ORIGINAL PAPER

(Thio)urea containing quaternary ammonium salts for the CO_2-fixation with epoxides

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Abstract

A detailed screening of differently substituted chiral and achiral (thio)urea-containing quaternary ammonium salts revealed their potential as catalysts for the CO_2-fixation with epoxides to obtain cyclic carbonates in high yields under operationally simple atmospheric pressure conditions. Additional DFT calculations substantiate a mechanism involving an initial addition of the nucleophilic iodide counter anion of the ammonium salt to the H-bonding activated epoxide, followed by stepwise CO_2-fixation and cyclization.

Graphical abstract
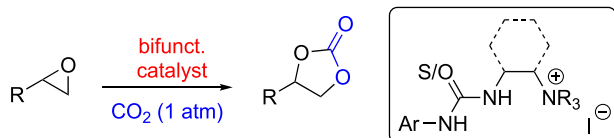
Introduction

Reactions of CO_2 with epoxides to form either cyclic carbonates, or polycarbonates are transformations that have attracted much interest over the last years [1–11]. A broad variety of different catalysts has been used to facilitate these reactions and especially metal complexes (usually in combination with nucleophilic additives) have been very carefully studied for the formation of cyclic carbonates **2** by CO_2

insertion into epoxides **1** [9, 10]. Besides that, also metal-free approaches, mostly using ionic liquids [11, 12] or small molecule organocatalysts [6], were systematically tested for this transformation. Among the used organocatalysts, especially dual catalyst systems or bifunctional organocatalysts consisting of a nucleophilic motive and an acidic functionality (that is supposed to activate the epoxide opening by the nucleophilic group leading to an alkoxide which then reacts with CO_2) have shown high potential for these reactions under mild atmospheric pressure conditions [13–25]. Our group has a fundamental interest in bifunctional ammonium salt catalysis (i.e., for asymmetric catalysis [26–28]), and we have recently also carried out CO_2-fixation reactions with epoxides in the presence of quaternary ammonium salt catalysts [22, 29, 30]. Based on a recent collaborative study with the Kass group wherein we demonstrated the potential of charge-containing thioureas for the CO_2-fixation with epoxides **1** under mild conditions [22], we have now carried out detailed experimental and theoretical investigations on the general use of urea- and thiourea containing chiral

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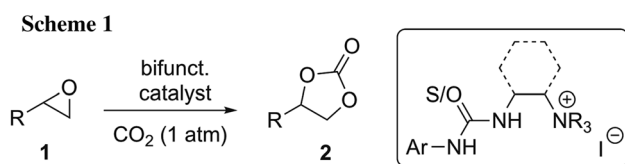
Scheme 1

and achiral quaternary ammonium salts as catalysts for this CO_2-fixation reaction (Scheme 1).

Results and discussion

Catalyst identification, optimization of reaction conditions, and application scope

It has been well documented in the past that simple achiral ammonium halides can be used to facilitate the CO_2-fixation with epoxides **1** [31–33], but it was also clearly shown that Lewis and/or Bronsted acids do significantly improve the reaction's performance (see Refs. [23, 29] for two examples). We thus decided to first carry out a systematic screening of the CO_2-fixation potential of all the differently functionalized catalysts shown in Fig. 1. As a test reaction, we hereby chose the reaction of neat styrene oxide (**1a**) in the presence of 1 mol% of catalyst at 60 °C under an atmospheric pressure of CO_2 (balloon) for 6 h (unless otherwise stated).

