Self-Assembling Nickel Clusters Form Binding Sites for Alkali Metal Cations: Novel Analogs of Enolate Aggregates

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Received December 17, 1992

Abstract: Salicylaldimine ligands having 3-methoxy or 3-(2-methoxyethoxy) side arms react with $NiSO_4$ or $Ni(OAc)_2$ to form novel bimetallic cage structures involving ligands, nickel atoms, and one or more types of counteranions. The cluster structures exhibit complexation properties and are of general interest because of their similarity to known alkali organometallic aggregates. Mixed transition metal–alkali metal aggregates of this type are very little known. In the present case, one aggregate is a donor–acceptor array comprised of four ligands, two nickel atoms, two sodium atoms, integral picrate anions, and water. This previously unknown complexation mode was verified in the solid state by X-ray structure analysis and in the solution state by a variety of techniques. Although the two complexes reported here have different stoichiometries and arise from different nickel reagent starting materials, the overall form of the cation-coordinating cage structure in each case is nearly identical, suggesting that the structural array is of a general type. Inferences about solution structure have been drawn from cation complexation profiles. Previous structural suggestions have proved incorrect, and follow-up work has failed to provide any structural alternative to that shown here.

Introduction

Nature sets the structural stage for protein or enzymatic function with the primary amino acid sequence. Once this is done, such feeble forces[1,2] as hydrogen-bonding, salt bridge formation, π-stacking, etc., control the final shape (protein secondary, tertiary, and quaternary structure) and, thus, the function of the material. Several groups[3] have been interested in this phenomenon and have worked to achieve biologically-inspired function in systems that bear little apparent structural relation to their natural counterparts.

Electrostatic interactions are involved in the recognition, binding, and transport of metal ions and *inter alia* determine the binding and selectivity properties displayed by such membrane-active substances as valinomycin[4] and the channel-former gramicidin A.[5] These two natural systems exhibit spherical recognition. The organization of their structural elements into a prebinding conformation is a distinctive feature of these ion complexers. More than 150 unique protein structures are known that contain one or more of seven different types of bound metal ions. Iron, calcium, and zinc, the most commonly observed,[6] modulate conformational and electronic properties in the systems that contain them. An excellent example is the "zinc finger" motif of certain DNA regulatory proteins.[7] The Zn^{2+} ion modulatesthe electronic distribution of attached histidine residues and enhances their hydrogen-bonding properties. Its coordination geometry fosters the exposure of other key residues and orients the "finger" for site-specific recognition of DNA.[8]

As part of an effort to understand ionophores[9] and molecular complexation, we have developed relatively small molecular hosts that can assemble, organize, and complex various substrates.[10] Some systems self-assemble and bind with little structural change.[3b] On the other hand, there are hosts such as carboxypeptidase A that undergo significant structural change ("induced-fit systems") when a guest is bound.[11] A model in the former category was devised by Reinhoudt et al., who used macrocyclic salen–polyether–UO_2 complexes to afford a binding site for urea.[12] We have previously reported a crown ether system in which adenine and thymine side arms were used to organize an induced-fit receptor to accommodate α,Ω-diammonium dications.[10a] In addition to enhancing hydrogen-bonding, the use of transition or other heavy metals to organize a binding site is an attractive notion. In the work discussed below, we show that nickel may be so used and that when it is incorporated into salicylaldimine complexes, novel bimetallic cage structures form that bind alkali metal cations and make them an integral part of the cage structure.

The present work is of interest well beyond the intended purpose, however. These nickel–alkali metal clusters are similar in many respects to the structures known for such alkali metal aggregates as those formed from lithium, sodium, or potassium enolates.[13] Although some examples of transition metal–alkali metal mixed aggregates are known,[14] none to our knowledge has previously been reported involving the alkali metal as a "bound" species.

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(1) Gokel, G. W.; Nakano, A. Feeble Forces and Flexible Frameworks. In *Crown Compounds: Toward Future Directions*; Cooper, S., Ed.; Verlag Chemie: in press.

(2) Schneider, H.-J. *Angew. Chem., Int. Ed. Engl.* **1991**, *30*, 1417.

(3) (a) Roberts, S. M. *Molecular Recognition: Chemical and Biochemical Problems*; Royal Society of Chemistry: London, 1989. (b) Hamilton, A. D. In *Advances in Supramolecular Chemistry*; Gokel, G. W., Ed.; JAI Press: Greenwich, CT, 1990; Vol. 1, p 1. (b) Feng, Q.; Park, T. K.; Rebek, J., Jr. *Science* **1992**, *256*, 1179.

(4) (a) Ovchinnikov, Y. A.; Ivanov, W. T.; Shkrob, A. M. *Membrane-Active Complexones*; Elsevier: Amsterdam, 1974. (b) Pointer, G. R.; Pressman, B. C. *Top. Curr. Chem.* **1981**, *101*, 83.

(5) Urry, D. W. *Proc. Natl. Acad. Sci. U.S.A.* **1971**, *68*, 672.

(6) Christianson, D. W.; Alexander, R. S. *J. Am. Chem. Soc.* **1989**, *111*, 6412.

(7) (a) Berg, J. M. *Science* **1986**, *232*, 485. (b) Brown, R. S.; Sander, C.; Argos, P. *FEBS Lett.* **1985**, *186*, 271.

(8) Pavletich, W. P.; Pabo, C. O. *Science* **1991**, *242*, 809.

(9) Gokel, G. W. *Chem. Soc. Rev.* **1992**, *21*, 39–47.

(10) (a) Kim, M.; Gokel, G. W. *J. Chem. Soc., Chem. Commun.* **1987**, 1686. (b) Gokel, G. W.; Echegoyen, L.; Kim, M. S.; Hernandez, J.; deJesus, M. *J. Inclusion Phenom.* **1989**, *7*, 73. (c) Medina, J. C.; Li, C.; Bott, S. G.; Atwood, J. L.; Gokel, G. W. *J. Am. Chem. Soc.* **1991**, *113*, 366. (d) Medina, J. C.; Goodnow, T. T.; Bott, S.; Atwood, J. L.; Kaifer, A. E.; Gokel, G. W. *J. Chem. Soc., Chem. Commun.* **1991**, 290. (e) Gokel, G. W.; Medina, J. C.; Li, C. *Synlett* **1991**, 677–683. (f) Schall, O.; Gokel, G. W. *J. Chem. Soc., Chem. Commun.* **1992**, 748–750.

(11) (a) Hartsuck, J. A.; Lipscomb, W. N. *Enzymes* **1971**, *3*, 1. (b) Quiocho, F. A.; Lipscomb, W. N. *Adv. Protein Chem.* **1971**, *25*, 1. (c) Lipscomb, W. N. *Proc. Natl. Acad. U.S.A.* **1980**, *77*, 3875. (d) Christianson, D. W.; Lipscomb, W.N. *Acc. Chem. Res.* **1989**, *22*, 62–69.

(12) Van Staveren, C. J.; Van Eerden, J.; Van Veggel, F. C. J. M.; Harkema, S.; Reinhoudt, D. N. *J. Am. Chem. Soc.* **1988**, *110*, 4994.

(13) (a) Williard, P. G.; Carpenter, G. B. *J. Am. Chem. Soc.* **1985**, *107*, 3345. (b) Williard, P. G.; Carpenter, G. B. *J. Am. Chem. Soc.* **1986**, *108*, 462.

