is known, Δm and K can be determined at constant Δ .

Armitage et.al. have also reported an elaborate procedure which attempts to describe the equilibrium between the LSR and the substrate⁽³⁵⁾. They show how to calculate the equilibrium binding constant, K_B , and the bond or limiting chemical shift, Δm , of the substrate molecule when it is associated with the lanthanide. The binding constant, K_B , for the process in equation 2 is defined as

$$K_B = \frac{[LS]}{[L][S]} = \frac{[LS]}{([K] - [LS])([S] - [LS])} \quad (14)$$

Equation 5, $\Delta = \Delta m S_b/St$, can be rewritten as

$$\Delta = \Delta m \frac{[LS]}{[S]} \quad (5b)$$

When equation 14 is solved for $[LS]$, and substituted for $[LS]$ in equation 5b (the $[LS]^2$ term is neglected), then

$$\Delta = \frac{K_B [L] \Delta m}{1 + K_B [S] + K_B [L]} \quad (15)$$

This can be rearranged to yield

$$[S] = [L] \Delta m \left(\frac{1}{\Delta} \right) - \left[\left(1/K_B \right) + [L] \right] \quad (16)$$

Equation 16 shows that a plot of $[S]$ versus $(1/\Delta)$ gives a straight line whose slope is $[L] \Delta m$ and whose y intercept is $- ((1/K_B) + L)$. Such a plot, it is claimed, can yield unambiguous values of Δm and K_B . The actual experimental procedure involves varying the substrate concentration at a constant LSR concentration with the restriction of $S \gg L$.

Shapiro and Johnston⁽³⁶⁾ have investigated the two step LSR-substrate interaction mechanism (equations 2 and 4),



The induced shift via the two-step interaction is defined as

$$\Delta = \frac{1}{S} (x \Delta_1 + 2y \Delta_2) \quad (17)$$

where X is the molar concentration of LS , Δ_1 the limiting shift of the LS complex (Δm), y the molar concentration of LS_2 complex and Δ_2 the limiting shift of the LS_2 complex.

Plots of $1/\Delta$ versus S at constant L under the conditions $S \gg L$ and plots of Δ versus L/S at constant S (also $S \gg L$) were observed to give reliable values of the limiting LIS value for the LS_2 species⁽³⁶⁾.

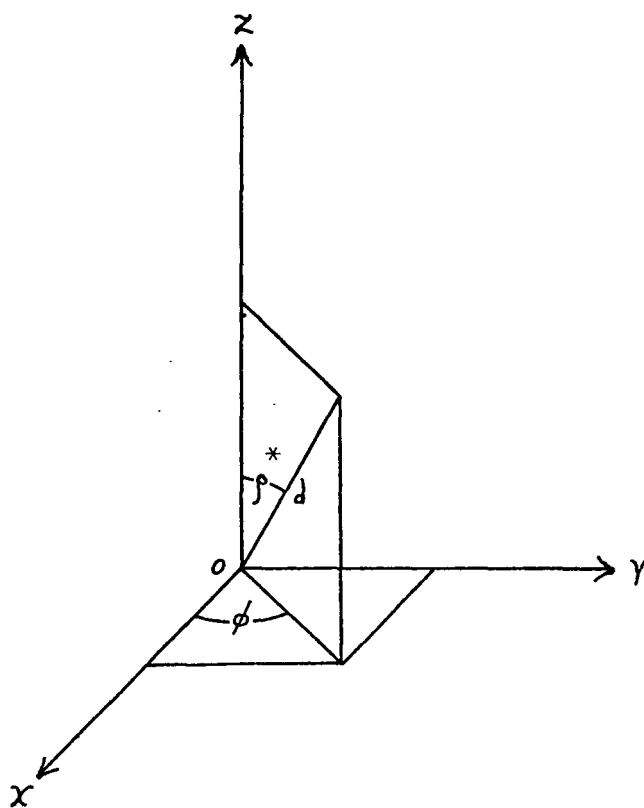
ApSimon has developed a heuristic method of LIS data reduction⁽³⁷⁾. A set of internally scaled parameters is generated by plotting the shift of a given resonance, Δ_i , against the sum of all observed shifts, $\sum \Delta_i$, for each L/S ratio. Errors in LSR and substrate weighings or concentrations do not effect the results. The slopes of the resulting straight lines are a set of internally scaled shift parameters for all protons in the substrate. The main disadvantage of this method lies in the fact that absolute values of Δ m and K values cannot be derived by this method. The real advantages of this method are (a) the exact concentrations of LSR or substrate need not be known, (b) solvent effects or water need not effect the result, (c) shift data from several separate runs can be combined in one data work-up.

F. Application of LSR

The LIS phenomenon has, perhaps, its greatest potential as a tool for organic structural determination.

Willcott and coworkers have presented one attractive method for comparing reduced experimental LIS data with shifts calculated from the simplified McConnell-Robertson pseudocontact equation, equation (1)⁽³⁸⁾. This approach places the substrate at the center of a Cartesian coordinate system (Figure 1). The lanthanide is then incrementally moved over the surface of a sphere at

Figure 1. The Coordinate System



radius, d , where d is the assumed lanthanide to substrate distance. As the lanthanide is moved about the sphere's surface, its location is described in terms of ρ (the colatitude measured from the positive Z axis) and ϕ (the azimuth, measured counterclockwise from the X - Z plane)⁽³⁸⁾.

A computer evaluation of the McConnell-Robertson variable is performed at each lanthanide position for all i protons assuming the principal axis is through the origin of the coordinate system. These numbers are then scaled by least squares against the relative observed shifts $(\Delta H/H)_{oi}$ to give a set of calculated shifts $(\Delta H/H)_{ci}$. The agreement between generated and observed data is represented by an agreement factor, R , defined as

$$R = \left[\frac{\sum_i ((\Delta H/H)_{oi}^2 - (\Delta H/H)_{ci})^2 W_i}{\sum_i (\Delta H/H)_{oi}^2 W_i} \right]^{1/2} \quad (18)$$

where W_i is a weighting factor.

Willcott et.al. have reported minimum agreement factors ranging from 0.032 for 2-adamantanol to 0.092* for cyclooctanetetraene dimer epoxide⁽³⁸⁾.

* Refinements have yielded agreement factors of 5% for the dimer epoxide. M. R. Willcott and R. E. Davis, Private Commun.

G. Statement of Purpose

Quantitative LIS data reduction methods and their application have been discussed. To date, no statistical evaluation of the various data reduction methods has appeared.

It was the purpose of this work to perform repetitive LIS experiments on four rigid organic molecules, 1-adamantanol, 2-adamantanol, 1-adamantanamine and 2-adamantanamine. $\text{Eu}(\text{fod})_3$ and $\text{Yb}(\text{fod})_3$ were used to determine data consistency between different lanthanides. LIS data reduction was via the Demarco⁽³²⁾ and experimentally less demanding ApSimon⁽³⁷⁾ methods for all data sets. Where possible, calculated shift parameters were scaled for comparison to typical data reported in the literature.

Observed LIS data reduction must consider the following statistics concepts:

1. Appropriateness. Do the chosen variables actually relate to and describe the phenomenon of interest:
(Do the LIS parameters relate to the McConnell-Robertson model?) This question is a justification for the present work but is beyond its scope.
2. Accuracy. Do the measurements approach the actual values of the chosen variables? This, again, cannot be determined without comparison to the McConnell-Robertson model.

3. Preciseness. How repeatable are the measurements?

That was the primary intent of this work.

II.

EXPERIMENTAL

EXPERIMENTAL

All Nuclear Magnetic Resonance (NMR) spectra were recorded on a Varian A-60 spectrometer at a constant probe temperature of 30°C. Both tetramethylsilane (TMS) and benzene were used as internal references for all measurements. All chemical shifts, Δ , are reported in Hertz (Hz) downfield from TMS.

The LSR's used in these studies were Eu(III) tris-1,1,1,2,2,-3,3-heptafluoro-7,7-dimethyl-4,6-octanedione and Yb(III) tris-1,1,1,2,2,3,3-heptafluoro-7,7-dimethyl-4,6-octanedione, hereafter denoted as Eu(fod)₃ and Yb(fod)₃ respectively. These LSR's were obtained commercially and used without further purification. Prior to each set of runs, the LSR was dried over P₄O₁₀ in vacuo and aliquots of 10,10,20,40 and 80 mg were weighed out, placed into "home made" 6 mm test tubes and sealed with Parafilm. These manipulations were performed in a nitrogen-purged glove box to minimize the possibility of contamination by atmospheric moisture.

Substrate samples of 1-adamantanol, 2-adamantanol and 1-adamantanamine were obtained commercially. 2-Adamantanamine was prepared from 2-adamantanamine hydrochloride by a procedure analogous to that reported by Smith and Williams⁽³⁷⁾. Five grams (0.026 moles) of amine hydrochloride in 25 mls of distilled water were neutralized with 10% NaOH solution. The free amine was extracted with petroleum ether, washed four times with distilled water, dried over magnesium sulfate and rotary evaporated to yield 3.6 grams of crude 2-adamantanamine.

Stock solutions of the alcohols and amines were prepared to assure uniform substrate concentrations for all eight runs in each series. The solutions were prepared as follows:

1-Adamantanol and 2-Adamantanol

After drying in vacuo, 0.381 grams (0.0026 moles) of alcohol were weighed out into a dry 5 ml volumetric flask. Commercial CDCl_3 (1% TMS) was added to make 5 mls of 0.5 molar solution. The stock solutions were prepared and stored in a nitrogen atmosphere.

1-Adamantanamine and 2-Adamantanamine

The 1-adamantanamine stock solution was prepared by weighing out 0.68 g (0.0045 moles) of freshly sublimed amine to a dry 5 ml volumetric flask. Molecular sieve dried CCl_4 with 1% TMS and 1% benzene was added to make 5 mls of 0.9 molar solution. A 0.88 molar 2-adamantanamine stock solution was prepared in the same manner. Freshly sublimed 2-adamantanamine (0.67 g) was dissolved in CCl_4 to make 5 mls of stock solution. The stock solution was prepared and stored in a nitrogen atmosphere.

Experiments were conducted in the following manner: Each sample was prepared by transferring 0.5 ml of substrate stock solution to a clean, nitrogen purged NMR tube via syringe. The substrate NMR spectrum was obtained. Then, the first 10 mg increment

of LSR was added. The sample was given five minutes to reach probe temperature (30°C) prior to running the spectrum. This procedure was repeated for additional increments of 10, 20, 40 and 80mg of LSR. In some experiments, particularly those involving $\text{Yb}(\text{fod})_3$, a smaller total of LSR, only four increments (10, 10, 20 and 40 mg), was used in order to minimize line broadening.

The observed shift data from each run were linearized via a computer least-squares procedure. The best fits for Δ obs. versus L/S ratio (Method I) and Δ obs. versus $\sum \Delta$ obs. (Method II) were calculated for each proton. These computations were performed on an IBM 1130 digital computer using a single precision, multiple regression program written by R. A. Issacs (copy in Appendix).

III.

RESULTS AND DISCUSSION

RESULTS AND DISCUSSION

A. General

Four repetitive, incrementally altered spectra were obtained for each of the substrate-LSR combinations listed in Table 2. Observed chemical shifts, Δ obs (in Hertz relative to TMS) and the results of the Demarco and ApSimon data reductions are presented in the tables. Combined data from all spectra in each set were evaluated. These results are presented in a separate table following each set.

Substrate protons have been numbered according to their distances from the oxygen or nitrogen atom, as determined by measurement of Dreiding stereomodels. The closest proton was assigned the smallest number*.

Four distinct, separate, first-order proton resonances are observable in LSR modified spectra of 1-adamantanol, I, and 1-adamantanamine, II. Figure 2 illustrates the numerical proton assignments*.

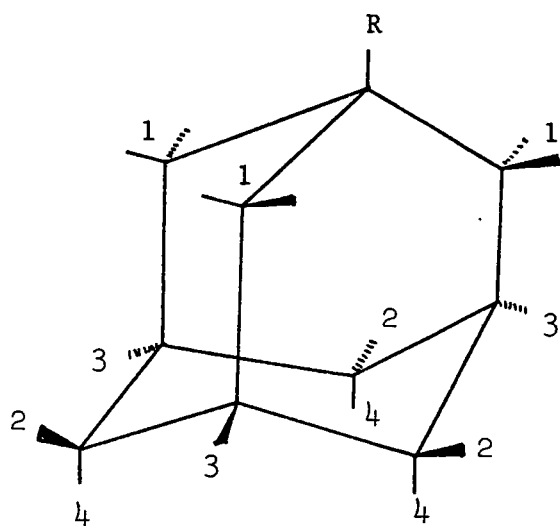
At the highest LSR concentration, nine proton resonances are distinguishable in the spectra of 2-adamantanol, VII, and 2-adamantanamine, VIII. Figure 3 shows these proton assignments.

* This is not according to IUPAC convention but simplifies the assignment of shift parameters.

Table 2. Index of Observed and Calculated Data Tables

<u>LSR</u> <u>Substrate</u>	<u>Eu(fod)₃</u> <u>Table Nos.</u>	<u>Yb(fod)₃</u> <u>Table Nos.</u>
1-Adamantanol, V Combined Runs	3-6 7	8-11 12
1-Adamantanamine, VI Combined Runs	13-16 17	18-21 22
2-Adamantanol, VII Combined Runs	23-26 27	28-31 32
2-Adamantanamine, VIII Combined Runs	33-36 37	38-41 42
Comparison of Demarco Eu and Yb Shift Parameters		
1-Adamantanol		43
1-Adamantanamine		
2-Adamantanol		44
2-Adamantanamine		
Comparison of ApSimon Eu and Yb Shift Parameters		
1-Adamantanol		45
1-Adamantanamine		
2-Adamantanol		46
2-Adamantanamine		

Figure 2. Proton Assignments for 1-Adamantananol and 1-Adamantanamine



V, R = -OH
VI, R = -NH₂

Prior to describing the data reduction, a brief outline of concepts is in order. The three most important concepts are:

1. The mathematical relationship of $(3\cos^2\theta - 1)/r^3$ is assumed to correlate LIS with the structure of the substrate.
2. Accurate LIS data are then the sets of numbers which give good correlations with $(3\cos^2\theta - 1)/r^3$.
3. The precision of these LIS parameters is described by the deviation of the computation. The accuracy must be similar because deviations of the same magnitude are obtained for McConnell-Robertson correlations.

