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Synthesis and Lanthanide Coordination Properties of New 2,6-Bis(*N*-*tert*-butylacetamide)pyridine and 2,6-Bis(*N*-*tert*-butylacetamide)pyridine-*N*-oxide Ligands

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The compound 2,6-bis(*N*-*tert*-butylacetamide)pyridine (**2**) was obtained via a Ritter synthesis, and oxidation with oxone provided the title pyridine-*N*-oxide (**3**). The compounds were characterized by spectroscopic methods, and the molecular structure of the *N*-oxide was determined by single-crystal X-ray diffraction methods. The coordination chemistry with $Eu(NO_3)_3$ was examined by using 1:1 and 2:1 ligand/Eu ratios, and a single-crystal X-ray analysis for $Eu(\mathbf{3})(NO_3)_3(H_2O)$ was completed. The ligand **3** is found to chelate in a tridentate fashion on the Eu(III).

Introduction

One method of treatment under consideration for processing of high-level radioactive fuel materials involves nuclear incineration.[1] The success of the approach, in part, depends on the separation of minor actinides Am and Cm from the dominant actinides U and Pu prior to incineration. Therefore, there is fundamental interest, as well as practical demands, for the development of new selective coordination and separations chemistry for these species in aqueous solutions.[2−4] Several families of ligands such as carbamoylmethylphosphonates (CMP), $(RO)_2P(O)CH_2C(O)NR_2$,[5] carbamoylmethylphosphine oxides (CMPO), $R_2P(O)CH_2C(O)NR_2$,[6−9] and alkyl malonamides,[10−17] $[RR'NC(O)]_2CR''H$, have attracted the greatest attention as selective actinide ion chelators due in part to their stability toward strong radiation fields, as well as their ability to function in contact with the acidic aqueous solutions typically used to handle the actinide ions. In our group, we have been developing another family of ligands that offer promising performance in actinide separations: phosphinomethylpyridine-*N*-oxides, **NOPO** and **NOPOPO**.[18−28]

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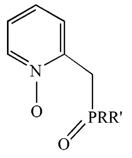
(1) Draganic, I. G.; Draganic, Z. D.; Adloff, J. P. *Radiation and Radioactivity on Earth and Beyond*; CRC Press: Boca Raton, FL, 1990.
(2) Madic, C.; Hudson, M. J.; Liljenzin, J. O.; Glatz, J. P.; Nannicini, R.; Kolarik, Z.; Odoj, R. *New Partitioning Techniques for Minor Actinides*; Project Report EUR 19149 En; European Commission: Luxembourg, 2000.
(3) Mathur, J. N.; Murali, M. S.; Nash, K. L. *Solvent Extr. Ion Exch.* **2001**, *19*, 357−390.
(4) Nash, K. L.; Madic, C.; Mathur, J. N. Actinide Separation Science and Technology. In *The Chemistry of the Actinide and Transactinide Elements*; Springer: Berlin, in press, Chapter 24.
(5) Horwitz, E. P.; Martin, K. A.; Diamond, H.; Kaplan, H. *Solvent Extr. Ion Exch.* **1986**, *4*, 449−494.
(6) Horwitz, E. P.; Kalina, D. G.; Diamond, H.; Vandegrift, G. F.; Schulz, W. W. *Solvent Extr. Ion Exch.* **1985**, *3*, 75−109.
(7) Ozawa, M.; Koma, Y.; Nomura, K.; Tanaka, Y. *J. Alloys Compd.* **1988**, *271−273*, 538−543.
(8) Mathur, J. N.; Murali, M. S.; Natarajan, P. R.; Badheka, L. P.; Bannerji, A.; Ramanujam, A.; Dhami, P. S.; Gopalakrishnan, V.; Dhumwad, R. K.; Rao, M. K. *Waste Manage. (Oxford)* **1993**, *13*, 317−325.
(9) Myasoedov, B. F.; Chmutova, M. K.; Smirnov, I. V.; Shadrin, A. U. In *Global '93: Future Nuclear Systems: Emerging Fuel Cycles and Waste Disposal Options*; American Nuclear Society: La Grange Park, IL, 1993.
(10) Cuillerdier, C.; Musikas, C.; Hoel, P.; Nigond, L.; Vitart, X. *Sep. Sci. Technol.* **1991**, *26*, 1229−1244.
(11) Tan, X. F.; Wang, Y. S.; Tan, T. Z.; Zhou, G. F.; Bao, B. R. *J. Radioanal. Nucl. Chem.* **1999**, *242*, 123−126.
(12) McNamara, B. K.; Lumetta, G. J.; Rapko, B. M. *Solvent Extr. Ion Exch.* **1999**, *17*, 1403−1421.
(13) Lumetta, G. J.; McNamara, B. K.; Rapko, B. M.; Hutchinson, J. M. *Inorg. Chim. Acta* **1999**, *293*, 195−205.
(14) Spjuth, L.; Liljenzin, J. O.; Hudson, M. J.; Drew, M. G. B.; Iveson, P. B.; Madic, C. *Solvent Extr. Ion Exch.* **2000**, *18*, 1−23.
(15) Facchini, A.; Amato, L.; Modolo, G.; Nannicini, R.; Madic, C.; Baron, P. *Sep. Sci. Technol.* **2000**, *35*, 1055−1068.
(16) Courson, O.; Lebrun, M.; Malmbeck, R.; Pagliosa, G.; Romer, K.; Satmark, B.; Glatz, J. P. *Radiochim. Acta* **2000**, *88*, 857−863.
(17) Lumetta, G. J.; Rapko, B. M.; Garza, P. A.; Hay, B. P.; Gilbertson, R. D.; Weakley, T. J. R.; Hutchinson, J. E. *J. Am. Chem. Soc.* **2002**, *124*, 5644−5645.
(18) Rapko, B. M.; Duesler, E. N.; Smith, P. H.; Paine, R. T.; Ryan, R. R. *Inorg. Chem.* **1993**, *32*, 2164−2174.
(19) Englehardt, U.; Rapko, B. M.; Duesler, E. N.; Frutos, D.; Paine, R. T. *Polyhedron* **1995**, *14*, 2361−2369.
(20) Bond, E. M.; Duesler, E. N.; Paine, R. T.; Nöth, H. *Polyhedron* **2000**, *19*, 2135−2140.