(14) Williard, P. G. In *Comprehensive Organic Synthesis*; Schrieber, S. L., Ed.; Pergamon: Oxford, Vol. 1, p 1.

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Results and Discussion

The intent of this project was two-fold. First, we wished to assess the binding profiles of nickel–alkali metal cluster compounds using both the picrate extraction and homogeneous binding constant methods to see if there was a difference in the information obtained. Second, we wished to explore how binding actually occurred, as we felt that the model proposed originally was incorrect. This required the preparation of several nickel salicylaldimine complexes. Experimental details for these were unavailable, and we obtained some unusual results while in pursuit of what we thought were simple dimers.

Preparation of Schiff Bases. 3-Methoxy-*N*-methylsalicylaldimine (**1**) was prepared directly from *o*-vanillin and methylamine, and 3-(2-methoxyethoxy)-*N*-methylsalicylaldimine (**2**) was obtained in two steps from 2,3-dihydroxybenzaldehyde. Preparation (see Figure 1) and characterization of these monomers was straightforward.

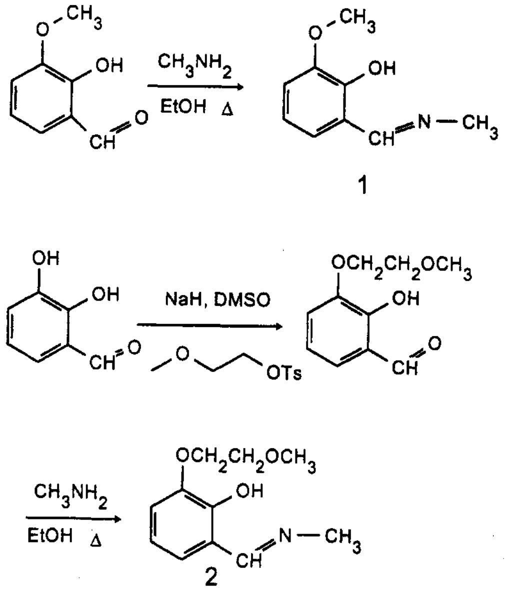

Figure 1. Preparation of Schiff bases.

Formation of Nickel Complexes from 1 and 2. In the studies reported here, salicylaldimine ligands **1** and **2** were allowed to react with either NiSO$_4$ or Ni(OAc)$_2$, as shown in Figure 2. Procedures for complex formation were based on reports from Holm and others.[15] The reaction of methoxysalicylaldimine **1** with nickel sulfate in a 1:0.5 ratio (**1**:Ni) afforded complex **1**$_2$·Ni (**3**, see Experimental Section and Figure 2), which was isolated as dark green needles (mp 205–206 °C).

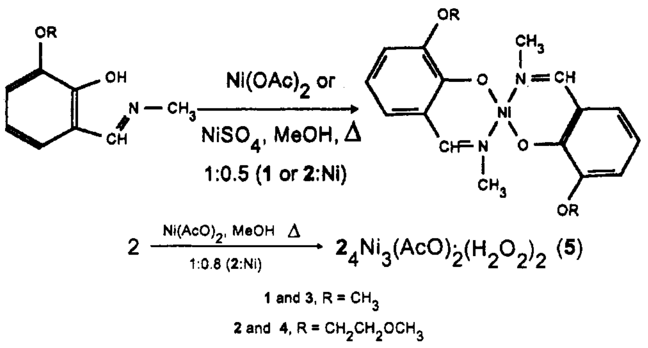

Figure 2. Preparation of **3**, **4**, and **5**.

A more complicated situation was observed in the attempted synthesis of **2**$_2$·Ni (**4**). When Ni(OAc)$_2$ was used as the nickel source, we isolated emerald green plates (mp 116–120 °C) that were found to have the stoichiometry **2**$_4$·Ni$_3$(OAc)$_2$(H$_2$O)$_2$ (**5**). At first, the difference in stoichiometry was thought to result from the change in anion from sulfate to acetate. In fact, two variables in this preparation had been altered: the anion and the *ratio* of reactants. The latter, a change in ratio of ligand:nickel from 1:0.5 to 1:0.8 was not anticipated to be important. Our expectations notwithstanding, a variety of trinuclear salicylaldimine nickel complexes has been reported[16,17] to result when compounds such as **3** or **4** react in the presence of an excess of nickel. When an identical preparation was conducted in which the ratio was returned to the original (1:0.5) value, we obtained fine green needles (mp 157–158 °C) having the stoichiometry **2**$_2$·Ni and the structure shown as **4**. The structures of **3** and **4** were confirmed by ^{1}H NMR, UV–visible–NIR, mass spectral, and elemental analyses. Complete characterization of these compounds is included in the Experimental Section because experimental details have not, to our knowledge, been previously reported.

Preparation of Nickel Cluster Compounds. Ni$_3$2$_4$(AcO)$_2$·2H$_2$O (5). We prepared the Ni(II) complexes **3** and **4** as described above. After slow evaporation (*ca* 168 h) of a cyclohexane solution, emerald green crystals of **5** were collected. X-ray crystallography revealed that the complex, C$_{48}$H$_{66}$N$_4$O$_{18}$Ni$_3$ (FW 1163.14 g mol^{-1}), included four salicylaldimine rings, three Ni(II) atoms, two H$_2$O, and two AcO$^-$ molecules. The solid-state structure is shown in its entirety in Figure 3 (top) along with a schematic representation (bottom) of the nickel cluster's local coordination sphere. In this illustration, "sal" represents the salicylaldimine ring and "ether" or "PhO" refers to the oxygen of precursor **2** that coordinates. Note that in this structure, ether refers to the –OCH$_2$CH$_2$– oxygen and PhO means that the phenoxide oxygen coordinates. Further, O(Ac) means that the coordinating oxygen derives from the acetate anion.

The ORTEP plot of the structure is somewhat complicated, and reference to the schematic shown in Figure 3 (bottom) should clarify ligand–metal relationships. It is interesting to note that the stereochemistry of each nickel in this complex is octahedral, as opposed to either square planar or tetrahedral geometry. The oxygenated side arms are involved in metal cation binding in a way different from that anticipated. Two of the oxygenated side arms are involved in Ni(II) coordination, while the other two are simply hovering about the structure.

Two Ni(II) atoms (*i.e.* atoms 2 and 3) are approximately within the same plane, while the third (nickel-1) is located above and to the left (as viewed in Figure 3). Two water molecules are present in the coordination spheres of these atoms. Nickel(II) atoms 2 and 3 share one water molecule, while nickels 1 and 2 share a second. Two acetate residues complete the octahedral array: one coordinates to Ni(1) and the other coordinates to Ni(3). Although the hydrogen atoms in the water molecules were not located, the position and orientation of the water oxygen suggests hydrogen-bonding to the acetate residues. Finally, the two salicylaldimine rings shown at the upper right of Figure 3 are parallel and partially stacked. The mean distance between their atomic planes is ~3.9 Å. A direct stacking interaction is usually ascribed to aromatics having parallel planes and a separation of *ca.* 3.4 Å.

Sodium-Nickel Bimetallic Cluster. Nickel dimer **3** and sodium picrate (1:1) were dissolved in chloroform:acetone (1:1) and heated

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(15) (a) Holm, R. H.; O'Connor, M. J. *Prog. Inorg. Chem.* **1971**, *14*, 241 and references therein. (b) Sacconi, L.; Paoletti, P.; Del Re, G. *J. Am. Chem. Soc.* **1957**, *79*, 4062. (c) Holm, R. H. *J. Am. Chem. Soc.* **1961**, *83*, 4683. (d) Holm, R. H.; Everett, G. W., Jr. *Inorg. Chem.* **1966**, *7*, 83–214.

