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RESEARCH ARTICLE

Ga-catalyzed Temperature-dependent Oxazolidinone/Piperazine Synthesis from Phenyl Aziridines Involving a Divergent Ligand-assisted Mechanism

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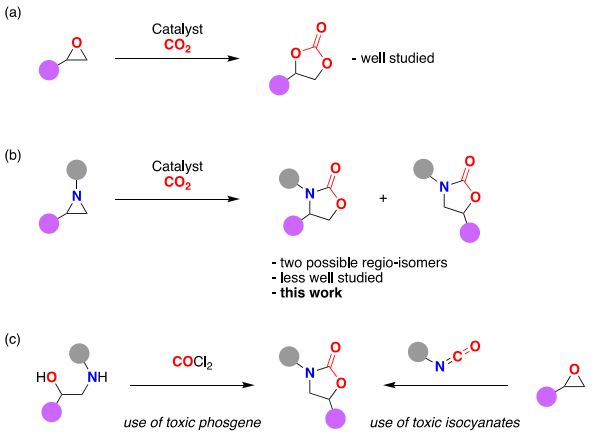
Supporting information for this article is given via a link at the end of the document.

Abstract: Application of a binary Ga-based catalyst system for the coupling of CO_2 and aziridines to form oxazolidinones is presented. It has been possible to optimize the catalyst system for the selective formation of a single regioisomer, in excellent yield, under relatively mild reaction conditions. The optimized catalyst system has been successfully applied to a range of substituted aziridines derived from styrene oxide. It has been observed that aziridines bearing two aromatic substituents result in piperazine formation through an unexpected dimerization reaction. These piperazine products can be selectively formed in the absence of CO_2 or are favored at lower reaction temperatures. A detailed DFT study into the reaction mechanism for the formation of both products has been carried out and an unusual ligand assistance in the case of oxazolidinone synthesis has been identified. More specifically, this ligand interaction promotes the initial ring-opening of the aziridine and this work presents the first fully elucidated mechanism involving this intermediate.

Introduction

Carbon dioxide (CO_2) is a highly attractive chemical feedstock and C_1 source as a result of its wide availability/low price, and also its relative non-toxicity. However, CO_2 is a rather inert molecule and therefore requires high energy consumption for its activation. There are several possible approaches to resolving this issue in order to provide processes for its application under less harsh reaction conditions; (i) react the CO_2 with high energy molecules, such as, epoxides which have high ring-strain, (ii) the use of catalysts, or (iii) combination of both of these two approaches, as has been successfully achieved in the field of cyclic carbonate synthesis. The synthesis of cyclic carbonates through the atom-efficient coupling of CO_2 and epoxides has attracted significant attention (Scheme 1a) and a large number of catalyst systems have been developed.[1] These cyclic products have found use as electrolytes in Li-ion batteries and monomers for polymer synthesis, amongst other applications. Another family of high energy molecules, analogous to epoxides, are aziridines (Scheme 1b). These compounds are three-membered heterocycles bearing a N-atom (which may be substituted) and exhibit significant ring-strain, in similarity to epoxides.[2] It has already been demonstrated that these aziridines can be reacted with CO_2 or carbamates to form oxazolidinones with a range of substituents, resulting in a diverse group of important heterocyclic products.[3-5] Like cyclic carbonates, these compounds have also found a range of applications, with particular use as scaffolds in drug molecules[6] and as chiral auxiliaries.[7] It should be noted that this approach to the synthesis of oxazolidinones is an attractive way to replace traditional methods for their synthesis, which include reactions of amino alcohols with toxic phosgene[8] or epoxides with toxic isocyanates (Scheme 1c).[9]

One of the key challenges in the synthesis of oxazolidinones from CO_2 and aziridines is that two distinct regioisomers are possible (Scheme 1b). Selectivity towards a single regioisomer



Scheme 1. (a) Synthesis of cyclic carbonates from CO_2 and epoxides. (b) Synthesis of the two possible regioisomers of oxazolidinones from CO_2 and aziridines. (c) Less-favourable routes for the synthesis of oxazolidinones.

can be achieved through the careful optimization of the reaction conditions. Recently, we have developed a Ga-based catalyst which we found to be highly active for the formation of cyclic carbonates from CO_2 and epoxides[10] and we therefore decided to evaluate if it could also be applied to the coupling of CO_2 and aziridines. This report presents the results obtained from this study focusing on the use of aziridines which are readily prepared from amines and styrene oxide.

Results and Discussion

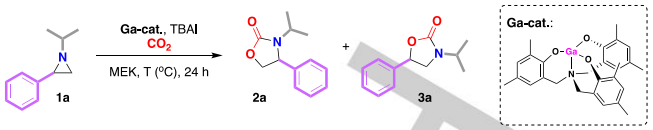
Initially it was necessary to prepare the styrene oxide-derived aziridines, **1a**-**i**. This was achieved through a two-step process as has been previously described by He and co-workers (see Supporting Information; Scheme S1).[11] Firstly, the styrene oxide was reacted with a primary amine in the presence of a catalytic amount of LiBr forming an intermediate amino alcohol.[12] Thereafter, the desired aziridine was formed by reaction with Br_2, PPh_3 and Et_3N in MeCN.

