Synthesis and Structure of a New Tripodal Polypyridine Copper(II) Complex That Enables to Recognize a Small Molecule

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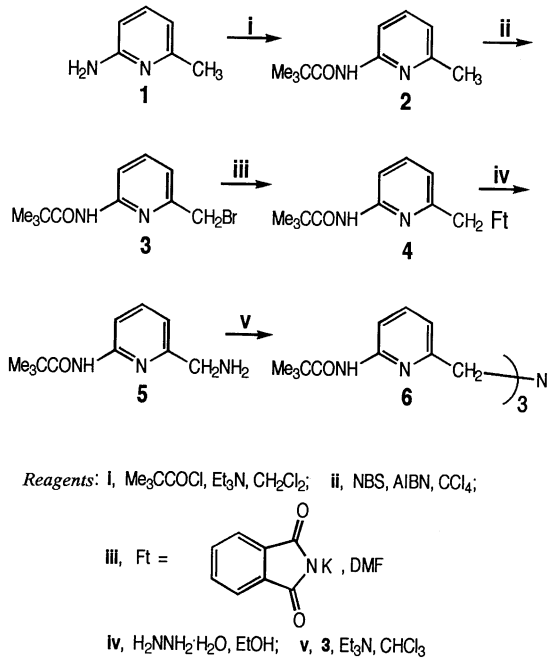
With a view to constructing an artificial metalloenzyme model complex which can recognize and capture a small molecule, a new tripodal ligand, tris(6-pivaloylamino-2-pyridylmethyl)amine, and its mononuclear copper(II) complex has been synthesized, and they were characterized by ^{1}H-NMR and positive-ion FAB mass spectra, cyclic voltammetry and X-ray structure analysis.

The enzymatic reactions in biological systems are initiated with the formation of enzyme-substrate complexes, which are achieved by the presence of an appropriate vacant space and of an accurate molecular recognition system for the substrates.[1-3] The relevant arrangement of bulky hydrophobic tert-butyl and/or phenyl groups and a combination of non-covalently interacting groups, such as hydrogen bonding, electrostatic bonding, hydrophobic bonding, and coordinative bonding, are essential for host-guest chemistry that accompanies the molecular recognition; it leads to the construction of an artificial enzyme model. Here we report the synthesis of a new tripodal tetradentate ligand, tris(6-pivaloylamino-2-pyridylmethyl)amine (TPPA), and the structural characterization of its copper(II) complex, which has some non-covalent interaction sites. These interaction sites play a specific function for (i) the formation of a stable tetradentate chelate complex with metal ion, (ii) the fixation of an externally-introduced small molecule by three hydrogen-bonding NH groups, (iii) the binding of the small molecule in an appropriate coordination sphere, and (iv) prevention of dinuclear complex formation.



Scheme 1.

TPPA was prepared from 2-amino-6-methylpyridine **1** in five steps, as shown in Scheme 1. To a CH_2Cl_2 (100 mL) solution of **1** (100 mmol) was added dropwise pivaloyl chloride (110 mmol) in the presence of triethylamine (130 mmol), and then stirred at room temperature for 2 h. The crude product obtained was purified by recrystallization with ether to give **2** (83.6 % yield). **2** (55 mmol) was brominated with NBS (27.5 mmol) and catalytic amount of AIBN in CCl_4 under a nitrogen atmosphere. The reaction mixture of monobromide **3**, dibromide (by-product), and unreacted **2** was separated by silica gel column chromatography with a hexane/AcOEt eluate. The compound **3** (22.6 mmol) was treated with potassium phthalimide (22.6 mmol) in DMF solution (150 mL) under reflux for 30 min to give **4**. The ethanol solution (100 mL) of **4** (10 mmol) and hydrazine monohydrate (10 mmol) was refluxed for 2 h to give the primary amine product **5** (74.7 % yield). The amine **5** (4 mmol) was coupled with an excess of the bromide **3** in $CHCl_3$ solution (50 mL) in the presence of triethylamine (12 mmol) at 50 °C for 3 h. After the usual workup, the transparent needle-like crystal of **6** (TPPA)[4] was isolated (30.2 % yield) through recrystallization from $CHCl_3$/AcOEt/hexane (1:1:10) solution.

The copper(II) complex with TPPA was prepared by the addition of TPPA (1.5×10^{-2} mmol) to an acetone solution (2 mL) of anhydrous $CuCl_2$ (1.5×10^{-2} mmol) at room temperature, which resulted in an immediate color change from yellow to green. The resulting solution was treated by $NaClO_4$ (1.65×10^{-2} mmol). After the addition of methanol (1 mL) and water (1 mL), the solution was allowed to stand for a few days in a refrigerator to give a yellowish green crystal **7** (83.0 % yield).[5]

