Reaction of *N*-nitro-*O*-(4-nitrophenyl)hydroxylamine with phosphorus pentoxide in the presence of nitriles. New method for the generation of aryloxenium ion*

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A reaction of *N*-nitro-*O*-(4-nitrophenyl)hydroxylamine with nitriles RCN (R = Me, Et, Ph) in the presence of P_4O_{10} in excess amount at 0 °C leads to the formation of 2-R-5-nitro-1,3-benzoxazoles. The reaction presumably takes place through the intermediate (phenoxy)oxodiazonium ion $[NO_2C_6H_4O—N=N=O]^+$, which eliminates an N_2O molecule to form the aryloxenium ion $[NO_2C_6H_4O]^+$. The latter reacts with nitriles RCN at the *ortho*-carbon atom of the phenyl ring giving 2-R-5-nitro-1,3-benzoxazoles.

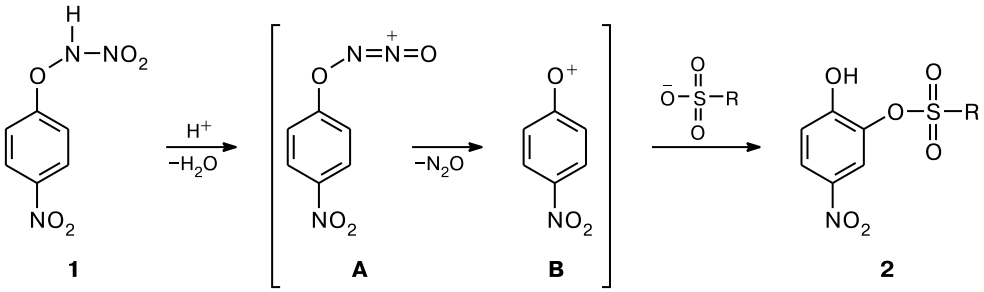
Key words: hydroxylamines, 1,3-benzoxazoles, nitriles, oxodiazonium ion, aryloxenium ion, ^1H, ^{13}C, ^{14}N NMR spectra.

In our preceding work,[1] we studied a possibility of generation of the earlier unknown (phenoxy)oxodiazonium ion $[Ar—O—N=N=O]^+$ (**A**). The ion **A** (Scheme 1) is presumably generated from *N*-nitro-*O*-(4-nitrophenyl)-hydroxylamine (**1**) upon the action of a sulfonic acids (RSO_3H, R = CH_3, CF_3) with liberation of N_2O and formation of the oxenium ion **B**, which reacts with the sulfonic acid anion to give 2-hydroxy-5-nitrophenyl-R-sulfonates **2**. A possibility of formation of (phenoxy)oxodiazonium ion **A** as a kinetically independent species was confirmed by our quantum chemical calculations.[1]

Such a method for the generation of oxenium ions has not been known before our works. At the same time, it has been shown earlier[2] that thermolysis of *N*-(*p*-nitrophenoxy)pyridinium tetrafluoroborate (**3**) leads to 5-nitro-2-phenyl-1,3-benzoxazole (**4a**) in 35% yield (Scheme 2). This reaction presumably proceeds *via* the intermediate *p*-nitrophenyloxenium ion **B**, which reacts with PhCN at the *ortho*-position of the phenyl ring giving rise to oxazole **4a**.

The purpose of the present work was to obtain additional confirmation of formation of the oxenium ion **B** (and, respectively, the intermediate (phenoxy)oxodiazonium ion **A**) in the reaction of compound **1** with nitriles, which gives benzoxazoles **4** similarly to the reaction shown in Scheme 2. To generate the (phenoxy)oxodiazonium ion **A**, we used a method developed by us earlier[3,4] for the generation of aryloxodiazonium ions $[Ar—N=N=O]^+$, *i.e.*, the reaction of nitramines $ArNHNO_2$ with P_4O_{10}. In this connection, in the present work we studied the reaction of *N*-nitrohydroxylamine **1** with nitriles in the presence of P_4O_{10}.

Scheme 1



* Dedicated to Academician of the Russian Academy of Sciences O. M. Nefedov on the occasion of his 80th birthday.

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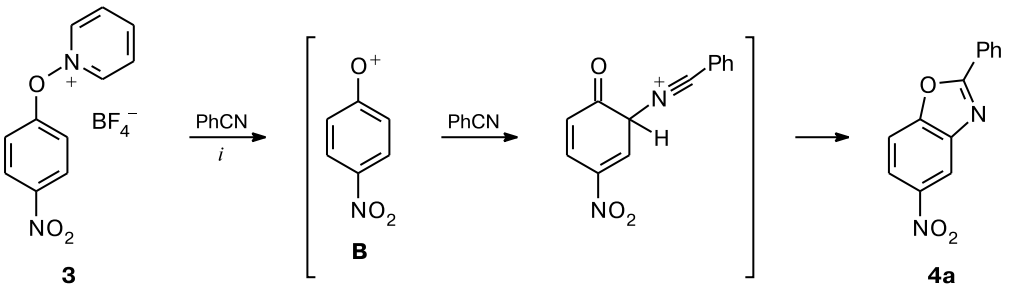
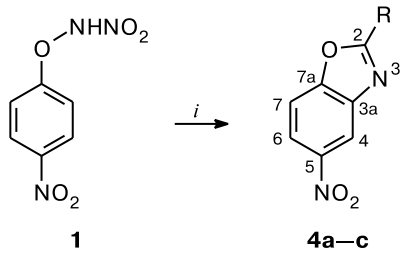
Scheme 2



i. 180 °C, 72 h.

