# Solution and solid-state characterization of a dicopper receptor for large substrates

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**Abstract**: Ligand **2** contains two metal-binding domains separated by a rigid spacer and assembles into a dicopper receptor with a large central cavity with no evidence of catenation.

*Key words*: copper complex, coordination, X-ray crystallography, molecular recognition.

**Résumé** : Le ligand **2** contient deux groupement pour coordonner des métaux séparer par un espaceur rigide et s'auto-assemble avec le cuivre(II) pour former un récepteur avec un grand cavité centrale avec aucune evidence pour la formation de caténane.

*Mots clés* : complex de cuivre, coordination, crystallographie rayons-X, reconnaissance moléculaire.

## Introduction

The metal-directed self-assembly of discrete supramolecular structures, e.g., triangles (1), squares (2), and grids (3), has attracted considerable interest in recent years. When properly designed, discrete supramolecular structures may serve as metalloreceptors for small organic and bio-organic molecules (4). A key advantage of metallomacrocycles over similarly sized organic receptors is the higher yields associated with metal-directed self-assembly compared with conventional macrocycle synthesis (5). One drawback, however, is that dimetallic receptors have a tendency to form interlocking rings depending on their concentration and the size of the receptor site (6). Although templation of the metalloreceptor around a guest molecule(s) may eliminate catenation, it may in turn diminish or eliminate further guest binding by occupying the receptor site.

Since metalloreceptors capable of binding functionalized substrate can perform catalysis and behave as artificial enzymes (7), receptors for larger substrate would increase the diversity of possible substrate and, therefore, products obtained. Early work with dimetallic receptors proved the importance of metal-directed self-assembly; however, it focused on systems with small receptor sites (8). Thus the binding of substrates larger than a single heterocycle was precluded, and the formation of catenanes was impossible. Although reports of dimetallic receptors with large cavities have recently appeared in the literature, no confirmation of host–guest binding in the solid state was presented (9). Herein we present solution and solid-state evidence for the assembly of a dimetallic receptor with a large cavity that displays no evidence of catenation, yet requires no template for its formation.

## Results and discussion

The organic framework for our dimetallic receptor is based on *m*-terphenyl, synthesized by the uncatalyzed reaction of aryllithium or arylmagnesium reagents with *m*-dichlorobenzene (the Hart reaction) (10). The Hart reaction allows facile entry into large substructures suitable for further functionalization, since R groups may be readily incorporated in the ligand framework (Scheme 1). Thus, 4,4′-bis(bromomethyl)-1,1′:3′,1″-terphenyl (**1**) was synthesized from 4,4′-dimethyl-1,1′:3′,1″ -terphenyl by radical bromination with NBS in 67% yield (11). Allowing **1** to react with two equivalents of potassium acetylacetonate in *tert*-butanol afforded ligand **2** in 91% yield after extraction with methanol (Scheme 1).[2] In solution, ligand **2** exists in its keto and enol forms. Integration of the two methyl peaks at 2.12 and 2.17 ppm supports an approximate 1:1 of the two forms. A singlet and doublet for H-3 and H-3′, respectively, and a triplet for H-2, also supports this assignment. In the IR region, both O–H and C–O stretches confirm the keto–enol formulation.

The dicopper receptor is readily synthesized in near quantitative yield from **2** and $Cu(NH_3)_4SO_4$ in a biphasic $H_2O$–$CHCl_3$ reaction mixture (8).[3] Upon layering **2** in chlo-

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[2]Selected data for **2**: $^1$H NMR ($CDCl_3$) δ: 2.12 (s, 3H, H-1, keto), 2.17 (s, 3H, H-1, enol), 3.21 (d, 2H, H-3, keto), 3.72 (s, 2H, H-3, enol), 4.03 (t, 1H, H-4, keto), 7.23–7.75 (m, 12H, H-4,) 16.8 (s, 1H, H-7, -OH enol). FAB-MS *m*/*z*: 455.0 $[M + H]^+$.
[3]Selected data for **3**: ESI-MS *m*/*z*: 1055.46 $[M + Na]^+$ Anal. calcd. for **3**·0.5$CHCl_3$: C 66.31, H 5.56; found: C 66.60, H 5.48.

