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Reduction of Azides to Amines by Samarium Diiodide

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Abstract: Amines can be prepared by reduction with samarium diiodide under mild conditions and in good yields.

Samarium diiodide is known to be a powerful electron-donor able to promote a wide range of reductions and coupling reactions.¹ The reactivity of samarium diiodide towards various nitrogen compounds including nitro compounds, azocompounds, hydrazines, oximes and imines has already been examined and shown to be of synthetic interest especially in the conversion of nitroarenes^{2,3} and nitroalkanes⁴ to hydroxylamines and/or amines. However, to our knowledge, there are no literature precedents for the reduction of azides to amines by this reagent. We found that phenyl azides bearing a variety of electron-donating and electron-withdrawing substituents can be cleanly reduced to the respective anilines upon reaction with samarium diiodide at room temperature. In a typical procedure a carefully degassed solution of 2-azidobiphenyl (0.5 mmol) in anhydrous THF (5 ml) was treated under nitrogen with 15 ml of a commercial 0.1M solution of SmI₂ in THF. The resulting mixture was stirred at room temperature for ca. 30 min., whereupon was hydrolyzed with water and some 5% aqueous sodium carbonate (to ensure basic conditions). Extraction with diethyl ether and removal of the solvent gave crude 2-aminobiphenyl in virtually quantitative yield. Filtration of the crude through silica gel furnished the pure amine in 96% yield. Our results are collected in the Table (entries 1-11).

As shown in the Table (entries 7-11) even aromatic azido-aldehydes and -ketones are selectively transformed to the amines, despite the fact that (aromatic) aldehydes and ketones undergo rapid pinacol coupling in the presence of the iodide.⁵ On the other hand, 4-nitrophenyl azide affords only little amounts of 4-nitroaniline and instead leads to a rather complex mixture of unidentified products probably arising from competing reduction of the nitro moiety. Similar to aryl azides, toluene-4-sulfonyl azide undergoes fast and clean reduction with SmI₂ at room temperature (Table, entry 12), whereas under analogous conditions 1-azidoadamantane remains largely unchanged. However, in boiling THF this poorly electron acceptor alkyl azide also is converted to 1-aminoadamantane in satisfactory yield (Table, entry 13), though under these thermal conditions it shows a tendency to suffer fragmentation to some undetermined product other than the amine. Our method requires at least 3 mol of SmI₂ per mole of the azide. The use of a lesser amount of the reagent normally results in significant recovery of the starting azide. The mechanism of these azide reductions presumably involves initial electron transfer from SmI₂ to give an azide and thence a nitrene radical anion,⁶ but the subsequent role of this possible intermediate and samarium salt(s) is unclear at this stage.

Thus, we have provided a novel, efficient protocol for the reduction of (aromatic) azides to amines employing SmI_2 which is a commercially available, rather inexpensive, non-toxic and non-stinking reagent. Our protocol compares favourably to most previous procedures reported in the literature⁷ using a variety of reagents including, *inter alia*, LiAlH₄, NaBH₄, catalytic hydrogenation, Ph₃P, Na₂S/NEt₃, diborane, Bu₃SnH and, more recently, SnCl₂⁸ and H₂S/piperidine.⁹ It is noteworthy that our method enables effective conversion of \underline{o} -azidoto \underline{o} -aminobenzaldehyde and therefore adds to the very recently reported one using (stinking and toxic) hexamethyldisilathiane.¹⁰ Selective reduction of \underline{o} -azidobenzaldehyde is of special interest since, coupled with its ready availability from \underline{o} -nitrobenzaldehyde,¹⁰ it offers a clean method for the formation of \underline{o} -aminobenzaldehyde from the nitro derivative.¹¹

Entry	Amine ^c	time (min)	yield, ^d %
1	2-aminobiphenyl	30	96
2	4-methoxyaniline	100	95
3	α -(phenylsulfanyl)- <u>o</u> -toluidine ^e	60	98
4	2-chloroaniline	70	90
5	3-chloroaniline	120	98
6	4-chloroaniline	75	92
7	2-aminoacetophenone	60	98
8	3-aminoacetophenone	75 ^f	89
9	4-aminoacetophenone	120 ^f	90
10	2-aminobenzaldehyde	10 ^f	79
11	2-amino-5-formylthiopheneg	180 ^f	73
12	toluene-4-sulfonamide	5	92
13	1-aminoadamantane	90 ^h	58

Table. Synthesis of Amines from Azides^a and SmI₂^b.

^a All the examined azides were previously known, except α -(phenylsulfanyl)- $\underline{0}$ -azidotoluene which was prepared from the corresponding amine by means of a standard procedure. ^b The procedure described in the text was normally employed, unless noted otherwise. ^c Amines identified by spectral comparison with authentic samples commercially available or independently prepared. ^d Yields isolated by column cromatography. ^e Ref. 12. ^f Reaction performed on 0.5 mmol of azide in 10 ml of THF. ^g Ref. 10. ^h Reaction run in refluxing THF.

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