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# Guanidine-Catalyzed Reductive Amination of Carbon Dioxide with Silanes: Switching between Pathways and Suppressing Catalyst Deactivation

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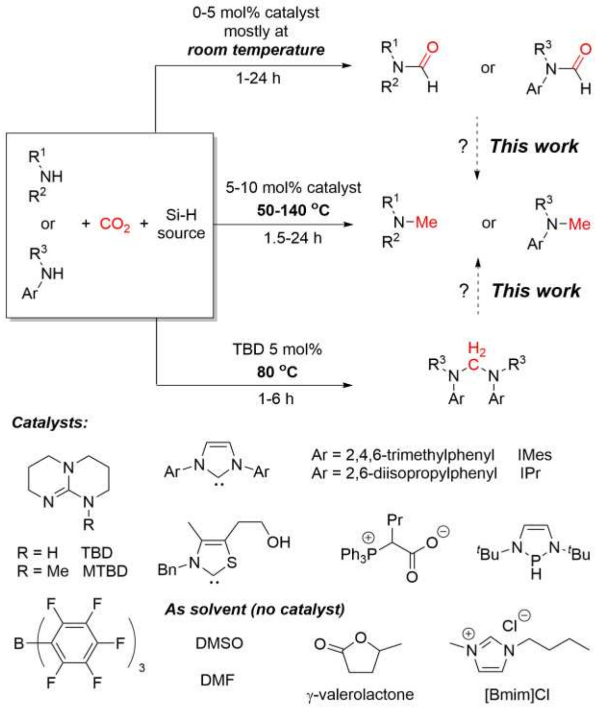
**ABSTRACT:** A mechanistic investigation into the guanidine catalyzed reductive amination of $CO_2$, using a combination of $^1H$, $^{29}Si$ NMR, FT-IR, MS and GC profiling, is reported. Inexpensive and readily available *N,N,N',N'*-tetramethylguanidine (TMG) was found to be an equally effective catalyst compared to more elaborate cyclic guanidines. Different catalytic pathways to formamide **2**, aminal **4** and *N*-methylamine **3**, were identified. A pathway to formamide product **2** dominates at 23 °C. Increasing the reaction temperature to 60 °C enables a competitive, higher energy pathway to **4** and **3**, which requires direct reduction of $CO_2$ with $PhSiH_3$ to formoxysilane **E**. Reduction of aminal **4**, in the presence of $CO_2$ and the catalyst, led to formation of a 1 : 1 ratio of **2** and **3**. The catalyst itself can be formylated under the reaction conditions, resulting in its deactivation. Thus, alkylated TMGs were found to be more stable and more active catalysts than TMG, leading to a successful organocatalyzed reductive functionalization of $CO_2$ with silane at 0.1 mol% catalyst loading (TON = 805 and TOF = 33.5 $h^{-1}$).

**Keywords:** *Carbon dioxide utilization, reductive functionalization, guanidine, mechanism, silanes.*

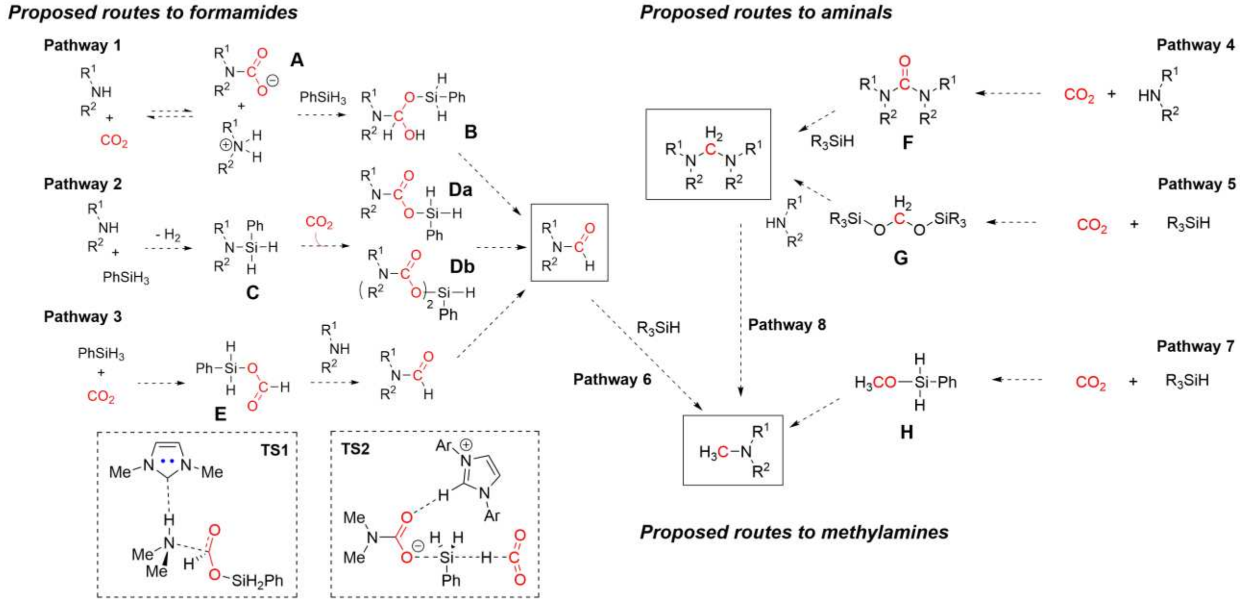
## INTRODUCTION

Conversion of $CO_2$ from industrial processes into useful compounds is a major contemporary research challenge, in which understanding reactivity in $CO_2$-based processes is essential. Whilst the majority of the studies focus on metal catalyzed reduction and functionalization of $CO_2$,[1] organocatalyzed reactions of $CO_2$ are also a highly active area of research. Compared to metal-based catalysts, organocatalysts are, with the exception of carbenes, more tolerant towards common contaminants of industrial $CO_2$ waste streams such as moisture, $SO_2$ and $NO_x$, requiring less costly pre-reaction purification.[2] Thus, these reactions can provide complementary technologies in $CO_2$ utilization to those based on metal-catalyzed processes.

