



Single-step conversion of *N*-benzyl, *N*-trityl and *N*-diphenylmethyl amines to *t*-butyl carbamates using polymethylhydrosiloxane[☆]

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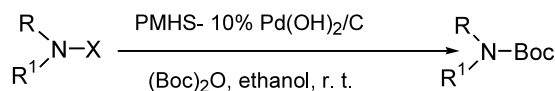
Abstract—*t*-Butyl carbamates were obtained efficiently in high yields from the corresponding *N*-benzyl, *N*-trityl and *N*-diphenylmethyl precursors in a single-step reductive transformation employing polymethylhydrosiloxane and di-*t*-butyl dicarbonate under Pd(OH)₂/C catalysis. © 2003 Elsevier Science Ltd. All rights reserved.

The protection, deprotection and interconversion of protecting groups form an integral part of multistep organic synthesis. A direct method for interconversion of one protecting group to another is often a desired transformation as it increases synthetic efficiency by avoiding the intermediate steps.¹ Amines are an important part of many bio-active natural products and they are useful intermediates both in protected as well as unprotected forms, in basic as well as in applied research.² Among various *N*-protecting groups, the *t*-butyloxycarbonyl group is one of the most commonly and frequently used protecting groups due to its reasonable stability and ease of cleavage under mild conditions. Besides this, the presence of Boc protection in the Taxol side chain (Taxotere[®]) is important.

A literature search showed that, there are few examples of the conversion of *N*-benzyl and *N*-trityl amines to *t*-butyl carbamates.³ There are, to our knowledge, no reports presenting the direct conversion of *N*-diphenylmethyl amines to *t*-butyl carbamates. Consequently, the development of new and general methods for these purposes is being pursued. In our development of new reduction procedures for the synthesis of *t*-butyl carbamates,⁴ we were especially interested in exploring the potential use of polymethylhydrosiloxane (PMHS) which has gained prominence as a safe and economic reagent in recent times as a versatile reductant in

organic synthesis.^{5,6} In continuation of these studies, herein we wish to report a new and efficient protocol for the one-pot reductive transformation of *N*-benzyl, *N*-trityl and *N*-diphenylmethyl amines to the corresponding *t*-butylcarbamates using polymethylhydrosiloxane and di-*t*-butyl dicarbonate in the presence of Pd(OH)₂/C catalysis (Scheme 1).

The scope and generality of this reagent system is illustrated with several examples and the results are summarized in Tables 1 and 2. Initially, *N,N*-dibenzyl phenyl glycine methyl ester was treated with PMHS and (Boc)₂O in the presence of Pd(OH)₂/C in absolute ethanol at room temperature to afford the corresponding *t*-butyl carbamate in 90% isolated yield, with the ester functionality being unaffected (entry 1, Table 1).⁷ Interestingly, it was found that the transformation proceeded smoothly without affecting the commonly used hydroxyl protecting groups MPM, MOM and TBS ethers (entries 3, 4 and 6, Table 1). This conversion is also effective in the presence of a free hydroxyl group (entry 5, Table 1). We have observed that when a benzyl ester is present within the substrate, the resultant product was devoid of it affording the corresponding acid (entry 7, Table 1). As a minor limitation, we found that double bond reduction occurred in the case of the



X= Bn or Tr or DPM

R, R¹= Aryl, alkyl, H

Scheme 1.

Keywords: polymethylhydrosiloxane; di-*tert*-butyl dicarbonate.

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Table 1. Conversion of NBn_2 and NBn to $NHBoc$ and $NBoc$ protected amines

entry	substrate	time (h)	product	yield (%) ^a
1		3		90
2		4		88
3		3		84
4		3		82
5		4		88
6		4		92
7		5		86
8		5		90
9		3		85
10		5		86

^aAll the yields refer to pure isolated products characterized by ¹H NMR and mass spectroscopy.

N-allyl substituted amines (entry 8, Table 1). The stability of the aromatic ring and aliphatic ketone is an added advantage of this protocol (entries 9 and 10, Table 1).

Encouraged by these findings we have extended the reaction conditions to *N*-trityl and *N*-diphenylmethyl amine substrates and it was found that this protocol holds equally well with respect to aliphatic as well as aromatic substrates (entries 1–10, Table 2). It is worth mentioning that the halo functionality was also stable to the present reaction conditions (entry 6, Table 2).

In conclusion, we have developed a new and convenient method for the direct conversion of *N*-benzyl, *N*-trityl and *N*-diphenylmethyl amines to *t*-butyl carbamates. We firmly believe that the present protocol has potential utility in organic synthesis due to its chemoselectivity, efficiency, economy, simplicity and safety.

Typical experimental procedure: To a stirred solution of the substrate (1 mmol) in ethyl alcohol (10 mL) was added PMHS (180 mg, 3 mmol) and 10% Pd(OH)₂/C

Table 2. Conversion of trityl (Tr) and diphenylmethane (DPM) protected amines to Boc protected amines

entry	substrate	time (h)	product	yield (%) ^a
1		2		92
2		5		88
3		8		90
4		6		86
5		5		86
6		8		87
7		5		88
8		5		89
9		4		88
10		3		87

^aAll the yields refer to pure isolated products characterized by ¹H NMR and mass spectroscopy.

(~15 mg). Di-*t*-butyl dicarbonate (240 mg, 1.1 mmol) was added and the reaction mixture was stirred at room temperature for the given time (see Tables 1 and 2). After completion of the reaction, the mixture was filtered and the filtrate was evaporated in vacuo. The residue was purified by column chromatography on silica gel to give the corresponding NH-Boc or N-Boc products in excellent yields.⁸

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7. The same reaction was also carried out in the presence of 10% Pd/C catalysis, wherein we observed that, the reaction takes longer (8 h) and heating (45°C) was necessary.
8. Spectroscopic data of the products: (entry 3, Table 1): ¹H NMR (CDCl₃): δ 7.2 (d, *J*=8.6 Hz, 2H), 6.82 (d, *J*=8.6 Hz, 2H), 4.4 (s, 2H), 3.78 (s, 3H), 3.47 (t, *J*=4.8 Hz, 2H), 3.27 (m, 2H), 1.43 (s, 9H); EIMS (*m/z*): 137 (M⁺–144). (Entry 4, Table 1): ¹H NMR (CDCl₃): δ 4.61 (s, 2H), 3.59 (t, *J* = 4.4 Hz, 2H), 3.36–3.28 (m, 5H), 1.46 (s, 9H); EIMS (*m/z*): 206 (M⁺+1). (Entry 2, Table 2): ¹H NMR (CDCl₃): δ 3.6 (broad s, 1H), 1.59–1.49 (m, 14H), 1.43 (s, 9H); EIMS (*m/z*): 227 (M⁺).