Synthesis, Structure, and Properties of {*N,N′*-Bis[2-(2-pyridyl)ethyl]pyridine-2,6-dicarboxamido}copper(II)

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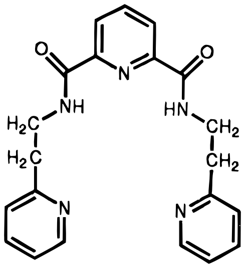
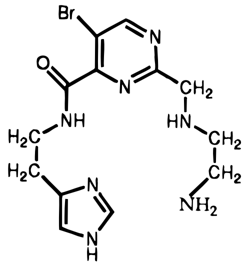
Introduction

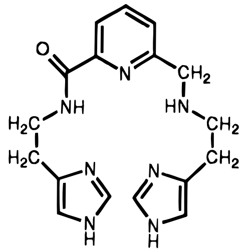
Our interest in metal complexes of ligands that contain amide moieties stems from their occurrence in metalloproteins and metal complexes of glycopeptide antibiotics like bleomycin (BLM).[1] In such pursuit, we have synthesized a designed dipeptide ligand *N,N′*-bis(2-(2-pyridyl)ethyl)pyridine-2,6-dicarboxamide (Py_3PH_2 (**1**); two dissociable amide protons are denoted as H_2). We report in this account the synthesis, structure, and properties of [Cu(Py_3P)] (**2**), the Cu(II) complex of this new ligand. **2** is the first example of a dipeptide complex of copper comprising a $[CuN_5]$ chromophore.[2] We have also compared the structural and spectroscopic parameters of the distorted square-pyramidal complex **2** with those of two other Cu(II) complexes, namely, [Cu(PMA)]X (X = ClO_4^-, BF_4^-)[3] and $[Cu(HAPH)][ClO_4]\cdot 1.6H_2O$,[4] that contain $[CuN_5]$ chromophores of similar geometry and one deprotonated amido N donor in the first coordination sphere.



Py_3PH_2 (**1**)



PMAH



HAPH

Experimental Section

Preparation of Compounds. 2,6-Pyridinedicarbonyl dichloride (**3**) and 2-(2-aminoethyl)pyridine (**4**) were procured from Aldrich Chemical Co. and used without further purification. ACS reagent grade copper(II) acetate hydrate (Aldrich) was recrystallized before use. The solvents were dried and freshly distilled.

Py_3PH_2 (1). A batch of 3.87 g (0.018 mol) of **3** was dissolved in 120 mL of chloroform in a 250 mL round-bottom flask and cooled to 0 °C. To this was added dropwise 6.95 mL (0.055 mol) of **4**, and the resulting yellow solution was stirred. After 30 min, a condenser was attached and the solution was heated to reflux for 5 h. Following a brief period of cooling, it was filtered and the filtrate was washed twice with 70 mL of water. The chloroform layer was then evaporated under vacuum. The residual foam was triturated twice with chloroform and placed under high vacuum for 48 h, during which a beige solid (mp 106−110 °C) was obtained. Total yield: 5.98 g (87%). The compound was stored at −20 °C. ^1H NMR ($CDCl_3$, 500 MHz), δ (from TMS): 3.14 (t, 4H, CH_2), 3.91 (q, 4H, CH_2), 7.13 (q, 2H, py), 7.20 (d, 2H, py), 7.60 (t, 2H, py), 7.99 (t, 1H, py), 8.31 (d, 2H, py), 8.49 (d, 2H, py), 8.79 (t, 2H, NH). ^{13}C NMR ($CDCl_3$, 500 MHz), δ (from TMS): 37.15, 39.04, 121.70, 123.57, 124.60, 136.67, 138.81, 148.83, 149.20, 159.44, 163.64. Selected IR bands (KBr pellet, cm^{-1}): 3320 (m), 2930 (w), 1654 (ν_{CO}, vs), 1593 (s), 1542 (vs), 1475 (s), 1438 (s), 1357 (m), 1306 (m), 1240 (m), 1150 (w), 1071 (w), 1000 (m), 847 (m), 746 (s), 670 (m), 507 (w).

