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Pushing the Limits with Squaramide-Based Organocatalysts in Cyclic Carbonate Synthesis

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ABSTRACT: Squaramides are presented as modular, easy to optimize and effective catalysts for the conversion of epoxides and carbon dioxide into cyclic organic carbonates (COCs). The catalytic potential of these squaramides, in combination with a suitable halide nucleophile, is particularly noted when internal epoxides are examined as substrates and their transformation into disubstituted COCs marks a rare case of an effective organocatalyst for these challenging conversions. Control experiments support the mechanistic view that the squaramides are predominantly involved in the stabilization of intermediate oxo- and carbonato-anions which, after their formation, are able to displace a bromide nucleophile from an initially formed 1:1 assembly comprising the squaramide host.

Keywords: *carbon dioxide, cyclic carbonates, homogenous catalysis, organocatalysis*, *squaramides*

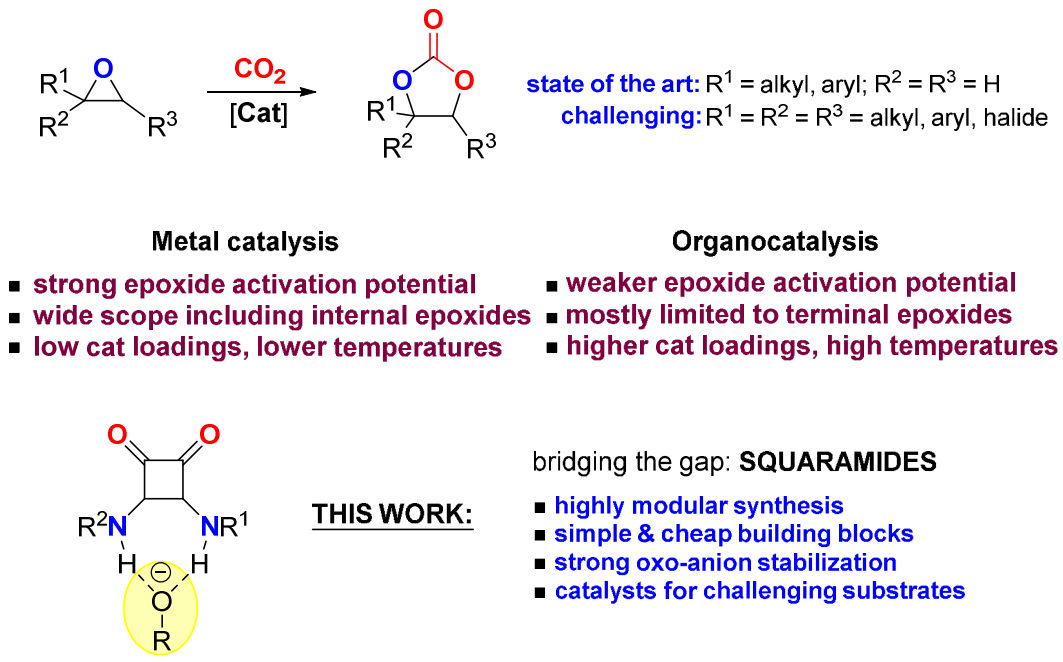
■ INTRODUCTION

Small molecule activation,[1] and particularly carbon dioxide (CO_2) conversion, continues to challenge the synthetic communities to devise more efficient and sustainable catalysis protocols. CO_2 is a renewable carbon feed stock that has shown potential to provide an alternative for some fossil fuel based chemical synthesis,[2] though generally there still exists a requirement for new catalyst development to expand on the portfolio of organic compounds that are derived from this waste molecule.[3] Despite the high kinetic stability, catalysis has manifested itself as the primary technology for the conversion and fixation of CO_2. Among the most widely studied reactions that utilize CO_2 as a substrate are those that lead to either cyclic[4] or poly-carbonates,[5] using cyclic ethers as reaction partners. Both categories of these organic carbonates have attracted interest from academic and industrial communities, and various commercial processes have now been developed.[6]

The synthesis of cyclic organic carbonates (COCs) has witnessed a spectacular progress over the last decade with the field being clearly dominated by metal-catalyzed approaches.[7] Indeed, homogeneous metal catalysis has demonstrated to solve a series of important challenges in the area including the use more challenging cyclic ether substrates such as internal di-[8] and trisubstituted epoxides,[9] and oxetanes.[10] Recently, metal-free approaches have been presented as sustainable alternatives for metal-catalyzed formation of COCs.[11] Intrinsically, organocatalytic activation of the cyclic ether substrates is less powerful compared to metal-based conversions: as a result, poorer overall kinetics and substrate scope are typically observed requiring thus significantly higher catalyst loading and/or reaction temperatures. Among the substrate activation strategies, hydrogen-bonding (HB) has been prevalent and has delivered a simple

though effective means towards organocatalytic formation of COCs from CO_2 and mostly terminal epoxides.[12] However, in order to uplift the potential of organocatalysis, new strategies are warranted in order to be more competitive to metal catalyzed COC synthesis. Principally, the coupling of internal epoxides and CO_2 remains a challenging task with limited evolution in COC product scope observed over the years.[13]

Scheme 1. Comparison of Organocatalytic and Metal-based Approaches in COC Formation



