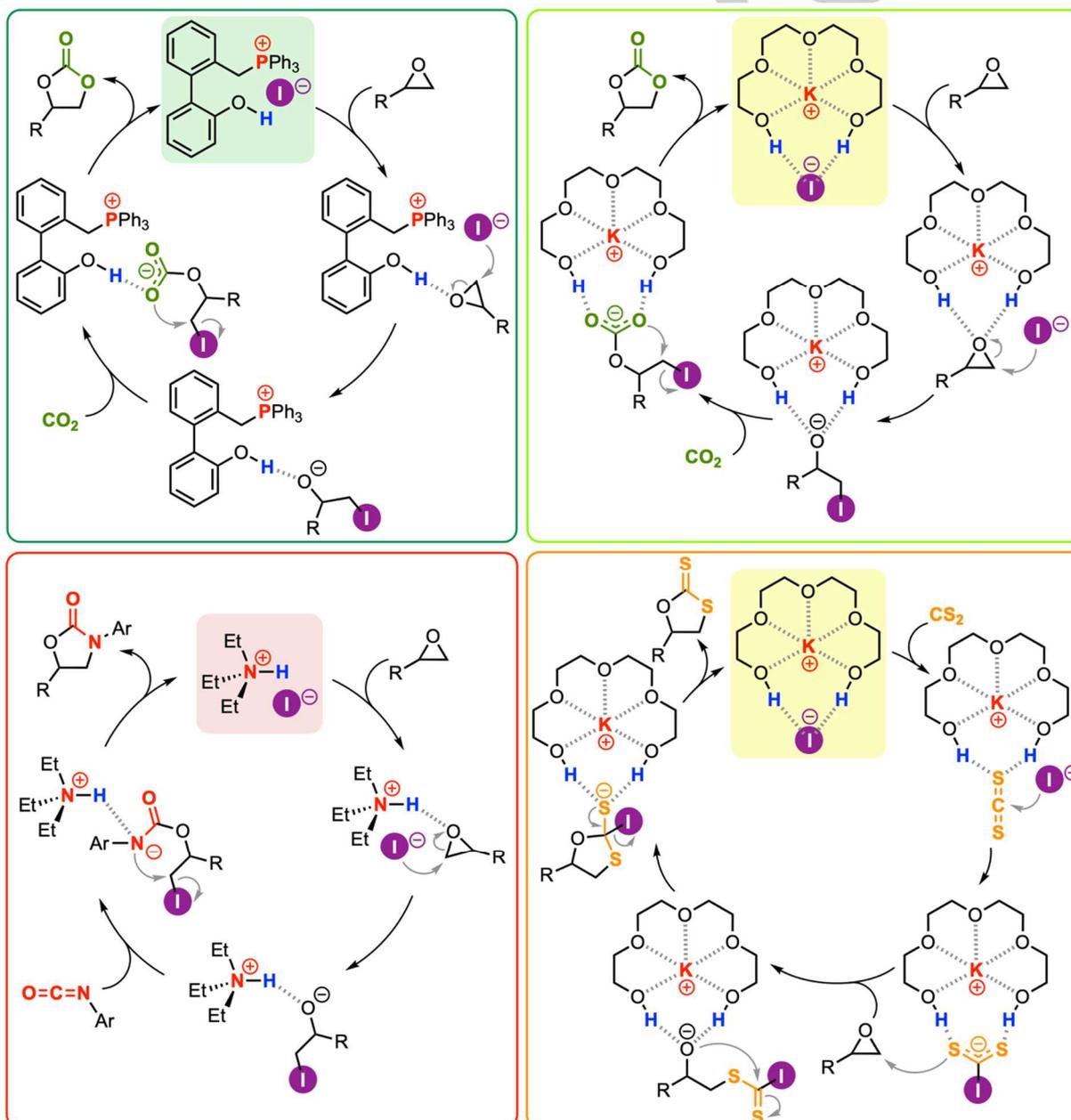# Bifunctional Onium and Potassium Iodides as Nucleophilic Catalysts for the Solvent-Free Syntheses of Carbonates, Thiocarbonates, and Oxazolidinones from Epoxides

Seiji Shirakawa*[a]

*Dedicated to Professor Keiji Maruoka on the occasion of his 70th birthday*

Abstract: The catalytic potential of organo-onium iodides as nucleophilic catalysts is aptly demonstrated in the synthesis of cyclic carbonates from epoxides and carbon dioxide (CO_2), as a representative CO_2 utilization reaction. Although organo-onium iodide nucleophilic catalysts are metal-free environmentally benign catalysts, harsh reaction conditions are generally required to efficiently promote the coupling reactions of epoxides and CO_2. To solve this problem and accomplish efficient CO_2 utilization reactions under mild conditions, bifunctional onium iodide nucleophilic catalysts bearing a hydrogen bond donor moiety were developed by our research group. Based on the successful bifunctional design of the onium iodide catalysts, nucleophilic catalysis using a potassium iodide (KI)-tetraethylene glycol complex was also investigated in coupling reactions of epoxides and CO_2 under mild reaction conditions. These effective bifunctional onium and potassium iodide nucleophilic catalysts were applied to the solvent-free syntheses of 2-oxazolidinones and cyclic thiocarbonates from epoxides.

1. Introduction

Catalysis of organo-halogen compounds has gained much attention in recent years. Halogen-bonding catalysis of organo-iodine compounds, which activate electrophiles via donor-accepter interactions at the σ-hole on the iodine atom, has been extensively investigated in the field of organo-halogen chemistry.[1] The development of oxidative reactions using hypervalent organo-iodine catalysts is another emerging research area,[2] and the design of chiral hypervalent organo-iodine catalysts for use in catalytic asymmetric reactions has become an important research topic.[3] Although these two catalytic modes are now attracting much attention in organo-halogen chemistry, the nucleophilic catalysis of organo-onium iodides and other iodide compounds is another important feature in halogen catalysis. The catalytic potential of organo-onium iodides as nucleophilic catalysts was well demonstrated in the synthesis of cyclic carbonates from epoxides and carbon dioxide (CO_2), as a representative CO_2 utilization reaction.[4,5] Catalytic CO_2 utilization reactions using organo-onium iodide nucleophilic catalysts have been extensively investigated in the field of green and sustainable chemistry due to the importance of research into the utilization of CO_2. Controlling the concentration of CO_2 has become one of the most important tasks for the protection of planetary health, and organo-onium iodide-catalyzed CO_2 utilization reactions with epoxides that transform CO_2 to useful molecules could contribute to this important task. In this context, our research group became interested in the development of effective organo-onium iodide nucleophilic catalysts to realize efficient coupling reactions of CO_2

