Inorg. Chem. **2002**, *41*, 1120−1127

Synthesis, Structure, and Preparative Transamination of Tetrazinc Carbamato Complexes Having the Basic Zinc Carboxylate Structure

C. Shawn McCowan, Thomas L. Groy, and M. Tyler Caudle*

Department of Chemistry and Biochemistry, Arizona State University, Box 871604, Tempe, Arizona 85287-1604

Received August 22, 2001

The series of tetranuclear zinc(II) carbamato complexes $(Zn_4O)(O_2CR)_6$, (**1**, R = diethylamino; **2**, R = piperidino; **3**, R = pyrrolidino) was prepared. Complexes **2** and **3** were crystallographically characterized and shown to have the same tetrahedral Zn_4O^{6+} core. Complex **2** crystallizes in the cubic space group $I\bar{4}3d$, $a = 24.0131(5)$ Å, $V = 13846.6(5)$ Å^3, R(1976 observed reflections) = 0.0194, and GOF = 1.013. Complex **3** crystallizes in the triclinic space group $P\bar{1}$, $a = 10.3178(6)$ Å, $b = 10.6962(6)$ Å, $c = 19.5130(11)$ Å, $\alpha = 81.9070(10)°$, $\beta = 75.4880(10)°$, $\gamma = 81.6540(10)°$, $V = 2050.4(2)$ Å^3, R(6141 observed reflections) = 0.0334, and GOF = 0.979. NMR spectroscopy was used to show that the $(Zn_4O)L_6$ structure was maintained in nonpolar solvents. The complexes reacted with free amine in nonpolar solvents, which resulted in facile conversion of one member of the series to another. For example, reacting **1** with a stoichiometric amount of pyrrolidine in tetrahydrofuran followed by workup resulted in the quantitative formation of **3** with liberation of diethylamine. Formally, this is a transamination metathesis reaction between the diethylcarbamate ligand and pyrrolidine. The reaction is complete within 3 min at room temperature, in marked contrast to the extreme conditions required to effect transamination on organic carbamates. The complexes also undergo a facile transcarboxylation reaction with carbon dioxide which results in scrambling of the carboxyl group of the carbamate ligand with free CO_2, also complete in about 3 min. Both transamination and transcarboxylation reactions are consistent with the intermediacy of free CO_2. However, because of the propensity for the complexes to hydrolyze to liberate CO_2, the role of adventitious moisture in facilitating the reaction cannot presently be rejected.

Introduction

Divalent metal carbamates are formed either by direct insertion into a metal−nitrogen bond or via condensation of CO_2 directly with an amine in the presence of the divalent metal cation. Their formation is important in the assembly of the magnesium center in ribulose 1,5-bisphosphate carboxylase/oxygenase,[1] the nickel center in urease,[2] and the zinc center in the zinc-dependent phosphotriesterase.[3] Carbon dioxide fixation by the magnesium-dependent biotin carboxylase enzymes also results in the formation of a critical carbamate functional group.[4] Synthetically, the formation of urethanes from amines and CO_2 can be mediated by metal ions,[5] and likely involves metal carbamate intermediates as well. Since urethanes have traditionally been prepared from reactive carbonyl compounds such as phosgene, a toxic and noxious gas, CO_2-dependent formation of carbamates and urethanes holds the promise of replacing phosgene-dependent processes with more benign processes. However, despite a

* To whom correspondence should be addressed. E-mail: tcaudle@asu.edu.

(1) (a) Belknap, W. R.; Portis, A. R., Jr. *Biochemistry* **1986**, *25*, 1864−1869. (b) Schreuder, H. A.; Knight, S.; Curmi, P. M. G.; Andersson, I.; Cascio, D.; Bränden, C.-I.; Eisenberg, D. *Proc. Natl. Acad. Sci. U.S.A.* **1993**, *90*, 9968−9972. (c) Cleland, W. W.; Andrews, T. J.; Gutteridge, S.; Hartman, F. C.; Lorimer, G. H. *Chem. Rev.* **1998**, *98*, 549−561.

(2) (a) Park, I.-L.; Carr, M. B.; Hausinger, R. P. *Proc. Nat. Acad. Sci. U.S.A.* **1994**, *91*, 3233−3237. (b) Park, I.-L.; Hausinger, R. P. *Science* **1995**, *267*, 1156−1158. (c) Pearson, M. A.; Schaller, R. A.; Michel, L. O.; Karplus, P. A.; Hausinger, R. P. *Biochemistry* **1998**, *37*, 6214−6220.

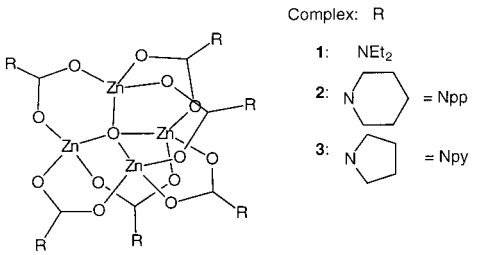
(3) (a) Shim, H.; Raushel, F. M. *Biochemistry* **2000**, *39*, 7357−7364. (b) Hong, S.-B.; Kuo, J. M.; Mullins, L. S.; Raushel, F. M. *J. Am. Chem. Soc.* **1995**, *117*, 7580−7581.

(4) (a) Knowles, J. R. *Annu. Rev. Biochem.* **1989**, *58*, 195−221. (b) Jitrapakdee, S.; Wallace, J. C. *Biochem. J.* **1999**, *340*, 1−16.

(5) (a) Alessio, R.; Belli Dell_Amico, D.; Calderazzo, F.; Englert, U.; Guarini, A.; Labella, L.; Strasser, P. *Helv. Chim. Acta* **1998**, *81*, 219−230. (b) McGhee, W. D.; Riley, D. P.; Christ, M. E.; Christ, K. M. *Organometallics* **1993**, *12*, 1429−1433. (c) McGhee, W. D.; Riley, D. P. *Organometallics* **1992**, *11*, 900−907. (d) Tsuda, T.; Washita, H.; Watanabe, K.; Miwa, M.; Saegusa, T. *J. Chem. Soc., Chem. Commun.* **1978**, 815−816.

