Short Communication

A structural and computational study of tetraaqua[2,6-diacetylpyridinebis-(semicarbazone)]-gadolinium(III) trinitrate

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Abstract

An X-ray structural analysis of tetraaqua[2,6-diacetylpyridinebis(semicarbazone)]-gadolinium(III)trinitrate, $GdC_{11}H_{21}N_{10}O_{15}$, $FW = 690.59$ g/mol, $P2_1/n$, $a = 10.021(7)$, $b = 22.944(3)$, $c = 10.185(2)$ Å, $\beta = 96.91(4)°$, $V = 2325(2)$ Å^3, $Z = 4$, $D_x = 1.973$ g/cm^3, Mo Kα radiation ($\lambda = 0.71073$ Å), $\mu = 29.2$ cm^{-1}, $F(000) = 1364$, and $R = 0.036$ for 3875 reflections, revealed at Gd(III) cation in a nine-coordinate environment displaying pseudo-tricapped trigonal prismatic geometry. The coordination sphere consists of 3N and 6O. Four of the oxygen donors are coordinated water molecules. A relativistic extended Huckel (REX) calculation at the experimental geometry indicates that the 4f electrons mix only slightly with the ligand orbitals. A calculation of the bond overlap population (BOP) reinforces the highly ionic nature of the Gd–ligand bonds in the complex.

Introduction

The chemistry of the lanthanides has undergone a resurgence in recent years due to the increasing importance of their compounds in advanced materials [1], catalysis [2], and especially biochemistry. The highly paramagnetic Gd(III) ion has been of great interest since it can induce an efficient relaxation mechanism on the protons in inner-sphere (and to a lesser extent outer-sphere) water molecules when its complexes are localized in certain types of tissues.

The effectiveness of a particular species as a relaxation agent has been shown to be influenced by many factors, including the coordination environment of the central metal cation [3]. Hence, the preparation of complexes with multiple coordination sites available for water molecules has been suggested as a strategy to obtaining improved contrast agents [3, 4].

Macrocyclic Schiff base complexes of the lanthanides have been researched as an answer to the water coordination problem of GdDTPA (which has only one). Smith *et al.* have analyzed the hexamine Schiff base (HAM) complex of Gd(III), and found a greater relaxivity in a 0.47T field for GdHAM versus GdDTPA [4]. Vallarino and co-workers [5] and Jackels and co-workers [6] have also extensively researched the use of macrocyclic Schiff base complexes as potential MRI contrast agents.

Acyclic Ln Schiff base complexes have received much less attention since they are, in general, more prone to hydrolysis than their macrocyclic counterparts [5, 7]. A stable, acyclic Schiff base complex of Gd(III) could however have advantages as an MRI contrast agent due to its natural flexibility. With this goal in mind, a study of acyclic Schiff base complexes which have the potential to be improved MRI contrast agents has been initiated.

The pentadentate ligand 2,6-diacetylpyridinebis(semicarbazone), DAPSC, reacts with all the metals of the first transition series to form stable complexes [8]. The ability of DAPSC to complex different ions suggests a degree of flexibility, structurally and chemically, which makes in an attractive candidate for our studies. With the larger 3+ ions of the lanthanide series, higher coordination numbers (CNs) are found in DAPSC complexes [9, 10] and the report of two isostructural Ln complexes, $M(DAPSC)(H_2O)_4(NO_3)_3$ where M = Eu or Yb) [10], is of particular interest due to the relatively high number of coordinated water molecules. We have extended this chemistry to Gd(III) and report here the structure and preliminary computational studies of $Gd(DAPSC)(H_2O)_4(NO_3)_3$.

Experimental

Materials

All chemicals were reagent grade and used as supplied from Aldrich.

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Preparation of [Gd(DAPSC)(H₂O)₄](NO₃)₃

Gadolinium nitrate, prepared from the oxide (0.75 mmol) and nitric acid, was added to 0.430 g DAPSC (1.55 mmol) prepared by a method previously described [11], in 40 ml deionized H₂O. The mixture was heated to 52 °C and stirred for approximately 1 h. A yellow solution resulted which was filtered while still warm and allowed to slowly evaporate. After 5 days, clear colorless crystals suitable for X-ray diffraction studies were obtained.