B. Data Reduction with the DeMarco-Wenkert method.

The Demarco-Wenkert method of data reduction, Method I on the data tables (Tables 3-42), was chosen because it is experimentally the easiest. Observed LIS, Δ obs, was plotted via least-squares against the LSR to substrate ratio, L/S. The resulting shift parameters are summarized for V and VI in Table 43 and for VII and VIII in Table 44.

There are two runs with unusually large deviations in shift parameters compared to the remaining runs in their respective sets. The first $\text{Yb}(\text{fod})_3$ altered V (Table 8) has larger LIS than other runs of the set (Tables 9-11). This is

Table 3

Run No. 1

Eu (FOD)₃ Induced Proton Shifts^{a/} in 1-Adamantanol, in CDCl₃ at 60 MHz

Eu (FOD) ₃ (Total mg.)	Proton				$\sum \Delta$ Obs.	Mole Ratio L/S
	<u>1</u>	<u>3</u>	<u>2</u>	<u>4</u>		
10	124	134	104	104	462	0.038
20	152	142	112	108	514	0.077
40	198	156	127	125	606	0.154
80	294	184	168	142	788	0.308
160	486	241	228	192	1147	0.616
<u>Slopes</u>						
<u>Method I</u>	618.9	183.0	215.8	150.3		
Confidence Level						
90%	4.17	1.35	11.6	9.57		
99%	7.42	2.4	20.7	17.0		
<u>Method II</u>	0.5281	0.1572	0.1842	0.1282		
Confidence Level						
90%	0.0021	0.0081	0.0046	0.0040		
99%	0.0053	0.0145	0.0116	0.0101		

^{a/} Hz downfield from TMS.

Table 4

Run No. 2

Eu (FOD)₃ Induced Proton Shifts^{a/} in 1-Adamantanol, in CDCl₃ at 60 MHz

Eu (FOD) ₃ (Total mg.)	Proton				$\sum \Delta$ Obs.	Mole Ratio L/S
	<u>1</u>	<u>3</u>	<u>2</u>	<u>4</u>		
10	121	134	104	100	459	0.038
20	146	143	111	107	507	0.077
40	196	155	132	116	599	0.154
80	297	186	166	144	793	0.308
160	484	242	228	192	1146	0.616
<u>Slopes</u>						
<u>Method I</u>	624.3	184.9	214.1	158.7		
Confidence Level						
90%	10.2	3.78	8.47	5.8		
99%	18.1	6.72	15.1	10.3		
<u>Method II</u>	0.5281	0.1564	0.1811	0.1342		
Confidence Level						
90%	0.0009	0.0014	0.0027	0.0021		
99%	0.0023	0.0036	0.0068	0.0052		

a/ Hz downfield from TMS.

Table 5

Run No. 3

Eu (FOD)₃ Induced Proton Shifts^{a/} in 1-Adamantanol, in CDCl₃ at 60 MHz

<u>Eu (FOD)₃</u> <u>(Total mg.)</u>	<u>Proton</u>				<u>Σ Δ Obs.</u>	<u>Mole Ratio</u> <u>L/S</u>
	<u>1</u>	<u>3</u>	<u>2</u>	<u>4</u>		
10	126	135	105	101	467	0.038
20	151	141	112	108	512	0.077
40	200	156	133	118	607	0.154
80	302	187	167	144	800	0.308
160	476	238	226	188	1128	0.616
<u>Slopes</u>						
<u>Method I</u>	602.6	178.7	208.9	149.5		
<u>Confidence Level</u>						
90%	18.4	7.07	10.3	4.14		
99%	32.7	12.6	18.3	7.36		
<u>Method II</u>	0.5287	0.1568	0.1834	0.1311		
<u>Confidence Level</u>						
90%	0.0009	0.0007	0.0021	0.0015		
99%	0.0016	0.0013	0.0034	0.0027		

a/ Hz downfield from TMS.

Table 6

Run No. 4

Eu (FOD)₃ Induced Proton Shifts^{a/} in 1-Adamantanol, in CDCl₃ at 60 MHz

<u>Eu (FOD)₃</u> <u>(Total mg.)</u>	<u>Proton</u>				<u>Σ Δ Obs.</u>	<u>Mole Ratio</u> <u>L/S</u>
	<u>1</u>	<u>3</u>	<u>2</u>	<u>4</u>		
10	133	135	107	103	478	0.038
20	154	143	114	109	520	0.077
40	205	158	116	110	589	0.154
80	311	189	171	147	818	0.308
160	517	250	239	199	1205	0.616
 <u>Slopes</u>						
<u>Method I</u>	664.4	197.4	235.3	167.9		
<u>Confidence Level</u>						
90%	16.3	2.20	30.9	21.5		
99%	28.9	3.92	54.9	38.2		
 <u>Method II</u>	 0.5235	 0.1554	 0.1866	 0.1343		
<u>Confidence Level</u>						
90%	0.0097	0.0034	0.0079	0.0052		
99%	0.0241	0.0085	0.0198	0.0130		

a/ Hz downfield from TMS.

Table 7

Run Nos. 1-4 Combined

Eu (FOD)₃ Induced Proton Shifts in 1-Adamantanol, in CDCl₃ at 60 MHz

Eu (FOD) ₃ (Total mg.)	Proton				$\sum \Delta$ Obs.	Mole Ratio L/S
	<u>1</u>	<u>3</u>	<u>2</u>	<u>4</u>		
10	124	134	104	104	462	0.038
20	152	142	112	108	514	0.077
40	198	156	127	125	606	0.154
80	294	184	168	142	788	0.308
160	486	241	228	192	1147	0.616
10	121	134	104	100	459	0.038
20	146	143	111	107	507	0.077
40	196	155	132	116	599	0.154
80	297	186	166	144	793	0.308
160	484	242	228	192	1146	0.616
10	126	135	105	101	467	0.038
20	151	141	112	108	512	0.077
40	200	156	133	118	607	0.154
80	302	187	167	144	800	0.308
160	476	238	226	188	1128	0.616
10	133	135	107	103	478	0.038
20	154	143	114	109	520	0.077
40	205	158	116	110	589	0.154
80	311	189	171	142	818	0.308
160	517	250	239	199	1205	0.616
<u>Slopes</u>						
<u>Method I</u>	627.5	186.0	218.5	156.6		
<u>Confidence Level</u>						
90%	10.7	2.9	6.0	4.4		
99%	15.1	4.2	8.5	6.2		
<u>Method II</u>	0.5272	0.1562	0.1838	0.1316		
<u>Confidence Level</u>						
90%	0.0018	0.0006	0.0016	0.0014		
99%	0.0025	0.0009	0.0023	0.0020		

Table 8

Run No. 1

Yb (FOD)₃ Induced Proton Shifts^{a/} in 1-Adamantanol, in CDCl₃ at 60 MHz

<u>Yb (FOD)₃</u> <u>(Total mg.)</u>	<u>1</u>	<u>3</u>	Proton	<u>2</u>	<u>4</u>	<u>Σ Δ Obs.</u>	<u>Mole Ratio</u> <u>L/S</u>
10	184	154		123	119	580	0.038
20	266	180		156	136	698	0.076
40	405	224		201	175	1005	0.151
80	638	300		282	248	1468	0.302
<u>Slopes</u>							
<u>Method I</u>	1698.9	546.7		588.2	491.3		
Confidence Level							
90%	132.8	37.8		57.0	9.60		
99%	282.5	80.3		121.3	20.4		
<u>Method II</u>	0.5007	0.1610		0.1732	0.1445		
Confidence Level							
90%	0.0170	0.0053		0.0093	0.0050		
99%	0.0577	0.0182		0.0316	0.0172		

a/ Hz downfield from TMS.

Table 9

Run No. 2

Yb (FOD)₃ Induced Proton Shifts^{a/} in 1-Adamantanol, in CDCl₃ at 60 MHz

<u>Yb (FOD)₃</u> <u>(Total mg.)</u>	<u>Proton</u>				<u>ΣΔ Obs.</u>	<u>Mole Ratio</u> <u>L/S</u>
	<u>1</u>	<u>3</u>	<u>2</u>	<u>4</u>		
10	142	142	111	106	501	0.038
20	176	152	120	116	564	0.076
40	259	178	153	136	726	0.151
80	408	227	203	176	1014	0.302
<u>Slopes</u>						
<u>Method I</u>	1015.2	325.5	355.9	265.3		
<u>Confidence Level</u>						
90%	29.9	10.1	27.8	0.46		
99%	63.8	21.6	59.1	0.98		
<u>Method II</u>	0.5174	0.1658	0.1816	0.1351		
<u>Confidence Level</u>						
90%	0.0014	0.0014	0.0037	0.0020		
99%	0.0048	0.0050	0.0128	0.0069		

a/ Hz downfield from TMS.

Table 10

Run No. 3

Yb (FOD)₃ Induced Proton Shifts^{a/} in 1-Adamantanol, in CDCl₃ at 60 MHz

<u>Yb (FOD)₃</u> <u>(Total mg.)</u>	<u>Proton</u>				<u>Σ Δ Obs.</u>	<u>Mole Ratio</u> <u>L/S</u>
	<u>1</u>	<u>3</u>	<u>2</u>	<u>4</u>		
10	144	144	111	107	506	0.038
20	184	154	123	118	579	0.076
40	268	181	156	138	743	0.151
80	427	231	209	180	1047	0.302
<u>Slopes</u>						
<u>Method I</u>	1073.8	333.5	375.3	275.7		
<u>Confidence Level</u>						
90%	16.2	11.6	21.3	3.0		
99%	34.5	24.8	45.2	6.4		
<u>Method II</u>	0.521645	0.162061	0.182423	0.133870		
<u>Confidence Level</u>						
90%	0.0019	0.0019	0.0031	0.0019		
99%	0.0067	0.0065	0.0108	0.0067		

a/ Hz downfield from TMS.

Table 11

Run No. 4

Yb (FOD)₃ Induced Proton Shifts^{a/} in 1-Adamantanol, in CDCl₃ at 60 MHz

<u>Yb (FOD)₃</u> <u>(Total mg.)</u>	<u>Proton</u>				<u>Σ Δ Obs.</u>	<u>Mole Ratio</u> <u>L/S</u>
	<u>1</u>	<u>3</u>	<u>2</u>	<u>4</u>		
10	142	142	111	106	501	0.038
20	179	152	122	117	570	0.076
40	267	180	156	137	740	0.151
80	406	226	202	176	1010	0.302
<u>Slopes</u>						
<u>Method I</u>	1004.3	322.0	349.4	263.9		
<u>Confidence Level</u>						
90%	63.3	16.7	35.7	5.6		
99%	134.6	35.6	75.8	11.9		
<u>Method II</u>	0.5178	0.1659	0.1804	0.1357		
<u>Confidence Level</u>						
90%	0.0015	0.0019	0.0035	0.0032		
99%	0.0051	0.0065	0.0120	0.0109		

a/ Hz downfield from TMS.

Table 12

Run Nos. 1-4 Combined

Yb (FOD)₃ Induced Proton Shifts in 1-Adamantanol, in CDCl₃ at 60 MHz

<u>Yb (FOD)₃</u> <u>(Total mg.)</u>	<u>Proton</u>				<u>Σ Δ Obs.</u>	<u>Mole Ratio</u> <u>L/S</u>
	<u>1</u>	<u>3</u>	<u>2</u>	<u>4</u>		
10	184	154	123	119	580	0.038
20	266	180	156	136	698	0.076
40	405	224	201	175	1005	0.151
80	638	300	282	248	1468	0.302
10	142	142	111	106	501	0.038
20	176	152	120	116	564	0.076
40	259	178	153	136	726	0.151
80	408	227	203	176	1014	0.302
10	144	144	111	107	506	0.038
20	184	154	123	118	579	0.076
40	268	181	156	138	743	0.151
80	427	231	209	180	1047	0.302
10	142	142	111	106	501	0.038
20	179	152	122	117	570	0.076
40	267	180	156	137	740	0.151
80	406	226	202	176	1010	0.302
<u>Slopes</u>						
<u>Method I</u>	1198	381.9	417.3	324.0		
<u>Confidence Level</u>						
90%	165.5	52.5	57.3	48.9		
99%	236.1	75.0	81.7	69.7		
<u>Method II</u>	0.5138	0.1637	0.1785	0.1415		
<u>Confidence Level</u>						
90%	0.0031	0.0009	0.0016	0.0013		
99%	0.0044	0.0013	0.0023	0.0019		

Table 13

Run No. 1

Eu (FOD)₃ Induced Proton Shifts^{a/} in 1-Adamantanamine, in CCl₄ at 60 MHz

<u>Eu (FOD)₃</u> <u>(Total mg.)</u>	<u>Proton</u>				<u>ΣΔ Obs.</u>	<u>Mole Ratio</u> <u>L/S</u>
	<u>1</u>	<u>3</u>	<u>2</u>	<u>4</u>		
10	112	127	102	102	443	0.020
20	135	135	109	109	488	0.043
40	176	145	121	121	563	0.085
80	263	170	157	138	728	0.171
160	423	213	208	178	1022	0.341
<u>Slopes</u>						
<u>Method I</u>	969.9	266.6	335.6	232.4		
<u>Confidence Level</u>						
90%	13.4	7.81	18.9	9.95		
99%	23.9	13.9	33.5	17.7		
<u>Method II</u>	0.537	0.148	0.186	0.128		
<u>Confidence Level</u>						
90%	0.0016	0.0009	0.0035	0.0029		
99%	0.0028	0.0017	0.0063	0.005		

a/ Hz downfield from TMS.