and epoxides under atmospheric pressure. Herein, we summarize our approaches to the designs of bifunctional onium iodide nucleophilic catalysts that possess hydrogen bond donor sites that allow them to achieve efficient coupling reactions of CO_2 and epoxides. We then used our experience in the design of bifunctional onium iodide nucleophilic catalysts to also develop a potassium iodide–tetraethylene glycol complex catalyst for use in CO_2 utilization reactions. Additionally, these bifunctional onium and potassium iodide catalysts could be applied to the solvent-free syntheses of 2-oxazolidinones and thiocarbonates as useful 5-membered heterocyclic compounds (Scheme 1).
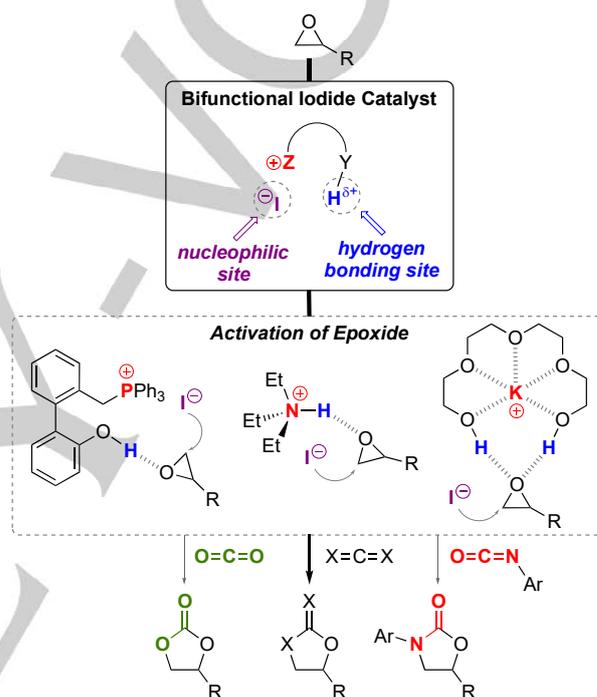
Scheme 1. Bifunctional onium and potassium iodide nucleophilic catalysts for the activation of epoxides.

2. Bifunctional Quaternary Phosphonium Bromide and Iodide Nucleophilic Catalysts for the Synthesis of Cyclic Carbonates

2.1. Design of Bifunctional Quaternary Phosphonium Salt Catalysts

A wide variety of metal- and organo-catalyzed coupling reactions of epoxides and CO_2 have been developed for the synthesis of cyclic carbonates as useful building blocks.[6] Quaternary onium bromides and iodides are representative organocatalysts for CO_2 utilization reactions.[4] Although these onium halide catalysts are metal-free environmentally benign catalysts, harsh reaction conditions are required to efficiently promote the coupling reactions of epoxides and CO_2 (Scheme 2), and the design of new organocatalysts that could be effective for CO_2 utilization reactions under atmospheric pressure and milder temperature is

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highly desired.[6e] To realize these ideal reaction conditions, hydrogen bond donor molecules such as phenols, alcohols, and silanols were employed as co-catalysts with quaternary onium halide catalysts.[4d] These binary organo-catalytic systems significantly improved the catalytic efficiency, and the binary catalysts promoted the coupling reactions of epoxides and CO_2 under milder reaction conditions. Reports about the positive effects of hydrogen bonding co-catalysts picked our interest in the design of bifunctional quaternary onium halide catalysts bearing a hydrogen bond donor moiety. We have designed and synthesized bifunctional quaternary phosphonium halides **1** possessing a phenolic hydroxy group.[7,8] The bifunctional quaternary phosphonium halides **1** with a biphenyl backbone were readily prepared from triphenylphosphine and the corresponding arylmethyl halides.
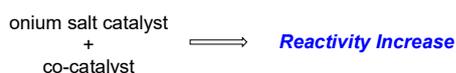
Earlier Catalytic Method
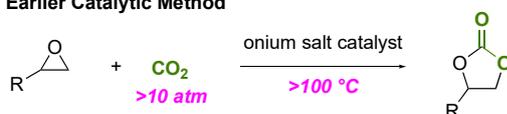
onium salt catalysts : $R_4N^+Br^-$, $R_4N^+I^-$, $R_4P^+I^-$

Harsh Reaction Conditions

Improved Method using Co-catalyst

co-catalysts : Ar–O**H**, R–O**H**, R_3Si–O**H**

Our Catalyst Design

bifunctional onium salt

Realize Milder Reaction Conditions

Scheme 2. Quaternary onium salt-catalyzed coupling reactions of epoxides and CO_2.

Seiji Shirakawa received his Ph.D. from Kyoto University under the guidance of Prof. Keiji Maruoka. He was awarded JSPS postdoctoral fellow to carry out postdoctoral work with Prof. James L. Leighton at Columbia University and Prof. Shū Kobayashi at The University of Tokyo. He was appointed as an assistant professor at Nihon University, and as an associate professor at Kyoto University. He is currently an associate professor in Nagasaki University since 2014. His current interests are organocatalysis, green chemistry, and planetary health.
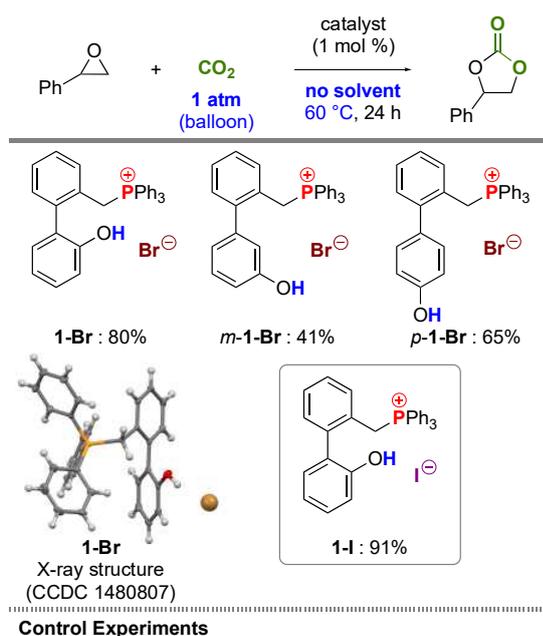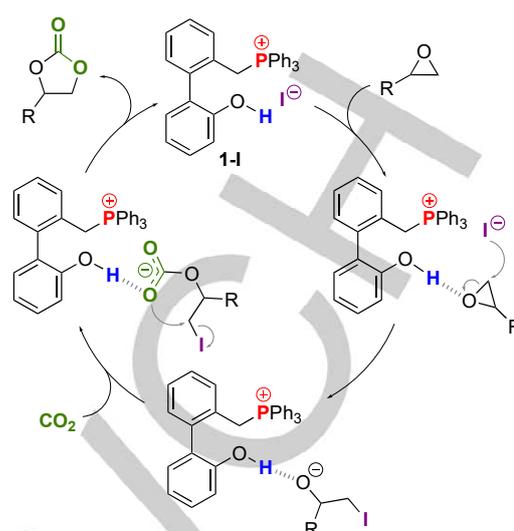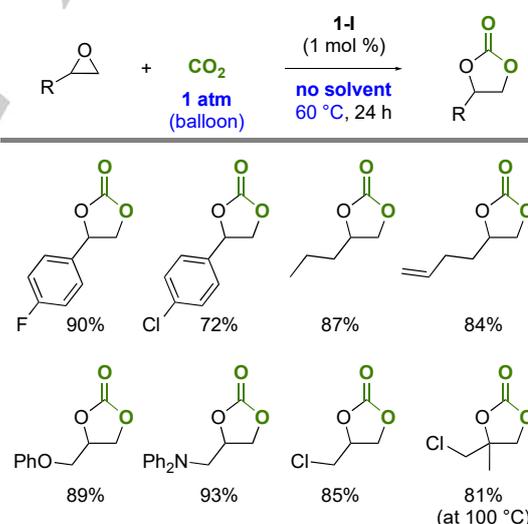
The catalytic performance of bifunctional quaternary phosphonium bromides **1** was investigated in the coupling reaction of styrene oxide and CO_2 under atmospheric pressure (Scheme 3).[7] When styrene oxide and bifunctional quaternary phosphonium bromide **1-Br** (1 mol %) were mixed at 60 °C for 24 hours under a CO_2 atmosphere (1 atm, using a balloon) without the use of a solvent, the target cyclic carbonate product was obtained in an 80% yield. The effects from the position of the hydroxy group in bifunctional quaternary phosphonium bromide catalysts with a biphenyl backbone were examined. The regioisomeric phosphonium bromide catalysts *m*-**1-Br** and *p*-**1-Br** showed lower catalytic activities than catalyst **1-Br**. These results suggest that fine tuning of the catalyst structure improves the catalytic activity. An exchange of the bromide counter anion with iodide (**1-I**) further improved the catalytic activity. Several control experiments were performed to clarify the utility of bifunctional quaternary phosphonium salt catalysts. A commercially available simple benzyltriphenylphosphonium bromide showed quite low catalytic activity under the mild reaction conditions (3% yield). A binary catalytic system using benzyltriphenylphosphonium bromide (1 mol %) and phenol (1 mol %) was also submitted to the CO_2 utilization reaction. Although the reaction was accelerated by the effect of a phenol co-catalyst (51% yield), the activity was lower than that of bifunctional quaternary phosphonium bromide **1-Br**. To clarify the effect of a hydroxy group on **1-Br**, the catalytic activity of hydroxy-protected quaternary phosphonium bromide was also investigated. As expected, the hydroxy-protected catalyst provided the target product only in a 16% yield. The structure of the bifunctional quaternary phosphonium bromide **1-Br** was confirmed via X-ray diffraction analysis.