[Cu(Py_3P)] (2). To a solution of 106.5 mg of copper(II) acetate hydrate (0.53 mmol) in 15 mL of methanol was added dropwise with stirring a solution of 200 mg (0.53 mmol) of **1** in 5 mL of methanol. The resulting deep blue solution was stirred at 25 °C for 2 h. The methanol was then removed under vacuum, and the residue was redissolved in 2 mL of a 1:1 (v/v) methanol/acetonitrile mixture. The blue solution thus obtained was filtered to remove any suspended particles. Slow diffusion of diethyl ether into this solution afforded blue blocks, which were collected after 48 h. Total yield: 170 mg (73%). Selected IR bands (KBr, cm^{-1}): 3421 (m, br), 1626 (s), 1609 (ν_{CO}, vs), 1578 (s), 1478 (m), 1445 (m), 1420 (m), 1380 (s), 1326 (m), 1296 (m), 1210 (w), 1118 (w), 1066 (m), 1016 (m), 860 (w), 834 (w), 782 (m), 750 (m), 685 (m), 639 (w), 597 (m), 514 (w). Electronic absorption spectrum, λ_{max}, nm (ϵ, M^{-1} cm^{-1}): water, 612 (190), 770 sh, 256 (19 000); methanol, 613 (220), 740 sh, 258 (18 800). μ_{eff}(298 K, polycryst): 1.88 μ_B.

Physical Measurements. Absorption spectra were recorded on a Perkin-Elmer Lambda 9 spectrophotometer. A Perkin-Elmer 1600 FTIR spectrophotometer was employed to monitor the infrared spectra. EPR spectra at X-band frequencies were obtained with a Bruker ESP-300 spectrometer. ^1H and ^{13}C NMR spectra were recorded at 25 °C on a Varian 500 MHz Unity Plus machine (interfaced with a Sun OS 4.1.3 computer). Electrochemical measurements were performed with standard Princeton Applied Research instrumentation using a Pt electrode and an aqueous SCE. Room-temperature magnetic susceptibility was measured with a Johnson Matthey magnetic susceptibility balance.

X-ray Data Collection and Structure Solution and Refinement. Blue blocks of **2** suitable for X-ray analysis were obtained by slow diffusion of diethyl ether into a 1:1 (v/v) methanol/acetonitrile solution. Diffraction experiments were performed on a Siemens P4 diffractometer equipped with a Siemens rotating anode, nickel filter, and modifed LT-1 low-temperature apparatus. Cu Kα radiation (λ = 1.541 78 Å) was employed. Only random fluctuations of less than 4% in the intensities of two standard reflections were observed during the course of data collection. The structure was solved by direct methods (SHELXTL v.5, Sheldrick, 1994). Non-hydrogen atoms were refined anisotropically. Hydrogen atoms were included at calculated positions by using a riding model. A total of 2372 reflections with $F > 2\sigma(F)$ were used

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(2) A survey of the existing literature reveals that although structural data for Cu(II) complexes containing $n \geq 1$ deprotonated amido N donor atoms are available, there is no example of a 5-coordinate Cu(II) complex with two deprotonated amido N and three other N donors in the first coordination sphere.

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Table 1. Summary of Crystal Data and Intensity Collection and Structure Refinement Parameters for [Cu(Py$_3$P)] (**2**)

formula (mol wt)	$C_{21}H_{19}N_5O_2Cu$ (436.95)	α, deg	73.550(14)
cryst color, habit	dark blue, block	β, deg	82.460(14)
T, K	130	γ, deg	69.980(14)
cryst system	triclinic	V, Å^3	912.0(3)
space group	$P\bar{1}$	Z	2
a, Å	8.695(2)	d_{calcd}, g cm^{-3}	1.591
b, Å	9.020(2)	abs coeff, μ, cm^{-1}	19.39
c, Å	12.914(2)	R^a	0.0334

^{a} $R = (\sum||F_o| - |F_c||)/\sum|F_o|$.

