

Selective Retention of Methanol over Ethanol by a Cyclen-Based Cryptand/Copper(II) Complex

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Supporting Information

ABSTRACT: A cyclen-based cryptand (**2**) was prepared in a two-step synthesis from dioxocyclen. When a $\text{Cu}(\text{CF}_3\text{SO}_3)_2$ complex with **2** was prepared in methanol, the $2/\text{Cu}(\text{CF}_3\text{SO}_3)_2$ complex incorporated one methanol in the cavity formed by the diethyleneoxy unit and the NH group of the cyclen. When prepared in ethanol, the $2/\text{Cu}(\text{CF}_3\text{SO}_3)_2$ complex similarly incorporated one ethanol. Cold electrospray ionization mass spectrometry (ESI-MS) of the $2/\text{Cu}(\text{CF}_3\text{SO}_3)_2/\text{alcohol}$ complexes selectively retains methanol over ethanol under ESI-MS conditions.

Cyclic polyamines, such as cyclam (14-membered cyclic polyamine) and cyclen (12-membered cyclic polyamine), can potentially bind heavy-metal ions and exhibit host–guest interactions.¹ Other research groups have added to these basic cyclic polyamines and have reported the syntheses of bicyclic,^{2a–e} tricyclic,^{2f,g} and tetracyclic^{2f} compounds derived from cyclam and cyclen. During our efforts to functionalize cyclen, we found that quadruple- and double-armed cyclens with aromatic side arms behave like insectivorous plants (e.g., Venus flytrap) when forming complexes with Ag^+ ions.³ We called these quadruple- and double-armed cyclens “argentivorous molecules”. To extend this research, we have prepared a cyclen-based cryptand (**2**) that incorporates a bridging diethyleneoxy unit between two aromatic side arms at the 1 and 7 positions of the cyclen ring (Figure 1).

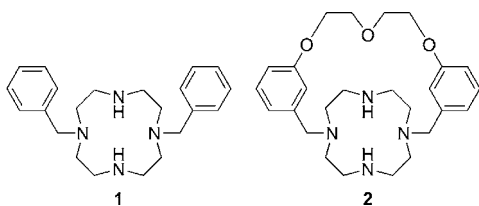


Figure 1. Double-armed cyclen (**1**) and cyclen-based cryptand (**2**).

The new cryptand has two binding moieties, a cyclen and a diethyleneoxy unit. We expected that the conformation of the diethyleneoxy unit would allow inclusion of a neutral guest, such as an alcohol, when the cyclen moiety has formed a complex with a metal ion. Here, we report the first example of a complex employing the cyclen-based cryptand, which selectively retains methanol over ethanol.

The new cryptand **2** was prepared in a two-step synthesis from dioxocyclen (**7**; see the Supporting Information, SI). The bicyclic precursor **3** was prepared by the reaction of 1,1'-[oxybis(ethane-

2,1-diyloxy)]bis[3-(chloromethyl)benzene] (**6**) with 1,4,7,10-tetraazacyclododecane-2,6-dione (**7**). **3** was finally reduced with DIBAL-H to give **2**. The structures of **2** and **3** were confirmed by ¹H and ¹³C NMR, fast atom bombardment mass spectrometry, elemental analysis, and X-ray crystallography. As shown in Figure 2, the diethyleneoxy unit of **2** adopts a twisted conformation.

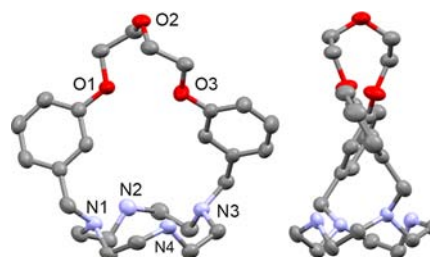


Figure 2. Ellipsoid plot of **2**. Hydrogen atoms and the solvent acetonitrile have been omitted for clarity.

We prepared the $2/\text{Cu}(\text{CF}_3\text{SO}_3)_2$ complex using methanol and ethanol as solvents. Structures of a methanol-containing $\text{Cu}(\text{CF}_3\text{SO}_3)_2$ complex [$2/\text{Cu}(\text{CF}_3\text{SO}_3)_2/\text{MeOH}$] and an ethanol-containing $\text{Cu}(\text{CF}_3\text{SO}_3)_2$ complex [$2/\text{Cu}(\text{CF}_3\text{SO}_3)_2/\text{EtOH}$] were confirmed by elemental analysis and X-ray crystallography. Elemental analysis revealed that one molecule of methanol or ethanol was contained in each complex. Figures 3

