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Regioselective synthesis of 5-aryl-2-oxazolidinones from carbon dioxide and aziridines using $Br^{-}Ph_3{}^{+}PPEG_{600}P^{+}Ph_3Br^{-}$ as an efficient, homogenous recyclable catalyst at ambient conditions

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ABSTRACT

Polyethylene glycol functionalized phosphonium salt ($Br^{-}Ph_3{}^{+}PPEG_{600}P^{+}Ph_3Br^{-}$) was found to be an efficient, homogenous, recyclable catalyst for coupling of CO_2 with a variety of aziridines producing corresponding 5-aryl-2-oxazolidinones with good yields and excellent regioselectivity under relatively mild and solvent free conditions. Furthermore, the catalyst was effectively recycled for four consecutive cycles without any significant loss in its catalytic activity and selectivity.

Stabilizing and reducing atmospheric carbon dioxide (*Green house gas*) levels have emerged as a pressing global issue for mitigating the effects of climate change. In addition, due to its non-toxic, abundant, and renewable carbon resource, development of commercially viable routes to basic chemicals that employ carbon dioxide as the starting material becomes of practical value for synthetic chemists.[1] In particular, one of the attractive routes for the chemical fixation of CO_2 is to efficiently convert CO_2 into five-membered heterocycles such as oxazolidinones. The importance of 5-membered oxazolidinones has been emphasized in organic synthesis. They have been widely used as chiral synthons, chiral auxiliaries, and as synthetic intermediates in several asymmetric transformations.[2,3] Moreover, some substituted oxazolidinones are also being used as building blocks for the synthesis of biologically active compounds.[4]

Although oxazolidinones have been known for their great variety of applicability, merely only few preparative methods exist for the target compounds from C_1 sources including amino alcohols with phosgene and CO,[5] propargylamines, or propargylic alcohols with CO_2[6], insertion of CO_2 into the aziridines, etc. Synthesis of oxazolidinones utilizing CO_2 as a feedstock is more attractive in comparison to other processes. In this regard, numerous homogeneous catalysts were reported for the synthesis of oxazolidinones from CO_2 and aziridines such as alkali metal halide,[7] iodine,[8] naturally occurring amino acids,[9](salen)-Cr(III)/DMAP,[10] phenol/DMAP,[11] quaternary ammonium bromide functionalized polyethylene glycol,[12] zirconyl chloride,[13] polystyrene supported amino acid,[14], and $[C_4DABCO]Br$.[15] Although significant advances have been made, still there are some disadvantages like requirement of high reaction temperature, longer reaction time, toxic organic solvents, and co-catalysts to achieve higher yields. Hence, development of an efficient, environmental benign, thermo-stable, recyclable catalyst for the synthesis of oxazolidinones from CO_2 and aziridines under milder reaction condition is still desirable.

In recent years, ionic liquids (ILs) have attracted significant attention from the scientific community due to its distinctive properties such as low viscosity, high thermal stability, negligible vapor pressure, high loading capacity, ease in recyclability, and as environmentally benign solvents.[16] Various chemical reactions with high conversion and selectivity have been smoothly performed using ILs as a catalyst or reaction medium.[17] We previously reported that polyethylene glycol functionalized phosphonium salt derived ILs can efficiently catalyze the coupling of carbon dioxide with epoxide for the synthesis of cyclic carbonate.[18a] The wide application of PEG in organic synthesis is closely related to its broad range of solubility. We envisage the phosphonium halide as a catalytically active species which is covalently grafted onto highly CO_2-philic polymer PEG, expected to enhance the catalytic activity for coupling of carbon dioxide with aziridine to afford 2-aryl oxazolidinones synthesis. We were delighted to find that

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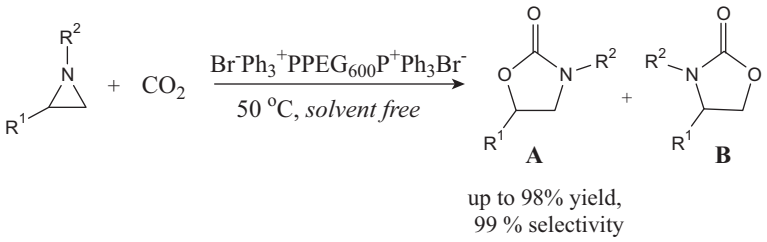