Scheme 3. Effects of quaternary phosphonium halide catalysts in the coupling reaction of styrene oxide and CO_2.

Scheme 4. Proposed catalytic cycle for the bifunctional phosphonium iodide-catalyzed coupling reactions of epoxides and CO_2.

The substrate scope in the bifunctional quaternary phosphonium iodide **1-I**-catalyzed coupling reactions of epoxides and CO_2 was examined under solvent-free conditions (Scheme 5). The target cyclic carbonates bearing various functionalities were prepared under atmospheric CO_2 pressure in good to high yields.

Based on the results in Scheme 3, we proposed a catalytic cycle for the CO_2 utilization reaction catalyzed by bifunctional quaternary phosphonium iodide **1-I** (Scheme 4). In this reaction, epoxide is activated via hydrogen bonding with a phenolic hydroxy group on the bifunctional catalyst. The activated epoxide then undergoes nucleophilic attack by an iodide counter anion. The resulting alkoxide attacks CO_2, and a subsequential intramolecular ring-closing reaction affords the cyclic carbonate product with a regeneration of the phosphonium iodide catalyst **1-I**. Compared with the use of a bromide anion (**1-Br**), as shown in Scheme 3, the positive effect of the iodide anion (**1-I**) could be explained by a lower ability to coordinate with phenolic hydrogen in the iodide nucleophilic attack step. Another explanation could be based on the ability of the higher leaving groups in the ring-closing step.

Scheme 5. Generality of the substrates in the bifunctional quaternary phosphonium iodide-catalyzed coupling reactions of epoxides and CO_2.

2.2. Kinetic Resolution of Epoxide by Chiral Bifunctional Quaternary Phosphonium Salt

Once we had established an effective design of bifunctional quaternary phosphonium salt catalysts **1-I** and **1-Br** with a biphenyl backbone, we next became interested in the

development of a "chiral" bifunctional quaternary phosphonium salt for the kinetic resolution of epoxides via a coupling reaction with CO_2 (Scheme 6).[7] The biphenyl backbone in the catalyst **1-Br** was simply exchanged for a binaphthyl backbone to prepare the target chiral bifunctional quaternary phosphonium bromide catalyst (*S*)-**2a**. The catalytic ability for a kinetic resolution of epoxide was examined under atmospheric CO_2 pressure.[9] Although the ability of (*S*)-**2a** as an asymmetric catalyst was insufficient, a certain level of enantioselectivity was observed in both the cyclic carbonate product and in recovered starting epoxide. It should be noted that with respect to kinetic resolution the chiral recognition ability of bifunctional quaternary phosphonium bromide (*S*)-**2a** was better than that of the hydroxy-protected chiral quaternary phosphonium bromide (*S*)-**2b**. These results suggest the potential utility of the bifunctional catalyst design for the kinetic resolution of epoxides.
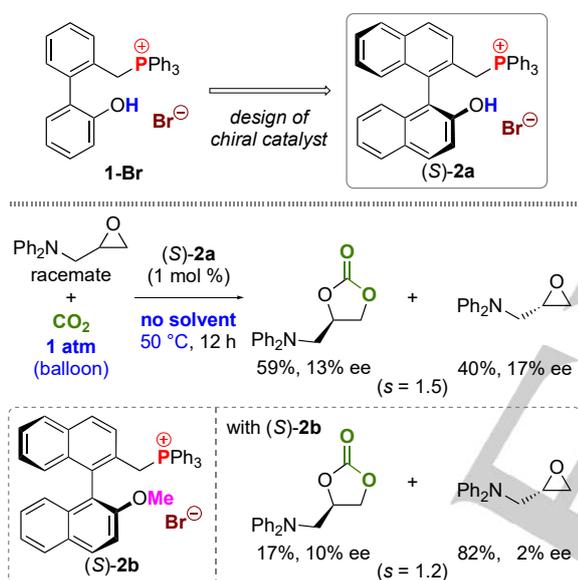

Scheme 6. Kinetic resolution of epoxide by chiral bifunctional quaternary phosphonium bromide via a coupling reaction with CO_2.

3. Triethylamine Hydroiodide as a Simple Yet Effective Bifunctional Nucleophilic Catalyst

3.1. Synthesis of Cyclic Carbonates using a Triethylamine Hydroiodide Catalyst

The design concept for the bifunctional quaternary phosphonium iodide **1-I** prompted our interest in the catalytic activity of triethylamine hydroiodide as a readily available bifunctional catalyst for the CO_2 utilization reactions (Scheme 7).[10,11] Triethylamine hydroiodide is easily prepared via a simple mixing of triethylamine and hydroiodic acid. The reported pK_a value of hydrogen on the nitrogen atom of triethylamine hydroiodide is sufficiently acidic to activate epoxides. Thus, we expected that triethylamine hydroiodide could work as a simple yet effective