Organocatalyzed reactions of $CO_2$ can be broadly divided into three main approaches: direct functionalization, *e.g.* into carbonates,[3] carbamates;[4] reduction into formaldehyde, formic acid and methanol;[5] and reductive functionalization.[6] The latter, with an amine as a reactant, gives formamides, *N*-methylamines or aminals, which can be valuable synthetic intermediates (Scheme 1). Polysiloxanes, such as polymethylhydrosiloxane (PMHS), are particularly attractive as reductants as they themselves are waste by-products of the silicone industry.[7]



**SCHEME 1. Organocatalyzed reductive functionlization of $CO_2$ using silanes**



**SCHEME 2. Proposed mechanistic pathways to reductive functionalization products of $CO_2$ and amine**

Consequently, reductive functionalization of $CO_2$ has been reported using various guanidines,[8] carbenes,[9] phosphorus ylides,[10] 1,3,2-diazaphospholene,[11] carboxylate,[12] fluoride and hydroxide anions,[13] and $B(C_6F_5)_3$,[14] as catalysts and DMSO,[15] DMF,[16] γ-valerolactone,[17] or [Bmim]Cl as solvents.[18] Despite such progress, and in contrast to metal-catalyzed 'activation' of $CO_2$, little is understood about the mechanism of these reactions, particularly the relationship between the different products from reactions under seemingly very similar conditions (Scheme 1).

**Previously proposed catalytic pathways**: The previously proposed catalytic pathways for these reactions are summarized by Scheme 2. For the synthesis of formamides, **Pathway 1** starts with formation of an ammonium carbamate **A**, stabilized by polar solvents, followed by its reduction with $PhSiH_3$ to **B,** and finally formamide.[8a] **Pathway 2** is a direct reaction between the amine and $PhSiH_3$, generating $H_2$ and a silylamine **C**, which can react with $CO_2$ to give silylcarbamate **D**.[15] Lastly, $CO_2$ and $PhSiH_3$ may react with each other to produce formoxysilane **E**, which can then react with the amine to produce a formamide (**Pathway 3**). This pathway through **TS1** was found to be the lowest energy pathway in a computational study on reactions between amines, $CO_2$ and $PhSiH_3$ with NHC catalysts.[19] Furthermore, another computational study by Li on the same pathway suggested that the NHC pre-catalyst activates neither $CO_2$ nor silane, but acts as a base to form a carbamate species which catalyzes the reduction of $CO_2$ to a formoxysilane species (**TS2**), followed by transamidation by the amine giving the formamide product.[20]

The pathway to aminals in particular, is still unexplored experimentally. While reduction of a urea (**Pathway 4**), *i.e.* a possible product in reactions between an amine and $CO_2$, to an aminal with $LiAlH_4$ is well-established,[21] the only precedents with a silane as reductant require a ruthenium catalyst,[22] or much higher temperature.[14b] An alternative proposal *via* a bis(silylacetal) species has been proposed by Cantat *et. al.* (**Pathway 5**), although no experimental evidence supporting this pathway was provided.[8b]

Finally, several routes to *N*-methylamines (**Pathways 6-8**) have been proposed including reduction of formamides,[14b, 23] reaction of amines with PhSiH2(OMe),[16] or through reduction of the aminal product.[6] However, definitive mechanistic and kinetic evidence has been scarce and mainly limited to observation of proposed intermediates **C**, **D**, **E** and **G** using $^1H$, $^{13}C$ or $^{29}Si$ NMR.[5a, 15, 18] This was due to complex equilibria in these systems, low stability of intermediates and difficulties collecting reliable kinetic data for the gas-liquid reaction systems.

We report here our experimental mechanistic investigation into guanidine-catalyzed reductive functionalization of $CO_2$ using silanes. Kinetic evaluation of individual pathways and that of the overall reaction led to conclusive evidence of the most active pathways at low and high temperature. A catalyst deactivation pathway was identified, and was subsequently prevented leading to the identification of much more active and readily accessible guanidines as catalysts for these types of reactions with TON = 805 and TOF = 33.5 $h^{-1}$.

## RESULTS AND DISCUSSION

**Preliminary studies on catalytic activity**:

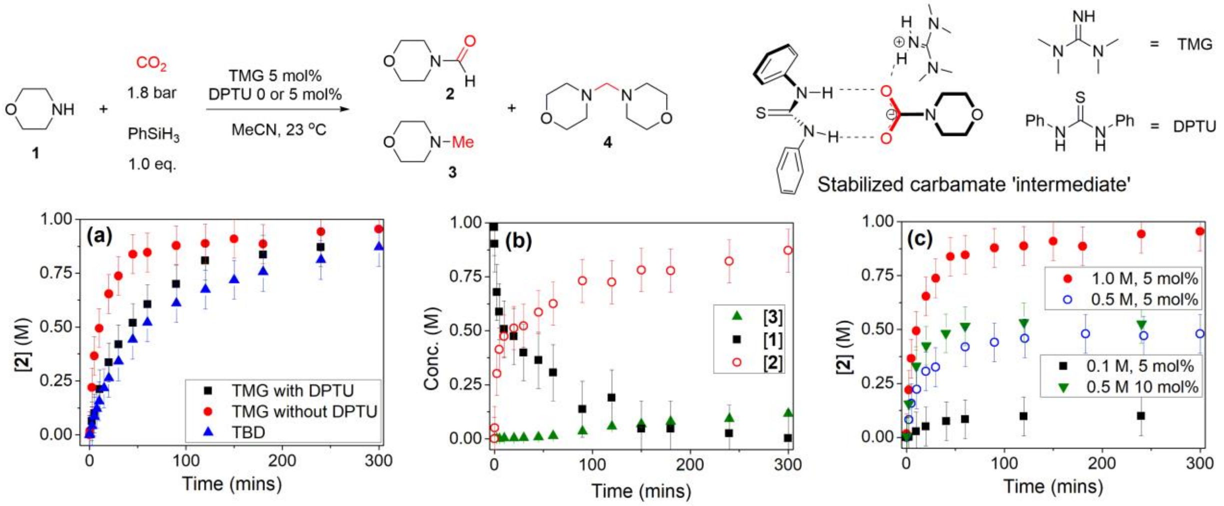


**FIGURE 1. Reductive amination of CO2 using TMG and its kinetic profiles (a) [2] *vs* time, at 5 mol% catalyst loading and 23 °C; (b) [1], [2] and [3] *vs* time, using 5 mol% of TMG as catalyst at 60 °C; (c) reaction profiles at different starting concentrations in [2] at 23 °C.**

