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# Synthesis and characterization of asymmetric substituted dicarbamates

Chao Zhao, Peng Fei Yang *, Shun Ping Wang, Jun Ying Li, Tian Duo Li *

*Shandong Provincial Key Laboratory of Fine Chemicals, Shandong Polytechnic University, Jinan 250353, China*

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**Abstract**

Several new asymmetric substituted dicarbamates were synthesized with a convenient route. Firstly, tolylene-2, 4-diisocyanate dimmer was obtained from monomer with tributylphosphine as catalyst. Then, the dimmer reacted with alcohol ($R^1OH$) to prepare carbamate substituted uretidione. Finally, uretidione ring was opened and the released isocyanate reacted with another alcohol ($R^2OH$, $R^1 \neq R^2$).



*Keywords:* Asymmetric substituted dicarbamates; Tolylene-2, 4-diisocyanate; Uretidione

Carbamates are a kind of significant compounds which have been used in many areas, such as intermediates of organic synthesis, pesticides and weedicides [1,2]. As a kind of special carbamate, asymmetric substituted dicarbamate has been continuously investigated [3–5]. There are two traditional routes to synthesize asymmetric substituted dicarbamate (Scheme 1). In the early days, they were prepared from 2, 4-dinitrotolylene and carbon monoxide. Lick [6] used 2, 4-dinitrotolylene and carbon monoxide to react with ethanol (125 °C, 3000 psi) and methanol (175 °C, 4775 psi) in the presence of amorphous rhodium sesquioxide, respectively. The mixture of **4a** and **4b** was acquired with that method. However, it was very difficult to separate those two compounds and the reaction condition was very harsh. Afterwards, Schulze [7,8] prepared asymmetric substituted dicarbamates with 2-nitro-4-aminotolylene. Firstly, amido was transformed into isocyanate and reacted with $R^1OH$, or amido reacted with $R^1OCOCl$ directly, through which the first carbamate group was introduced; secondly, nitryl was reduced to amido, transformed into isocyanate and reacted with $R^2OH$, or the amino reacted with $R^2OCOCl$ directly, through which the second carbamate group was introduced. Pure compounds could be obtained, but it was very inconvenient in procedure and harsh in reaction conditions.

In this paper, we synthesized several asymmetric substituted dicarbamates with a convenient route (Scheme 2). It was divided into three steps. Firstly, tolylene-2, 4-diisocyanate was dimerized with tributylphosphine as catalyst. Then, tolylene-2, 4-diisocyanate dimmer reacted with alcohol ($R^1OH$) to prepare carbamate substituted uretidione. Finally, uretidione ring was opened with tributylphosphine as catalyst, in order that the released isocyanate reacted

* Corresponding authors.
*E-mail addresses:* ypfyyh@gmail.com (P.F. Yang), litianduo@163.com (T.D. Li).

