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Catalytic, Enantioselective Synthesis of Cyclic Carbamates from Dialkyl Amines by CO_2-Capture: Discovery, Development, and Mechanism

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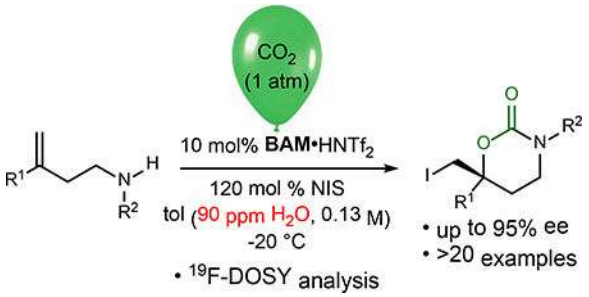
Abstract

Cyclic carbamates are a common feature of small molecule therapeutics, offering a constrained hydrogen bond acceptor that is both polar and sterically small. Methods for their preparation most often focus first on aminoalcohol synthesis and then reaction with phosgene or its equivalent. This report describes an enantioselective synthesis of cyclic carbamates in which carbon dioxide engages an unsaturated basic amine, facilitated by a bifunctional organocatalyst designed to stabilize a carbamic acid intermediate while activating it toward subsequent enantioselective carbon-oxygen bond formation. Six-membered cyclic carbamates are prepared in good yield with high levels of enantioselection, as constrained 1,3-amino alcohols featuring a chiral tertiary alcohol carbon. Spectroscopic analysis (NMR, DOSY) of various substrate-reagent combinations provides insight into the dominant species under the reaction conditions. Two peculiar requirements were identified to achieve highest consistency: a 'Goldilocks' amount of water and the use of a non-crystalline form of the ligand. These atypical features of the final protocol notwithstanding, a diverse range of products could be prepared. Their functionalizations illustrate the versatility of the carbamates as precursors to enantioenriched small molecules.

Graphical Abstract



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ASSOCIATED CONTENT

Preparative information and analytical data provided for all new compounds; details of spectroscopic measurements (pK_a determination and F-DOSY); X-ray data (cif) for **7c**, **29b**. This material is available free of charge via the Internet at http://pubs.acs.org.

INTRODUCTION

Carbon dioxide is an abundant, nontoxic, inexpensive and renewable carbon-based feedstock that can be used as a C1 building block in organic synthesis.[1] By measure of reagent cost alone, CO_2 ($0.00066/mol) compares favorably to common alternatives (triphosgene: $553/mol, CDI: $223/mol). The low reactivity of CO_2 is often overcome by the use of potently nucleophilic reactants, such as Grignard reagents, or electrophilic/redox active metal complexes.[2] 'Carbon dioxide fixation' describes a heterogeneous collection of CO_2 manipulations,[3] including immobilization by amine–based materials.[4] We envisioned the possibility that amines might instead be used as substrates, and their carbamic acid adducts used productively in a non-redox transformation. However, to the best of our knowledge, the use of CO_2 as a carbon and/or oxygen donor in an enantioselective reaction with amines at atmospheric pressure is unprecedented.[1,5,6] In contrast, propargylic and homoallylic alcohol substrates can be converted to enantioenriched carbonate products using CO_2 and chiral silver(I)[7] and protic acid complexes,[8] respectively. An enantioselective CO_2-fixation reaction based on an alkene-amine platform (e.g. **1**) and electrophile (X^+)-based activation could lead to an enantioenriched carbamate (**3**) ready for further functionalization (Scheme 1A). Linezolid[9] and Efavirenz[10] are representative drugs[11] that prominently display a cyclic carbamate derived from a chiral aminoalcohol, and whose absolute configuration modulates receptor binding.

In order to achieve CO_2-capture with an unsaturated alcohol or amine (**1**) (Scheme 1A), alkene haloetherification and haloamination pathways (Scheme 1B, blue boxes) must be subverted by an intermolecular CO_2-capture step (Scheme 1B).[12] Indeed, enantioselective halofunctionalizations of alkenes with both oxygen[8,13,14,15] and nitrogen[16]nucleophiles have witnessed success in recent years. Electron-withdrawing groups (EWG) at nitrogen enable N-C bond formation with an activated alkene, but cannot be employed as a design element here (Scheme 1A, R'=EWG), as it would slow, if not prevent CO_2-capture. Prior work has not involved nucleophilic, Lewis basic alkyl amines due to their incompatibility with many catalysts. Nucleophilic aziridines are competent substrates for aziridine-CO_2 insertion reactions to form 5-membered cyclic carbamates (oxazolidones), but an enantioselective variant is not yet known.[5] Generally speaking, the emerging understanding in halogen-initiated alkene functionalization is that protected amines remain sufficiently nucleophilic for alkene haloamination, but not for alkene halocarbamation.

Additional differences between alcohol-CO_2 capture and amine-CO_2 enantioselective reaction design result from the nature of the intermediates. Alkyl amines engage carbon dioxide to form carbamic acids[17] (**5**, Scheme 1B), and typically react further to generate the carbamic acid salt (e.g. **5**·HNR_2).[18] A chiral Brønsted base catalyst would need to compete with the amine of **5**·HNR_2, since the latter would be inert or a competent precursor to racemic product in most subsequent functionalizations driven by the nucleophilicity of the carbamic acid oxygen. Indeed, we ultimately observed several of these species in the work reported here (Scheme 4).

