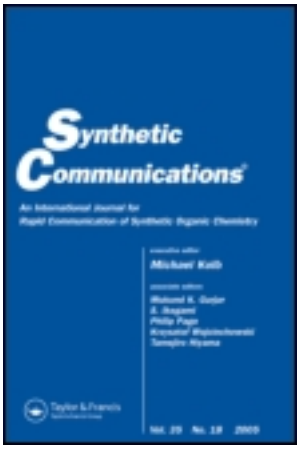

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REDUCTION OF NITROARENES TO AZOXYBENZENES BY NaOH-PEG 400

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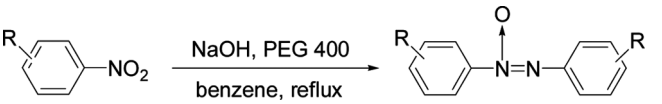
GRAPHICAL ABSTRACT



Abstract *The reduction of nitroarenes to azoxybenzenes by NaOH-PEG 400 in benzene is described. The protocol is facile, economical, and effective.*

Keywords Azoxybenzenes; benzene; nitroarenes; poly(etheylene glycol 400); sodium hydroxide

INTRODUCTION

Conversion of nitroarenes into the corresponding azoxybenzenes can be carried out with a variety of reducing reagents such as alkaline metal borohydrides,[1] sodium arenetellurolate,[2] phosphine,[3] $InBr_3$-Et_3SiH,[4] and metals such as samarium,[5] thallium,[6] and nickel.[7] However, most of these methods suffer from drawbacks such as high costs, lengthy reactions, poor yields, or inconvenient workup procedures; therefore, there is a need for a facile, economical, and effective synthetic procedure for the preparation of azoxybenzenes.

The reduction of aldehydes and ketones to the corresponding alcohols by KOH-isopropanol has been recently reported, in which isopropanol is used as a hydrogen source and solvent. This protocol is unprecedented, simple, economical, and effective.[8] Thus, we attempt the reduction of nitroarenes to azoxybenzenes by the analogical reducing system. Here, we first designed the reduction of nitroarenes by NaOH-poly(ethylene glycol 400) (PEG 400) in benzene, and the corresponding azoxybenzenes were obtained in moderate to good yields (Scheme 1).

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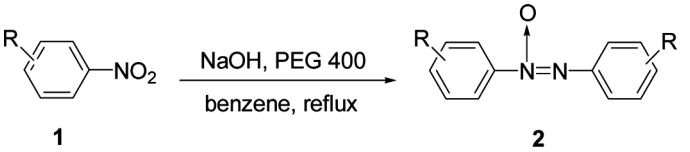

1 2

Scheme 1. Reduction of nitroarenes to azoxybenzenes.

Aprotic benzene was selected as a solvent to reduce the solvent effects of alcohol on the reduction; the widely available and inexpensive PEG 400 could not only play a role as hydrogen source but also transfer NaOH into the organic phase and promote the reductions as a phase-transfer catalyst similar to crown ethers.[9]

RESULTS AND DISCUSSION

At the beginning of our work, we chose to study the reduction of *m*-bromonitrobenzene as a model reaction. The effects of the reaction temperature and the amounts of PEG 400 and NaOH on the reaction were investigated, and the results from our optimization studies are listed in Table 1.

Initially, both the reaction rates and yields increased with increasing amounts of NaOH (entries 1-1 and 1-2); however, beyond a certain value, it appeared that increasing the amounts of NaOH had no effect on the reaction (entry 1-3).

While maintaining the optimized amount of NaOH, we found that no reaction (NR) took place in the absence of PEG 400 (entry 1-4). By increasing the amount of PEG 400 to 0.5 mmol (entry 1-2), a good yield (80%) was achieved. When the amount of PEG 400 was further increased to 0.6 mmol (entry 1-6), only 74% yield was observed, which may be the result of further reductions of the azoxybenzenes by a superfluous hydrogen source.

The effects of reaction temperature were also investigated (entries 1-2, 1-7, and 1-8). We found that no reaction (NR) occured when the temperature was not higher than 60 °C (entry 1-7), but the reaction yields dramatically increased with increasing temperature, indicating the reaction has a high activation energy.

The reductions of a variety of nitroarenes were studied under the optimal conditions, and the corresponding azoxybenzenes were obtained in moderate to good

Table 1. Optimization of reaction conditions[a]

Entry	NaOH (mmol)	PEG 400 (mmol)	Temperature (°C)	Time (h)	Yield (%)[b]
1-1	5	0.5	Reflux	4	63
1-2	8	0.5	Reflux	1	80
1-3	10	0.5	Reflux	1	80
1-4	8	0	Reflux	12	NR
1-5	8	0.4	Reflux	1	69
1-6	8	0.6	Reflux	1	74
1-7	8	0.5	60	12	NR
1-8	8	0.5	70	4	57

[a]Reaction conditions: *m*-bromonitrobenzene (1 mmol), benzene (20 mL).
[b]Isolated yields of *m,m′*-dibromoazoxybenzene after recrystallization.

