Available online at www.sciencedirect.com
ScienceDirect
Tetrahedron
Tetrahedron 63 (2007) 8723–8726

Silica supported perchloric acid ($HClO_4$–SiO_2): an efficient reagent for the preparation of primary carbamates under solvent-free conditions

Ali Reza Modarresi-Alam,* Ferydoon Khamooshi, Mahmoud Nasrollahzadeh and Homeyra Alsadat Amirazizi

Department of Chemistry, University of Sistan and Baluchestan, Zahedan 98135, Iran

Received 26 March 2007; revised 28 May 2007; accepted 14 June 2007
Available online 21 June 2007

Abstract—The synthesis of primary carbamates from structurally diverse compounds containing a hydroxyl group has been performed in high yields and purity, and without any epimerization under solvent-free conditions using $HClO_4$–SiO_2 as a mild, convenient, and effective reagent. The procedure is operationally simple, efficient, and environmentally benign.

1. Introduction

Carbamates (urethanes) are widely used nowadays. Apart from the use of polyurethanes in plastics,[1–3] they are also common components of agrochemicals such as herbicides, fungicides, and pesticides,[1,2,4–6] or drug intermediates in the pharmaceuticals industry.[1,2,7] Their ability to cyclize to heterocyclic compounds is widely exploited in organic syntheses.[4] In addition, among the various amine-protecting groups, carbamates are commonly used due to their chemical stability toward acids, bases, and hydrogenation.[8] Their conventional synthesis is based on the use of phosgene in organic solvents, a toxic chemical, which suffers from stringent transportation and stocking limitations. To substitute phosgene with a less noxious starting material may represent an important industrial target for the future, in addition to meet the raw material diversification goal. Carbon dioxide and organic carbonates are good candidates as phosgene substitutes.[9] However, these methods cannot produce *N*-unsubstituted (primary) carbamates. Synthesis of *N*-unsubstituted carbamates **1** from alcohols has also been accomplished by several-pot reaction methods such as trichloroacetyl isocyanate,[10,11] chloroformates (starting from toxic phosgene),[12] chlorosulfonyl isocyanate,[13] and cyanogen chloride.[14]

Loev and co-workers reported the synthesis of *N*-unsubstituted carbamates from alcohols by treatment with sodium cyanate and trifluoroacetic acid in certain organic solvents such as benzene, methylene chloride, and tetrachloride carbon.[15] These solvents are toxic and are not eco-friendly. In addition, trifluoroacetic acid is very expensive. From the standpoint of 'green chemistry', significant efforts have been made to find an alternative to organic solvents. A very attractive substitute for these solvents is a solvent-free reaction (industrially important due to reduced pollution, low cost, and simplicity in processing and handling).[16–21]

In attempts to synthesize primary carbamates from phenols and alcohols under solvent-free conditions, we have recently reported a method for the conversion of compounds containing a hydroxyl group to primary carbamates at room temperature in the absence of solvent using trichloroacetic acid.[22,23] Since this acid is relatively toxic and corrosive, we were interested in developing methods for the synthesis of carbamates utilizing solid acids, as they are industrially important due to their potential in replacing conventional acid/base catalysts.[19–21,24–27]

Solid supported reagents are unique catalysts or reagents that have become popular over the last two decades.[19–21,24–27] The high catalytic activity, low toxicity, moisture, air tolerance, their recyclability, and particularly low price make the use of solid supported reagents attractive alternatives to conventional acids. Although the catalytic applications of solid supported reagents for organic synthesis have been well established, relatively few examples are reported on the use of $HClO_4$–SiO_2.[28] Silica supported perchloric acid ($HClO_4$–SiO_2) has received considerable attention as an inexpensive, non-toxic, and recyclable catalyst for various organic transformations, affording the corresponding products

