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1,2-Eliminations in a Novel Reductive Coupling of Nitroarenes to Give Azoxy Arenes by Sodium Bis(trimethylsilyl)amide

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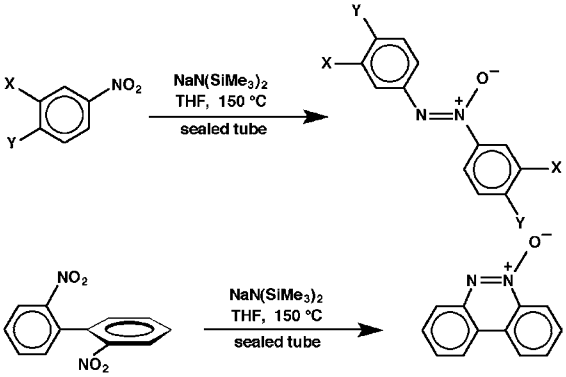
ABSTRACT



Symmetric azoxy arenes were successfully prepared in one step from 2 equiv of the corresponding nitroarenes by use of sodium bis(trimethylsilyl)amide as the deoxygenating agents in THF at 150 °C in a sealed tube.

Sodium bis(trimethylsily)amide often acts as a strong base in organic transformations.[1−6] Because of its nucleophilicity, this commercially available reagent is also used to provide for addition of a nitrogen atom to organic compounds.[7−9] Transformation of aromatic esters to nitriles in one flask represents a recent application of sodium bis(trimethylsily)amide.[7] Moreover, this silicon-containing reagent exhibits a selective monodemethylating ability in dimemthoxy aromatic compounds.[10] Thus, it can be applied as an efficient deprotecting agent. In our investigation of new applications of silicon-containing compounds, we considered the potential deoxygenation ability of sodium bis(trimethylsily)amide. Consequently, an unprecedented deoxygenation reaction was developed for the conversion of nitroarenes to azoxy compounds by use of sodium bis(trimethylsily)amide. The reaction mechanism is intriguing since it may invole three sequential 1,2-eliminations.

Current interest in azoxy compounds is increasing dramatically because of their physiological activities and ap-

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plications to liquid crystals.[11−13] They are also utilized as DNA cleavers, polymerization inhibitors, stabilizers, dyes, and analytical reagents.[14] Azoxy compounds can be prepared from amines,[14,15] hydroxylamines,[16,17] nitrosohydroxylamine ammonium salts,[18] and azo,[19,20] nitro,[21−23] and nitroso compounds.[24,25] Those methods often require reducing agents, oxidizing agents, or UV light.

In the newly developed method, we treated a THF solution of a nitroarene with 1.0 equiv of $NaN(SiMe_3)_2$ in a sealed tube at 150 °C for 12 h. After normal workup and purification with silica gel column chromatography, the desired azoxy arene was often isolated in solid form (see Scheme 1 and Table 1). Among various solvents, including THF, *p*-dioxane, DMF, and HMPA, we found that the use of THF or a mixture of THF/HMPA gave the best results. The coupling reaction required 12 h for completion. A shorter reaction time led to a lower yield for the desired azoxy arenes, yet a longer time gave over-reduced azo compounds as the byproducts in a significant amount. In a control experiment, we performed the reaction involving **1b** in THF at reflux (~65 °C) under an N_2 atmosphere. The desired product **2b** was produced in 32% yield (versus 45% in Table 1). Moreover, the same reaction did not proceed at room temperature.

Scheme 1

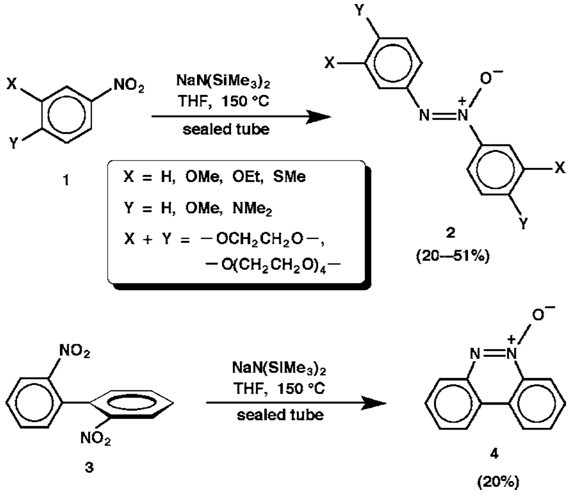

Table 1. Transformations of Nitroarenes to the Corresponding Azoxy Arenes by Use of $NaN(SiMe_3)_2$ (1.0 equiv) in THF at 150 °C