10.1021/ic060389c CCC: $33.50



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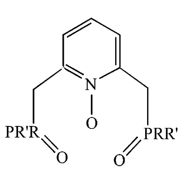

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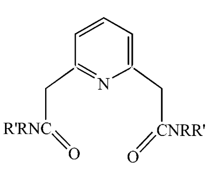

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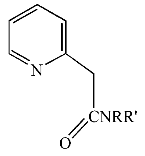

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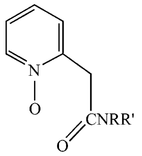

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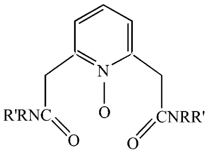

NOCOCO

The **NOPO** and **NOPOPO** ligands form very stable complexes which, in the solid state, adopt bidentate and tridentate chelate interactions on lanthanide, Ln(III), plutonium(IV), and thorium(IV) ions.[18−24] Furthermore, the **NOPOPO** ligands act as excellent liquid−liquid extractants for trivalent actinide ions present in strongly acidic aqueous solutions.[25−28] We are also engaged in the development of additional classes of acyclic ligands that might serve to partition Am and Cm. Two such target ligand systems attempt to combine, in a single platform, beneficial aspects of the well-studied malonamide ligands and the pyridine-*N*-oxide fragment. These acyclic ligands are the previously unknown 2-(N-alkylacetamide)pyridine-*N*-oxides, **NOCO**, and 2,6-bis(N-alkylacetamide)pyridine-*N*-oxides, **NOCOCO**. We report here the synthesis of the first examples of the **NCOCO** precursor ligand (R = *t*-Bu, R′ = H), 2,6-bis(*N*-*tert*-butylacetamide)pyridine (**2**), and the **NOCOCO** ligand (R = *t*-Bu, R′ = H), 2,6-bis(*N*-*tert*-butylacetamide)pyridine-*N*-oxide (**3**), and initial coordination chemistry observations of both with $Eu(NO_3)_3$.

Experimental Section

General Information. The organic reagents used in the syntheses were purchased from Aldrich Chemical Co., and organic solvents were obtained from VWR. Solvents were dried and distilled using standard procedures. The $Eu(NO_3)_3 \cdot 6H_2O$ was obtained from Ventron. Infrared spectra were recorded on a Bruker Tensor 27 benchtop spectrometer, and NMR spectra were obtained from a Bruker FX-250 spectrometer using Me_4Si (^1H, ^{13}C) as the external standard. All downfield shifts from the reference were assigned $+\delta$ values. Mass spectra were obtained from the Midwest Center for Mass Spectrometry at the University of Nebraska, and elemental analysis services were acquired from Galbraith Laboratories.

Ligand Synthesis. 2,6-Bis(chloromethyl)pyridine was prepared as described previously.[19] ***CAUTION:*** *Handling of this reagent and its solutions should be performed in a well-ventilated fume hood. Skin and eye contact must be carefully avoided since the compound is an aggressive skin irritant with variable individual response symptoms. It has a small vapor pressure at 23 °C and can cause bronchial irritation as well.*

2,6-Bis(*N-tert*-butylacetamide)pyridine (2). A sample of 2,6-bis(chloromethyl)pyridine (8.0 g, 0.045 mol) and excess KCN (17.75 g, 0.27 mol) were combined in dimethylformamide (DMF) (120 mL) at 23 °C and stirred (18 h). A brown solution formed to which water (50 mL) and CH_2Cl_2 (50 mL) were added and stirred (15 min). The phases were separated, and the water phase washed with CH_2Cl_2 (2 × 50 mL). The combined organic phases were retained, washed with water (70 mL), and dried over anhydrous $NaHCO_3$. Following evaporation of the solvent, a brown solid (6.7 g) was recovered. Column chromatography (silica gel, 70−230 mesh, elution with CH_2Cl_2) resulted in isolation of 2,6-bis(cyanomethyl)pyridine (**1**) as a tan powder: yield 5.3 g, 75%; mp 96−97 °C. Anal. Calcd for $C_9H_7N_3$: C, 68.77; H, 4.49; N, 26.73. Found: C, 68.41; H, 4.40; N, 26.90. NMR spectra ($CDCl_3$): ^1H δ 3.93 (CH_2), 7.37 (d, $J = 7.8$ Hz, $C_{3,5}H$), 7.76 (t, $J = 7.7$ Hz, C_4H). $^{13}C\{^1H\}$ δ 27.1 (CH_2), 117.3 ($C{\equiv}N$), 122.2 (C_3), 139.5 (C_4), 151.6 (C_2). Infrared spectrum (KBr, cm^{-1}): 2255 (ν_{CN}).

A sample of **1** (2.3 g, 0.014 mol) partially dissolved in glacial acetic acid (18 mL) was mixed with *t*-BuOH (2.8 mL, 0.029 mol). Concentrated H_2SO_4 (1.5 mL) was then added dropwise (0.5 h) at 23 °C, and the mixture was heated (55 °C, 8h). Upon cooling, an off-white precipitate formed. The solvent was removed by vacuum distillation, and then water (20 mL) and CH_2Cl_2 (100 mL) were added. The pH was adjusted to 8 by addition of $NaHCO_3$ solution, the phases separated, and the water phase washed with CH_2Cl_2 (3 × 50 mL). The combined organic phase was dried over anhydrous $NaHCO_3$, leaving a light green powder (3.83 g). The powder was combined with boiling ethanol (100 mL), and toluene was added dropwise until the powder dissolved. The hot solution was filtered and cooled to 23 °C leaving a light yellow powder (**2**): yield 3.0 g (67%); mp 171−172 °C. Anal. Calcd for $C_{17}H_{27}N_3O_2$: C, 66.85; H, 8.91; N, 13.76. Found: C, 66.75; H, 9.10; N, 13.71. NMR spectra ($CDCl_3$): ^1H δ 1.28 (CH_3), 3.58 (CH_2), 6.59 (NH), 7.13 (d, $J = 7.6$ Hz, $C_{3,5}H$), 7.58 (t, $J = 7.7$ Hz, C_4H). $^{13}C\{^1H\}$ δ 29.4 (CH_3), 47.0 (CH_2), 51.8 (CCH_3), 122.8 ($C_{3,5}$), 138.6 (C_4), 156.2, ($C_{2,6}$), 168.8 (CO). Infrared spectrum (KBr, cm^{-1}): 1655 (ν_{CO}).