Recent developments in the area of HB catalysis of COC formation have demonstrated that catalyst design plays an imperative role to boost activity. For instance, Dufaud reported on cavitand based hosts for ammonium guests thereby increasing the reactivity of the counter-anion (nucleophile) towards ring-opening of the epoxide and subsequent COC formation.[14] Jerome, Tassaing, Detrembleur and coworkers developed binary catalysts based on fluorinated alcohols that are highly active catalysts for terminal epoxide/CO_2 couplings,[15] whereas Werner

communicated the use of various attractive, modular bifunctional phosphonium and ammonium based organocatalysts.[16] However, organocatalysts that are able to mediate the coupling reaction between internal epoxides and CO_2 under comparatively mild conditions remain scarce.[17] In this context, we recently reported cavitand based polyphenols as binary catalysts systems that show interesting potential towards internal epoxide/CO_2 couplings, and these systems also showed very high turnover numbers (TONs) and initial turnover frequencies (TOFs up to around 500/h) for terminal epoxide conversion into mono-substituted COCs.[17a]

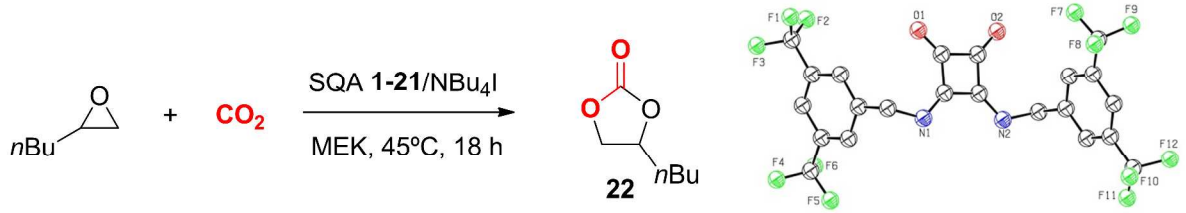
In our quest towards more powerful catalysts for COC formation, we considered the use of squaramides (Scheme 1) as these structures have been shown to have excellent substrate activation potential in the area of organocatalysis.[18] Importantly, these squaramides have highly modular properties and can be build up stepwise[19] providing either symmetrical or nonsymmetrical, sterically/electronically tunable structures. Squaramides have previously been shown to strongly bind halide anions[20,21] which are useful nucleophilic components of binary catalysts for COC formation. We anticipated that oxoanions, which are *in situ* produced by epoxide ring-opening, could easily displace the halide nucleophile thereby forming a conceptually new catalytic approach in COC synthesis. Oxoanions have a typically stronger interaction with squaramides compared to halides and the stabilization of oxoanionic species thus offers new unexplored potential to pre-organize both nucleophile and substrate favoring the preparation of COCs. In this work we will demonstrate that squaramide based binary catalysts have exceptional potential for COC preparation, and moreover show unique behavior to facilitate the conversion of both terminal as well as internal epoxide substrates with high efficiency, thereby illustrating that organocatalysis can offer a competitive and sustainable alternative to metal catalysis in this area of CO_2 conversion.

■ RESULTS AND DISCUSSION

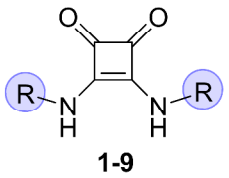
Catalyst Screening Phase. A series of symmetrically and non-symmetrically disubstituted squaramides **1–21** (see Table 1, Supporting Information (SI) for more experimental details) were prepared to investigate the influence of their substitution on the catalytic performance of the squaramide when combined with NBu_4I as nucleophilic additive. Both symmetrical (**1–9**) as well as nonsymmetrical substitutions (**10–21**) were considered. In order to facilitate a fair comparison between all binary catalyst systems, a solvent was required (MEK) to maintain homogeneous solutions during the catalytic reactions.[22] Under comparatively mild conditions (45ºC, 10 bar) formerly used for polyphenol based binary catalysts[12e] the use of squaramide/NBu_4I combinations based on **1–9** (Table 1, entries 1–9) resulted in various yields for cyclic carbonate **22** (4–58%). Both binary systems **6**/NBu_4I and **7**/NBu_4I gave the best results and comprise of secondary amide groups substituted by (2-pyridyl)methylene and bis-3,5-di-trifluoromethyl-aryl groups (X-ray structure for **7** was determined). Therefore, we prepared nonsymmetrical squaramides in a subsequent screening stage using at least one of these aforementioned substitutions, and the catalytic efficiency of compounds **10–21** was investigated in the formation of cyclic carbonate **22** (Table 1, entries 10–21). The most satisfactorily results (yield of **22** up to 75%) were obtained with squaramides **15** and **16** that have both one amide unit substituted by a bis-3,5-di-trifluoromethyl-aryl group flanked by a second amide unit having dimethylaminoethylene or a (2-pyridyl)methylene substitution, respectively (Table 1, entries 15 and 16). Thus, for the best catalytic efficiency the presence of both electron-withdrawing and electron-donating NR-groups in the squaramide scaffold seems a requisite.

