Direct Conversion of Azides and Benzyl Carbamates to *t*-Butyl Carbamates Using Polymethylhydrosiloxane and Pd-C

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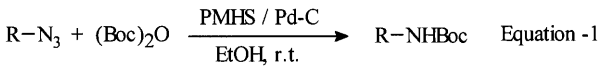
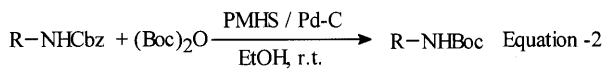
One step direct conversion of azides and benzyl carbamates to *t*-butyl carbamates is achieved using inexpensive and safe hydride source namely polymethylhydrosiloxane (PMHS) under Pd-C catalysis.

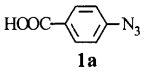
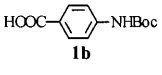
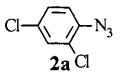
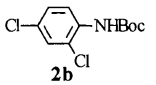
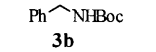
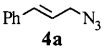
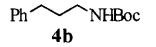
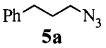
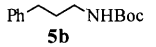
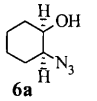
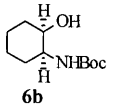
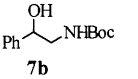
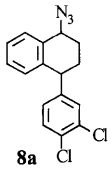
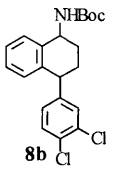
N-(*t*-Butoxycarbonyl) functionality plays a major role as the protective group for amines in the synthesis of unusual amino acids and also in peptide chemistry.[1] This is due to its reasonable stability and easy removal under mild conditions. In the former case an amino group is generally introduced through azide and then reduced to amine followed by blocking preferably as *t*-butyl carbamate. A few attempts have been made recently to achieve this transformation in "one-pot".[2] Similarly interconversion of one protective group to other especially direct conversion of benzyl carbamates to *t*-butyl carbamates has been gaining prominence.[3] The activity of clinically used anticancer compound Taxotere® is attributed to *t*-Boc present in side chain amino acid of Taxol.[4] This back ground of *N*-Boc in organic and medicinal chemistry and also our own interest in making amino containing clinically useful compounds has prompted us to develop a new and efficient "one pot" protocol for direct conversion of azides and benzyl carbamates to *t*-butyl carbamtes (Equations 1 and 2). Our efforts in this direction have resulted in identifying PMHS as an efficient reagent[5] under Pd-C catalysis. The findings are documented herein. PMHS is gaining prominence in the recent times especially as a safe, economic alternative in reductions.[6]





The results pertaining to both these transformations are summerized in Tables 1 and 2 respectively. Interestingly, hydrogenation sensitive substrates (entries 3 and 7 of Table 1 and entries 3, 4, 5 and 6 of Table 2) underwent smooth chemoselective conversions. Also other protective groups viz., TBDMS ether (entry 8 of Table 2), ester substrates (entries 5, 6, 8 and 10 of Table 2) and acetal group (entry 9 of Table 2) were unaffected. Entry 8 (Table 1) demonstrates smooth reductive protection to generate a Sertraline intermediate,[7] a powerful clinically used antidepressant. The halo aromatics (entries 2 and 8 of Table 1) were also stable to present protocol. Reduction of double bond in the substrate (entry 4 of Table 1 and entry 6 of Table 2) is however noted as a minor limitation of this reaction.

Table 1. Conversion of azides to *t*-butyl carbamates

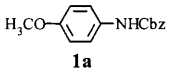
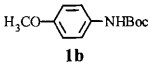
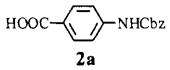
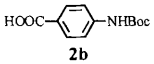
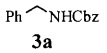
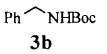
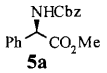
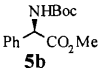
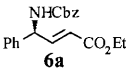
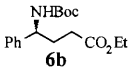
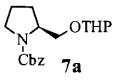
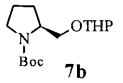
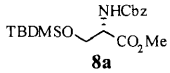
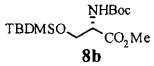
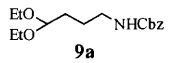
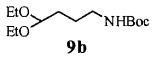
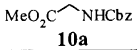
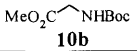
Entry	Substrate	Time/ h	Product	Yield/ %
1.	 **1a**	3	 **1b**	90
2.	 **2a**	3	 **2b**	88
3.	 **3a**	4	 **3b**	94
4.	 **4a**	4	 **4b**	89
5.	 **5a**	4	 **5b**	90
6.	 **6a**	5	 **6b**	90
7.	 **7a**	4	 **7b**	88
8.	 **8a**	5	 **8b**	85

A typical experimental procedure for both the transformations is as follows: To a solution of substrate (1.0 mmol) in ethyl alcohol (10 mL) was added 10% Pd-C (~15 mg), PMHS (0.180 g, 3 mmol) and di-*t*-butyl dicarbonate (0.240 g, 1.1 mmol). After stirring for given time (see Tables), the reaction mixture was filtered and filtrate was evaporated *in vacuo*. The residue was chromatographed on silica gel to the corresponding *N*-Boc products in excellent yields[8] (see tables).

In conclusion, we have developed a convenient method for direct conversion of azides and *N*-Cbz protected amines to more useful *N*-Boc protected amines. We believe that the reagent system described here has tremendous potential for use in organic synthesis due to its high chemoselectivity, efficiency, economy, simplicity, and safety. The application of the present methodology to the natural product synthesis is currently underway.

We thank INSA (New Delhi) for research grant and CSIR, New Delhi for fellowship to three of us (LC, CRR and MVR).

Table 2. Conversion of benzyl carbamates to *t*-butyl carbamates

Entry	Substrate	Time/ h	Product	Yield/ %
1.	 **1a**	4	 **1b**	94
2.	 **2a**	3	 **2b**	93
3.	 **3a**	3	 **3b**	92
4.	 **4a**	4	 **4b**	91
5.	 **5a**	5	 **5b**	86
6.	 **6a**	6	 **6b**	90
7.	 **7a**	8	 **7b**	87
8.	 **8a**	6	 **8b**	87
9.	 **9a**	5	 **9b**	88
10.	 **10a**	4	 **10b**	86

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8 All the products were characterized after chromatography by IR, ^{1}H NMR and mass spectroscopy.

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