The X-ray crystal structure established for [Cu(tppa)Cl]ClO_4 **7**,[6] as shown in Figure 1, revealed that the coordination environment around the central copper atom is an axially-compressed trigonal-bipyramid with three pyridine nitrogen atoms in the equatorial positions (Cu - N(2a) = 2.148(5), Cu - N(2b) = 2.137(5), Cu - N(2c) = 2.314(6) Å) and with *tert*-amine nitrogen (Cu - N(1) = 1.955(5) Å) and chloride atoms (Cu - Cl = 2.206(2) Å) in the axial positions. Such a structural geometry is also supported from the well-separated *d-d* band in the absorption spectrum (740 and 860 nm). The copper atom is displaced by 0.40 Å toward the chloride atom from the mean plane defined by three pyridine-nitrogen atoms. All three N-H vectors directed toward the chloride anion (Cl···N(3a) = 3.19, Cl···N(3b) = 3.15, Cl···N(3c) = 3.24 Å), which suggests the formation of hydrogen bonding with the chloride anion. The three *tert*-butyl groups approach one another and form a hydrophobic space in such a manner that they protect the chloride atom, which implies that the copper coordination sphere surrounded by three pivaloylamino groups can hold a relevant-sized molecule such as chloride anion.

The complex exhibits a very interesting one-electron redox reversible cyclic voltammogram in CH_3CN/0.1 M (n-Bu_4N)BF_4.

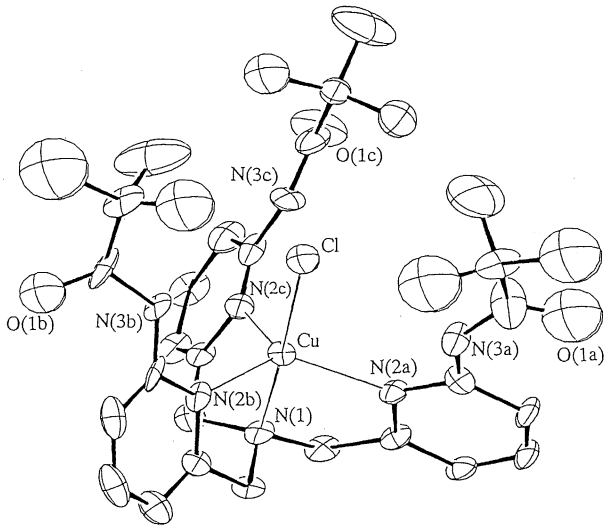


Figure 1. ORTEP representation of the structure of the $[Cu(tppa)Cl]^+$ cation (**7**) with atom-labeling scheme. Thermal ellipsoids are drawn at the 50 % probability level.

The observed redox potential is +0.225 V vs. Ag/AgCl (or +0.447 V when converted to the NHE scale by the addition of +0.222 V), which is much significantly higher than that observed for $[Cu(tpa)Cl]PF_6$ (-0.39 V vs. NHE).[7] This high anodic potential value may have been caused by the unique coordination geometry and sphere, which is favourable for the Cu(I) complex and leads to a mild affinity for dioxygen molecule.[8]

Current efforts are being devoted to further exploring the recognition ability of **7** with various small guest molecules by use of convergent non-covalent interaction groups.

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References and Notes

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4 *Physical and spectroscopic data* for **6**: Positive-ion FAB mass m/z = 588 $[TPPA + H]^+$ and 610 $[TPPA + Na]^+$. Anal. Calcd for $C_{33}H_{45}N_7O_3$: C, 67.44; H, 7.72; N, 16.68;. Found: C, 67.24; H, 7.61; N, 16.60; ^{1}H-NMR: δ(CD_3CN) 8.18 (s, 3H, N-H), 7.99 (d, J 7.8 Hz, 3H, 5-H(py)), 7.70 (t, J 7.8 Hz, 3H, 4-H(py)), 7.33 (d, J 7.8 Hz, 3H, 3-H(py)), 3.74 (s, 6H, -CH_2-), 1.27 (s, 27H, t-Bu).

5 *Physiscal and spectroscopic data* for **7**: Positive-ion FAB mass m/z = 685 $[Cu(tppa)Cl]^+$; Anal. Calcd for $C_{33}H_{45}N_7O_7CuCl_2$: C, 50.40; H, 5.78; N, 12.47; Cl, 9.02. Found for crystals of **7**: C, 50.30; H, 5.65; N, 12.55; Cl, 8.98.

6 *Crystal data* for **7**: $C_{33}H_{45}N_7O_7CuCl_2$, M_W = 786.30, orthorhombic, space group *Pccn*; a = 11.601(2), b = 35.355(5), c = 18.401(2) Å, V = 7547.1 Å^3, Z = 8, D_C = 1.384 g cm^{-3}; Mo-Kα (λ = 0.71073 Å); μ = 8.09 cm^{-1}, 3 < 2θ < 55°. Intensity data collected at room temperature on an Enraf-Nonius CAD4-EXPRESS four-circle diffractometer; structure solved and refined using SDP-MolEN program system, absorption correction was applied by DIFABS. 11080 Unique reflections of which 5486 [$I > 3\sigma(I)$] are observed. The structure was solved by the heavy-atom method and refined anisotropically. Hydrogen atoms were included in the calculation, but they were not refined. Final R and R_W factors were 0.0818 and 0.1158, respectively.

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