Copper(I) Chelate Complexes with Novel π-Conjugated 1,2-Bis(2-pyridylethynyl)benzene Ligands: Synthesis, Structure, and Reactivity

Tomikazu Kawano, Jun Kuwana, Tatsuji Shinomaru, Chong-Xu Du, and Ikuo Ueda*
The Institute of Scientific and Industrial Research, Osaka University, 8-1 Mihogaoka, Ibaraki, Osaka 567-0047

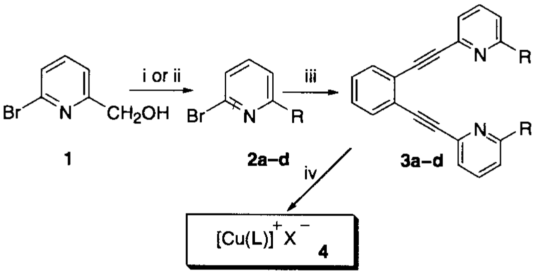
(Received September 13, 2001; CL-010905)

Novel π-conjugated nitrogen ligands, 1,2-bis(2-pyridylethynyl)benzenes, and their Cu(I) complexes have been synthesized and structurally characterized: the reactivity of the complexes for radical cyclization has also been examined.

Cu(I) complexes with polydentate nitrogen ligands have received considerable attention within the fields of supramolecular chemistry[1] and bioinorganic chemistry.[2] Among these complexes, some two-coordinate Cu(I) complexes have been shown to be effective in transition-metal-catalyzed reactions due to their enhanced reactivity.[3] In these catalytic reactions, C_2-symmetric nitrogen ligands, which act in a chelating mode, play an important role in the catalytic activity of the complex. However, few extensive structural studies of the complexes derived from the chelating nitrogen ligands have been reported.[4] In this study, 1,2-bis(2-pyridylethynyl)benzene ligands bearing an extended π-conjugated system were designed as a new class of nitrogen ligands. The ligands and their complexes might be expected to have potential as catalysts, antitumor agents, electrochemical and photochemical devices. We herein describe the syntheses and structural characterizations of the novel ligands and their Cu(I) complexes, along with the reactivity of the complexes in radical cyclization.

The new ligands (**3a–d**) were synthesized according to the procedure outlined in Scheme 1. Reaction of the sodium salt of 2-bromo-6-(hydroxymethyl)pyridine (**1**)[5] with methyl iodide afforded the 6-(methoxymethyl) derivative in 97% yield. Reaction of sodium salts of phenol or *i*-PrOH with the 6-(iodomethyl) derivative, which was obtained by mesylation of **1**, followed by treatment of the mesylated derivative with sodium iodide, gave the 6-(phenoxy)methyl and 6-(isopropoxy)methyl derivatives in 93% and 95% yields, respectively. The latter synthetic protocol allows the preparation of bromopyridine derivatives with a variety of substituents at the 6-position. The cross-coupling reaction of 1,2-bis(ethynyl)benzene[6] with the corresponding 2-bromopyridine derivatives (**2a–d**) in the presence of a catalytic amount of $Pd(PPh_3)_4$ in diethylamine at 80 °C afforded the desired ligands in good yields. All new ligands obtained were characterized by spectroscopy (NMR, IR, and FABMS) and elemental analysis.

The reaction of the ligand (**3b**) with an equimolar quantity of $[Cu(CH_3CN)_4]X$ ($X = PF_6$ or ClO_4) in dichloromethane at room temperature proceeded smoothly to afford yellow mononuclear Cu(I) complexes [Cu(**3b**)](PF_6), **4bA**, and [Cu(**3b**)](ClO_4), **4bB**, in 90% and 67% yields, respectively. The molecular formulas of **4bA** and **4bB** were determined on the basis of FAB mass spectroscopy and elemental analysis. Complexes **4aA**, **4cA**, **4cB** and **4dA** were obtained in a similar manner in 87%, 100%, 61% and 71% yields, respectively. On the other hand, the isolation of [Cu(**3b**)]Cl, **4bC**, was unsuccessful when CuCl was used as the Cu(I) salt. During the reaction of **4b** with CuCl in chloroform, a yellow solution of **4bC** was initially obtained, which gradually turned into a blue-green solution. Under anaerobic conditions, however, the yellow color of **4bC** remained unchanged. This indicates that **4bC** is remarkably air-sensitive and highly reactive in solution. By contrast to **4bC**, both **4bA** and **4bB** were found to be very air-stable even if oxygen gas was bubbled into the reaction solution.



