

Communications to the Editor

**Organization of Chiral Pyridine-Containing
Bisbipyridino Podands by Cu(I) and Their
Enantiomeric Recognition of (*R*)- and
(*S*)- α -Phenylethylammonium Perchlorates**

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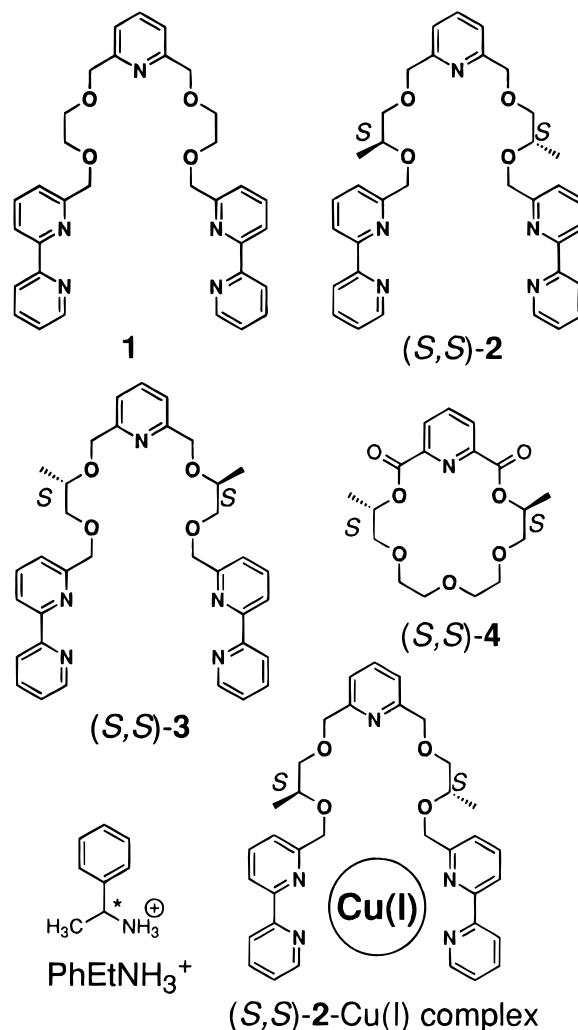
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Attention has been focused on the organization of host molecules by complexation with metal ions. Kobuke et al. reported that podands having catechol and β -diketone units were organized by boron or Cu(II) to give a host molecule which exhibited high extractability of metal ions and high metal ion selectivity.¹ Nabeshima et al. reported that podands having bipyridyl units were organized by Cu(I) to give K⁺ selectivity in liquid membrane transport.² In this case, K⁺ transport was considerably less than that by the ligands containing no Cu(I). To the best of our knowledge, no metal ion-organized host molecule which exhibits enantiomeric recognition of optically active guests such as chiral organic ammonium ions has been reported. When a crown ether ligand binds a primary alkylammonium ion, a *three-point binding site* in the ligand is needed to facilitate the formation of a stable complex.³ Thus, one would expect drastic changes in the interactive ability toward ammonium ions for a host molecule before and after metal organization of the host. It is possible for such host molecules to achieve enantiomeric recognition of chiral guest molecules by the introduction of chiral barriers to the binding site. Herein, we report the first example of recognition for the enantiomers of chiral α -phenylethylammonium (PhEtNH₃⁺) perchlorate by Cu(I)-organized chiral pyridine-containing bisbipyridino podands.

Podands **1** and (*S,S*)-**2** (Chart 1) were prepared by the reaction of 6-bromomethyl-2,2'-bipyridyl and the appropriate pyridine-containing diols. Podand (*S,S*)-**3** was obtained by the reaction of 2,6-pyridinedimethanol ditosylate with (*S*)-(+)-6-(2''-oxa-4''-hydroxypentyl)-2,2'-bipyridyl. The structures of the podands were confirmed by ¹H NMR, high-resolution MS, and elemental analyses.⁴ To see if the podands form complexes with Cu(I) using the two bipyridyl portions of the molecule,⁵ high-resolution MS and ¹H NMR spectra of a 1:1 mixture of (*S,S*)-**2** and CuCl were measured. As shown in Figure 1, parent ion peaks arising from [(*S,S*)-**2**+⁶³Cu]⁺ and [(*S,S*)-**2**+⁶⁵Cu]⁺ in the high-resolution MS were observed at *m/z* 654 (100%) and 656 (57%), respectively.⁶ On the other hand, a parent ion peak arising from [(*S,S*)-**2**+H]⁺ appeared at *m/z* 592 in only a 10% intensity. In the ¹H NMR spectrum of the (*S,S*)-**2**-Cu(I) mixture in CDCl₃, signals for protons at positions 4, 5, 4', and 5' on the bipyridyl units appeared at a lower field by 0.15, 0.07, 0.15, and 0.12 ppm, respectively, than those of (*S,S*)-**2**, while the

