

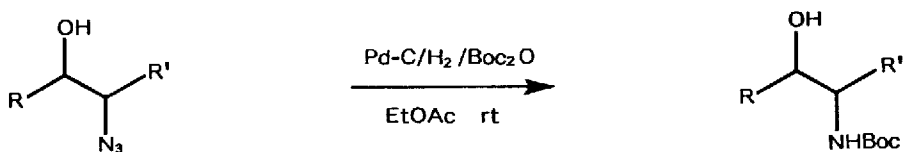
ONE-POT TRANSFORMATION OF AZIDO-GROUP TO N-(t-BUTOXYCARBONYL)AMINO GROUP

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Abstract: A convenient one-pot protocol for the conversion of azido-group to N-Boc amino group has been described.

Nucleophilic substitution of halides, sulfonates, or oxiranes with azide anion is a well-established route leading to primary amines. In particular, the oxirane route has been universally recognized as the general method for introducing 1,2-amino alcohol functionality, which is usually encountered during total synthesis of alkaloids, amino sugars, amino acids, etc.. If protection of an amino group is required, an appropriate protecting group can be introduced after converting the azido group to the corresponding amine in a separate experiment. In this case, because of the highly polar property of thus-obtained 1,2-amino alcohol functionality and its high solubility in aqueous media, its purification through any available means may be tedious and time-consuming. Furthermore, an amine protection like t-butoxycarbonyl group (Boc) sometimes requires a base such as sodium hydroxide or triethylamine as a promoter,¹⁾ which in some cases may cause undesired side reaction. Thus, practical one-pot entry which could be executed totally under neutral conditions to overcome such a two-stage process would be very useful, if realized. Here, we disclose a convenient one-pot protocol to convert a vicinal azido alcohol into the corresponding amino alcohol in which the amino group is protected by Boc, one of the most representative protecting groups for amines.¹⁾



Commercially available palladium (10%) on charcoal (Pd/C) is sufficient for the present transformation. A suspension of Pd/C in ethyl acetate was vigorously stirred under hydrogen atmosphere until the uptake of hydrogen ceased.²⁾ To this was added a mixture of 1,2-azido alcohol and di-t-butyl dicarbonate (Boc_2O) in ethyl acetate, the resulting solution being stirred under hydrogen at room temperature until disappearance of the azido alcohol as monitored by tlc diagnosis. To the reaction was added celite powder and the mixture was filtered through a celite pad to eliminate the catalyst, the filtrate being concentrated *in vacuo* to give rise to the desired product. In order to separate the pure product from unchanged Boc_2O , only short-path silica gel chromatography was usually required. The results are summarized in Table 1. As a general trend,

TABLE 1. One-pot conversion of 2-azido alcohols into 2-N-Boc-amino alcohols^a

Entry	Azido alcohol	Time hr	RNHBoc Yield/% ^b	Entry	Azido alcohol	Time hr	RNHBoc Yield/% ^b
1		19	71	5		26	73
2		21	95	6		3	85
3		40	73	7		4	86
4		30	89	8		4	93

^a All experiments conducted under conditions: Pd/C=0.1 g/g of substrate; EtOAc=10 ml/g of substrate; Boc₂O=1.2 eq. ^b For the pure product isolated by Si₂O chromatography.

the azido groups neighboring the ester groups (entries 6-8) were rapidly hydrogenolyzed and subsequently protected under the given reaction conditions to afford the corresponding N-Boc amino alcohols. Surprisingly, the reaction time required for the present one-pot two stage transformation was almost the same as that required for the first stage (hydrogenolysis) conducted without Boc₂O. Accordingly, there emerges an important corollary that the protection step may be accelerated by the palladium catalyst, though details remain unclear. The traditional protocol for the conversion of azido-group to amino-group using Pd/C catalyst thus turned out, if performed in the presence of Boc₂O,³⁾ to provide a short-cut azido to the N-Boc-amino route which should be synthetically highly useful.

References and notes

- Green, T.W. "Protective Groups in Organic Chemistry"; John Wiley & Sons: New York, 1981, p.232.
- This pre-saturation step is important. Otherwise palladium can act as a dehydrogenation catalyst to furnish not amine but nitrile in a significant amount under the given reaction conditions.
- Protecting group switching from N-Z to N-Boc under hydrogenolysis conditions in the presence of Boc₂O has been published in this journal: Sakaitani, M.; Hori, M.; Ohfuné, Y. *Tetrahedron Lett.*, 1988, 29, 2983. We thank Dr. Y. Ohfuné of Suntory Institute for Bioorganic Research, for sending us their manuscript prior to publication.

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