

Modeling Lanthanide Coordination Complexes. Comparison of Semiempirical and Classical Methods

Thomas R. Cundari* and L. C. Saunders

Department of Chemistry, University of Memphis, Memphis, Tennessee 38152-6060

Received September 12, 1997

A variety of approximate methods for *efficient* modeling of large lanthanide (Ln) complexes were studied. Attention was paid to ligand motifs prevalent in Ln coordination chemistry. Gadolinium was chosen given its central location in the Ln series and its importance in areas such as magnetic resonance imaging. A semiempirical approach based on a technique first described for europium was extended to gadolinium. Comparison with *ab initio*, molecular mechanics, and PM3 methods was performed for experimental and model complexes. Electrostatic models were found to be most reliable for cationic, large coordination number complexes with hard nitrogen and oxygen donors—an important subset of lanthanide complexes. When used for appropriate target complexes electrostatic models, particularly when used in conjunction with molecular mechanics, can be an effective and efficient technique for the study of large, experimentally relevant lanthanide coordination complexes.

INTRODUCTION

Lanthanide chemistry has come under increasing study. Experimentalists have sought to exploit their unique chemical and magnetic properties for a variety of advanced materials, catalysis, and biomedical applications.¹ For example, compounds of gadolinium (Gd) are currently used in all commercial magnetic resonance imaging (MRI) contrast agents.² If the structure of potential contrast agents could be successfully determined, the relationship between chemical properties and relaxivity, which is currently unclear, could be deduced and improved agents developed. Similarly, rational design of lanthanide complexes with important applications in other areas could be pursued.

This research seeks to develop and assess *computationally efficient* methods for modeling lanthanide (Ln) complexes. These techniques could then be used for rational design of Ln materials. The lanthanides have been little studied computationally. Challenges in application of quantum methods to lanthanides include: large numbers of electrons, the electron correlation problem, and the importance of relativistic effects.³ The majority of *ab initio* calculations on lanthanides have employed effective core potentials (ECPs).⁴ Despite the great computational savings effected by replacing core electrons with an ECP, such calculations remain prohibitive for large Ln complexes. Semiempirical methods, on the other hand, are much more feasible, although applications to lanthanide chemistry are rare.⁵ A major difficulty in quantum calculations on lanthanides arises from the highly contracted 4f orbitals that overlap weakly with ligating atoms. Some workers have employed ECPs in which the 4f manifold is included in the core and found that in the appropriate circumstances accurate modeling is achieved.^{4c} In research by de Andrade et al.⁵ on semiempirical methods they studied [Eu(dipivaloylmethanato)₃-(terpyridine)], [Eu(piccolinate-*N*-oxide)₃(terpyridine)], and [Eu(acetylacetonate)₃(phenanthroline)] using a derivative of

the semiempirical AM1 method in which the lanthanide europium is treated as a point charge (referred to as a sparkle in MOPAC⁶). In this technique Eu interacts with other atoms in the complex in an electrostatic fashion.

All lanthanides favor a formal oxidation state of +3, high coordination numbers, and hard donors such as oxygen and nitrogen. Given their similar properties, it is reasonable to inquire whether the method developed by de Andrade et al. for europium^{5a–c} can be extended to other lanthanides. Additionally, this research strives to compare predicted structures with those derived from a published molecular mechanics (MM) force field.⁷ Given the high degree of ionic bonding common to lanthanides the de Andrade method deserves consideration as a technique for rapid and effective modeling of Ln complexes.

COMPUTATIONAL METHODS

Starting geometries were taken from X-ray crystal structures.⁸ Input files were created with gadolinium replaced by the “++” sparkle.^{5b} The files were sent to an IBM RS-6000 workstation, and MOPAC⁶ was employed to optimize the geometries. The semiempirical method employed by de Andrade et al. was based on the sparkle method.⁵ This was accomplished by defining a +3 charge on the lanthanide and allowing for no orbitals. Other atoms in the complex behave in a normal, quantum mechanical fashion.

The LEAH (lanthanide electrostatic AM1 Hamiltonian) model for the calculation of lanthanide complexes developed by de Andrade et al. for europium⁵ was extended to gadolinium. This involved determination of several parameters: EHEAT (heat of sublimation of gadolinium plus the sum of the first three ionization potentials) was set to 991.2 kcal mol⁻¹, the sparkle charge for gadolinium (CORE) was set to +3, and the atomic mass (AMS) was set to that of gadolinium (157.25 AMU). The following MOPAC6 keywords were employed in optimization: AM1, PRECISE, XYZ, EF, MMOK, CHARGE (overall charge of the complex), and *T* = 36000.⁹ In addition, two AM1 parameters

* Address correspondence to this author.

Table 1. ALPAM1 and AMAM1 Grid Search^a

ALPAM1 (Å ⁻¹)	AMAM1 (au)	RMS _{hvy} (DAPSC) (Å)
2.0	2.0	0.234
2.0	3.0	0.230
2.0	4.0	0.229
2.5	2.0	0.300
2.5	3.0	0.308
2.5	4.0	0.312

^a The parameters ALPAM1 and AMAM1 are described in Computational Methods; RMS_{hvy} is the root mean square deviation in heavy atom positions between the experimental^{8a} and LEAH-calculated structures of [Gd(DAPSC)(OH₂)₄]³⁺.

were adjusted as described below. ALPAM1, which is used in calculation of core–core repulsion, was changed to 2.0 Å⁻¹. AMAM1 is derived from *g*_{ss}, a one-center, two-electron integral, and was adjusted to a value 4.0 au; the parameter AMAM1 has units of energy.⁶

RESULTS AND DISCUSSION

1. Tetra(aqua)diacetylpyridinebis(semicarbazone)-gadolinium(III). The parameters ALPAM1 and AMAM1 were estimated based on a grid search (Table 1) conducted on [Gd(DAPSC)(OH₂)₄]³⁺, DAPSC = diacetylbis(semicarbazone). The initial portion of the present research focused on this complex since Gd(III) complexes of DAPSC, and its derivatives, have shown promise in recent experiments as MRI contrast agents.¹⁰ Also, this complex contains prototypical hard, oxygen and nitrogen-based ligands common in lanthanide chemistry. In a previous work^{3a-c} optimum ALPAM1 and AMAM1 were selected based on a 3² factorial design involving interatomic distances for the coordination polyhedra of two complexes: [Eu(acetylacetonate)₃(phenanthroline)] and a nine-coordinate analogue [Eu(dipivaloylmethanato)₃(terpyridine)]. In this research, optimum ALPAM1 and AMAM1 were selected based on the LEAH-predicted geometry that shows the best correspondence with experiment as measured by the root-mean-square deviation in heavy atom positions (RMS_{hvy}). Based on the results in Table 1, ALPAM1 and AMAM1 values of 2.0 Å⁻¹ and 4.0 au, respectively, were selected for further study.