Chart 1



proton signals for methylene, methyl, and pyridine ring protons shifted to higher fields (-0.01 to -0.15 ppm).⁷ Therefore, the MS and ¹H NMR experiments show that (*S,S*)-**2** forms a complex with Cu(I) through coordination with the bipyridyl moieties.

(4) Compound **1**: pale yellow oil; ¹H NMR (δ ppm, CDCl₃) 8.68 (d, *J* = 4.4 Hz, 2H), 8.39 (d, *J* = 7.8 Hz, 2H), 8.27 (d, *J* = 7.8 Hz, 2H), 7.82 (t, *J* = 7.7 Hz, 2H), 7.79 (t, *J* = 7.7 Hz, 2H), 7.69 (t, *J* = 7.6 Hz, 1H), 7.52 (d, *J* = 7.8 Hz, 2H), 7.41 (d, *J* = 7.8 Hz, 2H), 7.31 (d, *J* = 7.6 Hz, 2H), 4.80 (s, 4H), 4.71 (s, 4H), 3.80 (s, 8H); HRMS (thioglycerol as matrix) calcd for C₃₃H₃₄N₅O₄ 564.2611; found 564.2628 (100%, [M + H]⁺). Anal. Calcd for C₃₃H₃₃N₅O₄: C, 70.32; H, 5.90. Found: C, 70.38; H, 5.85. Compound **2**: pale yellow oil; ¹H NMR (δ ppm, CDCl₃) 8.68 (d, *J* = 4.2 Hz, 2H), 8.38 (d, *J* = 7.8 Hz, 2H), 8.25 (d, *J* = 8.0 Hz, 2H), 7.80 (t, *J* = 7.7 Hz, 4H), 7.66 (t, *J* = 7.6 Hz, 1H), 7.56 (d, *J* = 7.8 Hz, 2H), 7.38 (d, *J* = 7.8 Hz, 2H), 7.31 (d, *J* = 7.6 Hz, 2H), 4.80 (s, 4H), 4.68 (s, 4H), 3.91 (hex, *J* = 5.6 Hz, 2H), 3.74–3.60 (m, 4H), 1.29 (d, *J* = 6.2 Hz, 6H); HRMS (thioglycerol as matrix): calcd for C₃₅H₃₈N₅O₄ 592.2924, found 592.2927 (100%, [M + H]⁺); [α]_D²⁵ = +18.9° (*c* = 5.07, CHCl₃). Anal. Calcd for C₃₅H₃₇N₅O₄: C, 71.05; H, 6.30. Found: C, 71.03; H, 6.26. Compound **3**: pale yellow oil; ¹H NMR (δ ppm, CDCl₃) 8.68 (d, *J* = 3.8 Hz, 2H), 8.39 (d, *J* = 8.0 Hz, 2H), 8.27 (d, *J* = 7.8 Hz, 2H), 7.82 (t, *J* = 7.7 Hz, 2H), 7.80 (hexat, *J*_{ortho} = 7.7 Hz, *J*_{meta} = 1.8 Hz, 2H), 7.66 (t, *J* = 7.6 Hz, 1H), 7.51 (d, *J* = 7.8 Hz, 2H), 7.44 (d, *J* = 7.8 Hz, 2H), 7.32 (d, *J* = 7.6 Hz, 2H), 4.78 (s, 4H), 4.77 (s, 4H), 3.89 (hex, *J* = 5.6 Hz, 2H), 3.76–3.59 (m, 4H), 1.29 (d, *J* = 6.2 Hz, 6H); HRMS (thioglycerol as matrix) calcd for C₃₅H₃₈N₅O₄ 592.2924; found 592.2921 (100%, [M + H]⁺); [α]_D²⁵ = -8.76° (*c* = 5.08, CHCl₃). Anal. Calcd for C₃₅H₃₇N₅O₄: C, 71.05; H, 6.30. Found: C, 71.24; H, 5.74.

