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LANTHANIDE SHIFT REAGENTS INVOLVING CROWN ETHERS

DAVID J. LONG

AUGUST, 1977

THESIS

SUBMITTED IN PARTIAL FULFILLMENT OF THE  
REQUIREMENTS FOR THE DEGREE OF MASTER OF SCIENCE

APPROVED:

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Appreciation is also extended to Rochester Institute of Technology for support of this work.

## ABSTRACT

Complexes between lanthanide nitrates and the cyclic polyethers 18-crown-6 and dicyclohexano-18-crown-6 have been synthesized; the reactions occur rapidly and in high yield.

The crown ether-salt complexes have been characterized by melting point, infrared and ultraviolet spectrophotometry, conductance analysis, and nuclear magnetic resonance spectrometry. NMR spectra of uncomplexed and complexed crown ethers were identical; the uncomplexed salts were more soluble in NMR solvents than were the complexes.

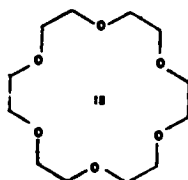
In most cases the crown ether-salt complexes are usable shift reagents and induce greater shifts than do the uncomplexed lanthanide salts in both proton and carbon magnetic resonance spectrometry. Of the substrates studied, triglycine was affected by these shift reagents to the greatest degree.

Contact and pseudo-contact shift contributions were estimated and consistent with the literature.

## HISTORICAL

The cyclic polyethers synthesized by Pederson<sup>1</sup> have been shown to be a remarkable class of compounds as demonstrated by the ability of these ethers to cause a variety of inorganic compounds to dissolve via complexation in nonpolar organic solvents. These "crown ethers", so named because their geometry as a result of coordination resembles a regal crown, were the first neutral molecules to form stable crystalline complexes with alkali metal ions.

Since the systematic names of the polyethers were typically too cumbersome for routine use, Pederson suggested an alternate form of nomenclature.



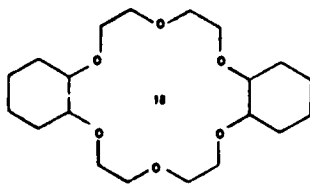
I

18-crown-6 (I) is so named because: (1) it has eighteen atoms in the ring, (2) it is a member of the "crown" class of polyethers, and (3) it has six oxygens within the ring.

The cations of the alkali and of the alkaline earth elements were the first inorganic substrates studied. It was shown<sup>1</sup> that potassium hydroxide could be dissolved in toluene which contained 18-crown-6. The resulting crown-complexed potassium hydroxide was found to be a powerful base apparently due to the enhanced reactivity



of the hydroxide anion. Similarly, potassium permanganate was a much more effective oxidizing agent when solution in nonpolar solvents was induced by dicyclohexano-18-crown-6 (IA).



IA

Sam and Simmons<sup>2</sup> observed that the resulting solution, known as "purple benzene", was able to oxidize a variety of organic compounds under mild conditions in 95-100% yields.

The complexation of appropriately sized cations with crown ethers appears to involve Lewis acid-base complexation. The oxygen atoms of the ether ring surround the metal cation and assumedly the electrostatic forces between the metal and each heteroatom are virtually equal.

Pederson advanced several conditions that affected complex formation and stability. Among these were: (1) the relation of physical size between the cation and the cavity of the crown ether ring, (2) the basicity of the ring oxygen atoms, and (3) the valence of the cation.

It was experimentally determined that a complex of greatest relative stability was formed when the ionic radius of the cation

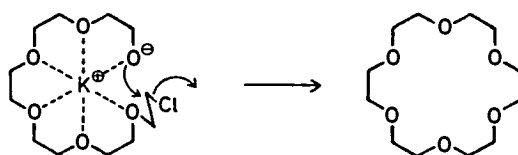
TABLE I

POLYETHER RING SIZES AND IONIC DIAMETERS<sup>4</sup>

<u>Polyether Ring</u>	<u>Ether Hole Diameter (A)</u>	<u>Ion</u>	<u>Ionic Diameter in Crystal (A)</u>
12-crown-4	1.2 - 1.5	Li <sup>+</sup>	1.36
15-crown-5	1.7 - 2.2	Na <sup>+</sup>	1.94
18-crown-6	2.6 - 3.2	K <sup>+</sup>	2.66
21-crown-7	3.4 - 4.3	Rb <sup>+</sup>	2.94
		Cs <sup>+</sup>	3.34

most closely matched the cavity size of a crown ether<sup>3</sup> (see Table I). Gokel and Durst obtained the stability constants,  $\log_{10} K$  ( $K$  in  $M^{-1}$  at 25° C), for polyether-cation complexes between 18-crown-6 and  $Na^+$  ( $\log K = 4.3$ ),  $K^+$  (6.1), and  $Cs^+$  (4.6). The crown hole diameter of 18-crown-6 (2.6-3.2 Å) corresponds most closely to the ionic diameter of potassium ion (2.66 Å) as shown in Table I.

The apparent specificity of a cation for a particular crown ether lead to the so-called "templated syntheses" for the corresponding crowns:



The reaction proceeds via the Williamson ether synthesis and during the last step the polyheteroatom chain wraps around the template cation. This allows the alkoxide and the carbon bearing the leaving group to approach one another and complete the cyclization.

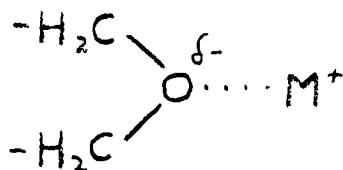
Pederson<sup>1</sup> was able to synthesize dibenzo-18-crown-6 in 39-48 % yields using reactant concentrations of 0.75-1.00 M. Such yields for eighteen-membered rings, which are difficult to make due to competing polymerization at these high concentrations, were much superior to yields reported for procedures using high dilution techniques.

R. N. Greene<sup>5</sup> synthesized 18-crown-6 by two methods, each involving a different base, and the results of these syntheses supported the template effect theory. When bases that provide potassium ion were used, yields up to 93% were obtained. When tetra-n-butylammonium hydroxide was used, the yield was much lower and polymerization often accompanied cyclization.

In other related work<sup>6</sup>, Cook and co-workers found that 15-crown-5 could be synthesized in highest yield when sodium ion bases were used. This smaller fifteen-membered ring apparently favored the smaller sodium cation. It was also found that the next smallest polyether, 12-crown-4, was obtained in highest yield when a lithium ion was acting as a template in the synthesis. Thus, there is a continuing trend of cyclization of smaller rings facilitated by the correspondingly smaller cations.

The quantity and basicity of ring oxygen atoms play an important role in the formation and stability of salt-polyether complexes. 18-Crown-6 is able to assume the configuration that places all six oxygen atoms coplanar to one another. Each is separated from the next by two methylene groups. It is reasonable to expect that an ion-dipole attraction takes place when a suitably sized cation is properly located in the center of the crown ether. The interaction between the metal ion and the oxygen of the carbon-

oxygen dipole can be visualized as follows:



X-ray crystallography has been performed on several crown complexes<sup>7,22</sup> and it was determined that the metal cation lies just above the plane of the oxygen atoms for a six-oxygen cyclic ether (see Figure 1).

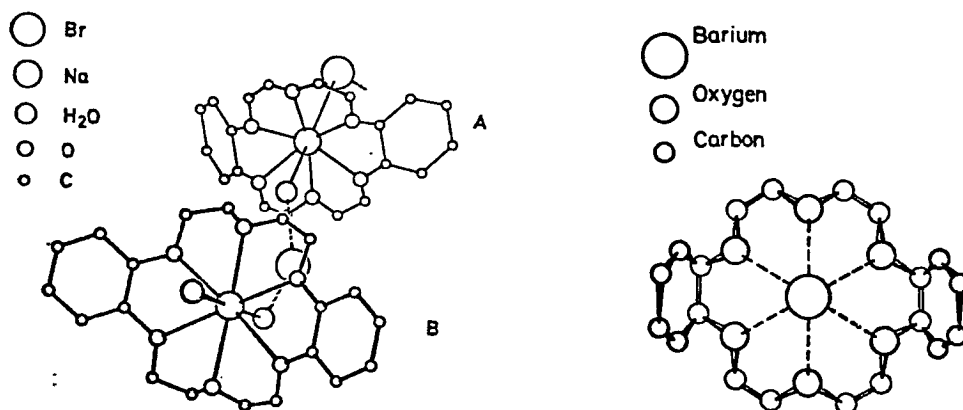


Figure 1. Crown-complex Structures

A complex between dibenzo-18-crown-6 and alkali thiocyanate was examined by three-dimensional X-ray analysis<sup>8</sup>. The unit cell was found to be comprised of four molecules of salt-ether complex and two molecules of uncomplexed ether. The two types of crown ether had identical bond lengths and angles (within experimental error) but different conformations. An accompanying diagram depicted

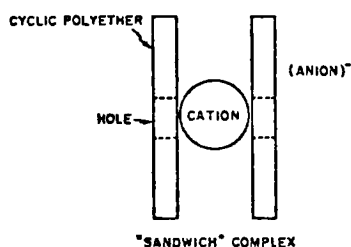
the uncomplexed ether as a relatively flat structure compared to the complexed version.

Pederson observed the extent of solubility of both complexed and uncomplexed crown ethers. Dibenzo-18-crown-6 was found to be more soluble in chloroform, dichloromethane, and pyridine, but only slightly soluble in alcohols and water. The saturated analog, dicyclohexano-18-crown-6, was found to be more soluble in solvents of both high and low dielectric constant, especially in alcohols, than the aromatic polyether. A complex between dibenzo-18-crown-6 and potassium isothiocyanate dissolved in dimethylsulfoxide at 26 °C up to 0.27 M concentration. In the same solvent and temperature, a complex between dicyclohexano-18-crown-6 and potassium hydroxide dissolved up to concentrations of about 0.4 M. Generally, both complexed and uncomplexed saturated polyethers were more soluble than the corresponding aromatic compounds.

The valence of the complexed cation appeared, in an earlier work<sup>1</sup>, to have little effect upon the stoichiometry and stability of the crown complexes. It was originally reported that the stable complexes that had been thusfar prepared involved one molecule of polyether per cation regardless of the valence of the metal cation. Pederson amended his initial proposals concerning stoichiometry in a later publication<sup>9</sup>. An overestimation of the hole diameter

of eighteen-membered crown ethers led Pederson to assume that only one polyether molecule was associated with a cation. A revised estimate of the diameter (2.6 - 3.2 Å) indicated that a cesium ion (3.34 Å) may be too large to accommodate a single molecule of dicyclohexano-18-crown-6. Elemental analyses and powder X-ray diffraction patterns suggested that a 2:1 polyether:cation ratio was the actual stoichiometry. Since no elements of uncomplexed polyether were observed in the pattern, a simple mixture of free ether and complex was considered unlikely. In addition, an infrared band at 10.02 micrometers, observed in the spectrum of dibenzo-18-crown-6, was not evident in the spectrum of the 2:1 complex prepared from that crown ether.

A "sandwich" structure, consisting of a spherical cation situated between two relatively flat polyether molecules, was suggested as a possible arrangement for the 2:1 complex:



It was concluded that stoichiometry appears to be controlled by the relative sizes of the metal cation and the polyether holes.

