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Author(s)	Fujita, Shin-ichiro; Bhanage, Bhalchandra M.; Arai, Masahiko
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Synthesis of *N,N'*-Disubstituted Urea from Ethylene Carbonate and Amine Using CaO

Shin-ichiro Fujita,^{*†} Bhalchandra M. Bhanage,^{†,††} and Masahiko Arai^{†,††}

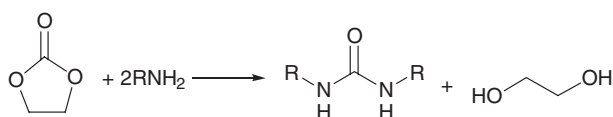
[†]Division of Materials Science and Engineering, Graduate School of Engineering, Hokkaido University, Sapporo 060-8628

^{††}CREST, JST

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Calcium oxide has been proved to be an excellent solid catalyst for the synthesis of *N,N'*-disubstituted ureas from ethylene carbonate and primary amines under mild conditions.

Substituted ureas have found extensive applications such as dyes, antioxidants, corrosion inhibitor, intermediates for the preparation of pharmaceuticals, and agricultural chemicals.¹ They can be synthesized from amines via phosgenation,² reductive carbonylation,³ or oxidative carbonylation.⁴ However, these reactions are not eco-friendly because of risks associated with using the poisonous compounds of phosgene and carbon monoxide and/or a potentially explosive mixture of carbon monoxide and oxygen. The reactions of amines with dialkyl or diaryl carbonate also produce substituted ureas or substituted carbamates.^{5,6} The latter compounds further reacts with amines producing substituted ureas. However, the carbonates are currently produced via similar hazardous routes of phosgenation or oxidative carbonylation.^{5,6} *N,N'*-Disubstituted ureas can be synthesized via the reaction of ethylene carbonate and amine in the presence of homogeneous base catalysts such as sodium methoxide and triethylamine (Scheme 1).⁷ However, no one has used solid base catalysts for this reaction. The solid base catalysts are more easily separable and recyclable than the homogeneous catalysts and are still gaining much attention.⁸ In the present work, it has been shown that calcium oxide is an excellent solid catalyst for the synthesis of the disubstituted ureas from ethylene carbonate and primary amines.



Scheme 1. Synthesis of *N,N'*-disubstituted urea from EC and amine.

Table 1 lists the reaction results for the *N,N'*-dibutylurea synthesis from ethylene carbonate (EC) and butylamine using various catalysts.⁹ It is seen that among the catalysts used only CaO is a good catalyst. *N,N'*-Dibutylurea is obtained in a yield of 49% after the reaction for 1 h with CaO (Entry 1). When the reaction time is lengthened from 1 to 3 h, the yield increases from 49 to 78% (Entry 2). In contrast to these, ZnO gives a very poor yield and the other catalysts do not produce the disubstituted urea (Entries 3–5). To elucidate the difference among the catalysts, basic properties of the catalysts were examined by temperature programmed desorption of adsorbed CO₂.¹⁰ For CaO, CO₂ desorption peaks were observed at 585 and 650 °C. For ZnO and MgO, peaks appeared below 500 °C. ZrO₂ had a trace amount of CO₂ desorption at 580 °C. These results suggest that CaO has larger amounts of strongly basic sites as compared with

Table 1. *N,N'*-Dibutylurea synthesis using various catalysts^a

Entry	Catalyst	Yield / %
1	CaO	49
2	CaO ^b	78
3	ZnO	6
4	MgO	0
5	ZrO ₂	0

^a Catalyst, 0.5 g; EC, 40 mmol; butylamine 80 mmol; temperature, 100 °C; time 1 h. ^b The reaction was carried out for 3 h.

the other catalysts, resulting in its higher activity observed.

The reactions of EC with various amines were also carried out using CaO. The results obtained are represented in Table 2.¹¹ It is seen that CaO is effective for the synthesis of various disubstituted amines. Propylamine and butylamine give good yields for the corresponding disubstituted ureas at a reaction temperature of 100 °C (Entries 1 and 2). Slightly higher reaction temperatures are required to obtain the substituted ureas from hexylamine and benzylamine with good yields (Entries 3 and 5). Unfortunately, from aniline, diphenylurea was not produced even at 125 °C (Entry 6). The product observed was 2-(phenylamino)ethanol. Probably, EC should decompose to ethylene oxide¹² and this decomposition product should further react with aniline, producing 2-(phenylamino)ethanol. Aniline might catalyze the former reaction.

