

A Protic Ionic Liquid Catalyzes CO₂ Conversion at Atmospheric Pressure and Room Temperature: Synthesis of Quinazoline-2,4-(1*H*,3*H*)-diones**

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Abstract: The chemical fixation of CO₂ under mild reaction conditions is of significance from a sustainable chemistry viewpoint. Herein a CO₂-reactive protic ionic liquid (PIL), [HDBU⁺][TFE⁻], was designed by neutralization of the superbase 1,8-diazabicyclo[5.4.0]undec-7-ene (DBU) with a weak proton donor trifluoroethanol (TFE). As a bifunctional catalyst for simultaneously activating CO₂ and the substrate, this PIL displayed excellent performance in catalyzing the reactions of CO₂ with 2-aminobenzonitriles at atmospheric pressure and room temperature, thus producing a series of quinazoline-2,4(1*H*,3*H*)-diones in excellent yields.

Chemical conversion of CO₂ is an alternative for CO₂ utilization, and has been paid much attention in the past decades.^[1] In comparison with toxic phosgene and CO, CO₂ is an abundant, easily available, environmentally friendly, and renewable C1 building block. However, CO₂ conversion is limited because of its inherent thermodynamic stability, thus resulting in low reactivity. In this context, the key issue to convert CO₂ into useful chemicals under mild reaction conditions will inevitably rely on its activation. Therefore, effective catalytic systems are highly required. So far, many efficient catalysts have been developed for CO₂ conversion into high-value chemicals such as methanol,^[2] formic acid,^[3] and others.^[4] However, high temperature and pressure are generally needed. In recent years, researchers have paid much attention to chemically converting CO₂ under mild reaction conditions, especially at atmospheric pressure and room temperature.^[5] Kimura et al. reported [(n-C₄H₉)₄N]₂⁺[WO₄]²⁻ as a bifunctional catalyst which could catalyze the reactions of CO₂ with various aromatic diamines at atmospheric pressure around 100 °C.^[5g] More recently, cobalt-coordinated conjugated microporous polymers were reported to function as heterogeneous catalysts for the reaction of CO₂ with propylene oxide at atmospheric pressure and room temperature.^[5h] Though much progress has been made, the chemical con-

version of CO₂ at atmospheric pressure and room temperature is still a challenge.

Ionic liquids (ILs) composing of organic cations and inorganic/organic anions have unique features such as high thermal and chemical stability, negligible vapor pressure, easy recyclability, and tunable properties, which have been applied in many areas.^[6] Specifically, task-specific ILs have displayed superior performance for CO₂ capture and conversion through careful design and choice of novel component ions to endow them with unique properties.^[4c,d,h,7] For example, superbase-derived protic ionic liquids (PILs) were presented to be excellent media for rapid and reversible capture of CO₂ under mild reaction conditions.^[7b] CO₂ could react with PILs to form liquid carbonate, carbamate, or phenolate salts, which might result in activation of CO₂, thus rendering the chemical transformation of CO₂ under mild reaction conditions. Inspired by this progress, we designed a CO₂-reactive PIL using 1,8-diazabicyclo[5.4.0]undec-7-ene (DBU) as a superbase and trifluoroethanol (TFE) as a proton donor, denoted as [HDBU⁺][TFE⁻]. This PIL could adsorb CO₂ with maximum molar ratio CO₂/IL of 1.01 at atmospheric pressure and room temperature (see the Supporting Information), thus suggesting that it was a good absorbent for CO₂ with a capacity comparable to those reported PILs.^[7b]

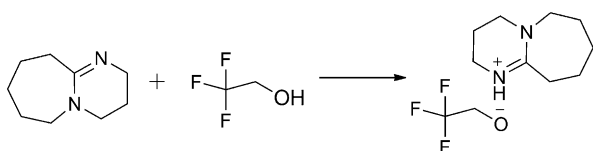
Quinazoline-2,4(1*H*,3*H*)-diones can serve as intermediates for the synthesis of pharmaceuticals.^[8] The reaction of CO₂ with 2-aminobenzonitriles is an atom-economical route for the synthesis of these compounds, and it has been widely investigated using various catalysts including DBU,^[9] Cs₂CO₃,^[10] MgO-ZrO₂,^[11] [Bmim]OH,^[12] *N*-methyl-tetrahydropyrimidine,^[13] guanidines,^[14] [(n-C₄H₉)₄N]₂⁺[WO₄]²⁻,^[5g,15] and 1-butyl-3-methylimidazolium acetate ([Bmim]Ac).^[16] However, in these studies a high CO₂ pressure and temperature were generally required. In this work, we have found that by using [HDBU⁺][TFE⁻] as the catalyst and solvent, the CO₂ reaction with 2-aminobenzonitriles at atmospheric pressure and room temperature produces a series of quinazoline-2,4(1*H*,3*H*)-diones in excellent yields. Moreover, the IL could be easily recovered and reused without activity loss.

