Ionic Liquids

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Transformation of Atmospheric CO_2 Catalyzed by Protic Ionic Liquids: Efficient Synthesis of 2-Oxazolidinones**

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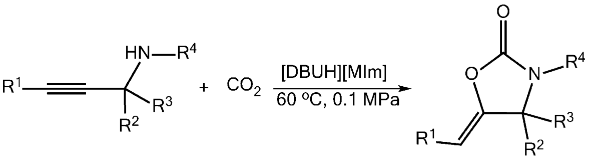
Abstract: *Protic ionic liquids (PILs), such as 1,8-diazabicyclo-[5.4.0]-7-undecenium 2-methylimidazolide [DBUH][MIm], can catalyze the reaction of atmospheric CO_2 with a broad range of propargylic amines to form the corresponding 2-oxazolidinones. The products are formed in high yields under mild, metal-free conditions. The cheaper and greener PILs can be easily recycled and reused at least five times without a decrease in the catalytic activity and selectivity. A reaction mechanism was proposed on the basis of a detailed DFT study which indicates that both the cation and anion of the PIL play key synergistic roles in accelerating the reaction.*

Carbon dioxide (CO_2) is an abundant, nontoxic, nonflammable, easily available, and renewable C1 resource.[1] CO_2 chemistry has become one of the most important branches of chemistry.[2] CO_2 has been transformed into various useful chemicals, such as dimethyl carbonate,[3] urethanes,[4] formic acid,[5] methanol,[6] cyclic carbonates,[7] polycarbonates,[8] and others. As it is thermodynamically stable and kinetically inert, harsh reaction conditions, such as using high-pressure CO_2,[9] metal complexes,[10] and strong bases,[11] have to be applied. The exploration of new, green, and metal-free catalysts for the reaction of atmosphere CO_2 is a very interesting topic.

2-Oxazolidinones[12] are important heterocyclic compounds having many applications in organic synthesis[13] and pharmaceutical chemistry.[14] For example, they can be used as cholesteryl ester transfer protein inhibitors[15] and monoamine oxidase inhibitors.[16] Therefore, many efforts have been made to synthesize these useful heterocyclic compounds, for example through the allylic C−H oxidation reaction of N-Boc amines[17] and the formal [3+2] cycloaddition reaction,[18] among others.[19] Recently, the cyclization of CO_2 with propargylic amines to obtain 2-oxazolidinones has attracted much attention. So far, a variety of effective catalytic systems, such as silver/1,8-diazabicyclo-[5.4.0]undec-7-ene (DBU)[20] and NHC–gold complexes (NHC = N-heterocyclic carbene),[21] have been used to promote this type of reaction. Although CO_2 can be efficiently transformed using these catalytic systems, the metal catalysts used in the reactions are both expensive and toxic. In particular, it is difficult to recover and reuse these catalysts. Therefore, the exploration of efficient, cheap, green, reusable, and metal-free catalysts for this class of reaction is of great importance.

Ionic liquids (ILs) have some very attractive properties, such as negligible vapor pressure and nonflammability. They are excellent solvents for both organic and inorganic substances and their functions can be tuned by changing the structures of their cations or anions.[22] ILs have been recently explored as novel and green materials for the capture and fixation of CO_2.[23] They have also been used in materials synthesis and in chemical reactions[24] especially as effective catalysts and additives in CO_2 reactions, such as the hydrogenation of CO_2 to formic acid[25] and in the synthesis of quinazoline-2,4(1*H*,3*H*)-diones[26] and disubstituted ureas.[27]

We demonstrate herein for the first time the use of ILs as both the catalyst and solvent for the cyclization reaction of CO_2 with propargylic amines to form 2-oxazolidinones under metal-free conditions (Scheme 1). Several ILs were found that could be used as both catalyst and solvent for the reactions. In particular, 1,8-diazabicyclo[5.4.0]-7-undecenium 2-methylimidazolide [DBUH][MIm] was very effective for this kind of reaction, giving the desired product in high yield under mild conditions, and could be easily recovered and reused. DFT studies indicated that the cation and anion have a synergistic effect in catalyzing the reactions.



Scheme 1. The reaction of CO_2 with propargylic amines to form 2-oxazolidinones.

