Inorg. Chem. **1996,** *35,* 3−4

Benzimidazol-2-ylcarbinols and Benzimidazol-2-yl Ketones: Novel Bifunctional Chelating Ligands for Copper

Sergiu M. Gorun* and Robert T. Stibrany

Corporate Research, Exxon Research and Engineering Company, Annandale, New Jersey 08801

Alan R. Katritzky,* Jaroslaw J. Slawinski,[⊥] Hassan Faid-Allah,[‡] and Frédéric Brunner[§]

Department of Chemistry and Center for Heterocyclic Compounds, University of Florida, Gainesville, Florida 32611-7200

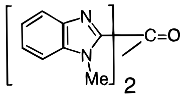
Received June 2, 1995

Imidazole (histidine) coordination is well recognized for many copper-containing enzymes that bind O_2, O_2^-, or O_2^{2-} ions. Many of these enzymes function as oxidases or oxygenases for hydrocarbon substrates.[1] Interestingly, copper also catalyzes undesirable oxidations of hydrocarbons used as fuels, lubricants, etc.[2] Strong chelation by N-heterocycles of Cu (II)[3] or Cu(I) (the latter from Cu-containing impervious films formed on metal surfaces)[4] seems to be a common requirement for a "deactivator" of such oxidations, and we have shown that bioinspired imidazole ligands indeed prevent copper-induced oxidations.[5] Benzimidazole ligands are also known as Cu deactivators.[7] Chelating bis- or tris(benzimidazoles) have received little attention compared to polyimidazoles.

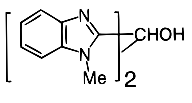
Additional carbinol and carbonyl functionalities should allow further derivatization (for example, to enhance ligand lipophilicity) or red-shift the MLCT bands (believed important in artificial photosynthesis[8]) of their Cu(I) complexes.

This paper describes the preparation of representative examples of compounds of three new classes of benzimidazoles and the preparation and structural and spectroscopic characterization of some of their copper complexes.

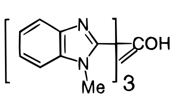
1-Methylbenzimidazole,[9] **1**, is known to undergo lithiation at the 2-position, and the lithio derivative **2** was previously reacted with carbon dioxide[11] leading to 1-methylbenzimidazole-2-carboxylic acid. We have now found that **2** reacts with $^1/_2$ mol of diethyl carbonate to give ketone **3**, **BBIK**, in 48% yield.[12] Secondary alcohol **4**, **BBICOH**, was prepared from **2** and ethyl formate[15] while tertiary alcohol **5**, **TBICOH**, was obtained in moderate yield by reacting **2** with ethyl chloroformate.[16] All of the ligands are white crystalline solids which are stable in air.



3



4



5

The copper (II) complex, $[Cu(BBIK)_2(NO_3)](NO_3)$, **6**, was prepared by reacting 170 mg (0.62 mmol) $Cu(NO_3)_2{\cdot}3H_2O$, dissolved in 20 mL of a 1:1 methanol/acetonitrile mixture, with 361 mg (1.24 mmol) of **3**. Evaporation of the solvent[17] gave green, X-ray quality crystals. The Cu coordination sphere (see Figure 1) incorporates four N imidazoles and at least one O from a coordinated nitrate. The two BBIK ligands bind Cu(II) in an axial−equatorial mode, with a 88° bite angle; the Cu−N bond lengths, 1.987(2)−2.088(3)Å, are normal. If the O15 coordination is ignored, the coordination geometry can be described as square pyramidal. The rings of the ligand are noncoplanar (24° and 31°) leading to a reduction in the exocyclic conjugation of aromatic rings with ketone carbonyl. However,

---

[⊥] Present address: Department of Drug Technology, Medical Academy Gdansk, K. Marksa 107, 80-416 Gdansk, Poland.

[‡] Present address: Chemistry Department, Alexandria University, Alexandria, Egypt.

[§] Present address: CIBA-GEIGY Limited CH-4002 Basel, Switzerland.