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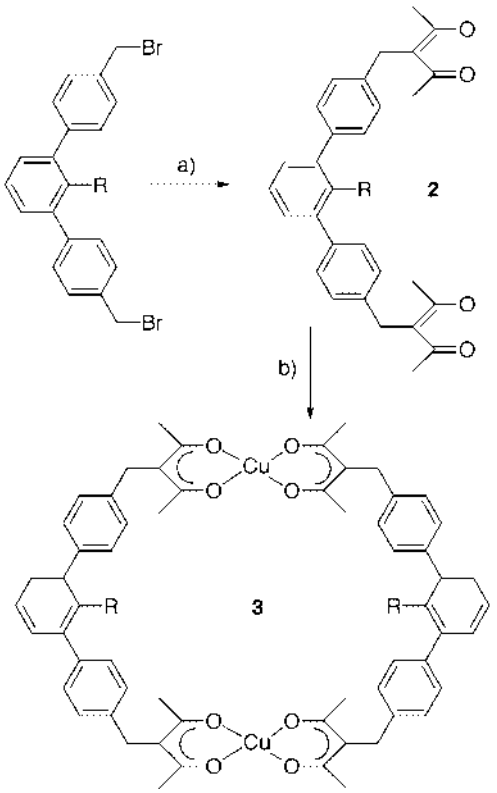
**Scheme 1.** Synthesis of ligand **2** and metallomacrocycle **3** (R = H). Reagents and conditions: (*a*) KO-*t*-Bu and 2,4-pentanedione in *t*-BuOH; (*b*) $Cu(NH_3)_4SO_4 \cdot H_2O$ in $H_2O$–$CHCl_3$.

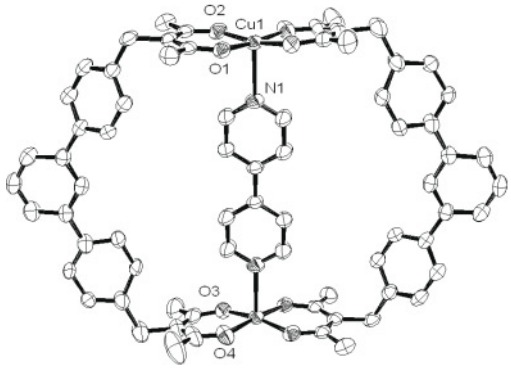



roform with $Cu(NH_3)_4SO_4$ in $H_2O$, the organic-soluble olive-green $Cu_2\mathbf{2}_2$ complex (**3**) is produced (Scheme 1). The IR spectrum of **3** confirms the presence of metal-bound acetylacetonate moieties, while electrospray mass spectrometry verified the molecular structure of complex **3**. Since the complex is charge neutral, the molecular ion was obtained as the $Na^+$ adduct of the complex.[3]

The electronic absorption spectrum of **3** contains an absorption band at 644 nm associated with metal-based *d*–*d* transitions. The addition of nitrogen-containing bases to a chloroform solution of **3** produces a turquoise solution and a concomitant shift in the metal-based transition to higher energy. (An isosbestic point in the titration is an indication of a two-species system.) A more detailed binding study with 4,4′-bipyridine reveals a binding constant of 250 $M^{-1}$. Monoaza guests, such as pyridine and substituted pyridines, bind much more poorly to the dicopper complex, with binding constants of ≈1.

X-ray quality crystals of **3** as its 4,4′-bipyridine adduct (**4**) are obtained by slow evaporation of a 1:1 mixture of 4,4′-bipyridine and **3** in $CHCl_3$ (Scheme 1, Fig. 1).[4] The solid-state structure of **4** clearly delineates the size of the cavity

**Fig. 1.** X-ray crystal structure of **4** showing 50% probability ellipsoids for all nonhydrogen atoms. H atoms and $CHCl_3$ have been omitted for clarity. Only the N, O, and Cu of the asymmetric unit are labelled. Selected bond distances (Å) and angles (°): Cu(1)—N(1): 2.338(5); Cu(1)—O(1): 1.926(4); Cu(1)—O(2): 1.921(4); Cu(1)—O(3): 1.921(5); Cu(1)—O(4): 1.912(4); O(1)-Cu(1)-O(2): 91.61(17)°; O(3)-Cu(1)-O(4): 90.8(2)°.

