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A New Reaction of the Azoxy Group with Alkyl Thiolates: Reduction to Amino *via* a Sulfenamido Intermediate

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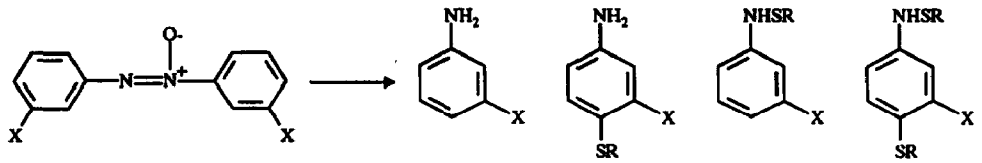
Abstract: A novel alkyl thiolate-induced reduction of azoxybenzenes is reported to yield anilines via *in situ* decomposition of the corresponding sulfenamides formed as primary reaction products.

The cleavage of N-N and N-O bonds is an important step in synthesis.[1] Azoxy to amino reduction is usually carried out under acidic conditions,[2] only a few alternative methods being known which do not require the use of acids.[1,3-4] In protic solvents aromatic azoxy compounds are inert to treatment with strong bases even at high temperatures, deoxygenation to N=N being very slow in the absence of a metal.[2] Thus, symmetrically substituted azoxybenzenes are conveniently prepared by reduction of the corresponding nitro compounds in refluxing alkaline/alcoholic solutions.[5] We now report that, in contrast to the behaviour of alkoxide ions,[5-6] aliphatic thiol anions bring about reduction of aromatic azoxy compounds, the products depending on the R group of the thiolate reagent (Table1). Thus, while MeSNa and 2-PrSNa yield anilines **2** and **3**, the sulfenamide **4** is the major product in the reactions with *t*-BuSNa.[7] Disulfides (RSSR) are also formed in considerable amounts as well as some minor products in trace amounts. Notably, reduction of the azoxy function is accompanied by some alkylthio-*de*-hydrogenation limited to the position *para* to the aza-substituent (products **3** and **5**). Examples of nucleophilic aromatic substitutions of hydrogens in the reactions of activated arenes with nucleophiles are numerous.[8]

Table 1 Reactions of Azoxybenzenes **1** (0.019 M) with RSNa (0.19 M) in Refluxing 2-Propanol.

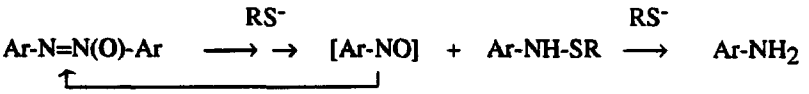


1 **2** **3** **4** **5**

Substrate, X	RSNa, R	Reaction time, h	Products (%-yield)[a]			
Cl	Me	1	**2** (60)	**3** (5)		
Cl	2-Pr	1	**2** (51)	**3** (9)		
Cl	*t*-Bu	1.5	**2** (trace)	**3** (5)	**4** (65)	
H	Me	9.5	**2** (65)			
H	*t*-Bu	37.5			**4** (44)	**5** (5)

[a] Yields refer to isolated products.

This promising novel reduction of the NNO group, which employs slightly basic conditions, cheap and common reagents and a very simple procedure, is also of considerable interest from the mechanistic point of view. The recovery of sulfenamides from some of these reactions implies that direct interaction has occurred between the anionic sulfur center and the electrophilic NNO function leading to a new N-S bond. This type of reactivity of the azoxy functionality is unprecedented. Specific questions concern the possible intermediates involved (*i.e.* whether reduction of N=NO proceeds via initial deoxygenation to N=N) and the relation existing between the *t*-BuS$^-$ reactions, producing sulfenamides, and the 2-PrS$^-$ and MeS$^-$ reactions, giving anilines. The intermediacy of the azo group is ruled out since 3,3'-dichloroazobenzene is recovered quantitatively after treatment with MeSNa in 2-propanol at reflux for 6 hours. The involvement of sulfenamides **4** as reaction intermediates was considered next. When subjected to typical reaction conditions sulfenamides **4** display very different reactivity depending on the substituent R. Thus, while the *t*-Bu-substituted compund (**4**: X = Cl, R = *t*-Bu)[9] is very stable (1%-conversion in 7 h), the 2-propyl derivative (**4**: X = Cl, R = 2-Pr)[9] is quantitatively converted to the corresponding aniline in less than 20 min. Steric factors are likely at the origin of this behaviour, the bulky *t*-Bu group hindering attack of the nucleophile. These results are consistent with the idea that sulfenamides **4** are the primary products in the reaction under investigation; depending on their reactivity, they either accumulate and can be isolated (R = *t*-Bu) or proceed to anilines as sketched below.



It is suggested that reaction is initiated by coupling of the thiol anion with the nitrogen α to the NO group to form a covalent adduct[11] which decomposes to a nitroso- and a sulfenamido- intermediates. Under the reaction conditions used these presumed intermediates would undergo very rapid reductive dimerization to azoxybenzene[14] and reduction to aniline, respectively. The scope and mechanism of this novel reaction are currently investigated in our laboratories.

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