COMPLEXATION OF METAL IONS WITH AZACROWN ETHERS BEARING AN 8-HYDROXYQUINOLINE SIDE ARM

Xian Xin Zhang, Jerald S. Bradshaw,* Andrei V. Bordunov,† and Reed M. Izatt*
Department of Chemistry and Biochemistry
Brigham Young University
Provo, UT 84602, USA

Abstract. Thermodynamic quantities (log K, ΔH, and $T\Delta S$) for the interactions of six azacrown ethers each bearing an 8-hydroxyquinoline (CHQ) side arm (1–6) with Na^+, K^+, Ba^{2+}, and Cu^{2+} were determined by calorimetric titration in methanol solution at 25°C. The results indicate that these ligands form stable complexes with the cations studied. Ligands 1 and 3 that have CHQ attached through position 7 (next to the OH group) show high selectivity for Cu^{2+} (log K values of 8.12 and 9.44, respectively) over Na^+, K^+, and Ba^{2+} by more than four orders of magnitude. On the other hand, ligands 2 and 4 that have CHQ attached through position 2 (next to the quinoline nitrogen group) form more stable complexes with Na^+, K^+, and Ba^{2+}, but less stable complexes with Cu^{2+}, than ligands 1 and 3. All ligands interact more strongly with K^+ than with Na^+. The K^+/Na^+ selectivity for ligands 4 and 5 is about 1.5 log K units. All complexation reactions display negative enthalpy changes. In most cases the entropy changes are also negative, indicating that formation of the complexes is enthalpy driven. ^1H NMR spectral experiments demonstrate coordination of the cations by all donor atoms of the ligands including those of the CHQ arm. In all cases, the OH signal is observed in the ^1H NMR spectra, suggesting that the complexation with the cations does not involve deprotonation of the CHQ groups in the ligands.

Key words: Crown ether, metal ion selectivity, equilibrium constant, enthalpy change, entropy change, 8-hydroxyquinoline side arm.

1. Introduction

Attachment of various functional groups to azacrown ethers often results in some unique complexing properties of the macrocyclic ligands [1–9]. Monoazacrown and diazacrown ethers containing phenolic groups have been shown to have strong binding ability for alkali and alkaline-earth cations [3–5] and to be effective reagents for extraction of these cations from water into an organic phase [4,5]. The presence of UV or fluorescent active side arms on lariat ethers allows the analytical determination of certain cations by spectrophotometric methods because of the selectivity of the ligands for the

---

† Present address: Division of Chemistry and Chemical Engineering 210-41, California Institute of Technology, Pasadena, CA 91125.

cations and the specific UV or fluorescence response of the complexed species [6–9].

8-Hydroxyquinoline and its derivatives are another type of widely used chromogenic reagents. Since 8-hydroxyquinoline forms a stable five-membered chelate ring with a metal cation through coordination of quinoline nitrogen and hydroxy oxygen atoms [10], 8-hydroxyquinoline-substituted lariat ethers should possess strong metal-ion complexing ability. Such behavior has been demonstrated in two of our recent publications [11,12]. Compared with other alkali and alkaline-earth metal ions, the higher stability of the Mg^{2+} complex with a diazacrown ether bearing two 5-chloro-8-hydroxyquinoline (CHQ) arms (7, see Figure 1) resulted in a unique UV-visible absorption spectrum of the Mg^{2+}-7 complex in methanol [12]. Diazacrown ethers 7 and 8 with two CHQ attached as side arms exhibited high cation selectivities for Mg^{2+}, Cu^{2+}, and Ni^{2+} (by 7) and K^+ and Ba^{2+} (by 8) [11,12]. High complex stability and selectivity for K^+ and Ba^{2+} by 8 were attributed to the formation of a pseudo second macroring through π-π stacking between the two CHQ rings of 8 [11].

