

# Synthesis of urea derivatives from amines and CO<sub>2</sub> in the absence of catalyst and solvent†

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Received 29th April 2010, Accepted 12th August 2010

DOI: 10.1039/c0gc00059k

Urea derivatives are obtained in mild to good yield from the reactions of primary aliphatic amines with CO<sub>2</sub> in the absence of any catalysts, organic solvents or other additives. To optimize reaction conditions, experimental variables including temperature, pressure, the concentration of amine, reaction time *etc.* were studied. Satisfactory yields were obtained at the optimized conditions that are comparable to the presence of catalyst and solvent. The preliminary investigation of the reaction mechanism showed that alkyl ammonium alkyl carbamate was quickly formed as the intermediate, and then the final product was formed by the intramolecular dehydration.

## Introduction

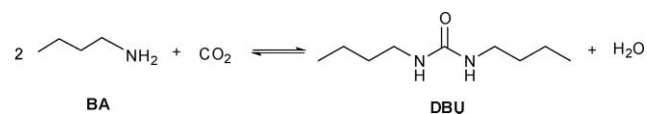
The increasing levels of carbon dioxide in the atmosphere has a detrimental effect on the climate and is the major contributing factor to recent global warming.<sup>1</sup> It is imperative that new reactions and processes are developed for the efficient storage or utilization of the abundant and renewable CO<sub>2</sub> resource in an environmentally friendly manner. For the carbon dioxide capture and storage (CCS),<sup>2</sup> amine scrubbing<sup>3</sup> will probably be the dominant technology for CO<sub>2</sub> capture from coal-fired power plants. Chemical utilization of CO<sub>2</sub><sup>4–8</sup> could also help to reduce its concentration in the atmosphere while at the same time exploiting it as a carbon feedstock for the production of useful organic compounds. Herein we describe a technology that combines CO<sub>2</sub> capture and utilization into one process with the formation of useful urea derivatives but not for geologic sequestration.

Urea derivatives are widely used in a variety of areas,<sup>9</sup> such as pharmaceuticals, agricultural pesticides, antioxidants in gasoline and corrosion inhibitors. Traditional synthesis of urea derivatives involves the reaction of amines with phosgene, CO<sup>10</sup> or isocyanate,<sup>11</sup> which has tremendous toxicological and environmental problems. Alternative routes have also been developed, which involve amines reacting with urea,<sup>12</sup> ethylene carbonate<sup>13</sup> or diethyl carbonate.<sup>14</sup> However, these expensive reagents originate from CO<sub>2</sub> reacting with ammonium,<sup>15</sup> ethylene oxide or ethanol.<sup>5</sup> Some researchers have synthesized urea derivatives through amines reacting with CO<sub>2</sub> in the presence of catalysts, such as 1,8-diazabicyclo[5.4.0]undec-7-ene,<sup>16</sup> CsOH,<sup>17</sup> Cs<sub>2</sub>CO<sub>3</sub>,<sup>18</sup> Au/poly,<sup>19</sup> [Bmim]OH<sup>20</sup> or KOH/PEG1000,<sup>21</sup> using ionic liquids, *N*-methylpyrrolidone or CO<sub>2</sub> as solvent. We show

a neat and effective route for the synthesis of urea derivatives from amines and CO<sub>2</sub> in the absence of any catalyst, organic solvent or other additives, with satisfactory yields comparable to that reported in literature with these additives.

## Results and discussion

During the initial research of this work, we tried to perform the reaction by using solid base catalysts. A lot of product was formed when a blank reaction was carried out in the absence of catalyst. With the assurance that no impurities or other factors could promote the reaction, we examined the catalytic possibility of the stainless steel wall of the reactor as our previous observation.<sup>22</sup> Similar yields of 29.8% and 30.2% were obtained for *n*-butylamine (BA) reacting with CO<sub>2</sub> in a stainless steel reactor with and without setting Teflon inner liner at conditions of 180 °C, 10 MPa, 1.0 mmol ml<sup>−1</sup> BA for 4 h. Thus, there was no reactor wall effect and the reaction could occur in the absence of any catalyst. So the effect of reaction parameters were studied using BA as a model substrate with the formation of *N,N'*-dibutylurea (DBU) as the main-product and no by-products detected except water (Scheme 1).