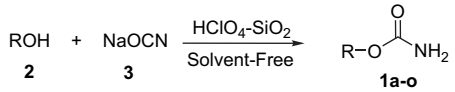
Keywords: Solvent-free conditions; *N*-Unsubstituted carbamates; Compounds containing a hydroxyl group; Silica supported perchloric acid ($HClO_4$–SiO_2); Solid acid.
* Corresponding author. Tel.: +98 541 2431146; fax: +98 541 2450995; e-mail: modaresi@hamoon.usb.ac.ir

0040–4020/$ - see front matter © 2007 Elsevier Ltd. All rights reserved.
doi:10.1016/j.tet.2007.06.048

in excellent yields with high selectivity.[28] However, to the best of our knowledge there has been no report on the use of $HClO_4$–SiO_2 for primary carbamates' synthesis.

Furthermore, in the past decade the development of new technologies have been expedited to strive to eliminate the need for chromatographic separation of mixtures, especially impurities and this itself has led to the development of new technologies in synthetic organic chemistry.[29]

Herein, we report $HClO_4$–SiO_2 as an efficient reagent for the synthesis of primary carbamates **1** from structurally diverse compounds **2** with sodium cyanate in high yield and purity under solvent-free conditions (Scheme 1).



Scheme 1.

2. Results and discussion

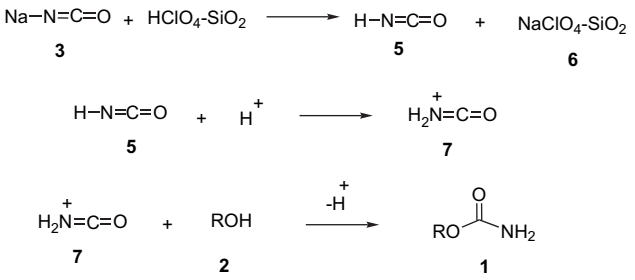
$HClO_4$–SiO_2 was prepared from silica gel and perchloric acid according to the literature.[28] Primary carbamates **1a–o** were purely obtained from reaction of alcohol or the phenol **2** with sodium cyanate **3** in the presence of $HClO_4$–SiO_2 at room temperature or 55–65 °C for appropriate time in high yields, as summarized in Table 1 and Scheme 1.

As shown in Table 1, several structurally varied substrates have been used for pure and clean synthesis of primary carbamates **1a–o** under this simple procedure. Primary, secondary, tertiary, allylic, benzylic alcohols, and phenols are all smoothly converted to the corresponding carbamates. It is remarkable to note that in the case of (−)-menthol **2a**, the reaction produced the corresponding (−)-menthyl carbamate **1a** without any epimerization. In most cases, the crude product was actually quite pure and did not require additional purification or work up. In aromatic compounds **1j–o** (entries 10–15), the yield and purity was improved at 55–65 °C for 1 h. Phenols containing electron-withdrawing groups (CN, COOR, and CHO) failed to react under our experimental conditions. Most likely these functional groups decrease the nucleophilicity of the phenol oxygen for effective attack to give intermediate **5** and/or **7** (Scheme 2). This may be the reason why compound **1l** (entry 12) was obtained in lower yield (58%). Also, the reaction conditions tolerate moieties such as *O*-isopropyl (**1h**, entry 8), which often undergoes cleavage in strongly acidic media. Furthermore, it is worthy to mention that reaction of α- and β-naphthol (entries 14 and 15) did not proceed completely in trichloroacetic acid (the recently reported method[22,23]). Indeed, considerable amounts of starting material remained even after long times, and/or at high temperatures. Moreover, this method is more effective than that recently reported[22,23] in terms of the removal of trichloroacetic acid, and the reaction times, which have been shortened from 12 to 1 h (Table 1).