In a previous study, we linked the origin of catalytic activity in the reaction between propargyl amines and $CO_2$ to the superbasicity of guanidine catalysts.[24] Consequently, *N*,*N*,*N'*,*N'*-tetramethylguanidine (TMG) was demonstrated to be an inexpensive, stable and superior catalyst when compared with elaborate cyclic guanidines, for the formation of cyclic carbamates using $CO_2$.[24] This led to our interest in using TMG as a catalyst in the reductive amination of $CO_2$.

The previously proposed mechanism by Cantat and coworkers,[8a] based on the observation of a guanidinium carbamate species in step-wise addition experiments, suggested stabilization of a carbamate intermediate is required (Scheme 2, **Pathway 1**). Thus, *N,N'*-diphenylthiourea (DPTU) was included as a co-catalyst in a reaction between morpholine, $PhSiH_3$ and $CO_2$ (Scheme 3, for crystal structure of the carbamate-DPTU-TMG complex, see ESI). The conversion of morpholine to formamide **2** and *N*-methylamine **3** was successful (quantified by gas chromatography). However, to our surprise it proceeded faster without DPTU, suggesting stabilization of the carbamate species is non-essential, and potentially detrimental to the reaction (Fig. 1a). Comparing the reaction profiles of reactions using TMG and TBD as catalyst (5 mol%) at room temperature showed that TMG is the much superior catalyst, reaching completion within 50 minutes compared to > 300 minutes with TBD.

Kinetic profiling a liquid-gas reaction requires establishing the pre-reaction phase transfer equilibrium of $CO_2$ between the gas phase and solution, and various equilibria between the reagents and $CO_2$. Thus, the reaction was performed with a 15-minute equilibration period to enable equilibration of the carbamate species (and temperature) before initiation of the reaction by addition of $PhSiH_3$ (Table 1, entry 1). The reaction rate was found to be dependent on the pressure of $CO_2$. Reaction at 1.2 bar $CO_2$ proceeds more slowly than one performed at 1.8 bar, but both achieve full conversion within 6 hours (ESI, section 7.1.6). Variable Time Normalization Analysis of data in Fig. 1c showed approximate first order dependence on [TMG], [**1**] and [$PhSiH_3$],[25] although the fit was not perfect and more complex kinetics can be expected (see ESI, Fig. S9 and S10).

Increasing the reaction temperature to 60 °C resulted in a two-stage kinetic profile (Fig. 1b), a slower overall reaction and a significant amount of the *N*-methylmorpholine product **3** (12 %) formed during the second stage of the reaction (Table 1, entry 1 and 2). Increasing the amount of $PhSiH_3$ from 1 to 2 equivalents led to an increased yield of *N*-methylamine **3** from 12% to 27% after 6 hours (Table 1, entry 2 and 3). Uncatalyzed reactions were slow, giving 23% and 15% yield after 28 hours of **2** at 60 °C and 23 °C, respectively. Inclusion of water (10 mol%, entry 4) in the reaction at 60 °C had no effect on the reaction kinetics or the overall conversion to **2** and **3**. This rules out moisture sensitive intermediates, and highlights the stability of the TMG catalyst against hydrolysis under the reaction conditions.[24]

**TABLE 1. Product distribution in TMG catalysed reductive amination of $CO_2$[a]**

| Entry | Protocol | **1 : 2 : 3 : 4** (%) |
|---|---|---|
| 1 | $\mathbf{1} + CO_2 \xrightarrow[\text{15 mins}]{\text{TMG}} \xrightarrow[\text{23 °C}]{PhSiH_3}$ | 0 : 98 : 2 : 0[b] |
| 2 | $\mathbf{1} + CO_2 \xrightarrow[\text{15 mins}]{\text{TMG}} \xrightarrow{PhSiH_3}$ | 0 : 88 : 12 : 0[b] |
| 3 | $\mathbf{1} + CO_2 \xrightarrow[\text{15 mins}]{\text{TMG}} \xrightarrow{PhSiH_3\text{, 2 eq.}}$ | 0: 73 : 27 : 0[b] |
| 4 | $\mathbf{1} + CO_2 + \text{0.1 eq. } H_2O \xrightarrow[\text{15 mins}]{\text{TMG}} \xrightarrow{PhSiH_3}$ | 0 : 86 : 14 : 0[b] |
| 5 | $\mathbf{1} + PhSiH_3 + CO_2 \xrightarrow[\text{10 mins}]{} \xrightarrow{\text{TMG}}$ | 0 : 86 : 14 : 0[b] |
| 6 | $PhSiH_3 + CO_2 \xrightarrow[\text{15 mins}]{\text{TMG}} \xrightarrow{\mathbf{1}}$ | 0 : 75 : 1 : 24[c] |

| | | |
|---|---|---|
| 7 | $PhSiH_3 + CO_2 \xrightarrow[60\ mins]{TMG} \xrightarrow{N_2\ flush} \xrightarrow{1}$ | 51 : 26 : 0: 23[c] |

[a] $CO_2$ (1.8 bar), **1** (2.0 mmol), TMG (5 mol%), MeCN (2.0 mL), 60 °C, 360 mins after addition of the last component; [b] Determined by GC; [c] Determined by $^1H$ NMR.