In general, large cations and small polyethers cause polyether-cation ratios higher than 1:1.

The preparation of a lanthanide salt-crown ether complex was first reported by Pederson in his original publication<sup>1</sup> on the complexing abilities of the crown ethers. The effect of lanthanum acetate on the ultraviolet spectrum of dibenzo-18-crown-6 was the only characteristic described for this complex.

The complexation of lanthanide nitrates and isothiocyanates with two representative crown ethers, benzo-15-crown-5 and dibenzo-18-crown-6, was reported by DePaoli and co-workers<sup>10</sup>. They reported that all complexes with both crown ethers possessed a 1:1 stoichiometry based upon carbon, hydrogen, nitrogen, and lanthanide quantitative analyses. The compounds exhibited only moderate solubility in polar solvents (e.g. alcohols and acetonitrile) and were largely insoluble in benzene and carbon tetrachloride. Experimental details on solubility determinations and conductivity measurements were not outlined in this publication; however, it was stated that nonelectrolytic behavior was exhibited by the complexes in acetonitrile solution.

This thesis discusses the synthesis and characterization of novel lanthanide-crown ether complexes. This research was of



interest since: (1) DePaoli's and Pederson's results suggested that such complexes could be made, (2) Pederson's studies showed that proper matching of ether hole size and cation size could guide the research and, most importantly (3) such complexes when formed could very well provide new and useful lanthanide shift reagents. Since inorganic salts complexed with crown ethers exhibited enhanced solubility in chloroform, benzene, and other nonpolar solvents that are typically used in the nuclear magnetic resonance experiment, it seemed reasonable to expect similar desirable solubility characteristics from the crown-complexed lanthanide ions. In addition, the enhanced reactivity due to anion separation in these complexes conveniently provided a highly accessible, Lewis acidic lanthanide cation to interact with a Lewis basic substrate.

Crown ether complexes of lanthanide ions possessing unpaired  $f$  electrons are of interest due to their potential use in NMR spectrometry as shift reagents. The unpaired  $f$  electrons of lanthanide ions are a source of a secondary magnetic field. Thus when an organic compound is treated with such lanthanide ions, signals due to this organic compound are shifted relative to their positions in the absence of the lanthanide ions. It should be noted here that this effect is common and is usually the result of a pseudo-contact mechanism of interaction as described below. Since the influence of the secondary magnetic

field decreases rapidly with distance, it is desirable to place the Lewis acidic atom in the LSR, on the average, in close proximity with the nucleus ( $^1\text{H}$  or  $^{13}\text{C}$ ) being examined. Thus, organic molecules possessing a more Lewis basic site are affected by LSR to a greater degree due to the stronger acid-base interaction.

Induced chemical shifts caused by lanthanide shift reagents can be interpreted in terms of two mechanisms. One of these involves a contact interaction mechanism and occurs via covalent bond formation; electron density is delocalized between the metal ion and the substrate nuclei. The other mechanism involves a dipolar, or pseudo-contact, interaction due to the magnetic moment of the unpaired electron in the metal ion. Since the 4f electrons of lanthanide ions are highly shielded, induced chemical shifts in proton magnetic resonance arise predominantly from the dipolar mechanism<sup>11</sup>. Lanthanide induced shifts of  $^{13}\text{C}$  nuclei have, however, been studied for pyridine in the presence of the  $\beta$ -diketonate complexes of europium, praseodymium, and ytterbium and a dipolar mechanism alone could not account for the observations; significant contact interaction was apparent for carbons ortho to the nitrogen atom<sup>12</sup>.

The shift reagent experiment typically involves the incremental addition of known weights of solid LSR to a solution of known amounts of the organic substrate of interest. The induced

shifts are tabulated after each addition as displacement of a resonance from its original position, i.e. from the resonance in the absence of LSR. These data are usually plotted versus the mole ratio of LSR to substrate. The slope of the linear portion of the curve for each nucleus set yields qualitative information in regard to the relative shifting capabilities of a particular LSR.

The majority of studies involving LSR has utilized six-coordinate metal complexes with various derivatives of fluorinated and nonfluorinated  $\beta$ -diketonate ligands<sup>13,14</sup>. These were used mainly with substrates in nonpolar solution, e.g. deuteriochloroform, carbon tetrachloride, and benzene- $d_6$ . When polar solvents were required, e.g. deuterium oxide, the ionic lanthanide salts, such as praseodymium nitrate, were used. Hydrated chlorides and nitrates were found to induce smaller shifts than the corresponding  $\beta$ -diketonate LSR, probably due to the reduced Lewis acidity of the ion caused by such hydration<sup>15</sup>. Europium ions usually induce shifts to high field and praseodymium ions to low field. In contrast,  $\beta$ -diketonate complexes of praseodymium normally shift proton resonances to higher field and the  $\beta$ -diketonate complexes of europium shift protons to lower field.

## EXPERIMENTAL

Proton magnetic resonance ( $^1\text{H}$  NMR) spectra were obtained on a Varian CFT-20 (80 MHz) instrument and a Perkin-Elmer (60 MHz) instrument. Carbon magnetic resonance ( $^{13}\text{C}$  NMR) spectra were obtained on a Varian CFT-20 (20 MHz) spectrometer and, unless otherwise indicated, are proton spin decoupled. Chemical shifts are expressed, for both proton and carbon nuclei, as parts per million relative to internal tetramethylsilane, TMS ( $\delta 0.00$ ). Multiplicity notations are: s, singlet; d, doublet; t, triplet; m, multiplet.

Infrared (IR) spectra were obtained on a Perkin-Elmer 621 instrument. Absorptions are reported in wavenumbers ( $\text{cm}^{-1}$ ). The spectral notations used are: s, strong; m, medium; w, weak; br, broad; sh, shoulder.

Melting points were determined using a Mel-Temp capillary melting point apparatus and are corrected.

Microanalyses were done by Baron Consulting Corporation, Orange, Connecticut.

Conductance measurements were made in acetonitrile at  $25.00 \pm 0.05$  °C with a YSI Company, Incorporated Model 31 B- conductivity bridge.

Mass spectral analyses were obtained using an AEI Scientific Apparatus, Inc. Model MS-902 instrument with a Scientific Research Instruments chemical ionization source at Cornell University, Ithaca, New York. This lab is directed by Timothy Wachs.

Data from shift reagent studies were developed with a least squares fit program, written by Dr. William Hayles of RIT, on a Hewlett-Packard Model 9820 calculator.

## Synthesis of a Complex (II) between Praseodymium Nitrate and 18-Crown-6

A solution of 992 mg. (3.0 mmol) of green praseodymium nitrate hexahydrate (K&K Labs) dissolved in 25 ml. of anhydrous methanol was prepared. Upon addition of 797 mg. (3.0 mmol) of 18-crown-6 (I, Aldrich Chemical Co.) at 25 °C, the green homogeneous solution effervesced for 1-2 minutes with no observable temperature change. When this effervescence subsided, a pale green solid had precipitated from the now colorless solution. The precipitate was suction-filtered through a Buchner funnel, washed with cold anhydrous methanol, and gently dried on a watch glass over a steam bath to yield 1.082 g. (61% yield) of pale green II which did not melt below 360 °C; the sample became light brown at 310 °C but remained solid up to 360 °C (the upper limit of the thermometer). The product was dried at 100 °C over phosphorus pentoxide under a vacuum for 72 hours.

<sup>1</sup>H NMR (dimethylsulfoxide-d<sub>6</sub>): δ 3.52, s, OCH<sub>2</sub>; δ 2.56, m, CD<sub>3</sub>SOCD<sub>2</sub>H. <sup>13</sup>C NMR (dimethylsulfoxide-d<sub>6</sub>): δ 69.79, OCH<sub>2</sub>; δ 39.46, CD<sub>3</sub>SOCD<sub>3</sub>. IR (KBr disc): 2950, 2880 m (aliphatic C-H stretch); 1420 s, 1375 s, 810 w (nitrate stretch and bend); 1055 s (ether linkage stretch). Microanalysis - Calculated for a 1:1 salt-crown ether adduct C<sub>12</sub>H<sub>24</sub>N<sub>3</sub>O<sub>15</sub>Pr: C, 24.37; H, 4.06; N, 7.11. Calculated for a 5:4 salt-crown ether adduct C<sub>48</sub>H<sub>96</sub>N<sub>15</sub>O<sub>69</sub>Pr<sub>5</sub>: C, 21.40; H, 3.57; N, 7.80. Found: C, 21.88; H, 3.35; N, 7.19.

A gravimetric analysis of Pr<sup>3+</sup> was performed on three samples

of II.<sup>16</sup> Calculated %: 20.2 Found %: 22.9, 19.8, 21.8 Average 21.5.

### Synthesis of a Complex (III) between Europium Nitrate and 18-Crown-6

A solution of 528 mg. (2.0 mmol) of 18-crown-6 dissolved in 20 ml. of anhydrous methanol was prepared; to this colorless, homogeneous solution was added 893 mg. (2.0 mmol) of europium nitrate hexahydrate (K&K Labs). The salt dissolved with effervescence at ca. 25 °C with no apparent temperature change and a white solid immediately precipitated. The reaction mixture was heated to reflux and sufficient methanol was added to just effect a homogeneous solution. Upon cooling to room temperature a solid product crystallized; the product was separated by suction-filtration and dried on a watch glass over a steam bath. The first crop weighed 521 mg. and sublimed during melting point analysis at 353 °C; in addition, sample discoloration (white to brown) was observed at 300 °C. The methanolic filtrate was evaporated from an Erlenmeyer flask over a steam bath to a volume of ca. 20 ml. to yield, via the workup described above, additional crops of product which sublimed during melting point analysis between 353-360 °C. The total yield of the reaction was 746 mg. (62%).

<sup>1</sup>H NMR (dimethylsulfoxide-d<sub>3</sub>): δ 3.49, s, OCH<sub>2</sub>; δ 2.48, m, CD<sub>3</sub>SOCD<sub>2</sub>H. <sup>13</sup>C NMR (dimethylsulfoxide-d<sub>3</sub>): δ 69.75, OCH<sub>2</sub>; δ 39.46, CD<sub>3</sub>SOCD<sub>3</sub>. IR (fluorolube mull): 2956 m, 2882 m (aliphatic C-H stretch); 1430 m, 1325 m (nitrate stretch and bend); 1045 s

(ether linkage stretch). Microanalysis - Calculated for a 1:1 salt-crown ether adduct  $C_{12}H_{24}N_3O_{15}Eu$ : C, 23.93; H, 4.02; N, 6.98. Calculated for a 5:4 salt-crown ether adduct  $C_{48}H_{96}N_{15}O_{69}Eu_5$ : C, 20.96; H, 3.50; N, 7.65. Found: C, 20.02; H, 3.32; N, 6.67. Duplicate Found: C, 19.66; H, 3.61; N, 6.61.