Since 8-hydroxyquinoline and its derivatives are UV active and fluorescent compounds, a study of the metal-ion complexation properties of CHQ-substituted macrocycles is important since these materials could be used for sensing and detecting metal ions. In this paper, we present thermodynamic
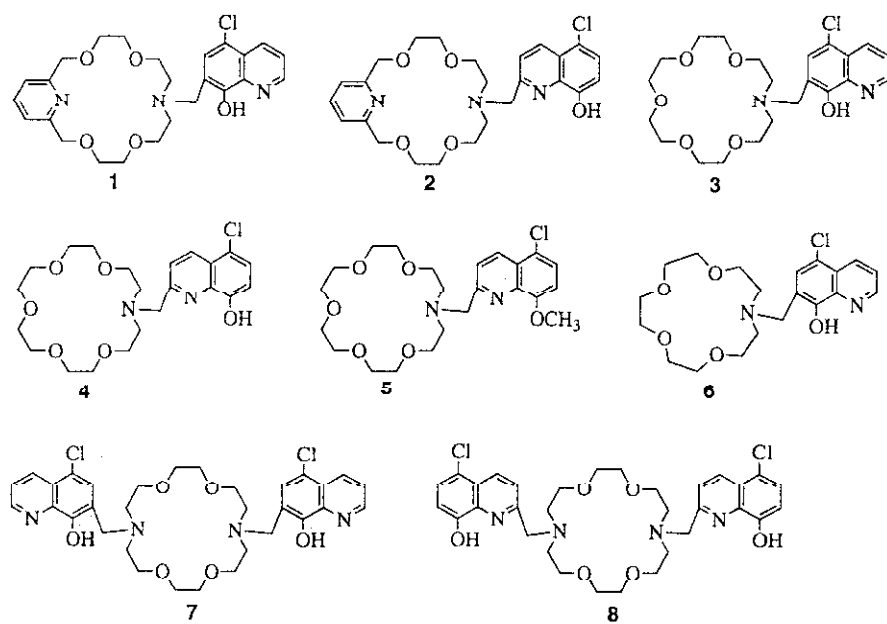

Figure 1. Structures of azacrown and diazacrown ethers.

(log K, ΔH, and ΔS) and ^1H NMR spectral data for the interactions of six azacrown ethers each bearing a CHQ side arm (1-6, see Figure 1) with Na^+, K^+, Ba^{2+}, and Cu^{2+}. The results show that these CHQ-substituted azacrown ethers form stable complexes with the cations studied in absolute methanol (MeOH). High Cu^{2+} selectivity is observed in several cases. The ^1H NMR spectra indicate coordination of the cation by all donor atoms of the ligand including those of the CHQ arm.

2. Experimental

2.1. MATERIALS

The syntheses of CHQ-substituted compounds 1-5 have been reported [12,13]. Compound 6, 13-((5-chloro-8-hydroxy-7-quinolinyl)methyl)-1,4,7,10-tetraoxa-13-azacyc-lopentadecane, was prepared and isolated according to the procedure reported for 3 [12] to give an oil. ^1H NMR (CDCl$_3$): δ 2.95 (t, J = 5.2 Hz, 4 H), 3.71 (m, 16 H), 4.00 (s, 2 H), 7.34 (s, 1 H), 7.50 (m, 1 H), 8.47 (d, 1 H), 8.91 (m, 1 H); MS: m/z 412 (M$^+$ + 1). Anal. Calcd for $C_{20}H_{27}N_2O_5Cl$: C, 58.47; H, 6.58. Found: C, 58.46; H, 6.62.

Reagent grade chemicals were obtained from the indicated sources and used without further purification: NaBr (J. T. Baker), KBr (Wasatch), BaBr$_2$ (Johnson Matthey), and CuCl$_2$ (Aldrich). The MeOH (Fisher HPLC grade) used had a water content of less than 0.05%.

2.2. DETERMINATION OF THERMODYNAMIC QUANTITIES

Log K, ΔH, and $T\Delta S$ values were determined as described earlier [14] in MeOH at 25.0 ± 0.1°C by titration calorimetry using a Tronac Model 450 calorimeter equipped with a 20-mL reaction vessel. The metal ion solutions (0.10 M) were titrated into the crown ether solutions (3.0 x 10^{-3} M) and the titrations were carried out to a two-fold excess of the metal ions. For interactions of Cu^{2+} with ligands 1-4 and 6 which exhibited very large exothermic effects, both Cu^{2+} (0.062 M) and ligand (8.0 x 10^{-4}–1.5 x 10^{-3} M) concentrations were decreased to avoid a large temperature increase during the reaction in order to obtain accurate thermodynamic quantities. Thermodynamic quantities for reactions for which log K > 6 were determined by a cation competition technique wherein a solution containing ligand and one cation was titrated with a solution of a second cation having a larger log K value than the former one [15]. The methods used to process the calorimetric data and to calculate the log K and ΔH values have been described [16].

