Organocatalysis

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N-Heterocyclic Carbenes as Efficient Organocatalysts for CO_2 Fixation Reactions**

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During the last decade, N-heterocyclic carbenes (NHCs) have attracted attention because of the intensive development of general synthetic methods and wide applications in the field of molecular catalysis.[1] The unique properties of the unsaturated NHC carbon atom, stabilized by the electron-donating heteroatoms on either side, are highlighted by their utilization as versatile ligands for transition metals[2] and organocatalysts[3] as they exhibit strong basicity. Most NHC-mediated organocatalysis includes the formation of covalent, active intermediates by their addition to C=O bonds as the key step, leading to nucleophilic incorporation of the carbonyl functional group. Such an apparent σ-donor character of NHCs has also been applied to CO_2 capture, and the resulting imidazolium-2-carboxylates are identified as the typical NHC–CO_2 adducts (Figure 1).[4] Whereas the reverse reaction has been proven to be decisive for delivering a number of NHC complexes,[5] in principle, the zwitterionic CO_2 adduct could be utilized as a convenient CO_2 carrier to accomplish CO_2 fixation through the nucleophilic incorporation of the O=C=O unit as proposed for various Lewis base catalyst systems.[6]

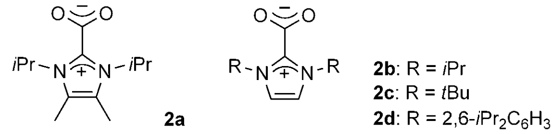
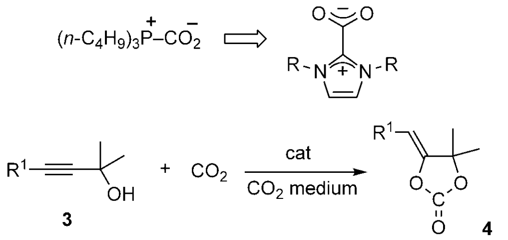


Figure 1. Imidazolium-2-carboxylates as NHC–CO_2 adducts.

During our studies on CO_2 fixation to produce highly valuable chemicals, we reported the carboxylative cyclization of propargylic alcohols catalyzed by nBu$_3$P in supercritical CO_2.[7,8] Although the role of the tertiary phosphane catalyst has not been fully understood, we proposed a reaction mechanism involving a putative zwitterionic phosphane–CO_2 adduct which promotes nucleophilic addition of the CO_2 fragment to the unsaturated alcoholic substrate. The fact that NHCs exhibit similar chemical properties to those of tertiary phosphanes, prompted us to investigate new CO_2 transformation catalyst systems using NHCs. We have reported some preliminary results in a patent application,[9a] and herein we report that NHCs (1,3-dialkylimidazol-2-ylidene; **1**) and the corresponding CO_2 adducts (1,3-dialkylimidazolium-2-carboxylates; **2**) act as effective catalysts for carbonate synthesis using CO_2 under relatively mild reaction conditions as shown in Scheme 1.[9b]



Scheme 1. Carboxylative cyclization of propargylic alcohol with CO_2.

We first examined the carboxylative cyclization of 2-methyl-3-propyn-2-ol (**3a**, $R^1 = H$; 5.0 mmol) with a catalytic amount (5.0 mol%) of a parent carbene, 1,3-diisopropyl-4,5-dimethylimidazol-2-ylidene (**1a**), under identical reaction conditions to those used for the nBu$_3$P-catalyzed reaction in supercritical CO_2 (Table 1). When the reaction was carried out at 100°C and 10.0 MPa for 15 hours, a five-membered cyclic carbonate, 5-methylene-4,4-dimethyl-1,3-dioxolan-2-one (**4a**), was obtained in 80% yield (Table 1, entry 1). The corresponding NHC–CO_2 adduct **2a** also showed comparable

Table 1: Carboxylative cyclization of **3a** and CO_2 (see Scheme 1 for reaction, $R^1 = H$). [a]

Entry	Catalyst	P [MPa]	T [°C]	Yield [%][b]
1	**1a**	10.0	100	80
2	**2a**	10.0	100	85
3	nBu$_3$P	10.0	100	99
4	**2a**	4.5	100	88
5	**2a**	2.5	100	62
6	**2a**	4.5	60	90
7	**2a**	4.5	40	82
8	**2b**	4.5	60	90
9	**2c**	4.5	60	99
10	**2d**	4.5	60	5

[a] Reaction conditions: The reaction was carried out in a 50 mL stainless-steel reactor containing **3a** (5.0 mmol) and the catalyst (0.25 mmol) for 15 h. [b] Determined by ^1H NMR methods, using durene as an internal standard.