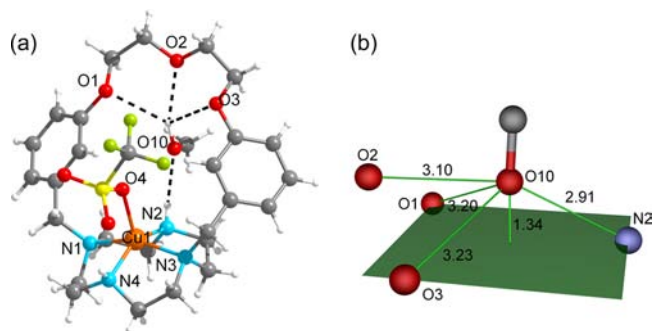


Figure 3. Ball and stick plot (a) and skeletal drawing (b) of the $2/\text{Cu}(\text{CF}_3\text{SO}_3)_2/\text{MeOH}$ complex. Hydrogen atoms and the non-coordinating CF_3SO_3^- anion have been omitted from the ball and stick plot for clarity. Figure S7 in the SI shows an ORTEP diagram with the hydrogen atoms of $2/\text{Cu}(\text{CF}_3\text{SO}_3)_2/\text{MeOH}$.

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and S7 in the SI show the structure of $2/\text{Cu}(\text{CF}_3\text{SO}_3)_2/\text{MeOH}$. In this complex, Cu1 is five-coordinated by the four nitrogen atoms of the cyclen and one oxygen atom of the CF_3SO_3 anion. The Cu1–N1, Cu1–N2, Cu1–N3, and Cu1–N4 bonds are 1.9879(16)–2.0713(16) Å, and the Cu1–O4 bond is 2.2121(13) Å. The Cu1–N (N1, N2, N3, and N4) distances are comparable with those of the copper(II) complex with a double-armed cyclen previously reported.^{3b} The diethyleneoxy unit of the complex is not disordered, and the oxygen atom (O10) of the methanol forms hydrogen bonds with the three oxygen atoms (O1, O2, and O3) of the diethyleneoxy unit and with one nitrogen atom (N2) of the cyclen. As shown in Figure 3b, the O10(methanol)–O1, O10–O2, and O10–O3 distances are in the range 3.10–3.23 Å, and the O10–N2 distance is 2.91 Å. These O–O and O–N distances are comparable with the O–O and O–N hydrogen-bond distances in complexes of 18-crown-6^{4a–d} and diaza-18-crown-6^{4e–g} derivatives. The methanol oxygen O10 is above the mean plane of the bonding atoms (green square, O1, O3, and N2) at a distance of 1.34 Å.

When ethanol was used as a solvent to prepare the $\text{Cu}(\text{CF}_3\text{SO}_3)_2$ complex, an ethanol-containing $\text{Cu}(\text{CF}_3\text{SO}_3)_2$ complex [$2/\text{Cu}(\text{CF}_3\text{SO}_3)_2/\text{EtOH}$] was obtained. As shown in Figures 4a and S7 in the SI, Cu1 is again five-coordinate, with

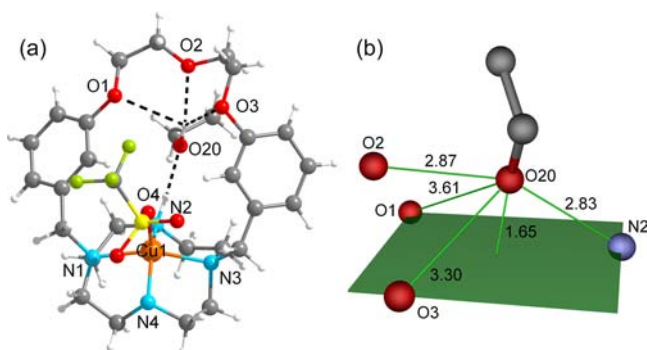


Figure 4. Ball and stick plot (a) and skeletal drawing (b) of $2/\text{Cu}(\text{CF}_3\text{SO}_3)_2/\text{EtOH}$. Hydrogen atoms and one CF_3SO_3 anion have been omitted in the ball and stick plot for clarity. Figure S7 in the SI shows an ORTEP diagram with the hydrogen atoms of $2/\text{Cu}(\text{CF}_3\text{SO}_3)_2/\text{EtOH}$.