Table 14

Run No. 2

Eu (FOD)₃ Induced Proton Shifts^{a/} in 1-Adamantanamine, in CCl₄, at 60 MHz

Eu (FOD) ₃ (Total mg.)	Proton				$\sum \Delta$ Obs.	Mole Ratio L/S
	1	3	2	4		
10	108	124	100	100	432	0.020
20	125	125	106	106	462	0.043
40	161'	141	117	117	536	0.085
80	235	162	138	138	673	0.171
160	380	201	195	166	942	0.341
<u>Slopes</u>						
<u>Method I</u>	851.5	245.8	294.7	205.4		
Confidence Level						
90%	7.03	16.4	19.3	20.4		
99%	12.5	29.3	34.3	36.3		
<u>Method II</u>	0.5329	0.1540	0.1844	0.1286		
Confidence Level						
90%	0.0026	0.0037	0.0058	0.0054		
99%	0.0047	0.0066	0.0103	0.0096		

^{a/} Hz downfield from TMS.

Table 15

Run No. 3

Eu (FOD)₃ Induced Proton Shifts^{a/} in 1-Adamantanamine, in CCl₄ at 60 MHz

Eu (FOD) ₃ (Total mg.)	Proton				$\sum \Delta$ Obs.	Mole Ratio L/S
	<u>1</u>	<u>3</u>	<u>2</u>	<u>4</u>		
10	103	125	100	100	428	0.020
20	117	129	104	104	454	0.043
40	154	140	115	115	524	0.085
80	223	160	136	136	655	0.171
160	357	195	187	174	913	0.341

Slopes

<u>Method I</u>	797.4	202.0	272.9	232.0
Confidence Level				
90%	12.0	7.73	14.1	5.69
99%	21.4	13.7	25.1	10.1
<u>Method II</u>	0.5235	0.1444	0.1792	0.1529
Confidence Level				
90%	0.0017	0.0019	0.0039	0.0011
99%	0.0009	0.0034	0.0069	0.0020

^{a/} Hz downfield from TMS.

Table 16

Run No. 4

Eu (FOD)₃ Induced Proton Shifts^{a/} in 1-Adamantanamine, in CCl₄ at 60 MHz

<u>Eu (FOD)₃</u> <u>(Total mg.)</u>	<u>Proton</u>				<u>Σ Δ Obs.</u>	<u>Mole Ratio</u> <u>L/S</u>
	<u>1</u>	<u>3</u>	<u>2</u>	<u>4</u>		
10	99	123	99	99	420	0.020
20	115	127	103	103	448	0.043
40	140	132	111	111	494	0.085
80	206	158	133	133	630	0.171
160	354	194	187	173	908	0.341
<u>Slopes</u>						
<u>Method I</u>	797.3	227.3	276.9	233.8		
<u>Confidence Level</u>						
90%	42.5	17.4	23.1	7.9		
99%	75.5	30.9	41.2	14.1		
<u>Method II</u>	0.519	0.148	0.1807	0.1521		
<u>Confidence Level</u>						
90%	0.0036	0.0045	0.0032	0.0020		
99%	0.0064	0.008	0.0056	0.0035		

a/ Hz downfield from TMS.

Table 17

Run Nos. 1-4 Combined

Eu (FOD)₃ Induced Proton Shifts in 1-Adamantanamine, in CCl₄ at 60 MHz

Eu (FOD) ₃ (Total mg.)	Proton				$\Sigma \Delta$ Obs.	Mole Ratio L/S
	1	3	2	4		
10	112	127	102	102	443	0.020
20	135	135	109	109	488	0.043
40	176	145	121	121	563	0.085
80	263	170	157	138	728	0.171
160	423	213	208	178	1022	0.341
10	108	124	100	100	432	0.020
20	125	125	106	106	462	0.043
40	161	141	117	117	536	0.085
80	235	162	138	138	673	0.171
160	380	201	195	166	942	0.341
10	103	125	100	100	428	0.020
20	117	129	104	104	454	0.043
40	154	140	115	115	529	0.085
80	223	160	136	136	655	0.171
160	357	195	187	174	913	0.341
10	99	123	99	99	420	0.020
20	115	127	103	103	448	0.043
40	140	132	111	111	494	0.085
80	206	158	133	133	630	0.171
160	354	194	187	173	908	0.341

Slopes

Method I	854.0	239.9	295.1	226.1
Confidence Level				
90%	39.5	11.4	14.4	6.9
99%	55.9	16.2	20.4	9.8
Method II	0.5299	0.1488	0.1831	0.1382
Confidence Level				
90%	0.0015	0.0011	0.0013	0.0020
99%	0.0021	0.0015	0.0019	0.0029

Table 18

Run No. 1

Yb (FOD)₃ Induced Proton Shifts^{a/} in 1-Adamantanamine, in CCl₄ at 60 MHz

Yb (FOD) ₃ (Total mg.)	Proton				$\Sigma \Delta$ Obs.	Mole Ratio L/S
	<u>1</u>	<u>3</u>	<u>2</u>	<u>4</u>		
10	124	129	106	106	465	0.021
20	150	143	115	115	523	0.042
40	204	157	130	130	621	0.084
80	308	190	174	150	822	0.167
<u>Slopes</u>						
<u>Method I</u>	1261.9	403.3	465.9	295.7		
Confidence Level						
90%	7.89	42.3	47.6	44.3		
99%	16.8	89.9	101.3	94.3		
<u>Method II</u>	0.5198	0.1664	0.1918	0.1219		
Confidence Level						
90%	0.005	0.0109	0.0077	0.0064		
99%	0.0107	0.0052	0.0164	0.0137		

a/ Hz downfield from TMS.

Table 19

Run No. 2

Yb (FOD)₃ Induced Proton Shifts^{a/} in 1-Adamantanamine, in CCl₄ at 60 MHz

<u>Yb (FOD)₃</u> <u>(Total mg.)</u>	<u>Proton</u>				<u>Σ Δ Obs.</u>	<u>Mole Ratio</u> <u>L/S</u>
	<u>1</u>	<u>3</u>	<u>2</u>	<u>4</u>		
10	120	128	104	104	456	0.021
20	145	140	112	112	509	0.042
40	206	159	132	132	629	0.084
80	315	193	176	152	836	0.167
160	501	248	239	202	1190	0.334
<u>Slopes</u>						
<u>Method I</u>	1221.4	378.4	437.4	306.6		
<u>Confidence Level</u>						
90%	55.5	28.1	28.5	23.4		
99%	98.7	49.9	50.6	41.7		
<u>Method II</u>	0.5209	0.1617	0.1866	0.1308		
<u>Confidence Level</u>						
90%	0.0025	0.0024	0.0032	0.0041		
99%	0.0044	0.0043	0.0058	0.0074		

a/ Hz downfield from TMS.

Table 20

Run No. 3

Yb (FOD)₃ Induced Proton Shifts^{a/} in 1-Adamantanamine, in CCl₄ at 60 MHz

<u>Yb (FOD)₃</u> <u>(Total mg.)</u>	<u>Proton</u>				<u>Σ Δ Obs.</u>	<u>Mole Ratio</u> <u>L/S</u>
	<u>1</u>	<u>3</u>	<u>2</u>	<u>4</u>		
10	124	130	106	106	466	0.021
20	152	140	114	114	520	0.042
40	207	159	132	132	630	0.084
80	307	191	174	150	822	0.167
160	485	245	232	198	1160	0.334
<u>Slopes</u>						
<u>Method I</u>	1149.4	364.4	408	286.8		
<u>Confidence Level</u>						
90%	45.7	23.6	28.6	20.9		
99%	81.2	41.9	50.9	37.3		
<u>Method II</u>	0.5202	0.1652	0.1849	0.1298		
<u>Confidence Level</u>						
90%	0.0019	0.0015	0.0039	0.0041		
99%	0.0034	0.0027	0.0069	0.0072		

^{a/} Hz downfield from TMS.

Table 21

Run No. 4

Yb (FOD)₃ Induced Proton Shifts^{a/} in 1-Adamantanamine, in CCl₄ at 60 MHz

<u>Yb (FOD)₃</u> <u>(Total mg.)</u>	<u>Proton</u>				<u>Σ Δ Obs.</u>	<u>Mole Ratio</u> <u>L/S</u>
	<u>1</u>	<u>3</u>	<u>2</u>	<u>4</u>		
10	128	131	107	107	473	0.021
20	152	141	115	115	523	0.042
40	211	159	132	132	634	0.084
80	317	194	176	153	840	0.167
160	502	251	239	203	1195	0.334
<u>Slopes</u>						
<u>Method I</u>	1199.3	382.1	428.3	301.3		
<u>Confidence Level</u>						
90%	47.4	20.8	25.0	15.7		
99%	84.3	37.0	44.5	27.9		
<u>Method II</u>	0.5189	0.1654	0.1854	0.1303		
<u>Confidence Level</u>						
90%	0.0012	0.0014	0.0035	0.0061		
99%	0.0021	0.0025	0.0061	0.0034		

a/ Hz downfield from TMS.

Table 22

Run Nos. 1-4 Combined

Yb (FOD)₃ Induced Proton Shifts in 1-Adamantanamine, in CCl₄ at 60 MHz

Yb (FOD) ₃ (Total mg.)	Proton				$\sum \Delta$ Obs.	Mole Ratio L/S
	1	3	2	4		
10	124	129	106	106	465	0.021
20	150	143	115	115	523	0.042
40	204	157	130	130	621	0.084
80	308	190	174	150	822	0.167
10	120	128	104	104	456	0.021
20	145	140	112	112	509	0.042
40	206	159	132	132	629	0.084
80	315	193	176	152	836	0.167
160	501	248	239	202	1190	0.334
10	124	130	106	106	466	0.021
20	152	140	114	114	520	0.042
40	207	159	132	132	630	0.084
80	307	191	174	150	822	0.167
160	485	245	232	198	1160	0.334
10	128	131	107	107	473	0.021
20	152	141	115	115	523	0.042
40	211	159	132	132	634	0.084
80	317	194	176	153	840	0.167
160	502	251	239	203	1095	0.334

Slopes

<u>Method I</u>	1194.8	376.7	426.7	298.3
Confidence Level				
90%	18.8	8.4	9.8	7.2
99%	26.6	11.9	13.9	10.2
<u>Method II</u>	0.5407	0.1706	0.1933	0.1349
Confidence Level				
90%	0.0061	0.0021	0.0024	0.0021
99%	0.0087	0.0029	0.0033	0.0030

Table 23

Run No. 1

Eu (FOD)₃ Induced Proton Shifts^{a/} in 2-Adamantanol, in CDCl₃ at 60 MHz

Eu (FOD) ₃ (Total mg.)	Proton									$\Sigma \Delta_{\text{Obs.}}$	Mole Ratio L/S
	1	2	3	4	5	6	7	8	9		
10	274	154	140	114	114	114	114	114	114	1252	0.038
20	310	180	165	121	121	121	121	121	121	1381	0.077
40	372	222	205	145	145	132	132	132	132	1617	0.154
80	498	308	286	186	176	162	158	154	148	2076	0.308
160	771	491	460	271	258	226	214	208	192	3091	0.616
200	886	564	531	307	288	250	236	227	205	3494	0.772
<u>Slopes</u>											
<u>Method I</u>	837	561	534	266	240	189	168	156	125		
Confidence Level											
90%	13	11	9	6	8	6	4	5	5		
99%	22	18	15	9	13	10	7	8	9		
<u>Method II</u>	0.2719	0.1824	0.1736	0.0865	0.0781	0.0614	0.0546	0.0507	0.0406		
Confidence Level											
90%	0.0008	0.0005	0.0005	0.0007	0.0008	0.0007	0.0003	0.0004	0.0006		
99%	0.0013	0.0009	0.0008	0.0012	0.0014	0.0011	0.0005	0.0006	0.0010		

^{a/} Hz downfield from TMS.

Table 24

Run No. 2

Eu (FOD)₃ Induced Proton Shifts^{a/} in 2-Adamantanol, in CDCl₃ at 60 MHz

Eu (FOD) ₃ (Total mg.)	Proton									$\sum \Delta$ Obs.	Mole Ratio L/S
	1	2	3	4	5	6	7	8	9		
10	273	154	140	114	114	114	114	114	114	1251	0.038
20	316	184	169	122	122	122	122	122	122	1401	0.077
40	385	231	213	150	150	136	136	136	136	1673	0.154
80	549	342	319	198	198	170	168	164	158	2266	0.308
160	828	528	496	290	275	238	225	217	199	3296	0.616

SlopesMethod I
Confidence Level

90%	25	19	18	9	17	7	4	2	7.4
99%	45	33	32	17	29	12	7	4	13

Method II
Confidence Level

90%	0.0009	0.0008	0.0009	0.0012	0.0016	0.0014	0.0003	0.0003	0.0010
99%	0.0017	0.0014	0.0015	0.0022	0.0031	0.0025	0.0005	0.0007	0.0017

^{a/} Hz downfield from TMS.