#### Synthesis of a Complex (IV) between Gadolinium Nitrate and 18-Crown-6

A solution of 905 mg. (2.0 mmol) of gadolinium nitrate hexahydrate (K&K Labs, Inc.) dissolved in 20 ml. of anhydrous methanol was prepared. To this homogeneous solution was added 529 mg. (2.0 mmol) of 18-crown-6 which readily dissolved at ca. 25 °C with swirling. A white solid precipitated within 1-2 minutes; the solid was filtered with suction and dried in a vacuum oven at 110 °C over  $P_2O_5$  for 1.5 hours. The first crop weighed 475 mg. and melted (with decomposition from a white solid to a brown oil) at 290 °C. The methanolic filtrate was evaporated under vacuum with a rotary evaporator to yield, via the workup described for II, 295 mg. of white powder which melted with decomposition at 280 °C. The total yield of white solid was 770 mg. (63%).

$^1H$  NMR of IV exhibited a very broadened resonance at  $\delta$ 3.50 which was observed only when the RF field of the instrument was increased by a factor of ten.  $^{13}C$  NMR exhibited only a random noise baseline with no resonances observed. IR (KBr disc): 2950 w, 2875 w (aliphatic C-H stretch); 1450 m, 1315 m (nitrate



stretch and bend); 1055 m (ether C-O stretch). Microanalysis-  
Calculated for a 1:1 salt-crown ether adduct  $C_{12}H_{24}N_3O_{15}Gd$ :  
C, 23.71; H, 3.95; N, 6.92. Calculated for a 5:4 salt-crown  
ether adduct  $C_{48}H_{96}N_{15}O_{69}Gd_5$ : C, 20.77; H, 3.46; N, 7.57.  
Found: C, 20.02; H, 3.85; N, 6.88.

Synthesis of a Complex (V) between Praseodymium Nitrate and  
Dicyclohexano-18-crown-6

A solution of 1.756 g. (4.7 mmol) of dicyclohexano-18-crown-6 (Aldrich Chemical Co., Inc.) dissolved in 15 ml. of absolute methanol was prepared and to this was added 2.047 g. (4.7 mmol) of praseodymium nitrate hexahydrate. The green homogeneous solution was gently heated on a steam bath for 5 minutes and then allowed to cool to room temperature. Upon standing overnight a light green solid had precipitated; the supernatant liquid was separated by suction filtration. The crystals were washed with 3 x 20 ml. portions of diethyl ether and then allowed to dry in air on a watch glass. The yield was 2.106 g. (93%) and the product melted between 275-280 °C with decomposition to give a brown oil. The product was recrystallized from absolute methanol, suction filtered, dried on a watch glass, then placed in a drying pistol under vacuum over  $P_2O_5$  at 100 °C for 18 hours. The recrystallized product melted at 310-311 °C with decomposition.

$^1H$  NMR (Acetonitrile- $d_3$ ):  $\delta$  3.55, s, 20 H,  $OCH_2$ ;  $\delta$  1.2-1.8,

m, 16 H, CH<sub>2</sub>. Off-resonance decoupled <sup>13</sup>C NMR (Dimethylsulfoxide-d<sub>6</sub>): δ76.56, d, C<sub>1,9,14,22</sub>; δ70.12, t, C<sub>4,6,17,19</sub> of isomer A; δ69.82, t, C<sub>4,6,17,19</sub> of isomer B; δ67.62, t, C<sub>3,7,16,20</sub> of isomer A; δ67.48, t, C<sub>3,7,16,20</sub> of isomer B; δ39.45, m, CD<sub>3</sub>SOCD<sub>3</sub>; δ27.30, t, C<sub>10,13,23,26</sub>; δ21.60, t, C<sub>11,12,24,25</sub>. IR (KBr disc): 2932 m, 2860 m (aliphatic C-H stretch); 1510 s, 1305 sh, 1265 s, 810 s (nitrate stretch and bend); 1070 s, 1045 s, 1020 s (ether C-O stretch). Microanalysis - Calculated for a 3:2 salt-crown ether adduct C<sub>40</sub>H<sub>72</sub>N<sub>9</sub>O<sub>39</sub>Pr<sub>3</sub>: C, 27.83; H, 4.17; N, 7.30; Pr, 24.52. Found: C, 27.87; H, 4.15; N, 7.33; Pr, 24.88.

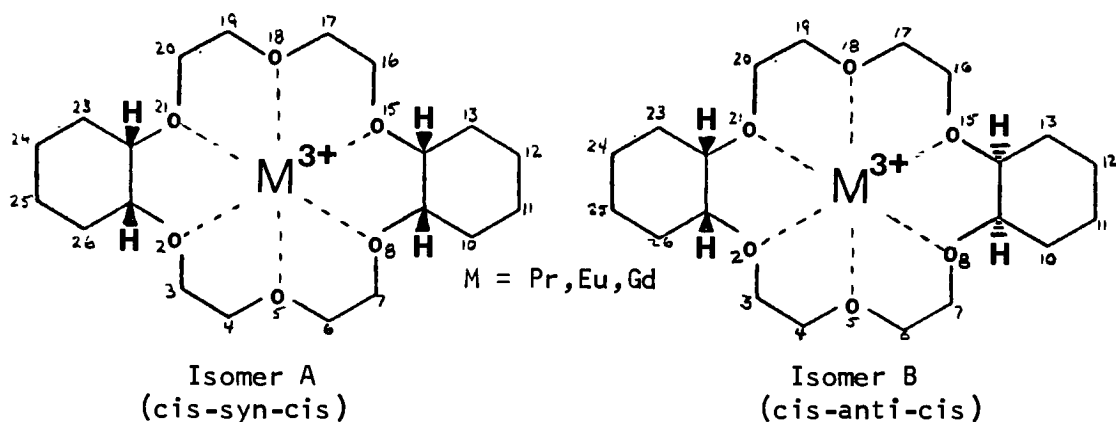


Figure 2. Isomeric Complexes between Lanthanide Nitrates and Ether IA

Synthesis of a Complex (VI) between Europium Nitrate and

Dicyclohexano-18-crown-6

Europium nitrate hexahydrate (PCR, Inc., 2.23 g., 5.0 mmol) and 1.86 g. (5.0 mmol) of dicyclohexano-18-crown-6 (Parish Chemical Co.) were dissolved in 10 ml. of absolute methanol. The colorless homogeneous solution was evaporated on a steam bath to ca. 4 ml. and a first crop of white crystals appeared. These were suction filtered and recrystallized from absolute methanol. The filtrate was evaporated on a rotary evaporator and the remaining solid was washed with ethyl ether and dried in air on a watch glass. The combined crops weighed 2.87 g. (99% yield) and melted between 234-241 °C into a bubbling brown oil.

<sup>1</sup>H NMR (Dimethylsulfoxide-d<sub>6</sub>): δ 3.51, s, 20 H, OCH<sub>2</sub>; δ 2.31, m, CD<sub>3</sub>SOCD<sub>2</sub>H; δ 1.36, m, 16 H, CH<sub>2</sub>. Off-resonance decoupled <sup>13</sup>C NMR (Dimethylsulfoxide-d<sub>6</sub>): δ 76.57, d, C<sub>1,9,14,22</sub>; δ 70.09, t, C<sub>4,6,17,19</sub> of isomer A; δ 69.81, t, C<sub>4,6,17,19</sub> of isomer B; δ 67.61, t, C<sub>3,7,16,20</sub> of isomer A; δ 67.48, t, C<sub>3,7,16,20</sub> of isomer B; δ 39.14, m, CD<sub>3</sub>SOCD<sub>3</sub>; δ 27.31, t, C<sub>10,13,23,26</sub>; δ 21.61, t, C<sub>11,12,24,25</sub>. IR (KBr disc): 2940 m (aliphatic C-H stretch); 1490 m, 1313 m, 810 w (nitrate stretch and bend); 1070 m, 1029 m (ether C-O stretch). Microanalysis - Calculated for a 3:2 salt-crown ether adduct C<sub>40</sub>H<sub>72</sub>N<sub>9</sub>O<sub>39</sub>Eu<sub>3</sub>: C, 27.31; H, 4.10; N, 7.17. Found: C, 27.60; H, 4.23; N, 7.11

Synthesis of a Complex (VII) between Gadolinium Nitrate and  
Dicyclohexano-18-crown-6

Gadolinium nitrate hexahydrate (1.359 g., 3.0 mmol) and dicyclohexano-18-crown-6 (2.102 g., 3.0 mmol) were dissolved in 20 ml. of absolute methanol and the homogeneous solution was heated to boiling for 10 minutes. The volume was reduced by evaporation over a steam bath to ca. 15 ml. and the product began to crystallize. The reaction mixture was allowed to cool to room temperature and the solid was suction filtered, washed with ethyl ether, and dried on a watch glass over a steam bath for 1-2 minutes. The fine white crystals weighed 786 mg. (44% yield) and melted at 256-258 °C to give a brown oil.

<sup>1</sup>H and <sup>13</sup>C NMR of VII exhibited only a random noise baseline with no resonances observed. IR (KBr disc): 2953 m (aliphatic C-H stretch); 1480 s, 1297 s (nitrate stretch and bend); 1053 m, 1011 m (ether C-O stretch). Microanalysis - Calculated for a 3:2 salt-crown ether adduct C<sub>40</sub>H<sub>72</sub>N<sub>9</sub>O<sub>39</sub>Gd<sub>3</sub>: C, 27.06; H, 4.06; N, 7.10. Found: C, 26.98; H, 4.16; N, 7.02.

Conductance Measurements of Praseodymium Nitrate and its Crown Complexes

Three acetonitrile solutions each were prepared of praseodymium nitrate, complex II, and complex V in the concentration range 10<sup>-3</sup> to 10<sup>-5</sup> molar. The cell constant was calculated for

the system from a standard aqueous solution 0.0200 M in potassium chloride. The conductivity of each solution was measured and the equivalent conductance was then calculated<sup>31</sup> from these data (see Table III).

Sample Calculations:

$$\text{Cell Constant} = k = \frac{\bar{L}}{L} = \frac{2.768 \times 10^{-3} \text{ mho cm}^{-1}}{1.320 \times 10^{-3} \text{ mho}} = 2.097 \text{ cm}^{-1}$$

$$\begin{aligned} \text{Equivalent Conductance} &= \frac{10^3 k L}{c} = \frac{10^3 (2.097) (2.1 \times 10^{-6} \text{ mho})}{3 \times 10^{-4} \text{ N Pr}(\text{NO}_3)_3} \\ &= 14.77 \end{aligned}$$

L is defined as conductance in ohms<sup>-1</sup> or mho

$\bar{L}$  is defined as specific conductance in mho cm<sup>-1</sup>

c is defined as solute concentration in equivalents/liter

### General Procedure for a Shift Reagent Experiment

A known amount (50-200 mg.) of the substrate to be studied (e.g. 50 microliters of dimethylsulfoxide) was accurately measured with an analytical balance or microliter syringe and then dissolved in a known volume (e.g. 500 microliters of acetonitrile-d<sub>3</sub>) of a deuterated solvent. The <sup>1</sup>H or <sup>13</sup>C NMR spectrum was taken and the chemical shifts of the nuclei of interest were tabulated.