four nitrogen atoms of the cyclen and one oxygen atom of the CF_3SO_3 anion. The Cu1–N (N1, N2, N3, and N4) distances are similar to those of $2/\text{Cu}(\text{CF}_3\text{SO}_3)_2/\text{MeOH}$ and are in the range 1.988(6)–2.079(6) Å, and the Cu1–O4 distance is 2.195(5) Å. Interestingly, the ethanol molecule is encapsulated in the cavity formed by the three oxygen atoms (O1, O2, and O3) of the diethyleneoxy unit and the nitrogen atom (N2) of the cyclen. The distance (1.65 Å) between the O20(ethanol) and the mean plane of the ligand (O1, O3, and N2) is longer than that in $2/\text{Cu}(\text{CF}_3\text{SO}_3)_2/\text{MeOH}$. In addition, some disorder is observed in the ethanol molecule [see the CIF file of $2/\text{Cu}(\text{CF}_3\text{SO}_3)_2/\text{EtOH}$ in the SI]. These results indicate that the interaction between ethanol and the $2/\text{Cu}(\text{CF}_3\text{SO}_3)_2$ complex is weaker than that between methanol and the $2/\text{Cu}(\text{CF}_3\text{SO}_3)_2$ complex. The $2/\text{Cu}(\text{CF}_3\text{SO}_3)_2$ complex therefore distinguishes the methyl and ethyl groups by the difference in steric bulk. Lippard and co-workers have reported that a dicopper(II) complex with a dinucleating hexaimidazole ligand includes one MeOH molecule.^{4h} The example differs from $2/\text{Cu}(\text{CF}_3\text{SO}_3)_2/\text{MeOH}$ because the MeOH molecule is bound by hydrogen bonding in our case.

To see if the copper(II) complex with **2** can retain methanol and ethanol, CSI-MS of a mixture of **2** and $\text{Cu}(\text{CF}_3\text{SO}_3)_2$ was measured in methanol or ethanol at 298 K. Figure 5 (top) shows

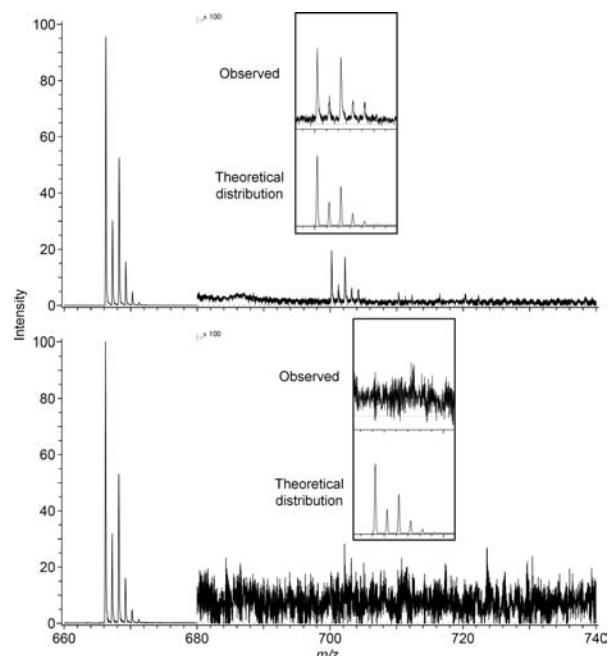


Figure 5. CSI-MS (298 K) of a mixture of **2** and $\text{Cu}(\text{CF}_3\text{SO}_3)_2$ in methanol (top) and ethanol (bottom). [**2**] = $[\text{Cu}(\text{CF}_3\text{SO}_3)_2]$ = 100 $\mu\text{mol/L}$.

CSI-MS of a mixture of **2** and $\text{Cu}(\text{CF}_3\text{SO}_3)_2$ in methanol. The fragment ion peak arising for $[\mathbf{2} + \text{Cu}^{2+} + \text{CF}_3\text{SO}_3^-]^+$ was observed at m/z 666, and the peak for $[\mathbf{2} + \text{Cu}^{2+} + \text{CF}_3\text{SO}_3^- + \text{MeOH} + 2]^+$ was observed at m/z 700.⁵ The fragment ion peak patterns agree with theoretical distributions. On the other hand, no fragment ion peak for $[\mathbf{2} + \text{Cu}^{2+} + \text{CF}_3\text{SO}_3^- + \text{EtOH} + 2]^+$ (m/z 714) was observed in the corresponding ethanol solution (Figure 5 bottom). These results suggest that the $2/\text{Cu}(\text{CF}_3\text{SO}_3)_2/\text{alcohol}$ complex is more stable with methanol than ethanol under CSI-MS conditions at 298 K.