2,6-Bis(*N-tert*-butylacetamide)pyridine-*N*-oxide (3). A sample of **2** (1.0 g, 3.2 mmol) was combined with water (4.9 mL), methanol (15.8 mL), $NaHCO_3$ (0.57 g, 6.8 mmol), and oxone (1.44 g, 2.4 mmol) under nitrogen atmosphere. The mixture was stirred (24 h) at 45−50 °C, and then the methanol was evaporated. CH_2Cl_2 (15 mL) was added to the residue, the phases separated, and the water phase washed with CH_2Cl_2 (10 × 15 mL). The extraction was monitored by UV emission from aliquots spotted on a TLC plate. The combined organic phases were dried over anhydrous $NaHCO_3$, leaving a white powder (**3**): yield 1.0 g (97%); mp 232−233 °C. Soluble in $CHCl_3$, CH_3OH, CH_2Cl_2. Anal. Calcd for $C_{17}H_{27}N_3O_3$: C, 63.53; H, 8.47; N, 13.07. Found: C, 63.52; H, 8.94; N, 12.97. NMR spectra ($CDCl_3$): ^1H δ 1.22 (CH_3), 3.74 (CH_2), 7.18−7.32 (m), 7.45 (NH). $^{13}C\{^1H\}$ δ 29.4 (CH_3), 42.1 (CH_2), 51.8 (CCH_3), 126.6 ($C_{3,5}$), 128.0 (C_4), 147.6, ($C_{2,6}$), 167.7 (CO). Mass spectrum (HR-FAB) Calcd for $^{12}C_{17}H_{28}{}^{14}N_3{}^{16}O_3$: 322.21307. Found: 322.21317 ($M + H^+$). Infrared spectrum (KBr, cm^{-1}): 1654 (ν_{CO}), 1251 (ν_{NO}).

Preparation of Complexes. A sample of **2** (180 mg, 0.58 mmol) in CH_2Cl_2 (3 mL) was added to an ethanol solution (3 mL)

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(21) Gan, X. M.; Parveen, S.; Smith, W. L.; Duesler, E. N.; Paine, R. T. *Inorg. Chem.* **2000**, *39*, 4591−4598.

(22) Bond, E. M.; Duesler, E. N.; Paine, R. T.; Neu, M. P.; Matonic, J. H.; Scott, B. L. *Inorg. Chem.* **2000**, *39*, 4152−4155.

(23) Gan, X.; Duesler, E. N.; Paine, R. T. *Inorg. Chem.* **2001**, *40*, 4420−4427.

(24) Gan, X.; Paine, R. T.; Duesler, E. N.; Nöth, H. *J. Chem. Soc., Dalton Trans.* **2003**, 153−159.

(25) Bond, E. M.; Englehardt, U.; Deere, T. P.; Rapko, B. M.; Paine, R. T.; FitzPatrick, J. R. *Solvent Extr. Ion Exch.* **1997**, *15*, 381−400.

(26) Bond, E. M.; Englehardt, U.; Deere, T. P.; Rapko, B. M.; Paine, R. T.; FitzPatrick, J. R. *Solvent Extr. Ion Exch.* **1998**, *16*, 967−983.

(27) Bond, E. M.;. Gan, X.; FitzPatrick, J. R.; Paine, R. T. *J. Alloys Compd.* **1998**, *271*−*273*, 172−175.

(28) Nash, K. L.; Lavallette, C.; Borkowski, M.; Paine, R. T.; Gan, X. *Inorg. Chem.* **2002**, *41*, 5849−5858.

Table 1. Crystallographic Data for **3** and Eu(**3**)$(NO_3)_3(H_2O)$

	3	Eu(**3**)$(NO_3)_3(H_2O)$
formula	$C_{17}H_{27}N_3O_3$	$C_{17}H_{29}EuN_6O_{13}$
fw	321.42	677.42
space group	$P\bar{1}$	*Pnma*
a, Å	7.0703(6)	12.2060(9)
b, Å	9.373(1)	16.4583(13)
c, Å	14.355(3)	13.1838(11)
α, deg	94.016(13)	90
β, deg	102.593(11)	90
γ, deg	90.140(9)	90
V, Å^3	926.0(2)	2648.5(4)
Z	2	4
d_{calc}, g/cm^3	1.153	1.699
T, °*C*	20	−50
μ, *mm*$^{-}$1	0.08	2.44
R1	0.0425	0.0236
wR2	0.1076	0.0574

containing $Eu(NO_3)_3{\cdot}6H_2O$ (315 mg, 0.58 mmol). The solution was stirred and the solvent evaporated, leaving a white powder which was recrystallized from EtOH or THF: yield, 0.35 g (85%). Anal. Calcd for Eu(**2**)$(NO_3)_3(H_2O)$(EtOH), $C_{19}H_{35}EuN_6O_{13}$: C, 32.26; H, 4.99; N, 11.88. Found: C, 32.32; H, 4.71; N, 12.12. Infrared spectrum (KBr, cm^{-1}): 1627 cm^{-1} (ν_{CO}).

A sample of **2** (372 mg, 1.2 mmol) in CH_2Cl_2 (5 mL) was added to $Eu(NO_3)_3{\cdot}6H_2O$ (325 mg, 0.6 mmol) in EtOH (3 mL). The solution was stirred (10 min) and the solvent evaporated, leaving a colorless powder: yield, 0.53 g (88%). Anal. Calcd for Eu(**2**)$_2$-$(NO_3)_3(H_2O)$(EtOH), $C_{36}H_{60}EuN_9O_{14}$: C, 43.46; H, 6.08; N, 12.67. Found: C, 44.11; H, 6.13; N, 14.02. Infrared spectrum (KBr, cm^{-1}): 1627 (ν_{CO}).