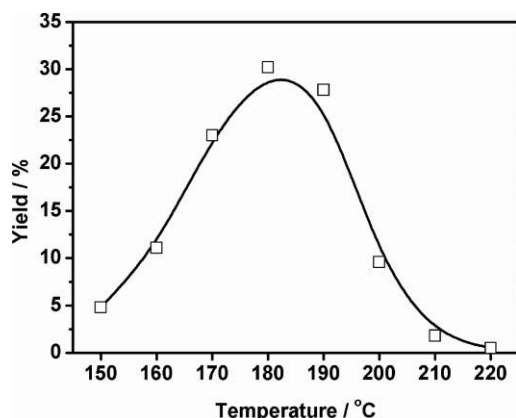
Scheme 1 Reaction of *n*-butylamine with CO<sub>2</sub>.

Increasing the temperature led to a rise then fall in the isolated yield of DBU, reaching a maximum yield at around 180 °C (Fig. 1). The decrease of the yield at high temperatures was ascribed to the idea that it is a reversible and exothermic reaction; its equilibrium constant decreases as temperature increases. The reactions of 5 mmol DBU and 100 mmol H<sub>2</sub>O were examined at different temperatures from 180 to 220 °C. The hydrolyzation content increased with increasing and nearly completed at 220 °C (data not shown), indicating that it is a reversible reaction. The industrial production of urea from NH<sub>3</sub> and CO<sub>2</sub> occurs

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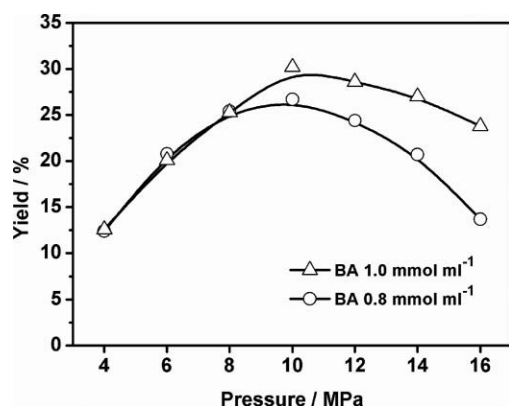
† Electronic supplementary information (ESI) available: Spectroscopic data for the products. See DOI: 10.1039/c0gc00059k



**Fig. 1** Effect of temperature on the isolated yield of DBU. The selectivity of DBU was 100% at all the conversion values. Conditions: BA 1.0 mmol ml<sup>-1</sup>; pressure 10 MPa; time 4 h.

in two steps *via* the intermediate ammonium carbamate. The conversion of NH<sub>3</sub> and CO<sub>2</sub> into ammonium carbamate is highly exothermic, while the dehydration to urea is endothermic. The overall process is exothermic and no urea was formed at high temperatures.<sup>15,18</sup> The production of DBU may have a similar thermal effect. As the overall process is exothermic, a shift of the equilibrium to the left with the increase in temperature is reasonable.