[HDBU⁺][TFE⁻] was synthesized by neutralization of DBU and TFE, as illustrated in Scheme 1. The characterization for this IL is given in the Supporting Information, and the ¹H NMR data (Figure S1) and FTIR (Figure S2) analysis confirm its formation. For comparison, other three ILs with different cations and anions, including, [HDBU⁺][CH₃COO⁻], [HTMG⁺][TFE⁻], and [Et-DBU⁺][TFE⁻]

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Scheme 1. Preparation of [HDBU⁺][TFE⁻].

Table 1: Reaction of 2-aminobenzonitrile with CO₂ catalyzed by different IL catalysts.^[a]

Entry	Catalyst/Solvent	Yield [%] ^[b]
1	—	0
2	[HDBU ⁺][TFE ⁻]	97
3	[HDBU ⁺][CH ₃ COO ⁻]	15
4	[HTMG ⁺][TFE ⁻]	67
5	[Et-DBU ⁺][TFE ⁻]	7 ^[c]
6 ^[d]	[(<i>n</i> -C ₄ H ₉) ₄ N] ₂ ⁺ [WO ₄] ²⁻	90

[a] Reaction conditions: 2-aminobenzonitrile (1 mmol), catalyst (3 mmol), CO₂ (0.1 MPa), 303 K, 24 h. [b] Yield of isolated product.

[c] determined by LC analysis. [d] DMSO (1 mL), catalyst (0.02 mmol), CO₂ (0.1 MPa), 373 K, 120 h.^[5g]

(TMG = 1,1,3,3-tetramethylguanidine), were synthesized (see the Supporting Information).

The reaction of CO₂ with 2-aminobenzonitrile was carried out in the absence and presence of the as-synthesized ILs, and the results are listed in Table 1. This reaction did not proceed in the absence of any catalyst. To our delight, [HDBU⁺][TFE⁻] as the catalyst showed high efficiency for this reaction (see Figures S3 and S4 in the Supporting Information), thus producing quinazoline-2,4-(1*H*,3*H*)-dione in 97 % yield, without any byproducts, within 24 hours (Table 1, entry 2). Moreover, [HDBU⁺][TFE⁻] served as a solvent, which allowed the reaction to proceed more rapidly than the reported systems.^[5g] For comparison, three other ILs were examined for catalyzing this reaction. It was indicated that they were also effective, however, they showed lower activities (Table 1, entries 3–5). The differences in their chemical structures may be responsible for their activities. [HDBU⁺][CH₃COO⁻], having the same cation as [HDBU⁺][TFE⁻], afforded a much lower product yield (15 %), thus indicating that the anions of the PILs influence the activities of the catalysts. Additionally, [HTMG⁺][TFE⁻] and [Et-DBU⁺][TFE⁻], which have the same anion as [HDBU⁺][TFE⁻], also gave lower product yields (67 and 7 %, respectively), thus suggesting that the cations of the ILs affected the activities of the catalysts as well. From the above findings, it can be inferred that both the cations and anions of these ILs played important role in the reaction.

The [HDBU⁺][TFE⁻]-catalyzed system could be applied to various 2-aminobenzonitriles reacting with CO₂ at atmospheric pressure and room temperature (Table 2). It was demonstrated that all reactions proceeded smoothly, thus producing the corresponding quinazoline-2,4-(1*H*,3*H*)-diones. With the exception of 4-methyl-2-aminobenzonitrile (Table 2, entry 2), the other 2-aminobenzonitriles, having substituents including methoxy, fluoro, chloro, and bromo groups, generated the corresponding products in excellent yields within

Table 2: Synthesis of various quinazoline-2,4-(1*H*,3*H*)-diones.^[a]

Entry	Substrate	Product	Yield [%] ^[b]
1 ^[c]			97
2			68 ^[d]
3			92
4			96 ^[d]
5			92
6			90
7			95
8 ^[e]			95

[a] Reaction conditions: Reactant (1 mmol), [HDBU⁺][TFE⁻] (6 mmol), CO₂ (0.1 MPa), 303 K, 24 h. [b] Yield of isolated product. [c] [HDBU⁺][TFE⁻] (3 mmol). [d] Determined by LC analysis. [e] [HDBU⁺][TFE⁻] used for the fifth time.

