Inorganic Chemistry
Article
pubs.acs.org/IC

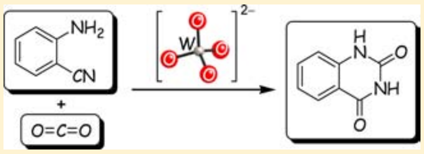
Efficient $[WO_4]^{2-}$-Catalyzed Chemical Fixation of Carbon Dioxide with 2-Aminobenzonitriles to Quinazoline-2,4(1*H*,3*H*)-diones

Toshihiro Kimura, Hanako Sunaba, Keigo Kamata, and Noritaka Mizuno*

Department of Applied Chemistry, School of Engineering, The University of Tokyo, 7-3-1 Hongo, Bunkyo-ku, Tokyo 113-8656, Japan

Supporting Information

ABSTRACT: A simple monomeric tungstate, $TBA_2[WO_4]$ (**I**, TBA = tetra-*n*-butylammonium), could act as an efficient homogeneous catalyst for chemical fixation of CO_2 with 2-aminobenzonitriles to quinazoline-2,4(1*H*,3*H*)-diones. Various kinds of structurally diverse 2-aminobenzonitriles could be converted into the corresponding quinazoline-2,4(1*H*,3*H*)-diones in high yields at atmospheric pressure of CO_2. Reactions of inactive 2-amino-4-chlorobenzonitrile and 2-amino-5-nitrobenzonitrile at 2 MPa of CO_2 also selectively proceeded. The present system was applicable to a g-scale reaction of 2-amino-5-fluorobenzonitrile (10 mmol scale) with CO_2 and 1.69 g of analytically pure quinazoline-2,4(1*H*,3*H*)-dione could be isolated. In this case, the turnover number reached up to 938 and the value was the highest among those reported for base-mediated systems so far. NMR spectroscopies showed formation of the corresponding carbamic acid through the simultaneous activation of both 2-aminobenzonitirile and CO_2 by **I**. Kinetic and computational studies revealed that **I** plays an important role in conversion of the carbamic acid into the product.



INTRODUCTION

Quinazoline-2,4(1*H*,3*H*)-diones are important key intermediates in pharmaceutical synthesis.[1] They are conventionally synthesized by stoichiometric reactions of anthranilamides with phosgene[2] or anthranilic acids with urea,[3] potassium cyanate,[4] and chlorosulfonyl isocyanate.[5] These methodologies, however, require specialized and/or very toxic reagents. In contrast, Mizuno and co-workers have reported atom-efficient synthesis of quinazoline-2,4(1*H*,3*H*)-diones from 2-aminobenzonitriles and CO_2 with a stoichiometric amount of 1,8-diazabicyclo[5.4.0]undec-7-ene (DBU).[6−8] To date, various kinds of organic and inorganic base catalysts such as DBU,[9] Cs_2CO_3,[10] MgO/ZrO_2,[11] 1-butyl-3-methylimidazolium hydroxide,[12] *N*-methyltetrahydropyrimidine,[13] and 1,1,3,3-tetramethylguanidine[14] have been used to synthesize quinazoline-2,4-(1*H*,3*H*)-diones. However, these systems have disadvantages (see the Supporting Information, Table S1): their low turnover numbers (TONs, 1−79), high pressures of CO_2 (1−10 MPa), narrow applicability to substrates, and low reusability of catalysts. Especially, there have been only a few reports on catalytic systems using CO_2 at atmospheric pressure or those applicable to substrates with low basicities of amino groups (e.g., 2-amino-5-nitrobenzonitrile). Therefore, developments of efficient catalysts are still challenging subjects.

Polyoxometalates (POMs) are a large family of anionic metal−oxygen clusters of early transition metals and have stimulated many current research activities in broad fields such as catalysis, material science, and medicine, because their chemical and physical properties can finely be tuned by choosing constituent elements and counter cations.[15] Due to their unique properties, isopoly- and heteropolyoxometalates, mixed-addenda POMs, lacunary POMs, transition-metal-substituted POMs, and peroxometalates have been used as catalysts for various acid-catalyzed, photocatalytic, and oxidation reactions.[15,16] On the other hand, base catalysis by POMs including chemical fixation of CO_2 has scarcely been reported.[17] We have previously reported highly efficient chemical fixation of CO_2 at atmospheric pressure with aromatic diamines to cyclic urea derivatives catalyzed by a simple monomeric tungstate, $TBA_2[WO_4]$ (**I**, TBA = tetra-*n*-butylammonium).[17a] Bifunctional activation of both CO_2 and an aromatic diamine by a tungsten-oxo moiety in **I** results in high yields and TONs. Compound **I** has been reported to show catalytic activities for chemical fixation of CO_2 with only two kinds of 2-aminobenzonitriles (2-aminobenzonitrile and 2-amino-5-chlorobenzonitrile) to the corresponding quinazoline-2,4(1*H*,3*H*)-diones, and the reaction mechanism is still unclear.

In this paper, we expand the scope of the **I**-catalyzed chemical fixation of CO_2 with various kinds of structurally diverse 2-aminobenzonitriles. In addition, the reaction mechanism is investigated in detail on the basis of ^{1}H, ^{13}C, and ^{183}W NMR spectroscopies, kinetics, and density functional theory (DFT) calculations.

EXPERIMENTAL SECTION

Materials. Solvents and substrates were obtained from Kanto, TCI, or Aldrich (Reagent grade) and purified prior to the use.[18] Products were isolated and identified by comparison of their ^{1}H and ^{13}C NMR signals with literature data (see the Suppoting Information). Deuterated solvents (D_2O, $CDCl_3$, DMSO-d_6, and DMF-d_7) were purchased from ACROS, C/D/N Isotopes, or Aldrich and used as received. Polyoxotungstates ($TBA_2[W_6O_{19}]$, $TBA_4[W_{10}O_{32}]$, and

Received: September 28, 2012
Published: November 13, 2012

dx.doi.org/10.1021/ic302110a | Inorg. Chem. 2012, 51, 13001−13008

$TBA_4[\alpha\text{-}SiW_{12}O_{40}]$) were synthesized according to literature procedures[19] and characterized by IR, NMR (^{29}Si and ^{183}W), and elemental analysis.

Instruments. IR spectra were measured on a Jasco FT/IR-460 spectrometer Plus using KBr disks. NMR spectra were recorded on a JEOL JNM-EX-270 spectrometer (^1H, 270.0 MHz; ^{13}C, 67.80 MHz; ^{29}Si, 53.45 MHz; ^{183}W, 11.20 MHz) by using 5 mm tubes (for ^1H and ^{13}C) or 10 mm tubes (for ^{29}Si and ^{183}W). Chemical shifts (δ) were reported in ppm downfield from $Si(CH_3)_4$ (solvent, $CDCl_3$) for ^1H, ^{13}C, and ^{29}Si NMR spectra and 2 M Na_2WO_4 (solvent, D_2O) for ^{183}W NMR spectra. For NMR measurements of the reaction of **I** with CO_2, pressure-resistant or J.YOUNG valve NMR tubes were used: DMF solution of **I** was evacuated at 233 K followed by quick introduction of CO_2 (0.1−0.6 MPa). ICP-AES analyses were performed with a Shimadzu ICPS-8100 spectrometer. GC analyses were performed on Shimadzu GC-2014 with a flame ionization detector equipped with an InertCap-5 capillary column (internal diameter = 0.25 mm, length = 60 m) or a TC-1 capillary column (internal diameter = 0.25 mm, length = 30 m). Mass spectra were recorded on a Shimadzu GCMS-QP2010 equipped with a TC-5HT capillary column at an ionization voltage of 70 eV. Argon filled MBraun Labmaster 130 and VAC Omni-Lab glove boxes were employed for manipulation and storage of all oxygen and moisture sensitive compounds.

