Conversion of Azobenzenes into *N*,*N*′-Diarylhydrazines by Sodium Dithionite

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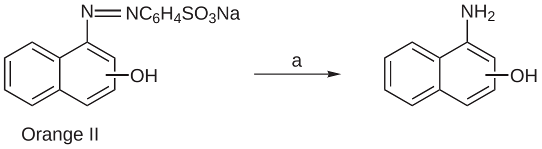
Received 7 March 2007

Abstract: A number of chloro-, methyl- and methoxy-substituted azobenzenes have been reduced to the corresponding hydrazines by using an aqueous solution of $Na_2S_2O_4$. The yield is generally excellent, but two compounds, viz. 4,4-dimethoxyazobenzene and 2,2,4,4,6,6-hexamethylazobenzene, gave no hydrazine at all.

Key words: azobenzenes, sodium dithionite, reduction, hydrazines

Sodium dithionite ($Na_2S_2O_4$) is a versatile and cheap reagent, which has been employed to reduce, among a variety of compounds,[1] aldehydes,[2] ketones,[2,3] unsaturated ketones,[4] and a range of unsaturated nitrogen compounds.[5,6] The latter group includes a large number of azoarenes, which gave the corresponding aminoarenes when treated with an excess of an aqueous solution of the sulfur compound at elevated temperature;[6i–r] a representative example is shown in Scheme 1.[5]

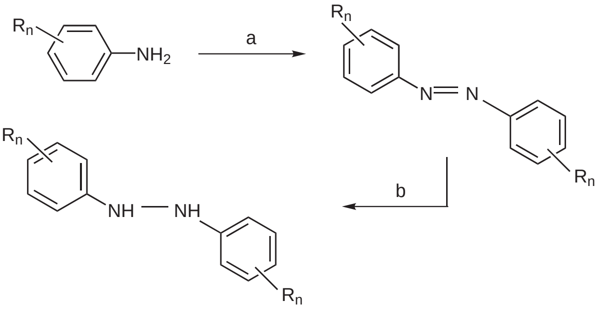


Scheme 1 *Reagents and conditions*: (a) $Na_2S_2O_4$, H_2O.

On this basis we expected that 2,2′,3,3′-tetramethylazobenzene (**1a**) would be converted into 2,3-dimethylaniline when treated with the reducing reagent under similar conditions, but to our surprise that appeared not to be the case; instead, the corresponding hydrazine was obtained.

In order to explore if this particular reduction with dithionite is a special case or not, several azobenzenes **1**, prepared by oxidation of aniline derivatives using oxygen, cuprous chloride, and pyridine as described by Terentiev and Mogiljanskji,[7–9] were investigated. Exploratory experiments with **1a** revealed two important features. First, water, the solvent used by Fieser in his reduction of Orange II,[5] had to be replaced by a mixture of water and one or several organic solvents to achieve consumption of the azobenzene at a reasonable rate under reflux. We settled for a 3:20:20 mixture of dichloromethane, methanol, and water, which proved to be a useful solvent system. Secondly, when the dithionite–azobenzene molar ratio was approximately 2.2, which was the value used by Fieser,[5] the consumption of the azobenzene was very sluggish. The ratio was therefore increased, and when it was 5.5 or above the conversion appeared to proceed at a satisfactory rate.

Selected substituted azobenzenes[10] were then reacted under conditions identical or very similar to those found to be the best for **1a**.[11] The results, which are summarized in Scheme 2 and Table 1, show that most of the azobenzenes were converted into the corresponding *N*,*N*′-diarylhydrazines[12,13] in excellent yield and, consequently, deviate from the course of reaction reported by Fieser and others, for similar azo compounds.[5,6i–q] The products were easy to isolate and purify, but the stability was variable. Thus, whereas the methylated and methoxylated *N*,*N*′-diarylhydrazines (**2a**–**d**,**i**,**j**) are fairly stable at room temperature even in the presence of air, the chloro-substituted analogues **2f**–**h** reacted with oxygen[8b,13i,14] to furnish the starting azobenzenes.



Scheme 2 *Reagents and conditions*: (a) O_2, $(CuCl)_2$, pyridine, r.t.; (b) $Na_2S_2O_4$, H_2O, MeOH, CH_2Cl_2, reflux; n = 1 or 2.

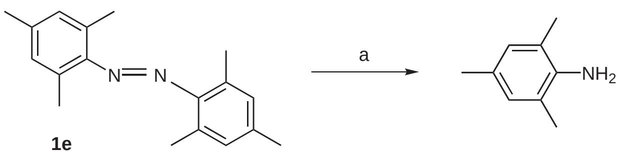
Two of the azobenzene investigated failed to give the corresponding hydrazines. One compound, **1e**, reacted as expected on the basis of Fieser's report[5] and afforded 2,4,6-trimethylaniline in 96% yield (Scheme 3);[15] no *N*,*N*′-bis(2,4,6-trimethylphenyl)hydrazine was isolated. Another deviation was observed with 4,4′-dimethoxyazobenzene (**1k**); this compound reacted slowly and gave a complex product mixture, which contained neither the hydrazine nor the corresponding aniline derivative. This is somewhat surprising considering the fact that the 2,2′- and 3,3′-analogues gave the corresponding hydrazines in excellent yields (Table 1).