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 (1) (a) Kobuke, Y.; Sumida, Y.; Hayashi, M.; Ogoshi, H. *Angew. Chem., Int. Ed. Engl.* **1991**, *30*, 1496. (b) Kobuke, Y.; Satoh, Y. *J. Am. Chem. Soc.* **1992**, *114*, 789. (c) Kobuke, Y.; Kokubo, K.; Munakata, M. *J. Am. Chem. Soc.* **1995**, *117*, 12751.

 (2) (a) Nabeshima, T.; Inaba, T.; Furukawa, N. *Tetrahedron Lett.* **1987**, *28*, 6211. (b) Nabeshima, T.; Inaba, T.; Furukawa, N.; Hosoya, T.; Yano, Y. *Inorg. Chem.* **1993**, *32*, 1407.

 (3) (a) Davidson, R. B.; Bradshaw, J. S.; Jones, B. A.; Dalley, N. K.; Christensen, J. J.; Izatt, R. M.; Morin, F. G.; Grant, D. M. *J. Org. Chem.* **1984**, *49*, 353. (b) Izatt, R. M.; Zhu, C. Y.; Dalley, N. K.; Curtis, J. C.; Kou, K. L.; Bradshaw, J. S. *J. Phys. Org. Chem.* **1992**, *5*, 656.

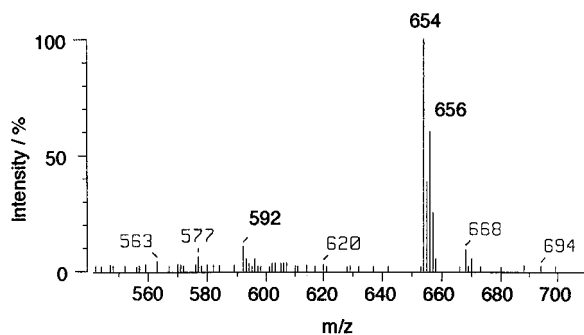


Figure 1. High-resolution mass spectra of the (*S,S*)-2-Cu(I) complex.

Enantiomeric recognition toward PhEtNH₃⁺ by podands **1**, (*S,S*)-**2**, and (*S,S*)-**3**, and their Cu(I) complexes in MeOH has been evaluated using a calorimetric titration procedure (Table 1).⁸ When the podands without Cu(I) were used, no interactions with PhEtNH₃⁺ were observed ($\Delta H \approx 0$). On the other hand, the 1:1 podand–Cu(I) complexes exhibited strong interactions with PhEtNH₃⁺ in MeOH ($\log K = 3.08–3.64$). These $\log K$ values are higher than those for the interaction of PhEtNH₃⁺ with some chiral pyridino-18-crown-6 ligands.⁹ The calorimetric and spectroscopic results provide strong evidence for organization of the podands with assistance from Cu(I) to form adequate structures for the typical three-point binding needed by primary alkylammonium ions.^{3,9} The Cu(I)-organized chiral complexes, (*S,S*)-2-Cu(I) and (*S,S*)-3-Cu(I), favor the (*S*)-PhEtNH₃⁺ and (*R*)-PhEtNH₃⁺ salts, respectively, while achiral complex, **1**-Cu(I), does not exhibit enantiomeric recognition. The enantiomeric recognition shown by (*S,S*)-2-Cu(I) and (*S,S*)-

(5) Diamagnetic Cu(I) was used since it forms a four-coordinate complex with nitrogen ligands and little or no change is observed in the ¹H NMR spectra of Cu(I) complexes.

(6) HRMS for the (*S,S*)-2-CuCl complex: calcd for C₃₅H₃₇N₅O₄⁶³Cu 654.2137, found 654.2137 (100%, [(*S,S*)-2+⁶³Cu]⁺); calcd for C₃₅H₃₇N₅O₄⁶⁵Cu 656.2123, found 656.2143 (57%, [(*S,S*)-2+⁶⁵Cu]⁺).