bifunctional nucleophilic catalyst to promote CO_2 utilization reactions under atmospheric pressure.
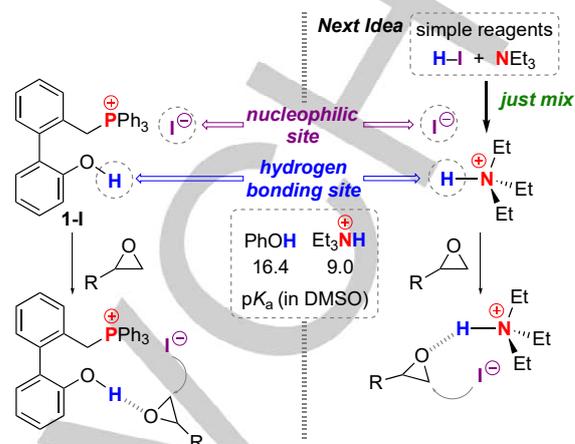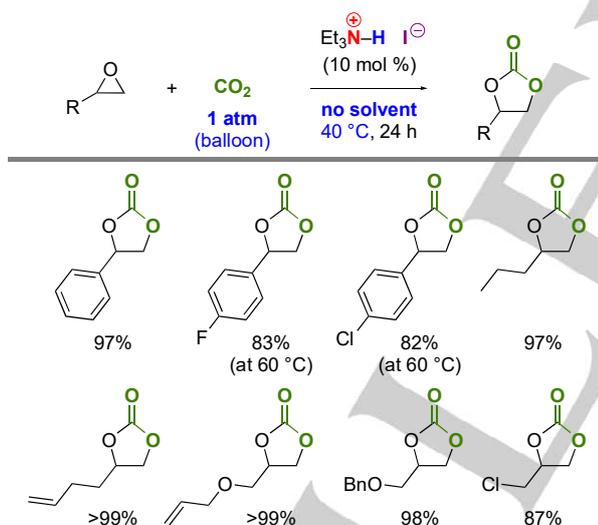

Scheme 7. Triethylamine hydroiodide as a simple bifunctional onium salt catalyst.

To prove the utility of our design for a simple nucleophilic iodide catalyst, triethylamine hydroiodide was used as a catalyst in the coupling reaction of styrene oxide and CO_2 (Scheme 8).[10] As expected, the CO_2 utilization reaction was efficiently promoted by triethylamine hydroiodide (10 mol %) under mild reaction conditions (1 atm using a CO_2 balloon, at 35 °C, without a solvent) to provide the corresponding cyclic carbonate product in a 92% yield. On the other hand, triethylamine hydrobromide and chloride catalysts showed catalytic activity that was at best modest to low under same reaction conditions. Several control experiments were also performed to clarify the importance of the bifunctional nature of the triethylamine hydroiodide catalyst. Almost no catalytic activity was observed when the reactions were performed with a catalytic amount of either triethylamine or hydroiodic acid. Furthermore, tetraethylammonium iodide catalyst sluggishly promoted the reaction under mild reaction conditions. These results clearly suggest the importance of the bifunctional properties of triethylamine hydroiodide for the efficient promotion of the CO_2 utilization reaction under mild reaction conditions.
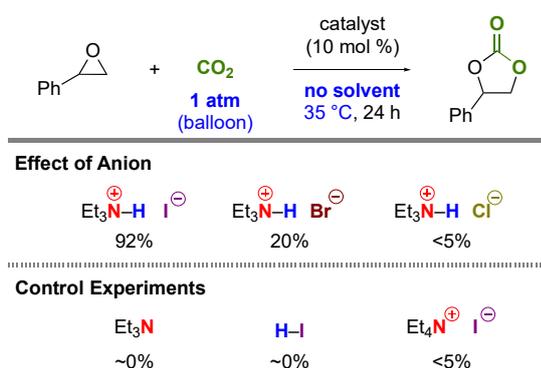
Scheme 8. Effects of ammonium salt catalysts in the coupling reaction of styrene oxide and CO_2.

The generality of epoxides in the CO_2 utilization reaction under atmospheric pressure and mild temperature was examined in the presence of the triethylamine hydroiodide nucleophilic catalyst (Scheme 9). The target cyclic carbonates bearing various functionalities were obtained in good to high yields under solvent-free conditions.

Scheme 9. Substrate generality in the triethylamine hydroiodide-catalyzed coupling reactions of epoxides and CO_2.

The utility of the present catalytic system using a triethylamine hydroiodide nucleophilic catalyst was further demonstrated in the synthesis of optically active cyclic carbonates (Scheme 10). The proposed catalytic cycle of the onium iodide-catalyzed coupling reactions of CO_2 and epoxides, as shown in Scheme 4, does not involve nucleophilic attacks at the chiral carbon center. The reaction mechanism suggests that stereochemical information of a chiral carbon center on epoxide
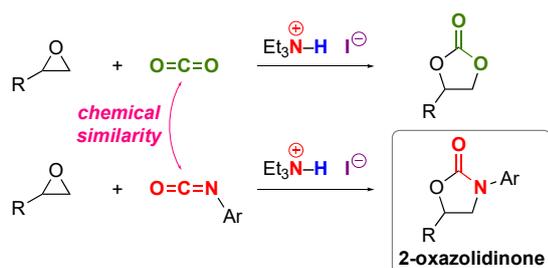
substrates, such as glycidyl ethers, will be kept after the formation of cyclic carbonate products. As expected, the coupling reactions with optically active epoxides and CO_2 were efficiently promoted by triethylamine hydroiodide under mild reaction conditions to produce the targeted optically active products with no loss of enantiomeric purity.
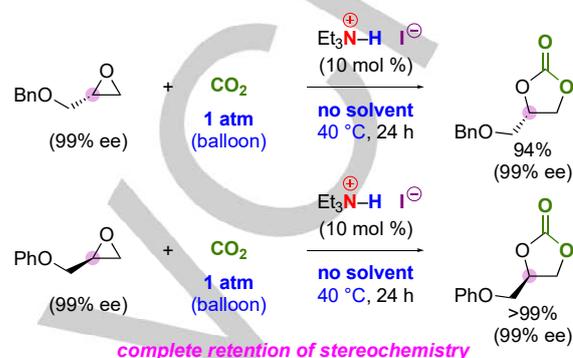

Scheme 10. Coupling reactions with optically active epoxides and CO_2, as promoted by the triethylamine hydroiodide catalyst.

3.2. Synthesis of 2-Oxazolidinones using a Triethylamine Hydroiodide Catalyst

Triethylamine hydroiodide worked as an effective bifunctional nucleophilic catalyst in the CO_2 utilization reactions via the activation of epoxides. To expand the utility of the triethylamine hydroiodide catalyst for the activation of epoxides, we next attempted the synthesis of 2-oxazolidinones from epoxides and isocyanates under the influence of the triethylamine hydroiodide catalyst (Scheme 11).[12,13] The chemical similarity between CO_2 and isocyanates was recognizable when considering the electronic properties of the sp-carbon atoms in these compounds. The 2-oxazolidinones are among the most important 5-membered heterocycles in medicinal chemistry,[14] and their efficient formation by the reactions of epoxides and isocyanates was expected to be accomplished using the same catalytic system as that used in the CO_2 utilization reactions.
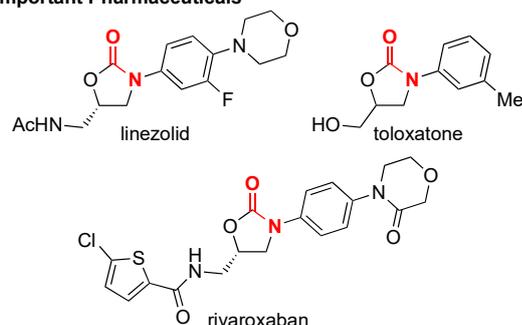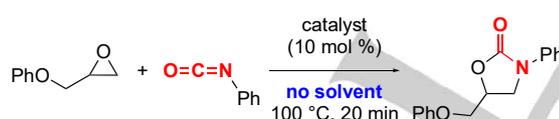
Scheme 11. Triethylamine hydroiodide-catalyzed coupling reactions of epoxides and isocyanates for the synthesis of 2-oxazolidinones as pharmaceutical building blocks.
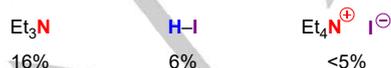
Based on discussion of the coupling reactions of epoxides and isocyanates, the catalytic ability of a triethylamine hydroiodide catalyst was investigated in the reaction of glycidyl phenyl ether and phenyl isocyanate under solvent-free conditions (Scheme 12).[12] To our delight, the targeted 2-oxazolidinone product was obtained in a good yield (83% yield). The effects of triethylamine hydrobromide and chloride catalysts as well as several control experiments were examined. Similar tendencies on catalytic activities in comparison with the CO_2 utilization reaction as shown in Scheme 8 were observed.