^{1}H NMR spectra were recorded using a Varian Gemini 200 (200 MHz) spectrometer in deuterated dimethylsulfoxide (DMSO-d_6). Tetramethylsilane (TMS) was used as the internal standard. Concentrations of the ligands were *ca.* 0.01 M and those of the metal ions were 3~6-fold greater than those of the ligands. The DMSO-d_6 was used since the OH proton signals could be observed in this solvent [17,18].

3. Results and Discussion

In Table I are listed log K, ΔH, and $T\Delta S$ values for the interactions of CHQ-containing azacrown ethers with Na$^+$, K$^+$, Ba^{2+}, and Cu^{2+}. Single-CHQ-armed ligands 1–6 form stable complexes with these cations in McOH (log K values range from 3.00 to 9.44). The two 18-membered-ring ligands 1 and 3 show high selectivity for Cu^{2+} (log K values of 8.12 and 9.44, respectively) over the other metal ions studied by more than four orders of magnitude, while a 15-membered-ring ligand 6 selectively binds Cu^{2+} (log K = 7.88) over the other cations by more than three log K units. Ligand 4 selectively binds Ba^{2+} (log K = 6.20) over the other cations studied. All ligands in Table I form more stable complexes with K$^+$ than with Na$^+$. Good K$^+$/Na$^+$ selectivity is observed for ligands 4 and 5 with a selectivity factor of about 1.5 log K units. Nevertheless, as shown in Table I, the single-CHQ-armed ligands 1–6 exhibit lower K$^+$/Na$^+$ selectivity than the double-CHQ-armed ligand 8.

3.1. EFFECT OF THE LIGAND STRUCTURE ON METAL ION COMPLEXATION

Ligands 1-2 and 3-4 are two pairs of isomers. They differ only in the attachment site of the CHQ unit to the parent macrorings. Compounds 2 and 4 have CHQ attached through its position 2 (next to the quinoline nitrogen atom) and form more stable complexes with Na$^+$, K$^+$, and Ba^{2+} than compounds 1 and 3. The opposite is true for Cu^{2+}. Ligands 1 and 3 which have CHQ attached through its position 7 (next to the OH group) bind Cu^{2+} significantly stronger than do ligands 2 and 4. The same effect has been noted for double-CHQ-armed isomers 7 and 8 [12] (see Table I). Ligand 6 with the CHQ arm attached through its position 7, like 1 and 3, also forms a very stable complex with Cu^{2+}.

The difference between 1 and 3 and between 2 and 4 is that a pyridine group is incorporated into the 18-membered-ring backbone of 1 and 2. A comparison of 1 with 3 and of 2 with 4 shows that incorporation of the pyridine ring increases the stability of the Na$^+$ complexes and decreases the

Table I. Log K, ΔH (kJ/mol), and $T\Delta S$ (kJ/mol) values for interactions of macrocyclic ligands with metal ions in methanol at 25.0°C