Table 2. Atomic Coordinates ($\times 10^4$) and Equivalent Isotropic Displacement Coefficients (Å^2 $\times$ 10^3) for **2**

	x	y	z	U(eq)
Cu	7262(1)	85(1)	2768(1)	22(1)
O1	8734(3)	−1504(3)	5869(2)	33(1)
O2	3458(2)	4309(2)	1909(2)	27(1)
N1	7411(3)	−2022(3)	2332(2)	22(1)
N2	8607(3)	−1233(3)	4044(2)	24(1)
N3	6123(3)	1280(3)	3829(2)	22(1)
N4	5507(3)	1869(3)	1862(2)	22(1)
N5	9033(3)	943(3)	1627(2)	23(1)
C1	6098(4)	−2190(4)	1993(2)	23(1)
C2	6011(4)	−3681(4)	1969(2)	25(1)
C3	7330(4)	−5060(4)	2321(2)	28(1)
C4	8693(4)	−4908(4)	2665(2)	26(1)
C5	8716(4)	−3371(3)	2654(2)	23(1)
C6	10187(4)	−3143(4)	2992(2)	28(1)
C7	9928(4)	−2755(4)	4090(2)	29(1)
C8	8143(4)	−795(3)	4967(2)	24(1)
C9	6704(4)	759(3)	4819(2)	23(1)
C10	5974(4)	1627(4)	5578(2)	27(1)
C11	4665(4)	3035(4)	5276(2)	30(1)
C12	4086(4)	3547(4)	4239(2)	28(1)
C13	4852(3)	2624(3)	3517(2)	23(1)
C14	4508(3)	3010(3)	2336(2)	22(1)
C15	5516(4)	2292(4)	686(2)	26(1)
C16	7191(4)	1437(4)	214(2)	26(1)
C17	8596(4)	1728(3)	601(2)	24(1)
C18	9413(4)	2757(4)	−59(2)	29(1)
C19	10734(4)	2920(4)	330(3)	32(1)
C20	11200(4)	2099(4)	1374(3)	29(1)
C21	10306(4)	1142(4)	2000(2)	27(1)

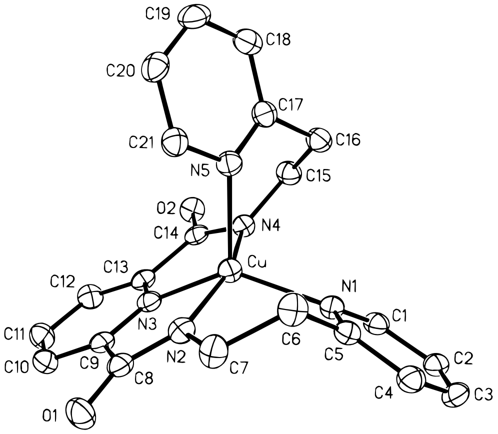

Figure 1. Thermal ellipsoid plot of **2** (50% probability level) showing the numbering scheme. H atoms are omitted for the sake of clarity.

Table 3. Selected Bond Distances (Å) and Angles (deg) for [Cu(Py$_3$P)] (**2**)

Bond Distances			
Cu−N1	2.089(2)	N3−C13	1.332(4)
Cu−N2	1.985(2)	N4−C14	1.339(4)
Cu−N3	1.942(2)	N4−C15	1.457(4)
Cu−N4	2.003(2)	N5−C17	1.347(4)
Cu−N5	2.172(2)	N5−C21	1.347(4)
N1−C1	1.344(4)	O1−C8	1.241(3)
N1−C5	1.354(4)	O2−C14	1.242(3)
N2−C8	1.331(4)	C6−C7	1.525(4)
N3−C9	1.332(4)	C15−C16	1.533(4)
Bond Angles			
N1−Cu−N2	91.21(9)	C1−N1−Cu	121.3(2)
N1−Cu−N3	139.21(9)	C5−N1−Cu	118.0(2)
N1−Cu−N4	104.76(9)	C9−N3−Cu	118.2(2)
N2−Cu−N3	79.68(10)	C13−N3−Cu	118.4(2)
N2−Cu−N5	102.06(9)	C17−N5−Cu	118.8(2)
N3−Cu−N4	79.96(10)	C21−N5−Cu	119.3(2)
N3−Cu−N5	119.62(9)	N2−C8−O1	128.1(3)
N4−Cu−N2	159.63(10)	N2−C8−C9	111.4(2)
N4−Cu−N5	87.40(9)	N4−C14−O2	127.9(3)
N5−Cu−N1	101.15(9)	N4−C14−C13	112.0(2)

in the refinement (full-matrix least-squares), and the data were corrected for absorption effects by the use of the program XABS 2.[5]