Increments of solid shift reagent (e.g. 16.5 and 34.2 mg. of praseodymium nitrate hexahydrate) were added to the sample, the spectrum taken again after each addition, and the induced chemical shift of each desired nucleus in the substrate was again tabulated. The mole ratio of shift reagent to substrate was then calculated at each stage of addition and these data were used, with the corresponding chemical shifts, in a least squares fit computer program to determine the slope for each nucleus of a plot of chemical shifts vs. mole ratio of shift reagent to substrate.

Sample Data:	Least Squares Fit program $Y = mX + b$	
	<u>X (mole ratio)</u>	<u>Y (chemical shift, ppm)</u>
	0.00	2.50
	$5.6 \times 10^{-2}$	2.88
	$1.2 \times 10^{-1}$	3.25
	$m = \text{slope} = 6.24$	

#### Shift Reagent Solubility Determinations

Approximately 100 mg. of shift reagent was mixed with about 1 ml. of solvent and the extent of solubility was visually observed and recorded.

## Nuclear Magnetic Resonances of the Uncomplexed Crown Ethers

### 18-crown-6

$^1\text{H}$  NMR (Dimethylsulfoxide- $d_6$ ):  $\delta$ 3.51, s,  $\text{OCH}_2$ ;  
 $\delta$ 2.35, m,  $\text{CD}_3\text{SOCD}_2\text{H}$ .

$^{13}\text{C}$  NMR (Dimethylsulfoxide- $d_6$ ):  $\delta$ 69.89, t,  $\text{OCH}_2$ ;  
 $\delta$ 39.67, m,  $\text{CD}_3\text{SOCD}_3$ .

### Dicyclohexano-18-crown-6

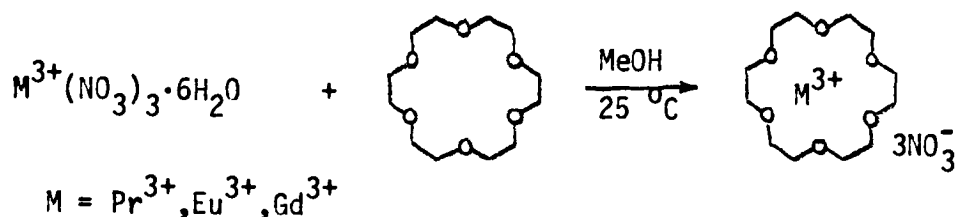
$^1\text{H}$  NMR (Dimethylsulfoxide- $d_6$ ):  $\delta$ 3.51, s, 20 H,  $\text{OCH}_2$ ;  
 $\delta$ 2.31, m,  $\text{CD}_3\text{SOCD}_2\text{H}$ ;  $\delta$ 1.40, m, 16 H,  $\text{CH}_2$ .

$^{13}\text{C}$  NMR (Dimethylsulfoxide- $d_6$ ):  $\delta$ 76.57, d,  $\text{C}_{1,9,14,22}$ ;  
 $\delta$ 70.16, t,  $\text{C}_{4,6,17,19}$  of isomer A;  $\delta$ 69.81, t,  $\text{C}_{4,6,17,19}$   
of isomer B;  $\delta$ 67.67, t,  $\text{C}_{3,7,16,20}$  of isomer A;  $\delta$ 67.49,  
t,  $\text{C}_{3,7,16,20}$  of isomer B;  $\delta$ 39.62, m,  $\text{CD}_3\text{SOCD}_3$ ;  $\delta$ 27.34,  
t,  $\text{C}_{10,13,23,26}$ ;  $\delta$ 21.64, t,  $\text{C}_{11,12,24,25}$ .

## RESULTS AND DISCUSSION

### I. Synthesis and Purification of the Lanthanide Salt-Crown Ether Complexes

The general method for the preparation of salt-crown ether complexes described by DePaoli<sup>10</sup> was followed at the initial stages of this research. We soon found, however, that the product precipitated spontaneously upon combination of the two reactants at room temperature in methanol;



this was in contrast to the published procedure which indicated a gradual precipitation of the product from hot (50-60 °C) acetonitrile. The crystalline product was filtered from the supernatant methanol through a Buchner funnel, washed with cold methanol, and dried on a watch glass over a steam bath. The filtrate was evaporated on a rotary evaporator to recover the product in solution which was then prepared via the work-up described above. The amorphous solid recovered from the filtrate melted over a much broader range than the first crop. This recovered solid was generally crystallized by trituration in chloroform before the two crops were combined. Yields ranged from 80-95% depending upon the purity of both reactants (more highly purified crown ethers



became commercially available as the research progressed).

Lanthanide nitrates were used as reactants in all syntheses. Syntheses involving lanthanide nitrates are of greatest interest since the resulting complexes were very useful. However, in an effort to prepare salt-crown ether complexes of higher solubility, lanthanide acetates were synthesized from the corresponding oxides (as well as purchased from PCR, Inc.) and used in place of the nitrates in a trial synthesis. The acetate anions proved to be less desirable because the solubility of the resulting complex was even less than that of the nitrate analog.

It should be noted here that a 1:1 salt-crown ether complex was expected in view of the quantitative elemental analyses published by DePaoli<sup>10</sup>. Thus, equimolar amounts of both reactants were used in all syntheses. Carbon, hydrogen, and nitrogen analyses of the products indicated that the stoichiometry of the complexes was other than simply one molecule of crown ether per molecule of lanthanide salt; since these complexes (see Table II) appear to contain fewer crown ether ligands than praseodymium atoms, we had in effect used an excess of crown ether reactant in this reaction. Evaporation of the methanol filtrate in each synthesis typically yielded an oil or amorphous solid (probably a mixture of complex and unreacted crown ether) and this solid was triturated in a minimum of chloroform or petroleum ether.

The complex crystallized and was filtered; the unreacted starting material (including the excess crown ether) apparently remained in solution, hence eluding detection.

## II. Characterization of the Lanthanide Salt-Crown Ether Complexes

Six complexes were prepared; europium, praseodymium, and gadolinium nitrates were each complexed by 18-crown-6 and dicyclohexano-18-crown-6. Elemental analysis results are listed in Table II. When it was determined that all of the complexes exhibited analyses other than percentages calculated for a 1:1 salt-crown ether complex, various ratios of ligand to salt were considered until a reasonable agreement could be made. The complexes made with dicyclohexano-18-crown-6 appeared to fit the observed analyses when it was assumed that each complex was composed of two molecules of crown ether and three molecules of lanthanide salt<sup>17</sup>. No X-ray crystallography was performed on any of the complexes and thus a structure such as the following is merely suggested as a possible arrangement of the molecules in the solid complex (see Figure 3).

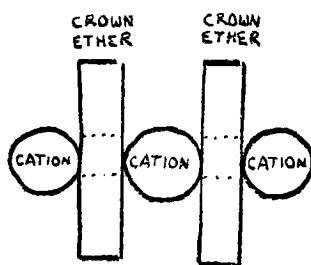


Figure 3.

TABLE II  
ANALYTICAL DATA OF THE SALT-CROWN ETHER COMPLEXES

<u>Compound</u>	<u>Formula</u>	<u>Mol Ratio</u> <u>(Salt:Ether)</u>	<u>Calc.</u> <u>MW</u>	<u>Carbon, %</u> <u>Found</u> <u>Calcd</u>	<u>Hydrogen, %</u> <u>Found</u> <u>Calcd</u>	<u>Nitrogen, %</u> <u>Found</u> <u>Calcd</u>
II	$C_{12}H_{24}N_3O_{15}Pr$	1:1	591	21.88	3.35	7.19
	$C_{48}H_{96}N_{15}O_{69}Pr_5$	5:4	2691	21.40	3.57	7.80
III	$C_{12}H_{24}N_3O_{15}Eu$	1:1	602	20.02	3.32	6.67
	$C_{48}H_{96}N_{15}O_{69}Eu_5$	5:4	2746	20.96	3.50	7.65
IV	$C_{12}H_{24}N_3O_{15}Gd$	1:1	607	20.02	3.85	6.88
	$C_{48}H_{96}N_{15}O_{69}Gd_5$	5:4	2773	20.77	3.46	7.57
V	$C_{20}H_{36}N_3O_{15}Pr$	1:1	700	27.87	4.15	7.33
	$C_{40}H_{72}N_6O_{30}Pr_3$	3:2	1725	27.83	4.17	7.30
VI	$C_{20}H_{36}N_3O_{15}Eu$	1:1	710	27.60	4.23	7.11
	$C_{40}H_{72}N_6O_{30}Eu_3$	3:2	1758	27.31	4.10	7.17
VII	$C_{20}H_{36}N_3O_{15}Gd$	1:1	715	26.98	4.16	7.02
	$C_{40}H_{72}N_6O_{30}Gd_3$	3:2	1774	27.06	4.06	7.10

The idea for this proposed structure appeared in Pederson's publication concerning variable stoichiometry in crown complexes<sup>9</sup>.

A close agreement was not obtained with complexes prepared with 18-crown-6 when a 3 to 2 ratio of salt to crown ether was assumed. Calculations assuming a 5 to 4 ratio showed the best correlation but even these did not closely agree with the observed percentages.

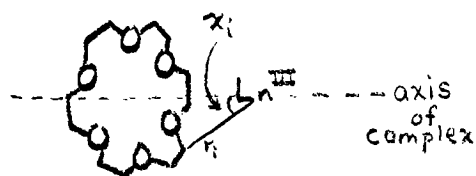
In addition to elemental analysis, the complexes were characterized by melting point, proton (pmr) and carbon (cmr) magnetic resonance spectroscopy, infrared and ultraviolet spectrophotometry, mass spectrometry, and conductometric analysis.

The proton magnetic resonances of the complexed polyether ring nuclei in dimethylsulfoxide- $d_6$  were found to be virtually identical in position to the resonances of the same nuclei in the free polyether (see Experimental); the same identity held for the carbon resonances. The carbon-hydrogen coupling constant,  $J_{C-H}$ , in the cmr spectrum of free 18-crown-6 was 140 Hz and in the praseodymium complex (II) it was 141 Hz (both spectra in dimethylsulfoxide- $d_6$ ). It can be proposed that the geometry of the crown complex may be the cause of the lack of induced shift (induced by the metal ion). The McConnell-Robertson equation<sup>18</sup>

should hold for these complexes:

$$\Delta H_i/H = K( 3\cos^2 \chi_i - 1/r_i^3 )_{\text{avg.}}$$

In this equation,  $\Delta H_i/H$  represents the induced shift and  $r_i$  represents the internuclear distance between the lanthanide ion and the carbon or hydrogen nucleus in question. The principal magnetic axis is generally chosen such as to cause the complex to have nearly axial symmetry about the axis. In this case, the principal magnetic axis likely connects the center of the lanthanide ion and the center of the crown ether ring (see Figure 4).



Distance between ether and lanthanide is exaggerated.

(See text for positioning of the axis)

Figure 4. Principal Magnetic Axis

$\chi_i$  is defined as the angle between the distance scalar  $r_i$  and the principal magnetic axis. A critical angle of  $\chi = 54^\circ 44'$  causes  $3\cos^2 \chi - 1$  and thus the right hand side of the McConnell-Robertson equation to equal zero and, consequently, an induced shift of zero is expected.