Ligand	Cation	log K	ΔH	$T\Delta S$
1	Na^+	3.85 ± 0.02	-17.5 ± 0.6	4.47
	K^+	4.01 ± 0.05	-28.3 ± 0.4	-5.41
	Ba^{2+}	4.12 ± 0.07	-32.7 ± 0.9	-9.18
	Cu^{2+}	8.12 ± 0.09^a	-95.1 ± 0.7^a	-48.8
2	Na^+	4.20 ± 0.03	-23.6 ± 0.4	0.37
	K^+	5.16 ± 0.03	-38.8 ± 0.1	-9.35
	Ba^{2+}	5.49 ± 0.05	-37.1 ± 0.6	-5.76
	Cu^{2+}	3.72 ± 0.08	-103.1 ± 4.1	-81.9
3	Na^+	3.60 ± 0.02	-27.5 ± 0.4	-5.15
	K^+	4.47 ± 0.02	-40.0 ± 0.2	-14.5
	Ba^{2+}	4.08 ± 0.08	-39.3 ± 0.8	-16.5
	Cu^{2+}	9.44 ± 0.15^a	-89.0 ± 1.2^a	-35.1
4	Na^+	3.98 ± 0.03	-27.4 ± 0.5	-4.68
	K^+	5.42 ± 0.04	-52.1 ± 0.3	-21.2
	Ba^{2+}	6.20 ± 0.07^a	-40.6 ± 0.7^a	-5.21
	Cu^{2+}	5.52 ± 0.11	-99.5 ± 2.5	-68.0
5	Na^+	4.06 ± 0.05	-20.2 ± 0.7	2.97
	K^+	5.64 ± 0.08	-45.8 ± 0.4	-13.6
	Ba^{2+}	5.02 ± 0.09	-30.6 ± 1.1	-1.95
	Cu^{2+}	4.25 ± 0.06	-40.5 ± 0.5	-16.2
6	Na^+	3.00 ± 0.08	-17.8 ± 0.8	-0.68
	K^+	3.17 ± 0.07	-19.4 ± 0.7	-1.31
	Ba^{2+}	4.28 ± 0.08	-20.6 ± 0.9	3.82
	Cu^{2+}	7.88 ± 0.10^a	-105.6 ± 3.3^a	-60.7
7[b]	Na^+	2.89 ± 0.05	-14.1 ± 0.8	2.4
	K^+	3.39 ± 0.03	-24.4 ± 0.7	-5.0
	Ba^{2+}	3.60 ± 0.05	-11.6 ± 0.5	8.9
	Cu^{2+}	10.1 ± 0.1^a	-92.5 ± 0.6^a	-34.9
8[b]	Na^+	3.74 ± 0.01	-26.4 ± 0.3	-5.1
	K^+	6.61 ± 0.03^a	-58.1 ± 0.1^a	-20.4
	Ba^{2+}	12.2 ± 0.4^a	-76.1 ± 0.7^a	-6.5
	Cu^{2+}	4.7 ± 0.2	-116 ± 4	-89

[a] Quantities were determined by competitive calorimetric titration.
[b] Reference 12.

stability of the K^+ and Cu^{2+} complexes. Ligand **5** bears a methoxyquinoline instead of hydroxyquinoline (CHQ) side arm. This structural change, as compared with **4**, results in a stabilization effect for the interactions with Na^+ and K^+ and a destabilization effect with Ba^{2+} and Cu^{2+}. Ligands **3** and **6** have the same CHQ side arm and attachment position, but different macroring

sizes. The 15-membered-ring 6 forms less stable complexes with Na$^+$, K$^+$, and Cu^{2+} than the 18-membered-ring 3.

The complexation behavior of single-CHQ-armed ligands is different from that of the double-CHQ-armed ligands. Compared with 7, ligand 3 shows increased log K values for interactions with Na$^+$, K$^+$, and Ba^{2+}, but a decreased log K value with Cu^{2+}. On the other hand, ligand 4 forms more stable complexes with Na$^+$ and Cu^{2+}, but less stable complexes with K$^+$ and Ba^{2+} than ligand 8. The high stability of the K$^+$ and Ba^{2+} complexes with 8 is attributed to the formation of a pseudo second macroring through π-π stacking between the two CHQ rings [11]. This effect is not possible for single-CHQ-armed compounds 1–6 (see the ^{1}H NMR spectral data in Section 3.3).

3.2. ENTHALPIC AND ENTROPIC EFFECTS OF COMPLEXATION

Thermodynamic data in Table I show the complexation of the metal ions with CHQ-substituted azacrown ethers to be exothermic in each case. The $T\Delta S$ values are negative except in the cases of Na$^+$ interaction with 1, 2, 5, and 7 and of Ba^{2+} with 6 and 7. These facts indicate that the formation of the complexes in most cases is enthalpy driven.

