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Synthesis, selected coordination chemistry and extraction behavior of a (phosphinoylmethyl)pyridyl N-oxide-functionalized ligand based upon a 1,4-diazepane platform

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ABSTRACT

Syntheses for the new multidentate chelating ligands ((6,6′-((1,4-diazepane-1,4-diyl)bis(methylene))-bis(pyridine-6,2-diyl))bis(methylene))bis(diphenylphosphine oxide) (**2**) and 6,6′-((1,4-diazepane-1,4-diyl)bis(methylene))bis(2-((diphenylphosphoryl)methyl)pyridine 1-oxide) (**3**), based upon a 1,4-diazepane platform functionalized with 2-(diphenylphosphinoylmethyl)pyridine P-oxide and 2-(diphenylphosphinoylmethyl)pyridine N,P-dioxide fragments, respectively, are reported. Results from studies of the coordination chemistry of the ligands with selected lanthanide nitrates and $Cu(BF_4)_2$ are outlined, and crystal structures for two complexes, $[Cu(\mathbf{2})](BF_4)_2$ and $[Cu(\mathbf{3})](BF_4)_2$, are described along with survey Eu(III) and Am(III) solvent extraction analysis, for **3**.

1. Introduction

Current practical needs for efficient chemical separation processes that result in selective recognition and binding of *f*-element ions in harsh environments is driving revived interest in the design and synthesis of new, robust multidentate organic chelating ligands [1–11]. In recent contributions we have described the development of several new multidentate phosphine oxide ligands that are based upon pyridine and pyridine N-oxide platforms including molecules of types **A**–**E** as shown in Fig. 1. As expected, the coordination chemistry of these ligands with *f*-element ions has proven to be intriguing [12–25]. In particular, the N-oxide ligands (designated as NOPO ligands) of types **A** and **C**, generally form bidentate O_PO_N chelates while examples of **E** (designated as NOPOPO ligands) produce tridentate $O_PO_NO_P$ chelates. Furthermore, both ligand classes display unique solvent extraction performance [26–29]. The molecular structures of isolated solid-state coordination complexes and solvent extraction complexes in organic solutions typically contain two to four of these chelating ligands in the *f*-element ion inner coordination sphere. As a result, it is of interest to graft two or more of the chelating fragments onto a backbone that would position the collected donor centers for enhanced, pre-organized coordination interactions. Numerous possible backbones, with varying degrees of flexibility or rigidity, can be considered for this ligand construction objective, and several options are currently under study in our group. In particular, cyclic diamines such as piperazine, 1,4-diazacycloheptane, **F**, and 1,5-diazacyclooctane rings have been used extensively as platforms to assemble various donor groups that provide pre-organized multidentate chelate structures. Directly pertinent to our studies, pyridyl-2-yl-methyl [30–38], pyridyl-2-yl-ethyl [35], quinoyl-2-yl-methyl [32] and imidazol-2-yl-methyl [36] fragments have been grafted onto one or more of these diamines, and their multidentate coordination interactions explored primarily with transition metal cations. In other cases, various carboxylic acid fragments have been attached to diamine platforms, and the coordination chemistry of these ligands with lanthanide ions examined with primary relevance to the development of MRI reagents [39–42]. In the present report, we describe the synthesis of two new ligands that contain two **B** (NPO) or **C** (NOPO) fragments appended to the 1,4-diazacy-

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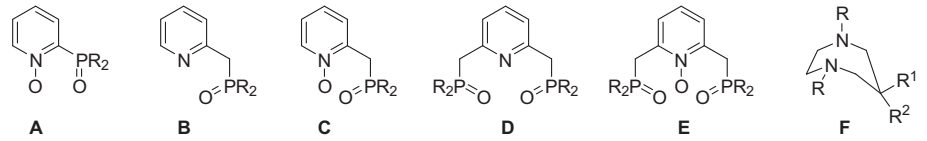

Fig. 1. Chelating phosphinopyridine and pyridine N-oxide ligand structure types **A–E** and the 1,4-diazacycloheptane (DACH), **F**, platform.

cloheptane **F** (DACH) backbone (R′ = R″ = H), along with selected coordination chemistry and preliminary screening of the Eu(III)/Am(III) extraction performance of the ligand containing the **C** fragments.

2. Experimental

2.1. Materials and general procedures

Organic reagents (Aldrich Chemical Co.) and metal salts (Ventron) were used as received, and organic solvents (VWR) were dried by using standard methods. Unless noted otherwise, reactions were performed under a dry nitrogen atmosphere by using Schlenk methods. The 2,6-bis(chloromethyl)pyridine was purchased or prepared as described previously [13]. Infrared spectra were recorded from KBr pellets on a Bruker Tensor 27 FTIR spectrometer. The FT-NMR spectra were recorded with Avance 300 and 500 spectrometers by using Me_4Si (^1H and ^{13}C) and 85% H_3PO_4 as external chemical shift standards. Downfield shifts were assigned +δ values. The atom numbering systems used in the shift assignments for the new compounds are provided in the Supplementary Data. Mass spectra were obtained from the UNM Mass Spectrometry Center, and elemental analyses were performed by Galbraith Laboratories.