Synthesis and Characterization of $TBA_2[WO_4]$ (I). Tetra-*n*-butylammonium salt of a monomeric tungstate **I** was synthesized according to literature procedure.[20] Because of the highly hygroscopic property, **I** was stored and handled in glovebox. IR (KBr, ν): 2990, 2958, 2945, 2919, 2874, 1474, 1464, 1455, 1379, 1364, 1240, 1166, 1109, 1069, 1058, 1031, 992, 838, 738 cm^{-1}. ^{183}W NMR (11.2 MHz, DMSO-d_6, 298 K): δ = 16.5 ppm. Anal. Calcd for $TBA_2[WO_4]$: C, 52.45, H, 9.90; N, 3.82; W, 25.09. Found: C, 52.20; H, 9.93; N, 3.84; W, 24.91.

Typical Procedure for the I-Catalyzed Reaction of CO_2 (0.1 MPa) with 2-Aminobenzonitriles. 2-Aminobenzonitrile (1 mmol), **I** (0.02 mmol), and DMSO (1 mL) were charged in a Schlenk tube with a magnetic stir bar. CO_2 (0.1 MPa) was introduced by a balloon, and the reaction mixture was stirred at 373 K. The reaction solution was periodically analyzed by GC, LC, GC-MS, or NMR. The reaction mixture was added into 1 M HCl aqueous solution (5 mL) and then the resulting precipitates were collected by filtration, washed with water (2 mL), toluene (2 mL), and diethyl ether (2 mL), and dried in vacuo to give the analytically pure products. Isolated products were identified by comparison of ^1H and ^{13}C NMR spectra with literature data.

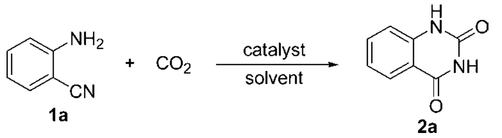
Typical Procedure for the I-Catalyzed Reaction of CO_2 (2 MPa) with 2-Aminobenzonitriles. 2-Aminobenzonitrile (1 mmol), **I** (0.02 mmol), and DMSO (1 mL) were charged in a Teflon vessel placed in a stainless steel autoclave with a magnetic stir bar. CO_2 (2 MPa) was introduced to autoclave and the reaction mixture was stirred at 373 K. After reaction was completed, autoclave was cooled to room temperature and CO_2 was slowly vented. Products were isolated and idetified by the ^1H and ^{13}C NMR spectroscopies.

Quantum Chemical Calculations. DFT calculations were carried out at the B3LYP level theory[21] (6-31++G* basis sets for H, C, N, and O atoms and the double-ξ quality basis sets with effective core potentials proposed by Hay and Wadt[22] for W atoms) by using conductor-like polarizable continuum model (CPCM) with parameters of the United Atom Topological Model (UAKS). 2-Aminobenzonitrile was used as a model substrate. Transition state structure was searched by numerically estimating the matrix of second-order energy derivatives at every optimization step and by requiring exactly one eigenvalue of this matrix to be negative. For transition state, the frequency analysis was conducted at the same level at the final geometry. Optimized geometries were shown in Table S2 and Figure 7b (see the Supporting Information). The zero-point vibrational energies were not included. All calculations were performed with the Gaussian09 program package.[23]

■ RESULTS AND DISCUSSION

Catalytic Chemical Fixation of CO_2 with 2-Aminobenzonitriles to Quinazoline-2,4(1*H*,3*H*)-diones. Effects of solvents on the **I**-catalyzed chemical fixation of CO_2 (2 MPa) with 2-aminobenzonitrile (**1a**) to quinazoline-2,4(1*H*,3*H*)-dione (**2a**) were investigated. Among the solvents tested, dimethyl sulfoxide (DMSO) was the most effective solvent and **2a** was obtained in the highest yield of 90% (Table 1, entry 1). *N*,*N*-Dimethylacetamide (DMA), *N*,*N*-dimethylformamide (DMF), toluene, and acetonitrile gave **2a** in 77, 75, 49, and 29% yields, respectively, whereas 1,2-dichloroethane was a poor solvent (Table 1, entries 4−8). Effects of catalysts on the reaction of CO_2 with **1a** in DMSO were investigated. Compound **I** showed the highest catalytic activity among the catalysts tested. Reactions hardly proceeded in the absence of **I** or in the presence of isopoly- and heteropolyoxotungstates ($TBA_2[W_6O_{19}]$, $TBA_4[W_{10}O_{32}]$, and $TBA_4[\alpha\text{-}SiW_{12}O_{40}]$), the catalyst precursor of H_2WO_4, and TBABr (Table 1, entries 9−14).[24] Catalytic activities of $TBA_6[\gamma\text{-}H_2GeW_{10}O_{36}]$ and TBAOH, which have been reported to be active for Knoevenagel condensation of active methylene compounds with carbonyl compounds,[17b,25] were lower than that of **I** (Table 1, entries 15 and 16). After the **I**-catalyzed reaction was completed, **1a** (1 mmol) was added to the reaction mixture and the reaction was again carried out under the same conditions. The reaction proceeded with almost the same yield and selectivity as those observed for the first run (Table 1, entries 1 and 2). Thus, **I** is intrinsically reusable.[26] Even at atmospheric pressure of CO_2 (0.1 MPa), the catalytic reaction of CO_2 with

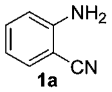
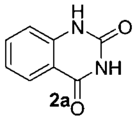
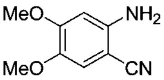
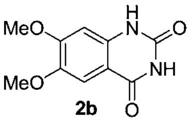
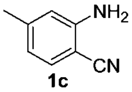
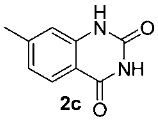
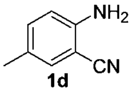
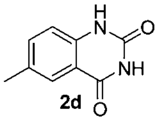
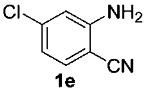
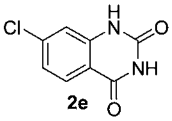
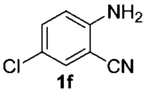
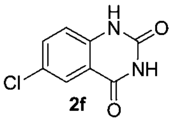
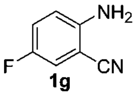
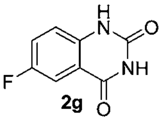
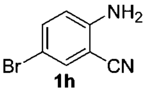
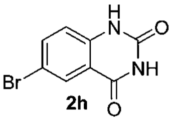
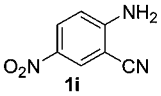
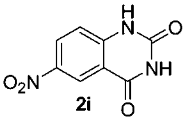
Table 1. Effects of Catalysts and Solvents on Chemical Fixation of CO_2 with 1a[a]



entry	catalyst	solvent	yield of **2a** (%)
1	**I**	DMSO	90
2[b]	**I**	DMSO	92
3[c]	**I**	DMSO	90
4	**I**	DMA	77
5	**I**	DMF	75
6	**I**	Toluene	49
7	**I**	Acetonitrile	29
8	**I**	1,2-dichloroethane	1
9	Without	DMSO	<1
10	$TBA_2[W_6O_{19}]$	DMSO	<1
11	$TBA_4[W_{10}O_{32}]$	DMSO	<1
12	$TBA_4[\alpha\text{-}SiW_{12}O_{40}]$	DMSO	<1
13	H_2WO_4	DMSO	<1
14[d]	TBABr	DMSO	<1
15	$TBA_6[\gamma\text{-}H_2GeW_{10}O_{36}]$	DMSO	5
16[d]	$TBAOH{\cdot}30H_2O$	DMSO	63