(1) (a) *Bioinorganic Chemistry of Copper*; Karlin, K. D., Tyeklar, Z., Eds.; Chapman & Hall: New York, 1993. (b) *Copper Proteins and Copper Enzymes*; Lontie, R., Ed.; CRC Press: Boca Raton, FL, 1984. (c) *Copper Proteins*; Siger, H., Ed.; Metal Ions in Biological Systems 13; M. Dekker: New York, 1981.

(2) Scott, G. *Atmospheric Oxidation and Antioxidants*; Elsevier: New York, 1965.

(3) (a) da Costa, S. L. F. A.; Agosthino, S. M. L. *Corrosion* **1989**, *45*, 472. (b) Collie, M. J. *Corrosion Inhibitors-Development Since 1980;* Noyes Data Corporation: Park Ridge, NJ, 1983. (c) Chakravorty, N. K. *J. Inst. Petrol.* **1963**, *49*, 353.

(4) (a) Tornkvist, C.; Thierry, D.; Bergman J.; Liedberg, B.; Leygraf, C. *J. Electrochem. Soc.* **1989,** *136*, 58. (b) Rubin, J.; Gutz, I. G. R.; Orville-Thomas, W. J. *J. Mol. Struct.* **1983**, *100*, 571. (c)Searle, A. R.; Velapoldi, R. A.; Erickson, N. *Inorg. Nucl. Chem. Lett.* **1979**, *15,* 33.

(5) Gorun, S. M.; Frankenfeld, J. W. U.S. Patent 4,869,838 1989. A general synthetic route to the more basic polyimidazol-4-yl ligands has also been described.[6]

(6) Katritzky, A. R.; Slawinski, J. J.; Brunner, F.; Gorun, S. M. *J. Chem. Soc., Perkin Trans. I* **1989**, 1139.

(7) (a) Thierry, D.; Leygraf, C. *J. Electrochem. Soc.* **1985,** *132*, 1009 (b) Cotton, J. B.; Scholes, I. R. *Br. Corr. J.* **1967**, *2*, 1. (c) Elliot, J. S.; Davis, B. T. UK Patent 1,061,904. 1967.

(8) Recent reviews: (a) Kalyanasundaram, K. *Photochemistry of Polypyridine and Porphyrin Complexes;* Academic Press: London, 1992; Chapter 9. (b) McMillin, D. R.; Kirchhoff, J. R.; Goodwin, K. V. *Coord. Chem. Rev.* **1985**, *64*, 83.

(9) 1-Methylbenzimidazole **1** was synthesized according to a literature[10] procedure; mp 58−60 °C (lit. 60−61 °C).

(10) Pozharskii, A. F.; Simonov, A. M. *J. Gen. Chem. USSR* **1963**, *33*, 172.

(11) Alley, P. W.; Shirley, D. A. *J. Org. Chem.* **1958**, *23*, 1791.

(12) (a) Bis(1-methylbenzimidazol-2-yl) ketone, **3, BBIK**, was prepared by lithiation of 1-methylbenzimidazole, **1**, followed by reaction with diethyl carbonate and quenching with HCl. Experimental details are given in the Supporting Information. (b) **BBIK** was previously reported to form in a multistep procedure by the condensation of 1-amino-2-(methylamino)benzene with diethyl malonate followed by catalyzed autoxidation of the product.[13] NMR data for **BBIK** have not been reported. A second procedure using **1** and phosgene[14] claims **BBIK** in 8% yield, but the only evidence reported, its melting point, is about 95 deg higher than the true 190−191 °C. The above papers do not report metal complexation properties of **BBIK.**

(13) Sprecher, A. C.; Zuberbühler, A. D. *Angew. Chem., Int. Ed. Engl.* **1977,** *16*, 189.

(14) Regel, E.; Büchel, K-H. *Liebigs Ann. Chem.* **1977,** 145.

