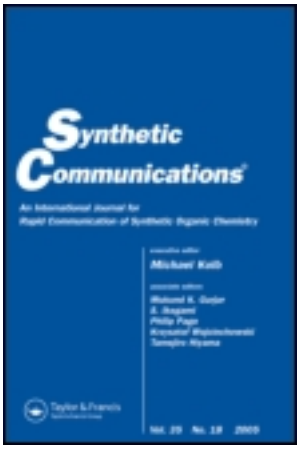


Synthetic Communications: An International Journal for Rapid Communication of Synthetic Organic Chemistry

Publication details, including instructions for authors and subscription information:
http://www.tandfonline.com/loi/lsyc20

(Bromodimethyl)sulfonium Bromide Mediated Rapid and Facile Protection of Amines

M. Shailaja [a], A. Manjula [a] & B. Vittal Rao [a]

[a] Organic Chemistry Division II, Indian Institute of Chemical Technology, Hyderabad, India

Published online: 20 May 2011.

To cite this article: M. Shailaja , A. Manjula & B. Vittal Rao (2011) (Bromodimethyl)sulfonium Bromide Mediated Rapid and Facile Protection of Amines, Synthetic Communications: An International Journal for Rapid Communication of Synthetic Organic Chemistry, 41:14, 2073-2080, DOI: 10.1080/00397911.2010.497592

To link to this article: http://dx.doi.org/10.1080/00397911.2010.497592

Synthetic Communications®, 41: 2073–2080, 2011

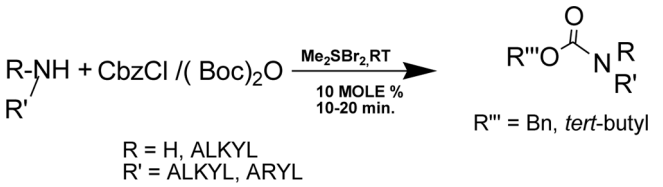
ISSN: 0039-7911 print/1532-2432 online
DOI: 10.1080/00397911.2010.497592

Taylor & Francis
Taylor & Francis Group

(BROMODIMETHYL)SULFONIUM BROMIDE MEDIATED RAPID AND FACILE PROTECTION OF AMINES

M. Shailaja, A. Manjula, and B. Vittal Rao
Organic Chemistry Division II, Indian Institute of Chemical Technology, Hyderabad, India

GRAPHICAL ABSTRACT



Abstract *A new clean protocol for protection of aryl and aliphatic amines with t-butoxycarbonyl (t-BOC) and benzyloxycarbonyl (Cbz) catalyzed by simple (bromodimethyl)sulfonium bromide has been developed. Rapid protection of amines in excellent yields in totally solvent-free conditions has been achieved.*

Keywords Amine; benzyloxycarbonyl chloride; (bromodimethyl)sulfonium bromide; di-*tert*-butyldicarbonate; protection

INTRODUCTION

Protecting groups play vital roles in carrying out reactions selectively at one reactive site in a multifunctional compound. The significance of protecting groups can be judged by the numerous literature reports appearing on new groups as well as many new methods of introduction or removal of them.[1] Efficient protection of amines is a key step in organic synthesis, more so because it has become an essential tool in contemporary peptide[2] and organic chemistry.[3] t-Butoxycarbonyl (t-BOC) and benzyloxycarbonyl (Cbz) are among the favorite protecting groups for protection of amines.[4] The acid labile nature of the t-BOC has both advantages and disadvantages as it can be used as a deprotection method. Cbz, on the other hand, is stable to basic and most aqueous acidic media, cleaved by either photolysis or hydrogenolysis.

The protection of amines by the Cbz group has been achieved in a variety of base-mediated reaction conditions[5] whereas very few reports exist for the protection

Received December 14, 2009.