a: R = H; **b**: R = CH_2OMe; **c**: R = CH_2OPh; **d**: R = CH_2O-*i*-Pr
A: X = PF_6; **B**: X = ClO_4; **C**: X = Cl

Scheme 1. Reagents and conditions: i) a)NaH, THF, 0 °C, b) MeI (97%). ii) a) MsCl, DMAP, CH_2Cl_2, −40°C (95%), b) NaI, acetone, 60 °C (98%), c) PhONa or *i*-PrONa,THF, 0 °C (93%, 95%). iii) 1,2-bis(ethynyl)benzene, $Pd(PPh_3)_4$, Et_2NH, 80 °C (72% for **3a**, 92% for **3b**, 95% for **3c**, 75% for **3d**), iv) $Cu(CH_3CN)_4PF_6$, $Cu(CH_3CN)_4ClO_4$, or CuCl,CH_2Cl_2, rt.

The structures of the complexes thus obtained were unambiguously assigned on the basis of ^1H NMR, UV and X-ray crystallography. The ^1H NMR spectra of **4bA** in dichloromethane-d_2 solution consisted of a simple pattern of peaks corresponding to **3b**, indicative of the formation of a symmetric species. However, ^1H NMR measurement of **4bA** at higher concentration (about 10 mM) resulted in the appearance of new peaks, which implies the formation of a different Cu(I) complex from **4bA**. Concentration-dependent behavior was also observed in the case of **4cA** and **4dA**, where, in particular, a new complex was generated as the main product at concentrations above 16 mM solution of **4cA**. This finding will be reported in detail elsewhere. The UV electronic spectra of **4bA** displayed a new absorption at 360 nm, which was assigned to a metal-to-ligand charge-transfer band. The NMR spectra and electronic spectra of other complexes mentioned above indicated a similar behavior. Further structural information came from the single crystal X-ray analysis of **4bB** and **4cA**. The X-ray quality crystals were obtained from **4bB** and **4cA** by recrystallization from dichloromethane–hexane and acetone, respectively. Figure 1 shows the crystal structure of **4bB**.[7] The complex **4bB** consists of one ligand (**3b**), one two-coordinate Cu(I) ion, and one perchlorate anion. The ligand coordinates Cu(I) ions in a trans-chelating mode. The average dihedral angle between the aromatic rings in **4bB** is 3.63°, indicative of the formation of a planar complex. The bond length of Cu–N is 1.935 Å and the bite angle of N–Cu–N is 170.28(7)°. The ClO_4^- anion adopts position nearly perpendicular to the N–Cu–N axis. The distance between the Cu(I) ion and the adjacent oxygen atom of the ClO_4^- anion is 2.43 Å, indicative of the presence of a relatively strong interaction. The crystal structure of the cation of **4cA** also had a planar structure similar to that of **4bB**.

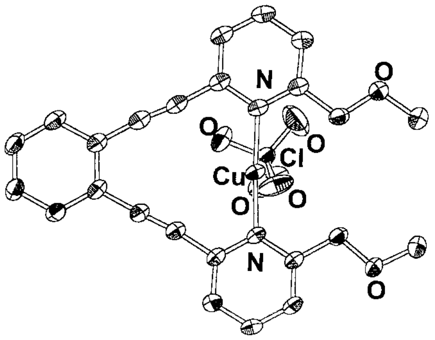
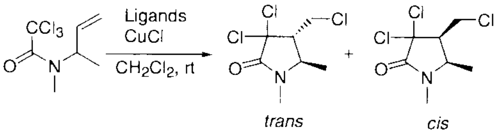


Figure 1. Crystal structure of **4bB**.