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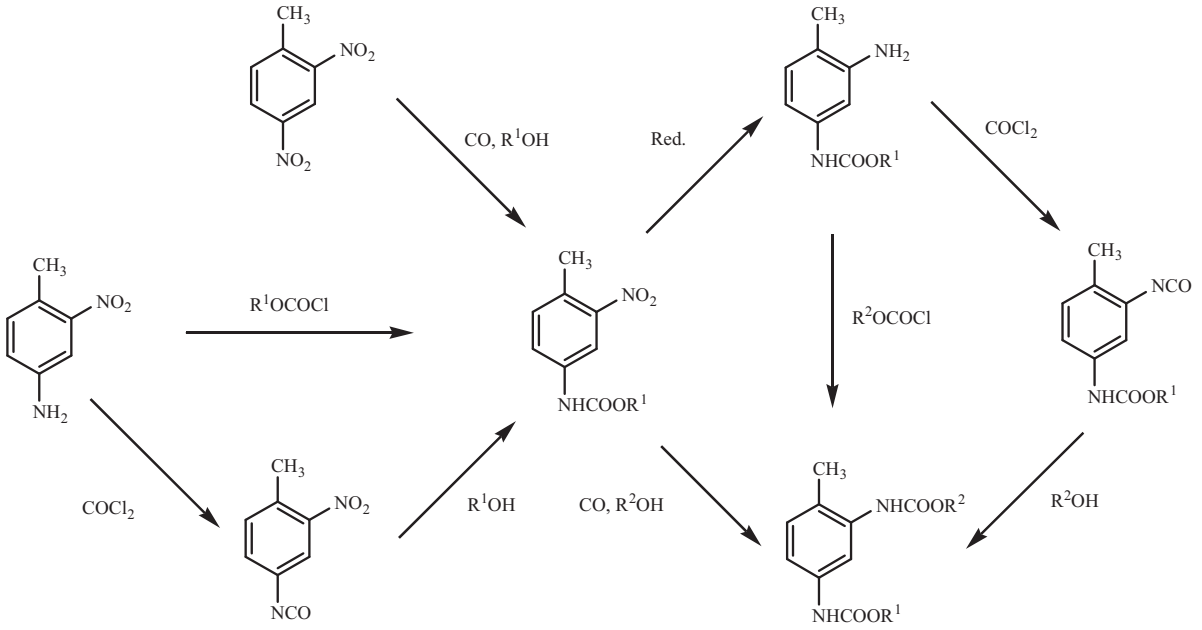
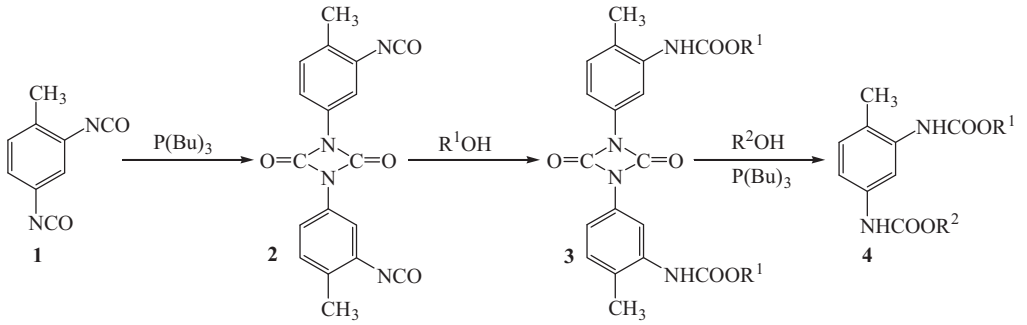



Scheme 1. Traditional synthetic routes of asymmetric substituted dicarbamate.




Scheme 2. New synthetic route of asymmetric substituted dicarbamate.

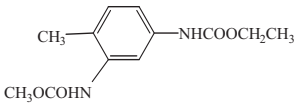
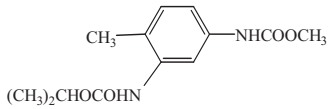
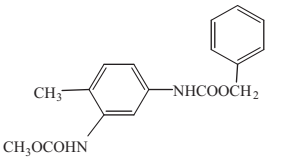
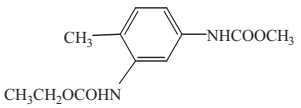
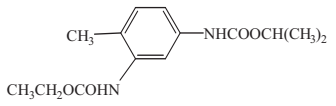
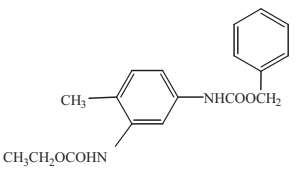
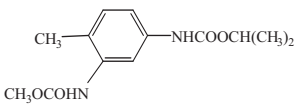
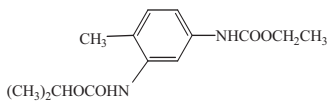
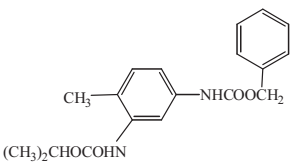
with another alcohol ($R^2OH$, $R_1 \neq R_2$). A series of asymmetric substituted dicarbamates was prepared, four of which was not reported before.

Tolylene-2, 4-diisocyanate dimmer **2** was obtained from monomers **1**. Dimerization of isocyanate was a reversible reaction in the presence of catalysts or elevated temperature [9]. In order to get a better yield, tributylphosphine was used as catalyst and the reaction was carried on at relatively low temperature. The dimerization reaction was used to protect one active isocyanate group, and make the other isocyanate reacted with $R^1OH$. IR, NMR and elemental analysis showed that the protected isocyanate could not react with $R^1OH$ [10].

After dimmerization and carbamation with $R^1OH$, uretidione ring must be opened to generate asymmetric substituted dicarbamate. It was reported that [11] uretidione ring could broken at above 150 °C. In the presence of catalyst, such as trialkylphosphines, the dissociation temperature maybe decreased. For example, uretidione dissociated slightly at 25 °C and completely dissociated at 80 °C in the presence of trialkylphosphines [12]. Thus, tributylphosphine was used once again, yet the purpose was to open uretidione ring at elevated temperature after **3a**–**3c** were synthesized. The blocked isocyanate could be set free and react with $R^2OH$ to synthesize **4a**–**4i** (Table 1). **4f, 4g, 4h, 4i** were not reported before.