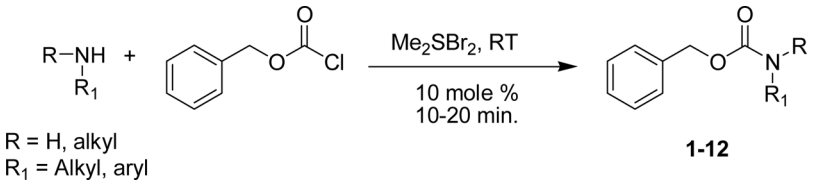
Address correspondence to B. Vittal Rao, Organic Chemistry Division II, Indian Institute of Chemical Technology, Hyderabad 500 607, India. E-mail: vittalrao@iict.res.in; raobommena@gmail.com

of amines in an acid medium.[6] In pursuit of our endeavor to develop novel and environmentally friendly methods, we herein report an operationally facile, rapid, efficient, and high-yielding protocol for protection of amines by the Cbz group using catalytic amounts of (bromodimethyl)sulfonium bromide[7] (Me_2SBr_2) reagent. (Bromodimethyl)sulfonium bromide, which is easy to prepare, has several attractive features as a catalyst, such as clean reaction conditions, versatility, mildness, and ease of handling, added to the fact that the reagent has not been fully exploited yet. Our earlier experience with it proved its versatility for development of cleaner synthetic methods including solventless approaches.

RESULTS AND DISCUSSION

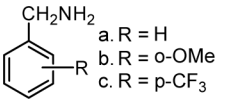
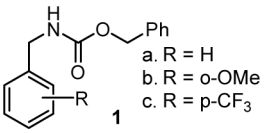
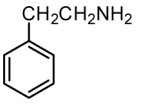
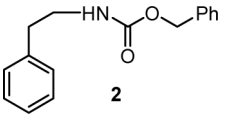
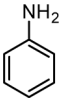
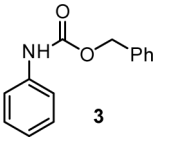
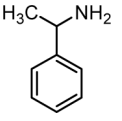
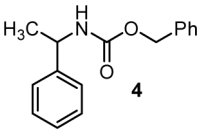
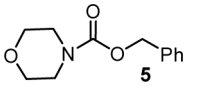
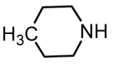
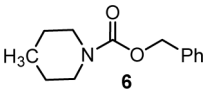
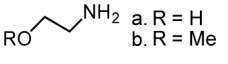
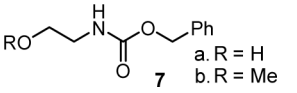
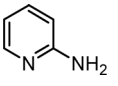
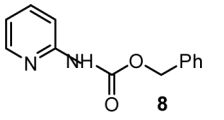
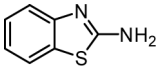
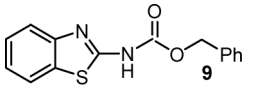
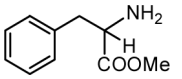
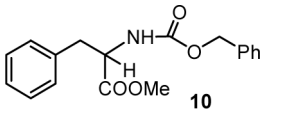
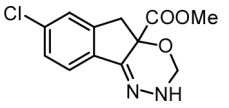
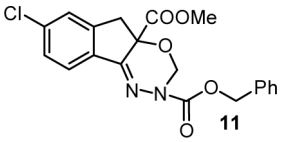
Benzylamine and benzyloxycarbonyl chloride (CbzCl, 50% solution in toluene) were treated with 10 mol% of Me_2SBr_2 at room temperature to afford the corresponding Cbz protected amine in good yield (Table 1) in 10 min. Further reactions were carried out to test the generality of the method using a variety of substrates and substitutions. In each case, the reaction proceeded efficiently at ambient temperature and afforded the corresponding Cbz-protected amine. Protection is equally effective with secondary amines such as piperidine and morpholine (entries 5 and 6). The interesting feature was the facile protection of the amino group of α-amino acid ester (entry 10) as well as β-amino acid esters derived from sugars, which could find applications in peptide chemistry. Additionally, the method is highly chemoselective, as only amine functionality is protected even in the presence of alcohol functionality (entry 7). All products were characterized by ^{1}H NMR, infrared (IR), and mass spectrometry data. Reaction rate and conversion yields were dependent on the nature of the amines. In general, primary amines react faster and give better yields.

