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1,2-Bis(4-(1,3-dioxolan-2-yl)phenyl)diazene Oxide

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Abstract: A simple approach to synthesizing 1,2-bis(4-(1,3-dioxolan-2-yl)phenyl)diazene oxide was developed in this study, based on glucose as an eco-friendly reductant.

Keywords: azoxybenzene; 1,3-dioxolane; glucose; reduction reaction

1. Introduction

Azoxybenzenes are widely used as liquid crystals [1,2], natural and synthetic compounds with various biological activities (insecticidal activity, plant growth stimulators) [3–6] (Figure 1), ligands for preparing coordination polymers [7], and polyvinyl chloride stabilizers [8]. The reactivity of the azoxy group allows them to be used as building blocks in fine organic synthesis [9–11].

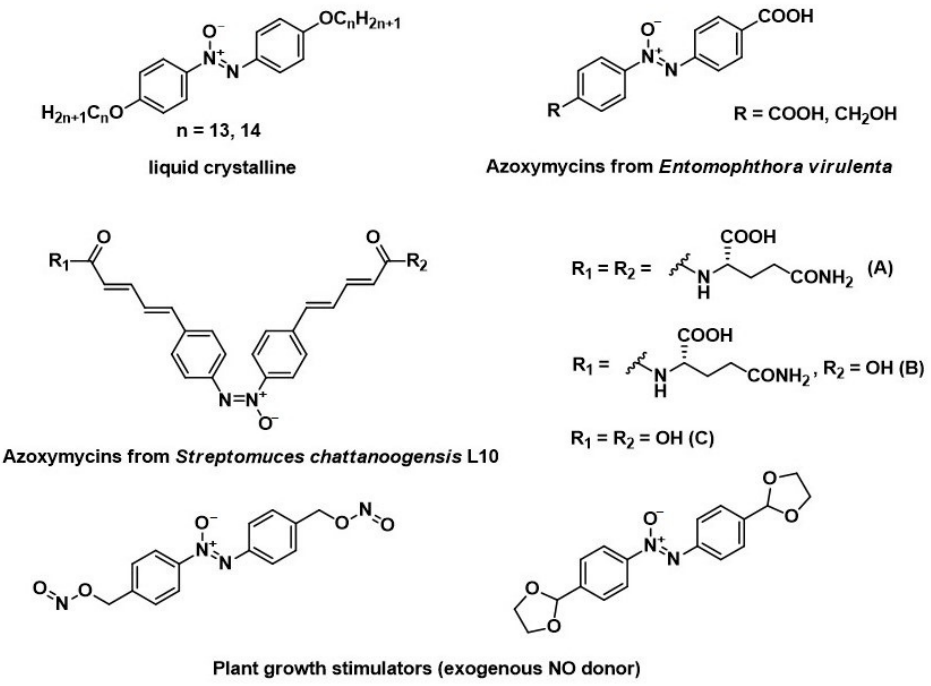

Figure 1. Examples of liquid crystalline and bioactive natural and synthetic azoxybenzenes.

The main methods for synthesizing azoxybenzenes are the oxidation of aromatic amines [12,13] and azo compounds [14], and the reduction of nitroso compounds [15]. The reduction of nitro compounds is the most widely used method. The classic version uses sodium arsenite [16], sodium alkoxides [17], alkali metal borohydrides [18–20], Zn-$BiCl_3$ [21], and Zn/NH_4Cl in a mixture with 1-butyl-3-methylimidazolium tetrafluoroborate ([bmim][BF_4]) and water [22], or selective catalytic hydrogenation [23,24]. This method cannot be employed for substrates containing other functional groups that are

