reflect improved overlap of the central bond with the aromatic $\pi$-system,[26] as well as weakening of this bond,[27] in the trans compound.

In summary, we have uncovered a remarkably efficient photochemical route to the strained *trans*-bicyclo[5.1.0]octene ring system. Efforts to synthesize theoretically interesting unnatural products via extensions of this approach are underway in our laboratory.

**Acknowledgment.** Support for this work was provided by the National Institutes of Health (National Cancer Institute) through Grant 22807.

**Registry No.** (+)-**1**, 101836-56-0; (+)-**2**, 120666-81-1; (-)-**2**, 120710-33-0; (±)-**2**, 120710-31-8; (-)-**7**, 120666-82-2; (+)-**8**, 105990-58-7; (+)-**9**, 120666-83-3; **10**, 120666-84-4; **11**, 120666-85-5; (+)-**14**, 120710-35-2; (-)-**14**, 120710-34-1; (±)-**14**, 120710-32-9; (±)-**15**, 120666-86-6; **16**, 120666-87-7.

**Supplementary Material Available:** Spectroscopic data (IR, UV, $^1$H NMR, $^{13}$C NMR, and HRMS) for **2**, **7-11**, **14-16** (3 pages). Ordering information is given on any current masthead page.

(25) In isomerizations involving central bond cleavage, radical inversions at C(1) and C(11) were assumed to be equally probable.
(26) For pertinent discussion, see ref 15a and 10.
(27) See, for example: Gassman, P. G.; Bonser, S. M. *J. Am. Chem. Soc.* **1983**, *105*, 667.

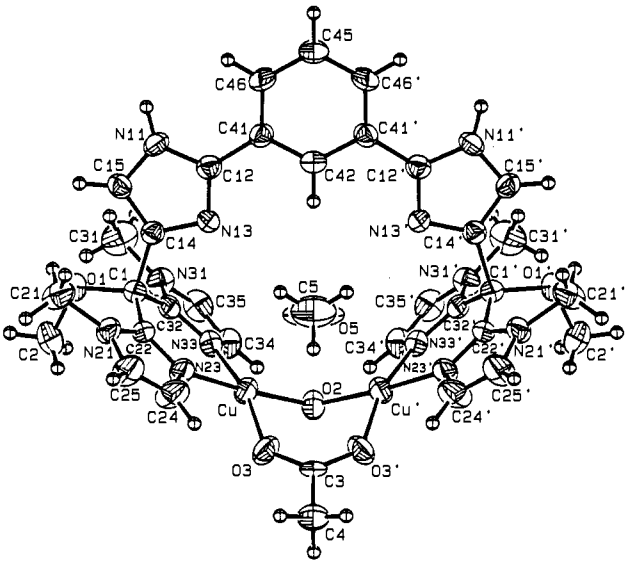



**Figure 1.** ORTEP drawing of **2**·1.5THF·MeOH showing the 40% probability thermal ellipsoids and atom labels for all non-hydrogen atoms (excluding the perchlorate counterions and THF solvate molecules). Selected interatomic distances (Å) and angles (deg) are as follows: Cu-O(2), 1.934 (5); Cu-O(3), 1.937 (7); Cu-N(23), 1.973 (8); Cu-N(33), 1.979 (8); Cu···Cu′, 3.156 (3); Cu···N(13), 4.132 (8); Cu-O(2)-Cu′, 109.3 (4); O(3)-Cu-O(2), 91.6 (4); O(3)-Cu-N(23), 87.9 (3); N(23)-Cu-N(33), 89.1 (3); N(33)-Cu-O(2), 92.7 (4).

## A Dinucleating Hexaimidazole Ligand and Its Dicopper(II) Methanol Inclusion Complex

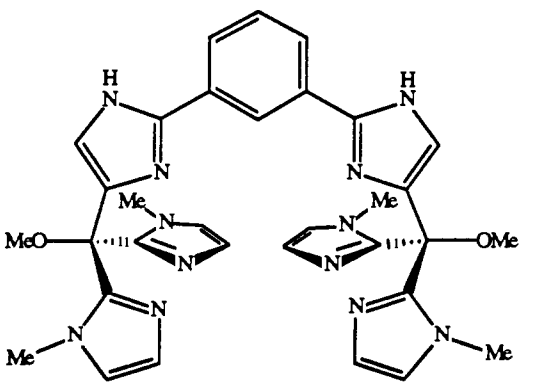
William B. Tolman, R. Lynn Rardin, and Stephen J. Lippard*