In an additional investigation and application of the catalyst, the amine protection was also attempted with $(Boc)_2O$ by employing Me_2SBr_2 under similar conditions. The reaction was attempted at room temperature with di-*tert*-butyldicarbonate, amine, and 10 mol% Me_2SBr_2. The process proceeds smoothly to generate N-Boc amines in good yields almost instantaneously. All the products were characterized by the ^{1}H NMR, IR, and mass spectrometry, and the data were in full agreement with the literature data. The protocol, N-boc protection of amines, is of general applicability with a variety of amines protected in a facile manner (Table 2). In addition, the Boc protection was equally effective in the case of amino acid esters (Table 2, entry 7) as well as chemoselective (Table 2, entry 5). The yields were greater for Boc protection, and reaction times are shorter when compared to the Cbz protection. Compared to the other



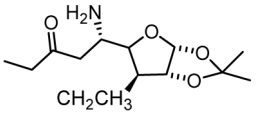
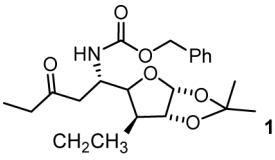
Scheme 1. Me_2SBr_2-catalyzed Cbz protection of amines.

Table 1. Me_2SBr_2-catalysed Cbz protection of amines

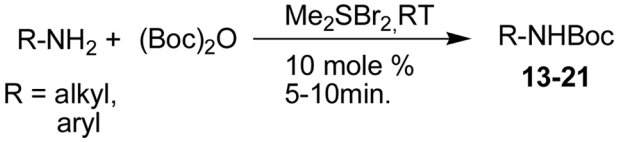
Entry	Amine	Product	Time (min)	Yield (%)
1.			12 10 15	89 84[13] 85
2.			10	83[6a]
3.			10	74[12]
4.			15	90[13]
5.			10	72[13]
6.			15	76[14]
7.			12 18	87[13] 88
8.			10	86[6a]
9.			20	83[6a]
10.			15	20[13]
11.			15	88

(*Continued*)

Table 1. Continued

Entry	Amine	Product	Time (min)	Yield (%)
12.		 **12**	20	75

Note: The superscript number in yield column is the reference number for reported compounds.



Scheme 2. Me_2SBr_2-catalyzed Boc protection of amines.

reagents and methods known for Boc protection of amines such as base catalyzed,[8] neutral,[9] yittria–zirconia[10] mediated, or Lewis acid catalyzed,[11] the Me_2SBr_2-catalyzed protocol has distinct advantages such as simplicity, short reaction times, environmentally friendly, clean approach.

The role of the catalyst, (bromodimethyl)sulfonium bromide, is somewhat like that of Lewis acid: an electrophilic activation of benzyloxycarbonyl chloride and di-*tert*-butyldicarbonate.

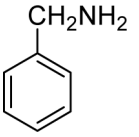
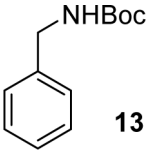
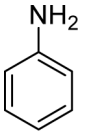
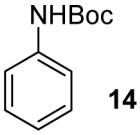
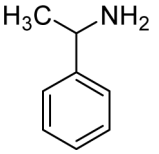
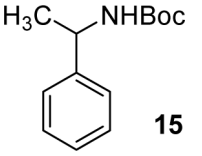
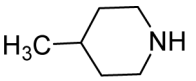
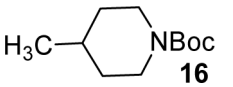
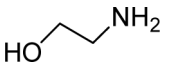
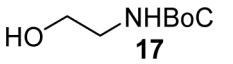
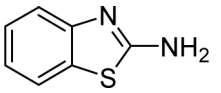
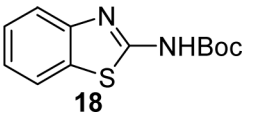
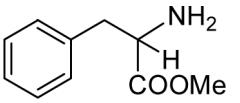
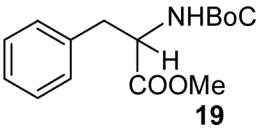
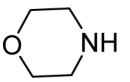
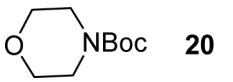
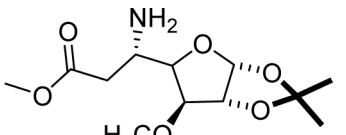
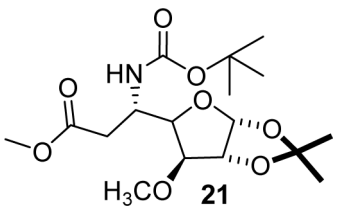
In conclusion, the Me_2SBr_2-catalyzed direct protection of amines by both CbZ and Boc groups is an operationally facile, rapid, mild, and environmentally friendly clean synthetic method. The protocol is general and applicable to a variety of alkyl, and substituted alkyl, aryl, substituted aryl amines, and amino acid esters.

