



Iodotrimethylsilane : A Mild and Efficient Reagent for the Reduction of Azides to Amines

Ahmed Kamal*, N. Venugopal Rao and E. Laxman

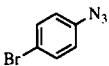
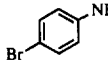
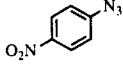
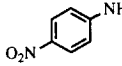
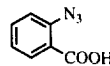
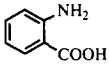
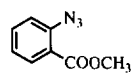
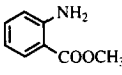
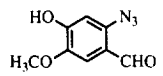
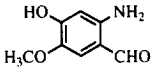
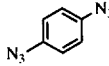
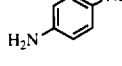
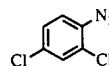
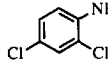
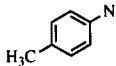
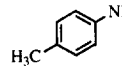
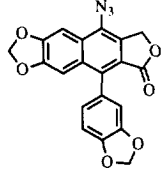
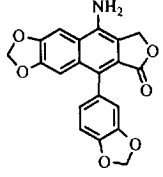
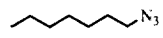

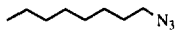
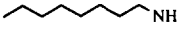




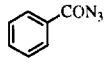
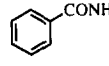
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Abstract : Chlorotrimethylsilane - sodium iodide reagent (*in situ* generation of iodotrimethylsilane) in acetonitrile reduces alkyl and aryl/aroyl azides to the corresponding amines/amides in excellent yields under neutral and mild conditions. © 1997 Elsevier Science Ltd.

The reduction of azides to amines is an important reaction for the synthesis of a variety of organic compounds. The azides can be prepared with good regio, stereo, and enantioselectivity and their transformation to the amino group provides a wide scope of applications in organic synthesis. As a result, a number of reagents have been reported in the literature¹ for this reductive process. An exhaustive review² has described various aspects of such reductions. Some of the recent reagents include the borohydrides³⁻⁵ benzyltriethylammonium tetrathiomolybdate⁶, hexamethyldisilathiane^{7,8} and samarium iodide^{9,10}. In spite of a large number of methods reported for this conversion there has been considerable interest to explore more milder and selective reagents.

In the last two decades an explosive growth has been witnessed in the use of organo-silicon reagents in organic synthesis. Iodotrimethylsilane with remarkable reactivity as a hard-soft reagent has been known for a wide spectrum of synthetic applications^{11,12}. Literature studies^{13,14} have demonstrated that *in situ* generation of iodotrimethylsilane using chlorotrimethylsilane-sodium iodide reagent system is desirable because of its near neutral conditions, more reactive nature and commercial viability from practical point of view¹⁵, in comparison to the use of iodotrimethylsilane directly. In our recent studies on the synthesis of some natural products, we were confronted with the challenge of exploring a mild and versatile method for the reduction of azido group without affecting the other susceptible functionalities. In this connection, we report an efficient reduction of alkyl, aryl and aroyl azides upon treatment with chlorotrimethylsilane and sodium iodide (*in situ* generation of iodotrimethylsilane) in acetonitrile at room temperature to provide the corresponding primary amines and amides. To our knowledge there is no previous precedent reported for this type of reduction with iodotrimethylsilane or by its *in situ* generation. The results have been summarised in the Table. Similar results have also been obtained by using iodotrimethylsilane directly.

Table. Reduction of azides^a to amines by chlorotrimethylsilane-sodium iodide reagent system
(*in situ* generation of iodotrimethylsilane)

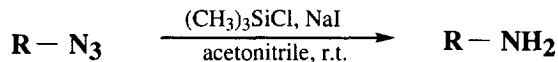
Entry	Substrate	Time (min)	Product ^b	Yield % ^c
1		10		97
2		10		96
3		5		98
4		5		98
5		5		98
6 ^d		10		96
7		10		97
8		5		97
9		5		94
10		15-20		92
11		15-20		90
12		15		93
13		15		92
14		10		95

^aRef 16

^bAmines identified by spectral comparison with authentic samples commercially available or independently prepared.

^cIsolated yields (approximately).

^dReaction performed on 1 mmol of diazide using 3 mmol of reagent system.



R = alkyl, aryl and aroyl

In a typical procedure; to a solution of 2-azido benzoic acid (1 mmol) in acetonitrile (10 ml), sodium iodide (1.5 mmol) was added and stirred for 5 minutes. To this stirred suspension, a solution of chlorotrimethylsilane (1.5 mmol) in acetonitrile (2 ml) was added dropwise and the stirring continued for another 10 minutes. On the completion of the reaction as indicated by TLC (ethylacetate-hexane, 7:3), the reaction mixture was quenched with 10% sodium thiosulphate solution and it was extracted with ethyl acetate (20 ml). The organic layer was washed with brine solution, dried over anhydrous Na_2SO_4 and concentrated under vacuum to give the crude product. This was purified by column chromatography (ethyl acetate-hexane, 1:1) to afford pure 2-amino benzoic acid (anthranilic acid) as white solid (98% yield).

Various azides¹⁶ upon reduction in presence of iodotrimethylsilane gives the corresponding amines in almost quantitative yields (above 90%). These reactions are spontaneous and are found to be almost complete within few minutes as monitored by TLC. Moreover, this reagent is known in the literature for the cleavage of esters¹⁷ as well as ethers¹⁸. Interestingly, under the present conditions this reagent did not cleave the ether or ester functionality, hence providing a selective azido reduction (entries 4 & 5). Further, as a part of the ongoing medicinal chemistry programme this selective reduction has also been applied for the reduction of 4-azidopodophyllum lignan (entry 9) to its corresponding amine without the opening of γ -lactone ring, though this reagent is known for γ -lactone ring cleavage¹⁹. In contrast to other azido reducing agents^{2,9}, this reagent does not affect the aldehyde, nitro and halo functionalities (entries 1, 2, 5 & 7). The secondary alkyl azides (entries 12 & 13) have also given the corresponding amines in good yields. Furthermore, unlike the only other organo-silicon reagent known for aromatic azide reduction i.e., HMDST⁷, this reagent has broader applicability as it reduces the alkyl, aryl and as well as aroyl azides in excellent yields as seen in the Table.

The present approach which is carried out under extremely mild and neutral conditions has provided a novel as well as efficient and chemoselective protocol for the reduction of alkyl/aryl azides to the corresponding amines. The reagent employed for this process is rather inexpensive, non-stinking and non-toxic. Our present method compares favourably to most of the earlier literature reported procedures. Though this reagent is extensively employed in organic synthesis, this new finding further broadens its versatility.

References and Notes

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IICT commun. No. 3846

(Received in UK 30 June 1997; revised 4 August 1997; accepted 8 August 1997)