A sample of **3** (1.0 g, 3.1 mmol) in ethanol (15 mL) was combined with $Eu(NO_3)_3{\cdot}6H_2O$ (1.4 g, 3.1 mmol) in ethanol (15 mL), and the mixture stirred for 1 h. The solvent was evaporated, leaving a white solid. This was redissolved in a minimum of ethanol, treated with ethyl acetate, and cooled to −20 °C. Colorless crystals formed on standing (12 h): yield 1.5 g, 73%. Anal. Calcd for Eu-(**3**)$(NO_3)_3(H_2O)$, $C_{17}H_{29}EuN_6O_{13}$: C, 30.14; H, 4.32; N, 12.41. Found: C, 29.73; H, 4.48; N, 11.82. Infrared spectrum (KBr, cm^{-1}): 1638 (ν_{CO}) and 1224 (ν_{NO}).

A sample of **3** (0.25 g, 0.75 mmol) in ethanol (3 mL) was combined with $Eu(NO_3)_3{\cdot}6H_2O$ (0.21 g, 0.38 mmol) in ethanol (15 mL), and the mixture stirred for 1 h. The solvent was concentrated, and EtOAc (3 mL) was added. The mixture was cooled (−20 °C) and allowed to stand overnight. A colorless powder formed and was collected: yield 0.36 g, 95%. Anal. Calcd for Eu(**3**)$_2(NO_3)_3$-(H_2O), $C_{34}H_{56}EuN_9O_{16}$: C, 40.88; H, 5.65; N, 12.62. Found: C, 40.44; H, 6.05; N, 12.34. Infrared spectrum (KBr, cm^{-1}): 1635(ν_{CO}) and 1228(ν_{NO}).

X-ray Diffraction Analyses. Compound **3** was recrystallized from isopropyl alcohol, a blocky crystal (0.47 × 0.28 × 0.23 mm^3) was mounted on a glass fiber, and X-ray diffraction data were collected on a Siemens R3 m/V X-ray diffractometer at 23 °C using graphite-monochromated Mo K_α radiation ($\lambda = 0.71073$ Å). Selected crystal and refinement data are collected in Table 1. A small absorption correction was applied on the basis of ψ scans. The structure was solved by direct methods and refined by full matrix least-squares techniques.[29] The refinement was well behaved, and all hydrogen atoms were located in difference maps after anisotropic refinement of the non-hydrogen atoms.

Table 2. Selected Bond Distances (Å) for **3** and Eu(**3**)$(NO_3)_3(H_2O)$

	3		
N1−O1	1.2995(15)	C13−O3	1.2264(17)
N1−C1	1.3629(18)	C12−C13	1.523(2)
N1−C5	1.3656(19)	C7−N2	1.333(2)
C1−C6	1.476(2)	C13−N−3	1.333(2)
C5−C12	1.491(2)	C8−N2	1.478(2)
C6−C7	1.529(2)	C14−N3	1.479(2)
C7−O2	1.2253(18)		
	Eu(3)$(NO_3)_3(H_2O)$		
Eu−O1	2.3710(15)	N1−O1	1.332(2)
Eu−O2	2.3939(11)	N1−C1	1.3582(18)
Eu−O3	2.4680(17)	C1−C4	1.488(2)
Eu−O4	2.5060(14)	C4−C5	1.521(2)
Eu−O7	2.5659(16)	C5−O2	1.2399(19)
Eu−O6	2.6097(18)	C5−N2	1.322(2)
		C6−N2	1.479(3)

Needles of Eu(**3**)$(NO_3)_3(H_2O)$ were obtained by very slow evaporation of a hexane/EtOAc solution of the complex that was prepared by using a deficiency of **3** over that required for the formation of the 1:1 complex. A crystal was cut to size (0.25 × 0.12 × 0.04 mm^3) and mounted on a glass fiber. X-ray diffraction data were collected on a Bruker ×8 Apex 2 CCD-based diffractometer equipped with an Oxford Cryostream 700 low-temperature device and normal focus Mo-target X-ray tube ($\lambda = 0.71073$Å) operated at 1500 W power (50 kV, 30 mA). The X-ray intensities were measured at 223(2) K, and the detector was placed at a distance 6.002 cm from the crystal. A full sphere of data consisting of 2222 frames was collected with a scan width of 0.5° in ω and ϕ with an exposure time of 20 s/frame. The frames were integrated with the Bruker SAINT software package[30] with a narrow-frame algorithm. The integration of the data yielded a total of 39 154 reflections to a maximum $2\theta = 71.98°$ of which 6001 reflections were independent and 5082 were greater than $2\sigma(I)$. There is a 93% completion for 2θ, max > 71 ° and 99.8% for 2θ, max = 65 °.

The final cell parameters were based on the *xyz* centroids of 6837 reflections above $10\sigma(I)$. Analysis of the data showed negligible decay during the data collection. The data were processed with SADABS and corrected for absorption.[31] The structure was solved and refined with the Bruker SHELXTL (version 6.12) software package[32] using the orthohombic space group *Pnma*. There is disorder in the hydrogen positions of N2 and O3. The N2 hydrogen is spread over a large area and was not localized. The hydrogen positions on O3 are mostly in two positions, H1O [60% occupancy] and H2O [40% occupancy]. These H positions were fixed in the final refinements, but the U_{iso}'s were allowed to vary. The CH_2 and pyridine H atoms were allowed to vary in position and U_{iso}'s while the terminal methyl H atoms were placed in idealized positions and U_{iso}'s set to $1.5U_{equiv}$ of the parent atom.

Results and Discussion

Syntheses of variously substituted (*N*-alkylacetamide) and (*N*,*N*-dialkylacetamide) pyridines (**NCO**) from DCC-promoted coupling of 2-pyridyl acetic acid and alkyl amines have been previously developed due to the utility of the amides as starting materials for the synthesis of 4*H*-quinolizin-4-one compounds used in pharmaceutical com-

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(29) Sheldrich, G. M. *Nicolet SHELXTL Operations Manual*; Nicolet XRD Corp.: Cupertino, CA, 1981. The least squares refinement minimizes $\sum\omega(|F_o| - |F_c|)^2$, where $\omega = 1/[\sigma(F)^2 + gF^2]$.