*Tolylene-di-*(2-*isopropyl-4-ethyl*)*-carbamate* (**4f**): colorless crystal, yield 89%, mp 142–143 °C. Calcd. C, 59.96; H, 7.18; N, 9.99. Found: C, 59.86; H, 7.07; N, 10.04. $^1$H NMR (400 MHz, DMSO-$d_6$): $\delta$ 1.22 (d, 6H, $J$ = 6.5 Hz),

Table 1
Asymmetric substituted dicarbamates (**4f, 4g, 4h, 4i** were not reported before).

| Compound | Structure | Compound | Structure | Compound | Structure |
|---|---|---|---|---|---|
| **4a** |  | **4d** |  | **4g** |  |
| **4b** |  | **4e** |  | **4h** |  |
| **4c** |  | **4f** |  | **4i** |  |

2.09(s, 3H), 4.06(q, 2H, $J$ = 7.1 Hz), 4.83(m, 1H, $J$ = 6.2 Hz), 7.02–7.48(m, 3H), 8.66(s, 1H), 9.47(s, 1H). $^{13}$C NMR (100 MHz, DMSO-$d_6$): $\delta$ 13.99, 16.57, 21.45, 59.44, 66.79, 114.43, 114.47, 125.06, 129.57, 136.02, 136.66, 152.98, 153.36. IR (KBr, cm$^{-1}$): 3331.07, 3302.13, 1695.43.

*Tolylene-di-*(2-*methyl*-4-*benzyl*)-*carbamate* (**4g**): colorless crystal, yield 72%, mp 129–130 °C. Calcd. C, 64.96; H, 5.77; N, 8.91. Found: C, 64.88; H, 5.72; N, 9.03. $^1$H NMR (400 MHz, DMSO-$d_6$): $\delta$ 2.03(s, 3H), 3.56(s, 3H), 5.05(s, 2H), 6.97–7.44 (m, 8H), 8.74(s, 1H), 9.60(s, 1H). $^{13}$C NMR (100 MHz, DMSO-$d_6$): $\delta$ 16.53, 51.05, 65.07, 114.37, 114.53, 125.16, 127.43, 127.45, 127.88, 129.69, 135.94, 136.20, 136.56, 152.80, 154.18. IR (KBr, cm$^{-1}$): 3259.70, 1712.79, 1693.50.

*Tolylene-di-(2-ethyl*-4-*benzyl*)-*carbamate* (**4h**): colorless crystal, yield 68%, mp 119–120 °C. Calcd. C, 65.84; H, 6.14; N, 8.53. Found: C, 65.62; H, 6.14; N, 8.55. $^1$H NMR (400 MHz, DMSO-$d_6$): $\delta$ 1.15 (t, 3H, $J$ = 6.9 Hz), 2.04 (s, 3H), 4.02 (q, 2H, $J$ = 6.9 Hz,), 5.05 (s, 2H), 6.97–7.44 (m, 8H), 8.68 (s, 1H), 9.59 (s, 1H). $^{13}$C NMR (100 MHz, DMSO-$d_6$): $\delta$ 14.06, 16.56, 59.55, 65.06, 114.40, 114.46, 125.16, 127.42, 127.44, 127.87, 129.66, 136.01, 136.20, 136.53, 152.80, 153.73. IR (KBr, cm$^{-1}$): 3271.27, 1710.86, 1693.50.

*Tolylene-di-*(2-*isopropyl*-4-*benzyl*)-*carbamate* (**4i**): colorless crystal, yield 78%, mp 130–131 °C. Calcd. C, 66.65; H, 6.48; N, 8.18. Found: C, 66.62; H, 6.44; N, 8.17. $^1$H NMR (400 MHz, DMSO-$d_6$): $\delta$ 1.15 (d, 6H, $J$ = 6.2 Hz), 2.04 (s, 3H), 4.78 (m, 1H, $J$ = 6.2 Hz, 12.5 Hz), 5.06 (s, 2H), 6.97–7.45 (m, 3H), 8.62 (s, 1H), 9.60 (s, 1H). $^{13}$C NMR (100 MHz, DMSO-$d_6$): $\delta$ 16.59, 21.45, 65.06, 66.81, 114.41, 125.16, 126.02, 127.42, 127.44, 127.87, 129.64, 136.09, 136.21, 136.51, 152.81, 153.36. IR (KBr, cm$^{-1}$): 3331.07, 3302.13, 1695.43.

## 1. Experimental

IR: Bruker TENSOR27. NMR: Bruker AVANCE II 400. Elemental analysis: Elementar VARIOE III.

