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Stereognostic Coordination Chemistry. 1. The Design and Synthesis of Chelators for the Uranyl Ion

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Abstract: A new approach to the molecular recognition of metal oxo cations is introduced based on a ligand design strategy that provides at least one hydrogen bond donor for interaction with oxo group(s) as well as conventional electron pair donor ligands for coordination to the metal center. This concept of stereognostic coordination of oxo metal ions is exemplified in the design of four tripodal ligands—tris[2-(2-carboxyphenoxy)ethyl]amine [NEB], tris[3-(2-carboxyphenoxy)propyl]amine [NPB], tris[3-(2-carboxynaphthyl-3-oxy)propyl]amine [NPN], and tris[3-(2-carboxy-4-octadecylphenoxy)propyl]amine [NPodB]—for sequestration of the uranyl ion. The ligands NEB, NPB, and NPN form 1:1 complexes with UO_2^{2+}. The bidentate coordination of carboxyl groups of these compounds is indicated by the infrared spectra, which offer some support for the presence of a hydrogen bond to the uranyl group. Mass spectral data corroborate CPK model predictions that more than five intervening atoms between the tertiary nitrogen atom and the carboxylate groups are required for metal ion incorporation and monomeric complex formation. Solvent extractions of aqueous UO_2^{2+} into chloroform solutions of the ligands have shown them to be powerful extractants. In the case of the very hydrophobic ligand NPodB the stoichiometry of the complexation reaction is shown to be a 1:1 UO_2/ligand complex formed by the release of 3 protons. The extraction is quantitative at pH 2.5, and an effective extraction coefficient of about 10^{11} is estimated for neutral aqueous solutions of UO_2^{2+}.

Introduction

Selectivity of metal complexation by ligands is a chemical feature that has long been valued by chemists and one which has many important technological applications. Examples include metal ore processing, analytical and environmental applications, and pharmaceuticals. The standard approach in the design of metal ion selective complexing agents relies on two basic tenets: (1) the construction of a ligand cavity of appropriate size[1] consisting of convergant donor groups;[2] and (2) a match of the metal ion and ligand electronic properties summarized by the principle of hard and soft acids and bases.[3] Both of these considerations essentially treat the metal ion as a hard sphere whose properties are defined by a fixed charge and radius.

Metal oxo cations such as VO^{2+}, TcO^{3+}, and UO_2^{2+} have pronounced three-dimensional anisotropy that in principle allows for a kind of molecular recognition approach in their selective complexation. The coordination chemistry and ligand preparation for these metal ions have usually treated the metal oxo group as an occupied coordination site of the metal. Our goal is to approach the recognition of these metal oxo cations utilizing the oxo group(s) as a means of providing both additional binding strength and selectivity in forming the ion–ligand complex. The dipolar nature of the metal–oxygen bond produces a partial negative charge on the oxo group that can be exploited in the design of specific complexing agents. Supplying a hydrogen bond donor group to interact with an oxo group (within a ligand that also provides donor groups for coordination to the metal center) is a means of improving molecular recognition. This approach recognizes oxo cations by something like three-dimensional, tactile recognition (stereognosis)[4] and we therefore describe it as stereognostic coordination chemistry. Initial investigation of this concept involves the complexation of uranyl ion, UO_2^{2+}.

It is estimated that 4.5 × 10^{12} kg of uranium is dissolved in seawater.[5] This represents approximately one thousand times that available from terrestrial sources. Virtually all of the uranium is present as the very stable tris(carbonato) complex $[UO_2(CO_3)_3]^{4-}$.[6] However, at a concentration of 3.3 ppb, the utilization of this resource depends upon the development of an efficient, selective means of complexation. The oxidizing environment of seawater assures the uranium present is in the form of U(VI) as the uranyl ion, UO_2^{2+}. This has spurred interest in the development of "uranophiles"—i.e. uranyl-specific complexing agents.[7] The low marine concentration of UO_2^{2+} and the high concentration of other cations exacerbates the problem of selectivity. The design of earlier complexing agents intended to be specific for UO_2^{2+} relied upon recognition of the uranyl equatorial coordination plane (perpendicular to the *trans*-oxo groups) as the sole means of interacting with the metal center. Several macrocycles were designed to encompass precisely the circumference of the uranyl ion equatorially. Some of these showed high affinities for UO_2^{2+},[7-16] even though several of these ligands proposed a coordination behavior never seen in UO_2^{2+} complexes (equatorial six coordination is only achieved with bidentate ligands with small bite angles such as CO_3^{2-} and NO_3^-). In any case, the underlying approach of that strategy is essentially just size selectivity.

The short uranium–oxygen bonds characteristic of the uranyl ion are indicative of a strong multiple bond to the oxo groups.[7,17-19] The dipolar nature of these U–O bonds gives rise to an effective charge on the metal cation larger than the dipositive net charge on the uranyl ion.[17,20-26] This greater charge manifests itself in

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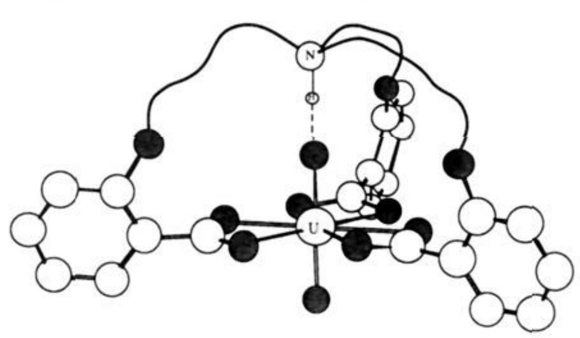
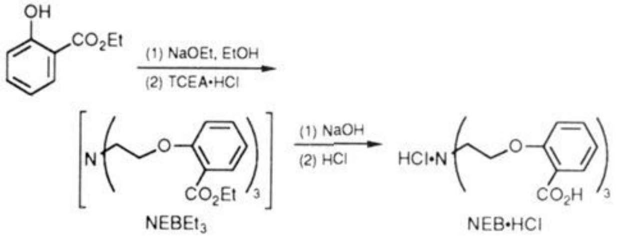


Figure 1. Schematic diagram of a stereognostic ligand for $\mathrm{UO_2^{2+}}$ incorporating three donor carboxylate groups and an ammonium hydrogen bond donor.

the relative ordering the strengths of complexation and hydrolysis for various oxidation states of uranium: $\mathrm{U^{4+}} > \mathrm{UO_2^{2+}} > \mathrm{U^{3+}}$. The fact that $\mathrm{UO_2^{2+}}$ falls between $\mathrm{U^{4+}}$ and $\mathrm{U^{3+}}$ in acidity suggests that the effective charge at the metal center is greater than 3, which results in increased binding strength of ligands in the equatorial plane.[24–26] Furthermore, the excess positive charge at the uranium atom is prima facie evidence for partial negative charge on each of the uranyl oxygen atoms. This partial negative charge makes the uranyl oxo group a potential hydrogen bond acceptor. Indeed, single-crystal X-ray and neutron diffraction studies of many uranyl complexes show hydrogen bonding between a hydrogen bond donor and a uranyl oxo receptor. Examples of such interactions are presented in Table I.[27–48] The role hydrogen bonding might play in $\mathrm{UO_2^{2+}}$ complexation seems to have been overlooked (with the exception that intramolecular hydrogen bonding has been suggested as contributing to the stability of uranyl–EDTA complexes.)[49–50]

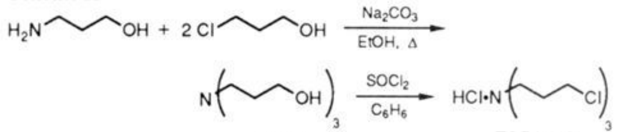
It is anticipated that both the stability and selectivity of uranyl chelates will be enhanced when provision is made for oxo group interaction in addition to coordinative interactions to the metal center. The gain in stability contributed by a hydrogen bond may be small in relation to the metal binding interactions, but the net gain in specificity can be expected to be significant, since a positively charged hydrogen bond donor group both contributes to the stability of the uranyl complex and at the same time destabilizes complexes with non-oxo cations through electrostatic repulsion, thus the overall increase in selectivity is expected to exceed the hydrogen bond energy in a defined structure.

Scheme I



NEBEt$_3$ NEB•HCl

Scheme II



THPA TCPA•HCl

The coordination geometry of $[\mathrm{UO_2(CO_3)_3}]^{4-}$ is characterized by bidentate carbonate coordination of D_{3h} symmetry of the complex anion.[48] Carboxylate complexes such as the uranyl acetate anion $[\mathrm{UO_2(O_2CCH_3)_3}]^{-}$[51] have essentially the same coordination geometry and are also very stable;[52] hence our ligand design concept for the uranyl ion has begun with tripodal tricarboxylic acid ligands in which the three carboxylic acid groups are linked together at a tertiary amine bridgehead, such that, when protonated, the latter can act as a hydrogen bond donor. The proposed geometry of the resulting uranyl complexes with such ligands is presented schematically in Figure 1. It was anticipated that the length of the ligand arms can be adjusted to optimize the ligand cavity size while incorporation of an aromatic ring as part of the ligand arm provides a means of increasing the ligand rigidity, thereby offsetting the entropic disadvantage of the long ligand arm.