First, the catalytic activity of various typical ILs, acting as both catalyst and solvent, for the reaction between atmospheric CO_2 and the propargylic amine butyl-(1-phenylethynyl-butyl)-amine (**1a**) was investigated at 60 °C for 6 h (Table 1). The structures of all of the ILs are given in the Supporting Information. In the absence of an IL, the reaction did not occur (Table 1, entry 1). For imidazolium-based ILs (entries 2–6), the use of neutral ILs 1-butyl-3-methylimidazolium perchlorate ([Bmim][ClO_4]), 1-butyl-3-methylimidazolium bis((trifluoromethyl)sulfonyl)imide ([Bmim][Tf_2N]),

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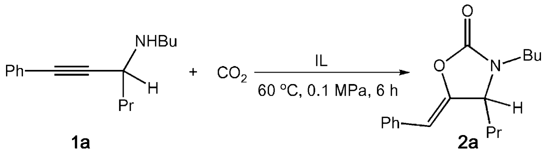
Table 1: Reaction of CO_2 with propargylic amine **1a** in various ILs.[a]



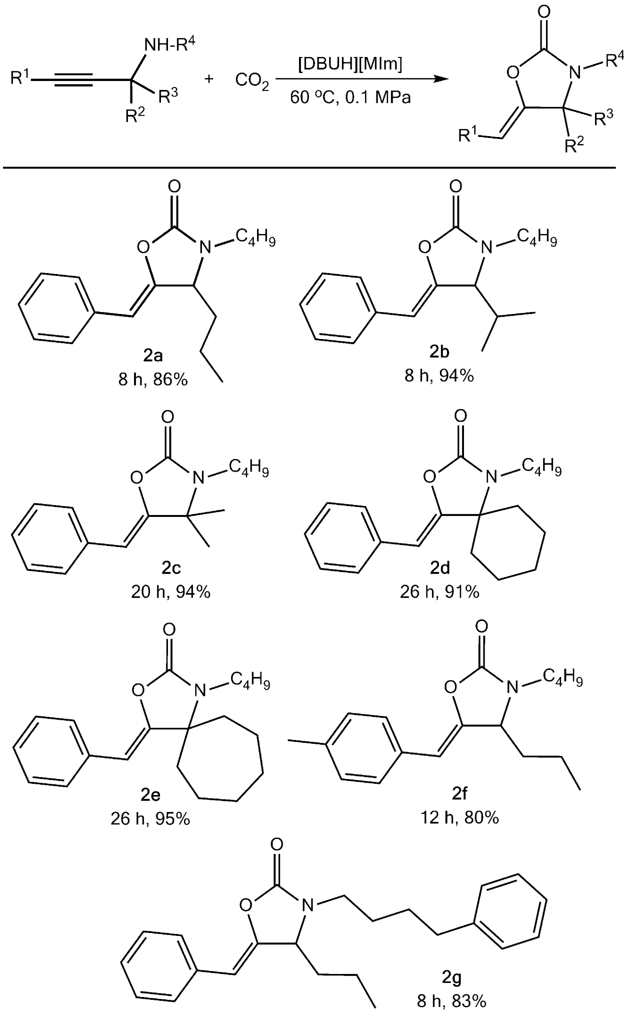
Entry	ILs	Yield[b] [%]
1	–	0
2	$[Bmim][ClO_4]$	0
3	$[Bmim][Tf_2N]$	0
4	[Bmim][Cl]	0
5	$[Bmim]_2[WO_4]$	29
6	[Bmim][OAc]	37
7	[DBUH][OAc]	45
8	[DBUH][Im]	64
9	[DBUH][PhE]	79
10	[DBUH][*i*PrIm]	82
11	[DBUH][MIm]	85
12[c]	[DBUH][MIm]	90

[a] Reaction conditions: **1a** (0.5 mmol), IL (1 mmol), CO_2 (0.1 MPa), 60°C, 6 h. [b] The yield was determined by ^1H NMR spectroscopy using 1,3,5-trioxane as an internal standard. [c] The reaction time was 8 h.

