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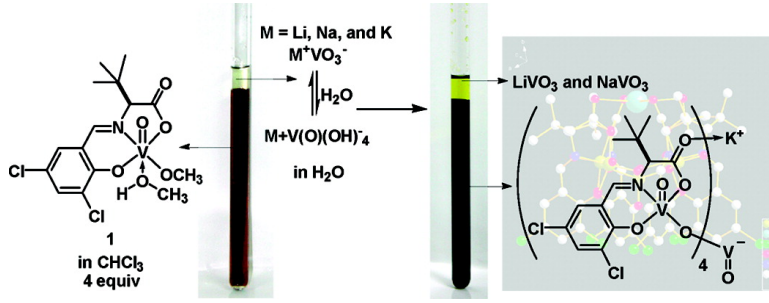

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Directed Assembly of Chiral Oxidovanadium(V) Methoxides into C_4-Symmetric Metal(I) Vanadate-Centered Quadruplexes: Synergistic K^+- and Ag^+-specific Transport

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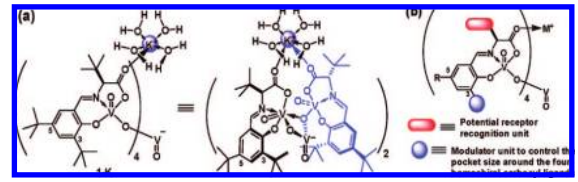
Synergistic self-assembly of proteins facilitated by a specific metal ion often results in a new and unique biological function in nature. One intriguing example is the synergistic K^+-specific transport from extracellular media into the cell thru a tetrameric, KcsA membrane protein (i.e., a K^+ channel membrane protein from *Streptomyces lividans*) with a synergistic binding of K^+ by four homochiral glycine residues near the opening site in KcsA.[1] In marked contrast, artificial C_4-symmetric oligonuclear assemblies that exhibit specific molecular or K^+-specific recognition, biological functions, or asymmetric catalysis in a synergistic mode are rarely explored.[2]

As part of our ongoing programs by using chiral oxidovanadium(V) complexes in catalyzing asymmetric aerobic oxidation[3] and oxidative coupling of 2-naphthols,[4] we have been engaged in the structural identification of a chiral oxidovanadium(V) methoxide bearing 3,5-di-*tert*-butyl-*N*-salicylidene-L-*tert*-butylglycinate. A K^+-solvated C_4-symmetric vanadate-center tetrameric cluster **1-K** was accidentally isolated.[3c] The K^+ exists in a unique solvation environment and is sandwiched between four water molecules and four homochiral carboxyl units (Scheme 1a). This type of complexation is similar to a 1:2 complex of a sandwich structure between K^+ and 12-crown-4[5] or between K^+ and (iso)G-quartet analogues.[2,6] More importantly, the C3-*tert*-butyl group at the salicylidene template in the cluster is positioned underneath the next flanking salicylidene unit. This unique structural assembly and stoichiometry between the monomeric oxidovanadium(V) complex and the central $K^+[(V{=}O)(-O-)_4]^-$ unit are inspirational. We figured that a judicious modulation of the C(3)-substituent at the salicylidene template in the parent oxidovanadium(V) methoxide complex may delicately control the size of the pocket domain among the four homochiral carboxyl units, thus allowing for potential metal-specific ion capture (Scheme 1b).

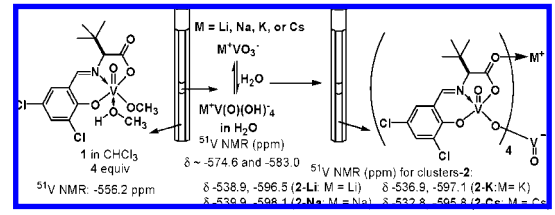
We recently discovered that a specific *N*-salicylidene-*tert*-butylglycinate-based chiral oxidovanadium(V) methoxide can self-assemble into an ion-specific, alkali metal vanadate-centered, C_4-symmetric tetrameric cluster by a concept similar to the directed assembly mastered by chemistry researchers.[7] The artificial, directed assembly process, for the first time, in chiral oxidovanadium(V) complex allows for highly efficient K^+- and Ag^+-specific transport from aqueous phase containing other three alkali metal cations into organic solvents. We report herein our preliminary results of these findings.

A solution of the oxidovanadium(V) 3,5-dichloro-*N*-salicylidene-L-*tert*-butylglycinate **1** (4 equiv) in $CDCl_3$ is partitioned with an aqueous solution containing respective alkali metal metavanadate [$MVO_3{-}2H_2O$ or $MV(O)(OH)_4$, M = Li, Na, K, or Cs], Scheme 2. ^{51}V NMR spectroscopic analyses of these respective clusters in $CDCl_3$ show complete conversion of **1** (δ −556.2 ppm) into the corresponding clusters **2** in 10 min. All the clusters **2** show two distinctive signals around -536.3 ± 3.5 and -597 ± 1 ppm in a 1:4 ratio, corresponding to the central vanadate and the four flanking oxidovanadium units, respectively.

