

UC Berkeley

UC Berkeley Previously Published Works

Title

Bond Covalency and Oxidation State of Actinide Ions Complexed with Therapeutic Chelating Agent 3,4,3-LI(1,2-HOPO)

Permalink

<https://escholarship.org/uc/item/4tc1b0xz>

Journal

Inorganic Chemistry, 57(9)

ISSN

0020-1669

Authors

Kelley, Morgan P
Deblonde, Gauthier J-P
Su, Jing
[et al.](#)

Publication Date

2018-05-07

DOI

10.1021/acs.inorgchem.8b00345

Peer reviewed

1 Bond Covalency and Oxidation State of Actinide Ions Complexed 2 with Therapeutic Chelating Agent 3,4,3-LI(1,2-HOPO)

3 Morgan P. Kelley,[†] Gauthier J.-P. Deblonde,[‡] Jing Su,[†] Corwin H. Booth,[‡] Rebecca J. Abergel,[‡]
4 Enrique R. Batista,^{*,†} and Ping Yang^{*,†}

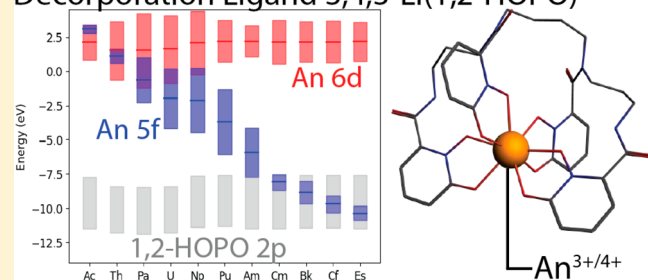
5 [†]Theoretical Division, Los Alamos National Laboratory, Los Alamos, New Mexico 87544, United States

6 [‡]Chemical Sciences Division, Lawrence Berkeley National Laboratory, Berkeley, California 94720, United States

7 **S** Supporting Information

8 **ABSTRACT:** The hydroxypyridinone ligand 3,4,3-LI(1,2-
9 HOPO) is a promising agent for biological decorporation of
10 radionuclides, and allows spectroscopic detection of many
11 lanthanide (Ln) and actinide (An) species via sensitized
12 luminescence. Despite the manifest uses of this ligand, the
13 structural and thermodynamic properties of its complexes
14 across the An series remain understudied. Theoretical
15 investigations of the binding of An(III) and An(IV) ions,
16 from actinium to einsteinium, by the 3,4,3-LI(1,2-HOPO)
17 ligand, as well as experimental extended X-ray absorption fine
18 structure (EXAFS) studies on the trivalent americium, curium,
19 and californium complexes were employed to address the
20 resulting structures, thermodynamic parameters, redox proper-
21 ties, and corresponding electronic configurations. An(IV) ions were found to form much stronger complexes than An(III) ions,
22 consistent with experimental measurements. Complexation of both An(III) and An(IV) ions generally becomes more favorable
23 for heavier actinides, reflecting increased energy degeneracy driven covalency and concomitant orbital mixing between the 5f
24 orbitals of the An ions and the π orbitals of the ligand. Notably, the ability of this ligand to either accept or donate electron
25 density as needed from its pyridine rings is found to be key to its extraordinary stability across the actinide series.

Covalency in Actinide Complexes of Decorporation Ligand 3,4,3-LI(1,2-HOPO)



26 **■** INTRODUCTION

27 Radiological contamination incidents can result in widespread
28 radiation exposure to both local and remote regions.
29 Representing an extreme recent example, the 2011 Fukushima
30 Daiichi Nuclear Power Plant accident resulted in the dispersal
31 of several radionuclides across a wide area, including portions of
32 the continental U.S.¹ Actinide (An) and lanthanide (Ln) fission
33 product species are likely to be major components of such
34 contamination events, and it is therefore necessary to
35 thoroughly understand and study the behavior of these ions
36 in environmental and biological systems.²

37 Internal contamination of human populations in the event of
38 a radiological incident, whether accidental or intentional, is of
39 critical concern. Once internalized, An ions transit rapidly
40 throughout the bloodstream and are primarily deposited in the
41 liver and bones (uranium is an exception and preferentially
42 deposits in the kidneys rather than in the liver), from which
43 elimination occurs very slowly.^{3,4} Uptake and deposition of
44 these ions present severe health risks due to both their
45 radiological and chemical toxicities.³ Medical treatments for
46 removal of An ions from the body are deemed essential in
47 limiting radiation exposure. Decorporation is primarily done
48 through chelation therapy, in which a ligand is introduced into
49 the body to complex the ions; the ions are then expelled from
50 the body concurrently with the ligand in either the urine or

51 feces. Stemming from the similar charge to ionic radius ratios
52 and coordination behaviors of Fe(III) and Pu(IV),⁵ a promising
53 class of compounds for the purpose of decorporation are the
54 siderophore-inspired⁶ multidentate hydroxypyridinonate
55 (HOPO) ligands, which have a peerless affinity for the An
56 ions.⁷

57 HOPO chelators coordinate isotopes of the An and Ln series
58 exceptionally well both *in vitro* and *in vivo*, and have been
59 shown to be effective decorporation agents in multiple animal
60 models.^{8–19} Two hydroxypyridinonate ligands have undergone
61 preclinical development as potential therapeutic agents for
62 actinide decorporation: the tetradentate chelator 5-LIO(Me-
63 3,2-HOPO) and the octadentate chelator 3,4,3-LI(1,2-
64 HOPO),¹⁷ with the latter now entering a first-in-human clinical
65 phase. Both of these ligands have been shown to be significantly
66 more effective An decorporation agents than the only approved
67 and used drug so far: the diethylenetriaminepentaacetic acid
68 (DTPA).¹⁷ Further, HOPO ligands have potentially a wide
69 array of additional medical uses. A HOPO ligand has been
70 proposed as a Gd(III) chelator for use as a contrast agent in
71 magnetic resonance imaging,^{20–23} and HOPO ligands have
72 been suggested as complexants in radiopharmaceutical treat-

Received: February 7, 2018

73 ments using $^{89}\text{Zr(IV)}$, $^{225}\text{Ac(III)}$, and $^{227}\text{Th(IV)}$.^{24,25} In
 74 addition to their manifest medical utility, HOPO ligands have
 75 analytical uses. 3,4,3-LI(1,2-HOPO) is known to sensitize the
 76 luminescence of several Ln(III), An(III), and An(IV) cations
 77 through the antenna effect,^{26–33} allowing these systems to be
 78 characterized spectroscopically and opening up a range of
 79 innovative applications including fluorescence-based bioas-
 80 says.^{31,32,34–38} A recent report has shown 3,4,3-LI(1,2-
 81 HOPO) capable of stabilizing Bk in the +4 oxidation state—
 82 the first stable Bk(IV) species observed in solution—a
 83 development potentially leading to novel Bk separation and
 84 purification techniques.³³

85 Despite the promising applications of HOPO ligands, a
 86 number of gaps in knowledge of their fundamental chemistry
 87 remain. Thermodynamic measurements have been performed
 88 with 3,4,3-LI(1,2-HOPO) across the Ln(III) series, and with
 89 Am(III), Cm(III), Ce(IV), Th(IV), and Pu(IV).^{8–11,39,40}
 90 However, the stability constants of M(IV)–3,4,3-LI(1,2-
 91 HOPO) complexes have proven more difficult to measure, as
 92 they exceed the stability of any known ligand with these
 93 ions.^{8,9,39} Furthermore, while the primary uses of HOPO
 94 ligands are in biological systems, thermodynamic measurements
 95 have necessarily been performed *in vitro*, and current
 96 knowledge of *in vivo* complex stability is derived solely from
 97 the decorporation profiles of the ions.^{8,11–17} *In vivo*, the
 98 oxidation state of the Ln and An ions is uncertain upon
 99 complexation, as there is some evidence suggesting HOPO may
 100 induce the oxidation or reduction of the metal ions.^{9,39,41}

101 Finally, the structure and bonding of the 3,4,3-LI(1,2-HOPO)
 102 complexes have not yet been fully investigated. To our
 103 knowledge, only the single-crystal X-ray structure of Eu(III)
 104 complexed with 3,4,3-LI(1,2-HOPO) has been obtained,³¹
 105 while structures of Sm(III), Eu(III), Gd(III), Am(III), Cm(III),
 106 and Cf(III) complexes have been determined when bound to
 107 the protein siderocalin (Scn).^{33,42} Currently, the only reported
 108 structure for a tetravalent metal ion complex of 3,4,3-LI(1,2-
 109 HOPO) is with Zr(IV).⁴³ Due, in part, to the large amount of
 110 material needed, no crystal structure of a free (non-protein-
 111 bound) An-3,4,3-LI(1,2-HOPO) complex has ever been
 112 reported. Some of the actinide contaminants potentially
 113 requiring decorporation have had neither structural nor
 114 thermodynamic measurements performed; this gap in knowl-
 115 edge can be addressed well with computational studies.
 116 Furthermore, the underlying causes of complexation, including
 117 the role of covalency in the An–ligand interaction, can be
 118 investigated via electronic structure calculations.

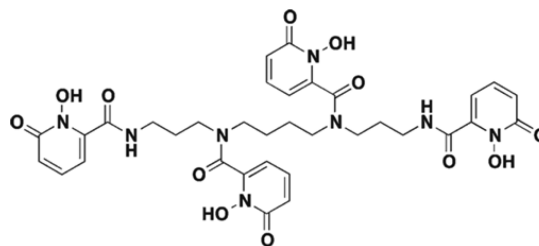
119 The present work uses density functional theory (DFT)
 120 combined with extended X-ray absorption fine structure
 121 (EXAFS) measurements to advance our current understanding
 122 of An-3,4,3-LI(1,2-HOPO) complexes. Their structure, ther-
 123 modynamics, electronic structures, and redox properties are
 124 investigated across the An series up to Es, with both formally
 125 An(III) and An(IV) ions. The similarity of 3,4,3-LI(1,2-
 126 HOPO) to other biological complexants and the wealth of
 127 excellent experimental information on this system ensures that
 128 a fundamental understanding of An-3,4,3-LI(1,2-HOPO)
 129 complexation will have applications beyond this single ligand,
 130 and presents an opportunity to study trends in An-ligand
 131 binding across the actinide series that can inform future work
 132 developing An complexants.