EXPERIMENTAL

To 1 mmol of an amine, 1 mmol of the protecting group [CBzCl, 50% solution in toluene or $(Boc)_2O$] was added dropwise, followed by 10 mol% of Me_2SBr_2 catalyst. The reaction mixture stirred at room temperature, and the progress of the reaction was monitored by thin-layer chromatography (TLC). After completion of the reaction as indicated by the disappearance of the amine, the reaction mixture was quenched with water and extracted with ethyl acetate. The organic layer washed with water and brine, dried over anhydrous sodium sulfate, filtered, and concentrated under reduced pressure to yield the product.

Physical and spectroscopic data of compounds are in full agreement with those reported in literature; citations have been included in both Tables 1 and 2. Spectral data for **1b**, **1d**, **11**, and **12**, which are new, and a few other important compounds are given below.

Table 2. Me_2SBr_2-catalyzed Boc protection of amines

Entry	Amine	Product	Time (min)	Yield (%)
1		 **13**	5	85[9]
2		 **14**	6	77[9]
3		 **15**	8	92[9]
4		 **16**	5	81[11]
5		 **17**	8	82[11]
6		 **18**	10	80[9]
7		 **19**	10	80[9]
8		 **20**	7	80[9]
9		 **21**	10	75[11]

Note: The superscript number in yield column is the reference number for reported compounds.

Compounds in Table 1

Benzyl 2-methoxybenzylcarbamate 1b. Oil; IR (ν cm^{-1}): 3335, 3030, 2925, 1726; ^{1}H NMR ($CDCl_3$, 200 MHz, δ): 7.40–7.20 (m, 5H, Ar), 6.90 (m, 3H, Ar), 5.02 (s, 2H, Bn), 4.30 (d, 2H, CH_2, $J = 5.76$ Hz), 4.20 (brs, 1H, NH), 3.80 (s, 3H, OCH3). ^{13}C NMR ($CDCl_3 + DMSO$, 75 MHz, δ): 45.22, 59.60, 110.15, 119.86, 125.08, 126.73, 127.89, 128.74, 130.43, 132.45, 132.15, 137.83, 158.50; EI mass (m/z): 272 (M + 1). CHN analysis: calcd. C, 62.13; H, 4.56; N, 4.53. Found: C, 61.59; H, 4.45; N, 4.38.

Benzyl [4-(triflouromethyl)benzyl]carbamate 1c. Mp 43 °C; IR (ν cm^{-1}): 3300, 1720; ^{1}H NMR ($CDCl_3 + DMSO$, 300 MHz, δ): 7.56 (d, 2H, Ar, $J = 8.29$ Hz), 7.42 (d, 2H, Ar, $J = 8.29$ Hz), 7.30 (m, 5H, Ar), 5.02 (s, 2H, Bn), 4.80 (brs, 1H, NH), 4.30 (d, 2H, CH_2, $J = 6.03$ Hz); ^{13}C NMR ($CDCl_3 + DMSO$, 75 MHz, δ): 44.72, 66.64, 125.39, 126.56, 127.60, 128.56, 128.60, 129.81, 136.62, 143.38, 156.68; EI mass (m/z): 332 (M + Na). CHN Analysis: calcd. C, 70.80; H, 6.31; N, 5.16. Found: C, 70.01; H, 6.42; N, 5.09.

Benzyl (2-phenylethyl)carbamate 2. Mp 55 °C; IR (ν cm^{-1}): 3303, 3033, 1735; ^{1}H NMR ($CDCl_3 + DMSO$, 300 MHz, δ): 7.34 (m, 10H, Ar), 5.03 (s, 2H, Bn), 4.25 (brs, 1H, NH), 3.40 (t, 2H, CH_2, $J = 13.03$ Hz), 2.80 (t, 2H, CH_2, $J = 6.99$ Hz); EI mass (m/z): 241 (M^+). CHN Analysis: calcd. C, 75.30; H, 6.66; N, 5.49. Found: C, 74.01; H, 6.62; N, 5.43.

Benzyl (1-phenylethyl)carbamate 4. Mp 46 °C; IR (ν cm^{-1}): 3327, 3029, 2929, 1688; ^{1}H NMR ($CDCl_3 + DMSO$, 300 MHz, δ): 7.30 (m, 10H, Ar), 5.10 (s, 2H, Bn), 4.60 (brs, 1H, NH), 4.38 (q, 1H, CH), 2.40 (d, 3H, CH_3, $J = 4.80$ Hz); EI mass (m/z): 278 (M + Na).

