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Crown-Ether-Functionalized Nickel Salicylaldimine Complexes. Structural Characterization of Their Potassium, Cesium, and Hexylammonium Derivatives and Their Use in the Transport of Amino Acids

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Complexes of crown-ether functionalized planar multidentate complexes include derivatives of salicylideneimines,[1] porphyrins,[2] and phthalocyanines.[3] Our recent interest in the coordination chemistry of crown-ether-functionalized tetra-*tert*-butylsalicylideneimines, ^{t}Bu$_4$salphen, derives from the anticipated importance of these compounds in selective complexation[4] and transport.[5] The crown-ether-functionalized ^{t}Bu$_4$salphen complexes combine the electron-pair-donor characteristics of the crown ether component[6] and the metal-dependent electron-pair-acceptor properties of the salphen-bound metal ions. As ditopic receptors, these molecules are expected to recognize and specifically bind to zwitterions such as amino acids or other molecules that contain both basic and acidic sites. The molecules reported herein are conceptually similar to a known receptor of ω-amino carboxylates that consists of a macrotricyclic quaternary ammonium unit bridged via a xylyl bridge to an aza crown ether.[7] The assembly of this receptor, "tetazac", is quite complex however, and its synthesis in a small overall yield involves 28 steps.

In this communication we report our synthetic and structural studies of the 18-crown-6-Ni^{t}Bu$_4$salphen complex and its K^+, Cs^+, and n-$C_6H_{13}NH_3^+$ derivatives and preliminary results of amino acid transport by these molecules.

The4,5-bis(3,5-di-*tert*-butylsalicylideneimino)benzo-18-crown-6 ligand, **I**, is obtained by a Schiff base condensation reaction between 4,5-diaminobenzo-18-crown-6 and 3,5-di-*tert*-butylsalicylaldehyde.[8,9] The reaction of **I** (in CH_2Cl_2) with nickel acetate (in CH_3OH) affords, after evaporation of the solvents, crystalline Ni-**I** in 70% yield.[9] The latter reacts with KI and CsI to give crystalline (K-Ni-**I**)$^+$Cl$^-$·H$_2$O[9] and (Cs-Ni-**I**)$^+$I$^-$,[9] respectively. The reaction of Ni-**I** with CsI in a 2:1 molar ratio gave crystalline [Cs(Ni-**I**)$_2$]$^+$I$^-$. Slow evaporation of an acetone solution of Ni-**I** that contained hexylammonium chloride gave large crystals of the Ni-**I**-HexNH$_3^+$Cl$^-$ derivative.

The structures of (K-Ni-**I**)$^+$Cl$^-$, (Cs-Ni-**I**)$^+$I$^-$, and (Ni-**I**-HexNH$_3$)$^+$Cl$^-$ (Figure 1) and of [Cs(Ni-**I**)$_2$]$^+$ I$^-$ have been determined.[10] In the monomeric (K-Ni-**I**)$^+$Cl$^-$ complex, the seven-coordinate K^+ ion is bound to a water molecule ($K{-}O_{H_2O}$ = 2.687(4) Å) in addition to the six crown-ether oxygen donors (Figure 1A) ($\overline{K{-}O}$ = 2.83(2) Å; range 2.751(4)−2.899(4) Å) The chloride anion is found 3.478(1) Å from the K^+ ion and 7.102(1) Å from the Ni^{2+} ion and is hydrogen-bonded to the K^+ bound water molecule at 3.409(3) Å. The basic structural features of the Cs^+ derivatives are determined by the coordination requirements of the large Cs^+ ions that are coordinatively unsaturated when bound only by the oxygen donors of a single 18-crown-6 unit. This is the case with the (Cs-Ni-**I**)$^+$I$^-$, complex where the presence of one Cs^+ ion per Ni-**I** results in dimer formation (Figure 1B). The Cs^+ ions in each of the two Cs-Ni-**I** units, in addition to being coordinated by the 18-crown-6 moiety ($\overline{Cs{-}O}$ = 3.08(3) Å; range 3.021(4)−3.177(4) Å), also are coordinated by two salphen ligand oxygen atoms at 3.298 and 3.226 Å. The strength of these interactions becomes apparent in the appearance of a "parent" ion peak in the FAB mass spectrum of the compound at a mass of 1928 (corresponding to the (Cs-Ni-**I**)$_2^+$ dimer. The I^- ion is found 7.246(4) Å from the Cs^+ ion and close to five ligand carbon atoms atoms at distances that range from 3.762(4) to 3.984(4) Å. An examination of the ^{1}H NMR spectra of Cs-Ni-**I** shows that the dimer persists in CH_2Cl_2 but dissociates in $(CH_3)_2SO$ solution. In the structure of the Ni-**I**-HexNH$_3^+$Cl$^-$ complex, the NH_3^+ unit of the HexNH$_3^+$ guest hydrogen-bonds in a symmetric fashion to the 18-crown-6 unit and the C_6 chain lies parallel to the salphen-crown backbone of the host molecule (Figure 1C). The mean N−O distance in Ni-**I**-HexNH$_3^+$ ($\overline{N{-}O}$ = 2.92(4) Å) is slightly shorter than the corresponding distance reported[11] for the 9-anthracenylmethylbenzylammonium "adduct" of dibenzo-24-crown-8 (N−O range 2.98−3.15 Å).