To account for the absence of induced shift in the NMR spectra of the crown ether complexes, it was proposed that the complex may dissociate into free molecules of crown ether and lanthanide nitrate when dissolved in polar solvents (e.g., acetonitrile or water). An acetonitrile solution of praseodymium nitrate and one of complex V were analyzed by ultraviolet spectrophotometry and a single band was observed in each spectrum. This occurred at a wavelength of 231 nanometers in each and corresponded to an ionic nitrate absorption. A comparison UV spectrum of an aqueous sodium nitrate solution confirmed the nitrate ion assignment. The shape of each absorption band was identical within experimental error. The visible spectrum of  $\text{Pr}^{3+}$  has been reported to exhibit a band at 442 nanometers ( $\log \epsilon = 6.3$ )<sup>32</sup> however no band was observed at this wavelength in the visible spectrum of complex V.

It was proposed that a substrate such as dimethylsulfoxide might alter the ultraviolet spectrum of the lanthanide-crown ether complex if it formed an adduct with the complex. When an amount of dimethylsulfoxide corresponding to the amount of shift reagent in a typical shift experiment was added to the acetonitrile solution of complex V, the absorption band remained unchanged in both wavelength and shape. The addition of this substrate, which would compete for the available coordination sites of the lanthanide ion, apparently made no effect upon the nitrate UV absorptions.

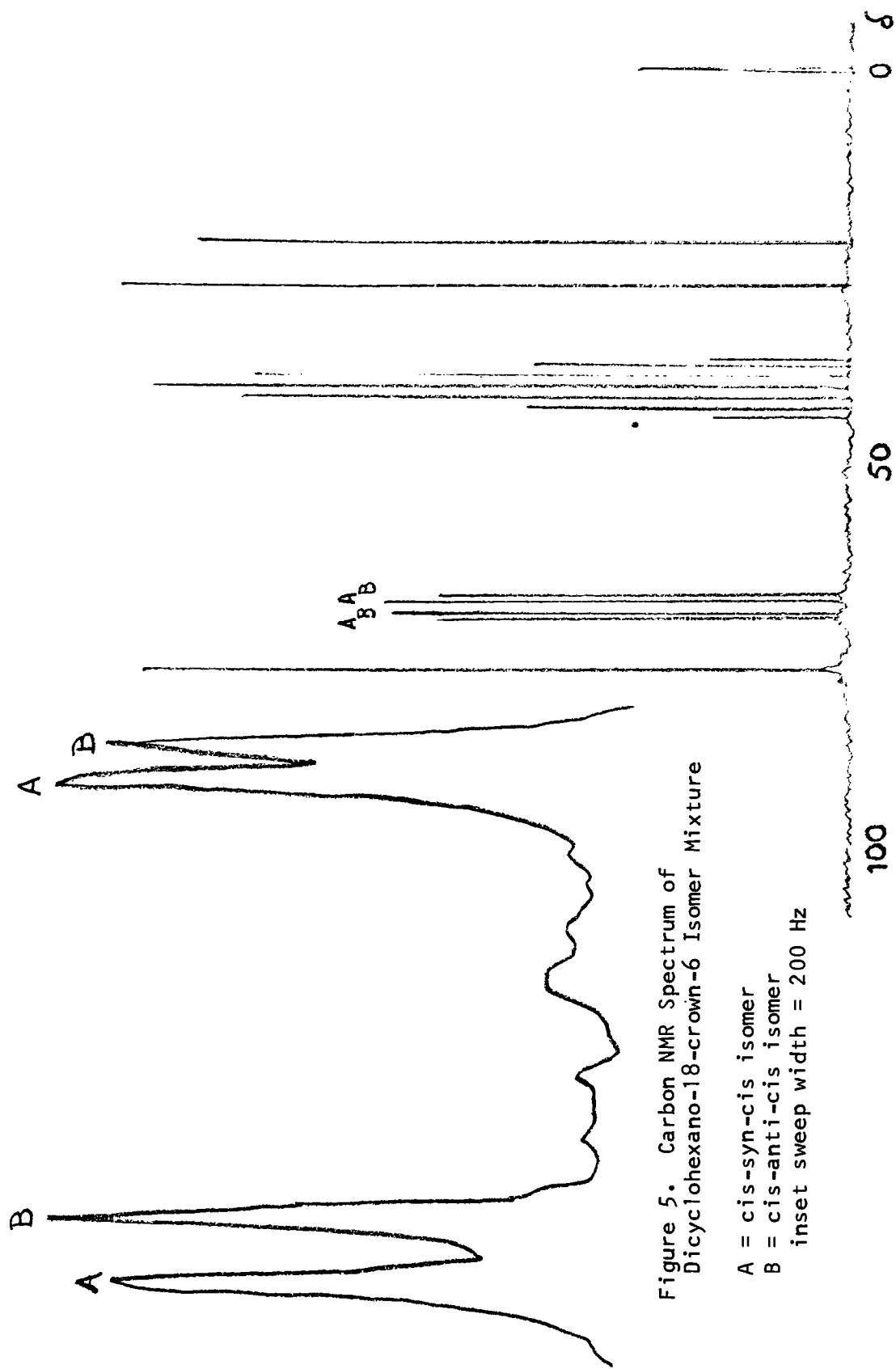


Figure 5. Carbon NMR Spectrum of Dicyclohexano-18-crown-6 Isomer Mixture

A = cis-syn-cis isomer  
 B = cis-anti-cis isomer  
 inset sweep width = 200 Hz

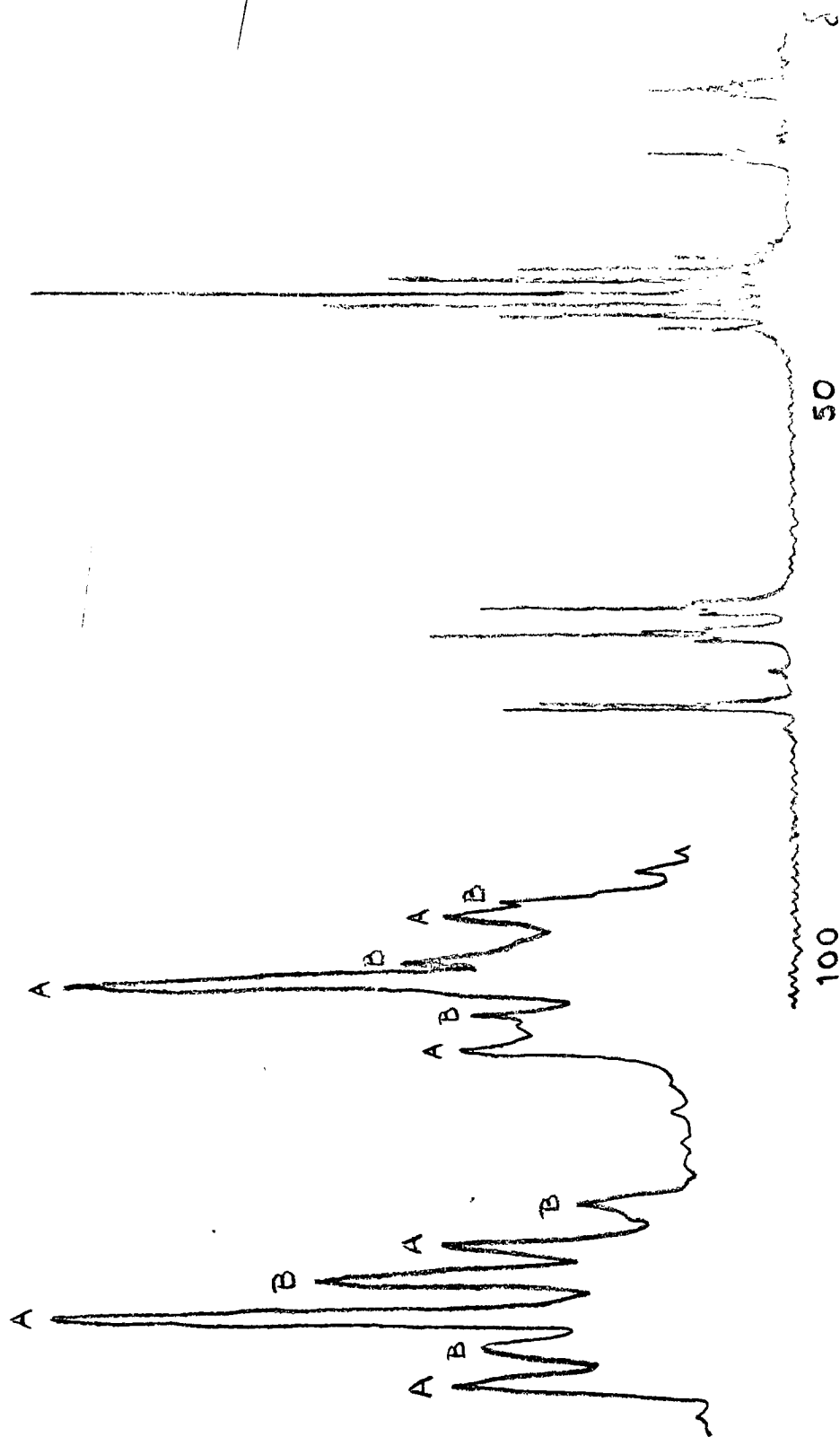


Figure 6. Off-Resonance Decoupled Spectrum of Isomeric Carbons in Complex V

A = cis-syn-cis isomer triplet

B = cis-anti-cis isomer triplet inset sweep width=300 Hz



The decoupled carbon magnetic resonance spectra of dicyclohexano-18-crown-6 and of complexes with praseodymium and europium each showed two pairs of resonances in a region that indicated that these signals were due to carbons attached to oxygen (see Figure 5). It was determined (see below) that one set corresponded to carbons  $C_{3,7,16,20}$  and the other set to carbons  $C_{4,6,17,19}$  (see Figure 2). The multiplicity of each of the four resonances in the cmr spectrum of complex V was determined with the off-resonance decoupling technique<sup>19</sup> as two sets of two overlapping triplets (indicating that each of the carbons in question was consistent with four nonequivalent methylene carbons--see Figure 6). It was subsequently determined through correspondence with Parish Chemical Company, the manufacturer of this sample of crown ether, that this ether was prepared by catalytic hydrogenation of dibenzo-18-crown-6. A cis relation is expected at each site of ring fusion to the larger ether cycle and two isomers are still possible. The two cis-fused cyclohexane rings may be "syn" or "anti" to one another (see Figure 2).

B. Haymore developed a technique to separate the two isomers by preparing lead perchlorate and hydronium perchlorate complexes<sup>20</sup>. A sample of each isomer was kindly provided by Dr. Haymore and the carbon NMR of each enabled us to confirm the assignment of each carbon atom in the mixture.