and 1-butyl-3-methylimidazolium chloride ([Bmim][Cl]) had no catalytic effect on the reaction. To our delight, the basic ILs 1-butyl-3-methylimidazolium tungstate ($[Bmim]_2[WO_4]$) and 1-butyl-3-methylimidazolium acetate ([Bmim][OAc]) could catalyze the reaction, with the yields of the target product 5-benzylidene-3-butyl-4-propyl-oxazolidin-2-one (**2a**) being 29% and 37%, respectively. The protic ionic liquid (PIL) 1,8-diazabicyclo[5.4.0]- 7-undecenium acetate ([DBUH][OAc]) showed catalytic activity and gave product **2a** in 45% yield, which was much higher than that of [Bmim][OAc]. This result suggests that with the same anion the catalytic activity of the DBU-based PIL is better than the imidazolium-based IL. With this in mind, some DBU-based PILs were synthesized by neutralization reactions, and the activity order of anions was found to follow the order: MIm^- > 2-isopropylimidazolide ($iPrIm^-$) > phenolate (PhE^-) > imidazolide (Im^-). This result implies that the nucleophilic strength of anions is an important factor in determining the catalytic activity of the PILs. In contrast to the imidazolide anion, the alkyl-substituted imidazolide anion was found to be a stronger nucleophile and showed excellent activity for this reaction (Table 1, entries 8, 10, and 11). As a result of the steric hindrance imposed by the substituent, [DBUH][MIm] showed the best activity for the reaction giving **2a** in 85% yield (entry 11), better than the result obtained for 1,8-diazabicyclo[5.4.0]-7-undecenium 2-isopropylimidazolide ([DBUH][*i*PrIm]). Additionally, traditional strong bases including the organic base triethylamine, DBU, and 1,5,7-triazabicyclo[4.4.0]dec-5-ene (TBD), which are catalytically active for the transformation of *N*-alkylprop-2-ynylamines,[28] and the inorganic base Cs_2CO_3 which also acts as a nucleophile, were used to catalyze this reaction. However, the highest yield obtained was only 37% (see Table S1 in the Supporting Information) and it is very difficult to recover these bases after the reaction. Thus, to study the effects of temperature and time and the effect of changing the concentration of PIL employed, the PIL [DBUH][MIm] was used as the catalyst for the reaction under an atmospheric pressure of CO_2 (see Figure S1-S3). Under these optimized conditions, the yield of the desired product could reach 90% (Table 1, entry 12).

The reusability of [DBUH][MIm] was tested under the optimized reaction conditions and the results are given in Figure S4. The catalytic activity and selectivity of the PIL did not change notably after being reused five times, suggesting that the PIL maintained its original performance and was recyclable.

The reactions of CO_2 with a range of different substituted propargylic amines were then conducted under the optimized reaction conditions and the yields of the isolated target products are summarized in Scheme 2. In general, the reactivity of the propargylic amines depended strongly on the nature of the R^2 and R^3 substituents. When the R^2 group was hydrogen and R^3 was an alkyl group, the reactions went to completion within 12 h (**1a**, **1b**, **1f**, **1g**). When R^2 was an alkyl group (and therefore with a stronger electron-donating ability than hydrogen), a significantly longer time was required to