10.1021/ic010885v CCC: $22.00
Published on Web 02/14/2002

Chart 1



large number of divalent metal carbamate complexes that have been structurally characterized, there is remarkably little literature detailing the special chemical reactivity of such compounds. The carbon−nitrogen bond in carbamates possesses considerable lability, and under moderately acidic conditions, it is cleaved to liberate CO_2 and the amine.[6] The liberation of CO_2 from carbamates is of particular relevance to the biotin enzymes.[7] It has been established that the carbamate functional group in N^1-carboxybiotin donates the carboxyl group to a carbon nucleophile, resulting in net CO_2 transfer to form a new C−C bond. When applied to simple metal carbamate complexes, this biochemical model for CO_2 transfer suggests a pathway by which carbamates might be activated for synthetic chemistry, highlighting the importance of understanding the reactivity of metal carbamate complexes.

Zinc carbamato compounds include tetranuclear complexes with a Zn_4O^{6+} core that can be considered analogues of the basic zinc carboxylate structure,[8−10] Chart 1. This motif has several advantages as a platform for studying transformations occurring at the carbamate group. The complexes are diamagnetic and so are amenable to study by nuclear magnetic resonance. They are also highly symmetrical, having only a single type of carbamate ligand and thus simple NMR spectra. Finally, they are structurally stable as a result of the Zn_4O^{6+} core, and decomposition problems are minimized.

In this paper we report the synthesis, structure, and reactivity of a series of complexes having the general formula $(Zn_4O)(O_2CR)_6$, where R is an amino group, Chart 1. In a rudimentary model for the reaction of carbamate complexes with nucleophiles, we observe that these complexes undergo a facile transamination reaction that results in metathesis of the carbamate amino group with free amine. This reaction permits us to readily convert one member of this series into another in quantitative yield in some cases. We also find that these complexes readily react with free $^{13}CO_2$ in solution, which reveals scrambling between the carboxyl group of the carbamate ligand and free CO_2. This latter reaction has precedent in the carbamate complexes of high-valent early transition metals, which were studied extensively by Extine and Chisholm.[11,12] These studies indicated that the reaction between free amine and free CO_2 competes with CO_2 insertion/elimination, complicating the study of the mechanism as shown by Chisholm and more recently by Darensbourg.[13] Both the CO_2 exchange and transamination are closely related to the lability of the O_2C-N bond in $(Zn_4O)(O_2CR)_6$ complexes and are expected to yield insight into the enigmatic CO_2 insertion/elimination reactions of metal carbamate complexes.

Experimental Section

Materials. Dimethylzinc as a 2 M solution in toluene (*Caution*: dimethyl zinc is pyrophoric and should be handled with care under a nitrogen atmosphere), diethylamine, pyrrolidine, and piperidine were obtained from Aldrich. Amines were stored over 4 Å molecular sieves. Solvents used in the preparative work were distilled by standard methods. Chloroform-d_6 was obtained from Cambridge Isotope Laboratories and distilled from calcium hydride before being stored in a glovebox. All synthetic and analytical manipulations were carried out under a nitrogen atmosphere, either in a glovebox or by standard Schlenk techniques.

$(Zn_4O)(O_2CNEt_2)_6$ (1). Dimethylzinc (5 mL, 10 mmol) was reacted with 2 equiv of neat diethylamine (2.1 mL, 20.3 mmol) under nitrogen in a room temperature water bath. After 16 h, 5 mL of tetrahydrofuran (THF) was added and the solution was exposed to CO_2 gas. After 5 h, 0.25 equiv of distilled water (45 μL, 2.5 mmol) was added. After another 19 h at room temperature and positive CO_2 pressure, the reaction mixture was evaporated to dryness under vacuum to give 2.14 g (88% yield) of **1**. IR (KBr, cm^{-1}): 1567, 1509, 796. ^1H NMR (ppm in $CDCl_3$): 3.28 (q, 4H), 1.08 (t, 6H). ^{13}C NMR (ppm in $CDCl_3$): 162.53, 41.61, 13.63. Anal. Found (calcd) for $C_{30}H_{60}N_6Zn_4O_{13}$ (%): C, 37.3 (37.0); H, 6.3 (6.2); N, 8.6 (8.6).

$(Zn_4O)(O_2CNpp)_6$ (2). Dimethylzinc (10 mL, 20 mmol) was reacted with 2 equiv of piperidine (4.0 mL, 40 mmol) in 150 mL of THF under nitrogen. After 16 h, the mixture was evaporated to dryness under vacuum. The solid residue was dissolved in 175 mL of acetonitrile and exposed to CO_2 gas, giving a white precipitate within 5 min. The solution was allowed to stand under positive pressure of CO_2 for 16 h and then filtered to give 3.90 g (74% yield) of **2**. IR (KBr, cm^{-1}): 1566, 1498, 1444, 1291, 788. ^1H NMR (ppm in $CDCl_3$): 3.42 (t, 4H), 1.49 (m, 6H). ^{13}C NMR (ppm in $CDCl_3$): 162.20, 45.03, 25.69, 24.6. Anal. Found (calcd) for $C_{36}H_{60}N_6Zn_4O_{13}$ (%): C, 41.2 (41.3); H, 6.0 (5.8); N, 8.4 (8.0).

$(Zn_4O)(O_2CNpy)_6$ (3). Dimethylzinc (10 mL, 20 mmol) was reacted with 2 equiv of pyrrolidine (3.4 mL, 40 mmol) in 175 mL of THF under nitrogen. After 16 h, the mixture was evaporated to dryness under vacuum. The solid residue was dissolved in 175 mL of acetonitrile and exposed to CO_2, giving a white precipitate within 5 min. After 5 h, 0.25 equiv of distilled water (90 μL, 5 mmol) was added. The solution was allowed to stand under a positive pressure of CO_2 for 16 h and then filtered to give 3.02 g (62.8% yield) of **3**. IR (KBr, cm^{-1}): 1566, 1506, 1476, 1457, 793. ^1H NMR (ppm in $CDCl_3$): 3.32 (t, 4H), 1.77 (p, 4H). ^{13}C NMR (ppm in

