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Metal binding studies using spiroacetal thiacrown ethers

Marica Nikac [a,b], Margaret A. Brimble [a,*], Robyn L. Crumbie [b], Trevor D. Bailey [b]

[a] Department of Chemistry, The University of Auckland, 23 Symonds St., Auckland 1043, New Zealand
[b] School of Biomedical and Health Sciences, University of Western Sydney, Locked Bag 1797, Penrith South DC 2560, Australia

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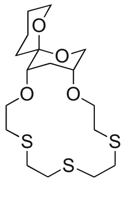
ABSTRACT

The binding ability of a series of spiroacetal thiacrown ethers with Li^+, Na^+, K^+, Cs^+, Co^{2+}, Cd^{2+}, Ag^+ and Pb^{2+} is reported. The thiacrown ethers showed an affinity for the heavy metals. The interaction of the three thiacrown ethers **1**–**3** and $[Al(acac)_3]$ **5**, $[Co(NH_3)_5NO_2](BPh_4)_2$ **6** and $[Co(en)_3](BPh_4)_3$ **7** complexes is also investigated.

The increasing pharmacological importance of compounds containing a spiroacetal framework has prompted significant interest in both their synthesis and reactivity.[1] Since the isolation of monensin, a spiroacetal-containing ionophore,[2] and the discovery of its cation binding properties, extensive interest in the synthesis of spiroacetal-containing ionophores has been noted. We have previously reported the synthesis of a novel class of spiroacetal thiacrown **1**–**3** and azacrown ethers[3] that have the potential to provide attractive possibilities for environmental and medicinal chemistry due to their ability to act as pH dependent ionophores.[4] We herein, report the ability of the spiroacetal thiacrown ethers to act as ligands for binding to metal ions and complexes. As primary receptors, crown compounds can complex simple organic and inorganic cations, anions and neutral molecules, whilst as second-sphere ligands they can interact with metal complexes.[5]

We determined the conditional stability constants exhibited by the spiroacetal thiacrown ethers **1**–**3** and 18-S-6 **4** towards Li^+, Na^+, K^+, Cs^+, Co^{2+}, Cd^{2+}, Ag^+ and Pb^{2+} using the ultraviolet spectroscopic method devised by Cram and co-workers[6] The results are summarised in Table 1 and show the association constant (K_a) for the equilibrium and the free energy of complexation (ΔG).

In accordance with the HSAB theory[7] spiroacetal thiacrown ethers **1**–**3** exhibited an affinity for the heavy metals, particularly silver. It is believed that electrostatic interactions do not predominate in the complexation of silver by thiacrown macrocycles.[8] The interaction is thought to be largely covalent based on the Ag–S bond length.[9] Thiacrown ethers **1**–**3** showed a lower binding affinity for silver than 18-S-6. The most likely explanation for this is the difference in conformation of thiacrowns **1**–**3** and the presence of the two oxygen atoms. In general, thiacrown compounds tend to bridge metal ions rather than chelate to them because the sulfur atoms have been shown to exist outside (exodentate) the cavity in many cases.[10]



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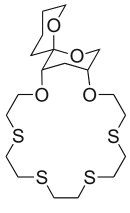

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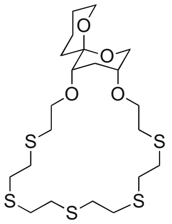

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The large difference in the complexation of silver over lead cannot be completely explained using the HSAB theory. Lead is considered a borderline acid and this may partly explain the lower association constant. However, lead and silver are both thiophilic metals, that is, they have an affinity for sulfur donor groups.[11] One possible explanation is the difference in the oxidation states. Generally, metal ions with lower oxidation states exert less electrostatic attraction, however, thiacrown ethers are known to stabilise lower oxidation states of metals due to their Π-acidity.[12]

We next investigated the possibility of these thiacrown compounds **1**–**3** to act as secondary ligands. The idea of second-sphere coordination was first postulated by Alfred Werner[13] in 1912 to explain a number of phenomena he observed. Second-sphere coordination can generally be described as the 'non-covalent bonding of chemical entities to the first coordination sphere of a transition metal complex.'[14] The adducts formed through second-sphere interactions have found applications in a variety of areas because they can result in a modification of the properties of the metal complexes and macrocycles.

The interaction of **1**–**3** and 18-S-6 **4** with readily available $[Al(acac)_3]$ **5**, $[Co(NH_3)_5NO_2](BPh_4)_2$ **6** and $[Co(en)_3](BPh_4)_3$ **7** complexes was thus examined using ^1H NMR spectroscopy at 25 °C in either chloroform-d_3 or dimethylsulfoxide-d_6. The choice of solvent was dependent primarily on its ability to solubilise the complexes. Proton NMR spectroscopy was used to measure small chemical shift or line width differences between the complexed and uncomplexed species. The further advantage of using the cobalt complexes was

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[*] Corresponding author. Tel.: +64 9 3737599; fax: +64 9 3737422.
E-mail address: m.brimble@auckland.ac.nz (M.A. Brimble).