(15) Bis(1-methylbenzimidazol-2-yl)carbinol, **4, BBICOH**, was prepared by lithiating 1-methylbenzimidazole, **1**, followed by reaction with ethyl formate and quenching with ammonium chloride. Experimental details are given in the Supporting Information.

(16) Tris(1-methylbenzimidazol-2-yl)carbinol, **5, TBICOH**, was prepared by lithiating **1**, followed by reaction with ethyl chloroformate and quenching with ammonium chloride. Experimental details are given in the Supporting Information.

(17) Anal. Calcd for **6**, $[Cu((C_8H_7N_2)_2CO)_2(NO_3)][NO_3]{\cdot}0.5\ H_2O$ ($C_{34}H_{29}CuN_{10}O_{8.5}$): C, 52.02; H, 3.70; N, 17.84. Found: C, 52.23; H, 3.86; N, 17.80. Crystal data for **6**$\cdot$MeCN: monoclinic, space group $P2_1/n$ (alternative of $P2_1/c$, No. 14); $a = 11.222(2)$ Å, $b = 17.140(4)$ Å, $c = 9.365(4)$ Å, $\beta = 98.10(2)°$, $V = 3688(1)$ Å^3; $d_{calc} = 1.458$ g cm^{-3} for $Z = 4$. A total of 6779 independent reflections were collected. The structure was solved using direct methods techniques. R_1 (unweighted, based on F) = 0.048 for 4914 independent reflections with $I > 3\sigma(I)$.

0020-1669/96/1335-0003$12.00/0

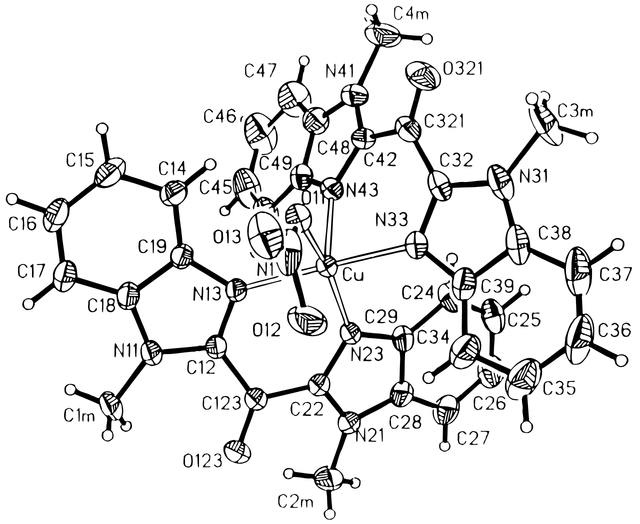


Figure 1. View of the $[Cu(BBIK)_2(NO_3)]^+$ cation. The predominant (52%) coordination mode of the nitrate is specified by oxygen atoms at O11, O12, and O13 and a nitrogen atom at N1. Selected bond lengths (Å) and angles (deg): Cu−N13 = 1.987(2), Cu−N23 = 2.039(3), Cu−N33 = 2.002(3), Cu−N43 = 2.088(3), Cu−O11 = 2.075(4), Cu−O15 = 2.086(20), O123−C123 = 1.216(4), O321−C321 = 1.212(4); N13−Cu−N23 = 88.3(1), N13−Cu−N33 = 169.9(1), N23−Cu−N33 = 96.7(1), N13−Cu−N43 = 100.0(1), N23−Cu−N43 = 101.8(1), N33−Cu−N43 = 87.6(1), N13−Cu−O11 = 88.9(1), N23−Cu−O11 = 161.5(1), N33−Cu−O11 = 83.6(1), N43−Cu−O11 = 96.7(1), C12−C123−C22 = 118.3(3), C32−C321−C42 = 117.7(3).

unlike dipyridyl ketones[18] or other N-heterocycles,[3a] neither carbonyl hydration nor metal−oxygen bond formation is observed for **6**.[19]