(16) (a) Miners, J. O.; Sinn, E.; Coles, R. B.; Harris, C. M. *J. Chem. Soc., Dalton Trans.* **1972**, 1149. (b) Butcher, R. J.; Sinn, E. *J. Chem. Soc., Chem. Commun.* **1975**, 832. (c) Butcher, R. J.; Jasinski, J.; Mockler, G. M.; Sinn, E. *J. Chem. Soc., Dalton Trans.* **1979**, 1099. (d) Casellato, U.; Vigato, P. A.; Fenton, D. E.; Vidali, M. *Chem. Soc. Rev.* **1979**, *8*, 199.

(17) Sacconi, L.; Mani, F.; Benuni, A. In *Comprehensive Coordination Chemistry*; Wilkinson, G., Gillard, R., McCleverty, J., Eds.; Pergamon Press: New York, 1987; Vol. 5, pp 221–225.

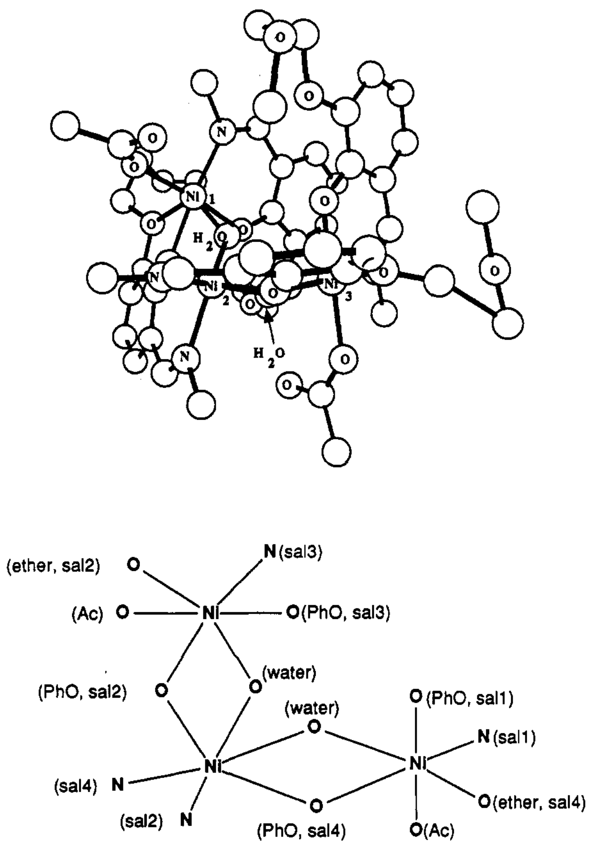


Figure 3. Solid-state structure (top) and schematic (bottom) of the coordination sphere about complex **5**.

at reflux for 15 min. The reaction mixture was allowed to stand for 72 h, after which reddish-brown prisms of **6** (mp 165–175 °C, soften at 160 °C, stoichiometry $1_4{\cdot}Ni_2(NaPic)_2{\cdot}H_2O$) were deposited. Compound **6** was subjected to X-ray analysis. A schematic of nickel's local coordination sphere and a complete ORTEP plot are shown in Figure 4. In the schematic, part of the Na^+ coordination sphere in each case has been omitted and is due to coordination by either a picrate hydroxyl or nitro group. The abbreviations sal, ether, etc., are as noted above.

The structure of **6** is quite different from what might have been expected. The most striking feature is that the picrate counteranion is an integral part of the bimetallic complex. The nickel cluster also contains a water molecule that is directly involved in the formation (and organization) of the bimetallic (Ni–Na) complex. The methoxy side arms that were designed to participate in binding by forming a pseudocrown subunit that binds Na^+ actually coordinate very differently. Two of the methoxy groups bind Na, and one binds Ni, but the fourth is too far away (≈4 Å) from Na^+ to be directly involved in binding. Each nickel atom in **6** is six-coordinate as observed in **5** (see Figure 3) rather than four-coordinate as in complex **3**. It should also be noted that both aromatic rings shown at the bottom of Figure 4 are essentially parallel (stacked), and their planes are separated by an average distance of 3.8 Å.

Cage Comparison. The striking similarity between structures **5** and **6** (Figure 5) suggests that the cage arrangement observed here may be more common than might have been imagined. This is especially surprising since **5** and **6** differ substantially in the metal ions that are present. Although both exhibit a rhombus formed from two nickel and two oxygen atoms, the overall cluster is completed in one case by one of two sodium cations and in the other by a third nickel atom. The salicylaldimine units play a remarkably similar role in coordinating the metals (see cage comparison in Figure 5 and individual schematics). In **5**, the binding site of Ni(1) (upper left) corresponds very closely to that

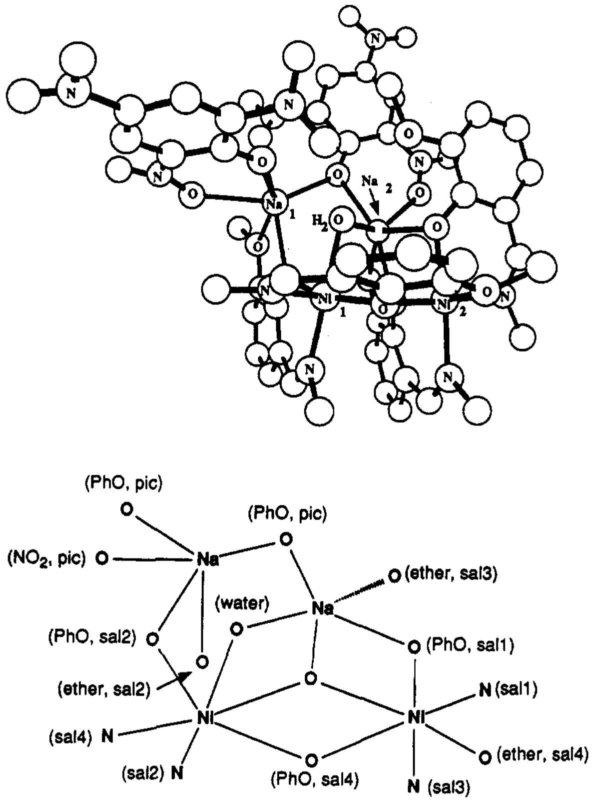
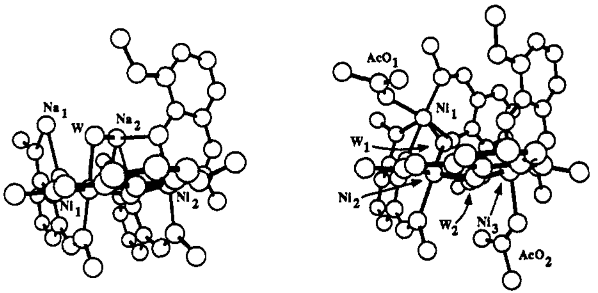


Figure 4. Solid state structure (top) and schematic (bottom) of the coordination sphere about bimetallic complex **6**.