[a] Reaction conditions: **1a** (1 mmol), catalyst (W: 2 mol % with respect to **1a**), solvent (2 mL), CO_2 (2 MPa), 373 K, 12 h. Yields were determined by GC analysis. [b] Reuse experiment. Reaction conditions are the same as those in entry 1. [c] Reaction conditions: **1a** (1 mmol), **I** (2 mol % with respect to **1a**), DMSO (2 mL), CO_2 (0.1 MPa), 373 K, 120 h. [d] Catalyst (2 mol % with respect to **1a**).

Table 2. Chemical Fixation of CO_2 with Various 2-Aminobenzonitriles Catalyzed by I[a]

Entry	Substrate	Product	CO_2 (MPa)	Time (h)	Isolated yield (%)
1	 1a	 2a	0.1	144	77
2			2	12	85
3	 1b	 2b	0.1	96	96
4			2	12	96
5	 1c	 2c	0.1	168	83
6			2	18	85
7	 1d	 2d	0.1	96	91
8			2	12	87
9[b,c]	 1e	 2e	2	28	69
10	 1f	 2f	0.1	120	93
11			2	12	95
12	 1g	 2g	0.1	72	93
13			2	12	91
14	 1h	 2h	0.1	120	88
15			2	12	95
16[c,d]	 1i	 2i	2	24	74

[a] Reaction conditions: Substrate (1 mmol), **I** (2 mol % with respect to substrate), DMSO (2 mL), 373 K. Purities of isolated products were determined by ^{1}H NMR (≥95% in all cases). [b] **I** (10 mol % with respect to **1e**), 413 K. Conversion of **1e** (96%). [c] Yields were determined by ^{1}H NMR analysis of the reaction solution. [d] **I** (10 mol % with respect to **1i**), 393 K. Conversion of **1i** (80%).

1a efficiently proceeded to give **2a** in 90% yield (Table 1, entry 3).

The **I**-catalyzed system could be applied to chemical fixation of CO_2 with various kinds of structurally diverse 2-aminobenzonitriles (Table 2). Various 2-aminobenzonitriles with electron-donating and electron-withdrawing substituents were converted into the corresponding quinazoline-2,4(1*H*,3*H*)-diones in good to excellent yields at atmospheric pressure of CO_2 (Table 2, entries 1, 3, 5, 7, 10, 12, and 14), whereas higher pressures of CO_2 (1−10 MPa) are generally required to attain high yields with the other catalysts (see the Supporting Information, Table S1). 2-Amino-4,5-dimethoxybenzonitrile (**1b**) gave 6,7-dimethoxyquinazoline-2,4(1*H*,3*H*)-dione (**2b**), which is a key intermediate toward Prazosin, IAAP, and Doxazosin,[27] in 96% yield (Table 2, entry 3). 5-Halogen-susbstituted 2-aminobenzonitriles (**1f**−**1h**) were efficiently converted into the corresponding quinazoline-2,4(1*H*,3*H*)-diones (**2f**−**2h**) in excellent yields (Table 2, entries 10, 12, and 14). In addition, reactions more efficiently proceeded at 2 MPa of CO_2 and were completed within 28 h (Table 2, entries 2, 4, 6, 8, 9, 11, 13, 15, and 16). Notably, inactive 4-chloro-2-aminobenzonitrile (**1e**) and 5-nitro-2-aminobenzonitrile (**1i**) were selectively converted into the corresponding 7-chloroquinazoline-2,4(1*H*,3*H*)-dione (**2e**, 69% yield) and 6-nitroquinazoline-2,4(1*H*,3*H*)-dione (**2i**, 74% yield), respectively, while a complex mixture of products has been reported to be formed by the reaction of CO_2 with **1i**, even in the presence of a stoichiometric amount of DBU.[9]

To further confirm the effectiveness of the present system, we carried out 10 mmol scale reactions of CO_2 (2 MPa) with **1a**, **1b**, and **1g** (Figure 1). Analytically pure **2a**, **2b**, and **2g** could be isolated in 93% (1.52 g), 98% (2.18 g), and 94% (1.69

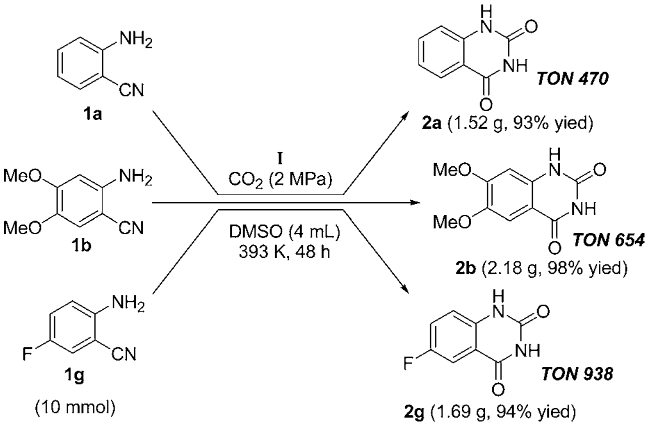


Figure 1. Larger-scale reactions of CO_2 with **1a**, **1b**, and **1g** catalyzed by **I** (0.20, 0.15, and 0.10 mol % with respect to **1a**, **1b**, and **1g**, respectively).

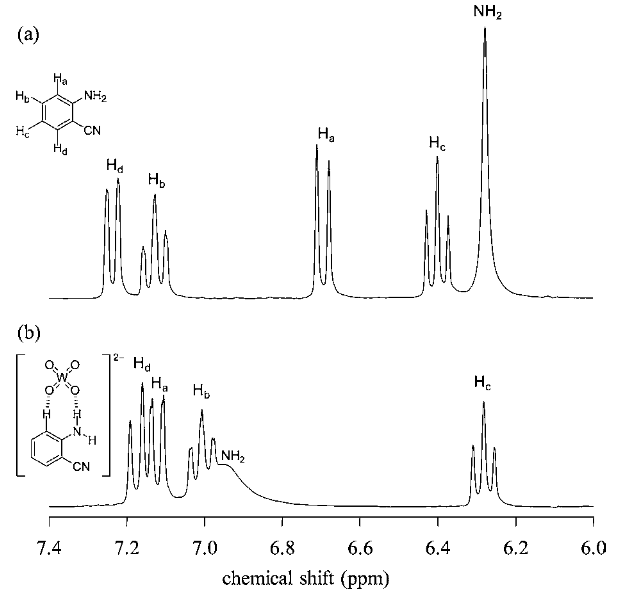


Figure 2. ^1H NMR spectra of (a) **1a** and (b) **1a** in the presence of **I**. Solvent (DMF/DMF-d_7 (0.4/0.2 mL)), 233 K, **1a** (0.9 M), **I** (0.2 M).

