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Bifunctional Organocatalyst for Activation of Carbon Dioxide and Epoxide To Produce Cyclic Carbonate: Betaine as a New Catalytic Motif

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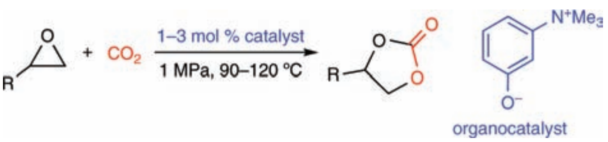
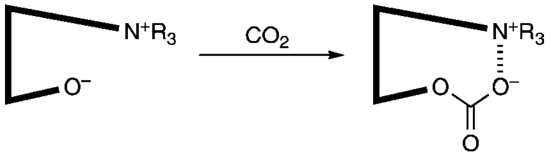
ABSTRACT



Bifunctional organocatalysts bearing an ammonium betaine framework have been developed as a new catalytic motif for the activation of carbon dioxide and epoxides to produce cyclic carbonates.

Activation and fixation of carbon dioxide (CO_2) has been a challenging subject in organic synthesis because of the poor reactivity of CO_2.[1] The importance of this subject is growing steadily because of the utility of CO_2 as a renewable carbon source. Among various methods, catalytic conversion of CO_2 is extremely significant from the chemical and industrial viewpoints.[1,2] To address this subject, we focused on organocatalysis, which has achieved a remarkable development in a decade by the ingenious designs of catalysts.[3] Scheme 1 illustrates an ammonium betaine framework for the cooperative activation of CO_2 to give a reactive intermediate that may be useful for various transformations. We envisioned that the aryloxide anion would have both nucleophilic and leaving abilities, both of which are essential for catalysis, and that the quaternary ammonium cation might stabilize the anion formed by the nucleophilic addition to CO_2.

Scheme 1. CO_2 Activation by Ammonium Betaine Organocatalyst



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Extensive studies have been done to achieve clean, selective, and atom-economic coupling reactions of CO_2 with epoxides to give cyclic carbonates, which are useful as synthetic intermediates, aprotic polar solvents, and feedstocks for engineering plastics.[4−9] To test our strategy for the direct activation of CO_2 (Scheme 1), we decided to employ this coupling reaction. When we initiated this study, no betaines had been reported as catalysts for this reaction. Although betaine-acid salts have been reported to act as catalysts,[8] ammonium halides bearing the carboxyl group are generated in situ, and the proposed mechanism is different from our strategy outlined in Scheme 1. During this study, Ooi and co-workers have revealed the great potential of betaines as catalysts for asymmetric Mannich-type reactions.[10] Here we report bifunctional organocatalysts functioning as metal-free, halogen-free, and solvent-free catalysts for the coupling reactions of CO_2 with epoxides.

Betaines **1**−**8** (Figure 1) were synthesized as described in the Supporting Information, and they were screened for catalytic activity toward the conversion of 1,2-epoxyhexane (**9a**) into **10a**. A stainless autoclave was charged with epoxide **9a**, catalyst, and then CO_2 (initial pressure 1 MPa), and the mixture was stirred at 120 °C for 24 h. The results are summarized in Table 1. Among ortho-substituted betaines **1**−**3**, **3** with the trimethylammonium group gave the best result (entries 1−3). The bulky substituent, such as the allyl and benzyl groups, is likely to hinder the access of CO_2/epoxide to the phenolate anion. Next, we tried to tune the distance between the two functional groups in the catalyst in two ways: one is to employ meta- and para-isomers **4** and **5**, and the other is to examine biaryl systems **6**−**8**. To our delight, biphenyl compound **6** gave a higher yield than **3** (entries 3 and 10). To suppress the rotational flexibility determining the distance between the two functional groups, we replaced the phenyl group by the naphthyl group. As expected, catalytic activity increased in the following order: **6** < **7** < **8** (entries 10−12). In the case of **8**, the catalyst loading could be reduced to 1 mol % although the yield decreased a little (entry 13). We anticipated that because of

