Fixation of CO_2 by Hydroxozinc(II) Complex with Pyridylamino Type Ligand

Syuhei Yamaguchi, Teppei Takahashi, Akira Wada, Yasuhiro Funahashi, Tomohiro Ozawa, Koichiro Jitsukawa, and Hideki Masuda*
Department of Applied Chemistry, Graduate School of Engineering, Nagoya Institute of Technology, Showa-ku, Nagoya 466-8555

(Received April 16, 2007; CL-070411; E-mail: masuda.hideki@nitech.ac.jp)

Reaction of hydroxozinc(II) complex bearing amino group with CO_2 gave carbamate product, whose generation and reaction mechanism have been studied structurally and spectroscopically as a structural/functional model of biotin-dependent carboxylase.

Carbon is an essential element for all the lives on the earth, the most of which is locked in highly oxidized forms such as carbon dioxide and carbonate minerals in air and the earth, respectively.[1] In order to utilize them effectively, the living things employ them by change into organic compounds that are rich in carbon–carbon bonds and are decorated with hydrogen atoms, through biological systems such as photosynthesis and syntheses.[1] Carbamato moieties are key components in these biological CO_2 fixation to organic substrates, which are catalyzed by magnesium-containing enzymes such as ribolose-1,5-bisphosphate carboxylase/oxygenase (rubisCO) and biotin-dependent enzymes (pyruvate carboxylase, etc.).[2] The mechanism of the transfer reaction and the role of metal ions are not well understood yet, although many chemists study hard for converting carbon dioxide into carbamato derivatives.[3] Carbamato moieties are also found out in dinickel–urease and dizinc–phosphotriesterase, hydrolytic enzymes, in which carbamato ligands are formed by reaction of lysine residue with CO_2 to play as the bridging ligand for the two metal ions.[2]

In the course of model study for carbonic anhydrase[4] using the hydroxozinc(II) complex containing tripodal ligand, tris(6-amino-2-pyridylmethyl)amine (TAPA),[5] we discovered quite unique reactions between the pyridyl amino group of $[Zn(tapa)(OH)]^+$ and carbon dioxide, which is very similar to that between biotin and carbon dioxide in pyruvate carboxylase reaction.[2] The structure and binding behavior are considered to be a good structure and reaction model for the biotin-Mg–H_2O system in the biological system. Here, we describe the binding reaction of carbon dioxide by hydroxozinc(II) complex of TAPA on the basis of ^{1}H and ^{13}C NMR and ESI mass spectroscopic and X-ray structure analytical methods and discuss the reaction mechanism in biotin-dependent carboxylase.

The Zn^{II}–OH complex $[Zn(tapa)(OH)]ClO_4$ (**1**) was prepared from reaction of $Zn(ClO_4)_2 \cdot 6H_2O$ with TAPA by subsequent addition of KOH in acetonitrile, and then a colorless single crystal was obtained by standing the resultant solution for a few days.[6] The crystal structure of **1** revealed that the Zn^{II} complex has a trigonal-bipyramidal geometry (τ value of 1.0)[7] with three pyridine nitrogen atoms in trigonal plane (Zn(1)–N(2) = 2.140(7), Zn(1)–N(3) = 2.144(8), Zn(1)–N(4) = 2.082(9) Å), and tertiary amine nitrogen and hydroxo oxygen atoms in the axial positions (Zn(1)–N(1) = 2.204(7), Zn(1)–O(1) = 1.961(6) Å) (Figure S1).[5,16] The hydroxo ion is surrounded with three amino NH groups of TAPA by intramolecular hydrogen bonds; O(1)···N(5) = 2.95(1), O(1)···N(6) = 2.91(1), O(1)···N(7) = 2.76(1) Å. As seen in many cases,[8–11] it has been indicated that the hydrogen-bonding interaction between hydroxo oxygen atoms and NH groups makes metal–hydroxo species stabilize.

