

Communication

A Direct Method for the Efficient Synthesis of Hydroxyalkyl-Containing Azoxybenzenes

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Abstract: Reaction of nitrobenzyl alcohol with glucose (200 mol%) in the presence of NaOH in water-ethanol medium gave 1,2-bis(4-(hydroxymethyl)phenyl)diazene oxide, 1,2-bis(2-(hydroxymethyl)phenyl)diazene oxide and 1,2-bis(4-(1-hydroxyethyl)phenyl)diazene oxide in 76%, 76% and 72% yields, respectively.

Keywords: azoxybenzenes; nitrobenzyl alcohol; reduction



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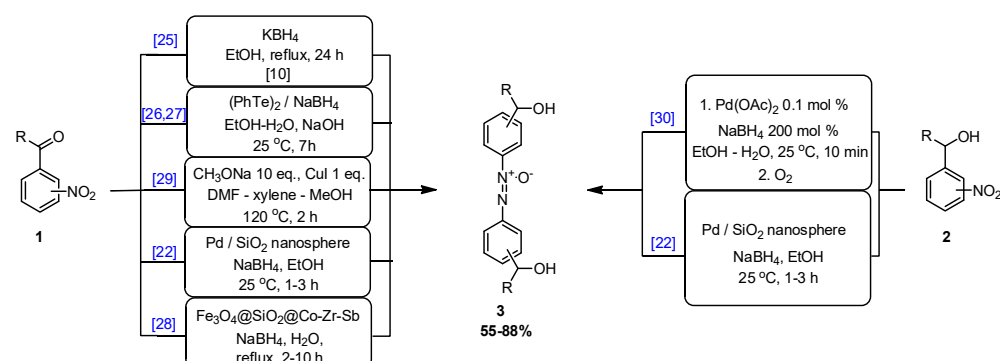
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1. Introduction

The azoxybenzene moiety is a part of many compounds with practically valuable properties: liquid crystalline compounds [1–3] and bioactive substances [4–6]. Classical approaches to the synthesis of azoxybenzenes are based on numerous versions of the reduction of nitroaromatic substrates [7–9] or the oxidation of aminoarenes [10–14] and other methods [15]. However, such a route is not optimal where substrates contain functional groups susceptible to reduction or oxidation conditions. For this reason, it seems interesting to increase the molecular complexity of azoxybenzenes bearing reactive functions, such as carboxy- [16], formyl- [17], amino- [18,19], alkyne- [12,20,21], hydroxyl- [22], and other groups. Earlier, we demonstrated an example of the azoxybenzene preparation through reduction with glucose [23] in the presence of sodium hydroxide in the water-ethanol medium to synthesize 1,3-dioxolanyl-containing azoxybenzenes [24]. In the present work, this method was extended to the preparation of hydroxyalkyl-containing azoxybenzenes **3**, some of which were synthesized earlier using different methods [22,25–30] (Scheme 1).

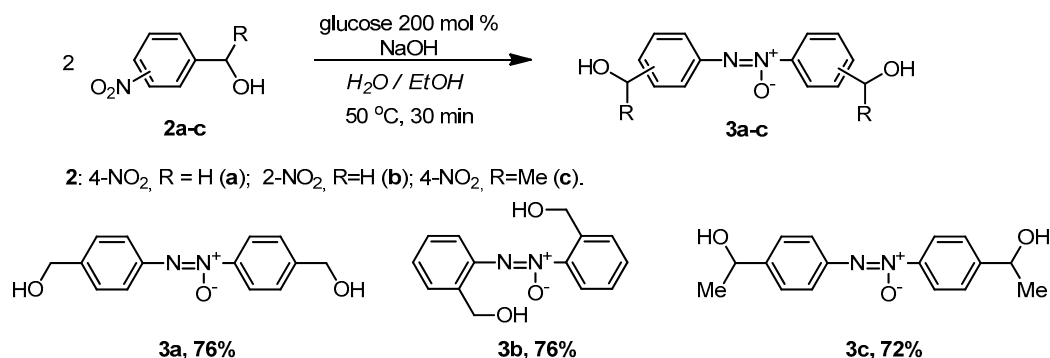


Scheme 1. Examples of preparation hydroxyalkyl-containing azoxybenzenes.

2. Results and Discussion

Various nitroaryl-containing benzyl alcohols **2** (commercially available or easy synthesizable by known methods in high yields [31–33]) can serve as convenient starting compounds for the synthesis of hydroxyalkyl-containing azoxybenzenes.