Ni-Na Bimetallic Cage (6)

Trinuclear Ni(II) Cluster (5)

Figure 5. Comparison of nickel(II) cages of complexes **5** and **6**. The picrate anions have been removed from the figure on the left. Parts of the ethyleneoxychain in **5** (right) were removed as well.

of one of the Na ions in **6**. In the former, the presence of a third nickel atom and acetate residues apparently dictates the stacking pattern and the orientation of the fourth ring (Figure 3). Ni(3), on the right, coordinates to one of the acetate anions in preference to nitrogen as in **6**. The donor atoms in the third ring should not display any preference in their arrangement around Ni(1) (*i.e.*, axial N-equatorial O over axial O–equatorial N). However, if the latter arrangement were present, the stacking interaction might be lost (at least as judged by an examination of Cochrane molecular models). π-Stacking may enforce such a disposition of donor atoms, because a loss in stabilization energy would likely result if the aromatic ring was inverted.

Solution Structure. A large and historically important body of literature exists that describes various aspects of nickel salen complexes. Systems related to those described here were extensively investigated 20–30 years ago, particularly by Holm and co-workers and Sacconi and co-workers.[15] The latter group also published an extensive review on the coordination chemistry of nickel.[17] According to the literature, $Ni(Me\text{-}sal)_2$ derivatives normally possess a planar or stepped coordination sphere, with a *trans* disposition of donor atoms. This arrangement minimizes unfavorable interactions between the methyl groups. The complexes are diamagnetic and square planar in the solid state but become partially paramagnetic when dissolved in poorly coordinating solvents such as C_6H_6 and $CHCl_3$ and fully paramagnetic in coordinating solvents such as pyridine. In the latter, paramagnetism arises from axial coordination of solvent molecules. If the systems are sterically hindered, an equilibrium between tetrahedral and square planar species accounts for the paramagnetism. When the *N*-substituent is not very bulky, the observed paramagnetic behavior is attributed to molecular association. Holm[15c] proposed that two (or possibly more) planar complexes stack upon each other, converting tetracoordinate Ni(II) into a species that is, at least, pentacoordinated. It is these pentavalent Ni(II) atoms that display paramagnetic behavior (Figure 6). Additional evidence for this aggregation has been gathered by different authors[13a,b,18] and has been supported by the observation that bis(salicylaldehyde)ethylenediimino–Cu(II) associates in this fashion in the solid state: the association occurs by weak bonding between a copper atom in one and a donor oxygen atom ($d_{Cu\cdots O}$ 2.41 Å) in another molecule.[19]

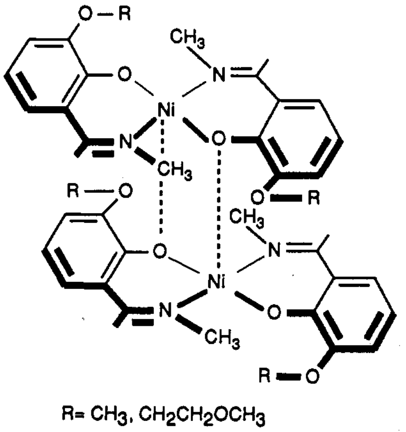


Figure 6. Proposed association of $Ni(Me\text{-}sal)_2$ derivatives.

The paramagnetic behavior of **3** and **4** is still detectable, as seen in the ^1H NMR spectra. The 400-MHz NMR spectrum of **3** (DMSO-d_6 and $CDCl_3$) shows line width increases and downfield shifts (compared to **1** or **2**) that suggest paramagnetic behavior. The methine proton in **1** appears as a sharp singlet at 8.30 ppm ($CDCl_3$ solution). In complex **3**, the same resonance has broadened and now appears 1.5 ppm more downfield. Some broadening is observed for all resonances. In DMSO-d_6, the proton in the residual CD_3SOCD_2H was poorly resolved, almost certainly due to coordination of the sulfoxide oxygen. The same methine proton (of **3**) appears at about 10.6 ppm in DMSO-d_6; its resonance is broadened (along with all others in the spectrum) as a consequence of this paramagnetism.

Vapor pressure osmometry (VPO) yielded results compatible with little association for complex **3**, with an average degree of association value, $n = 1.08 \pm 0.03$. However, compounds known to aggregate to some extent (*e.g.*, by cryoscopic and magnetic measurements)[20] have shown osmometric results similar to those we obtained. Bis(*N*-methylsalicylaldimino)Ni(II) and bis(*N*-cyclopropylsalicylaldimino)Ni(II) display n values of 1.02 and 1.06 when studied by osmometric measurements. Nonetheless, in the former complex paramagnetism does arise from an aggregation phenomenon *per se*. In the latter complex, paramagnetism was ascribeed to an equilibrium between planar diamagnetic (monomeric), associated paramagnetic, and tetrahedral species. In any event, the concentration of these paramagnetic aggregates may be too low at room temperature for the VPO technique to be suitable for their detection.

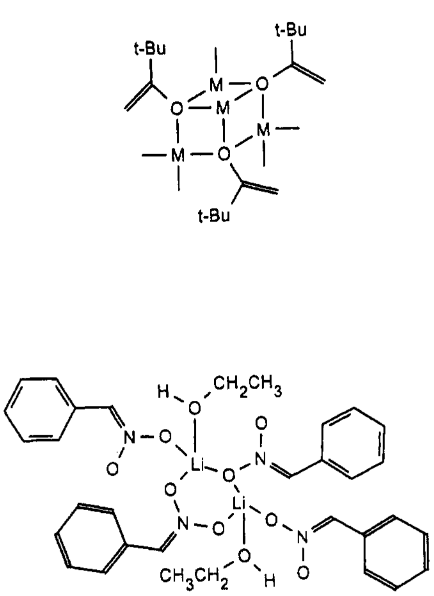


Figure 7. (Top) Typical metal–oxygen organization in known mixed transition–alkali metal clusters. (Bottom) Structure of the lithium nitronate salt.

Two mechanisms for the assembly of these cages seem plausible to us. One possible mechanism is that observed for salen derivatives. These compounds form interesting di- and trinuclear heterometal complexes with both transition- and non-transition-metal cations.[15] Solid-state structures of these Na^+ complexes display four sp^2, *cis*-oriented, oxygen atoms from two different molecules surrounding the cation. The latter is further coordinated to two solvent molecules (MeCN or THF). Solvation (coordination) of the K^+ and NH_4^+ cations requires six oxygens from three different molecules. This is likely due to the larger size of K^+ and NH_4^+ compared to Na^+ and their consequently different solvation requirements. In the case of Li^+, two or four oxygens are sufficient for proper solvation, depending upon the solvent and the counteranion. In our complexes, the initial binding may be accomplished by approach to the metal cations, followed by self-assembly into the final structure.

It is also possible that complexes **3** and **4** aggregate, however little, as stacks (see Figure 6). This may enhance the metal-binding ability by making available a larger number of donor atoms. Once the metal cation approaches the ligand, self-assembly of the aggregates occurs to afford structures **5** and **6** (observed for X-ray analysis). Based upon the evidence in hand, we cannot currently distinguish stacking from other aggregation. Whichever mechanism leads to complexes **5** and **6**, stabilization is due to the forces associated with aggregation as well as to electrostatics involving the cations, anions, and ligands which are all involved in the same complex species.