g) yields, respectively, showing that the present system is applicable to g-scale reactions. The TONs for reactions of **1a**, **1b**, and **1g** reached up to 470, 654, and 938, respectively, and these values were much larger than those (1−79 (**2a**), 1−48 (**2b**), and 3−53 (**2g**)) of the reported systems (see the Supporting Information, Table S1).[28]

Reaction Mechanism. Although a carbamic acid has been postulated as an intermediate for chemical fixation of CO_2 with 2-aminobenzonitrile to quinazoline-2,4(1*H*,3*H*)-dione,[6,9−14] its formation and the mechanism for successive conversion into the product have never been investigated. To investigate the mechanism, we investigated reactivities of **1a** with **I** in the absence and presence of CO_2 by ^1H and ^{183}W NMR spectroscopies. The ^1H NMR spectrum of **1a** showed downfield shifts of NH_2 protons (from 6.28 to 6.95 ppm) and a 3-H proton (from 6.69 to 7.16 ppm) upon addition of **I** (Figure 2), indicating hydrogen bonding interaction between **I** and **1a** to form a **I**−**1a** adduct as shown in Figure S1 (see the Supporting Information). The downfield shift of NH_2 protons ($\Delta\delta$ = +0.67 ppm) upon addition of **I** was much larger than

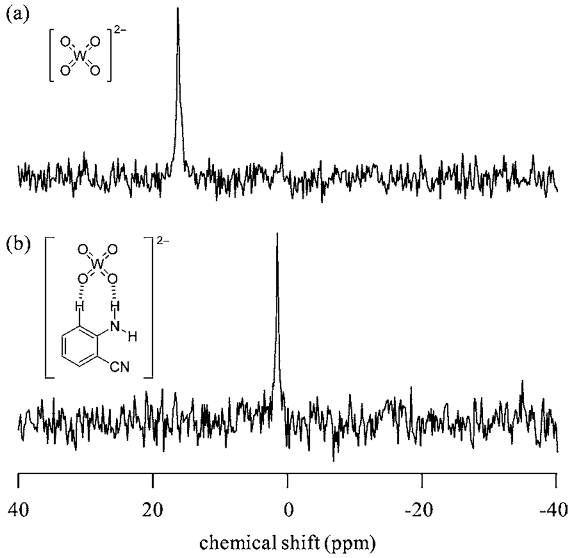


Figure 3. ^{183}W NMR spectra of (a) **I** and (b) **I** in the presence of **1a**. Solvent (DMF/DMF-d_7 (1.3/0.7 mL)), 233 K, **1a** (0.5 M), **I** (0.5 M).

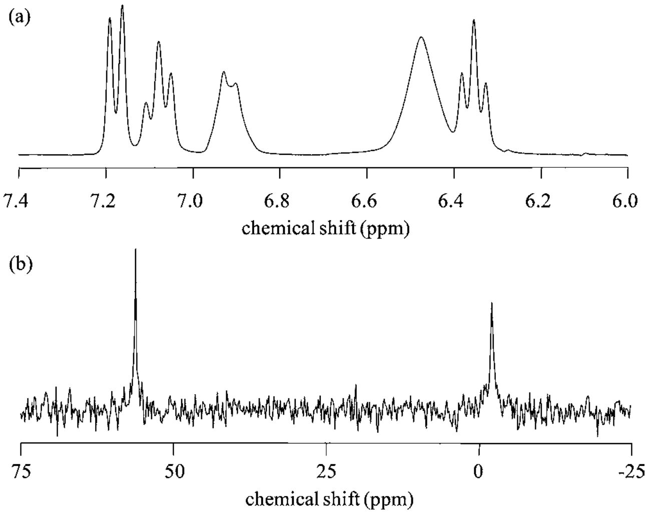


Figure 4. (a) ^1H and (b) ^{183}W NMR spectra of **I** in the presence of **1a** and CO_2. (a) Solvent (DMF/DMF-d_7 (0.4/0.2 mL)), 233 K, **1a** (0.9 M), **I** (0.2 M), CO_2 (0.1 MPa). (b) Solvent (DMF/DMF-d_7 (1.3/0.7 mL)), 233 K, **1a** (0.5 M), **I** (0.5 M), CO_2 (0.1 MPa).

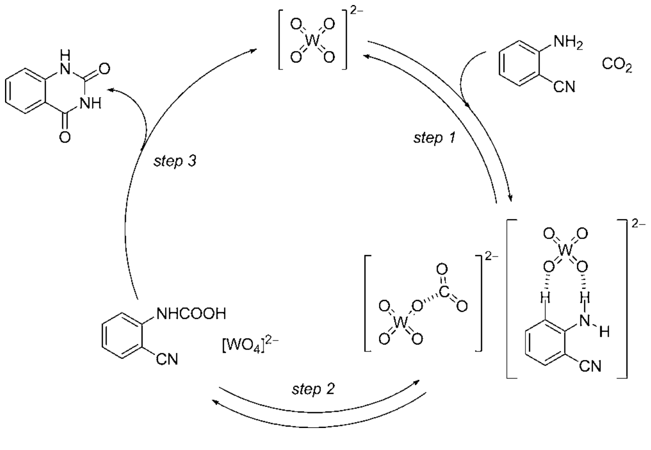


Figure 5. Proposed reaction mechanism for chemical fixation of CO_2 with **1a** catalyzed by **I**.

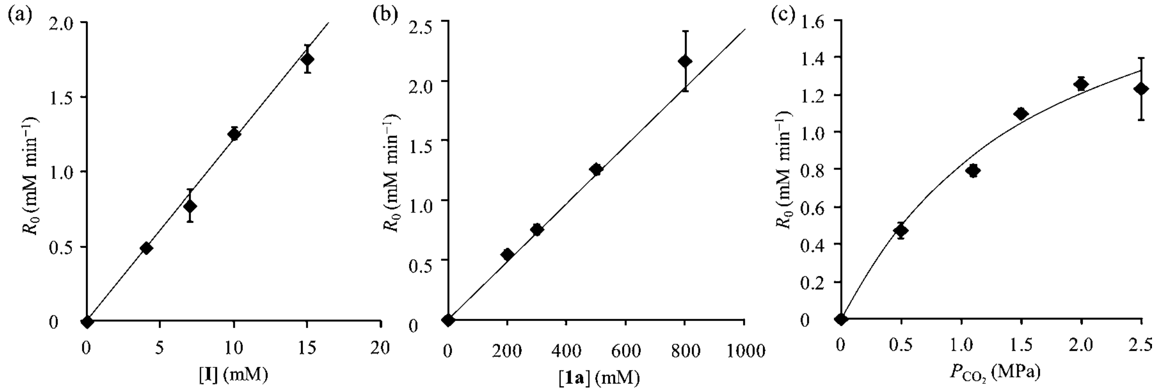


Figure 6. Dependences of reaction rates on concentrations of (a) **I** and (b) **1a** and (c) pressure of CO_2 for reaction of CO_2 with **1a** catalyzed by **I**. Reaction conditions for (a): **I** (4–15 mM), **1a** (0.5 M), CO_2 (2.0 MPa), DMSO (2 mL), 373 K. Reaction conditions for (b): **I** (10 mM), **1a** (0.2–0.8 M), CO_2 (2.0 MPa), DMSO (2 mL), 373 K. Reaction conditions for (c): **I** (10 mM), **1a** (0.5 M), CO_2 (0–2.5 MPa), DMSO (2 mL), 373 K. Solid lines were calculated with eq 3.

that ($\Delta\delta$ = +0.05 ppm) upon addition of DBU, suggesting stronger interaction of **1a** with **I**. The 16.4 ppm ^{183}W signal of **I** also shifted to 1.6 ppm upon addition of **1a** (Figure 3).