Similar to 2-(4-nitrophenyl)-1,3-dioxolane [24], the reduction of nitrobenzyl alcohols **2** readily proceeds on exposure to glucose (200 mol%) in the presence of sodium hydroxide in the water–ethanol medium. The TLC or GC/MS control of the reaction course shows that complete conversion of the substrate occurs within 30 min of keeping the reaction mixture at 50 °C and vigorous stirring (Scheme 2).



Scheme 2. Reaction of nitrobenzyl alcohol **2a–c** with glucose.

The target products **3** precipitate as a crystalline solid after dilution of the reaction mass with water. Products were filtered off, washed with water, and further purified by recrystallization or flash chromatography.

The structure of **3** was confirmed by ¹H and ¹³C-NMR spectroscopy, IR spectroscopy, and high-resolution mass spectrometry.

In this case, successful reduction to azoxy derivatives was due to a combination of experimental conditions, namely the reaction time, reaction medium and lack of aeration. It is also known that the reduction of nitroarenes by glucose can be carried out to obtain azo compounds [34–36] and aromatic amines [37].

3. Materials and Methods

The reactions were monitored by thin-layer chromatography (Sorbfil, Imid Ltd., Krasnodar, Russia). The ¹H-NMR, ¹³C-NMR spectra were acquired on ECA400 (JEOL) (400 and 100 MHz, respectively) spectrometers in (CD₃)₂SO at room temperature. The chemical shifts δ were measured in ppm with reference to the residual solvent resonances (¹H: (CD₃)₂SO, δ = 2.49 ppm; ¹³C: (CD₃)₂SO, δ = 39.5 ppm). The splitting patterns are referred to as s—singlet; d—doublet; t—triplet; m—multiplet. Coupling constants (J) are given in hertz. IR spectra were recorded on an IR Prestige (Shimadzu), using tablets of samples with KBr. High-resolution and accurate mass measurements were carried out using a Bruker MaXis Impact (electrospray ionization/time of flight). The melting points were determined on Stuart SMP30 apparatus and left uncorrected. The commercial reagents employed in the synthesis were 2-Nitrobenzaldehyde (98%, Aldrich, St. Louis, MS, USA), 4-Nitrobenzaldehyde (98%, Aldrich, St. Louis, MS, USA), 4'-Nitroacetophenone (98%, Aldrich, St. Louis, MS, USA), Sodium borohydride (powder, 98%, ABCR) and D-(+)-Glucose monohydrate (≥99%, Vekton, Russia).

General Procedure for the Preparation of Hydroxyalkyl-Containing Azoxybenzenes (3)

Nitrobenzyl alcohol **2** (3.26 mmol) in ethanol (6 mL) was added to 30% aq. NaOH (7.5 mL). At 50 °C, a solution of glucose monohydrate (1.29 g, 6.5 mmol) in water (1 mL) was added. The mixture was stirred for 30 min at 50 °C. The reaction was cooled, diluted with water, and the formed precipitate was filtered and washed with distilled water. The resulting residue was purified via recrystallization from EtOH.

1,2-bis(4-(hydroxymethyl)phenyl)diazene oxide **3a**. Yield 0.32 g (76%); light beige crystals; mp 163–164 °C (EtOH). IR (KBr): ν = 3284 (OH), 3055 (Csp²-H), 2974, 2933, 2899, 2872 (Csp³-H), 1600, 1498 (Csp²-Csp²), 1465, 1408, 1327, 1278, 1199, 1159, 1035, 1010, 825 cm⁻¹ (Supplementary Materials, Figure S1). ¹H-NMR ((CD₃)₂SO, 399.78 MHz):

δ = 4.57 (s., 2H, CH₂), 4.62 (s., 2H, CH₂), 5.33 (br. s., 1H, OH), 5.43 (br. s., 1H, OH), 7.45–7.50 (m., 2H, CH), 7.52–7.56 (m., 2H, CH), 8.07–8.11 (m., 2H, CH), 8.18–8.23 (m., 2H, CH) (Supplementary Materials, Figure S2). ¹³C-NMR ((CD₃)₂SO, 100.5 MHz): δ = 62.1 (CH₂), 62.5 (CH₂), 121.8 (CH), 125.0 (CH), 126.6 (CH), 126.7 (CH), 142.2 (C), 144.6 (C), 146.3 (C), 147.0 (C) (Supplementary Materials, Figure S3). HRMS ESI TOF: m/z = 259.1082 [M+H]⁺ (259.1077 calc. for C₁₄H₁₄N₂O₃) (Supplementary Materials, Figure S4).