With the styrene oxide-derived aziridines in hand, we embarked on an optimisation of the catalytic cycloaddition with CO_2 to form the oxazolidinone products (Table 1). For this we applied our previously reported Ga-based catalyst system that was shown to be highly active for the corresponding cycloaddition of epoxides and CO_2 to form cyclic carbonates.[10,13] We selected aziridine **1a** for this optimisation as it presents a simple structure. As mentioned above, the cycloaddition of aziridines and CO_2 is more complex than that of epoxides and CO_2 due the fact that two distinct oxazolidinone regioisomers can be formed (in this work denoted as **2** and **3**). We sought to optimise the reaction for the selective synthesis of oxazolidinone regioisomer **3a** from aziridine **1a**. This regioisomer is formed as there is preferential attack at the benzylic position of styrene oxide (electronic factors are dominant over steric effects in this substrate). This result has already been studied and explained for the analogous cyclic carbonate formation by Kleij/Bo and co-workers.[14] This regioisomer is of interest as it is the predominant regioisomer present in the structure of many drug molecules.[6]

Initially a binary catalyst system loading of 1.0 mol% Ga-catalyst and 2.0 mol% tetrabutylammonium iodide (TBAI) was employed at 90, 80 and 70 °C (Table 1, entries 1, 2 and 3, respectively). These experiments provided yields of greater than 90 %, although small amounts of the undesired regioisomer, **2a**, were obtained. From these results it can be seen that decreasing the temperature results in improved yield and selectivity towards the desired oxazolidinone regioisomer, **3a**. Further reduction in the temperature to 60 °C resulted in a yield of >99 % and excellent selectivity (>99 %) towards the desired product (Table 1, entry 4). Decrease in reaction time to 16 hours resulted in a slightly lower yield of 96 %, whilst maintaining the excellent selectivity towards **3a** (Table 1, entry 5). At this point, reduction in binary catalyst system loading was also studied (Table 1, entries 6, 7 and 8).

Reduction of the Ga-catalyst loading to 0.5 mol%, whilst maintaining the TBAI co-catalyst loading furnished quantitative yield and excellent selectivity (Table 1, entry 6). Further reduction of the TBAI co-catalyst loading to 1.0 mol% with a Ga-catalyst loading of 0.5 mol% resulted in a decrease in the yield to 93 % (Table 1, entry 7). A similar outcome was obtained when the Ga-catalyst loading was reduced to 0.25 mol% at a TBAI co-catalyst loading of 2.0 mol% (Table 1, entry 8). The reaction was also

Table 1. Reaction condition optimization for the selective formation of regioisomer **3a** from **1a** using a Ga-based catalyst system.[a]



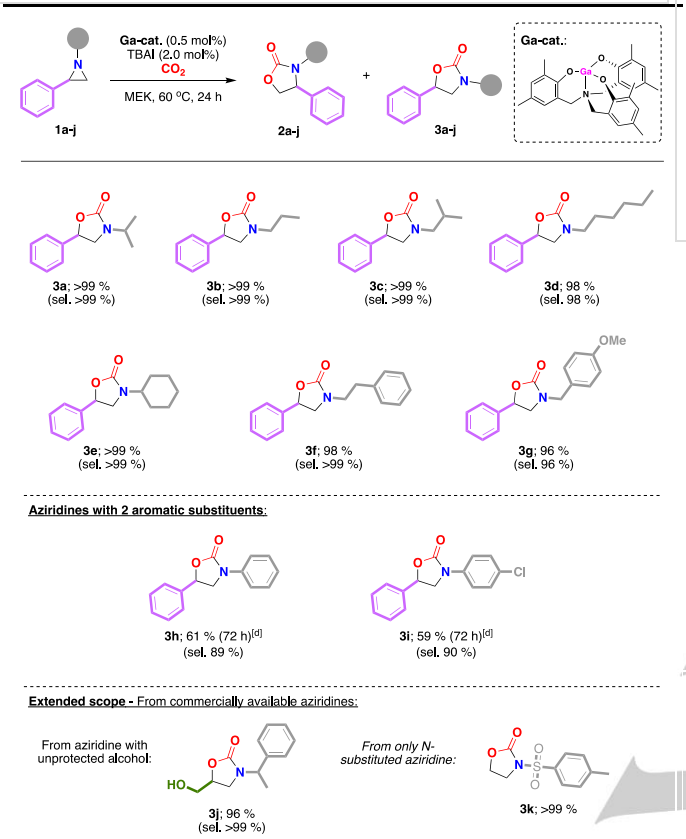
Entry	Ga-catalyst [mol%]	TBAI [mol%]	T [°C]	Yield [%][b]	Selectivity **2a**/**3a**[c]
1	1.0	2.0	90	91	9/91
2	1.0	2.0	80	92	8/92
3	1.0	2.0	70	98	2/98
4	1.0	2.0	60	>99	<1/>99
5[d]	1.0	2.0	60	96	<1/>99
6	**0.5**	**2.0**	**60**	**>99**	**<1/>99**
7	0.5	1.0	60	93	<1/>99
8	0.25	2.0	60	91	<1/>99
9	0.5	-	60	20	<1/>99
10	-	2.0	60	27	<1/>99
11	0.5	2.0 (TBAB)	60	85	<1/>99