Cundari et al. have reported an extension of the MM2 force field for gadolinium.⁷ This force field provided accurate structural prediction for high coordination number Gd(III) complexes with a variety of ligating atom types. Both LEAH and MM provide excellent structural prediction for [Gd(DAPSC)(OH₂)₄]³⁺. The average absolute difference (Δ) between theory and experiment for bond lengths is 0.03 Å (MM), 0.05 Å (LEAH); for Gd–ligand bond lengths, Δ_r = 0.06 Å (MM), 0.09 Å (LEAH). Bond angles (Δ_θ) are predicted to within 4° of experiment (MM, LEAH). Modeling of Gd-dependent bond angles is also very good (X–Gd–Y: Δ_θ = 4° (MM), 6° (LEAH); Gd–X–Y: Δ_θ = 3° (MM and LEAH)). The MM force field does slightly better than LEAH in prediction of dihedral angles (Δ_r = 5° (MM), 7° (LEAH)), although given the very soft metal–ligand bond torsional potentials in coordination complexes, both values are excellent. To put the results into perspective, the average LEAH-predicted geometry corresponds to differences of 2–3% versus experiment, competitive with that seen in

Table 2. Lanthanide Trihalides: Theory vs Experiment^a

X	LEAH (Å)	PM3 ^b	EXP ^c	ECP ^d (Å)
F	1.90	2.03 Å (2.01 Å, 108°)	2.05 Å, 108°	2.06
Cl	1.99	2.36 Å (2.36 Å, 116°)	2.49 Å, 113°	2.53
Br	1.97	2.42 Å (2.41 Å, 112°)	2.64 Å, 114°	2.68
I	2.00	2.75 Å (2.75 Å, 114°)	2.84 Å, 108°	2.91

^a Predicted Gd–X (X = halide) bond lengths are given at several levels of theory. ECP and LEAH calculations obtain *D*_{3h} symmetry lowest energy structures. The methods are described in the text. ^b PM3 geometry optimizations were carried out at planar (*D*_{3h}) and pyramidal (*C*_{3v}) geometries. The former are calculated to be transition states, while the latter are minima. The Gd–X bond lengths (Å) and X–Gd–X bond angles (deg) for the *C*_{3v} minima are given in parentheses. ^c Experimental LnX₃ bond lengths are measured in the gas-phase by electron diffraction techniques and are taken from the review by Hargittai. The Molecular Geometry of Gas-Phase Metal halides. Hargittai, M. *Coord. Chem. Rev.* **1988**, 91, 35–88. ^d Ab initio calculations were carried out using effective core potential (ECP) methods and the valence basis sets described in ref 4f.

extensive ECP studies of lanthanide and transition metal complexes.³ Hence, preliminary results suggest that LEAH deserves consideration as a technique for modeling Gd(III) complexes.

2. Trihalides and Related Model Complexes. Before further assessing LEAH for larger Gd(III) coordination complexes, calculations were carried out to probe the effect of alteration of the chemical environment on predictive ability. Lanthanide trihalides and related complexes were studied since experimental and ECP data are available. By altering the halide the degree of ionic and covalent bonding in Ln–ligand bonds can be methodically changed. Although the work of de Andrade et al.⁵ suggests sparkle methods are not likely useful for low coordination number complexes, we wish to simply assess the effect of metal–ligand bond covalency on predictive ability.

In each case, LEAH-optimized structures (done in *C*₁ symmetry) of LnX₃ (X = F, Cl, Br, I) were trigonal planar with equivalent Ln–halide bond lengths. The Gd–F distance was predicted much more accurately (Δ_r = 0.15 Å or 7%) than the other halides (Table 2). The LEAH-optimized structure of GdF₃ was trigonal planar regardless of whether the starting geometry was trigonal planar or trigonal pyramidal. Hence for these complexes, the best predictive ability is found when the Ln–ligand bond is the most ionic.

Gadolinium trihalides were also optimized using a semiempirical PM3 method¹¹ to provide another point of comparison. Trihalides were initially PM3-optimized under *D*_{3h} symmetry; PM3-predicted bond lengths are in better agreement with experiment than those obtained using the electrostatic AM1 approach, Table 2. However, the lowest energy PM3 structures were not planar (*D*_{3h}) but pyramidal (*C*_{3v}). Prediction of a pyramidal structure is in opposition to ECP calculations, which yield *D*_{3h} minimum energy LnF₃ geometries.^{4g}

To assess the effect of coordination number on predictive ability the complex GdCl₆³⁻ was studied. This trianion is present in the crystal structure of HAMZIE.^{8b} The experimental Gd–Cl bond lengths in GdCl₆³⁻ are between 2.67 and 2.68 Å. The LEAH-calculated structure of GdCl₆³⁻ is octahedral with GdCl = 2.34 Å (Δ_r ≈ 13%); recall from Table 2 that the theory-experiment difference for GdCl₃ is Δ_r ≈ 20%. PM3 optimization of *O*_h-GdCl₆³⁻ results in Gd–