Tolylene-2, 4-diisocyanate was purchased from Sigma–Aldrich Co., Ltd. and used after vacuum distillation. Tributylphosphine was purchased from TCI (Shanghai) Development Co., Ltd. and used received. Other organic solvents were purchased from Sinopharm Chemical Reagent Co. Ltd. and used after distillation or vacuum distillation.

*Synthesis of tolylene-2, 4-diisocyanate dimmer* **(2)**: Tolylene-2, 4-diisocyanate **1** (8.708 g, 50 mmol) was fully dissolved in toluene (50 mL), to this was added tributylphosphine (3% m/m). The reaction was carried on with magnetic stirrer at 0 °C for 3 h. After that, the mixture was filtered, washed for three times and dried. The product **2** was recrystallized from petroleum ether and dried in vacuum for 24 h.

*Synthesis of 1, 3-Diazetidine-2, 4-dione, 1, 3-bis(3-lcarbamato-4-methylphenyl)* **(3)**: Tolylene-2, 4-diisocyanate dimer **2** (0.696 g, 2.0 mmol) was fully dissolved in chlorobenzene (50 mL), to this was added R$^1$OH (10 mmol). The

reaction was carried on with magnetic stirrer at 60 °C for 3 h. The mixture was filtered and the residue **3** was washed with chlorobenzene, dried under vacuum at 60 °C for 24 h.

*Synthesis of asymmetric substituted dicarbamates* **(4)**: **3** (1.0 mmol) was fully dissolved in DMF (15 mL). $R^2OH$ ($R^1 \neq R^2$) (10 mmol) and tributylphosphine (3% m/m) was added. The reaction was carried on with magnetic stirrer at 60 °C for 3 h. The mixture was filtered and the filtrate **4** was dried under vacuum at 90 °C for 48 h to remove the solvent. The remaining solid was recrystallized in DMF/$H_2O$ (3:7).

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## References

[1] J.J. D'Amico, F.G. Bollinger, Synth. Chem. Agrochem. II 443 (1991) 300.
[2] T.C. Jeong, S.W. Cha, J.I. Park, Int. J. Immunopharmacol. 17 (1995) 1035.
[3] V. Singh, P. Vedantham, P.K. Sahu, Tetrahedron 60 (2004) 8161.
[4] T. Yuge, T. Sakai, N. Kai, et al. Chem. Eur. J. 14 (2008) 2984.
[5] M. Sato, Y. Kitamura, N. Yoshimura, et al. J. Org. Chem. 74 (2009) 1268.
[6] G.C. Lick, Oxford, Mich, U.S. Patent 4,052,420 (1977).
[7] W.D.D. Schulze, D.D. Patent 299,032 (1983).
[8] R. Schirmer, D.E. Wurzer, D.E. Patent 2,703,838 (1983).
[9] H.J. Laas, R. Halpaap, J. Pedain, Adv. Synth. Catal. 336 (1994) 185.
[10] Select data of compounds: **3a**: white powder, yield 96%. Calcd. C, 58.23; H, 4.82; N, 13.40. Found: C, 58.15; H, 4.78; N, 13.39. $^1$H NMR (400 MHz, DMSO-$d_6$): $\delta$ 2.18 (s, 3H), 3.67 (s, 3H), 7.11–7.57 (m, 3H), 8.94 (s, 1H). IR (KBr, cm$^{-1}$): 3295.96, 1779.55, 1703.32. **3b**: white powder, yield 94%. Calcd. C, 59.97; H, 5.50; N, 12.73. Found: C, 59.71; H, 5.37; N, 12.57. $^1$H NMR (400 MHz, DMSO-$d_6$): $\delta$ 1.24 (t, 3H, $J$ = 7.0 Hz), 2.17 (s, 3H), 4.09 (q, 2H, $J$ = 6.9 Hz), 7.10–7.57 (m, 3H), 8.92 (s, 1H). IR (KBr, cm$^{-1}$): 3296.51, 1780.50, 1699.14. **3c**: white powder, yield 91%. Calcd. C, 61.50; H, 6.03; N, 11.96. Found: C, 61.29; H, 6.21; N, 11.88. $^1$H NMR (400 MHz, DMSO-$d_6$): $\delta$ 1.24 (d, 6H, $J$ = 6.2 Hz), 2.17 (s, 3H), 4.85 (m, 1H, $J$ = 12.4), 7.07–7.57 (m, 3H), 8.83 (s, 1H). IR (KBr, cm$^{-1}$): 3288.72, 1785.85, 1695.95.
[11] A.W. Hofmann, Ber. 4 (1871) 246.
[12] E. Querat, L. Tighzert, J.P. Pascault, Angew. Makromol. Chem. 242 (1996) 1.