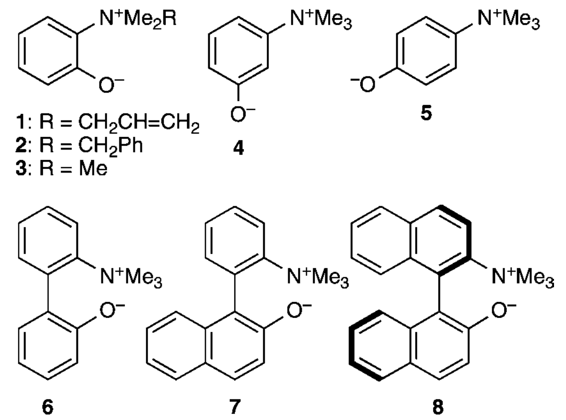
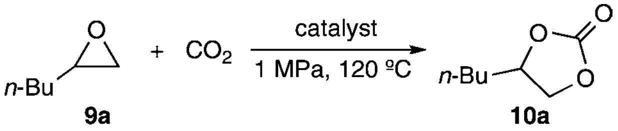


Figure 1. Bifunctional organocatalysts bearing an ammonium betaine framework.

Table 1. Synthesis of Cyclic Carbonate **10a** from CO_2 and 1,2-Epoxyhexane (**9a**) with Organocatalysts[a]



entry	catalyst	loading (mol %)	yield (%)[b]
1	**1**	3	61
2	**2**	3	60
3	**3**	3	76
4	**4**	3	>99
5	**4**	2	>99
6	**4**	1	88
7	**5**	3	>99
8	**5**	2	>99
9	**5**	1	88
10	**6**	3	84
11	**7**	3	93
12	**8**	3	99
13	**8**	1	77
14	L-Phe	3	11
15	*o*-dimethylaminophenol	3	4
16	*p*-$MeOC_6H_4OH$/DMAP[7a,c]	3	61
17	$PhN^+Me_3{\cdot}PhO^-$	3	15

[a] Conditions: **9a** (1.2 mL, 10 mmol), catalyst (quantity indicated above), 1 MPa CO_2, 120 °C, 24 h, in a 50-mL autoclave. [b] Determined by ^1H NMR, using 2-methoxynaphthalene as an internal standard.

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the long distance between the two functional groups in the catalyst, meta- and para-isomers **4** and **5** would show lower catalytic activity than ortho-isomer **3**. Contrary to our expectation, however, **4** and **5** even showed higher catalytic activity (entries 4 and 7). We suppose that this is because the oxyanion moiety in **4** and **5** is sterically less hindered than that in **3**. In both cases, when the catalyst loading was reduced to 2 mol % and 1 mol %, respectively, the product was obtained in >99% and 88%, the latter of which was higher than that attained by **8** (entries 5, 6, 8, and 9).

Amino acids are zwitterions capable of showing high catalytic activity yet under more harsh conditions.[7d] To directly compare the catalytic powers, we used L-phenylalanine under the same reaction conditions (entry 14). As a result, the product **10a** was obtained in a much lower yield (11%), which suggests that the phenolate anion is a better nucleophile than the carboxylate anion. Next, we examined *o*-dimethylaminophenol, where the hydroxy group can be activated by the dimethylamino group via the intramolecular hydrogen bonding (entry 15). Despite structural similarity to **3**, *o*-dimethylaminophenol gave **10a** in only 4% yield, which indicates the importance of the naked phenolate anion. A highly active cocatalyst system with *p*-methoxyphenol (Lewis acid) and 4-(dimethylamino)pyridine (DMAP, Lewis base) has been reported.[7a,c] We used this catalytic system under the same conditions to obtain **10a** in 61% yield (entry 16). Finally, phenyltrimethylammonium phenoxide ($PhN^+Me_3{\cdot}PhO^-$) was examined. This ion-paired complex was found to be much inferior to the betaine counterpart such as **3**−**5** (entry 17). We suppose that ion-pair formation occurs tightly in $PhN^+Me_3{\cdot}PhO^-$, hindering the insertion of CO_2/epoxide, while the betaine structure is more favorable because the phenolate anion is remote from the quaternary ammonium cation. On the basis of these observations, we conclude that the nucleophilicity of the phenolate anion is the most important factor and that electrostatic stabilization of the anion generated by attacking CO_2/epoxide is less important.