Table 3. Predicted Structures of $\text{GdCl}_3\text{Dme}_2$ and Derivatives

	VAKMID-Xtal	LEAH-GdCl ₃ dme ₂	PM3-GdCl ₃ dme ₂	LEAH-GdF ₃ dme ₂	PM3-GdF ₃ dme ₂
Gd–O (Å) ^a	2.46 ± 0.03	3.01 ± 0.22	2.71 ± 0.09	2.77 ± 0.07	2.80 ± 0.09
Gd–halide (Å) ^a	2.63 ± 0.01	2.04 ± 0.01	2.57 ± 0.08	1.97 ± 0.01	2.15 ± 0.12
	LEAH-GdF ₃ (OH ₂) ₄	PM3-GdF ₃ (OH ₂) ₄	ECP-GdF ₃ (OH ₂) ₄	Xtal	
Gd–O (Å) ^b	2.52 ± 0.14	2.71 ± 0.05	2.57 ± 0.03	2.42 ± 0.03 ¹²	
Gd–F (Å) ^b	2.00 ± 0.05	2.08 ± 0.01	2.14 ± 0.00	NA	
	LEAH-GdF ₇ ^{4–}		PM3-GdF ₇ ^{4–}	ECP-GdF ₇ ^{4–}	
Gd–F (Å) ^c			2.48 ± 0.22	2.40 ± 0.02	

^a Geometry optimization of $\text{GdCl}_3\text{dme}_2$ (VAKMID) by LEAH and PM3 was begun from the experimental structure.^{8c} For GdF_3dme_2 the experimental structure of VAKMID was used with chlorines replaced by fluorines and Gd-F distances initialized to 2.05 \AA . ^b The starting geometry for optimization of $\text{GdF}_3(\text{OH}_2)_4$ was taken from VAKMID with chlorines modified as fluorines as described above and aqua ligands occupying the coordination sites of the ether ligands of dme (Gd-O distances unchanged from experiment). ^c Geometry optimization of GdF_7^{4-} was carried out under C_{2v} (capped octahedron, with Gd-F = 2.05 \AA) since this polytope most closely approximates that observed in VAKMID.

Cl = 2.63 \AA , much closer to experiment. The complex GdCl_6^{3-} was also ECP-optimized under O_h symmetry using valence basis sets akin to those described previously.^{4f} ECP-predicted Gd-Cl bond lengths are 2.85 \AA or 7% too long. The calculations highlight the difficulties in application of any quantum method to large coordination number lanthanide complexes. The data also suggest that prediction by the LEAH model improves as coordination number increases.

Calculations were conducted on seven-coordinate compounds (VAKMID^{8c} ($\text{GdCl}_3\text{dme}_2$), GdF_3dme_2 , $\text{GdF}_3(\text{OH}_2)_4$, and GdF_7^{4-} , dme = dimethoxyethane) to study the effect of charge. The inability of LEAH to accurately model the Gd-Cl bond (as indicated by trihalides) prohibited reasonable geometrical prediction of $\text{GdCl}_3\text{dme}_2$. The crystal structure of $\text{GdCl}_3\text{dme}_2$ has average Gd-Cl and Gd-O bond lengths of 2.63 \pm 0.01 \AA and 2.46 \pm 0.03 \AA , respectively; the LEAH-calculated Gd-Cl and Gd-O bond lengths are 2.04 \pm 0.01 \AA and 3.01 \pm 0.22 \AA , 22% too short and 22% too long, respectively (Table 3). Clearly, PM3 predicts the bond lengths of $\text{GdCl}_3\text{dme}_2$ much more accurately than LEAH with Gd-Cl and Gd-O lengths at 2.57 \pm 0.08 \AA (5% short) and 2.71 \pm 0.09 \AA (10% long). However, replacement of the Cl in $\text{GdCl}_3\text{dme}_2$ with F improves LEAH's predictive ability with respect to Gd-O bond lengths; the Gd-O bond distance in GdF_3dme_2 is 2.77 \pm 0.07 \AA , \approx 0.2 \AA shorter than in $\text{GdCl}_3\text{dme}_2$. Due to the lack of experimental data on Gd-F bonds the accuracy of these bond lengths cannot be adequately analyzed, although the experimental Gd-F bond length in GdF_3 (2.05 \AA) suggests the LEAH value of 1.97 \pm 0.01 \AA in GdF_3dme_2 (Table 3) is reasonable.

The results for $\text{GdF}_3(\text{OH}_2)_4$ indicated that LEAH accurately predicted the Gd-O bond lengths (2.52 \pm 0.14 \AA) as compared to experiment. Analysis of a structural database¹² yielded an average Gd-O bond length of 2.42 \pm 0.03 \AA (24 samples) for Gd(III)-O_{aqua} linkages. The PM3 predicted bond length was 2.71 \pm 0.05 \AA . The LEAH calculation was unsuccessful for GdF_7^{4-} as the compound dissociated into GdF_6^{3-} and F^- , suggesting that highly anionic systems are best approached with caution using electrostatic models.

In sum, test calculations indicated that the sparkle technique can provide efficient modeling of lanthanide complexes. In general, the method is more reliable as the coordination number increases and for systems in which the lanthanide is coordinated to a hard, electronegative atom.