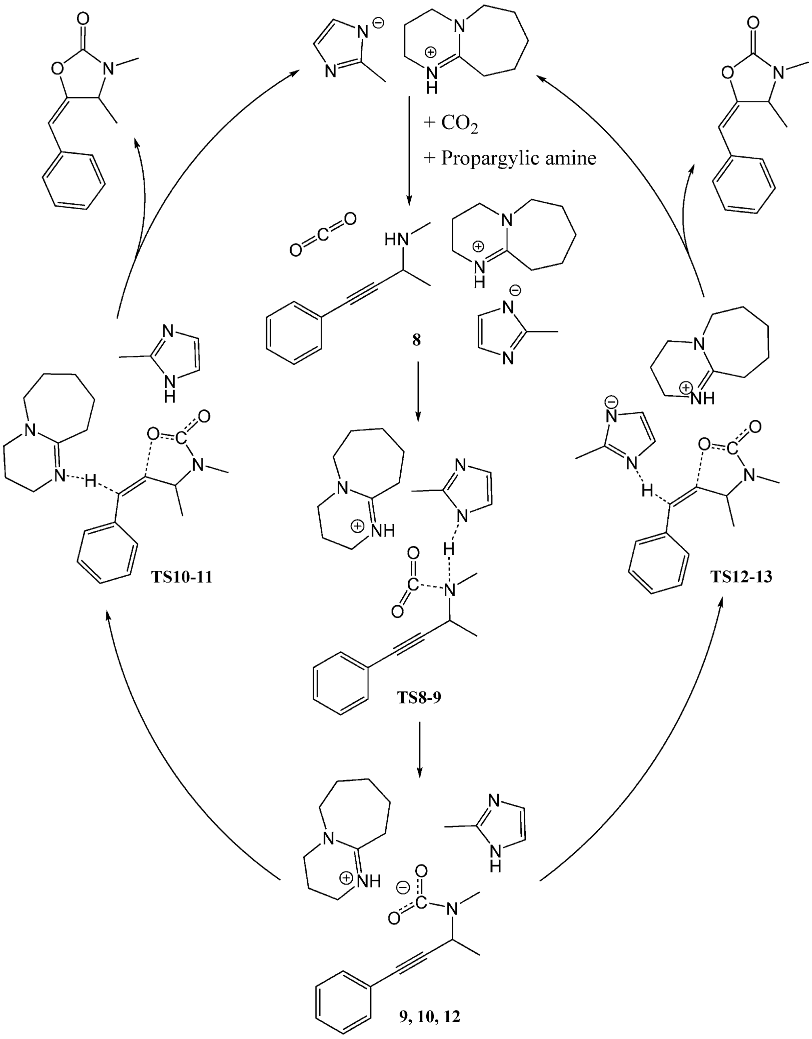


Scheme 2. Scope of the propargylic amine substrate for the reaction. Optimized reaction conditions: substrate (0.5 mmol), [DBUH][MIm] (1 mmol; 0.2342 g), CO_2 (0.1 MPa), 60°C.

complete the reactions (**1c**–**e**) and higher yields were also obtained. According the above results, we can see that the stronger the electron-donating ability of R^2 and R^3, the higher the yield of the desired product, although the reaction then required a much longer time to go to completion. Additionally, propargylic amines with different R^1 and R^4 groups were also studied (**1f** and **1g**), and good yields of the corresponding 2-oxazolidinones (**2f** and **2g**) were obtained. The above results confirmed the versatility of the new catalytic method for producing 2-oxazolidinones.

Subsequently, the catalytic mechanism of [DBUH][MIm] was investigated in detail by employing the DFT method and the Gaussian 09 package.[29] At first, the noncatalyzed cycloaddition of CO_2 and propargylic amine (**1a**) was studied. Scheme S2 shows clearly that the target product from the reaction of CO_2 and the propargylic amine is formed when the amino group undergoes electrophilic attack by the CO_2 molecule followed by subsequent intramolecular cyclization steps. Figure S5 suggests that the intramolecular cyclization step with an energy barrier of 42.7 kcal mol^{-1} is the rate-determining step. The overall energy barrier for the cycloaddition is 52.1 kcal mol^{-1}, which is too high for the reaction to occur. The theoretical calculation result is consistent with the experimental results that the reaction did not occur without the catalyst (Table 1, entry 1). Catalysts should be introduced to decrease the energy barrier for the reaction.

Both the CO_2 and the amino group on the propargylic amine can be activated by [DBUH][MIm], so the mechanisms of both CO_2- and amino-activated reaction pathways were investigated, respectively. Scheme S3 show clearly that there are three steps in the CO_2-activated mechanism: CO_2 capture,[30] attack on the C≡C bond, and the intramolecular cyclization steps. First, the PIL can capture CO_2 and form the ion pair [DBUH][MIm-CO_2], in which CO_2 is activated by having more negative charge on the O atoms. In the subsequent attack of the captured CO_2 on the C≡C bond of propargylic amine, the H atom of the cation [DBUH]$^+$ attacks the C≡C bond synchronously. This corresponds to the transition state of TS4–5. The energy barrier of this step is 46.8 kcal mol^{-1}. In the last intramolecular cyclization step via transition state TS6–7, the target product is formed and the PIL [DBUH][MIm] is regenerated. The results of the energy calculations are shown in Figure S6, which suggest that the attack on the C≡C bond is the rate-determining step and the overall energy barrier for the CO_2-activated mechanism is 46.8 kcal mol^{-1}. Although the energy barrier of the CO_2-activated mechanism is relatively high, it is less than that of the non-catalyzed one (52.1 kcal mol^{-1} in Figure S5).



Scheme 3. The amino-activated mechanism for the [DBUH][MIm]-promoted cycloaddition of CO_2 with propargylic amine substrates.