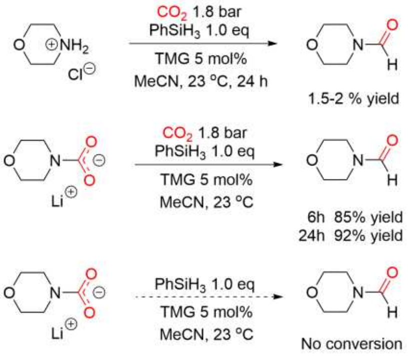
As the reaction was found to be dependent upon $CO_2$ pressure, a possible explanation for the two stage nature of the reaction at 60 °C, comparing to that at 23 °C (Fig. 1a and Fig. 1b), is the lower solubility of $CO_2$ at the higher temperature. However, FT-IR experiments showed that the rate of $CO_2$ transfer into solution was much faster (30 seconds to reach saturation) than the observed reaction rate. Alternatively, rapid reaction between morpholine and $CO_2$ giving the morpholinium morpholinecarbamate will lead to a 50% conversion of morpholine to the carbamate. The observed kinetics above thus may be attributed to rapid reduction of the carbamate species **Mor-A** at 60 °C or catalyst deactivation as the reaction progresses.

The product selectivity was also found to be dependent upon the order of addition of reagents (Table 1). The addition of TMG last, after 10 minutes at 60 °C, led to no change in conversion compared to when $PhSiH_3$ was added last (entry 5 & 1). However, on mixing morpholine, $PhSiH_3$ and $CO_2$ without the catalyst, the production of gas and an exothermic reaction was observed, suggesting an uncatalyzed reaction occurring between reagents. Finally, pre-mixing $CO_2$ and $PhSiH_3$ for 15 minutes in the presence of TMG led to the formation of aminal **4** (24 %) as a side product instead of methylamine **3** (entry 6). While formation of formamide product **2** is faster, a slower reduction of $CO_2$ to **E** and **G** (catalyzed by TMG) may be responsible for the formation of aminal **4** (**Pathway 5**).

The findings above suggest that the mechanism of the reaction and interplay between products **2**, **3** and **4** are complex, and reactions between subsets of reactants have significant impact on the overall reaction outcome. Thus, a more thorough investigation was required to understand these complex reaction pathways. Consequently, further characterization of the proposed pathways and their dependence on temperature was carried out. The potentially complex parallel pathways, particularly at higher temperature, rules out a traditional kinetic investigation. Instead, a combination of spectroscopic and kinetic techniques was employed to evaluate the various proposed pathways.

### Evaluation of catalytic pathways and their temperature dependence

***Pathways 1 and 2***: The role of the morpholinium carbamate **Mor-A** (Pathway 1) in the mechanism was investigated experimentally. Reaction between morpholinium hydrochloride, $CO_2$ and $PhSiH_3$ in the presence of TMG (5 mol%) in MeCN gave little product (1.5-2.0 % of **2**, after 24 h, 23 °C). A similar reaction with lithium carbamate Li/**Mor-A** gave formamide **2** in 85% yield after 6 hours and 92% yield after 24 hours. Without $CO_2$ (under nitrogen), the reaction gave no conversion to **2** under otherwise identical conditions (Scheme 3). Thus, **Pathway 1** is feasible under the reaction conditions with an additional requirement of $CO_2$ involvement after intermediate **Mor-A**, e.g. **TS2**. This will be referred to as **Pathway 1'**.



**SCHEME 3. Reactions of intermediate Mor-A.**

The relevance of a silylamine species (***Pathway 2***) was investigated through reaction of **1** and $PhSiH_3$ in the presence of TMG at 60 °C under $N_2$. After 6 hours, <8% conversion to silylamine **C** was observed. Although insertion of $CO_2$ into independently prepared **C** to give silylcarbamate species **D** was facile, the moisture sensitivity of intermediate **C** and the tolerance of the reaction to moisture rules out ***Pathway 2*** in our catalytic system.

To probe other possible intermediates, the reaction was monitored by *in situ* FT-IR spectroscopy, $^1H$ and $^{29}Si$ NMR. This highlighted two significant intermediates which were initially attributed to silylcarbamate **Mor-Da/Mor-Db** (1698 $cm^{-1}$, see Fig. 2), despite the lack of evidence for **Pathway 2**, and to formoxysilane **E** (1723 $cm^{-1}$).

Morpholine **1** was reacted with $CO_2$ and 1.0 equivalent of $PhSiH_3$ at 23 °C without TMG. The $^{29}Si$ NMR spectrum of the reaction mixture showed partial consumption of $PhSiH_3$ and formation of a monohydride silane species (−31.1 ppm, $J_{Si,H}$ = 281 Hz, Fig. 2c). The stoichiometry of the reaction was confirmed in a similar experiment, using only 0.5 equivalents of $PhSiH_3$ (to 1.0 eq. of **1**) which showed complete conversion of $PhSiH_3$ to the monohydride species. This species is tentatively assigned to be **Mor-Db** (Fig. 2c, $\delta_H$ ($d_3$-MeCN) 5.47 ppm (Si–H)).

FT-IR analysis of the reaction between **1**, $CO_2$ and $PhSiH_3$ (1.0 eq.) at 23 °C (Fig. 2) showed formation of a silylcarbamate species (1698 $cm^{-1}$, 1242 $cm^{-1}$) in the first 10 minutes.[26] This signal quickly disappeared once TMG (5 mol%) was introduced, as expected from the $^{29}Si$ NMR results. This led to the formation of formamide **2** (1678 $cm^{-1}$, Fig. 2a) within 120 minutes in 98% yield (with 2% of *N*-methylamine **3**). The silylcarbamate signal was assigned to **Mor-Db** based on the stoichiometry of the reagents and the corresponding $^1H$ and $^{29}Si$ NMR data above. Repeating the reaction between **1**, $CO_2$ and $PhSiH_3$ at 23 °C, followed by flushing with $N_2$ and addition of TMG (5 mol%), led to ~5% of product **2** by GC after 300 minutes. Thus, the reduction of **Mor-Db** requires $CO_2$ to proceed, in agreement with the reduction of Li/**Mor-A** (Scheme 3). For the reaction under $CO_2$, a small signal corresponding to formoxysilane **E** (1725 $cm^{-1}$), whose assignment was based on the reported $\nu_{C=O}$ of $HCO_2SiEt_3$ 1708 $cm^{-1}$ and that of $HCO_2SiH_2Me$ 1727 $cm^{-1}$,[27] slowly built up over the first 100 minutes. These results indicated that reactions to form intermediates **Mor-Db**, through ***Pathway 1'***, instead of ***Pathway 2***, is rapid at 23 °C, even without the catalyst, and this may be the dominant pathway for the formation of product **2**. However, involvement of formoxysilane **E** at this temperature cannot be completely discounted.