The difference in the catalytic activity of **4** and **5** became clear as the reaction temperature was decreased (Figure 2); meta-isomer **4** was found to be more active than para-isomer **5**. This can be partially ascribed to the higher nucleophilicity of the phenolate anion of **4** because of the lack of the conjugation stabilization. Interestingly, the yields dropped sharply around 70−90 °C for unknown reasons. The catalyst might precipitate below the critical temperature. The use of 2 mol % of **4** at 90 °C afforded **10a** in 98% yield. Using the most active catalyst **4** (3 mol %), the substrate scope was explored. The results are summarized in Table 2. Various epoxides **9b**−**f** were converted into the corresponding cyclic carbonates **10b**−**f** in excellent yields (80−99%).

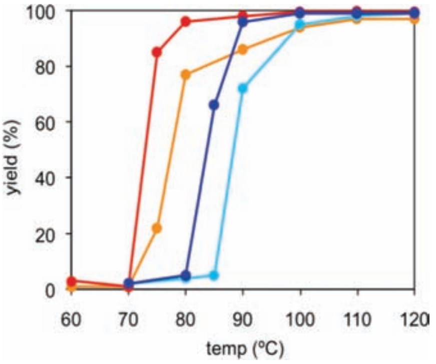
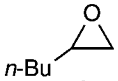
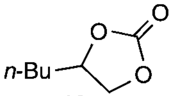
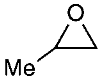
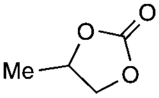
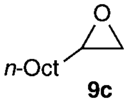
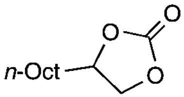
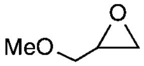
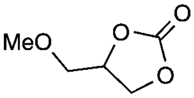
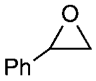
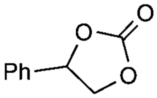
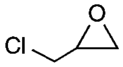
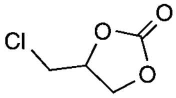


Figure 2. The catalytic activity for the synthesis of **10a** is compared between **4** (red: 2 mol %; orange: 1 mol %) and **5** (blue: 2 mol %; light blue: 1 mol %) by changing the reaction temperature. The NMR yield was determined by using 2-methoxynaphthalene as an internal standard.

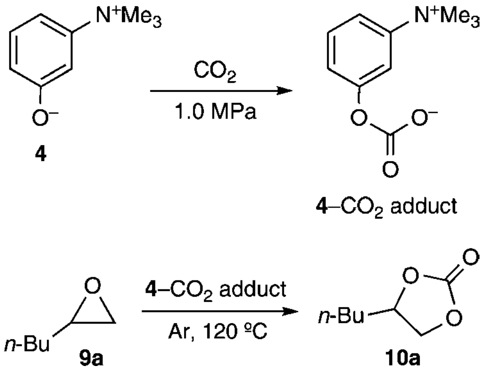
Table 2. Synthesis of Various Cyclic Carbonates with Catalyst **4**[a]

substrate	product	yield (%)[b]
 **9a**	 **10a**	99
 **9b**	 **10b**	99
 **9c**	 **10c**	80
 **9d**	 **10d**	99
 **9e**	 **10e**	98
 **9f**	 **10f**	85

[a] Conditions: **9** (10 mmol), catalyst **4** (3 mol %), 1 MPa CO_2, 120 °C, 24 h, in a 50-mL autoclave. [b] Isolated yield.