nitroarene	X	Y	azoxy product[a]	yield (%)
1a	H	H	**2a**	21
1b	OMe	H	**2b**	45
1c	H	OMe	**2c**	40
1d	OMe	OMe	**2d**	51
1e	OEt	H	**2e**	42
1f	SMe	H	**2f**	46
1g	H	NMe_2	**2g**	25
1h	$-OCH_2CH_2O-$		**2h**	22
1i[b]	$-O(CH_2CH_2O)_4-$		**2I**	>20

[a] Compounds **2a**−**g** were reported previously;[21b] our spectroscopic data are consistent with those in the literature. [b] Use of DMEU as the cosolvent and 2.5 equiv of $NaN(SiMe_3)_2$ for 48 h.

In addition to the intermolecular couplings, we found that cyclization took place on 2,2′-dinitrobiphenyl (**3**) under the same thermal conditions (Scheme 1). It gave the intramolecular coupling product **4** in 20% yield.

The azoxy arenes **2a**−**i** and **4** were fully characterized by spectroscopic methods. For example, compound **2d** possessed characteristic resonance at δ 150.23 ppm for the aromatic $^{13}C-N^+(O-)=N$ and at δ 148.26 ppm for the aromatic $^{13}C-N=N^+(O-)$. Its IR absorptions showed peaks at 1455 cm^{-1} for antisymmetric stretching and at 1278 cm^{-1} for symmetric stretching of the $N^+(O-)=N-$ functional group. The exact masses for these zwitterionic type compounds were obtained by mass spectrometer.

A plausible pathway for the conversion of nitroarenes **5** to symmetric azoxy arenes **13** is shown in Scheme 2, which accounts for our original design. The lack of acidic protons in nitroarenes **5** allows them to undergo nucleophilic attack by $NaN(SiMe_3)_2$ to give adducts **6**. We supposed that the first intramolecular 1,2-elimination took place at the $Si-N-N^+-O-$ moiety of **6** to give azoxysilanes **7** and Me_3SiO-. This is analogous to Krüger's[26] report on a deoxy-

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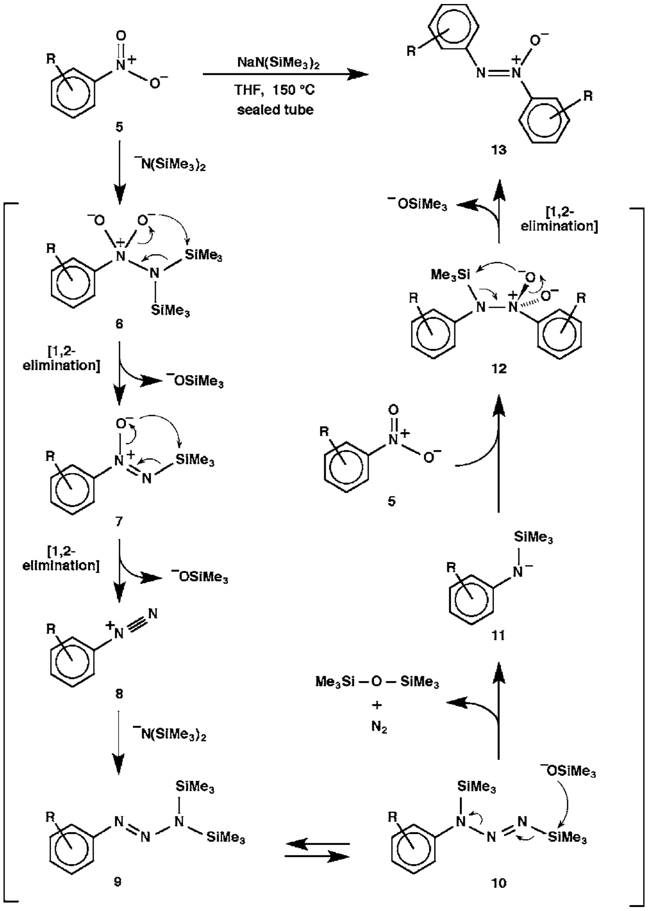
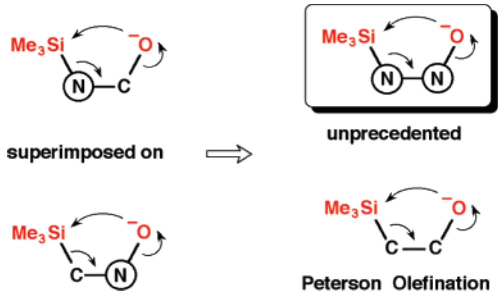
Scheme 2