Many structural studies involving di- and trinuclear homo- or heterometal complexes of Ni(II) or Cu(II) are available.[14,15] It is interesting to note that, to our knowledge, all of these complexes have as integral components an anion and/or solvent molecules. The anion neutralizes the metal cation's charge. The coordinating solvent may complete the solvation sphere. Such solvents vary over the broad range from water and alcohols to nitriles, ethers, and ketones. The presence of solvent molecules must generally play a coordinating and stabilizing role in these complexes, as they are nearly always observed in the solid-state structures.

The present case is the first example of these well-known ligands forming mixed transition–alkali metal clusters. In recent years, a number of alkali metal carbanion and alkoxide anion structures have been reported. A typical example of the metal–oxygen organization can be seen at the top of Figure 7. In that case, the

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(18) (a) Fergunson, J. *Spectrochim. Acta* **1961**, *17*, 316. (b) MacVicar, H. C. C.; O'Brien, R. J. *Can. J. Chem.* **1962**, *40*, 822.

(19) Hall, D.; Walters, T. J. *J. Chem. Soc.* **1960**, 2644.

(20) (a) Holm, R. H.; Swaminathan, K. *Inorg. Chem.* **1962**, *1*, 599. (b) Holm, R. H.; Swaminathan, K. *Inorg. Chem.* **1963**, *2*, 181.

Table I. Cation Binding by Crowns and Cage Molecules

		% or log K_{ex} (picrate)[a]				
ligand	cation	other refs	this work	picrate concn	ligand concn	log K_S in MeOH
12-crown-4	Li	0.77				<1.7
12-crown-4	Na	0.95				1.7
12-crown-4	K	0.57				1.74
15-crown-5	Li	1.29				≈0
15-crown-5	Na	3.90				3.24
15-crown-5	K	2.58				3.43
18-crown-6	Li	1.92				≈0
18-crown-6	Na	3.39				4.35
18-crown-6	K	5.97				6.08
1	Li[b]	63%				≈3[c]
1	Na	40%	65 ± 3%	8 mM	25 mM	2.62 ± 0.07
			20 ± 1%	80 μM	75 μM	
2	Li	30%				
2	Na	44%	75 ± 5%	8 mM	25 mM	2.58 ● 0.09
			25 ± 1%	80 μM	75 μM	
1	K	16%				1.4 ● 0.38

[a] Picrate extraction percentages are indicated by %; other values are $\log_{10} K_{ex}$ (in benzene/water) as reported by Takeda, Y. *Bull. Chem. Soc. Jpn.* **1979**, *52*, 1920; **1980**, *53*, 2393. [b] Values from ref 22 are estimated from bar graph. [c] This value was obtained as 2.96 ± 0.01 by the ISE method described in the Experimental Section, but it is not calibrated in the usual fashion due to the poor Li^+ binding of 18-crown-6 and should be considered approximate.

sodium salt of pinacolone enolate organizes in a cubic array. A similar phenomenon is observed for both the lithium and potassium salts, although in both cases the aggregation is hexameric.

A second example especially relevant to our own work is the structure reported for the lithium nitronate salt[21] shown at the bottom of Figure 7. In our case, we have observed direct participation by the nitro groups of picrate anion, a fact that might seem surprising in the absence of this well-established precedent. In this case, two molecules of ethanol participate as seconadry donors, just as water molecules invariable participate in our nickel–sodium aggregate formation.

It is of interest and importance to note that the Coulombic cation-binding profile of these nickel complexes can be appreciated from the structures shown. In all cases, there is direct interaction between a phenoxide anion and the bound (sodium) cation. Even though the counteranion may be altered from picrate (which can participate in binding via nitro and phenoxide) to perchlorate, which is a poor donor generally, the selectivity order ($Li^+ > Na^+ > K^+$) is maintained. Furthermore, the alternating O–metal–O–metal motif is obvious here as it is known to occur in carbanion and enolate aggregates.

Binding Constants and Complex Structure. Our interest in this system was initially piqued by a report that compounds such as **1** react with nickel to form cation-binding pseudocrown cavities.[22] This is certainly the case in structures such as those devised by Reinhoudt and co-workers that are based on the salen system in which the salicylaldimine residues are held together covalently. The notion of using nickel to organize salicylaldimines into a cation-binding donor group array is a clever one, but the cation-binding data for the system did not appear to us to correspond to those expected for a neutral, crown ether-like system. If **1** or **2** did form a pseudocavity when complexed by nickel, it should display crown-ether-like binding selectivity. We have shown[23] that in solutions such as methanol, neutral crown ethers favor K^+ over Na^+ or Li^+ (order of diminishing solvation enthalpy), but charged systems exhibit the Coulombic order[24] $Li^+ > Na^+ > K^+$. Complexation data for these compounds determined by picrate extraction[25] and ion-selective methods[26] are recorded in Table I. Note that log K_S values are for $(ligand)_2$:Ni (or its dimer) complex binding the specified cation in methanol solution. The picrate extraction values refer to extraction of $M^+picrate^-$ from water into $CHCl_3$.

Subsequent to our preliminary report[27] of the present study, the original nickel salicylaldimine complexation studies were reexamined by the original group[28] with the goal of determining what species in solution accounts for alkali metal complexation and whether the anion is required for complexation.

Two important observations result from that effort. First, our finding[22] that the complexing species is dinuclear was confirmed (for acetone). Second, since $Na^+ClO_4^-$ was the cation source, it was asserted that "binding of the alkali-metal cation is not contingent upon the presence of picrate anion or a coordinating solvent." The contention[28] seems to be that nickel dimers of the type known for many years are responsible for the cation binding and that the structure we reported is not. It is certainly true that structures observed in the solid state and in solution may differ. Unfortunately, the authors of that work provided no physical evidence of stacked dimer formation and failed to resolve the key question of why the simple Holm dimers, if binding alkali metal cations, show a binding profile that differs from the expected one.

The question of cation binding by crowns or by these more complex species is also complicated. Literally hundreds of papers have addressed cation binding in cryptand, crown, or pseudocrown (podand) compounds, and much of what is currently known is summarized in a recent monograph on the subject.[29] The two most popular methods for determining cation-binding strengths involve either a direct measurement in homogeneous solution (by NMR, ion selective electrode methods, calorimetry, etc.) or by use of the so-called picrate extraction technique. When the former method is used, equilibrium binding constants for the reaction,

$$\text{cation} + \text{crown} \rightleftarrows \text{complex}$$

usually designated K_S, are obtained that generally agree in magnitude irrespective of the method used in their determination. Likewise, values obtained by the picrate extraction technique usually agree as well so long as all variables are controlled. Typical, but not standard, conditions for picrate extraction are as follows.

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[21] Klebe, G.; Bohn, K. H.; Marsch, M.; Bosch, G. *Angew. Chem., Int. Ed. Engl.* **1987**, *26*, 78.

[22] Schepartz, A.; McDevitt, J. P. *J. Am. Chem. Soc.* **1989**, *111*, 5976.

[23] Gokel, G. W.; Goli, D. M.; Minganti, C.; Echegoyen, L. *J. Am. Chem. Soc.* **1983**, *105*, 6786.

[24] Kaifer, A.; Gustowski, D. A.; Echegoyen, L.; Gatto, V. J.; Schultz, R. A.; Cleary, T. P.; Morgan, C. R.; Goli, D. M.; Rios, A. M. *J. Am. Chem. Soc.* **1985**, *107*, 1958.