(6) (a) Caplow, M. *J. Am. Chem. Soc.* **1968**, *90*, 6795−6803. (b) Ewing, S. P.; Lockshon, D.; Jencks, W. P. *J. Am. Chem. Soc.* **1980**, *102*, 3072.
(7) Tipton, P. A.; Cleland, W. W. *J. Am. Chem. Soc.* **1988**, *110*, 5866−5869.
(8) Cotton, F. A.; Daniels, L. M.; Falvello, L. R.; Matonic, J. H.; Murillo, C. A.; Wang, X.; Zhou, H. *Inorg. Chim. Acta* **1997**, *266*, 91−102.
(9) Clegg, W.; Harbron, D. R.; Homan, C. D.; Hunt, P. A.; Little, I. R.; Straughan, B. P. *Inorg. Chim. Acta* **1991**, *186*, 51−60.
(10) Belforte, A.; Calderazzo, F.; Englert, U.; Strähle, J. *Inorg. Chem.* **1991**, *30*, 3778−3781.
(11) Chisholm, M. H.; Extine, M. *J. Am. Chem. Soc.* **1977**, *99*, 792−802.
(12) (a) Chisholm, M. H.; Extine, M. *J. Chem. Soc., Chem. Commun.* **1975**, 438−439. (b) Chisholm, M. H.; Extine, M. *J. Am. Chem. Soc.* **1977**, *99*, 782−792.
(13) Darensbourg, D. J.; Frost, B. J.; Larkins, D. L. *Inorg. Chem.* **2001**, *40*, 1993−1999.

Table 1. Crystallographic Parameters

	2	3
empirical formula	$C_{36.79}H_{60}N_{6.40}O_{13}Zn_4$	$C_{32}H_{51}N_7O_{13}Zn_4$
fw	1061.47	1003.28
cryst size (mm)	0.28 × 0.28 × 0.28	0.35 × 0.26 × 0.20
cryst syst	cubic	triclinic
space group	$I\bar{4}3d$	$P\bar{1}$
color	colorless	colorless
a (Å)	24.0131(5)	10.3178(6)
b (Å)	24.0131(5)	10.6962(6)
c (Å)	24.0131(5)	19.5130(11)
α (deg)	90	81.9070(10)
β (deg)	90	75.4880(10)
γ (deg)	90	81.6540(10)
V (Å^3)	13846.6(5)	2050.4(2)
Z	12	2
temp (K)	173(2)	173(2)
λ (Å)	0.71073	0.71073
measd reflcns	53,566	16,747
independ reflcns	2046	7241
obsd reflcns	1976	6141
R_{all}	0.0201	0.0334
R_{obs}	0.0194	0.0281
wR_{all}	0.0442	0.0728
wR_{obs}	0.0440	0.0714
GOF	1.013	0.979
x[a]	0.003(10)	

[a] Flack, H. D. *Acta Crystallogr.* **1983**, *A39*, 876−881.

$CDCl_3$): 161.94, 46.45, 25.56. Anal. Found (calcd) for $C_{30}H_{48}N_6Zn_4O_{13}$(%): C, 38.1 (38.3); H, 5.2 (5.1); N, 9.8 (9.8).

Crystallography. Crystals of **2** and **3** were prepared by recrystallization in acetonitrile at 70 °C in a sealed thick-walled pressure flask. Single crystals of suitable dimensions were coated in mineral oil and mounted on the tip of a glass fiber. See Table 1 for information about data collection parameters. Refinement of F^2 data was against all reflections. The weighted R and goodness-of-fit are based on F^2, and conventional R factors are based on F, with F set to zero for negative F^2. The threshold expression of $F^2 > 2\sigma(F^2)$ was used only for calculating R factors and is not relevant to the choice of reflections for refinement.

In **2**, the atoms in the piperidyl group, N(2)−C(8)-C(9)−C(10)−C(11)−C(8′), are disordered in the ratio of 0.5/0.5 with their symmetry generated equivalents N(2a)−C(8a)−C(9a)−C(10a)−C(11a)−C(8′a). These two disordered groups form opposing chair configurations. The atoms C(8) and C(8′) are symmetry equivalent atoms included at relative occupancies of 0.5/0.5 and were constrained to have the same anisotropic displacement parameters. This was done so that the SHELX AFIX command calculated the hydrogen positions on the piperidyl ring correctly. There were 0.40(1) acetonitrile solvent molecules per **2** included in the structure.

In refinement of **3**, the atom groups C(1c)−C(1d) and C(1c′)−C(1d′) are disordered atoms related by a twist of the N(1a)−C(1b)−C(1c)−C(1d)−C(1e) ring. These have refined occupancy ratios of 0.53/0.47, respectively, with the constraints that the prime atoms have the same anisotropic displacement parameters as the nonprime atoms. There was one acetonitrile solvent molecule per **3** included in the structure.

Preparative Transamination Reactions. In an example of a typical preparative transamination, 0.25 g of **1** was dissolved in 25 mL of THF and reacted with 6.5 equiv of pyrrolidine. After 18 h, all of the solvent and free amine was removed by evaporation and the solid residue dried in vacuo. NMR analysis of the product in $CDCl_3$ showed the product to consist of greater than 94% **3**, with a trace of unreacted **1** remaining. No other products were observed by NMR spectroscopy. Typically, the amount of **3** + **1** recovered

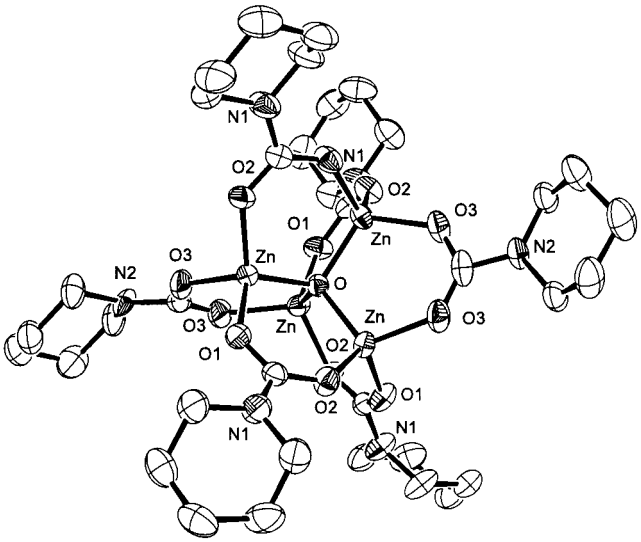


Figure 1. Molecular structure of **2** (50% ellipsoids). Only non-carbon atoms are labeled. Important bond lengths (Å): Zn−O, 1.9420(2); Zn−O(2), 1.9415(15); Zn−O(3), 1.9465(16); Zn···Zn 3.1467(5). Important bond angles (deg): Zn−O−Zn, 110.101(8); Zn−O−Zn, 108.220(16); O(3)−C(7)−O(3), 125.2(3); O(1)−C(1)−O(2), 124.7(2); O(3)−C(7)−N(2), 107.7(4). Important torsion angles (deg): O(3)−C(7)−N(2)−C(8′), 6.4; O(3)−C(7)−N(2)−C(8), 1.9; O(2)−C(1)−N(1)−C(6), 3.6; O(1)−C(1)−N(1)−C(2), 0.5.

was quantitative. Other transamination reactions leading to formation of **1** and **2** were carried out by the same method.