Here we report the synthesis of four examples of this ligand design concept as applied to the development of uranyl chelators. These are tris[2-(2-carboxyphenoxy)ethyl]amine, tris[3-(2-carboxyphenoxy)propyl]amine, tris[3-(2-carboxynaphthyl-3-oxy)propyl]amine, and tris[3-(2-carboxy-4-octadecylphenoxy)-propyl]amine, referred to as NEB, NPB, NPN, and NPodB, respectively (Schemes I–V). The uranyl complexes of NEB, NPB, and NPN also have been prepared (Schemes VI–VIII) and the uranyl solvent extraction capabilities of NPodB determined.

Experimental Section

(A) Synthesis. (I) General. All reactions were carried out under an argon or nitrogen atmosphere unless otherwise noted. Analytical thin-layer chromatography (TLC) was performed with Analtech silica gel GHLF glass-backed plates. Visualization was accomplished via iodine vapor or UV light. Flash chromatography was performed as described by Still[53] using 230–400 mesh silica gel 60. Infrared spectra, ^{1}H-NMR spectra, mass spectra, and elemental analyses consistent with proposed ligand structures were obtained.[54] Infrared spectra were obtained on a Nicolet 5-DXB FTIR spectrometer as Nujol or Fluorolube mulls. The Raman spectra were obtained from powdered samples placed in glass

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(54) Elemental analyses, some ^{1}H-NMR assignments, and complete mass spectral data are included as Supplementary Material. See the supplementary material paragraph for ordering information.

Table I. Evidence for Hydrogen Bonding to the Uranyl Ion in Single-Crystal Diffraction Studies of Various Complexes

compd	U–O, Å	donor[a] (D)	UO···D, Å	UO···H, Å	ref
α-$UO_2(OH)_2$	1.71 (3)	O	2.88 (4)		27
β-$UO_2(OH)_2$	1.81 (2)	O	2.82 (3)		28
γ-$UO_2(OH)_2$	1.81 (2)	O	2.77 (2)		29
$H_2U_3O_{10}$	1.83 (2)	O	2.88 (3)		30
$(UO_2SO_4)_2 \cdot 7H_2O$	1.75 (2)	W	2.94 (3)		31
	1.76 (2)	W	2.90 (3)		
	1.77 (2)				
	1.74 (2)	W	2.92 (3)		
$(NH_4)_2UO_2(SO_4)_2 \cdot H_2O$	1.818 (14)	N	2.900 (25)		32
	1.819 (13)	W	2.820 (22)		
$UO_2(HPO_3)(PO_3)_2$[b]	1.751 (6)				33
	1.784 (5)	O	2.639 (7)	1.665 (13)	
	1.774 (6)	O	2.696 (7)	1.714 (12)	
	1.748 (6)				
$UO_2(H_2PO_4)_2 \cdot 3H_2O$	1.773 (10)	W	2.886		34
	1.774 (11)				
$UO_2(urea)_2(NO_3)_2$	1.764 (6)	N	3.149 (12)	2.36 (3)	35
	1.744 (6)				
$UO_2(urea)_4(H_2O)(NO_3)_2$	1.77 (2)				36
	1.78 (2)	N[c]	3.13 (2)	2.26 (3)	
		N	3.17 (1)	2.39 (3)	
$UO_2(urea)_3SO_4$	1.772 (3)	N	3.090 (6)	2.14 (5)	37
	1.765 (3)				
$(NH_4)_2[UO_2(malonate)_2]$	1.77 (1)	N	2.83 (2)	1.93	38
	1.75 (1)				
$(UO_2)_2(OH)_2Cl_2(H_2O)_4$	1.821 (21)	W	2.85 (3)		39
	1.752 (15)				
	1.812 (20)	W	2.93 (3)		
	1.760 (20)				
$(CN_3H_6)_4[UO_2(O_2)(CO_3)_2] \cdot 2H_2O$	1.75 (2)	N[c]	2.97		40
		N	2.99		
	1.82 (2)	N[c]	3.00		
		N	2.92		
$Et_2NH_2[UO_2(Et_2NCOS)_2(OEt)]$	1.79 (1)	N	2.85 (2)		41
	1.77 (1)				
$Pr_2NH_2[UO_2(Pr_2NCOS)_2(OEt)]$	1.80 (1)	N	2.87 (2)		42
	1.77 (1)				
$(Pr_2NH_2)_2[UO_2(Pr_2NCOS)_2(S_2)]$	1.815 (6)	N	2.78 (2)		43
			2.92 (2)		
$UO_2(NH_2O)_2 \cdot 3H_2O$[b]	1.769 (9)	N		1.98 (2)	44
$UO_2(NH_2O)_2 \cdot 4H_2O$[b]	1.826 (6)	N[c]		2.02 (2)	45
		W		2.14 (2)	
$UO_2(NH_2O)_2(HOCH_2CH_2OH)$	1.81 (1)	N	2.92 (2)		46
$UO_2(4\text{-aminobutanoate})_3(ClO_4)_2$	1.76 (1)	N	2.74		47
$[NH_4]_4[UO_2(CO_3)_3]$	1.79 (1)	N	2.96 (2)		48

[a] Hydrogen bond donor moieties are as follows: (O) non-water oxygen atom, (W) water molecule, or (N) nitrogen atom. [b] Denotes results of a single crystal neutron diffraction study; all other data were obtained from X-ray diffraction. [c] Hydrogen bonding suggested between two different donor groups and the same uranyl oxygen atom.

capillaries. Excitation was supplied by a Spectra Physics 165 krypton ion laser at 676.4 nm. The scattered light was measured by a Photometrics multichannel CCD detector.

(II) **Materials.** All solvents were used as received from commercial sources. Thionyl chloride was freshly distilled prior to use. 2-Aminopropanol and 3-chloropropanol were obtained from Fluka and were used without further purification. Ethyl salicylate was used as received from Aldrich. Tris(2-chloroethyl)amine hydrochloride [CAUTION, extremely toxic material] was prepared according to literature methods.[55,56] Stearoyl chloride was prepared from stearic acid (Aldrich) and freshly distilled thionyl chloride.

Sodium uranyl triacetate was prepared from uranyl acetate dihydrate (Allied) and sodium acetate in dilute acetic acid. A stock solution of 0.1 M uranyl nitrate was prepared from reagent grade $UO_2(NO_3)_2 \cdot 6H_2O$ (Baker). This solution was standardized according to the method of Davies and Gray.[57]

(III) **Ligands.** **(a) Tris[2-(2-carboxyphenoxy)ethyl]amine Hydrochloride (NEB·HCl, Scheme I).** Ethyl salicylate (28.27 g, 0.170 mol) was added to a warm solution of sodium ethoxide prepared from sodium metal (3.91 g, 0.170 mol) and 200 mL of absolute ethanol. After the solution was stirred for 10 min, tris(2-chloroethyl)amine hydrochloride (10.00 g, 0.042 mol) was added and the completed reaction mixture was heated to reflux for 24 h. Saponification of the ester groups was accomplished by the addition of excess 3 N NaOH and refluxing for an additional 5 h. Acidification with 6 M HCl resulted in the formation of a sticky mass. The supernatant was decanted and the mass was dissolved in 400 mL of warm acetone. Crystallization occurred upon standing to afford 17.44 g (77%) of small white needles. Mp 192–193 °C. IR (Nujol) cm^{-1}: 1602 vs, 1580 m, 1286 s, 743 s. ^{1}H-NMR (DMSO-d_6, 250 MHz): δ 12.8 (broad, 3 H, CO_2H), 7.74 (dd, $J = 7.5$ and 1.6 Hz, 3 H, ArH ortho to acid), 7.57 (dt, $J = 8.0$ and 1.6 Hz, 3 H, ArH para to acid), 7.18 (d, $J = 8.4$ Hz, 3 H, ArH ortho to RO), 7.08 (t, $J = 7.5$ Hz, 3 H, ArH para to RO), 4.59 (apparent s, 6 H, NCH_2), 4.07 (app. s, 6 H, CH_2OAr). MS (+FAB, thioglycerol/glycerol) *m/e* 510 $(M - Cl)^+$.

(b) Tris(3-hydroxypropyl)amine (Scheme II). A mixture of 3-amino-1-propanol (39.27 g, 0.523 mol), 3-chloro-1-propanol (108.74 g, 1.15 mol), and Na_2CO_3 (125 g, 1.2 mol) in 300 mL of absolute ethanol was heated to reflux for 24 h. The reaction mixture was cooled and 400 mL of chloroform added. Filtration and concentration of the filtrate afforded a yellow syrup. Vacuum distillation yielded 83.16 g (83%) of a colorless, viscous syrup. This material was identified by ^{1}H-NMR as predominantly tris(3-hydroxypropyl)amine and was used without further purification. Bp 150–170 °C (0.03 mmHg). ^{1}H-NMR ($CDCl_3$, 250 MHz): δ 4.5 (broad, 3 H, OH), 3.70 (t, 6 H, CH_2O), 2.59 (t, 6 H, NCH_2), 1.73 (m, 6 H, $NCH_2CH_2CH_2$).