The numbering system employed in Figure 2 is derived from a publication by Meinwald and Crandall<sup>21</sup> concerning the systematic nomenclature of bridged polycyclic compounds. The two isomers each possess four centers of chirality (at each point of cis-fusion); the "cis-syn-cis" and "cis-anti-cis" names can be replaced by the more systematic R-S notation<sup>23</sup>. Thus, isomer A in Figure 2 and its enantiomer may be named 1(R)-9(S)-14(R)-22(S)-2,5,8,15,18,21-hexaoxatricyclo[20,4,0,0<sup>9,14</sup>]hexacosane; isomer B of Figure 2 and its enantiomer would be 1(R)-9(R)-14(S)-22(S)-2,5,8,15,18,21-hexaoxatricyclo[20,4,0,0<sup>9,14</sup>]hexacosane.

The infrared spectra of complexed and uncomplexed crown ethers were, apart from nitrate absorptions, significantly different from one another. Uncomplexed 18-crown-6 exhibited a strong, broad ether linkage (C-O stretch band) at 1120 cm<sup>-1</sup>; when complexed with one of the lanthanide ions this absorption was shifted to about 1050 cm<sup>-1</sup> and fine splitting was now observed. A moderate hydroxyl stretch absorption in the uncomplexed crown ether, probably due to the presence of water in the sample, was observed to be relatively weak in the IR spectra of the complexes. (Although the latter were obtained as KBr discs, a blank KBr disc displayed no hydroxyl band indicating that the bromide salt was quite dry.) Consequently, the complexes were thought to be free of any associated water or solvent methanol.

Mass spectral analysis of complex V by chemical ionization techniques apparently resulted in dissociation of the praseodymium ion from the crown ether due to elevated temperatures (300-450 °C). The molecular ion of dicyclohexano-18-crown-6 (MW 372.5) appeared at  $m/e$  373 accompanied by a smaller M+1 peak. The base peak of the spectrum occurred at  $m/e$  45 corresponding to a  $^+CH_2CH_2OH$  moiety.

Conductometric analysis of praseodymium nitrate and complexes II and V were performed in acetonitrile. Concentrations ranging from  $10^{-3}$  to  $10^{-5}$  molar were employed and a plot of equivalent conductance,  $\Lambda$ , versus the square root of the concentration was prepared. Weak electrolytic behavior was exhibited by both complexes and the lanthanide salt as the slope of their curves tended toward infinity at infinite dilution. It was suggested that this weak electrolytic behavior was caused by extensive ion-pairing in the acetonitrile solution (see Table III). The fact that the complex dissolved in acetonitrile gave rise to somewhat different conductance than praseodymium nitrate in acetonitrile suggests that the complex does not completely dissociate in acetonitrile, if it dissociates at all.

In summary, the conductance data, infrared absorptions, and melting points distinguish the complexes from the free crown ethers and serve to support the existence of salt-crown ether adducts.

TABLE III

## CONDUCTANCE DATA IN ACETONITRILE

<u>Compound</u>	<u>Conc. (M)</u>	<u>Conductance, L (<math>\mu</math>mho)</u>	<u>Equivalent Conductance, <math>\Lambda</math></u>
Pr(NO <sub>3</sub> ) <sub>3</sub>	1 x 10 <sup>-3</sup>	7.6	5.4
	1 x 10 <sup>-4</sup>	2.1	14.8
	1 x 10 <sup>-5</sup>	1.7	116.2
Complex II*	1 x 10 <sup>-3</sup>	17.2	12.1
	1 x 10 <sup>-4</sup>	4.6	32.2
	1 x 10 <sup>-5</sup>	1.9	133.0
Complex V*	4 x 10 <sup>-4</sup>	57.7	101.2
	4 x 10 <sup>-5</sup>	7.0	123.1
	4 x 10 <sup>-6</sup>	2.1	364.9
KCl (aq.)	2.0 x 10 <sup>-2</sup>	1310.0	

$$k = 2.113 \text{ cm}^{-1} = \text{cell constant}$$

\* Calculations are based on the molecular formulae for complex II (1:1 adduct) and complex V (3:2 adduct) described on pp. 15 and 19, respectively, and are adjusted per atom of lanthanide in complex V.

Standard aqueous KCl was used in determining the cell constant since KCl is insoluble in acetonitrile.

### III. Application of the Lanthanide-Crown Ether Complexes

It seemed reasonable to assume that the crown-complexed lanthanide ions might exhibit the same enhanced solubility in nonpolar solvents (e.g. benzene and chloroform) that was observed with the crown-complexed alkali cations. When the lanthanide complexes were prepared with 18-crown-6 they were found to be appreciably soluble only in polar solvents (e.g. water, methanol, dimethylsulfoxide, and acetonitrile). This insolubility in nonpolar solvents was thought to be due, at least in part, to the high charge of the lanthanide cation (3+). DePaoli and co-workers<sup>10</sup> reported that their lanthanide (III) nitrate complexes with dibenzo-18-crown-6 were soluble in methanol, slightly soluble in acetonitrile, and insoluble in benzene and carbon tetrachloride. Pederson<sup>1</sup> reported increased solubility in methanol of the divalent salts strontium and barium chloride when they were complexed by dibenzo-18-crown-6. In an effort to create a more oleophilic complex, a series of lanthanide ions complexed by the saturated dicyclohexano-18-crown-6 was prepared. These were moderately soluble in acetone but remained insoluble in the nonpolar solvents including benzene and chloroform. We have only partly succeeded in enhancing the solubility of lanthanide ions in nonpolar organic solvents via complexation. It could well be that substitution of cyclohexane rings of the crown ether with large nonpolar groups (e.g. t-butyl groups) could lead to com-

plexes that are soluble in solvents as nonpolar as deuteriochloroform.

Both the dicyclohexano-18-crown-6 complex of praseodymium nitrate and the free praseodymium nitrate hexahydrate were added to acetonitrile until saturation. The free nitrate salt could be dissolved in concentrations up to 4.1 molar but complex V could be dissolved only up to 0.6 molar. Since quantitative elemental analysis indicated that the formula of complex V was  $\text{Pr}_3(\text{dicyclohexano-18-crown-6})_2(\text{NO}_3)_9$ , a 0.6 molar solution of the complex was 1.8 molar in praseodymium atoms. Despite the lower solubility for complex V, this solubility was sufficient to produce significant lanthanide shifts with organic substrates.

Since a primary objective of this research was to prepare a novel and useful lanthanide shift reagent via crown ether complexation, high solubility of these complexes in nonpolar solvents was most desirable. Since Lewis acid-base coordination is the type of interaction that leads to substrate coordination with lanthanide shift reagents, it is important that the solvent used for these shift studies be a poor Lewis acid, such as benzene- $d_6$  or deuteriochloroform, rather than a stronger Lewis base, such as dimethylsulfoxide- $d_6$ .

It was proposed that a lanthanide salt with a more highly polarizable anion than nitrate might allow the crown complex to dissolve in chloroform or other suitable nonpolar NMR solvent. A compound such as europium triiodide might be a suitable choice since the large anion is highly polarizable and contributes no resonances to the NMR spectrum. This proposal, however, has not been investigated.

The utility of the lanthanide-crown ether complexes as NMR shift reagents was investigated by attempts to shift both the proton and carbon NMR spectra of a number of substrates. These shifts were compared to those obtained from substrates shifted by the ionic lanthanide nitrates and, in some cases, the  $\beta$ -diketonate reagents  $\text{Eu}(\text{fod})_3$  and  $\text{Pr}(\text{fod})_3$ .

Each shift study was conducted in the same general manner; weighed increments of solid shift reagent were added to a substrate solution of known concentration. Slopes of plots of lanthanide-induced chemical shifts versus the mole ratio of shift reagent to substrate were determined with a least-squares computer program. The slopes of the resulting plots were tabulated for comparison and are listed in Table IV.

## A. Triglycine

Of the substrates studied, N(N-glycylglycyl)glycine, or "triglycine", exhibited the largest induced NMR shifts of nuclei near the site of coordination. Since the samples of triglycine were dissolved in deuterium oxide, exchangeable protons were replaced by deuterium and the zwitterion form of the molecule existed in this solution:

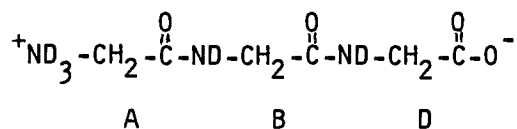


Figure 7. Structure of Triglycine in Deuterium Oxide

The nomenclature of the three methylene sets and carbonyl sets was derived from a publication by Kim and Martell<sup>24</sup>. The letter "A" is assigned to the methylene protons and to the carbonyl carbon located nearest the terminal amino group. The methylene protons nearest the terminal carboxyl group and the carbonyl carbon of the carboxyl group are labeled with the letter "D". The intermediate NMR nuclei are labeled in alphabetical sequence.

The assignment of the methylene proton resonances in the pmr spectrum of triglycine (in the absence of shift reagent) were compared to the assignments made by Kim and Martell<sup>24</sup>.



These assignments were made, in the latter case, on the basis of NMR experiments in which it was determined that as the solution pH increased, the pmr resonances of triglycine methylene protons nearest the site of proton dissociation shifted to higher field. The methylene groups, in the former case, showed proton resonances in the region  $\delta$ 3.6-4.0. Methylene group B was assigned the lowest field signal,  $\delta$ 3.91, in this region. Methylene group A was assigned to the  $\delta$ 3.79 signal and methylene group D\* was correlated with the  $\delta$ 3.66 signal.

The shifting abilities of complex V and complex VI were compared to each other and to their respective salts, praseodymium nitrate and europium nitrate. All of these shift studies were conducted in deuterium oxide solution. Triglycine was an excellent substrate for this comparison since it possessed three proton sets and six carbon sets of nuclei at various distances from the site of shift reagent coordination. The resulting slopes shown in Table IV correspond to the induced chemical shifts of the substrate versus the mole ratio of shift reagent to substrate. When the slopes of the experiments involving complex V or VI were calculated, these were divided by three since three lanthanide ions were present in each mole of complex, and it is of interest to compare all slopes based on one mole of lanthanide atom. These adjusted slopes are the ones listed in Table IV involving complex V or VI.

TABLE IV  
RESULTS OF NMR SHIFT STUDIES

<u>Substrate</u>	<u>Shift Reagent</u>	<u>Nucleus / Slope</u>	<u>Conc. (M) / Solvent</u>	
Triglycine (see Fig. 7)	Complex V* <sup>1</sup> H Methylene	Group A: + 0.66	0.25 Deuterium Oxide	
		B: + 2.77	" "	
		D: +18.30	" "	
	<sup>13</sup> C Carbonyl	Group A: + 0.59	" "	
		B: + 4.57	" "	
		D: + 3.57	" "	
	<sup>13</sup> C Methylene	Group A: + 0.31	" "	
		B: + 1.30	" "	
		D: +35.70	" "	
	Praseodymium Nitrate#	<sup>1</sup> H Methylene	Group A: + 0.06	" "
		B: + 0.67	" "	
		D: + 5.31	" "	
<sup>13</sup> C Carbonyl	Group A: + 0.36	" "		
	B: + 2.31	" "		
	D: +19.20	" "		

TABLE IV, con't.

