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Selective Reduction of an Aromatic Nitro Group to an Azoxy Unit in the Presence of an Aliphatic Nitro Group

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Summary. Chemoselective reduction of 1-nitro-2-(2-nitro-2-methylpropyl)-benzene to 2,2′-di-(2-nitro-2-methylpropyl)-azoxybenzene was achieved with sodium borohydride in methanol in the presence of substoichiometric amounts of bismuth, whereas reduction with zinc in hydrochloric acid gave a mixture of the latter, 1-amino-2-(2-amino-2-methylpropyl)-benzene, and 3,3-dimethyl-3,4-dihydrocinnoline, and showed poor reproducibility. The crystal structure of the azoxybenzene was determined by single-crystal X-ray diffraction.

Keywords. Azoxybenzene; Bismuth; Nitro compounds; Reductions; X-Ray structure determination.

Introduction

Aromatic azoxy compounds are of great current interest because of their physiological activities and their use in liquid crystal systems [1]. The most convenient method for their synthesis is the reduction of nitroarenes [1, 2]. However, this may also lead to hydroxylamines, hydrazines, azoarenes, and, eventually, to anilines [3]. Not surprisingly, therefore, only very few methods have been reported for the selective reduction of nitroarenes to azoxy compounds [4]. The problem of chemoselectivity is further exacerbated by the presence of functional groups which must remain intact during the reduction. The most promising method appears to be the catalytic reduction with sodium borohydride in the presence of bismuth which has been shown to tolerate ester and nitrile functionalities [4]. A particularly challenging case is the selective reduction of a nitroarene containing an aliphatic nitro group. We here report the first example of such a transformation.

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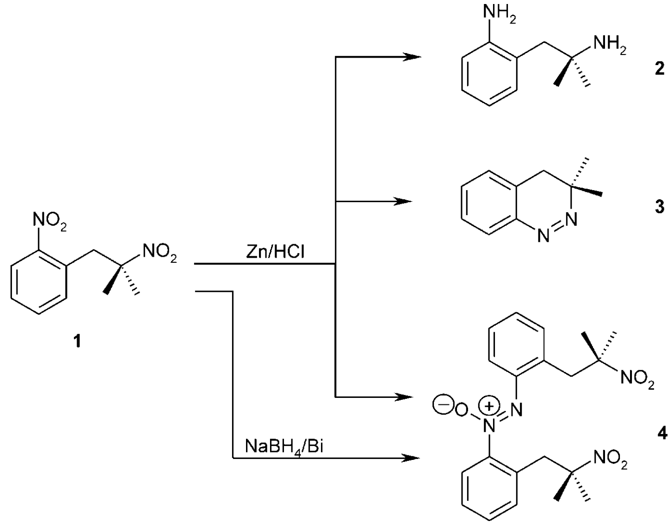
Results and Discussion

1-Nitro-2-(2-nitro-2-methylpropyl)-benzene (**1**) [5] was reduced unselectively with zinc in hydrochloric acid. The three products isolated were the aniline



Scheme 1. Synthesis of **2**–**4**

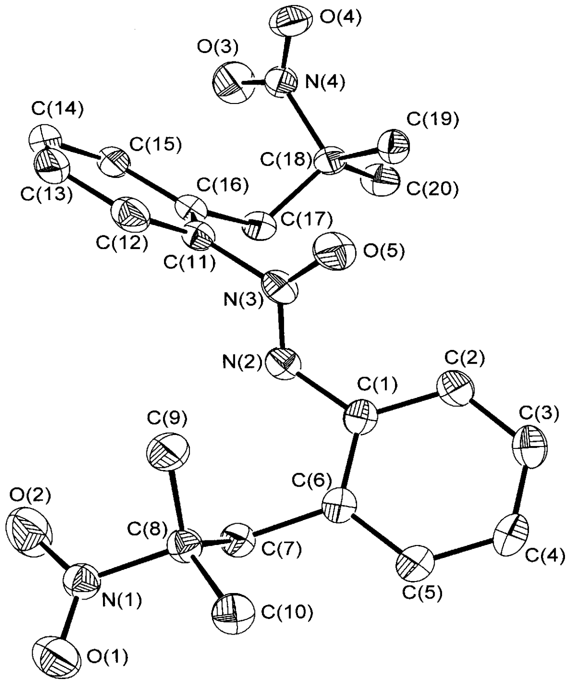


Fig. 1. Molecular structure of **4** (non-centrosymmetric molecule). Selected bond lengths (pm) and angles (°): N(1)–C(8) 154.4(2), N(2)–C(1) 143.7(2), N(3)–C(11) 143.7(2), N(4)–C(18) 153.7(2); N(2)–N(3)–O(5) 127.85(14), N(2)–N(3)–C(11) 115.75(13), C(11)–N(3)–O(5) 116.13(14), C(1)–N(2)–N(3) 116.52(14)

