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Protic ionic liquids-promoted efficient synthesis of quinazolines from 2-aminobenzonitriles and CO_2 at ambient conditions

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ABSTRACT

Despite recent renaissance of CO_2 chemistry, transformation of CO_2 at ambient conditions remains still of great challenge. In this work, an easily prepared protic ionic liquid *e.g.* 1,1,3,3-tetramethylguanidinium imidazolide [HTMG][Im] was developed as highly efficient, recyclable and bifunctional catalyst for the carboxylative cyclization of 2-aminobenzonitriles with CO_2 at atmospheric pressure and room temperature. The catalytic protocol was found to be applicable to various 2-aminobenzonitriles bearing electron-withdrawing or electron-donating substituents, affording the corresponding quinazoline-2,4(1H,3H)-diones in moderate to excellent yields. In addition, the catalyst could be conveniently recovered and reused for five cycles with almost consistent activity. Consequently, this process represents an alternative approach for the efficient and greener chemical fixation of CO_2 to afford valuable heterocycles.

1. Introduction

Over the past several decades, atmospheric CO_2 concentration has been increasing at an alarming rate primarily due to consumption of fossil fuels for energy requirements. Consequently, as a major contributor to greenhouse effect, CO_2 is closely implicated with negative environmental burdens and energy crisis such as global warming, sea-level-rise and species extinction. On the other hand, CO_2 can also be regarded as a sustainable C_1 resource from the standpoint of synthetic chemistry due to several characteristics such as low cost, nontoxicity, non-flammability, easy accessibility and so on. [1]. Therefore, highly efficient transformations of CO_2 into value-added chemicals such as heterocycles [2], formic acids [3], methanol [4], dimethyl carbonate [5], cyclic carbonate [6], polycarbonates [7], ureas [8], urethanes [9], α,β-unsaturated carbonyl compounds [10], and carbon monoxide [11], which enjoy a wide application in organic synthesis and pharmaceutical discovery, can fulfill the requirements of green chemistry and sustainable development. Nevertheless, despite the great strides we have witnessed in CO_2 transformations, development of highly efficient catalytic systems that promote the reactions involving CO_2 under ambient conditions especially at atmospheric pressure and room temperature is still limited and highly desired due to the inertness of CO_2 [12].

Among multiple heterocyclic compounds from CO_2, quinazoline-2,4(1H,3H)-diones have drawn much attention due to their wide range of biological and pharmacological activities. For instance, a range of commercially accessible antihypertensive agents such as Prazosin (Minipress*R*), Bunazosin (Detantol*R*) and Doxazosin (Cardenalin*R*) have been synthesized with 6,7-dimethoxyquinazoline-2,4(1H,3H)-dione derivative as a building block. As to the synthesis of quinazoline-2,4(1H,3H)-diones, since Mizuno pioneered the carboxylative cyclization of 2-aminobenzonitriles and CO_2 [13], which is a green strategy with 100% atom efficiency, a plethora of basic compounds such as 1,1,3,3-tetramethylguanidine (TMG) [14], Cs_2CO_3 [15], poly(amidine) [16], MgO/ZrO_2 [17], monomeric tungstate [18], 1-butyl-3-methylimidazolium hydroxyl ([BMIm]OH) [19], [BMIm]OAc [20], amine-functionalized MCM-41 [21], mesoporous smectites [22], TBD-functionalized Fe_3O_4 [23], Choline hydroxide [24], NHCs [25] and ionic liquids (ILs) [26] have been explored as efficient catalysts. For example, Han and co-workers found that the cyclization of CO_2 and 2-aminobenzonitriles could proceed efficiently in water without any catalyst [27]. Density functional theory (DFT) calculations revealed that the *in situ* generation of carbonic acid from CO_2 and H_2O is the fundamental step for the reaction [28]. Recently, cooperative catalysis has been emerged as promising strategy in CO_2 transformations. Through simultaneous activation of both 2-aminobenzonitriles and CO_2, $TBA_2[WO_4]$ [18] and easily prepared protic IL [$HDBU^+$][TFE^-] [26] promoted the cyclization under ambient conditions even at atmospheric pressure and room temperature.