Next, the catalytic protocol towards the formation of carbonate **22** was optimized using **15**/NBu_4I as a binary catalyst under *neat* conditions (Table 2). The coupling of 1,2-epoxyhexane

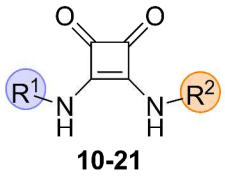
Table 1. Screening of Binary Catalysts based on **1-21** and NBu_4I in the Conversion of 1,2-Epoxyhexane and CO_2 into the Cyclic Carbonate **22** under various Reaction Conditions.[a]



1. R = *n*-Pr
2. R = CH_2CH_2OH
3. R = $CH_2CH_2NMe_2$
4. R = Ph
5. R = *p*-MeO-C_6H_4
6. R = CH_2(2-pyridyl)
7. R = 3,5-di-CF_3-C_6H_3
8. R = CH_2(3,5-di-CF_3-C_6H_3)
9. R = Bn



1-9



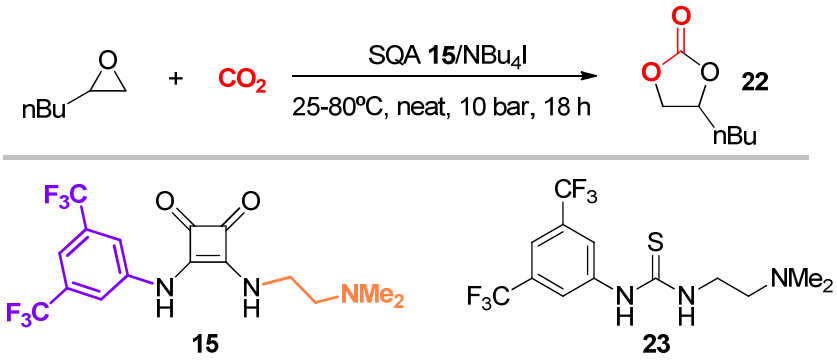
10-21

10. R^1 = CH_2(2-pyridyl); R^2 = *n*-Pr
11. R^1 = CH_2(2-pyridyl); R^2 = CH_2CH_2OH
12. R^1 = CH_2(2-pyridyl); R^2 = $CH_2CH_2NMe_2$
13. R^1 = 3,5-di-CF_3-C_6H_3; R^2 = *n*-Pr
14. R^1 = 3,5-di-CF_3-C_6H_3; R^2 = CH_2CH_2OH
15. R^1 = 3,5-di-CF_3-C_6H_3; R^2 = $CH_2CH_2NMe_2$
16. R^1 = 3,5-di-CF_3-C_6H_3; R^2 = CH_2(2-pyridyl)
17. R^1 = 3,5-di-CF_3-C_6H_3; R^2 = Bn
18. R^1 = 4-CF_3-C_6H_4; R^2 = $CH_2CH_2NMe_2$
19. R^1 = CH_2(3,5-di-CF_3-C_6H_3); R^2 = $CH_2CH_2NMe_2$
20. R^1 = 4-CF_3-C_6H_4; R^2 = CH_2(2-pyridyl)
21. CH_2(3,5-di-CF_3-C_6H_3); R^2 = CH_2(2-pyridyl)

Entry	SQA	Yield 22(%)[b]	Entry	SQA	Yield 22 (%)[b]
1	**1**	36	12	**12**	30
2	**2**	4	13	**13**	53
3	**3**	46	14	**14**	56
4	**4**	16	15	**15**	75
5	**5**	54	16	**16**	74
6	**6**	58	17	**17**	59
7	**7**	52	18	**18**	58
8	**8**	28	19	**19**	42
9	**9**	10	20	**20**	65
10	**10**	44	21	**21**	36
11	**11**	16	22	–	0

[a]Reaction conditions: 1,2-epoxyhexane (2.0 mmol), squaramide (5.0 mol%), NBu_4I (5.0 mol%), MEK (5.0 mL), pCO_2 = 10 bar, 45ºC, 18 h, mesitylene (15 mol%); MEK = methylethyl ketone, SQA = squaramide. [b]Determined by ^1H NMR ($CDCl_3$) using mesitylene as internal standard. The selectivity towards **22** was >99%. The inset (top) shows the X-ray structure for squaramide **7**.

Table 2. Optimization of the Catalytic Formation of Cyclic Carbonate **22** using **15**/NBu_4I as Binary Catalyst.[a]



Entry	15 (mol%)	NBu_4I (mol%)	T (ºC)	t (h)	Yield 22 (%)[b]
1	2.0	2.0	25	18	64
2[c]	2.0	2.0	25	18	53
3	4.0	2.0	25	18	67
4	1.0	2.0	25	18	47
5	2.0	6.0	25	18	79
6	2.0	4.0	25	18	72
7	2.0	1.0	25	18	38
8	–	4.0	25	18	0
9	–	2.0	25	18	0
10	2.0	2.0	45	18	100
11	2.0	2.0	80	1	100[d]
12	–	2.0	80	1	11
13	3.0	6.0	25	18	86
14	–	6.0	25	18	0
15[e]	2.0	2.0	25	18	36

[a]Reaction conditions: 1,2-epoxyhexane (8.0 mmol), **15** (2.0 mol%), NBu_4I (2.0 mol%), neat, pCO_2° = 10 bar, 18 h, mesitylene (15 mol%). [b]Determined by ^1H NMR ($CDCl_3$) using mesitylene as internal standard. The selectivity towards **22** was >99%. [c]Initial pressure was 30 bar. [d]Yield was 85% after 0.5 h, calculated TOF = 85/h. [e]Using **23** (2.0 mol%).