Computational methods

Molecular mechanics calculations were carried out using the standard MM2 program [12a] at Memphis State University. The program Macro Model [12b] was used as a graphical user interface to facilitate the input of the complexes studied. One modification of the approach of Hay [13] was employed, i.e. the Ln–ligand interactions were treated as entirely electrostatic. Thus, the present approach is similar in spirit to the points-on-a-sphere approach employed with great success by Kepert [14]. The PPITEREX program of Pyykko [15a] was employed for electronic structure calculations since this method has the added advantage that it is a relativistically-parameterized variant of extended Huckel [15b, c].

X-ray crystallography

A crystal of dimensions 0.50 × 0.40 × 0.35 mm suitable for X-ray diffraction studies was mounted on the end of a glass fiber. All subsequent measurements were made using a Nicolet P3 diffractometer with graphite-monochromated Mo Kα radiation (λ = 0.71073 Å). The cell dimensions were determined by a least-squares refinement of 25 automatically centered reflections. A variable-speed (1–29.3°) 2θ scan technique was used to measure the intensity data from 3.5 to 55.0° in 2θ. Three standard reflections were measured every 250 reflections to monitor for any crystal decomposition during the X-ray analysis. An absorption correction was made using a psi scan and the correction is given along with the other pertinent crystal data in Table 1.

Structure refinement

The data reduction was performed using SHELXTL PLUS [16a]. Structure solution and final refinement were performed using the NRCVAX (PC-Version) [16b] package of programs. The Gd atoms and all non-hydrogen atoms were located by Patterson and Fourier syntheses and refined anisotropically by full-matrix least-squares. The hydrogen atoms were located using a difference Fourier map and refined in *x*, *y* and *z* only. The model converged to an *R* of 0.036 and an *R*ᵥᵥ of 0.039. Selected final positional parameters, bond dis-

TABLE 1. Crystal data

Empirical formula	$GdC_{11}H_{21}N_{10}O_{15}$
Formula weight	690.59
a (Å)	10.021(7)
b (Å)	22.944(3)
c (Å)	10 185(2)
β (°)	96.91(4)
V (Å³)	2325(2)
Z	4
Temperature (°C)	22
ρ_{calc} (g/cm³)	1 973
Crystal system	monoclinic
Space group	$P2_1/n$
μ (cm⁻¹)	29 2
No. data collected	5309
No. unique ($I \geqslant 2.5\sigma I$)	3875
Final shift/error ratio	0.024
R, R_w	0.036, 0.039

tances and bond angles are listed in Tables 2 and 3, respectively.

Results and discussion

The crystals were found to contain monomeric $Gd(DAPSC)(H_2O)_4^{3+}$ cations balanced by three non-coordinating NO_3^- anions. The gadolinium ion resides in a nine-coordinate ligand environment comprised of three nitrogen (N3, N4, N5) and six oxygen (O1, O2, W1, W2, W3, W4) donors. The DAPSC moiety is essentially planar as can be seen in the ORTEP view of the cation, Fig. 1. A molecular mechanics (MM) optimization of $[Gd(DAPSC)]^{3+}$ shows the DAPSC ligand to be planar with the Gd(III) ion in the DAPSC plane. The average deviation between the MM and X-ray structures for the five Ln–ligand bond lengths and five ligand–Ln–ligand bonds angles is 0.04 Å and 3°, respectively, in excellent agreement. In the crystal structure, the Gd is displaced from the DAPSC plane towards the three water ligands. Again, an MM experiment on $[Gd(DAPSC)(H_2O)_4]^{3+}$ is able to reproduce this feature. The deviation in Ln–OH₂ bond lengths between the MM and X-ray determined structures is larger than found above for the other ligands, 0.12 Å (~5%), but still significant given the approximations made. These results suggest that the MM method is able to describe the bonding in these Ln complexes, at least qualitatively.