Table 1. Preparation of primary carbamates **1a–o**[a]

Entry	Compound	R	Time (min)	Yield (%)
1	**1a**	(−)-Menthyl	45	82
2	**1b**	CH_3CH_2	45	73
3	**1c**	$CH_3CH_2CH_2$	45	81
4	**1d**	$CH_3CH_2CH_2CH_2$	45	77
5	**1e**	C_6H_{11}	45	80
6	**1f**	$(CH_3)_3C$	45	74
7	**1g**	$PhCH_2$	45	78
8	**1h**	$(CH_3)_2CHOCH_2CH_2$	45	81
9	**1i**	$H_2C{=}CHCH_2$	45	79
10	**1j**	C_6H_5[b]	60	79
11	**1k**	4-$CH_3C_6H_4$[b]	60	83
12	**1l**	4-BrC_6H_4[b]	60	58
13	**1m**	2-$C(CH_3)_3$–4-$CH_3C_6H_4$[b]	60	75
14	**1n**	α-Naphthyl[b]	60	72
15	**1o**	β-Naphthyl[b]	60	82

[a] See Refs. 22, 30, and 31 for carbamates **1a–m**, **1n**, and **1o**, respectively.
[b] By heating at 55–65 °C for 1 h.



Scheme 2.

The products were identified by comparison of their IR and physical properties with those of authentic samples.[22,30,31] In addition, they have also been characterized by ^1H NMR (500 MHz) and ^{13}C NMR (125 MHz). ^{13}C NMR spectra display signals for carbonyl carbons of aliphatic or aromatic carbamate in the range of δ 146–157 ppm.

The possible reaction mechanism is similar to that recently reported,[22] and is depicted in Scheme 2. The first step could be the reaction of sodium cyanate **3** with an acid ($HClO_4$–SiO_2) to give isocyanic acid **5**.[22,32,33] In the second step, the proton of $HClO_4$–SiO_2 is added to isocyanic acid **5** to yield the intermediate **7** (N-protonation is favored[34]). Finally, formation of carbamate **1** may occur by a nucleophilic attack of alcohol **2** on the carbon of the intermediate **7** (Scheme 2).

3. Conclusion

In conclusion, we have developed a novel and highly efficient method for the synthesis of various primary carbamates by the treatment of structurally varied alcohols and phenols with sodium cyanate in the presence of $HClO_4$–SiO_2 as an effective reagent. The solvent-free conditions, mildness of the conversion, simple experimental procedure, clear reaction profiles, high yields and purity, and short reaction times are the noteworthy advantages of the protocol. Furthermore, this method does not have disadvantages such as involvement of toxic solvents, expensive starting materials, formation of any undesirable side products, and epimerization. Further studies are in progress.

4. Experimental

4.1. General

^{1}H NMR and ^{13}C NMR spectra were recorded by Bruker Avance DRX500 (500 MHz). The IR spectra were obtained on a Shimadzu-470. Melting points were recorded by Electrothermal 9100 and were uncorrected. Thin layer chromatography (TLC) was carried out using plastic sheets precoated with silica gel 60 F. All starting materials such as alcohols, phenols, NaOCN, and solvents were purchased from Fluka, Merck, and Aldrich chemical companies and were purified with the proper purification techniques before use.[35,36] The products **1** were identified through comparison of their spectral data, IR, ^{1}H NMR, ^{13}C NMR, TLC, and physical properties with those of authentic samples.[22,30,31] $HClO_4$–SiO_2 was prepared from silica gel and perchloric acid according to the literature.[28]

4.2. General procedure

In a typical procedure, to a mixture of sodium cyanate (2 mmol) and $HClO_4$–SiO_2 (2 g, 1 mmol), alcohol or phenol (1.0 mmol) was added and the mixture was pulverized in a mortar at room temperature or 55–65 °C for appropriate time (Table 1). The reaction was monitored in TLC. After completion of the reaction, $CHCl_3$ was added and the mixture was filtered for separation of the reagent. The solvent ($CHCl_3$) was evaporated to give the product. Pure products were obtained in high yields, as summarized in Table 1.