2 [6], the cinnoline derivative **3** [7], and the desired azoxy compound **4** (Scheme 1). The reaction proved to be somewhat temperamental, giving varying yields of these compounds. Such poor reproducibility is not unusual for heterogeneous reactions. The best result obtained with respect to the azoxy species **4** was 12% of **2**, 28% of **3** and 56% of **4**. Tedious work-up involving distillation and chromatography was necessary for separating this product mixture. In contrast to this, reduction of **1** according to the protocol by *Ren et al.* [7] (sodium borohydride in the presence of substoichiometric amounts of bismuth powder in methanol) gave **4** in 70% yield after simple recrystallisation (Scheme 1).

The identity of the product was confirmed by a single-crystal X-ray structure analysis. **4** adopts the (*Z*)-configuration (Fig. 1).

Two individual molecules are present whose bond parameters are almost identical. The asymmetric unit contains 1.5 molecules. Structural parameters are unexceptional and compare well to those obtained for related species such as azoxybenzene [8] and 4,4′-azoxydianisole [9]. The N–N distance is 126.9(2) and 128.4(3) pm corresponding to a double bond. The azoxy N–O distance has a value of 126.05(18) and 126.4(3) pm, which is slightly, but significantly, longer than the N–O distances of the nitro groups which range from 121.99(19) to 122.48(19) pm.

Experimental

NMR: Bruker Avance DRX 500 (500.13 MHz, ^{1}H, ext. *TMS* 125.04 MHz, ^{13}C, ext. *TMS*). MS: VG Autospec (70 eV). Elemental analyses agreed favourably with the calculated values.

1-Amino-2-(2-amino-2-methylpropyl)-benzene (**2**), *3,3-Dimethyl-3,4-dihydrocinnoline* (**3**, $C_{10}H_{16}N_2$) *and 2,2′-Di-(2-nitro-2-methylpropyl)-azoxybenzene* (**4**, $C_{20}H_{24}N_4O_5$) *by Reduction of 1-Nitro-2-(2-nitro-2-methylpropyl)-benzene* (**1**, $C_{10}H_{12}N_2O_4$) *with Zinc in Hydrochloric Acid*

A mixture of 40 cm^3 6 *N* hydrochloric acid, 2.0 g **1** [5] (8.92 mmol) and 8.0 g Zn powder (122 mmol) was heated to reflux for 1 h. The mixture was allowed to cool to room temperature. Undissolved Zn was removed by decanting and washed with 20 cm^3 of water. After alkalisation by addition to an excess of 2 *N* NaOH solution the mixture was extracted with 3 × 40 cm^3 of diethyl ether. The combined extracts were dried with Na_2CO_3. The solvent was removed *in vacuo*. 1-Amino-2-(2-amino-2-methylpropyl)-benzene (**2**) and 3,3-dimethyl-3,4-dihydrocinnoline (**3**) were distilled off at 0.1 Pa at a bath temperature of 60°C. The distillate was separated chromatographically using a silica gel column: 417 mg of **2** (28%) was eluted with CH_2Cl_2 and 165 mg of **3** (12%) with ethyl acetate. Recrystallisation of the distillation residue from ethanol afforded 2.01 g of **4** (56%). In other runs the yield of **4** varied and was as low as 10%.

2: The compounds was characterised by comparison with an authentic sample prepared by the established route [6].

3: ^{1}H NMR ($CDCl_3$): $\delta = 1.33$ (s, 6H, 2 Me), 2.51 (s, 2H, CH_2), 7.04 (d, 1H, $J = 7.5$ Hz, CH), 7.35 (t, 1H, $J = 7.5$ Hz, CH), 7.42 (t, 1H, $J = 7.5$ Hz, CH), 7.94 (d, 1H, $J = 7.5$ Hz, CH) ppm; ^{13}C NMR ($CDCl_3$): $\delta = 24.7$ (Me), 31.9 (CH_2), 60.4 (CMe_2), 121.8 (ring C), 127.9 (ring C), 128.0 (ring C), 128.8 (ring C), 131.4 (ring C), 141.2 (ring C) ppm; EI-MS: m/z (%) = 160 [M^+] (11), 132 [M^+-N_2] (40), 117 [M^+-N_2-Me].

