Molecular Recognition by a Cu(II)-2,2′-bipyridine Complex Involving Coordination and Hydrogen Bonding

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A novel Cu(II) complex bearing a 2,2′-bipyridine derivative with malonylamide moieties showed regioselective molecular recognition behaviour toward *m*-aminobenzoic acid by both coordination and hydrogen bonding and this recognition should be an induced fit to the flexible recognition site of the Cu(II) complex.

Multipoint molecular recognition is a ubiquitous and indispensable event in catalysis of selective chemical conversion by enzymes, transport of ions and materials, and construction of highly organized structures as observed in proteins and DNA.[1] Metal complexes as host molecules allow us to use ligation of guest molecules as stronger interaction between host and guest molecules as observed in Rh(III)–porphyrin systems reported by Aoyama and co-workers,[2] Zn(II)–polyamine complexes by Kimura and co-workers,[3] and a Cd(II) complex by Chin and co-workers.[4] Concerning the choice of a metal ion in a host molecule, substitution-labile metal ions such as Cu(II) are useful to gain high selectivity in guest binding by strong requirement for combination of both coordination and noncovalent interaction, in contrast to substitution-inert metal ions which could hold the external guest only by coordination. In the case of Cu(II) complex, an axial coordination is essentially weakened by Jahn–Teller effect and, therefore, the aid of noncovalent interaction is necessary toward the axial binding of the guest molecule.

Toward our goal to perform highly selective molecular recognition based on complementary binding of a guest molecule by metal coordination concomitant with noncovalent interaction, we have synthesized a novel 2,2′-bipyridine (bpy) derivative having two ethyl dimethylmalonylamide moieties, bembpy (6,6′-bis(ethyl dimethylmalonylamido)-2,2′-bipyridine), and its Cu(II) complex.[5] We present herein molecular recognition by the complex toward carboxylic acids through weak metal coordination at an axial position and hydrogen bonding to the malonyl moiety. In our present system, in the case of aminobenzoic acids as substrates, only the *m*-isomer binds in the recognition site of the complex.

A molecular recognition device (**1**), $[Cu(NO_3)_2(bembpy)]$, was synthesized via the reaction of bembpy with $Cu(NO_3)_2$ in MeOH in good yield. The crystal structure of **1** was determined by X-ray crystallography and its ORTEP drawings are shown in Figure 1.[6] Selected bond lengths and angles are listed in the figure caption.

In solution, the apical nitrate ligands were found to dissociate to form vacant sites for substrate binding, judging from ESIMS spectrum[7] of **1** in MeOH in which peaks due to $\{[Cu(bembpy)]^{2+}\text{-}H^+\}^+$ were observed and no NO_3^--bound species.

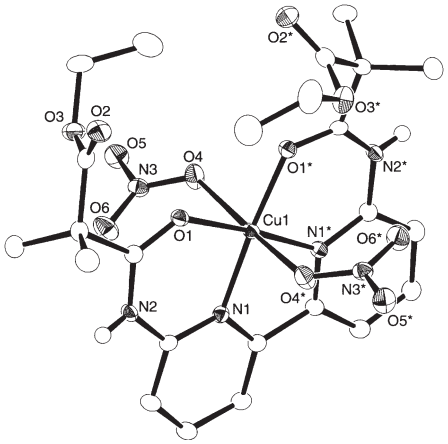


Figure 1. An ORTEP drawing of **1** with 50% probability thermal ellipsoids. Selected bond lengths (Å) and angles (deg): Cu(1)–O(1), 1.936(1); Cu(1)–N (1), 1.953(2); Cu(1)–O(4), 2.407(2); N(1)–Cu(1)–N(1*), 83.63(9); O(1)–Cu(1)–N(1), 91.89(6); O(1)–Cu(1)–O(1*), 92.62(8).

We examined **1** as a receptor for carboxylic acids and revealed interesting feature of molecular recognition by **1**. Aminobenzoic acids were submitted as guest molecules (Scheme 1) in the presence of equimolar 2,6-dimethylpyridine and it was found that only *m*-aminobenzoic acid formed 1:1 and 1:2 adducts among three isomers. UV–vis spectra of the mixtures of **1** and *m*-aminobenzoic acid showed spectral change; the original host complex showed absorption maxima due to d–d transitions at 642 nm ($\varepsilon = 1.2 \times 10^2\,M^{-1}cm^{-1}$) and 388 nm ($\varepsilon = 3.2 \times 10^2\,M^{-1}cm^{-1}$) in MeOH. Upon adding the *m*-aminobenzoic acid (0.5 to 10-fold relative to **1**) to the solution, the spectrum was changed to show absorption maxima at 633 and 404 nm without having clear isosbestic point. These results suggest that *m*-aminobenzoic acid is bound to the Cu(II) center of **1** by coordination to be recognized. ESIMS spectrum of the reaction mixture of **1** (1×10^{-4} M) and *m*-aminobenzoic acid in DMF and also in MeOH showed signals assigned to [Cu(*m*-aminobenzoato)(bembpy)]$^+$ (**2**; Figure 2) at 669.4 which were consistent with a computer simulation. In addition to that, weaker signals due to a protonated form of a 1:2 adduct ($\{[Cu(m\text{-aminobenzoato})_2(bembpy)]+H^+\}^+$) were observed at 807.3, which was also consistent with its simulation. In sharp contrast, *o*- and *p*-aminobenzoic acids did not show any spectral change in UV–vis spectra and any peaks assigned to their adducts in ESIMS spectra. The selectivity of **1** toward aminobenzoic acids is different from the system reported by Aoyama and co-workers.[2] It should be noted that a remote functional group could