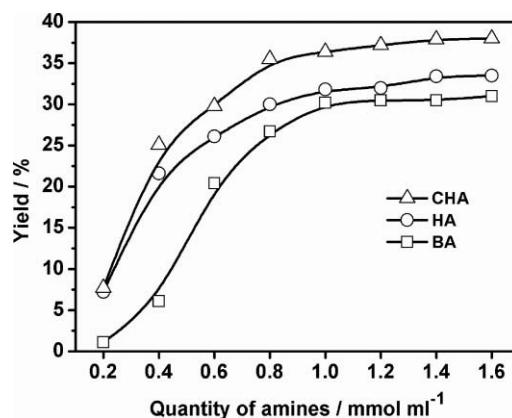
The isolated yield of DBU reached a maximum value at supercritical region, *ca.* 10 MPa, and then decreased with increasing pressure (Fig. 2). At pressures above 10 MPa, the superfluous CO<sub>2</sub> dissolved into the liquid phase of butyl ammonium butyl carbamate (BABC), this resulted in an expansion of the liquid and then caused a dilution effect as observed in our previous work.<sup>23</sup> The dilution effect was less obvious for the case of 1.0 mmol ml<sup>-1</sup> BA and the yield decreased slowly at higher pressures compared with 0.8 mmol ml<sup>-1</sup> BA. Based on the role of amine, it is a reactant and also a promoter or catalyst of the reaction (as discussed later). The catalytic effect is more obvious for the high concentrations of BA, so the negative dilution effect is less obvious, leading to a slow decrease of the yield.



**Fig. 2** Effect of pressure on the isolated yield of DBU. The selectivity of DBU was 100% at all the conversion values. Conditions: BA 1.0 mmol ml<sup>-1</sup>; temperature 180 °C; time 4 h.

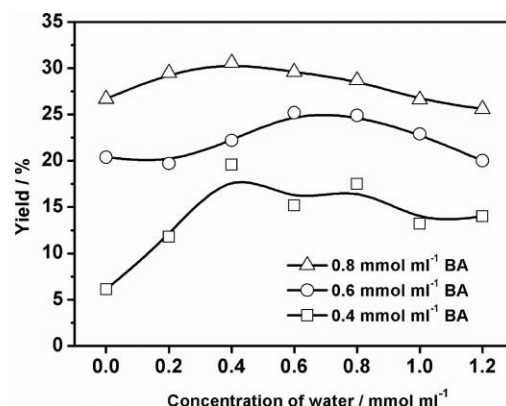
The concentration of BA had a great effect on the isolated yield of DBU, which increased drastically and then reached a plateau slightly with increasing of the concentration of BA

(Fig. 3). The results for the reactions of hexylamine (HA) and cyclohexylamine (CHA) with CO<sub>2</sub> showed that the yield of the product was also greatly dependent on the concentration of the reactant similar to BA. Aria and co-workers<sup>24</sup> have reported that cyclic ureas could be formed from alkylene diamines and CO<sub>2</sub> at 150 °C in the absence of catalyst in methanol solvent. The industrial production of urea also operates at elevated temperatures (150–220 °C) and pressures (15–25 MPa) with the precise control of the amount of ammonia and CO<sub>2</sub> without using any catalyst.<sup>15</sup> So it seems to be reasonable for synthesizing urea derivatives without catalyst by finely controlling the reaction conditions.



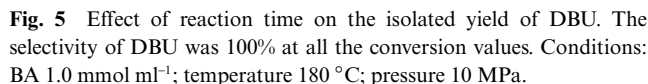
**Fig. 3** Effect of quantity of amines on the isolated yield of urea derivatives. The selectivity of DBU was 100% at all the conversion values. Conditions: temperature 180 °C; pressure 10 MPa; time 4 h. HA: hexylamine, CHA: cyclohexylamine.

The isolated yield of DBU could be enhanced by adding a small amount of water, especially at low concentrations of BA, but it decreased slightly at large quantity of water (Fig. 4). The positive effect of water was ascribed to the interaction of water with BABC; while the reaction equilibrium would shift to the left with an excess amount of water, resulting in a reduction of the yield of DBU.



**Fig. 4** Effect of additional water on the isolated yield of DBU. The selectivity of DBU was 100% at all the conversion values. Conditions: temperature 180 °C; pressure 10 MPa; time 4 h.

