Angewandte Chemie

Helicate Ligands

DOI: 10.1002/ange.200502571

Allosteric-Controlled Metal Specificity of a Ditopic Ligand**

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There are numerous examples in the field of metallosupramolecular chemistry that demonstrate that careful design of ligands can produce species that are selective to certain metal ions.[1] For example, Lehn et al. demonstrated that a mixture of two ligands that contain three bipyridine units and are linked either by aliphatic or ether units form only homonuclear and homoleptic trinuclear double and triple helicates upon reaction with Cu^+ and Ni^{2+} ions, respectively.[2] Another approach to enhance metal specificity is to introduce discrete binding domains within a ligand strand such that each domain is specific to a particular metal ion.[3] However, when using the latter strategies, the information contained within the ligand system, that is, its "programming", is finalized at the synthetic stage and cannot be altered thereafter. Herein, we describe a ditopic ligand L^1, whose selectivity for different transition-metal ions can effectively be "reprogrammed" by the addition of the larger s-block-metal ions to the crown ether moiety. This approach is related to the allosteric effect demonstrated by Rebek et al., in which the ability of a crown ether to coordinate Group 1 metal ions is influenced by coordination of a remote bipyridine coordination domain.[4] In this case, however, the reverse occurs as coordination of the crown ether unit controls the ability of a remote nitrogen-donor unit to act as either a tetradentate or bisbidentate domain. Other reprogrammable systems have been shown to control the formation of helicates[5] and modulate their pitch length.[6]

The reaction of L^1 (Scheme 1) with an equimolar amount of $[Cu(MeCN)_4]PF_6$ in MeCN gave a dark-red solution, and ESI-mass-spectrometric analysis showed the formation of a dinuclear double helicate with an ion at m/z 1497 consistent with $\{[Cu_2(L^1)_2](PF_6)\}^+$. In addition, the crown ether moiety

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[**] We thank the EPSRC and the University of Huddersfield for financial support.

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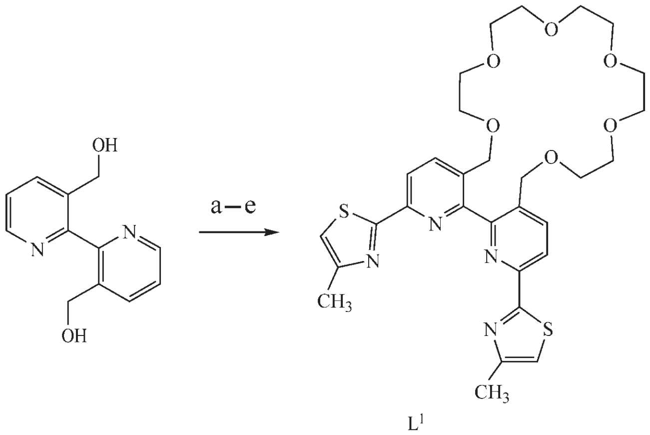

Scheme 1. Conditions: a) penta(ethylene glycol) di-*para*-toluenesulfonate, DMF, NaH (60/45 %); b) *m*CPBA, CH_2Cl_2 (70 %); c) TMSCN, PhCOCl, CH_2Cl_2 (83 %); d) H_2S, Et_3N, EtOH (90 %); e) chloroacetone, EtOH (76 %). DMF = dimethylformamide, *m*CPBA = *meta*-chloroperoxybenzoic acid , TMSCN = trimethylsilyl cyanide.

can coordinate barium ions as the reaction of this copper-containing helicate with excess $Ba(ClO_4)_2$ gives rise to ions in the ESI mass spectrum of *m*/*z* 1788 and 2124, which correspond to $\{[Cu_2(L^1)_2Ba](ClO_4)_3\}^+$ and $\{[Cu_2(L^1)_2Ba_2](ClO_4)_5\}^+$, respectively. The formation of the complex $[Cu_2(L^1)_2Ba_2(H_2O)](ClO_4)_6\cdot 2\,MeCN\cdot 0.5\,Et_2O$ has been established by a single-crystal X-ray diffraction study (Figure 1).[7] In the solid state, the ligand splits into two bisbidentate binding domains with two Cu^I ions coordinated by two bridging ligands in a double helicate arrangement with an average interdomain torsion angle of 108.9° (N-C-C-N). Each of the Cu^I centers has a distorted-tetrahedral geometry formed by coordination of one bidentate pyridyl–thiazole nitrogen-donor unit from each ligand (Cu–N: 1.985(7)–2.158(8) Å). Furthermore, both of the crown ether units coordinate to barium ions ($O{-}BaO_{(crown\ ether)}$: 2.760(8)–2.978(12) Å), with the longest bonds arising from coordination of the "benzylic" oxygen atoms ($Ba{-}O_{(methylene)}$: 2.791(9)–2.978(12) Å).