Table 25

Run No. 3

Eu (FOD)₃ Induced Proton Shifts^{a/} in 2-Adamantanol, in CDCl₃ at 60 MHz

Eu (FOD) ₃ (Total mg.)	Proton									$\Sigma \Delta$ Obs.	Mole Ratio L/S
	1	2	3	4	5	6	7	8	9		
10	293	168	152	117	117	117	117	117	117	1315	0.038
20	322	188	172	122	122	122	122	122	122	1414	0.077
40	396	238	219	154	154	138	138	138	138	1713	0.154
80	537	334	312	195	195	167	165	162	158	2225	0.308
160	845	534	506	295	280	241	228	221	201	3351	0.616

SlopesMethod I
Confidence Level

90%	32	16	16	16	15	14	8	7	7
99%	57	29	28	28	27	25	14	13	12

Method II
Confidence Level

90%	0.0016	0.0009	0.0011	0.0012	0.0020	0.0013	0.0004	0.0004	0.0012
99%	0.0028	0.0017	0.0019	0.0022	0.0036	0.0024	0.0007	0.0008	0.0021

^{a/} Hz downfield from TMS.

Table 26

Run No. 4

Eu (FOD)₃ Induced Proton Shifts^{a/} in 2-Adamantanol, in CDCl₃ at 60 MHz

Eu (FOD) ₃ (Total mg.)	Proton									$\sum \Delta$ obs.	Mole Ratio L/S
	1	2	3	4	5	6	7	8	9		
10	273	155	140	113	113	113	113	113	113	1246	0.038
20	307	179	162	120	120	120	120	120	120	1368	0.077
40	375	214	206	146	146	133	133	133	133	1619	0.154
80	517	321	298	187	188	163	160	158	153	2145	0.308
160	819	523	490	286	272	236	224	216	198	3264	0.616

Slopes

<u>Method I</u>	939	636	602	298	275	211	190	176	144	
Confidence Level										
90%	27	29	15	14	9	14	9	6	3	
99%	48	51	27	25	15	25	16	11	6	
<u>Method II</u>	0.2703	0.1832	0.1733	0.0861	0.0792	0.0608	0.0548	0.0507	0.0414	
Confidence Level										
90%	0.0003	0.0026	0.0005	0.0012	0.0016	0.0012	0.0006	0.0004	0.0009	
99%	0.0005	0.0047	0.0009	0.0021	0.0029	0.0022	0.0011	0.0007	0.0018	

^{a/} Hz downfield from TMS.

Table 27

Run Nos. 1-4 Combined

Eu (FOD)₃ Induced Proton Shifts in 2-Adamantanol, in CDCl₃ at 60 MHz

Eu (FOD) ₃ (Total mg.)	Proton									$\Sigma \Delta$ Obs.	Mole Ratio L/S
	1	2	3	4	5	6	7	8	9		
10	274	154	140	114	114	114	114	114	114	1252	0.038
20	310	180	165	121	121	121	121	121	121	1381	0.077
40	372	222	205	145	145	132	132	132	132	1617	0.154
80	498	308	286	186	176	162	158	154	148	2076	0.308
160	771	491	460	271	258	226	214	208	192	3091	0.616
200	886	564	531	307	288	250	236	227	205	3494	0.772
10	273	154	140	114	114	114	114	114	114	1251	0.038
20	316	184	169	122	122	122	122	122	122	1401	0.077
40	385	231	213	150	150	136	136	136	136	1673	0.154
80	549	342	319	198	198	170	168	164	158	2266	0.308
160	828	528	496	290	275	238	225	217	199	3296	0.616
10	293	168	152	117	117	117	117	117	117	1315	0.038
20	322	188	172	122	122	122	122	122	122	1414	0.077
40	396	238	219	154	154	138	138	138	138	1713	0.154
80	537	334	312	195	195	167	165	162	158	2225	0.308
160	845	534	506	295	280	241	228	221	201	3351	0.616
10	273	155	140	113	113	113	113	113	113	1246	0.038
20	307	179	162	120	120	120	120	120	120	1368	0.077
40	375	214	206	146	146	133	133	133	133	1619	0.154
80	517	321	298	187	188	163	160	158	153	2145	0.308
160	819	523	490	286	272	236	224	216	198	3264	0.616
<u>Slopes</u>											
<u>Method I</u>	892.8	589.1	517.3	285.8	259.9	201.3	179.7	166.5	134.3		
Confidence Level											
90%	23.7	16.1	15.3	7.8	8.6	5.5	4.9	4.7	4.4		
99%	33.3	22.7	21.5	11.0	12.1	7.8	6.8	6.5	6.2		
<u>Method II</u>	0.2712	0.1820	0.1736	0.0868	0.0791	0.0611	0.0546	0.0506	0.0409		
Confidence Level											
90%	0.0003	0.0005	0.0002	0.0003	0.0005	0.0004	0.0001	0.0001	0.0003		
99%	0.0005	0.0006	0.0003	0.0005	0.0007	0.0005	0.0002	0.0002	0.0004		

Table 28

Run No. 1

Yb (FOD)₃ Induced Proton Shifts^{a/} in 2-Adamantanol, in CDCl₃ at 60 MHz

Yb (FOD) ₃ (Total mg.)	Proton									$\Sigma \Delta$ Obs.	Mole Ratio L/S
	1	2	3	4	5	6	7	8	9		
10	363	217	198	140	138	138	134	134	134	1596	0.038
20	482	298	274	179	179	161	161	151	151	2036	0.076
40	698	446	412	243	238	208	208	192	192	2937	0.151
80	984	648	602	337	322	273	273	250	235	3924	0.302

Slopes

Method I	2320	1612	1511	733	678	508	518.5	411	382
Confidence Level									
90%	334	215	199	92	107	59	70	42	73
99%	711	458	422	196	228	126	150	90	154
Method II	0.2667	0.1852	0.1734	0.0842	0.0780	0.0582	0.0595	0.0504	0.0440
Confidence Level									
90%	0.0012	0.0002	0.0004	0.0009	0.0018	0.0008	0.0002	0.0016	0.0016
99%	0.0026	0.0006	0.0009	0.002	0.0038	0.0017	0.0004	0.0034	0.0035

a/ Hz downfield from TMS.

Table 29

Run No. 2

Yb (FOD)₃ Induced Proton Shifts^{a/} in 2-Adamantanol, in CDCl₃ at 60 MHz

Yb (FOD) ₃ (Total mg.)	Proton									$\Sigma \Delta$ Obs.	Mole Ratio L/S
	1	2	3	4	5	6	7	8	9		
10	392	238	217	145	145	140	140	134	134	1685	0.038
20	513	324	297	190	179	168	168	157	157	2153	0.076
40	712	460	424	250	244	211	211	196	196	2904	0.151
80	1042	696	644	359	342	286	286	262	245	4161	0.302

Slopes

Method I
Confidence Level
90%
99%

2427	1708	1593	790	740	544	544	479	412
209	135	125	78	71	45	45	36	70
446	287	267	166	151	96	96	76	150

Method II
Confidence Level
90%
99%

0.2627	0.1848	0.1723	0.0856	0.0802	0.0588	0.0588	0.0518	0.0449
0.0005	0.0010	0.0009	0.0013	0.0013	0.0003	0.0003	0.0004	0.0022
0.0011	0.0021	0.0019	0.0029	0.0027	0.0007	0.0007	0.0008	0.0046

a/ Hz downfield from TMS.

Table 30

Run No. 3

Yb (FOD)₃ Induced Proton Shifts^{a/} in 2-Adamantanol, in CDCl₃ at 60 MHz

Yb (FOD) ₃ (Total mg.)	Proton									$\sum \Delta$ Obs.	Mole Ratio L/S
	1	2	3	4	5	6	7	8	9		
10	335	198	181	138	128	128	128	128	128	1492	0.038
20	456	285	260	172	172	155	155	146	146	1947	0.076
40	628	404	370	222	217	193	193	179	179	2585	0.151
80	923	607	560	318	309	257	257	236	222	3689	0.302

Slopes

<u>Method I</u>	2178	1511	1402	670	659	477	477	406	351		
Confidence Level											
90%	224	169	147	43	86	53	53	23	52		
99%	476	360	312	90	183	112	112	50	111		
<u>Method II</u>	0.2678	0.1859	0.1724	0.0822	0.0811	0.0587	0.0587	0.0497	0.0433		
Confidence Level											
90%	0.0003	0.0009	0.0002	0.0019	0.0022	0.0003	0.0003	0.0014	0.0017		
99%	0.0007	0.0020	0.0004	0.0040	0.0049	0.0005	0.0005	0.0031	0.0036		

a/ Hz downfield from TMS.

Table 31

Run No. 4

Yb (FOD)₃ Induced Proton Shifts^{a/} in 2-Adamantanol, in CDCl₃ at 60 MHz

Yb (FOD) ₃ (Total mg.)	Proton									$\sum \Delta$ Obs.	Mole Ratio L/S
	1	2	3	4	5	6	7	8	9		
10	326	194	175	135	135	126	126	126	126	1469	0.038
20	448	278	254	169	169	153	153	145	145	1914	0.076
40	632	406	273	224	218	194	194	180	180	2501	0.151
80	960	630	580	329	316	255	255	243	228	3796	0.302

Slopes

Method I	2360	1623	1484	726	674	478	478	441	382		
Confidence Level											
90%	188	135	430	34	39	64	64	19	50		
99%	400	287	914	73	83	137	137	41	106		
Method II	0.2729	0.1878	0.1716	0.0839	0.0779	0.0553	0.0553	0.0509	0.0441		
Confidence Level											
90%	0.0085	0.0064	0.0284	0.0017	0.0010	0.0036	0.0036	0.0015	0.0031		
99%	0.0181	0.0136	0.0605	0.0035	0.0022	0.0076	0.0076	0.0032	0.0066		

a/ Hz downfield from TMS.

Table 32

Run Nos. 1-4 Combined

Yb (FOD)₃ Induced Proton Shifts in 2-Adamantanol, in CDCl₃ at 60 MHz

Yb(FOD) ₃ (Total mg.)	Proton									ΣΔ Obs.	Mole Ratio L/S
	1	2	3	4	5	6	7	8	9		
10	363	217	198	140	138	138	138	134	134	1596	0.038
20	482	298	274	179	179	161	161	151	151	2036	0.076
40	698	446	412	243	238	208	208	192	192	2937	0.151
80	984	648	602	337	322	273	273	250	235	3924	0.302
10	392	238	217	145	145	140	140	134	134	1685	0.038
20	513	324	297	190	179	168	168	157	157	2153	0.076
40	712	460	424	250	244	211	211	196	197	2904	0.151
80	1042	696	644	359	342	286	286	262	245	4161	0.302
10	335	198	181	138	128	128	128	128	128	1492	0.038
20	456	285	260	172	172	155	155	146	146	1947	0.076
40	628	404	370	222	217	198	198	179	179	2585	0.151
80	923	607	560	318	309	257	257	236	222	3689	0.302
10	326	194	175	135	135	126	126	126	126	1469	0.038
20	448	278	254	169	169	153	153	145	145	1914	0.076
40	632	406	273	224	218	194	194	180	180	2501	0.151
80	960	630	580	329	316	255	255	243	228	3796	0.302

Slopes

<u>Method I</u>	2321.4	1613.7	1497.5	730.0	688.1	501.8	501.8	441.7	381.7
Confidence Level									
90%	106.3	74.2	98.1	31.7	30.1	26.3	26.3	19.4	22.1
99%	151.5	105.9	140.0	45.3	42.8	37.5	37.5	27.7	31.6
<u>Method II</u>	0.2671	0.1857	0.1733	0.0839	0.0790	0.0579	0.0579	0.0507	0.0442
Confidence Level									
90%	0.0012	0.0009	0.0035	0.0005	0.0006	0.0005	0.0005	0.0003	0.0005
99%	0.0018	0.0013	0.0049	0.0007	0.0008	0.0007	0.0007	0.0005	0.0007

Table 33

Run No. 1

Eu (FOD)₃ Induced Proton Shifts^{a/} in 2-Adamantanamine, in CCl₄ at 60 MHz

<u>Eu (FOD)₃</u> <u>(Total mg.)</u>	<u>Proton</u>									<u>Σ Δ Obs.</u>	<u>Mole Ratio</u> <u>L/S</u>
	<u>1</u>	<u>3</u>	<u>2</u>	<u>4</u>	<u>5</u>	<u>6</u>	<u>7</u>	<u>8</u>	<u>9</u>		
10	195	118	138	113	113	113	113	113	113	1129	0.022
20	216	130	150	115	115	115	115	115	115	1186	0.044
40	258	168	176	122	122	122	122	122	122	1334	0.088
80	347	238	232	149	147	147	142	138	138	1678	0.175
160	526	382	344	208	200	200	177	172	172	2381	0.350
200	600	442	391	235	227	222	194	187	187	2685	0.439
<u>Slopes</u>											
<u>Method I</u>	984	791.4	615.9	302.7	280.4	271.9	198.9	181.8	181.8		
<u>Confidence Level</u>											
90%	18.1	15.8	11.1	17.1	14.9	13.7	5.81	5.07	5.07		
99%	29.8	26.0	18.3	28.2	24.5	22.5	9.55	8.32	8.32		
<u>Method II</u>	0.2572	0.2065	0.1614	0.0803	0.0751	0.0715	0.0521	0.0479	0.0479		
<u>Confidence Level</u>											
90%	0.0016	0.0013	0.0008	0.0012	0.0012	0.0008	0.0003	0.0002	0.0002		
99%	0.0024	0.0020	0.0012	0.0019	0.0019	0.0013	0.0005	0.0003	0.0003		

^{a/} Hz downfield from TMS.