SYNLETT 2007, No. 11, pp 1695–1698
Advanced online publication: 25.06.2007
DOI: 10.1055/s-2007-982565; Art ID: D07007ST

Table 1 Conversion of Substituted Azobenzenes **1** into the Corresponding *N*,*N*′-Diarylhydrazines **2** by Sodium Dithionite Treatment

Substituents of **1**	Molar ratio of $Na_2S_2O_4$:**1**	Reaction at reflux (h)	Isolated yield of **2** (%)[a]
1a: 2,2′,3,3′-Me_4	5.5	2.0	81
1b: 2,2′,4,4′-Me_4	9.1	1.6	86
1c: 2,2′,6,6′-Me_4	9.1	1.6	80
1d: 3,3′,5,5′-Me_4	9.1	1.8	89
1e: 2,2′,4,4′,6,6′-Me_6	6.1	3.0	0
1f: 2,2′-Cl_2	10.0	1.5	90
1g: 3,3′-Cl_2	11.3	1.5	88
1h: 4,4′-Cl_2	11.3	6.0	80
1i: 2,2′-$(MeO)_2$	11.5	1.5	83
1j: 3,3′-$(MeO)_2$	9.3	1.5	94
1k: 4,4′-$(MeO)_2$	9–18	1.5	0

[a] The products were characterized by IR, ^1H NMR, and ^{13}C NMR spectroscopy, mass spectrometry, and melting points (when appropriate), and compared with literature data. All the products are known from the literature, see ref. 1.



Scheme 3 *Reagents and conditions*: (a) $Na_2S_2O_4$, H_2O, MeOH, CH_2Cl_2, reflux.

The reduction of azobenzene derivatives to the corresponding *N*,*N*′-diarylhydrazines reported here is a cheap, simple, and convenient alternative to a number of methods already available.[13d,16] Overreduction to anilines, which is the main or a significant reaction when other reducing agents are used,[5,6i–r,8h,17] is barely observed. It is also noteworthy that the reaction conditions are slightly basic and therefore prevent benzidine rearrangement of the hydrazobenzenes.[13i,j,18]

In this context a paper by Park and Han is quite interesting.[13c] They found that azobenzenes dissolved in aqueous acetonitrile were reduced by sodium dithionite to the corresponding hydrazobenzenes when dioctyl viologen, an electron-transfer catalyst, was present. However, in the absence of this catalyst no reaction occurred. Thus, the reducing power of $Na_2S_2O_4$ is influenced by solvent effects.

In conclusion, the paper describes a high-yield method for the preparation of diarylhydrazines from the corresponding azobenzenes. It has been reported previously that the same reduction can be achieved with $Na_2S_2O_4$ provided an electron-transfer catalyst is added. By changing from homogeneous (aq MeCN) to two-phase (aq MeOH–CH_2Cl_2) conditions we have achieved reduction without adding an electron-transfer catalyst.

Acknowledgment

Financial support from the former Nycomed Imaging (now GE Healthcare) is highly appreciated. Thanks are also due to Ann Margot Whyatt at the University of Bergen, and Dr. Dag Ekeberg at the Norwegian University of Life Sciences, for skillful technical assistance.

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(9) **General Procedure for the Preparation of Azobenzenes 1a–k from Anilines**
Oxygen was bubbled through a mixture of an aniline derivative (20 mmol), $(CuCl)_2$ (0.20 g, 2.0 mmol), and dry pyridine (20 mL), which was stirred at r.t. for 1–3 h. The reaction was quenched by addition of H_2O (20 mL), which in some cases gave a precipitate, in other cases not. When no precipitate was formed, the hydrolyzate was extracted with Et_2O (3 × 10 mL) and the combined extracts were dried ($MgSO_4$), filtered, and concentrated on a rotary evaporator. Purification by flash chromatography (silica, hexane–EtOAc in a ratio of 90:10) gave a solid, which was recrystallized from EtOH and dried under vacuum. When the azobenzene precipitated during the hydrolysis, the precipitate was filtered, washed with H_2O on the filter, and dried under vacuum. The products were characterized by IR, ^1H NMR, and ^{13}C NMR spectroscopy, mass spectrometry, and melting points (when appropriate), which were compared with literature data.

