Design of bifunctional quaternary phosphonium salt catalysts for CO₂ fixation reaction with epoxides under mild conditions

Received 00th January 20xx,
Accepted 00th January 20xx

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DOI: 10.1039/x0xx00000x

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An efficient synthesis of cyclic carbonates from epoxides and CO₂ under mild reaction conditions was achieved via the use of a newly designed bifunctional quaternary phosphonium iodide catalyst. The importance of the bifunctional design of the catalysts was clearly demonstrated in the present work by control experiments. Furthermore, a chiral version of the bifunctional phosphonium salt could be applied to a kinetic resolution of this reaction.

Carbon dioxide (CO₂) is recognized as an unfavorable industrial waste due to its greenhouse effect, and the reduction of CO₂ emissions has become integral to the creation of a sustainable society.¹ From a different point of view, however, CO₂ is also recognized as an ideal C1 source for chemical synthesis because it is inexpensive, abundant, and nontoxic. In this context, the development of chemical transformations to useful compounds via the use of CO₂ as a reactant has become a hot topic in the field of green sustainable chemistry.² Among these transformations, the synthesis of cyclic carbonates **2** from epoxides **1** and CO₂ has been the most extensively studied due to their high utility in industrial processes.³ Although a wide variety of metal catalysts and organocatalysts such as quaternary onium salts have been developed to promote this reaction, high temperature (>100 °C) and pressure (>10 atm) are often required to produce the products **2** in satisfactory yields.⁴ Therefore, the development of catalysts that can be effective for this reaction under mild conditions continues to be highly desired. To achieve this desirable task, we became interested in the design of new bifunctional quaternary onium salt catalysts possessing a phenolic hydroxy group when a binary catalyst system with

onium salts and phenols was reported to have effectively promoted the reaction under relatively mild conditions (Scheme 1).^{5,6} Herein, we report the development of effective bifunctional quaternary phosphonium salts⁷ for the synthesis of cyclic carbonates **2** with epoxides **1** under atmospheric CO₂ pressure, mild temperature (60 °C), and low catalyst loading (1 mol %). The utility of a bifunctional design for the catalyst in this reaction was clearly demonstrated in the present work.⁸ Furthermore, a chiral version of the bifunctional organocatalyst was also developed, and we applied the chiral catalyst to a kinetic resolution in this reaction.⁹

Scheme 1 Synthesis of cyclic carbonates **2** under mild reaction conditions.

To achieve an efficient synthesis of cyclic carbonates **2** under mild reaction conditions, we designed bifunctional quaternary phosphonium bromides **3** possessing a phenolic hydroxy group. The phosphonium salts **3** with a biphenyl backbone were readily prepared via the reaction with triphenylphosphine and corresponding arylmethyl bromides. There was a concern that the distance between the phosphonium salt moiety and the hydroxy group on catalyst **3** could affect the catalytic activity, and therefore, we prepared regioisomers: *o*-**3**, *m*-**3**, and *p*-**3** (Scheme 2). The structure of the phosphonium salt *o*-**3** was confirmed via X-ray diffraction analysis, and a hydrogen-bonding interaction between the hydroxy group and the counter-anion (Br[−]) was observed in the crystal structure.¹⁰

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Electronic Supplementary Information (ESI) available: Experimental details and characterization data for new compounds. See DOI: 10.1039/x0xx00000x

Scheme 2 Synthesis and structure of bifunctional quaternary phosphonium bromides **3**.