The amino-activated mechanism and its potential energy curves are illustrated in Scheme 3 and Figure 1, respectively. As a result of the hydrogen atom of the amino group being captured by the 2-methylimidazolide anion of [DBUH][MIm], the CO_2 electrophilic attack on the amino group is more favorable, having an energy barrier of 6.3 kcal mol^{-1} (via transition state TS8–9). After this step a 2-methylimidazole molecule and a new ion pair ([DBUH]$^+$ and the carbamate anion) are formed (Scheme 3, structure 9). In the following intramolecular cyclization step, the attack of the O atom and the proton transfer to the C≡C bond occurs simultaneously. Depending on the sources of the proton, there are two potential routes for this intramolecular cyclization step, as shown in Scheme 3. For the route via transition state TS10–11, the [DBUH]$^+$ provides the proton with an energy barrier of 30.5 kcal mol^{-1}. For the second route, the proton transfers from a 2-methylimidazole molecule to the C≡C bond, via transition state TS12–13, with an energy barrier of 31.0 kcal mol^{-1}. Both routes render the attack of the O atom on the C atom in the C≡C bond easier and lead to the target product and the regeneration of the catalyst [DBUH][MIm]. These

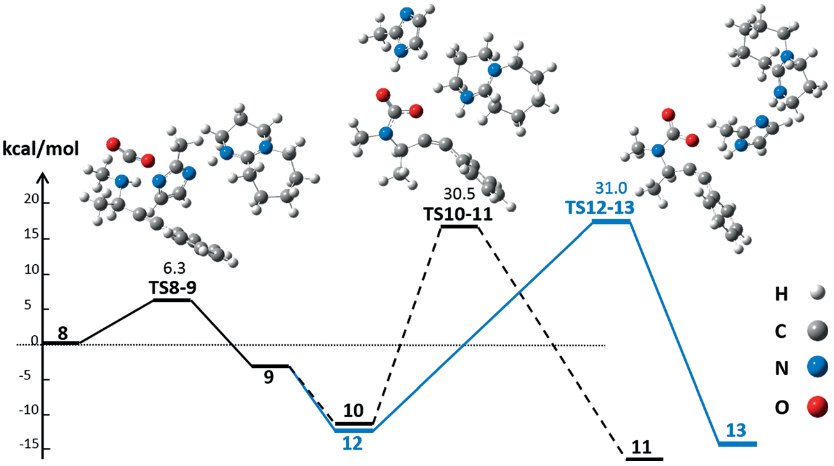


Figure 1. Potential energy curves of amino-activated reaction pathways.

results indicate clearly that both the cation and the anion of the PIL play important roles in accelerating the reactions. These calculations are in good agreement with the experimental results which show that the PILs (Table 1, entries 7–11) show better performance for the transformation of CO_2 than the aprotic ionic liquids (Table 1, entries 2–6). Figure 1 shows that the intramolecular cyclization step is the rate-determining step and that the overall energy barrier for the amino-activated mechanism is 31 kcal mol^{-1}.

By comparing the overall energy barrier of the [DBUH][MIm]-promoted mechanisms, the amino-activated mechanism is more favorable than the CO_2-activated one which has an overall energy barrier of 46.8 kcal mol^{-1}. In the amino-activated mechanism, [DBUH][MIm] promoted both the CO_2 electrophilic attack step and the intramolecular cyclization step by capturing and providing protons, respectively. As a result, the overall energy barrier of the cycloaddition of CO_2 with propargylic amine is lowered from 52 to 31 kcal mol^{-1}.

In conclusion, we have developed a new strategy to utilize ILs as both the catalyst and the solvent to promote the synthesis of 2-oxazolidinones from atmosphere CO_2 and propargylic amines effectively and selectively under mild conditions. Among the ILs studied, [DBUH][MIm] shows the best performance and this PIL can be easily recovered and reused. Theoretical studies reveal that both the cation and anion are crucial in catalyzing the reaction and that the PIL promotes both the CO_2 electrophilic attack and the intramolecular cyclization step by capturing and providing proton, respectively. We believe that this simple, metal-free, and greener route to produce 2-oxazolidinones may have important future applications.

Keywords: carbon dioxide fixation · density functional calculations · heterocycles · ionic liquids · reaction mechanisms

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