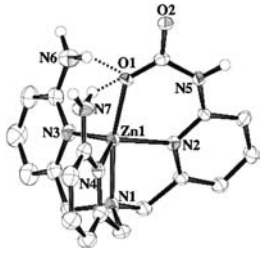
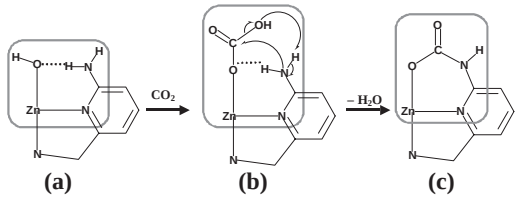


Figure 1. ORTEP view of cation part of **2**. The counter anions and hydrogen atoms are omitted except for NH hydrogens for clarity.

Interestingly, the reaction of hydroxozinc(II) complex **1** with CO_2 gas in acetonitrile gave unique CO_2 adduct **2** (Figure 1).[6] X-ray structure of **2** revealed that the Zn^{II} complex has a trigonal-bipyramidal geometry (τ value = 0.79)[7] with three pyridine nitrogen atoms in trigonal plane (Zn(1)–N(2) = 2.059(4), Zn(1)–N(3) = 2.059(5), Zn(1)–N(4) = 2.055(5) Å) and tertiary amine nitrogen and carbamic acid oxygen atoms in the axial positions (Zn(1)–N(1) = 2.170(5), Zn(1)–O(1) = 1.995(4) Å). The ligated carbamate oxygen atom hydrogen-bonded intramolecularly with the two amino NH groups; O(1)···N(6) = 2.886(7), O(1)···N(7) = 2.888(7) Å. The generation is also confirmed from the ESI-mass spectrum and elemental analysis of **2**.[6] It is obvious that the carbamoyl group has been formed by the reaction of amino group of hydroxozinc(II) complex **1** with CO_2.

In order to elucidate the reaction mechanism, the reaction process was followed by ^{1}H NMR spectroscopy. The bubbling of CO_2 gas into an acetonitorile-d_3 solution of complex **1** in an ice bath exhibited an interesting spectral change. The N–H proton peak initially observed at 7.30 ppm showed definitive up-field shift to 6.10 ppm by addition of dry CO_2 gas after 5 min, although the other proton peaks also exhibited slight shifts except for disappearance of the OH proton peak detected at 1.51 ppm (Figures 2a and 2b). After 2 h, further remarkable spectral change was observed (Figure 2c), which was identical to that of **2**.[6] Thus, the species observed in Figure 2b must be a reaction intermediate that was generated in the course of



Scheme 1.

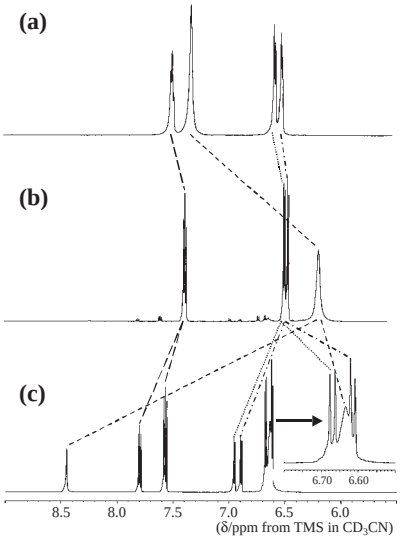
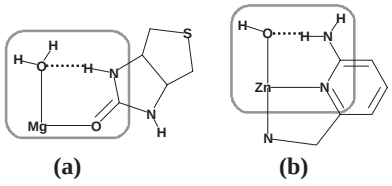