Formation of a **I**–CO_2 adduct was confirmed by ^{13}C and ^{183}W NMR spectroscopies in a similar way to the **I**-catalyzed chemical fixation of CO_2 with an aromatic diamine:[17a] When DMF solution of **I** was exposed to CO_2 (0.1 MPa), new 163.6-ppm ^{13}C and 57.8-ppm ^{183}W signals of **I**–CO_2 appeared with decrease in the 16.4-ppm ^{183}W signal intensity of **I** (see the Supporting Information, Figures S2 and S3). Upon further introduction of CO_2 (0.6 MPa), a new ^{13}C signal appeared at 160.9 ppm with disappearance of the 163.6-ppm signal. The 160.9-ppm signal also exhibited satellites with a coupling constant of $^2J_{W-C}$ = 6.1 Hz (14% satellite intensity), of which the value was close to that (6.7 Hz) of **I**–CO_2. Similarly, a new ^{183}W signal appeared at 22.6 ppm with disappearance of the 16.4- and 57.8-ppm signals of **I**–CO_2 and **I**, respectively. Therefore, these two new signals would be assignable to a **I**–$(CO_2)_2$ adduct formed by the reaction of **I**–CO_2 with CO_2.

Next, ^{1}H, ^{13}C, and ^{183}W NMR spectra of **I** in the presence of both **1a** and CO_2 were measured. When CO_2 (0.1 MPa) was introduced into DMF solution containing **I** and **1a** at 233 K, the 6.45-ppm ^{1}H signal of hydrogen-bonded NH_2 protons and the 163.6-ppm ^{13}C signal of a **I**–CO_2 adduct were still observed (see the Supporting Information, Figures S3 and 4a). The ^{183}W NMR spectrum also showed signals at 55.9 and −2.8 ppm assignable to **I**–**1a** and **I**–CO_2, respectively (Figure 4b). All these NMR results support bifunctionality of **I**. The hydrogen bond would weaken the N–H bond and facilitate nucleophilic attack of the NH_2 group in **1a** on the carbon atom of CO_2 to form the corresponding carbamic acid. Upon heating reaction solution containing **I**, **1a**, and CO_2 to 298 K, new eight ^{13}C signals appeared at 155.5, 148.4, 133.8, 132.0, 118.6, 118.1, 117.7, and 96.1 ppm (see the Supporting Information, Figure S4). It has been reported that a ^{13}C signal of a carboxy carbon in a carbamic acid appears in the range of 157–160 ppm.[29] Therefore, these eight ^{13}C signals are likely assignable to the carbamic acid.[30] New ^{1}H signals also appeared at 8.52, 7.20, and 6.52 ppm assignable to aromatic protons of the carbamic acid, whereas the other signals of the carbamic acid overlapped with those of **1a**. On the other hand, the ^{13}C and ^{1}H signals of the carbamic acid were not observed in the absence of **I**, suggesting that formation of carbamic acid requires the presence of **I** and that **I**–**1a** and/or **I**–CO_2 likely play important roles in formation of the carbamic acid.

On the basis of these spectroscopic results, we propose a possible reaction mechanism for the **I**-catalyzed chemical fixation of CO_2 with **1a** (Figure 5). First, activation of both **1a** and CO_2 by **I** facilitates nucleophilic attack of the NH_2 group on the carbon atom of CO_2 to give a carbamic acid (eq 1). Then, the carbamic acid is converted into **2a** (eq 2). Kinetic studies showed the first-order dependences of the reaction rates (R_0) on concentrations of **I** (4–15 mM) and **1a** (0.2–0.8 M) and pressure of CO_2 (P_{CO_2}, 0–1.5 MPa) (see the Supporting Information, Figures S6 and 6). The overall reaction rate is expressed by eq 3 (see details in Supporting Information). Dependences of the reaction rates on concentrations of **I** and **1a** and pressure of CO_2 were fairly well reproduced by using eq 3, K_1 = 5.8 × 10^{-1} MPa^{-1}, and k_1 = 4.5 × 10^{-4} mM^{-1} min^{-1} (shown by the solid lines in Figure 6), and the conversion of the carbamic acid into the product (step 3 in Figure 5) would be the rate-determining step:

$$\mathbf{1a} + CO_2 \overset{K_1}{\rightleftarrows} \text{carbamic acid} \tag{1}$$

$$\text{carbamic acid} + \mathbf{I} \xrightarrow{k_1} \mathbf{2a} + \mathbf{I} \tag{2}$$

$$R_0 = \frac{d[\mathbf{2a}]}{dt} = k_1[\mathbf{I}][\mathbf{1a}]_0\left(\frac{1}{1 + \frac{1}{K_1 P_{CO_2}}}\right) \tag{3}$$

To investigate the reaction mechanism in more detail, we carried out DFT calculations taking into account solvation in toluene using the conductor-like polarizable continuum model (CPCM) with parameters of the united atom topological model (UAKS).[31] Energies of reaction steps were calculated according to Figure 7(a), and the results are summarized in Figure 7b. The reaction of $[WO_4]^{2-}$ with a carbamic acid forms $[HWO_4]^-$ interacting with a carbamate (**A**) and was calculated to be exothermic by 78 kJ mol^{-1}. The intramolecular attack of the carbamate on the nitrile group takes place to form the cyclic intermediate **B**. This is the rate-determining step for the present reaction, and the activation barrier of the transition-state (**TS1**) was calculated to be 107 kJ mol^{-1}, much lower than that (189 kJ mol^{-1}) for the cyclization of the carbamic acid in the absence of $[WO_4]^{2-}$ (see the Supporting Information, Figure S7). A monomeric tungstate works not only as a base