2.2. Experimental procedures

2.2.1. Ligand syntheses

*2.2.1.1. 2-(diphenylphosphinoylmethyl)-6-(chloromethyl)pyridine (**1a**).* Ethyl diphenylphosphinite (4.7 mL, 21.76 mmol) was combined with a solution of 2,6-bis(chloromethyl)pyridine (15.7 g, 89.18 mmol) [13] in *o*-xylene (60 mL) under a nitrogen atmosphere, and the mixture was stirred (120 °C, 2 h). After evaporation of solvent, the residue was purified by column chromatography (silica gel (230 g), CH_2Cl_2/MeOH, 100/0 to 97/3) leaving **1a** as a white powder. Yield: 6.64 g, 89%. Mp 118–120 °C. Single crystals of **1a** were obtained by slow evaporation of a CH_2Cl_2/Et_2O (10/90) solution. $^{31}P\{^1H\}$ NMR (121.5 MHz, $CDCl_3$): δ = 30.5. ^1H NMR (300 MHz, $CDCl_3$): δ = 7.75–7.69 (m, 4H, H_9), 7.52 (t, J_{HH} = 7.8 Hz, 1H, H_4), 7.46–7.33 (m, 7H, $H_{10,11}$ and H_3 or H_5), 7.18 (d, J_{HH} = 7.8 Hz, 1H, H_3 or H_5), 4.42 (s, 2H, H_7), 3.89 (d, J_{HP} = 14.4 Hz, 2H, H_1). $^{13}C\{^1H\}$ NMR (75.4 MHz, $CDCl_3$): δ = 155.9 (C_6), 152.4 (d, J_{CP} = 7.0 Hz, C_2), 137.4 (C_4), 132.3 (d, J_{CP} = 100.4 Hz, C_8), 131.8 (C_{11}), 131.1 (d, J_{CP} = 9.5 Hz, C_9), 128.4 (d, J_{CP} = 11.9 Hz, C_{10}), 124.2 (d, J_{CP} = 3.2 Hz, C_5), 120.8 (C_3), 46.5 (C_7), 40.9 (d, J_{CP} = 64.0 Hz, C_1). IR (KBr, cm^{-1}): ν = 3057, 2923, 1612, 1589, 1575, 1483, 1455, 1433, 1397, 1293, 1268, 1249, 1225, 1200 ($\nu_{P=O}$), 1161, 1118, 1084, 1066, 1024, 992, 963, 858, 827, 813, 753, 734, 714, 699, 690, 618, 575, 543, 519, 490, 452, 435, 410. HRMS (ESI): *m*/*z* (%) = 342.0826 (100) [M+H$^+$]. $C_{19}H_{18}NOPCl$ requires 342.0815; 364.0635 (40) [M+Na$^+$]. $C_{19}H_{17}NOPClNa$ requires 364.0634. *Anal.* Calc. for $C_{19}H_{17}ClNOP$: C, 66.77; H, 5.01; N, 4.10. Found: C, 66.66; H, 4.86; N, 3.50%.

*2.2.1.2. ((6,6′-((1,4-diazepane-1,4-diyl)bis(methylene))bis(pyridine-6,2-diyl))bis(methylene))bis(diphenylphosphine oxide) (**2**).* To a solution of homopiperazine (293 mg, 2.92 mmol) and NaOH (468 mg, 11.7 mmol) in a mixture of CH_2Cl_2 (25 mL) and water (15 mL) was added **1a** (2.00 g, 5.85 mmol). The mixture was stirred (23 °C, 4 d) and then additional NaOH (500 mg, 12.5 mmol) was added and the mixture stirred (6 d). The phases were separated and the aqueous layer extracted with CH_2Cl_2 (3 × 20 mL). The combined organic layer was dried with $MgSO_4$, filtered and the solvent evaporated under reduced pressure. Purification of the residue, performed by column chromatography (silica gel (60 g), eluant CH_2Cl_2/MeOH, 90/10 to 80/20), afforded **2** as an orange solid. Yield: 1.05 g, 51%. Mp 74–76 °C. $^{31}P\{^1H\}$ NMR (121.49 MHz, $CDCl_3$): δ = 29.6. ^1H NMR (300 MHz, $CDCl_3$): δ = 7.66–7.60 (m, 8H, H_{12}), 7.38 (t, J_{HH} = 7.8 Hz, 2H, H_7), 7.26–7.13 (m, 16H, $H_{6,8,13,14}$), 3.81 (d, J_{HP} = 14.1 Hz, 4H, H_{10}), 3.53 (s, 4H, H_4), 2.56–2.45 (m, 8H, $H_{1,2}$), 1.63–1.56 (m, 2H, H_{13}). $^{13}C\{^1H\}$ (75.4 MHz, $CDCl_3$): δ = 158.3 (C_5), 151.1 (d, J_{CP} = 6.9 Hz, C_9), 136.2 (C_7), 131.9 (d, J_{CP} = 99.9 Hz, C_{11}), 131.2 (C_{14}), 130.6 (d, J_{CP} = 9.4 Hz, C_{12}), 127.9 (d, J_{CP} = 11.8 Hz, C_{13}), 122.7 (d, J_{CP} = 1.8 Hz, C_8), 120.7 (C_6), 63.3 (C_4), 54.3 (C_1), 53.8 (C_2), 40.2 (d, J_{CP} = 64.4 Hz, C_{10}), 26.7 (C_3). IR (KBr, cm^{-1}): ν = 3054, 2932, 2813, 1589, 1573, 1483, 1454, 1436, 1394, 1341, 1267, 1192 ($\nu_{P=O}$), 1120, 1069, 1027, 994, 924, 832, 722, 693, 641, 605, 519. HRMS (ESI): *m*/*z* (%) = 711.3015 [M+H$^+$] (90). $C_{43}H_{45}N_4O_2P_2$ requires 711.3018; 733.2847 [M+Na$^+$] (100). $C_{43}H_{44}N_4O_2NaP_2$ requires 733.2837. *Anal.* Calc. for **2**·2CH_2Cl_2, $C_{45}H_{48}Cl_2N_4O_2P_2$: C, 61.37; H, 5.49; N, 6.36. Found: C, 62.49; H, 5.37; N, 6.27%.