RESULTS AND DISCUSSION

133

Structure. The 3,4,3-LI(1,2-HOPO) ligand (Scheme 1; 134 s1
 henceforth referred to as “HOPO” to simplify the notation) 135

Scheme 1. Structure of 3,4,3-LI(1,2-HOPO)



incorporates four hydroxypyridinone 1,2-HOPO groups linked 136
 through a polyamine scaffold, and is capable of forming 137
 octadentate complexes with An ions, occupying all—or nearly 138
 all—of the first coordination shell of the ion. Ions are bound 139
 through the oxygen atoms within the 1,2-HOPO units, O(C) 140
 and O(N) (the carbonyl and hydroxyl groups within the 141
 hydroxamate, respectively). When fully deprotonated, HOPO 142
 carries four negative charges. 143

Density functional theory has frequently been applied to 144
 complicated An systems with good results,^{44–52} and has 145
 previously been used to study HOPO complexes. Daumann 146
 et al. used DFT to optimize the structure of the [Eu(HOPO)][−] 147
 complex, resulting in a gas phase geometry consistent with the 148
 crystal structure and a calculated UV–vis spectra matching 149
 experimental measurements.³¹ DFT was also used by Deri et al. 150
 to study the [Zr(HOPO)]⁰ complex, using their computational 151
 results to direct the synthesis of improved ligands for Zr(IV) 152
 complexation.²⁵ Several studies have used time dependent DFT 153
 to study lanthanide luminescence sensitization by ligands 154
 containing the 1,2-HOPO unit,^{26,40,53–55} in addition to 155
 calculations on Am and Cm.⁴⁰ These results suggest that 156
 DFT is a useful method for studying the metal–HOPO system. 157

Figure 1 shows the ion–oxygen distances in structures 158 ft
 optimized in the gas phase and utilizing implicit solvation 159
 models (polarizable continuum model) with the dielectric 160
 constant of water and that of a protein environment, as the 161
 HOPO ligand is frequently used *in vivo*. The results presented 162
 in Figure 1 show excellent agreement with available 163
 experimental crystal structures.^{15,24,31,32,42,56–59} The optimized 164
 aqueous [Eu(HOPO)][−] complex has an average Eu–O 165
 distance of 2.45 ± 0.01 Å, within uncertainty of the 166
 experimentally determined average of 2.40 ± 0.04 Å.³¹ Several 167
 other experimental studies have determined coordination 168
 structures of individual 1,2-HOPO units (without the poly- 169
 amine scaffold) in tetrakis-bidentate complexes.^{57–59} The 170
 average Pu(IV)–O distances in these structures are $2.33 \pm$ 171
 0.02 Å, compared to 2.36 ± 0.02 Å for the calculated distances 172
 (Figure 1). Experimentally determined Fe(III)–O, Ce(IV)–O, 173
 and Th(IV)–O distances in the 1,2-HOPO complexes are 174
 likewise consistent with our calculations of 3,4,3-LI(1,2- 175
 HOPO) complexes. 176

The An–O(C) and An–O(N) distances are generally not 177
 statistically distinct in measured crystal structures, as is 178
 generally the case in our results. Furthermore, the structure 179
 of the aqueous [Zr(HOPO)]⁰ complex matches nearly exactly 180
 that of the B3LYP optimized structure of Deri et al., who 181
 calculated average Zr–O(C) and Zr–O(N) distances of $2.22 \pm$ 182

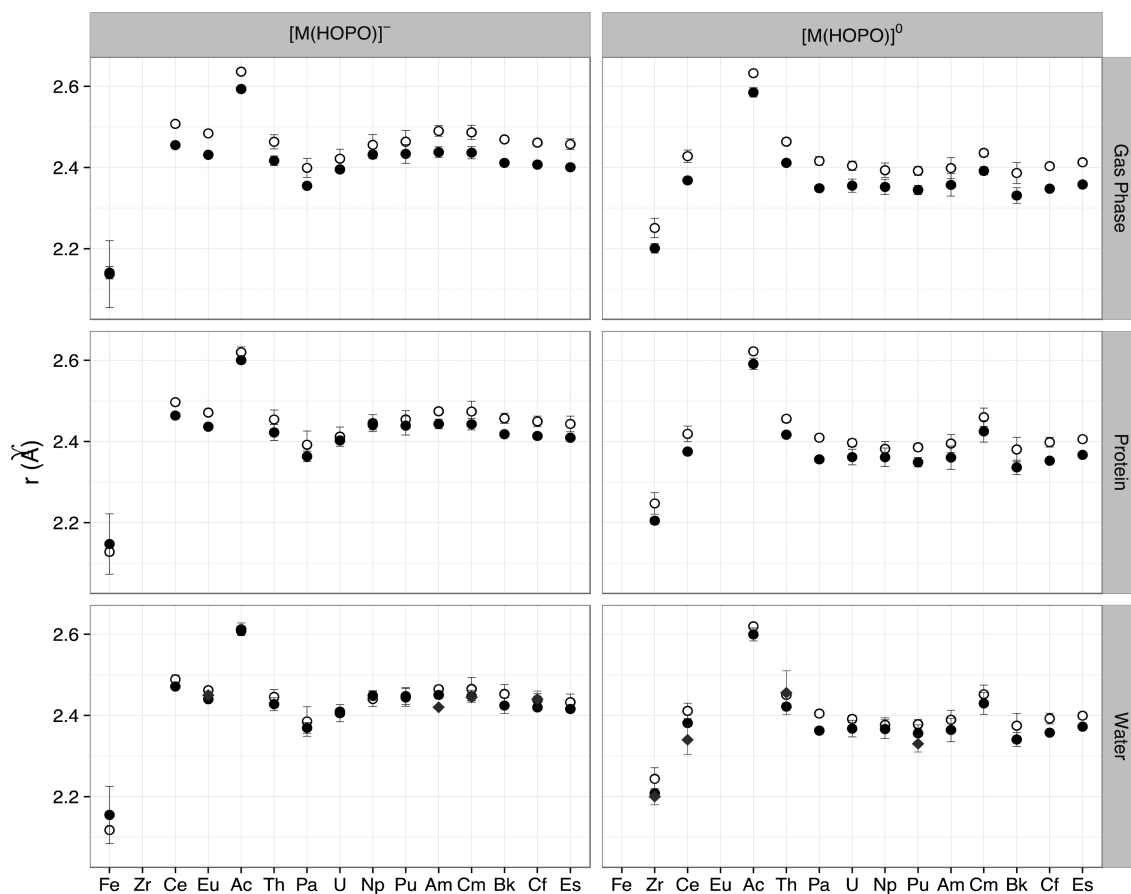


Figure 1. Ion-oxygen distances, M–O(N) (○) and M–O(C) (●), in $[M(\text{HOPO})]^{-}$ and $[M(\text{HOPO})]^{0}$ complexes. Experimental M–O distances (red ◆) are included when available, for Eu, Zr (crystal structures),^{31,43} Ce, Th, and Pu (crystal structures from the bidentate 1,2-HOPO ligand),^{56,58} and Am, Cm, and Cf (EXAFS data from this work). Error bars depict the standard deviation of ion–oxygen distances in the complex or the experimental uncertainty.

183 0.05 and $2.27 \pm 0.04 \text{ \AA}$, respectively, compared with $2.208 \pm$
 184 0.007 \AA and $2.24 \pm 0.03 \text{ \AA}$ in the present study.²⁵ Sturzbecher-
 185 Hoehne et al. optimized structures of $[\text{Eu}(\text{HOPO})]^{-}$, $[\text{Am}$ -
 186 $(\text{HOPO})]^{-}$, and $[\text{Cm}(\text{HOPO})]^{-}$ in the gas phase using the
 187 PBE functional. Ion-oxygen distances are nearly identical to the
 188 gas phase structures presented here for all three ions.⁴⁰

189 **EXAFS Measurements.** To further verify the DFT/PBE
 190 structures, EXAFS measurements were performed on the later
 191 actinides, as no experimental structural data were available in
 192 the literature for comparison. Usable EXAFS data were
 193 obtained on HOPO complexes formed *in situ* with Am, Cm,
 194 and Cf (the amount of Bk material available for these
 195 experiments was too limiting). The data quality is best for
 196 the Am and Cm spectra, allowing for sharper spectra and a
 197 confident comparison to the fit model. The $[\text{Cf}(\text{HOPO})]^{-}$ data
 198 are of lesser quality (only $\sim 3 \mu\text{g}$ available for measurements),
 199 limiting the range in wave vector k (Figure 2, top). Though
 200 details of the fitting models are provided in the Supporting
 201 Information, we describe several important features here. The
 202 fitting model for the Am and Cm data is derived from a
 203 simplification of the M^{3+} calculations described above. In
 204 particular, each scattering shell is modeled by a single atom pair,
 205 which is multiplied by the nominal coordination number and
 206 Gaussian broadened by a Debye–Waller factors, σ^2 , to account
 207 for any distribution of such bonds, as well as thermal
 208 broadening. This assumption, namely that the distribution of
 209 bonds is narrow enough that a Gaussian will describe the

structure adequately, can be considered justified by the 210
 relatively small values of σ^2 (less than 0.02 \AA^2 for all shells) 211
 and the overall good quality of the fits. In addition, the second 212
 shell near 3.3 \AA in the calculation includes both 4 C and 4 N 213
 neighbors. Since these species are virtually indistinguishable in 214
 this measurement, their bond lengths are constrained together 215
 and their Debye–Waller factors, σ^2 , set equal, so any differences 216
 in the An–C and An–N distributions for this shell are reflected 217
 in the average σ^2 . In addition, the Cm data require an additional 218
 shell, corresponding to a bond length near 3.0 \AA (98% 219
 confidence level⁶⁰). Since Cm^{3+} luminescence lifetime measure- 220
 ments indicate the presence of inner-sphere water,¹⁰ we 221
 tentatively ascribe this peak to an oxygen scatterer, although 222
 we note the long bond length and large error in σ^2 , which may 223
 be a consequence of a dynamic coordination. We also find such 224
 a peak improves the fits to the $[\text{Am}(\text{HOPO})]^{-}$ data, although 225
 with less confidence (75% confidence level). We emphasize 226
 that the presence of this peak in the spectrum has no effect on 227
 the bond lengths reported below. 228

To further consider inner-sphere water coordination, we 229
 used a number of different strategies to optimize the calculated 230
 $[\text{Am}(\text{HOPO})(\text{H}_2\text{O})]^{-}$ structure, but none was successful. In 231
 the absence of constraints, the added water molecule moved 232
 away from the ion to a distance of approximately 4.3 \AA , where it 233
 formed two hydrogen bonds with HOPO oxygen atoms 234
 coordinating to the Am ion. It is possible that solution dynamic 235
 effects would establish an equilibrium in which a water 236

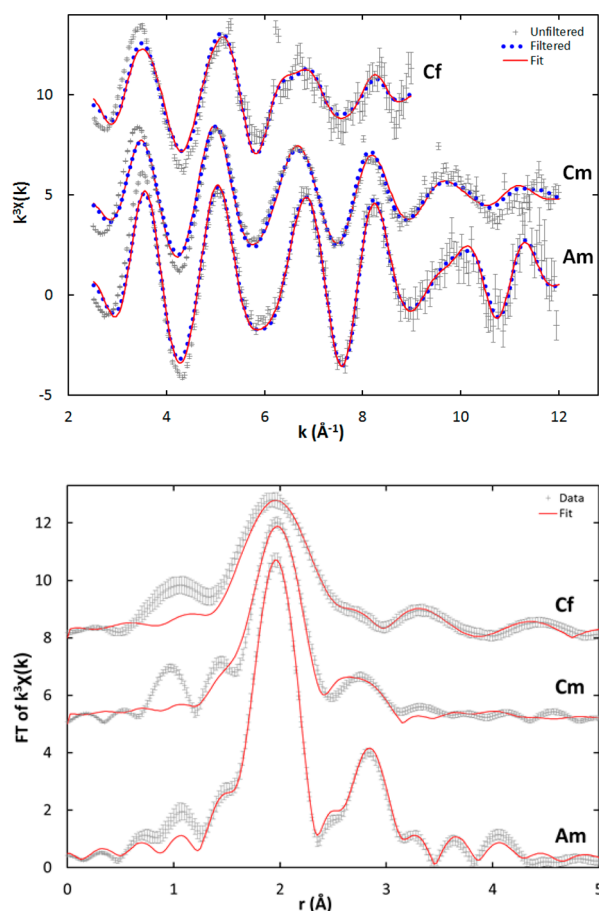


Figure 2. EXAFS data and fit results from the An L_{III} edge of [An(III)(HOPO)][−] (An = Am, Cm, or Cf). The upper panel shows the results in *k*-space. The raw (unfiltered) data reveal error bars estimated by the reproducibility of 16 (Am, Cm) to 21 (Cf) averaged traces. The bottom panel shows the data and fit are transformed from 2.5 to 12.0 Å^{−1} (from 2.5 to 9.0 Å^{−1} for Cf) and fit between 1.5 and 4.3 Å (between 1.4 and 5.0 Å for Cf). The filtered data and fit in the top panel are back-transformed over the fit range. See Tables S3 and S4 for fit details.