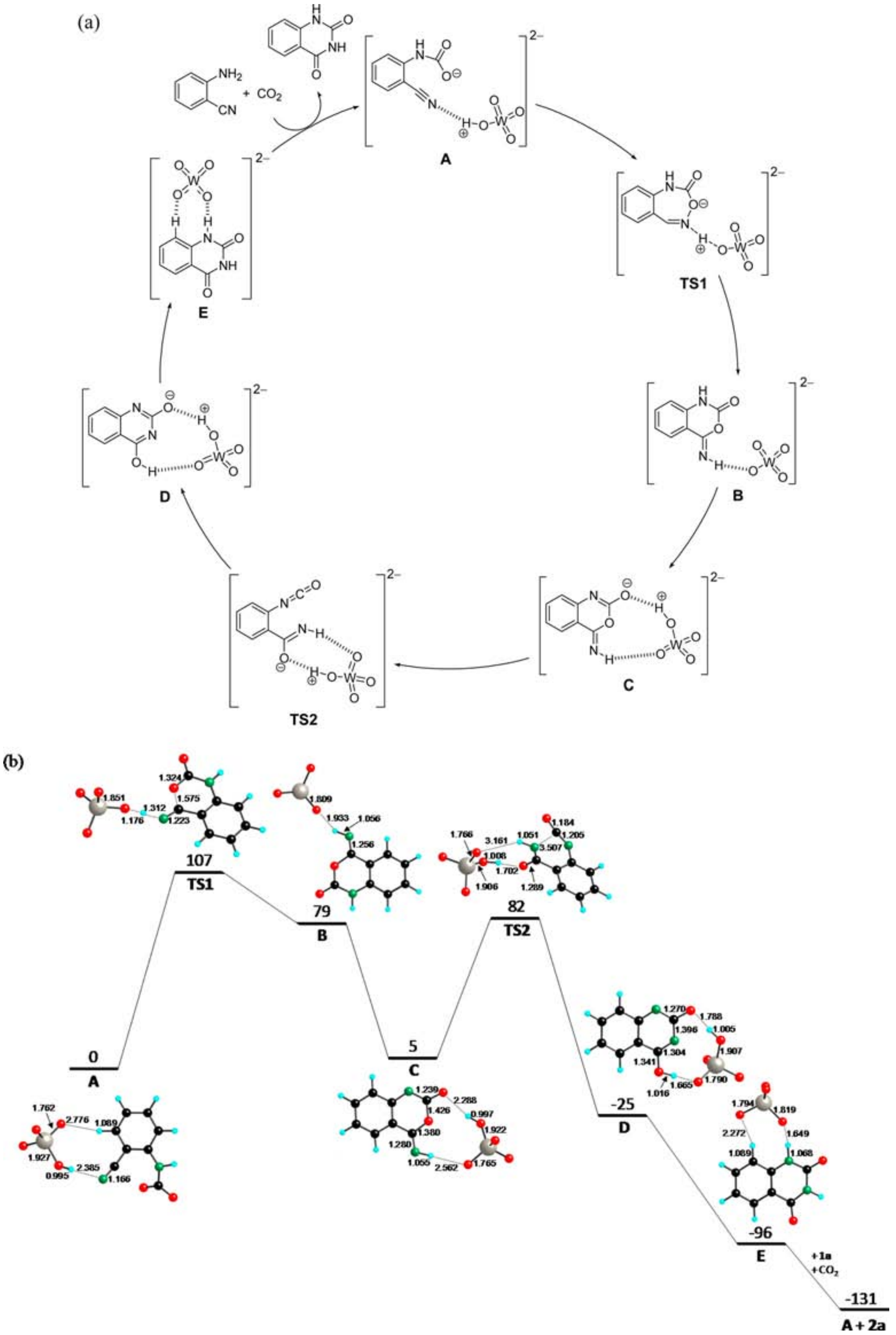


Figure 7. (a) Proposed reaction mechanism for the conversion of the carbamic acid to **2a** (step 3 in Figure 5) catalyzed by **I** and (b) calculated energy diagram of reaction of CO_2 with **1a** to **2a** catalyzed by $[WO_4]^{2-}$ (energies and lengths in kJ mol^{-1} and Å, respectively). Gray, red, black, green, and light blue balls represent tungsten, oxygen, carbon, nitrogen, and hydrogen atoms, respectively.

(proton abstraction of the carbamic acid by $[WO_4]^{2-}$) but also as an acid (activation of the nitrile group by $[HWO_4]^{-}$). Therefore, the nucleophilic attack of the negatively charged oxygen atom of the carbamate on the positively charged carbon atom of the nitrile group easily takes place, resulting in the low activation barrier. Then, **B** was isomerized to the imidic acid intermediate (**C**). Intermediate **C** followed by the conversion into the isomeric product adduct (**D**) through the isocyanate intermediate. Then, **D** was converted into the $[WO_4]^{2-}$–product adduct (**E**). The activation barrier (**TS2**, 77 kJ mol^{-1}) from **C** to **D** was lower than that of **TS1**. Quinazoline-2,4(1*H*,3*H*)-dione **2a** was eliminated through **E** followed by the reaction of $[WO_4]^{2-}$ with **1a** and CO_2, accomplishing the catalytic cycle. These computational results support that $[WO_4]^{2-}$ plays an important role in conversion of the carbamic acid into the product.

■ CONCLUSIONS

In summary, a simple monomeric tungstate **I** showed high catalytic activity for chemical fixation of CO_2 with various kinds of structurally diverse 2-aminobenzonitriles including inactive **1e** and **1i** to the corresponding quinazoline-2,4(1*H*,3*H*)-diones. The TONs reached up to 470, 654, and 938 for g-scale reactions of **1a**, **1b**, and **1g**, respectively, and these values were much higher than those reported for base-mediated systems. On the basis of NMR results, the carbamic acid was formed through the simultaneous activation of both 2-aminbenzonitrile and CO_2 by **I**. Kinetics and DFT calculations showed that **I** plays an important role in conversion of the carbamic acid into the product.

■ ASSOCIATED CONTENT

Ⓢ Supporting Information

Kinetic derivation, data of products, Cartesian coordinates of the calculated structures, and the complete citation of ref 23. This material is available free of charge via the Internet at http://pubs.acs.org.

■ AUTHOR INFORMATION

Corresponding Author

*E-mail: tmizuno@mail.ecc.u-tokyo.ac.jp.

Notes

The authors declare no competing financial interest.

■ ACKNOWLEDGMENTS

This work was supported in part by the Japan Society for the Promotion of Science (JSPS) through its "Funding Program for World-Leading Innovative R&D on Science and Technology (FIRST Program)" and Grants-in-Aid for Scientific Research from the Ministry of Education, Culture, Science, Sports, and Technology of Japan.

■ REFERENCES

(1) (a) Fujino, K.; Takami, H.; Atsumi, T.; Ogasa, T.; Mohri, S.; Kasai, M. *Org. Process Res. Dev.* **2001**, *5*, 426−433. (b) Kayser-Bricker, K. J.; Glenn, M. P.; Lee, S. H.; Sebti, S. M.; Cheng, J. Q.; Hamilton, A. D. *Bioorg. Med. Chem.* **2009**, *17*, 1764−1771.

(2) Michman, M.; Patai, S.; Wiesel, Y. *Org. Prep. Proced. Int.* **1978**, *10*, 13−16.

(3) (a) Pastor, G.; Blanchard, C.; Montginoul, C.; Torreilles, E.; Giral, L.; Texier, A. *Bull. Chem. Soc. Chim. Fr.* **1975**, 1331−1338. (b) Khalifa, M.; Osman, A. N.; Ibrahim, M. G.; Ossman, A. R. E.; Ismail, M. A. *Pharmazie* **1982**, *37*, 115−117.

(4) Lange, N. A.; Sheibley, F. E. *Org. Synth.* **1943**, *2*, 79−80.

(5) Vorbrueggen, H.; Krolikiewicz, K. *Tetrahedron* **1994**, *50*, 6549−6558.

(6) (a) Mizuno, T.; Okamoto, N.; Ito, T.; Miyata, T. *Tetrahedron Lett.* **2000**, *41*, 1051−1053. (b) Mizuno, T.; Okamoto, N.; Ito, T.; Miyata, T. *Heteroat. Chem.* **2000**, *11*, 428−433.