The yield increased smoothly with the reaction time and reached to 72.9% after 24 h (Fig. 5). The control experiments with catalysts and solvents showed that the yield was enhanced



Entry	Catalyst & additive	Quantity/mmol	Yield/%
1	None	—	30.2
2	NaOH	1	31.2
3	KOH	1	33.4
4	CsOH	1	37.8
5	Na <sub>2</sub> CO <sub>3</sub>	1	36.6
6	K <sub>2</sub> CO <sub>3</sub>	1	38.7
7	Cs <sub>2</sub> CO <sub>3</sub>	1	41.3
8	NMP	100	37.5
9	Cs <sub>2</sub> CO <sub>3</sub> + NMP	1 + 100	55.3
10	[Bmim]Cl	1	31.8
11	[Bmim]OH	1	37.0

slightly with the presence of these additives (Table 1). But the increase was at the expense of additional procedure to separate the catalyst and additives from product and the cost of economy *etc.* Additives are necessary only when a remarkable enhancement of the yield could compensate these drawbacks. So the optimized reaction condition is *ca.* 180 °C, 10 MPa.

The scope of this reaction was examined (Table 2). A wide range of primary aliphatic amines bearing different chain length and/or substituents could undergo the target reaction smoothly, delivering the corresponding dialkyl ureas in moderate to good yields (entries 1–12). The conversions of isopropylamine and

$$\begin{array}{c}
 \text{H}_2\text{N}-\text{C}(\text{R})=\text{CH-X} + \text{CO}_2 \rightleftharpoons \begin{cases} 
 \text{R}-\text{NH}-\text{C}(=\text{O})-\text{NH-R} + \text{H}_2\text{O} & n=0; X=\text{H} \\
 \text{R}-\text{NH}-\text{C}(=\text{O})-\text{CH(X)-CH}_2\text{-R} + \text{H}_2\text{O} & n=1, 2 \\
 & X=\text{NH}_2 \text{ or OH}
 \end{cases}
 \end{array}$$

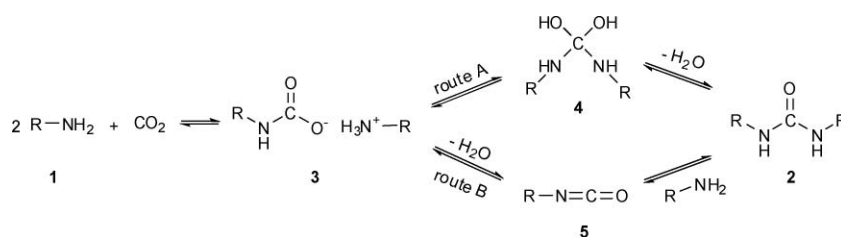
<sup>a</sup> Conditions: amine 1.0 mmol ml<sup>-1</sup>; temperature 180 °C; pressure 10 MPa; time 24 h. The selectivity of listed product was 100% at all the conversion values.

**Table 3** Synthesis of urea derivatives from different amines and CO<sub>2</sub><sup>a</sup>

$n\text{-Bu-NH}_2 + \text{HN} \begin{matrix} \text{R}^1 \\ \text{R}^2 \end{matrix} + \text{CO}_2 \rightleftharpoons n\text{-Bu-NH-C(=O)-NH-n-Bu} + n\text{-Bu-NH-C(=O)-N} \begin{matrix} \text{R}^1 \\ \text{R}^2 \end{matrix} + \begin{matrix} \text{R}^1 \\ \text{R}^2 \end{matrix} \text{-N-C(=O)-N} \begin{matrix} \text{R}^1 \\ \text{R}^2 \end{matrix} + \text{H}_2\text{O}$						
		Conv./%		Select./%		
Entry	B	A	B	A-A	A-B	B-B
1	isopropylamine	74.3	41.4	42.9	46.4	10.6
2	sec-butylamine	40.5	26.1	37.3	47.1	15.6
3	hexylamine	72.7	80.1	18.6	51.4	30.1
4	cyclohexylamine	77.5	60.3	27.8	50.3	21.8
5	benzylamine	76.9	56.6	24.2	57.8	18.0
6	diethylamine	62.5	7.8	77.8	22.2	—
7	dipropylamine	39.2	6.6	68.1	31.9	—
8	dibutylamine	39.4	4.2	78.1	21.9	—
9	pyrrolidine	51.0	33.8	20.4	79.6	—
10	piperidine	46.7	13.9	52.5	47.5	—
11	morpholine	58.1	13.3	60.8	39.2	—