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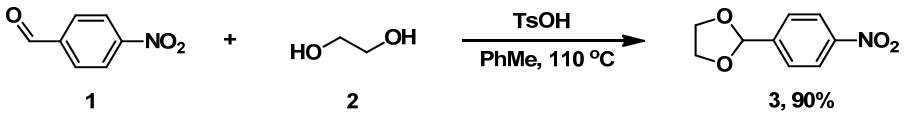
sensitive to reduction. For instance, when reducing nitroaromatic aldehydes or ketones, the carbonyl group is simultaneously reduced [25–28]. In addition, the reaction is often accompanied by the formation of significant amounts of azo compounds, which complicates the isolation of pure azoxy compounds. In this case, azoxybenzenes with carbonyl groups can be used as starting compounds for the synthesis of analogs of natural and synthetic azoxymycins and other practically useful compounds, such as cyclic acetal prepared from 1,2-bis(4-formylphenyl)diazenoxide and ethylene glycol, which are able to stimulate the growth of grain crops [6].

We are interested in synthesizing 1,2-bis(4-(1,3-dioxolan-2-yl)phenyl)diazene oxide by reducing 2-(4-nitrophenyl)-1,3-dioxolane, using glucose as an eco-friendly reductant in alkaline medium. The reduction of nitro compounds under the action of glucose has been previously described [29]; however, despite its simplicity, the method is not widely used. In addition, in some cases, depending on the conditions of the reduction, the reaction products can be both aromatic amines [30] and azo compounds [31]. The reduction of 2-(4-nitrophenyl)-1,3-dioxolane under $Li[AlH_4]$ is accompanied by the formation of azo compounds [32].

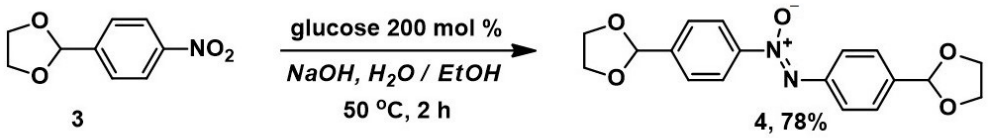
2. Results and Discussion

To begin, 2-(4-nitrophenyl)-1,3-dioxolane **3** was synthesized from commercial 4-nitrobenzaldehyde **1** via acetalization with ethylene glycol **2** in a toluene medium (Scheme 1) [33]. Its physical constants and spectral data are in agreement with the literature data. [33].



Scheme 1. Synthesis of dioxolane **3**.

The reduction of 2-(4-nitrophenyl)-1,3-dioxolane **3** was carried out by mixing it with ethanol in a 30% NaOH solution at 50 °C, along with a solution of 200 mol% glucose. Monitoring of the reaction by analytical thin-layer chromatography (TLC) showed that complete conversion is achieved after 2 h of stirring the reaction mixture at 50 °C (Scheme 2).



Scheme 2. Synthesis of azoxybenzene **4** from 2-(4-nitrophenyl)-1,3-dioxolane **3**.

We found that conducting experiments in a water–ethanol medium is optimal for carrying out the reduction, since it provides the highest yield of the desired product **4** and minimizes undesirable reactions and the resinification of the reaction mixture. Exchange of ethanol for *iso*-propanol or tetrahydrofuran leads to the partial destruction of the starting compound **3**; it thus incompletely converts, and the yield of the desired product is sharply reduced. When the reaction is carried out at the boiling point, the target compound is contaminated with resinous impurities that are difficult to separate. For complete conversion of the starting compound at room temperature, a time of more than 36 h is necessary; therefore, the reaction was carried out at 50 °C.

The target azoxybenzene **4** was purified by recrystallization from ethanol.

The structure of 1,2-bis(4-(1,3-dioxolan-2-yl)phenyl)diazene oxide **4** was unambiguously confirmed by single-crystal X-ray analysis (Figure 2).