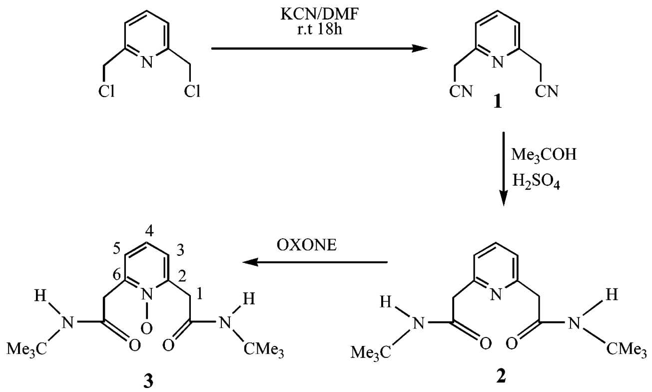
(30) *SAINT Pius*, v. 701; Bruker Analytical X-ray: Madison, WI, 2003.

(31) Sheldrick, G. M. *SADAB5*, v. 2.10, *Program for Empirical Absorption Correction of Area Detector Data*; University of Göttingen: Göttingen, Germany, 2003.

(32) Sheldrick, G. M. *SHELXTL*, v. 6.12; Bruker Analytical X-ray: Madison, WI, 2001.

positions.[33] The oxidation of the 2-(acetamide) pyridines (**NCO**) to 2-(acetamide) pyridine *N*-oxides (**NOCO**) and the subsequent use of these compounds as ligands has not been reported, but that chemistry is under development in our group at this time.[34] Despite the relative ease of the syntheses of the **NCO** compounds, the corresponding syntheses for 2,6-bis(*N*-alkylacetamide)pyridine or 2,6-bis(*N*,*N*-dialkylacetamide)pyridine (**NCOCO**) ligands have received limited development[35] and syntheses for their *N*-oxide derivatives (**NOCOCO**) have not been described. As it turns out, the syntheses are not as straightforward as expected due in part to the acidity of the methylene "elbow" carbon atoms in these molecules. Herman and co-workers[35] have briefly reported the formation of two macrocyclic **NOCOCO**-like ligands that contain a pyridine ring in the macrocycle backbone. The ligands were obtained via substitution reactions between the dimethyl ester of 2,6-pyridine diacetic acid and triethylene tetramine or *N*,*N′*-bis(3-aminopropyl)-ethane-1,2-diamine. However, the macrocyclic structure in these ligands precludes chelation interactions involving the amido carbonyl oxygen atoms and the pyridine fragment. Related substitution reactions using simple primary and secondary monoamines and the dimethyl ester of 2,6-pyridine-*N*-oxide diacetic acid were briefly examined in our group, but the reactions were found to be sluggish. Subsequently, attempts to obtain **NCOCO** ligands via DCC coupling of amines with 2,6-pyridine diacetic acid were also not fully satisfactory in part due to the reactivity of the diacid. As a result, while still pursuing the ester substitution and amide coupling chemistry, we turned our attention to alternative synthetic routes. One alternative approach to **NCOCO** ligands involves the Ritter reaction between a dinitrile and an alcohol in the presence of strong acid that generates a carbonium ion intermediate from the alcohol.[36,37] In the present study, the appropriate dinitrile reagent 2,6-bis(cyanomethyl) pyridine (**1**) was obtained by substitution on 2,6-bis(chloromethyl)pyridine using a modification of a previously described synthesis.[38] Compound **1** was obtained in good yield (75%) as an analytically pure tan solid. Spectroscopic data (^{1}H and ^{13}C NMR and IR) for **1** were obtained since these were not provided in the patent literature. Most notably, the ^{1}H and ^{13}C{^{1}H} NMR resonances for the methylene group, δ 3.93 and 27.1, respectively, are observed upfield of the corresponding resonances for 2,6-bis(chloromethyl)pyridine, δ 4.64, and 46.4, respectively. The ^{13}C{^{1}H} NMR resonance for the cyanide group appears at δ 117.3, and the infrared stretching frequency, $\nu_{C\equiv N}$, is assigned to an absorption at 2255 cm^{-1}.

Scheme 1



Previous studies of the Ritter reaction suggest that a number of alcohols capable of forming a carbonium ion in the presence of strong acids such as H_2SO_4 can be used to generate amides.[37] In the present case, **1** and *t*-BuOH were combined (1:2) in acetic acid, concentrated H_2SO_4 was added dropwise, and the combination heated (55 °C, 8 h) as depicted in Scheme 1. Following workup, 2,6-bis(*N*-*tert*-butylacetamide)pyridine (**2**) was obtained as an analytically pure light yellow powder. The ^{1}H and ^{13}C{^{1}H} NMR spectra are consistent with the expected structure. The methylene groups display a diagnostic single ^{1}H NMR resonance at δ 3.58 and a single ^{13}C NMR resonance at δ 47.0. The ^{13}C NMR resonance assigned to the cyano groups in **1** is no longer present. The infrared spectrum also shows the absence of the ν_{CN} band that is replaced by a band at 1655 cm^{-1} assigned to ν_{CO} of the amide groups. Compound **2** was then oxidized with oxone giving 2,6-bis(*N*-*tert*-butylacetamide)-pyridine-*N*-oxide (**3**) in high yield as an analytically pure white powder. A high-resolution FAB-MS spectrum shows a parent ion ($M + H^+$, $m/e = 322.21317$) in good agreement with the calculated mass. The ^{1}H and ^{13}C{^{1}H} NMR spectra were fully assigned and, as expected from our studies of (phosphinomethyl)pyridine-*P*-oxides and (phosphinomethyl)-pyridine-*N*,*P*-oxides,[18,19,23] the ^{1}H NMR resonance for the methylene groups in **3**, δ 3.74, is slightly downfield from the corresponding resonance in the pyridine precursor **2**. In addition, the ^{13}C{^{1}H} NMR resonance for the methylene groups in **3**, δ 42.1, is upfield of the resonance in the precursor **2**.[39] The infrared spectrum of **3** contains bands at 1654 and 1251 cm^{-1} that are assigned to ν_{CO} and ν_{NO}, respectively.

Single crystals of **3** were obtained by recrystallization from isopropyl alcohol, and the molecular structure was determined by X-ray diffraction techniques. The molecule crystallizes in the triclinic space group $P\bar{1}$ with two formula units in the unit cell. A view of the molecule is shown in Figure 1. The molecule has a 2-fold axis along O1−N1−C3. The pyridine-*N*-oxide ring is planar (mean deviation 0.0048 Å) as are the amido groups (mean deviation for C6−C7−(O2)−N2(H)−C8, 0.0339 Å and for C12−C13−(O3)−N3(H)C14, 0.0332 Å) and the angles between the pyridine-*N*-oxide plane

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(33) Kurashina, Y.; Miyata, H.; Momose, D. U.S. Patent 4,877,795, October 31, 1989.