Scheme 1. (a) K^+-Solvated C_4-Symmetric Vanadate-Centered Tetrameric Cluster **1-K**; (b) Design Concept Thru Metal Metavanadate-Directed Assembly for Metal Ion Encapsulation and Potential Ion-Channel Models



Scheme 2. Alkali Metal Metavanadate-Directed Assembly of Clusters in $H_2O/CHCl_3$ and Their Respective Chemical Shifts in ^{51}V NMR



X-ray crystallographic analyses of the K^+ and Cs^+-containing clusters **2-K** and **2-Cs** reveal that the central C_4-symmetric vanadate(V) unit serves to grip four homochiral oxidovanadium(V) units together through vanadate μ-oxo linkages in a covalent fashion, Figure 1a.[8] The positive charge on K^+ or Cs^+ is balanced by the negative charge in the central vanadate. More importantly, the K^+ or Cs^+ is chelated *in a unique square planar scaffold* by four carboxyl units in the four flanking chiral oxidovanadium(V) subunits through simultaneous carboxyl coordination. The binding profile is in close similarity to the K^+ transport mode exerted by four homochiral glycine residues of the opening site in KcsA (Figure 1b,c).[1] The respective μ-oxo bridge units are coordinated anti to the next V=O unit and serve to hold the whole cluster by cooperation with the K^+ or Cs^+.

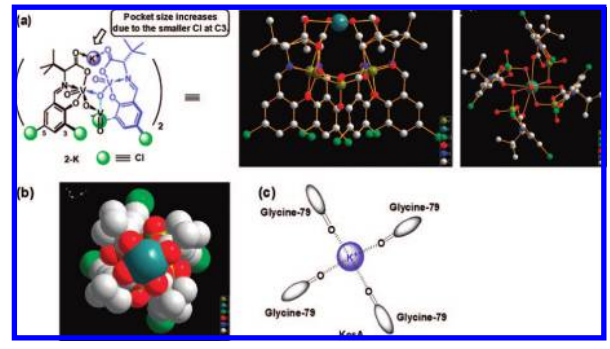


Figure 1. X-ray crystal structure of **2-K** (hydrogens omitted for clarity): (a) side view and bottom view; (b) top view of **2-K**; (c) KcsA local K^+-chelated domain.

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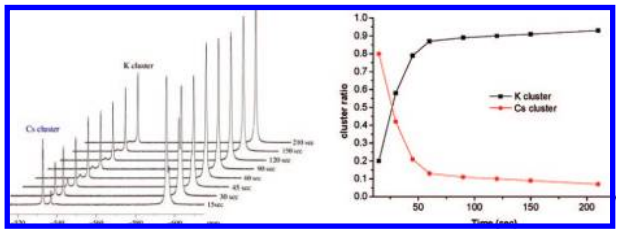

Figure 2. Dynamic trace study by ^{51}V NMR spectroscopic analyses on the distribution of **2-K** and **2-Cs** in $CDCl_3$ layer in the swapping experiment between **2-Cs** and KCl or KVO_3.

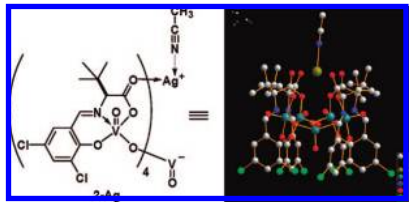

Figure 3. X-ray crystal structure of **2-Ag** (hydrogens omitted for clarity).

To evaluate if the 3,5-dichloro-substituted oxidovanadium(V) methoxide **1** can act as a potential K^+-specific ion transporter (i.e., an artificial KcsA mimetic) from the aqueous solution, competitive partitioning studies between K^+ and other alkali metal ions in the presence of **1** in $H_2O/CDCl_3$ mixture were further carried out. A 1:1 (i.e., equimolar) mixture of aqueous $LiVO_3$ and KVO_3 solution is partitioned with a solution of **1** (4 equiv) in $CDCl_3$. The competitive, directed assembly progress was monitored by ^{51}V NMR spectroscopic analysis of the mixture in a NMR tube. It was found that exclusive formation of the K^+ encapsulated cluster **2-K** was resulted in $CDCl_3$ in 10 min.[9] Remarkably, similar observation was also found in the competitive partitioning between K^+ and Na^+ under the same directed assembly conditions. Only the K^+ encapsulated cluster **2-K** was formed in $CDCl_3$ in 10 min. Furthermore, a competitive partitioning among a mixture of Li^+, Na^+, and K^+ also led to the same K^+-specific encapsulation to form **2-K**. To our knowledge, this is first successful exclusive recognition of K^+ in a mixed solution of K^+ and Na^+ with spontaneous assembly of a tetrameric cluster similar to the KcsA open-site K^+-binding regime.