*Department of Chemistry*
*Massachusetts Institute of Technology*
*Cambridge, Massachusetts 02139*

*Received March 10, 1989*

Notable progress has been made using dinucleating ligands to model features of $Cu_2$ cores in hemocyanin and tyrosinase[1-3] and of $Fe_2$ centers in iron-oxo proteins[4] such as semimethemerythrin.[5] Little work has yet been reported with polyimidazole ligands,[6] however, and none with dinucleating species containing imidazoles as the sole N-donors. Application of the latter class to mimic the chemical and physical properties of dinuclear metalloproteins with histidine-dominated cores could ultimately prove to be as important as using porphyrins, rather than other tetraaza macrocycles, in biomimetic heme research.

In this communication we wish to report the synthesis of hexaimidazole **1**, a molecule specifically designed to encapsulate two metals in a biomimetic environment. In particular, **1** is preorganized to inhibit formation of undesired polynuclear species, an outcome previously encountered in attempts to prepare dimetallic complexes using multidentate N-donor ligands lacking a coordinating bridge atom.[7] As proof of its dinucleating ability, we present the synthesis, X-ray crystal structure, and physical characterization of a dicopper(II) complex of **1** which, as an added feature of interest, contains an included methanol.




**1**

Compound **1** was obtained upon dual metalation (potassium diisopropylamide)[8] at C5 of the N-protected imidazoles in a 1,3-bis(2-imidazolyl)benzene[9,10] followed by condensation with

(1) (a) Karlin, K. D.; Cruse, R. W.; Gultneh, Y.; Farooq, A.; Hayes, J. C.; Zubieta, J. *J. Am. Chem. Soc.* **1987**, *109*, 2668. (b) Karlin, K. D.; Haka, M. S.; Cruse, R. W.; Meyer, G. J.; Farooq, A.; Gultneh, Y.; Hayes, J. C.; Zubieta, J. *Ibid.* **1988**, *110*, 1196. (c) Cruse, R. W.; Kaderli, S.; Karlin, K. D.; Zuberbühler, A. D. *Ibid.* **1988**, *110*, 6882.
(2) (a) Sorrell, T. N.; O'Connor, C. J.; Anderson, O. P.; Reibenspies, J. H. *J. Am. Chem. Soc.* **1985**, *107*, 4199. (b) Review: Sorrell, T. N. *Tetrahedron* **1989**, *45*, 3.
(3) McKee, V.; Zvagulis, M.; Dadgegian, J. V.; Patch, M. G.; Reed, C. A. *J. Am. Chem. Soc.* **1984**, *106*, 4765.
(4) Review: Lippard, S. J. *Angew. Chem., Int. Ed. Engl.* **1988**, *27*, 344.
(5) (a) Suzuki, M.; Vehara, A.; Endo, K. *Inorg. Chim. Acta* **1986**, *123*, L9. (b) Borovik, A. S.; Que, L., Jr. *J. Am. Chem. Soc.* **1988**, *110*, 2345. (c) Borovik, A. S.; Que, L., Jr.; Papaefthymiou, V.; Münck, E.; Taylor, L. F.; Anderson, O. P. *Ibid.* **1988**, *110*, 1986.
(6) (a) Tang, C. C.; Davalian, D.; Huang, P.; Breslow, R. *J. Am. Chem. Soc.* **1978**, *100*, 3918. (b) Breslow, R.; Hunt, J. T.; Smiley, R.; Tarnowski, T. *Ibid.* **1983**, *105*, 5337. (c) Brown, R. S.; Huguet, J. *Can. J. Chem.* **1980**, *58*, 889. (d) Slebocka-Tilk, H.; Cocho, J. L.; Frakman, Z.; Brown, R. S. *J. Am. Chem. Soc.* **1984**, *106*, 2421. (e) Sorrell, T. N.; Borovik, A. S. *Ibid.* **1986**, *108*, 2479; 4255. (f) Gomez-Romero, P.; DeFotis, G. C.; Jameson, G. B. *Ibid.* **1986**, *108*, 851. (g) Gomez-Romero, P.; Casan-Pastor, N.; Ben-Hussein, A.; Jameson, G. B. *Ibid.* **1988**, *110*, 1988. (h) Suzuki, M.; Oshio, H.; Uehara, A.; Endo, K.; Yanaga, M.; Kida, S.; Saito, K. *Bull. Chem. Soc. Jpn.* **1988**, *61*, 3907. (i) Gorun, S. M.; Lippard, S. J. *Inorg. Chem.* **1988**, *27*, 149. (j) Potvin, P. G.; Wong, M. H. *J. Chem. Soc., Chem. Commun.* **1987**, 672.
(7) (a) Toftlund, H.; Murray, K. S.; Zwack, P. R.; Taylor, L. F.; Anderson, O. P. *J. Chem. Soc., Chem. Commun.* **1986**, 191. (b) Hartman, J. R.; Lippard, S. J. Unpublished results. (c) See, however: Wieghardt, K.; Tolksdorf, I.; Herrmann, W. *Inorg. Chem.* **1985**, *24*, 1230 for a possible exception.
(8) (a) Raucher, S.; Koolpe, G. A. *J. Org. Chem.* **1978**, *43*, 3794. (b) Gawley, R. E.; Termine, E. J.; Aube, J. *Tetrahedron Lett.* **1980**, *21*, 3115.
(9) Prepared by dehydrogenation of the corresponding bis(imidazoline)[10a] with $BaMnO_4$[10b-d] followed by dialkylation with NaH/2-(trimethylsilyl)ethoxymethyl chloride.[10e,f]