Figure 2. ^{1}H NMR spectra of (a) **1** in CD_3CN; (b) after bubbling CO_2 gas into an CD_3CN solution of **1** for 5 min; (c) after 2 h at 300 K. Detailed ^{1}H and ^{13}C NMR spectra were deposited (Figures S3–S6).[16]

carbamoylation from **1** to **2**, which is assigned to a hydrogen–carbonatozinc(II) species (**1-CO_2**, Scheme 1b). The formation of hydrogencarbonato species is also confirmed from good agreements in ^{1}H, ^{13}C NMR, and ESI mass spectral data for $[Zn(TNPA)(HCO_3^-)]^+$ complex with similar hydrogen-bonding interaction sites; TNPA = tris(6-neopentylamino-2-pyridylmethyl)amine.[11] Judging from the ^{1}H NMR spectral behavior observed every 30 min for 2 h, the hydrogencarbonato species **1-CO_2** was completely converted to **2** through the generation of **1-CO_2** species, which was irreversible. The generation of carbamato carboxyl has also been confirmed from ^{13}C NMR spectrum appeared at 156.4 ppm (Figure S6),[16] which is obviously distinguished from that of carbonato carboxyl group generally appearing at ca. 175 ppm.[3] The consumption process of **1-CO_2**, as estimated by ^{1}H NMR, was analyzed using the first-order kinetics (Figure S2).[16] Thus, it is clear that the reaction from **1-CO_2** to **2** is intramolecular condensation accompanied by dehydration.

This is the first report that the crystal structures of both the precursor complex and produced carbamic acid from the reaction of amino group and CO_2 have been established and that the reaction mechanism has been elucidated, although similar reaction products have been reported previsouly.[3,12] These findings suggest that such a divalent metal ion is required for the fixation of CO_2 and stabilization of the carbamate product as the binding and assisting site. Considering that Zn^{2+} ion exhibits sometimes similar enzymatic activity to Mg^{2+} and judging from the structural similarity between the reaction product, carbamic acid, and native carboxybiotin obtained from biotin and carbon dioxide (Scheme 2), the essence of this reaction mechanism will give good information for interpretation of that in biotin-dependent carboxylase (Scheme S1).[16]

In conclusion, we have studied the preparation of carbamic acid from reaction of hydroxozinc(II) complex containing amino group with CO_2 and confirmed the reaction mechanism structurally and spectroscopically. In pyruvate carboxylase, which is a kind of biotin-dependent carboxylase that converts from pyruvic acid and carbon dioxide to oxaloacetate in presence of Mg^{2+} ions, the biotin participates in fixation and activation of carbon



Scheme 2.

dioxide as a cofactor,[1,13] and the two Mg^{2+} ions are assumed to play the following two roles; one is involved in conversion from ATP to ADP and another is associated with the formation of biotin carboxylate intermediate derived from biotin. The form of biotin-Mg–H_2O system bound to the urea oxygen has been proposed as the active species (Scheme 2a).[14,15] However, there is almost no information about the detailed mechanism on the binding of biotin and carbon dioxide, except for the structure and characterization of the apo forms of the enzymes.[14] The present results will give a better understanding for the mechanism.

This work was supported partly by a Grant-in-Aid for Scientific Research from the Ministry of Education, Culture, Sports, Science and Technology, Japan and supported in part by a grant from the NITECH 21st Century COE Program, to which our thanks are due.

