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LETTERS

Deprotection of Sulfonamides Using Iodotrimethylsilane

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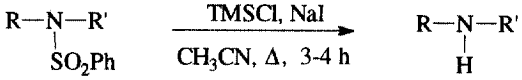
Abstract : The deprotection of sulfonamides is achieved under neutral conditions by reaction with iodotrimethylsilane in acetonitrile at reflux. © 1999 Published by Elsevier Science Ltd. All rights reserved.

Keywords *: Amines; Sulfonamides; Iodotrimethylsilane; Acetonitrile.*

The protection of amines by sulfonyl groups is often used in organic synthesis [1], because the resultant sulfonamides are crystalline and more resistant to nucleophilic attack. Moreover, sulfonamides derived from primary amines can be easily deprotonated and the anions serve as nucleophiles in reactions with alkylating reagents [2]. Previously reported methods for deprotection required drastic conditions (lengthy reaction times, strongly basic conditions) [3] e.g sodium naphthalenide [4], sodium in liquid ammonia and refluxing in strong acid [5]. Therefore, there is much interest in the development of new deprotection methods which include SmI_2 [6], Mg in methanol [7] and TBAF [8].

In continuation of our work dealing with the reductive cleavage of phthalides [9], we now report a simple and mild deprotective method of sulfonamides using iodotrimethylsilane in acetonitrile. Iodotrimethylsilane is an extremely useful and versatile reagent in organic synthesis [10].



$$R{-}\underset{SO_2Ph}{N}{-}R' \xrightarrow[CH_3CN,\ \Delta,\ 3\text{-}4\ h]{TMSCl,\ NaI} R{-}\underset{H}{N}{-}R'$$

Scheme

The desulfonylation proceeds with 1.5 eq. of iodotrimethylsilane in acetonitrile, refluxing for 3-4 hr in good yields. The mild reaction conditions employed in this deprotection method allow the selective deprotection of sulfonamides in the presence of N-alkyl and N-benzyl groups. (For yields and conditions, see, table). However, the deprotection of secondary sulfonamides did not take place under similar conditions.

In conclusion, the reagent used for this cleavage is inexpensive, non-toxic and the cleavage is carried out under mild and neutral conditions.

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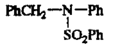
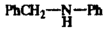
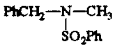
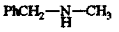
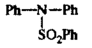
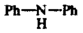
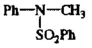
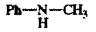
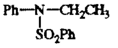
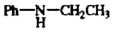
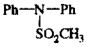
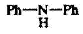
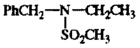
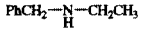
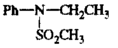
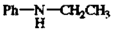
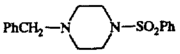
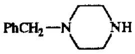
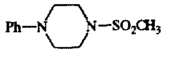
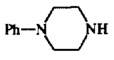
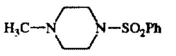
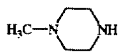
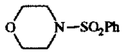
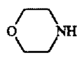
Table 1 Deprotection of Sulfonamides with Iodotrimethylsilane

Entry	Sulfonamide	Product[a]	Yield[b] (%)
1.	 $\mathrm{PhCH_2{-}\underset{SO_2Ph}{N}{-}Ph}$	 $\mathrm{PhCH_2{-}\underset{H}{N}{-}Ph}$	88
2.	 $\mathrm{PhCH_2{-}\underset{SO_2Ph}{N}{-}CH_3}$	 $\mathrm{PhCH_2{-}\underset{H}{N}{-}CH_3}$	86
3.	 $\mathrm{Ph{-}\underset{SO_2Ph}{N}{-}Ph}$	 $\mathrm{Ph{-}\underset{H}{N}{-}Ph}$	88
4.	 $\mathrm{Ph{-}\underset{SO_2Ph}{N}{-}CH_3}$	 $\mathrm{Ph{-}\underset{H}{N}{-}CH_3}$	86
5.	 $\mathrm{Ph{-}\underset{SO_2Ph}{N}{-}CH_2CH_3}$	 $\mathrm{Ph{-}\underset{H}{N}{-}CH_2CH_3}$	86
6.	 $\mathrm{Ph{-}\underset{SO_2CH_3}{N}{-}Ph}$	 $\mathrm{Ph{-}\underset{H}{N}{-}Ph}$	88
7.	 $\mathrm{PhCH_2{-}\underset{SO_2CH_3}{N}{-}CH_2CH_3}$	 $\mathrm{PhCH_2{-}\underset{H}{N}{-}CH_2CH_3}$	84
8.	 $\mathrm{Ph{-}\underset{SO_2CH_3}{N}{-}CH_2CH_3}$	 $\mathrm{Ph{-}\underset{H}{N}{-}CH_2CH_3}$	84
9.			74
10.			76
11.			74
12.			70

a) All the products were characterised by IR and ^{1}HNMR. b) Isolated yields

In a typical procedure; to a suspension of sodium iodide (1.5 mmol) in acetonitrile (10 mL) chlorotrimethylsilane (1.5 mmol) was added dropwise and stirred for 10 minutes at 0°C under a N_2 atmosphere. To this stirred suspension, a solution of N,N-diphenylsulfonamide (1 mmol) in acetonitrile (5 mL) was added and refluxed for 3 hrs. The reaction mixture was quenched with water and extracted with ethylacetate (25 mL). The organic layer was washed with 10% sodium thiosulphate solution, brine, dried over anhydrous Na_2SO_4 and concentrated under vacuum to give the crude product. This was purified by column chromatography to afford pure N,N-diphenylamine (88% yield).

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