(c) Tris(3-chloropropyl)amine Hydrochloride (TCPA·HCl, Scheme II). A mechanically stirred mixture of tris(3-hydroxypropyl)amine (83.16 g, 0.435 mol) in 300 mL of benzene was treated by the dropwise addition

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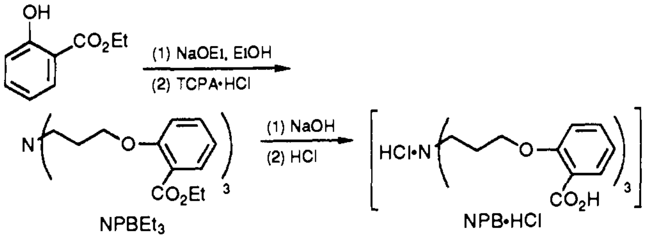
Scheme III



of a 1:1 (v/v) solution of freshly distilled thionyl chloride (175 mL, 2.40 mol) in benzene over a 30-min period. The reaction mixture was slowly heated and then maintained at reflux for 3 h. The excess thionyl chloride was destroyed by careful addition of sufficient ethanol and heating for 1 h. Most of the solvent was removed by distillation leading to crystallization of the crude hydrochloride salt upon cooling. Recrystallization from ethyl acetate afforded 97.92 g (80%) of tris(3-chloropropyl)amine hydrochloride as small white crystals. Mp 86–87 °C (lit.[58] mp 85–87 °C). IR (Nujol) cm^{-1}: 2450 br, 1489 m, 801 m, 778 m. ^{1}H-NMR (CDCl$_3$, 250 MHz): δ 12.7 (broad, 1 H, NH), 3.72 (t, 6 H, CH$_2$Cl), 3.29 (dt, 6 H, NCH$_2$), 2.42 (m, 6 H, NCH$_2$C*H*$_2$CH$_2$).

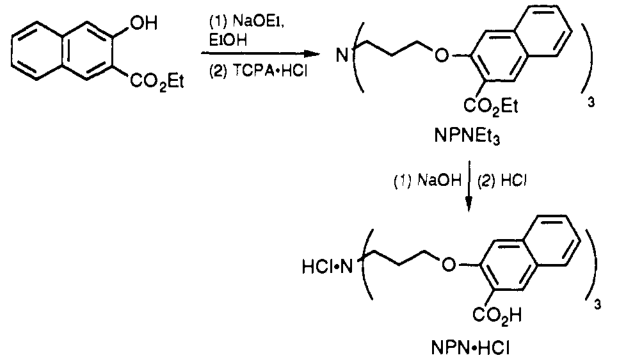
(d) Tris[3-(2-(ethoxycarbonyl)phenoxy)propyl]amine (NPBEt$_3$, Scheme III). Ethyl salicylate (44.91 g, 0.270 mol) was added to a solution of sodium ethoxide prepared by the dissolution of sodium metal (6.21 g, 0.270 mol) in 300 mL of absolute ethanol. Tris(3-chloropropyl)amine hydrochloride (15.00 g, 0.053 mol) was then added and the mixture was heated at reflux for 42 h. After cooling, the mixture was extracted from 400 mL of water with CH$_2$Cl$_2$ (2 × 300 mL). The CH$_2$Cl$_2$ phase was dried (Na$_2$SO$_4$) and the solvent evaporated. The residue was recrystallized from hexane, affording 18.37 g (55%) of white prisms. Mp 74–76 °C. IR (Nujol) cm^{-1}: 1720 s, 1598 s, 1581 s, 1241 s, 1080 s, 755 s. ^{1}H-NMR (CDCl$_3$, 250 MHz) δ 7.78 (dd, J = 7.7 and 1.8 Hz, 3 H, ArH ortho to ester), 7.19 (dt, J = 8.5 and 1.7 Hz, 3 H, ArH para to ester), 6.94 (t, J = 7.5 Hz, 3 H, ArH para to RO), 6.03 (d, J = 8.4 Hz, 3 H, ArH ortho to RO), 4.33 (q, 6 H, CO$_2$CH$_2$), 3.61 (t, 6 H, CH$_2$OAr), 2.59 (t, 6 H, NCH$_2$), 1.90 (m, 6 H, NCH$_2$C*H*$_2$CH$_2$), 1.35 (t, 9 H, CH$_3$).

(e) Ethyl 3-Hydroxy-2-naphthanoate. Thionyl chloride (46 mL, 0.63 mol) was added dropwise to a solution of 3-hydroxy-2-naphthanoic acid (78.35 g, ca. 0.42 mol) in 300 mL of dichloromethane. After 3 h, 300 mL of absolute ethanol was added along with triethylamine (93 mL, 0.66 mol). The mixture was heated to reflux for 6 h and then allowed to stand at room temperature for 72 h. The reaction mixture was partitioned between water and dichloromethane (2×); the organic phase was washed with 10% NaHCO$_3$, dried (Na$_2$SO$_4$), and evaporated. The residue was recrystallized twice from ethanol to yield 49.50 g (55%) of large pale yellow prisms of ethyl 3-hydroxy-2-naphthanoate. Mp 80–81 °C. IR (Nujol) cm^{-1}: 1680 s, 1514 m, 1284 s, 1213 s, 788 m. ^{1}H-NMR (CDCl$_3$, 250 MHz): δ 10.53 (s, 1 H, ArOH), 8.45 (s, 1 H, ArH), 7.77 (d, J = 8.3 Hz, 1 H, ArH), 7.65 (d, J = 8.3 Hz, 1 H, ArH), 7.47 (ddd, J = 8.0, 8.1, 1.0 Hz, 1 H, ArH), 7.29 (overlapping resonances, 2 H, ArH), 4.45 (q, 2 H, CO$_2$CH$_2$), 1.46 (t, 3 H, CH$_3$).

(f) Tris[3-(2-(ethoxycarbonyl)naphthyl-3-oxy)propyl]amine (NPNEt$_3$, Scheme IV). Sodium metal (1.59 g, 69.4 mmol) was dissolved in 200 mL of absolute ethanol. To this solution was added ethyl 3-hydroxy-2-naphthanoate (15.0 g, 69.4 mmol), and the resulting suspension was heated to reflux for 10 min. The reaction mixture was cooled briefly and tris(3-chloropropyl)amine hydrochloride (3.93 g, 13.8 mmol) was added. The reaction mixture was heated to reflux for 24 h. After cooling, the reaction mixture was partitioned between water and ethyl acetate (3 × 100 mL). The organic layer was washed with brine, dried (Na$_2$SO$_4$), and evaporated. The residue was recrystallized from ethanol/toluene to afford 5.67 g (52%) of large white prisms. Mp 143–144 °C. IR (Nujol) cm^{-1}: 1700 m, 1629 m, 1596 m, 1263 s. ^{1}H-NMR (CDCl$_3$, 250 MHz) δ 8.28 (s, 3 H, ArH), 7.81 (d, J = 7.9 Hz, 3 H, ArH), 7.33 (dd, J = 8.0 Hz, 3 H, ArH), 7.07 (dd, J = 7.9 Hz, 3 H, ArH), 5.84 (s, 3 H, ArH), 5.76 (d, J = 8.1 Hz, 3 H, ArH), 4.40 (q, 6 H, CO$_2$CH$_2$), 3.65 (t, 6 H, ArOCH$_2$), 2.67 (t, 6 H, NCH$_2$), 2.00 (m, 6 H, NCH$_2$C*H*$_2$CH$_2$), 1.41 (t, 9 H, CH$_3$). MS (+FAB, thioglycerol/glycerol) *m/e* 786 (MH$^+$).

(g) Tris[3-(2-carboxynaphthyl-3-oxy)propyl]amine Hydrochloride (NPN·HCl, Scheme IV). A mixture of NPNEt$_3$ (3.23 g, 4.10 mmol), 60 mL of ethanol, and 20 mL of 3 N NaOH was heated at reflux for 4 h with the periodic addition of 2–3 mL of water to dissolve any precipitates that formed. The mixture was cooled and acidified with aqueous HCl. The resulting precipitate was then recrystallized from methanol/water and dried in vacuo to yield 2.33 g (77%) of NPN·HCl. Mp 180–184 °C. IR (Nujol) cm^{-1}: 1713 s, 1630 s, 1256 s, 1064 s, 834 m. ^{1}H-NMR (DMSO-d_6, 250 MHz) δ 8.31–7.38 (m, 18 H, ArH), 4.30 (broad, unresolved, 6 H, NCH$_2$), 3.52 (t, 6 H, CH$_2$OAr), 2.34 (m, 6 H, NCH$_2$C*H*$_2$CH$_2$). MS (+FAB, thioglycerol/glycerol) *m/e* 703 (MH$^+$).

Scheme IV



(h) 5-Stearoylsalicylic Acid. To a mixture of stearoyl chloride (80.0 g, 0.264 mol) and salicylic acid (38.3 g, 0.278 mol) in 300 mL of nitrobenzene was added aluminum trichloride (60 g, 0.45 mol) over a 15-min period. The reaction mixture was stirred overnight at 25 °C and then quenched by carefully pouring onto 400 mL of water. This mixture was then allowed to stand overnight and the supernatant was decanted. The remaining gray mass was recrystallized twice from glacial acetic acid and recrystallized twice from methanol to afford 74.83 g (70%) of 5-stearoylsalicylic acid. Mp 128–129 °C. IR (Nujol) cm^{-1}: 1683 s, 1610 m, 1580 m, 1204 s. ^{1}H-NMR (acetone-d_6, 250 MHz): δ 8.29 (d, J = 2.3 Hz, 1 H, ArH ortho to acid), 7.91 (dd, J = 2.3 and 8.7 Hz, 1 H, ArH para to acid), 6.79 (d, J = 8.7 Hz, 1 H, ArH meta to acid), 2.74 (t, 2 H, ArCH$_2$), 1.43 (m, 2 H, ArCH$_2$C*H*$_2$), 1.01 (apparent singlet, 30 H, –(C*H*$_2$)$_{15}$CH$_3$), 0.60 (t, 3 H, CH$_3$).