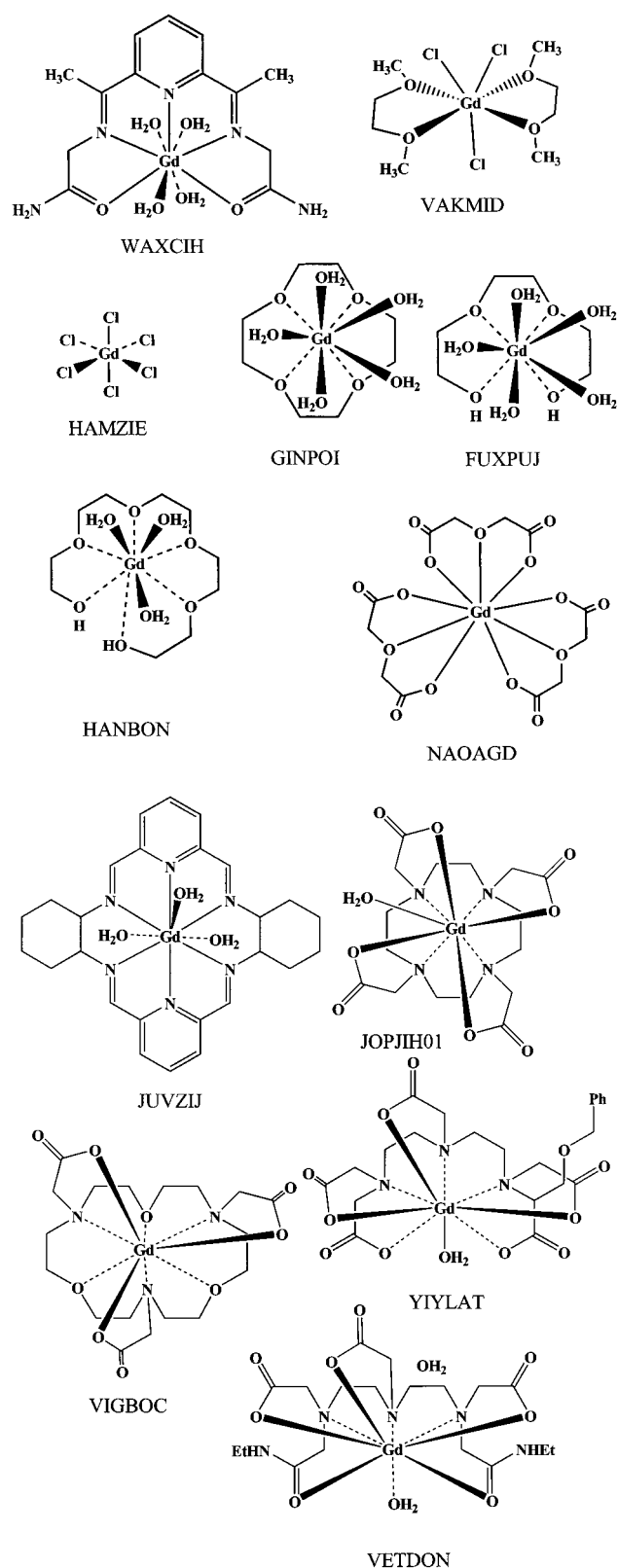
As this is the norm in lanthanide coordination chemistry, LEAH would seem to be a tool worthy of further investigation in the modeling of such complexes. On the other hand, the method seems to become less reliable as the overall charge on the complex becomes anionic and for softer donor ligands (e.g., chloride).

3. Lanthanide Coordination Complexes. Molecular mechanics⁷ and LEAH calculations were conducted on representative complexes found in the Cambridge Crystallographic Database.⁸ The references codes are FUXPUJ, GINPOI, HANBON, WAXCIH, JUVZIJ, NAOAGD, VETDON, VIGBOC, JOPJIH01, YIYLAT, Scheme 1.⁸ The first five complexes all have an overall charge of +3 and ligating atom types that are neutral sp^3 oxygen (aqua, alcohol, and ether ligands) or neutral sp^2 nitrogen (pyridine and imine ligands). It will be seen that the LEAH method worked considerably better for these complexes than those which were either neutral or anionic and contained carboxylate and amine ligands.

LEAH calculations conducted on the crown ether complex GINPOI provided very accurate results. The AM1 derived bond lengths had a mean theory experiment absolute difference in bond lengths (Δ_r) of 0.05 \AA , $\Delta_\theta = 5^\circ$, and $\Delta_\tau = 17^\circ$. Likewise, LEAH also gave good prediction for the ether complex HANBON ($\Delta_r = 0.03$ \AA , $\Delta_\theta = 5^\circ$, $\Delta_\tau = 11^\circ$) as indicated by the data in Table 4. HANBON, unlike GINPOI, is an acyclic polyether complex. One expects such acyclic systems to have more conformational flexibility than macrocycles, thus the observation of good modeling for HANBON was promising. The LEAH predicted structure of the acyclic polyether complex FUXPUJ ($\Delta_r = 0.04$ \AA , $\Delta_\theta = 9^\circ$, $\Delta_\tau = 17^\circ$), however, was considerably worse than for the related complexes GINPOI and HANBON.

Due to reasonable prediction of bond lengths and poor prediction of bond angles in FUXPUJ, the latter metric parameters were examined more closely. The analysis suggested that differences among the complexes was due to the X-Gd-Y angles. In particular, the largest theory-experiment differences ($\Delta \approx 11^\circ$ for each) were seen in O_w -Gd- O_w (O_w = oxygen of ligating water). In HANBON, there are three aqua ligands and hence only three (out of 36) X-Gd-Y angles involving these ligands. Both GINPOI and FUXPUJ are pentaqua complexes and hence the less accurately predicted O_w -Gd- O_w angles comprise a large percentage of the X-Gd-Y angles. Modeling of X-Gd-Y

Scheme 1



angles in FUXPUJ is worse than GINPOI since the former also shows poor prediction for O—Gd—O angles involving aqua and alcohol or ether ligands of the acyclic tetraethyl-ene glycol ligand. Analysis of Gd(III)—ether(aqua) complexes suggests that LEAH is more reliable in describing the angular orientation of ligands about a metal for polydentate versus monodentate ligands and macrocyclic versus acyclic ligands.

WAXCIH ($[\text{Gd}(\text{DAPSC})(\text{OH}_2)_4]^{3+}$) was also accurately predicted by LEAH as described above: $\Delta_r = 0.05 \text{ \AA}$, $\Delta_\theta = 4^\circ$, $\Delta_\tau = 7^\circ$. Another complex with imine (sp^2 nitrogen) ligands is JUVZIJ. The overall predictive ability of LEAH with respect to JUVZIJ is excellent ($\Delta_r = 0.03 \text{ \AA}$, $\Delta_\theta = 3^\circ$, $\Delta_\tau = 7^\circ$), even superior to that for WAXCIH. Semiempirical methods have long been used for accurate prediction of organic molecules. The comparable predictive ability for both the metal dependent and independent metric data, Table 4, for polyether and polyimine complexes is encouraging with respect to the application of LEAH to lanthanide complexes.