Machine parameters, crystal data, and data collection parameters are summarized in Table 1. Positional coordinates are included in Table 2, while selected bond distances and angles are listed in Table 3. The rest of the crystallographic data have been submitted as Supporting Information.

Results and Discussion

The presence of a base in the reaction mixture facilitates coordination of the deprotonated amido nitrogens to metal ions.[6] This fact makes copper (II) acetate an excellent starting material in methanol since acetate ions make the reaction medium sufficiently basic to allow coordination of the deprotonated amido nitrogens to copper.[3,7] In the present study, reaction of Py_3PH_2 with copper(II) acetate in methanol also affords [Cu(Py$_3$P)] (**2**) in high yield. When $Cu(ClO_4)_2 \cdot 6H_2O$ is used as the starting material, the desired complex **2** is formed only upon addition of 2 equiv of sodium acetate to the reaction mixture.

Structure of [Cu(Py$_3$P)] (2). The X-ray crystallographic study reveals that the crystals are composed of [Cu(Py$_3$P)] units. An ORTEP drawing of **2** is shown in Figure 1, and the metric parameters are listed in Table 3. The Cu(II) ion is coordinated to five N atoms, and the coordination geometry around Cu is distorted square-pyramidal. Two deprotonated amido nitrogens and two nitrogens from the pyridine rings reside in the basal plane while one pyridine nitrogen occupies the axial position. The central pyridine ring and the two deprotonated amido moieties are essentially coplanar, and the two N−Cu−N angles associated with this portion of **2** are considerably smaller (∼80°) than the ideal value of 90° (Table 3). The N−Cu−N angles in the six-membered chelate rings are however close to 90° except for N1−Cu−N4, which is quite large (104.7°). Deviations from idealized square-pyramidal geometry are evident in the way the basal plane is drawn away from the axial N (N1−Cu−N3 angle is 139.2°), and the central copper atom is located 0.41 Å above the mean basal plane (Figure 1). The average Cu−N(peptide) bond distance (1.994(2) Å) of **2** is well within the range noted for peptide complexes of bivalent copper.[3,4,7,8] Three noticeably different Cu−N(pyridine) bond lengths are observed in **2**. The long Cu−N5 bond 2.172(2) Å reflects weak axial interaction which is typical for Jahn−Teller-sensitive copper (II) complexes. The Cu−N1(pyridine) bond length (2.089(2) Å) is however

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close to the typical Cu−N(pyridine) distances (2.0−2.1 Å).[4,9−12] Quite in contrast, the Cu−N3 bond length of **2**, which is part of two five-membered chelate rings with delocalized electron density, is considerably shorter (1.942(2) Å).[13] Similar short and long Cu−N(pyridine) bond lengths are also observed in the Cu(II) complex of a Schiff base derived from 2,6-diacetylpyridine and 2-(2-aminoethyl)pyridine.[10]