Scheme 12. Effects of ammonium salt catalysts in the coupling reaction of glycidyl phenyl ether and phenyl isocyanate.

The assumed catalytic cycle for the synthesis of 2-oxazolidinone catalyzed by a triethylamine hydroiodide appears

in Scheme 13. It should be noted that the reaction mechanisms for cyclic carbonate synthesis with CO_2 and that of 2-oxazolidinone synthesis with isocyanates were expected to be quite similar.
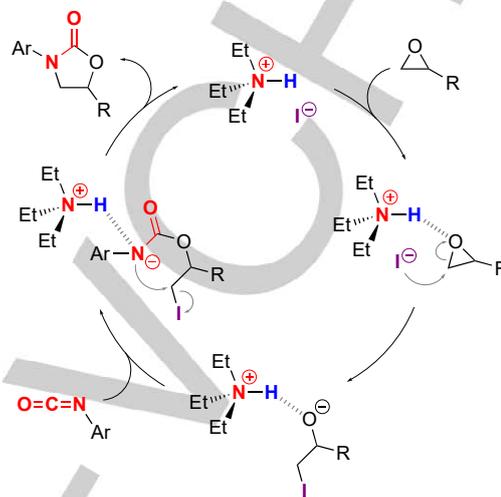

Scheme 13. Assumed catalytic cycle for the triethylamine hydroiodide-catalyzed coupling reactions of epoxides and isocyanates.

The scopes of both epoxides and isocyanates were investigated, and the selected examples appear in Scheme 14. A wide variety of 2-oxazolidinones, which include pharmaceutical building blocks, were synthesized in good to high yields under the influence of a triethylamine hydroiodide catalyst.
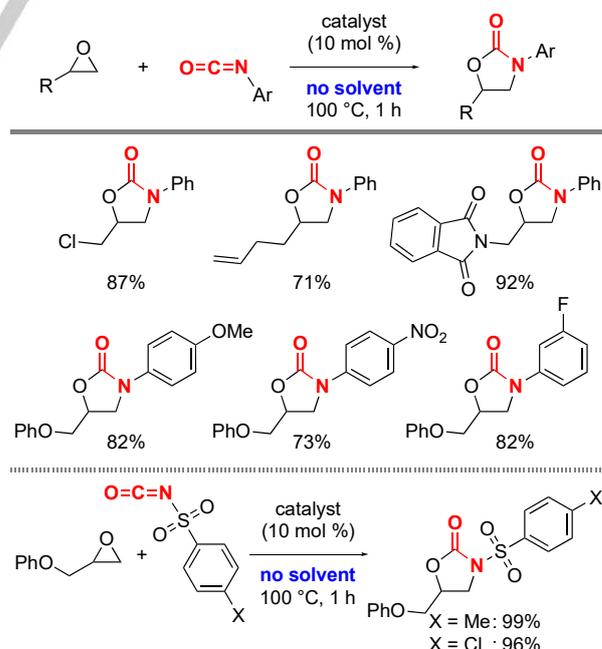
Scheme 14. Substrate generality in the synthesis of 2-oxazolidinones under the influence of a triethylamine hydroiodide catalyst.

Based on the discussion about reaction mechanism in Scheme 13, it is expected that stereochemical information of epoxide substrates, such as glycidyl ethers, will be kept after the formation of 2-oxazolidinone products as same as cyclic carbonate synthesis with CO_2. As expected, optically active 2-oxazolidinones could be synthesized from optically active epoxides in the catalytic system that uses a triethylamine hydroiodide (Scheme 15).
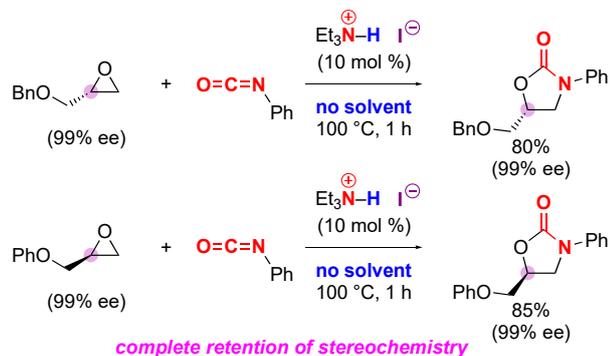

Scheme 15. Optically active 2-oxazolidinone synthesis promoted by a triethylamine hydroiodide catalyst.

4. Potassium Iodide-Tetraethylene Glycol Complex as a Catalyst

4.1. Synthesis of Cyclic Carbonates using a KI–Glycol Complex as a Catalyst

Bifunctional quaternary phosphonium iodide **1-I** and triethylamine hydroiodide functioned as effective organocatalysts in the coupling reactions of epoxides and CO_2 under atmospheric pressure. The design concept of these two bifunctional onium iodide nucleophilic catalysts piqued our interest in the catalytic ability of a potassium iodide (KI)–tetraethylene glycol complex (Scheme 16).[15,16] Tetraethylene glycol forms a complex with KI that increases the nucleophilic ability of an iodide anion. Additionally, the hydroxy groups of tetraethylene glycol complex activate epoxide substrates via hydrogen bonding interactions. Thus, as a catalyst the KI–tetraethylene glycol complex promotes practical coupling reactions of epoxides and CO_2 under mild reaction conditions.
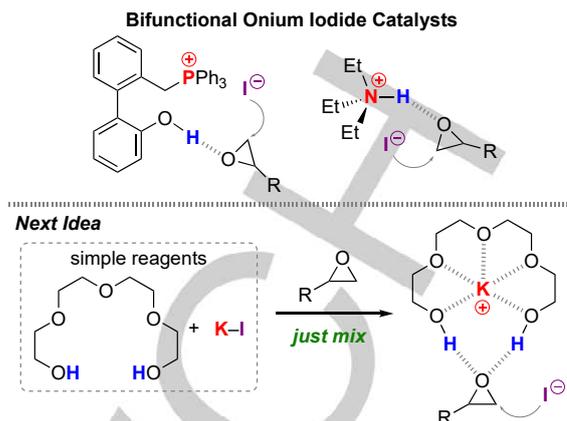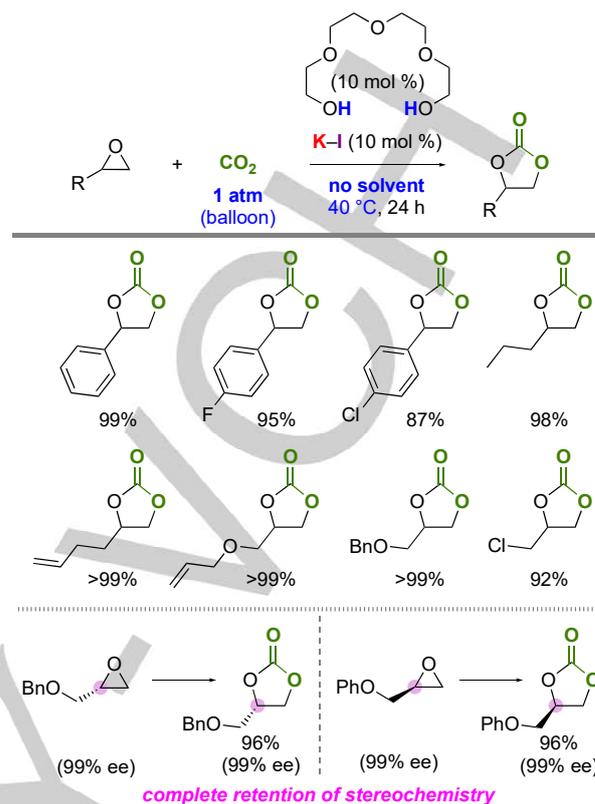

