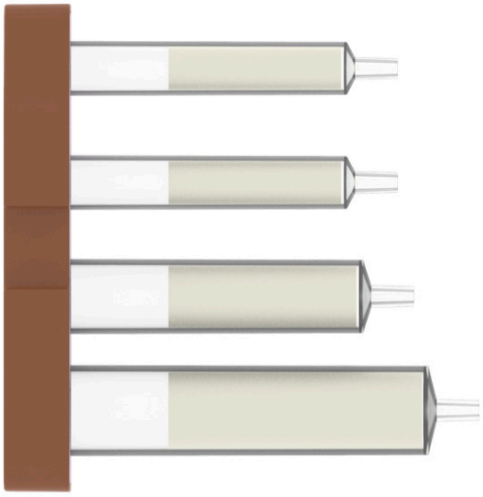
Application Note – N-Boc deprotection

Introduction

N-Boc deprotection involves the reaction between an N-Boc protected amine and acid (TFA, HCl, TsOH and etc…) to generate the corresponding free amine salt.
Using the approach in this application note, the Synple Chem synthesizer offers an easy and quick automated method for the N-Boc deprotection of primary and secondary amines and avoid the handling of volatile and corrosive acids such as TFA or HCl.

Cartridge Contents

The cartridge contains a set of reagents to carry out a N-Boc deprotection reaction on a scale up to 0.5 mmol for B011.



***p*TsOH•H$_2$O**

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Solid supported triethylamine

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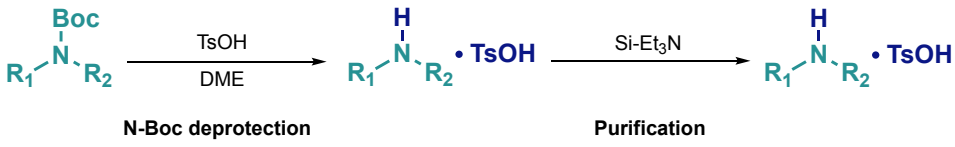
This method can be used for the following transformations:

- Boc deprotection with primary amines
- Boc deprotection with secondary amines

Reaction Scheme

This section describes the general course of the N-Boc deprotection:



In a standard N-Boc deprotection, the N-Boc product is deprotected with volatile acids (TFA, HCl,…) and then the acid is removed under vacuum to afford the corresponding free amine salt.

Reaction Procedure

1) N-Boc deprotection

$TsOH \cdot H_2O$ is solubilized (compartment 1) to the vial using DME (1 mL) at 1 mL/min at 40°C. The reaction is stirred for 2 hours at 40°C.

2) Purification

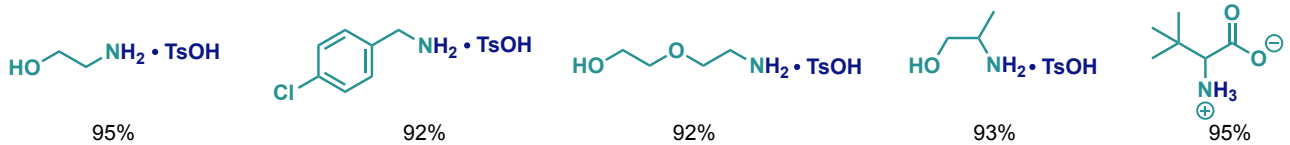
12 mL of MeOH is added to the vial. In order to remove the excess of TsOH, the solution from the vial is then passed five times through compartment 3 (solid supported triethylamine) at 2 mL/min. The compartment is washed with MeOH (2.4 mL) five times. The solution in the vial contains the free amine salt.

Substrate Scope

Tolerated functional groups

A wide range of different functional groups are tolerated.

Example substrate scope – free amines



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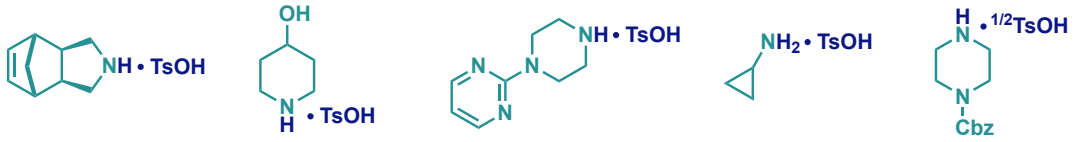

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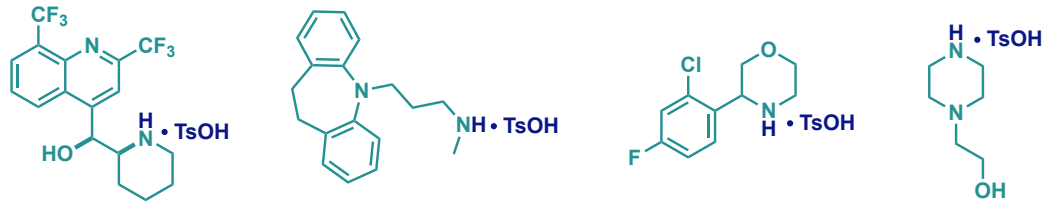

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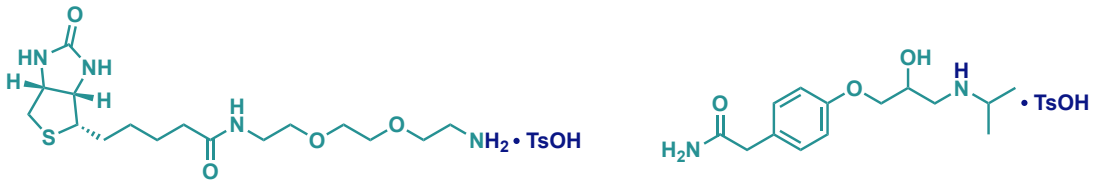

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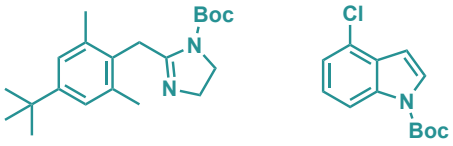
Known Chemistry-Limitations

Not supported substrates example



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Reaction Parameter Editing

Editing parameters:

Parameter 1	Reaction time of Boc deprotection step

Enabling and Disabling parts:

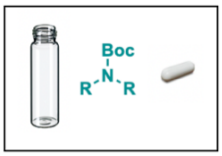
No parts to disable.

Sample Preparation

Setup

Components for sample preparation:

- Vial
- N-Boc product (up to 0.5 mmol)
- Stir bar
- No solvent



Machine Solvents for the use with Boc deprotection cartridges

Please connect the following solvent to the color-coded solvent lines:

	S1: Dichloromethane, anhydrous
	S2: Dimethoxyethane (DME)
	S3: MeOH
	S4: –
	S5: –