1,2-bis(2-(hydroxymethyl)phenyl)diazene oxide **3b**. Yield 0.32 g (76%); light beige crystals; mp 118–120 °C (EtOH). IR (KBr): ν = 3230 (OH), 2922, 2864 (Csp³-H), 1483, 1458, 1440, 1365, 1330, 1184, 1039, 1012, 921, 750 cm⁻¹ (Supplementary Materials, Figure S5). ¹H-NMR ((CD₃)₂SO, 399.78 MHz): δ = 4.58 (d., 5.7 Hz, 2H, CH₂), 4.74 (d., 5.7 Hz, 2H, CH₂), 5.20 (t., 5.7 Hz, 1H, OH), 5.41 (t., 5.7 Hz, 1H, OH), 7.35–7.42 (m., 2H), 7.45–7.51 (m., 1H), 7.58–7.62 (m., 2H), 7.70–7.74 (m., 1H), 7.77–7.82 (m., 1H), 7.88–7.92 (m., 1H) (Supplementary Materials, Figure S6). ¹³C-NMR ((CD₃)₂SO, 100.5 MHz): δ = 59.22 (CH₂), 59.35 (CH₂), 121.0 (CH), 123.4 (CH), 126.8 (CH), 127.2 (CH), 127.6 (CH), 128.1 (CH), 128.4 (CH), 130.5 (CH), 135.6 (C), 137.6 (C), 140.8 (C), 147.0 (C) (Supplementary Materials, Figure S7). HRMS ESI TOF: m/z = 241.0978 [(M-H₂O)+H]⁺ (calc. 241.0971 for C₁₄H₁₂N₂O₂ [3b-H₂O]) (Supplementary Materials, Figure S8).

1,2-bis(4-(1-hydroxyethyl)phenyl)diazene oxide **3c**. Yield 0.34 g (72%); light beige crystals; mp 105–106 °C (EtOH). IR (KBr): ν = 3327 (OH), 3074, 3053, 3034 (Csp²-H), 2970, 2924 (Csp³-H), 1602, 1498 (Csp²-Csp²), 1462, 1409, 1367, 1327, 1286, 1203, 1083, 1010, 896, 840 cm⁻¹ (Supplementary Materials, Figure S9). ¹H-NMR ((CD₃)₂SO, 399.78 MHz): δ = 1.34 (d., 2.3 Hz, 3H, CH₃), 1.35 (d., 2.5 Hz, 3H, CH₃), 4.57–4.87 (m, 2H, CH), 5.30 (d., 4.3 Hz, 1H, OH), 5.40 (d., 4.4 Hz, 1H, OH), 7.48–7.52 (m, 2H, CH), 7.54–7.58 (m, 2H, CH), 8.06–8.09 (m, 2H, CH), 8.17–8.20 (m, 2H, CH) (Supplementary Materials, Figure S10). ¹³C-NMR ((CD₃)₂SO, 100.5 MHz): δ = 25.78 (CH₃), 25.82 (CH₃), 67.47 (CH), 67.51 (CH), 67.77 (CH), 67.80 (CH), 121.8 (CH), 125.0 (CH), 125.7 (CH), 126.0 (CH), 142.1 (C), 146.2 (C), 149.4 (C), 151.7 (C) (Supplementary Materials, Figure S11). HRMS ESI TOF: m/z = 287.1397 [M+H]⁺ (287.1390 calc. for C₁₆H₁₈N₂O₃) (Supplementary Materials, Figure S12).

Supplementary Materials: The following can be downloaded online. Figure S1: IR-spectrum of 3a; Figure S2: ¹H-NMR of 3a; Figure S3: ¹³C-NMR of 3a; Figure S4: HRMS of 3a; Figure S5: IR-spectrum of 3b; Figure S6: ¹H-NMR of 3b; Figure S7: ¹³C-NMR of 3b; Figure S8: HRMS of 3b; Figure S9: IR-spectrum of 3c; Figure S10: ¹H-NMR of 3c; Figure S11: ¹³C-NMR of 3c; Figure S12: HRMS of 3c.

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