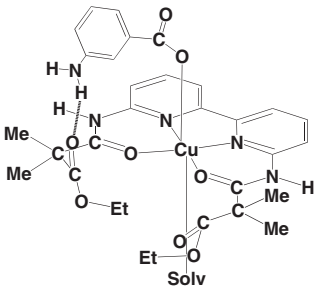
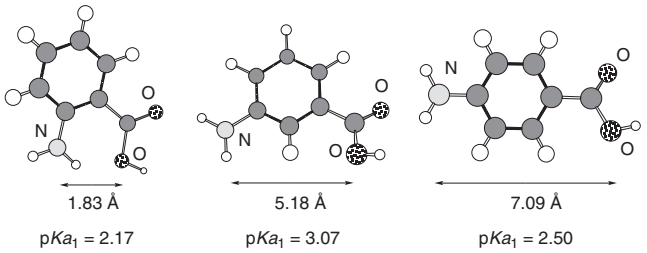


Figure 2. A proposed structure of the adduct **2**.

be recognized in our system. In addition, Fish and co-workers have reported that a Rh–nucleoside trimer host could recognize aminobenzoates with mainly π–π interaction in water and the *o*-isomer was found the most favorable guest because of stronger hydrophobic interaction with the host molecule.[8] In this case, the amino and carboxyl groups direct to aqueous phase to form hydrogen bonding with H_2O and no significant interaction with host molecules. Thus, the selectivity and recognition mode in our present system are unique in recognition systems reported so far.

In order to ascertain the factors of recognition behavior of **1**, several experiments were examined. When *m*-diaminobenzene was submitted as a substrate, no adduct was observed in ESIMS spectrum of the reaction mixture to indicate that the carboxyl group is necessary to be recognized. On the other hand, carboxylic acids without any other functional groups such as isobutylic acid and benzoic acid did not afford any adducts either, pointing out that the hydrogen bonding is concomitantly required for the recognition. A Cu(II) complex without recognition sites, $[Cu(NO_3)_2(babpy)]$ (babpy = 6,6′-bis(acetoamido)-2,2′-bipyridine),[9] was exmanined as a host molecule. In contrast to the case of **1**, no spectral change was observed in UV–vis spectrum upon the addition of *m*-aminobenzoic acid in methanol. This result indicates that the malonyl moieties are required to recognize the guest and to form the adduct. In addition, *m*-pivalamide-benzoic acid was also adopted as a guest molecule under the same conditions to exhibit no adduct formation. This indicates that steric effects is also important for the recognition behaviour of **1**. Thus, we propose the structure of the adduct between **1** and *m*-aminobenzoic acid as shown in Scheme 1. In the adduct, the hydrogen bonding should be formed with the ester C=O oxygen rather than the C–O oxygen because the basicity of the C=O oxygen is larger than that of the C–O oxygen as observed in a mechanism of acid-catalyzed ester hydrolysis.[10]

The recognition behavior by **1** toward *m*-aminobenzoic acid was given further scrutiny in viewpoint of structural aspects. The distance between the Cu(II) center of **1** and one of carbonyl oxygen of the ester moieties was found to be 5.08 Å by X-ray crystallography. On the other hand, the distances between carboxyl oxygen of aminobenzoic acids and their amino hydrogen was estimated by MM2 calculations to be 1.83 Å for the *o*-isomer, 5.18 Å for the *m*-isomer, and 7.09 Å for the *p*-isomer, respectively, as shown in Scheme 1. Obviously, only the *m*-isomer fits to the receptor sites of **1**. Concerning the acidity of the guest molecule, the *m*-isomer is least acidic in comparison of pK_a values of



Scheme 1. MM2-optimized structures of aminobenzoic acids.

the three isomers as shown in Scheme 1. This suggests that the acidity is not responsible in the guest binding and the selectivity. As the ethyl dimethylmalonyl functionality should have certain flexibility in solution, the fixation of the *m*-aminobenzoic acid is thought to be an induced fit. In sharp contrast to the substitution-inert Rh(III) center,[2] the lability of the axial position at the Cu(II) center enhances the selectivity of **1** because the complementary noncovalent interaction such as hydrogen bonding in this case is indispensable to achieve the adduct formation in addition to the coordination of the carboxyl group.

In conclusion, the complex **1** can recognize *m*-aminobenzoic acid selectively via a two-point recognition by means of coordination of the carboxyl group and probably hydrogen bonding between the amino group and the carbonyl oxygen of the ester moiety of the side arm.

References and Notes

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