Analytical Transamination Reactions. In a typical experiment, 0.06 mmol of **1** was dissolved in 1.0 mL of $CDCl_3$ containing 10 μL (0.093 mmol) of cyclohexane as a calibration standard. The precise amount of **1** was determined by integrating the diethyl signals and comparing with the cyclohexane resonance. A 6 equiv amount of pyrrolidine was added and the solution permitted to stand for 18 h, after which the proton NMR spectrum of the solution was measured. There was no evidence for loss of CO_2 during this experiment. Mass balance was established by showing that the amount of diethylamine liberated was equal to the amount of pyrrolidine carbamate formed. The equilibrium constant K_{eq} was determined from the integrated intensities of the signals arising from free amine and carboxylated amine. The consistency of the equilibrium constant was demonstrated by showing that reaction between **3** and diethylamine gave the same value for K_{eq}. Analytical transamination reactions for **2** and **3** were carried out by the same method.

Results

The molecular structures of **2** and **3** are shown in Figures 1 and 2. The molecular structure of **1** has been previously reported[10] and was not redetermined for this work. The structures of **1**−**3** are reminiscent of the tetranuclear basic zinc carboxylate structure. From the point of view of the zinc coordination polyhedra, the structure can be described as consisting of four ZnO_4 tetrahedra sharing a single oxygen-centered vertex. The zinc atoms are supported by six carbamato ligands which each point at the vertex of an octahedron. The complexes possess approximate cubic symmetry, and the details of the solid-state structural parameters are best discussed in terms of their deviation from idealized cubic symmetry. In **3**, all four $Zn-O_{central}$ bonds are essentially equivalent in length, and the average of the

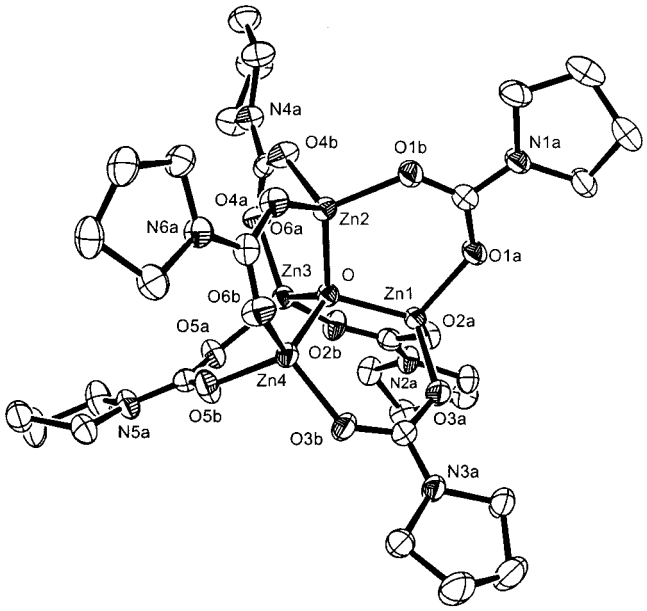
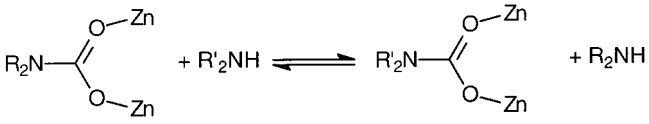


Figure 2. Molecular structure of **3** (50% ellipsoids). Only non-carbon atoms are labeled. Important bond lengths (Å): Zn(1)−O, 1.947(2); Zn(2)−O, 1.946(2); Zn(3)−O, 1.943(2); Zn(4)−O, 1.9555(2); Zn···Zn (av), 3.18(2). Important bond angles (deg): Zn−O−Zn (av), 109.6(7); O−C−O (av), 125.8(2). The average O−C−N−C torsion angle is 3.8°.

$Zn-O_{central}-Zn$ bond angles is 109.6(7)°. The Zn_4O^{6+} core in crystalline **3** is therefore a nearly perfect tetrahedron. The carbamate groups are expected to be planar as a result of partial double bond character in the C−N bond. The average O−C−N−C torsion angle in **3** is 3.8°, indicative of slight deviation from planarity resulting from strain in the five-membered pyrrolidine ring. The Zn_4O^{6+} core in crystalline **2** is a flattened tetrahedron with two Zn−O−Zn bond angles of 108.22(2)° and four of 110.101(8)°. The two trans ligands bridging the smaller Zn−O−Zn bond angles exhibit considerable disorder, and satisfactory refinement of the structure is achieved only when the entire piperidine moiety is permitted to float over two equivalent positions. This results in a piperidine carbamate ligand that is substantially distorted when compared to the other four ligands, reflected in the unusually small O(3)−C(7)−N(2) angle of 107.7(4)°. Examination of the packing diagram suggests that this results from a network of close contacts involving the distorted ligands and acetonitrile molecules of crystallization, which reside in 3-fold channels formed by the distorted piperidine groups. There are no such close interactions with the undistorted ligands. The molecular structure of **2** is otherwise analogous to **1** and **3**. The Zn···Zn distances in **2** and **3** are 3.15−3.20 Å, in line with typical complexes having the Zn_4O^{6+} core.[9]

In solution, proton and ^{13}C NMR spectroscopy shows that the $(Zn_4O)L_6$ molecular architecture is maintained for **1**−**3**. For example, **1** exhibits a very simple proton NMR spectrum showing a single upfield triplet and downfield quartet, confirming the existence of a single type of diethyl carbamate ligand as required by symmetry. Importantly, there is no NMR evidence for residual amine in any of the purified preparations of **1**−**3**. The ^{13}C NMR spectra of **1**−**3** also show a single type of ligand and, more significantly, exhibit a single very sharp carboxyl signal in the range from 161.9 to 162.5 ppm, even with a natural abundance of ^{13}C. Stereochemical nonrigidity in carbamate complexes is readily observed by broadening of this signal,[14] sometimes to the point that it is not observed at all. The sharpness of the carboxyl signal is then significant since it indicates considerable structural integrity and lack of fluxionality in solution.