Except for 5, all complexation reactions of the ligands with Cu^{2+} exhibit large negative enthalpy changes (-ΔH values $\geq$ 90 kJ/mol). The lower log K values for Cu^{2+}-2, Cu^{2+}-4, and Cu^{2+}-8 interactions are due to larger negative $T\Delta S$ values, indicating a larger conformational change of these ligands when coordinated with Cu^{2+}. The stronger interactions of 1-6 with K$^+$ than with Na$^+$ are attributed to larger enthalpy gains due to K$^+$ complexation. In every case, there are larger entropy losses for K$^+$ than for Na$^+$ complexation. A similar situation has been noted previously for the different thermodynamic behavior when lariat ethers complex with K$^+$ and Na$^+$ [19].

3.3. ^{1}H NMR SPECTRA

^{1}H NMR spectra of free and complexed 2 and 4 are shown in Figures 2 and 3, respectively. Chemical shifts of aromatic and hydroxyl protons of free and complexed ligands are listed in Table II. Upon complexation with the metal ions, all proton signals of the ligands undergo chemical shift changes of varying magnitudes indicating the interactions of the cations with both macroring and CHQ side arms [12,20–22]. It is seen in Figures 2 and 3 that the spectra of the complexed ligands are different from those of the free ones.

The free and complexed ligands 2 and 4 show OH proton signals (Figures 2 and 3). This observation demonstrates that the CHQ-armed azacrown ethers

exist in a neutral phenol form and that the interactions with the cations do not result in the loss of the CHQ protons. The same effect has been observed for other phenol-containing macrocycles [11,12]. Upon complexation with a metal ion, two significant changes in the OH peak of the ligands can be seen. First, the OH signal experiences a large downfield shift (to a larger δ (ppm) value, see Figures 2 and 3). Second, the OH peaks are sharper in complexed ligands than in free ones.

Except for proton H_d, all aromatic protons of 2 and 4 undergo downfield shifts as the ligands form complexes with K^+ or Ba^{2+} (see Table II, negative CIS values in parentheses). This is not surprising since the electron-donating interactions of the donor atoms of CHQ and pyridine rings with the cations result in a magnetic deshielding effect. We previously observed large upfield shifts of the CHQ protons in the 8 complexes with K^+ and Ba^{2+} (up to 100 Hz) [11,12], which was an evidence of π-π interaction between the two CHQ rings of compound 8. This interaction resulted in a pseudo second macroring
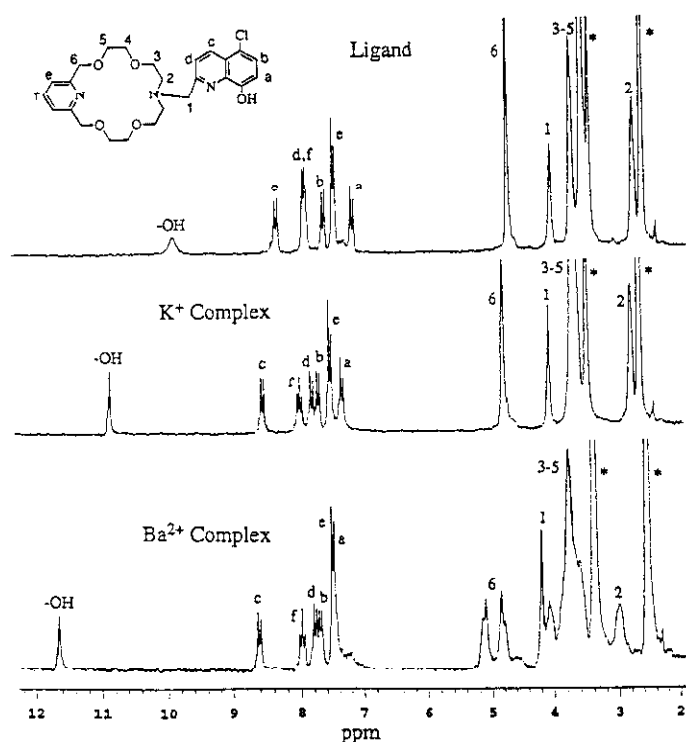