The catalytic ability of bifunctional quaternary phosphonium bromides **3** was investigated in the synthesis of cyclic carbonate **2a** (Table 1). The reaction was quite simple and easy. A mixture of styrene oxide **1a** and catalyst *o*-**3** (1 mol %) was stirred at 60 °C for 24 h under a CO₂ atmosphere (1 atm, using a balloon), and we obtained the target product **2a** in an 80% yield (entry 1). Other regioisomeric catalysts, *m*-**3** and *p*-**3**, were also examined for this reaction, but these catalysts showed activities that were inferior to catalyst *o*-**3** (41% and 65% yields, respectively, entries 2 and 3). These results clearly indicated that the tuning of the distance between the two functionalities on the bifunctional catalyst was important in the design of highly active catalysts for this reaction. To clarify the importance of the hydroxy group on the catalyst *o*-**3**, we compared the results with the catalytic activity of the hydroxy group protecting catalyst *o*-**4** and a simple benzyltriphenylphosphonium bromide (entries 4 and 5). As expected, these catalysts showed very low reactivities, and the product **2a** was obtained in only low yields (16% and 3% yields, respectively). Furthermore, a binary catalyst system with benzyltriphenylphosphonium bromide and phenol gave product **2a** in only a moderate yield (51% yield, entry 6). Based on these results, we concluded that a bifunctional design with an appropriate arrangement of functionalities was essential in the design of effective catalysts. An exchange of the counter-anion from bromide (*o*-**3**) to iodide (*o*-**5**) further improved the catalytic activity to obtain product **2a** in a high yield (91% yield, entry 7).¹¹ The reaction profiles with phosphonium salts *o*-**3**, *p*-**3**, *o*-**4**, and *o*-**5** are shown in Fig. 1.¹²

Table 1. Effect of quaternary phosphonium salt catalysts^a

Entry	Catalyst	Yield ^b (%)
1	<i>o</i> - 3	80
2	<i>m</i> - 3	41
3	<i>p</i> - 3	65
4	<i>o</i> - 4	16
5	BnPh ₃ P ⁺ Br ⁻	3
6	BnPh ₃ P ⁺ Br ⁻ + PhOH (1 mol %)	51
7	<i>o</i> - 5	91

^aReaction conditions: **1a** (2.0 mmol), catalyst (0.020 mmol, 1 mol %), CO₂ (1 atm, using a balloon), 1,3,5-trimethoxybenzene (0.10 mmol, internal standard), 60 °C, 24 h. ^bYield was determined via ¹H NMR analysis using 1,3,5-trimethoxybenzene as an internal standard.

Fig. 1 Hydrogen-bonding interactions on the α -hydrogens of tetraalkylammonium salts.

Based on the X-ray crystal structure shown in Scheme 1 and on the results listed in Table 1, the assumed catalytic cycle for the present reaction was proposed, as shown in Scheme 3.³ Epoxide **1** is activated via hydrogen bonding with a phenolic hydroxy group on catalyst *o*-**5** (intermediate **A**). The activated epoxide then undergoes nucleophilic attack from an iodide counter-anion to form intermediate **B**. The reactive alkoxide in intermediate **B** attacks CO₂ to yield intermediate **C**. The intramolecular ring-closing of intermediate **C** affords cyclic carbonate **2** with a regeneration of phosphonium iodide catalyst *o*-**5**.

Scheme 3 Assumed catalytic cycle.

With the effective catalyst and assumed catalytic cycle in hand, the substrate generality of epoxides **1** was examined with catalyst *o*-5 (Table 2). Not only styrene oxide derivatives (**1a–1c**) but also epoxides possessing an alkyl chain (**1d** and **1e**) could be employed for the reaction to obtain cyclic carbonates **2a–2e** in good to high yields (72–92% yields, entries 1–5).¹³ Epoxides containing various functional groups (**1f–1h**) could also be applied to this reaction to give products **2f–2h** in good to high yields (85–93% yields, entries 6–8). Furthermore, this reaction system could be applied to the reaction with 2,2-disubstituted epoxides, such as **1i** (Scheme 4). Although yield of the product **2i** was moderate under mild reaction temperature (26% yield at 60 °C), the yield of **2i** was improved at higher reaction temperature (81% yield at 100 °C).¹⁴

Table 2. Substrate scope^a

Entry	R	Yield ^b (%)
1 ^c	Ph (1a)	92 (2a)
2	4-F-C ₆ H ₄ (1b)	90 (2b)
3	4-Cl-C ₆ H ₄ (1c)	72 (2c)
4	CH ₃ CH ₂ CH ₂ (1d)	87 (2d)
5	CH ₂ =CHCH ₂ CH ₂ (1e)	84 (2e)
6	ClCH ₂ (1f)	85 (2f)
7	PhOCH ₂ (1g)	89 (2g)
8	Ph ₂ NCH ₂ (1h)	93 (2h)