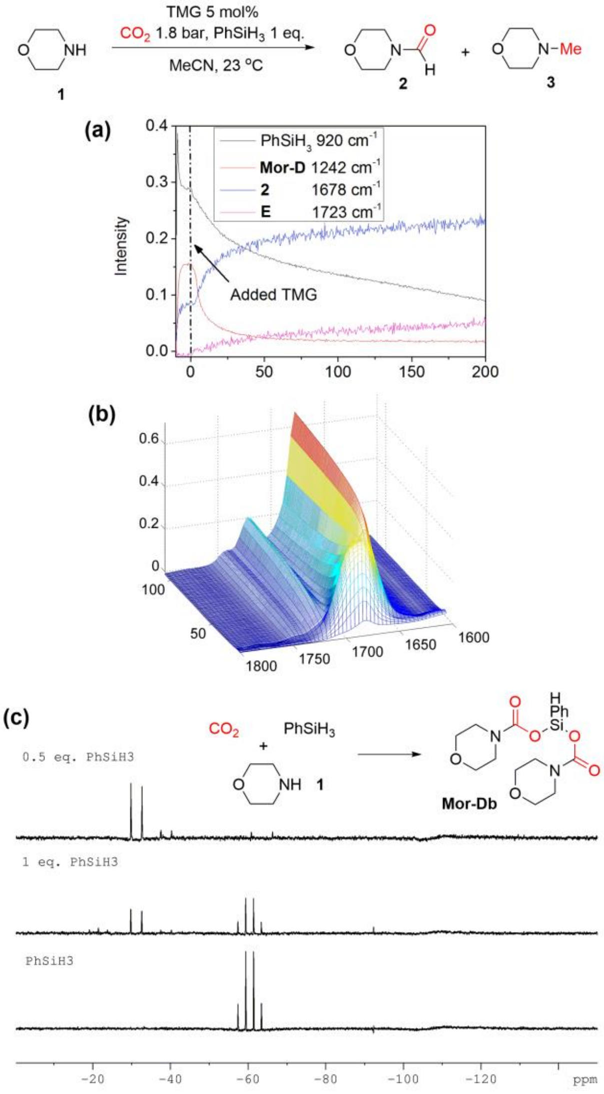


**FIGURE 2. (a) FT-IR data of a reaction using 5 mol% TMG, 23 °C; (b) time evolution of the carbonyl region of a reaction using 5 mol% TMG, 60 °C; (c) $^{29}$Si NMR spectra of a reaction between 1, $CO_2$ and $PhSiH_3$.**

***Pathway 3***: When $CO_2$ was reacted with $PhSiH_3$ in the presence of the TMG catalyst (5 mol%) at 60 °C, an IR signal corresponding to formoxysilane **E** (***Pathway 3***) was observed to build up, while the $PhSiH_3$ signal at 920 $cm^{-1}$ dissipated over 50 minutes. An identical reaction at 23 °C was much slower, achieving < 20% conversion after 2 hours (Fig. 3a, single wavenumber plots). Little conversion was observed in the absence of the catalyst. After flushing the reaction at 60 °C with nitrogen (60 minutes), introduction of morpholine **1** led to very rapid consumption of **E** and concurrent formation of formamide **2** and aminal **4** (Fig. 3b and Table 1, entry 7). Post reaction analysis by $^1$H NMR showed a ratio **1** : **2** : **4** = 51 : 26 : 23. Thus, formation of **E** and ***Pathway 3*** requires higher temperature than ***Pathway 1***. A recent computational study by Kim and Li also indicated that the lowest energy pathway to formamide **2** involves formation of formoxysilane **E** as the rate determining step.[28] However, their results suggested subsequent reduction of formamide **2** is rapid, in contrast with our experimental results.

Thus, evaluation of the three proposed pathways to formamide **2** ruled out ***Pathway 1*** and ***Pathway 2***. ***Pathway 3*** is feasible, but slow at 23 °C. ***Pathway 1'*** is likely the dominant pathway at this temperature but proceeds via the rapid formation of **Mor-Db**, which surprisingly requires $CO_2$ for its subsequent conversion to **2**.

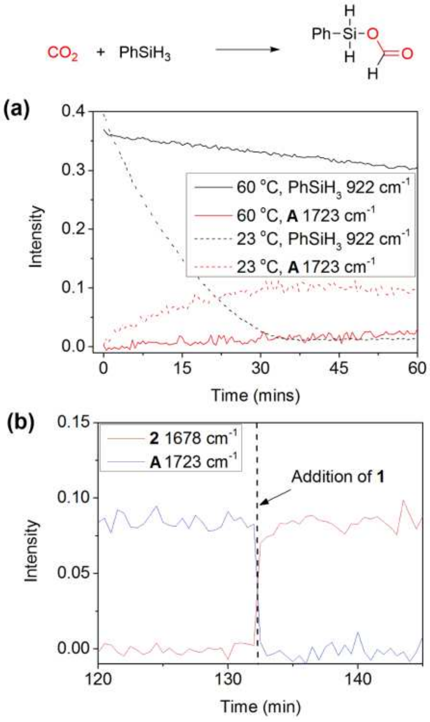


**FIGURE 3. FT-IR data of (a) a reaction between $CO_2$ and $PhSiH_3$, using 5 mol% TMG, at 23 °C and 60 °C; (b) changes upon addition of amine 1 to reaction mixture between $CO_2$ and $PhSiH_3$.**

### Pathway to aminal 4 and methylamine 3

The findings above suggest that the mechanism of the reaction, and interplay between products **2**, **3** and **4** are complex, and reactions between subsets of reactants have a significant impact on the reaction outcome. Entries 1 and 6 of Table 1 support a link between silylated-$CO_2$ products **E** or **G** and aminal **4** (**Pathway 5**), rather than a route to aminal **4** *via* urea **F** and its subsequent reduction. Indeed, subjecting urea **F** to the reaction conditions (60

°C) resulted in no reduction to aminal **4** after 27 hours. Consequently, further characterization of the routes to products **3** and **4**, and their dependence on temperature, was carried out.