[25] Eisenmann, G.; Ciani, S. M.; Szabo, G. *J. Membr. Biol.* **1969**, *1*, 294. (b) Pedersen, C. J. *J. Am. Chem. Soc.* **1970**, *92*, 391. (c) Frensdorff, H. K. *J. Am. Chem. Soc.* **1971**, *93*, 4684.

[26] Arnold, K. A.; Gokel, G. W. *J. Org. Chem.* **1986**, *51*, 5015.

[27] Schall, O. F.; Robinson, K.; Atwood, J. L.; Gokel, G. W. *J. Am. Chem. Soc.* **1991**, *113*, 7434.

[28] Jones, M. W.; Gupta, N.; Schepartz, A.; Thorp, H. H. *Inorg. Chem.* **1992**, *31*, 1308–1310.

[29] Inoue, Y., Gokel, G. W., Eds. *Cation Binding by Macrocycles*; Marcel Dekker: New York, 1990.

An aqueous solution of cation$^+$picrate$^-$ and a CH_2Cl_2 solution of ligand are shaken together. The ligand complexes the cation and draws it into the nonpolar solution. The yellow picrate anion is likewise drawn in to maintain electroneutrality, and its concentration is assessed by UV–vis spectroscopy from its known spectrum and extinction coefficient. The picrate extraction constant reflects the amount of picrate extracted from aqueous solution relative to the total picrate available. Unless all variables in the picrate extraction experiment are held constant in separate experiments, the data may not be directly comparable. An informative discussion of this method may be found in a review by Takeda.[30]

A second and important issue is the role of picrate itself in the binding process. We have shown in crown ether–cation complexation studies conducted in polar solvents (e.g., methanol) that a change in counteranion from perchlorate to chloride does not affect K_S. In the picrate extraction, the anion is hydrophobic, soluble in such poorly solvating media as chloroform or dichloromethane, and may play a direct role in cation complexation. This is likely to be true for any anion that has sufficient solubility to be extracted into the nonpolar solution under study. Indeed, this may also be the case if the overall complex, including the non-hydrophobic anion, is more soluble and stable in the presence of the anion than in its absence.

We have shown previously[23] that the 3*n*-crown-*n* (n = 4–8) compound series does not show the so-called hole size selectivity relationship (in polar solution) for the cations Na^+, K^+, Ca^{2+}, and NH_4^+. Rather, the correlation of binding strength is roughly with the solvation enthalpy order of the cations involved rather than with hole size. Thus, the binding order observed for the spherical cations Na^+, Ca^{2+}, and K^+ (in MeOH at 25 °C), was $K^+ > Na^+ > Ca^{2+}$. Peak binding was observed for 18-crown-6 for all of the cations examined in this case. In general, the binding strength of Li^+ was so low that it could not be determined by ISE methods, although Hopkins and Norman[31] reported Li^+ complexation data for 12-crown-4, tetramethyl-12-crown-4, 15-crown-5, and 18-crown-6 in acetonitrile at 25 °C. They reported a crown size stability constant order for Li^+ of $12 < 15 < 18$ for this series. Thus, the lithium data show a binding selectivity similar to that noted for the larger cations. It should also be noted that data exist for binding of Li^+ in the gas phase.[32]

In contrast, much information concerning Li^+ binding determined by the two-phase extraction technique has been reported in the literature. Thus 12-crown-4 shows no Li^+ selectivity in MeOH but does in certain two-phase systems. An important difference between the two methods is the presence of picrate as counteranion in a nonpolar solvent and its influence on the binding complex. Simple 12-crown-4 does not extract lithium into the organic phase, however, presumably because the cation's solvation enthalpy is too high.

In polar solutions such as anhydrous methanol, changing the counteranion from Cl^- to Br^- does not affect the equilibrium constant. This is presumably because the polar solvent fills the vacant apical sites when cation complexation involves the ligand in an essentially two-dimensional sense. This role of solvent is often apparent in solid-state structures.[33] In a nonpolar solvent such as $CHCl_3$, the anion is critically important because stabilization of the cation·ligand complex cannot be achieved by solvent. Thus, the phenoxide anion of picrate is almost certainly in the cation's coordination sphere. The binding selectivity is thus dominated by Coulombic interactions rather than the solvation enthalpy of the cation.

A consideration of charge density alone is insufficient to account for selectivity in the two-phase extraction method. It is also important to consider that a minimum number of donor groups is required in a macroring in order to complex a cation. There is a paucity of solid-state structural data on lithium cation complexes. Recent work on certain metalation reagents[34] has shown that complexation of lithium cation by 12-crown-4 is usually of the sandwich type when the anion is weakly donating but of the stoichiometry 12-crown-4·Li^+·anion$^-$ when the anion is in the cation's coordination sphere. This suggests that four oxygen donor atoms are insufficient to solvate lithium cation. The same is surely true in nonpolar solvents which can make little contribution to the overall complex stabilization. Takagi and Ueno have noted in their review of crowns as chromogenic reagents[35] that a "localized negative charge (high basicity) strengthens the coordination interaction and favors the extraction of lighter alkali metal ions."

It thus seems likely to us that a charged species plays a key role in binding by these molecules. A compelling prospect is structure **6**. It seems difficult to imagine that association of the nickel·$(sal)_2$ system does not at some juncture pass through Holm's dimer. Osmometric molecular weight may confirm this if reliable (*vide supra*), but there is no reason to suppose that the aggregation ceases at this stage. It is not unreasonable to assume that water plays a key role in complexation as observed in **6**. Acetone may serve as a donor group in the absence of a strongly coordinating ligand, since even the weakly donating nitro group of picrate coordinates in **6**.

Conclusions

Two examples of nickel cage complexes have been prepared, purified, characterized, and studied. Their structures have been confirmed by X-ray crystallography. In one case, the cage involves three nickel atoms and in the other two niickel atoms and one sodium atom. The key feature is that the cage structures, although being of different constitution, are nearly identical in the placement of metals and salicylaldimine ligands. Complexation of the sodium cation in one of these cage structures occurs in a novel and fundamentally different way from that originally proposed. The ability of these novel aggregates to bind alkali metal cations suggests that other examples of this new class of clusters may also be at hand.

Experimental Section

^1H NMR spectra were recorded on a Varian VXR-400 high-resolution spectrometer at 399.95 MHz unless otherwise specified. ^1H NMR spectra were recorded at 60 MHz on a Hitachi Perkin-Elmer R-600 spectrometer. $CDCl_3$ was used as solvent, unless otherwise specified. Chemical shifts (δ) in ppm downfield from internal Me_4Si (TMS) or from residual, nondeuterated solvent are reported in the following order: chemical shift, peak multiplicity (broad; s = singlet; d = doublet; t = triplet; m = multiplet), integration, and assignment. Infrared (IR) spectra were recorded in KBr on a Perkin-Elmer 599 spectrophotometer and are reported in cm^{-1}, calibrated against the 1601-cm^{-1} band of polystyrene. DCl mass spectra were determined on a VG Trio-2 spectrometer, using methane or ammonia as the reagent gas. UV–vis–NIR measurements were determined on a Perkin-Elmer Lambda 9 spectrophotometer, interfaced to an IBM PC/XT, with the slit set in automatic servocontrol. VPO measurements were carried out using a Wescor 5100c vapor pressure osmometer in $CHCl_3$ (HPLC grade) as solvent. The repeatability and accuracy of the same was tested by running samples of known molecular weight prior to running an unknown. Melting points were determined on a Thomas-Hoover 6406-K capillary melting point apparatus and are uncorrected. Combustion analyses were performed at Atlantic Microlab,

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(30) Takeda, Y. *Top. Curr. Chem.* **1984**, *121*, 1.