Table 1. Comparison between Measured (EXAFS) and Calculated M³⁺ Nearest-Neighbor Bond Lengths

number	bond type	R_{EXAFS} (Å) ^a	R_{DFT} (Å) ^b
8	Am–O	2.420(6)	2.46(1)
8	Am–C/N	3.292(7)	3.33(3)
8	Cm–O	2.444(6)	2.46(2)
8	Cm–C/N	3.24(2)	3.31(3)
8	Cf–O	2.45(2)	2.43(2)
8	Cf–C/N	3.54(10)	3.29(3)

^aValues in parentheses indicate fit error. ^bValues in parentheses indicate standard deviation of bond length distribution.

significantly smaller than the next smallest ion in Figure 1, Zr⁴⁺ 259 (IR = 0.84 Å).⁶¹ Calculations performed on main group cations, 260 K⁺, Ca²⁺, and Al³⁺, revealed similar trends. Al³⁺ (IR = 0.535 261 Å)⁶¹ has a coordination number of 6, with two O(N) groups 262 rotating away from the ion. Ca²⁺ is much larger (IR = 1.12 Å)⁶¹ 263 but has a significantly lower charge density, resulting in a loose 264 8 coordinate complex in which the average distance to the 265 oxygen atoms is greater than 2.5 Å. K⁺, with the lowest charge 266 density and the largest ionic radius (IR = 1.38 Å)⁶¹ of any ion 267 examined here, forms a 6 coordinate complex. This is achieved 268 not by rotating two oxygen atoms away, as Al³⁺ does to 269 accommodate its smaller ionic radius, but by the disengagement 270 of an entire 1,2-HOPO unit from the ion. This results in a very 271 loose 6-coordinate complex with average coordinated K⁺–O 272 distances greater than 2.8 Å. The structural deformities seen 273 here for other ions commonly found in biological systems could 274 represent an advantage for An complexation, minimizing 275 competition with ions naturally present in the bloodstream, 276 as the size and conformation of the complex is likely to impact 277 its interaction with proteins like Scn,⁴² therefore leading to 278 selectivity of An ions. Some of these complexes are illustrated in 279 Figure 3. Additionally, the structures of the Al³⁺ and Fe³⁺ 280

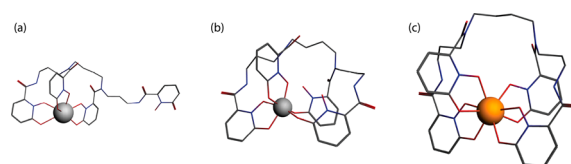


Figure 3. Ion-HOPO structures for complexes with (a) K⁺, (b) Al³⁺, and (c) Cm³⁺. Metal ions are represented by spheres, HOPO^{4−} atoms by sticks; red = oxygen, blue = nitrogen, gray = carbon. Hydrogen atoms omitted for clarity. Structure c is representative of all Ln and An complexes, which can be found in the Supporting Information, along with coordinates for all structures.

237 molecule is sometimes in the first coordination shell of the ion 238 and sometimes in the second coordination shell. To fully 239 investigate this question, it is necessary to include both explicit 240 solvents and dynamic simulation which is beyond the scope of 241 this work.

242 Other than the exceptions described above, the fit model 243 obtained from calculated structures describes the data well 244 (Figure 2). Generally speaking, the EXAFS data are consistent 245 with the HOPO complex structure calculations for the nearest 246 neighbor M(III)–O pair distances with the largest deviation 247 occurring with [Am(HOPO)][−]. In addition, the Cf–C/N 248 average bond length differs from calculation, but the calculation 249 also shows a broad distribution width for the 8 bonds in this 250 shell. Table 1 compares the EXAFS bond length results to 251 those derived from the DFT calculations for the first two shells. 252 Further details of the methods and results are available in 253 Supporting Information (pp S11–S15).

254 **DFT Structure.** The ions shown in Figure 1 maintain a 255 coordination number of 8, with the exception of the 7 256 coordinate Fe³⁺, in which one of the O(N) groups is rotated 257 away from the ion with an Fe³⁺–O distance of 3.6 Å. This is 258 consistent with the ionic radius (IR) of Fe³⁺, 0.78 Å, which is

complexes, with the O(N) groups rotating away to 281 accommodate the smaller ions, imply that the M–O(N) 282 bonds are slightly weaker than the M–O(C) bonds. 283

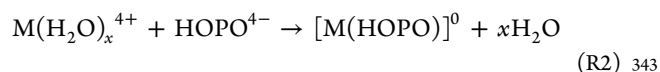
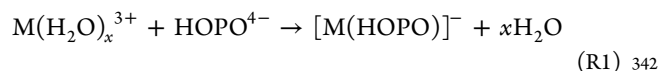
The [An(HOPO)][−] complexes show a fairly small but 284 consistent increase in An–O distances starting with Th and 285 leveling off around Am. While this is the opposite trend 286 expected from the decrease in ionic radii across the series due 287 to the contraction of the *Sf* orbitals, it can be understood via the 288 electronic structure of the earlier An ions, many of which 289 strongly disfavor the An(III) oxidation state. These ions are 290 essentially oxidized to An(IV), matching the An–O distances of 291 the [An(HOPO)]⁰ complexes; this is explored in subsequent 292 sections. Ac³⁺ is significantly further from the oxygen atoms in 293 line with its larger ionic radius and consistent with recent 294

295 EXAFS measurements showing Ac(III)–H₂O and Ac³⁺–Cl
 296 distances to be 0.1–0.2 Å greater than corresponding Am³⁺
 297 complexes.^{44,62} [An(HOPO)]⁰ complexes behave more pre-
 298 dictably, with An(IV)–O distances initially decreasing as the
 299 ionic radius decreases and then remaining nearly constant
 300 beyond U(IV). [Cm(HOPO)]⁰ is a notable exception to this
 301 trend, having an increase in An–O distance inconsistent with
 302 the rest of the series. The reasons behind this discrepancy will
 303 be covered in the discussion of electronic structure.

304 There are only minor differences—like the convergence of
 305 the M–O(N) and M–O(C) distances in water—between the
 306 structures optimized in the gas phase, the protein-like
 307 environment, and water using the implicit solvation model
 308 employed here, as shown in Figure 1. Upon binding by a
 309 protein, it is important to note that the HOPO ligand is flexible
 310 and therefore the complex structures can be influenced by
 311 strong explicit interactions occurring between the metal
 312 complex and the protein. Hence the structures of complexes
 313 identified in proteins may show larger deviation from the data
 314 in this report.

315 **Thermodynamics.** The free energies of complexation by
 316 the HOPO^{4−} ligand were calculated at the DFT/PBE0 level to
 317 compare with experimental thermodynamic measurements of
 318 the stability constants across the An series. These computed
 319 free energies between the hydrated ions (using both an explicit
 320 first solvation shell of water and the implicit polarizable
 321 continuum model) and HOPO^{4−} Reactions R1 and R2 are
 322 shown in Figure 4. As with the ion-oxygen distances presented

which have measured log(β_{101}) values for HOPO with M(IV) 333
 ions nearly double those of M(III) complexes.^{9,39} For example, 334
 the log(β_{101}) for Ce³⁺ is 17.4(5) while that for Ce⁴⁺ is 41.5(5), 335
 corresponding to an energy difference of approximately 33
 336 kcal/mol.³⁹ This is the same order of magnitude as the 337
 difference in Ce³⁺ vs Ce⁴⁺ calculated here, despite these 338
 calculations considering only the solvated ion within a 339
 polarizable continuum without counterions or other aspects 340
 of solvation. 341



The above reactions denote the number of water molecules as 344
 “*x*”, with *x* = 6 for Fe and *x* = 9 for all other ions. While the 345
 assumption of *x* = 9 is confirmed for the two Ln and the early 346
 An ions, later An ions have experimentally debated hydration 347
 numbers between eight and nine.^{51,63–65} Precise determination 348
 of the number of water molecules within the first solvation shell 349
 of An ions is a challenging computational problem^{49,50,66,67} 350
 beyond the scope of the current work. Additionally, the 351
 difference in complexation energy between a hydration number 352
 of eight or nine amounts only to the order of 3–4 kcal/mol, 353
 which is small enough to have no impact on conclusions 354
 concerning the complexation energy across the An series 355
 despite potential changes in coordination number. Fe³⁺ has a 356
 hydration number of only six, with a high spin ground state for 357
 both the hydrated ion and the Fe(HOPO)[−] complex. 358

The left panel of Figure 4 depicts the Gibbs free energy 359
 (ΔG) of reaction R1, where An(HOPO)[−] complexes have a 360
 presumed oxidation state of + III at the metal center. 361
 Reassuringly, the difference between the two trivalent Ln ions 362
 calculated here, Ce and Eu, matches experiments showing an 363
 increase in stability constants across the Ln series.¹¹ Complex- 364
 ation of the early An(III) ions is very favorable, becoming less 365
 so as the series is traversed. These early actinides—Th, Pa, and 366
 U—readily form An(IV) complexes instead of An(III) species, 367
 and the comparative favorability of complexation is due to 368
 electron donation to the HOPO stabilizing the ion. The 369
 binding energy does not significantly change after Cm³⁺. 370
 Formation of the [Ac(HOPO)][−] complex is less favorable than 371
 other An complexes, in line with the increased ionic radius and 372
 Ac–O distances described in the preceding section. The cause 373
 behind this decrease requires a discussion of the electronic 374
 structures of the complexes, and is provided in greater detail in 375
 the Electronic Structure section. 376

Formation of the [M(HOPO)]⁰ complexes (right panel of 377
 Figure 4; reaction R2) shows ΔG of complexation for the 378
 formally An(IV) ions, which is significantly more favorable than 379
 the formally An(III) complexation of HOPO, consistent with 380
 experimental observations.⁹ Complexation energy becomes 381
 more favorable as the series is traversed, but unlike the trend 382
 observed for the An(III) ions, this starts near the beginning of 383
 the series with Th. The trend is not consistent across the series, 384
 however, with Bk(IV) complexation becoming less favorable 385
 than Cm(IV). Additionally, the behavior of Ac, which changes 386
 based on the oxidation state of the ion, requires some 387
 explanation. The formation of the [Ac(HOPO)][−] complex is 388
 unfavorable compared to the rest of the An series, an 389
 unsurprising observation given the significantly longer Ac–O 390
 bond lengths. Formation of the [Ac(HOPO)]⁰ complex, 391

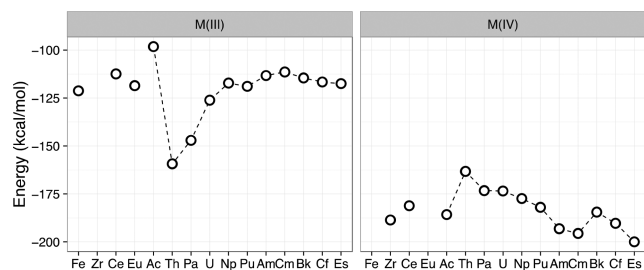


Figure 4. Free energy (ΔG) of complexation between the hydrated ions and the HOPO^{4−} ligand in implicit water solvent.

323 above, the trends between the gas phase calculations, the
 324 calculations including the implicit water solvent, and those with
 325 a protein-like solvent are similar, most likely because the
 326 complex is not very polarizable (see Supporting Information,
 327 Figure S6 for thermodynamic calculations in the two solvation
 328 environments and the gas phase using the bare ions); therefore,
 329 only those using implicit water solvation are shown in Figure 4.
 330 The calculated ΔG of complexation for the M(IV) ions is
 331 significantly lower than that of the M(III) ions. This matches
 332 well with experimental thermodynamic studies (Table 2),

Table 2. Experimentally Measured Stability Constants for Relevant Ln and An ions with HOPO.^a

M ³⁺	log(β_{101})	M ⁴⁺	log(β_{101})
Ce ³⁺	17.4(5) ³⁹	Ce ⁴⁺	41.5(5) ^{39,42}
Eu ³⁺	20.2(2) ^{11,28}	Th ⁴⁺	40.1(5) ^{9,39}
Am ³⁺	20.4(2) ⁴⁰	Pu ⁴⁺	43.5(7) ⁹
Cm ³⁺	21.8(4) ¹⁰	Bk ⁴⁺	44.7 ^{b33}

^aSuperscripts indicate reference from which data is cited. ^bEstimation based on a linear ionic radius correlation.

