Selective Removal of *N*-Boc Protecting Group from Aromatic Amines Using Silica Gel-Supported Sodium Hydrogen Sulfate and HY-Zeolite as Heterogeneous Catalysts[1]

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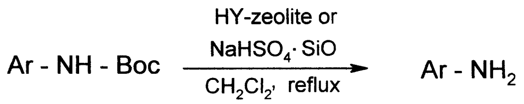
Abstract: Silica gel-supported sodium hydrogen sulfate and HY-zeolite were found to be efficient catalysts for the selective removal of the *N*-Boc protecting group from aromatic amines keeping intact the aliphatic *N*-Boc amines. HY-zeolite was used as a reusable catalyst.

Keywords: HY-zeolite; *N*-Boc aliphatic amines; *N*-Boc aromatic amines; selective deprotection; silica gel-supported $NaHSO_4$

The *tert*-butoxycarbonyl (Boc) group is extensively used as a protecting group for amines and amino acids in organic synthesis.[2] This group is stable to mildly acidic and basic conditions. There are a number of methods for removal of this group.[3] However, the reagents used in most of these methods work under homogeneous conditions. Recently silica gel under reduced pressure [4] and clay [5] have been used as solid reagents for removal of the *N*-Boc group from aromatic amines. In connection with our recent work on the application of heterogeneous catalysts we have observed that silica gel-supported sodium hydrogen sulfate ($NaHSO_4 \cdot SiO_2$) and HY-zeolite are efficient catalysts for the selective deprotection of *N*-Boc aromatic amines.

Several *N*-Boc aromatic and aliphatic amines were refluxed with HY-zeolite or $NaHSO_4 \cdot SiO_2$ in CH_2Cl_2 (Table 1). Deprotected aromatic amines were obtained in excellent yields while *N*-Boc aliphatic amines remained unchanged. This selectivity was also observed by considering a starting molecule containing both aromatic and aliphatic *N*-Boc groups (entries 9 and 10). The product was found to be an aromatic amine having a protected aliphatic amine group. To define the selectivity intermolecular competition experiments with mixture of aromatic and aliphatic amines with *N*-Boc groups were also performed (entries 14 and 15). Deprotection of aromatic amines was observed but *N*-Boc aliphatic amines remained intact. Different acid-sensitive groups like ether (entry 2), acetate (entry 5) and ester (entry 6) also remained unchanged. The electron-rich indole moiety was not at all affected during deprotection of *N*-Boc-indoles due to the attack of the *tert*-butyl cation (formed from the Boc group at the time of deprotection) under the present experimental conditions. The structures of all the products were derived from their spectral (IR, ^1H NMR and MS) data and by direct comparison with authentic samples.



Scheme 1.

Both the catalysts, $NaHSO_4 \cdot SiO_2$ and HY-zeolite acted as solid reagents under mild experimental conditions (see Experimental Section). They can be removed at ease from the reaction mixture after completion of reaction just by filtration. The first catalyst can easily be prepared[6] from the readily available reagents, $NaHSO_4$ and silica gel (finer than 200 mesh) and the second catalyst is commercially available. In most of the earlier methods[3] the recovery of the catalyst for reuse was a problem but HY-zeolite can conveniently be recovered and reused.

In conclusion, we have applied two heterogeneous catalysts, $NaHSO_4 \cdot SiO_2$ and HY-zeolite for selective removal of Boc groups from aromatic amines. The method is mild and the yields of the deprotected amines are very high. The great advantage is that one of the catalysts, HY-zeolite, can be recycled. We feel the present protocol will find practical application in organic synthesis involving deprotection of *N*-Boc aromatic amines.