(i) 5-Octadecylsalicylic Acid (Scheme V). Amalgamated zinc was prepared by treating zinc metal (mossy, 100 g, 1.53 mol) with a solution of HgCl$_2$ (10.0 g, 0.037 mol) in 200 mL of 6 M HCl. After 5 min of swirling, the solution was decanted and 5-stearoylsalicylic acid (60.0 g, 0.148 mol), 150 mL of toluene, 30 mL of glacial acetic acid, and 350 mL of 9 M HCl were added. The reaction mixture was then heated at reflux and vigorously mechanically stirred. Additions of 15 mL of concentrated HCl were periodically made and heating continued for 48 h. After the mixture was cooled to 25 °C, the organic layer was removed and the aqueous phase was extracted with ether (3 × 300 mL) with the combined organic phase being washed with brine and dried (Na$_2$SO$_4$). After evaporation of the solvents the residue was recrystallized twice from methanol to afford 50.07 g (86%) of a white crystalline powder that was used without further purification. Mp 95–96 °C. IR (Nujol) cm^{-1}: 1674 s, 1616 m, 1586 m, 1377 s. ^{1}H-NMR (acetone-d_6, 250 MHz) δ 7.44 (d, J = 2.2 Hz, 1 H, ArH ortho to acid), 7.11 (dd, J = 2.2, 8.5 Hz, 1 H, ArH para to acid), 6.60 (d, J = 8.5 Hz, 1 H, ArH meta to acid), 2.31 (t, 2 H, ArCH$_2$), 1.30 (m, 2 H, ArCH$_2$C*H*$_2$), 1.01 (apparent singlet, 30 H, –(C*H*$_2$)$_{15}$CH$_3$), 0.60 (t, 3 H, CH$_3$).

(j) Ethyl 5-Octadecylsalicylate (Scheme V). A solution of 5-octadecylsalicylic acid (42.26 g, 0.118 mol) and 60 mL of concentrated H$_2$SO$_4$ in 600 mL of absolute ethanol was heated at reflux for 24 h. Most of the solvent was removed under reduced pressure and the remaining material was carefully added to 200 mL of water with external cooling. Extraction with ether (3 × 200 mL) followed by washing the organic phase with brine, drying (Na$_2$SO$_4$), and evaporation afforded 43.59 g (88%) after recrystallization from ethanol. Mp 51–52 °C. Further purification to remove an unsaturated byproduct of the Clemmensen reduction was carried out on a portion of the ethyl 5-octadecylsalicylate (31.32 g) by addition of bromine to a CCl$_4$ solution of the ester until the orange color persisted. Destruction of excess Br$_2$ with cyclohexene, evaporation, and recrystallization from acetone afforded 29.11 g (93% recovery) of small white needles. Mp 52.5–53.5 °C. IR (Nujol) cm^{-1}: 1681 s, 1613 m, 1592 m, 1208 s, 1088 s. ^{1}H-NMR (CDCl$_3$, 250 MHz): δ 10.68 (s, 1 H, ArOH), 7.62 (d, J = 2.2 Hz, 1 H, ArH ortho to ester), 7.26 (dd, J = 2.2 and 8.6 Hz, 1 H, ArH para to ester), 6.90 (d, J = 8.5 Hz, 1 H, ArH meta to ester), 4.40 (q, 2 H, CO$_2$CH$_2$), 2.53 (t, 2 H, ArCH$_2$), 1.59 (m, 2 H, ArCH$_2$C*H*$_2$), 1.42 (t, 3 H, ester CH$_3$), 1.25 (apparent singlet, 30 H, –(C*H*$_2$)$_{15}$CH$_3$), 0.88 (t, 3 H, octadecyl CH$_3$).

(k) Tris[3-(2-(ethoxycarbonyl)-4-octadecylphenoxy)propyl]amine (NPodBEt$_3$, Scheme V). Tris(3-chloropropyl)amine hydrochloride (1.02 g, 3.60 mmol) was added to a mixture of ethyl 5-octadecylsalicylate (7.51 g, 17.9 mmol) and Na$_2$CO$_3$ (2.8 g, 26 mmol) in 60 mL of absolute ethanol. The mixture was heated at reflux for 48 h. After the mixture

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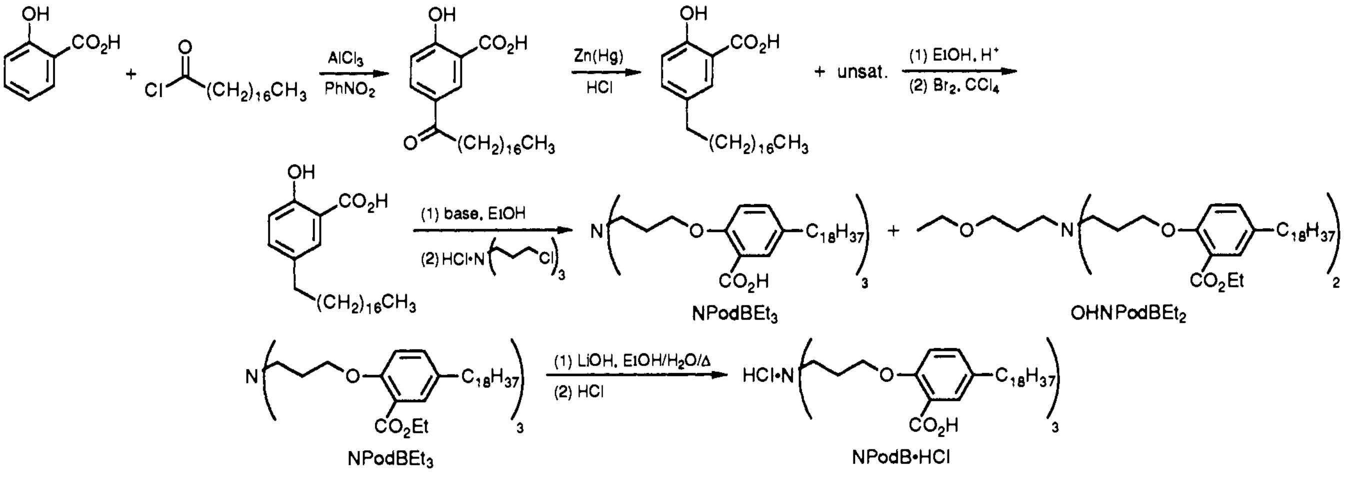
[58] Dei, A.; Morassi, R. *J. Chem. Soc.* **1971**, 2024.

Scheme V



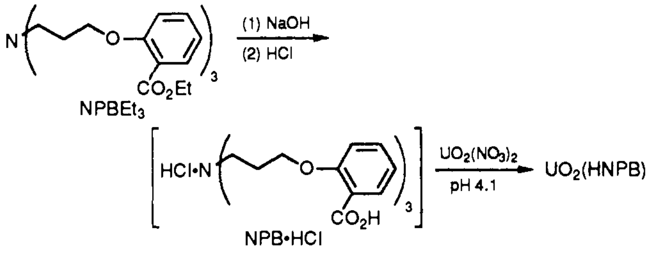
was cooled to 25 °C, 100 mL of chloroform was added and the mixture filtered. Evaporation of the filtrate and purification by flash chromatography (25% ethyl acetate/hexanes) afforded 1.98 g (40%) of NPodBEt$_3$. Recrystallization from petroleum ether yielded 1.81 g of small white needles. Mp 70.0–70.5 °C. TLC $R_f = 0.47$ (40% ethyl acetate/hexanes). IR (Nujol) cm^{-1}: 1699 s, 1614 m, 1575 m, 1502 s, 1255 s, 1092 s. ^{1}H-NMR (CDCl$_3$, 250 MHz) δ 7.57 (d, $J = 2.3$ Hz, 3 H, ArH ortho to ester), 7.04 (dd, $J = 2.2$ and 8.4 Hz, 3 H, ArH para to ester), 6.88 (d, $J = 8.5$ Hz, 3 H, ArH meta to ester), 4.32 (q, 6 H, CO_2CH_2), 3.51 (t, 6 H, $ArOCH_2$), 2.57 (overlapping resonances, 12 H, NCH_2 and $ArCH_2$), 1.85 (m, 6 H, $NCH_2C\mathit{H}_2CH_2$), 1.61 (m, 6 H, $ArCH_2C\mathit{H}_2$), 1.35 (t, 9 H, ester CH_3), 1.25 (apparent singlet, 90 H, $-(C\mathit{H}_2)_{15}CH_3$), 0.88 (t, 9 H, octadecyl CH_3). MS (+FAB) *m/e* 1392 (MH$^+$).