392 however, is more favorable compared to its neighbors in the
 393 early part of the series— exactly the opposite behavior expected
 394 from the geometry. To explain this behavior and other
 395 observations mentioned above, it is necessary to delve deeper
 396 into the electronic structure of the An-HOPO complexes.

397 **Electronic Structure.** Charge donation from the ligand to
 398 the ion occurs primarily into the 6d orbitals of the metal ion in
 399 $[\text{An}(\text{HOPO})]^-$ complexes, with 5f participation increasing and
 400 6d decreasing slightly across the actinide series up to Am
 401 (Figure 5). An exception to this is Ac, which resembles the later

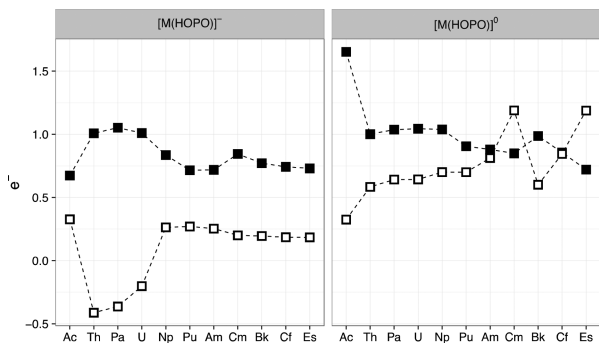


Figure 5. Electron donation into the valence d (■) and f (□) orbitals (6d/5f for An ions—note that a single electron is donated into the 5d orbital of Ac in the $[\text{Ac}(\text{HOPO})]^0$ complex). The change in population (Δd and Δf ; actual populations minus the formally expected An(III) or An(IV) population) is plotted here.

402 actinides despite its position at the beginning of the series.
 403 There is also a slight decrease in donation into the 5f between
 404 Am and Cm, possibly due to the fact that Cm^{3+} is $5f^7$ and
 405 adding an additional electron into the half-filled 5f shell is less
 406 favorable than adding into the 6d. The dual participation of the
 407 5f and 6d orbitals matches recent experimental and theoretical
 408 studies showing participation of both the f and d orbitals in
 409 uranium complexation,⁶⁸ in addition to theoretical work on
 410 solid state and molecular structures across the An series.^{46,69,70}

411 It is important to note that it is not the absolute values of the
 412 Mulliken populations shown in Figure 5 that are important to
 413 our analyses here, but rather the trends between the An ions.
 414 The oxidation state of the metal center is better described using
 415 spin density, as in Figures 6 and 7; we note that calculated S^2
 416 values are uniformly within 0.15 of the expectation value.

417 An interesting feature of the 6d and 5f populations in the
 418 $[\text{An}(\text{HOPO})]^-$ complexes (Figure 5) is that Th, Pa, and U
 419 have a decrease in their 5f populations upon complexation ($\Delta 5f$
 420 < 0). This is reflective of the fact that all three of these ions are
 421 more stable as An(IV) species than An(III), and when these

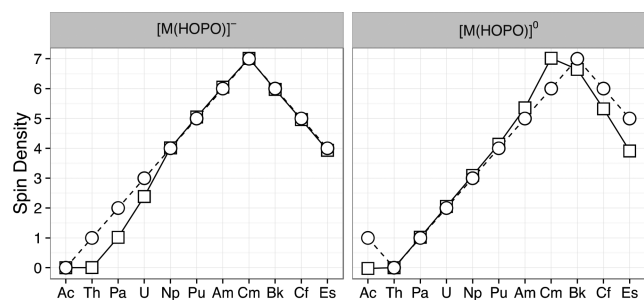


Figure 6. Actual (□) and formal (○) spin densities on the An ions in the $[\text{An}(\text{HOPO})]^-$ and $[\text{An}(\text{HOPO})]^0$ complexes.

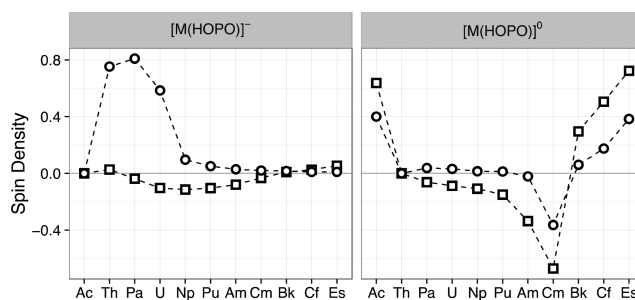


Figure 7. Total spin densities on the complexing 1,2-HOPO units of the HOPO^{4-} molecule, grouped into total oxygen (□) and total pyridine (○) contributions.

422 formally An(III) ions are complexed by the HOPO^{4-} ligand
 423 they are oxidized, giving up spin density to the ligand. Figure 6
 424 shows that the actual spin density of Th, Pa, and U in the
 425 $[\text{An}(\text{HOPO})]^-$ complexes is significantly lower than their
 426 formal spin densities as An(III) ions. The surrendered spin
 427 density moves from the ions into the HOPO^{4-} ligand, where it
 428 is taken into the pyridine rings of two of four coordinating 1,2-
 429 HOPO units (Figure 7). The spin density in the pyridine ring
 430 increases, making up for the decrease in spin density on the ion
 431 (a breakdown of Figure 7 into different groups within each 1,2-
 432 HOPO unit can be found in the Supporting Information,
 433 Figure S5). Despite the oxidation of these ions, significant
 434 electron donation to the 6d orbitals from the ligand still occurs,
 435 making this exchange 5f-to-ligand back bonding. This has the
 436 effect of stabilizing the ion, resulting in the favorable
 437 complexation energy observed in Figure 4. It is clear that the
 438 ability of the pyridine ring to take electron density from the
 439 metal center contributes to the stability of the $[\text{An}(\text{HOPO})]^-$
 440 complexes with the early actinides. Introducing an even better
 441 electron-withdrawing group could be a path toward creating
 442 better chelators for the low oxidation states of early actinides.

443 Actinide ions in the $[\text{An}(\text{HOPO})]^0$ complexes have levels of
 444 electron donation into their 6d orbitals comparable to those in
 445 the $[\text{An}(\text{HOPO})]^-$ complexes, but significantly greater
 446 donation into the 5f orbitals. Electron donation into the 5f
 447 orbitals (relative to the formal An(IV) expectation) increases
 448 across the series, a trend briefly reversed at Bk. This is because
 449 unlike other late actinides, Bk maintains a + IV oxidation state,
 450 as demonstrated by the spin density. The trend of increasing 5f
 451 participation continues in Cf and Es.

452 The unexpected increase in the Cm(IV)–O distances relative
 453 to the other An (HOPO)⁰ complexes (Figure 1) can be
 454 explained by examining Figure 6 and Figure 7. Our observed
 455 increase in Cm–O distances matches observations from
 456 calculations on solid-state AnO_2 structures, that predict an
 457 increase in the lattice constant of CmO_2 relative to the rest of
 458 the series. This was explained by Prodan et al.⁷⁰ as being due to
 459 the electronic configuration of Cm(IV), $5f^6$. This less stable
 460 electron configuration leads Cm(IV) to borrow α spin density
 461 from the coordinating oxygen atoms in order to approach the
 462 stability of the $5f^7$ subshell, resulting in a spin density on the
 463 Cm atom between the formal Cm(III) and Cm(IV). The spin
 464 density on the Cm atom in the $[\text{Cm}(\text{HOPO})]^0$ complex is
 465 nearly 7, indicating that the Cm(IV) has been reduced by
 466 HOPO^{4-} to Cm(III). Unlike the solid CmO_2 , the 1,2-HOPO
 467 units have other atoms aside from oxygen to donate spin
 468 density; an increase in spin density on the pyridine ring, in
 469 addition to the coordinating oxygen atoms, is observed. We

Table 3. Calculated Free Energy (ΔG) of Oxidation for the $[\text{An}(\text{HOPO})]^-$ Complexes to $[\text{An}(\text{HOPO})]^0$, in Water Relative to Ferrocene (eV)

	Ac	Th	Pa	U	Np	Pu	Am	Cm	Bk	Cf	Es
ΔG	1.19	-1.76	-1.95	-1.99	-1.01	-0.20	0.72	1.23	0.01	1.32	1.24

note that the majority of the donated spin density comes from the oxygen atoms rather than the pyridine ring, though both groups participate. Increasing the electron donation ability of the coordinating atoms could result in a stronger complex. This trend continues for the later actinides, which are also essentially reduced to An(III). However, with an already half-filled 5f subshell, the actinides after Cm take β spin from the 1,2-HOPO units, resulting in a spin density lower than what would be expected for a formally An(IV) ion and a corresponding increase in spin density on the HOPO⁴⁻.

The ability of the HOPO⁴⁻ ligand to allow coordinating actinide ions to attain their most stable oxidation states by either accepting or donating electron density also explains the behavior of Ac, where the formation of the $[\text{Ac}(\text{HOPO})]^0$ complex was significantly more favorable than any other complex, counter to expectations from trends in the optimized geometries and inconsistent with the formation of the $[\text{Ac}(\text{HOPO})]^-$ complex. Ac(IV) has a formal 6p⁵5f⁰ electron configuration, which is very unstable. Ac(IV) is, as expected, quite easily reduced to Ac(III) by the ligand, completing the 6p shell to become 6p⁶5f⁰. The spin density on Ac(IV) is zero, reduced from a formal spin density of 1 (Figure 6), which is compensated by an increase in spin density on the HOPO⁴⁻ ligand (Figure 7). Spin density from both coordinating oxygen atoms and the pyridine ring of all four 1,2-HOPO units is taken to reduce Ac(IV). Since the Ac(IV) ion is unstable, complexation with HOPO is more favorable due not to the increased stability of the complex but rather the instability of the Ac(IV) ion; by reducing Ac(IV) and filling the 6p shell, the HOPO stabilizes the Ac ion as Ac(III), resolving the previously anomalous trend in Figure 4.

Table 3 shows the free energy of the oxidation potentials of the $[\text{M}(\text{HOPO})]^-$ complexes to $[\text{M}(\text{HOPO})]^0$, relative to ferrocene/ferrocenium (Fc^0/Fc^+ ; ΔG for the ferrocene redox couple was calculated as 4.52 eV). The $[\text{Ce}(\text{HOPO})]^-/[\text{Ce}(\text{HOPO})]^0$ redox couple has been measured experimentally³⁹ as -0.3(1) eV when adjusted relative to Fc^0/Fc^+ ; this is a good match with the -0.55 eV value calculated here. The difference between the calculated result and experimental measurements is within the uncertainty of the applied method.⁷¹ The redox potentials of all early actinide complexes, up to Pu, are negative compared to ferrocene (with the exception of Ac), while all later actinide complexes have positive redox potentials relative to the Fc^0/Fc^+ couple. The complexes with ions having more stable An(IV) oxidation states (i.e., Th, Pa, and U) are significantly easier to oxidize to $[\text{M}(\text{HOPO})]^0$; this is because in the $[\text{M}(\text{HOPO})]^-$ complexes, the metal centers are already in oxidation state IV resulting in additional electron density residing on the HOPO ligand, leading to the ease of removal of the electron during the oxidation process and the negative oxidation potential. For Np and Pu complexes, it is the metal center being oxidized. In contrast, the late actinide ions in $[\text{M}(\text{HOPO})]^0$ mentioned above (Cm, Cf, Es) are reduced to An(III) during complexation with HOPO⁴⁻, and are the least likely to form the $[\text{M}(\text{HOPO})]^0$ complex. For these complexes, it is the HOPO ligand being oxidized instead of metal center. Bk is somewhat

of an exception to this trend, as the Bk center is being oxidized, with a ΔG of oxidation of only 0.01 eV, essentially the same as that of Fc^0/Fc^+ couple and contrasting with its neighbors Cm and Cf which both have values over 1 eV. Metal oxidation states are known to have some dependence on complexing ligands,^{72,73} and this redox data gives further evidence of the stabilization of An(IV) ions by HOPO, recently observed by Deblonde et al. in their investigation of Bk⁴⁺ complexation by HOPO.³³ These differences in redox potential correspond to the changes in the An spin density observed in Figure 6.