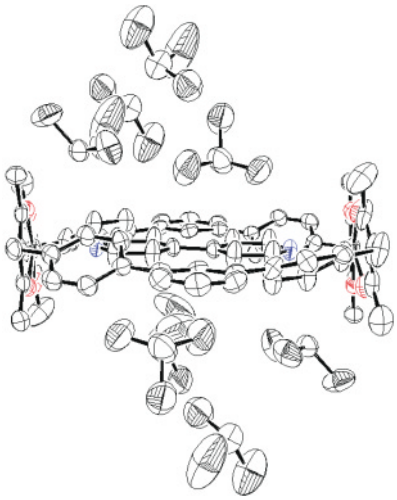



produced by the assembly of the complex: the Cu—Cu distance is 11.8 Å, while the cross-cavity distance, measured from the central benzene 2-positions, is 14.0 Å, and the peripheral phenyl groups are separated by 12.6 Å. The metal ions are not only directing the assembly of the receptors, but they are also binding the substrate, 4,4′-bipyridine, into their primary coordination sphere. The Cu—N bond length is 2.338 Å, and the Cu—O bond lengths vary between 1.912 and 1.926 Å. The Cu(II) ions are pulled slightly out of the basal plane (0.15 Å), maintaining a typical metal–metal distance for 4,4′-bipyridine bridged-metal ions. The angle at the benzyl carbon that connects the acetylacetonate and terphenyl moieties is distorted from a tetrahedral geometry to 115°. The unit cell is over 2500 $Å^3$; ten chloroform molecules are also present.

The large hexagonal cavity delineated by the two terphenyl groups and the $Cu(acac)_2$ moieties encompasses a volume of approximately 400 $Å^3$ when extended to the acetylacetonate methyl groups (Fig. 2). Crystallization solvent (10 × $CHCl_3$) is also found within this cavity. The $Cu(acac)_2$ moieties are approximately perpendicular to the central phenyl ring, whereas the two other phenyl rings are tilted away from the plane. Molecular modelling based on the $Cu_2\mathbf{2}_2$ framework suggests that the $Cu(acac)_2$ moities are sufficiently bulky to preclude catenane formation in **4**. This bodes well for the use of this framework in secondary sphere coordination studies, since R groups such as -$CO_2H$, -$CO_2Me$, and -$CONH_2$ may be readily introduced using existing methodology (Scheme 1). Furthermore, extending the cavity volume may also be possible by introducing bulkier aliphatic groups to the metal-binding acetylacetonate

[4] Crystal data for **4**: $C_{70}H_{64}N_2O_8Cu_2$ (10 × $CHCl_3$), M = 2381.99, triclinic, space group $P\bar{1}$; $a$ = 12.0488(5), $b$ = 14.5721(6), $c$ = 15.0139(6) Å; α = 104.141(1), β = 95.203(1), γ = 95.569(1)°; $V$ = 2526.20(18) $Å^3$; $Z$ = 1; $D_c$ = 1.566 g $cm^{-3}$; μ = 1.265 $mm^{-1}$; $T$ = 180(1) K; $R_1$ = 0.0880 for 8929 data with $I > 2\sigma(I)$. Supplementary material may be purchased from the Depository of Unpublished Data, Document Delivery, CISTI, National Research Council Canada, Ottawa, ON K1A 0S2, Canada. For information on obtaining material electronically go to http://www.nrc.ca/cisti/irm/unpub_e.shtml. Crystallographic information has also been deposited with the Cambridge Crystallographic Data Centre (CCDC No. 179443). Copies of the data can be obtained free of charge via www.ccdc.cam.ac.uk/conts/retrieving.html (or from the Cambridge Crystallographic Data Centre, 12, Union Road, Cambridge CB2 1EZ, U.K.; fax: +44 1223 336033; or deposit@ccdc.cam.ac.uk).

**Fig. 2.** View of the X-ray crystal structure of **4** along the plane containing the *m*-terphenyl framework. Eight of the 10 chloroform solvent molecules are shown. The solvent is found above and below a cavity delineated by the acetylacetonate groups of the metallomacrocycle.



moities. We are currently pursuing these two avenues and will present our results in due course.