R<sup>1</sup> = H, alkyl  
R<sup>2</sup> = alkyl

<sup>a</sup> Conditions: A (BA) 1.0 mmol mL<sup>-1</sup>; B 1.0 mmol mL<sup>-1</sup>; temperature 180 °C; pressure 10 MPa; time 24 h.

**Scheme 2** Proposed reaction mechanism.

sec-butylamine were low due to the steric hindrance effect (entries 2 & 5). Alkylene diamines or alcohol amines reacted with CO<sub>2</sub> under the same conditions producing corresponding cyclic ureas (entries 13–16) and urethanes (entries 17–20) as reported in literature.<sup>24</sup> The observation that diamine is more reactive than monoamine was ascribed to it bearing two amino groups with the formation of stable five- or six-membered rings. However, no products were detected at the same reaction conditions for the secondary and aromatic amines. Based on the reaction mechanism, the formation of the intermediate of alkyl isocyanate (*vide infra*) was the prerequisite of the reaction, which could not form in the case of secondary amines. The base dissociation constant of aromatic amines is 10<sup>6</sup> times smaller than the aliphatic amines (aniline pK<sub>b</sub> = 9.37 vs. BA pK<sub>b</sub> = 3.34), which may be the reason for the inactivity of aromatic amines. Therefore, the reaction largely depends on the structure and the basicity of the reactant.

Moreover, urea derivatives were synthesized from different amines with CO<sub>2</sub> under the same reaction conditions (Table 3). Amine A and amine B with different substituents could react with CO<sub>2</sub> to produce, theoretically, three kinds of corresponding urea derivatives, *i.e.* symmetric A–A, B–B and asymmetric A–B. Different primary aliphatic amines reacted with BA to produce urea derivatives, and the selectivity of the asymmetric products was higher (entries 1–5). Interestingly, the corresponding A–A and A–B urea derivatives could be produced from the secondary

aliphatic amines with BA and CO<sub>2</sub>, but B–B products were not detected (entries 6–11). As shown in the above paragraph, the secondary aliphatic amines could not react with CO<sub>2</sub>, but the asymmetric A–B products were formed in the presence of primary aliphatic amine (BA). It could illustrate the reaction mechanism as discussed below.

The reaction mechanism is proposed in Scheme 2. Primary aliphatic amine **1** reacted with CO<sub>2</sub> rapidly to form alkyl ammonium alkyl carbamate (AAAC) **3**, an intermediate, and then form the final product **2** via the subsequent dehydration. Two possible dehydrating steps were proposed, intermolecular route A and intramolecular route B through the intermediate **4** or **5**. It was witnessed through the following experiments.

First of all, the phase-behavior of the reaction of BA and CO<sub>2</sub> was observed in a high pressure view-cell. 15 ml BA was preset into an 80 ml view-cell at room temperature (Fig. 6A). With charging CO<sub>2</sub> into the reactor, the gas phase turned into black rapidly (Fig. 6B). As the pressure reached to 2 MPa, at which the charging was stopped, the black phase turned into gray gradually (Fig. 6C) and finally into bright within 2 min and the pressure decreased to *ca.* 1 MPa (Fig. 6D). The color change of the gas phase was due to the quick formation of BABC, the intermediate, and then sank down to the bottom, forming a viscous liquid. It indicates that the formation of the intermediate **3** is a fast step. The existence of **3** was examined by the experiment of using 5 ml cyclohexylamine or piperidine to