(7) Recent books and review articles for chemical fixation of CO_2: (a) Sakakura, T.; Choi, J.-C.; Yasuda, H. *Chem. Rev.* **2007**, *107*, 2365−2387. (b) Peters, M.; Köhler, B.; Kuckshinrichs, W.; Leitner, W.; Markewitz, P.; Müller, T. E. *ChemSusChem* **2011**, *4*, 1216−1240. (c) Cokoja, M.; Bruckmeier, C.; Rieger, B.; Herrmann, W. A.; Kühn, F. E. *Angew. Chem., Int. Ed.* **2011**, *50*, 8510−8537. (d) Aresta, M. *Carbon Dioxide as Chemical Feedstock*; Wiley-VCH: Weinheim, Germany, 2010. (g) Riduan, S. N.; Zhang, Y. *Dalton Trans.* **2010**, *39*, 3347−3357. (h) Ackermann, L. *Angew. Chem., Int. Ed.* **2011**, *50*, 3842−3844. (i) North, M. *Angew. Chem., Int. Ed.* **2009**, *48*, 4104−4105. (j) Yang, Z.-Z.; Zhao, Y.-N.; He, L.-N. *RSC Adv.* **2011**, *1*, 545−567. (k) Federsel, C.; Jackstell, R.; Beller, M. *Angew. Chem., Int. Ed.* **2010**, *49*, 6254−6257.

(8) Recent examples of catalytic systems for chemical fixation of CO_2: (a) Fujihara, T.; Nogi, K.; Xu, T.; Terao, J.; Tsuji, Y. *J. Am. Chem. Soc.* **2012**, *134*, 9106−9109. (b) Williams, C. M.; Johnson, J. B.; Rovis, T. *J. Am. Chem. Soc.* **2008**, *130*, 14936−14937. (c) Yeung, C. S.; Dong, V. M. *J. Am. Chem. Soc.* **2008**, *130*, 7826−7827. (d) Inamoto, K.; Asano, N.; Nakamura, Y.; Yonemoto, M.; Kondo, Y. *Org. Lett.* **2012**, *14*, 2622−2625. (e) Kayaki, Y.; Yamamoto, M.; Ikariya, T. *Angew. Chem., Int. Ed.* **2009**, *48*, 4194−4197. (f) Yu, K. M. K.; Yeung, C. M. Y.; Tsang, S. C. *J. Am. Chem. Soc.* **2007**, *129*, 6360−6361. (g) Wong, W.-L.; Cheung, K.-C.; Chan, Z.-Y.; Zhou, K.-H.; Lee, K.-Y. W. *Chem. Commun.* **2007**, 2175−2177. (h) K. Mori, Y.; Mitani, P.-H.; Hara, T.; Mizugaki, T.; Ebitani, K.; Kaneda, K. *Chem. Commun.* **2005**, 3331−3333. (i) Mizuno, H.; Takaya, J.; Iwasawa, N. *J. Am. Chem. Soc.* **2011**, *133*, 1251−1253. (j) Riduan, S. N.; Zhang, Y.; Ying, J. Y. *Angew. Chem., Int. Ed.* **2009**, *48*, 3322−3325. (k) Kikuchi, S.; Sekine, K.; Ishida, T.; Yamada, T. *Angew. Chem., Int. Ed.* **2012**, *51*, 6989−6992. (l) Gomes, C. D. N.; Jacquet, O.; Villiers, C.; Thuéry, P.; Ephritikhine, M.; Cantat, T. *Angew. Chem., Int. Ed.* **2012**, *51*, 187−190.

(9) (a) Mizuno, T.; Ishino, Y. *Tetrahedron* **2002**, *58*, 3155−3158. (b) Mizuno, T.; Iwai, T.; Ishino, Y. *Tetrahedron Lett.* **2004**, *45*, 7073−7075. (c) Mizuno, T.; Mihara, M.; Nakai, T.; Iwai, T.; Ito, T. *Synthesis* **2007**, 2524−2528.

(10) Patil, Y. P.; Tambade, P. J.; Jagtap, S. R.; Bhanage, B. M. *Green Chem. Lett. Rev.* **2008**, *1*, 127−132.

(11) Patil, Y. P.; Tambade, P. J.; Parghi, K. D.; Jayaram, R. V.; Bhanage, B. M. *Catal. Lett.* **2009**, *133*, 201−208.

(12) Patil, Y. P.; Tambade, P. J.; Deshmukh, K. M.; Bhanage, B. M. *Catal. Today* **2009**, *148*, 355−360.

(13) Nagai, D.; Endo, T. *J. Polym. Sci., Part A: Polym. Chem.* **2009**, *47*, 653−657.

(14) Gao, J.; He, L.-N.; Miao, C.-X.; Chanfreau, S. *Tetrahedron* **2010**, *66*, 4063−4067.

(15) (a) Okuhara, T.; Mizuno, N.; Misono, M. *Adv. Catal.* **1996**, *41*, 113−252. (b) Kozhevnikov, I. V. *Catalysts for Fine Chemical Synthesis, Vol. 2, Catalysis by Polyoxometalates*; John Wiley & Sons: Chichester, U.K., 2002. (c) Hill, C. L. In *Comprehensive Coordination Chemistry II*; McCleverty, J. A., Meyer, T. J., Eds.; Elsevier Science: New York, 2004; Vol. *4*, pp 679−759. (d) Neumann, R.; Khenkin, A. M. *Chem. Commun.* **2006**, 2529−2538. (e) Mizuno, N.; Yamaguchi, K.; Kamata, K. In *Topics in Organometallics Chemistry−Chemistry of Bifunctional Molecular Catalysis*; Ikariya, T., Shibasaki, M., Eds.; Springer-Verlag: Berlin, 2011; pp 127−160.

(16) Recent examples of POM-based catalytic systems: (a) Inumaru, K.; Ishihara, T.; Kamiya, Y.; Okuhara, T.; Yamanaka, S. *Angew. Chem., Int. Ed.* **2007**, *46*, 7625−7628. (b) Macht, J.; Janik, M. J.; Neurock, M.; Iglesia, E. *J. Am. Chem. Soc.* **2008**, *130*, 10369−10379. (c) Long, D.-L.; Song, Y.-F.; Wilson, E. F.; Kögerler, P.; Guo, S.-X.; Bond, A. M.; Hargreaves, J. S. J.; Cronin, L. *Angew. Chem., Int. Ed.* **2008**, *47*, 4384−4387. (d) Kikukawa, Y.; Yamaguchi, S.; Nakagawa, Y.; Uehara, K.; Uchida, S.; Yamaguchi, K.; Mizuno, N. *J. Am. Chem. Soc.* **2008**, *130*, 15872−15878. (e) Sartorel, A.; Carraro, M.; Scorrano, G.; De Zorzi, R.; Geremia, S.; McDaniel, N. D.; Bernhard, S.; Bonchio, M. *J. Am. Chem. Soc.* **2008**, *130*, 5006−5007. (f) Ishimoto, R.; Kamata, K.; Mizuno, N. *Angew. Chem., Int. Ed.* **2009**, *48*, 8900−8904. (g) Leng, Y.; Wang, J.; Zhu, D.; Ren, X.; Ge, H.; Shen, L. *Angew. Chem., Int. Ed.* **2009**, *48*, 168−171. (h) Kamata, K.; Hirano, T.; Kuzuya, S.; Mizuno, N. *J. Am. Chem. Soc.* **2009**, *131*, 6997−7004. (i) Khenkin, A. M.; Leitus, G.; Neumann, R. *J. Am. Chem. Soc.* **2010**, *132*, 11446−11448. (j) Kamata, K.; Yonehara, K.; Nakagawa, Y.; Uehara, K.; Mizuno, N. *Nat. Chem.* **2010**, *2*, 478−483. (k) Murakami, M.; Hong, D.; Suenobu, T.; Yamaguchi, S.; Ogura, T.; Fukuzumi, S. *J. Am. Chem. Soc.* **2011**, *133*, 11605−11613. (l) Nisar, A.; Lu, Y.; Zhuang, J.; Wang, X. *Angew. Chem., Int. Ed.* **2011**, *50*, 3187−3192. (m) Huang, Z.; Luo, Z.; Geletii, Y. V.; Vickers, J. W.; Yin, Q.; Wu, D.; Hou, Y.; Ding, Y.; Song, J.; Musaev, D. G.; Hill, C. L.; Lian, T. *J. Am. Chem. Soc.* **2011**, *133*, 2068−2071. (n) Hirano, T.; Uehara, K.; Kamata, K.; Mizuno, N. *J. Am. Chem. Soc.* **2012**, *134*, 6425−6433. (o) Antonova, N. S.; Carbo, J. J.; Kortz,