This report establishes the feasibility of an enantioselective amine CO_2-capture/cyclization reaction. The carbamates so formed are enantioenriched, validating a bifunctional Brønsted

acid/base catalyst for effective alkene halocarbamation. Furthermore, mechanism-guided analysis of the reaction provides insight to several dominant catalyst-substrate species in solution. Importantly, these studies were carried out over several years, during which inconsistent conversions were observed. An optimized and highly reproducible reaction was ultimately achieved by ligand preparation as an amorphous solid form, and the use of a precise amount of water in the reaction. A collection of product functionalizations establish the value of this approach, providing enantioenriched cyclic carbamates and acyclic amino alcohols. Insofar as cyclic carbamates of this type are often prepared by the use of electrophilic phosgene equivalents, the use of carbon dioxide in this way provides a compelling mild and inexpensive alternative.

RESULTS AND DISCUSSION

The point of origin for these studies was the application of conditions optimal for homoallylic alcohol-CO_2 capture/cyclization, for which **7a**·$HNTf_2$ was highly effective.[8] Using an analogous amine substrate (**8a**), this catalyst resulted in low enantioselection (50%) and yield (15%) (Table 1, entry 4). Behavior of the substrate was benchmarked under the same conditions but with a series of substitutions. For example, treatment of amine **8a** with NIS in toluene without catalyst provided products consistent with *N*-halamine formation[19] or alkene iodoamination,[20] but rate is slow at low temperature. Further exploration of the reaction of amine **8a** with carbon dioxide and various potential catalysts was pursued (Table 1).[21] Evidence for formation of a competent CO_2 adduct was obtained by using a full equivalent of TBD (**6**) (Table 1, entry 2), producing carbamate **8b** in 79% yield.

Reflecting on the contrasting behavior of **7a**·$HNTf_2$ with alcohols and amine **8a**, we reasoned that the carbamic acid intermediate is less acidic relative to an alkyl carbonic acid,[14c] and that use of a more Brønsted basic bifunctional catalyst might recover this loss of reactivity while maintaining selectivity (Figure 1). Although an acidic catalyst could better activate the electrophilic NIS, binding to the Brønsted basic amine substrate would lower its nucleophilic character. Methodically increasing catalyst basicity, while diminishing its acidity, may identify an optimal level of activation for both electrophile and nucleophile (Figure 1). Notably, this line of thought is counter to the prevailing wisdom encountered with many Brønsted acid catalyzed reactions.[22,23,24] In the event, the analogous catalyst **7b** bearing a methyl group at the quinoline 7-position led to higher yield (31%) and enantioselection (81% ee) (Table 1, entry 5) that improved further with the C7-methoxy catalyst **7c** (75% yield, 89% ee) (Table 1, entry 6).[25] Interestingly, higher substrate concentrations led to diminished yield and selectivity (Table 1, entries 7–8), concomitant with signs that the reaction mixtures were more heterogeneous due to insolubility of one or more reagents. Although the bis(amidine) free base is also capable of hydrogen bond-donor/acceptor interactions, low yield (44%) and selectivity (32% ee) were observed (Table 1, entry 9).[26]

A second obstacle to development was the observation that yields could vary dramatically, with stirring efficacy, reaction time, and ligand purification method each contributing to degrees of conversion. It was straightforward to achieve yields in the 20–30% range, but

>60% yield was achieved sporadically. Oddly, no single variable among these appeared dominant, although ligand recrystallization clearly affected the degree of reaction heterogeneity, causing *greater* heterogeneity and *lower* conversions (measured by ^{1}H NMR using an internal standard). The most effective catalyst form was amorphous in nature, prepared using trituration. This material appeared identical in key aspects (i.e. ^{1}H NMR, LCMS) to recrystallized material, but provided less heterogeneous reaction mixtures. Extensive investigation (*vide infra*) ultimately led to a straightforward protocol for the highest rates and conversion: use of wet toluene (90 ppm water, 0.13 M in substrate) provided highly reproducible yield and selectivity across a broad range of substrates.