(34) Binyamin, I.; Duesler, E. N.; Paine, R. T. manuscript to be submitted.

(35) Herman, G. G.; Blaton, N.; Dierck, I.; Steenland, M. W. A.; Lippens, W. *Challenges for Coordination Chemistry in the New Century*; Melnik, M., Sirota, A., Eds.; Slovak Technical University Press: Bratislava, 2001; p 189.

(36) Plant, H.; Ritter, J. J. *J. Am. Chem. Soc.* **1951**, *73*, 4076−4077.

(37) Krimen, L. I.; Cota, D. J. In *Organic Reactions*; Dauben, W. G., Ed.; J. Wiley: New York, 1969; Vol. 17, pp 213−325.

(38) Hertel, C.; Hoffmann, T.; Jakob-Roetne, R.; Norcross, R. D. European Patent 6,262,089.

(39) *N*-Oxidation of (phosphinomethyl)pyridine-*P*-oxides to give (phosphinomethyl)pyridine-*N*,*P*-oxides typically results in 7−10 ppm upfield shifts in the ^{13}C NMR resonance of the methylene carbon atom.[23]

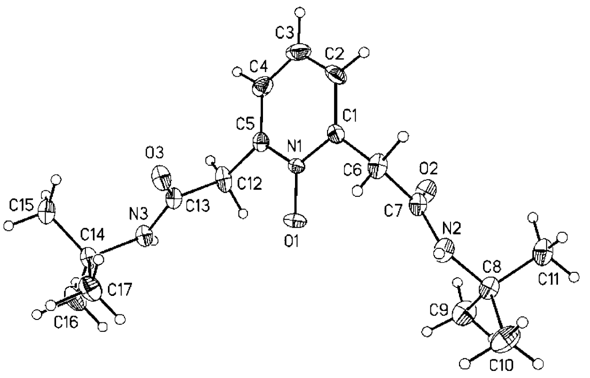

Figure 1. Molecular structure and atom-labeling scheme for compound **3** (30% thermal ellipsoids).

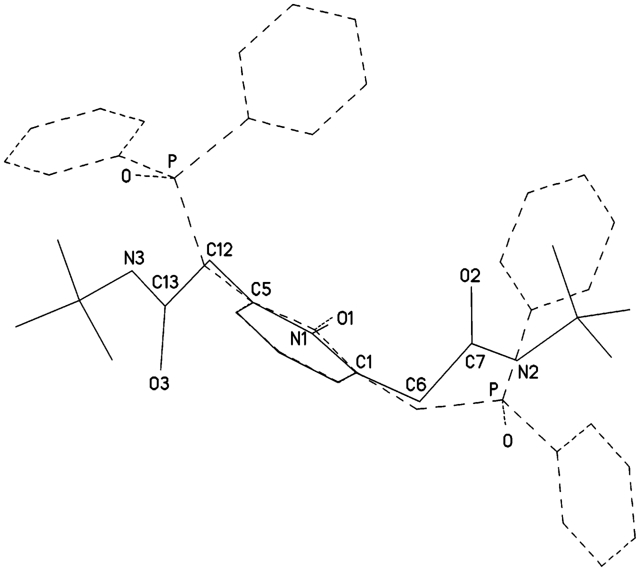

Figure 2. Framework structural overlay of compounds **3** and **4**.

and the amide planes are 78.1° and 80.7°. The C═O bond vectors are rotated away from the N−O bond vector with one carbonyl oxygen atom "up" and one "down" relative to the pyridine-*N*-oxide plane. The angle between the two amide group planes in 86.3°. This orientation is stabilized by extensive N−H$\cdots$O(C) hydrogen bonding (e.g., N2−H2$\cdots$O3 [$-x$, $1 - y$, $-z$] and N3H3$\cdots$O2 [$-x$, $-y$, $-z$]) that produces chains along the *b* axis. There are three groups of N−C bond lengths in **3**. The N−C(O) bond length, 1.333(2) Å, is the shortest and it is typical of distances found in organic amide compounds. The average N−C bond length in the pyridine-*N*-oxide ring, 1.364(2) Å, is typical of the distances found in the (phosphinomethyl)pyridine-*N*-oxide ligands.[18−24] The average N−C bond length in the *t*-BuN(H) groups is 1.479 Å. Finally, the average C═O bond length, 1.225(2) Å and the N−O bond length, 1.300 Å, are typical of distances found in organic amides and pyridine-*N*-oxides, respectively.

It is instructive to compare this structure against the molecular structure of the **NOPOPO** derivative $[Ph_2P(O)CH_2]_2C_5H_3NO$ (**4**),[19] and a superposition of the atom positions is shown in Figure 2. Unlike **3**, in the solid state, **4** does not adopt a structure with a 2-fold rotation axis. Instead, the molecule has a mirror plane passing through O1−N1−C3. The two P═O bond vectors are rotated away from the N−O bond vector but in a fashion that places them on the same side of the plane formed by the pyridine-*N*-oxide ring. Of course, in the **NOPOPO** molecule there are no strong hydrogen-bonding interactions that influence the lattice superstructure. However, in **3** there are strong hydrogen-bond interactions between the molecular units, as shown in Figure 3: N2−H2$\cdots$O3 [$-x$, $1 - y$, $-z$] 164°, N2$\cdots$O3, 2.936 Å, H2$\cdots$O3, 2.11 Å; N3−H3$\cdots$O2 [$-x$, $-y$, $-z$] 168°, N3$\cdots$O2, 2.936 Å, H3$\cdots$O2, 2.15 Å. These result in a chain arrangement along the *b* axis. Each molecule in the chain is related to its neighbors by an inversion center. It should also be noted that the C3H3$\cdots$O1 separation is short, 2.17 Å, with C3$\cdots$O1 = 3.094 Å (sum of van der Waal radii = 3.25 Å). This may indicate a weak hydrogen bond between the *N*-oxide oxygen atom in one molecule and pyridine ring H atom in a neighboring molecule.