The geometry around the Gd can be described as a slightly distorted tricapped trigonal prism with the N3, N5 and W2 forming the three rectangular face caps. Least-squares planes which included the two atoms of the prism edge, the Gd(III), and the face capping atom of the rectangular face perpendicular to the prism edge were calculated for each of the three edges and the dihedral angles formed were found to be 120.7(2), 116.0(2) and 123.1(2)°, respectively. A comparison of

TABLE 2. Atomic positional parameters and U_{eq} for non-hydrogen atoms

	x	y	z	U_{eq}[a]
Gd	0.21430(3)	0.10893(2)	0.21715(3)	0.0303(1)[b]
O1	0.1278(5)	0.1673(2)	0.0319(5)	0.043(2)
O2	0.0909(4)	0.0254(2)	0.1397(5)	0.040(2)
N1	0.0783(6)	0.2548(3)	−0.0643(6)	0.052(3)
N2	0.1543(6)	0.2506(2)	0.1590(5)	0.040(3)
N3	0.1923(4)	0.2155(2)	0.2698(5)	0.034(2)
N4	0.2368(4)	0.1397(2)	0.4636(5)	0.035(2)
N5	0.1652(5)	0.0334(2)	0.3949(5)	0.038(2)
N6	0.1213(6)	−0.0190(2)	0.3427(6)	0.046(2)
N7	0.0251(7)	−0.0675(3)	0.1537(7)	0.052(3)
C1	0.1200(6)	0.2220(3)	0.0393(6)	0.038(3)
C2	0.2236(6)	0.2387(3)	0.3853(6)	0.038(2)
C3	0.2271(14)	0.3038(4)	0.4145(8)	0.077(6)
C4	0.2528(6)	0.1957(3)	0.4972(6)	0.039(3)
C5	0.2891(8)	0.2132(3)	0.6298(7)	0.052(3)
C6	0.3042(8)	0.1710(4)	0.7290(7)	0.058(3)
C7	0.2817(7)	0.1145(4)	0.6966(6)	0.051(3)
C8	0.2452(5)	0.0992(3)	0.5615(6)	0.039(3)
C9	0.2069(6)	0.0387(3)	0.5208(6)	0.039(3)
C10	0.2172(8)	−0.0090(4)	0.6213(8)	0.057(4)
C11	0.0794(6)	−0.0192(3)	0.2066(6)	0.039(2)
W1	−0.0165(5)	0.1284(2)	0.2513(5)	0.051(2)
W2	0.3048(6)	0.0613(3)	0.0253(5)	0.051(2)
W3	0.4133(5)	0.1654(2)	0.1790(5)	0.049(2)
W4	0.4178(5)	0.0596(3)	0.3040(7)	0.052(2)
N1N	0.4379(5)	0.3165(3)	0.0777(6)	0.049(3)
N1O1	0.4313(5)	0.3655(2)	0.0234(5)	0.070(3)
N1O2	0.4319(6)	0.2718(2)	0.0115(6)	0.080(3)
N1O3	0.4532(6)	0.3145(3)	0.2044(5)	0.080(3)
N2N	0.0888(7)	0.4046(4)	0.1030(9)	0.081(4)
N2O1	0.0453(7)	0.4525(2)	0.0843(7)	0.098(4)
N2O2	0.1532(10)	0.3882(6)	0.1935(11)	0.26(10)
N2O3	0.0635(9)	0.3712(3)	0.0101(13)	0.19(9)
N3N	0.6776(6)	0.0801(3)	0.0942(6)	0.048(2)
N3O1	0.6644(4)	0.1214(2)	0.1721(5)	0.056(2)
N3O2	0.5802(5)	0.0580(3)	0.0304(7)	0.095(4)
N3O3	0.7898(4)	0.0609(2)	0.0820(5)	0.058(2)

[a]U_{eq} is defined as one third of the trace of the orthogonalized U_{ij} tensor. [b]In this and subsequent tables e.s.d.s in the least significant figure are given in parentheses.

TABLE 3. Selected bond distances (Å) and angles (°)