Using triturated **7c** to prepare **7c**·$HNTf_2$ was broadly effective and employed toluene spiked with water (2.7 μL H_2O in 30 mL tol: 90 ppm ≈ 4 mol % at 0.13 M) (Table 2). Generous changes at nitrogen (Table 2, entries 1–10) and alkene substituents (Table 2, entries 11–25) were allowed. At the nitrogen, the electronic nature of the benzyl substituent affected selectivity minimally in most cases. An *ortho*-tolyl group also provided the carbamate in high ee (94% ee) and yield (72%), but the reaction time was extended to 5 days (Table 2, entry 3). This suggests that the steric nature of the nitrogen has greater impact on reactivity - perhaps in the rate of CO_2-capture - than it does on the subsequent enantioselectivity-determining step. Substituents at the alkene affected the outcome more significantly, consistent with the preference for an unhindered π-nucleophile to engage NIS. Not unexpectedly, electron-donating groups (Table 2, entries 11–16) led to carbamates in high yield and enantioselectivity (85–93% ee). Highly electron rich *para*-methoxy (**23a**) and sterically demanding 2-naphthalene (**21a**) analogues gave the desired product in 85 and 93% ee, respectively. Unfortunately substitution near the alkene was less tolerated, as the *ortho*-tolyl case was unreactive (Table 2, entry **20a**). Aryl rings with electron-withdrawing groups (Table 2, entries 19–22) also showed high enantioselectivity (85–95% ee) but longer reaction times were needed (120 h) for *meta*-chloro (**27**), *meta*-fluoro (**28**), and *para*-(trifluoromethyl)phenyl (**29**) substrates (Table 2, entries 20–22). Alkenes bearing aliphatic substituents are challenging substrates, but were converted to desired carbamates in moderate (60% ee) and low (41% ee) enantioselectivity (Table 2, entries 23–24). Although not a focus of these studies, an allylic amine (**33a**, Scheme 2) reacted sluggishly to produce oxazolidinone **33b** in low ee. The qualified success with more electron-deficient olefins is notable, as is the trisubstituted alkene **34a** (Scheme 2). Despite its increased steric demands and aliphatic substituents, trisubstituted alkene **34a** exhibited an encouraging level of reactivity and selectivity to produce spirocycle **34b** (Scheme 2, 74% yield, 78% ee).

Mechanistic Considerations.

Scheme 3 is a basic outline of the species expected to be present during these transformations. In the absence of a catalyst, formation of the alkyl amine salt (**37**) of the carbamic acid intermediate **36** is anticipated, as its role in the formation of formamide derivatives by the action of the guanidine base TBD is well-precedented.[27] Intervention by a chiral catalyst (**38**) to form **39** is unprecedented, but could be the basis for the enantioselective transformations described here.

The bifunctional nature of the most active and selective catalyst (**7c**·$HNTf_2$) can be inferred by comparison to the free base (**7c**) performance (Table 1, entry 9), as well as the behavior of the diprotonated ligand (**7c**·[$HNTf_2$]$_2$). The latter was minimally productive, and was rendered completely inactive with a 1:3 ratio of **7c**:acid. These behavior extremes of a single catalyst's basicity and acidity are consistent with their dual importance to activity and selectivity. Discussion of the precise catalyst protonation state should consider the change in (basic) amine substrate concentration as the reaction proceeds, particularly at early stages when an excess of amine is present relative to acid catalyst, whether intentionally mono- or polyprotonated.

The mechanistic hypothesis that a more Brønsted basic Brønsted acid catalyst might be needed, to better ion pair with the carbamic acid vis-à-vis a carbonic acid, led to the trend of increasing reactivity and selectivity noted above (Table 1, entries 4–6 and Figure 1). Evidence supporting the hypothesis and the species outlined in Scheme 3 was pursued. In one case, experiments (see Supporting Information) in this series revealed that the disubstituted amine **8a** forms a carbamic acid salt (i.e. **37**, Scheme 3) implicated by ^{1}H NMR and a peak at 161 ppm (^{13}C NMR, N-*C*O_2H) under the reaction conditions but in the absence of catalyst. Furthermore, the reversibility of its formation17 was established by replacing the CO_2 atmosphere with argon, resulting in its return to **8a**. Addition of **7c**·$HNTf_2$ to **8a**·CO_2 resulted in only peak broadening, owing to the insolubility in this attempt to prepare a stoichiometric amount of the protic acid complex (**39**). While conditions support the formation of **37**, its conversion to carbamate is slow (non-productive) with an achiral base,[28] offering an intervention point for a suitable catalyst. Importantly, the formation and stability of **37** under these conditions may account for the lack of intramolecular haloamination (Scheme 1B). However, its interconversion with complex **39** is essential for productive carbamate formation. Whether an equilibrium between species **37** and **39** might be observed became a line of investigation.

We sought evidence for the existence of **37** and **39** in solution through the use of fluorine-containing substrate **29a** and a series of ^{19}F-DOSY experiments that could approximate the molecular weight of the dominant fluorine-containing species in solution (Scheme 4, see Supporting Information).[29] Analysis of a mixture of **29a** and CO_2 enabled observation of a species with FW = 986, closely resembling Complex I (Scheme 4, FW = 960). Furthermore, when **7c**·$HNTf_2$ is added to this mixture, this species is replaced by two new species of higher FW (1485 & 1640). Each contained component fluorines of **29a** and Tf_2NH, and could be constructed from a common unit of **C** (Scheme 4, FW = 1295). The difference between this FW and the observed species could be due to the hydrogen bond donating ability of **C**, unsatisfied by the absent NIS in these experiments, resulting in **C**$(H_2CO_3)_3$ (FW = 1481) and **C**·**B** (FW = 1644). Since the experiment precluded the use of a desiccant, the postulated carbonic acid-solvated complex is possible. Similarly, carbamic acid **B** may effectively bind to **C** until NIS is present. Although these assignments are not exclusive of alternatives, these experiments successfully documented the existence of species in solution whose size is consistent with those hypothesized in Schemes 3–4. The finding that 90 ppm water (4 mol % relative to 10 mol % catalyst) provided consistent and highest conversions is

also aligned with the observation of the carbonic acid salt and the role it might play in maintaining solubility of the catalyst and/or its resting state.