The characterization of the coordination behavior of **2** toward lanthanide ions and the comparison of the behavior against the bonding performance of **NPOPO** ligands is of central interest. Therefore, 1:1 and 2:1 combinations of **2** with $Eu(NO_3)_3$ were examined. Colorless complexes were isolated in high yield following evaporation of the combining solvent (CH_2Cl_2 or EtOH). Recrystallizations by slow solvent evaporation led to deposition of microcrystalline solids that so far have proven unsuitable for single-crystal X-ray diffraction analyses. Elemental analyses for the 1:1 and 2:1 complexes obtained from ethanol solution are consistent with compositions corresponding to Eu(**2**)$(NO_3)_3(H_2O)$(EtOH) and Eu(**2**)$_2(NO_3)_3$(EtOH), respectively. Infrared spectra obtained for the solids in KBr pellets show small down-frequency shifts, -27 cm^{-1}, in a band tentatively assigned to the amide carbonyl stretch. This is consistent with metal binding to this group, but without a crystallographic structure determination for either of these complexes, the ligand denticity of **2** remains uncertain. On the basis of the knowledge that neutral amides are generally considered to be moderately good ligands toward aquated, hard Ln(III) cations,[40] it is anticipated that the **NCOCO** ligand **2** probably binds in a bidentate fashion to Eu(III) through the carbonyl oxygen atoms in the two *t*-Bu amide arms. However, the pyridine N atom may not be entirely silent. Instead, it may be involved in hydrogen bonding with an inner-sphere coordinated water or ethanol molecule. This proposal is supported by a recent crystal structure determination for the closely related complex $[Nd\{[Ph_2P(O)CH_2]_2C_5H_3N\}_2(NO_3)(OH)(H_2O)]\cdot(NO_3)(MeOH)(H_2O)$.[41] In this case, the **NPOPO** ligand bonds with the Nd(III) cation in a bidentate mode through the two phosphoryl oxygen donor atoms while the pyridine N atom participates in hydrogen bonding with an inner-sphere water molecule.

The pyridine-*N*-oxide ligand, **3**, should be more likely to produce complexes that display tridentate coordination. Indeed, a 1:1 combination of **3** with $Eu(NO_3)_3$ produces a colorless, microcrystalline solid in high yield. Elemental

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(40) Hart, F. A. Scandium, Yttrium and Lanthanides. In *Comprehensive Coordination Chemistry*; Wilkinson, G., Ed.; Pergamon: New York, 1987; Vol. 3, p 1059.

(41) Gan, X.; Duesler, E. N.; Paine, R. T. manuscript in preparation.

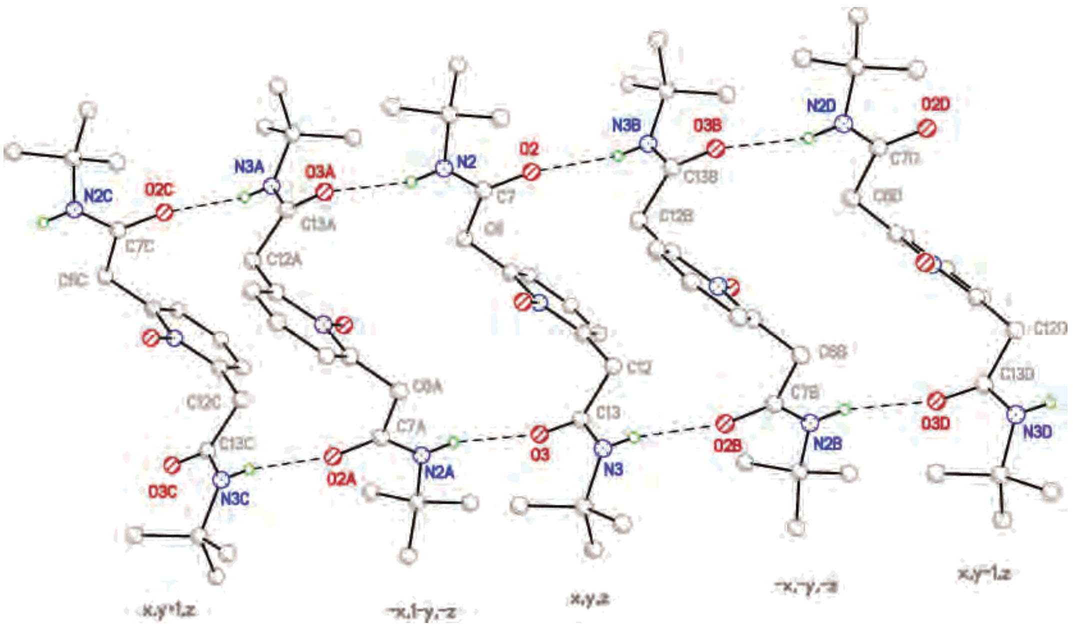

Figure 3. Hydrogen-bond interactions between molecules of **3** shown along the *b* axis. The oxygen atoms are shown in red, the nitrogen atoms in blue, and amide H atoms in green.

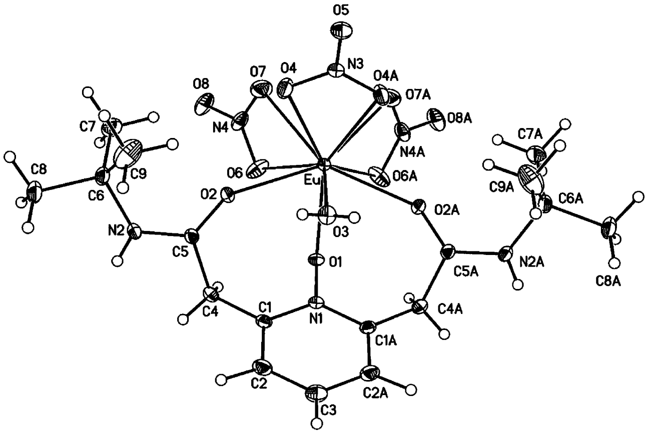

Figure 4. Molecular structure and atom labeling scheme for Eu(**3**)$(NO_3)_3$-(H_2O).

analyses are in good agreement with the composition Eu(**3**)$(NO_3)_3(H_2O)$. Infrared spectra of the solids obtained from KBr pellets show down-frequency shifts for the bands tentatively assigned to ν_{NO} and ν_{CO} stretching frequencies: $\nu_{NO} = 1224$ cm^{-1} ($\Delta\nu_{NO} = -27$ cm^{-1}); $\nu_{CO} = 1638$ cm^{-1} ($\Delta\nu_{CO} = -16$ cm^{-1}). These data are similar to coordination shifts found for **NOPOPO**/Ln complexes, and they are consistent with tridentate chelation by the ligand. Crystallographic quality single crystals of the 1:1 complex were not obtained by slow crystallization from EtOH, EtOH/CH_2Cl_2, or EtOH/EtOAc solutions; however, suitable crystals were obtained from a sample of the complex prepared with a deficiency of ligand over the stoichiometric 1:1 amount.

