Reaction of Hydroxo Complexes of Divalent Metal Ions with Amide

Shiro Hikichi, Masako Tanaka, Yoshihiko Moro-oka and Nobumasa Kitajima*

Research Laboratory of Resources Utilization, Tokyo Institute of Technology, 4259 Nagatsuta, Midori-ku, Yokohama 227, Japan

Reaction of hydroxo complexes of copper(II) and nickel(II) with *p*-nitroacetanilide gave chelated amido complexes and the structure of the copper(II)–amido complex was determined by X-ray crystallography.

Many hydrolytic metalloenzymes possessing divalent metal ions (Zn, Mg, Mn, Co and Ni) at the reactive centre are known.[1] It has been suggested that a metal hydroxide intermediate which is produced by the deprotonation of metal-coordinated water attacks the substrate nucleophilically in the catalytic process.[2] We have recently reported that a series of hydroxo complexes of Mn^{II}, Fe^{II}, Co^{II}, Ni^{II}, Cu^{II} and Zn^{II} with the tripodal ligand L [L = hydrotris(3,5-diisopropylpyrazol-1-yl)borate] exhibit very high nucleophilic reactivities, even reacting with atmospheric CO_2.[3]† Furthermore, the P–O bond in tris- and bis-phosphate esters is cleaved by the hydroxozinc(II) complex.[4] The reactivity of these hydroxo complexes toward *p*-nitroacetanilide is reported in this communication.[5]

Treatment of the bis(μ-hydroxo)copper(II) complex $[\{CuL(OH)\}_2]$ **1**[6] with 2 equiv. of *p*-nitroacetanilide in Et_2O under argon yielded a deprotonated amido complex **2** quantitatively.‡ The structure of **2** was determined by X-ray crystallography and a perspective view is given in Fig. 1. The geometry of copper ion is best described as square-pyramidal with one nitrogen atom from the tris(pyrazolyl)borate at an apical position. Both amide nitrogen and oxygen are bound to the copper equatorially, leading to the formation of a four-membered ring. The amide methyl and phenyl groups lie on the plane consisting of the four-membered ring and adopt a *cis*-configuration, whereas alkyl groups on amides usually strongly favour a *trans* arrangement. Although a number of copper(II) peptide or amido complexes with deprotonated amides have been reported, a chelated coordination mode for amides as found in **2** has been reported only very recently by Chin and coworkers.[8] To our knowledge, this cobalt(III) benzamido complex[8] is the only previous example of a structurally characterized chelated transition metal–amido complex. Bond lengths and angles in the amide group of **2** are summarized in Table 1 and are compared with those reported for the cobalt(III) benzamido complex. It is known that the C–N and C–O bonds of free amide possess comparable amounts of single and double bond character (40% double bond character in C–N).[7] In the amido chelated complex **2** and the cobalt(III) complex, both of the C–N and C–O bonds are intermediate between typical single and double bond values as found in free amides. The C–O bond lengths of both amido chelated complexes are slightly elongated relative to the amide, which implies a greater degree of delocalization of negative charge. The O–C–N angles found in **2** and the cobalt(III) complex are smaller than that of free amide owing to chelation (Table 1).

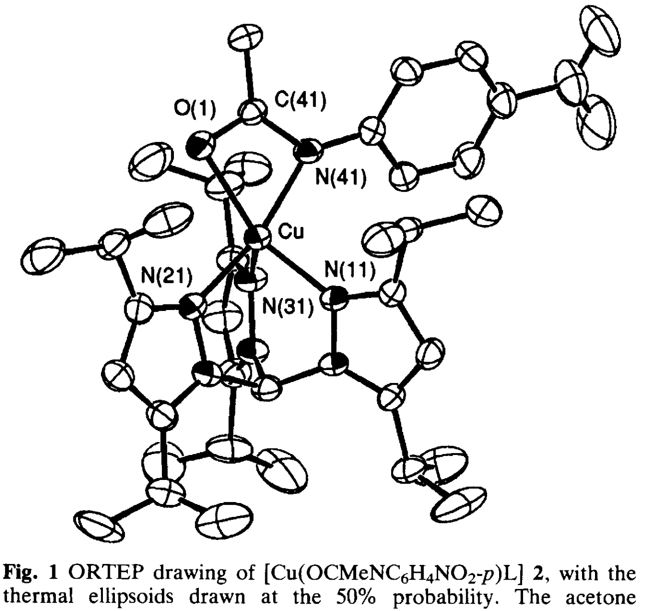
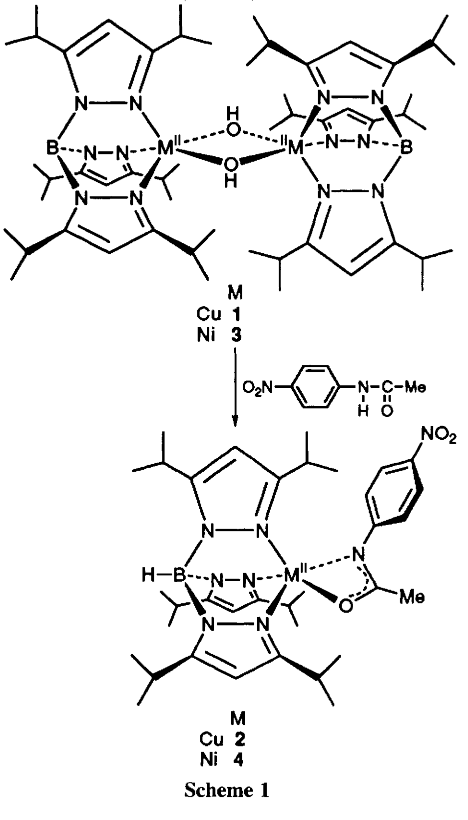