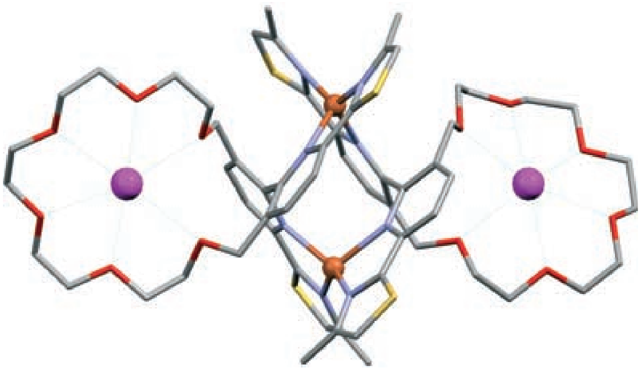

Figure 1. Crystal structure of the complex cation in $[Cu_2(L^1)_2Ba_2](ClO_4)_6\cdot 2\,MeCN\cdot 0.5\,Et_2O$.

The ^1H NMR spectrum of $[Cu_2(L^1)_2]^{2+}$ in CD_3CN shows three aromatic signals for the pyridyl–thiazole moiety, consistent with a highly symmetrical double helicate complex in which all four of the thiazole–pyridyl fragments are chemically equivalent (Figure 2 a). The two doublets ascribed to the pyridyl protons show a characteristic upfield shift that arises because these protons are shielded by the aromatic-ring currents of a thiazole moiety in the adjacent ligand strand. In addition, the diastereotopic "benzylic" -CH_2O- protons give rise to two comparatively upfield doublets. The addition of barium ions affords a similar ^1H NMR spectrum, in which the "benzylic" -CH_2O- protons show a characteristic downfield shift because of the coordination of the electronegative Ba^{2+} ions in the crown ether cavities (Figure 3 a).

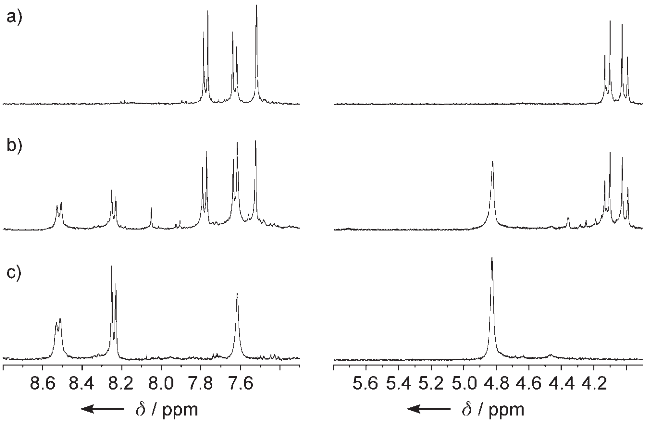

Figure 2. Selected regions of the ^1H NMR spectra (CD_3CN) of a) $[Cu_2(L^1)_2]^{2+}$, b) $L^1 + Cu^+ + Zn^{2+}$, and c) $[Zn(L^1)]^{2+}$.

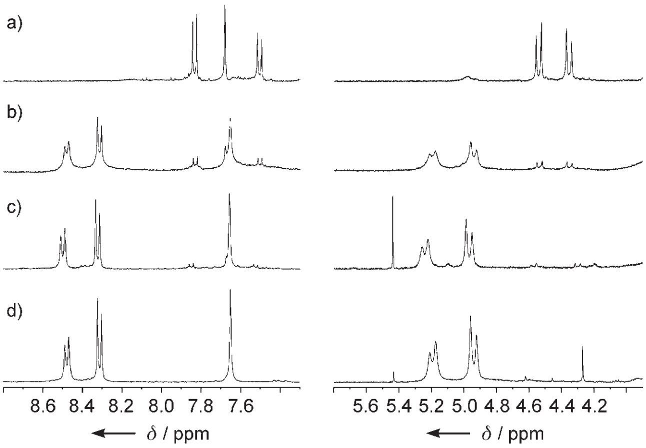

Figure 3. Selected regions of the ^1H NMR spectra (CD_3CN) of a) $[Cu_2(L^1)_2]^{2+}$ + excess Ba^{2+} ions, b) $L^1 + Cu^+ + Zn^{2+}$ + excess Ba^{2+} ions, c) $L^1 + Cu^+ + Zn^{2+}$ + excess Sr^{2+} ions, and d) $[Zn(L^1)]^{2+}$ + excess Ba^{2+} ions.