Covalency across the An Series. As the An series is traversed, the energy of the An 5f orbitals decreases and aligns better with that of the ligand orbitals, enhancing orbital mixing between the metal center and the ligand. This effect can be seen in Figure 8 for both the $[\text{An}(\text{HOPO})]^-$ and $[\text{An}(\text{HOPO})]^0$ complexes. The descending energy levels of the 5f orbitals across the An series and their corresponding increase in degeneracy with the conjugated π orbital of the 1,2-HOPO units in the HOPO⁴⁻ ligand yield the increase in charge donation into the 5f orbitals with the 6d orbitals maintaining a

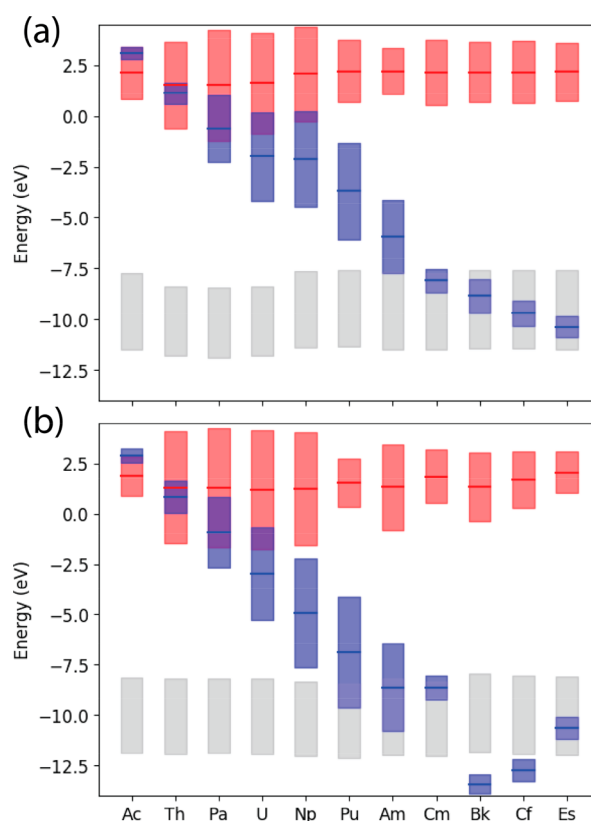


Figure 8. Average energy levels of the 5f (blue) and 6d (red) orbitals in the (a) $[\text{An}(\text{HOPO})]^-$ and (b) $[\text{An}(\text{HOPO})]^0$ complexes. The conjugated π orbital of the 1,2-HOPO units in the HOPO⁴⁻ ligand (which includes the pyridine ring and the coordinating oxygen atoms) are also shown for each complex (gray). Darker lines represent the average energy value of the orbitals, while the shaded regions give the standard deviation. Averages and standard deviations of the orbital energies are weighted by MO composition.

constant energy and population across the series, as observed in Figure 5. These findings across the entire An series corroborate the work of Sturzbecher-Hoehne et al., who found increased orbital overlap in the [Cm(HOPO)]⁻ complex relative to the [Am(HOPO)]⁻ complex, suggesting that this might be responsible for the increase in binding constant between the two actinides.⁴⁰ This decrease in An 5f energy has been observed previously in a number of different studies, including oxygen ligands in both solid state and molecular systems.^{46,69,70,74,75} Comparing Figure 8, parts a and b, one notes that the change of 5f orbital energy across the series is oxidation state dependent; for example, the sudden drop in 5f energy between Cm and Bk in Figure 8b occurs because Cm is actually Cm(III) and Bk is Bk(IV) in the [An(HOPO)]⁰ complexes. Comparing Figure 8b with solid state AnO₂ systems where the metal centers are all formally oxidation state IV shows that the energy degeneracy to 5f orbitals displays strong dependency to the ligand type—in the solid-state system, the 5f orbitals interact with the oxygen 2p orbitals only, while here they interact with the conjugated π orbital formed by the oxygen of the pyridine ring.

As the An 5f orbitals become more degenerate with the π orbital of the 1,2-HOPO units in the HOPO⁴⁻ ligand, significant mixing between the An 5f and the ligand orbitals occurs. Until Am³⁺, each [An(HOPO)]⁻ complex has all of its occupied f molecular orbitals localized in the metal. As the series is traversed, however, the 5f orbitals become increasingly mixed with the ligand orbitals. For example, in [Bk(HOPO)]⁻, the 5f orbitals are spread across 29 molecular orbitals, each with at least 5% f participation. A similar trend is observed in the [An(HOPO)]⁰ complexes starting at Pu, consistent with the overall lower energy of the 5f orbitals in the [An(HOPO)]⁰ complexes. This explains why the complexes become more stable across the latter part of the An series, despite the 6d orbitals remaining at a constant energy level. Additional data on the delocalization of the 5f orbitals, including molecular orbital diagrams, is available in the Supporting Information (Figures S1–S4). The changing energy levels of the 5f orbitals also sheds light on the unexpected break in the thermodynamic trends at Bk(IV), where an increase in ΔG of complexation (that is, ΔG becomes less negative) between Cm and Bk in [An(HOPO)]⁰ is observed (Figure 4). This corresponds to the 5f orbitals of Bk (Bk(IV) is 5f⁷) decreasing by approximately 5 eV from the Cm level, so that they are nearly below the range of the ligand orbitals in energy. As briefly discussed above, this is due to Cm having a +III oxidation state, while Bk has a +IV oxidation state within their respective [An(HOPO)]⁰ complexes. Cf and Es likewise favor the +III oxidation state, increasing the energy of the 5f orbitals in [Cf(HOPO)]⁰ and [Es(HOPO)]⁰ complexes, relative to Bk. The change in behavior between Cm and Bk can therefore be traced back to the oxidation state of the ion.

In their study of the f and d orbital contributions to covalency, Minasian et al. described covalent bonds using a mixing coefficient, λ , defined as

$$\lambda = \frac{H_{ML}}{|E_M^0 - E_L^0|} \quad (1)$$

where λ ranges between zero and one depending on the degree of covalent contribution to the bond, H_{ML} is the off diagonal matrix element of the Hamiltonian (proportional to the overlap integral between the two atoms making up the bond), and E_M^0

and E_L^0 are the metal and ligand orbital energies, respectively.⁶⁸ From eq 1, there are two ways in which a covalent bond can be achieved. Overlap driven covalency is realized in the presence of a significant matrix element (H_{ML}), indicating increased spatial overlap of orbitals. Energy degeneracy driven covalency is attained when the metal and ligand orbital energy levels are nearly degenerate; that is when the denominator $E_M^0 - E_L^0$ approaches zero. It should be noted that without a nonzero value for H_{ML} —at least some orbital overlap— λ is zero and covalency of either type is not possible.

The later actinide complexes display strong energy degeneracy driven covalency as described previously by Minasian and others,^{68,70,75,76} as opposed to the more traditional overlap driven covalency typical of the early actinides. Later actinide ions, which are significantly contracted relative to their earlier peers, have less spatial overlap and therefore are often thought to have primarily ionic interactions. The mixing of the 5f orbitals of later actinides with the ligand orbitals is energy degeneracy covalency in nature. Additionally, this increased orbital mixing correlates with the enhanced stability of the complexes. These results support the idea that ligand dependent energy degeneracy driven covalency is an important feature of the chemistry of the later actinides, supplanting the more traditional covalency derived from the spatial overlap of orbitals, and these results match recent calculations on the heavy actinides with dipicolinate ligands.⁷⁶ The later actinides are an ideal place to study these competing factors of covalent bonds.

CONCLUDING REMARKS

The data presented in this study provide a thorough examination of the fundamental interactions between the HOPO ligand and actinide ions across oxidation states and solvation environments, including changes in the covalency of the actinide-ligand interactions and the ability of the ligand to oxidize or reduce ions as necessary upon complexation. Calculated structures corroborate well with experimental values, including unprecedented EXAFS data on the Am(III), Cm(III), and Cf(III) complexes. The HOPO ligand is shown to be able to both oxidize early actinide ions and reduce later actinide ions, a key to its unparalleled complexation across the series. Charge donation from the ligand occurs largely from the coordinating oxygen atoms, while charge acceptance is driven almost entirely by the pyridine ring. These properties of the HOPO ligand—which is among the strongest actinide complexing ligands known—provide insight into future ligand design. These results also highlight the importance of energy degeneracy driven covalency for the later actinides. The increase in orbital mixing between the actinide 5f orbitals and the conjugated π orbital of the 1,2-HOPO units in the HOPO⁴⁻ ligand as the actinide series is traversed is an important part of the chemistry of the middle and later actinides and a likely target to be exploited by future ligands designed to separate these elements.

METHODS

Calculations. Structures of the metal–3,4,3-LI(1,2-HOPO) complexes were optimized using density functional theory (DFT) with the PBE functional,⁷⁷ relativistic ZORA Hamiltonian, and triple- ζ plus two polarization function (TZ2P) basis sets with the frozen core approximation applied to the inner shells [1s²–4f¹⁴] for actinide atoms and [1s²] for C, N and O atoms.^{78,79} Crystal structures for HOPO complexes have been found in two different conformers, termed A and

668 B for Ln complexes by Daumann et al., who determined that A is a
669 kinetic isomer that converts into B over time, which is the more
670 thermodynamically stable isomer based on DFT calculations.³¹ Similar
671 isomers have been observed for Sn⁴⁺ and Zr⁴⁺.^{43,80} The more
672 thermodynamically stable of these Ln-HOPO structures matches well
673 with available crystal structures of An–HOPO complexes inside the
674 protein siderocalin, which have only been found in this config-
675 uration.^{32,42} These structures were used as a starting point for the DFT
676 optimizations. Frequency calculations were performed to determine
677 thermodynamic properties of each structure. Calculations using the
678 hybrid PBE0 functional were used to determine thermodynamic and
679 electronic properties. The COSMO implicit solvation model^{81–84} was
680 used to model the complexes in aqueous and protein-like environ-
681 ments, using a dielectric constant of 4 and a radius of 3.45 Å for the
682 protein-like environment. All calculations were performed using ADF
683 2016.^{85,86}

684 **X-ray Absorption Spectroscopy.** Solution samples of Am, Cm,
685 and Cf complexed with HOPO were all prepared within 10 days of the
686 synchrotron measurements and loaded into triply contained aluminum
687 holders with kapton windows. The Am, Cm, and Cf masses were 27.1,
688 10.9, and 3.3 μg, respectively. The concentrations were 1.840, 0.614,
689 and 0.207 mM. The ratio ligand/metal was 1.3 to ensure total binding
690 of the radionuclides, and the pH was comprised between 7 and 8
691 (CAPS buffer).

692 X-ray absorption data were collected on BL 11–2 at the Stanford
693 Synchrotron Radiation Lightsource at the Am, Cm, and Cf L_{III} edges
694 using a Si(220) double-crystal monochromator. Harmonic rejection
695 was achieved with a Rh-coated mirror for the Am and Cm data, while
696 the monochromator was half-tuned for the Cf data.