LEAH, however, failed to accurately determine the geometry of JOPJIH01 ($\Delta_r = 0.10 \text{ \AA}$, $\Delta_\theta = 6^\circ$, $\Delta_\tau = 10^\circ$), VETDON ($\Delta_r = 0.09 \text{ \AA}$, $\Delta_\theta = 5^\circ$, $\Delta_\tau = 11^\circ$), VIGBOC ($\Delta_r = 0.08 \text{ \AA}$, $\Delta_\theta = 4^\circ$, $\Delta_\tau = 14^\circ$), and YIYLAT ($\Delta_r = 0.12 \text{ \AA}$, $\Delta_\theta = 6^\circ$, $\Delta_\tau = 15^\circ$) all of which contain carboxylate and amine ligands. Geometrical prediction for NAOAGD, which consists of both neutral sp^3 oxygen and carboxylate ligands, was very poor ($\Delta_r = 0.22 \text{ \AA}$, $\Delta_\theta = 17^\circ$, $\Delta_\tau = 44^\circ$). For these compounds the Gd—O carboxylate bonds Gd—O_c were too short by an average of approximately 0.33 \AA . Faulty prediction of Gd—O_c bonds caused the overall metric prediction for the aminocarboxylates to be inaccurate. Furthermore, as seen in model calculations on GdCl_3dme , poor description of one Gd—ligand bond type can set off a chain reaction of faulty prediction. In the case of aminocarboxylates, other Gd—X bonds involving ligands other than carboxylates are typically too long, due most likely to steric repulsion caused by the short Gd—O_c bonds.

4. Comparison with Molecular Mechanics. Cundari et al.⁸ have developed a MM force field capable of describing the following ligating atom types: amine N, imine N, carboxylate O, carbonyl O, and neutral sp^3 O. Hence, the following complexes were studied with the force field and then compared to the LEAH method: FUXPUJ, GINPOI, HANBON, WAXCIH, JUVZIJ, NAOAGD, VETDON, VIGBOC, JOPJIH01, YIYLAT. As with the LEAH method, geometry optimization was started from the reported X-ray structure.⁸ The MM minimization was conducted in two steps with hydrogens being optimized first and then the entire complex. In general, as found earlier paper, MM provides accurate and efficient structural prediction of Gd(III) compounds: $\Delta_r = 0.02 \text{ \AA}$ (JOPJIH01, NAOAGD) — 0.05 \AA (GINPOI, FUXPUJ, HANBON); $\Delta_\theta = 1^\circ$ (NAOAGD) — 8° (FUXPUJ); $\Delta_\tau = 4^\circ$ (JUVZIJ) — 16° (FUXPUJ). Structural prediction by MM was comparable to LEAH for compounds with neutral, sp^3 oxygen (aqua, ether and alcohol ligands) or neutral, sp^2 nitrogen (imines) ligating atom types, Table 4. MM showed better predictive ability than LEAH for aminocarboxylate complexes (NAOAGD, VETDON, VIGBOC, JOPJIH01, YIYLAT).

5. Comparison with a Semiempirical PM3 Method. The semiempirical PM3¹¹ method (gadolinium is not treated as a sparkle and can interact with other atoms covalently) was used for geometry optimization of Ln complexes. A subset of Gd(III) complexes that were accurately modeled by LEAH were studied (GINPOI, WAXCIH, JUVZIJ) as well as VIGBOC whose modeling was found to be inaccurate. The PM3 method proved to be unreliable for structural prediction of these complexes: $\Delta_r = 0.04 \text{ \AA}$ (VIGBOC) — 0.06 \AA (WAXCIH); $\Delta_\theta = 5^\circ$ (JUVZIJ) — 10° (GINPOI); $\Delta_\tau = 16^\circ$ (GINPOI) — 18° (VIGBOC, WAX-