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## References

1. (*a*) S. Leininger, B. Olenyuk, and P.J. Stang. Chem. Rev. **100**, 853 (2000); (*b*) J.A.R. Navarro and B. Lippert. Coord. Chem. Rev. **185–186**, 653 (1999); (*c*) B. Olenyuk, A. Fechtenkotter, and P.J. Stang. J. Chem. Soc. Dalton Trans. 1707 (1998); (*d*) A. Sautter, D.G. Schmid, G. Jung, and F. Wuerthner. J. Am. Chem. Soc. **123**, 5424 (2001); (*e*) R.-D. Schnebeck, E. Freisinger, and B. Lippert. Chem. Commun. 675 (1999); (*f*) R.-D. Schnebeck, E. Freisinger, F. Glahe, and B. Lippert. J. Am. Chem. Soc. **122**, 1381 (2000).
2. (*a*) S.-S. Sun and A.J. Lees. J. Am. Chem. Soc. **122**, 8956 (2000); (*b*) S.-S. Sun and A.J. Lees. Inorg. Chem. **40**, 3154 (2001); (*c*) S.-S. Sun, A.S. Silva, I.M. Brinn, and A.J. Lees. Inorg. Chem. **39**, 1344 (2000); (*d*) P.J. Stang, D.H. Cao, S. Saito, and A.M. Arif. J. Am. Chem. Soc. **117**, 6273 (1995); (*e*) M. Fujita, J. Yazaki, and K. Ogura. J. Am. Chem. Soc. **112**, 5645 (1990).
3. (*a*) L. Zhao, Z. Xu, L.K. Thompson, and D.O. Miller. Polyhedron, **20**, 1359 (2001); (*b*) P.N.W. Baxter, J.-M. Lehn, G. Baum, and D. Fenske. Chem. Eur. J. **6**, 4510 (2000); (*c*) J. Rojo, F.J. Romero-Salguero, J.-M. Lehn, G. Baum, and D. Fenske. Eur. J. Inorg. Chem. 1421 (1999); (*d*) D.M. Bassani, J.-M. Lehn, K. Fromm, and D. Fenske. Angew. Chem. Int. Ed. **37**, 2364 (1998); (*e*) G.S. Hanan, D. Volkmer, U.S. Schubert, J.-M. Lehn, G. Baum, and D. Fenske. Angew. Chem. Int. Ed. Engl. **36**, 1842 (1997).
4. (*a*) J.A. Whiteford, C.V. Lu, and P.J. Stang. J. Am. Chem. Soc. **119**, 2524 (1997); (*b*) M. Fujita, J. Yazaki, and K. Ogura. Tetrahedron Lett. **32**, 5589 (1991).
5. (*a*) M. Fujita. *In* Comprehensive supramolecular chemistry. Vol. 9. *Edited by* J.A. Atwood and J.-M. Lehn. Pergamon Press, New York. 1996. p. 25; (*b*) D.H. Cao, K. Chen, J. Fan, J. Manna, B. Olenyuk, J.A. Whiteford, and P.J. Stang. Pure Appl. Chem. **69**, 1979 (1997).
6. (*a*) W.J. Hunks, M.C. Jennings, and R.J. Puddephatt. Inorg. Chem. **39**, 2699 (2000); (*b*) W.J. Hunks, M.-A. MacDonald, M.C. Jennings, and R.J. Puddephatt. Organometallics, **19**, 5063 (2000); (*c*) M. Fujita and K. Ogura. Coord. Chem. Rev. **148**, 249 (1996); (*d*) M. Fujita and K. Ogura. Supramol. Sci. **3**, 37 (1996); (*e*) M. Fujita, M. Aoyagi, F. Ibukuro, K. Ogura, and K. Yamaguchi. J. Am. Chem. Soc. **120**, 611 (1998); (*f*) C. Dietrich-Buchecker, J.-P. Sauvage, N. Geum, A. Hori, M. Fujita, S. Sakamoto, and K. Yamaguchi. Chem. Commun. 1182 (2001); (*g*) G.J.E. Davidson, S.J. Loeb, N.A. Parekh, and J.A. Wisner. J. Chem. Soc. Dalton Trans. 3135 (2001).
7. (*a*) W.B. Motherwell, M.J. Bingham, and Y. Six. Tetrahedron, **57**, 4663 (2001); (*b*) J. Suh. Adv. Supramol. Chem. **6**, 245 (2000).
8. (*a*) A.W. Maverick and F.E. Klavetter. Inorg. Chem. **23**, 4129 (1984); (*b*) A.W. Maverick, S.C. Buckingham, Q. Yao, J.R. Bradbury, and G.G. Stanley. J. Am. Chem. Soc. **108**, 7430 (1986).
9. (*a*) L.H. Uppadine, J.M. Weeks, and P.D. Beer. J. Chem. Soc. Dalton Trans. 3367 (2001); (*b*) K. Fujimoto and S. Shinkai. Tet. Lett. **35**, 2915 (1994).
10. (*a*) T.K. Vinod, P. Rajakumar, and H. Hart. Tetrahedron, **51**, 2267(1995); (*b*) A. Saednya and H. Hart. Synthesis, 1455 (1996).
11. H. Hart and P. Rajakumar. Tetrahedron, **51**, 1313 (1995).