That Complexes I and II might exist in solution led us to consider their relevance to the formation of carbamate, including the potential for Complex I (similar to **37**, Scheme 3) to serve as a nonselective pathway to product; this avenue appears to be relatively slow under catalyst-free conditions (with NIS present) at −20 °C (Table 1, entry 1). Addition of an effective catalyst (Table 1, entries 3–6) chaperones it through a product-forming pathway, by formation of productive chiral complex **C** (i.e. **39**). Successful modulation of reactivity and selectivity can be achieved by tuning the Brønsted basicity of the catalyst further in favor of formation of complex **C** through the use of methoxy substituents. Furthermore, we speculate that in some manner the triflimide salt is favored over a carbamic acid salt of the chiral ligand, as the latter's behavior is characterized by lower yield and ee (Table 1, entry 9).

Critical Determinants of Reproducibility: Ligand Solubility and Water's 'Goldilocks Effect'.

As noted earlier, astonishing differences in conversion were realized over the course of these studies, with low (<40%) yields common, but higher (>60%) yields recorded as well, all using protocols employing ligand **7c**. The varying yields tracked closely with conversion, rather than varying degrees of product selectivity (i.e. competition by alkene iodoamination). Of greatest concern was the inconsistency observed across years of study. Among the countless hypotheses that were tested to address the problem of inconsistency, the ligand purification protocol exhibited the greatest correlation. Oddly, catalyst sourced from crystallized **7c** was associated with low conversions, while purification of **7c** by trituration provided material that led to high conversions. It was also noted that triturated **7c** reliably led to a catalyst that appeared completely soluble in toluene, and gave the least heterogeneous reactions mixtures, the highest conversions, and highest enantioselection.[30] Careful comparison of 7c (^{1}H NMR and LCMS were used to assay purity[31]) resulting from trituration or crystallization revealed no significant differences, arguing against the presence of an impurity that might be responsible for behavioral differences.[31] Ligand **7c** is soluble in dichloromethane and gives visually homogeneous solutions regardless of purification technique. Catalyst batches were routinely prepared by treatment of ligand **7c** with triflimidic acid in dichloromethane, giving the catalyst salt as an amorphous solid after solvent removal. However, catalyst behavior in toluene was different at this point, providing a visually transparent solution when prepared from triturated ligand, but a turbid solution when prepared from recrystallized ligand.

We hypothesized that catalyst speciation was related directly to the method of purification of **7c**. The amorphous nature of the triturated solid ligand (**7c**) likely renders it more readily soluble, whereas the recrystallized catalyst was slow to solubilize. Slow or incomplete dissolution would lead to both low conversion and low reproducibility. This apparent difference in solubility for **7c**·$HNTf_2$ would suggest that the difference in speciation is persistent through the protonation step. Structural support for this hypothesis was sought by growth of a single crystal of **7c** and its analysis by X-ray diffractometry (Figure 2). In the solid state, two molecules interlocked through complementary hydrogen bond donor-acceptor interactions are observed. N-N distances measure 3.022–3.093 Å for each hydrogen

bond donor-acceptor interaction, alongside N-H-N angles ranging from 167–176°. The stilbene diamine N-C-C-N torsional angles measured 62° and 69°. A total of eight molecules of **7c** in the form of interlocked pairs fill the unit cell, accompanied by numerous dichloromethane solvent molecules to give an overall density of 1.348 g/cm^3. Insofar as hydrogen bonding is entirely intradimer in this crystal packing, dissolution to the dimer form may be straightforward, but further solvation to monomeric **7c** might occur less readily.

The tight packing theory to explain differences in catalyst (**7c**·HNTf$_2$) activity was appealing and circumstantially supported by the interlocked dimer observed in crystalline **7c**, from which the acid salt must form. However, from this point we can only speculate that crystalline **7c** leads to **7c**·HNTf$_2$ with distinct speciation compared with that prepared from its triturated counterpart. The observation that stirring efficacy could impact conversion, noted earlier, is likely due to a combination of factors, including reaction heterogeneity and the gas-solution nature of the protocol. [31]

Armed with an understanding of the molecular packing for **7c**, and a hypothesis that its crystalline form translates to catalyst solubility in toluene, we hypothesized that the water effect may also relate to catalyst solubility, aggregation, and/or the solubility of its reactant-bound forms. Without concern for a precise mechanism of its action, we probed the effect of water on conversion and selectivity further to find that yield generally correlated well with conversion.[31] Use of substrate **8a** and otherwise optimized conditions, anhydrous toluene provided the carbamate product in 47% yield. At 44 ppm water in toluene, the yield was slightly enhanced to 52%. At 90 ppm water in toluene, the yield improved further to 75%. Beyond this level, however, the yield dropped to 65% and 57% at 104 and 130 ppm water in toluene, respectively. This trend was charted for numerous substrates, but peak conversion for some (i.e. **9a**) occurred at slightly higher dilution (0.08 M, 6 mol % H_2O). This may be due to the overall solubility of specific components, as they vary from substrate to substrate. Another observation consistent with the catalyst aggregation theory and water additive effect is that the highest enantioselection in each case correlated with the greatest conversion, suggesting that enhanced catalyst availability was responsible for the water effect. At non-optimal water concentrations, the selectivity could either be similar (**8b**) or lower (**9b**).