<u>Substrate</u>	<u>Shift Reagent</u>	<u>Nucleus / Slope</u>	<u>Conc. (M) / Solvent</u>
Triglycine, con't.	Praseodymium Nitrate	<sup>13</sup> C Methylene Group A: + 0.10	0.25 Deuterium Oxide
		B: + 0.57	" "
		D: +15.10	" "
Complex VI*	<sup>1</sup> H Methylene Group	A: - 0.06	" "
		B: - 0.26	" "
		D: - 1.31	" "
<sup>13</sup> C Carbonyl	Group	A: - 1.64	" "
		B: - 9.40	" "
		D: + 65.80	" "
<sup>13</sup> C Methylene	Group	A: + 0.06	" "
		B: - 0.65	" "
		D: - 74.30	" "
Europium Nitrate#	<sup>1</sup> H Methylene Group	A: - 0.01	" "
		B: - 0.22	" "
		D: - 0.94	" "

TABLE IV, con't.

<u>Substrate</u>	<u>Shift Reagent</u>	<u>Nucleus / Slope</u>	<u>Conc. (M) / Solvent</u>
Triglycine, con't.	Europium Nitrate	<sup>13</sup> C Carbonyl Group A: - 0.26	0.25 Deuterium Oxide
		B: - 1.51	" "
		D: +55.90	" "
Dimethylsulfoxide $\text{H}_3\text{C}-\overset{\text{O}}{\parallel}{\text{S}}-\text{CH}_3$	Complex V*	<sup>13</sup> C Methylene Group A: + 0.06	" Acetonitrile-d <sub>3</sub>
		B: - 0.62	" "
		D: -65.70	" "
		<sup>1</sup> H Methyl: + 6.64	1.4
Praseodymium Nitrate	Pr(fod) <sub>3</sub>	<sup>13</sup> C Methyl: - 2.74	" "
		<sup>1</sup> H Methyl: + 6.24	" "
		<sup>13</sup> C Methyl: + 1.60	" "
Complex VI*	Europium Nitrate	<sup>1</sup> H Methyl: -13.10	0.7
		<sup>13</sup> C Methyl: -20.90	1.4
		<sup>1</sup> H Methyl: - 3.13	" "
		<sup>1</sup> H Methyl: - 4.77	0.7

TABLE IV, con't.

<u>Substrate</u>	<u>Shift Reagent</u>	<u>Nucleus / Slope</u>	<u>Conc. (M) / Solvent</u>
Acetone	Complex V*	<sup>1</sup> H Methyl: + 0.32	1.4 Acetonitrile-d <sub>3</sub>
$\begin{array}{c} \text{O} \\ \parallel \\ \text{H}_3\text{C}-\text{C}-\text{CH}_3 \end{array}$		<sup>13</sup> C Methyl: + 0.45	" "
		<sup>13</sup> C Carbonyl: + 0.92	" "
	Praseodymium Nitrate	<sup>1</sup> H Methyl: 0.00	" "
		<sup>13</sup> C Methyl: - 0.14	" "
		<sup>13</sup> C Carbonyl: + 4.95	" "

\* All slopes for complexes V and VI were divided by 3 in order to compare each shift reagent on the basis of one mole of lanthanide ion.

# See reference 25

Positive (+) slopes indicate a low-field shift; negative (-) slopes indicate a high-field shift.

Error estimates are found in Appendix I and Appendix II.

No precision measurement can be made since the slopes are the result of a single determination.

The proton data indicate that proton set D was shifted by all shift reagents to the greatest degree; methylene set B was shifted more than set A but less than set D. This is consistent with the assignments that place methylene group D closest to the Lewis basic coordination site, followed by B and A (see Figure 7). Assuming that paramagnetic shift reagents involve primarily a pseudo-contact mechanism in pmr spectra and, thus, conform to the McConnell-Robertson equation<sup>18</sup>, increased distance of a nucleus set from the substrate-shift reagent coordination site decreases the induced shift of that nucleus set. This assumes that the angle factor does not change appreciably in these cases.

The direction for induced shift for each proton set was always the same for both praseodymium complex V and the praseodymium salt, i.e., downfield, and it was upfield for both the europium complex VI and the europium salt.

In the case of both lanthanide ions, it appears that the shifting ability of the ionic salts on the pmr spectrum of triglycine is improved when these salts are complexed by dicyclohexano-18-crown-6.

The assignment of all resonances in the carbon spectrum of triglycine was aided by the use of model compounds and off-reson-

ance decoupling of the carbon spectrum. In off-resonance decoupled spectra, the multiplicities of the carbonyls would still be singlets; the three methylene carbons would, however, couple with their attached hydrogens to form a triplet in each case. All three of the methylene carbon resonances were closely spaced in the narrow region of  $\delta$ 40.0 to  $\delta$ 44.5; thus any assignment made by chemical shift alone seemed difficult.

A technique known as a "crossover experiment" was performed to support the assignment of the methylene protons and methylene carbons. Since the proton chemical shifts of the three methylene groups were accurately known, the carbon chemical shifts could be determined for these same groups as follows: 1) the decoupler frequency is offset in increments of 100 Hz. As this frequency deviates from a condition of complete proton-spin decoupling, residual splittings are observed at each methylene resonance. 2) The variation of the coupling constant,  $J_{C-H}$ , is plotted against the proton irradiating frequency. A computer program was used to produce the data from such plots<sup>27</sup>. TMS is placed by convention at a proton irradiating frequency of 4800 Hz. 3) The decoupler frequency at which the signal collapses into a singlet is noted for each carbon. This frequency corresponds to the exact frequency resonance of the connected proton. Such a frequency is determined by subtracting 4800 Hz from the known

proton chemical shift. The value 4800 Hz thus corresponds to the position of TMS relative to the shifts of these protons.

The carbon spectrum of triglycine, as mentioned previously, exhibited all three methylene resonances within several parts per million of one another. Since the coupling constants typically found with carbon spectra are large (50-250 Hz), overlapping multiplicities would present problems in the crossover study. This was resolved by the addition of complex V to the triglycine sample causing methylene set D to shift away from sets B and A by about 15 ppm; this allowed the residual splitting of B and A to be more clearly seen during the crossover studies. For comparison, the proton chemical shifts of these remaining two sets were determined by obtaining the pmr spectrum of an identical mole ratio of complex V to triglycine in D<sub>2</sub>O. As a result, methylene sets B and A appeared at  $\delta$ 4.50 and  $\delta$ 3.95, respectively. When the residual splitting and decoupler offset data were obtained for the cmr sample of triglycine containing complex V, it was determined via the crossover procedure that the carbon resonances at  $\delta$ 43.19 and  $\delta$ 40.83 corresponded to proton resonances at  $\delta$ 4.56 and  $\delta$ 3.97, respectively. Thus, it was concluded that the most downfield resonance of the methylene sets was set D, the intermediate signal was set B, and the most upfield methylene signal was set A in the cmr spectrum of triglycine.



When considering induced shifts in the cmr spectrum of triglycine a contact shift mechanism, as well as the pseudo-contact mechanism, must be considered. Carbon atoms closest to the site of coordination have the greatest potential to be involved in the delocalization of electron density that is associated with contact shifts<sup>28</sup>. For triglycine, carbonyl set D and methylene set D may exhibit this effect. Gansow and co-workers<sup>29</sup> determined that europium ion induced a contact shift that was about five times the magnitude of that produced by praseodymium ion; thus, we could expect a more pronounced contact shift contribution with the europium complex VI and europium nitrate than with their praseodymium counterparts (see below).

Referring again to Table IV, the crown-complex shift reagents, V and VI, induced greater carbon shifts of the three methylene groups than did the corresponding ionic salts. The direction of the shift with both praseodymium compounds is toward low field and, except for methylene carbon A, the shifts for both europium compounds are toward high field. The positive slope of methylene carbon A in the latter case may be due to experimental error since the induced shift is relatively small. The praseodymium complex V induces a shift about twice that of the praseodymium salt; the europium complex VI induces slightly larger shifts than europium nitrate. The carbonyl carbons D, B, and A were tentatively assigned through comparison

with model compounds. Carbonyl set D was assigned to the most downfield resonance since carboxylate anions are generally more deshielded than the carbonyls of amides<sup>30</sup>. Complex V shifted sets A and B to a greater degree than praseodymium nitrate shifted them but the nitrate appeared to shift carbonyl set D more than complex V did. Shifts for all of these carbonyl carbons were to lower field with both praseodymium reagents. The europium complex VI shifted all three carbonyl sets to a greater degree than did europium nitrate. However, the shift direction of carbonyl set D was toward low field for both europium reagents as opposed to the upfield shifts for carbonyl sets B and A. It has been pointed out that europium produces a greater amount of contact shift<sup>29</sup> and carbonyl set D, being immediately adjacent to the site of shift reagent-substrate coordination, would be most susceptible to this interaction.

A method of measuring the relative amounts of contact and pseudo-contact mechanisms that affect a selected nucleus has been published<sup>28</sup>. This method indicates that nuclei within four bond lengths of the shift reagent-substrate coordination site are susceptible to contact shifts. It was based upon the McConnell-Robertson equation for pseudo-contact shifts<sup>18</sup>. When the induced shifts caused by two different shift reagents (e.g., by complex V and by praseodymium nitrate) are compared, the ratio of their respective McConnell-Robertson equations should be constant. This

assumes: 1) that angle  $\alpha_i$  and distance  $r_i$  are the same in both substrate-shift reagent adducts i.e., only a ratio of the constant terms K need be regarded, and 2) the shift has been induced by a pseudo-contact mechanism. Since  $\Delta H_i/H$  is effectively the slope of a shift study at a mole ratio of one, the overall ratio is:

$$\frac{(\Delta H_i/H)_{\text{LSR 1}} = K(3\cos^2 \alpha_i - 1/r_i^3)}{(\Delta H_i/H)_{\text{LSR 2}} = K'(3\cos^2 \alpha_i - 1/r_i^3)} =$$

$$\frac{\text{slope}_{\text{LSR 1}}}{\text{slope}_{\text{LSR 2}}} = \frac{K}{K'} = \text{constant}$$

In other words, for a given substrate, a constant ratio should be obtained when comparing the slopes caused by one shift reagent versus the slopes caused by another for all nuclei in the substrate.

For triglycine, four possible shift reagent comparisons to be made are: 1) complex V versus praseodymium nitrate 2) complex VI versus europium nitrate 3) complex V versus complex VI and 4) praseodymium nitrate versus europium nitrate. Table V lists these four types of ratios with individual slopes taken from Table IV.