Scheme 1



The previous synthesis of **1** was accomplished by the reaction of zinc metal with diethylamine and CO_2 at 150 °C and 50 atm pressure in a bomb reactor.[10] In this case there was considerable interest in the origin of the central oxide anion, which was established to arise from CO_2 by reductive deoxygenation, with the reduced product being diethylformamide. This is chemically reasonable in light of the reducing power of metallic zinc and the precedent for deoxygenation of CO_2 by zinc at high temperature.[15] In the case of our preparations of **1**−**3**, this is an unlikely scenario, and a hydrolytic process involving trace amounts of adventitious water is the most likely source of the oxide dianion. This is supported by the observation that yields of the target complexes are improved by addition of stoichiometric amounts of water to the reaction mixture.

It was found that the carbamate ligands in complexes **1**−**3** are readily interconverted from one to another simply by reacting with the appropriate different secondary amine, as shown in Scheme 1. Note that this is not a simple ligand exchange but requires metathesis of the $N-CO_2^-$ bond of the carbamate ligand. This reaction may formally be considered a transamination (by analogy with transesterification in esters) in which one carbamate amino moiety is exchanged for another. For example, **1** is converted almost quantitatively to **3** upon reaction with 6 equiv of pyrrolidine, as described in the Experimental Section. Transamination of **1** is clearly shown by the NMR spectra in Figure 3. Figure 3a shows the ^1H NMR spectrum of **1** prior to reaction with pyrrolidine. Reaction with pyrrolidine, workup as described in the Experimental Section and analysis of the resulting residue by NMR gave a new spectrum, Figure 3b, which is compared with a spectrum of **3** prepared independently, Figure 3c. The NMR data show essentially complete conversion to **3** with only a trace of diethyl carbamate remaining. Mass balance in the $(Zn_4O)L_6$ complex is demonstrated by in situ NMR tube experiments. For example, reaction between **1** and pyrrolidine in $CDCl_3$ shows that 1 equiv of free diethylamine is liberated for each equivalent of pyrrolidinecarbamate formed, consistent with the stoichiometry in Scheme 1. There is no detectable formation of side products. These in situ transamination experiments also demonstrate that transami-

(14) Caudle, M. T.; Kampf, J. W. *Inorg. Chem.* **1999**, *38*, 5474−5475.
(15) (a) Murgulescu, I. G.; Cismaru, D. *J. Chim. Phys.* **1961**, *58*, 181−185. (b) Maier, C. G.; Ralston, O. C. *J. Am. Chem. Soc.* **1926**, *48*, 364.

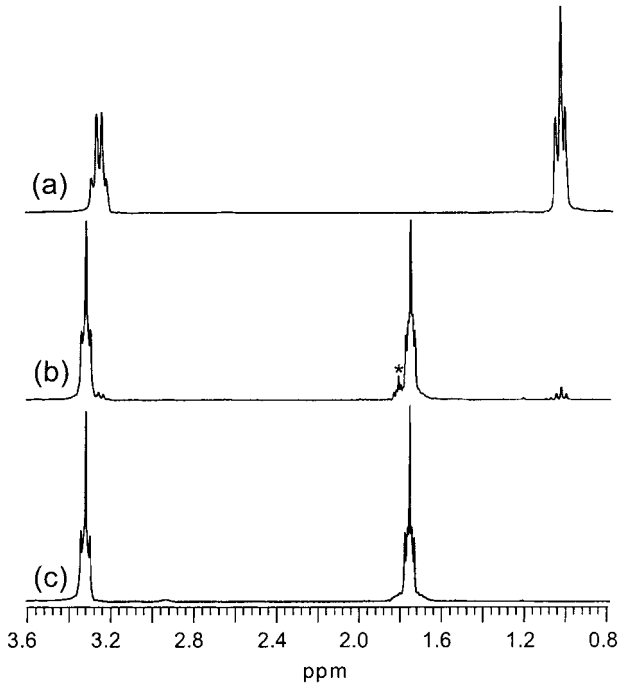


Figure 3. Proton NMR spectra (300 MHz, $CDCl_3$) showing conversion from **1** to **3** by reaction with pyrrolidine: (a) **1**; (b) **1** + 6 equiv of pyrrolidine; (c) **3**. The asterisk (*) indicates residual THF from the preparative transamination reaction.

Table 2. Yield Data for Transamination of **1**−**3**

complex	amine	equiv[a]	product	% conversion[b] (%)	K_{eq}[b,c]
1	pyrrolidine	6.5	**3**	94.9	14(4)
1		16.5	**3**	100.0	
1	piperidine	6.7	**2**	74.0	1.8(5)
1		16.5	**2**	96.7	
3	piperidine	6	**2**	25.4	0.14(4)
3		16.3	**2**	38.4	
3	diethylamine	30	**1**	14.7	0.07(2)
2	diethylamine	10	**1**	1.5	0.5(1)
2		30	**1**	46.0	
2		100	**1**	52.2	
2	pyrrolidine	6	**3**	81.9	7(2)
2		10	**3**	87.0	

[a] Per $(Zn_4O)L_6$ complex. [b] Based on total conversion of carbamate ligand measured by NMR on isolated products. [c] Measured by in situ NMR.

nation is kinetically facile, being complete within the time required to obtain a single NMR spectrum (about 5 min).

Preparative transamination reactions starting from **1** to give **2** or **3** proceed essentially to completion even with stoichiometric amounts of pyrrolidine or piperidine. On the other hand, the reverse reactions require a large excess of diethylamine to obtain isolable quantities of **1**. Yield data for preparative transamination reactions are tabulated in Table 2. These data qualitatively show that the pyrrolidinecarbamate derivative **3** is formed in high yield (>80%) by the reaction of stoichiometric amounts of pyrrolidine with **1** or **2** but that yields are lower for conversions leading to formation of **1**.

