



Carbamate synthesis from amines and dimethyl carbonate under ytterbium triflate catalysis

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Abstract—A facile synthesis of carbamates from amines and dimethyl carbonate has been achieved using ytterbium triflate as catalyst. © 2002 Elsevier Science Ltd. All rights reserved.

Carbamates are compounds of great interest because of their important application as intermediates¹ for the synthesis of pesticides, fungicides, herbicides,² medical drugs,³ polyurethane based polymers and as protecting groups of amine function.⁴

Initially carbamates were almost exclusively synthesised by the reaction of amines with phosgene or its derivatives.⁵ This procedure had several drawbacks, among which the extreme toxicity of phosgene and generation of by-products. So, several efforts have been made for the preparation of title compounds using non-toxic reagents and for the development of novel environmentally friendly methodologies.

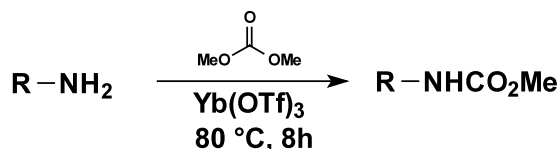
Carbamate synthesis has been accomplished by reductive carbonylation of nitro aromatics,⁶ oxidative carbonylation of amines catalysed by various transition metal complexes,⁷ zinc-promoted amino group protection with chloroformates,⁸ reaction of azides and chloroformates in the presence of Me₃P,⁹ reaction of tetraethylammonium hydrogen carbonate with amines,¹⁰ Cs₂CO₃ induced reaction of amines, alkyl halides and CO₂,¹¹ 1,1-carbonyldiimidazole-promoted reaction between alcohols and amines.¹² Some of these methods however have some limitations such as formation of inorganic salts as by-products. Very recently, the carbamate synthesis from dialkyl carbonates and amines in the presence of a catalyst, such as silica gel,¹³ lead(II) nitrate,¹⁴ γ -Al₂O₃,³ or MCM-41-TBD¹⁵ has been reported. The use of dialkyl carbonates instead of phosgene or chloroformates represents a good alterna-

tive, because the only by-product of this reaction is an alcohol, that can be easily removed from the reaction medium.

As a part of our ongoing studies to investigate the use of lanthanide triflates as catalyst in solvent-free conditions, we recently reported the synthesis of 1,5-benzodiazepines,¹⁶ 1,2,3,6-tetrahydropyridazines¹⁷ and glycidic esters¹⁸ catalysed by La(OTf)₃ or Yb(OTf)₃ hydrate. Herein we report that Yb(OTf)₃ can be efficiently used for the preparation of carbamates from amines and dimethyl carbonate (DMC) in solvent-free conditions (Scheme 1).¹⁹

The reaction was carried out at 80°C for 8 h using neat DMC (5.0 mmol) and amine (1.0 mmol) in the presence of Yb(OTf)₃ hydrate (0.05 mmol) as catalyst. The results are summarised in Table 1.

Yields obtained from primary, secondary or aromatic amines were high and similar, except for the less nucleophilic *p*-nitroaniline. Best results were obtained using 0.05 equiv. of Yb(OTf)₃ hydrate; if the reaction was carried out using 0.1 equiv. of the catalyst no significant improvements in terms of yields or time were observed, while minor amounts decreased yields and prolonged reaction times. It is important to note that addition of



Scheme 1.

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Table 1. Carbamate synthesis catalysed by Yb(OTf)₃

Substrate	Product	Yield (%) ^a
<i>n</i> -Butylamine	1	93
Cyclohexylamine	2	89
Benzylamine	3	95
α -Methylbenzylamine	4	92
Piperidine	5	87
Aniline	6	96
<i>p</i> -Anisidine	7	88
<i>p</i> -Nitroaniline	8	61

^a Yields of isolated products.

few mL of CH₂Cl₂ to the reaction mixture precipitated the catalyst with the consequence of its simple recovery by filtration in nearly quantitative yield. The catalyst could be reused several times without any loss of activity: the reaction to give compound **1** has been in fact repeated five times through the catalyst washed with CH₂Cl₂ and dried at 70°C for 2 h, with the following yields: 92, 91, 91, 89, and 91%. The filtrate, washed with a solution of citric acid, afforded after evaporation the pure carbamate, without the need of further purification.

In summary, the method of carbamate synthesis described herein compares favourably with heretofore reported methodologies, especially in terms of product yields, easy work-up procedure, absence of toxic or hardly removable by-products and simple recovery and complete recyclability of the catalyst used.