24 hours. For example, 2-amino-4,5-dimethoxybenzonitrile afforded a 96 % yield of 6,7-dimethoxyquinazoline-2,4-(1*H*,3*H*)-dione (Table 2, entry 3), which is a key intermediate in the synthesis of Prazosin, IAAP, and Doxazosin.^[8b] The above results indicate that the substituents in the phenyl ring of 2-aminobenzonitriles have little effect on the reactivity with CO₂, and [HDBU⁺][TFE⁻] was highly efficient for catalyzing these reactions.

In addition, the reusability of [HDBU⁺][TFE⁻] was evaluated for the synthesis of quinazoline-2,4-(1*H*,3*H*)-dione

from CO₂ and 2-aminobenzonitrile. It was demonstrated that the product yield almost remained unchanged as the same IL was used for five reactions (Table 2, entry 8), thus suggesting the designed IL maintained its original performance and was recyclable.

To explore the reaction mechanism, the interactions of [HDBU⁺][TFE⁻] with CO₂ and substrate were examined by NMR spectroscopy and IR analysis. The absorption of CO₂ by [HDBU⁺][TFE⁻] was examined by FTIR and NMR analyses. In the ¹³C NMR spectrum, a new signal appeared at δ = 167.7 ppm (Figure 1), which was attributed to the carbonyl

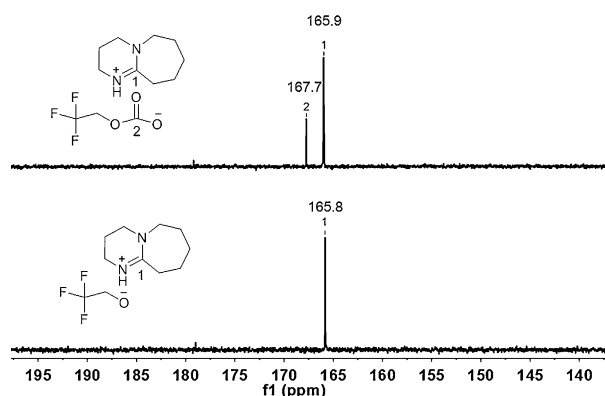


Figure 1. ¹³C NMR spectrum of pure [HDBU⁺][TFE⁻] and the intermediate derived from exposure of [HDBU⁺][TFE⁻] to CO₂ (0.1 MPa; D₂O, 0.6 mL, 298 K).

carbon atom of the carbonate and suggests that CO₂ was activated by the anion [TFE⁻], thus forming a carbonate intermediate. This intermediate in agreement with those previously reported.^[7b] In our previous work we found that [HDBU⁺] could activate CO₂ at 9 MPa and thus had a ¹³C NMR signal at δ = 172.3 ppm,^[4h] however, in this work the absence of this signal implies that at atmospheric pressure [HDBU⁺] could not activate CO₂. In the FTIR spectrum a new band appeared at 1702 cm⁻¹ (see Figure S5 in the Supporting Information), which is assigned to the stretching vibration of the C=O bond of carbonate, thus confirming the formation of carbonate and the ¹³C NMR data. This carbonate may be the key intermediate for the CO₂ conversion.

The ¹H, ¹³C, and ¹⁵N NMR analyses for [HDBU⁺][TFE⁻], 2-aminobenzonitrile, and their mixture were carried out. The ¹H NMR signal of the NH₂ of 2-aminobenzonitrile in the mixture shifted from δ = 5.98 (the shift of NH₂ in pure 2-aminobenzonitrile) to 6.03 ppm, and showed broadening (see Figure S6 in the Supporting Information), thus suggesting the hydrogen bonding between the IL and the substrate. In contrast, all the ¹⁵N NMR signals assigned to the N atoms of the IL and 2-aminobenzonitrile shifted accordingly upon the mixing these two compounds (Figure 2). Specifically, the ¹⁵N NMR signals for NH₂ of 2-aminobenzonitrile and for NH of [HDBU⁺] shifted significantly, thus indicating the hydrogen bonding between [HDBU⁺] and the substrate. Considering that [Et-DBU⁺][TFE⁻] afforded a much lower yield of quinazoline-2,4(1*H*,3*H*)-dione as compared with [HDBU⁺][TFE⁻] (Table 1, entries 2 and 5), it can be deduced that the