4: ^{1}H NMR ($CDCl_3$): $\delta = 1.51$ (s, 6H, 2 Me), 1.53 (s, 6H, 2 Me), 3.42 (s, 2H, CH_2), 3.63 (s, 2H, CH_2), 7.18 – 7.22 (m, 2H, 2 CH), 7.31 – 7.34 (m, 1H, CH), 7.38 – 7.44 (m, 3H, 3 CH), 7.66 – 7.86 (m, 1H, CH), 8.39 – 8.41 (m, 1H, CH) ppm; ^{13}C NMR ($CDCl_3$): $\delta = 25.5$ (Me), 25.6 (Me), 40.6 (CH_2), 41.3 (CH_2), 88.7 (*C*Me_2), 121.7 (ring C), 124.2 (ring C), 127.8 (ring C), 128.4 (ring C), 128.6 (ring C), 129.5 (ring C), 130.5 (ring C), 131.4 (ring C), 131.9 (ring C), 132.5 (ring C), 142.6 (ring C), 149.8 (ring C) ppm; CI-MS: m/z (%) = 401 [$M^+ + 1$] (2), 354 [M^+–NO_2].

2,2′-Di(2-nitro-2-methylpropyl)azoxybenzene (**4**) *by Reduction of 1-Nitro-2-(2-nitro-2-methylpropyl)benzene* (**1**) *with Sodium Borohydride in the Presence of Bismuth*

1 [5] (1.12 g, 5.00 mmol) was dissolved in 20 cm^3 of methanol under Ar. The stirred solution was cooled to 0°C with an ice bath. Bismuth powder (522 mg, 2.50 mmol) was added, followed by 567 mg of sodium borohydride (15.2 mmol). After 0.5 h at room temperature the mixture was filtered. A small amount of NaOH was added and stirring was continued for 4 h at room temperature in the air. Ice-cold 1 *M* HCl (100 cm^3) was added and the mixture was stirred for 0.5 h. Crude **4** separated as a yellow solid which was filtered off with suction, washed with water, dried in vacuo and recrystallised from methanol. Yield 701 mg (70%). Spectroscopic data were identical to those described above. Single crystals for an X-ray crystal structure determination were obtained by slow evaporation of a methanol solution.

X-Ray Crystallography

The crystal structure of **4** was determined at 100 K using a STOE IPDS II diffractometer with graphite-monochromated Mo-Kα radiation ($\lambda = 0.71073$ Å). Details of the structure determination are collected in Table 1. Additional material to the structure determination can be obtained from the Cambridge Crystallographic Data Centre (CCDC), 12 Union Road, Cambridge CB2 1EZ (UK), Tel.: (+44) 1223/336-408, Fax: (+44) 1223/336-033, E-mail: deposit@ccdc.cam.ac.uk, World Wide Web: http://www.ccdc.cam.ac.uk, referring to the deposition number CSD 192454. Atomic scattering factors were taken from standard sources [10]. The program package used was SHELXL 97 [11].

Table 1. Crystal data and structure refinement parameters for **4**

Formula	$C_{20}H_{24}N_4O_5$
Formula weight	400.43
Crystal system	Monoclinic
Space group	$P2_1/n$
a/nm	1.55325(14)
b/nm	1.24842(7)
c/nm	1.63609(15)
β/°	111.059(6)
V/nm^3	2.9607(4)
Z	6
μ/mm^{-1}	0.098
Crystal size/mm	0.45×0.35×0.15
Reflections collected/unique	22329/6348
R(int)	0.0447
Goodness-of-fit on F^2	0.977
$R1$[a] [$I > 2\sigma(I)$], $wR2$[b]	0.0431, 0.1148

[a] $R1 = \sum||F_o| - |F_c||/\sum|F_o|$; [b] $wR2 = \{\sum[w(F_o^2 - F_c^2)^2]/\sum[w(F_o^2)^2]\}^{0.5}$

Acknowledgments

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