Benzyl morpholine-1-carboxylate 5. Oil; IR (ν cm^{-1}): 3440, 2910, 2852, 1697; ^{1}H NMR ($CDCl_3$, 200 MHz, δ): 7.30 (m, 5H, Ar), 5.10 (s, 2H, Bn), 3.60 (br, 4H, N-CH_2), 3.40 (t, 4H, $J = 4.91$ Hz, CH_2); EI mass (m/z): 221 (M^+).

Benzyl 4-methylpiperazine-1-carboxylate 6. Oil; IR (ν cm^{-1}): 3440, 2923, 2853, 1700; ^{1}H NMR ($CDCl_3$, 300 MHz, δ): 7.30 (m, 5H, Ar), 5.09 (s, 2H, Bn), 4.14 (t, 2H, CH_2, $J = 4.72$ Hz), 2.68 (t, 2H, CH_2, $J = 4.76$ Hz), 1.60 (m, 2H, CH_2), 1.10 (t, 2H, CH_2, $J = 4.56$ Hz), 0.96 (S, 3H, CH_3, $J = 6.60$ Hz); EI mass (m/z): 234 (M^+).

Benzyl (2-methoxyethyl)-1-carbamate 7b. Oil; IR (ν cm^{-1}): 3337, 3033, 2925, 1708; ^{1}H NMR ($CDCl_3$, 200 MHz, δ): 7.50 (m, 5H, Ar), 5.02 (s, 2H, Bn), 4.20 (brs, 1H, NH), 3.40 (t, 2H, CH_2, $J = 5.29$ Hz), 3.30 (t, 2H, CH_2, $J = 5.29$ Hz,), 3.22 (s, 3H, OCH_3); EI mass (m/z): 208 (M − 1), 167 (M-OCH_3).

4a-Methyl-2-phenyl-7-chloroindeno[1,2-d][1,2,3]oxadiazine-2,4a(4H,5H)-dicarboxylate 11. Mp 122–125 °C; IR (ν cm^{-1}): 3454, 3032, 2951, 1746; ^{1}H NMR ($CDCl_3 + DMSO$, 300 MHz, δ): 7.64 (d, 2H, $J = 8.12$ Hz Ar), 7.50 (S, 1H, Ar), 7.40–7.20 (m, 5H, Ar), 5.50 (d, 1H, $J = 10.0$ Hz, OCH), 5.30 (s, 2H, Bn), 5.10 (d, 1H, $J = 10.0$ Hz, OCH), 3.63 (s, 3H, OCH_3), 3.42 (d, 1H, $J = 18$ Hz, CH), 3.20 (d, 1H, $J = 18$ Hz, CH); FAB mass: 401 $(M + 1)^+$. CHN analysis: calcd. C, 59.90; H, 4.27; N, 6.96. Found: C, 58.68; H, 4.22; N, 6.82.

Benzyl (S)-1-((3aR,6S,6aR)-6-methoxy-2,2-dimethyltetrahydrofuro[3,2-d][1,3]dioxol-5-yl)-3-oxopentylcarbamate 12. ^{1}H NMR ($CDCl_3$ + DMSO, 200 MHz, δ): 7.35–7.20 (m, 5H, Ar), 5.85 (d, 1H, $J = 3.30$ Hz), 5.35 (s, 1H), 5.21 (s, 2H, OCH_2 Bn), 4.50 (d, 1H, $J = 3.33$ Hz), 4.30 (brs, 1H, NH), 4.23–4.05 (q, 2H, $J = 6.66$, 13.32 Hz, OCH_2), 3.62 (m, 1H), 3.42 (s, 3H, OCH_3), 2.70–2.52 (m, 2H, CH_2), 1.45 (s, 3H, CH_3), 1.30 (s, 3H, CH_3), 1.28 (t, 3H, $J = 6.65$ Hz $OCH_2\underline{CH_3}$); ESI mass: 421 ($M + 1^+$). CHN analysis: calcd. C, 60.01; H, 6.24; N, 3.33. Found: C, 59.39; H, 6.05; N, 3.28.