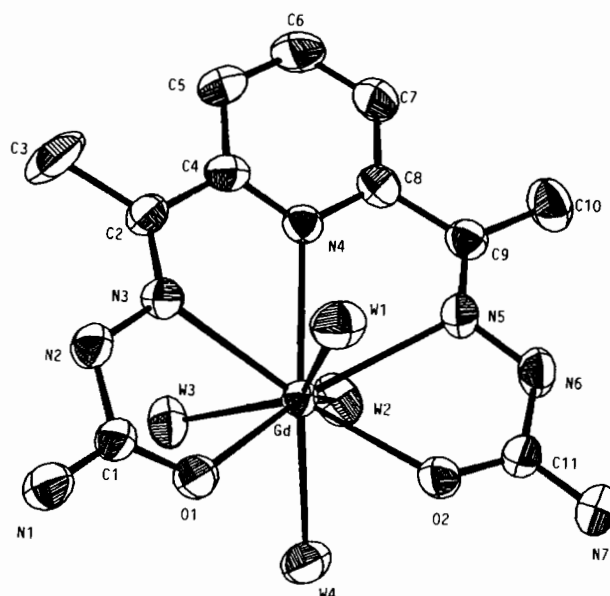|			
Gd–O1	2.390(4)	Gd–O2	2.364(4)
Gd–N3	2.519(5)	Gd–N4	2.591(5)
Gd–N5	2.595(5)	Gd–W3	2.443(5)
Gd–W2	2.503(6)	Gd–W1	2.421(5)
Gd–W4	2.405(5)		
O1–Gd–O2	93.74(14)	O1–Gd–W3	78.74(16)
O1–Gd–W2	76.11(17)	O1–Gd–W1	75.37(17)
O1–Gd–W4	139.90(19)	O2–Gd–W1	74.17(16)
O2–Gd–W3	141.08(16)	O2–Gd–W2	67.01(17)
O2–Gd–W4	97.36(21)	W3–Gd–W2	74.13(20)
W2–Gd–W1	129.41(18)	W2–Gd–W4	73.18(18)
W1–Gd–W4	144.71(21)		

Fig. 1. ORTEP view of the cation with ellipsoids drawn at the 50% probability level.

the Gd–N bond lengths to those of Gd–O shows that the former are the longest in the coordination sphere. However, these Gd–N bond distances are somewhat shorter ($\sim$0.05 Å) than those reported recently [17] for a structurally related Gd complex with a $CN = 9$. Long Gd–N bonds are not uncommon and Palenik has pointed out the fact that long Ln–N distances have been observed in virtually all lanthanide complexes with nitrogen donors [18]. The shortest contacts are the Gd–O (carbonyl) at 2.390(5) and 2.364(5) Å with the Gd–water contacts ranging from 2.405(5) to 2.503(6) Å. The longest Gd–water contact involves W2 which is the lone oxygen in a rectangular face capping site. This observation is reasonable since the capping atoms are usually at longer distances than the atoms forming the prism [18].

A relativistic extended Huckel (REX) calculation on the Gd complex, at the experimental geometry, indicates that the 4f electrons mix only slightly with the ligand orbitals. As expected for Ln coordination compounds, the predominant mixing between metal and ligand is through the more diffuse 5d AOs; however, the occupation of the 5d manifold is only 0.6 electrons as determined by a Mulliken population analysis (MPA). Calculation of bond overlap population (BOPs) from the MPA reinforces the highly ionic nature of the Ln–ligand bonds. The average values for the different ligating atom types are Gd–N = 0.08; Gd–O = 0.02; Gd–W = 0.01. The larger BOP for Gd–N versus Gd–O and Gd–W indicates that the Gd–nitrogen interactions are more ionic than Gd–oxygen, as expected given the larger size and lower electronegativity of N versus O. The calculated atomic charge on the Gd is +2.52, as

determined by the MPA. Thus, the high coordination number and ionic Ln–ligand bonds suggest that there is only a small (if any) barrier to conversion between the TTP and CSAP isomorphs, and that the solution structure of the complex is probably quite dynamic.

Two noteworthy structural points are the fact that four of the nine donors are water molecules and that the nitrate anions are not coordinated to the metal. The hydrophilic tendencies of the DAPSC complex are probably a result of the terminal amino groups. One area for future exploitation is the planarity of the DAPSC ligand. Vallarino and co-workers [5] and Hart and co-workers [19] have shown that large geometric distortions can be induced by changing the central Ln(III) ion in macrocyclic, Ln Schiff base complexes. Given a fixed central ion, greater deviations from planarity must be induced through modification of the ligand, in this case DAPSC. Presently, we are using MM experiments to suggest modifications to DAPSC which can induce non-planarity and perhaps increased coordination number [20].

Supplementary material

Complete listings of the atomic coordinates, bond distances, bond angles, hydrogen atomic coordinates, anisotropic thermal parameters, and a listing of observed and calculated structure factors are available from the authors on request.

Acknowledgements

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