Table 34

Run No. 2

Eu (FOD)₃ Induced Proton Shifts^{a/} in 2-Adamantanamine, in CCl₄ at 60 MHz

Eu (FOD) ₃ (Total mg.)	Proton									$\Sigma \Delta$ Obs.	Mole Ratio L/S
	1	3	2	4	5	6	7	8	9		
10	194	112	136	111	111	111	111	111	111	1108	0.022
20	221	135	154	117	117	117	117	117	117	1212	0.044
40	266	174	182	126	126	126	126	126	126	1378	0.088
80	359	247	240	154	150	150	141	141	141	1723	0.175
160	537	393	353	214	207	203	180	174	174	2435	0.350
200	613	442	407	243	235	230	200	192	192	2754	0.439

Slopes

Method I	1008.6	800.9	647.1	320.3	299.2	286.3	210.3	190.0	190.0
Confidence Level									
90%	20.9	31.9	6.9	10.9	11.1	8.5	5.4	3.3	3.3
99%	34.4	52.4	11.4	17.9	18.3	13.9	8.8	5.4	5.4
Method II	0.2552	0.2027	0.1637	0.0810	0.0757	0.0724	0.0532	0.0481	0.0481
Confidence Level									
90%	0.0018	0.0032	0.0007	0.0015	0.0015	0.0012	0.0008	0.0006	0.0006
99%	0.0029	0.0053	0.0011	0.0024	0.0025	0.0020	0.0013	0.0009	0.0009

a/ Hz downfield from TMS.

Table 35

Run No. 3

Eu (FOD)₃ Induced Proton Shifts^{a/} in 2-Adamantanamine, in CCl₄, at 60 MHz

Eu (FOD) ₃ (Total mg.)	Proton									$\Sigma \Delta$ Obs.	Mole Ratio L/S
	1	3	2	4	5	6	7	8	9		
10	198	112	140	112	112	112	112	112	112	1122	0.022
20	226	138	156	116	116	116	116	116	116	1216	0.044
40	275	180	188	128	128	128	128	128	128	1411	0.088
80	392	273	261	163	157	157	150	145	145	1843	0.175
160	600	439	389	233	225	220	192	195	185	2668	0.350
200	682	505	440	259	252	244	209	208	201	2993	0.439

Slopes

Method I	1178.4	950.5	731.3	366.5	346.1	326.9	236.8	215.7	215.7
Confidence Level									
90%	35.1	30.1	22.5	14.4	13.4	11.1	6.4	5.2	5.2
99%	53.5	49.5	37.0	23.6	22.0	18.2	10.5	8.6	8.6
Method II	0.2580	0.2081	0.1601	0.0802	0.0757	0.0716	0.0518	0.0472	0.0472
Confidence Level									
90%	0.0013	0.0018	0.0010	0.0013	0.0016	0.0011	0.0005	0.0006	0.0006
99%	0.0022	0.0029	0.0016	0.0021	0.0027	0.0018	0.0003	0.0009	0.0009

^{a/} Hz downfield from TMS.

Table 36

Run No. 4

Eu (FOD)₃ Induced Proton Shifts^{a/} in 2-Adamantanamine, in CCl₄ at 60 MHz

Eu (FOD) ₃ (Total mg.)	Proton									$\sum \Delta$ Obs.	Mole Ratio L/S
	1	3	2	4	5	6	7	8	9		
10	197	119	137	111	111	111	111	111	111	1111	0.022
20	222	136	154	116	116	116	116	116	116	1208	0.044
40	275	180	187	128	128	128	128	128	128	1410	0.088
80	466	334	309	187	182	177	166	161	161	2143	0.175
160	566	414	370	223	216	210	197	190	190	2576	0.350
200	648	478	421	251	242	239	203	196	196	2874	0.439
<u>Slopes</u>											
<u>Method I</u>	1082.2	875.2	680.2	341.1	318.4	306.9	231.9	212.7	212.7		
Confidence Level											
90%	162.3	135.2	105.6	42.8	39.1	33.5	35.1	30.6	30.6		
99%	266.7	222.1	173.6	70.4	64.3	55.0	57.6	50.3	50.3		
<u>Method II</u>	0.2545	0.2061	0.1602	0.0769	0.0742	0.0712	0.0514	0.0497	0.0497		
Confidence Level											
90%	0.0016	0.0019	0.0013	0.0010	0.0012	0.0017	0.0016	0.0015	0.0015		
99%	0.0026	0.0030	0.0022	0.0023	0.0019	0.0029	0.0026	0.0024	0.0024		

^{a/} Hz downfield from TMS.

Table 37

Run Nos. 1-4 Combined

Eu (FOD)₃ Induced Proton Shifts in 2-Adamantanamine, in CCl₄ at 60 MHz

Eu (FOD) ₃ (Total mg.)	Proton									$\Sigma \Delta$ Obs.	Total Ratio L/s
	1	2	3	4	5	6	7	8	9		
10	195	118	138	113	113	113	113	113	113	1129	0.022
20	216	130	150	115	115	115	115	115	115	1186	0.044
40	258	168	176	122	122	122	122	122	122	1334	0.088
80	347	238	232	149	147	147	142	138	138	1678	0.175
160	526	382	344	208	200	200	177	172	172	2381	0.350
200	600	442	391	235	227	222	194	187	187	2685	0.439
10	194	112	136	111	111	111	111	111	111	1108	0.022
20	221	135	154	117	117	117	117	117	117	1212	0.044
40	266	174	182	126	126	126	126	216	126	1378	0.088
80	359	247	240	154	150	150	141	141	141	1723	0.175
160	537	393	353	214	207	203	180	174	174	2435	0.350
200	613	442	407	243	235	230	200	192	192	2754	0.439
10	198	112	140	112	112	112	112	112	112	1122	0.022
20	226	138	156	116	116	116	116	116	116	1216	0.044
40	275	180	188	128	128	128	128	128	128	1411	0.088
80	392	273	261	163	157	157	150	145	145	1843	0.175
160	600	439	389	233	225	220	192	185	185	2668	0.350
200	682	505	440	259	252	244	209	201	201	2993	0.439
10	197	111	137	111	111	111	111	111	111	1111	0.022
20	222	136	154	116	116	116	116	116	116	1208	0.044
40	275	180	187	128	128	128	128	128	128	1410	0.088
80	466	334	309	187	182	177	166	161	161	2143	0.175
160	566	414	370	223	216	210	197	190	190	2576	0.350
200	648	478	421	251	242	239	203	196	196	2874	0.439

Slopes

<u>Method I</u>	1063	854	668	332.7	311.0	298.0	219.5	200.1	200.1
Confidence Level									
90%	43	35.3	26.6	12.9	12.2	10.6	9.3	8.4	8.4
99%	60.3	49.4	37.3	18.0	17.2	14.9	13.1	11.8	11.8
<u>Method II</u>	0.2565	0.2062	0.1612	0.0801	0.0749	0.0716	0.0529	0.0482	0.0482
Confidence Level									
90%	0.0006	0.0008	0.0004	0.0005	0.0005	0.0005	0.0004	0.0004	0.0004
99%	0.0009	0.0012	0.0006	0.0007	0.0007	0.0007	0.0005	0.0005	0.0005

Table 38

Run No. 1

Yb (FOD)₃ Induced Proton Shifts^{a/} in 2-Adamantanamine, in CCl₄ at 60 MHz

Yb (FOD) ₃ (Total mg.)	Proton									$\Sigma \Delta$ Obs.	Mole Ratio L/S
	1	3	2	4	5	6	7	8	9		
10	261	155	173	122	122	122	118	118	118	1309	0.021
20	356	218	227	143	143	143	143	134	134	1641	0.043
40	568	353	345	197	188	188	188	169	169	2365	0.086
80	1065	672	620	338	320	300	280	253	243	4091	0.172
160	2007	1281	1138	606	544	504	466	412	384	7342	0.343
<u>Slopes</u>											
Method I	5477.1	3529.0	3025.1	1528.3	1334.1	1200.0	1078.6	922.5	830.9		
Confidence Level											
90%	120.6	77.7	60.7	61.2	53.8	30.2	5.6	22.1	8.5		
99%	214.6	138.2	107.9	108.9	95.7	53.7	9.9	39.3	15.2		
Method II	0.2894	0.1865	0.1598	0.0808	0.0705	0.0634	0.0569	0.0487	0.0438		
Confidence Level											
90%	0.0003	0.0004	0.0004	0.0012	0.0012	0.0003	0.0010	0.0001	0.0005		
99%	0.0006	0.0007	0.0007	0.0022	0.0021	0.0005	0.0019	0.0001	0.0009		

^{a/} Hz downfield from TMS.

Table 39

Run No. 2

Yb (FOD)₃ Induced Proton Shifts^{a/} in 2-Adamantanamine, in CCl₄, at 60 MHz

Yb (FOD) ₃ (Total mg.)	Proton									$\Sigma \Delta$ Obs.	Mole Ratio L/S
	1	3	2	4	5	6	7	8	9		
10	299	180	194	130	130	130	124	124	124	1435	0.021
20	422	260	268	163	158	158	158	146	146	1879	0.043
40	750	484	456	256	250	228	228	202	202	3056	0.086
80	1427	938	852	456	419	389	361	323	305	5470	0.172
<u>Slopes</u>											
<u>Method I</u>	7572.1	5096.2	4410.3	2193.7	1951.7	1737.0	1571.8	1334.4	1210.9		
Confidence Level											
90%	379.2	265.7	215.5	144.2	111.1	121.3	19.8	73.9	36.8		
99%	806.5	565.1	458.3	306.7	236.2	257.9	42.1	157.1	78.3		
<u>Method II</u>	0.2796	0.1882	0.1629	0.0810	0.0721	0.0642	0.0579	0.0492	0.0447		
Confidence Level											
90%	0.0005	0.0008	0.0008	0.0013	0.0016	0.0016	0.0025	0.0005	0.0013		
99%	0.0012	0.0017	0.0018	0.0027	0.0034	0.0034	0.0052	0.0011	0.0028		

^{a/} Hz downfield from TMS.

Table 40

Run No. 3

Yb (FOD)₃ Induced Proton Shifts^{a/} in 2-Adamantanamine, in CCl₄, at 60 MHz

Yb (FOD) ₃ (Total mg.)	Proton									$\sum \Delta_{\text{obs.}}$	Mole Ratio L/S
	1	3	2	4	5	6	7	8	9		
10	332	205	214	138	138	138	138	128	128	1559	0.021
20	465	287	287	175	166	166	166	152	152	2016	0.043
40	755	478	454	255	248	226	226	201	201	3044	0.086
80	1499	971	880	466	428	394	368	328	310	5644	0.172

Slopes

Method I	7799.0	5132.6	4458.9	2192.5	1954.0	1712.3	1534.0	1333.0	1210.0
Confidence Level									
90%	676	486.9	400.3	205.8	145.9	188.5	94.0	111.0	46.0
99%	1438	1035.5	851.3	437.7	310.5	400.9	200	236	97
Method II	0.2854	0.1879	0.1632	0.0803	0.0714	0.0627	0.0560	0.0488	0.0442
Confidence Level									
90%	0.0008	0.0013	0.0005	0.0006	0.0019	0.0012	0.0010	0.0004	0.0016
99%	0.0016	0.0029	0.0011	0.0013	0.0039	0.0027	0.0023	0.0008	0.0035

a/ Hz downfield from TMS.

Table 41

Run No. 4

Yb (FOD)₃ Induced Proton Shifts^{a/} in 2-Adamantanamine, in CCl₄ at 60 MHz

<u>Yb (FOD)₃</u> <u>(Total mg.)</u>	<u>Proton</u>									<u>Σ Δ obs.</u>	<u>Mole Ratio</u> <u>L/S</u>
	<u>1</u>	<u>3</u>	<u>2</u>	<u>4</u>	<u>5</u>	<u>6</u>	<u>7</u>	<u>8</u>	<u>9</u>		
10	332	206	215	139	139	139	139	129	129	1567	0.021
20	501	313	308	186	173	173	173	158	158	2143	0.043
40	830	521	490	272	265	240	240	211	211	3280	0.086
80	1541	975	880	469	431	399	372	332	312	5711	0.172
<u>Slopes</u>											
<u>Method I</u>	8017	5100	4410	2184	1957	1728	1543	1344	1207		
<u>Confidence Level</u>											
90%	190	136	95	79	72	93	6.2	47	29		
99%	404	289	203	168	154	197	13	100	62		
<u>Method II</u>	0.2916	0.1855	0.1604	0.0795	0.0712	0.0629	0.0561	0.0489	0.0439		
<u>Confidence Level</u>											
90%	0.0006	0.0007	0.0001	0.0009	0.0023	0.0015	0.0006	0.0006	0.0015		
99%	0.0012	0.0015	0.0003	0.0021	0.0050	0.0033	0.0024	0.0012	0.0032		

a/ Hz downfield from TMS.