First control experiments with tetraethylammonium iodide (**A**) and thiourea **B** showed that only the synergistic combination of both motives allows for notable conversion after 6 h reaction time, substantiating the need for two complementary modes of activation. Switching to our chiral cyclohexanediamine-based systems **C** next [27], we immediately realized that both functional groups, the (thio)urea and the quaternary ammonium iodide are crucial to reach reliable conversions. While the urea **C1**, which is missing in the ammonium group, did not give any product at all, the quaternary ammonium salt **C2** without a urea moiety performed better, but not as good as the hybrid catalyst **C3**. The importance of a nucleophilic counter anion, i.e., iodide, was clearly demonstrated when using the analogous trifluoroacetate-containing **C4**, which did not lead to any formation of the product at all. When changing the ammonium group from trimethylamine (**C3**) to benzyldimethylamine (**C5**) the reactions became slightly faster under standard conditions (29% conv. instead of 26%) and nearly complete conversion to the carbonate **2a** could be reached by either prolonging the reaction time at 60 °C, or by raising the temperature to 120 °C. Noteworthy, the beneficial nature of both NH-groups of the urea moiety was demonstrated when testing the mono-methylated **C6** instead. Changing from ureas to thioureas, next, another slight improvement in conversion could be achieved, especially when increasing the acidity of the thiourea by incorporation of electron-poor aryl groups (see catalyst **C8**). However, also in this case longer

Fig. 1 Initial catalyst screening for the CO_2-fixation with epoxide **1a** (values in brackets give the conversion of **1** to **2**)
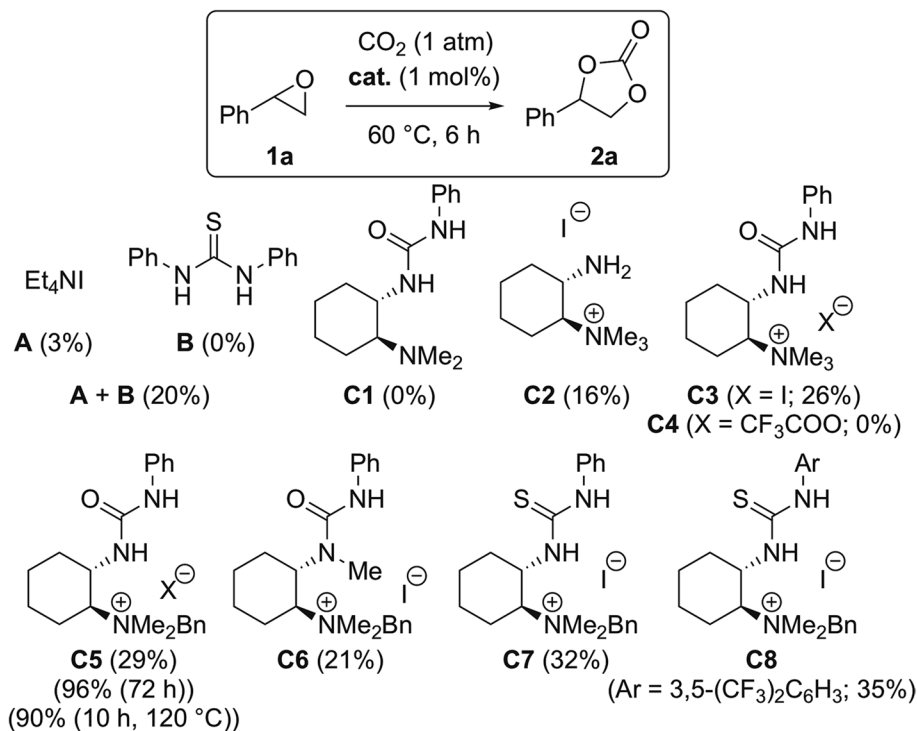
reaction times or higher temperatures were necessary to reach complete conversion.

As the bifunctional ammonium salt catalysts **C** have recently demonstrated their potential for asymmetric transformations of three-membered ring heterocycles (i.e., for the kinetic resolution of oxaziridines [26]), we were interested to see if we can also achieve a kinetic resolution in the CO_2-fixation of epoxides **1** (for selected recent examples by others see Refs. [16, 34–36]). We tested several epoxides **1** with different chiral catalysts **C**, but unfortunately in neither case any enantiomeric enrichment of the recovered starting epoxide **1** or the formed carbonate **2** could be achieved.