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References

- Adams, P.; Baron, F. A. *Chem. Rev.* **1965**, *65*, 567–602.
- (a) Tai-The, W.; Huang, J.; Arrington, N. D.; Dill, G. M. *J. Agric. Food Chem.* **1987**, *35*, 817; (b) Piccardi, P. *Chim. Ind.* **1986**, *68*, 108–117.
- (a) Vauthey, I.; Valot, F.; Gozzi, C.; Fache, F.; Lemaire, M. *Tetrahedron Lett.* **2000**, *41*, 6347–6350; (b) Barthelemy, J. *Lyon. Pharm.* **1986**, *37*, 249–263.
- Greene, T. W.; Wuts, P. G. M. *Protective Groups in Organic Synthesis*, 3rd ed.; J. W. Wiley and Sons: New York, 1999; pp. 503–550 and references cited therein.
- (a) Eckert, H.; Foster, B. *Angew. Chem., Int. Ed. Engl.* **1987**, *26*, 894; (b) Cotarca, L.; Delogu, P.; Nardelli, A.; Sunjic, V. *Synthesis* **1996**, 553–576.
- (a) Cenini, S.; Crotti, C.; Pizzotti, M.; Porta, F. *J. Org. Chem.* **1988**, *53*, 1243–1250 and references cited therein; (b) Ragaini, F.; Cenini, S. *Organometallics* **1994**, *13*, 1178–1189; (c) Paul, F.; Fischer, J.; Ochsenbein, P.; Osborn, J. A. *Organometallics* **1998**, *17*, 2199–2206 and references cited therein.
- Wan, B.; Liao, S. L.; Yu, D. *Appl. Catal. A: Gen.* **1999**, *183*, 81–84.
- Yadav, J.; Reddy, G.; Reddy, M.; Meshram, H. *Tetrahedron Lett.* **1998**, *39*, 3259–3262.
- Ariza, X.; Urpi, F.; Villarassa, J. *Tetrahedron Lett.* **1999**, *40*, 7515–7517.
- Inesi, A.; Mucciante, V.; Rossi, L. *J. Org. Chem.* **1998**, *63*, 1337–1338.
- (a) Salvatore, R. N.; Ledger, J. A.; Jung, K. W. *Tetrahedron Lett.* **2001**, *42*, 6023–6025; (b) Salvatore, R. N.; Shin, S. I.; Nagle, A. S.; Jung, K. W. *J. Org. Chem.* **2001**, *66*, 1035–1037; (c) Salvatore, R. N.; Chu, F.; Nagel, A. S.; Kapxhiu, E. A.; Cross, R. M.; Jung, K. W. *Tetrahedron* **2002**, *58*, 3329–3347.
- D'Addona, D.; Bochet, C. G. *Tetrahedron Lett.* **2001**, *42*, 5227–5229.
- Gupte, S. P.; Shivarkar, A. B.; Chaudhari, R. V. *J. Chem. Soc., Chem. Commun.* **2001**, 2620–2621.
- Baba, T.; Fujiwara, M.; Oosaku, A.; Kobayashi, A.; Deleon, R. G.; Ono, Y. *Appl. Catal. A: Gen.* **2002**, *227*, 1–6.
- Carlioni, S.; De Vos, D. E.; Jacobs, P. A.; Maggi, R.; Sartori, G. *J. Catal.* **2002**, *205*, 199–204.
- Curini, M.; Epifano, F.; Marcotullio, M. C.; Rosati, O. *Tetrahedron Lett.* **2001**, *42*, 3193–3195.
- Curini, M.; Epifano, F.; Marcotullio, M. C.; Rosati, O. *Heterocycles* **2001**, *55*, 1599–1604.
- Curini, M.; Epifano, F.; Marcotullio, M. C.; Rosati, O. *Eur. J. Org. Chem.* **2002**, *9*, 1562–1568.
- General procedure:** To a solution of amine (1.0 mmol) in dimethyl carbonate (5.0 mmol), Yb(OTf)₃ (0.05 mmol) was added and the resulting mixture stirred for 8 h at 80°C; CH₂Cl₂ (2 mL) was added at room temperature, the catalyst so precipitated was filtered under vacuum;

the filtrate was diluted with CH₂Cl₂ (20 mL), washed twice with a 2% solution of citric acid, dried over Na₂SO₄ and evaporated to give pure carbamate.

Analytical data for selected compounds:

Compound 2: IR (cm⁻¹) 1688; ¹H NMR (CDCl₃, 200 MHz): δ 1.13–2.20 (m, 10H), 3.44–3.52 (m, 1H), 3.68 (s,

3H), 4.68 (s br, 1H); ¹³C NMR (CDCl₃, 50 MHz): δ 24.7, 25.4, 33.4, 49.8, 51.8, 152.7.

Compound 7: IR (cm⁻¹) 1682; ¹H NMR (CDCl₃, 200 MHz): δ 3.62 (s, 3H), 3.71 (s, 3H), 6.84–7.46 (m, 4H), 8.55 (s br, 1H); ¹³C NMR (CDCl₃, 50 MHz): δ 52.7, 55.9, 118.4, 121.2, 134.8, 154.6, 157.0.