Table 42

Run Nos. 1-4 Combined

Yb (FOD)₃ Induced Proton Shifts in 2-Adamantanamine, in CCl₄ at 60 MHz

<u>Yb (FOD)₃</u> <u>(Total mg.)</u>	<u>Proton</u>									<u>ΣΔ Obs.</u>	<u>Total Ratio</u> <u>L/S</u>
	<u>1</u>	<u>2</u>	<u>3</u>	<u>4</u>	<u>5</u>	<u>6</u>	<u>7</u>	<u>8</u>	<u>9</u>		
10	261	155	173	122	122	122	118	118	118	1309	0.021
20	356	218	227	143	143	143	143	134	134	1641	0.043
40	568	353	345	197	188	188	188	169	169	2365	0.086
80	1065	672	620	338	320	330	280	253	243	4091	0.172
10	299	180	194	130	130	130	124	124	124	1435	0.021
20	422	260	268	163	158	158	158	146	146	1879	0.043
40	750	484	456	256	250	228	228	202	202	3056	0.086
80	1427	938	852	456	419	389	361	323	305	5470	0.172
10	332	205	214	138	138	138	138	128	128	1559	0.021
20	465	287	287	175	166	166	166	152	152	2016	0.043
40	755	478	454	255	248	226	226	201	201	3044	0.086
80	1499	971	880	466	428	394	368	328	310	5644	0.172
10	332	206	215	139	139	139	139	129	129	1567	0.021
20	501	313	308	186	173	173	173	158	158	2143	0.043
40	830	521	490	272	265	240	240	211	211	3280	0.086
80	1541	975	880	469	431	399	372	332	312	5711	0.172
<u>Slopes</u>											
<u>Method I</u>	7190	4694	4065	2005	1797	1591	1429	1229	1115		
<u>Confidence Level</u>											
90%	529	353	305	155	135	115	106	90	81		
99%	755	504	435	222	193	164	152	129	116		
<u>Method II</u>	0.2876	0.1868	0.1610	0.0805	0.0710	0.0633	0.0568	0.0489	0.0440		
<u>Confidence Level</u>											
90%	0.0012	0.0003	0.0004	0.0003	0.0005	0.0003	0.0004	0.0001	0.0003		
99%	0.0017	0.0005	0.0006	0.0005	0.0007	0.0005	0.0006	0.0002	0.0004		

Table 43. Comparison of Shift Parameters ^{a/} Generated by the Demarco-Wenkert Method for 1-Adamantanol (V) and 1-Adamantanamine (VI)

Slopes	Proton			
	<u>1</u>	<u>3</u>	<u>2</u>	<u>4</u>
<u>V - Eu(fod)₃</u>	627.5	186.0	218.5	156.6
Confidence Level				
90%	10.7	2.9	6.0	4.4
99%	15.1	4.2	8.5	6.2
<u>V - Yb(fod)₃</u>	1198	381.9	417.3	324.0
Confidence Level				
90%	165.5	52.5	57.3	48.9
99%	236.1	75.0	81.7	69.7
<u>VI - Eu(fod)₃</u>	854.0	239.9	295.1	226.1
Confidence Level				
90%	39.5	11.4	14.4	6.9
99%	55.9	16.2	20.4	9.8
<u>VI - Yb(fod)₃</u>	1194.8	376.7	426.7	298.3
Confidence Level				
90%	18.8	8.4	9.8	7.2
99%	26.6	11.9	13.9	10.2

^{a/} Based on combined data from four runs.

Table 44. Comparison of Shift Parameters ^{a/} Generated by the Demarco-Wenkert Method for 2-Adamantanol (VII) and 2-Adamantanamine (VIII)

<u>Slopes</u>	<u>Proton</u>								
	<u>1</u>	<u>2</u>	<u>3</u>	<u>4</u>	<u>5</u>	<u>6</u>	<u>7</u>	<u>8</u>	<u>9</u>
<u>III - Eu(fod)₃</u>	892.8	589.1	517.3	285.8	259.9	201.3	179.7	166.5	134.3
<u>Confidence Level</u>									
90%	23.7	16.1	15.3	7.8	8.6	5.5	4.9	4.7	4.4
99%	33.3	22.7	21.5	11.0	12.1	7.8	6.8	6.5	6.2
<u>III - Yb(fod)₃</u>	2321.4	1613.7	1497.5	730.0	688.1	501.8	501.8	441.7	381.7
<u>Confidence Level</u>									
90%	106.3	74.2	98.1	31.7	30.1	26.3	26.3	19.4	22.1
99%	151.5	105.9	140.0	45.3	42.8	37.5	37.5	27.7	31.6
<u>IV - Eu(fod)₃</u>	1063	854	668	332.7	311.0	298.0	219.5	200.1	200.1
<u>Confidence Level</u>									
90%	43	35.3	26.6	12.9	12.2	10.6	9.3	8.4	8.4
99%	60.3	49.4	37.3	18.0	17.2	14.9	13.1	11.8	11.8
<u>IV - Eu(fod)₃</u>	5951	3843.9	3317.3	1661.9	1462.7	1310.3	1172.3	1009.6	908.6
<u>Confidence Level</u>									
90%	509	342.3	299.3	145.9	133.5	112.8	103.5	88.2	81.1
99%	724	487.1	425.9	207.6	198.9	160.6	147.9	125.5	115.8

a/ Based on combined data from four runs.

due to a manipulative error. The low solubility of V in CDCl_3 required slight heating of the solvent. Transfer of heated stock solution to the NMR tube via a cool syringe resulted in crystallization and partial loss of V. This larger L/S ratio caused a larger LIS.

The other noticeable deviation is in the first run of VIII with $\text{Yb}(\text{fod})_3$ (Table 38). This run is possibly the best in the set (Tables 39-41). It was the only one run with freshly prepared stock solution. An NMR break-down delayed runs 2-4 for three days. During this time a small amount of white precipitate formed in the stock solution, in spite of its storage under nitrogen. This probable loss of VIII may have caused larger LIS.

The precision of this method ranges from 0.6 per cent (Table 18) to 15 per cent (Table 36) at the 90 per cent confidence level. The majority of deviations are between 2 and 5 per cent. It has been determined in these laboratories that the agreement between the experimental and the computed McConnell-Robertson model has been between 3 and 8 per cent. It therefore seems likely that Demarco-Wenkert shift parameters with a precision of 2 to 5 per cent can be successfully employed for structural determination. Experimental data with 2 per cent precision might be expected to give 2 per cent agreement factors.

It is apparent that the precision of the shift parameters (Demarco-Wenkert) is not increased by replication of data runs using our methodology. The precision of shift parameters from combined data runs (Tables 7, 12, 17, 22, 27, 32, 37, and 42) makes this point clear.

Note that our data were carefully obtained. All variables were controlled (i.e. same stock solution for all runs, dried and sublimed reagents, the same instrument, etc.). These experiments were done much more carefully than the lab data on which many uses of the computational model are based. Furthermore, the lack of detailed experimental description in the current literature might indicate that the reported LIS data were not carefully generated. There are obvious exceptions, Kelsey⁽³³⁾, Armitage⁽³⁵⁾ and Shapiro⁽³⁶⁾. Their data are very precise within the particular data sets and are probably accurate. However, even these carefully produced shift indexes were usually only determined once for each compound.

C. Data Reduction with the ApSimon Method

The heuristic ApSimon method of data reduction, Method II, (Tables 3 to 42), was applied to data previously examined by Method I. The shift parameters calculated via this method are summarized for V and VI in Table 45 and for VII and VIII in Table 46. .

Table 45. Comparison of Shift Parameters ^{a/} Generated by the ApSimon Method for 1-Adamantanol (V) and 1-Adamantanamine (VI)

<u>Slopes</u>	<u>Proton</u>			
	<u>1</u>	<u>2</u>	<u>3</u>	<u>4</u>
<u>V - Eu(fod)₃</u>	0.5272	0.1562	0.1838	0.1316
<u>Confidence Level</u>				
90%	0.0018	0.0006	0.0016	0.0014
99%	0.0025	0.0009	0.0023	0.0020
<u>V - Yb(fod)₃</u>	0.5138	0.1637	0.1785	0.1415
<u>Confidence Level</u>				
90%	0.0031	0.0009	0.0016	0.0013
99%	0.0044	0.0013	0.0023	0.0019
<u>VI - Eu(fod)₃</u>	0.5299	0.1488	0.1831	0.1382
<u>Confidence Level</u>				
90%	0.0015	0.0011	0.0013	0.0020
99%	0.0021	0.0015	0.0019	0.0029
<u>VI - Yb(fod)₃</u>	0.5407	0.1706	0.1933	0.1349
<u>Confidence Level</u>				
90%	0.0061	0.0021	0.0024	0.0021
99%	0.0087	0.0029	0.0033	0.0030

a/ Based on combined data from four runs.

Table 46. Comparison of Shift Parameters ^{a/} Generated by the ApSimon Method for 2-Adamantanol (VII) and 2-Adamantanamine (VIII)

Slopes	Proton								
	<u>1</u>	<u>2</u>	<u>3</u>	<u>4</u>	<u>5</u>	<u>6</u>	<u>7</u>	<u>8</u>	<u>9</u>
VII - Eu(fod) ₃	0.2712	0.1820	0.1736	0.0868	0.0791	0.0611	0.0546	0.0506	0.0409
Confidence Level									
90%	0.0003	0.0005	0.0002	0.0003	0.0005	0.0004	0.0001	0.0001	0.0003
99%	0.0005	0.0006	0.0003	0.0005	0.0007	0.0005	0.0002	0.0002	0.0004
VII - Yb(fod) ₃	0.2671	0.1857	0.1733	0.0839	0.0790	0.0579	0.0579	0.0507	0.0442
Confidence Level									
90%	0.0012	0.0009	0.0035	0.0005	0.0006	0.0005	0.0005	0.0003	0.0005
99%	0.0018	0.0013	0.0049	0.0007	0.0008	0.0007	0.0007	0.0005	0.0007
VIII - Eu(fod) ₃	0.2565	0.2062	0.1612	0.0801	0.0749	0.0716	0.0529	0.0482	0.0482
Confidence Level									
90%	0.0006	0.0008	0.0004	0.0005	0.0005	0.0005	0.0004	0.0004	0.0004
99%	0.0009	0.0012	0.0006	0.0007	0.0007	0.0007	0.0005	0.0005	0.0005
VIII - Yb(fod) ₃	0.2876	0.1868	0.1610	0.0805	0.0710	0.0633	0.0568	0.0489	0.0440
Confidence Level									
90%	0.0012	0.0003	0.0004	0.0003	0.0005	0.0003	0.0004	0.0001	0.0003
99%	0.0017	0.0005	0.0006	0.0005	0.0007	0.0005	0.0006	0.0002	0.0004

^{a/} Based on combined data from four runs.

The increased precision (0.5 to 2 per cent at the 90 per cent confidence level) is very evident, particularly in runs that have significant deviations with Method I. The average deviation for this method is approximately 1 per cent. This increased precision is not surprising since the ApSimon method inherently has fewer sources of error. The Demarco-Wenkert procedure requires precise knowledge of the substrate concentration, the LSR concentration and the precise LIS of all protons at each lanthanide to substrate ratio. The ApSimon method requires only precise knowledge of the resonance position.

The precision of the ApSimon procedure places limits on the precision of structural determinations. The quality of observed data cannot be exceeded by the precision of the structural determination via the McConnell-Robertson model.

Tables 47 to 50 give a comparison of Demarco-Wenkert LIS parameters (I) and scaled ApSimon LIS parameters (II) for all four compounds. The scaling factor was obtained for the first proton. Agreement factors, R, were calculated using a simplified form of equation 18,

$$R = \sqrt{\frac{(\text{LIS I} - \text{LIS II})^2}{(\text{LIS II})^2}}, \quad (19)$$

where LIS I and LIS II are the corresponding Demarco and ApSimon LIS parameters. Agreement between I and II is better

Table 47. Comparison of Demarco-Wenkert and Scaled ApSimon LIS
Parameters* for 1-Adamantanol

<u>Proton</u>	<u>Eu(fod)₃ LIS Parameters</u>		
	<u>Method II</u>	<u>Method I</u>	<u>Method II</u> <u>(Scaled) a/</u>
1	0.5272	627.5	627.5
3	0.1562	186	186
2	0.1838	218.5	218.8
4	0.1316	156.6	156.6

Agreement factor, $R = 0.0004$

a/ Scaling factor = 1190

	<u>Yb(fod)₃ LIS Parameters</u>		
1	0.5138	1198	1198 <u>b/</u>
3	0.1637	381	381.7
2	0.1785	417.3	416.2
4	0.1415	324.	329.9

Agreement factor, $R = 0.004$

b/ Scaling factor = 2331.6

* From combined runs, Tables 7 and 12.

Table 48. Comparison of Demarco-Wenkert and Scaled ApSimon LIS
Parameters* for 1-Adamantanamine

<u>Proton</u>	<u>Eu(fod)₃ LIS Parameters</u>		
	<u>Method II</u>	<u>Method I</u>	<u>Method II</u> <u>(Scaled) a/</u>
1	0.5299	854.	854.
3	0.1488	239.9	239.8
2	0.1831	295.1	295.1
4	0.1382	226.1	222.7

Agreement factor, $R = 0.003$

a/ Scaling factor = 1611.6

	<u>Yb(fod)₃ LIS Parameters</u>		
1	0.5407	1194.	1194. <u>b/</u>
3	0.1706	376.	376.
2	0.1933	426.	426.
4	0.1349	298.3	298.

Agreement factor, $R = 0.0002$

b/ Scaling factor = 2208.2

* From combined runs, Tables 17 and 22.

Table 49. Comparison of Demarco-Wenkert and Scaled ApSimon LIS Parameters* for 2-Adamantanol

<u>Proton</u>	<u>Eu(fod)₃ LIS Parameters</u>		
	<u>Method II</u>	<u>Method I</u>	<u>Method II</u> <u>(Scaled) ^{a/}</u>
1	0.2712	892.8	892.8
2	0.1820	589.1	599.1
3	0.1736	517.3	571.5
4	0.0868	285.8	285.7
5	0.0791	259.9	260.4
6	0.0611	201.3	201
7	0.0546	179.7	179.7
8	0.0506	166.5	166.6
9	0.0409	134.3	134.6

Agreement factor, $R = 0.04$

a/ Scaling factor = 3292

	<u>Yb(fod)₃ LIS Parameters</u>		
			<u>b/</u>
1	0.2671	2321.4	2321.4
2	0.1857	1613.7	1613.9
3	0.1733	1497.5	1506
4	0.0839	730.0	729
5	0.0790	688.1	687
6	0.0579	501.8	503
7	0.0579	501.8	503
8	0.0507	441.7	441
9	0.0442	381.7	384

Agreement factor, $R = 0.003$

b/ Scaling factor = 8691.1

* From Combined runs, Tables 27 and 32.