Because of this disappointing result we then decided to move away from the chiral catalysts and investigated analogous simple achiral bifunctional thioureas **D** next (for a previous report by others describing the synthesis of an analogous system see Ref. [37]). It should be clearly pointed out that some of the early results obtained with catalysts **D1** and **D2** were already reported in a recent collaborative publication with the Kass group [22], but they will briefly be mentioned here as well together with the new results to provide a comprehensive overview and to illustrate our motivation to carry out the detailed computational studies reported in the second part of this article. The ammonium salts **D** were easily accessible from the simple commercially available diamine **3** on gram-scale (Fig. 2). In general, the introduction of different ureas and thioureas, as well as different ammonium substituents is possible by this synthesis strategy. Given the observed higher activity of chiral electron-poor thioureas **C** (see Fig. 1), we hereby primarily

focused on the achiral thiourea-containing salts **D1** and **D2**. Both of them gave around 30% conversion at 60 °C after 6 h reaction time and it was shown that either increasing the reaction temperature to 120 °C and/or prolonging the reaction time allowed for quantitative conversion of epoxide **1a** to carbonate **2a** even with only 0.5 mol% of catalyst (with isolated yields higher than 90% after a short filtration over a plug of silica gel to remove the catalyst). It should be noted that we also tested the catalyst scaffold **D1** with different benzyl substituents of the ammonium cation as well, but no significant difference in catalytic activity could be observed.

Very interestingly, we could show that the direct use of a mixture of the thiourea-containing amine **5** and benzyl bromide (**6**) allowed for the in situ generation of the active catalyst **D1** (with bromide as the counter anion) under the CO_2 fixation conditions, which gave reasonable (but lower) conversions as well (for a related recent report on CO_2 fixation with an in situ prepared onium salt catalyst see Ref. [38]).

With the catalytic potential of the simple achiral bifunctional ammonium salts **D1** and **D2** clearly proven, we next investigated the application scope for the atmospheric pressure CO_2 fixation with different epoxides to access the carbonates **2a**–**2i** (Fig. 3). All reactions were carried out under solvent-free conditions with 1 mol% of the catalyst by simply using a balloon of CO_2. Catalyst **D1** turned out to be more reliable at 60 °C (96% conversion after 24 h) while catalyst **D2** usually gave complete conversion within 4–8 h at 120 °C (which may be attributed to the better solubility of this compound at higher temperatures compared to **D1**).