697 Data were reduced using standard procedures^{87–89} using the
698 REXAFS suite of XAFS analysis codes.⁹⁰ In particular, after a pre-edge
699 subtraction using the Victoreen formula,⁸⁷ a 5 knot cubic spline (Am
700 and Cm) or a fifth order Chebychev polynomial (Cf) was used to
701 describe the embedded atom absorption μ_a when determining the
702 EXAFS function $\chi(k) = [\mu(k) - \mu_a(k)]/\mu_a(k)$, where $\mu(k)$ is the total
703 absorption after the pre-edge subtraction (that is, the absorption due
704 to the element and absorption edge of interest) and k is the
705 photoelectron wave vector given by $k = [(2m_e/\hbar)(E - E_0)]^{1/2}$, where
706 E is the incident energy, E_0 is the photoelectron threshold energy
707 arbitrarily defined by the energy at the half-height of the absorption
708 edge, and m_e is the rest mass of the electron.

709 Scattering phases and amplitudes were calculated using FEFF
710 10.0.1,⁹¹ and all fits were carried out in r -space using RSFIT within the
711 REXAFS suite of XAFS analysis codes.

712 EXAFS fit models were derived from the DFT results. It is
713 important to note that while the DFT models were used in the
714 calculation, the fitting methodology is only very weakly dependent on
715 the DFT geometry, as it reduces the complicated structure to only a
716 few pairs and models the bond length distribution with those shells
717 without further reference to the calculated geometry.

718 A more complete exposition of the EXAFS methods and results is
719 presented in the [Supporting Information](#).

720 ■ ASSOCIATED CONTENT

721 ■ Supporting Information

722 The Supporting Information is available free of charge on the
723 [ACS Publications website](#) at DOI: [10.1021/acs.inorgchem.8b00345](https://doi.org/10.1021/acs.inorgchem.8b00345).

725 Molecular orbital diagrams, delocalization of 5f orbitals
726 across the An series, Mulliken valence populations of An
727 ions in complexes, spin density on HOPO groups,
728 oxidation energy of bare ions, complexation energy in
729 differing solvation environments, Cartesian coordinates
730 of selected structures, EXAFS spectra, and fit results.
731 (PDF)

■ AUTHOR INFORMATION

Corresponding Authors

*(P.Y.) E-mail: pyang@lanl.gov.

*(E.R.B.) E-mail: erb@lanl.gov.

ORCID

Morgan P. Kelley: 0000-0001-5196-9821

Jing Su: 0000-0002-6895-2150

Rebecca J. Abergel: 0000-0002-3906-8761

Enrique R. Batista: 0000-0002-3074-4022

Ping Yang: 0000-0003-4726-2860

Notes

The authors declare no competing financial interest.

■ ACKNOWLEDGMENTS

We thank M. Antonio of Argonne National Laboratory for
sharing his Mo calibration data and his Mo foil. This work was
supported by the U.S. Department of Energy, Office of Science,
Office of Basic Energy Sciences, Heavy Elements Chemistry
Program at Los Alamos National Laboratory under contract
number DE-AC52-06NA25396 (M.P.K, E.R.B., and P.Y.) and
at the Lawrence Berkeley National Laboratory under Contract
DE-AC02-05CH1123 (R.J.A. and C.H.B.). Los Alamos Na-
tional Laboratory is operated by Los Alamos National Security,
LLC, for the National Nuclear Security Administration of U.S.
Department of Energy. Portions of this work were supported at
LANL by the Glenn T. Seaborg Institute Postdoctoral
Fellowship (J.S.). Calculations were completed using the
Molecular Science Computing Facilities in the William R.
Wiley Environmental Molecular Sciences Laboratory, a national
scientific user facility sponsored by the U.S. DOE BER and
located at Pacific Northwest National Laboratory. Use of the
Stanford Synchrotron Radiation Lightsource, SLAC National
Accelerator Laboratory, is supported by the U.S. DOE, Office
of Science, Office of Basic Energy Sciences under Contract No.
DE-AC02-76SF00515.

■ REFERENCES

- (1) Whitcomb, R. C.; Ansari, A. J.; Buzzell, J. J.; McCurley, M. C.; Miller, C. W.; Smith, J. M.; Evans, D. L. A Public Health Perspective on the U.S. Response to the Fukushima Radiological Emergency. *Health Phys.* **2015**, *108* (3), 357–363.
- (2) Silva, R. J.; Nitsche, H. Actinide Environmental Chemistry. *Radiochim. Acta* **1995**, *70–71* (S1), 377–396.
- (3) *Management of Persons Contaminated with Radionuclides Handbook: Recommendations of the National Council on Radiation Protection and Measurements*; National Council on Radiation Protection and Measurements: Bethesda, MD, 2009.
- (4) Durbin, P. W. Actinides in Animals and Man. *Chemistry of the Actinide and Transactinide Elements* **2006**, *5*, 3339–3440.
- (5) Raymond, K. N.; Matzanke, B.; Müller, G. Complexation of Iron by Siderophores: A Review of Their Solution and Structural Chemistry and Biological Function. *Top. Curr. Chem.* **1984**, *123*, 49–102.
- (6) White, D. L.; Durbin, P. W.; Jeung, N.; Raymond, K. N. Specific Sequestering Agents for the Actinides. 16. Synthesis and Initial Biological Testing of Polydentate Oxohydroxypyridinecarboxylate Ligands. *J. Med. Chem.* **1988**, *31*, 11–18.
- (7) Gorden, A. E. V.; Xu, J.; Raymond, K. N.; Durbin, P. Rational Design of Sequestering Agents for Plutonium and Other Actinides. *Chem. Rev.* **2003**, *103* (11), 4207–4282.
- (8) Sturzbecher-Hoehne, M.; Deblonde, G. J. P.; Abergel, R. J. Solution Thermodynamic Evaluation of Hydroxypyridinonate Chelators 3,4,3-LI(1,2-HOPO) and 5-LIO(Me-3,2-HOPO) for UO₂(VI) and Th(IV) Decorporation. *Radiochim. Acta* **2013**, *101* (6), 359–366.

- 793 (9) Sturzbecher-Hoehne, M.; Choi, T. A.; Abergel, R. J.
794 Hydroxypyridinone Complex Stability of Group (IV) Metals and
795 Tetravalent F-Block Elements: The Key to the next Generation of
796 Chelating Agents for Radiopharmaceuticals. *Inorg. Chem.* **2015**, *54* (7),
797 3462–3468.
- 798 (10) Sturzbecher-Hoehne, M.; Kullgren, B.; Jarvis, E. E.; An, D. D.;
799 Abergel, R. J. Highly Luminescent and Stable Hydroxypyridinone
800 Complexes: A Step towards New Curium Decontamination Strategies.
801 *Chem. - Eur. J.* **2014**, *20* (32), 9962–9968.
- 802 (11) Sturzbecher-Hoehne, M.; Ng Pak Leung, C.; D'Aléo, A.;
803 Kullgren, B.; Prigent, A.-L.; Shuh, D. K.; Raymond, K. N.; Abergel, R.
804 J. 3,4,3-LI(1,2-HOPO): In Vitro Formation of Highly Stable
805 Lanthanide Complexes Translates into Efficacious in Vivo Europium
806 Decorporation. *Dalton Trans.* **2011**, *40* (33), 8340–8346.
- 807 (12) Durbin, P. W.; Kullgren, B.; Xu, J.; Raymond, K. N. In Vivo
808 Chelation of Am(III), Pu(IV), Np(V), and U(VI) in Mice by TREN-
809 (Me-3,2-HOPO). *Radiat. Prot. Dosim.* **1994**, *53* (1–4), 305–309.
- 810 (13) An, D. D.; Kullgren, B.; Jarvis, E. E.; Abergel, R. J. From Early
811 Prophylaxis to Delayed Treatment: Establishing the Plutonium
812 Decorporation Activity Window of Hydroxypyridinone Chelating
813 Agents. *Chem.-Biol. Interact.* **2017**, *267*, 80–88.
- 814 (14) Xu, J.; Kullgren, B.; Durbin, P. W.; Raymond, K. N. Specific
815 Sequestering Agents for the Actinides. 28. Synthesis and Initial
816 Evaluation of Multidentate 4-Carbamoyl-3-Hydroxy-1-Methyl-2(1H)-
817 Pyridinone Ligands for in Vivo plutonium(IV) Chelation. *J. Med.*
818 *Chem.* **1995**, *38* (14), 2606–2614.
- 819 (15) Xu, J.; Raymond, K. N. Uranyl Sequestering Agents: Correlation
820 of Properties and Efficacy with Structure for UO₂²⁺ + Complexes of
821 Linear Tetradentate 1-Methyl-3-Hydroxy-2(1H)-Pyridinone Ligands
822 1. *Inorg. Chem.* **1999**, *38* (20), 308–315.
- 823 (16) An, D. D.; Villalobos, J. A.; Morales-Rivera, J. A.; Rosen, C. J.;
824 Bjornstad, K. A.; Gauny, S. S.; Choi, T. A.; Sturzbecher-Hoehne, M.;
825 Abergel, R. J. ²³⁸Pu Elimination Profiles after Delayed Treatment with
826 3,4,3-LI (1,2-HOPO) in Female and Male Swiss-Webster Mice. *Int. J.*
827 *Radiat. Biol.* **2014**, *90* (11), 1055–1061.
- 828 (17) Abergel, R. J.; Durbin, P. W.; Kullgren, B.; Ebbe, S. N.; Xu, J.;
829 Chang, P. Y.; Bunin, D. I.; Blakely, E. A.; Bjornstad, K. A.; Rosen, C. J.;
830 Shuh, D. K.; Raymond, K. N. Biomimetic Actinide Chelators: An
831 Update on the Preclinical Development of the Orally Active
832 Hydroxypyridinone Decorporation Agents 3,4,3-LI(1,2-HOPO) and
833 5-LIO(Me-3,2-HOPO). *Health Phys.* **2010**, *99* (3), 401–407.
- 834 (18) Choi, T. A.; Furimsky, A. M.; Swezey, R.; Bunin, D. I.; Byrge, P.;
835 Iyer, L. V.; Chang, P. Y.; Abergel, R. J. In Vitro Metabolism and
836 Stability of the Actinide Chelating Agent 3,4,3-LI(1,2-HOPO). *J.*
837 *Pharm. Sci.* **2015**, *104* (5), 1832–1838.
- 838 (19) Durbin, P. W.; Kullgren, B.; Xu, J.; Raymond, K. N.
839 Development of Decorporation Agents for the Actinides. *Radiat.*
840 *Prot. Dosim.* **1998**, *79* (1–4), 433–443.
- 841 (20) Xu, J.; Churchill, D. G.; Botta, M.; Raymond, K. N.
842 Gadolinium(III) 1,2-Hydroxypyridinone-Based Complexes: Toward
843 MRI Contrast Agents of High Relaxivity. *Inorg. Chem.* **2004**, *43* (18),
844 5492–5494.
- 845 (21) Datta, A.; Raymond, K. N. Gd-Hydroxypyridinone (HOPO)-
846 Based High-Relaxivity Magnetic Resonance Imaging (MRI) Contrast
847 Agents. *Acc. Chem. Res.* **2009**, *42* (7), 938–947.
- 848 (22) Thompson, M. K.; Botta, M.; Nicolle, G.; Helm, L.; Aime, S.;
849 Merbach, A. E.; Raymond, K. N. A Highly Stable Gadolinium
850 Complex with a Fast, Associative Mechanism of Water Exchange. *J.*
851 *Am. Chem. Soc.* **2003**, *125* (47), 14274–14275.
- 852 (23) Werner, E. J.; Datta, A.; Jocher, C. J.; Raymond, K. N. High-
853 Relaxivity MRI Contrast Agents: Where Coordination Chemistry
854 Meets Medical Imaging. *Angew. Chem., Int. Ed.* **2008**, *47* (45), 8568–
855 8580.
- 856 (24) Captain, I.; Deblonde, G. J.-P.; Rupert, P. B.; An, D. D.; Illy, M.
857 C.; Rostan, E.; Ralston, C. Y.; Strong, R. K.; Abergel, R. J. Engineered
858 Recognition of Tetravalent Zirconium and Thorium by Chelator-
859 Protein Systems: Toward Flexible Radiotherapy and Imaging Plat-
860 forms. *Inorg. Chem.* **2016**, *55* (22), 11930–11936.
- (25) Deri, M. A.; Ponnala, S.; Zeglis, B. M.; Pohl, G.; Dannenberg, J. 861
J.; Lewis, J. S.; Francesconi, L. C. Alternative Chelator for ⁸⁹Zr 862
Radiopharmaceuticals: Radiolabelling and Evaluation of 3,4,3-(LI-1,2- 863
HOPO). *J. Med. Chem.* **2014**, *57*, 4849–4860. 864
- (26) Daumann, L. J.; Tatum, D. S.; Andolina, C. M.; Pacold, J. I.; 865
D'Aléo, A.; Law, G. L.; Xu, J.; Raymond, K. N. Effects of Ligand 866
Geometry on the Photophysical Properties of Photoluminescent 867
Eu(III) and Sm(III) 1-Hydroxypyridin-2-One Complexes in Aqueous 868
Solution. *Inorg. Chem.* **2016**, *55* (1), 114–124. 869
- (27) Daumann, L. J.; Werther, P.; Ziegler, M. J.; Raymond, K. N. 870
Siderophore Inspired Tetra- and Octadentate Antenna Ligands for 871
Luminescent Eu(III) and Tb(III) Complexes. *J. Inorg. Biochem.* **2016**, 872
162, 263–273. 873
- (28) Abergel, R. J.; D'Aleo, A.; Ng Pak Leung, C.; Shuh, D. K.; 874
Raymond, K. N. Using the Antenna Effect as a Spectroscopic Tool: 875
Photophysics and Solution Thermodynamics of the Model Lumines- 876
cent Hydroxypyridinone Complex [Eu III(3,4,3-LI(1,2-HOPO))].- 877
Inorg. Chem. **2009**, *48* (23), 10868–10870. 878
- (29) Agbo, P.; Xu, T.; Sturzbecher-Hoehne, M.; Abergel, R. J. 879
Enhanced Ultraviolet Photon Capture in Ligand-Sensitized Nano- 880
crystals. *ACS Photonics* **2016**, *3* (4), 547–552. 881
- (30) Agbo, P.; Abergel, R. J. Ligand-Sensitized Lanthanide Nano- 882
crystals: Merging Solid-State Photophysics and Molecular Solution 883
Chemistry. *Inorg. Chem.* **2016**, *55* (20), 9973–9980. 884
- (31) Daumann, L. J.; Tatum, D. S.; Snyder, B. E. R.; Ni, C.; Law, G. 885
L.; Solomon, E. I.; Raymond, K. N. New Insights into Structure and 886
Luminescence of Eu(III) and Sm(III) Complexes of the 3,4,3-LI(1,2- 887
HOPO) Ligand. *J. Am. Chem. Soc.* **2015**, *137* (8), 2816–2819. 888
- (32) Moore, E. G.; Xu, J.; Jocher, C. J.; Werner, E. J.; Raymond, K. N. 889
Cymothoe Sangaris": An Extremely Stable and Highly Luminescent 890
1,2-Hydroxypyridinone Chelate of Eu(III). *J. Am. Chem. Soc.* **2006**, 891
128 (33), 10648–10649. 892
- (33) Deblonde, G. J.-P.; Sturzbecher-Hoehne, M.; Rupert, P. B.; An, 893
D. D.; Illy, M.-C.; Ralston, C. Y.; Brabec, J.; de Jong, W. A.; Strong, R. 894
K.; Abergel, R. J. Chelation and Stabilization of Berkelium in Oxidation 895
State + IV. *Nat. Chem.* **2017**, *9*, 843–849. 896
- (34) Zwier, J. M.; Bazin, H.; Lamarque, L.; Mathis, G. Luminescent 897
Lanthanide Cryptates: From the Bench to the Bedside. *Inorg. Chem.* 898
2014, *53* (4), 1854–1866. 899
- (35) Bünzli, J.-C. G.; Eliseeva, S. V. Intriguing Aspects of Lanthanide 900
Luminescence. *Chem. Sci.* **2013**, *4* (5), 1939–1949. 901
- (36) Butler, S. J.; Parker, D. Anion Binding in Water at Lanthanide 902
Centres: From Structure and Selectivity to Signalling and Sensing. 903
Chem. Soc. Rev. **2013**, *42*, 1652–1666. 904
- (37) Faulkner, S.; Pope, S. J. A.; Burton-Pye, B. P. Lanthanide 905
Complexes for Luminescence Imaging Applications. *Appl. Spectrosc.* 906
2005, *40* (1), 1–31. 907
- (38) Wang, X.; Chang, H.; Xie, J.; Zhao, B.; Liu, B.; Xu, S.; Pei, W.; 908
Ren, N.; Huang, L.; Huang, W. Recent Developments in Lanthanide- 909
Based Luminescent Probes. *Coord. Chem. Rev.* **2014**, *273–274*, 201– 910
212. 911
- (39) Deblonde, G. J.-P.; Sturzbecher-Hoehne, M.; Abergel, R. J. 912
Solution Thermodynamic Stability of Complexes Formed with the 913
Octadentate Hydroxypyridinone Ligand 3,4,3-LI(1,2-HOPO): A 914
Critical Feature for Efficient Chelation of Lanthanide(IV) and 915
Actinide(IV) Ions. *Inorg. Chem.* **2013**, *52*, 8805–8811. 916
- (40) Sturzbecher-Hoehne, M.; Yang, P.; D'Aleo, A.; Abergel, R. J. 917
Intramolecular Sensitization of Americium Luminescence in Solution: 918
Shining Light on Short-Lived Forbidden 5f Transitions. *Dalt. Trans.* 919
2016, *45*, 9912. 920
- (41) Xu, J.; Radkov, E.; Ziegler, M.; Raymond, K. N. Plutonium (IV) 921
Sequestration: Structural and Thermodynamic Evaluation of the 922
Extraordinarily Stable Cerium (IV) Hydroxypyridinone Complexes 923
1. *Inorg. Chem.* **2000**, *39* (iv), 4156–4164. 924
- (42) Allred, B. E.; Rupert, P. B.; Gauny, S. S.; An, D. D.; Ralston, C. 925
Y.; Sturzbecher-Hoehne, M.; Strong, R. K.; Abergel, R. J. Siderocalin- 926
Mediated Recognition, Sensitization, and Cellular Uptake of Actinides. 927
Proc. Natl. Acad. Sci. U. S. A. **2015**, *112* (33), 10342–10347. 928