Reaction of L^1 with an equimolar amount of $[Zn(H_2O)_6](ClO_4)_2$ in MeCN gave a pale-yellow solution, and ESI-MS analysis showed an ion of *m*/*z* 776 consistent with the formation of the mononuclear $\{[Zn(L^1)](ClO_4)\}^+$ complex. The ^1H NMR spectrum of $[Zn(L^1)]^{2+}$ in CD_3CN (Figure 2 c) shows more deshielded pyridyl proton resonances than the Cu helicate $[Cu_2(L^1)_2]^{2+}$, thus reflecting an absence of the aromatic shielding caused by interstrand π stacking of the ligands in the latter complex. In addition, the "benzylic" -CH_2O- protons appear as a broad singlet, which indicates that rapid conformational movement about the bipyridyl backbone occurs on the NMR timescale, thus rendering these methylene protons chemically equivalent. Upon addition of $Ba(ClO_4)_2$ to $[Zn(L^1)]^{2+}$, an ion of m/z 1112 that corresponds to $\{[Zn(L^1)Ba](ClO_4)_3\}^+$ is observed in the ESI mass spectrum, thus indicating that a Ba^{2+} ion is again coordinated in the host cavity of the crown ether. Consistent with this observation, the ^1H NMR spectrum in CD_3CN shows small but significant changes as the "benzylic" -CH_2O- protons resolve into two doublets on addition of Ba^{2+} ions (Figure 3d). This change could be ascribed to the restricted conformational mobility induced by coordination of a Ba^{2+} ion into the crown host cavity. Treatment of $[Zn(L^1)]^{2+}$ with excess $Ba(ClO_4)_2$ followed by crystallization afforded the complex $[Zn(L^1)Ba(H_2O)_2](ClO_4)_4{\cdot}MeCN{\cdot}0.5\,Et_2O{\cdot}0.75\,H_2O$, the structure of which has been established by single-crystal X-ray diffraction studies.[8] In the solid state, the ligand coordinates to the equatorial plane of the Zn^{2+} center through all four nitrogen-donors, and two water molecules occupy the axial positions (Figure 4). The ligand is almost planar and exhibits only a shallow helical twist about the metal center, which is caused by unfavorable steric interactions between the methylene substituents on the central bipyridine core (N-C-C-N dihedral angle is approximately 31.0°). The arrangement of equatorial nitrogen-donors and axial water ligands generates a distorted-tetragonal geometry about the Zn^{2+} center (Zn–N: 2.178(5)–2.237(6) Å; Zn–O: 2.060(5) and 2.095(5) Å) similar to the geometry observed by Baxter et al. for the Zn^{II} complex of the analogous crown-free ligand.[9] The Ba–O separations are distributed over a narrower range than for $[Cu_2(L^1)_2Ba_2]^{6+}$ (Ba–O in $[Zn(L^1)Ba]^{4+}$: 2.803(4)–2.893(4) Å), which is consistent with the barium ion being located more centrally within the crown ether in $[Zn(L^1)Ba]^{4+}$ (compare with, the range 2.736–2.875 Å for the Ba–O separations observed in the barium complex of [18]crown-6).[10]

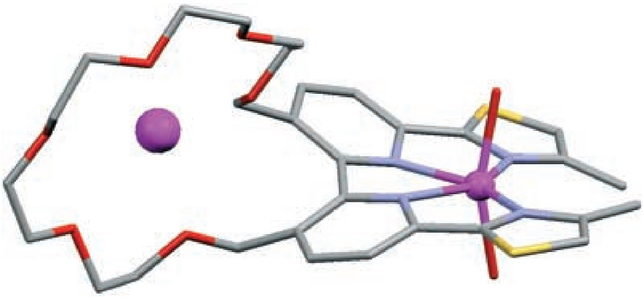

Figure 4. Crystal structure of the complex cation in $[Zn(L^1)Ba(H_2O)_2](ClO_4)_4{\cdot}MeCN{\cdot}0.5\,Et_2O{\cdot}0.75\,H_2O$.