Figure 2. ^1H NMR spectra of free 2 and its K^+ and Ba^{2+} complexes in DMSO-d_6. Peak assignments were determined from the spectra of model compounds and are shown for all protons. The peaks labeled with an asterisk are attributed to the solvent.
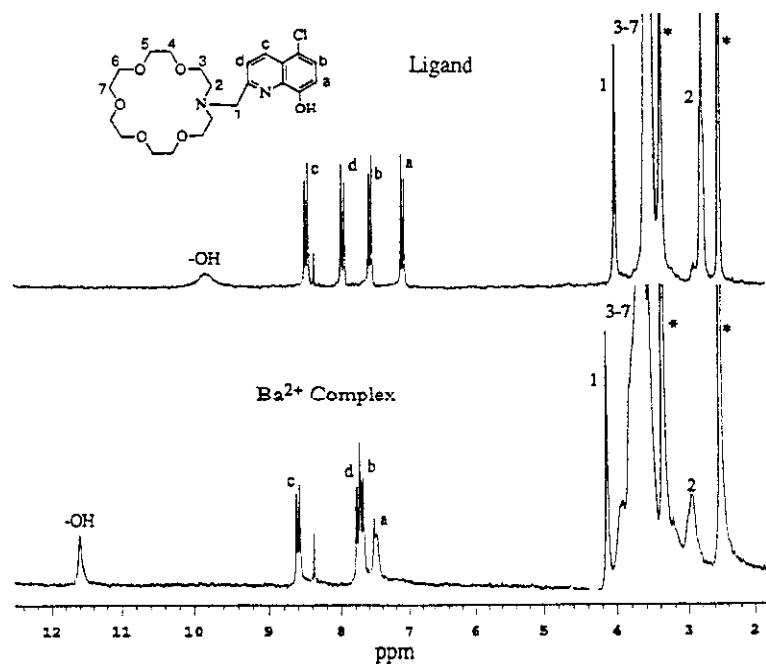
Figure 3. ^{1}H NMR spectra of free 4 and its Ba^{2+} complex in DMSO-d_6. Peak assignments were determined from the spectra of model compounds and are shown for all protons. The peaks labeled with an asterisk are attributed to the solvent.

Table II. Chemical shifts (δ in ppm)^a of aromatic and hydroxyl protons of free and complexed ligands 2 and 4 and cation-induced shifts (CIS)^b in DMSO

Compound	H$_a$	H$_b$	H$_c$	H$_d$	H$_e$	H$_f$	H$_{OH}$
2	7.050	7.523	8.246	7.821	7.353	7.817	9.803
2-K$^+$	7.188	7.573	8.413	7.681	7.381	7.872	10.731
	(-27.5)	(-10.0)	(-33.3)	(28.1)	(-5.50)	(-11.0)	(-186)
2-Ba^{2+}	7.481	7.692	8.611	7.777	7.481	7.981	11.634
	(-86.1)	(-33.7)	(-73.0)	(8.90)	(-25.6)	(-32.8)	(-366)
4	7.068	7.543	8.433	7.928	-	-	9.826
4-Ba^{2+}	7.502	7.707	8.597	7.753	-	-	11.592
	(86.6)	(32.7)	(32.8)	(35.0)			(358)

^{a} Concentrations of the ligands were ca. 0.01 M and those of the metal ions were 0.05~0.07 M. The chemical shifts are referred to internal Me$_4$Si .

^{b} CIS (Hz) = 200 x [δ_{lig} (ppm) - δ_{compl} (ppm)]. The CIS values (in Hz) are given in parentheses. A negative value indicates a downfield shift, while a positive value indicates an upfield shift.

[11]. No upfield shifts are observed for the aromatic protons of **2** and **4** (except H_d) because the tether connecting the CHQ group in **2** to the macroring is not long enough to allow π-π interaction between CHQ and pyridine rings and **4** has only one aromatic ring. Thus, a pseudo second macroring cannot form in **2** or **4** and, consequently, **2** and **4** do not have high selectivity for K^+ and Ba^{2+}.