genating step involving the Si−N−C−O− moiety (Scheme 3). Moreover, a related 1,2-elimination of α-trimethylsilyl *N*-oxide, Si−C−N−O−, has also been developed as the key step in monodeoxygenations of nitroalkanes, nitrones, and heterocyclic *N*-oxides.[27,28] These intramolecular 1,2-eliminations and the Peterson olefination[29,30] (involving Si−C−C−O−) share a common feature in that a siloxide is excluded from the Si−X−Y−O− moieties. For X and Y, both of them are carbon atoms in the Peterson olefination. Nevertheless, at least one of them is a nitrogen atom in the other three 1,2-eliminations (see Scheme 3).

Scheme 3



At elevated temperature, the second intramolecular 1,2-elimination may occur to azoxysilanes **7** to give diazonium arenes **8** and Me_3SiO- (see Scheme 2). Reaction of **8** with the second equivalent of $NaN(SiMe_3)_2$ provides triazenes **9**, in which a terminal silyl group can undergo migration to give the isomers **10**.[31] Then, Me_3SiO-, which is generated in situ during the conversions of **6** → **7** → **9**, attacks the terminal silyl group in **10** to afford anilides **11** and N_2. The oxidation state of the nitrogen atoms in $NaN(SiMe_3)_2$ is thus increased by two. The reactant $NaN(SiMe_3)_2$ in the entire transformation can be regarded as a reducing agent. In the next step, the anilides are coupled with the second molecules of **5** to give the unstable intermediates **12**. Finally, the third intramolecular 1,2-elimination takes place at the $Si-N-N^+-O-$ moiety to generate the target azoxy arenes **13**.

In a control experiment for the conversion of **1a** → **1b**, we were able to identify *N*,*N*-bis(trimethylsilyl)aniline (bp 54 °C) as the byproduct by GC−mass spectroscopic techniques. The *N*,*N*-bis(trimethylsilyl)aniline may come from silylation of the anilide **11** (R = H). Alternatively, diazonium arenes **8** could decompose to give N_2 and the corresponding phenylium species. Trapping of this active species with $NaN(SiMe_3)_2$ in situ could also give *N*,*N*-bis(trimethylsilyl)aniline.

A key step for the formation of azoxy arenes **13** is the coupling of anilides **11** with nitroarenes **5** (see Scheme 2). We found two factors that retarded the coupling efficiency. The first factor is the ortho effect. Our experimental results showed that a nitrobenzene with an −OMe or −OEt at the ortho position cannot be converted to the corresponding azoxy arenes. In sharp contrast, nitroarenes with the same substituents at a meta or para position were dimerized successfully (see rows 2−5 of Table 1). The second factor is the electronic effect from an electron-withdrawing substituent. Placement of a $-NO_2$ group at the para or ortho position in nitrobenzene made the conversion unfeasible. These substituents in **11** would deactivate their nucleophilicity. On the other hand, substituents with electron-donating ability (e.g., −OMe, −OEt, −SMe, and $-NMe_2$) promoted the coupling process.

For the same chemical transformation, the established methods often give azoxy products in higher yield than those by our method. However, some of them require a strong reducing agent such as $LiAlH_4$;[23a] some of them involve heterogeneous reaction conditions such as the use of Zn[22c] and Bi metals.[21]

In conclusion, sodium bis(trimethylsily)amide was developed as a deoxygenating agent for the coupling of nitroarenes to azoxy arenes. This newly developed reaction proceeded

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in a sealed tube at 150 °C. The entire process involved three deoxygenating steps, during which the silyl groups removed oxygen atoms from the intermediates through intramolecular 1,2-eliminations.

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Supporting Information Available: Synthetic and experimental procedures, analytical data, and NMR spectra. This material is available free of charge via the Internet at http://pubs.acs.org.

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