Compounds in Table 2

***tert*-Butyl (1-phenylethyl)carbamate 15.** Mp 65 °C; IR (ν, cm^{-1}): 3388, 3031, 2932, 1684; ^{1}H NMR ($CDCl_3$ + DMSO, 200 MHz, δ): 7.30 (m, 5H, Ar), 5.40 (br, 1H, CH), 4.70 (br, 1H, NH), 2.58 (s, 3H, CH_3), 1.40 (s, 9H, t-Bu). CHN Analysis: calcd. C, 65.30; H, 7.70; N, 5.90. Found: C, 66.64; H, 7.74; N, 5.96.

***tert*-Butyl morpholine-4-carboxylate 20.** Mp 54 °C; IR (ν, cm^{-1}): 3443, 2929, 2866, 1697; ^{1}H NMR ($CDCl_3$ + DMSO, 200 MHz, δ): 3.60 (t, 4H, $J = 5.28$ Hz, N-CH_2), 3.38 (t, 4H, $J = 5.32$ Hz, CH_2), 1.49 (s, 9H, t-Bu). CHN Analysis: calcd. C, 56.01; H, 8.71; N, 7.05. Found: C, 56.97; H, 8.75; N, 7.11.

REFERENCES

1. Greene, T. W.; Wuts, P. G. M. *Protecting groups in Organic Synthesis*, 2nd ed.; John Wiley: New York, 1999; pp. 309–406.
2. (a) Xiuo, X.-Y.; Ngu, K.; Choa, C.; Patel, D. V. Selective solid-phase synthesis of ureas and hydantoins from common phenyl carbamate intermediates. *J. Org. Chem.* **1997**, *62*, 6968; (b) Merrifield, R. B. Solid-phase peptide synthesis, I: The synthesis of a tetrapeptide. *J. Am. Chem. Soc.* **1963**, *85*, 2149; (c) Merrifield, R. B. Solid-phase peptide synthesis, II: The synthesis of bradykinin. *J. Am. Chem. Soc.* **1964**, *86*, 304.
3. Sharma, G. V. M.; Reddy, K. R.; Krishna, P. R.; Shankar, A. R.; Narsimulu, K.; Kumar, S. K.; Jayaprakash, P.; Jagannadh, B.; Kunwar, A. C. Robust mixed 10/12 helices promoted by "alternating chirality" in a new family of C-linked carbo-β-peptides. *J. Am. Chem. Soc.* **2003**, *125*, 13670.
4. (a) Chen, G.-H.; Pan, P.; Chen, Y.; Meng, X.-B.; Li, Z.-J. Selective deprotection of the Cbz amine protecting group for the facile synthesis of kanamycin A dimers linked at N-3″ position. *Tetrahedron* **2009**, *65*, 5922; (b) Chakraborti, A. K.; Chankeshwara, S. V. $HClO_4$–SiO_2 as a new, highly efficient, inexpensive, and reusable catalyst for *N-tert*-butoxycarbonylation of amines. *Org. Biomol. Chem.* **2006**, *4*, 2769; (c) Varala, R.; Nuvula, S.; Adapa, S. R. Molecular iodine–catalyzed facile procedure for N-Boc protection of amines. *J. Org. Chem.* **2006**, *71*, 8283; (d) Chankeshwara, S. V.; Chakraborti, A. K. Catalyst-free chemoselective N-*tert*-butyloxycarbonylation of amines in water. *Org. Lett.* **2006**, *8*, 3259.
5. (a) Chang, M.-Y.; Pai, C.-L.; Kung, Y.-H. Synthesis of (±)-coerulescine and a formal synthesis of (±)-horsfiline. *Tetrahedron Lett.* **2005**, *46*, 8463; (b) Roos, G. H. P.; Dastlik, K. A. Highly diastereoselective alkylation of the dellaria oxazinone template with bifunctional electrophiles. *Synth. Commun.* **2003**, *33*, 2197; (c) Dendrinos, K. G.; Kalivretenos, A. G. Convenient protection of amines as carbamates using polymer-bound HOBT as catalyst. *J. Chem. Soc., Perkin Trans. 1* **1998**, 1463; (d) Sennyey, G.; Barcelo, G.; Senet,

J. P. Synthesis and use of dibenzylpyrocarbonate: preparation of dipeptide free n-benzyloxycarbonyl glycine. *Tetrahedron Lett.* **1986**, *27*, 5375; (e) Sharma, S. K.; Miller, M. J.; Payne, S. M. Spermexatin and spermexatol: New synthetic spermidine-based siderophore analogs. *J. Med. Chem.* **1989**, *32*, 357.