The copper (I) complex $[Cu(BBIK)_2](BF_4)$·solvent, **7**, was prepared by mixing *aerobically* 586 mg (2.02 mmol) of **3** with a 20 mL acetonitrile solution containing 268 mg of $CuBF_4$·4MeCN (1.01 mmol), which instantly developed a dark blue color. Liquid diffusion of cosolvents (diethyl ether, ethanol) overnight formed black X-ray quality crystals.[21] The structure of the cation of **7**, shown in Figure 2, exhibits normal Cu−N distances ranging from 1.987(5) to 2.019(5)Å.[22a] The ligand bite angle of 90° is about 14° smaller than the ideal value required for regular tetrahedral geometry but 5−10 deg. larger than those encountered for α-diimines.[22] The geometry around the Cu is pseudotetrahedral (D_{2d}), with a dihedral angle of 88.1° between the intraligand N−Cu−N planes.

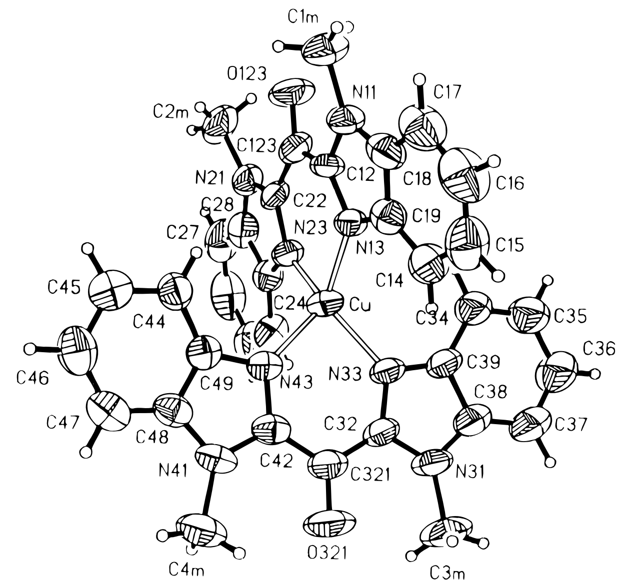


Figure 2. View of the $[Cu(BBIK)_2]^+$ cation. Selected bond lengths (Å) and angles (deg): Cu−N13 = 2.011(6), Cu−N33 = 1.987(5), Cu−N22 = 2.014(6), Cu−N43 = 2.019(5), O123−C123 = 1.224(10), O321−C321 = 1.221(10); N13−Cu−N23 = 90.4(2), N13−Cu−N33 = 120.0(2), N23−Cu−N33 = 124.5(2), N13−Cu−N43 = 117.0(2), N23−Cu−N43 = 116.6(2), N33−Cu−N43 = 91.0(2), C12−C123−C22 = 119.8(7), C32−C321−C42 = 121.4(7).

While the **BBIK** bite angle is similar for both Cu(II) and Cu(I), aromatic−carbonyl conjugation is favored only for the Cu(I) complex (the aromatic rings deviate by only 5 ± 1° from coplanarity). This is reflected both in the air stability of **7** and in its intense color. Both **6** and **7** are stable in solution; **7** is slowly oxidized in air to Cu(II) over a period of days. The electronic spectroscopy and NMR of a deep purple MeCN solution of **7** suggest that the solid state Cu coordination is maintained in solution.[23] No free ligand or coordinated MeCN is observed by NMR. The presence of a 623 nm absorption, most likely a d−π^* MLCT transition, combined with the hydrolytic stability of the carbonyl group suggests that metal complexes of **BBIK** or its derivatives may be candidates for photochemical scission of water.

In conclusion, new bifunctional tri- and bidentate N ligands have been prepared. The coordination properties of **BBIK** have been elucidated via the preparation and spectroscopic and structural characterization of its first metal complexes. The preparation, using a similar synthetic strategy, of unalkylated-polybenzimidazole ligands as well as metal complexes of the carbinol ligands will be reported elsewhere.

Acknowledgment. We thank the Crystalytics Co. for the X-ray data.