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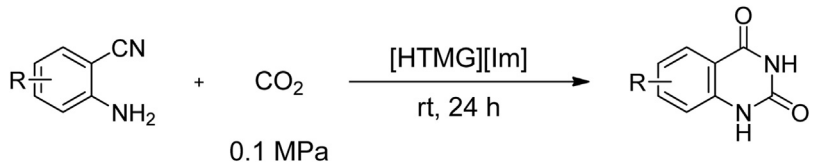
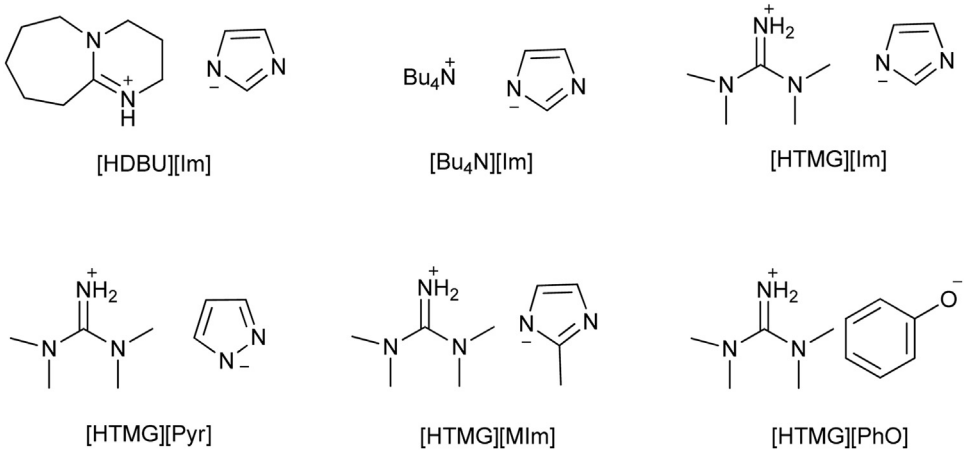


Scheme 1. Cyclization of 2-aminobenzonitriles with CO_2 catalyzed by [HTMG][Im] under mild conditions.



Scheme 2. The PILs prepared in current study.

As a subset of ILs, many remarkable properties of protic ionic liquids (PILs) have been identified and utilized during the past few years [29]. First of all, PILs can be prepared through a facile proton transfer from the acid to the base, leading to the presence of proton-donor and proton-acceptor sites, which allow structure-property correlations to be regulated. Secondly, due to the distinguished properties PILs bearing, their significant chemical potentials have been extended to equimolar CO_2 absorption [30] and ring-closure reactions from CO_2 to form heterocycles such as quinazoline-2,4(1H,3H)-diones [26], 2-oxazolidinones [31] and 2-benzimidazolones [32] under mild reaction conditions. Inspired by the structure-property correlation of PILs, we designed and synthesized a protic ionic liquid [HTMG][Im] via easy neutralization of TMG and imidazole, whose catalytic property was tested for the cyclization of 2-aminobenzonitrile and CO_2 (Scheme 1). The experimental results showed that [HTMG][Im] rendered a smooth-performing reaction between various 2-aminobenzonitriles with electron-withdrawing groups or electron-donating groups and CO_2 at room temperature and atmospheric pressure. Besides, ease of recovery and being reused for five consecutive cycles without any appreciable deactivation are additional eco-friendly attributes of this catalytic system. To shed light on the reaction mechanism, NMR, *in-situ* FT-IR spectroscopy and detailed DFT study were also performed.

2. Experimental

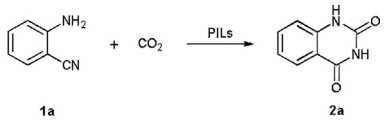
2.1. Materials and methods

All starting materials were obtained from TCI, Aladdin or Alfa Aesar Company and used as received. ^{1}H NMR spectra were recorded on Bruker 400 MHz spectrometer using $CDCl_3$ or DMSO-d_6 as solvent referenced to $CDCl_3$ (7.26 ppm) or DMSO-d_6 (2.50 ppm). ^{13}C NMR spectra were recorded at 100.6 MHz in $CDCl_3$ (or DMSO-d_6) using $CDCl_3$ (77.0 ppm) (or DMSO-d_6, 39.5 ppm) as an internal reference. Infrared (IR) spectra were recorded on a Bruker Tensor 27 FT-IR spectrophotometer with KBr pellets. All the products were characterized by ^{1}H, ^{13}C NMR and FT-IR analysis here and were identified by comparison of their characterized data with those reported in the literature.

2.2. Preparation and characterization of the protic ionic liquids

[HTMG][Im] was synthesized according to the reported procedures [26,28–30]. In a typical process, equimolar imidazole (20 mmol, 1.36 g) was added to the 1,1,3,3-tetramethylguanidine (20 mmol, 2.30 g) solution in ethanol. The mixture was stirred at 25 °C for 24 h. After reaction, ethanol and water were removed under reduced pressure. The product thus obtained in quantitative yield was then dried in vacuum for 24 h at 80 °C. Other PILs were

Table 1
Catalyst screening and condition optimization[a].



Entry	ILs	T (°C)	Yield[b] (%)
1	–	120	0
2	[HTMG][Im]	120	96
3	[HDBU][Im]	120	84
4	[Bu_4N][Im]	120	26
5	[HTMG][Pyr]	120	64
6	[HTMG][PhO]	120	0
7	[HTMG][MIm]	120	92
8	[HTMG][Im]	90	96
9	[HTMG][Im]	60	94
10	[HTMG][Im]	25	90

[a] Reaction conditions: 2-aminobenzonitrile (0.5 mmol, 0.0591 g), CO_2 (0.1 MPa), 24 h, IL amount (4 equiv.).
[b] Isolated yield.