Scheme 1. Synthesis of 2-oxazolidinones from aziridines and CO_2.

polyethylene glycol functionalized phosphonium salt provided excellent catalytic activity toward the selective synthesis of 5-aryl-2-oxazolidinones from aziridine and CO_2 under relatively milder reaction condition. Our strategy is also called as 'mono-phase reaction, two-phase separation'.[18b]

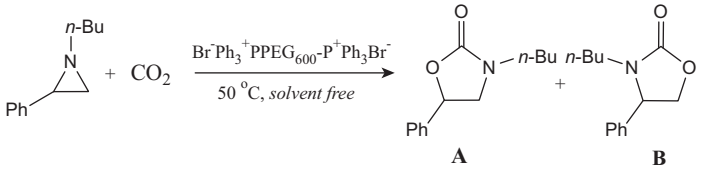
Herein, we report the use of $Br^{-}Ph_3^{+}PPEG_{600}P^{+}Ph_3Br^{-}$ as a highly efficient catalyst for the synthesis of 5-substituted-2-oxazolidinone under mild reaction conditions, without the need of any additives providing high yield or excellent regioselectivity (Scheme 1). In addition, the catalyst was effective for the synthesis of a wide range of substrates under solvent-free conditions.

To optimize the reaction conditions, the reaction of 1-butyl-2-phenylaziridine with CO_2 in the presence of $Br^{-}Ph_3^{+}PPEG_{600}P^{+}Ph_3Br^{-}$ as a catalyst was chosen as a model reaction for the synthesis of 5-aryl-2-oxazolidinones. Various reaction parameters such as catalyst loading, effect of CO_2 pressure, reaction temperature, and time were studied and the results obtained are summarized in Table 1.

The concentration of the catalysts has a strong influence on the yield of 5-aryl-2-oxazolidinones from CO_2 and aziridine. The concentration of catalyst was optimized by employing the reaction with 5, 10, 15, and 20 wt % of catalyst. It was observed that 10 wt % of catalyst provided excellent yield (98%) and selectivity (99%) toward the desired product while further increase in the catalyst loading had no significant effect on catalyst activity and selectivity (Table 1, entries 1–4). The effect of the reaction temperature ranging from 25 to 100 °C on the cycloaddition reaction of aziridine catalyzed by $Br^{-}Ph_3^{+}PPEG_{600}P^{+}Ph_3Br^{-}$ at 5 MPa CO_2 pressure was investigated (Table 1, entries 5–7). We observed that at room temperature (25 °C), 77% conversion with excellent regioselectivity of desired product (99%) was obtained after the reaction time of 16 h (Table 1, entry 5). The yield of oxazolidinones increased with increasing temperature up to 50 °C, while on further increase in reaction temperature the yield and selectivity decreased considerably due to the formation of side products.

Next, we studied the effect of CO_2 pressure on the conversion of product using $Br^{-}Ph_3^{+}PPEG_{600}P^{+}Ph_3Br^{-}$ as a catalyst at 50 °C in the pressure range of 2–7 MPa (Table 1, entries 8–11). The 5-aryl-2-oxazolidinones yield increases in the pressure range of 5–6 MPa and remained unchanged with the further increase in pressure. The yield of 3-butyl-5-phenyl-2-oxoazolidinone was maximum at 5 MPa CO_2 pressures (98%) after 6 h (Table 1, entry 2). In addition, we also performed the reaction at 2 MPa CO_2 pressure at 50 °C where the 3-butyl-5-phenyl-2-oxoazolidinone yields 72% with a

Table 1
Effect of reaction parameters on the synthesis of 2-oxazolidinones from CO_2[a]