Next, we decided to isolate and characterize a key intermediate, a betaine-CO_2 adduct (Scheme 2). A stainless autoclave was charged with catalyst **4** (151 mg, 1.00 mmol) and CO_2 (1 MPa), and the mixture was stirred at a constant temperature (7−90 °C) for 24 h. Careful release of CO_2 gave a white powder. The product was characterized by an absorption at 1655 cm^{-1} (C═O stretching vibration) in the IR spectrum and an additional signal at 161.2 ppm (carbonyl C) in the ^{13}C NMR spectrum, which strongly support the formation of a **4**-CO_2 adduct.[11] To examine whether the **4**-CO_2 adduct is the reaction intermediate, we heated this adduct with an excess amount of epoxide **9a** (10.0 mmol) under Ar in an autoclave at 120 °C for 24 h (Scheme 2). As

Scheme 2. Formation of Betaine-CO_2 Adduct and Demonstration of Reaction Intermediate



a result, cyclic carbonate **10a** was obtained. The yields are shown in Figure 3, where the reaction temperature for the formation of the **4**-CO_2 adduct is shown in the horizontal axis. Figure 3 clearly indicates that the **4**-CO_2 adduct was formed most efficiently at 15 °C, which indicates that the nucleophilicity of the aryloxide of betaine **4** is very high.[11] At higher temperatures, the decarboxylation reaction seems to proceed faster. We consider that the rate-determining step is the epoxide ring-opening step because the catalytic reaction proceeded well above 90 °C (Figure 2). On the basis of these observations, we propose the catalytic cycle as shown in Scheme 3.

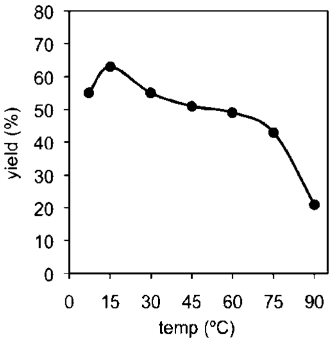
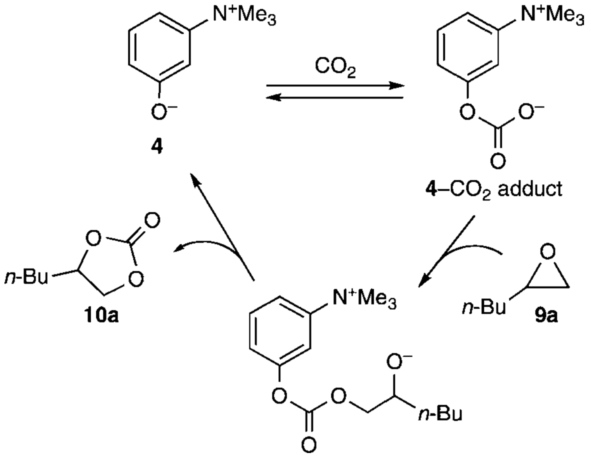


Figure 3. The synthesis of **10a** by the reaction of the **4**-CO_2 adduct with an excess amount of epoxide **9a** under Ar in a 30-mL autoclave at 120 °C for 24 h. The reaction temperature for the formation of the **4**-CO_2 adduct is shown in the horizontal axis.

Scheme 3. Proposed Catalytic Cycle



In summary, we have proposed a new catalytic motif for CO_2 activation. Bifunctional organocatalysts bearing an ammonium betaine framework have been developed for the activation of carbon dioxide and epoxides to produce cyclic carbonates. Among them, betaine **4** is one of the most active catalysts that can function under the metal-free, halogen-free, and solvent-free conditions. The betaine-CO_2 adducts will be used for various purposes. In particular, the fact that the **4**-CO_2 adduct was formed even at 15 °C is promising because this type of betaine may also be useful for carbon capture and storage (CCS).[12]

Acknowledgment. We are grateful to the SC-NMR Laboratory of Okayama University for the measurement of NMR spectra.

Supporting Information Available: Synthetic procedures, synthesis of CO_2 adducts and subsequent reaction with epoxide, optimization of the reaction conditions, and copies of NMR spectra of all new compounds. This material is available free of charge via the Internet at http://pubs.acs.org.

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[11] The weight of the powder was increased by 28 mg at 15 °C, and the subsequent reaction with **9a** gave **10a** in 63%. Similar results were obtained for catalyst **5** (weight increase: 29 mg; IR: 1631 cm^{-1}; NMR: 161.2 ppm; formation of **10a**: 41%) and catalyst **6** (weight increase: 30 mg; IR: 1655 cm^{-1}; NMR: 161.3 ppm; formation of **10a**: 65%).

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