^aReaction conditions: **1** (2.0 mmol), catalyst *o*-5 (0.020 mmol, 1 mol %), CO₂ (1 atm, using a balloon), 60 °C, 24 h. ^bYield of isolated products **2**. ^cReaction was performed on 10 mmol scale (**1a**, 10 mmol; *o*-5, 0.10 mmol).

Scheme 4 Application to 2,2-disubstituted epoxide **1i**.

To expand the utility of the bifunctional design of quaternary phosphonium salt catalysts, we developed chiral versions of the catalysts. Based on the design of effective catalysts *o*-3 and *o*-5, we prepared a chiral catalyst (*S*)-**6** with a chiral binaphthyl backbone (Scheme 5).¹⁵ The chiral catalyst (*S*)-**6** was applied to the kinetic resolution of epoxide **1h** with CO₂.¹⁶ The mixture of **1h** and catalyst (*S*)-**6** (1 mol %) was stirred at 50 °C for 12 h under a CO₂ atmosphere (1 atm, using a balloon), and cyclic carbonate **2h** was obtained in a 13% ee (59% yield) with recovery of the unreacted **1h** in a 17% ee (40% yield) (*s* = 1.5).¹⁷ On the other hand, the hydroxy group protecting the catalyst (*S*)-**7** showed low reactivity and selectivity (*s* = 1.2). A moderate level of enantioselectivity for the recovered epoxide **1h** (31% ee) was obtained in a higher conversion via a prolonged reaction time with catalyst (*S*)-**6**. The kinetic resolution of epoxide **1j** was also performed, and the reaction was promoted by catalyst (*S*)-**6** to give product **2j** in low selectivity (*s* = 1.2).¹⁸ Although the chiral recognition ability of the chiral bifunctional phosphonium salt (*S*)-**6** was insufficient, this is a valuable example of an organocatalyzed kinetic resolution for this reaction.

Scheme 5 Chiral version of phosphonium salt catalysts with application to kinetic resolutions.

Conclusions

In summary, we successfully achieved an efficient synthesis of industrially important cyclic carbonates **2** via a reaction of epoxides **1** and CO₂ under mild reaction conditions using newly designed bifunctional phosphonium salt catalysts. The importance of the bifunctional design of the catalysts was clearly demonstrated in the present work by comparison with other catalysts. Furthermore, a chiral version of the bifunctional phosphonium salt could be applied to a kinetic resolution in this reaction. Further studies will be directed toward improvement of the selectivity in the kinetic resolution.

Acknowledgements

This work was partially supported by a Grant-in-Aid for Scientific Research(C) from JSPS, The Naito Foundation, and the Cooperative Research Program of "Network Joint Research Center for Materials and Devices". We thank Dr. Kazunobu Igawa (Kyushu University) for helpful discussion, and Junko Nagaoka (Nagasaki University) for X-ray diffraction analysis.

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- Almost no side products were observed in the ¹H NMR spectra of the crude reaction mixture.
- Reusability of catalyst **o-5** was examined in the reaction of entry 1 (table 2). The catalyst was recovered in 73% yield after flash column chromatography on silica gel. The recovered catalyst showed same reactivity with fresh catalyst in the next run.
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- 17 The selectivity factor (s) was calculated as follows.⁹ $s = k_{\text{fast}}/k_{\text{slow}} = \ln[1 - C(1 + ee_{2h})] / \ln[1 - C(1 - ee_{2h})] = \ln[(1 - C)(1 - ee_{1h})] / \ln[(1 - C)(1 + ee_{1h})]$; $C = ee_{1h} / (ee_{1h} + ee_{2h})$.
- 18 The kinetic resolution of styrene oxide **1a** was also examined, and almost no selectivity ($s \approx 1.0$) was observed.