Reduction of Aromatic Nitro Compounds to Aromatic Amines by Sodium Trimethylsilanethiolate

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Introduction

Primary aliphatic nitro compounds have been found to react with thiosilanes, including $Me_3SiSSiMe_3$, $MeSSiMe_3$, and $PhSSiMe_3$, under alkaline conditions to give thiohydroxamic acids and thiohydroximates in high yields.[1] Primary nitro compounds can also be converted to the corresponding nitriles by $Me_3SiSSiMe_3$.[2] Secondary nitro compounds, however, react with $Me_3SiSSiMe_3$ or $MeSSiMe_3$ to give oximes under alkaline conditions.[1] A recent paper reported that Me_3SiSNa can be used to remove two methyl groups sequentially from an aryl methyl ether to give the parent arenediol in good to excellent yields.[3]

Zon et al.[4] reported that reduction of nitroarenes with $Me_3SiSiMe_3$ at 240 °C affords predominantly the corresponding amines in addition to azo coupling byproducts. Conversion of nitroarenes to arylamines can also be accomplished by numerous other methods.[5-9] Herein we report that Me_3SiSNa can reduce various aromatic nitro compounds to the corresponding aromatic amines in high yields.

Results

Scheme I shows the newly developed method for the reduction of nitroarenes to amines. We first generated about 2 equiv of Me_3SiSNa by reacting $Me_3SiSSiMe_3$ with NaOMe in anhydrous 1,3-dimethyl-2-imidazolidinone at room temperature.[10] Nitroarenes were then treated with Me_3SiSNa at 185 °C in a sealed tube for 24 h. After aqueous workup, we isolated the corresponding arylamines in 83–98% yields (Table I).

We applied this method to nitrobenzenes with various substituents, including CH_3, C_2H_5, Ph, OCH_3, OC_2H_5, OPh, F, CF_3, and $N(CH_3)_2$ groups. These groups were attached at the ortho, meta, or para position (i.e., **1**, **3**, **5**, **7**, **9**, **11**, **13**, **15**, **17**, and **19**). The new reduction also succeeded with aromatic substrates having two substituents (see **21**, **23**, and **25** in Table I).

By employing the conditions shown in Scheme I, we were able to reduce nitropyridines **27**,[11] **29**,[12] and **31** in 2–3 h to the corresponding aminopyridines **28** (78%), **30** (68%), and **32** (70%), respectively. The yields of reduction products were lower for nitropyridines than for nitroarenes.

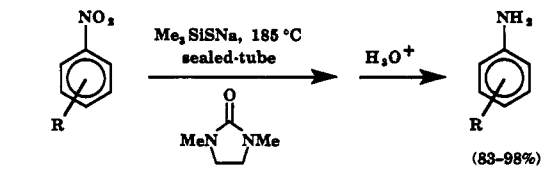
The reaction of Me_3SiSNa with 2-nitroanisole (**9**) often gave a mixture of 2-aminoanisole and 2-aminophenol (**10**). The ratio of the products depended upon the number of equivalents of Me_3SiSNa employed (see Table II). Nevertheless, we were able to obtain 2-aminophenol (**10**, 96% yield) exclusively using 4.0 equiv of Me_3SiSNa.

Discussion

Nature of the Nitro Reduction. We found that 2 equiv of the reducing reagent Me_3SiSNa was necessary for obtaining arylamines in high yields from nitroarenes. The reduction generated S_8 as a yellow solid, which was identified by mass spectrometry. Consequently, we propose the mechanism shown in Scheme II, in which 1,1-eliminations occurred in the steps **33** → **34** and **35** → **36**. Similar 1,1-elimination processes have been proposed before for the formation of S_8 from sulfide species.[1,13] In addition, the conversion of nitrene intermediates **36** to the final product anilines by hydrogen abstraction from the solvent is a well-defined reaction mode.[4,14]

While deoxygenating nitroarenes with hexamethyldisilane ($Me_3SiSiMe_3$) at 240 °C, Zon et al.[4] obtained arylamines along with azoarenes as the byproduct. Under our conditions with Me_3SiSNa at 185 °C, we isolated aryl-