[a] General conditions: **1a** (1.0 g, 6.2 mmol), Ga-catalyst, TBAI, 24 h, temperature, 1 mL MEK, CO_2 (15 bar) in a sealed 50 mL high-pressure reactor. [b] Yield calculated from the ^{1}H NMR spectra of the crude reaction mixture, with mesitylene as internal standard. [c] Calculated from the crude ^{1}H NMR spectra. [d] Reaction time of 16 h. TBAI = *tert*-butylammonium iodide, TBAB = *tert*-butylammonium bromide, MEK = 2-butanone.

studied in the absence of TBAI co-catalyst (Table 1, entry 9) and in the absence of Ga-catalyst (Table 1, entry 10). In both these cases appreciable amounts of product **3a** were obtained, indicating that (i) the TBAI co-catalyst can promote the reaction and (ii) that there appears to be some reaction with the catalyst alone. This latter observation will be reasoned in the DFT study later in this report. Finally, replacement of TBAI with tetrabutylammonium bromide (TBAB) resulted in an appreciable decrease in the yield to 85 %, although maintaining the complete selectivity for oxazolidinone **3a** (Table 1, entry 11). As a result of this study, the optimal reaction conditions were found to be 0.5 mol% Ga-catalyst, 2.0 mol% TBAI, 60 °C for 24 hours, whereby >99 % yield was obtained with an excellent selectivity towards the desired regioisomer, **3a**.

With the optimized reaction conditions in hand, we then set out to explore the substrate scope (Table 2) by converting all the aziridines previously prepared (Scheme 2; **1a**-**i**). It was found that all the aziridines derived from styrene oxide and aliphatic amines (N-alkyl aziridines **3a**-**g**) could be readily converted in quantitative or close to quantitative yields. These aziridines were also converted to the corresponding oxazolidinone products with excellent selectivity towards the desired regioisomer **3**. In contrast, aziridines derived from styrene oxide and anilines could not be smoothly converted (Table 2, compounds **3h** and **3i**). In these cases, incomplete conversion of the starting aziridine was observed and a significant amount of a piperazine side product was detected (other remaining products in the crude reaction mixture).[15] Furthermore, selectivities towards the regioisomer **3**

Table 2. Substrate scope using the substituted aziridines prepared in Scheme 1 and the Ga-based catalyst system from Table 1.[a,b,c]

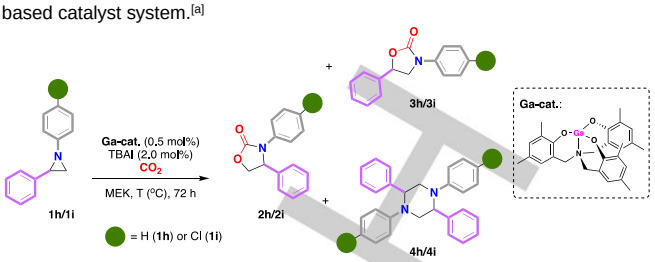


[a] Reaction conditions (unless otherwise stated): **1** (6.2 mmol), Ga-catalyst (0.5 mol%), TBAI (2.0 mol%), 24 h, 60 °C, 1 mL MEK, CO_2 (15 bar) in a sealed 50 mL high-pressure reactor. [b] Yields are NMR yields calculated from the ^{1}H NMR of the crude reaction mixture, using mesitylene as internal standard. [c] Selectivity refers to formation of regioisomer **3** *vs.* **2** and was calculated from the ^{1}H NMR spectra of the crude reaction mixture. [d] A mixture of products was formed in addition to **2** and **3**, with the rest found to be a piperazine (**4**).

were only around 90 %, compared to the general >99 % for the previously mentioned N-alkyl aziridines. The piperazines are likely to be formed from a dimerization-type reaction of two aziridines and were not observed in the products starting from **1a-g**. As a result, it appears that aziridines containing two aromatic groups directly attached to the aziridine display a more complex reactivity. The mechanism of this dimerization reaction is fully elucidated later in this report. Finally, two commercially available aziridines, one with a free alcohol group (**2j**) and one bearing a tosyl group and no other substituents (**2k**) were also studied and could be readily converted in high yield and selectivity, with no detection of any piperazine or other side products.