Properties. Coordination of the deprotonated amido nitrogens to copper in **2** is indicated by the shift of ν_{co} from 1654 cm^{-1} for the free ligand to 1609 cm^{-1} for the copper complex. In the visible region of the electronic absorption spectrum, **2** exhibits a broad band with maximum at ~613 nm ($\epsilon \approx 200$ $M^{-1}\ cm^{-1}$) with a shoulder around 750 nm. This spectrum is characteristic of a tetragonally distorted Cu(II) complex where the bands arise from the $d_{xz}(d_{yz}) \rightarrow d_{x^2-y^2}$ and $d_{xy} \rightarrow d_{x^2-y^2}$ transitions. The high extinction coefficient associated with the d−d transition(s) and the shoulder are both indicative of low-symmetry 5-coordinate copper complexes.[14] Comparison of the structural features of **2** with those of [Cu(PMA)]X (X = ClO_4^-, BF_4^-) reveals that the coordination geometry around copper is more distorted in **2**. Quite in line with this, [Cu(PMA)]X exhibits a more symmetric band at 612 nm with a lower extinction coefficient of 130 $M^{-1}\ cm^{-1}$.[3] Electrochemical measurements indicate that, in aqueous solution, **2** is irreversibly oxidized at a potential of 1.05 V (vs aqueous SCE). This value is close to the oxidation potentials of copper complexes of peptide ligands containing aromatic amino acids.[15]

The X-band EPR spectrum of **2** in methanol glass (100 K) is shown in Figure 2. The spectrum ($g_\perp = 2.20$ and $g_\| = 2.04$ with $A_\| = 154$ G) resembles the EPR spectra of monomeric tetragonal Cu(II) complexes with a $d_{x^2-y^2}$ ground state. Although no well-resolved superhyperfine coupling to first coordination sphere donor atoms is detected (Figure 2), some structural information could be inferred from the EPR parameters. The *g* values of **2**, which are very close to the *g* values of Cu(II)−BLM[16] and model complexes like [Cu(PMA)]X (X = ClO_4^-, BF_4^-),[3] [Cu(HAPH)][ClO_4]·1.6H_2O,[4] and others,[17,18] are indicative of a distorted square-pyramidal CuN_5 chromophore. The hyperfine coupling constant $A_{||}$ of **2** however, is significantly lower than the $A_\|$ values of Cu(II)−BLM and its models (range = 177−215 G).[3,4,17] The smaller $A_\|$ value of **2** is presumably associated with (a) the off-planar distortion observed in the crystal structure of this complex and (b) the weaker in-plane crystal field strength.[18] Since the Cu(II) center of **2** lies significantly above the mean basal plane, the in-plane crystal field strength appears to be weak despite coordination by deprotonated amido N's. Indeed, in $[Cu(HAPH)]^+$, the copper center resides in a more symmetric environment and exhibits an $A_{||}$ value of 215 G.[4] Miyoshi et al. have shown that stronger axial coordination results in lowering of $A_\|$ values in tetragonal Cu(II) complexes.[18] The axial donor groups in the three copper complexes $[Cu(PMA)]^+$, $[Cu(HAPH)]^+$, and **2** are a primary amine (NH_2), an imidazole, and a pyridine ring, respectively. That the pyridine N is the strongest donor in this list is evident from the lowest $A_\|$ value noted for **2**.

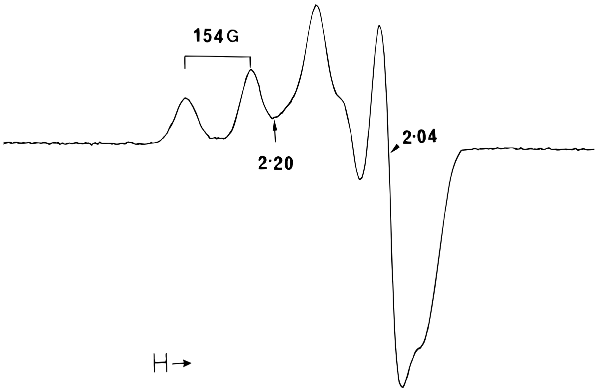

Figure 2. X-band EPR spectrum (100 K) of **2** in methanol glass. Selected *g* and *A* values are indicated. Spectrometer settings: microwave frequency, 9.43 GHz; microwave power, 13 mW; modulation frequency, 100 kHz; modulation amplitude, 2G.

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Supporting Information Available: Anisotropic thermal parameters for non-hydrogen atoms (Table S1), positional and isotropic hydrogen atom parameters (Table S2), and bond distances and angles (Tables S3 and S4) for complex **2** (4 pages). Ordering information is given on any current masthead page.

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