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catalytic activity (Table 1, entry 2), implying that imidazolium-2-carboxylates can be employed as NHC equivalents. Although the preceding $n\mathrm{Bu}_3\mathrm{P}$ catalyst afforded a satisfactory result (Table 1, entry 3) under the supercritical conditions, **2a** was found to be operative in a neat, homogeneous phase at 4.5 MPa CO_2 and 40 °C (Table 1, entries 4–7). In contrast, a sharp drop in the yield of **4a** was observed for the $n\mathrm{Bu}_3\mathrm{P}$ system as the reaction temperature fell below 80 °C (Figure 2). The advantageous catalytic results obtained with **2a** can be attributed to its superior nucleophilic properties. In fact, the presence of the $n\mathrm{Bu}_3\mathrm{P}$–CO_2 adduct derived from $n\mathrm{Bu}_3\mathrm{P}$ and supercritical CO_2 (35 °C, 10.0–20.0 MPa) was not confirmed by high-pressure NMR experiments.[10] In contrast to the reaction with $n\mathrm{Bu}_3\mathrm{P}$, the facile formation of the NHC–CO_2 adducts occurred under mild reaction conditions.

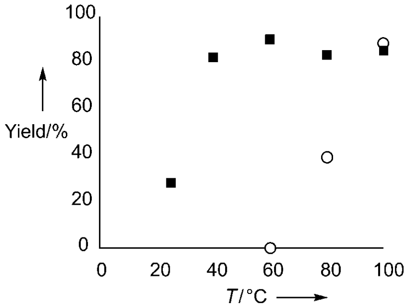
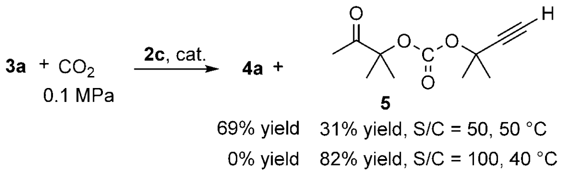


Figure 2. Reaction temperature dependence of the yield of **4a** for the catalyst system of $n\mathrm{Bu}_3\mathrm{P}$ (○; 10.0 MPa) and **2a** (■; 4.5 MPa). Reaction conditions: **3a** (5.0 mmol) and catalyst (0.25 mmol) for 15 h.

Screening tests, using a series of the NHC–CO_2 adducts **2** under the solvent-free reaction conditions at 4.5 MPa CO_2 and 60 °C, revealed that substituents on the nitrogen atoms of the NHC framework delicately influence the catalyst activity. The reproducible results obtained using 1,3-diisopropylimidazolium-2-carboxylate (**2b**) and **2a** suggests that a substitutent at the 4- and 5-positions of imidazolium ring do not affect the outcome of the reaction (Table 1, entries 6 and 8). The best yield of 99 % for the product was attained using 1,3-di-*tert*-butylimidazolium-2-carboxylate (**2c**), whereas the diaryl-substituted NHC–CO_2 adduct **2d** gave unsatisfactory results (Table 1, entries 9 and 10). Secondary and primary alcohols, as well as a homopropargylic alcohol, 2-methyl-4-pentyn-2-ol, were not transformed even in the presence of the catalyst **2c**; this lack of reactivity is in line with the trends observed for the $n\mathrm{Bu}_3\mathrm{P}$ system.[7]