We then sought to further study the formation of the piperazine side products from aziridines **1h/i** (Table 3). It should be noted that we have only observed one regioisomer of these piperazines in our product mixtures. First, we studied the effect of change in reaction temperature (Table 3). Increasing the temperature from 60 to 100 °C in both cases resulted in a decrease in the amount of piperazine product and an increase in the formation of oxazolidinones **3h** and **3i** (Table 3, entries 1, 2, 7 and 8). This allowed for the obtention of improved yields of oxazolidinones **3h/i**. Indeed, it appears that both of these aziridines react in a very similar fashion, with little effect of the substituent of the aromatic group attached to the nitrogen atom of

Table 3. Further study into the formation of products from **1h** and **1i** using a Ga-based catalyst system.[a]



Entry	Substrate	T [°C]	Yield of **2+3** [%][b]	Selectivity **2/3**[b]	Yield of **4** [%][b]
1	**1h**	60	61	11/89	29
2	**1h**	100	75	4/96	16
3	**1h**	45[c]	-	-	74
4[d]	**1h**	**60**	**-**	**-**	**81**
7	**1i**	60	59	10/90	31
8	**1i**	100	70	5/95	13
9[d]	**1i**	**60**	**-**	**-**	**82**

[a] General conditions: **1** (6.2 mmol), Ga-catalyst (0.5 mol%, TBAI (2.0 mol%), 72 h, temperature, 1 mL MEK, CO_2 (15 bar) in a sealed 50 mL high-pressure reactor. [b] Yield calculated from the ^{1}H NMR spectra of the crude reaction mixture, with mesitylene as internal standard. [c] reaction time = 48 h. [d] In the absence of CO_2, with a reaction time = 24 h.

the aziridine. With aziridine **1h**, we also attempted the reaction at 45 °C (Table 3, entry 3). After 48 hours, only piperazine product was observed in 74 % yield (aliquots taken from this reaction during this time did not contain oxazolidinone product, indicating that the piperazine is not produced by further reaction of an intermediate oxazolidinone). If the reaction of **1h** is carried out in the absence of CO_2 at 60 °C for 24 h, an 81 % yield of piperazine **4h** can be obtained with no other products (Table 3, entry 4). The reaction conditions for the clean preparation of piperazine **4h** from **1h** were then transferred to aziridine **1i** (Table 4). Reaction of this aziridine in the absence of CO_2 furnished a yield of 82 % for the desired piperazine product, with no other side products observed.

With these intriguing experimental results in hand, we sought to gain further insight through a detailed DFT study into the operative reaction mechanisms for the formation of both the oxazolidinone and piperazine products. Given the significant body of literature concerning the formation of cyclic carbonates from epoxides and CO_2, surprisingly, there are comparatively fewer mechanistic studies into the analogous aziridine reaction forming oxazolidinones. In the context of DFT studies, Ding and co-workers have explored the use of a range of HKUST-1 catalysts and fully studied the mechanisms.[16] Further to this, both Manca/Gallo and co-workers and Caselli and co-workers have studied metal-containing and metal-free catalysts, providing full DFT studies into the operative mechanisms.[3b,c,d,g] All of these reports describe an overall related mechanism to those expected from an epoxide/CO_2 cycloaddition reaction, although CO_2 activation by the N of the aziridine is implicated in some of these examples. Meanwhile, Baik/Nguyen and co-workers have presented the use of Cr-Salphen compounds as catalysts, proposing a reaction mechanism which is a little distinct from that of the corresponding reaction with epoxides.[17] We have recently