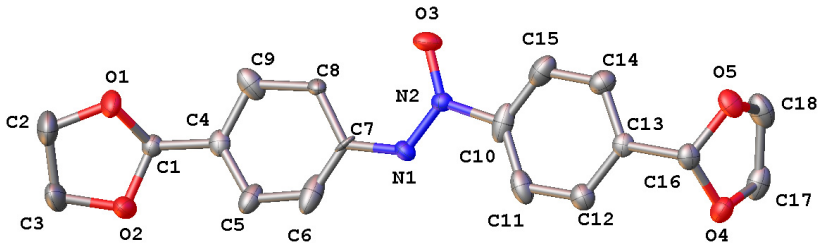
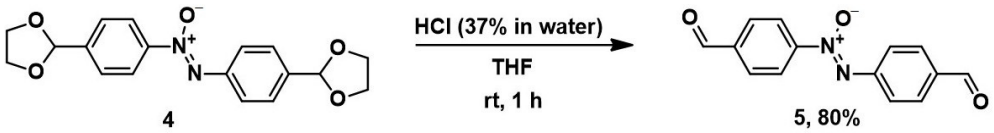


Figure 2. Crystal structure of compound **4** with labeling schemes and 50% thermal ellipsoids.

Deprotection of 1,3-dioxolane **4** was carried out with concentrated hydrochloric acid on a solution of **4** in tetrahydrofuran (THF) at room temperature (Scheme 3) [34]. The yield of *bis*-aldehyde **5** was 80% after recrystallization. Its structure was confirmed by ^{1}H and ^{13}C NMR and mass spectrometry.



Scheme 3. Deprotection of 1,3-dioxolane **4** resulting in *bis*-aldehyde **5**.

In summary, using glucose as an eco-friendly reagent allows for the selective reduction of 2-(4-nitrophenyl)-1,3-dioxolane **3** to the azoxy compound **4** with a high yield.

3. Materials and Methods

The reactions were monitored by thin-layer chromatography (Sorbfil, Imid Ltd., Krasnodar, Russia). The ^{1}H-NMR and ^{13}C-NMR spectra were acquired on ECA400 (JEOL) (400 and 100 MHz, respectively) spectrometers in $CDCl_3$ or $(CD_3)_2SO$ at room temperature (Figures S1–S6). The chemical shifts δ were measured in ppm with reference to the residual solvent resonances (^{1}H: $CDCl_3$, δ = 7.25 ppm; ^{13}C: $CDCl_3$, δ = 77.2 ppm; ^{1}H: $(CD_3)_2SO$, δ = 2.49 ppm; ^{13}C: $(CD_3)_2SO$, 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, Kyoto, Japan), 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). Mass spectra were recorded on a GCMS−QP2010 Plus (Shimadzu) via electron ionization (70 eV, ionization chamber temperature 250 °C). The melting points were determined on a Stuart SMP30 apparatus and left uncorrected. The commercial reagents employed in the synthesis were 4-Nitrobenzaldehyde (for synthesis, ≥98.0%, Aldrich, St. Louis, MO, USA), Ethylene glycol (99%, ABCR), and D-(+)-Glucose monohydrate (≥99.0%, Aldrich). CCDC 2,080,783 contains the supplementary crystallographic data for this paper. These data can be obtained free of charge at http://www.ccdc.cam.ac.uk/or (accessed date 28 April 2021) from the CCDC, 12 Union Road, Cambridge CB2 1EZ, UK; Fax: +44-1223-336033; E-mail: deposit@ccdc.cam.ac.uk.

*3.1. 1,2-Bis(4-(1,3-dioxolan-2-yl)phenyl)diazene Oxide (**4**)*

To 6 mL of ethanol, 7.5 mL of a 30% aqueous solution of sodium hydroxide and 0.5 g (2.56 mmol) of 2-(4-nitrophenyl)-1,3-dioxolane **3** were added. The reaction mixture was maintained at 50 °C, and a solution of 1 g (5.12 mmol) of glucose monohydrate in 1 mL of water was added, which was then stirred for 2 h at the specified temperature. Then, the reaction mixture was cooled and diluted with 50 mL of 2M hydrochloric acid, and the formed precipitate was filtered and washed on the filter with distilled water. The resulting residue was purified via recrystallization from EtOH, yielding azoxybenzene **4**. Yield 0.34 g (78%); yellowish solid; mp 117–118 °C. IR (KBr): ν = 3130, 3107, 3068 (Csp^2-H), 2958, 2893, 2736 (Csp^3-H), 1600, 1494 (Csp^2-Csp^2), 1467 (as N=N(O)), 1384 (sy N=N(O)) cm^{-1}.