We have further carried out a competitive partitioning experiment between K^+ and Cs^+. An equilibrium 95:5 mixture of K^+:Cs^+ encapsulated clusters **2-K** and **2-Cs** was obtained in $CDCl_3$ in 1 h (92:8 ratio in 8 min). Notably, the K^+-specific encapsulation process exerted by **1** is dynamically driven. In the first 10 s, about 50:50 mixtures of **2-K** and **2-Cs** were formed. The composition of **2-K** was enriched to 80% for the next 10 s and reaches about 90% for the following 100 s. About a 92:8 ratio of **2-K** and **2-Cs** was observed at 8 min of mixing time.[10] The result from this dynamic trace study indicates that there exists a dynamic swapping process of metal ions between **2-Cs** in $CDCl_3$ with the K^+ in the aqueous phase, allowing for further enrichment of **2-K** in the $CDCl_3$ layer.

To prove this unprecedented, facile metal ion swapping event in a biphasic system, we treated a pure Li^+ or Na^+ encapsulated cluster (**2-Li** or **2-Na**; 1 equiv) in $CDCl_3$ with an equimolar amount of KCl or KVO_3 in H_2O. Either Li^+ or Na^+ in the cluster was completely replaced by K^+ in 15 s with concomitant formation of **2-K**.[8] On the other hand, when Cs^+ encapsulated cluster **2-Cs** (1 equiv) in $CDCl_3$ was partitioned with an aqueous solution of KCl or KVO_3, a 90:10 mixture of K^+ and Cs^+ encapsulated clusters resulted in 2 min (Figure 2).[8] Notably, the negatively charged central vanadate unit in a given cluster serves as a handle for the facile dynamic swapping between metal ions in the biphasic interface.

Remarkably, the square planar type complexation of K^+ in the cluster **2-K** is at least 100 times stronger than that exerted by dicylohexano-18-crown-6[11] ($K_a \approx 10^8$ M^{-1}). No discernible change in the composition of the cluster **2-K** was detected when a large excess of dicylohexano-18-crown-6 (20 → 100 equiv) was administered to a $H_2O/CHCl_3$ (1/10) mixed solution containing **2-K**. Furthermore, a biphasic partitioning between an aqueous solution of $K^+VO_3^-$ containing dicylohexano-18-crown-6 (20 → 100 equiv) and a solution of the oxidovanadium(V) methoxide **1** (4 equiv) in $CDCl_3$ also led to an exclusive formation of the K^+-encapsulated cluster **2-K** in 10 min. On the other hand, the sandwich type, K^+-encapsulated cluster **1-K** (in Scheme 1) only shows comparable complexation ability to that exerted by dicylohexano-18-crown-6.

With this powerful dynamic metal ion swapping technique in hand, we are now able to encapsulate other +1 transition metal ions into the cluster at will. As a demonstration, Li^+ or Na^+ encapsulated clusters **2-Li** or **2-Na** (1 equiv) in $CDCl_3$ was treated with an equimolar amount of Ag_2SO_4 in H_2O. Complete swapping of Li^+ or Na^+ by Ag^+ was achieved in 3 or 43 h, respectively, leading to Ag^+-encapsulated cluster **2-Ag** (^{51}V NMR: δ −540.1 and −596.3 ppm) in quantitative yield. Notably, $AgVO_3$ is not soluble in water or $CHCl_3$ at all. This swapping protocol allows one to access the corresponding metal ion encapsulated clusters even with metal metavanadates which lack water and organic solvent solubility.

Finally, we were able to obtain the X-ray crystal structure of the Ag^+-encapsulated cluster **2-Ag** by recrystallization from CH_3CN. The key structural feature of **2-Ag** is similar to those for **2-K** and **2-Cs** except that an acetonitrile ligand is attached right on top of the encapsulated Ag^+ in a square pyramidal geometry, Figure 3. Notably, the unique square pyramidal geometry for the encapsulated Ag^+ is unprecedented. In addition, the acetonitrile ligand is situated in a C_4-symmetric environment created by the four flanking *tert*-butyl groups on the chiral oxidovanadium(V) templates, which poses a potential use of this C_4-symmetric silver vanadate **2-Ag** in asymmetric catalysis.

Acknowledgment. We thank the National Science Council of Taiwan for generous financial support of this research.

Supporting Information Available: Experimental procedures, X-ray data (cif and checkcif files), and spectroscopic characterization for **1**, **2-K**, **2-Cs**, and **2-Ag**. The material is available free of charge via the Internet at http://www.acs.org.

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