(l) *N*-(4-Oxahexyl)-*N*,*N*-bis[3-(2-(ethoxycarbonyl)-4-octadecylphenoxy)propyl]amine (OHNPodBEt$_2$, Scheme V). This compound has a lower R_f than NPodBEt$_3$ and eluted using 100% ethyl acetate after NPodBEt$_3$ had been recovered to afford 0.95 g (26%) of a white solid that yielded 0.81 g of a white crystalline powder after recrystallization from ethanol/ethyl acetate. Mp 47–49 °C. TLC $R_f = 0.10$ (40% ethyl acetate/hexanes). IR (Nujol) cm^{-1}: 1730 m, 1706 s, 1615 m, 1579 m, 1252 s, 1196 s, 957 m. ^{1}H-NMR (CDCl$_3$, 250 MHz) δ 7.56 (d, $J = 2.2$ Hz, 2 H, ArH ortho to ester), 7.18 (dd, $J = 2.2$ and 8.4 Hz, 2 H, ArH para to ester), 6.73 (d, $J = 8.6$ Hz, 2 H, ArH meta to ester), 4.33 (q, 4 H, CO_2CH_2), 3.95 (t, 4 H, $ArOCH_2$), 3.30 (apparent triplet 4 H, $C\mathit{H}_2OC\mathit{H}_2$), 2.64–2.47 (overlapping resonances, 10 H, NCH_2 and $ArCH_2$), 1.91 (m, 4 H, $NCH_2C\mathit{H}_2COAr$), 1.66–1.55 (overlapping resonances, 6 H, $NCH_2C\mathit{H}_2COEt$ and $ArCH_2C\mathit{H}_2$), 1.36 (t, 6 H, ester CH_3), 1.25 (apparent singlet, 60 H, $-(C\mathit{H}_2)_{15}CH_3$), 1.12 (t, 3 H, ether CH_3), 0.88 (t, 6 H, octadecyl CH_3). MS (+FAB) *m/e* 1020 (MH$^+$).

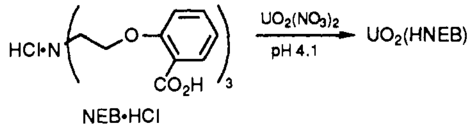
(m) Tris[3-(2-carboxy-4-octadecylphenoxy)propyl]amine Hydrochloride (NPodB·HCl, Scheme V). A solution of NPodBEt$_3$ (1.00 g, 0.718 mmol), lithium hydroxide (0.30 g, 13 mmol), 50 mL of absolute ethanol, and 3 mL of toluene was heated to reflux for 14 h. After cooling, the mixture was acidified with 6 M HCl and partitioned between 75 mL of water and chloroform (3 × 100 mL). The organic phase was washed with water and evaporated under reduced pressure. The residue was recrystallized from ethanol/ethyl acetate and yielded 0.95 g (98%) of a white crystalline powder. IR (Nujol) cm^{-1}: 1693 s, 1634 m, 1580 m, 1291 s, 1239 s. ^{1}H-NMR (CDCl$_3$, 250 MHz): δ 7.65 (d, $J = 2.1$ Hz, 3 H, ArH ortho to CO_2H), 7.14 (dd, $J = 2.0$ and 8.4 Hz, 3 H, ArH para to CO_2H), 6.73 (d, $J = 8.5$ Hz, 3 H, ArH meta to CO_2H), 4.11 (unresolved, 6 H, $ArOCH_2$), 3.61 (unresolved, 6 H, NCH_2), 2.47 (t, 6 H, $ArCH_2$), 2.39 (unresolved, 6 H, $NCH_2C\mathit{H}_2CH_2$). 1.51 (m, 6 H, $ArCH_2C\mathit{H}_2$), 1.25 (apparent singlet, 90 H, $(CH_2)_{15}$), 0.86 (t, 9 H, CH_3). UV–vis (CHCl$_3$): $\lambda_{max} = 304$ nm; $\epsilon_{304} = 8700$ cm^{-1} M^{-1}. MS (+FAB) *m/e* 1309 (MH$^+$).

(IV) Uranyl Complexes. (a) UO$_2$(HNPB) (Scheme VI). A solution of NEBEt$_3$ (0.406 g, 0.631 mmol), aqueous NaOH (1 N, 14 mL, 14 mmol), and 5 mL of ethanol was heated at reflux for 5 h. After the mixture was cooled to 25 °C, dilute HNO$_3$ was added to pH = 5 at which point some of the ligand began to precipitate and the solution became cloudy. Aqueous $UO_2(NO_3)_2$ (6.6 mL, 0.1009 M, 0.67 mmol) was added and a pale yellow precipitate formed immediately. This mixture was heated at reflux for 15 min, cooled to 25 °C, and adjusted to pH 4.1 with dilute NaOH. This procedure was repeated three times at which point the pH remained at 4.1 after heating. The precipitate was collected by filtration and washed with water, methanol, and ether. Further drying in vacuo afforded 0.467 g (89%) of a yellow powder. Mp 284 °C dec. MS (+FAB, nitrobenzyl alcohol) *m/e* 820 (MH$^+$).

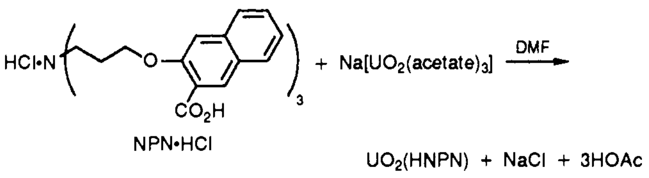
Scheme VI



Scheme VII



Scheme VIII



(b) UO$_2$(HNEB) (Scheme VII). An aqueous solution of $UO_2(NO_3)_2$ (7.0 mL, 0.1009 M, 0.710 mmol) was added to a solution of NEB·HCl (0.351 g, 0.643 mmol) dissolved in 120 mL of 20% ethanol/water. A milky yellow precipitate formed immediately. The mixture was heated to reflux for 15 min, allowed to cool to 25 °C, and adjusted to pH 4.1 by the careful addition of 0.10 M KOH. This procedure was repeated three times at which point the pH remained unchanged after heating. The precipitate was collected by filtration and washed with water, methanol, and finally ether. Further drying in vacuo afforded 0.418 g (84%) of a yellow powder. Mp 225 °C dec. MS (+FAB, thioglycerol/glycerol matrix) *m/e* 778 (MH$^+$).

(c) UO$_2$(HNPN) (Scheme VIII). To a solution of NPN·HCl (0.190 g, 0.258 mmol) in DMF was added Na[UO$_2$(acetate)$_3$] (0.121 g, 0.258 mmol). The mixture was warmed to 80 °C for 2 h, during which time the Na[UO$_2$(acetate)$_3$] dissolved and a fine yellow precipitate formed. The precipitate was collected and washed with water, methanol, and ether. Drying in vacuo afforded 0.214 g (86%) of a yellow microcrystalline powder. Mp > 250 °C dec. MS (+FAB, nitrobenzyl alcohol) *m/e* 970 (MH$^+$).

(B) Uranyl Extraction. Dilute uranyl nitrate solutions were prepared from the 0.1 M $^{238}UO_2(NO_3)_2$ stock solution described earlier; their concentrations were confirmed spectrophotometrically using arsenazo III as an indicator.[59,60]

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(59) Bhatt, V. J.; Agrawal, Y. K. *J. Radioanal. Nucl. Chem.* **1986**, *97*, 255.

(60) Kiriyama, T.; Kuroda, R. *Anal. Chim. Acta* **1974**, *71*, 375.

Partition experiments involving ^{238}U were performed at ambient temperature by placing 5.0 mL of chloroform with a known concentration of $HNPodBH_3^+Cl^-$ and 5.0 mL of an aqueous solution of known $UO_2(NO_3)_2$ concentration in a 16 × 150 mm screw-cap test tube. After vigorous shaking for 10 min and centrifugation, a suitable aliquot of the aqueous phase was removed to a 25-mL volumetric flask containing 2.0 mL of 0.10% (w/v) arsenazo III and 10.0 mL of 0.02 M HNO_3. The solution was diluted to 25 mL with water; the concentration of uranium was determined by measuring the absorbance at 652 nm and comparing it with a calibration curve. The distribution coefficient (D_{ex}) is defined as

$$D_{ex} = ([UO_2^{2+}]_i - [UO_2^{2+}]_{aq})/[UO_2^{2+}]_{aq} \qquad (1)$$

where

$$[UO_2^{2+}]_i = \text{initial } [UO_2^{2+}]_{aq} \qquad (2)$$

Experiments involving ^{235}U used a stock solution of 1.0 mM $^{235}UO_2Cl_2$ prepared by dissolution of a weighed amount of ^{235}U metal (Lawrence Berkeley Laboratory) in concentrated nitric acid followed by repeated evaporation and redissolution in 0.010 M HCl. All extractions were performed at ambient temperature.

Extraction experiments involving constant initial ligand and UO_2^{2+} concentration but variable acid concentrations were performed by placing 1000 μL of 5.2 mM $HNPodBH_3^+Cl^-$ chloroform in a polyethylene centrifuge tube. The aqueous phase consisted of 500 μL of the 1.0 mM $^{235}UO_2Cl_2$ stock solution and 500 μL of the stock HCl solution. After the solution was mixed vigorously with a vortex mixer for 20 min and centrifuged, equal volume aliquots of the organic and aqueous phase were removed and evaporated under an infrared lamp. The uranium was measured by counting the ^{235}U γ-photopeak at 185.7 keV. The distribution coefficient, D_{ex}, of uranium between the two phases was calculated by

$$D_{ex} = \{(\text{counts})_{org}/(\text{count time})_{org}\}/\{(\text{counts})_{aq}/(\text{count time})_{aq}\} \qquad (3)$$

Extraction experiments involving constant initial $[^{235}UO_2^{2+}]_{aq}$ and $[HCl]_{aq}$ but varying ligand concentration were performed by placing 1000 μL of an aqueous solution 0.5 mM in $^{235}UO_2Cl_2$ and 0.10 M in HCl in a polyethylene centrifuge tube and adding 1000 μL of a chloroform solution containing a known concentration of $HNPodBH_3^+Cl^-$. After vigorous mixing with a vortex mixer for 20 min, the phases were separated by centrifugation. Equal volume aliquots of both phases were removed, evaporated, and counted as described above.