The complex contains the Eu(III) bonded to three bidentate nitrate anions, a water molecule, and a tridentate chelated **NOCOCO** ligand. The molecule displays a mirror plane passing through Eu, O1, C3, N3, O5, and O_3. This structure very closely resembles the general features of the 1:1 complexes, Ln(**NOPOPO**)$(NO_3)_3$ (Ln = Nd, Er, Yb).[18,23] The latter are essentially isostructural despite the range of ionic radii for the Ln(III) ions.[42] However, there are important differences. It is immediately apparent that the Ln(**NOPOPO**)$(NO_3)_3$ complexes are all nine-coordinate with inner spheres composed of oxygen atoms from one neutral, tridentate **NOPOPO** ligand and three bidentate nitrate anions. There are no solvent molecules involved in inner-sphere coordination perhaps due to steric congestion imposed by the $Ph_2P(O)$ fragments. However, in Eu(**3**)$(NO_3)_3(H_2O)$, a water molecule resides in the inner-sphere environment, resulting in a 10-coordinate coordination polyhedron. This suggests that the coordination volume of **3**, even with the *t*-Bu groups both pointed toward the Eu(III) center, is less than that of the **NOPOPO** ligand. This is not completely unexpected since the amide group $-C(O)N(H)(^tBu)$ would be expected to be smaller than the $-P(O)Ph_2$ groups. Comparison of bond lengths and nonbonded contacts also support this suggestion. The Eu−O1(pyridine) bond length in Eu(**3**)$(NO_3)_3$, 2.3710(15) Å, is very similar to the Ln−O(pyridine) distances in Nd(**NOPOPO**)$(NO_3)_3$, 2.382(3) Å, and Er(**NOPOPO**)$(NO_3)_3$, 2.278(7) Å, when differences in ionic radii are accounted for.[42] The Eu−O2(carbonyl) bond length, 2.3939(11) Å, is similar to the average Ln−O(phosphoryl) bond lengths in Nd(**NOPOPO**)$(NO_3)_3$, 2.384(3) Å, and Er(**NOPOPO**)$(NO_3)_3$, 2.280(7) Å. In addition, the average Eu−O(nitrate) distance, 2.561(1) Å, is comparable to the average Ln−O(nitrate) distances in Nd(**NOPOPO**)$(NO_3)_3$, 2.461(7) Å, and Er(**NOPOPO**)$(NO_3)_3$, 2.542(3) Å. Despite the similarities in bond lengths, a striking difference appears in the size of the nonbonded triangular ligand “footprints” on the Ln(III) ions. For Eu(**NOCOCO**), the O1(N)···O2(C) and O2(C)···O2A(C) nonbonded distances are 2.923 and 4.353 Å, respectively. In Nd(**NOPOPO**)$(NO_3)_3$, the corresponding distances are 3.016 (av) and 3.389 Å, while in Er(**NOPOPO**)$(NO_3)_3$ the distances are 2.930 (av) and

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(42) Ionic radii for the subject Ln(III) ions all with the common coordination number eight are Nd, 1.26 Å; Eu, 1.21 Å; and Er, 1.14 Å.

3.239 Å. The differences between the latter two **NOPOPO** complexes reflect the smaller size of Er(III) relative to Nd(III).[42] It is apparent that the "footprint" triangle in the Eu(**NOCOCO**)$(NO_3)_3$ complex is spread open compared to those formed by the **NOPOPO** ligand. This is also indicated by the O2−O1−O2A angle that is 96.2° compared to 68.4° and 67.1° in the related **NOPOPO** complexes.

It is instructive to compare the donor group bond lengthening that occurs upon complexation of **NOCOCO**: free ligand: N1−O1, 1.2995(15) Å; C7−O2, 1.2253(18) Å; C13−O3, 1.2264(17) Å; complex: N1−O1, 1.322 (2) Å; C5−O2, 1.2399(19) Å. The coordination shift for N−O binding, ∼0.032(2) Å, is clearly larger than the shift for the amide carbonyl, ∼0.014 (2) Å, suggesting that the N-oxide is the stronger donor site in the **NOCOCO** complex. This is in agreement with the coordination shifts observed in the infrared spectra.

The 2:1 **NOCOCO**/$Eu(NO_3)_3$ combination produces a solid complex as well, and the CHN composition analysis is in good agreement with a formula Eu(**3**)$_2(NO_3)_3(H_2O)$. Unfortunately, single crystals of suitable quality for X-ray diffraction analyses have not been obtained. It is expected that both **NOCOCO** ligands are acting as tridentate chelates and, if the structure is related to those of Ln(**NOPOPO**)$_2(NO_3)_3$,[18,23] one or more of the nitrate ions resides in the outer coordination sphere. The structural details remain to be confirmed by future structural studies. It may be necessary to replace the *t*-Bu group on the ligand with another alkyl group in order to accomplish the isolation of a crystalline 2:1 complex, and that effort is underway in our group at this time.

As briefly mentioned in the Introduction, **NOPOPO** ligands have been found to display very interesting and potentially practical performance for the separation of trivalent f elements from acidic nuclear process waste solutions. They also discriminate to some degree between Eu(III) and Am(III); however, improved selectivity would be useful. The amide-substituted **NOPOPO** analogues, **NOCOCO**, produce a related chelation performance, as shown by the structural studies, and it will be of interest to determine if ligand binding preferences lead to more pronounced selectivity for Am(III). The extraction studies required to address this problem are planned for the future.

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Supporting Information Available: X-ray crystallographic files in CIF format. This material is available free of charge via the Internet at http://pubs.acs.org.

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