and CO_2 at 25ºC showed an encouraging 64% yield of carbonate **22** (Table 2, entry 1). Increasing the initial pressure to 30 bars did not improve this yield (Table 2, entry 2), but further variation of the **15**/NBu_4I ratio and reaction temperature proved to be beneficial (Table 2, entries 3–14). A NBu_4I loading of 6.0 mol% increased the yield to 79% (Table 2, entry 5) whereas higher reaction temperatures (45, 80ºC) gave as expected faster kinetics thereby shortening the required time towards full conversion of the epoxide substrate. For instance, the reaction performed at 80ºC with **15**/NBu_4I (both 2.0 mol%) was finished within 1 h with an appreciably high turnover frequency (Table 2, entry 11; TOF = 85/h).[23]

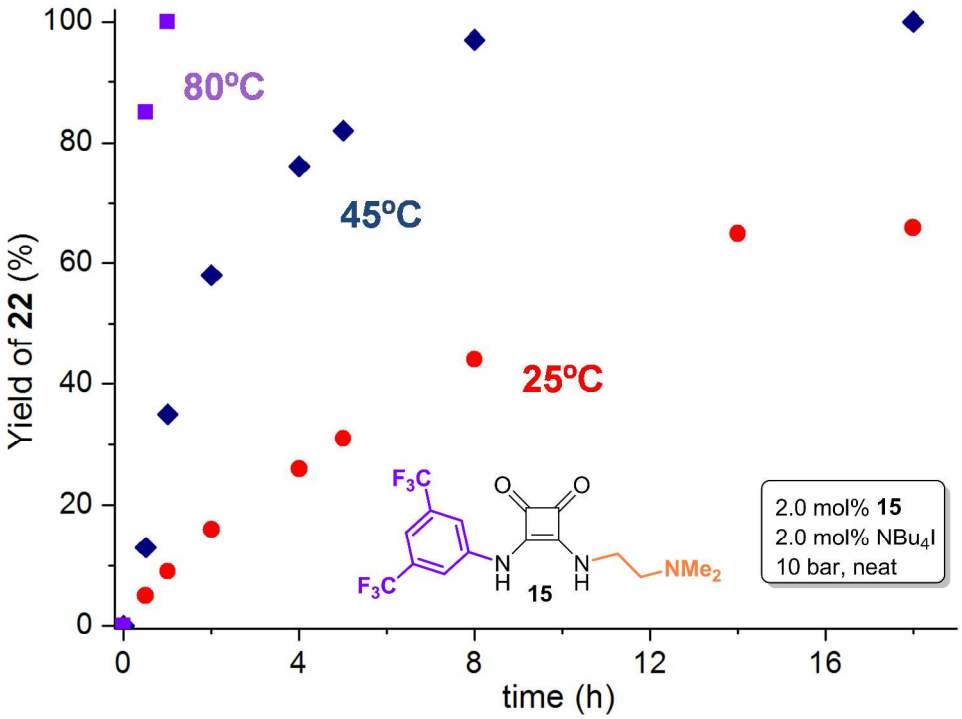


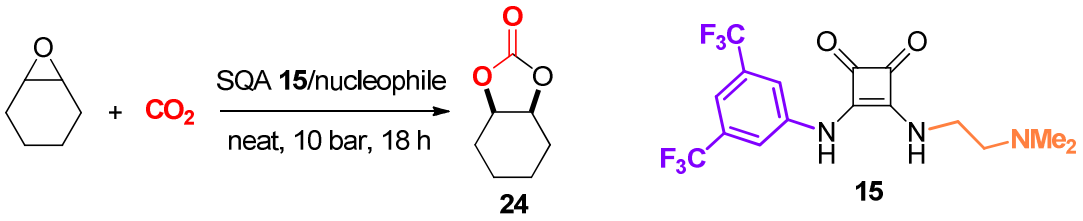
Figure 1. Kinetic profiles for the formation of carbonate **22** at different reaction temperatures using **15**/NBu_4I as binary catalyst.

Comparatively, the use of NBu_4I alone (*i.e.*, in the absence of the squaramide) only gave 11% yield of carbonate **22** (entry 12) thus clearly showing the beneficial presence of the squaramide. Interestingly, a thiourea-based hydrogen-bond epoxide activator (entry 15; **23**) displayed much lower reactivity towards COC formation compared to the structurally related squaramide **15** (*cf.*, entry 11), showing the crucial nature of the squaramide component towards the overall reactivity of the binary systems. The kinetic profiles for the preparation of carbonate **22** from 1,2-epoxyhexane and CO_2 were also determined at 25, 45 and 80ºC (see Figure 1). Importantly, the halide additive gave much poorer catalysis compared to thebinary system **15**/NBu_4I (Table 2; entries 8, 9, 12 and 14) in the temperature range 25–80ºC with, for instance, only 11% yield of **22** at 80ºC after 1 h. Therefore, the coupling of 1,2-epoxyhexane and CO_2 seems to be quite efficient at 80ºC using equimolar amounts (2.0 mol%) of **15** and NBu_4I.