Scheme 16. KI–tetraethylene glycol complex as a practical bifunctional catalyst.

To clarify the utility of a KI–tetraethylene glycol complex as the catalyst for the coupling reactions of epoxides and CO_2, the effects of glycols and alkali metal halides were investigated (Scheme 17).[15] When styrene oxide and KI alone were mixed under a CO_2 atmosphere (1 atm using a CO_2 balloon) at room temperature for 24 hours, almost none of the targeted cyclic carbonate was obtained. The effects of glycols were investigated using the same reaction system. The use of catalytic amounts of 1,2-dihydroxyethane and KI could only provide the product in a 6% yield, whereas a KI–tetraethylene glycol complex catalyst efficiently promoted the CO_2 utilization reaction under mild conditions to give the targeted cyclic carbonate in a 70% yield. To clarify the role of hydroxy groups in tetraethylene glycol, reactions using tetraethylene glycol dimethyl ether and monomethyl ether were performed. Catalytic activities that were lower than those for CO_2 utilization with tetraethylene glycol were observed in these reactions (17 and 34% yields, respectively). Furthermore, an 18-crown-6 complex with KI showed catalytic activity (24% yield) that was lower than that of the KI–tetraethylene glycol complex. These results suggest that the hydroxy groups in the KI–tetraethylene glycol complex catalyst are important for the efficient promotion of the coupling reaction. The effects of alkali metal halides were examined next. The KCl and KBr complex catalysts with tetraethylene glycol showed low levels of catalytic activity. On the other hand, the CO_2 utilization reaction using the NaI–tetraethylene glycol complex as a catalyst showed activity that was similar to that of using the KI complex as a catalyst. Butera and Detz performed computational studies for these catalytic systems to clarify the activation modes of epoxides by KI–tetraethylene glycol complex.[17]
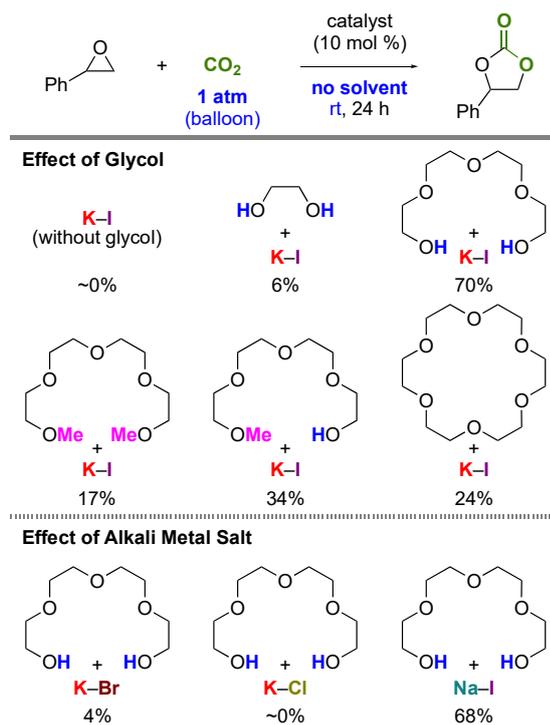
Scheme 17. The effects of glycols and alkali metal halides in the coupling reaction of styrene oxide and CO_2.

The generality of the epoxide substrates during the CO_2 utilization reaction under mild conditions (1 atm using a CO_2 balloon, at 40 °C, without a solvent) was examined using the KI–tetraethylene glycol complex as a catalyst (Scheme 18). The target cyclic carbonates bearing various functionalities were obtained in high yields under atmospheric CO_2 pressure. The optically active cyclic carbonate products were also obtained by the reactions using optically active epoxide substrates.


Scheme 18. Substrate generality in the KI-tetraethylene glycol complex-catalyzed coupling reactions of epoxides and CO_2.

The CO_2 utilization reaction with styrene oxide was conducted on a 50 mmol scale to demonstrate the practicality of the catalytic system when using a KI-tetraethylene glycol complex (Scheme 19). The target cyclic carbonate product (8.2 g) was obtained in a quantitative yield.

Scheme 19. The larger scale coupling reaction of styrene oxide and CO_2 when using a KI-tetraethylene glycol complex.
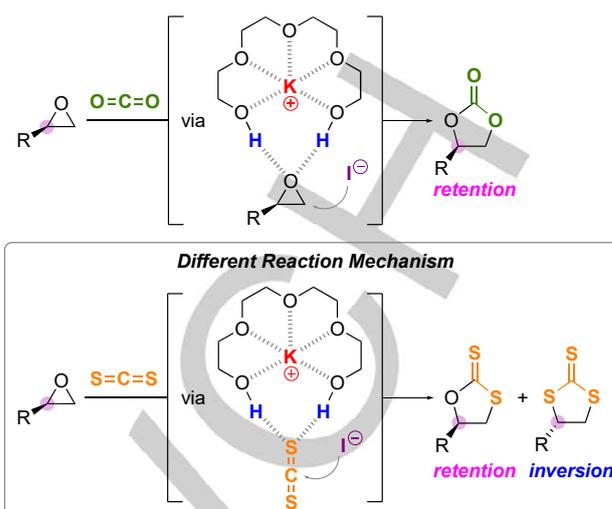
Recycling experiments using the KI-tetraethylene glycol complex catalyst were also performed to further demonstrate the practicality (Scheme 20). After recycling the catalyst ten times, we observed no significant loss of activity.
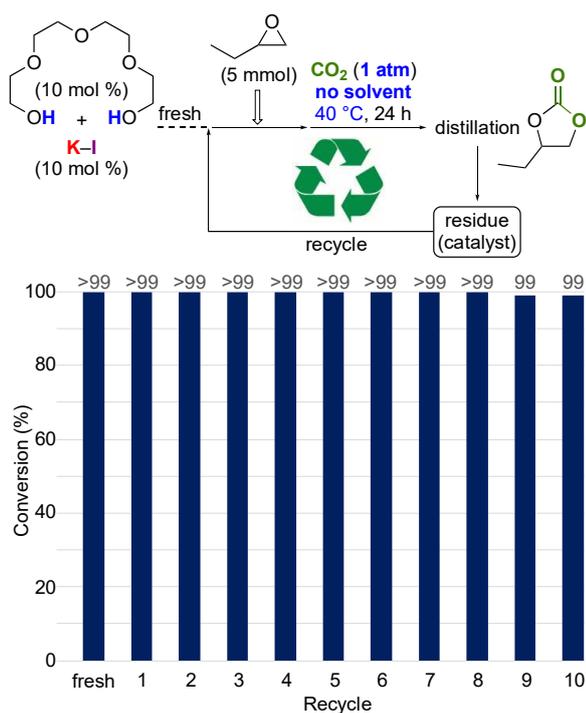
Scheme 20. Reusability of a KI-tetraethylene glycol complex as a catalyst.