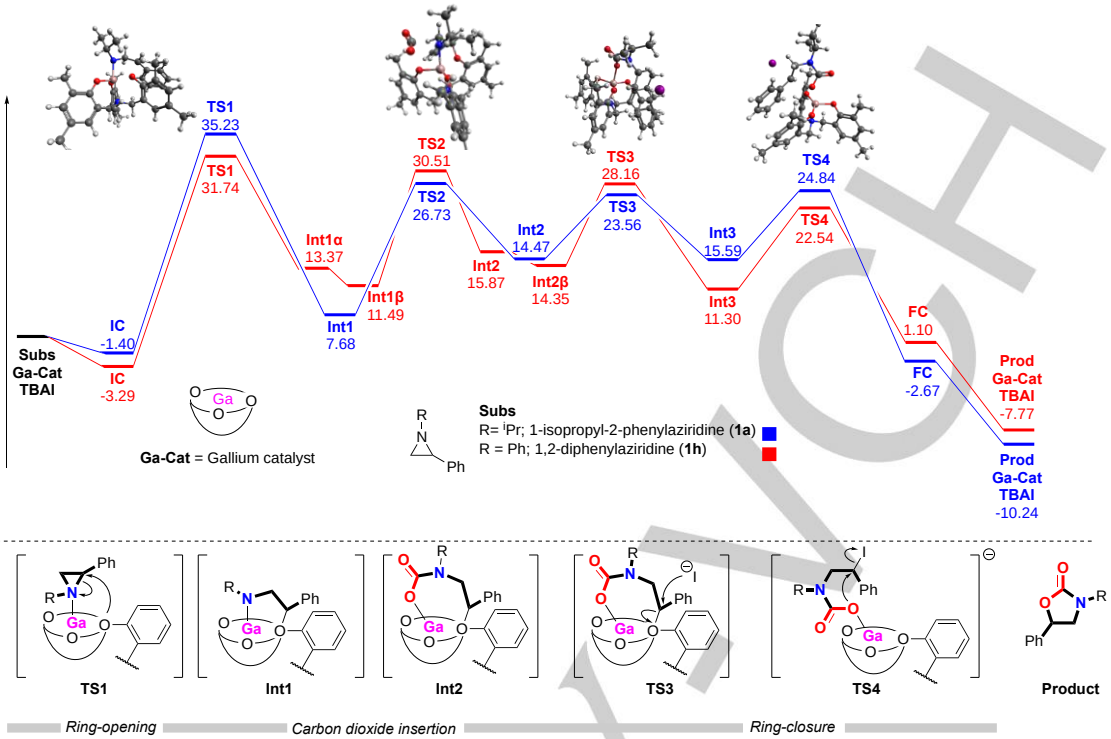


Figure 1. Calculated solvation optimised free energy surface ($\Delta G_{333\ K}$) at RIJCOSX-PWPB95-D3BJ/def2-TZVPP//RI-B97-D3/def2-SVP level of theory, for the synthesis of oxazolidinones **3a** and **3h** from CO_2 and **1a** (Blue) and **1h** (Red) respectively, catalysed by the Ga-catalyst and TBAI.

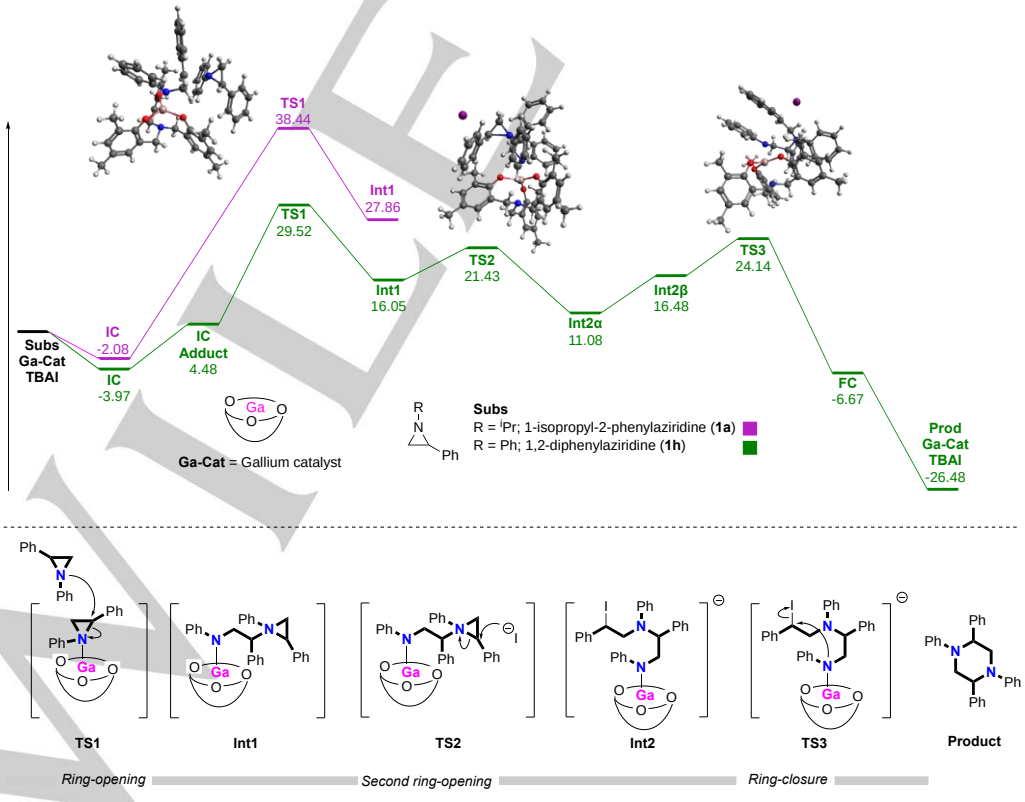


Figure 2. Calculated solvation optimised free energy surface ($\Delta G_{318\ K}$) at RIJCOSX-PWPB95-D3BJ/def2-TZVPP//RI-B97-D3/def2-SVP level of theory, for the synthesis of piperazine **4h** from CO_2 and **1h** (Green), catalysed by the Ga-catalyst and TBAI. Barrier for substrate assisted ring-opening of **1a** (Purple) is shown and is energetically inaccessible.