Screening of Internal Epoxides. The high activity profile for the squaramide based binary catalyst **15**/NBu_4I prompted us to investigate the potential of this system in the conversion of the more challenging internal epoxides and cyclohexene oxide (CHO) was chosen as a benchmark substrate (Table 3). Various co-catalytic nucleophiles including TBAB (tetrabutylammonium bromide) TEAB (tetraethylammonium bromide), KBr and PPNCl (bis[triphenylphosphine]iminium chloride) were examined.[24] First TBAB was considered (Table 3, entries 1–6) and the combination of 2.0 mol% of **15** with 4.0 mol% TBAB provided a 73% yield of carbonate **24** (Table 1, entry 1). Lowering the TBAB loading was not favorable towards product formation not even in the presence of a higher amount of **15** (Table 3, entries 2 and 4). The use of TBAB alone also gave an appreciable yield of carbonate **22** (Table 3, entries 5 and 6), and therefore too competitive interactions of the squaramide with the halide anion reduce the

ability to convert internal epoxides as the ring-opening of the latter is significantly slower compared with terminal

Table 3. Screening of the Catalytic Formation of Cyclic Carbonate **24** using **15** and various Nucleophiles as Binary Catalyst.[a]



Entry	15 (mol%)	Nu (mol%)	T (°C)	P (bar)	Yield 24 (%)[b]
1	2.0	TBAB, 4.0	80	10	73
2	2.0	TBAB, 2.0	80	10	37
3	2.0	TBAB, 2.0	80	30	55
4	4.0	TBAB, 2.0	80	10	51
5	–	TBAB, 2.0	80	10	36
6	–	TBAB, 4.0	80	10	50
7	2.0	PPNCl, 2.0	80	10	14
8	–	PPNCl, 2.0	80	10	57
9	2.0	KBr, 4.0	80	10	1[c]
10	–	KBr, 4.0	80	10	0[c]
11	2.0	TEAB, 4.0	80	10	59
12	–	TEAB, 4.0	80	10	1[c]
13	3.0	TEAB, 6.0	80	30	88
14	–	TEAB, 6.0	80	30	1[c]
15[d]	3.0	TEAB, 6.0	80	30	87
16[d]	–	TEAB, 6.0	80	30	18

[a]Reaction conditions: cyclohexene oxide (8.0 mmol), **15** (2.0–4.0 mol%), Nu (2.0–6.0 mol%), neat, pCO_2° = 10 bar, 18 h, mesitylene (15 mol%). Nu stands for the nucleophilic additive. [b]Determined by ^{1}H NMR ($CDCl_3$) using mesitylene as internal standard. The selectivity towards **24** was >99%, and only the *cis*-isomer was formed. [c]Not fully soluble. [d]Propylene carbonate (1.5 mL) was used as a solvent.

epoxides. This hypothesis was further supported by the use of a chloride based nucleophile (PPNCl; Table 3, entries 7 and 8); the binary catalyst **15**/PPNCl proved to be significantly less active than the nucleophilic additive itself and strong binding of the chloride by the squaramide is apparent.[21] Therefore, other bromide-based nucleophiles were then screened (Table 3, entries 9–16) to improve the dynamic exchange of the bromide anion by *in situ* generated oxoanions. Whereas the use of KBr was not productive, the presence of TEAB showed promise in terms of yield of carbonate **24**, and a clear positive influence of the squaramide **15** on the catalytic activity was noted. However, in several reactions, we noted that the nucleophilic additive alone was not (fully) soluble under neat conditions, which makes it difficult to assess the actual influence of the squaramide on the conversion kinetics. Fortunately, in the presence of propylene carbonate as a solvent we were able to assess this aspect properly (Table 3, entries 15 and 16), and about a five-fold increase in the yield of **24** was noted when the binary catalyst system was used (87 vs. 18%). This clearly demonstrates the beneficial character of using a binary system that comprises of a squaramide scaffold combined with a bromide-containing nucleophile (TEAB) exhibiting stronger ion pairing effect than in the presence of TBAB. The conditions reported in entries 13 and 15 of Table 3 thus seem to be optimal for the conversion of other internal epoxides as coupling partners for CO_2 using this organocatalytic binary system.

Scope in Cyclic Carbonate Products. Next, the scope in internal epoxide substrates was investigated (Figure 2, COCs **24–33**) to further evaluate the efficiency of binary catalyst system **15**/TEAB (3.0 and 6.0 mol%, respectively) at 80ºC and 30 bar. Various substitution patterns in the epoxide partner were examined and fortunately, the developed protocol proved to be beneficial towards the preparation of a wide variety of COC products in appreciable isolated yields (53–90%). Whereas the benchmark product, cyclohexene carbonate **24**, was isolated in

78% yield (*cis* isomer), also five-membered bicyclic epoxides could be converted into their COCs (**25** and **26**) in good yields despite the fact in the synthesis of **25** we observed slower conversion kinetics. COCs **26** and **27** that incorporate further heteroatoms were also isolated in similar yields as obtained for **24**. Next, a series of disubstituted acyclic epoxides with different size features were tested and could be converted into their COCs **28**–**32** in good yields and chemo-selectivities. Notable, epoxides with a higher degree of steric impediment were tolerated including those that can combine a phenyl and methyl fragment (**29**), a phenyl and ethyl ester substituent