Fig. 1 ORTEP drawing of $[Cu(OCMeNC_6H_4NO_2\text{-}p)L]$ **2**, with the thermal ellipsoids drawn at the 50% probability. The acetone molecule of crystallization is omitted for clarity. Selected bond distances (Å) and angles (°) are: Cu(1)–O(1) 2.109(3), Cu(1)–N(11) 1.983(3), Cu(1)–N(21) 1.964(3), Cu(1)–N(31) 2.184(3), Cu(1)–N(41) 1.994(3), O(1)–C(41) 1.278(4), N(41)–C(41) 1.326(5), O(1)–Cu(1)–N(11) 152.7(1), O(1)–Cu(1)–N(21) 102.6(1), O(1)–Cu(1)–N(31) 111.3(1), O(1)–Cu(1)–N(41) 64.2(1), N(11)–Cu(1)–N(21) 89.6(1), N(11)–Cu(1)–N(31) 92.8(1), N(11)–Cu(1)–N(41) 100.6(1), N(21)–Cu(1)–N(31) 90.1(1), N(21)–Cu(1)–N(41) 166.0(1), N(31)–Cu(1)–N(41) 98.9(1), Cu(1)–O(1)–C(41) 88.7(2), Cu(1)–N(41)–C(41) 92.4(2), O(1)–C(41)–N(41) 113.9(3).

In the reaction of $[\{NiL(OH)\}_2]$ **3**[3] with 2 equiv. of *p*-nitroacetanilide, a yellowish-green compound **4**§ was formed quantitatively. The FD-MS analysis suggested the formulation of **4** as $[Ni(OCMeNC_6H_4NO_2\text{-}p)L]$. The IR spectrum of **4** did not exhibit a band attributable to the amide ν(NH). In addition, the UV–VIS spectrum of **4** in toluene showed a band (ε = 70 $dm^3\ mol^{-1}\ cm^{-1}$) at 670 nm. This spectral feature is very similar to other structurally characterized five-coordinate nickel pyrazolylborate complexes **3** and $[(NiL)_2(\mu\text{-}CO_3)]$.[3] Based on these characteristics, **4** is identified as a deprotonated amido chelated complex which is isostructural with the copper complex **2**.



Scheme 1

Table 1 Bond lengths and angles of amido group

	C–N/Å	C–O/Å	O–C–N/°
2	1.326(5)	1.278(4)	113.9(3)
$[Co(PhCONH)L'']^{2+}$	1.32(1)	1.28(1)	111.5(9)
Free amide[7]	1.32	1.24	125
Double bond[7]	1.24	1.20	—
Single bond[7]	1.45	1.42	—

L″ = 1,4-dimethyl-1,4,7,10-tetraazacyclododecane

Whereas the copper(II) and nickel(II) complexes react with the amide readily, hydroxo complexes of Zn^{II}, Co^{II} and Mn^{II} did not react with amide to give deprotonated amido complexes. Mixtures of these hydroxo complexes and 2 equiv. of *p*-nitroacetanilide were stirred in Et_2O at room temperature for 12 hours, but only starting materials were recovered quantitatively. Although the acidity of the amide proton is low, the series of hydroxo complexes are highly basic so as to react with atmospheric CO_2; the order of reactivities toward CO_2 is $Zn > Cu > Ni \approx Co > Mn$.[3] Thus, the inertness of the hydroxo complexes Zn^{II}, Co^{II} and Mn^{II} is not due to their low nucleophilicity. The reaction pattern of these hydroxo complexes is also not correlated with the order of peptidase activities known for metal-substituted carboxypeptidase A (CPA); copper(II)-substituted CPA shows only a very low activity, whereas Ni^{II}–, Co^{II}– and Mn^{II}–CPA exhibit a catalytic activity comparable to native Zn^{II}–CPA.[9] Rather, the reactivity of hydroxo complexes towards amide is compatible with the degree of distortion in coordination observed for a series of μ-carbonato complexes $[(ML)_2(\mu\text{-}CO_3)]$: Zn (unidentate and bidentate) > Co ≈ Mn (unsymmetric bidentate) > Cu ≈ Ni (symmetric bidentate).[3] Similar geometric distortion has been reported for $[ML'(NO_3)][L' = HB(C_3N_2H_2Bu^t\text{-}3)_3]$, Zn (unidentate) > Co (unsymmetric bidentate) > Cu = Ni (symmetric bidentate).[10] Therefore, the reactivity of the hydroxo complexes toward the amide may be associated with the stability of the tightly bound four-membered ring of the formed chelated amido complexes.