Scheme 21. Synthesis of cyclic carbonates and thiocarbonates using a KI–tetraethylene glycol complex catalyst.

4.2. Synthesis of Cyclic Thiocarbonates using a KI–Tetraethylene Glycol Complex as a Catalyst

The effectiveness of the KI-tetraethylene glycol complex for the activation of epoxides was proven in the CO_2 utilization reactions. Based on these findings, we were next interested in the coupling reactions of epoxides and CS_2, which is an isoelectronic analogue of CO_2.[18,19] Although these two reactions for the synthesis of cyclic carbonates and thiocarbonates seem to be very similar, we nonetheless observed that the reaction mechanisms for CO_2 and CS_2 are totally different (Scheme 21).

When a mixture of optically active *N*-glycidylphthalimide as a substrate, CS_2 (1.2 equiv), KI (10 mol %), and tetraethylene glycol (10 mol %) was stirred for 5 hours at 80 °C under solvent-free conditions, the targeted optically active dithiocarbonate product was obtained in a 70% yield with complete "retention" of the stereochemistry (Scheme 22).[18] It is noteworthy that the corresponding trithiocarbonate was also isolated in this reaction as minor product (11% yield). Importantly, the trithiocarbonate product was obtained with complete "inversion" of the stereochemistry. These interesting observations prompted us to further investigate the stereochemical behavior in the coupling reaction of *cis*-epoxycyclohexane and CS_2. When the reaction of *cis*-epoxycyclohexane and CS_2 was performed at room temperature for 16 hours under the influence of a KI-tetraethylene glycol complex catalyst, *trans*-dithiocarbonate and *trans*-trithiocarbonate products were isolated in 41 and 15% yields, respectively. On the other hand, when the same *cis*-epoxycyclohexane was submitted to the reaction with CO_2 using the same catalytic system, only *cis*-carbonate product was produced.
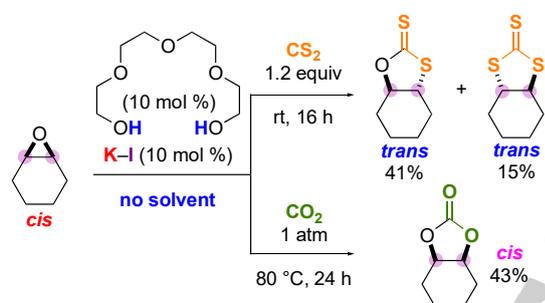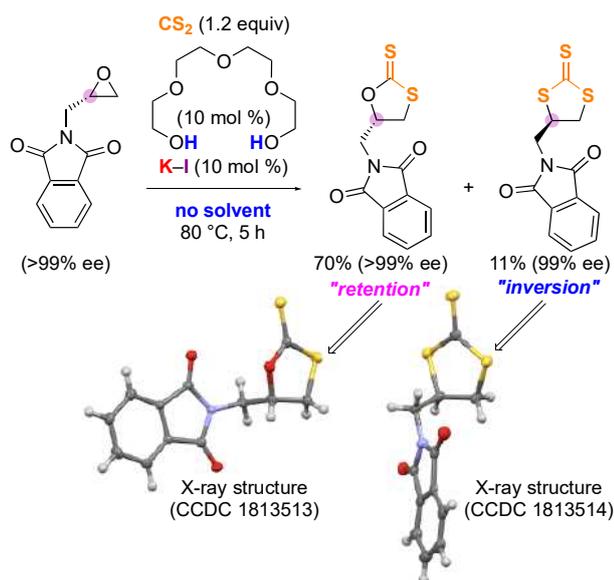
Scheme 22. Stereochemical behaviors in the coupling reactions of epoxides and CS_2 using a KI–tetraethylene glycol complex catalyst.

The retention of stereochemistry in the coupling reaction of *cis*-epoxycyclohexane and CO_2 was explained in basically the same reaction mechanism as that discussed in Scheme 4 for bifunctional phosphonium iodide **1-I**-catalyzed reactions. The *cis*-cyclic carbonate product was obtained via double S_N2 inversions with epoxide activation promoted by a KI-tetraethylene glycol complex catalyst (Scheme 23).
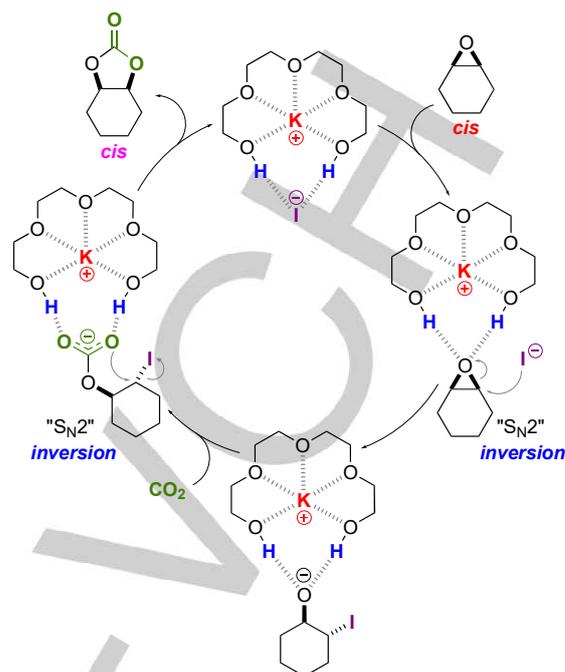
Scheme 23. Assumed catalytic cycle for the KI-tetraethylene glycol complex-catalyzed coupling reaction of *cis*-epoxycyclohexane and CO_2.