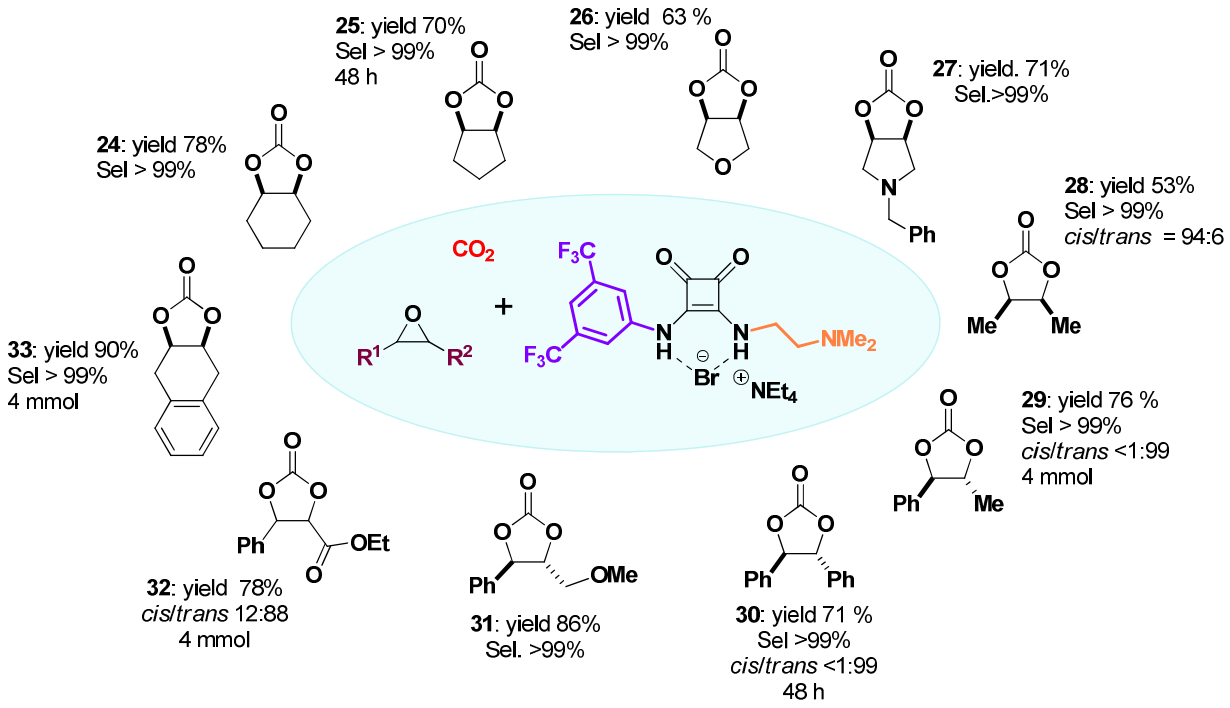


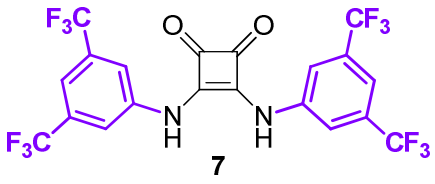
Figure 2. Substrate scope using **15**/TEAB (3.0/6.0 mol%) as binary catalyst at 80ºC, 30 bar initial pressure for 18 h, 8.0 mmol scale; deviations from this standard protocol are indicated in the Figure. All carbonate products **24**–**33** were isolated and fully characterized, see SI for details.

(**32**; original *cis*/*trans* ratio retained), two phenyl groups (**30**) or a phenyl/methoxymethyl combination (**31**). The scope in COC products displayed in Figure 2 is among the widest reported for organocatalyst systems in this area, and more specifically for the conversion of internal epoxides.

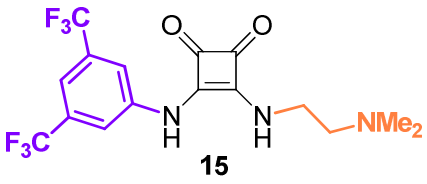
Titration Studies and Mechanism. In order to gain more insight into the operating mechanism, various titration studies were carried out using symmetrical and nonsymmetrical squaramides **7** and **15**, and different anionic guests (see Table 4). As may be expected from previous literature[20,21] describing the interaction between halides and symmetrical squaramide hosts, bromide anions interact strongly with host **7** and high association constants (K_{ass}) were determined when using either TBAB or TEAB (entries 1 and 2). Addition of a large excess (100 equiv) of CHO to host **7** did not provoke significant changes in the UV-vis spectrum (see SI) and apparently the interaction between **7** and CHO is mostly weak. This also becomes apparent from ^{1}H NMR titration experiments (CD_3CN) using higher concentrations of **7** showing virtually no displacement of the signals corresponding to the host molecule when adding up to 100 equiv of CHO. More importantly, in the presence of 4 equiv of TBAB compound **7** displays a significant downshift ($\Delta\delta$ = + 0.49 ppm) for the NH resonance (δ = 7.91 ppm) while the ArH signal (δ = 7.69 ppm) undergoes a modest upfield shift of –0.06 ppm. These characteristics do not change upon addition of 100 equiv of CHO to this 1:4 mixture of **7** and TBAB, suggesting that the epoxide is unable to compete with the bromide anion forming a hydrogen-bonded host-guest assembly. Consequently, this implies that the catalytic activity of squaramides in the formation of COCs does not relate to initial activation of the epoxide through hydrogen bonding but, instead, it is primarily associated to their stabilization potential of oxoanionic species which evolve after ring-opening of the epoxide substrate.