TABLE V

RATIO DATA FROM THE MCCONNELL-ROBERTSON EQUATIONS FOR TRIGLYCINE

<u>Nucleus</u>	<u>Comparison 1</u> $\frac{\text{Complex V}}{\text{Pr}(\text{NO}_3)_3}$	<u>Comparison 2</u> $\frac{\text{Complex VI}}{\text{Eu}(\text{NO}_3)_3}$	<u>Comparison 3</u> $\frac{\text{Complex V}}{\text{Complex VI}}$	<u>Comparison 4</u> $\frac{\text{Pr}(\text{NO}_3)_3}{\text{Eu}(\text{NO}_3)_3}$
$^1\text{H}$ Methylene Group A: B: D:	11.0	6.0	- 11.0	- 6.0
	4.1	1.2	- 10.6	- 3.1
	3.4	1.4	- 14.0	- 5.6
$^{13}\text{C}$ Carbonyl Group A: B: D:	1.6	6.3	- 0.4	- 1.4
	2.0	6.2	- 0.5	- 1.5
	0.2	1.2	0.1	0.3
$^{13}\text{C}$ Methylene Group A: B: D:	3.1	1.0	5.2	1.7
	2.3	1.1	- 2.0	- 0.9
	2.4	1.1	- 0.5	- 0.2

For example, in the case of pmr methylene set D:

$$\frac{\text{slope}_{\text{Pr}(\text{NO}_3)_3}}{\text{slope}_{\text{Eu}(\text{NO}_3)_3}} = \frac{5.31}{-0.94} = -5.6$$

In theory, all ratios in a series corresponding to a given nucleus shifted by two different reagents should be identical if only the pseudo-contact mechanism is in operation. If any ratio deviates from the constant value by a margin greater than the experimental error, one should suspect that a considerable amount of contact shift is involved<sup>28</sup>.

The results listed in Table V indicate the following general trends: 1) except for pmr methylene set A, the pmr methylene sets are fairly constant suggesting that a predominantly pseudo-contact mechanism prevails in the protons of triglycine. However, contact shifts are less likely in proton spectra compared to carbon spectra<sup>28</sup>; this explains the less constant slope ratios for the carbon spectra. 2) carbonyl carbon D stands alone in all four comparisons while the ratios for carbonyl carbons B and A are nearly identical. This is consistent with each set's proximity to the substrate coordination site which predicts that the greatest contact shift will be exhibited by carbonyl carbon D.

Considering the methylene carbons of triglycine, comparisons 1 and 2 of Table V indicate that a predominantly pseudo-contact mechanism for all three carbons is in operation; comparisons 3 and 4 are inconclusive for these carbon nuclei because the ratios are too widely scattered.

#### B. Dimethylsulfoxide, DMSO

Another substrate studied was DMSO (in acetonitrile- $d_3$  solution). Acetonitrile- $d_3$  was used as the NMR solvent since, being less Lewis basic than DMSO, it was sufficiently polar to dissolve the substrate and shift reagents but was not likely to compete with the substrate for the available shift reagent as would deuterium oxide. Substantial proton shifts were noted; the methyl group of DMSO was shifted slightly more by praseodymium complex V than by praseodymium nitrate. The reverse was true for europium complex VI and europium nitrate (see Table IV). For comparison, the  $\beta$ -diketonate shift reagent,  $\text{Pr}(\text{fod})_3$ , was also used to shift DMSO; the resulting slopes were much greater with  $\text{Pr}(\text{fod})_3$  than with either complex V or praseodymium nitrate. The DMSO methyl carbon was scarcely shifted by complex V or praseodymium nitrate, but  $\text{Pr}(\text{fod})_3$  caused a sizable shift of this nucleus.

### C. trans-Cinnamaldehyde

Cinnamaldehyde provides a carbonyl group of modest Lewis basicity to test the effectiveness of our shift reagents. Also, the pmr spectrum of this substrate was of interest because an olefinic proton was buried beneath the aromatic resonances. Efforts to shift this compound were hampered by the presence of an impurity, thought to be trans-cinnamic acid, in the sample. Thin-layer chromatography (silica gel; chloroform) of the aldehyde sample exhibited two spots; there was a large spot near the solvent front (the aldehyde component) and a relatively small spot at the origin (likely the acid impurity). Air-oxidation apparently caused this impurity in the reagent bottle. The substrate could also have been oxidized by the ionic nitrate groups from the shift reagents. A color change from yellow to yellow-brown was noted within the NMR sample tube. A sample of trans-cinnamaldehyde was distilled and collected as a pale yellow liquid; this compound also underwent a color change to yellow-brown when mixed with nitrate-bearing shift reagent. After several unsuccessful attempts at shifting cinnamaldehyde, it was decided to discontinue further studies on this substrate.

#### D. Acetone

Substantial carbon shifts for acetone were realized (see Table IV). The cmr spectra of this substrate indicated that the carbonyl carbon was shifted to a greater degree than the methyl carbons by both complex V and praseodymium nitrate (see Table IV). If we assume that the McConnell-Robertson pseudo-contact shift equation<sup>18</sup> is valid (angle  $\alpha_i$  undergoes negligible change), these results are consistent with the nuclei closer to the coordination site being shifted more. No effort was made to measure contact shift contributions using europium reagents, however. The methyl protons in the pmr spectra were not significantly shifted by either complex V or praseodymium nitrate at the shift reagent-substrate mole ratios employed. Additional work is needed on these proton shift studies.



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APPENDIX I

ERROR ANALYSIS OF OATA IN TABLE IV

<u>Substrate</u>	<u>Shift Reagent</u>	<u>Nucleus</u>	<u>Standard Deviation, <math>\sigma</math></u>	<u>Correlation Coefficient</u>		
Triglycine	Complex V	$^1\text{H}$ Methylene	A	$4.5 \times 10^{-5}$	0.999	
			B	$6.7 \times 10^{-4}$	0.999	
			D	$2.7 \times 10^{-1}$	0.996	
		$^{13}\text{C}$ Carbonyl	A	$3.5 \times 10^{-3}$	0.966	
			B	$7.6 \times 10^{-4}$	0.999	
			D	$2.3 \times 10^{-1}$	0.943	
		$^{13}\text{C}$ Methylene	A	$8.3 \times 10^{-4}$	0.971	
			B	$7.9 \times 10^{-4}$	0.998	
			D	$1.8 \times 10^{-1}$	0.999	
		$\text{Pr}(\text{NO}_3)_3$	$^1\text{H}$ Methylene	A	-	-
				B	-	-
				D	-	-
	$^{13}\text{C}$ Carbonyl		A	$4.0 \times 10^{-3}$	0.982	
			B	$9.8 \times 10^{-2}$	0.990	
			D	$7.1 \times 10^{-4}$	0.999	
	$^{13}\text{C}$ Methylene		A	$9.0 \times 10^{-5}$	0.995	
			B	$6.8 \times 10^{-3}$	0.988	
			D	$7.4 \times 10^0$	0.981	
	Complex VI		$^1\text{H}$ Methylene	A	$5.6 \times 10^{-5}$	-0.970
				B	$1.8 \times 10^{-4}$	-0.994
				D	$3.9 \times 10^{-3}$	-0.995
		$^{13}\text{C}$ Carbonyl	A	$1.3 \times 10^{-1}$	-0.945	
			B	$1.9 \times 10^{-1}$	-0.772	
			D	$6.5 \times 10^0$	-0.999	
$^{13}\text{C}$ Methylene		A	$2.4 \times 10^{-3}$	0.542		
		B	$1.1 \times 10^{-3}$	-0.996		
		D	$7.7 \times 10^0$	-0.998		
$\text{Eu}(\text{NO}_3)_3$		$^1\text{H}$ Methylene	A	-	-	
			B	-	-	
			D	-	-	
	$^{13}\text{C}$ Carbonyl	A	$1.7 \times 10^{-3}$	-0.968		
		B	$3.7 \times 10^{-3}$	-0.998		
		D	$6.8 \times 10^0$	-0.997		
	$^{13}\text{C}$ Methylene	A	$9.6 \times 10^{-5}$	-0.961		
		B	$4.2 \times 10^{-4}$	-0.999		
		D	$8.1 \times 10^0$	-0.997		

## APPENDIX I, con't.

<u>Substrate</u>	<u>Shift Reagent</u>	<u>Nucleus</u>	<u>Standard Deviation, <math>\sigma</math></u>	<u>Correlation Coefficient</u>	
DMSO	Complex V	$^1\text{H}$ Methyl	$8.9 \times 10^{-3}$	0.999	
		$^{13}\text{C}$ Methyl	$2.6 \times 10^{-2}$	0.985	
	$\text{Pr}(\text{NO}_3)_3$	$^1\text{H}$ Methyl	$7.1 \times 10^{-3}$	0.999	
		$^{13}\text{C}$ Methyl	$1.4 \times 10^{-3}$	0.704	
	$\text{Pr}(\text{fod})_3$	$^1\text{H}$ Methyl	$5.3 \times 10^{-2}$	-0.989	
		$^{13}\text{C}$ Methyl	$1.4 \times 10^{-3}$	-0.999	
	Complex VI	$^1\text{H}$ Methyl	$2.8 \times 10^{-2}$	0.989	
	$\text{Eu}(\text{NO}_3)_3$	$^1\text{H}$ Methyl	$2.6 \times 10^{-3}$	-0.999	
	Acetone	Complex V	$^1\text{H}$ Methyl	$1.3 \times 10^{-2}$	0.631
			$^{13}\text{C}$ Methyl	$1.5 \times 10^{-2}$	0.861
$^{13}\text{C}$ Carbonyl			$9.5 \times 10^{-3}$	0.976	
$\text{Pr}(\text{NO}_3)_3$		$^1\text{H}$ Methyl	-	-	
		$^{13}\text{C}$ Methyl	$5.0 \times 10^{-2}$	0.996	
		$^{13}\text{C}$ Carbonyl	$1.4 \times 10^{-4}$	0.986	

APPENDIX II

ERROR ANALYSIS OF SELECTED SLOPES IN TABLE IV

The uncertainty in the slope data of Tables IV and V was determined for certain shift studies; the shifts of triglycine proton sets A and B induced by praseodymium nitrate, europium nitrate, and complexes V and VI were examined by graphical analysis<sup>33</sup> to determine the uncertainty in each calculated slope. "Error bars" were drawn through each experimental point; these represented the limit of error in the observed chemical shift (0.01 ppm). Maximum and minimum values of the slope were drawn consistent with the requirement that both lines pass through every point. The difference between the slopes of the limiting lines can be taken as twice the limit of error in the best straight line. The slopes determined for the protons of methylene set A are apparently subject to a great deal of uncertainty compared to set B (see below) and, in view of this, quantities derived from set A slopes (see Table V) should be regarded with caution.

<sup>1</sup>H Methylene Set A

	<u>Complex V</u>	<u>Pr(NO<sub>3</sub>)<sub>3</sub></u>	<u>Complex VI</u>	<u>Eu(NO<sub>3</sub>)<sub>3</sub></u>
Maximum slope:	0.83	0.12	-0.09	-0.14
Minimum slope:	0.54	0.05	-0.04	-0.06
Limit of error:	0.15	0.04	0.03	0.04
Slope calculated from least-squares program: (see Table IV)	0.66± 0.15	0.06±0.04	-0.06±0.03	-0.01±0.04

<sup>1</sup>H Methylene Set B

	<u>Complex V</u>	<u>Pr(NO<sub>3</sub>)<sub>3</sub></u>	<u>Complex VI</u>	<u>Eu(NO<sub>3</sub>)<sub>3</sub></u>
Maximum slope:	2.92	0.71	-0.28	-0.39
Minimum slope:	2.67	0.63	-0.25	-0.24
Limit of error:	0.13	0.04	0.02	0.08
Slope calculated from least-squares program: (see Table IV)	2.77±0.13	0.67±0.04	-0.26±0.02	-0.22±0.08