Table 2. *N,N'*-Disubstituted urea synthesis from EC with various amines^a

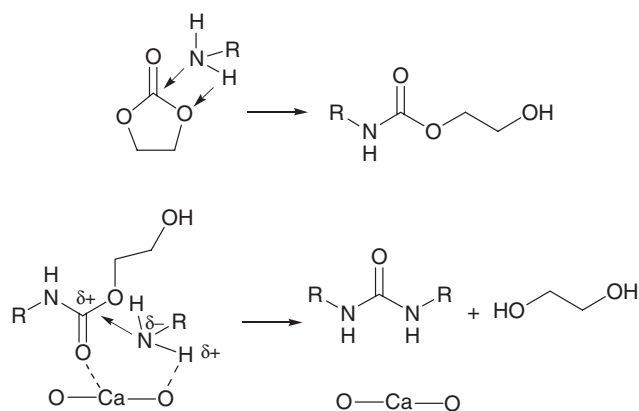
Entry	Amine	Yield / %
1	Propylamine	68
2	Butylamine	78
3	Hexylamine ^b	77
4	Benzylamine ^b	38
5	Benzylamine ^c	55
6	Aniline ^b	0

^a CaO, 0.5 g; EC, 40 mmol; amine 80 mmol; temperature, 100 °C; time 3 h. ^b at 125 °C. ^c at 150 °C.

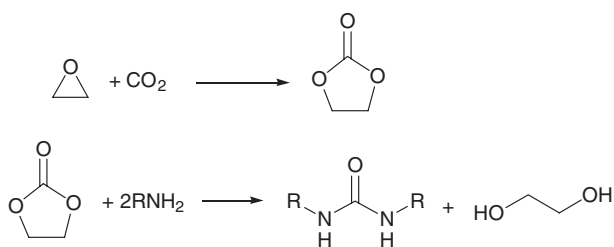
CaO was reused for the *N,N'*-dibenzylurea synthesis three times.¹³ The yields of *N,N'*-dibenzylurea obtained for the second and third runs were 56 and 55%, respectively. Thus, CaO retains its activity during the recycles. It is noted that the procedures for the recycle runs were carried out under ambient atmosphere. Exposing solid base catalysts to air sometimes causes their severe deactivation.⁸ However, such deactivation was not observed for the present reaction system.

For the experiment of Entry 1 in Table 1, compounds dissolved in water used for the post-reaction treatment were analyzed. It was found that all of EC was consumed and unreacted

amine, ethylene glycol, and 2-hydroxyethyl butylcarbamate presented in the water phase. This carbamate was considered to be intermediates species for the *N,N'*-dibutylurea formation. A plausible reaction mechanism for the title reaction is illustrated in Scheme 2. EC reacts with one molecule of amine, transforming to 2-hydroxyethyl alkylcarbamate. The carbamate reacts with another amine molecule, producing ethylene glycol and *N,N'*-dialkylurea. Since the carbamate formation from EC and amine proceeds rapidly around room temperature without any catalyst, as Kaupp et al. reported,¹⁴ the second reaction of carbamate and amine would be catalyzed by CaO and the rate determining step. CaO should activate both the amine and the carbamate as illustrated in Scheme 2.



Scheme 2. Reaction mechanism for *N,N'*-disubstituted urea synthesis from EC and amine.



Scheme 3. EC based carbon dioxide fixation.

In summary, this is the first paper reporting that CaO is an efficient solid catalyst for the synthesis of various *N,N'*-disubstituted ureas under mild conditions. It is noted that excess amine is not required under the present reaction conditions. This is more preferable from the viewpoint of economics. It should be noted that, since EC is prepared industrially from ethylene oxide and carbon dioxide, the title reaction will be EC based carbon dioxide fixation to important chemicals (Scheme 3).

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- 11 For the experiments with hexylamine and benzylamine, 50 mL of acetone was used instead of water for the post-reaction treatment of the products. The products were characterized by gas-chromatography, mass spectrometry, melting point measurements, ¹H NMR, and comparison with authentic samples whenever possible.
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