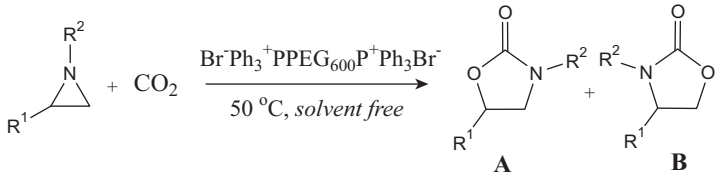


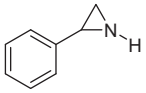
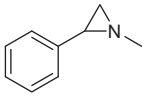
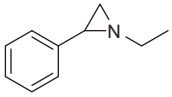
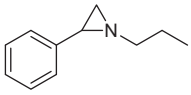
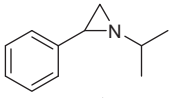
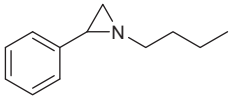
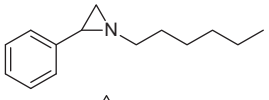
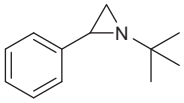
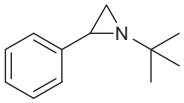
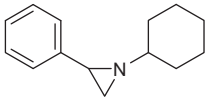
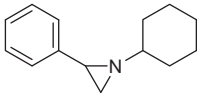
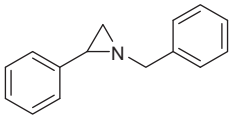
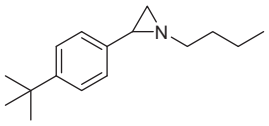
Entry	Catalyst loading (wt %)	Temp (°C)	Time (h)	Pressure (MPa)	Conv.[b] (%)	Selectivity A:B (%)
Catalyst loading						
1	5	50	6	5	63	91:9
2	10	50	6	5	97	98:2
3	15	50	6	5	98	99:1
4	20	50	6	5	98	99:1
Effect of temperature						
5	10	rt	16	5	77	99:1
6	10	80	6	5	94	97:3
7	10	100	6	5	92	90:10
Effect of pressure						
8	10	50	6	7	90	96:4
9	10	50	6	6	97	99:1
10	10	50	6	4	82	93:7
11	10	50	16	2	72	95:5
Effect of time						
12	10	50	12	5	96	97:3
13	10	50	3	5	74	97:3
14	10	50	2	5	62	92:8

[a] Reactions and conditions: 1-butyl-2-phenyl aziridine (1 mmol), catalyst, $Br^{-}Ph_3^{+}PPEG_{600}P^{+}Ph_3Br^{-}$ (10 wt %), CO_2 (5 MPa), 50 °C, time (6 h).
[b] Determined by GC analysis.

reaction time of 16 h (Table 1, entry 11), indicating that the reaction could be conducted effectively under milder reaction conditions. Furthermore, the effect of reaction time on the 5-aryl-2-oxazolidinones conversion was studied (Table 1, entries 12–14). The yield of oxazolidinones increased with increasing time and approached to 100% conversion after 6 h (Table 1, entry 2).

Table 2
Reaction of various aziridines with CO_2 using $Br^-Ph_3{}^+PPEG_{600}P^+PPh_3Br^-$ as catalyst under solvent-free conditions[a]



Entry	Substrates	Time (h)	Conversion (%)	Yield[b] (%)	Selectivity A:B (%)
1		6	99	80	95:5
2		6	100	89	92:8
3		6	100	95	97:3
4		6	100	95	99:1
5		6	99	89	99:1
6		6	100	93	99:1
7		6	99	98	99:3
8		8	15	10	99:1
9[c]		12	65	57	97:3
10		12	20	15	95:5
11[c]		8	67	59	95:5
12		6	99	91	96:4
13		6	99	95	98:2

[a] Reactions and conditions: aziridines (1 mmol), catalyst (10 wt %), CO_2 pressure (5 MPa), temperature (50 °C).
[b] Isolated yield.
[c] Temperature (110 °C).