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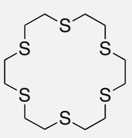
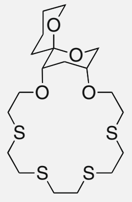
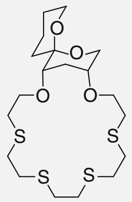
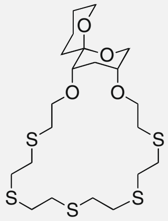
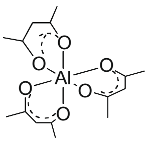
Table 1
Association constants (K_a) and binding free energies ($-\Delta G^\circ$) of hosts with metal picrates in $CHCl_3$ at 22 °C

Host	Cation	K_a ($M^{-1} \times 10^3$)	ΔG° (kJ mol^{-1})
 **4**	Li^+	0.05	−9.37
	Na^+	0.21	−13.08
	K^+	0.40	−14.71
	Cs^+	8.95	−22.32
	Co^{2+}	0.05	−9.82
	Cd^{2+}	8.25	−22.12
	Ag^+	3801.27[a]	−37.16
	Pb^{2+}	1.33	−17.64
 **1**	Li^+	0.11	−11.52
	Na^+	0.41	−14.78
	K^+	0.32	−14.16
	Cs^+	0.51	−15.27
	Co^{2+}	0.84	−16.51
	Cd^{2+}	1.19	−17.39
	Ag^+	3683.06	−37.08
	Pb^{2+}	35.71	−25.71
 **2**	Li^+	0.24	−13.49
	Na^+	1.83	−18.43
	K^+	0.45	−15.00
	Cs^+	0.66	−15.93
	Co^{2+}	1.10	−17.18
	Cd^{2+}	1.15	−17.28
	Ag^+	1576.61	−35.00
	Pb^{2+}	8.93	−22.31
 **3**	Li^+	0.09	−11.08
	Na^+	0.62	−15.78
	K^+	0.70	−16.05
	Cs^+	0.83	−16.49
	Co^{2+}	0.38	−14.60
	Cd^{2+}	1.30	−17.59
	Ag^+	922.85	−33.69
	Pb^{2+}	67.71	−27.28

[a] A 3×10^{-3} M solution of silver picrate and a 0.075 M solution of 18-S-6 **4** were used because at higher concentrations of silver picrate a precipitate formed.

that they had the potential to provide additional information through the direct observation of the metal ion using ^{59}Co NMR spectroscopy.



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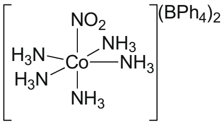

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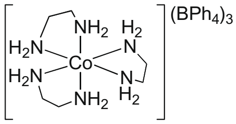

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Unfortunately, in this case the cobalt complexes **6** and **7** showed no interaction with thiacrown ethers **1**–**3** or 18-S-6 **4**. This may be due simply to weak or no interactions, anion effects on the possible interactions, or solvation which may affect the ability of the two species to interact as ion pairs. On the other hand, the experiments carried out with the neutral [Al(acac)$_3$] **5** complex did show second-sphere interactions with thiacrown compounds **2** and **3**. In the uncomplexed form, thiacrown **2** exhibited a sixteen-proton multiplet at δ_H 2.72–2.82 assigned to the protons next to the sulfur atoms (CH_2S). However, when [Al(acac)$_3$] **5** was added to the solution, the ^{1}H NMR spectrum showed a broadening of the signal to give a broad singlet at δ_H 2.77. Since no other signals were affected, this suggested an interaction between the components of the polythioether segment and the aluminium complex. Thiacrown **3** exhibited a similar type of interaction. A twenty-proton multiplet was observed at δ_H 2.69–2.84, which was assigned to the CH_2S groups in the free crown compound. Once again, the addition of [Al(acac)$_3$] **5** led to a broadening of the signal to produce a broad singlet at δ_H 2.78.

This interaction also provided information about the flexibility of the spiroacetal thiacrown ethers **1**–**3**. It suggested that thiacrown ethers **2** and **3** are much more flexible than the smaller thiacrown **1**. This greater flexibility enables the thiacrown ethers to adopt a conformation which maximises favourable interactions and minimises unfavourable interactions. It is likely that this also includes the conformation of the spiroacetal ring system. The greater flexibility of thiacrown ethers **2** and **3** allows the spiroacetal moiety to arrange itself in the most thermodynamically stable conformation while positioning itself away from the metal complex. The size of the cavity is thought to permit extra flexibility and is consistent with the results.

In summary, the present work constitutes a detailed analysis of the binding abilities of three spiroacetal thiacrown ethers **1**, **2** and **3**. The association constants were determined for Li^+, Na^+, K^+, Cs^+, Co^{2+}, Cd^{2+}, Ag^+ and Pb^{2+}. The superior complexing ability observed for **1**, **2** and **3** with Ag^+ is encouraging in terms of selective extraction. The interaction between thiacrown ethers **1**, **2** and **3** and $[Al(acac)_3]$ **5**, $[Co(NH_3)_5NO_2](BPh_4)_2$ **6** and $[Co(en)_3](BPh_4)_3$ **7** yielded promising results with the aluminium complex and provided a greater understanding of the flexibility of thiacrown ethers **2** and **3**.

Acknowledgements

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