Fig. 2 Syntheses of achiral catalysts **D** and screening for their CO₂-fixation potential
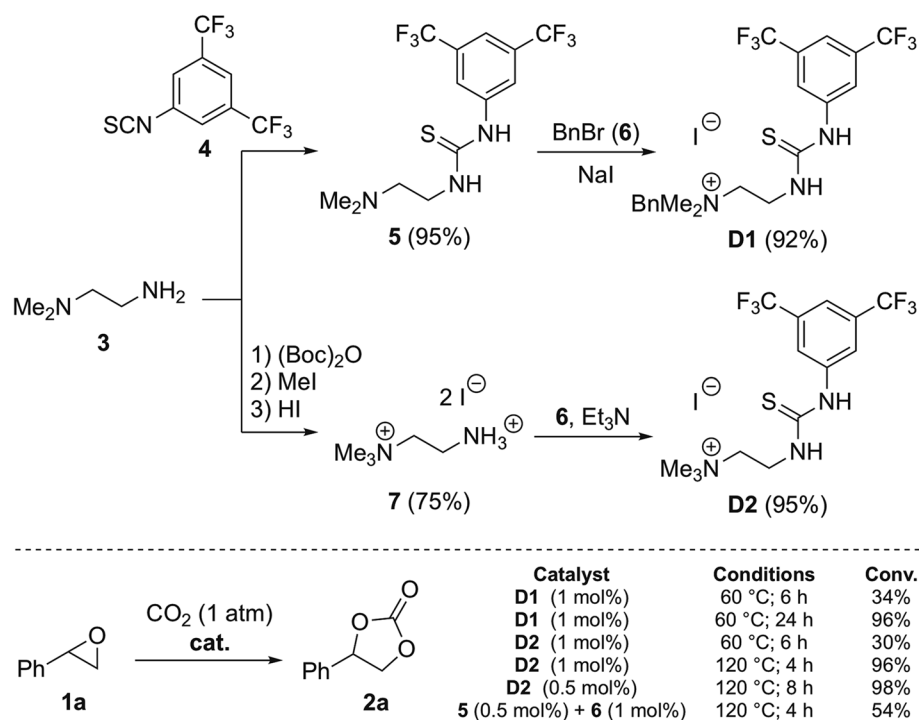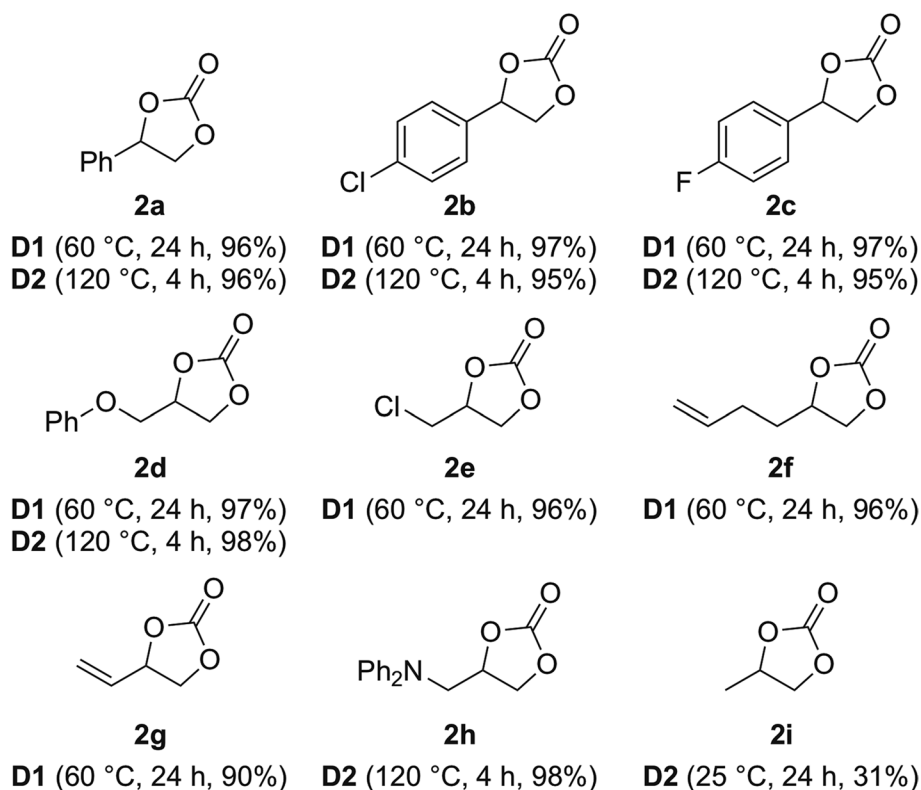
Catalyst	Conditions	Conv.
D1 (1 mol%)	60 °C; 6 h	34%
D1 (1 mol%)	60 °C; 24 h	96%
D2 (1 mol%)	60 °C; 6 h	30%
D2 (1 mol%)	120 °C; 4 h	96%
D2 (0.5 mol%)	120 °C; 8 h	98%
5 (0.5 mol%) + **6** (1 mol%)	120 °C; 4 h	54%

2a
D1 (60 °C, 24 h, 96%)
D2 (120 °C, 4 h, 96%)

2b
D1 (60 °C, 24 h, 97%)
D2 (120 °C, 4 h, 95%)

2c
D1 (60 °C, 24 h, 97%)
D2 (120 °C, 4 h, 95%)

2d
D1 (60 °C, 24 h, 97%)
D2 (120 °C, 4 h, 98%)

2e
D1 (60 °C, 24 h, 96%)

2f
D1 (60 °C, 24 h, 96%)

2g
D1 (60 °C, 24 h, 90%)

2h
D2 (120 °C, 4 h, 98%)

2i
D2 (25 °C, 24 h, 31%)

As can be seen in Fig. 3, a variety of different aromatic and aliphatic terminal epoxides were tolerated very well (internal epoxides did unfortunately not react, which is in analogy to our recent observations with other onium salt-based systems [22]).