^{1}H NMR ($CDCl_3$, 399.78 MHz): δ = 4.02–4.17 (m, 8H, CH_2), 5.86 (s, 1H, CH), 5.89 (s, 1H, CH), 7.57–7.63 (m, 4H, CH), 8.16–8.20 (m, 2H, CH), 8.29–8.33 (m, 2H, CH). ^{13}C NMR ($CDCl_3$, 100.5 MHz): δ = 65.35 (CH_2), 65.40 (CH_2), 102.7 (CH), 103.2 (CH), 122.4 (CH, Ar), 125.6 (CH, Ar), 126.8 (CH, Ar), 127.0 (CH, Ar), 139.3 (C, Ar), 141.8 (C, Ar), 144.5 (C, Ar), 148.7 (C, Ar). HRMS ESI TOF: m/z = 343, 1293 $[M+H]^+$ (343, 1289 calcd for $C_{18}H_{18}N_2O_5$). Crystal data for $C_{18}H_{18}N_2O_5$ (M = 342.34 g/mol): monoclinic, space group P21/c, a = 4.5333(7) Å, b = 21.946(4) Å, c = 15.968(3) Å, α = 90°, β = 95.627(4)°, γ = 90°, V = 1581.0(4) Å3, Z = 4, T = 120 K, μ = 1.06 cm^{-1}, Dcalc = 1.438 g/cm3. In total, 17,093 reflections were measured, 4876 of which were unique and used in all calculations. The final R_1 was 0.0636, and the wR_2 was 0.1635 (all data).

*3.2. 1,2-Bis(4-formylphenyl)diazenoxide (**5**)*

A solution was made of 0.5 g (1.46 mmol) of 1,2-bis(4-(1,3-dioxolan-2-yl)phenyl)diazen oxide **4** in 10 mL of tetrahydrofuran with 0.5 mL concentrated hydrochloric acid (37% in water). The reaction mixture was stirred for 1 h at room temperature. During this time, according to TLC (hexane/EtOAc, 8:4), complete conversion occurred **4**. The reaction mixture was diluted with 50 mL of water, and the formed precipitate was then filtered off and washed on a filter with water. The solid precipitate was recrystallized from the EtOH/EtOAc mixture. Yield 0.29 g (80%); yellowish solid; mp 188–190 °C (dec.) lit. [35] mp 178–180 °C (dec.). IR (KBr): ν = 3107 (Csp^2-H), 2850, 2789, 2742 (Csp^3-H), 1703, 1687 (C=O), 1597 (Csp^2-Csp^2), 1463 (as N=N(O)), 1390 (sy N=N(O)) cm^{-1}.^{1}H NMR (($CD_3)_2SO$, 399.78 MHz): δ = 8.05–8.08 (m, 2H, CH), 8.13–8.18 (m, 4H, CH), 8.43–8.47 (m, 2H, CH), 10.06 (s, 1H), 10.16 (s, 1H). ^{13}C NMR (($CD_3)_2SO$, 100.5 MHz): δ = 123.2 (CH, Ar), 125.4 (CH, Ar), 130.2 (CH, Ar), 130.5 (CH, Ar), 136.1 (C, Ar), 138.5 (C, Ar), 147.5 (C, Ar), 150.8 (C, Ar), 192.2 (C=O), 192.4 (C=O). MS (EI, 70 eV, I_{rel}, %): m/z = 254 (17) $[M^+]$, 226 (10), 169 (8), 133 (31), 105 (100).

Supplementary Materials: Figure S1: ^{1}H-NMR spectrum of **4**; Figure S2: ^{13}C-NMR spectrum of **4**; Figure S3: HRMS of 4; Figure S4: IR spectrum of 4; Figure S5.^{1}H-NMR spectrum of **5**; Figure S6: ^{13}C-NMR spectrum of **5**.

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