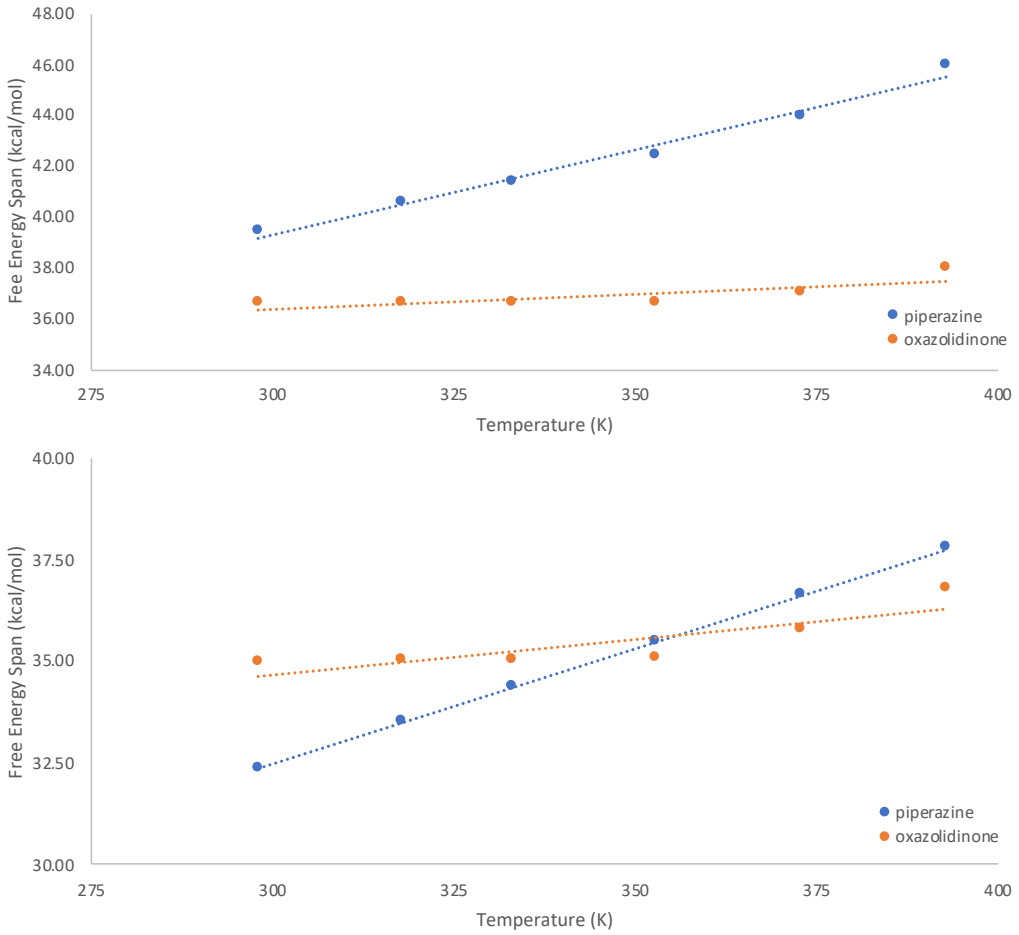


Figure 3. Temperature dependence of piperazine (blue) *vs*. oxazolidinone (orange) formation pathways for **1a** (top) and **1h** (bottom), showing free energy span ($\Delta G^{\ddagger}$) as a function of temperature.

reported the mechanism for the epoxide reaction with the Ga-catalyst used in this study,[10] and we initially assumed a straightforward transfer of reactivity and mechanism to the aziridine substrates used in this work. Following the expected mechanism, the coupling of the Ga-catalyst and aziridine should form the coordinated species (substrate-catalyst), which would then undergo a halide assisted ring opening step to form a Ga-amine intermediate. To our surprise the **Int1** structure was prohibitively high in energy (29.7 kcal mol^{-1} for substrate **1h**, and could not be located for substrate **1a**), and despite exhaustive investigation, the connecting **TS1** could not be identified. At this point, alternative adducts, and intermediates as proposed by Baik/Nguyen[17] were also investigated, but these also proved unsuccessful for this binary Ga-catalyst system. We then turned our attention to alternative approaches for the ring-opening of the aziridine. Previous work by Kleij/Licini and co-workers using a related V-aminotrisphenolate complex proposed that one of the phenolate moieties promotes the ring-opening of an epoxide for the synthesis of cyclic carbonates.[18] This approach to initial ring-opening was found to be favorable for this aziridine reaction with the Ga-catalyst and agrees with the experimental observation that moderate product yield can be obtained in the absence of co-catalyst, indicating that there must be an alternative to the standard nucleophile mediated (halide) ring-opening step.