As the ligand can partition into either tetradentate or bisbidentate binding domains, we decided to investigate its specificity towards different metal ions. The reaction of ligand L^1 with $[Cu(MeCN)_4]PF_6$ and $[Zn(CF_3SO_3)_2]$ (in the ratio 1:1:1) in CD_3CN gave an orange solution whose ^1H NMR spectrum showed six aromatic-proton environments that correspond to two different L^1-containing complexes. Comparison of the ^1H NMR spectrum of the mixed system with that of the individual $[Cu_2(L^1)_2]^{2+}$ and $[Zn(L^1)(H_2O)_2]^{2+}$ complexes showed that both these species were present in the ratio 1.5:1 (Figure 2b). This observation is also supported by the ESI mass spectrum, in which ions are present for both copper- and zinc-containing species. Upon the addition of $Ba(ClO_4)_2$, the color of the solution became paler and the ^1H NMR spectrum revealed new signals for the barium-containing species $[Cu_2(L^1)_2Ba_2]^{6+}$ and $[Zn(L^1)Ba]^{4+}$ in a 1:10 ratio, respectively (Figure 3b). Analysis by ESI MS showed that ions are present for the mononuclear zinc complex $\{[Zn(L^1)Ba](ClO_4)_3\}^+$, whereas ions that correspond to any copper-containing complexes were virtually nonexistent. Interestingly, the addition of excess $Sr(ClO_4)_2$ to a stoichiometric mixture of L^1, $[Cu(MeCN)_4]PF_6$, and $[Zn(CF_3SO_3)_2]$ resulted in virtually total conversion into the zinc-containing species ($[Cu_2(L^1)_2Sr_2]^{6+}/[Zn(L^1)Sr]^{4+}$, 1: > 20; Figure 3c).

Thus, upon addition of excess Zn^{2+} and Cu^+ ions, the ligand can act as either a tetradentate or bisbidentate donor unit to generate a mixture of the Cu^I helicate and Zn^{II} mononuclear species. However, upon addition of barium or strontium ions, the ligand is effectively reprogrammed to act as a tetradentate donor which is specific to Zn^{2+} ions.

As with similar systems,[5,6] such control over the ligand coordination domains may be attributed to one or two effects. Firstly, an electrostatic effect is plausible given that the copper helicate will form a 6+ ion $[Cu_2(L^1)_2M_2]^{6+}$ in the presence of excess Ba^{2+} or Sr^{2+} ions, whereas the zinc complex $[Zn(L^1)M]^{4+}$ carries an overall charge of only 4+. Thus, electrostatic destabilization of the highly charged helicate with respect to the mononuclear Zn^{2+} species results in the formation of the lesser charged species. However, the change in specificity could also be attributed to an allosteric effect, whereby coordination of a guest s-block ion to the crown ether unit is mechanically coupled to the bipyridine interannular bond in such a way as to impede the necessary partitioning required for helicate formation. Although the crystal structure of $[Cu_2(L^1)_2Ba_2(H_2O)](ClO_4)_6{\cdot}2\,MeCN{\cdot}0.5\,Et_2O$ clearly demonstrates that barium ions can coordinate to the crown ether region when the ligand is acting as a bisbidentate donor, careful comparison of the solid-state structures of the barium-containing helicate species $[Cu_2(L^1)_2Ba_2]^{6+}$ and monozinc(II) species $[Zn(L^1)Ba]^{4+}$ reveals that separations between the barium ions and the methylene oxygen atoms are marginally shorter for the latter (mean Ba–$O_{(methylene)}$ distances in $[Cu_2(L^1)_2Ba_2]^{6+}$: 2.895(2) Å; $[Zn(L^1)Ba]^{4+}$: 2.863(9) Å). Tentative extrapolation from these observations could imply that when acting as a tetradentate donor (compare with, bisbidentate), there is an effective contraction of the crown ether unit which serves to optimize the Ba^{2+}/etherate interactions. If sufficient, the difference in the binding energies between the barium/crown ether associations in the respective helicate and monomer (ligand) conformers could also account for the observed shift in equilibrium from the dicopper(I) helicate to the zinc(II) monomer. The apparent "mutual dependence" of effective crown ether size and remote binding events has been previously suggested for related ditopic systems[4] and is further supported by the observed increase in metal specificity when a smaller Sr^{2+} ion is employed (compare with, Ba^{2+} ions); therefore, the latter suggests that the Sr^{2+} ion is more sensitive to the difference in the effective size of the helicate and the monomer host cavities than the Ba^{2+} ion. Barium/strontium ion inclusion into the crown ether host of L^1, thus, appears to influence the conformational preferences of the nitrogen-donor domains, such that the preferred coordination mode is tetradentate in the presence of a guest ion.