Complex **4bC** might be expected to be useful for some organic reactions due to its high reactivity. Nagashima et al. established that the cyclization of *N*-allyltrichloroacetamides can be successfully achieved in the presence of a 1:1 mixture of CuCl and bipyridine under mild conditions.[8] The CuCl-bipyridine complex, which was prepared in the reaction mixture, plays an important role in this reaction. Therefore, radical cyclization of *N*-methyl-*N*-(1-methyl-2-propen)trichloroacetamide was examined using the complexes synthesized in this study (Scheme 2).



Scheme 2.

The acetamide was subjected to the complex **4dC**, generated in situ from CuCl and **3d**, in dichloromethane at room temperature to give trans-lactam as the major product (trans:cis = 93:7). Obviously, no radical cyclization using stable Cu(I) complexes such as **4bA** and **4bB** occurred. Table 1 summarizes the yields and diastereomer ratios of the reaction products.

Table 1. Radical cyclization of *N*-allylacetamide

Entry	Complexes	Time/h	Yield/%	Diastereomer ratio (trans:cis)
1	**4aC**	48	75	78:22
2	**4bC**	24	91	74:26
3	**4cC**	48	78	83:17
4	**4dC**	48	71	93:7
5	Cu-bipyridine	0.5	87	83:17

In conclusion, we have demonstrated that the reaction of a new class of π-conjugated nitrogen ligand, 1,2-bis(2-pyridylethynyl)benzenes, with Cu(I) salts proceeds smoothly to give novel planar two-coordinate Cu(I) complexes in good yields, and that radical cyclization of *N*-allyltrichloroacetamides using these complexes yields trans-lactam derivatives with good stereoselectivity.

We thank the Material Analysis Center of our institute for assisting with elemental analysis.

References and Notes

1 J. -M. Lehn, “Supramolecular Chemistry: Concepts and Perspectives,” VCH, Weinheim (1995); M. Fujita, K. Umemoto, M. Yoshizawa, N. Fujita, T. Kusukawa, and K. Biradha, *Chem. Commun.*, **2001**, 509.

2 W. Kaim and J. Rall, *Angew. Chem., Int. Ed. Engl.*, **35**, 43 (1996); W. B. Tolman, *Acc. Chem. Res.*, **30**, 227 (1997).

3 M. M. -C. Lo and G. C. Fu, *J. Am. Chem. Soc.*, **120**, 10270 (1998); D. A. Evans, M. M. Faul, M. T. Bilodeau, B. A. Anderson, and D. M. Barnes, *J. Am. Chem. Soc.*, **115**, 5328 (1993).

4 Cambridge Structural Database, Version 5.20, October 2000, CCDC, Cambridge, U.K.

5 D. Cai, D. L. Hughes, and T. R. Verhoven, *Tetrahedron Lett.*, **37**, 2537 (1996).

6 S. Takahashi, Y. Kuroyama, K. Sonogashira, and N. Hagihara, *Synthesis*, **1980**, 627.

7 Crystal data for **4bA**: $C_{24}H_{20}ClN_2O_6Cu$, M_r = 531.43, triclinic, space group $P\bar{1}$ (no. 2), a = 10.276(2), b = 12.226(2), c = 9.455(1) Å, α = 96.52(1), β = 91.81(1), γ = 71.93(1)°, V = 1121.9(3) Å^3, Z = 2, D_{calc} = 1.573 g cm^{-3}, μ(Mo Kα) = 11.37 cm^{-1}, T = 223 K, 5462 reflections measured, 5160 unique reflections, R_{int} = 0.011, 4250 observed reflections with $I > 3\sigma(I)$, Final R = 0.029 and R_w = 0.032. **CAUTION**. Perchlorate salts of metal complexes with organic ligands are potentially explosive. Only small amounts of materials should be prepared and handled with care.

8 H. Nagashima, N. Ozaki, M. Ishii, K. Seki, M. Washiyama, and K. Itoh, *J. Org. Chem.*, **58**, 464 (1993).