In cases of α- and β-naphthol (entries 14 and 15) after removing $CHCl_3$, petroleum ether and then ethyl acetate were added. The obtained solid was pure α- or β-naphthyl carbamate **1n** and **1o**.

Naphthalen-1-yl carbamate **1n**: reaction afforded white crystals **1n**, 72% yield, mp=178–180 °C.[30] IR (KBr, cm^{-1}): 3430 (m), 3343 (vw), 3275 (w), 3200 (w), 3055 (vw), 2920 (vw), 1698 (vs), 1603 (s), 1360 (vs), 1254 (s), 1222 (s), 1150 (m), 1082 (s), 1041 (m), 1010 (m), 958 (m), 801 (s), 773 (vs), 582 (m), 553 (w). ^{1}H NMR (500 MHz, $CDCl_3$) δ (ppm): 6.10 (br d, 2H), 7.20 (d, J=7.5 Hz, 1H), 7.35–7.45 (m, 3H), 7.63 (d, J=8.2 Hz, 1H), 7.78 (dd, J=9.3, 2.1 Hz, 1H), 7.92 (dd, J=8.8, 2.1 Hz, 1H). ^{13}C NMR (125 MHz, $CDCl_3$) δ (ppm): 117.7, 120.8, 124.8, 124.9, 125.6, 125.7, 126.9, 127.3, 134.0, 146.2, 154.7. Anal. Calcd for $C_{11}H_9NO_2$: C, 70.59; H, 4.81; N, 7.49. Found: C, 70.80; H, 4.71; N, 7.60%.

Naphthalen-2-yl carbamate **1o**: reaction afforded white crystals **1o**, 82% yield, mp=157–158 °C.[31] IR (KBr, cm^{-1}): 3405 (m), 3038 (w), 3270 (w), 3197 (vw), 3055 (vw), 1697 (vs), 1610 (w), 1506 (w), 1388 (s), 1355 (s), 1239 (s), 1206 (s), 1155 (m), 987 (s), 895 (m), 858 (m), 821 (m), 775 (m), 758 (w), 734 (m), 543 (w), 474 (m). ^{1}H NMR (500 MHz, $CDCl_3$) δ (ppm): 6.25 (br s, 2H), 7.20 (dd, J=8.7, 2.1 Hz, 1H), 7.34–7.41 (m, 2H), 7.49 (d, J=2.1 Hz, 1H), 7.71 (d, J=8.0 Hz, 1H), 7.75 (d, J=8.7 Hz, 2H). ^{13}C NMR (125 MHz, $CDCl_3$) δ (ppm): 117.9, 121.2, 124.8, 125.8, 126.9, 127.1, 128.5, 130.5, 133.1, 148.3, 154.9. Anal. Calcd for $C_{11}H_9NO_2$: C, 70.59; H, 4.81; N, 7.49. Found; C, 71.20; H, 4.65; N, 7.54%.

Menthyl carbamate **1a**: mp=166–168 °C and lit.,[37] 156–157 °C. Ethyl carbamate **1b**: mp=46–48 °C and lit.,[38] 48–50 °C. 1-Propyl carbamate **1c**: mp=58–59 °C and lit.,[38] 60 °C. 1-Butyl carbamate **1e**: mp=53–55 °C and lit.,[38] 54 °C. Cyclohexyl carbamate **1e**: mp=108–110 °C and lit.,[22] 108–110 °C. *tert*-Butyl carbamate **1f**: mp=106–108 °C and lit.,[15] 107–108 °C. Benzyl carbamate **1g**: mp=87–89 °C and lit.,[38] 91 °C. Ethylene glycol monoisopropyl ether carbamate **1h**: mp=57–59 °C and lit.,[39] 53 °C. Allyl carbamate **1i**: mp=19–21 °C and lit.,[22] 19–21 °C. Phenyl carbamate **1j**: mp=141–143 °C and lit.,[15] 145–148 °C. 4-Methylphenyl carbamate **1k**: mp=134–136 °C and lit.,[22] 134–136 °C. 4-Bromophenyl carbamate **1l**: mp=139–142 °C and lit.,[22] 139–142 °C. 2-*tert*-Butyl-4-methylphenyl carbamate **1m**: mp=143–144 °C and lit.,[22] 143–144 °C. Naphthalen-1-yl carbamate **1n**: mp=178–180 °C and lit.,[30] 175–177 °C. Naphthalen-2-yl carbamate **1o**: mp=157–158 °C and lit.,[31] 156–157 °C.