Mechanistic investigations

To obtain a better mechanistic understanding of this CO_2-fixation reaction (for three illustrative mechanistic studies of these reactions by others please see Ref. [39–41]), we carried out detailed computational studies of different possible mechanistic scenarios using DFT calculations (Fig. 4). In our previous contribution, we have already reported some of our preliminary results and observations of these mechanistic investigations [22]. Hereby kinetic isotope effects provided evidence that the reaction proceeds via opening of the H-bonding activated epoxide **Int-1** on the less-substituted carbon [22]. This ring opening can either occur via addition of the iodide to the activated epoxide (pathway A, **Int-2**) or via addition of the sulfur of the thiourea motive (pathway B, **Int-3**). Interestingly, **Int-3′** (which is obtained from **Int-3** by a barrierless proton transfer) is energetically significantly more stable than **Int-2**, **Int-2′** (after an almost barrierless proton transfer), or **Int-2″** (obtained after C–N bond rotation). In addition, **Int-3′** could be isolated after stirring the

catalyst **D2** with epoxide **1a** and also resubmitted to the reaction with CO_2 still providing the carbonate **2a** [22]. However, our first computations also suggested that pathway A (iodide attack) is kinetically favored over pathway B (compare TS1 and TS 2 in Fig. 4) and we were thus wondering if we can obtain further insights by investigating the different mechanistic scenarios shown in Fig. 4 by DFT calculations. It turned out that **Int-2′** can either undergo an intramolecular iodine replacement towards **Int-3′** (proceeding via the bond-rotated **Int-2″**), or it can directly add to CO_2 resulting in **Int-5**. This later pathway (TS 4) is kinetically clearly favored compared to the formation of the S-alkylated intermediate **Int-3′** (proceeding via TS6, **Int-2″** and TS7). In addition, also the final cyclization step from **Int-5** to the product **2a** is of lower barrier than the cyclization proceeding via **Int-4** (compare TS 9 and TS 5).

Accordingly, our calculations substantiate a mechanistic scenario that proceeds predominantly via pathway A (Fig. 4), while the experiment also observed **Int-3′** seems to play a minor contribution to the overall reaction only.

Conclusion

(Thio)urea-containing quaternary ammonium salts **C** and **D** revealed their potential for the CO_2-fixation with simple terminal epoxides **1** to obtain the corresponding carbonates **2**