A unifying hypothesis for the Goldilocks-water effect involves the catalyst solubility under the reaction conditions. We have noted previously that formation of a carbonic acid salt of the catalyst can be detrimental to alcohol→carbonate conversions. In those cases, water is minimized by the use of MS 4A. The situation here is clearly different and ligand-dependent, but formation of a carbonate salt of catalyst **7c**·HNTf$_2$ at low levels may *aid* in catalyst solubilization, or water may exert a beneficial role in maintaining solubility of the catalyst-carbamic acid complex (e.g. **C** in Scheme 4). Regardless of precise mechanism of action for water as an additive in these reactions, its benefit is evident when at a precise level. Water levels in toluene at 90 ppm and the concentration employed here equate to ≈4 mol %, and our observations suggest that water:catalyst ratios are optimal in the 0.5–1:1 range.

Carbamate Transformations.

In addition to the value afforded by a cyclic carbamate synthesis using carbon dioxide as a phosgene surrogate, Scheme 5 details several key product transformations. First, substitution of the neopentyl iodide in **8b** could be achieved in 65% yield using sodium methoxide to deliver **40**, or using sodium azide to furnish a new N-C bond in **41** in 86% yield. Alternatively, iodocarbamate reduction by stannane provided the protected tertiary alcohols **42a** and **42b** in 83% and 82% yield, respectively. These carbamates could be converted to their chiral 1,3-aminoalcohols **43a** and **43b** in 81% and 92% yield when $LiAlH_4$ was employed. The hydride reduction secures the CO_2 carbon as a methyl amine. Tertiary alcohol (*R*)-**43b** was prepared since it has been reported by Rossi to be a selective σ_1 inhibitor and in the more potent enantiomer series.[32]

CONCLUSION

In summary, a tandem CO_2-capture, enantioselective cyclization was developed to prepare 6-membered cyclic carbamates with high enantioselectivity. A metal-free, methoxy-quinoline-derived bifunctional bis(amidine)-triflimidic acid complex resulted from the hypothesis that the Brønsted basicity of the catalyst might be tuned to decouple the Brønsted basic amine substrate and its derived carbamate salt. This catalyst is superior to its congeners by measures of reactivity and selectivity. Measurements of pK_a support the hypothesis that it is a better Brønsted base than its less effective acid catalyst congeners, and NMR studies of species in solution provided evidence for catalyst-substrate complexes believed to be relevant to the catalyst-mediated enantioselective pathway. The ability of **C** to engage a Lewis basic reagent (e.g. NIS) follows from the two postulated complexes of **C** observed by ^{19}F-DOSY NMR. These achievements long stood as a Pyrrhic victory, due to low conversions, until they were correlated to observations that too much – or too little – water, and formation of a crystalline ligand form, led to limited conversion. The use of 90 ppm water as an additive, and ligand trituration, combined to give a highly reproducible protocol for achieving high conversions. The development of this transformation provides a convenient strategic and practical alternative to cyclic carbamates. A series of derivatizations of enantioenriched carbamates illustrate several CO_2-based alternatives to preparations that often involve phosgene and its equivalents.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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18. Alcohol- and amine-based CO2-fixation reactions substantially diverge at this intermediate, as the reactivity (as well as their formation constants) of a carbonic acid-alcohol complex (ref. 8) would be expected to be quite different from a carbamic acid-amine complex. The catalyst orchestrates several functions, and the dominant role may be different due to the difference in functional groups, despite otherwise similar transformations.
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28. In these experiments, the disubstituted amine substrate is an achiral amine base. A stronger base (i.e. TBD, Table 1, entry 2) can promote conversion to carbamate under these conditions.

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30. Selectivity was often affected as well, but this was deemed less informative since reactions with low conversion were more prone to non-catalyzed conversion to racemic product during the reaction quench stage. Product ee was still tracked (see SI).

31. See Supporting Information for data and commentary on procedural details.

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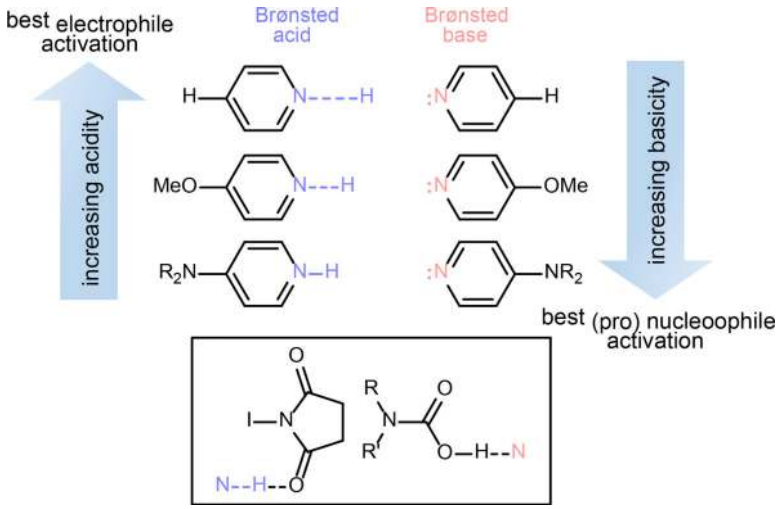


Figure 1.