(10) All the products were known from the literature: **1a** [29418-34-6]: ref. 8k, 8m; **1b** [29418-25-5]: ref. 8f, 8g, 8j; **1c** [29418-31-3]: ref. 8f, 8g, 8i, 8k, 8m; **1d** [77611-71-3]: ref. 8c, 8r, 8s; **1e** [5692-66-0]: ref. 6l, 8d, 8e, 8g, 8h; **1f** [7334-33-0]: ref. 8k, 8m, 8p, 8t, 8u, 8v; **1g** [15426-14-9]: ref. 8k, 8m, 8n, 8p, 8q, 8t; **1h** [1602-00-2]: ref. 8f, 8g, 8j–m, 8p, 8q, 8s, 8t; **1i** [613-55-8]: ref. 8k, 8m, 8n, 8p, 8t, 8u; **1j** [6319-23-9]: ref. 8t, 8u, 8v; **1k** [501-58-6]: ref. 8j, 8k–m, 8o, 8p, 8u.

(11) **General Procedure for the Reduction of Azobenzenes to *N,N′*-Diarylhydrazines**
Azobenzene **1** (0.4–2.1 mmol) was added to a mixture of H_2O (165 mL/mmol of **1**), MeOH (165 mL/mmol of **1**), and CH_2Cl_2 (25 mL/mmol of **1**). The resulting mixture was stirred and heated to reflux, and an excess of sodium dithionite (see Table 1) was added. After stirring at reflux (see Table 1), the product mixture was poured into ice and extracted with Et_2O (3 × 100 mL). The combined extracts were dried ($MgSO_4$) and filtered, and then the solvent was removed under reduced pressure to give a residue, from which the product **2** was isolated by flash chromatography (silica, hexane–EtOAc in a ratio of 90:10). The results are compiled in Table 1.

(12) All the *N,N′*-diarylhydrazines except 2,2′,4,4′-tetramethyl-(*N,N′*-diphenylhydrazine) (**2b**) are mentioned several times in the literature: **2a** [107418-14-4]: ref. 8c, 8m, 13f, 13j; **2c** [63615-06-5]: ref. 8m, 13f; **2d** [142068-90-4]: ref. 8c; **2e** [5692-66-0]: ref. 8m, 13a; **2f** [782-74-1]: ref. 8m, 13g, 13h; **2g** [953-01-5]: ref. 8m, 8n, 8q, 13e, 13g; **2h** [953-14-0]: ref. 8m, 8p, 8q, 13b–d, 13g, 13h; **2i** [787-77-9]: ref. 8m, 8n, 8p, 13e, 13g, 13h, 13j; **2j** [1027-32-3]: ref. 13g, 13h, 13j; **2k** [1027-40-3]: ref. 8m, 13b–d. The synthesis and isolation of **2b** have been reported by Nölting and Stricker,[8c] but no data except the melting point were given.
Data for **2b**: mp 119–121 °C (lit.[8c] mp 120–122 °C). IR (film): 3364, 3228, 3008, 1627, 1510, 1463, 1444, 1276, 1240, 1153, 1012, 875, 814 cm^{-1}. ^1H NMR (200 MHz, CCl_4): d = 2.16 (s, 6 H), 2.19 (s, 6 H), 5.19 (s, 2 H), 6.59–6.76 (m, 6 H). ^{13}C NMR (50 MHz, CCl_4): d = 16.9, 20.3, 111.1, 120.1, 127.4, 127.6, 130.7, 143.7. MS (EI): *m/z* (%) = 240 (0.5) [M^+], 194 (5), 182 (2), 172 (2), 163 (3), 147 (2), 131 (5), 110 (2), 107 (6), 106 (100), 105 (93), 98 (4), 88 (7), 87 (8), 85 (5), 78 (17), 77 (98), 76 (5), 74 (12). HRMS (EI): *m/z* calcd for $C_{16}H_{20}N_2$ [M^+]: 240.1626; found: 240.1622.

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(15) **Preparation of 2,4,6-Trimethylaniline**
2,2′,4,4′,6,6′-Hexamethylazobenzene (**1e**, 0.50 g, 1.88 mmol) was added to a mixture of H_2O (200 mL), MeOH (200 mL), and CH_2Cl_2 (30 mL). The resulting mixture was stirred and heated to reflux, and $Na_2S_2O_4$ (2.00 g, 11.5 mmol) was added. After stirring at reflux for 3 h, the product mixture was poured into ice and extracted with Et_2O (3 × 100 mL). The combined extracts were dried ($MgSO_4$) and filtered, and the solvent was subsequently removed under reduced pressure to give a residue, from which 0.42 g (82%) of 2,4,6-trimethylaniline was isolated by flash chromatography (silica, hexane–EtOAc in a 90:10 ratio). The spectroscopic and physical properties of the product were identical to those of the aniline derivative used to prepare azobenzene **1e**.

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