Thermogravimetric differential thermal analysis (TG-DTA) of the $2/\text{Cu}(\text{CF}_3\text{SO}_3)_2$ complexes containing methanol or ethanol were carried out in order to compare the binding of methanol and ethanol to the $2/\text{Cu}(\text{CF}_3\text{SO}_3)_2$ complex. As shown in Figures S7 and S8 in the SI, the weight losses at 180 °C in $2/\text{Cu}(\text{CF}_3\text{SO}_3)_2/\text{MeOH}$ and $2/\text{Cu}(\text{CF}_3\text{SO}_3)_2/\text{EtOH}$ are 3.88 and 5.56%, respectively. These weight losses correspond to one molecule of methanol (calcd 3.78%) and ethanol (calcd 5.34%). The weight loss at 120 °C, however, is ca. 0.5% in $2/\text{Cu}(\text{CF}_3\text{SO}_3)_2/\text{EtOH}$, while in $2/\text{Cu}(\text{CF}_3\text{SO}_3)_2/\text{MeOH}$, it is less than 0.1%. These results suggest that $2/\text{Cu}(\text{CF}_3\text{SO}_3)_2/\text{EtOH}$ loses alcohol molecules at a lower temperature than $2/\text{Cu}(\text{CF}_3\text{SO}_3)_2/\text{MeOH}$. The TG-DTA measurements therefore indicate that $2/\text{Cu}(\text{CF}_3\text{SO}_3)_2$ retains more strongly to methanol than ethanol.

In order to estimate the binding energies of the $2/\text{Cu}^{\text{II}}/\text{MeOH}$ and $2/\text{Cu}^{\text{II}}/\text{EtOH}$ complexes, the single-point-energy calculations for the X-ray structures were conducted using density functional theory (DFT; B3LYP/6-31G* and EDF2/6-31G*) methods with dual basis sets.⁶ As shown in Table 1, the binding energies ΔE_{MeOH} and ΔE_{EtOH} ($=E_{2/\text{Cu}^{\text{II}}/\text{ROH}} - E_{2/\text{Cu}^{\text{II}}} - E_{\text{ROH}}$) for the $2/\text{Cu}^{\text{II}}/\text{MeOH}$ and $2/\text{Cu}^{\text{II}}/\text{EtOH}$ complexes are ca. –22 and

Table 1. Binding Energies ($\Delta E_{\text{ROH}} = E_{2/\text{Cu}^{\text{II}}/\text{ROH}} - E_{2/\text{Cu}^{\text{II}}} - E_{\text{ROH}}$) and Binding Energy Differences ($\Delta\Delta E = \Delta E_{\text{MeOH}} - \Delta E_{\text{EtOH}}$) between 2/Cu^{II}/MeOH and 2/Cu^{II}/EtOH

compd	ΔE_{ROH} (kcal/mol)	
B3LYP/6-31G*	2/Cu ^{II} /MeOH	-21.69 (ΔE_{MeOH})
	2/Cu ^{II} /EtOH	-18.68 (ΔE_{EtOH})
	$\Delta\Delta E (= \Delta E_{\text{MeOH}} - \Delta E_{\text{EtOH}})$	-3.01
EDF2/6-31G*	2/Cu ^{II} /MeOH	-23.06 (ΔE_{MeOH})
	2/Cu ^{II} /EtOH	-17.61 (ΔE_{EtOH})
	$\Delta\Delta E (= \Delta E_{\text{MeOH}} - \Delta E_{\text{EtOH}})$	-5.45

-18 kcal/mol, respectively. These energies are greater than those in methanol/azacryptand systems (-9.94 to -12.78 kcal/mol) reported by Hossain et al.⁷ This is due to the four hydrogen bonds between the alcohols and the three oxygen atoms and one nitrogen atom in the diethyleneoxy unit and cyclen in the current system. In addition, the binding energy differences ($\Delta\Delta E = \Delta E_{\text{MeOH}} - \Delta E_{\text{EtOH}}$) are -3.0 (B3LYP/6-31G*) to -5.5 (EDF2/6-31G*) kcal/mol. These energy differences indicate that the stability of the methanol complex is greater than the ethanol complex by a factor of 5–10 (estimated from $\Delta G = -RT \ln K$, where $T = 298 \text{ K}$).

In conclusion, we have demonstrated that the $\text{Cu}(\text{CF}_3\text{SO}_3)_2$ complex with the cyclen-based cryptand, **2**, retains methanol but not ethanol in the CSI-MS conditions. This is the first instance for the preference between alcohols by a metal complex including a cryptand.

■ ASSOCIATED CONTENT

■ Supporting Information

Synthesis and spectral data of compounds **2**–**6**, X-ray structures of **2** and **3**, crystal data for 2/Cu(CF₃SO₃)₂/MeOH and 2/Cu(CF₃SO₃)₂/EtOH, crystallographic data of 2/Cu(CF₃SO₃)₂/MeOH and 2/Cu(CF₃SO₃)₂/EtOH in CIF format, TG-DTA analysis of 2/Cu(CF₃SO₃)₂/MeOH and 2/Cu(CF₃SO₃)₂/EtOH, and DFT calculations on 2/Cu^{II}/MeOH and 2/Cu^{II}/EtOH complexes. This material is available free of charge via the Internet at <http://pubs.acs.org>.

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Notes

The authors declare no competing financial interest.

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