Experimental Section

Deprotection of N-Boc Aromatic Amines

To a solution of Boc-protected aromatic amine (1 mmol) in CH_2Cl_2 (15 mL) HY-zeolite (200 mg) (PQ Corporation , USA)

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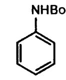
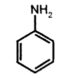
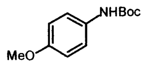
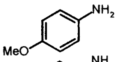
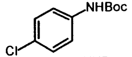
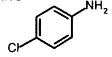
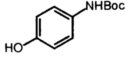
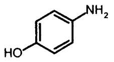
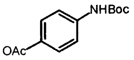
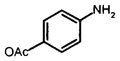
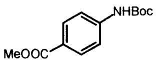
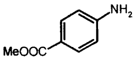
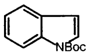
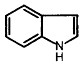
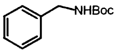
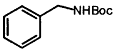
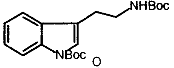
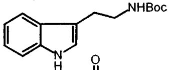
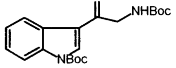
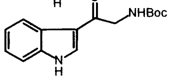
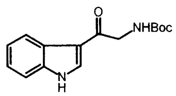
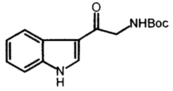
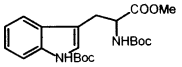
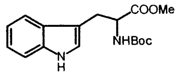
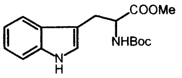
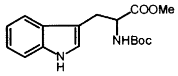
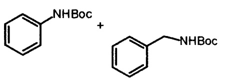
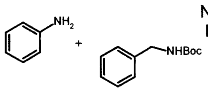
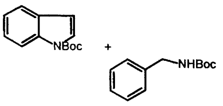
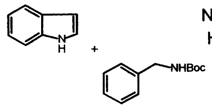
Table 1. Deprotection of the *N*-Boc group from aromatic amines.[a]

Entry	Substrate	Product	Catalyst (Time/h)	Isolated yield(%) of deprotected amine
1.			$NaHSO_4$. SiO_2 (2) HY-zeolite (1.5)	90 92
2.			$NaHSO_4$. SiO_2 (2) HY-zeolite (2)	94 96
3.			$NaHSO_4$. SiO_2 (2) HY-zeolite (2)	90 96
4.			$NaHSO_4$. SiO_2 (2) HY-zeolite (2)	90 92
5.			$NaHSO_4$. SiO_2 (2) HY-zeolite (2)	90 88
6.			$NaHSO_4$. SiO_2 (2) HY-zeolite (2)	85 86
7.			$NaHSO_4$. SiO_2 (4) HY-zeolite (3)	92 90
8.			$NaHSO_4$. SiO_2 (10) HY-zeolite (10)	– –
9.			$NaHSO_4$. SiO_2 (5) HY-zeolite (5)	88 92
10.			$NaHSO_4$. SiO_2 (5) HY-zeolite (5)	88 90
11.			$NaHSO_4$. SiO_2 (5) HY-zeolite (5)	- -
12.			$NaHSO_4$. SiO_2 (5) HY-zeolite	82 80
13.			$NaHSO_4$. SiO_2 (5) HY-zeolite	- -
14.			$NaHSO_4$. SiO_2 (10) HY-zeolite	90 92
15.			$NaHSO_4$. SiO_2 (10) HY-zeolite	88 90

[a] All the products were characterized from their spectral data and by comparison with authentic samples.

or $NaHSO_4 \cdot SiO_2$ (300 mg) was added and the mixture was refluxed (time is indicated in Table 1). After completion of reaction the mixture was cooled and filtered. The concentrated filtrate was chromatographed over silica gel to get the deprotected aromatic amine.

The recovered HY-zeolite was verified for three times to catalyze the deprotection of Boc-protected aromatic amine (following the above-mentioned procedure) without loosing its efficiency. The deprotected aromatic amine was obtained in each case in almost identical yield.

Competitive Experiment

To a solution of *N*-Boc aromatic amine (1 mmol) and *N*-Boc aliphatic amine (1 mmol) in CH_2Cl_2 (15 mL) HY-zeolite (200 mg) or $NaHSO_4 \cdot SiO_2$ (300 mg) was added and the mixture was refluxed for 10 h. The mixture was filtered and concentrated. The residue was chromatographed over silica gel to get the deprotected aromatic amine and the unchanged *N*-Boc aliphatic amine.

Acknowledgements

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References and Notes

[1] Part 19 in the series, "Studies on Novel Synthetic Methodologies", for part 18 see, C. Ramesh, G. Mahender, N. Ravindranath, B. Das, *Tetrahedron* **2003**, *59*, 1049. IICT Communication No. 4585.

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