Given the decreasing order of oxidation state $CO_2$ > formamide **2** > aminal **4** > *N*-methylamine **3**, it was surprising that aminal **4** was not detected in our initial reaction profiling by GC. The GC profile of authentic aminal **4** (prepared according to Huang)[29] showed that its peak overlapped significantly with that of starting material **1**, preventing accurate quantification. Thus, $^1H$ NMR spectroscopy was employed to characterize and quantify reaction intermediates, particularly any unstable species. In order to avoid changing the rate of $CO_2$ mass transfer into solution, which would have affected the product distribution, the reaction was performed in a Schlenk tube as normal using $d_3$-MeCN. Samples were taken and diluted with $d_3$-MeCN under nitrogen before measurement. Aminal **4** was shown to form at the beginning of the reaction, reaching a maximum at about 100 minutes and diminishing through further reaction (Fig. 4a). Importantly, the decrease in [**4**] was observed with a concomitant increase in [**3**]. A similar profile of [**4**] *vs* time was also observed for the reaction performed at 23 °C, albeit with much lower maximum concentration (0.02 M, see ESI). Thus, the pathway to product **3** is through apparent reduction of aminal **4**.[8b] This has also been very recently observed by He and co-workers, in a reaction between $CO_2$, methylaniline and $Ph_2SiH_2$ catalyzed by trimethylglycine betaine.[30]

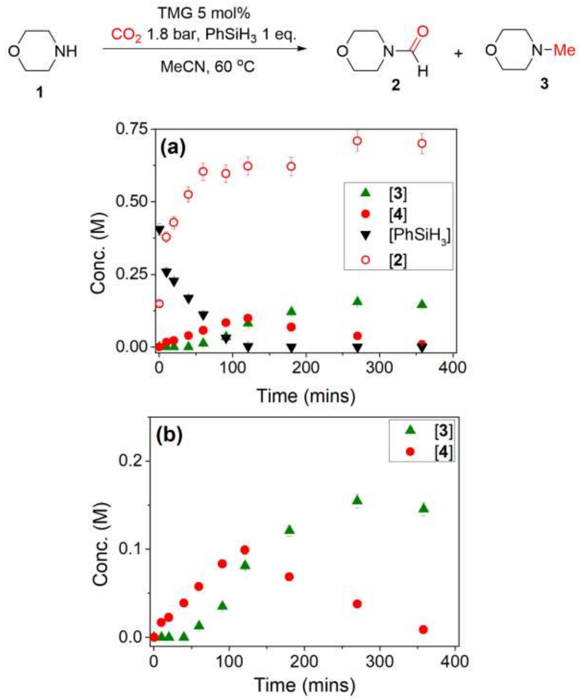
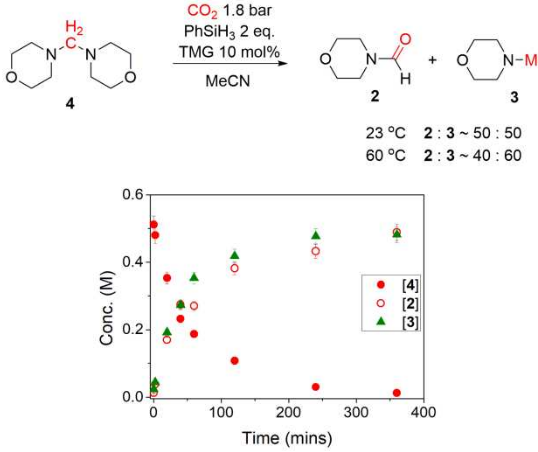


**FIGURE 4. Reaction profile by $^1H$ NMR (a) product formation *vs* time at 60 °C; (b) enlarged kinetic profile for *N*-methylamine 3 and aminal 4.**

To verify the relationship between aminal **4** and methylamine **3** in our reaction, aminal **4** was subjected to the reaction conditions (Scheme 4). No reaction was observed in the absence of $CO_2$. When $CO_2$ was included, in contrast to the finding of He group,[30] two products, formamide **2** and *N*-methylamine **3**, were obtained in ~ 50 : 50 and 40 : 60 ratios, at 23 °C and 60 °C respectively. The change in product ratio is consistent with the catalytic reaction in Scheme 2, with higher temperature resulting in a higher yield of **3**. The formations of products **2** and **3** follow similar kinetics, measured by $^1H$ NMR (Scheme 4).

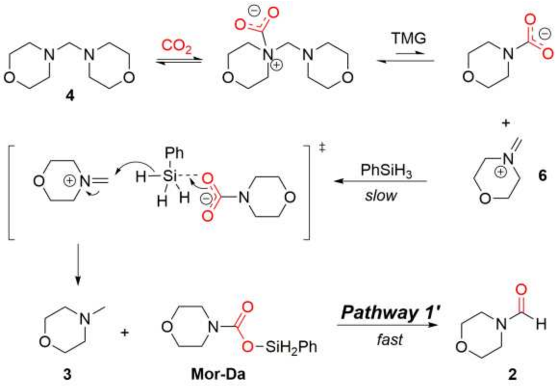
The enabling effect of $CO_2$ on this reaction can potentially be attributed to trace amounts of protons, generated from $CO_2$ and trace moisture, which can trigger fragmentation of aminal **4**.[31] Thus, a mixture of aminal **4**, $PhSiH_3$, and TMG (5 mol%) was treated with acetic acid (5 mol%) and monitored by $^1H$ NMR at 23 °C. No reaction was observed after 75 minutes, ruling out a Brønsted acid catalyzed mechanism. Thus, our experimental evidence indicated direct involvement of $CO_2$ in the later steps of the mechanisms, as a mediator/catalyst, to both formamide **2** and amine **3**, e.g. through **TS2** (Scheme 2).[20]