- 929 (43) Deri, M. A.; Ponnala, S.; Kozlowski, P.; Burton-Pye, B. P.; Cicek, 998
930 H. T.; Hu, C.; Lewis, J. S.; Francesconi, L. C. P-SCN-Bn-HOPO: A 999
931 Superior Bifunctional Chelator for 89Zr ImmunoPET. *Bioconjugate*
932 *Chem.* **2015**, *26* (12), 2579–2591.
- 933 (44) Ferrier, M. G.; Batista, E. R.; Berg, J. M.; Birnbaum, E. R.; Cross, 1000
934 J. N.; Engle, J. W.; La Pierre, H. S.; Kozimor, S. A.; Lezama Pacheco, J. 1001
935 S.; Stein, B. W.; Stieber, S. C. E.; Wilson, J. J. Spectroscopic and 1002
936 Computational Investigation of Actinium Coordination Chemistry. 1003
937 *Nat. Commun.* **2016**, *7*, 12312.
- 938 (45) Schnaars, D. D.; Gaunt, A. J.; Hayton, T. W.; Jones, M. B.; 1004
939 Kirker, I.; Kaltsoyannis, N.; May, I.; Reilly, S. D.; Scott, B. L.; Wu, G. 1005
940 Bonding Trends Traversing the Tetravalent Actinide Series: Synthesis, 1006
941 Structural, and Computational Analysis of An IV (Ar Acnac) 4 1007
942 Complexes (An = Th, U, Np, Pu; Ar Acnac = Ar N C(Ph)CHC(Ph) 1008
943 O; Ar = 3,5-T Bu 2 C 6 H 3. *Inorg. Chem.* **2012**, *51* (15), 8557–8566.
- 944 (46) Kaltsoyannis, N. Does Covalency Increase or Decrease across 1009
945 the Actinide Series? Implications for Minor Actinide Partitioning. 1010
946 *Inorg. Chem.* **2013**, *52*, 3407–3413.
- 947 (47) Bradley, J. A.; Yang, P.; Batista, E. R.; Boland, K. S.; Burns, C. J.; 1011
948 Clark, D. L.; Conradson, S. D.; Kozimor, S. A.; Martin, R. L.; Seidler, 1012
949 G. T.; Scott, B. L.; Shuh, D. K.; Tyliczszak, T.; Wilkerson, M. P.; 1013
950 Wolfsberg, L. E. Experimental and Theoretical Comparison of the O 1014
951 K-Edge Nonresonant Inelastic X-Ray Scattering and X-Ray Absorption 1015
952 Spectra of NaReO₄. *J. Am. Chem. Soc.* **2010**, *132* (39), 13914–13921.
- 953 (48) Minasian, S. G.; Keith, J. M.; Batista, E. R.; Boland, K. S.; Clark, 1016
954 D. L.; Kozimor, S. a.; Martin, R. L.; Shuh, D. K.; Tyliczszak, T. New 1017
955 Evidence for 5f Covalency in Actinocenes Determined from Carbon 1018
956 K-Edge XAS and Electronic Structure Theory. *Chem. Sci.* **2014**, *5*, 351.
- 957 (49) Gutowski, K. E.; Dixon, D. A. Predicting the Energy of the 1019
958 Water Exchange Reaction and Free Energy of Solvation for the Uranyl 1020
959 Ion in Aqueous Solution. *J. Phys. Chem. A* **2006**, *110* (28), 8840–8856.
- 960 (50) Parmar, P.; Samuels, A.; Clark, A. E. Applications of Polarizable 1021
961 Continuum Models to Determine Accurate Solution-Phase Thermo- 1022
962 chemical Values across a Broad Range of Cation Charge - The Case of 1023
963 U(III-VI). *J. Chem. Theory Comput.* **2015**, *11* (1), 55–63.
- 964 (51) Kelley, M. P.; Yang, P.; Clark, S. B.; Clark, A. E. Structural and 1024
965 Thermodynamic Properties of the Cm^{III} Ion Solvated by Water and 1025
966 Methanol. *Inorg. Chem.* **2016**, *55* (10), 4992–4999.
- 967 (52) Atta-Fynn, R.; Bylaska, E. J.; De Jong, W. A. Importance of 1026
968 Counteranions on the Hydration Structure of the Curium Ion. *J. Phys.*
969 *Chem. Lett.* **2013**, *4* (13), 2166–2170.
- 970 (53) D'Aléo, A.; Moore, E. G.; Szigethy, G.; Xu, J.; Raymond, K. N. 1027
971 Aryl Bridged 1-Hydroxypyridin-2-One: Effect of the Bridge on the 1028
972 Eu(III) Sensitization Process. *Inorg. Chem.* **2009**, *48* (19), 9316–9324.
- 973 (54) Moore, E. G.; Xu, J.; Jocher, C. J.; Corneille, T. M.; Raymond, 1029
974 K. N. Eu(III) Complexes of Functionalized Octadentate 1- 1030
975 Hydroxypyridin-2-Ones: Stability, Bioconjugation, and Luminescence 1031
976 Resonance Energy Transfer Studies. *Inorg. Chem.* **2010**, *49* (21), 1032
977 9928–9939.
- 978 (55) Moore, E.; Xu, J.; Jocher, C.; Castro-Rodriguez, I.; Raymond, K. 1033
979 N. Highly Luminescent Lanthanide Complexes of 1-Hydroxy-2- 1034
980 Pyridinones. *Inorg. Chem.* **2008**, *47*, 3105–3118.
- 981 (56) Gorden, A. E. V.; Shuh, D. K.; Tiedemann, B. E. F.; Wilson, R. 1035
982 E.; Xu, J.; Raymond, K. N. Sequestered Plutonium: [PuIV{SLIO(Me- 1036
983 3,2-HOPO)}₂] - The First Structurally Characterized Plutonium 1037
984 Hydroxypyridonate Complex. *Chem. - Eur. J.* **2005**, *11* (9), 2842– 1038
985 2848.
- 986 (57) Gorden, A. E. V.; Xu, J.; Szigethy, G.; Oliver, A.; Shuh, D. K.; 1039
987 Raymond, K. N. Characterization of a Mixed Salt of 1-Hydroxypyridin- 1040
988 2-One Pu (IV) Complexes. *J. Am. Chem. Soc.* **2007**, *129* (IV), 6674– 1041
989 6675.
- 990 (58) Riley, P. E.; Abu-dari, K.; Raymond, K. N. Specific Sequestering 1042
991 Agents for the Actinides. 9. Synthesis of Metal Complexes of 1- 1043
992 Hydroxy-2-Pyridinone and the Crystal Structure of Tetrakis(1-Oxy-2- 1044
993 pyridonato)aquothorium(IV) Dihydrate. *Inorg. Chem.* **1983**, *22* (2), 1045
994 3940–3944.
- 995 (59) Scarrow, R. C.; Riley, P. E.; Abu-Dari, K.; White, D. L.; 1046
996 Raymond, K. N. NC19-Ferric Ion Sequestering Agents. 13. Synthesis, 1047
997 Structures, and Thermodynamics of Complexation of cobalt(III) and 1048
iron(III) Tris Complexes of Several Chelating Hydroxypyridinones. 998
Inorg. Chem. **1985**, *24* (6), 954–967.
- (60) Downward, L.; Booth, C. H.; Lukens, W. W.; Bridges, F. A 999
1000 Variation of the F-Test for Determining Statistical Relevance of 1001
1002 Particular Parameters in EXAFS Fits. *AIP Conf. Proc.* **2006**, *882*, 129– 1003
131.
- (61) Shannon, R. D. Revised Effective Ionic Radii and Systematic 1004
1005 Studies of Interatomic Distances in Halides and Chalcogenides. *Acta*
Crystallogr., Sect. A: Cryst. Phys., Diffr., Theor. Gen. Crystallogr. **1976**, 1006
A32 (5), 751–767.
- (62) Ferrier, M. G.; Stein, B. W.; Batista, E. R.; Berg, J. M.; Birnbaum, 1007
1008 E. R.; Engle, J. W.; John, K. D.; Kozimor, S. A.; Lezama Pacheco, J. S.; 1009
1010 Redman, L. N. Synthesis and Characterization of the Actinium Aquo 1011
1012 Ion. *ACS Cent. Sci.* **2017**, *3* (3), 176–185.
- (63) Kimura, T.; Choppin, G. R. Luminescence Study on 1012
1013 Determination of the Hydration Number of Cm(III). *J. Alloys*
Compd. **1994**, *213-214*, 313–317.
- (64) Atta-fynn, R.; Bylaska, E. J.; Schenter, G. K.; de Jong, W. A. De. 1015
1016 Hydration Shell Structure and Dynamics of Curium (III) in Aqueous 1017
1018 Solution: First Principles and Empirical Studies. *J. Phys. Chem. A* **2011**, 1019
115 (Iii), 4665–4677.
- (65) D'Angelo, P.; Martelli, F.; Spezia, R.; Filippini, A.; Denecke, M. 1019
1020 A. Hydration Properties and Ionic Radii of actinide(III) Ions in 1020
1021 Aqueous Solution. *Inorg. Chem.* **2013**, *52* (18), 10318–10324.
- (66) Banik, N. L.; Vallet, V.; Réal, F.; Belmecheri, R. M.; 1022
1023 Schimmelpennig, B.; Rothe, J.; Marsac, R.; Lindqvist-Reis, P.; 1024
1025 Walther, C.; Denecke, M. a; Marquardt, C. M. First Structural 1026
1027 Characterization of Pa(IV) in Aqueous Solution and Quantum 1028
1029 Chemical Investigations of the Tetravalent Actinides up to Bk(IV): 1029
1030 The Evidence of a Curium Break. *Dalton Trans.* **2016**, *45* (2), 453– 1031
1032 457.
- (67) Wiebke, J.; Moritz, A.; Cao, X.; Dolg, M. Approaching 1032
1033 actinide(+III) Hydration from First Principles. *Phys. Chem. Chem.*
Phys. **2007**, *9*, 459–465.
- (68) Minasian, S. G.; Keith, J. M.; Batista, E. R.; Boland, K. S.; Clark, 1032
1033 D. L.; Conradson, S. D.; Kozimor, S. A.; Martin, R. L.; Schwarz, D. E.; 1034
1035 Shuh, D. K.; Wagner, G. L.; Wilkerson, M. P.; Wolfsberg, L. E.; Yang, 1036
1037 P. Determining Relative F and D Orbital Contributions to M-Cl 1037
1038 Covalency in MCl₆²⁻ (M = Ti, Zr, Hf, U) and UOCl₅⁻ Using Cl K- 1038
1039 Edge X-Ray Absorption Spectroscopy and Time-Dependent Density 1039
1040 Functional Theory. *J. Am. Chem. Soc.* **2012**, *134* (12), 5586–5597.
- (69) Tassell, M. J.; Kaltsoyannis, N. Covalency in AnCp₄ (An = Th– 1039
1040 Cm): A Comparison of Molecular Orbital, Natural Population and 1040
1041 Atoms-in-Molecules Analyses. *Dalt. Trans.* **2010**, *39*, 6719–6725.
- (70) Prodan, I. D.; Scuseria, G. E.; Martin, R. L. Covalency in the 1042
1043 Actinide Dioxides: Systematic Study of the Electronic Properties Using 1043
1044 Screened Hybrid Density Functional Theory. *Phys. Rev. B: Condens.*
Matter Mater. Phys. **2007**, *76* (3), 033101.
- (71) Roy, L. E.; Batista, E. R.; Hay, P. J. Theoretical Studies on the 1046
1047 Redox Potentials of Fe Dinuclear Complexes as Models for 1047
1048 Hydrogenase. *Inorg. Chem.* **2008**, *47* (20), 9228–9237.
- (72) Liu, J.-B.; Chen, G. P.; Huang, W.; Clark, D. L.; Schwarz, W. H. 1049
1050 E.; Li, J. Bonding Trends across the Series of Tricarbonato-Actinyl 1050
1051 Anions [(AnO₂)(CO₃)₃]⁴⁻ (An = U–Cm): The Plutonium Turn. 1051
1052 *Dalt. Trans.* **2017**, *46* (8), 2542–2550.
- (73) Huang, W.; Jiang, N.; Schwarz, W. H. E.; Yang, P.; Li, J. 1053
1054 Diversity of Chemical Bonding and Oxidation States in MS₄Molecules 1054
1055 of Group 8 Elements. *Chem. - Eur. J.* **2017**, *23* (44), 10580–10589.
- (74) Bursten, E.; Rhodes, F.; Strittmatter, J. The Bonding in Tris(n⁵- 1056
1057 Cyclopentadienyl Actinide Complexes IV: Electronic Structure Effects 1057
1058 in AnCl₃ and (n⁵-C₅H₅)₃An (An = Th–Cf) Complexes. *J. Less-Common*
Met. **1989**, *149*, 207–211.
- (75) Neidig, M. L.; Clark, D. L.; Martin, R. L. Covalency in F- 1060
1061 Element Complexes. *Coord. Chem. Rev.* **2013**, *257* (2), 394–406.
- (76) Kelley, M. P.; Su, J.; Urban, M.; Luckey, M.; Batista, E. R.; Yang, 1062
1063 P.; Shafer, J. C. On the Origin of Covalent Bonding in Heavy 1063
1064 Actinides. *J. Am. Chem. Soc.* **2017**, *139*, 9901–9908.