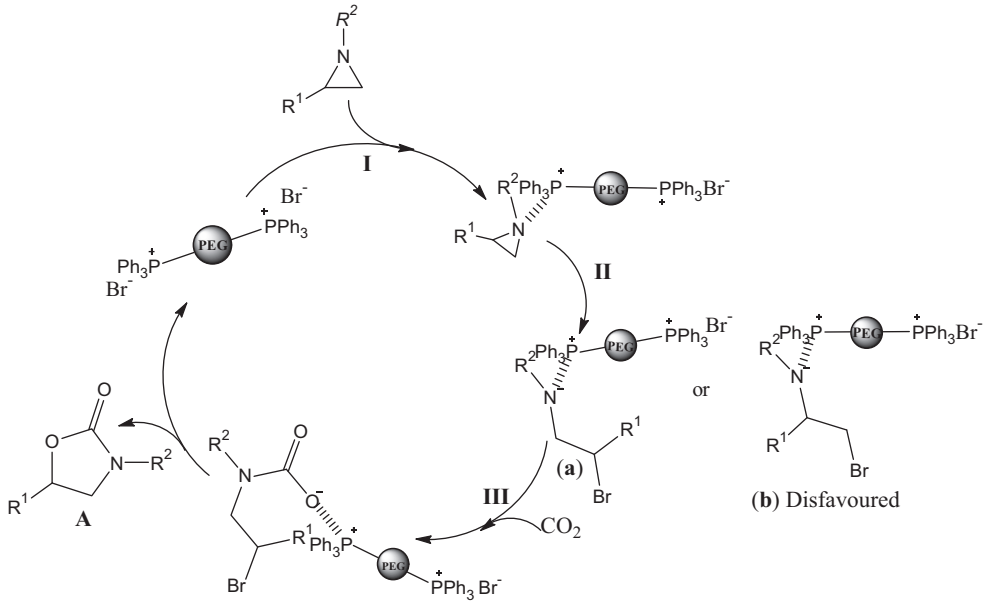


Figure 1. Plausible reaction mechanism.

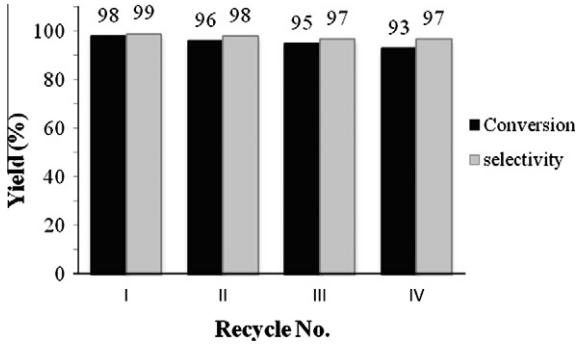


Figure 2. Catalyst reusability. [a]Reactions and condition: aziridines (1 mmol), catalyst (10 wt %), pressure (5 MPa), temperature (50 °C).

Hence, the final optimized reaction parameters for the synthesis of 5-aryl-2-oxazolidinones were aziridine (1 mmol), catalyst loading (10 wt %), CO_2 pressure (5 MPa), temperature (50 °C), and reaction time (6 h).

To broaden the scope and generality of the developed protocol, we screened variety of aziridines for oxazolidinones synthesis under optimized reaction conditions (Table 2, entries 1–13). The reaction of 2-phenylaziridine with CO_2 furnishes 80% yield of the corresponding desired product with good regioselectivity (Table 2, entry 1) while 1-methyl-2-phenylaziridine provided relatively similar yield (89%) of the desired products (Table 2, entry 2). With increase in the alkyl chain on nitrogen of aziridine, excellent yield of expected product with appreciable regioselectivity was obtained (Table 2, entries 3–7). Increase in the steric hindrance of R^2 group at nitrogen atom for substrate has lowered the yield of desired products (Table 2, entries 8 and 10). However, it was overcome with increase in the temperature and time which substantially increased the yield of desired product (Table 2, entries 9 and 11).