**SCHEME 4. Reaction of aminal 4 with $PhSiH_3$ and its kinetic profile.**

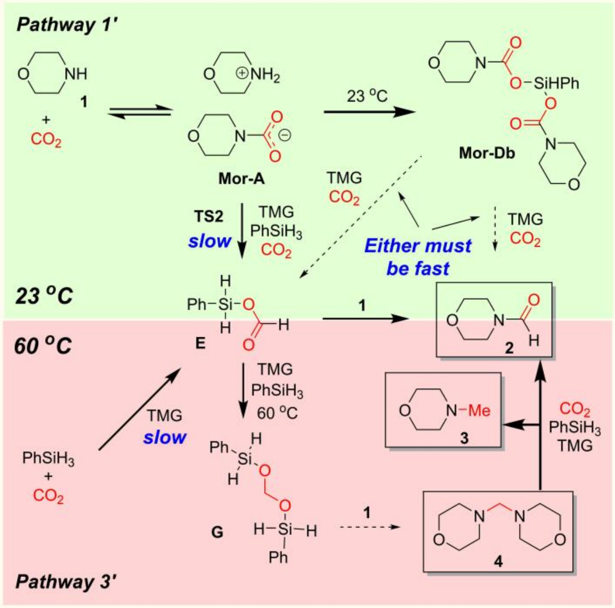
Based on the above results, a tentative mechanism can be proposed for the reduction of aminal **4** to products **2** and **3** (Scheme 5). Coordination with $CO_2$ activates the aminal to nucleophilic attack by the catalyst TMG, leading to formation of morpholine carbamate **Mor-Db** and iminium **6**. Activation of aminals with acetyl chloride and acetyl anhydride for functionalization is well-established.[32] This is followed by a reduction of **6** to **3** and **Mor-Da** by carbamate-activated silane, in a similar manner to **TS2**.[20] Subsequent reduction of silyl carbamate **Mor-Da** follows **Pathway 1'** to formamide **2**.

**Revised mechanism**: The results of our mechanistic investigations using reaction profiling, $^1H$, $^{29}Si$ NMR, FT-IR spectroscopy and mass spectrometry showed two possible catalytic pathways to reductive amination products **2**, **3** and **4** (Scheme 6). Product **2** is formed predominantly at lower temperatures (23 °C, **Pathway 1'**), most likely through carbamate intermediate **Mor-Db**. Product **4** is formed at elevated temperatures (60 °C, **Pathway 3'**, a combination of **Pathway 3** and **Pathway 5**) through intermediates **E** and **G**. Its subsequent reduction in the presence of $CO_2$ leads to a 1 : 1 ratio of **2** and **3** at 23 °C. Direct reduction of **2** to **3** cannot be ruled out at much higher temperatures, as demonstrated by other researchers,[33] but none was observed by us at 60 or 100 °C.



**SCHEME 5. Proposed mechanism for reduction of aminal 4**

Importantly, observation of formoxysilane **E** by FT-IR during the catalytic reaction at 23 °C suggests its involvement in the formation of formamide **2** through a combination of **Pathway 1'** and **Pathway 3**. Direct reduction of $CO_2$ with $PhSiH_3$ is slow at 23 °C (Fig. 4b). The need for extra $CO_2$ in the reduction of lithium carbamate Li/**Mor-A** supports a transition state similar to **TS2** (Scheme 2).[20] However, this reaction (reaching 85% conversion after 6 hours) is also much slower than the catalytic reaction (reaching completion in ~100 minutes). Thus, an alternative, faster route from **Mor-Db** to product **2**, either through formoxysilane **E** or not, must be operational at 23 °C.



**SCHEME 6. Revised mechanism for reductive amination of $CO_2$**

**Improving catalyst stability**: During the catalytic reaction (Fig. 4), the $^1$H NMR signal of TMG (2.94 ppm, 12H) slowly decreased in the first 100 minutes, while another N-Me signal (2.91 ppm) increased, along with a new signal at 8.52 ppm. No other $^1$H NMR signal was found to be associated with this species, leading to its assignment as formyl-TMG **7** (Fig. 5). This was confirmed by ESI-MS with the detection of a species at $m/z[M+H^+] = 144.1126$ (calcd. 144.1131) in the reaction mixture after 20 minutes. In addition, intermediate **8** ($m/z = 213.1706$) was also detected by MS, although its concentration was too low for detection by $^1$H NMR. These species are likely formed through transamidation under the reaction conditions.[34]

$^1$H NMR spectra of a reaction mixture at 23 °C showed that catalyst TMG was slowly converted to **7** over 60 minutes, with concomitant decrease in reaction rate (Fig. 5). These lead to loss of the nucleophilicity and superbasicity of the catalyst, which are essential to maintaining catalytic activity. We reasoned that alkylation of TMG at the NH position would increase both the superbasicity and nucleophilicity of the catalyst while suppressing its formylation, giving more active and stable catalysts.