- 1065 (77) Perdew, J. P.; Burke, K.; Ernzerhof, M. Generalized Gradient
1066 Approximation Made Simple. *Phys. Rev. Lett.* **1996**, *77* (18), 3865–
1067 3868.
- 1068 (78) Cao, X.; Dolg, M.; Stoll, H. Valence Basis Sets for Relativistic
1069 Energy-Consistent Small-Core Actinide Pseudopotentials. *J. Chem.*
1070 *Phys.* **2003**, *118* (2), 487–496.
- 1071 (79) Kuchle, W.; Dolg, M.; Stoll, H.; Preuss, H. Energy-Adjusted
1072 Pseudopotentials for the Actinides. Parameter Sets and Test
1073 Calculations for Thorium and Thorium Monoxide. *J. Chem. Phys.*
1074 **1994**, *100* (10), 7535–7542.
- 1075 (80) Deblonde, G. J.-P.; Lohrey, T. D.; An, D. D.; Abergel, R. J. Toxic
1076 Heavy Metal – Pb, Cd, Sn – Complexation by the Octadentate
1077 Hydroxypyridinonate Ligand Archetype 3,4,3-LI(1,2-HOPO). *New J.*
1078 *Chem.* **2018**, DOI: 10.1039/C7NJ04559J.
- 1079 (81) Klamt, A.; Schuurmann, G. COSMO: A New Approach to
1080 Dielectric Screening in Solvents with Explicit Expressions for the
1081 Screening Energy and Its Gradient. *J. Chem. Soc., Perkin Trans. 2* **1993**,
1082 *2*, 799.
- 1083 (82) Klamt, A. Conductor-like Screening Model for Real Solvents: A
1084 New Approach to the Quantitative Calculation of Solvation
1085 Phenomena. *J. Phys. Chem.* **1995**, *99* (7), 2224–2235.
- 1086 (83) Klamt, A.; Jonas, V. Treatment of the Outlying Charge in
1087 Continuum Solvation Models. *J. Chem. Phys.* **1996**, *105* (May), 9972–
1088 9981.
- 1089 (84) Pye, C. C.; Ziegler, T. An Implementation of the Conductor-like
1090 Screening Model of Solvation within the Amsterdam Density
1091 Functional Package. *Theor. Chem. Acc.* **1999**, *101*, 396–408.
- 1092 (85) Te Velde, G.; Bickelhaupt, F. M.; Baerends, E. J.; Fonseca
1093 Guerra, C.; van Gisbergen, S. J. a.; Snijders, J. G.; Ziegler, T. Chemistry
1094 with ADF. *J. Comput. Chem.* **2001**, *22* (9), 931–967.
- 1095 (86) Fonseca Guerra, F. C.; Snijders, J. G.; Te Velde, G.; Baerends, E.
1096 J. Towards an Order- N DFT Method. *Theor. Chem. Acc.* **1998**, *99* (6),
1097 391–403.
- 1098 (87) Li, G. G.; Bridges, F.; Booth, C. H. X-Ray-Absorption Fine-
1099 Structure Standards: A Comparison of Experiment and Theory. *Phys.*
1100 *Rev. B: Condens. Matter Mater. Phys.* **1995**, *52* (9), 6332–6348.
- 1101 (88) Hayes, T. M.; Boyce, J. B. EXAFS Spectroscopy. *Solid State Phys.*
1102 **1983**, *37*, 173.
- 1103 (89) Booth, C. H.; Hu, Y.-J. Confirmation of Standard Error Analysis
1104 Techniques Applied to EXAFS Using Simulations. *J. Phys. Conf. Ser.*
1105 **2009**, *190*, 012028.
- 1106 (90) Booth, C. H. RSXAP Analysis Package. [http://lise.lbl.gov/
1107 RSXAP/](http://lise.lbl.gov/R SXAP/) 2016.
- 1108 (91) Rehr, J. J.; Kas, J. J.; Vila, F. D.; Prange, M. P.; Jorissen, K.
1109 Parameter-Free Calculations of X-Ray Spectra with FEFF9. *Phys.*
1110 *Chem. Chem. Phys.* **2010**, *12* (21), 5503–5513.