Fig. 4 Calculated pathways for the CO$_2$-insertion into epoxide **1a** in the presence of the bifunctional catalyst **D2**
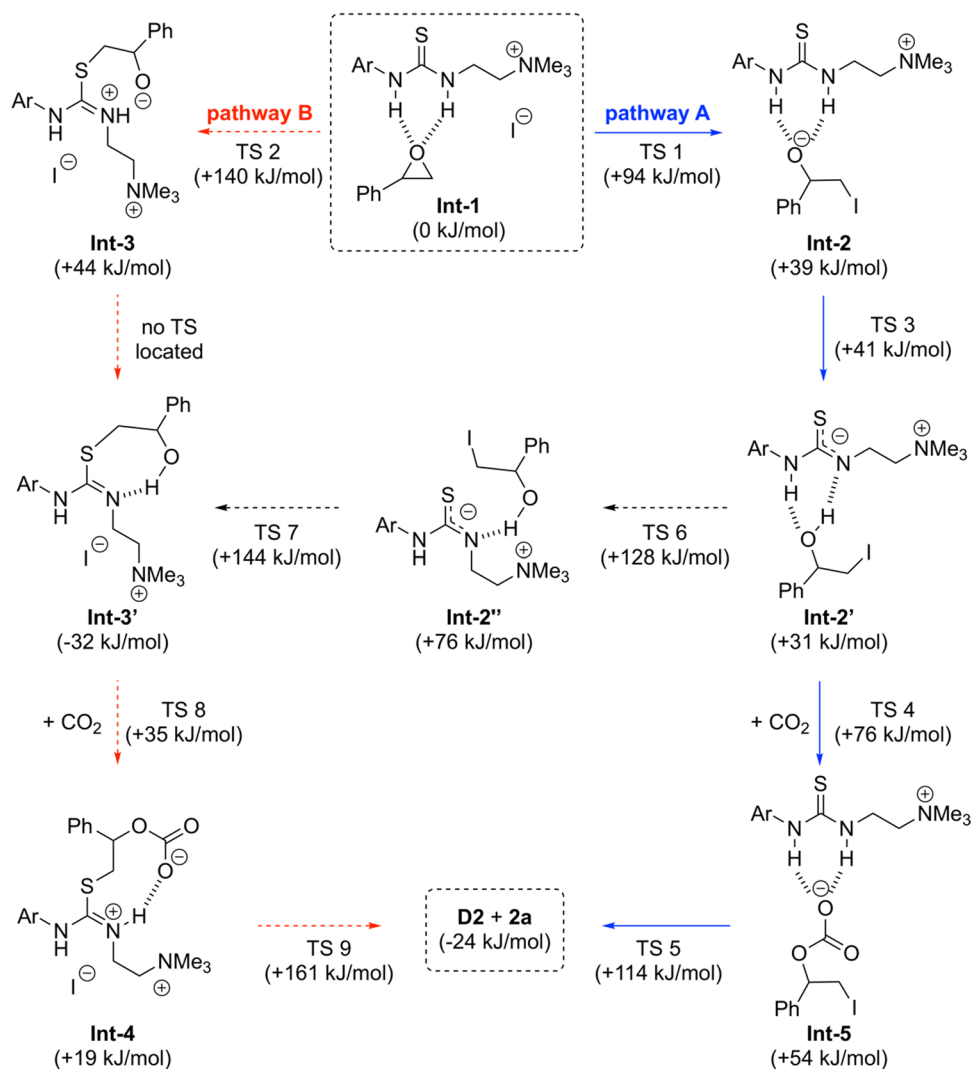
in high yields under operationally simple atmospheric pressure conditions. Detailed DFT calculations substantiate a mechanism involving an initial addition of the nucleophilic iodide counter anion of the ammonium salt to the H-bonding activated epoxide, followed by stepwise CO$_2$-fixation and cyclization.

Experimental

^{1}H and ^{13}C NMR spectra were recorded on a Bruker Avance III 300 MHz spectrometer and on a Bruker Avance III 700 MHz spectrometer with TCI cryoprobe. All NMR spectra were referenced on the solvent peak. High resolution mass spectra were obtained using a Thermo Fisher Scientific LTQ Orbitrap XL with an Ion Max API Source. The catalysts **C** and **D** were synthesized as described recently starting from commercially available cyclohexane diamine [22, 28]. All epoxides **1** were purchased from commercial

suppliers and the carbonates **2** are all known in literature and their NMR spectra fully matched those reported previously [16, 17, 22].

General CO$_2$-fixation procedure

A mixture of the epoxide **1** (4 mmol) and the hybrid catalyst **D** (0.04 mmol) was stirred at 1000 rpm at either 60 or 120 °C under one atmosphere of CO$_2$ (provided by using a balloon) for the time indicated in Fig. 3. After cooling to room temperature, the crude mixture was directly flushed through a short column of silica gel (heptanes/EtOAc = 10:1–3:1 as eluent) to afford the cyclic carbonates in the reported yields, fully matching the analytical data previously reported [16, 17, 22].

Computational methods

Calculations were performed using Gaussian 09 [42]: geometry optimisations were performed at the B3LYP/6–31G(d) level of theory using LANL2DZ for iodine and including an implicit description of styrene oxide as solvent by the polarized continuum model, as well as empirical dispersion as incorporated in Gaussian 09. The correct nature of the found transition states was checked by frequency calculations using the same method and basis set as the geometry optimisations. Then, the structures were reoptimised using B3LYP/6–31G(d,p)/LANL2DZ again including an implicit solvent description as well as dispersion. Gibbs free energies were obtained by vibrational frequency calculations using B3LYP/6–31+G(d,p)/LANL2DZ.

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