Figure 4 shows the ^1H NMR spectrum of a solution of **2** to which 6 equiv of pyrrolidine has been added. At equilibrium, the spectrum shows the presence of **2** and **3** as well as free pyrrolidine and piperidine. We defined K_{eq} for the **2** ⇌ **3** conversion according to

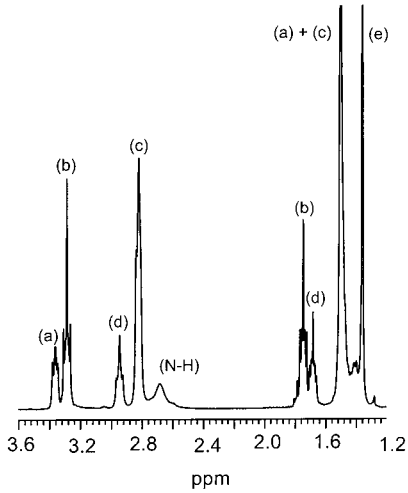


Figure 4. Equilibrium proton NMR spectrum ($CDCl_3$) of **3** to which 6 equiv of piperidine was added, showing transamination of the pyrrolidinecarbamate ligand, $pyNCO_2^-$, to piperidinecarbamate, $ppNCO_2^-$. Peaks are assigned as follows: (a) $ppNCO_2^-$; (b) $pyNCO_2^-$; (c) free piperidine; (d) free pyrrolidine; (e) cyclohexane, an internal concentration standard.

$$K_{eq} = [pyNCO_2^-][ppNH]/[ppNCO_2^-][pyNH] \qquad (1)$$

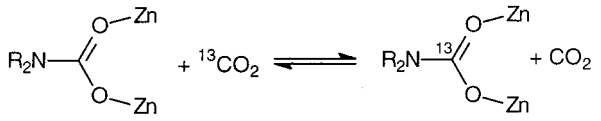
This equilibrium constant is based on total concentrations of ligand rather than on total concentrations of $(Zn_4O)L_6$. It is therefore a conditional equilibrium constant for conversion of piperidinecarbamate to pyrrolidinecarbamate under conditions where they are bound to the Zn_4O^{6+} core. Implicit in this definition of K_{eq} is that all six ligands on **2** are converted independently, although they can presumably be exchanged only one-at-a-time. The relative concentrations of free and carboxylated amine were determined by integrating the NMR peaks in Figure 4, and these values were used in eq 1 to determine K_{eq} for the interconversion **2** ⇌ **3**. In situ NMR data were likewise used to determine K_{eq} for all three possible transamination reactions, which are listed in Table 2 along with the preparative yield data.

The transamination yields are based on the total conversion of carbamate ligand as measured by NMR, which does not distinguish mixed-ligand complexes from homoleptic complexes in this case. We expect that heteroleptic complexes do form in the reactions that have not proceeded to completion since the alternative, that all ligands on a given complex are transaminated simultaneously, is chemically unlikely. Mass spectra by MALDI or electrospray techniques do not resolve the issue since the complexes themselves are neutral and only charged fragmentation products are observed, a common feature in the mass spectra of basic zinc carboxylates as well.[16]

Complexes **1**−**3** also undergo a transcarboxylation reaction with free CO_2, Scheme 2. This results in scrambling of the CO_2 moiety on the carbamate ligand with free CO_2 from solution and is readily observed in the ^{13}C NMR spectrum. Figure 5a shows the spectrum of **3,** and Figure 5b shows the same sample after exposure to $^{13}CO_2$. The signal arising

(16) (a) Charalambous, J.; Copperthwaite, R. G.; Jeffs, S. W.; Shaw, D. E. *Inorg. Chim. Acta* **1975**, *14*, 53−58. (b) Mead, W. L.; Reid, W. K.; Silver, H. B. *Chem. Commun.* **1968**, 573−574.

Scheme 2



from the carbamate carbon at 161 pm is enhanced in the second spectrum as a result of enrichment of that site in ^{13}C. Like transamination, transcarboxylation is rapid and the reaction has reached equilibrium within a matter of 5 min.

Discussion

The $(Zn_4O)L_6$ complexes function as a highly symmetric scaffold for carbamate ligands, where each ligand interacts with two of the zinc ions. Because each carbamate ligand is in a chemically equivalent environment, their chemical reactivity is not differentiated, which simplifies our understanding of the carbamate interconversions. To understand the transamination reaction, it is useful to compare the zinc carbamate complexes with simple organic carbamate esters where the labile zinc−oxygen interactions are replaced by inert carbon−oxygen bonds. Direct transamination of carbamic acid esters has been reported as a synthetic pathway to substituted urethanes,[17] but the reaction requires temperatures in excess of 150 °C and long reaction times. Reaction of organic carbamates with primary and secondary amines also tends to produce substituted ureas as byproducts, indicating a preference for elimination of the alcohol rather than the amine. This suggests partial dissociation of the alkoxide anion at elevated temperatures to produce the isocyanate as an intermediate, which reacts with the alcohol to regenerate the carbamate or with the amine to generate the substituted urea. Transamination in organic carbamates is therefore likely to proceed via direct nucleophilic attack by the entering amine on the carbamate carbon, followed by elimination of the leaving amino group. Because of the strong carbon oxygen bond in the carbamate esters, elimination of carbon dioxide from organic carbamates is unlikely to be kinetically viable. As a result, organic carbamates are stable to elimination of CO_2 by acids and do not scramble with free CO_2. On the other hand, metal carbamate complexes readily dissociate CO_2 when reacted with Brønsted acids and often do exhibit scrambling with CO_2. The kinetic lability of the $N-CO_2^-$ bond in metal carbamate complexes and the relative ease with which CO_2 can be eliminated is therefore the most likely explanation for the rapid transamination reactivity observed in the zinc carbamate complexes.