Table 4. Structural Prediction by LEAH

	all r		Gd-X		all Θ		X-Gd-Y		Gd-X-Y		all τ		X-Gd-Y-Z		Gd-X-Y-Z	
	MM	LEAH	MM	LEAH	MM	LEAH	MM	LEAH	MM	LEAH	MM	LEAH	MM	LEAH	MM	LEAH
GINPOI																
points	21	21	9	9	56	56	36	36	8	8	84	84	64	64	5	5
mean	0.05	0.05	0.06	0.08	5.93	4.85	7.49	6.11	3.68	2.90	8.85	16.72	8.99	8.20	9.00	
StDev	0.04	0.05	0.04	0.05	6.08	4.90	7.01	5.58	1.83	1.88	13.47	6.43	14.50	6.51	5.11	6.36
FUXPUJ																
points	18	18	9	9	50	50	36	36	6	6	61	61	48	48	6	6
mean	0.05	0.04	0.05	0.06	8.23	9.20	10.32	11.81	4.93	4.40	15.67	17.07	16.33	17.57	9.50	7.99
StDev	0.03	0.05	0.05	0.06	8.98	8.37	9.75	8.39	1.62	3.46	13.62	12.21	14.35	12.78	8.92	4.37
WAXCIH																
points	29	29	9	9	70	70	36	36	8	8	106	106	64	64	14	14
mean	0.03	0.05	0.06	0.09	3.68	4.27	4.41	5.73	2.65	3.45	4.84	7.24	6.24	9.37	4.23	4.79
StDev	0.03	0.04	0.04	0.05	2.69	4.04	3.08	4.75	0.93	2.74	4.60	5.90	5.14	5.95	3.39	5.29
JOPJIH01																
points	37	37	9	9	88	88	36	36	16	16	184	184	128	128	20	20
mean	0.02	0.103	0.026	0.35	2.03	6.43	2.56	10.08	1.80	7.73	4.54	9.61	4.46	10.22	6.50	9.53
StDev	0.01	0.148	0.015	0.06	1.60	6.70	1.94	8.01	0.96	5.64	4.27	8.88	3.77	9.22	6.73	6.71
HANBON																
points	24	24	9	9	60	60	36	36	10	10	103	103	80	80	10	10
mean	0.05	0.03	0.08	0.06	4.18	4.52	4.89	5.81	4.17	3.70	8.44	10.72	8.43	10.88	7.26	9.04
StDev	0.04	0.03	0.05	0.04	2.83	4.63	2.97	5.40	2.40	2.30	8.40	6.62	8.15	6.62	9.38	8.08
VETDON																
points	39	39	9	9	87	87	36	36	14	14	167	167	112	112	19	19
mean	0.03	0.09	0.05	0.30	2.59	5.47	3.40	7.32	1.85	8.10	8.28	11.09	7.50	9.77	10.38	14.48
StDev	0.02	0.13	0.02	0.13	2.36	4.28	3.06	4.36	1.18	4.73	8.67	11.08	6.92	9.64	9.07	13.07
JUVZIJ																
points	45	45	9	9	96	96	36	36	12	12	178	178	96	96	20	20
mean	0.04	0.03	0.04	0.08	2.64	2.72	3.06	4.09	2.16	1.70	3.71	7.26	4.39	8.72	2.87	5.90
StDev	0.03	0.03	0.02	0.04	2.34	2.68	3.11	3.66	1.29	1.13	3.20	5.26	3.44	5.57	2.59	4.81
VIGBOC																
points	39	39	9	9	90	90	36	36	16	16	201	201	144	144	21	21
mean	0.03	0.08	0.04	0.28	3.07	4.40	4.34	6.05	2.24	4.84	11.51	13.91	10.97	13.46	14.63	17.09
StDev	0.02	0.12	0.03	0.12	2.88	3.81	3.62	4.74	1.78	3.53	11.08	9.86	10.11	8.23	13.05	12.02
NAOAGD																
points	33	33	9	9	75	75	36	36	12	12	132	132	96	96	18	18
mean	0.02	0.22	0.05	0.77	1.29	16.62	1.42	20.04	1.22	41.33	12.60	44.46	11.91	41.51	10.18	27.82
StDev	0.02	0.51	0.02	0.77	0.85	18.08	1.12	14.37	0.04	15.53	7	34.14	6.52	34.80	9.12	24.25
YIYLAT																
points	45	45	9	9	96	96	36	36	14	14	180	180	112	112	20	20
mean	0.03	0.12	0.06	0.53	2.98	6.42	4.68	11.66	2.49	7.42	9.48	14.74	8.94	15.66	12.76	15.31
StDev	0.02	0.39	0.03	0.78	3.25	9.25	4.30	13.03	1.71	3.90	9.56	18.52	6.73	20.50	13.63	16.46

"Structural prediction for bond lengths (r , Å), bond angles (Θ , deg) and dihedral angles (τ , deg) is assessed for the LEAH method; "points" is the number of metric parameters of a specific type and is used in calculation of "mean" (the mean of the absolute value of the theory-experiment differences) and "StDev" (the standard deviation of the absolute value of the theory-experiment differences). A breakdown for metal-dependent bond lengths (Gd-X), bond angles (X-Gd-Y, Gd-X-Y), and dihedral angles (X-Gd-Y-Z and Gd-X-Y-Z) is also given. The same information is also provided for a molecular mechanics (MM) force field⁷ described earlier.

CIH). Consideration of these data indicates that torsional angles are the most poorly reproduced by the PM3 Hamiltonian, particularly in relation to LEAH and MM methods, although a more systematic analysis of gadolinium chemistry with the PM3 than was carried out here would be needed. Regardless, the limited results of this research show the MM and LEAH methods to be competitive with the PM3 approach.

SUMMARY AND CONCLUSIONS

A variety of approximate methods for *efficient* modeling of large lanthanide (Ln) complexes were studied. Attention was paid to ligand motifs prevalent in Ln coordination chemistry. Gadolinium was chosen given its central location in the Ln series and its importance in areas such as magnetic resonance imaging. A semiempirical approach based on a technique first described for Eu was extended to Gd.

Comparison with ECP, molecular mechanics, and PM3 methods was performed. Electrostatic models were found to be most reliable for cationic, large coordination number complexes with hard nitrogen and oxygen donors—an important subset of lanthanide complexes. Although this was not studied, the preceding conclusion suggests that electrostatic methods will be less reliable for Ln organometallics. The LEAH technique has the advantage of much greater speed than *ab initio* techniques even when the latter employ effective core potentials. For example, ECP^{4f} geometry optimization of GdF₃(OH₂)₄ required 1215 min on a Silicon Graphics O2 workstation; the same calculation requires 1.5 min on an IBM RS-6000/350 workstation with the LEAH method running in MOPAC. When used for appropriate target complexes electrostatic models, particularly in conjunction with molecular mechanics, can be an effective and efficient technique for the study of large, experimentally relevant lanthanide coordination complexes.

ACKNOWLEDGMENT

This work was supported in part by a grant from the University of Memphis (Faculty Research Grant) and the United State Department of Energy (Grant DE-FG02-97ER14811 from the Division of Chemical Sciences).