Diagram of expected substituent effects on hydrogen bond donor/acceptor interactions for bifunctional BAM catalysts.

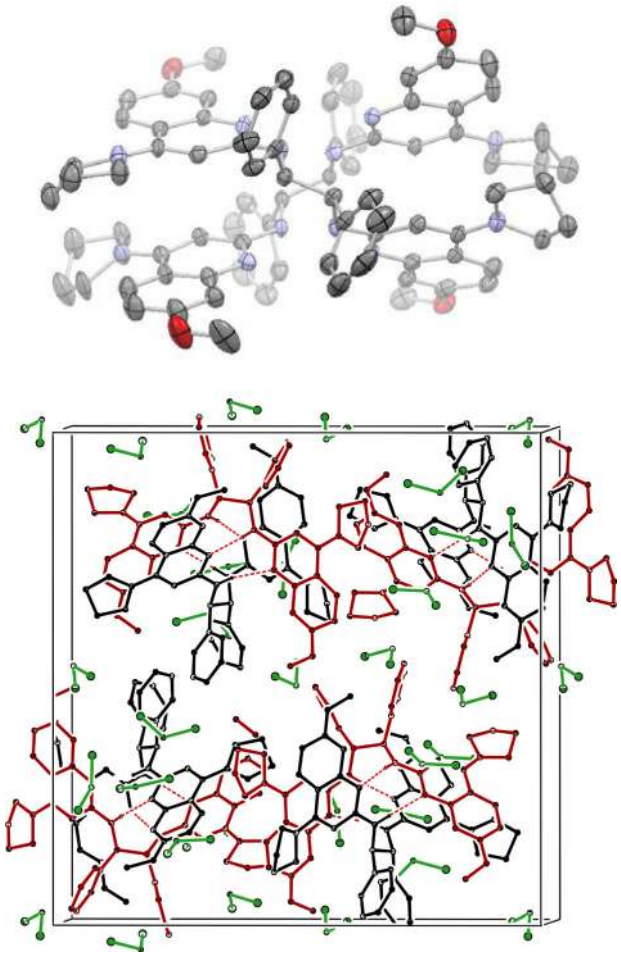
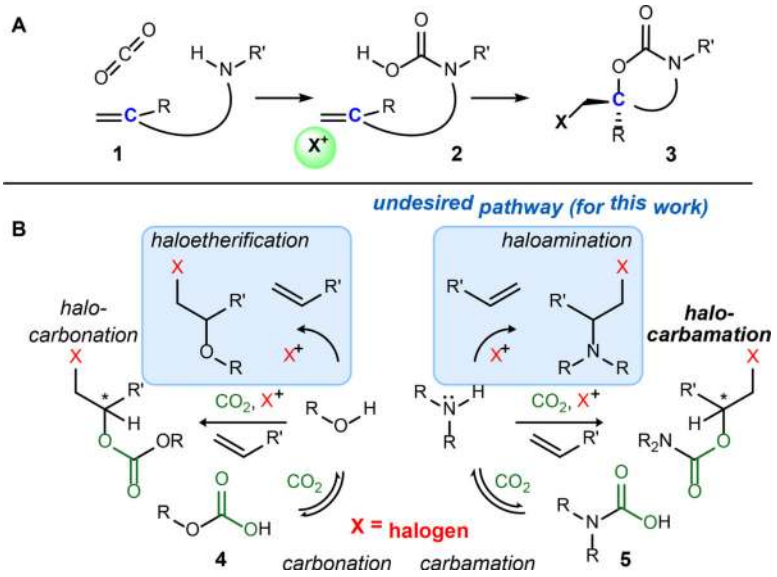


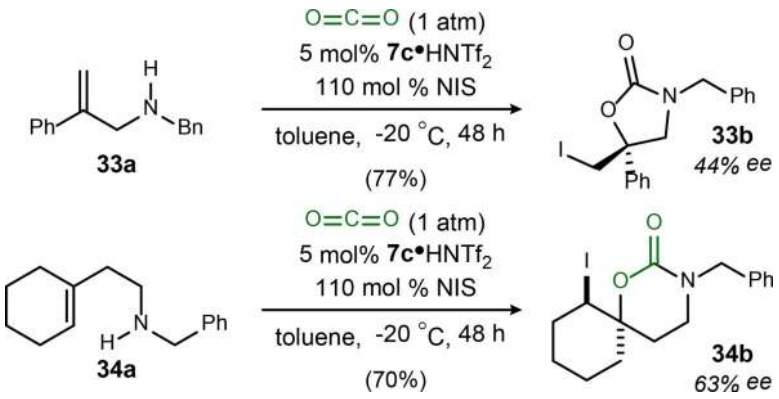
Figure 2.