Results and Discussion

Ligand Syntheses. For this ligand design, based on a tripodal coordination of carboxylate ligands with concomitant axial hydrogen bonding, the size of the uranyl ion and the required arm length of the tripod are the major structure determinants. Insufficient spacing between the tertiary nitrogen atom and the $-CO_2H$ groups will prohibit bidentate coordination of all three carboxylate groups. Conversely, providing excessive spacing between these functionalities diminishes the entropic force of the chelate effect. Examination of CPK molecular models indicated an optimum ligand arm length is achieved when atoms (e.g., six methylene groups) intervene between the nitrogen atom and the $-CO_2H$ groups. Shorter ligand arms of only 5-atom spacing were anticipated to be insufficient to allow bidentate coordination of all three acid groups. Two analogous ligands of different ligand arm length, NEB and NPB, were prepared to assess the effect of the cavity size. On the basis of CPK models of the ligands and the dimensions of the uranyl ion obtained from examination of crystallographic studies, the shorter ligand (NEB) cannot obtain the geometry depicted in Figure 1. In contrast, the longer ligand arms of NPB, NPN, and NPodB readily provide the necessary spacing to achieve this geometry.

Although we found no reference for the successful preparation of NEB[61] or any of the other ligands whose syntheses are presented here, various phenyl ether and tripodal ligands analogous to NEB have been prepared by Vögtle and co-workers.[61-63]

The synthesis of NEB (Scheme I) can be accomplished by first treating tris(2-chloroethyl)amine hydrochloride with an excess of the sodium, or other alkali metal, salt of ethyl salicylate. The hydrochloride salt of the nitrogen mustard was used because it is easier to handle and store for extended periods and because of the even higher toxicity of the free base. It proved convenient to saponify the crude reaction mixture and isolate NEB as the hydrochloride salt rather than purify the triethyl ester (that remains an oil). The removal of the excess ethyl salicylate and other reaction byproducts is easily accomplished by recrystallization from acetone.

The same general method utilized in the synthesis of NEB can be applied to the preparation of the longer-armed ligands by using the propyl analog of tris(2-chloroethyl)amine hydrochloride, TCPA·HCl. The convenient preparation of relatively large amounts of TCPA·HCl (Scheme II) is accomplished by the dialkylation of 3-amino-1-propanol with 3-chloro-1-propanol followed by the chlorination of the resulting triol with thionyl chloride.[64]

In the synthesis of NPB (Scheme III), isolation of the tetraprotonated form of the ligand proved difficult, due to the formation of a sticky, intractable material that resisted crystallization and purification. Therefore the triethyl ester, $NPBEt_3$, was isolated and the free ligand generated in situ by saponification and neutralization of $NPBEt_3$.

Saponification of $NPBEt_3$ followed by acidification introduces an appreciable amount of water into the sample that, due to the intractability of the acid form, cannot be completely removed. In order to study uranyl complexes prepared from both aqueous and nonaqueous solvent systems NPB derivatives were prepared that could be isolated in the acid form. A 6-atom-arm ligand that could be isolated in its acid form is the naphthalene analog of NPB (prepared according to Scheme IV). Dubbed NPN, this ligand is easily isolated as either the triethyl ester or hydrochloride salt of the free acid.

The preparation of the octadecyl derivative NPodB (Scheme V) began with the Friedel–Crafts acylation of salicylic acid with stearoyl chloride. Subsequent Clemmensen reduction of the aromatic ketone afforded an unsaturated byproduct as a minor impurity (ca. 5%) in the 5-octadecylsalicylic acid that could not be removed by recrystallization. Attempts to remove the impurity from the esterified acid by recrystallization and chromatography of ethyl 5-octadecylsalicylate failed. However, treatment with bromine and recrystallization afforded ethyl 5-octadecylsalicylate that was devoid of any detectable olefinic or brominated impurities.

Formation of the tripod was accomplished by treating tris(3-chloropropyl)amine hydrochloride (TCPA·HCl) with an excess of sodium 2-(ethoxycarbonyl)-4-octadecylphenoxide in ethanol. The first preparation of $NPodBEt_3$ utilized a stoichiometric amount of sodium ethoxide to generate the phenoxide and afforded a relatively low yield (19%) of $NPodBEt_3$. In addition to the desired triester, a large amount (30%) of the TCPA had reacted with sodium ethoxide or the ethanol solvent to produce the bis(aromatic ether), referred to as $OHNPodBEt_2$. An optimized preparation of $NPodBEt_3$ utilized excess sodium carbonate in ethanol to diminish ethoxide attack at the chloropropyl groups of TCPA. This gave an improved yield (40%) of $NPodBEt_3$. However, a significant amount (26%) of the bis(aromatic ether), $OHNPodBEt_2$, was still isolated, indicating that solvolysis of TCPA is a significant side reaction and the use of non-hydroxylic solvents such as DMF might be preferable.

Preparation of the free ligand from $NPodBEt_3$ via saponification with lithium hydroxide and acidification with HCl led to the isolation of NPodB as the hydrochloride salt, $HNPodBH_3^+Cl^-$. This material is freely soluble in chloroform at room temperature and will dissolve in other organic solvents such as warm toluene or hexane.

Uranyl Complexes. Comparison of uranyl complexation by NEB and NPB is a test of the prediction from CPK models that a 6-atom spacing is required to achieve full equatorial coordination of all three carboxylate groups to the uranium atom of a single uranyl ion. Unfortunately, such a comparison is hampered by

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[62] Trummler, B.; Maass, G.; Vöglte, F.; Sieger, H.; Heimann, U.; Weber, E. *J. Am. Chem. Soc.* **1979**, *101*, 2588.

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Table II. Some Relevant Absorbances Found in the Vibrational Spectra of Uranyl Complexes with Aromatic Ether Ligands

	carboxylate stretch		O═U═O stretch	
complex	asymmetric (IR, cm^{-1})	symmetric (IR, cm^{-1})	asymmetric (IR, cm^{-1})	symmetric (Raman, cm^{-1})
UO_2(HNEB)	1527	1421	913	*a*
UO_2(HNEB)	1526	1421	914	839
UO_2(HNPN)	1531	1416	910	838[b]

[a] Raman spectrum could not be obtained due to sample fluorescence. [b] Found in both the infrared and Raman spectra, see text.

differences in solubility of the two ligands and their uranyl complexes. Generation of NPB in situ from $NPBEt_3$ proceeds, as outlined in Scheme VI, by first saponifying to ensure complete removal of the ester protecting groups. Addition of UO_2^{2+} at pH = 4 avoids extensive hydrolysis of the uranyl ion[65,66] and ensures that the tertiary amine is protonated.

The uranyl complexes of NEB and NPB (Scheme VII)[67] were isolated as amorphous yellow powders that are essentially insoluble in water and organic solvents. The elemental analyses of the isolated materials were consistent with formation of UO_2(HNEB)[68] and UO_2(HNPB) from the 5- and 6-atom-spacing ligand, respectively.[54]

Preparation of the UO_2(HNPN) complex using the naphthalene analog of NPB according to the metathesis reaction shown in Scheme VIII allowed complexation in an aprotic solvent system. The yellow microcrystalline complex analyzed for the 1:1 UO_2(HNPN) complex.[54] The ready ability of NPN to displace acetate completely from UO_2^{2+} offers a qualitative measure of the binding strength of the chelating ligand.

(a) Vibrational Spectroscopy. Table II presents data for the uranyl stretching modes of vibration found in UO_2(HNEB), UO_2(HNPB), and UO_2(HNPN). The values were obtained from either the infrared (IR) or Raman spectra of the complexes with the exception of UO_2(HNEB), whose Raman spectrum could not be obtained because of interference from the fluorescence of the sample. The IR spectra of the complexes are quite similar with respect to the asymmetrical and symmetrical stretching modes of the carboxylate groups that occur at about 1530 and 1420 cm^{-1}, respectively. This is consistent with bidentate coordination of the carboxylate groups to the uranyl ion.[69]

The uranyl ion possesses two normal stretching modes of vibration: (1) the IR-active asymmetrical stretch, ν_3, and (2) the Raman-active totally symmetric stretch, ν_1. In a centrosymmetrical environment, ν_1 is not observed in the IR spectrum and ν_3 is not found in the Raman spectrum.[52] However, hydrogen bonding to one of the oxo groups of the uranyl ion breaks this symmetry, making ν_1 and ν_3 both IR- and Raman-active. Thus vibrational spectroscopy is a tool for evaluating the presence of a hydrogen bond to one of the apical oxygen atoms of a uranyl complex. Figure 2 is a comparison of the infrared and Raman spectra for UO_2(HNPB) in the region of the uranyl stretching modes. The prominent peak in the IR spectrum at 914 cm^{-1}, due to the asymmetric O═U═O stretching mode, is typical of uranyl complexes[52] and is not found in the Raman spectrum. The Raman-active uranyl symmetric stretch is found at 839 cm^{-1} and is not found in the IR spectrum. The mutual exclusion of these bands is consistent with a centrosymmetric uranyl group, although the fluorescence of the complex (the sloping baseline of the Raman spectrum in Figure 2) hampers the detection of weaker absorbances and thus may be obscuring them in the Raman spectrum. The coincidence of the moderate-to-weak infrared absorbance at 838 cm^{-1} with the strong O═U═O symmetric stretch, ν_1, found in the Raman spectrum of UO_2(HNPN) at 838 cm^{-1} (see Figure 3) is consistent with the occurrence of ν_1 in the IR spectrum caused by perturbation of the UO_2^{2+} symmetry by hydrogen bonding (although it could be due to ligand vibrations) since the infrared peak at 838 cm^{-1} also agrees well with naphthalene C–H out-of-plane bending vibrations[70] found in NPN·HCl at 834 cm^{-1}.