Table 2. Reductions of nitroarenes into the corresponding azoxybenzenes by NaOH-PEG 400 in benzene[a]

Entry	R	Nitroarenes	Reaction time (h)	Azoxybenzenes	Yield (%)[b]
2-1	H	**1a**	5	**2a**	90
2-2	*m*-Cl	**1b**	3	**2b**	85
2-3	*p*-Cl	**1c**	5	**2c**	44
2-4	*m*-Br	**1d**	1	**2d**	80
2-5	*p*-Br	**1e**	3	**2e**	43
2-6	*m*-I	**1f**	3	**2f**	76
2-7	*p*-I	**1g**	5	**2g**	40
2-8	*o*-CH_3	**1h**	4	**2h**	50
2-9	*m*-CH_3	**1i**	4	**2i**	86
2-10	*p*-CH_3	**1j**	2	—[c]	44[d]
2-11	*p*-OCH_3	**1k**	8	**2k**	50
2-12	*p*-OCH_2CH_3	**1l**	8	**2l**	64

[a]Reaction conditions: nitroarenes (1 mmol), NaOH (8 mmol), and PEG 400 (0.5 mmol) in benzene (20 mL) at reflux temperature.
[b]Isolated yields of azoxybenzenes after recrystallization.
[c]No *p,p′*-dimethylazoxybenzene was obtained.
[d]Yield refers to *p,p′*-dinitrobibenzyl.

yields (Table 2). These results suggest that the locations of substituent groups play an important role in determining the reduction efficiencies. Nitrobenzene and *meta*-substituted analogs were reduced efficiently, while *para*-substituted analogs were reduced in lower yields, which may be due to the presence of nucleophilic substitution side reactions in *para*-substituted nitroarenes. In addition, we found that the reactions of *o*-chloronitrobenzene, *o*-bromonitrobenzene, and *o*-iodonitrobenzene gave very complicated mixtures that were difficult to separate (not listed in Table 2; detailed studies are under way). For *p*-nitrotoluene (entry 2-10), no *p,p′*-dimethylazoxybenzene could be isolated, whereas *p,p′*-dinitrobibenzyl was obtained with 44% yield, which is because *p*-nitrotoluene (which possesses weakly acidic *a*-H) could spontaneously disproportionate in strongly basic medium to the reduced species, its radical anion, and as oxidized form *p,p′*-dinitrobibenzyl.[10]

In conclusion, we have developed a new method for synthesis of azoxybenzenes by the reduction of the corresponding nitroarenes with NaOH-PEG 400 in benzene at reflux temperature. The simple experimental procedure, the use of economically viable reagents, and the high efficiency of the reactions are advantages of this protocol, making this method useful for large-scale production of azoxybenzenes.

EXPERIMENTAL

All the reagents were obtained from commercial sources and used without further purification. Melting points of the compounds were measured using a Sanyo-Callenksmp apparatus and were uncorrected. The infrared (IR) spectra were recorded on a Perkin-Elmer 1700 spectrometer. ^{1}H NMR spectra in $CDCl_3$ were recorded on a Bruker DLX 300-MHz spectrophotometer. Elemental analysis was obtained from a VazioE elemental analyzer.

General Procedure for Synthesis of Azoxybenzenes

Nitroarenes (1 mmol) were added to a mixture of NaOH (8 mmol) and PEG 400 (0.5 mmol) in 20 mL benzene in a flask equipped with a condenser. The resultant solutions were magnetically stirred at reflux temperature until the nitroarenes were consumed, monitored by thin-layer chromatography (TLC). The solutions were filtered, rotary evaporated, and precipitated in water. The crude products were isolated by filtration and further purified by recrystallization in ethanol.

Compound 2a

Mp 35–36 °C (lit.[11] 35 °C); ^{1}H NMR (300 MHz, $CDCl_3$): $\delta = 7.40$–7.54 (m, 6H), 8.05–8.32 (m, 4H); IR, υ (KBr disc): 1572, 1474, 1425, 1329, 750, 670 cm^{-1}.

Compound 2b

Mp 97–98 °C (lit.[6] 96–97 °C); ^{1}H NMR (300 MHz, $CDCl_3$): $\delta = 7.36$–7.56 (m, 4H), 7.99 (d, $J = 7.5$ Hz, 1H), 8.19 (d, $J = 8.4$ Hz, 1H), 8.25 (s, 1H), 8.30 (s, 1H); IR, υ (KBr disc): 1556, 1470, 1421, 1302, 783 cm^{-1}.