To substantiate further this hypothesis, oxoanions were used as titrants and added to a solution of nonsymmetrical **15** (the squaramide used in the optimization and substrate scope phases) and the determined association constants compared to the ones derived from addition of either TBAB or TEAB (entries 4–7) to **15**. Interestingly, clearly weaker association of bromide anions with nonsymmetrical host **15** were revealed (entries 4 and 5) with K_{ass} about two orders of magnitude lower when compared with the titrations that involved symmetrical host **7** (*cf.*, entries 1 and 2). In the presence of model oxoanionic species tetrabutylammonium *p*ara-nitrophenolate [TBA(PNP)]

Table 4. Titration studies carried out with squaramides **7** and **15**, and various salts.[a]



7



15

Entry	Guest	Host/Guest	Log(K_{ass})	K_{ass} ($\times 10^5$ M^{-1})
1	TBAB	**7**·TBAB	5.57	3.72
2	TEAB	**7**·TEAB	5.55	3.55
3	CHO	**7**·CHO	–[b]	–[b]
4	TBAB	**15**·TBAB	3.48	0.030
5	TEAB	**15**·TEAB	3.58	0.038
6	TBA(PNP)	**15**·TBA(PNP)	4.43	0.269
7	TBA(OAc)	**15**·TBA(OAc)	6.38	23.9

[a]General conditions: [**7**] = 2.0×10^{-5} M or [**15**] = 2.5×10^{-5} M, CH_3CN, r.t. Stock solutions of the guests had a concentration 100–1000 times higher than the host concentration. SQA = squaramide, CHO = cyclohexene oxide, TBA(PNP) = tetrabutylammonium *p*-nitro-phenolate,

TBA(OAc) = tetrabutylammonium acetate. See SI for more details. [b]Interaction was too weak to determine a reliable association constant.

and tetrabutylammonium acetate [TBA(OAc)], significantly higher K_{ass} values are determined for 1:1 host-guest binding of PNP and OAc to **15** (entries 6 and 7). Despite some disparity between the nature of the oxoanions that evolve after epoxide ring-opening (alkoxide stage) and CO_2 insertion into the alkoxide species (linear carbonate stage), these results provide a rational explanation for the more preferred binding of oxoanions with host **15**, a result that closely follows literature precedent for substantially stronger binding of oxoanions compared to halides by symmetrical squaramides.[21] This preferred binding is also noted when analyzing NMR solutions (CD_3CN) of **15**/TBA(OAc) and **15**/TBA(OAc)/TBAB (1:5 mixtures of **15** and OAc or Br), respectively, and comparing these data with the spectroscopic features of **15**/TBAB. This comparison revealed that the chemical shifts noted in the ^{19}F and ^{1}H NMR spectra of the mixture of anions are closely related to those measured for **15**/TBA(OAc), and therefore this qualitative data is in line with the view that oxoanions indeed are able to compete for binding to the squaramide host in the presence of bromide (SI for more details)

From these titration studies and NMR control experiments a mechanistic profile for the binary catalysts **15**/TEAB is proposed. First, the squaramide **15** binds a bromide anion that originates from the TEAB additive that is present in excess to the host. Whereas epoxides are not likely to compete for binding to **15** in the presence of bromide, the excess of bromide can induce ring-opening of the epoxide substrate to give rise to an alkoxide species that can displace the bromide anion in the intermediate **15**·Br and evolves in the formation of an oxoanion-stabilized species. Subsequently, reaction of this species with CO_2 gives rise to a linear carbonate (a second, strongly binding oxoanionic intermediate) that undergoes cyclization to produce the COC product and regenerates the squaramide **15**. Since bromide binding to **15** is substantial, it is reasonable to suggest that the host-guest assembly **15**·Br can be considered as the resting state of

this catalytic system, with the bromide anion that is released in the ring-closing step affording the carbonate product being captured by the squaramide host **15**. Notably, the squaramide is thus primarily involved in the stabilization of oxanionic intermediates and not, as reported for the vast majority of organocatalysts in this area, in the initial activation step of the epoxide through hydrogen bonding. Squaramides **15** and **16** (with a pending 2-pyridyl group) were shown to be the best systems for COC formation and this is likely a result of intramolecular hydrogen-bonding (Figure 3, insert) of the alkyldimethylamino or pyridyl N-atom increasing to some extent the acidity of the involved NH fragment, therefore adding some further stabilization of the oxoanionic intermediates.[25]