(31) Hopkins, H. P., Jr.; Norman, A. B. *J. Phys. Chem.* **1980**, *84*, 309.

(32) (a) Staley, R. H.; Beauchamp, J. L. *J. Am. Chem. Soc.* **1975**, *97*, 5920. (b) Woodin, R. L.; Beauchamp, J. L. *J. Am. Chem. Soc.* **1978**, *100*, 501. (c) Meot-Ner, M. *J. Am. Chem. Soc.* **1983**, *105*, 4906. (d) Sharma, R. B.; Blades, A. T.; Kebarle, P. *J. Am. Chem. Soc.* **1984**, *106*, 510.

(33) (a) Dobler, M. *Ionophores and Their Structures*; Wiley-Interscience: New York, 1981. (b) Cram, D. J.; Trueblood, K. N. *Top. Curr. Chem.* **1981**, *98*, 43. (c) Hilgenfeld, R.; Saenger, W. *Top. Curr. Chem.* **1982**, *101*, 1.

(34) Power, P. L. *Acc. Chem. Res.* **1988**, *21*, 147.

(35) Takagi, M.; Ueno, K. *Top. Curr. Chem.* **1984**, *121*, 39.

Inc., Atlanta, GA. TLC analyses were performed on silica gel 60 F-254. Preparative chromatographic columns were packed with kieselgel 60 (70–230 mesh). All reactions were conducted under an atmosphere of dry nitrogen gas. All solvents were dried when required, by distillation over either CaH_2 or sodium benzophenone ketyl, and stored over activated molecular sieves (3Å). All reagents were of the best grade available and were used without further purification, unless otherwise stated.

2-Hydroxy-3-methoxy-*N*-methylsalicylaldimine (1). By the same procedure as for **2** (see below), *o*-vanillin (2.24 g, 14.7 mmol) and $MeNH_2$ (1.6 g of a 40% aqueous solution, 20.6 mmol) afforded **1** (2.38 g, 98%) as an orange solid (mp 72–74 °C). ^1H NMR (60 MHz): δ 3.45 (s, 3H, $-NCH_3$); 3.90 (s, 3H, $-OCH_3$); 6.85 (broad s, 3H, Ar-Hs); 8.30 (s, 1H, CH=N). IR: 2900 (br), 1600, 1450, 1405, 1390, 1370, 1240, 1160, 1075, 1000, 960, 860, 835, 780, and 730 cm^{-1}.

2-Hydroxy-3-(2-methoxyethoxy)-*N*-methylsalicylaldimine (2). A solution of 2,3-dihydroxybenzaldehyde (2.5 g, 18.1 mmol) in dry DMSO (25 mL) was added over a period of 2 h to an ice-cooled suspension of NaH (1.6 g of a 60% dispersion in oil, 40 mmol, previously washed with hexanes) in 25 mL of the same solvent. After addition, the mixture was kept at ambient temperature, (2-methoxyethoxy)-*p*-toluenesulfonate (4.6 g, 20.0 mmol) was added in one portion, and the solution was stirred mechanically for 26 h. Water (150 mL) was carefully added, and the solution was extracted with $CHCl_3$ (100 mL). The aqueous layer was acidified to pH 2 with 1 M aqueous HCl (color change to dark yellow) and then extracted with $CHCl_3$ (3 × 75 mL). The organic layer was then extracted with 1 M HCl (2 × 75 mL). Drying ($MgSO_4$) and removal of the solvent from the organic layer afforded an orange-brown oil, which solidified on standing. Column chromatography (SiO_2, $CHCl_3$) yielded 2-hydroxy-3-(2-methoxyethoxy)benzaldehyde as a light green-yellow solid (2.98 g, 84%, m.p. 58–60 °C). ^1H NMR: δ 3.48 (s, 3H, $-OCH_3$); 3.80 (t, 2H, $CH_3O\text{-}CH_2$); 4.22 (t, 2H, $O\text{-}CH_2\text{-}CH_2\text{-}O$); 6.94 (t, 1H, Ar 5H); 7.16–7.24 (2d, 2H, Ar 4H and 6H); 9.95 (s, 1H, CHO); 10.95 (s, 1H, Ar-OH). Anal. Calcd for $C_{10}H_{12}O_4$: C, 61.22; H, 6.17. Found: C, 61.15; H, 6.03.

The compound described above (2.88 g, 14.7 mmol) was dissolved in hot absolute EtOH (15 mL), and $MeNH_2$ (1.6 g of a 40% aqueous solution, 20.6 mmol), dissolved in 10 mL of the same solvent, was added dropwise. The color of the solution changed from yellow to deep orange. The solution was stirred at reflux for 15 min. After the solution was cooled, benzene (40 mL) was added, and the solvents were removed *in vacuo*, affording the product **2** as an orange oil (3.0 g, 98%). The imine appeared to undergo hydrolysis on either alumina or silica gel (TLC) and was thus used without further purification. ^1H NMR (60 MHz): δ 3.50 (broad s, 6H, $-NCH_3$ and $-OCH_3$); 3.95 (m, 4H, $O\text{-}CH_2\text{-}CH_2\text{-}O$); 6.90 (broad s, 3H, Ar-Hs); 8.40 (s, 1H, CH=N). IR: 3500 (br), 2950 (br), 1620, 1450, 1400, 1370, 1250, 1200, 1120, 1080, 1030, 1000, 900, 850, 780, and 740 cm^{-1}.

(3-Methoxy-*N*-methylsalicylaldimino)$_2$Ni(II) (3). By the same procedure as for **4**, **1** (1 g, 6.1 mmol) and $NiSO_4{\cdot}6H_2O$ (0.81 g, 3.1 mmol) afforded dark green needles (240 mg, 21%) (m.p. 205–206 °C). ^1H NMR: δ 3.710 (s, 6H, $-OCH_3$); 3.807 (broad s, 6H, $-NCH_3$); 6.315 (t, 2H, Ar 5H); 6.722–6.739 (broad d, 4H, Ar 4H and 6H); 9.787 (broad s, 2H, CH=N). IR: 3050–2800 (br), 1590, 1545, 1470, 1435, 1410, 1325, 1225, 1190, 1165, and 1095 cm^{-1}. MS (DCI) *m/z* (relative intensity): 387.0 (7), 300.2 (15), 166.1 (100). *Anal.* Calcd for $C_{18}H_{20}N_2O_4Ni$: C, 55.86; H, 5.21; N, 7.24. Found: C, 56.01; H, 5.24; N, 7.27.