6. (a) Yadav, J. S.; Reddy, G. S.; Reddy, M. M.; Meshram, H. M. Zinc-promoted simple and convenient synthesis of carbamates: An easy access for amino group protection. *Tetrahedron Lett.* **1989**, *39*, 3259; (b) Atwell, G. J.; Denny, W. A. Monoprotection of α,ω-Alkanediamines with the N-benzyloxycarbonyl group. *Synthesis* **1984**, 1032; (c) Fieser, L. F.; Fieser, M. *Reagents for Organic Synthesis*; John Wiley: New York, 1967; vol. 1, p. 109; (d) Bergmann, M.; Zervas, L. *Ber.* **1932**, *65*, 1192.
7. (a) Khan, A. T.; Parvin, T.; Choudhury, L. H. Bromodimethylsulfonium bromide–catalyzed three-component Mannich-type reactions. *Eur. J. Org. Chem.* **2008**, *5*, 834; (b) Olah, G. A.; Vankar, Y. D.; Arvanghi, M. Synthetic methods are reactions, 73: Conversion of epoxides and enamines into α-haloketones with halodimethylsulfonium halides. *Tetrahedron Lett.* **1979**, *38*, 3653; (c) Sucheta, K.; Vittal Rao, B. (Bromodimethyl) sulfonium bromide: An inexpensive reagent for the solvent-free, one-pot synthesis of α-aminophosphonates. *Tetrahedron Lett.* **2005**, *46*, 1209.
8. (a) Ponnusamy, E.; Fotadar, U.; Spisni, A.; Fiat, D. A novel method for the rapid, non-aqueous *t*-butoxycarbonylation of some ^{17}O-labeled amino acids and ^{17}O-NMR parameters of the products. *Synthesis* **1986**, *48*; (b) Kunieda, T.; Higuchi, T.; Abe, Y.; Hirobe, M. 3-Alkoxycarbonyl-2-oxazolones and their homopolymers as highly preservable amino-protecting reagents: *tert*-Butoxycarbonylation and benzyloxycarbonylation of amino groups. *Chem. Pharma. Bull.* **1984**, *32*, 2174; (c) Ishizuka, T.; Kunieda, T. Mild and selective ring cleavage of cyclic carbamates to amino alcohols. *Tetrahedron Lett.* **1987**, *28*, 4185.
9. Somireddy, M.; Narendar, M.; Nageswar, Y. V. D.; Rao, K. R. *N*-Boc protection of amines with di-*tert*-butyldicarbonate in water under neutral conditions in the presence of β-cyclodextrin. *Synlett* **2006**, 1110.
10. Pandey, K.; Dagade, S. P.; Upadhyay, R. K.; Dongare, M. K.; Pradeep, K. A facile procedure for *tert*-butoxycarbonylation of amines promoted by yttria-zirconia-based strong Lewis acid catalyst. *Arkivoc* **2002**, *8*, 28.
11. Sharma, G. V. M.; Reddy, J. J.; Sreelakshmi, P.; Radhakrishna, P. Rapid and facile Lewis acid–catalysed Boc protection of amines. *Tetrahedron Lett.* **2004**, *45*, 6963.
12. Mahesh, K. C.; Narasimhlu, M.; Reddy, T. S.; Suryakiran, N.; Venkateshwarlu, Y. A mild and efficient chemoselective protection of amines as N-benzyloxycarbonyl derivatives in the presence of $La(NO_3)_3 \cdot 6H_2O$ under solvent-free conditions. *Tetrahedron Lett.* **2007**, *48*, 55.
13. Gawande, M. B.; Polshettiwar, V.; Varma, R. S.; Jayaram, R. V. An efficient and chemoselective Cbz-protection of amines using silica–sulfuric acid at room temperature. *Tetrahedron Lett.* **2007**, *48*, 8170.
14. Varalu, R.; Enugula, R.; Adapa, S. R. Molecular iodine–catalyzed efficient N-Cbz protection of amines. *J. Iran. Chem. Soc.* **2007**, *4*, 370.