U.; Kholdeeva, O. A.; Poblet, J. M. *J. Am. Chem. Soc.* **2010**, *132*, 7488−7497. (p) Kamata, K.; Yamaura, T.; Mizuno, N. *Angew. Chem., Int. Ed.* **2012**, *51*, 7275−7279.

(17) (a) Kimura, T.; Kamata, K.; Mizuno, N. *Angew. Chem., Int. Ed.* **2012**, *51*, 6700−6703. (b) Sugahara, K.; Kimura, T.; Kamata, K.; Mizuno, N. *Chem. Commun.* **2012**, *48*, 8422−8424. (c) Kikukawa, Y.; Suzuki, K.; Sugawa, M.; Hirano, T.; Kamata, K.; Yamaguchi, K.; Mizuno, N. *Angew. Chem., Int. Ed.* **2012**, *51*, 3686−3690. (d) Suzuki, K.; Sugawa, M.; Kikukawa, Y.; Kamata, K.; Yamaguchi, K.; Mizuno, N. *Inorg. Chem.* **2012**, *51*, 6953−6961.

(18) Perrin, D. D.; Armarego, W. L. F. *Purification of Laboratory Chemicals*, 3rd ed.; Pergamon Press: Oxford, U.K., 1988.

(19) Tézé, A.; Hervé, G. *Inorg. Synth.* **1990**, *27*, 85−96.

(20) Che, T. M.; Day, V. W.; Francesconi, L. C.; Fredrich, M. F.; Klemperer, W. G.; Shum, W. *Inorg. Chem.* **1985**, *24*, 4055−4062.

(21) Becke, A. D. *J. Chem. Phys.* **1993**, *98*, 1372−1377.

(22) Hay, P. J.; Wadt, W. R. *J. Chem. Phys.* **1985**, *82*, 270−283.

(23) Frisch, M. J. et al. *Gaussian 09*; Gaussian, Inc.: Wallingford, CT, 2009. See the Supporting Information for complete reference.

(24) TBABr is active for cycloaddition of CO_2 with epoxides into cyclic carbonates: Caló, V.; Nacci, A.; Monopoli, A.; Fanizzi, A. *Org. Lett.* **2002**, *4*, 2561−2563.

(25) Balalaie, S.; Bararjanian, M. *Synth. Commun.* **2006**, *36*, 533−539.

(26) We attempted to investigate possible separation and recycling of the catalyst and explored appropriate solvents in which **I** or **2a** is insoluble after the reaction. Although **I** was easily soluble in various organic solvents such as DMSO, toluene, and dichloromethane, **2a** was insoluble in toluene and dichloromethane. Therefore, separation of **2a** from a reaction mixture was investigated. Toluene/DMSO (95/5, v/v) was used as a solvent because (i) chemical fixation of CO_2 with **1a** proceeded in both DMSO and toluene and (ii) **1a** and **I** were soluble in the solvent. Separation of **2a** from the toluene/DMSO (95/5, v/v) solution (1 mL) containing **I** (10 μmol) and **2a** (0.5 mmol, the amount corresponds to 100% yield under the conditions in Table 1) was demonstrated as follows: Insoluble precipitate **2a** was collected by filtration, washed with dichloromethane (6 mL), and evacuated to dryness. Analytically pure **2a** was recovered in 89% yield and the signals of **I** was not observed for ^{1}H NMR spectrum of recovered **2a**. Dichloromethane in the filtrate was easily removed by evaporation. Therefore, the filtrate containing **I** is possibly reusable by addition of **1a** (0.5 mmol).

(27) (a) Zunszain, P. A.; Federico, C.; Sechi, M.; Al-Damluji, S.; Ganellin, C. R. *Bioorg. Med. Chem.* **2005**, *13*, 3681−3689. (b) Andrus, M. B.; Mettath, S. N.; Song, C. *J. Org. Chem.* **2002**, *67*, 8284−8286. (c) Campbell, S. F.; Davey, M. J.; Hardstone, J. D.; Lewis, B. N.; Palmer, M. J. *J. Med. Chem.* **1987**, *30*, 49−57.

(28) The turnover frequencies for reactions of **1a**, **1b**, and **1g** were 19.5, 13.6, and 9.8 h^{-1}, respectively, and these values were larger than those (<0.1−6.6 h^{-1} (**2a**), <0.1−4.5 h^{-1} (**2b**), and <0.1−4.5 h^{-1} (**2g**)) of the reported systems.

(29) (a) Masuda, K.; Ito, Y.; Horiguchi, M.; Fujita, H. *Tetrahedron* **2005**, *61*, 213−229. (b) Knöfel, C.; Martin, C.; Hornebecq, V.; Llewellyn, P. L. *J. Phys. Chem. C* **2009**, *113*, 21726−21734. (c) Bacsik, Z.; Ahlsten, N.; Ziadi, A.; Zhao, G.; Garcia-Bennett, A. E.; Martín-Matute, B.; Hedin, N. *Langmuir* **2011**, *27*, 11118−11128.

(30) Formation of the carbamic acid in DMSO instead of DMF was confirmed by IR spectroscopy because IR bands of carbamic acids overlap with a strong absorption band at 1687 cm^{-1} of DMF. When DMSO-d_6 solution containing **I** (0.2 M) and **1a** (0.9 M) was exposed to CO_2 (0.1 MPa) at 298 K, eight new ^{13}C NMR signals appeared at 154.3, 147.2, 133.3, 131.4, 117.8, 117.6, 117.0, and 95.3 ppm in a similar way to that in DMF-d_7. Upon introduction of CO_2, a new IR band appeared at 1672 cm^{-1} (see the Supporting Information, Figure S5). Stretching vibration bands of C═O groups in carbamic acids and asymmetric stretching vibration bands of COO^- groups in carbamates have been observed in the range of 1700−1660 and 1570−1540 cm^{-1}, respectively.[29] Therefore, the 1672-cm^{-1} band is assigned to stretching vibration of the C═O group in the carbamic acid. These results support the formation of the carbamic acid as a key intermediate.

(31) The transition state structures could not successfully be optimized when solvation in DMSO was taken into consideration. It was confirmed that chemical fixation of CO_2 with **1a** to **2a** in toluene catalytically proceeded in the presence of **I** (Table 1, entry 6).