X-ray diffraction analysis of ^{7}MeO-StilbPBAM (**7c**) illustrating the (top) dimer and (bottom) solvent (CH_2Cl_2 in green)-filled unit cell (individual molecules of the dimer are colored red and black).

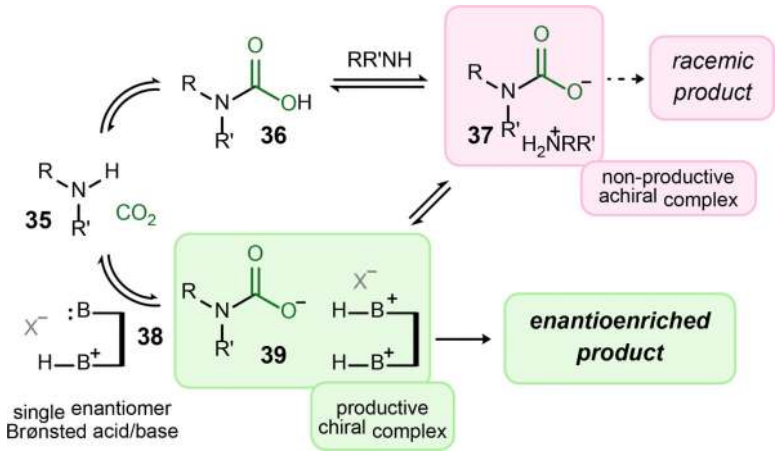


Scheme 1.

An approach to cyclic carbamates through CO_2-capture/electrophile-initiated cyclization (A), and illustration of significant competing reactions among etherification and carbonation pathways for alcohol and amine substrates (B).

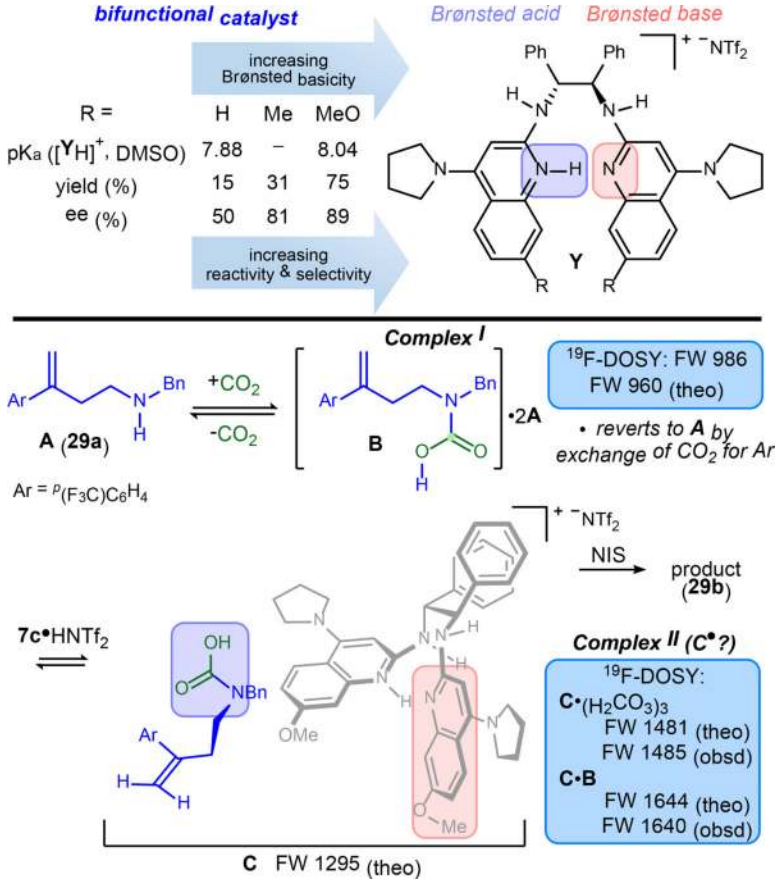


Scheme 2.
Iodocarbamation of an allylic amine and trisubstituted alkene.



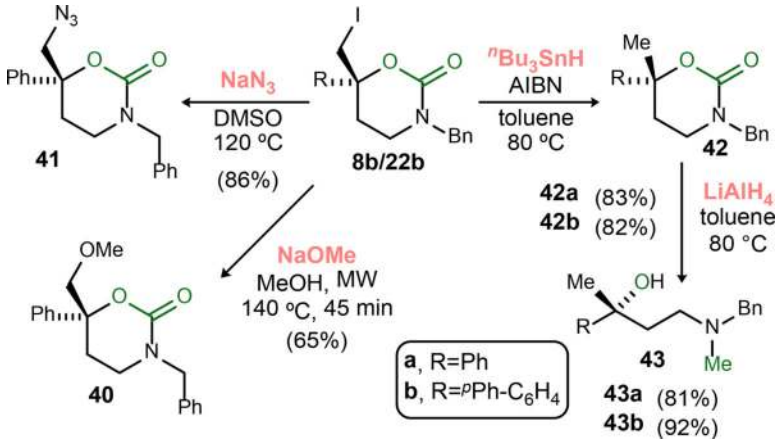
Scheme 3.

Outline of key mechanistic considerations, highlighting ion pairing competition between Brønsted basic substrate and catalyst.