Acknowledgment

References

1. M. Takagi and H. Nakamura: *J. Coord. Chem.* **15**, 53 (1986).
2. H. Tsukube: *Talanta* **40**, 1313 (1993).
3. N.G. Lukyanenko, V.N. Pastushok, A.V. Bordunov, V.I. Vetrogon, N.I. Vetrogon, and J.S. Bradshaw: *J. Chem. Soc. Perkin Trans. 1* 1489 (1994).
4. Y. Katayama, K. Fukuta, and M. Takagi: *Anal. Chim. Acta* **185**, 295 (1986).
5. Y. Katayama, R. Fukuta, T. Iwasaki, K. Nita, and M. Takagi: *Anal. Chim. Acta* **204**, 113 (1988).
6. Y. Sakai, N. Kawano, H. Nakamura, and M. Takagi: *Talanta* **33**, 407 (1986).
7. E. Chapoteau, B.P. Czech, C.R. Gebauer, A. Kumar, K. Leong, D.T. Mytych, W. Zazulak, D.H. Desai, E. Luboch, J. Krzykawski, and R.A. Bartsch: *J. Org. Chem.* **56**, 2575 (1991).
8. S. Shinkai, Y. Ishikawa, H. Shinkai, T. Tsuno, H. Makishima, K. Ueda, and O. Manabe: *J. Am. Chem. Soc.* **106**, 1801 (1984).
9. H. Nishida, Y. Katayama, H. Katsuki, H. Nakamura, M. Takagi, and K. Ueno: *Chem. Lett.* 1853 (1982).
10. J. Stary: *The Solvent Extraction of Metal Chelates*, Pergamon Press, New York (1964).
11. X.X. Zhang, A.V. Bordunov, J.S. Bradshaw, N.K. Dalley, X.-L. Kou, and R.M. Izatt: *J. Am. Chem. Soc.* **117**, 11507 (1995).
12. A.V. Bordunov, J.S. Bradshaw, X.X. Zhang, N.K. Dalley, X.-L. Kou, and R. M. Izatt: *Inorg. Chem.* **35**, 7229 (1996).
13. A.V. Bordunov, P.C. Hellier, J.S. Bradshaw, N.K. Dalley, X.-L. Kou, X.X. Zhang, and R.M. Izatt: *J. Org. Chem.* **60**, 6097 (1995).
14. (a) J.J. Christensen, J. Ruckman, D.J. Eatough, and R.M. Izatt: *Thermochim. Acta* **3**, 203 (1972). (b) R.M. Izatt, R.E. Terry, B.L. Haymore, L.D. Hansen, N.K. Dalley, A.G. Avondet, and J.J. Christensen: *J. Am. Chem. Soc.* **96**, 7620 (1976). (c) D.J. Eatough, R.M. Izatt, and J.J. Christensen: in N.D. Jespersen (ed.), *Biochemical and Clinical Applications of Thermometric and Thermal Analysis*, Elsevier, New York (1982), pp. 3–38.
15. (a) J.D. Lamb, R.M. Izatt, C.S. Swain, and J.J. Christensen: *J. Am. Chem. Soc.* **102**, 475 (1980). (b) H.-J. Buschmann: *Thermochim. Acta* **102**, 179 (1986).
16. D.J. Eatough, J.J. Christensen, and R.M. Izatt: *Thermochim. Acta* **3**, 219; 233 (1972).
17. O.L. Chapman and R.W. King: *J. Am. Chem. Soc.* **86**, 1256 (1964).
18. R.M. Silverstein, G.C. Bassler, and T.C. Morrill: *Spectrometric Identification of Organic Compounds*, 5th Ed., John Wiley & Sons, New York (1991), pp. 165-202.
19. R.M. Izatt, X.X. Zhang, H.Y. An, C.Y. Zhu, and J.S. Bradshaw: *Inorg. Chem.* **33**, 1007

(1994).

20. D. Live and S.I. Chan: *J. Am. Chem. Soc.* **98**, 3769 (1976).
21. Y. Takai, Y. Okumura, S. Takahashi, M. Sawada, M. Kawamura, and T. Uchiyama:
    J. Chem. Soc., Chem. Commun. 53 (1993).
22. C. Seel and F. Vögtle: in A.F. Williams, C. Floriani, and A.E. Merbach (eds.), *Perspectives in Coordination Chemistry*; VCH Publishers, New York (1992), pp. 47-48.