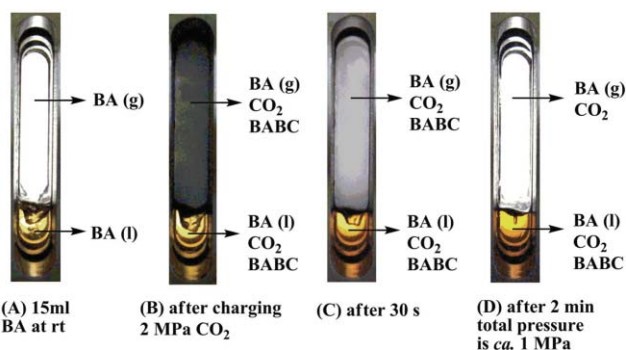


Fig. 6 Phase behavior of the reaction of BA with CO<sub>2</sub> to form butylammonium butylcarbamate (BABC).

react with 5 MPa CO<sub>2</sub> at room temperature for 10 min, with the subsequent characterization by solid-state <sup>13</sup>C CP/MAS NMR. The peaks at 162.23 ppm and 161.99 ppm clearly indicate the carbonyl group in **3** (Fig. 7). Thus amines reacted rapidly with CO<sub>2</sub> to form **3**, and it is not rate-determining step.

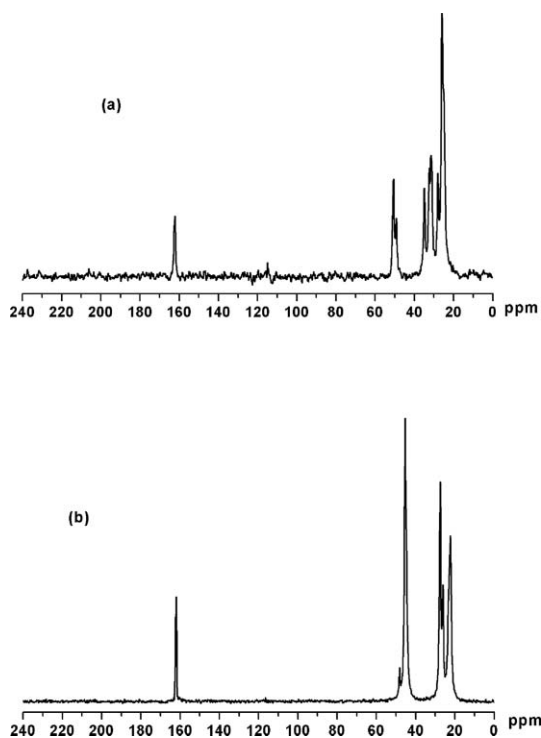
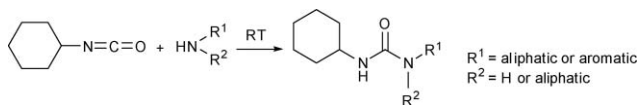


Fig. 7 Solid-state <sup>13</sup>C CP/MAS NMR spectrum of the products of (a) cyclohexylamine and (b) piperidine reacted with CO<sub>2</sub> at room temperature for 10 min.

Isocyanate was suspected to be the intermediate in the formation or the hydrolyzation of urea.<sup>24,25</sup> So alkyl isocyanate **5** was supposed to be the intermediate in this reaction. The reactivity of **5** was checked by using cyclohexylisocyanate to react with different amines at room temperature (Scheme 3). The reaction performed drastically to form the corresponding urea derivatives. It is widely accepted that **5** is very active and often used as building blocks to the synthesis of organics or polymers.<sup>27,28</sup> The intermediate **4** is not stable due to it bearing two hydroxy groups. The above results suggest that the rate-determining step is the formation of **4** or **5** from **3**.



Scheme 3 Reaction of cyclohexylisocyanate with different amines.