To understand the thermodynamics of transamination, it is useful to consider the relationship between **1**, **2,** and **3**

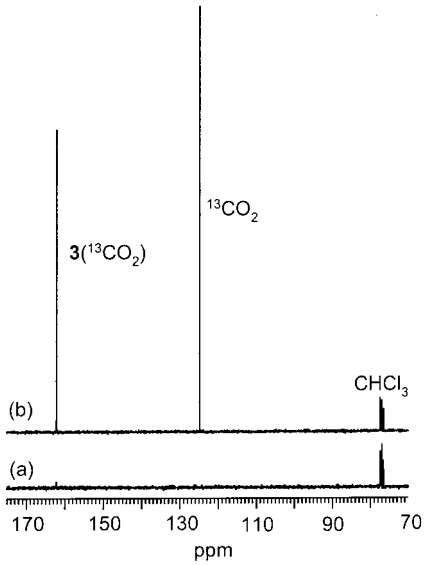
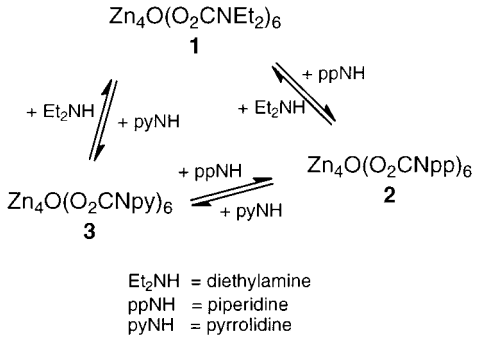


Figure 5. ^{13}C NMR spectra of **3** before (a) and 5 min after (b) exposure to $^{13}CO_2$. Solvent = $CDCl_3$. There was no change in the spectrum after (b) was collected.

Scheme 3



shown in Scheme 3. On the basis of values for K_{eq} in Table 2, the order of stability to transamination lies in the order **3** > **2** > **1**. This correlates with the trend in pK_a of pyrrolidine (19.6), piperidine (18.9), and diethylamine (18.7)[18] and suggests a linear free energy basis for the trend in stability. If $\log(K_{eq})$ for a transamination interconversion is plotted against the difference in pK_a for the two parent amines, a linear relationship is apparent, Figure 6. This correlation indicates that the stronger $N-CO_2^-$ bond is formed by the most basic amine, which explains the strong tendency to form the pyrrolidinecarbamate complex **3**. The slope is 1.2, and the intercept is essentially zero. The pK_a is a measure of the Brønsted acidity of the dialkylammonium ion and, hence, the σ-donor ability of the conjugate base. Inasmuch as ΔpK_a reflects the differing σ-donor strength of two amines, it is reasonable that ΔpK_a should correlate with the stability of the $N-CO_2^-$ bond in the carbamate. Given the substantial π-contribution in the $N-CO_2^-$ bond, it is surprising that a simple proton affinity parameter predicts so well the $N-CO_2^-$ interaction, which suggests that the π contribution is invariant for **1**, **2**, or **3**. This may arise from the fact that changes in the alkyl groups primarily affect steric constraints,

(17) (a) Knoefel, H.; Penninger, S.; Hammen, G.; Heitkamper, P. Nitrogen- and carbon-substituted di- and/or polyurethanes. Ep 60476 (Bayer A.-G., Fed. Rep. Ger.), 1982. (b) Merger, F.; Towae, F. Aryl mono- and polyurethanes. Ep 18583 (BASF A.-G., Fed. Rep. Ger, 1980. (c) Merger, F.; Towae, F. Aromatic di- and polyurethanes. De 2917568 (BASF A.-G., Fed. Rep. Ger.), 1980. (d) Falcone, S. J.; McCoy, J. J. N−Monosubstituted carbamic acid esters. Fr 2479209 (Atlantic Richfield Co., USA), 1981.

(18) Izutsu, K. *Acid−base dissociation constants in dipolar aprotic solvents*; Blackwell Scientific Publications: Oxford, U.K., 1990.

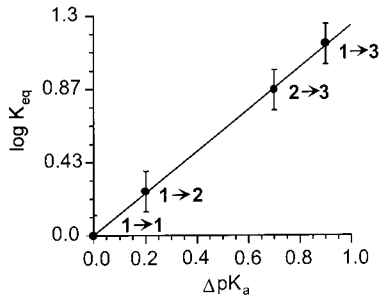


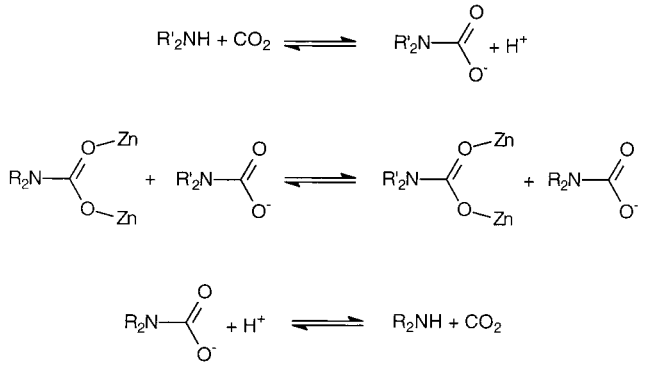
Figure 6. Transamination equilibrium constants log(K_{eq}) vs the pK_a difference ΔpK_a for the parent amines. K_{eq} was measured by proton NMR spectroscopy in $CDCl_3$. The amine pK_a data are referenced in acetonitrile.[18] Error bars give the average standard deviation over multiple measurements. The point 0,0 was included since log(K_{eq}) and ΔpK_a will be zero by definition for any self-exchange transamination. The best-fit line gives log(K_{eq}) = 1.2(1)ΔpK_a + 0.003(13).

which in turn have a greater impact on the σ-donor ability of the amines in this series.