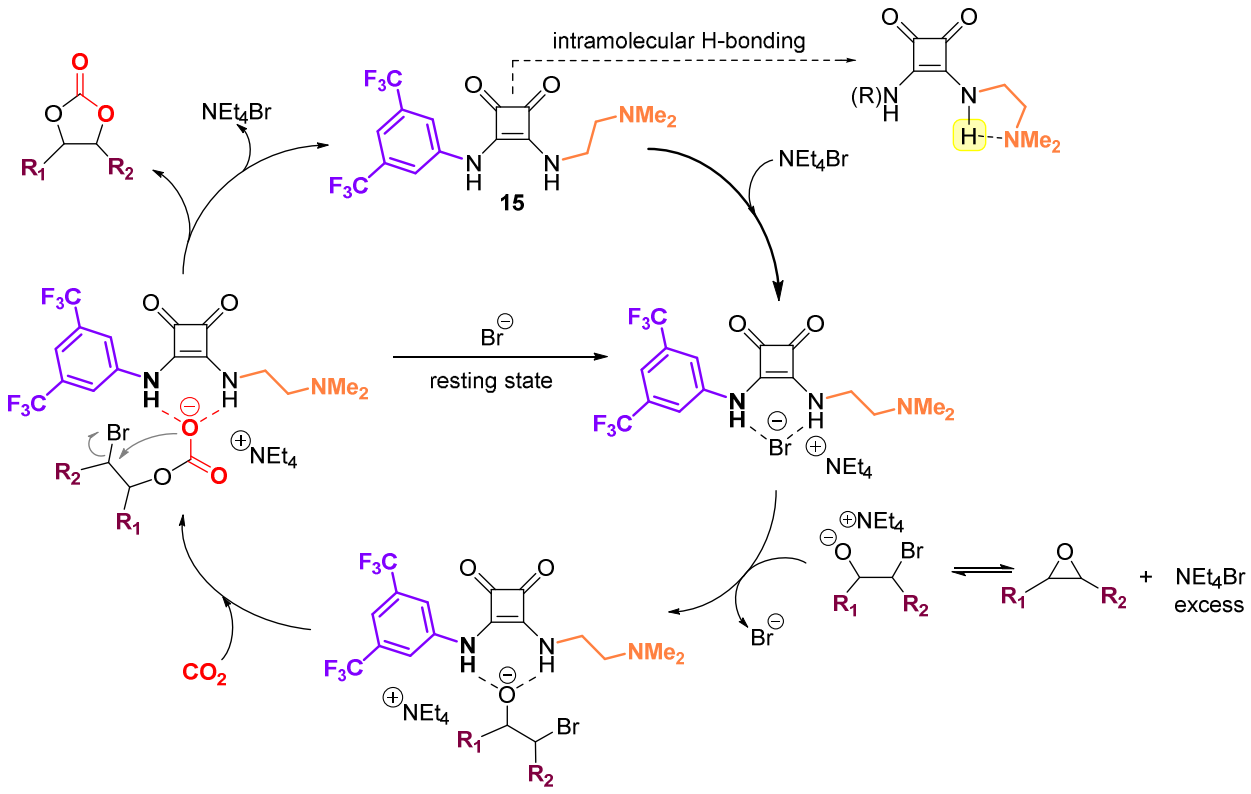


Figure 3. Proposed mechanistic manifold for the formation of COCs by the binary squaramide-based catalyst **15**/TEAB.

As observed for internal epoxide conversions (Figure 2), all reactions occur with retention of configuration pointing at a double-inversion mechanism in line with the proposal of Figure 3. Further experimental evidence is provided by the coupling of CO_2 with (*S*)-styrene oxide using **15**/NBu_4I at 45ºC and 10 bar: the product, styrene carbonate, was obtained with an *ee* of 99% in line with the retention of the original configuration present in the epoxide reagent.

■ CONCLUSION

In summary, squaramides are presented as modular and useful components of binary catalysts when combined with halides, and provide interesting new potential for the coupling of terminal and internal epoxides with CO_2 to prepare COCs. As opposed to many organocatalysts that activate the epoxide by hydrogen bonding, the squaramides are primarily involved in the stabilization of oxoanionic species during catalysis and thus offer new potential in this area. This potential is illustrated by the conversion of 10 internal epoxides which are generally difficult substrates to activate especially by organocatalytic systems. Therefore, new catalyst designs may help to bridge the gap between metal- and organo-catalysis aiming to improve the sustainability in COC synthesis and other related CO_2 conversion processes. Our focus is now on merging the concepts of sustainable organocatalytic CO_2 conversion, catalyst recycling and the development of continuous flow based processes.

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Notes

The authors declare no competing financial interest.

ASSOCIATED CONTENT

Supporting Information. Copies of analytical data/spectra for the squaramides **1–21** and COC products **24**–**33**, titration details and original spectra and cif file for **7**. This material is available free of charge via the Internet at http://pubs.acs.org.

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(22) Note that several symmetrical squaramides proved to be (partially) insoluble in neat 1,2-epoxyhexane and therefore MEK had to be added to solubilize these compounds.

(23) We also prepared a bifunctional version of **15** with a trimethylammonium iodide end-group, see the SI. This catalyst provided at a 0.05 mol% loading and 80ºC/10 bar a turnover number of 1100 in 66 h (average TOF/h = 17). The results indicate that supported versions of **15** (using for instance a benzyl bromide functionalized polystyrene commercially available at Sigma Aldrich) may hold promise to recycle these type of catalysts.

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