two molecules of bis(1-methylimidazolyl)ketone, methylation of the resulting diol, and deprotection.[11] Treatment of **1** in MeOH with 2 equiv of $Cu(OAc)_2 \cdot H_2O$ and an excess of $(Bu_4N)(ClO_4)$ caused the formation of a blue precipitate, which after crystallization from $CH_3CN$/THF yielded $[Cu_2(\mathbf{1})(\mu\text{-OH})(\mu\text{-OAc})](ClO_4)_2 \cdot 1.5THF$ (**2**·1.5THF) as blue plates (80%).[12] Crystallization from MeOH/THF afforded X-ray quality crystals of **2**·1.5THF·MeOH, the solid-state structure of which was determined (Figure 1).[13]

Molecule **2** has crystallographically required $C_s$ symmetry, with the mirror plane bisecting the phenyl ring and the hydroxo and acetato bridges. Only four of the six imidazole groups in **1** are coordinated to copper atoms, each of which adopts a $D_{2d}$ distorted square-planar geometry. The dihedral angle between the best least-squares planes through the two copper coordination spheres is 62.5°. Perchlorate counterions, hydrogen bonded to the uncoordinated imidazoles at N(11), and THF molecules are accommodated in the crystal lattice. Most interesting is a methanol solvent molecule located on the mirror plane and inserted into the cavity defined by the bis(imidazolyl)benzene linker. The resulting inclusion compound[14] resembles the vaulted lacunar cyclidenes studied by Busch and co-workers.[15] The location of O(5) in axial positions, the O(5)-Cu(Cu') distance being 2.59 (1) Å, suggests that inclusion of methanol is partly derived from weak ligation to the copper atoms. Alternative explanations, such as hydrogen bonding either to the uncoordinated imidazole or the bridging hydroxide ion, are precluded by the long O(5)-N(13) distance [3.34 (1) Å] and the location of the methanol opposite to the hydroxo bridge.

The X-band ESR spectrum of a frozen solution of **2**·1.5THF in $CH_3CN$ at 12 K has axial features ($g_\parallel = 2.33$, $g_\perp = 2.08$, $A_\parallel^{Cu} = 1.90\ (5) \times 10^{-2}$ cm$^{-1}$) characteristic of $N_2O_2$ coordination geometries in natural copper proteins.[16] In addition, we observe a $|\Delta M_S| = 2$ transition at $g \sim 4.3$, suggesting the presence of spin exchange coupling.[17] Solid-state magnetic susceptibility data for **2**·1.5THF, obtained between 6-300 K on a SQUID magnetometer, were fit to the Bleaney-Bowers expression.[18] The weak ferromagnetic coupling observed, $J = +1.3\ (1)$ cm$^{-1}$, differs from the moderate-to-strong antiferromagnetic interactions reported for many other hydroxo-bridged dicopper(II) complexes[19,20] but falls within the range of values found for ($\mu$-alkoxo)($\mu$-acetato)dicopper(II) species.[17] Consistent with the small $J$ value, the effective moment in solution at 294 K[21] is 1.7 $\mu_B$ per copper, close to the spin only value.