Table 50. Comparison of Demarco-Wenkert and Scaled ApSimon LIS Parameters* for 2-Adamantanamine

<u>Proton</u>	<u>Eu(fod)₃ LIS Parameters</u>		
	<u>Method II</u>	<u>Method I</u>	<u>Method II</u> (Scaled) <u>a/</u>
1	0.2565	1063	1063
2	0.2062	854	855
3	0.1612	668	668
4	0.0801	332.7	332
5	0.0749	311	310
6	0.0716	298	297
7	0.0529	219.5	219
8	0.0482	200.1	200
9	0.0482	200.1	200

Agreement factor, $R = 0.001$

a/ Scaling factor = 4144

<u>Yb(fod)₃ LIS Parameters</u>			
1	0.2876	7190	7190 <u>b/</u>
2	0.1868	4694	4670
3	0.1610	4065	4025
4	0.0805	2005	2013
5	0.0710	1797	1775
6	0.0633	1591	1583
7	0.0568	1429	1420
8	0.0489	1228	1223
9	0.0440	1115	1100

Agreement factor, $R = 0.005$

b/ Scaling factor = 25,000

* From combined runs, Tables 37 and 42.

than 1 per cent in most cases. This suggests that either method can be used to generate useful LIS parameters for structural determination via the McConnell-Robertson correlation.

The ease of the ApSimon method coupled with the fact that actual L/S ratios need not be known makes this a very attractive experimental technique of generating LIS parameters.

Preliminary investigations have indicated that shift parameters generated by the ApSimon method are as appropriate as those generated by other procedures to problems of structural determination⁽⁴⁰⁾.

D. Comparison to Other Data Reduction Methods

The observed LIS data manipulated via Method I and II do not lend themselves to work-up by the other methods discussed earlier in this paper. The Kelsey⁽³³⁾ method, for example, requires that the substrate be incrementally added to an LSR solution of known concentration. The method developed by Armitage and coworkers⁽³⁵⁾ involves varying the substrate concentration while maintaining a constant LSR concentration. Finally, Shapiro and Johnston⁽³⁶⁾ perform their experiments by keeping the concentration of substrate constant and varying only the LSR concentration. All three of these methods require more time for the experiment and the data reduction, but give LIS values with a defined physical significance.

E. Results Compared to Scaled Literature LIS Parameters

Several papers have investigated LSR effects on adamantyl derivatives. Wahl and Peterson⁽⁴¹⁾ have studied the effects of $\text{Eu}(\text{dpm})_3$ on CDCl_3 solutions of 1 and 2-adamantanol, V and VII. They reported the net shifts, ΔW , for all protons of V at an L/S molar ratio of 0.4:0.6 and all protons of VII at an L/S molar ratio of 1. Table 51 compares scaled $\text{Eu}(\text{dpm})_3$ shift parameters obtained from Wahl and Peterson to our $\text{Eu}(\text{fod})_3$ shift parameters calculated by Method I. The best agreement ($R = 0.022$) is evident for the LIS parameters of V determined by Method I. Method I parameters for VII are in reasonable agreement ($R = 0.065$). Shift parameters from Method I for VII diverge considerably from the literature data. The protons farthest away from the Ln appear to have the largest difference.

F. Comparison of Eu and Yb LIS Data

Reuben has suggested that observed lanthanide induced shifts might consist of both a contact and a pseudocontact term⁽³¹⁾. If all observed LIS is due to pseudocontact, then all internally scaled LIS parameters must agree for all lanthanides with the same substrate molecule. If the contact shift has the same behavior as the pseudocontact shift, then one cannot distinguish one from the other, although, variable amounts of each might be present. However, if contact shift behavior is radically

different from pseudocontact shift behavior, scaled data sets for different lanthanides such as Eu and Yb need not stand in a one to one correspondence for the same substrate.

Yb(dpm)_3 has been shown to induce the smallest amount of contact shift (vis. 2 to 4 per cent) in the proton spectrum⁽⁴⁰⁾. An estimate of the amount of contact shift present in ^{13}C LIS indexes of various pyridine bases in the presence of Ln(dpm)_3 LSR's has also been made⁽⁴⁰⁾.

The shift parameters obtained by Method I for Eu(fod)_3 were least-squares linearized against the corresponding Yb(fod)_3 shift parameters for compounds V-VIII (Table 52). The slopes obtained from this linearization were 1.86 for V, 1.38 for VI, 2.66 for VII and 6.40 for VIII. These slopes correspond to factors which can be used to convert Eu LIS parameters to Yb LIS parameters for the same substrate. A similar linearization of ApSimon LIS indexes (Table 53) gave values 0.949, 1.00, 0.998 and 1.07 for compounds V-VIII. Such results indicate that these proton shifts are either largely due to pseudocontact in both cases, or that the contact shift contribution mimics the pseudocontact behavior.

Table 51. Comparison of Shift Parameters to Scaled Literature LIS Parameters

<u>1-Adamantanol, V</u>			
<u>Proton</u>	<u>Ref. 40</u>	<u>Method I</u>	<u>Scaled^a/Ref. 40</u>
1	402	627	627
2	130	218	203
3	122	186	190
4	90	157	155

Agreement factor, $R = 0.022$

a/ Scaling factor = 1.56

<u>2-Adamantanol, VII</u>			
1	1500	893	893 ^{b/}
2	900	589	536
3	870	517	517
4	449	286	267
5	413	260	246
6	391	201	223
7	341	179	203
8	320	166	190
9	298	134	177

Agreement factor, $R = 0.065$

b/ Scaling factor = 0.595

Table 52. Least-Squares Correlation of Demarco Eu(fod)₃ Shift Indexes versus Yb(fod)₃ Shift Indexes

<u>1-Adamantanol (V)</u>	
627.5	1198.0
186.0	381.9
218.5	417.3
156.6	324.0
Slope =	1.865024
Deviation	
@ 90%	0.057
@ 99%	0.121

<u>1-Adamantanamine (VI)</u>	
854.0	1194.0
239.9	376.7
295.1	426.7
226.1	298.3
Slope =	1.379314
Deviation	
@ 90%	0.090
@ 99%	0.192

<u>2-Adamantanol (VII)</u>	
892.7	2321.0
589.1	1613.0
517.3	1497.0
285.8	730.0
259.9	688.1
201.3	501.8
179.7	501.8
166.5	441.7
134.3	381.7
Slope	2.659
Deviation	
@ 90%	0.082
@ 99%	0.123

<u>2-Adamantanamine (VIII)</u>	
1063.0	7190.0
854.0	4694.0
688.0	4065.0
332.0	2005.0
311.0	1797.0
298.0	1591.0
219.0	1429.0
200.0	1229.0
200.0	1115.0
Slope =	6.401608
Deviation	
@ 90%	0.379477
@ 99%	0.570219

Table 53. Least-Squares Correlation of ApSimon Eu(fod)₃ Shift Indexes versus Yb(fod)₃ Shift Indexes

<u>1-Adamantanol (V)</u>	
0.5272	0.5138
0.1562	0.1637
0.1838	0.1785
0.1316	0.1415
Slope =	0.949
Deviation	
@ 90%	0.034
@ 99%	0.073

<u>1-Adamantanamine (VI)</u>	
0.5299	0.5407
0.1488	0.1706
0.1831	0.1933
0.1382	0.1349
Slope =	1.004
Deviation	
@ 90%	0.061
@ 99%	0.130

<u>2-Adamantanol (VII)</u>	
0.2712	0.2671
0.1820	0.1857
0.1736	0.1733
0.0868	0.0839
0.0791	0.0790
0.0611	0.0579
0.0506	0.0507
0.0409	0.0442
Slope =	0.988
Deviation	
@ 90%	0.014
@ 99%	0.021

<u>2-Adamantanamine (VIII)</u>	
0.2565	0.2876
0.2062	0.1868
0.1612	0.1610
0.0801	0.0805
0.0749	0.0710
0.0716	0.0633
0.0529	0.0568
0.0482	0.0489
0.0482	0.0440
Slope =	1.065
Deviation	
@ 90%	0.063
@ 99%	0.095

IV.

CONCLUSION

CONCLUSION

The objects of this study were to find a readily workable method of obtaining relative LIS parameters, and determine how accurate and reliable this method is. A method requiring a minimum amount of experimental work and mathematical manipulation was desired.

This work has shown that relative shift parameters generated by the Demarco-Wenkert and ApSimon methods are essentially equivalent. Greater precision was realized with the ApSimon data manipulation in which observed LIS, Δ obs, was plotted against the sum of observed shifts, $\sum \Delta$ obs. The accuracy can best be determined by correlation with the McConnell-Robertson model via the method of Willcott, Davis and Lenkinski⁽³⁸⁾.

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APPENDIX

LIST OF ABBREVIATIONS

Δ , (Δ obs), δ ,	observed net chemical shift
Δ m	maximum shift of a given proton relative to its uncomplexed shift
Δ Eu	Demarco-Wenkert shift index
dpm	dipivaloylmethane
fod	1,1,1,2,2,3,3,-heptafluoro-7,7-dimethyl-4,6-octanedione
K	lanthanide shift reagent-substrate equilibrium constant
L	lanthanide shift reagent
L_t	total lanthanide shift reagent
LSR	lanthanide shift reagent
LIS	lanthanide induced shift
ρ	ratio of total lanthanide shift
φ^*	angle of the colatitude measured from the positive Z axis in the Willcott-Davis-Lenkinski structural model
S	substrate
S_b	bound substrate
S_f	free substrate
S_t	total substrate
σ	ratio of bound to total substrate, S_b/S_t
TMS	tetramethylsilane
θ	angular term of the McConnell-Robertson pseudocontact equation

// JOB

LOG-DRIVE---CART SPEC---CART-AVAIL---PHY DRIVE---
0000 0005 0005 0000

V2-M10---ACTUAL 16K CONFIG 16K

// FOR

*EXTENDED PRECISION

*ONE WORD INTEGERS

*IOCS(CARD,1132,PRINTER)

*LIST SOURCE PROGRAM

REAL MULT,NUM,INTER,X(40),Y(40),X2(40),Y2(40),CALCY(40),DIF(40)

INTEGER O,PT1,PT2,E,ANS,ANSS

COMMON TAB(34,5)

C WRITE(3,500)

C 500 FORMAT(' OPTION LIST',/,

C '\$' (F)REQUENCY',/,

C '\$' (M)MULTIPLIER FOR AUTOMATIC POINT DELETION',/,

C '\$' (C)CONFIDENCE LEVEL IN PERCENT',/,

C '\$' (X)- NEW X ARRAY, OLD Y',/,

C '\$' (Y)- NEW Y ARRAY, OLD X',/,

C '\$' (D)ATA X AND Y ARRAYS NEW',/,

C '\$' (R)EMOVE MAXIMUM DIFFERENCE',/,

C '\$' (P)RINT TABLE',/,

C '\$' (A)COMPUTE DATA POINT',/,

C '\$' (E)ND')

25 IL=0

K=0

READ(2,220)((TAB(I,J),I=1,34),J=1,5)

220 FORMAT(F5.1)

WRITE(3,221)TAB

221 FORMAT(' ',16F6.1)

WRITE(3,1)

1 FORMAT(' NMR & ')

READ(2,222)ANS

222 FORMAT(I2)

WRITE(3,223)ANS

223 FORMAT(' ',I2)

ANSS=11

FREQ=1.

995 FORMAT(1I2)

5 FORMAT(I2)

```

IF(ANS - 9 )777,786,777
786 WRITE(3,778)
778 FORMAT(' THE NUMBER OF ESTIMATES IS ')
READ(2,995)E
WRITE(3,223)E
990 FORMAT(2F5.1)
782 FORMAT(' THREE DATA POINTS IN ORDER 3F5.1')
783 FORMAT(' THE DATA POINT IS',1I5)
991 FORMAT(' THE TWO DATA POINTS IN ORDER,2F5.1')
785 FORMAT(3F5.1)
WRITE(3,779)
779 FORMAT(' DATA POINTS BEFORE =1, AFTER =0')
READ(2,5)ITEST
WRITE(3,223)ITEST
IF(ITEST - 0 )201,780,201
201 WRITE(3,991)
READ(2,990)P2A,P2B
WRITE(3,224)P2A,P2B
P2C=0
DO 781 J=1,E
WRITE(3,782)
READ(2,785)P1A,P1B,P1C
WRITE(3,224)P1A,P1B,P1C
FAC=(P1B-P1A)/(P2B-P2A)
P2C=((P1C-P1B)/FAC)+P2B)+P2C
PT1=P2C/E
781 CONTINUE
WRITE(3,783)PT1
GO TO 35
780 P2C=0
WRITE(3,991)
READ(2,990)P2A,P2B
WRITE(3,224)P2A,P2B
DO 784 J=1,E
WRITE(3,782)
READ(2,785)P1C,P1A,P1B
WRITE(3,224)P1C,P1A,P1B
FAC=(P1B-P1A)/(P2B-P2A)
P2C=((P1A-P1B)/FAC)+P2A)+P2C
PT2=P2C/E
784 CONTINUE
WRITE(3,783)PT2
GO TO 35

```

777 IF(ANS - 5)27;202,27

202 LL=1

WRITE(3,2)

2 FORMAT(' FREQUENCY IN MHZ=')

READ(2,220)FREQ

WRITE(3,221)FREQ

27 WRITE(3,7)

7 FORMAT(' MULTIPLIE- FOR AUTOMATIC DELETION OF POINT PAIR')

READ(2,220)MULT

WRITE(3,221)MULT

IF(ANSS - 2)100,900,100

100 WRITE(3,101)

101 FORMAT(' CONFIDENCE LEVEL IN PERCENT=')

READ(2,220)CONL

WRITE(3,221)CONL

IF(ANSS - 3)26,900,26

26 WRITE(3,29)

29 FORMAT(' NUMBER OF POINT PAIRS')

READ(2,222)N

WRITE(3,223)N

O=N

WRITE(3,3)

3 FORMAT(' DATA',/, ' X,Y-CARRIAGE RETURN',/,

\$' X,Y-CARRIAGE RETURN (INCLUDE DECIMAL POINTS)')

DO 4 J=1,N

READ(2,224)X(J),Y(J)

224 FORMAT(14F5.1)

WRITE(3,221)X(J),Y(J)

X2(J)=X(J)

Y2(J)=Y(J)

4 CONTINUE

900 DO 8 J=1,O

X(J)=X2(J)

Y(J)=Y2(J)

8 CONTINUE

K=0

N=0

LLL=0

24 IF(K - 4)203,203,31

203 IF(N - 4)33,602,602

602 CALL LEAS1(N,X,Y,SLOPE,INTER,CALCY,DIF)

YC=1.