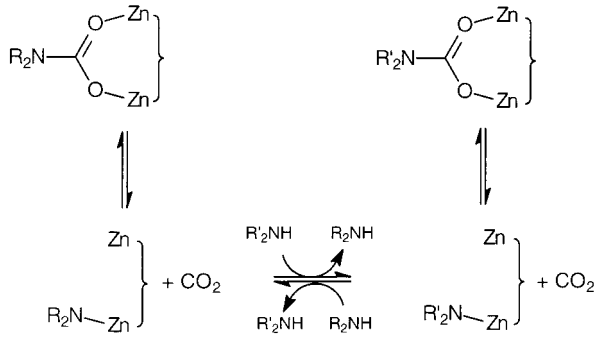
The equilibrium constants K_{eq} qualitatively correlate with the isolated yields of transamination products in Table 2. However, care must be exercised in the interpretation of the preparative yield data in terms of equilibrium thermodynamics. The preparative method involves a competition by the complex for two different amines, followed by removal of the unreacted amine in vacuo. The latter step favors release of the amine having the lower boiling point and may give rise to nonthermodynamic products when K_{eq} is small. The boiling points of diethylamine, pyrrolidine, and piperidine are 55, 87, and 106 °C, which should favor formation of **2** in general. This explains why the preparative conversion of **1** to **2** proceeds to >74% even though the equilibrium constant is only 1.8. However, K_{eq} clearly plays a dominant role in the preparation of **3** from **2**. K_{eq} for **2** ⇌ **3** is 7.3, so this conversion proceeds to better than 80% under stoichiometric conditions even though the boiling point of pyrrolidine is 19 °C lower than for piperidine.

While kinetics of transamination/transcarboxylation for this series is the subject of a forthcoming investigation, it is worthwhile at present to consider the observed reactions in the context of mechanistic information on other carbamate complexes. Observation of transcarboxylation in $(Zn_4O)L_6$ clearly requires the intermediacy of free carbon dioxide, and it is tempting to hypothesize a steady-state $N-CO_2^-$ bond cleavage step in transamination/transcarboxylation. However, the mechanism for transcarboxylation in metal carbamates was the subject of an extensive investigation by Chisholm and Extine,[11] who concluded that it proceeded via a preequilibrium between free amine and free CO_2 as shown in Scheme 4. The free CO_2 and amine were presumably generated from trace hydrolysis of the carbamate complexes by adventitious water. This is reasonable in the case of **1**−**3**, where we have observed that hydrolysis does result in the liberation of free CO_2. Furthermore, a very slight signal from CO_2 is observed in solution FTIR samples of the complexes even when precautions are taken to minimize the water content. The preequilibrium step is supported by chemical precedent in the formation of carbamates directly from amines and CO_2 in solution[19] and also provides a pathway

Scheme 4



Scheme 5



for transamination. Scheme 4 is therefore consistent with transamination/transcarboxylation and in fact requires that both reactions occur at comparable rates. It is therefore noteworthy that Chisholm and Extine did not observe transamination even in complexes undergoing facile transcarboxylation, except under conditions of excess CO_2.

The ease with which ligand hydrolysis takes place complicates any assessment of reactivity in this system, and we recognize a possible alternative reaction pathway that could lead to transamination/transcarboxylation directly from the $(Zn_4O)L_6$ complex, Scheme 5. In this mechanism, rate-limiting cleavage of the $^-O_2C-N_{leaving}$ bond precedes attack by the incoming amine in an S_N1-type reaction at the carbamate carbon. This reaction would be the formal the reverse of that proposed by Hartwig et al.[20] for insertion of CO_2 into metal−nitrogen bonds. It is in fact related to Scheme 4 since both proceed via free CO_2 but differ in the details of how free CO_2 is generated. The $N-CO_2^-$ bond breaking step need not necessarily be rate limiting if ligand dissociation must precede it, in which case Schemes 4 and 5 differ only by the dependence of the former on free amine. The specific role of the Zn_4O^{6+} core in the transamination/transcarboxylation process cannot be assessed on the basis of the present data, especially since there has yet to be a systematic survey of late transition metal carbamate reactivity. The metal centers would play a crucial role in stabilizing

(19) (a) Chakraborty, A. K.; Bischoff, K. B.; Astarita, G.; Damewood, J. R., Jr. *J. Am. Chem. Soc.* **1988**, *110*, 6947−6954. (b) Takeshita, K.; Kitamoto, A. *J. Chem. Eng. Jpn.* **1988**, *21*, 411−417. (c) Weiland, R. H.; Trass, O. *Can. J. Chem. Eng.* **1971**, *49*, 767−772.
(20) Hartwig, J. F.; Bergman, R. G.; Andersen, R. A. *J. Am. Chem. Soc.* **1991**, *113*, 6499−6508.

the amido intermediate generated in Scheme 5, but their function in Scheme 4 is not obvious beyond providing a scaffold for the carbamate ligand.

Transamination and transcarboxylation have important implications beyond the reactivity of the $(Zn_4O)L_6$ system. At the most fundamental level, insertion of CO_2 into metal−nitrogen bonds must be the microscopic reverse of the elimination of CO_2 from metal carbamates. Therefore, transamination/transcarboxylation in this system is relevant to longstanding questions concerning the mechanism of such insertion and exchange reactions in catalytic processes involving insertion of CO_2 into metal−nitrogen or metal−oxygen bonds and to the formation of metal−carbamate centers in biology. The transamination/transcarboxylation reaction also has implications for the mechanism by which the carbamate group in N^1-carboxybiotin transfers carbon dioxide to the terminal substrate in biotin-dependent enzymes. With these considerations in mind, we have planned a detailed mechanistic evaluation of the transamination/transcarboxylation activity of the $(Zn_4O)L_6$ series of complexes to follow this preparative report.

Summary

The series of complexes $(Zn_4O)L_6$ (L = diethylcarbamate (**1**), piperidinecarbamate (**2**), pyrrolidinecarbamate (**3**)) was prepared and crystallographically characterized. The complexes readily undergo transamination metathesis of the carbamate group to interconvert two members of the series. Equilibrium constants determined for transamination correlated linearly with the basicity of the parent amines, providing a linear free energy basis for the relative stability trend **3** > **2** > **1**. In addition, the complexes undergo a facile transcarboxylation reaction that scrambles the carboxyl group in the carbamate ligand with free carbon dioxide. This latter observation was placed in the context of proposed mechanisms for transamination/transcarboxylation. The potential importance of this system in the insertion of CO_2 into metal−nitrogen bonds was discussed.

Acknowledgment. The National Science Foundation is acknowledged for a grant to M.T.C. (Grant CHE-9985266 and for contribution toward the purchase of single crystal instrumentation used in this study (Grant CHE 9808440).

Supporting Information Available: Two X-ray crystallographic files in CIF format for complexes **2** and **3**. These materials are available free of charge via the Internet at http://pubs.acs.org.

IC010885V