(7) Nabeshima et al. reported that proton signals at positions 3, 3', 5, and 5' on the bipyridyl units in their bipyridyl podand–Cu(I) complex shifted to lower field by 0.02, 0.06, 0.34, and 0.29 ppm, respectively.²

(8) Izatt, R. M.; Wu, G. *Thermochim. Acta* **1989**, *154*, 161.

(9) (a) Izatt, R. M.; Wang, T.; Hathaway, J. K.; Zhang, X. X.; Curtis, J. C.; Bradshaw, J. S.; Zhu, C. Y. *J. Inclusion Phenom.* **1994**, *17*, 157. (b) Huszthy, P.; Bradshaw, J. S.; Zhu, C. Y.; Izatt, R. M.; Lifson, S. *J. Org. Chem.* **1991**, *56*, 3330.

Table 1. $\log K$, ΔH (kJ/mol), and $T\Delta S$ (kJ/mol) Values Determined by Calorimetric Titration for Interactions of **1**, (*S,S*)-**2**, (*S,S*)-**3**, and Their Cu(I) Complexes with (*R*)- and (*S*)- α -Phenylethylammonium (PhEtNH₃⁺) Perchlorate in MeOH at 25 °C

ligand	cation	$\log K$	ΔH	$T\Delta S$	$\Delta \log K$
1	(<i>S</i>)-PhEtNH ₃ ⁺		($\Delta H \sim 0$)		
	(<i>R</i>)-PhEtNH ₃ ⁺		($\Delta H \sim 0$)		
(<i>S,S</i>)- 2	(<i>S</i>)-PhEtNH ₃ ⁺		($\Delta H \sim 0$)		
	(<i>R</i>)-PhEtNH ₃ ⁺		($\Delta H \sim 0$)		
(<i>S,S</i>)- 3	(<i>S</i>)-PhEtNH ₃ ⁺		($\Delta H \sim 0$)		
	(<i>R</i>)-PhEtNH ₃ ⁺		($\Delta H \sim 0$)		
1 -Cu(I)	(<i>S</i>)-PhEtNH ₃ ⁺	3.53 ± 0.06	6.6 ± 0.7	27	
	(<i>R</i>)-PhEtNH ₃ ⁺	3.56 ± 0.06	7.1 ± 0.8	27	~0
(<i>S,S</i>)- 2 -Cu(I)	(<i>S</i>)-PhEtNH ₃ ⁺	3.64 ± 0.04	7.9 ± 0.7	29	
	(<i>R</i>)-PhEtNH ₃ ⁺	3.38 ± 0.05	6.8 ± 0.8	26	0.26
(<i>S,S</i>)- 3 -Cu(I)	(<i>S</i>)-PhEtNH ₃ ⁺	3.08 ± 0.04	4.8 ± 0.7	22	
	(<i>R</i>)-PhEtNH ₃ ⁺	3.25 ± 0.04	4.3 ± 0.8	23	0.17
(<i>S,S</i>)- 4 ^a	(<i>S</i>)-PhEtNH ₃ ⁺	2.11			
	(<i>R</i>)-PhEtNH ₃ ⁺	2.33			0.22

^a Reference 9.

3-Cu(I) is similar to that of (*S,S*)-dimethyl-substituted pyridino-18-crown-6, (*S,S*)-**4**.⁹ The $\Delta \log K$ values for the interactions of (*S,S*)-2-Cu(I) (0.26) and (*S,S*)-3-Cu(I) (0.17) with (*R*)- and (*S*)-PhEtNH₃⁺ are comparable to that of (*S,S*)-**4** (0.22).⁹ These results show that the binding sites in these Cu(I)-organized chiral podands are also good enantiomeric recognition sites for the chiral ammonium ions.

We have demonstrated that the chiral pyridine-containing bisbipyridino podands are organized by Cu(I) to give good enantiomeric recognition sites for chiral ammonium ions. Without the Cu(I) present, the podands do not interact with primary alkylammonium ions. This remarkable change in complexing ability and the observed enantiomeric recognition toward chiral ammonium ions demonstrate that this type of metal ion-organized system has potential for the design of new chiral supramolecular systems. Further studies of the new chiral podands are in progress.

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