Scheme I



Scheme II

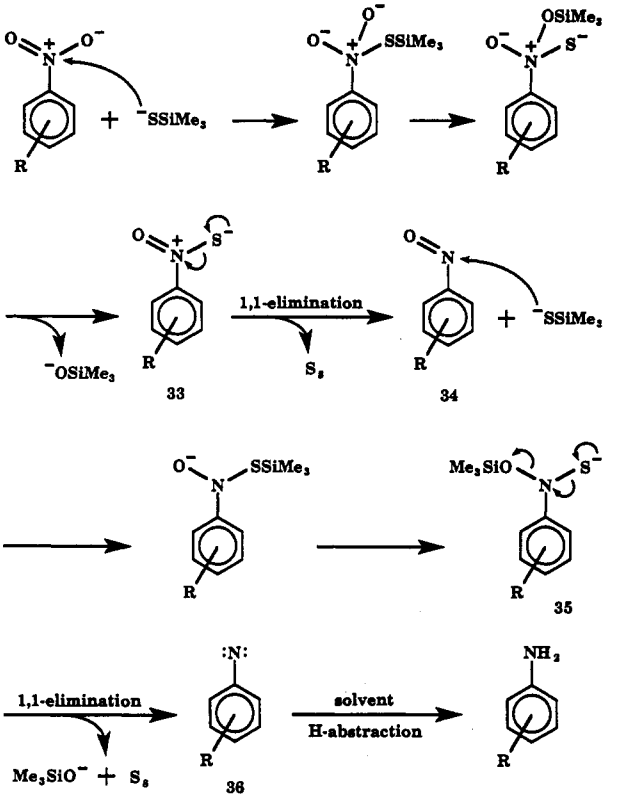


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Table I. Reduction of Aromatic Nitro Compounds to Aromatic Amines by Me_3SiSNa

nitro compound	amine	yield (%)
nitrobenzene (1)	aniline (2)	88
2-methylnitrobenzene (3)	2-methylaniline (4)	85
4-ethylnitrobenzene (5)	4-ethylaniline (6)	83
2-nitrobiphenyl (7)	2-aminobiphenyl (8)	93
2-nitroanisole (9)	2-aminophenol (10)	96
4-nitrophenyl phenyl ether (11)	4-phenoxyaniline (12)	88
1-fluoro-3-nitrobenzene (13)	3-fluoroaniline (14)	94
2-nitro-α,α,α-trifluorotoluene (15)	2-aminobenzotrifluoride (16)	87
3-nitro-α,α,α-trifluorotoluene (17)	3-aminobenzotrifluoride (18)	84
N,*N*-dimethyl-1,3-nitroaniline (19)	*N*,*N*-dimethyl-1,3-phenylenediamine (20)	93
4-nitro-*o*-xylene (21)	3,4-dimethylaniline (22)	86
2,5-diethoxynitrobenzene (23)	2,5-diethoxyaniline (24)	91
4-fluoro-2-nitrotoluene (25)	5-fluoro-2-methylaniline (26)	98
3-nitropyridine (27)	3-aminopyridine (28)	78
2-methoxy-3-nitropyridine (29)	3-amino-2-methoxypyridine (30)	68
2-methoxy-5-nitropyridine (31)	5-amino-2-methoxypyridine (32)	70

Table II. Yields of 2-Aminoanisole and 2-Aminophenol (10) Obtained from the Reaction of 2-Nitroanisole (9, 1.0 equiv) with Different Amounts of Me_3SiSNa

equiv of Me_3SiSNa	2-aminoanisole (%)	2-aminophenol (10, %)
1.0	57	9
1.5	51	37
2.1	34	50
3.1	3	84
4.0	not detectable	96

amines exclusively. For a special substrate 2-nitrobiphenyl, Zon et al.[4] reduced it with $Me_3SiSiMe_3$ at 240 °C to give some 9*H*-carbazole. This byproduct was not generated under our conditions, as determined by GC and TLC. The diversities between Zon's and our results may come from the difference of reaction temperature and solvent.