Now we give a brief comparison of the two possible dehydrating routes. Route A seems to be the only possible pathway for the secondary amines since they cannot form intermediate **5** through route B, while it is unlikely as no products were formed for the secondary amines. The two dehydrating routes are possible for primary aliphatic amines, but the formation of intermediate **4** needs two molecules, in contrast only one molecule is needed to form intermediate **5**. Moreover, intermediate **5** is more stable and readily formed compared to **4**, since it is difficult to form a four-substituted carbon atom bearing two hydroxyl groups. Intermediate **5** can react with another primary or secondary aliphatic amine to form the corresponding symmetric or asymmetric urea derivatives. And thus, the route B might be the predominant pathway.

Tsipis and co-worker investigated the mechanism of the production of urea from NH<sub>3</sub> and CO<sub>2</sub> by using electronic structure calculation methods.<sup>26</sup> They indicated that NH<sub>3</sub> and H<sub>2</sub>O could interact with the intermediate ammonium carbamate forming an active species, which acted as a catalyst to promote the reaction. A similar mechanism should be applicable to the present reaction, that amines interacted with AAC through hydrogen bonding or other means, and the interaction increased with increasing the concentration of amine, thus accelerated the dehydration to produce urea derivatives. Base was always used as a catalyst to accelerate this reaction in literature. As illustrated in Fig. 3, the amount of amine has a decisive effect on the reaction. Herein amine may therefore play a role of catalyst in present reaction, as amine is also a kind of strong base. More detailed mechanism is under investigation by using theoretical calculation methods.

## Conclusions

In summary, we developed a simple and green process that utilizes the captured CO<sub>2</sub> to synthesize useful urea derivatives, which avoids the use of toxic or expensive substrates. It is a parameter sensitive reaction, especially the concentration of the reactant. Satisfactory yields were obtained in the absence of any additives, which are comparable to those in the presence of catalyst and solvent. The preliminary study of the reaction mechanism showed that the formation of the intermediate **5** from **3** is the rate-determining step and the intramolecular dehydrating step (route B) is preferred. It is a green and facile route to the synthesis of urea derivatives, which has great potential for industrial application.

## Experimental

All the chemicals were used as received from commercial sources without further purification except aniline which was distilled before use. All the reactions were conducted in a 50 mL autoclave. The reactor was firstly charged with amines and/or additives, flushed with CO<sub>2</sub> three times, and then placed



into an oil batch preset to the reaction temperature. After heating for 20 min, CO<sub>2</sub> was introduced into the reactor with a high-pressure liquid pump (Jasco SCF-Get) to the desired pressure. The reaction was conducted while the mixture was stirred vigorously with a magnetic stirrer. After the reaction, the reactor was cooled to room temperature with an ice-water bath and then depressurized carefully. The products were washed with deionized (DI) water, recovered by filtration or rotary evaporation (depending on the solubility of product in water) and then dried in vacuum thoroughly. The powders were weighed to determine the isolated yields. All the samples were analyzed by gas chromatograph (Shimadzu GC-2010, Rtx-50 capillary column). The products were characterized by GC-MS (Agilent 5975/6890N). The solid-state <sup>13</sup>C CP/MAS NMR spectra were obtained on a Bruker Avance 400 WB spectrometer.

## Acknowledgements

This work was financially supported by the One Hundred Talent Program of CAS, and KJCX2, YWH16.