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Footnotes

† The hydroxo complexes, except for the zinc complex, have dinuclear structures bridged by a bis(hydroxo) unit as ascertained by X-ray analysis. The structure of the zinc complex is monomeric as established by spectroscopy.[11]

‡ *Spectroscopic and crystallographic data for* **2**: Satisfactory elemental analysis was obtained. IR (KBr pellet, ν/cm^{-1}); 2539 (BH), 1616, 1592, 1576, 1569, 1558, 1538, 1515. UV-VIS (CH_2Cl_2, λ/nm, ε/dm^3 mol^{-1} cm^{-1}); 338 (ε = 2700), 706 (150). FD-MS; *m/z* 708. **2**·Me_2CO crystallized in the triclinic space group $P\bar{1}$ with a = 13.050(6), b = 19.357(5), c = 9.267(3) Å, α = 98.02(3), β = 91.90(4), γ = 115.25(2)°, V = 2085(2) Å^3, Z = 2, D_c = 1.22 g cm^{-3}. The structure was solved by the Patterson method, and refined with anisotropic thermal parameters for all non-hydrogen atoms except the solvent molecule. The final R (R_W) value was 0.0521 (0.0486) for 5364 reflections [$I > 3\sigma(I)$, $3 \leq 2\theta \leq 50°$]. Atomic coordinates, bond lengths and angles, and thermal parameters have been deposited at the Cambridge Crystallographic Data Center. See Information for Authors, Issue No. 1.

§ *Spectroscopic data for* **4**: Satisfactory elemental analysis was obtained. IR (KBr pellet, ν/cm^{-1}); 2540 (BH), 1616, 1593, 1576, 1569, 1560, 1538, 1511. UV-VIS (CH_2Cl_2, λ/nm, ε/dm^3 mol^{-1} cm^{-1}); 341 (1500), 670 (70). FD-MS; *m/z* 703.

References

1 K. D. Karlin, *Science*, 1993, **261**, 701 and references cited therein.
2 D. W. Christianson and W. N. Lipscomb, *Acc. Chem. Res.*, 1989, **22**, 62.
3 N. Kitajima, S. Hikichi, M. Tanaka and Y. Moro-oka, *J. Am. Chem. Soc.*, 1993, **115**, 5496.
4 S. Hikichi, M. Tanaka, Y. Moro-oka and N. Kitajima, *J. Chem. Soc., Chem. Commun.*, 1992, 814.
5 Recent examples of amide hydrolysis with hydroxo–metal complexes: M. Ruf, K. Weis and H. Vahrenkamp, *J. Chem. Soc., Chem. Commun.*, 1994, 135; N. N. Murthy, M. Mahroof-Tahir and K. D. Karlin, *J. Am. Chem. Soc.*, 1993, **115**, 10404; B. K. Takasaki, J. H. Kim, E. Rubin and J. Chin, *J. Am. Chem. Soc.*, 1993, **115**, 1157; T. H. Fife, *Persp. Bioinorg. Chem.*, 1991, **1**, 43.
6 N. Kitajima, K. Fujisawa, C. Fujimoto, Y. Moro-oka, S. Hashimoto, T. Kitagawa, K. Toriumi, K. Tatsumi and A. Nakamura, *J. Am. Chem. Soc.*, 1992, **114**, 1277.
7 H. Sigel and R. B. Martin, *Chem. Rev.*, 1982, **82**, 385.
8 J. H. Kim, J. Britten and J. Chin, *J. Am. Chem. Soc.*, 1993, **115**, 3618.
9 J. E. Coleman and B. L. Vallee, *J. Biol. Chem.*, 1961, **236**, 2244; R. D. Dua and K. K. Gupta, *Biochem. Int.*, 1984, **9**, 379; M. D. Bond, B. Holmquist and B. L. Vallee, *J. Inorg. Biochem.*, 1986, **28**, 97; A. Schäffer and D. S. Auld, *Biochemistry*, 1986, **25**, 2476.
10 R. Han and G. Parkin, *J. Am. Chem. Soc.*, 1991, **113**, 9707.
11 [ZnL(OH)] has also been characterized independently by A. Looney, R. Han, K. McNeill and G. Parkin, *J. Am. Chem. Soc.*, 1993, **115**, 4690.