*2.2.1.3. 2-(chloromethyl)-6-((diphenylphosphoryl)methyl)pyridine 1-oxide (**1b**).* A mixture of **1a** (2.00 g, 5.85 mmol) and *m*CPBA (77%, 2.00 g, 8.78 mmol) in CH_2Cl_2 (50 mL) was stirred (18 h, 23 °C), and the resulting mixture was quenched with an aqueous solution of NaOH (2 M, 100 mL). After separation of the phases, the organic layer was washed with aqueous NaOH solution (2 M, 3 × 80 mL), and the combined organic layers were washed with brine (100 mL), dried over $MgSO_4$, filtered and evaporated to dryness to give **1b** as a white solid that doesn't require further purification. Yield: 2.00 g, 96%; Mp 138–140 °C. $^{31}P\{^1H\}$ NMR (121.5 MHz, $CDCl_3$): δ = 30.8. ^1H NMR (300 MHz, $CDCl_3$): δ = 7.75–7.87 (m, 4H, H_9), 7.62 (d, J_{HH} = 7.8 Hz, 1H, H_3 or H_5), 7.36–7.22 (m, 7H, H_3 or H_5 and $H_{10,11}$), 7.00 (t, J_{HH} = 7.8 Hz, 1H, H_4), 4.53 (s, 2H, H_7), 4.15 (d, J_{HP} = 14.1 Hz, 2H, H_1). $^{13}C\{^1H\}$ NMR (75.4 MHz, $CDCl_3$): δ = 146.5 (C_6), 143.9 (d, J_{CP} = 6.0 Hz, C_2), 131.8 (d, J_{CP} = 2.0 Hz, C_{11}), 131.7 (d, J_{CP} = 101.5 Hz, C_8), 130.5 (d, J_{CP} = 9.9 Hz, C_9), 128.3 (d, J_{CP} = 12.1 Hz, C_{10}), 126.5 (d, J_{CP} = 3.9 Hz, C_3), 124.3 (C_4 or C_5), 123.8 (C_4 or C_5), 40.1 (C_7), 31.2 (d, J_{CP} = 65.6 Hz, C_1). IR (KBr, cm^{-1}): ν = 2973, 1566, 1484, 1435, 1404, 1389, 1292, 1252, 1236, 1219, 1193 ($\nu_{P=O}$), 1165, 1118, 1104, 1070, 1026, 997, 974, 949, 931, 897, 852, 823, 785, 748, 735, 719, 692, 617, 590, 560, 541, 510, 462, 421. HRMS (ESI): *m*/*z* (%) = 358.0774 (20) [M+H$^+$]. $C_{19}H_{18}ClNO_2P$ requires 358.0758; 380.0588 (42) [M+Na$^+$]. $C_{19}H_{17}ClNNaO_2P$ requires 380.0578. 737.1294 (100) [2M+Na$^+$]. $C_{38}H_{34}Cl_2N_2NaO_4P_2$ requires 737.1263. *Anal.* Calc. for $C_{19}H_{17}ClNO_2P$: C, 63.79; H, 4.79; N, 3.92. Found: C, 63.46; H, 4.76; N, 3.34%.

*2.2.1.4. 6,6′-((1,4-diazepane-1,4-diyl)bis(methylene))bis(2-((diphenylphosphoryl)methyl)pyridine 1-oxide) (**3**).* In a fashion similar to that described for the synthesis of **2**, a sample of **1b** (2.3 g, 6.43 mmol) was combined with a mixture of homopiperazine (943 mg, 2.93 mmol) and NaOH (516 mg, 12.9 mmol) and stirred (7 d,