Scheme 4.

Summary of pK_a data, spectroscopic experiments, and key steps in carbon dioxide capture-cyclization reactions using a chiral Brønsted acid/base catalyst.



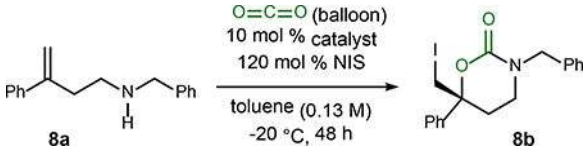
Scheme 5.

Nucleophilic (left) and reductive (right) functionalizations of carbamate **8b**.[a]

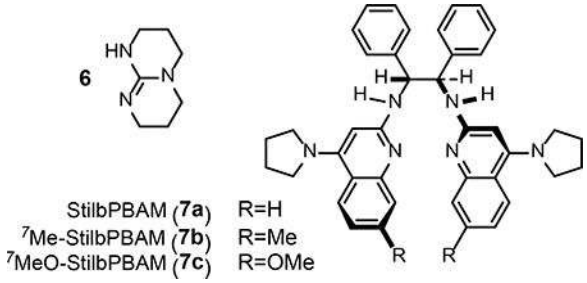
[a]For **22b**→**42b**→**43b**, the enantiomeric series was prepared.

Table 1

Development of an enantioselective CO_2-capture reaction using a homoallylic amine: effect of catalyst basicity/acidity on yield and selectivity.[a]



entry	catalyst	acid	yield (%)	ee (%)
1	none	–	0[b]	n/a
2	TBD (**6**, 1 equiv.)	–	79	n/a
3	StilbPBAM (7**a**)	–	35	30
4	StilbPBAM (7**a**)	$HNTf_2$	15	50
5	^{7}Me-StilbPBAM (7**b**)	$HNTf_2$	31	81
6	^{7}MeO-StilbPBAM (7**c**)	$HNTf_2$	75	89
7	^{7}MeO-StilbPBAM (7**c**)[c]	$HNTf_2$	46	82
8	^{7}MeO-StilbPBAM (7**c**)[d]	$HNTf_2$	23	70
9	^{7}MeO-StilbPBAM (7**c**)	–	44	32



[a] See Supporting Information for general experimental details.

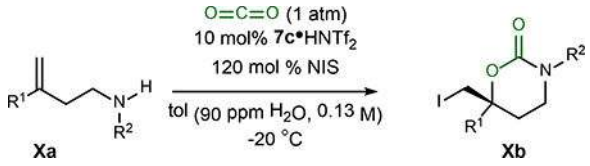
[b] Conversion to a mixture of products (consistent with iodamine formation and alkene iodoamination) is observed at higher temperatures, but is slower at −20 °C.

[c] 0.25 M.

[d] 0.4 M.

Table 2.

Initial scope of an enantioselective CO_2-capture reaction using homoallylic amines.[a]



entry	R^1	X	R^2	yield (%)	ee (%)
1	C_6H_5	**8**	Bn	75	89
2[b,e]	C_6H_5	**9**	^{p}MeBn	72	94
3[b]	C_6H_5	**10**	^{o}MeBn	70	94
4	C_6H_5	**11**	^{m}MeBn	76	88
5[c]	C_6H_5	**12**	^{p}MeOBn	64	73
6	C_6H_5	**13**	^{m}MeOBn	85	90
7	C_6H_5	**14**	^{p}ClBn	75	88
8	C_6H_5	**15**	^{p}FBn	60	91
9[b]	C_6H_5	**16**	^{n}Bu	59	81
10[b]	C_6H_5	**17**	^{n}Pr	55	40
11	$^{p}MeC_6H_4$	**18**	Bn	72	92
12[b]	$^{m}MeC_6H_4$	**19**	Bn	73	92
13[b]	$^{o}MeC_6H_4$	**20**	Bn	-	-
14	^{2}Np	**21**	Bn	72	93
15[e]	$^{p}PhC_6H_4$	**22**	Bn	77	91
16	$^{p}MeOC_6H_4$	**23**	Bn	60	85
17	$^{p}((CH_3)_3C)C_6H_4$	**24**	Bn	59	91
18	$^{m}MeOC_6H_4$	**25**	Bn	75	92
19	$^{p}FC_6H_4$	**26**	Bn	77	94
20[b]	$^{m}ClC_6H_4$	**27**	Bn	71	92
21[b]	$^{m}FC_6H_4$	**28**	Bn	62	85
22[b,f]	$^{p}CF_3C_6H_4$	**29**	Bn	67	95
23[b]	Me	**30**	Bn	77	41
24	Cy	**31**	Bn	59	60
25[b]	H	**32**	Bn	43	13

[a] Enantiomeric excess (ee) determined by HPLC using a chiral stationary phase. Reactions are 0.13 M in toluene. Isolated yields are listed. See SI for complete experimental details.

[b] Reaction time = 120 h.

[c] Reaction time = 72 h.

[d] Reaction concentration = 0.08 M.

[e] (*S,S*)-**7c** was used instead of (*R,R*).

[f] Absolute configuration for **29b** assigned using X-ray analysis, remaining examples assigned by analogy.