In control experiments, we reduced nitroarenes in 1,3-dimethyl-2-imidazolidinone at 185 °C by using $Me_3SiSSiMe_3$ alone (i.e., without adding NaOMe). The desired arylamines were obtained in 20–30% yields only. Thus we conclude that reduction of nitroarenes proceeds more efficient by using a sulfide[15] (e.g., Me_3SiSNa) than a thioether (RSR′).

Chemoselectivity and Rate. Reagent Me_3SiSNa can efficiently remove the methyl group from aryl methyl ethers.[3] For nitrobenzene containing a methoxy group (e.g., **9**), we found that reduction of the nitro group proceeded faster than O-demethylation. Table II lists the results from our systematic study.

Reduction of nitropyridines (2–3 h) proceeded faster than that of nitroarenes (~24 h). We believe that the nitrogen atom of the pyridine ring exerted some electronic and inductive effects to enhance the electrophilicity of the nitrogen atom of the nitro group. This rate enhancement may also be responsible for the successful reduction of the nitro group in methoxypyridines **29** and **31**, without competitive removal of the methyl unit. Thus the corresponding (amino)pyridines **30** and **32** were obtained in 68% and 70% yields, respectively.

Experimental Section

Standard Procedure for the Reduction of Aromatic Nitro Compounds to Aromatic Amines. A solution containing dry sodium methoxide (2.1 equiv), hexamethyldisilathiane (2.1 equiv), and anhydrous 1,3-dimethyl-2-imidazolidinone (2.0 mL) was stirred at room temperature under nitrogen for 1.5 h. The mixture was then transferred to a Pyrex combustion tube under argon. An aromatic nitro compound (1.0 equiv, ~100 mg) in 1,3-dimethyl-2-imidazolidinone (1.0 mL) was injected into the tube, which was then sealed. The sealed tube was heated in an oven at 185 °C (24 h for nitroarenes and 2–3 h for nitropyridines), during which the tube was shaken thoroughly once at 60 °C. The reaction mixture was diluted with water at room temperature, neutralized with 10% HCl, and extracted with Et_2O (15 mL × 5). The combined ethereal solutions were washed with water and saturated aqueous NaCl, dried over $MgSO_4$(s), filtered, and concentrated under reduced pressure. The residue was chromatographed on a column of silica gel to give a pure aromatic amine. The physical properties and spectroscopic characteristics of the isolated aromatic amines, including **2**, **4**, **6**, **8**,[4] **10**, **12**, **14**, **16**, **18**, **20**, **22**, **24**,[16] **26**, **28**, **30**,[17] and **32** were consistent with those of an authentic sample[18] or published data.[4,16,17]

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Registry No. 1, 98-95-3; 2, 62-53-3; 3, 88-72-2; 4, 95-53-4; 5, 100-12-9; 6, 589-16-2; 7, 86-00-0; 8, 90-41-5; 9, 91-23-6; 10, 95-55-6; 11, 620-88-2; 12, 139-59-3; 13, 402-67-5; 14, 372-19-0; 15, 384-22-5; 16, 88-17-5; 17, 98-46-4; 18, 98-16-8; 19, 619-31-8; 20, 2836-04-6; 21, 99-51-4; 22, 95-64-7; 23, 119-23-3; 24, 94-85-9; 25, 446-10-6; 26, 367-29-3; 27, 2530-26-9; 28, 462-08-8; 29, 20265-35-4; 30, 20265-38-7; 31, 5446-92-4; 32, 6628-77-9; Me_3SiSNa, 87495-22-5; $Me_3SiSSiMe_3$, 3385-94-2.

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Manzamenones A–F from the Okinawan Marine Sponges *Plakortis* sp.: Novel Dimeric Fatty Acid Derivatives Possessing a Bicyclo[4.3.0]nonane Skeleton

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Marine sponges of the genus *Plakortis* have been a rich source of unique bioactive secondary metabolites such as polycyclic aromatic alkaloids[1] or peroxy aliphatic acids and esters.[2] We have also isolated plakorin,[3] a cyclic peroxide

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