Encouraged by the dinucleating ability of **1**, as manifested by the unusual inclusion complex **2**·1.5THF·MeOH, we are currently exploring its reactions with a variety of metal ions found in dinuclear metalloprotein active sites.

**Acknowledgment.** This work was supported by U.S. Public Health Service Grant GM 32134 from the National Institute of General Medical Sciences. R.L.R. is grateful to the NIH for support under training Grant CA-09112 and W.B.T. to the American Cancer Society for a postdoctoral fellowship. We also thank Drs. D. P. Bancroft and J. G. Bentsen for assistance.

**Supplementary Material Available:** Spectroscopic data for **1**, solid-state magnetic susceptibility data for **2**, and tables of atomic positional and thermal parameters for **2**·1.5THF·MeOH (4 pages). Ordering information is given on any current masthead page.

(10) (a) Synthesized via the method of Oxley and Short (Oxley, P.; Short, W. F. *J. Chem. Soc.* **1947**, 497). (b) Hughey, J. L.; Knapp, S.; Schugar, H. *Synthesis* **1980**, 489. (c) Knapp, S.; Keenan, T. P.; Zhang, X.; Fikar, R.; Potenza, J. A.; Schugar, H. J. *J. Am. Chem. Soc.* **1987**, *109*, 1882. (d) Traylor, T. U.; Hill, K. W.; Tian, Z.-Q.; Rheingold, A. L.; Peisach, J.; McCracken, J. *Ibid.* **1988**, *110*, 5571. (e) Lipshutz, B. M.; Vaccaro, W.; Huff, B. *Tetrahedron Lett.* **1986**, *27*, 4095. (f) Whitten, J. P.; Matthews, D. P.; McCarthy, J. R. *J. Org. Chem.* **1986**, *51*, 1891.

(11) Further details of the preparation of **1** will be provided elsewhere. $^1H$ and $^{13}C\{^1H\}$ NMR, FTIR, and FAB-MS spectral data for **1** are included as Supplementary Material.

(12) Anal. ($C_{40}H_{50}N_{12}O_{14.5}Cl_2Cu_2$): C, H, N, Cl; FTIR (Nujol, cm$^{-1}$) 3563 (OH) (OD band obscured by Nujol envelope), 3225 (NH) [2405 (ND)], 3063, 2900-3000, 1570, 1507, 1468, 1449, 1427, 1284, 1103 ($ClO_4$), 1027, 989, 908, 807, 761, 710, 691, 624 ($ClO_4$) cm$^{-1}$; UV-vis ($CH_3CN$) [$\lambda_{max}$, nm ($\epsilon_M$/Cu cm$^{-1}$ M$^{-1}$)] 274 (17 700), 290 (sh), 315 (sh), 617 (74); magnetic susceptibility, solution (294 K, 2.5 mM in $CD_3CN$) 1.7 $\mu_B$/Cu.

(13) Crystal data for **2**·1.5THF·MeOH ($C_{41}H_{54}N_{12}O_{15.5}Cl_2Cu_2$, $M_r$ = 1160.94) at 296 K: size 0.46 × 0.26 × 0.11 mm, monoclinic, space group $P2_1/m$ (no. 11), $a = 8.529\ (4)$ Å, $b = 27.883\ (4)$ Å, $c = 11.133\ (5)$ Å, $\beta = 102.81\ (2)°$, $V = 2582\ (3)$ Å$^3$, $Z = 2$, $\rho_{calcd} = 1.493$ g cm$^{-3}$, $\rho_{meas} = 1.49\ (1)$ g cm$^{-3}$. For 2028 unique, observed reflections with $F^2 > 3\sigma(F^2)$ and 349 variable parameters, $R = 0.065$ and $R_w = 0.080$.

(14) (a) Cram, D. J. *Angew. Chem., Int. Ed. Engl.* **1988**, *27*, 1009. (b) Lehn, J.-M. *Ibid.* **1988**, *27*, 89.

(15) Ramprasad, D.; Lin, W.-K.; Goldsby, K. A.; Busch, D. H. *J. Am. Chem. Soc.* **1988**, *110*, 1480.

(16) Peisach, J.; Blumberg, W. E. *Arch. Biochem. Biophys.* **1974**, *165*, 691.

(17) Davis, W. M.; Lippard, S. J. *Inorg. Chem.* **1985**, *24*, 3688 and references therein.

(18) Bleaney, B.; Bowers, K. D. *Proc. R. Soc. London, A* **1952**, *214*, 451.