## References

- 1 J. Hansen, L. Nazarenko, R. Ruedy, M. Sato, J. Willis, A. Del Genio, D. Koch, A. Lacis, K. Lo, S. Menon, T. Novakov, J. Perlwitz, G. Russell, G. A. Schmidt and N. Tausnev, *Science*, 2005, **308**, 1431.
- 2 R. S. Haszeldine, *Science*, 2009, **325**, 1647.
- 3 G. T. Rochelle, *Science*, 2009, **325**, 1652.
- 4 T. Sakakura, J. C. Choi and H. Yasuda, *Chem. Rev.*, 2007, **107**, 2365.
- 5 T. Sakakura and K. Kohno, *Chem. Commun.*, 2009, 1312.
- 6 K. M. K. Yu, I. Curcic, J. Gabriel and S. C. E. Tsang, *ChemSusChem*, 2008, **1**, 893.
- 7 S. N. Riduan and Y. G. Zhang, *Dalton Trans.*, 2010, **39**, 3347.
- 8 M. Mikkelsen, M. Jorgensen and F. C. Krebs, *Energy Environ. Sci.*, 2010, **3**, 43.
- 9 F. Bigi, R. Maggi and G. Sartori, *Green Chem.*, 2000, **2**, 140.
- 10 D. J. Diaz, A. K. Darko and L. McElwee-White, *Eur. J. Org. Chem.*, 2007, 4453.
- 11 A. G. M. Barrett, T. C. Boorman, M. R. Crimmin, M. S. Hill, G. Kociok-Kohn and P. A. Procopiou, *Chem. Commun.*, 2008, 5206.
- 12 Z. Li, Z. Y. Wang, W. Zhu, Y. L. Xing and Y. L. Zhao, *Synth. Commun.*, 2005, **35**, 2325.
- 13 S. Fujita, B. M. Bhanage, H. Kanamaru and M. Arai, *J. Mol. Catal. A: Chem.*, 2005, **230**, 43.
- 14 R. Ballini, D. Fiorini, R. Maggi, P. Righi, G. Sartori and R. Sartorio, *Green Chem.*, 2003, **5**, 396.
- 15 (a) C. Bosch, W. Meiser, *US Pat.*, 1429483, 1922; (b) E. Otsuka, K. Kanal, T. Sakai, *US Pat.*, 3607937, 1971; (c) M. Karafian, C. S. Harbor, *US Pat.*, 3668250, 1969; (d) I. Mavrovic, *US Pat.*, 3759992, 1970.
- 16 C. F. Cooper and S. J. Falcone, *Synth. Commun.*, 1995, **25**, 2467.
- 17 F. Shi, Y. Q. Deng, T. L. SiMa, J. J. Peng, Y. L. Gu and B. T. Qiao, *Angew. Chem., Int. Ed.*, 2003, **42**, 3257.
- 18 A. Ion, V. Parvulescu, P. Jacobs and D. De Vos, *Green Chem.*, 2007, **9**, 158.
- 19 F. Shi, Q. H. Zhang, Y. B. Ma, Y. D. He and Y. Q. Deng, *J. Am. Chem. Soc.*, 2005, **127**, 4182.
- 20 T. Jiang, X. M. Ma, Y. X. Zhou, S. G. Liang, J. C. Zhang and B. X. Han, *Green Chem.*, 2008, **10**, 465.
- 21 D. L. Kong, L. N. He and J. Q. Wang, *Synlett.*, 2010, **8**, 1276.
- 22 J. M. Hao, H. Y. Cheng, H. J. Wang, S. X. Cai and F. Y. Zhao, *J. Mol. Catal. A: Chem.*, 2007, **271**, 42.
- 23 F. Y. Zhao, S. Fujita, S. Akihara and M. Arai, *J. Phys. Chem. A*, 2005, **109**, 4419.
- 24 B. M. Bhanage, S. Fujita, Y. Ikushima and M. Arai, *Green Chem.*, 2003, **5**, 340.
- 25 G. Estiu and K. M. Metz, *J. Am. Chem. Soc.*, 2004, **126**, 6932.
- 26 C. A. Tsipis and P. A. Karipidis, *J. Phys. Chem. A*, 2005, **109**, 8560.
- 27 R. G. Arnold, J. A. Nelson and J. J. Verbanc, *Chem. Rev.*, 1957, **57**, 47.
- 28 S. Subramani, Y. J. Park, Y. S. Lee and J. H. Kim, *Prog. Org. Coat.*, 2003, **48**, 71.