Supporting Information Available: Text giving preparation methods for **3**−**5** and some details of the structure determination for **7** and tables of atomic coordinates, bond distances and angles, anisotropic thermal parameters, and hydrogen atom coordinates for **6** and **7** (33 pages). Ordering information is given on any current masthead page.

IC950698V

---

[18] (a) Byers, P. K.; Canty, A. J.; Engelhardt, L. M.; Patrick, J. M.; White, A. H. *J. Chem. Soc., Dalton Trans.* **1985**, 981. (b) Annibale, G.; Canovese, L.; Cattalini L.; Natile G.; Biagini-Cingi, M.; Manotti-Lanfredi, A-M.; Tirripicchio, A. *J. Chem. Soc., Dalton Trans.* **1981**, 2280. (c) Fischer, B. E.; Sigel, H. *J. Inorg. Nucl. Chem.* **1975**, *37*, 2127. (d) See also Arali et al. (Arali, V. H.; Revankar, V. K.; Mahale, V. B.; Kulkarni, P. J. *Transition Met. Chem.* **1994**, *19*, 57) for N9-(benzimidazole), O(carbonyl) coordination to metals.

[19] In the preparation of **6**, the limited $Cu(NO_3)_2$ water of hydration is stoichiometrically sufficient for the formation of the *cis*-diols. Preservation of the carbonyl exocyclic conjugation is also observed in the $[Ru(BIK)_3]^{2+}$ cation (BIK is the parent bis(imidazol-2-yl) ketone).[20]

[20] (a) Gorun, S. M.; Greaney, M. A. **1990** ACS Meeting, Boston, MA (b) Gorun, S. M.; Greaney, M. A. To be submitted for publication.

[21] Anal. Calcd for **7**, $[Cu((C_8H_7N_2)_2CO)_2][BF_4]$·1.5MeCN·0.5EtOH ($C_{38}H_{35.5}BCuF_4N_{9.5}O_{2.5}$): C, 55.96; H, 4.39; B, 1.33; Cu, 7.29; F, 9.32; N, 16.31. Found: C, 55.93; H, 3.83; B, 1.38; Cu, 7.81; F,10.00; N, 16.20. Crystal data for **7**·MeCN·solvent: space group $P\bar{1}$ (No. 2); a = 14.079(3) Å, b = 11.623(3) Å, c = 14.524(3) Å, α = 108.35(2)°, β = 93.95(2)°, γ = 109.99(2)°, V = 2078.0(8) Å^3, d_{calc} = 1.30 g cm^{-3} for Z = 2. A total of 5701 independent reflections were collected. The structure was solved using direct methods techniques. R_1 (unweighted, based on F) = 0.058 for 2896 independent reflections with $I > 3\sigma(I)$.

[22] (a) Cu−N distances less than 2.0 Å are observed in CuN_x chromophores for other benzimidazole-containing ligands: Diguet, C.; Bernardinelli, A.; Bocquet, B.; Quattropani, A.; Williams; A. F. *J. Am. Chem. Soc.* **1992**, *114*, 7440 and references therein. See also: (b) Hendriks, H. M. J.; Birker, P. M. M. W. L; Van Rijn, J.; Verschoor, G. C.; Reedijk, J. *J. Am. Chem. Soc.* **1982,** *104*, 3607. (c) Patch, M. G.; Choi, H-K.; Chapman, D. R.; Bau, R.; McKee, V.; Reed, C. A. *Inorg. Chem.* **1990**, *29*, 110.

[23] ^{1}H-NMR, 25 °C, δ (MeCN), vs TMS: 4.39 (12 H, s); 7.07 - 7.71 (16 H, m). ^{13}C-NMR, δ (MeCN): 34.93; 112.76; 121.35; 125.67; 128.47; 137.52; 140.78; 145.82; 174.48. Variable temperature NMR experiments in various solvents are currently addressing the possibility of fast exchange. UV−vis (MeCN) (λ, nm (ϵ)): 623 (3740), 361 (47 350), 319 (29 270).