When the reaction of **3a** with **2c** was performed with a lower catalyst loading of 2 mol % under CO_2 at atmospheric pressure and 50 °C, an acyclic carbonate, 1,1-dimethyl-2-oxopropyl 1′,1′-dimethyl-2′-propynyl carbonate (**5**), was obtained in 31 % yield in addition to a 69 % yield of **4a** (Scheme 2). An additional decrease in the catalyst loading to 1 mol % and using a reaction temperature of 40 °C gave rise to **5** in 82 % yield (**4a**: 0 % yield). The carboxylative cyclization affording **4a** and the subsequent addition of **3a** to **4a** probably leads to **5** as a 2:1 coupling product of the propargyl alcohol and CO_2.[8b,11] The NHC derived from **2c** might promote the ring-opening transesterification[12] of **4a** in preference to the capture of CO_2 under moderate conditions.



Scheme 2. Carboxylation of **3a** under CO_2 atmosphere using **2c** with substrate/catalyst ratios (S/C) of 50 and 100 at temperatures of 50 and 40 °C, respectively.

The isolable NHC–CO_2 catalyst **2c** provides access to a variety of five-membered cyclic carbonates (**4b–j**) from substrates having internal alkynes (**3b–j**). As summarized in Table 2, **2c** exhibited better catalyst performance than the tertiary phosphane. The presence of electron-withdrawing groups conjugated to the triple bond led to a reduction in the reaction time or the reaction temperature (Table 2, entries 1–3). Notably, unlike the $n\mathrm{Bu}_3\mathrm{P}$ catalyst, **2c** is applicable to the reaction of **3g**, which has a *para*-methoxyphenyl group (Table 2, entry 6). The NHC catalyst also tolerates substrates bearing heterocycles such as pyridine and thiophene (Table 2, entries 7 and 8). The substrate **3j** having an olefinic group at the acetylenic terminus also provided the desired 5-*exo*-dig cyclization product **4j** in 84 % yield (Table 2, entry 9), whereas no carbonates were formed from allylic compounds including 2-methyl-3-buten-2-ol and 2-methyl-4-phenyl-3-buten-2-ol. In each product, the C=C double bond was found to have a *Z* configuration, as determined by NMR spectroscopy, indicating that the addition to the alkynes proceeded predominantly in a trans fashion, similar to the previous carboxylative cyclization.[7,13]

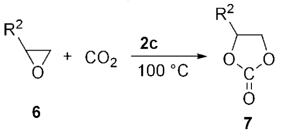
Table 2: Synthesis of *Z*-4-alkylidene-1,3-dioxolan-2-ones, **4**.[a]

Entry	R^1	T [°C]	t [h]	Yield [%][b,c]
1	p-$\mathrm{NO_2C_6H_4}$ (**3b**)	60	5	84 (77)
2	p-$\mathrm{CH_3COC_6H_4}$ (**3c**)	60	5	91 (82)
3	p-$\mathrm{ClC_6H_4}$ (**3d**)	60	15	86 (80)
4	$\mathrm{C_6H_5}$ (**3e**)	80	15	84 (88)[d]
5	p-$\mathrm{CH_3C_6H_4}$ (**3f**)	80	15	95 (62)
6	p-$\mathrm{CH_3OC_6H_4}$ (**3g**)	60	15	51[d] (0)
7	2-pyridyl (**3h**)	60	15	77 (64)
8	3-thienyl (**3i**)	60	45	94
9	*trans*-$\mathrm{C_6H_5CH{=}CH}$ (**3j**)	60	45	84

[a] Reaction conditions: The reaction was carried out with **3** (5.0 mmol) and **2c** (0.25 mmol) under CO_2 (4.5 MPa). [b] Yield of isolated product. [c] Yields in parentheses were obtained from the $n\mathrm{Bu}_3\mathrm{P}$ (5mol %) catalyst system with CO_2 (10 MPa), at 100 °C for 15 h. [d] Determined by ^{1}H NMR methods, using durene as an internal standard.