In summary, the O═U═O stretching frequencies for UO_2(HNEB), UO_2(HNPB), and UO_2(HNPN) are consistent with

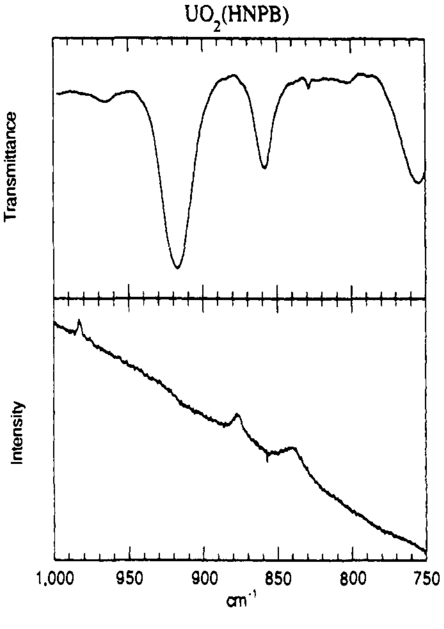

Figure 2. A comparison of the IR (top) and Raman (bottom) spectra for UO_2(HNPB) in the region of the O═U═O stretching frequencies. The $UO_{2\,asym}$ stretch occurs at 914 cm^{-1} in the IR spectrum and the $UO_{2\,sym}$ stretch is evident at about 838 cm^{-1} in the Raman spectrum.

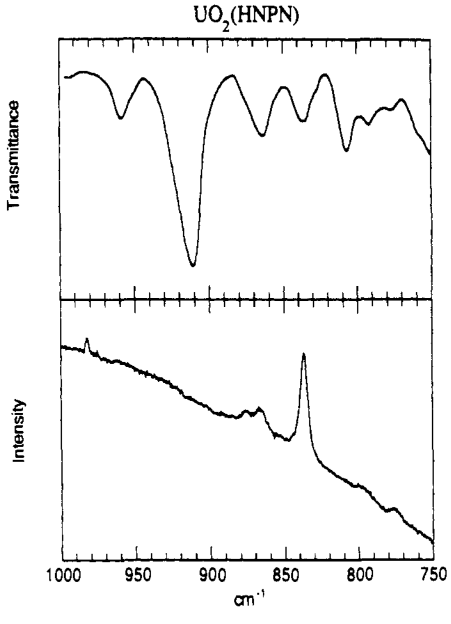

Figure 3. A comparison of the IR (top) and Raman (bottom) spectra for UO_2(HNPN) in the region of the O═U═O stretching frequencies. The $UO_{2\,asym}$ stretch occurs at 910 cm^{-1} in the IR spectrum. The $UO_{2\,sym}$ stretch is evident at about 838 cm^{-1} in the Raman spectrum and also has a corresponding peak in the IR spectrum.

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(67) An attempt to prepare UO_2(HNEB) via a metathesis reaction of NPB·HCl with Na[UO_2(acetate)$_3$] in DMF resulted in formation of a gelatinous precipitate, presumed to be polymeric in nature.

(68) The "H" shown in UO_2(HNEB), UO_2(HNPB), or UO_2(HNPN) reflects the fact that the tertiary amine of the ligand is protonated to provide a charge-neutral complex with UO_2^{2+}.

(69) The asymmetrical and symmetrical carboxylate stretching frequencies found in the structurally characterized complex of ammonium tris(2-methoxybenzoato)dioxouranium(VI) occur at 1524 and 1424 cm^{-1}, respectively: Franczyk, T. S.; Raymond, K. N. To be submitted for publication.

(70) Silverstein, R. M.; Bassler, G. C.; Morrill, T. C. *Spectroscopic Identifaction of Organic Compounds*, 4th ed.; Wiley and Sons: New York, 1981; pp 111 and 112.

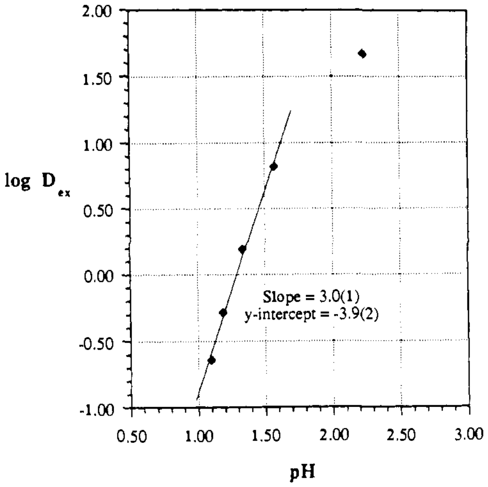

Figure 4. The dependence of uranyl distribution ratios on HCl activities. The symbols represent data points and the solid line is at least-squares linear regression of the four lower pH data.

hydrogen bonding in the case of NPN but do not provide definitive evidence of hydrogen bonding to the uranyl ion.

(b) Mass Spectroscopy. The nature of the uranyl complexes of the aromatic ether ligands, whether discreet 1:1 complexes or polymers, is of primary importance for the evaluation of the ligand architecture. The incorporation of the aromatic ring as part of the ligand arm increases ligand rigidity and favors monomeric complexation. Mass spectral analysis of $UO_2(HNEB)$ using fast atom bombardment ionization produced molecular ions corresponding to expected MH^+ species.[54] In addition to the MH^+ molecular ions, weak peaks at higher molecular mass were also detected. Some of these peaks were consistent with a 2:2 complex or fragments thereof, suggesting that the shorter armed ligand forms at least some oligomeric species.

Mass spectra of $UO_2(HNPB)$ and $UO_2(HNPN)$ showed distinct molecular ion (MH^+) peaks and no fragments corresponding to dimeric or oligomeric species. Although this represents only an absence of evidence for polymeric complex formation, it is an interesting contrast to the shorter armed ligand and is consistent with the evaluation of CPK models of the ligands and uranyl complexes that indicate the larger ligand arm is required for monomeric coordination.

Uranyl Extraction. The complexing and solvent extraction properties for UO_2^{2+} were investigated for the hydrophobic ligand HNPodB. The many potential variables involved in extraction of a metal from an aqueous solution are discussed in detail elsewhere.[71-74] For the extraction of UO_2^{2+} by NPodB, the overall distribution equilibrium can be considered a sum of partial equilibria:

$$\mathrm{HNPodBH}_n{}^{n-2}{}_{\mathrm{org}} \leftrightarrow \mathrm{HNPodBH}_n{}^{n-2}{}_{\mathrm{aq}} \qquad (4)$$

$$\mathrm{HNPodBH}_n{}^{n-2}{}_{\mathrm{aq}} \leftrightarrow \mathrm{HNPodB}^{2-}{}_{\mathrm{aq}} + n\mathrm{H}^+{}_{\mathrm{aq}} \qquad (5)$$

$$\mathrm{UO_2}^{2+}{}_{\mathrm{aq}} + \mathrm{HNPodB}^{2-}{}_{\mathrm{aq}} \leftrightarrow (\mathrm{UO_2(HNPodB)})_{\mathrm{aq}} \qquad (6)$$

$$(\mathrm{UO_2(HNPodB)})_{\mathrm{aq}} \leftrightarrow (\mathrm{UO_2(HNPodB)})_{\mathrm{org}} \qquad (7)$$

$$\mathrm{UO_2}^{2+}{}_{\mathrm{aq}} + \mathrm{HNPodBH}_n{}^{n-2}{}_{\mathrm{org}} \leftrightarrow (\mathrm{UO_2(HNPodB)})_{\mathrm{org}} + n\mathrm{H}^+{}_{\mathrm{aq}} \qquad (8)$$

Equation 4 represents the distribution of the ligand between the two phases. Equation 5 represents the deprotonation of the ligand in the aqueous phase. The proton stoichiometry (n) for the deprotonation of the ligand is dependent on the form of the ligand present in the organic phase; if the hydrogen ion concentration in the aqueous phase is sufficient, the ligand will exist as the monocation $HNPodBH_3^+$ in the organic phase and will require loss of three protons (i.e., $n = 3$) to allow binding of the three carboxyl groups. Lower hydrogen ion concentration in the aqueous phase will favor the overall charge-neutral, zwitterionic $HNPodBH_2$ in the organic phase and will result in a proton stoichiometry of two (i.e., $n = 2$) for complete binding of three carboxyl groups to the metal center. The complexation reaction represented by eq 6 assumes the binding of three deprotonated carboxyl groups to the uranyl ion; since the amine group is protonated the net charge on the complex is zero. Equation 7 is the distribution of the uranyl complex between the organic and aqueous phases. Finally, eq 8 represents the overall extraction equilibrium, a sum of eqs 4 through 7. The equilibrium constant (K_{ex}) for this extraction is defined as

$$K_{\mathrm{ex}} = ([\mathrm{UO_2(HNPodB)}]_{\mathrm{org}}[\mathrm{H}^+]^n{}_{\mathrm{aq}})/([\mathrm{UO_2}^{2+}]_{\mathrm{aq}}[\mathrm{HNPodBH}_n{}^{n-2}]_{\mathrm{org}}) \qquad (9)$$