Acknowledgements

The Sistan and Baluchestan University Graduate Council supported this research.

References and notes

1. Dibenedetto, A.; Aresta, M.; Fragale, C.; Narracci, M. *Green Chem.* **2002**, *4*, 439–443 and references therein.
2. Gupte, S. P.; Shivarkar, A. B.; Chaudhari, R. V. *Chem. Commun.* **2001**, 2620–2621.
3. Feldman, D.; Barbalata, A. *Synthetic Polymers, Technology, Properties, Applications*; Chapman and Hall: London, 1996; p 273.
4. Mindl, J.; Hrabík, O.; Stěrba, V.; Kaválek, J. *Collect. Czech. Chem. Commun.* **2000**, *65*, 1262–1272.
5. *Pesticide Chemistry*; Motolcsy, G., Nadasy, M., Andriska, V., Eds.; Academiai Kiado: Budapest, 1988; p 90.
6. Thompson, A. *Pesticide Outlook* **2002**, *13*, 84–86.
7. Martin, L. L.; Davis, L.; Klein, J. T.; Nemoto, P.; Olsen, G. E.; Bores, G. M.; Camacho, F.; Petko, W. W.; Rush, D. K.; Selk, D.; Smith, C. P.; Vargas, H. M.; Wilson, J. T.; Effland, R. C.; Fink, D. M. *Bioorg. Med. Chem. Lett.* **1997**, *7*, 157–162.
8. Greene, W. T.; Wuts, P. G. M. *Protective Groups in Organic Synthesis*, 2nd ed.; Wiley: New York, NY, 1991; p 327 and p 403.
9. Yoshida, M.; Hara, N.; Okuyama, S. *Chem. Commun.* **2000**, 151–152 and references therein.
10. Ichikawa, Y.; Osada, M.; Ohtani, I. I.; Isobe, M. *J. Chem. Soc., Perkin Trans. 1* **1997**, 1449–1455.
11. Kocovsky, P. *Tetrahedron Lett.* **1986**, *27*, 5521–5524.
12. Raucher, S.; Jones, D. S. *Synth. Commun.* **1985**, *15*, 1025.
13. Graf, R. *Chem. Ber.* **1963**, *96*, 56–67.
14. Fuks, R.; Hartemink, M. A. *Bull. Chim. Belg.* **1973**, *82*, 23.
15. Loev, B.; Kormendy, M. F. *J. Org. Chem.* **1963**, *28*, 3421–3426.
16. Tanaka, K. *Solvent-Free Organic Synthesis*; Wiley-VCH: Weinheim, 2003.
17. Nagendrappa, G. *Resonance* **2002**, *7*, 64–77.
18. Varma, R. S. *Green Chem.* **1999**, *1*, 43–55.
19. Varma, R. S. *Tetrahedron* **2002**, *58*, 1235–1255.