Compound 2c

Mp 154–156 °C (lit.[6]156–157 °C); ^{1}H NMR (300 MHz, $CDCl_3$): $\delta = 7.50$ (dd, $J = 9$, 9 Hz, 4H), 8.19 (d, $J = 8.7$ Hz, 2H), 8.28 (d, $J = 9$ Hz, 2H); IR, υ (KBr disc): 1583, 1481, 1404, 1323, 831 cm^{-1}.

Compound 2d

Mp 111–113 °C (lit.[6] 109–110 °C); ^{1}H NMR (300 MHz, $CDCl_3$): $\delta = 7.36$–7.45 (m, 2H), 7.56 (d, $J = 9.9$ Hz, 1H), 7.73 (d, $J = 9.9$ Hz, 1H), 8.06 (d, $J = 0.9$ Hz, 1H), 8.09 (d, $J = 1.2$ Hz, 1H), 8.24 (s, 1H), 8.29 (s, 1H); IR, υ (KBr disc): 1553, 1472, 1420, 1298, 781 cm^{-1}.

Compound 2e

Mp 171–173 °C (lit.[5]173–175 °C); ^{1}H NMR (300 MHz, $CDCl_3$): $\delta = 7.66$ (dd, $J = 9$, 9 Hz, 4H), 8.11 (d, $J = 8.7$ Hz, 2H), 8.21 (d, $J = 9$ Hz, 2H); IR, υ (KBr disc): 1575, 1465, 1398, 1319, 826 cm^{-1}.

Compound 2f

Mp 120–121 °C (lit.[6] 118–119 °C); ^{1}H NMR (300 MHz, $CDCl_3$): $\delta = 7.18$–7.27 (m, 2H), 7.71 (d, $J = 7.8$ Hz, 1H), 7.89 (d, $J = 7.8$ Hz, 1H), 8.08 (d, $J = 9$ Hz, 1H), 8.25 (d, $J = 8.1$ Hz, 1H), 8.55 (s, 1H), 8.63 (s, 1H); IR, υ (KBr disc): 1545, 1470, 1418, 1294, 783 cm^{-1}.

Compound 2g

Mp 205–207 °C (lit.[5] 208–210 °C); ^{1}H NMR (300 MHz, $CDCl_3$): $\delta = 7.78$ (dd, $J = 8.7$, 12.9 Hz, 4H), 7.87 (d, $J = 8.4$ Hz, 2H), 7.98 (d, $J = 8.4$ Hz, 2H); IR, υ (KBr disc): 1572, 1468, 1393, 1321, 829 cm^{-1}.

Compound 2h

Mp 59–60 °C (lit.[11] 60 °C); ^{1}H NMR (300 MHz, $CDCl_3$): $\delta = 2.37$ (s, 3H), 2.52 (s, 3H), 7.28–7.39 (m, 6H), 7.67 (d, $J = 7.5$ Hz, 1H), 8.03 (d, $J = 9.3$ Hz, 1H); IR, υ (KBr disc): 1485, 1420, 1381, 1329, 760 cm^{-1}.

Compound 2i

Mp 35–37 °C (lit.[6] 33–35 °C); ^{1}H NMR (300 MHz, $CDCl_3$): $\delta = 2.41$ (s, 3H), 2.44 (s, 3H), 7.18 (d, $J = 7.2$ Hz, 1H), 7.33–7.38 (m, 3H), 7.96-8.09 (m, 4H); IR, υ (KBr disc): 1603, 1493, 1458, 1414, 1306, 787 cm^{-1}.

Compound 2k

Mp 115–116 °C (lit.[6] 116.5–118.5 °C); ^{1}H NMR (300 MHz, $CDCl_3$): $\delta = 3.89$ (s, 6H), 6.97 (dd, $J = 7.2$, 8.7 Hz, 4H), 8.27 (dd, $J = 9$, 8.7 Hz, 4H); IR, υ (KBr disc): 1595, 1499, 1411, 1387, 1300, 1252, 839 cm^{-1}.

Compound 2l

Mp 137–139 °C; ^{1}H NMR (300 MHz, $CDCl_3$): $\delta = 1.43$–1.47 (m, 6H), 4.07–4.14 (m, 4H), 6.95 (dd, $J = 5.7$, 8.7 Hz, 4H), 8.24 (dd, $J = 9$, 11.1 Hz, 4H); IR, υ (KBr disc): 1598, 1500, 1473, 1411, 1390, 1300, 1256, 845 cm^{-1}; Anal. calcd. for $C_{16}H_{18}N_2O_3$: C, 67.12; H, 6.34; N, 9.78. Found: C, 66.86; H, 6.46; N, 9.69.

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