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[8] 4,5-Diaminobenzo-18-crown-6 is obtained by the 40 psi H_2 hydrogenation of 4,5-dinitrobenzo-18-crown-6 over palladium/activated carbon catalyst in methanol. The 4,5-dinitrobenzo-18-crown-6 reagent is obtained by nitration (concentrated HNO_3) of commercially available benzo-18-crown-6.

[9] Satisfactory elemental analyses, mass spectroscopic data, infrared spectroscopic data, and electronic spectroscopic data are available as Supporting Information.

[10] Crystal data: for K-Ni-**I**-Cl·H$_2$O·CHCl$_3$, space group $P1$, a = 10.3791(1) Å, b = 15.9553(2) Å, c = 18.4490(3) Å, α = 112.16(1)°, β = 102.97(1)°, γ = 96.43(1)°, Z = 2, R = 0.060; for (Cs-Ni-**I**-I)$_2$, space group $P1$, a = 10.0693(2) Å, b = 16.6268(1) Å, c = 19.2304(3) Å, α = 114.672(1)°, β = 102.098(1)°, γ = 93.290(1)°, Z = 1, R = 0.055; for Ni-**I**-HexNH$_3^+$-Cl$^-$, space group $P2_1/n$, a = 10.5888(1) Å, b = 19.1505(1) Å, c = 30.9815(4) Å, β = 93.714(1)°, z = 4, R = 0.056. The structure of the [Cs(Ni-**I**)$_2$]$^+$ I$^-$ complex has been determined and the pertinent data have been deposited as Supporting Information. The structure shows the 12-coordinate Cs^+ ion "sandwiched" between two, nearly parallel and staggered relative to each other, 18-crown-6 units.

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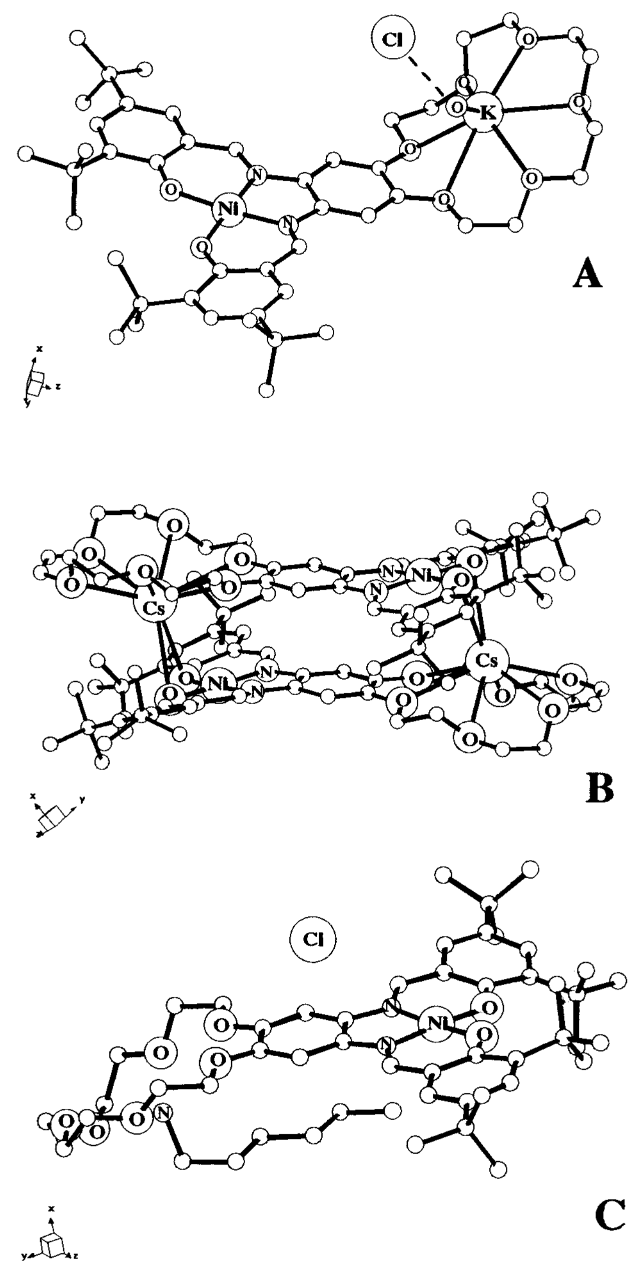