The full calculated mechanism for conversion of substrate **1a** at 333K is shown in Figure 1 (Blue). In full, from **IC**, dissociation of one of the phenolate moieties provides the nucleophilic site from which to activate the aziridine ring. This attack occurs at the more sterically hindered carbon, in agreement with selectivity obtained in the experimental part of this work. The ring-opened aziridine bridges the Ga and phenolate moiety of the ligand, allowing for reduced steric hinderance around the Ga atom. This intermediate (**Int1**) has an energy of 7.98 kcal mol^{-1}, which is significantly more stable than intermediates of the corresponding initially studied approach which was analogous to the cyclic carbonate mechanism. The transition state connecting **IC** and **Int1** is located at 35.23 kcal mol^{-1}, which although high in energy agrees with the elevated temperatures and times required for the reaction. This ligand-assisted ring-opening step is determined to be the energy span determining transition state. A direct comparison to the V=O catalyst reported by Kleij/Licini is provided in the Supporting Information (Figure S80, page S51). From **Int1** CO_2 then inserts into the Ga-N bond, forming **Int2**, with an energy barrier at 26.73 kcal mol^{-1}. Thereafter, from **Int2**, the iodide

nucleophile from TBAI, attacks the benzylic carbon, in an SN_2 type reaction step with a barrier at 23.56 kcal mol^{-1}, displacing the oxygen of the phenolate moiety, allowing for reformation of the Ga-O bond and the original catalyst structure. Finally, **Int3** can then undergo ring-closure, *via* **TS3** forming the oxazolidinone product releasing the iodide at **FC**. Exergonic dissociation of the product regenerates the catalyst, allowing for continued catalytic turnover, with an overall reaction free energy of -10.24 kcal mol^{-1}. From **Int3** this pathway is equivalent to the reaction between epoxides and CO_2. With this mechanistic approach now established, we returned to studies with substrate **1h**. The operative mechanism for formation of the equivalent oxazolidinone product (Figure 1, Red) follows a very similar pathway, albeit with minor conformation changes at **Int1α/β** and **Int2α/β** to account for non-covalent interactions between the two phenyl rings. Energetically the pathways for **1a** and **1h** are similar; at 333 K the ligand cooperative ring-opening step has rate determining energy spans of 36.63 and 35.03 kcal mol^{-1} respectively. To the best of our knowledge, this is the first full mechanistic elucidation involving a ligand assisted pathway in for this reaction. A comparison of the **aziridine-CO_2** adduct associative mechanism as proposed by Baik/Nguyen,[17] with the ligand cooperative mechanism proposed in this work is shown in the Support Information (Figure S79, page S50), for 1,2-diphenylaziridine at 333 K.

With the reaction mechanisms for the oxazolidinone formation understood, we then turned our attention to the more complex piperazine reaction. The operative mechanism for the formation of the piperazine product from **1h** at 318 K is shown in Figure 2 (Green). Interaction of the Ga-catalyst and **1h** furnishes **IC**, and from here a second molecule of **1h** can form an adduct and act as a nucleophile, activating the first aziridine ring to form **Int1**. This step occurs with a barrier of 33.49 kcal mol^{-1}, from **IC** which is the energy span determining intermediate (at -3.97 kcal mol^{-1}). From **Int1**, the iodide-assisted ring-opening of the second aziridine ring occurs with a barrier at 21.43 kcal mol^{-1} leading to **Int2α**. Conformational change and subsequent ring-closure, *via* **TS3** at 24.14 kcal mol^{-1}, forms the observed piperazine product, **4h**, and releases the iodide nucleophile. Thereafter, dissociation of **4h** from the FC intermediate regenerates the catalyst, with an overall reaction free energy of -26.48 kcal mol^{-1}. Alternatively, it could be foreseen how at **Int1** an additional molecule of **1h** could again act as a nucleophile leading to the formation of a polymeric chain. However, the barrier for this polymer forming step is less favorable at 3.0 kcal mol^{-1} higher in energy than that of the iodide assisted ring-opening of **Int1**, agreeing with the observed product formation and highlighting the important role of TBAI in the reaction. For substrate **1a**, the equivalent **TS1** leading to the piperazine product has a barrier of 40.52 kcal mol^{-1} at 318 K (Figure 2 Purple), making it energetically inaccessible and agreeing with the selectivity observed experimentally.

To further understand the temperature dependence of the reaction with substrate **1h**, we recalculated the thermal and entropic contributions to the free energy for each component of the competing reaction mechanisms. Given the observed product temperature dependence, subtle differences in barrier heights would be expected, with the preferential route changing upon increasing temperature. Based on the results in Table 3, it may be expected that, at 318 K the piperazine pathway should be favored, whereas at 373 K the oxazolidinone route should be favored; albeit with an energetically accessible $\Delta\Delta G^{\ddagger}$ accounting for the observed product selectivity in the region of 4:1 (Table 3, Entry 2). In addition, for **1a** the oxazolidinone route should be the most favorable at all temperatures as the piperazine product was not observed under any of the studied reaction conditions. Figure 3 shows the variation in free energy span upon increasing temperature from 298 K to 393 K. For substrate **1a**, it is clear the piperazine formation energy span is consistently larger, across the entire temperature range, compared to the observed oxazolidinone forming reaction. Whereas for substrate **1h**, at lower temperatures the piperazine route is favored, and then product selectivity switches to the oxazolidinone pathway as the temperature increases. This general trend agrees well with the experimental observations. The calculated $\Delta\Delta G^{\ddagger}$ at 318 K is 1.51 kcal mol^{-1} in favor of the piperazine product, whilst at 373 K it is 0.85 kcal mol^{-1} in favor of the oxazolidinone product. These values equate to a 20:80 and 60:40 (oxazolidinone:piperazine product ratio), respectively, in reasonable agreement, albeit a slight underestimation, of the experimental observations in this study. The temperature dependence can be explained by the different molecularity of the energy span determining step, whereby the bimolecular step for the piperazine pathway observes a greater entropic penalty as the temperature increases, making it less favorable at higher temperature.