[3-(2-Methoxyethoxy)-*N*-methylsalicylaldimino]Ni(II) (4). To a refluxing MeOH (70 mL) solution of **2** (1.50 g, 7.17 mmol) was added, in a slow stream, a hot solution of $NiSO_4{\cdot}6H_2O$ (0.94 g, 3.59 mmol) in 100 mL of the same solvent. Stirring and reflux were continued for 30 min, and the green solution was then cooled. Benzene (100 mL) was added, and the solvents were removed, affording a foamy green solid. This was kept *in vacuo* for 1 h. Cyclohexane (1 L) was used for digesting the residue for 3 h. After the solution was filtered and the solvent removed, a green solid remained. Crystallization from cyclohexane (150 mL) afforded the product as fine green needles (410 mg, 25%, m.p. 157–158 °C). ^1H NMR: δ 3.179 (s, 6H, $-OCH_3$); 3.359 (s, 6H, $-NCH_3$); 3.641 (t, 4H, $CH_3\text{-}O\text{-}CH_2$); 3.959 (t, 4H, $O\text{-}CH_2\text{-}CH_2\text{-}O$); 6.382 (t, 2H, Ar 5H); 6.633 (d, 2H, Ar 4H); 6.703 (d, 2H, Ar 6H); 7.723 (s, 2H, CH=N). MS (DCI) *m/z* (relative intensity): 475.2 (6), 211.3 (18), 210.2 (100). *Anal.* Calcd for $C_{22}H_{28}N_2O_6Ni$: C, 55.61; H, 5.94; N, 5.90. Found: C, 55.52; H, 5.96; N, 5.85.

Trinuclear [3-(2-Methoxy)ethoxy-*N*-methylsalicylaldimino]Ni(II) Derivative (5). Compound **2** (1.50 g, 7.17 mmol) was treated with $Ni(OAc)_2{\cdot}4H_2O$ (1.42 g, 5.70 mmol) and worked up in the same way as for **4**. Crystallization from cyclohexane (1 L) and slow evaporation (7 days) of the green solution to 200 mL afforded the product as emerald-green plates (150 mg, 8%, m.p. 116–120 °C). The structure of the compound was established by X-ray crystallography (see above). *Anal.* Calcd for $C_{48}H_{66}N_4O_{18}Ni_3$: C, 49.56; H, 5.72; N, 4.82. Found: C, 49.52; H, 5.61; N, 4.89.

Table II. Mean Instrument Responses at Varying Osmolality Values Used for Calibration in Organic Solvent

standard osmolality (mmol/kg)	mean instrument response
0.00	336 ± 8
30.76	540 ± 15
54.16	752 ± 7
72.18	1025 ± 40
92.06	1188 ± 30

Table III. Molecular Weight Measurements on **2a**

standard osmolality (mmol/kg)	mean instrument response (*X*-values (mmol/kg))	molecular weight (g mol^{-1})		error (%)
		theor	exptl (estd)	
38.54	644 ± 25 (26.87)	387.06	405	5
77.18	959 ± 29 (69.84)	387.06	428	10

Determination of Picrate Extraction Percentages.[25] A chloroform solution of the specified molarity (see Table I) was prepared for each of the Ni(II) complexes. Sodium picrate solutions were prepared by dissolving picric acid in aqueous NaOH solution (0.1050 M), and the concentrations were then determined spectrophotometrically (ϵ = 13 442 cm^{-1} M^{-1} at 356 nm). For concentrations of 80 and 75 μM (picrate and ligand, respectively), equal volumes (0.5 mL) of each solution were introduced into screw-capped vials containing a magnetic stirring bar. The two-phase system was stirred with a Thomas "MAGNEMATIC" stirrer Model 215, set at speed 8, for 3 min. The extent of metal cation extracted was evaluated spectrophotometrically, by measuring the loss of picrate absorbance at 356 nm in the aqueous layer, and the difference was expressed as percentages. For concentrations of 8 and 25 mM, the procedure was followed identically, but the volume of the Ni(II) complex solution was decreased to 0.4 mL in order to follow the conditions reported by the original authors.[22] All the extraction percentages are the average of five trials. Control experiments indicated that longer stirring time (10 min) did not cause an increase in the amounts of metal cation extracted. In the absence of ionophores, no $Na^+picrate^-$ was extracted from the aqueous layer.

Vapor Pressure Osmometric Determinations. Preliminary Calibration with Aqueous Standards. This was achieved by processing three standards of known osmolality: 100, 290, and 1000 mmol/kg. Subsequent measurements with organic systems are, in absolute terms, meaningless. Nevertheless, such aqueous standard precalibrations are a convenient way of establishing a reproducible "instrument response".

Direct Calibration in Organic Solvent. A pure solute of known molecular weight dissolved at precisely-known mass concentration levels in the chosen organic solvent is used for constructing a "calibration curve". Four solutions of 4,13-diaza-18-crown-6 in $CHCl_3$ (HPLC grade) were prepared: 30.76, 54.16, 72.18, and 92.06 mmol of solute/kg of solvent. A 0 mmol/kg reading was determined by running successive trials with pure solvent until a stable reading (±2 mmol/kg) was obtained during three consecutive trials. Each of the four solutions was processed at least five times, and a mean value was obtained. A calibration curve was obtained by plotting the obtained, experimental readings vs the standard osmolalities (mmol/kg). Typical values are shown in Table II. A linear regression of the data was obtained and used in the next steps: $Y = 9.56(X) + 291.57$; correlation coefficient = 0.99.

Molecular Weight Measurements. Next, a second, different solute of known molecular weight was processed, and the previous calibration curve was utilized to estimate its experimental molecular weight. *N,N′*-Bis(cyanomethyl)-4,13-diaza-18-crown-6 (**7**, F.W. 340.42 g mol^{-1})[36] was diissolved in $CHCl_3$ at a precisely known mmol/kg ratio. The calculations and results were as follows: standard osmolality, 63.16 mmol/kg; mean instrument response, 859 ± 19. Substituting the mean value into the linear regression equation gives $X = 59.375$ mmol/kg.

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[36] Gatto, V. J.; Arnold, K. A.; Viscariello, A. M.; Miller, S. R.; Morgan, C. R.; Gokel, G. W. *J. Org. Chem.* **1986**, *51*, 5373.

$$\mathrm{MW} = \frac{\text{mass concn (mg/kg)}}{\text{osmolality (mmol/kg)}} = \frac{21.50}{59.375} \times 1000 = 362$$

$$\text{error} = 7\%$$

The same procedure was repeated with the Ni(II) complex **2a**. These results are shown in Table III.

Crystal Structure Data for Compound 5. A suitable crystal was obtained from cyclohexane upon slow evaporation (7 days). Crystal data: $C_{48}H_{66}N_4O_{18}Ni_3$, FW = 1163.14 g mol^{-1}, space group $P2_1/n$, $a = 16.648$ Å, $b = 16.355$ Å, $c = 19.657$s Å, $V = 4535.3$ Å^3, $\beta = 99.04°$, 4 molecules/unit cell; measured by an Enraf–Nonius CAD-4F (κ geometry) X-ray spectrometer.

Crystal Structure Data for Compound 6. A suitable crystal was obtained from CH_2Cl_2:acetone (1:1, over 3 days) and found to have m.p. 165–175 (soften at 160) °C. Crystal data: $C_{48}H_{46}N_{10}O_{23}Na_2Ni_2$, FW = 1294.32 g mol^{-1}, tetragonal crystal system, space group $I41/a$, $a = b = 22.780(2)$ Å, $c = 46.284(4)$ Å, $V = 24018$ Å^3, $d_{\text{calcd}} = 1.437$ g cm^3, 16 molecules/unit cell; Mo Kα [μ(calcd) = 7.26 cm^{-1}], $R = 4.4$ for 2312 unique reflections with $I > 2(I)$ (of 6163 unique data) measured by an Enraf–Nonius CAD-4F (κ geometry) X-ray spectrometer using θ–2θ scans, $2 < \theta < 40°$; $R = 4.4$, $R_w = 4.9$.

Acknowledgment. We thank the NIH for a grant (GM 36262) that supported this work.