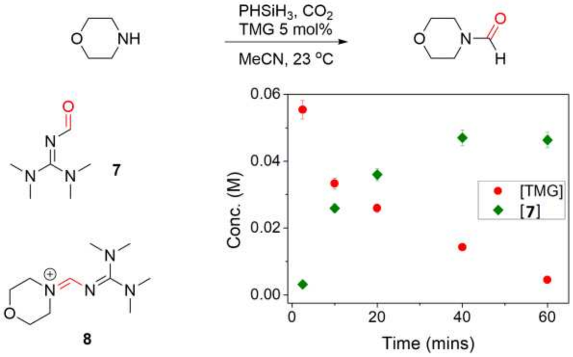


**FIGURE 5. Catalyst speciation *vs* time during reaction at 23 °C by $^1$H NMR.**

We reasoned that alkylation of TMG at the NH position would increase both the superbasicity and nucleophilicity of the catalyst while also suppressing its formylation, hence giving the more active and stable catalysts. Pentamethylguanidine (MTMG, Fig. 6) and *N*-butyl-*N',N',N'',N''*-tetramethylguanidine (BTMG) were prepared based on a procedure by Jessop.[35] Both of these new catalysts displayed faster kinetics at 1 mol% loading and 23 °C, particularly in the later stages where catalyst deactivation is evident with TMG (Fig. 6). Both MTMG and BTMG gave approximately 95% yield of **2** and 5% yield of **3** within 300 minutes. Increasing the catalyst loading to 5 mol% did result in a faster reaction with BTMG (ESI, Fig. S119). Decreasing the catalyst loading to 0.1 mol% led to longer reaction time, but still gave 80.5% yield of **2** and 3% yield of **3** after 24 hours. These correspond to TON = 805 and TOF = 33.5 h$^{-1}$, the highest TON value reported in reductive amination of $CO_2$ with a silane. In the context of the organocatalyzed reduction of $CO_2$ using silanes, only the NHC-catalyzed reduction reported by Zhang and Ying reached higher TON (1840).[5a] Typically reported non-metal catalyzed reductive amination of $CO_2$ employed 5-10 mol% of catalyst and 6-24 hours reaction time.

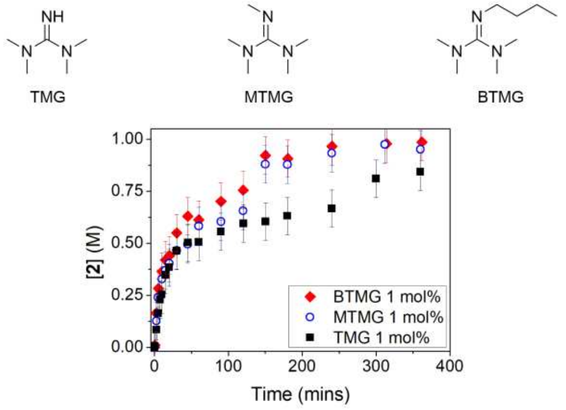
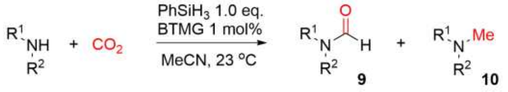
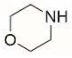
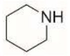
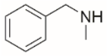
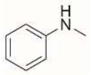
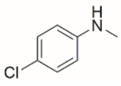
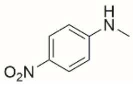
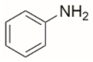
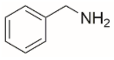
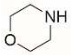


**FIGURE 6. Reaction profile by GC for reactions using 1 mol% catalyst loading, 23 °C.**

The substrate scope when using the new catalyst BTMG is summarized in Table 2. Secondary cyclic amines, benzylamines and anilines all gave good conversion after 8 hours at 23 °C, with **9** : **10** selectivity from 84 : 13 to 96 : 4 (entry 1-5 and 7). These selectivities are particularly good given that Cantat and co-workers reported very high selectivity for aminal products in similar reactions with *N*-methylanilines using TBD as the catalyst at 80 °C.[8b] Electron poor *p*-nitroaniline gave no reaction (entry 6). Benzylamine gave a complex mixture of products, which can be attributed to the multiple pathways of the mechanism (entry 8). Replacing $PhSiH_3$ with the more sustainable PMHS (poly(methylhydrosiloxane)) required an increase in reaction temperature to 60 °C to achieve comparable results in 22 hours.

**Table 2. Substrate scope with BTMG catalyst**[a]



| Entry | Substrate | Time (h) | **9** : **10** (%) |
|---|---|---|---|
| 1 |  | 8 | 96 : 4 |
| 2 |  | 8 | 84 : 6[b] |
| 3 |  | 8 | 90(73)[e] : 10 |
| 4 |  | 8 | 95(81)[e] : 5 |
| 5 |  | 22 | 84 : 13 |
| 6 |  | 22 | 0 |
| 7 |  | 22 | >95[c] |
| 8 |  | 22 | Mixture of formamide and urea |
| 9 |  | 22 | 83[d] |

[a]Yields were determined by $^1$H NMR using 1,3,5-trimethoxybenzene as internal standard; [b]determined by GC using 1,1'-biphenyl as internal standard; [c]with < 1% of di-formylated product; [d]using 3 Si-H eq. of PMHS instead of $PhSiH_3$, 60 °C, 5 mol% BTMG; [e]the numbers in brackets are isolated yields in %.

## CONCLUSIONS

In conclusion, our experimental investigation of the TMG-catalyzed reductive amination of $CO_2$ showed that reduction of $CO_2$ to formamide **2**, aminal **4** and then *N*-methylamine **3** is not sequential. Instead, separated catalytic pathways were identified giving **2** at lower temperature (23 °C), and **4** and **3** at higher temperature (60 °C). Importantly, reduction of aminal **4** was shown to proceed at 23 °C to give a 1 : 1 mixture of **2** and **3** as products. The lowest energy transition states suggested by DFT studies, albeit with NHC carbenes as catalysts,[20] have been shown to result in slower reaction than that measured experimentally with TMG as catalyst. Likely catalytic pathways to each product have been identified, which will guide further theoretical investigations of organocatalyzed reactions of $CO_2$. Importantly, $CO_2$ was found to be an essential mediator in the conversion of **Mor-Db** to **2** and the reduction of aminal **4**. Controlling the dual pathways of the mechanism will be important in achieving high selectivity between the three potential products in synthetic applications.

Furthermore, catalyst deactivation through formylation under reaction conditions was suppressed through alkylation of TMG. This led to identification of catalysts showing improved catalytic activity and stability, resulting in the highest recorded TON (805) in organocatalyzed reductive amination of $CO_2$ with a silane.

## ASSOCIATED CONTENT

**Supporting Information**. The Supporting information is available free of charge on http://pubs.acs.org at DOI: 10.1021/xxxxxxxx.
Kinetic data, spectra and characterization of compounds
Crystallographic data are included.

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## ABBREVIATIONS

TMG: *N,N,N',N'*-tetramethylguanidine; MTMG: *N,N,N',N',N"*-pentamethylguanidine; BTMG: *N*-butyl-*N',N',N",N"*-tetramethylguanidine; DPTU: *N,N'*-diphenylthiourea.

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SYNOPSIS TOC (Word Style “SN_Synopsis_TOC”).