REFERENCES AND NOTES

- Recent reviews of lanthanide chemistry can be found in the following papers. (a) Alexander, V. Design and Synthesis of Macrocyclic Ligands and Their Complexes of Lanthanides and Actinides. *Chem. Rev.* **1995**, 95, 273–343. (b) Gun'ko, Y. K.; Edelman, F. T. Lanthanide and Actinides. Annual Survey of their Organometallic Chemistry Covering the Year 1994. *Coord. Chem. Rev.* **1996**, 156, 1–89. (c) Hogerheide, M. P.; Boersma, J.; van Koten, G. Intramolecular Coordination in Group 3 and Lanthanide Chemistry. An Overview. *Coord. Chem. Rev.* **1996**, 155, 87–126. (d) Cotton, S. A. Aspects of the Lanthanide–Carbon σ -Bond. *Coord. Chem. Rev.* **1997**, 160, 93–127.
- Lauffer, R. B. Paramagnetic Metal Complexes as Water Proton Relaxation Agents for NMR Imaging: Theory and Design. *Chem. Rev.* **1987**, 87, 901–927.
- Benson, M. T.; Cundari, T. R.; Lutz, M. L.; Sommerer, S. O. Effective Core Potential Approaches to Computational Inorganic Chemistry. In *Reviews in Computational Chemistry*; Boyd, D., Lipkowsky, K., Eds.; 1996; Vol. 8, pp 145–202.
- (a) Ross, R. B.; Gayen, S.; Ermler, W. C. Ab initio Relativistic Effective Potentials with Spin–Orbit Operators. V. Ce through Lu. *J. Chem. Phys.* **1994**, 100, 8145–8155. (b) Dolg, M.; Stoll, H.; Preuss, H. Pseudopotential Study on Rare Earth Dihalides and Trihalides. *J. Mol. Struct. (THEOCHEM)* **1991**, 235, 67–79. (c) Dolg, M.; Stoll, H. Pseudopotential Study of the Rare Earth Monohydrides, Monoxides, and Monofluorides. *Theor. Chim. Acta* **1989**, 75, 369–387. (d) Dolg, M.; Stoll, H.; Preuss, H. Energy-adjusted Ab Initio Pseudopotentials for the Rare Earth Elements. *J. Chem. Phys.* **1989**, 90, 1730–1734. (e) Dolg, M.; Stoll, H.; Savin, A.; Preuss, H. Pseudopotential Study of Rare Earth Compounds. In *Quantum Chemistry – Basic Aspects, Actual Trends*; Carbo, R., Ed.; Elsevier: Amsterdam, 1989; pp 265–273. (f) Cundari, T. R.; Stevens, W. J. Effective Core Potential Methods for the Lanthanides. *J. Chem. Phys.* **1993**, 98, 5555–5565. (g) Cundari, T. R.; Sommerer, S. O.; Strohecker, L. A.; Tippet, L. Effective Core Potential Methods for the Lanthanides: The Trihalides. *J. Chem. Phys.* **1995**, 103, 7058–7063.
- (a) de Andrade, A. V. M.; Longo, R. L.; de Sa, G. F. Theoretical Model for the Prediction of Electronic Spectra of Lanthanide Complexes. *J. Chem. Soc., Faraday* **1996**, 92, 1835–1839. (b) de Andrade, A. V. M.; da Costa, N. B.; Simas, A. M.; de Sa, G. F. Sparkle Model for the Quantum Chemical Calculation of Europium Complexes of Coordination Number Nine. *J. Alloys Compds.* **1995**, 225, 55–59. (c) de Andrade, A. V. M.; da Costa, N. B.; Simas, A. M.; de Sa, G. F. Sparkle Model for the Quantum Chemical AM1 Calculation of Europium Complexes. *Chem. Phys. Lett.* **1994**, 227, 349–353. (d) Culbertson, J. C.; Knappe, P.; Rosch, N.; Zerner, M. C. An Intermediate Neglect of Differential Overlap (INDO) Technique for Lanthanide Complexes: Studies on Lanthanide Halides. *Theor. Chim. Acta* **1987**, 71, 21–39. (e) Jing-Qing, R.; Guang-Xian, X. Electronic Structure and Chemical Bonding of the Dimer of Bis(η^5 -cyclopentadienyl)-ytterbium Methyl. *Intern. J. Quantum Chem.* **1986**, 29, 1017–1024. (f) Hoffmann, R.; Ortiz, J. V. Hydride Bridges Between LnCp₂ Centers. *Inorg. Chem.* **1985**, 24, 2095–2104.
- Semiempirical calculations employed the MOPAC 6 program. Stewart, J. J. P. MOPAC: A Semiempirical Molecular Orbital Program. *J. Comput.-Aided Mol. Des.* **1990**, 4, 1–105.
- Cundari, T. R.; Moody, E. W.; Sommerer, S. O. Computer Aided Design of Metallopharmaceuticals: A Molecular Mechanics Force Field for Gadolinium Complexes. *Inorg. Chem.* **1995**, 34, 5989–5999.
- Structures were taken from the Cambridge Structural Database (version 5.1.3, Allen, F. H.; Kennard, O. 3D Search and Research Using the Cambridge Structural Database. *Chem. Des. Automation News* **1993**, 8, 31–37.). A search was done for Gd(III) complexes with either Gd–O or Gd–N bonds. The search was refined to include only complexes for which the atomic coordinates were available and excluded experimental structures with disorder, R factors of $\geq 10\%$, or which were polymeric. Furthermore, we focused on Gd(III) complexes with ligand types described in an extension of the MM2 force field,⁷ so as to permit comparison among a variety of techniques. (a) [Gd(DAPSC)(OH₂)₄][NO₃]₃ has the six-letter reference code WAXCIH. Sommerer, S. O.; Westcott, B. L.; Cundari, T. R.; Krause, J. A. A Structural and Computational Study of Tetraqua[2,6-Diacetylpyridine bis(semicarbazone)] gadolinium(III) Trinitrate. *Inorg. Chim. Acta* **1993**, 209, 101–104. (b) HAMZIE (Aqua-(18-crown-6)-dichlorogadolinium diaquachloro(18-crown-6)gadolinium hexachloro-