XINT =-INTER*(1./SLOPE)

```

XC=XINT
CALL PERC(INTER,CONL,N,X,Y,DIF,SLOPE,B,YC,YTOL,XC,XOP,XOM,D99)
99 CONTINUE
SSD=0.
DO 9 J=1,N
SSD=SSD+DIF(J)**2.
9 CONTINUE
NUM=N
VAR=SSD/(NUM-2.)
SD=SQRT(VAR)
RSLOP =1./((SLOPE*FREQ)
YTOLL=(B/SLOPE)*RSLOP
IF(LLL - 0)601,12,601
601 WRITE(3,600)N
600 FORMAT(' NUMBER OF POINTS=',I14)
WRITE(3,10)SSD,SD
10 FORMAT(' SSD=',F12.6,4X,' STANDARD DEVIATION=',F12.6)
12 WRITE(3,13)SLOPE,B,RSLOP,YTOLL
13 FORMAT(' SLOPE=',F12.6,' DEVIATION + OR - =',F12.6,/,
$' 1./((SLOPE*FREQUENCY)='F12.6,' DEVIATION + OR -',F12.6)
IF(LLL - 0)204,550,204
204 WRITE(3,50)INTER,YC,YTOL
50 FORMAT(' Y INTERCEPT=',F12.6,' RANGE FOR Y=',F12.6,
$' IS ',F12.6)
550 WRITE(3,51)XINT,XOP,XOM
51 FORMAT(' X INTERCEPT=',F12.6,' +',F12.6,' , -',F12.6)
IF(LLL - 0)205,35,205
205 DIFM=0.
DO 42 J=1,N
IF(DIFM - ABS(DIF(J)))206,206,42
206 DIFM=ABS(DIF(J))
I=J
42 CONTINUE
41 WRITE(3,14)
14 FORMAT(' ',10X,'INPUT DATA',9X,8X,'CALCULATED DATA',/,
$' ',7X,'X',14X,'Y',12X,'CALC Y',10X,'DIF')
DO 15 J=1,N
WRITE(3,16)X(J),Y(J),CALCY(J),DIF(J)
15 CONTINUE
16 FORMAT(' ',4F15.6)
IF(LLL - 1)44,207,44
207 LLL=0
GO TO 35

```

```

44 DO 17 J=1,N
   IF(ABS(DIF(J)) - (MULT*SD))17,17,20
17 CONTINUE
35 WRITE(3,19)
19 FORMAT(' OPTION& ')
   READ(2,222) ANSS
   WRITE(3,223) ANSS
   IF(ANSS - 1)208,25,208
208 IF(ANSS - 4)209,702,209
209 IF(ANSS - 5)210,703,210
210 IF(ANSS - 6)211,26,211
211 IF(ANSS - 12)212,26,212
212 IF(ANSS - 9)213,786,213
213 IF(ANSS - 2)214,27,214
214 IF(ANSS - 8)215,43,215
215 IF(ANSS - 3)216,100,216
216 IF(ANSS - 7)217,22,217
217 IF(ANSS - 10)218,28,218
218 GO TO 35
702 DO 704 J=1,0
   READ(2,705) X2(J)
   WRITE(3,221) X2(J)
704 CONTINUE
   GO TO 900
703 DO 706 J=1,0
   READ(2,705) Y2(J)
   WRITE(3,221) Y2(J)
706 CONTINUE
   GO TO 900
20 WRITE(3,21)
705 FORMAT(14F5.1)
21 FORMAT(' MAXIMUM POINT DELETED .GT. MULT*DIF')
22 CONTINUE
   DIFM=0.
   I=1
   DO 23 J=1,N
   IF(DIFM - ABS(DIF(J)))219,219,23
219 DIFM=ABS(DIF(J))
   I=J
23 CONTINUE
   WRITE(3,47)
47 FORMAT(' LINE DELETED')
   WRITE(3,16)X(I),Y(I),CALCY(I),DIF(I)

```

```

N=N-1
DO 40 J=1,N
X(J)=X(J+1)
Y(J)=Y(J+1)
40 CONTINUE
K=K+1
GO TO 24
31 WRITE(3,32)
32 FORMAT(' FOUR DATA POINTS HAVE BEEN DELETED;',/,
$' PLEASE REEVALUATE YOUR DATA')
GO TO 35
33 WRITE(3,34)
34 FORMAT(' THERE ARE LESS THAN FOUR DATA POINTS')
GO TO 35
43 LLL=1
GO TO 602
28 CONTINUE
CALL EXIT
END

```

UNREFERENCED STATEMENTS

99 41

FEATURES SUPPORTED

ONE WORD INTEGERS
EXTENDED PRECISION
IDCS

CORE REQUIREMENTS FOR

COMMON 510 VARIABLES 820 PROGRAM 1056

END OF COMPILATION

// DUP

*DELETE NMR
CART ID 0005 DB ADDR 4837 DB CNT 006F

*STORE WS UA NMR
CART ID 0005 DB ADDR 48CA DB CNT 006F

// JOB

LOG DRIVE	CART SPEC	CART AVAIL	PHY DRIVE
0000	0005	0005	0000

V2 M10 ACTUAL 16K CONFIG 16K

// FOR

*EXTENDED PRECISION

*ONE WORD INTEGERS

*LIST SOURCE PROGRAM

SUBROUTINE PERC(INTER,CONL,N,X,Y,DIF,SLOPE,B,YC,YTOL,XC,XOP,XOM,D)

REAL INTER,X(40),Y(40),DIF(40)

COMMON TAB(34,5)

C=N

LMN=0

TNM2=G-2.

SY=0.

SX=0.

SXX=0.

SDD=0.

DO 11 I=1,N

SX=SX+X(I)

SXX=SXX+X(I)**2.

SDD=SDD+DIF(I)**2.

SY=SY+Y(I)

11 CONTINUE

CALL STUDD(TNM2,CONL,DIST)

XDOT=SX/G

RM=(DIST*SQRT(SDD))/(SQRT(G)*SQRT(G-2.)*SQRT(SXX))

R=(DIST*SQRT(SDD))/(SQRT(G-2.)*SQRT(SXX))

XM=YC*(1./SLOPE)-INTER*(1./SLOPE)

YTOL=RM*SQRT(SXX+G*((XM-XDOT)**2.))

C CALCULATIONS FOR RANGE OF X FROM OBSERVED X

YDOT=INTER+SLOPE*XDOT

BP=SLOPE+B/2.

YDOTT=RM*SQRT(SXX)

XOP=(BP*XDOT-(YDOT-YDOTT/2.))/BP

BM=SLOPE-B/2.

XOM=(BM*XDOT-(YDOT+YDOTT/2.))/BM

RETURN

END

FEATURES SUPPORTED
ONE WORD INTEGERS
EXTENDED PRECISION

CORE REQUIREMENTS FOR PERC
COMMON 510 VARIABLES 58 PROGRAM 314

RELATIVE ENTRY POINT ADDRESS IS 0045 (HEX)

END OF COMPILATION

// DUP

*DELETE			PERC		
CART ID 0005	DB ADDR	4837	DB CNT	0019	

*STORE	WS	UA	PERC		
CART ID 0005	DB ADDR	4920	DB CNT	0019	

// JOB

LOG DRIVE	CART SPEC	CART AVAIL	PHY DRIVE
0000	0005	0005	0000

V2 M10 ACTUAL 16K CONFIG 16K

// FOR

*EXTENDED PRECISION
*ONE WORD INTEGERS
*LIST SOURCE PROGRAM

```
SUBROUTINE LEAS1(N,X,Y,SLOPE,B,CALCY,DIF)
  DIMENSION X(40),Y(40),CALCY(40),DIF(40)
  SUMX=0.
  SUMY=0.
  SUMXY=0.
  SUMXX=0.
  DO 10 J=1,N
    SUMX=SUMX+X(J)
    SUMY=SUMY+Y(J)
    SUMXX=SUMXX+X(J)**2.
10  SUMXY=SUMXY+X(J)*Y(J)
  G=N
  DENOM=SUMX**2.-G*SUMXX
  SLOPE=(SUMX*SUMY-G*SUMXY)/DENOM
  R=(SUMX*SUMXY-SUMY*SUMXX)/DENOM
  DO 11 J=1,N
    CALCY(J)=SLOPE*X(J)+B
11  DIF(J)=Y(J)-CALCY(J)
  RETURN
END
```

FEATURES SUPPORTED
ONE WORD INTEGERS
EXTENDED PRECISION

CORE REQUIREMENTS FOR LEAS1
COMMON 0 VARIABLES 24 PROGRAM 192

RELATIVE ENTRY POINT ADDRESS IS 001F (HEX)

END OF COMPILATION

// DUP

*DELETE LEAS1
CART ID 0005 DB ADDR 4837 DB CNT 000F

*STORE WS UA LEAS1
CART ID 0005 DB ADDR 492A DB CNT 000F

// JOB

LOG DRIVE	CART SPEC	CART AVAIL	PHY DRIVE
0000	0005	0005	0000

V2 M10 ACTUAL 16K CONFIG 16K

// FOR

*EXTENDED PRECISION

*ONE WORD INTEGERS

*LIST SOURCE PROGRAM

SUBROUTINE STUDD(TNM2,CONL,DIST)

DIMENSION CONLL(5),DF(34)

COMMON TAB(34,5)

CONLL(1)=90.

CONLL(2)=95.

CONLL(3)=99.

CONLL(4)=99.5

DO 5 K=1,30

G=K

DF(K)=G

5 CONTINUE

DF(31)=40.

DF(32)=60.

DF(33)=120.

DF(34)=10000.

DO 1 I=1,5

II = I

IF(ABS(CONL - CONLL(I)) - 0.01)2,2,1

1 CONTINUE

2 CONTINUE

DO 3 J=1,34

JJ = J

IF(ABS(TNM2 - DF(J)) - 0.01)4,4,3

3 CONTINUE

4 CONTINUE

DIST=TAB(JJ,II)

TNM2=DF(JJ)

CONL=CONLL(II)

RETURN

END

FEATURES SUPPORTED

ONE WORD INTEGERS
EXTENDED PRECISION

CORE REQUIREMENTS FOR STUDD
COMMON 510 VARIABLES 134 PROGRAM 220

RELATIVE ENTRY POINT ADDRESS IS 00A5 (HEX)

END OF COMPILATION

// DUP

*DELETE STUDD
CART ID 0005 DB ADDR 4837 DB CNT 0010

*STORE WS UA STUDD
CART ID 0005 DB ADDR 4929 DB CNT 0010

6.3	2.9	2.3	2.1	2.0	1.9	1.8	1.8	1.8	1.8	1.8	1.8	1.7	1.7	1.7	1.7	1.7
1.7	1.7	1.7	1.7	1.7	1.7	1.7	1.7	1.7	1.7	1.7	1.7	1.7	1.7	1.7	1.6	1.6
1.6	1.6	12.7	4.3	3.1	2.7	2.5	2.4	2.3	2.3	2.2	2.2	2.2	2.2	2.1	2.1	2.1
2.1	2.1	2.1	2.1	2.0	2.0	2.0	2.0	2.0	2.0	2.0	2.0	2.0	2.0	2.0	2.0	2.0
2.0	2.0	1.9	1.9	25.5	6.2	4.1	3.5	3.1	2.9	2.8	2.7	2.6	2.6	2.6	2.5	2.5
2.5	2.5	2.4	2.4	2.4	2.4	2.4	2.4	2.4	2.4	2.4	2.3	2.3	2.3	2.3	2.3	2.3
2.3	2.3	2.3	2.3	2.2	2.2	63.7	9.9	5.8	4.6	4.0	3.7	3.5	3.3	3.2	3.1	3.1
3.1	3.0	3.0	2.9	2.9	2.9	2.9	2.8	2.8	2.8	2.8	2.8	2.8	2.8	2.8	2.7	2.7
2.7	2.7	2.7	2.7	2.7	2.6	2.6	2.5	127.0	14.1	7.4	5.6	4.7	4.3	4.0	3.8	3.8
3.6	3.5	3.5	3.4	3.3	3.3	3.2	3.2	3.2	3.2	3.1	3.1	3.1	3.1	3.1	3.1	3.0
3.0	3.0	3.0	3.0	3.0	3.0	2.9	2.9	2.8	2.8							

NMR &

5

FREQUENCY IN MHZ=

60.0

MULTIPLIER- FOR AUTOMATIC DELETION OF POINT PAIR