Conclusion

In conclusion, we have demonstrated that a Ga-based catalyst system is capable of promoting the addition of aziridines and CO_2 to selectively form a single oxazolidinone regioisomer. To the best of our knowledge, this is the first report of a Ga-based catalyst system able to promote this conversion. Meanwhile, we have observed that aziridines containing two aromatic substituents (those derived from styrene oxide and aniline) do not cleanly form the desired oxazolidinone products, instead, furnishing mixtures of oxazolidinones and piperazines. We have been able to selectively form these piperazines by optimization of the reaction conditions (in the absence of CO_2 or at lower temperature). We will report a full synthetic investigation into these piperazine molecules in due course. In addition to the experimental results, we have also performed a full DFT study into the reaction mechanism and discovered a ligand assisted ring-opening step. We have compared the mechanisms for the oxazolidinone and piperazine synthesis and accounted for the reasons in the selectivities by the different substrates and the different temperatures.

Experimental Section

General Procedure for the Cycloaddition of CO_2 and Aziridines

A high-pressure reactor, equipped with a stirrer bar, was charged with Ga-catalyst, TBAI, MEK and aziridine. The reactor was then filled with CO_2. The reactor was heated and left stirring for the required time. At the end of the reaction the reactor was cooled and slowly vented before a known amount of mesitylene was added. An aliquot was then removed and dissolved in $CDCl_3$. The percentage conversion and NMR yield of the reaction was obtained from the ^{1}H NMR spectrum of this crude sample using the mesitylene as internal standard and compared to published spectra. In the case of products which required isolation, the crude reaction mixture was purified using column chromatography (hexane/ethyl acetate).

General Procedure for the Selective Synthesis of Piperazines from Aziridines (Absence of CO_2)

An ampoule, equipped with a stirrer bar, was charged with Ga-catalyst, TBAI, MEK and aziridine. The ampoule was sealed, and the reaction was then heated and left stirring for 24 hours at 60 °C. At the end of the reaction the ampoule was cooled before a known amount of mesitylene was added. An aliquot was then removed and dissolved in $CDCl_3$. The percentage conversion and NMR yield of the reaction was obtained from the ^1H NMR spectrum of this crude sample using the mesitylene as internal standard. In the case of product isolation, the MEK was removed under vacuum and the piperazines were then obtained by purification by column chromatography (hexane/ethyl acetate).

Computational Study Information

All DFT calculations undertaken using the ORCA 4.2.1 computational software.[19,20] Solvation optimizations and analytical frequency calculations were performed at the RI-B97-D3/def2-SVP (def2-TZVPP on the Ga metal centre) level of theory.[21-24] Final single-point energies and solvation corrections were calculated at RIJCOSX-PWPB95/def2-TZVPP level of theory.[23-26] All solvation corrections were calculated using the CPCM model with a dielectric constant value of 18.5 for MEK.[27] Analytical frequencies were calculated for inclusion of the Zero Point Energy (ZPE) correction and entropic contributions to the free energy term as well as confirming all intermediate were true with no imaginary modes and all transition states had the correct critical frequency of decomposition. Thermochemical parameters were evaluated across a temperature range from 298 K to 393 K, in 20 K increments, at a standard pressure (1.0 atm). Numerical precision integration grids were increased beyond the default settings, to Grid4 for the SCF step and Grid5 for the final energy evaluation. Concentration correction, to account for the low catalyst loading was applied as a free energy correction based on the Van't Hoff reaction quotient equation RT ln(Q)[28] where Q accounts for the 200-fold concentration gradient between the substrate and the catalyst. Graphical visualization and structural analysis performed from the DFT calculations using Avogadro 1.2.0.[29]

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Keywords: Gallium catalysis • Aziridines • Carbon dioxide • Oxazolidinones • Piperazines • DFT study

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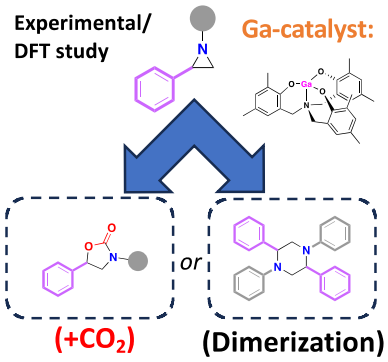

A Ga-based catalyst system for the regioselective coupling of CO_2 and aziridines to form oxazolidinones is presented. Unexpectedly, aziridines bearing two aromatic substituents result in piperazine formation. A detailed DFT study into the reaction mechanism of formation of both products is described, where an unusual ligand assistance during the initial ring-opening of the aziridine has been found.

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