Other s-block-metal ions also exert measurable effects: the addition of Li^+ and Na^+ ions result in the formation of equal amounts of copper and zinc complexes, whereas the zinc complex is again favored ($[Cu_2(L^1)_2K_2]^{6+}/[Zn(L^1)K]^{4+}$, 1:4) upon addition of K^+ ions. Comparison of the effects of the addition of Ba^{2+} versus K^+ ions shows that, although both significantly alter the equilibrium composition and favor the formation of the zinc-containing species, the change in monomer/helicate ratio is more apparent for Ba^{2+} ions. In view of the fact that both ions have similar ionic radii, the stronger influence of Ba^{2+} ions must reflect the difference in ionic charge, thus highlighting the importance of both electrostatic and allosteric factors in the modification of ligand specificity.

In conclusion, we have shown that a ditopic system can change its preference for different transition-metal ions upon addition of a range of s-block-metal ions at a remote site.

Received: July 22, 2005

Keywords: allosterism · copper · helicates · metal specificity · zinc

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[7] Single-crystal X-ray diffraction data were collected on a Bruker APEX-CCD area detector diffractometer under a stream of cold nitrogen. Crystal data for $[Cu_2(L^1)_2Ba_2(H_2O)](ClO_4)_6\cdot 2\,MeCN\cdot 0.5\,Et_2O$: $M_r = 2361.14$, triclinic, $P\bar{1}$, $a = 13.54(5)$, $b = 18.91(7)$, $c = 21.35(8)$ Å, $\alpha = 65.91(7)$, $\beta = 72.42(7)$, $\gamma = 85.18(7)°$, $V = 4754(31)$ Å^3, $Z = 2$, $\rho_c = 1.650$ Mg m^{-3}, $F(000) = 2374$, $\mu(Mo_{K\alpha}) = 1.602$ mm^{-1}, $T = 100$ K. A total of 54400 reflections were measured in the range $1.09 \leq \theta \leq 27.54°$ (*hkl* range indices $-17 \leq h \leq 17$, $-24 \leq k \leq 24$, $-27 \leq l \leq 27$), 21383 independent reflections ($R_{int} = 0.0386$). The structure was refined on F^2 to $R_w = 0.1603$ $R = 0.0582$ (16371 reflections with $I > 2\sigma(I)$) and GOF = 0.785 on F^2 for 1121 refined parameters, largest difference peak and hole 2.087 and −2.552 e Å^{-3}. As with many supramolecular crystal structures, all of those described herein contain regions of disorder associated with diffuse-lattice solvent species (acetonitrile/non-coordinating perchlorate counterions) and the conformationally flexible crown ether fragments. Accordingly, geometric restraints and/or constraints were employed (in several cases throughout all stages of refinement) in attempt to model disorder where appropriate. Where such attempts failed to account for persistent peaks in the electron density map, a diffuse solvent correction was applied by using the SQUEEZE routine in PLATON. A full description of the refinement details is given in the Supporting Information.

[8] Single-crystal X-ray diffraction data were collected on a Bruker SMART-CCD area detector diffractometer under a stream of cold nitrogen. Crystal data for $[Zn(L^1)(H_2O)_2Ba](ClO_4)_4\cdot MeCN\cdot 0.5\,Et_2O\cdot 0.75\,H_2O$; $M_r = 1340.66$, monoclinic, $P2_1/c$, $a = 18.431(1)$, $b = 17.981(1)$, $c = 17.614(1)$ Å, $\beta = 101.4330(10)°$, $V = 5721.5(6)$ Å^3, $Z = 4$, $\rho_c = 1.56$ Mg m^{-3}, $F(000) = 2705$, $\mu(Mo_{K\alpha}) = 1.442$ mm^{-1}, $T = 173$ K. A total of 59644 reflections were measured in the range $1.13 \leq \theta \leq 27.54°$ (*hkl* range indices $-23 \leq h \leq 23$, $-23 \leq k \leq 23$, $-22 \leq l \leq 22$), 13134 independent reflections ($R_{int} = 0.0858$). The structure was refined on F^2 to $R_w = 0.1888$ $R = 0.0702$ (7506 reflections with $I > 2\sigma(I)$) and GOF = 1.007 on F^2 for 667 refined parameters, largest difference peak and hole 1.347 and −1.045 e Å^{-3}. CCDC-278717 and -278718 contain the supplementary crystallographic data for this paper. These data can be obtained free of charge from the Cambridge Crystallographic Data Center via www.ccdc.cam.ac.uk/data_request/cif.

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