Equation 9 can be rearranged and expressed as

$$\log K_{\mathrm{ex}} = \log([\mathrm{UO_2(HNPodB)}]_{\mathrm{org}}/[\mathrm{UO_2}^{2+}]_{\mathrm{aq}}) + n \log [\mathrm{H}^+]_{\mathrm{aq}} - \log [\mathrm{HNPodBH}_n{}^{n-2}]_{\mathrm{org}} \qquad (10)$$

or

$$\log K_{\mathrm{ex}} = \log D_{\mathrm{ex}} + n \log [\mathrm{H}^+]_{\mathrm{aq}} - \log [\mathrm{HNPodBH}_n{}^{n-2}]_{\mathrm{org}} \qquad (11)$$

where

$$D_{\mathrm{ex}} = [\mathrm{UO_2(HNPodB)}]_{\mathrm{org}}/[\mathrm{UO_2}^{2+}]_{\mathrm{aq}} \qquad (12)$$

The extraction equilibrium presented in eq 8 and the subsequent equilibrium expression in eqs 9–12 encompass two key assumptions: (1) the only significant uranium-containing species in the organic phase is $UO_2(HNPodB)$; and (2) the only significant uranium-containing species in the aqueous phase is free, unbound UO_2^{2+}. These assumptions are based upon the ligand hydrophobicity and are tested by the subsequent fit of the model.

The proton stoichiometry (n in eq 8) can provide insight into the number of carboxyl groups bound to the uranyl ion in the extracted chelate; it is expected that $n = 3$ if the ligand is all in the organic phase as $HNPodBH_3^+$ and three protons are liberated upon uranyl binding—corresponding to coordination by all three carboxyl groups. Any other values for the apparent proton stoichiometry would invalidate the solution equilibrium model. To determine n, eq 11 can be rearranged as

$$\log D_{\mathrm{ex}} = -n \log [\mathrm{H}^+]_{\mathrm{aq}} + (\log [\mathrm{HNPodBH}_n{}^{n-2}]_{\mathrm{org}} + \log K_{\mathrm{ex}}) \qquad (13)$$

or

$$\log D_{\mathrm{ex}} = n\,\mathrm{pH} + (\log [\mathrm{HNPodBH}_n{}^{n-2}]_{\mathrm{org}} + \log K_{\mathrm{ex}}) \qquad (14)$$

If the ligand concentration is constant, a plot of the log distribution coefficient versus pH should yield a straight line of slope n and a y intercept of ($\log [HNPodBH_n{}^{n-2}]_{org} + \log K_{ex}$). Figure 4 displays the plot of $\log D_{ex}$ versus pH[75,76] for the extraction of $^{235}UO_2^{2+}$ by NPodB. The extractions were performed using an initial 4-fold excess of ligand. The four data points from the lower pH region were fit to a least-squares line giving a slope of 3.0 (1) and a y intercept of −3.9 (2). (The data point at pH 2.23 does not conform to the linear trend of the first four points; at low acid concentration the extraction of uranyl becomes nearly quantitative and the assumptions used in calculating D_{ex} are no longer valid.) The intercept corresponds to ($\log [NPodB]_{org} + \log K_{ex}$) which

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(74) Nakasuka, N.; Hirose, K.; Tanaka, M. *J. Inorg. Nucl. Chem.* **1973**, *35*, 265.

(75) The pH was calculated on the basis of the initial HCl concentration of the aqueous solution and was corrected for hydrogen ions generated from complexation of the ligand to the uranyl ion.

(76) The [HCl] was converted to pH using the activity coefficients for HCl found in the following: Harned, H. S.; Owen, B. B. *The Physical Chemistry of Electrolytic Solutions*; Reinhold: New York, 1950.

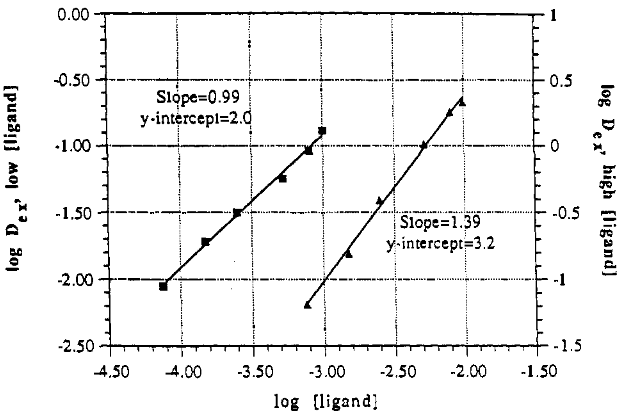

Figure 5. The dependence of uranyl distribution ratios on NPodB concentrations at [HCl] = 0.10 M and (right side) $[UO_2^{2+}]_{total}$ = 0.5 mM and (left side) $[UO_2^{2+}]_{total}$ = 0.05 mM. The symbols represent data points and the solid line is a least-squares linear regression of the data.

gives $\log K_{ex} \approx -1.2$. This value was only a first estimate since the ionic strength of the aqueous phase varied with the HCl concentration.

To evaluate the extraction constant at constant ionic strength and to see the effect of high electrolyte concentration (as in seawater) the extractions were repeated using 1 M aqueous NaCl. Formation of an emulsion at lower pH values limited these data to only two reliable points; however, they corroborate a proton stoichiometry of three and clearly demonstrate a suppression of UO_2^{2+} extraction by the presence of sodium chloride in the aqueous phase. Similar effects are known for other uranyl extractants[77-79] and are assigned to the complexing ability of chloride for the uranyl ion in the aqueous phase and the competition of the $>10^3$ excess of sodium ions with UO_2^{2+} for carboxyl groups of the ligand in the organic phase.

Determination of the UO_2/ligand stoichiometry can similarly be accomplished by measuring K_{ex} at constant acid concentration while varying the amount of ligand present in the organic phase. Rearrangement of eq 11 yields

$$\log D_{ex} = \log [\mathrm{HNPodBH_3^+}]_{org} + (\log K_{ex} - 3 \log [H^+]_{aq}) \qquad (15)$$

or

$$\log D_{ex} = \log [\mathrm{HNPodBH_3^+}]_{org} + (\log K_{ex} + 3\ \mathrm{pH}) \qquad (16)$$

Thus, a plot of $\log D_{ex}$ versus $\log [\mathrm{HNPodBH_3^+}]$ at a constant pH should yield a slope of one (the ligand/metal stoichiometry) and a y intercept that is $\log K_{ex} + 3$ pH. Figure 5 (right) depicts the double logarithmic plot of D_{ex} versus ligand concentration initially obtained from the extraction of UO_2^{2+} from a 0.1 M HCl aqueous solution by chloroform solutions of NPodB. The dependence is essentially linear, although the slope of the line obtained from a least-squares regression of the six data points is 1.39 (4). This result suggests more than one ligand, on average, is bound to the uranyl ion in the extracted complex. However, a subsequent set of extraction experiments performed at one-tenth the initial $[UO_2^{2+}]_{aq}$ (0.05 mM) was performed and a plot of log D_{ex} versus log [ligand] (Figure 5, left) yielded a slope of 0.99—the predicted metal–ligand stoichiometry of the extracted complex. The higher slope of the former first set of extraction experiments is apparently an artifact of the high concentration conditions.

Extrapolation of the log D_{ex} versus pH plot of Figure 4 can be used to estimate the extraction coefficient at neutral pH. Depending upon the estimated pK_a's of the ligand in water (compare 2-methoxybenzoic acid, for example),[80,81] values of approximately 10^{11} can be estimated, certainly high enough for quantitative complexation of even very dilute UO_2^{2+}.

Summary

Uranyl complexing agents have been developed which are intended to both coordinate to the central metal ion and hydrogen bond to the oxo group. This stereognostic coordination of the oxocation is a new way to achieve specificity of metal ion binding.

The ligands NEB, NPB, and NPN form 1:1 complexes with UO_2^{2+}. The bidentate coordination of carboxyl groups of these compounds is indicated by the infrared spectra, which offer some support for the presence of a hydrogen bond to the uranyl group. Mass spectral data corroborate CPK model predictions that more than five intervening atoms between the tertiary nitrogen atom and the carboxylate groups are required for metal ion incorporation and monomeric complex formation.

Solvent extraction of aqueous UO_2^{2+} into chloroform solutions of the ligands has shown them to be powerful extractants. In the case of the very hydrophobic ligand NPodB the stoichiometry of the complexation reaction is shown to be a 1:1 UO_2/ligand complex formed by the release of 3 protons.

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Supplementary Material Available: Text giving chemical analyses and ^{1}H-NMR assignments and a listing of additional vibrational data (3 pages). Ordering information is given on any current masthead page.

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