Figure 1. Structures and labeling scheme for derivatives of the 4,5-bis-(3,5-di-*tert*-butylsalicylideneimino)benzo-18-crown-6 ligand **I**: (A) the K-Ni-**I**-Cl·H_2O complex, (B) the Cs-Ni-**I**-I complex, and (C) the Ni-**I**-HexNH$_3^+$Cl$^-$ complex. (A) $K^+-Ni = 7.102(1)$ Å; closest $Ni-Ni = 8.098(1)$ Å; $\overline{K^+-O_{18\text{-}C\text{-}6}} = 3.08(3)$ Å (range 3.021(4)−3.177(4) Å); $K^+-Cl^- = 3.487(1)$ Å; $K^+-O_{H_2O} = 2.687(4)$ Å. In (B) $Cs^+-Ni = 3.437(1)$ Å; $Ni-Ni = 7.818(2)$ Å; $\overline{Cs^+-O_{18\text{-}C\text{-}6}} = 3.08(3)$ Å (range 3.021(4)−3.177(4) Å); $Cs^+-O_{salphen} = 3.298(4), 3.226(4)$ Å. In (C) $\overline{H_3N^+-O_{18\text{-}C\text{-}6}} = 2.92(4)$ Å (range, 2.849(3)−3.033(3) Å); $Ni-Cl^- = 6.454(1)$ Å.

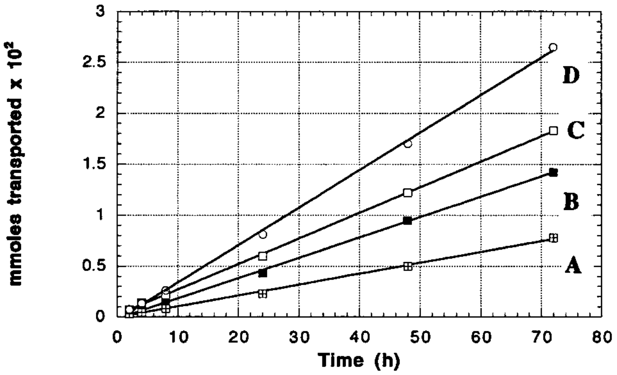

Figure 2. Transport of tryptophan by (A) the K-Ni-**I**-Cl·H_2O complex, (B) Ni-**I**, (C) K^+-Bz-18-crown-6, and (B) Bz-18-crown-6 (data taken from ref 12). The initial transport rates are $1.07(2) \times 10^{-4}$, 2.00×10^{-4}, 2.51×10^{-4}, and 3.67×10^{-4} mmol h^{-1}, respectively.

Preliminary studies on the carrier properties of the Ni-**I** complex and alkali metal ion derivatives show[12] effective transport of amino acids from acidic aqueous solutions to pure water. From an equimolar mixture of glycine, alanine, phenylalanine, histidine, and tryptophan in aqueous solution (pH 2.7) the hydrophobic amino acids phenylalanine and tryptophan are preferentially transported over the rest, which are either transported to a lesser extent or not transported at all. The transport of tryptophan from aqueous solution (isoelectric point pH 5.89) using Ni-**I** or its alkali metal derivatives as "carrier" molecules was found nearly 50% slower than that observed for benzo-18-crown-6 and the alkali metal ion loaded derivatives. (See Figure 2.) The origin of this difference is difficult to ascertain but very likely is due to differences in the interface behavior and guest−host interactions for the different carrier molecules. For all carriers, the rate of transport is slower in the presence of alkali metal ions. This inhibition undoubtedly is due to the competition between the amino acid NH_3^+ group and the alkali metal ion for the 18-crown-6 pocket. The Ni(^{t}Bu$_4$salphen)−veratrol complex, which does not contain a crown ether group, is inactive in the transport of tryptophan. This result indicates that the transport properties of Ni-**I** are due entirely to the 18-crown-6 group and the stability of the square planar Ni(II) site prevents coordination of the Ni(II) ion with moderately strong axial ligands[14] and precludes its involvement as an electron-accepting site in this molecule. A detailed systematic study of the transport of amino acids, dipeptides, and other zwitterionic molecules of varying sizes is currently in progress using the M-**I** complexes (M = Mn(III), Fe(III), Co(II)) which can readily accommodate axial ligands. Preliminary results show[15] the Mn-**I** complex to be a superior carrier of tryptophan when compared to the Ni-**I** complex.

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Supporting Information Available: Text giving detailed syntheses and characterizations of the compounds and tables of positional parameters, thermal parameters, and selected distances and angles for (K-Ni-**I**)$^+$Cl$^-$, Cs-Ni-**I**-I$^-$, Cs-(Ni-**I**)$_2$-I$^-$, and Ni-**I**-HexNH$_3^+$Cl$^-$ (56 pages). Ordering information is given on any current masthead page.

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[12] The transport studies were carried out at ambient temperature in systems where a compartment containing 10 mL of an aqueous 50 mM solution of tryptophan is separated from a compartment containing 10 mL of pure water by a layer (50 mL) of a 7.2 mM $CHCl_3$ solution containing the carriers (K-Ni-**I**, Ni-**I**, K-Bz-18-C-6, Bz-18-C-6). The cell used was similar to one described previously.[13] The concentration of the transported tryptophan was monitored by electronic spectroscopy. When a mixture of five amino acids was used, the initial concentration of each amino acid was 10 mM and the quantity transported was established by ^{1}H NMR spectroscopy.

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