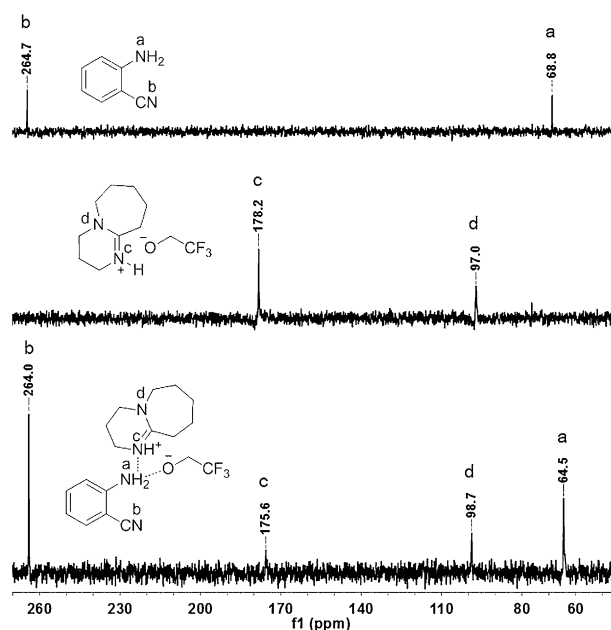
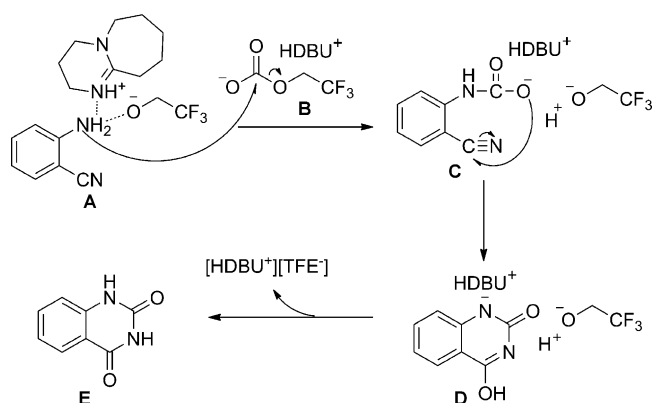


Figure 2. ¹⁵N NMR spectrum of [HDBU⁺][TFE⁻] and 2-aminobenzonitrile, with and without [HDBU⁺][TFE⁻] ([D₆]DMSO, 298 K).

hydrogen bonding between [HDBU⁺] and the substrate was very important for the synthesis of quinazoline-2,4(1*H*,3*H*)-dione from CO₂ reacting with 2-aminobenzonitrile. In addition, the ¹³C NMR signal, assigned to C1 in [TFE⁻], shifted downfield from δ = 58.94 to 58.98 ppm as the IL was mixed with 2-aminobenzonitrile (see Figure S7 in the Supporting Information), further indicating the formation of hydrogen bonding between [TFE⁻] and the substrate. The above results indicated that both the cation and anion of the IL could form hydrogen bonds with the substrate, and could weaken the N–H bond in NH₂ of 2-aminobenzonitrile, thus facilitating the nucleophilic attack of the NH₂ group in 2-aminobenzonitrile on the carbon atom of the activated CO₂. From the above analysis, it can be deduced that the IL can serve as a bifunctional catalyst for simultaneously activating CO₂ and the substrate at atmospheric pressure and room temperature.

On the basis of the experimental results and previous reports,^[5g,9–16] a possible mechanism for the [HDBU⁺][TFE⁻]-catalyzed reaction of CO₂ with 2-aminobenzonitrile to give quinazoline-2,4(1*H*,3*H*)-dione (**E**) is proposed (Scheme 2). In [HDBU⁺][TFE⁻], 2-aminobenzonitrile is activated by hydrogen bonding with both the cation and anion of the IL to form the intermediate **A**, while CO₂ is activated by the anion [TFE⁻] to form the intermediate **B**. The nucleophilic nitrogen atom of **A** attacks the carbon atom of **B** to form the intermediate **C**, with subsequent nucleophilic cyclization of **C** to produced **D**, which is subsequently converted into **E** after regeneration of [HDBU⁺][TFE⁻].

In summary, a bifunctional IL catalyst, [HDBU⁺][TFE⁻], was designed by neutralization of a superbase (DBU) and a weak proton donor (trifluoroethanol), and found to activate CO₂ and 2-aminobenzonitriles simultaneously to produce quinazoline-2,4(1*H*,3*H*)-diones in excellent yields under atmospheric pressure at room temperature. In addition, this



Scheme 2. Possible reaction pathway.

IL could be easily recovered and reused without loss in its activity. We believe that this kind of highly efficient, greener, and stable bifunctional IL catalytic system is promising for chemical fixation of CO₂ and generation of various useful chemicals under mild reaction conditions.

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