(19) A notable exception: Fallon, G. D.; Murray, K. S.; Spethmann, B.; Yandell, J. K.; Hodgkin, J. H.; Loft, B. C. *J. Chem. Soc., Chem. Commun.* **1984**, 1561.

(20) (a) Coughlin, P. K.; Lippard, S. J. *J. Am. Chem. Soc.* **1984**, *106*, 2328. (b) Benzekri, A.; Dubourdeaux, P.; Latour, J.-M.; Laugier, J.; Rey, P. *Inorg. Chem.* **1988**, *27*, 3710 and references therein. (c) Bertocello, K.; Fallon, G. D.; Hodgkin, J. H.; Murray, K. S. *Ibid.* **1988**, *27*, 4750 and references therein.

(21) (a) Evans, D. F. *J. Chem. Soc.* **1959**, 2003. (b) Live, D. H.; Chan, S. I. *Anal. Chem.* **1970**, *42*, 791.

## Rotamer Distribution Control and Double Michael Addition for Cyclopentane Annulation with Superb Selectivity

Seiki Saito,* Yohji Hirohara, Osamu Narahara, and Toshio Moriwake*

*Department of Applied Chemistry, Faculty of Engineering, Okayama University Tsushima, Okayama, Japan 700*

*Received December 27, 1988*

Michael addition of organocopper reagents to $\alpha,\beta$-unsaturated esters and subsequent intramolecular trapping of the intermediary ester enolate with an appropriately located electrophilic center (e.g., carbonyl or halide groups) constitutes efficient and reliable route to substituted cyclopentane frameworks.[1] Although the synthetic potential of this approach can be immediately recognized, methodology allowing access to related structures with the desired absolute configurations is still left to further exploration and challenge.[2] We disclose herein an extremely efficient entry leading to fully substituted cyclopentane derivatives (**2**)[3] from the axially dissymmetric acyclic precursor (**1**) via a tandem double Michael addition reaction with superb selectivity (>99% de). This approach involves a simple and promising method for controlling ground-state rotamer distribution, so that the diastereo-$\pi$-faces of carbon-carbon double bond of the enoate **1** can be differentiated.

It is well known that A is the most stable rotamer among rotamers A, B, and C for the rotational equilibrium of a *d,l*-ethane

(1) (a) Cooke, M. P., Jr. *Tetrahedron Lett.* **1979**, 2199-2202. (b) Little, R. D.; Dawson, J. R. *Ibid.* **1980**, 2609-2612. (c) Little, R. D.; Verhe, R.; Monte, W. T.; Nugent, S.; Dawson, J. R. *J. Org. Chem.* **1982**, *47*, 362-364. (d) Nugent, S. T.; Baizer, M. M.; Little, R. D. *Tetrahedron Lett.* **1982**, *23*, 1339-1342. (e) Nugent, W. A.; Hobbs, F. W., Jr. *J. Org. Chem.* **1983**, *48*, 5364-5366. See, also: *Org. Synth.* **1987**, *66*, 52-59. (f) Crimmins, M. T.; Mascarella, S. W.; DeLoach, J. A. *J. Org. Chem.* **1984**, *49*, 3033-3035. (g) Yamaguchi, M.; Tsukamoto, M.; Hirao, I. *Tetrahedron Lett.* **1985**, *26*, 1723-1726.

(2) For an approach to optically active cyclopentane frameworks by asymmetric synthesis relying on another method, see: (a) Danheiser, R. L.; Carini, D. J.; Basak, A. *J. Am. Chem. Soc.* **1981**, *103*, 1604-1606. (b) Winterfeldt, E.; Harre, M. *Chem. Ber.* **1982**, *115*, 1437-1447. (c) Danheiser, R. L.; Carini, D. J.; Fink, D. M.; Basak, A. *Tetrahedron* **1983**, *39*, 935-947. See, also: Danheiser, R. L.; Fink, D. M.; Tsai, Y.-M. *Org. Synth.* **1987**, *66*, 8-13. (d) Misumi, A.; Iwanaga, K.; Furuta, K.; Yamamoto, H. *J. Am. Chem. Soc.* **1985**, *107*, 3343-3345.

(3) For a carbohydrate approach to a fully substituted cyclopentane framework, see: RajanBabu, T. V. *J. Am. Chem. Soc.* **1987**, *109*, 609-610.

0002-7863/89/1511-4533$01.50/0 