References and Notes

1 D. Voet, P. G. Voet, *Biochemistry*, John Wiley & Sons, New York, **1990**, p. 561.
2 D. Walther, M. Ruben, S. Rau, *Coord. Chem. Rev.* **1999**, *182*, 67.
3 D. B. Dell'Amico, F. Calderazzo, L. Labella, F. Marchetti, G. Pampaloni, *Chem. Rev.* **2003**, *103*, 3857.
4 a) G. Parkin, *Chem. Rev.* **2004**, *104*, 699. b) H. Vahrenkamp, *Acc. Chem. Res.* **1999**, *32*, 589.
5 a) K. Jitsukawa, M. Harata, H. Arii, H. Sakurai, H. Masuda, *Inorg. Chim. Acta* **2001**, *324*, 108. b) A. Wada, Y. Honda, S. Yamaguchi, S. Nagatomo, T. Kitagawa, K. Jitsukawa, H. Masuda, *Inorg. Chem.* **2004**, *43*, 5725.
6 Detailed synthetic methods and crystallographic data of compounds, **1** and **2**, were deposited in Supporting Information.[16] Crystallographic data reported in this manuscript have been deposited with Cambridge Crystallographic Data Centre as supplementary publication nos. CCDC-260934 (**1**) and 260935 (**2**). Copies of the data can be obtained free of charge via www.ccdc.cam.ac.uk/conts/retrieving.html.
7 A. W. Addison, T. N. Rao, J. Reedijk, J. van Rijn, G. C. Verschoor, *J. Chem. Soc., Dalton Trans.* **1984**, 1349.
8 a) C. E. MacBeth, B. S. Hammes, V. G. Young, Jr., A. S. Borovik, *Inorg. Chem.* **2001**, *40*, 4733. b) C. E. MacBeth, A. P. Golomvek, V. G. Young, Jr., C. Yang, K. Kuczera, M. P. Hendrich, A. S. Borovik, *Science* **2000**, *289*, 938.
9 a) D. K. Garner, S. B. Fitch, L. M. McAlexander, L. M. Bezold, A. M. Arif, L. M. Berreau, *J. Am. Chem. Soc.* **2002**, *124*, 9970. b) K. J. Tubbs, A. L. Fuller, B. Bennett, A. M. Arif, L. M. Berreau, *Inorg. Chem.* **2003**, *42*, 4790.
10 a) S. Ogo, S. Wada, Y. Watanabe, M. Iwase, A. Wada, M. Harata, K. Jitsukawa, H. Masuda, H. Einaga, *Angew. Chem., Int. Ed.* **1998**, *37*, 2102. b) M. Harata, K. Hasegawa, K. Jitsukawa, H. Masuda, H. Einaga, *Bull. Chem. Soc. Jpn.* **1998**, *71*, 1031. c) M. Harata, K. Jitsukawa, H. Masuda, H. Einaga, *Bull. Chem. Soc. Jpn.* **1998**, *71*, 637. d) M. Harata, K. Jitsukawa, H. Masuda, H. Einaga, *Chem. Lett.* **1996**, 813. e) J. C. Mareque-Rivas, R. Prabaharan, S. Parsons, *Dalton Trans.* **2004**, 1648.
11 a) S. Yamaguchi, I. Tokairin, Y. Wakita, Y. Funahashi, K. Jitsukawa, H. Masuda, *Chem. Lett.* **2003**, *32*, 406. b) H. Masuda, I. Tokairin, K. Jitsukawa, H. Einaga, *J. Inorg. Biochem.* **1999**, *74*, 225.
12 a) E. García-Espana, P. Gaviña, J. Latorre, C. Soriano, B. Verdejo, *J. Am. Chem. Soc.* **2004**, *126*, 5082. b) H. Xu, E. M. Hampe, D. M. Rudkevich, *Chem. Commun.* **2003**, 2828.
13 a) J. R. Knowles, *Annu. Rev. Biochem.* **1989**, *58*, 195. b) S. Jitrapakdee, J. C. Wallace, *Biochem. J.* **1999**, *340*, 1. c) P. V. Attwood, *Int. J. Biochem. Cell Biol.* **1995**, *27*, 231.
14 a) B. G. Berneburg, D. Ash, *Biochemistry* **1997**, *36*, 14392. b) J. P. Branson, P. V. Attwood, *Biochemistry* **2000**, *39*, 7480.
15 a) E. R. Sanchez, M. C. Gessel, T. L. Groy, M. T. Caudle, *J. Am. Chem. Soc.* **2002**, *124*, 1933. b) F. J. Lihs, M. T. Caudle, *J. Am. Chem. Soc.* **2002**, *124*, 11334.
16 Supporting Information is available electronically on the CSJ-Journal Web site, http://www.csj.jp/journals/chem-lett/.

Published on the web (Advance View) June 2, 2007; doi:10.1246/cl.2007.842