On the basis of earlier reports and the experiment results,[12,18] we proposed a plausible reaction mechanism for the cycloaddition of CO_2 with aziridine (Fig.1). The coupling reaction is initiated by polarization of the C–N bond of aziridines through phosphonium cation which acts as a Lewis acidic site and this step activates the aziridine ring (Fig. 1, step I). Subsequently, the nucleophilic attack of bromide anion (Br^-) leads to the ring opening of aziridines providing the two different intermediates as represented as intermediate **a** and **b** mainly depending on the nature of the R^2 group present on the N-atom of aziridines (Fig. 1, step II). Insertion of CO_2 in to P–O bond to obtain carbamate salt could be stabilized by the phosphonium cation of $Br^-Ph_3{}^+PPEG_{600}P^+Ph_3Br^-$ and followed by cyclization leading to oxazolidinones and regeneration of the catalyst. The main product **A** could originate from the ring opening of aziridine at the most hindered carbon. Generally the three-membered heterocyclic ring opens by this route [19,20] and hence remains the most favorable route for the formation of oxazolidinones.

In an effort to craft the synthetic protocol more economical it is necessary to investigate the recyclability of the catalyst ($Br^-Ph_3{}^+PPEG_{600}P^+Ph_3Br^-$). [21] In each cycle, $Br^-Ph_3{}^+PPEG_{600}P^+Ph_3Br^-$ could be easily recovered and reused for the subsequent recycle. The yield of 5-aryl-2-oxazolidinones was consistent up to four consecutive recycles without any significant loss in its catalytic activity thus indicating high stability and activity of developed catalyst (Fig. 2). Therefore, immobilization of a phosphonium salt on a soluble polymer (e.g., PEG_{600}) provides an alternative pathway to demonstrate the recycling of homogeneous catalyst.

In conclusion, we have developed a highly efficient, homogeneous, and recyclable catalytic protocol for the synthesis of 5-aryl-2-oxazolidinones from CO_2 and aziridine with high conversion and excellent regioselectivity. To the best of our knowledge this is the first time, the coupling reactions using $Br^-Ph_3{}^+PPEG_{600}P^+Ph_3Br^-$ as a homogeneous recyclable catalyst under mild reaction conditions has been demonstrated without any significant loss in its catalytic activity. The developed methodology was effectively applicable for several aziridines affording good to excellent yield of desired products demonstrating a broad application of the methodology. Hence, the present methodology will sound to be viewed as a useful contribution for the utilization of CO_2 in the synthesis of industrially important chemicals.

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Supplementary data

Supplementary data (experimental procedures and characterization data of selected aziridines, oxazolidinones and copies of NMR spectra) associated with this article can be found, in the online version, at doi:10.1016/j.tetlet.2011.09.056.

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21. In a typical experimental procedure, coupling of CO_2 with aziridines was carried out in a 100 mL stainless steel autoclave reactor with a mechanical stirrer. The reactor was charged with aziridine (1 mmol) and catalyst (10 wt %) at room temperature. CO_2 gas was introduced into the autoclave and pressure was adjusted to desired pressure (5 MPa) and the mixture was stirred (550–600 rpm) continuously for desired time period. After completion of reaction, the reactor was cooled to room temperature and the remaining CO_2 was carefully vented and then reactor was opened. The product was extracted in diethyl ether (10 mL × 1). The solvent was evaporated in vacuum to obtain the crude product which was then purified by column chromatography silica gel, (100–200 mesh size) with petroleum ether/ethyl acetate (PE–EtOAc, 80:20) as eluent to afford pure product. The reaction mixture was analyzed by GC (Perkin–Elmer, Clarus 400) equipped with a flame ionization detector (FID) and a capillary column (Elite-1, 30 m × 0.32 mm × 0.25 μm). The products were confirmed by ^{1}H NMR (Varian 300 MHz NMR Spectrometer), ^{13}C NMR spectra (100 MHz) and GC–MS (Shimadzu GC–MS QP 2010) (Rtx-17, 30 m × 25mmID, film thickness 0.25 μm df) (column flow-2 mL/min, 80 °C to 240 °C at 10°/min rise.) which were consistent with those reported in the literature.
[Monophase reaction, two-phase separation: The catalyst has some solubility in the product. The catalyst was precipitated from the reaction mixture using antisolvent (e.g., diethyl ether) and thus the catalyst phase was used further for next recycle run. On the other hand the products were extracted in the diethyl ether phase.]