20. Tanaka, K.; Toda, F. *Chem. Rev.* **2000**, *100*, 1025–1074.
21. (a) Clark, J. H.; Macquarrie, D. J. *Chem. Soc. Rev.* **1996**, *25*, 303–310; (b) Clark, J. H.; Cullen, S. R.; Barlow, S. J.; Bastock, T. W. *J. Chem. Soc., Perkin Trans. 2* **1994**, 1117–1130; (c) Clark, J. H.; Macquarrie, D. J. *Chem. Commun.* **1998**, 853–860.
22. Modarresi-Alam, A. R.; Rostamizadeh, M.; Najafi, P. *Turk. J. Chem.* **2006**, *30*, 269–276.
23. Modarresi-Alam, A. R.; Najafi, P.; Rostamizadeh, M.; Keykha, H.; Bijanzadeh, H.-R.; Kleinpeter, E. *J. Org. Chem.* **2007**, *72*, 2208–2211.
24. Melero, J. A.; Grieken, R. V.; Morales, G. *Chem. Rev.* **2006**, *106*, 3790–3812.
25. Yadav, G. D. *Catal. Surv. Asia* **2005**, *9*, 117–137.
26. Okuhara, T. *Chem. Rev.* **2002**, *102*, 3641–3666.
27. Gorte, R. J. *Catal. Lett.* **1999**, *62*, 1–13.
28. (a) Kamble, V. T.; Jamode, V. S.; Joshi, N. S.; Biradara, A. V.; Deshmukh, R. Y. *Tetrahedron Lett.* **2006**, *47*, 5573–5576; (b) Das, B.; Venkateswarlu, K.; Majhi, A.; Reddy, M. R.; Reddy, K. N.; Rao, Y. K.; Ravikumar, K.; Sridhar, B. *J. Mol. Catal. A: Chem.* **2006**, *246*, 276–281; (c) Khan, A. T.; Choudhury, L. H.; Ghosh, S. *J. Mol. Catal. A: Chem.* **2006**, *255*, 230–235; (d) Narasimhulu, M.; Reddy, T. S.; Mahesh, K. C.; Prabhakar, P.; Rao, C. B.; Venkateswarlu, Y. *J. Mol. Catal. A: Chem.* **2006**, *266*, 114–117.
29. Moore, J. D.; Herpel, R. H.; Lichtsinn, J. R.; Flynn, D. L.; Hanson, P. R. *Org. Lett.* **2003**, *5*, 105–107 and references therein.
30. Fahmy, M. A. H.; Fukuto, T. R. *J. Agric. Food Chem.* **1972**, *20*, 168–169.
31. Barenes, J. H.; Chapman, M. V. A.; McCrea, P. A.; Marshall, P. G.; Walsh, P. A. *J. Pharm. Pharmacol.* **1961**, *13*, 39–48.
32. Lowenthal, M. S.; Khanna, R. K.; Moore, M. H. *Spectrochim. Acta, Part A* **2002**, *58*, 73–78.
33. Fischer, G.; Geith, J.; Klapotke, T. M.; Krumm, B. *Z. Naturforsch.* **2002**, *57b*, 19–24.
34. (a) Kabir-ud-Din; Owen, R. C.; Fox, M. A. *J. Phys. Chem.* **1981**, *85*, 1679–1682; (b) Nguyen, M. T.; Sengupta, D.; Vereecken, L.; Peeters, J.; Vanquickenborne, L. G. *J. Phys. Chem.* **1996**, *100*, 1615–1621.
35. Casey, M.; Leonard, J.; Lygo, B.; Procter, G. *Advanced Practical Organic Chemistry*; Chapman and Hall: New York, NY, 1990.
36. Armarego, W. L. F.; Perrin, D. D. *Purification of Laboratory Chemicals*; Butterworth-Heinmam: Oxford, 1996.
37. Oshikawa, T.; Yamashita, M. *Bull. Chem. Soc. Jpn.* **1989**, *62*, 3177–3181.
38. Weast, R. C.; Lide, D. R. *Handbook of Chemistry and Physics*, 70th ed.; CRC: Florida, FL, 1989–1990; C-194.
39. Ashburn, H. G.; Collett, A. R.; Lazzell, C. L. *J. Am. Chem. Soc.* **1938**, *60*, 2933–2935.