- gadolinium methanol solvate): Rogers, R. D.; Rollins, A. N.; Etzenhouser, R. D.; Voss, E. J.; Bauer, C. D. Structural Investigation into the Steric Control of Polyether Complexation in the Lanthanide Series: Macrocyclic 18-crown-6 versus Acyclic Pentaethylene Glycol. *Inorg. Chem.* **1993**, 32, 3451–3462. (c) VAKMID (Trichlorobis-(dimethoxyethane-*O,O'*)gadolinium(III)): Wei, G.; Gao, H.; Jin, Z.; Shen, Q. Crystal Structure of Trichlorobis(dimethoxyethane)gadolinium. *Jiegou Huaxue* **1989**, 8, 61–64. (d) FUXPUJ (Pentaqua-(triethylene glycol-*O,O',O'',O'''*)gadolinium trichloride): Rogers, R. D.; Voss, E. J.; Etzenhouser, R. D. F-element/Crown Ether Complexes. Synthetic and Structural Survey of Lanthanide Chloride Triethylene Glycol Complexes. *Inorg. Chem.* **1988**, 27, 533–542. (e) GINPOI ((12-Crown-4-*O,O',O'',O'''*)-pentaquagadolinium trichloride dihydrate): Roger, R. D.; Rollins, A. N.; Benning, M. M. F-element/Crown Ether Complexes. Preparation and Structural Characterization of Lanthanide Chloride Complexes of 12-crown-4. *Inorg. Chem.* **1988**, 27, 3826–3835. (f) HANBON (Triaqua(pentaethyleneglycol)gadolinium trichloride monohydrate): Rogers, R. D.; Rollins, A. N.; Etzenhouser, R. D.; Voss, E. J.; Bauer, C. D. Structural Investigation into the Steric Control of Polyether Complexation in the Lanthanide Series: Macrocyclic 18-crown-6 versus Acyclic pentaethylene glycol. *Inorg. Chem.* **1993**, 32, 3451–3462. (g) JUVZIJ ((2,3,5,6,8,9,11,12-Octadecahydro-3,5,9,11-tetra-aza-4,10-di(1,2)-cyclohexana-1,7-di(2,6)-pyridinaphane)triaquagadolinium(III) trichloride trihydrate(bis(cyclohexane-1,2-diamine)bis(2,6-diacylpyridine)triaquagadolinium(III) trichloride trihydrate): Bligh, S. W. A.; Choi, N.; Evagorou, E. G.; McPartlin, M.; Kelly, J. D. Synthesis and Crystal Structure of a Gadolinium(III) Complex of a Tetraimine Schiff-Base Macrocyclic. A Potential Contrast Agent for Magnetic Resonance Imaging. *Polyhedron* **1992**, 11, 2571–2573. (h) NAOAGD (Pentasodium tris-(oxydiacetato-*O,O',O''*)gadolinium diperchlorate hexahydrate): Structural Studies on Rare Earth Carboxylates. Albertsson, J. *Acta Chem. Scand.* **1968**, 22, 1563–1578. (i) VETDON (Aqua{(diethylenepentaacetato)bis(ethylamide)}gadolinium(III) hexahydrate): Konings, M. S.; Dow, W. C.; Love, D. B.; Raymond, K. N.; Quay, S. C.; Rocklage, S. M. Gadolinium Complexation by a New DTPA-amide Ligand. Amide Oxygen Coordination. *Inorg. Chem.* **1990**, 29, 1488–1491. (j) VIGBOC ((1,7,13-Triaza-4,10,16-trioxacyclooctadecane-*N,N',N''*-triacetato)gadolinium(III)): Chen, D.; Squattrito, F. J.; Martell, A. E.; Clearfield, A. Synthesis and Crystal Structure of a Nine-coordinate Gadolinium(III) Complex of 1,7,13-triaza-4,10,16-trioxacyclooctadecane-*N,N',N''*-triacetic acid. *Inorg. Chem.* **1990**, 29, 4366–4368. (k) JOPJIH01 (Sodium aqua(1,4,7,10-tetrakis(carboxymethyl)-1,4,7,10-tetraazacyclododecane)gadolinium tetrahydrate): Chang, C. A.; Francesconi, L. C.; Malley, M. F.; Kumar, K.; Gougoutas, J. Z.; Tweedle, M. F.; Lee, D. W.; Wilson, L. J. Synthesis, Characterization, and Crystal Structures of M(DO3A) (M = Fe, Gd) and Na(M(DOTA)) (M = Fe, Y, Gd). *Inorg. Chem.* **1993**, 32, 3501–3508. (l) YIYLAT (Disodium (4-carboxy-5,8,11-tris(carboxymethyl)-1-phenyl-2-oxa-5,8,11-triazatridecan-13-oato)gadolinium(III) sesquihydrate): Uggeri, F.; Aime, S.; Anelli, P. L.; Botta, M.; Brocchetta, M.; de Haen, C.; Ermondi, G.; Grandi, M.; Paoli, P. Novel Contrast Agents for Magnetic Resonance Imaging. Synthesis and Characterization of the Ligand BOPTA and its Ln(III) Complexes (Ln = Gd, La, Lu). X-ray Structure of Disodium (TPS-9-145337286-C-S)-(4-carboxy-5,8,11-tris(carboxymethyl)-1-phenyl-2-oxa-5,8,11-triazatridecan-13-ato(5-)) Gadolinolate(2-) in a Mixture with its Enantiomer. *Inorg. Chem.* **1995**, 34, 633–642.
- A short explanation of MOPAC keywords is given; consult ref 6 for more details. AM1: The AM1 semiempirical Hamiltonian is used. PRECISE: Tighten normal convergence criterion by 2 orders of magnitude. XYZ: Geometry optimization carried out using Cartesian coordinates. EF: The eigenvector following algorithm is used for geometry optimization. MMOK: A molecular mechanics correction is applied to CONH linkages. CHARGE: This is the overall charge of the target complex. T: This specifies the maximum CPU time in seconds.
- Benson, M. T.; Cundari, T. R.; Saunders, L. C.; Sommerer, S. O. Synthesis, Structure, Computational Studies and Magnetic Properties of a Ten-Coordinate Gadolinium Complex. *Inorg. Chim. Acta* **1997**, 257, 127–230.
- The PM3 method is described along with the AM1 method in ref 6.
- This search was conducted using version 5.1.3 of the Cambridge Structural Database.⁸ No limitation was placed on Gd(III) coordination number. The search excluded complexes for which atomic coordinates were not available, those with R factors of $\geq 10\%$, or polymers; Gd–O_{aqua} distances range from 2.37 to 2.50 Å.