We also examined another carbonate synthesis involving epoxides **6** and CO_2 with a NHC (Table 3).[14,15] By using the catalyst **2c** (5.0 mol %), styrene oxide was successfully converted into the corresponding carbonate within 24 hours under CO_2 (4.5 MPa) at 100 °C without using a solvent (Table 3, entry 1). The product was isolated in 89 % yield and with almost complete selectivity. The cycloaddition of CO_2 to

Table 3: Cycloaddition of CO_2 to epoxides **6**.[a]

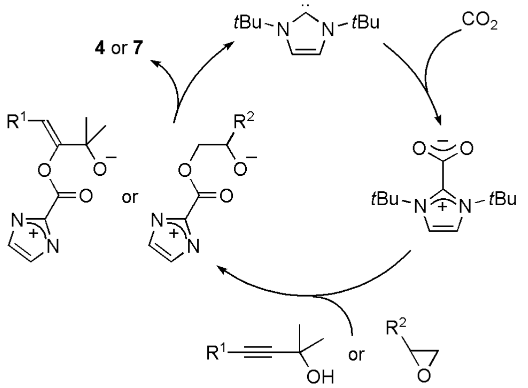


Entry	R^2	P [MPa]	t [h]	Yield [%][b,c]
1	C_6H_5 (**6a**)	4.5	24	89 (98)
2	$C_6H_5OCH_2$ (**6b**)	2.5	15	81
3	$ClCH_2$, (**6c**)	2.5	18	87
4	n-C_4H_9 (**6d**)	2.5	40	71

[a] Reaction conditions: The reaction was carried out with **6** (1.5 mmol) and **2c** (7.5×10^{-2} mmol) at 100 °C. [b] Yield of isolated product. [c] Yields in parentheses were determined by ^{1}H NMR methods, using durene as an internal standard.

other epoxides, including 2-(phenoxymethyl)oxirane, epichlorohydrin, and 2-butyloxirane, also proceeded at 2.5 MPa CO_2 to afford the desired carbonates **7** in yields ranging from 71 to 87 % (Table 3, entries 2–4). Very recently, Lu and coworkers reported the coupling of epoxides with CO_2 catalyzed by 1,3-diarylimidazolium-2-carboxylates at a higher reaction temperature of 120 °C.[4g]

The cyclic carbonate formations from either **3** or **6** using the NHC–CO_2 adduct can be explained by a mechanism involving the nucleophilic addition of the imidazolium-2-carboxylate to either the C$\equiv$C bond or the strained epoxide ring and subsequent intramolecular cyclization of alkoxide intermediates (Scheme 3). The significant positive effect of the electron-donating alkyl substituents on the NHC nitrogen atoms implies that the nucleophilic attack of the CO_2 moiety, bound to the NHC, onto the substrates is a possible rate-limiting step in the catalytic cycle.



Scheme 3. Plausible mechanism of the carboxylation catalyzed by the NHC–CO_2 adduct.

In summary, we have demonstrated that NHCs and NHC–CO_2 adducts serve as potent organocatalysts providing straightforward methods for solvent-free carbonate synthesis, and pave the way to utilizing CO_2 as a nucleophilic fragment in CO_2 fixation. In particular, the use of N,N′-dialkyl-substituted NHC derivatives has a significant advantage for the carboxylative cyclization relative to the earlier reported tertiary phosphane catalyst system because of their strong nucleophilic nature.

Experimental Section

General procedure for the carboxylative cyclization of **3**: A 50 mL stainless-steel autoclave equipped with a magnetic stirring bar was charged with argon gas in a desiccator. Catalyst **2a** (55 mg, 0.25 mmol), contained in the reactor, was purged with argon gas to remove oxygen. **3a** (0.5 mL, 5.0 mmol) was introduced into the autoclave with a syringe while the vessel was purged with argon. The vessel was charged with CO_2 (4.5 MPa) through a cooling apparatus with an HPLC pump. After stirring for 15 h at 40 °C, the reaction was stopped by cooling the autoclave in an ice bath. CO_2 was vented and the autoclave was slowly warmed to room temperature. The reaction mixture was analyzed by ^{1}H NMR spectroscopy using durene as an internal standard. The crude reaction mixture was purified by column chromatography on silica gel (n-hexane/ethyl acetate = 5:1) and then the isolated product was subjected to Kugelrohr distillation (80–85 °C, 18 mm Hg) to yield **4a** (526 mg, 82 %).

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