In sharp contrast, the coupling reaction of *cis*-epoxycyclohexane and CS_2 provided *trans*-dithiocarbonate and *trans*-trithiocarbonate products. Based on these results and those of previous related reports,[20] the assumed mechanisms for the reaction of epoxides and CS_2 are proposed in Scheme 24. The first step of the reaction with CS_2 is known to differ from the reaction with CO_2. At first, an iodide anion attacks CS_2, which is activated via hydrogen-bonding with the hydroxy groups of tetraethylene glycol (intermediate **A**). Subsequently, a S_N2-type nucleophilic attack by the resultant iododithioformate anion in intermediate **B** on the epoxide leads to intermediate **C** via a S_N2 inversion. Intramolecular cyclization (intermediate **C**) and the subsequent elimination of the iodide anion (intermediate **D**) lead to the attainment of a *trans*-dithiocarbonate product. On the other hand, a *trans*-trithiocarbonate minor product was obtained via the ring opening in intermediate **D** to form intermediate **E** (Scheme 24). The intramolecular S_N2 reaction of the thiolate anion in intermediate **E** afforded *cis*-thiirane. The reaction of *cis*-thiirane with CS_2 under the influence of a KI-tetraethylene glycol complex gave *trans*-trithiocarbonate product in the catalytic cycle, which is similar to the previously mentioned reaction mechanism in the formation of *trans*-dithiocarbonate. The proposed reaction mechanisms in Scheme 24 are supported by the stereochemistry observed in the coupling reaction of optically active *N*-glycidylphthalimide and CS_2, as shown in Scheme 22. The substrate scope for the KI-tetraethylene glycol complex-catalyzed coupling reactions of epoxides and CS_2 was also reported in our original manuscript.[18]
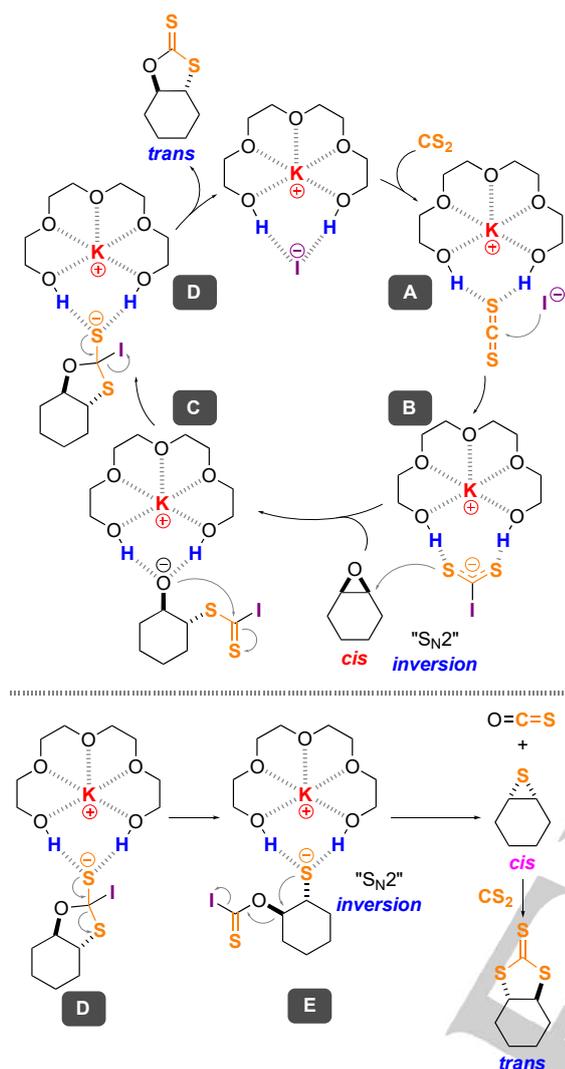
Scheme 24. Assumed reaction mechanisms for the KI-tetraethylene glycol complex-catalyzed coupling reaction of *cis*-epoxycyclohexane and CS₂.

5. Summary and Outlook

Three types of bifunctional iodide nucleophilic catalysts for the activation of epoxides were introduced herein. Previous reports of the positive effects of hydrogen bonding co-catalysts in the quaternary onium iodide-catalyzed coupling reactions of CO₂ and epoxides were consulted in the design of a bifunctional quaternary phosphonium iodide catalyst bearing a phenolic hydroxy group. The bifunctional quaternary phosphonium iodide with a biphenyl backbone efficiently promoted the coupling reactions of epoxides under atmospheric CO₂ pressure. BINOL-derived chiral bifunctional quaternary phosphonium salt was prepared and employed for the kinetic resolutions of epoxides via the CO₂ utilization reactions. The design of the effective bifunctional quaternary phosphonium salt catalysts prompted our interest in the catalytic ability of triethylamine hydroiodide to perform as a readily available bifunctional onium iodide catalyst. In this study,

we successfully used a simple triethylamine hydroiodide as an effective bifunctional nucleophilic catalyst for the coupling reactions of CO₂ and epoxides under mild reaction conditions. The utility of the triethylamine hydroiodide nucleophilic catalyst was further demonstrated in the solvent-free synthesis of 2-oxazolidinones, which are important pharmaceutical building blocks. The coupling reactions of epoxides and isocyanates were efficiently promoted by a simple triethylamine hydroiodide catalyst. The design concept of bifunctional onium iodide nucleophilic catalysts piqued our interest in the catalytic ability of a KI–tetraethylene glycol complex. The KI–tetraethylene glycol complex worked as a bifunctional nucleophilic catalyst to realize practical CO₂ utilization reactions of epoxides. The practicality of this reaction system was demonstrated on a larger scale in the synthesis and recycling experiments of the catalyst. The catalytic ability of the KI–tetraethylene glycol complex was also demonstrated in the coupling reactions of epoxides and CS₂, which is an isoelectronic analogue of CO₂. Although the two coupling reactions of epoxides with CS₂ or CO₂ seem similar, the reaction mechanisms proved to be totally different. The mechanistic differences of these two reactions were discussed based on the stereochemistry of cyclic thiocarbonate and carbonate products. Among the developed three types of bifunctional iodide nucleophilic catalysts, bifunctional quaternary phosphonium iodide with a biphenyl backbone efficiently promoted the coupling reactions of epoxides and CO₂ at lower catalyst loading (1 mol %) than other two catalysts (10 mol %). However, triethylamine hydroiodide catalyst and KI–tetraethylene glycol complex catalyst possess different advantages from viewpoint of the availability. KI–tetraethylene glycol complex catalyst, which is formed *in-situ* by simple mixing of KI and tetraethylene glycol, may be most practical catalyst from the viewpoint of availability and easy-to-handle.

The utility of the bifunctional design of onium and potassium iodide nucleophilic catalysts was clearly demonstrated in these studies. We have successfully developed efficient solvent-free methods for the syntheses of cyclic carbonates, cyclic thiocarbonates, and 2-oxizolidinones from epoxides using these bifunctional iodide catalysts. However, the substrates, which were activated by bifunctional iodide catalysts, were limited to epoxides in our reports. Further application of our bifunctional iodide catalytic system for the activation of other electrophilic substrates should be possible. Reactions with aziridines, as compounds that are related to epoxides, under the influence of iodide nucleophilic catalysts may provide attractive methods for the synthesis of nitrogen-containing compounds. The design and development of effective chiral iodide nucleophilic catalysts, for the kinetic resolution of epoxides via CO₂ utilization reactions and other asymmetric transformations, are another important topic for future research.

Acknowledgements

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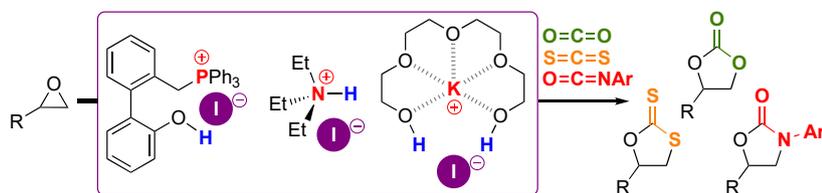
Prof. Dr. S. Shirakawa*

Bifunctional Onium and Potassium Iodides as Nucleophilic Catalysts for the Solvent-Free Syntheses of Carbonates, Thiocarbonates, and Oxazolidinones from Epoxides

Three types of bifunctional iodide nucleophilic catalysts bearing hydrogen bond donor site were developed for the solvent-free coupling reactions of epoxides and CO_2 under atmospheric pressure. These bifunctional iodide catalysts could also be applied to the solvent-free syntheses of thiocarbonates and 2-oxazolidinones, as useful 5-membered heterocyclic compounds, from epoxides.