The reactions of **1** with nitriles RCN (R = Me, Et, Ph) (Scheme 3) were carried out as follows. Compound **1** was dissolved in the corresponding nitrile at 0 °C, and the solution that obtained was added to a suspension of P_4O_{10} (14 equiv.) in RCN at 0 °C. The reaction time and yields of the 2-R-5-nitro-1,3-benzoxazoles **4a—c** thus formed are given in Table 1.

Scheme 3



i. P_4O_{10}/RCN, 0 °C.

The reaction of **1** with phosphorus pentoxide was the fastest in acetonitrile, the slowest in propio- and benzonitrile (see Table 1). Unidentified water-soluble products are formed in the side reactions, as well as 4-nitrophenol and 2,4-dinitrophenol in trace amounts due to the partial decomposition of **1** under the reaction conditions. In addition, when the reaction was carried out in benzonitrile, its partial trimerization occurs to yield 2,4,6-triphenyl-1,3,5-triazine (**5**).

Table 1. Reaction of **1** with RCN in the presence of P_4O_{10}

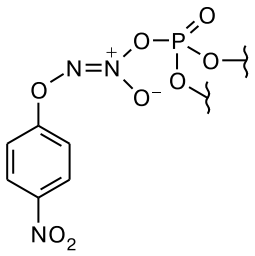
4	R	Reaction time	Yield of **4**[a] (%)
a	Ph	3 h	43
b	Et	2.5 h	52
c	Me	15 min	43 (59[b])

[a] The yields were calculated for the isolated product. The conversion of **1** was quantitative.

[b] The yield of 1,3-benzoxazole **4c** was determined from the ^{1}H NMR spectrum. The conversion of **1** was quantitative.

The structures of benzoxazoles **4a** and **4c** were confirmed by comparison with the known samples. The structure of the earlier unknown 2-ethyl-5-nitro-1,3-benzoxazole (**4b**) was confirmed by ^{1}H, ^{13}C, and ^{14}N NMR spectra.

A suggested scheme for the conversion of compound **1** to 2-R-5-nitro-1,3-benzoxazoles **4a—c** includes phosphorylation of **1** at the oxygen atom of the nitramine group with the formation of *O*-phosphorylated derivative **C**, which (possibly, after protonation) dissociates to give the ion **A**. The latter eliminates the molecule of N_2O with the formation of *p*-nitrophenyloxenium ion **B**, similarly to that shown in Scheme 1. The aryloxenium ion **B** thus formed reacts with the nitrile molecule, giving 1,3-benzoxazoles **4a—c** similarly to that shown in Scheme 2.



C

In conclusion, we discovered a new reaction of compound **1** with nitriles in the presence of phosphorus pentoxide leading to the formation of 2-R-5-nitro-1,3-benzoxazoles **4a—c**. The mechanism suggested for this conversion includes the intermediate formation of (phenoxy)-oxodiazonium ion **A** and aryloxenium ion **B**.

Experimental

^{1}H, ^{13}C, and ^{14}N NMR spectra were recorded on a Bruker DRX-500 spectrometer (500.13, 125.76, and 36.14 MHz, respectively). Chemical shifts are given relatively to $SiMe_4$ (^{1}H, ^{13}C) or $MeNO_2$ (^{14}N, external standard, the high-field chemical shifts are negative). IR spectra were recorded on a Specord M-80 spectrometer. Mass spectra were recorded on a Kratos MS-300 instrument (EI, 70 eV). High-resolution mass spectra were recorded on a Bruker micrOTOF II instrument using the electrospray ionization (ESI).[5] Reaction progress was monitored by thin-layer chromatography (Silufol UV-254 and Merck 60 F_{254}). Silica gel was used for preparative thin-layer chromatography.

Ethereal solution of **1** was obtained according to the procedure developed earlier.[6]

Reaction of *N*-nitro-*O*-(4-nitrophenyl)hydroxylamine (1) with RCN in the presence of P_4O_{10} (general procedure). A solution of **1** (50 mg, 0.25 mmol) in Et_2O (5 mL) was concentrated to dryness in the reaction flask *in vacuo* (1 Torr) at 0 °C for 5 min. A pre-cooled to 0 °C anhydrous RCN (5 mL) was added to the solid sample of **1** thus obtained under dry argon. The solution that obtained was added in one portion to a suspension of P_4O_{10} (1 g, 3.5 mmol) in anhydrous RCN (20 mL) at 0 °C with vigorous stirring under argon. The reaction mixture was vigorously stirred at 0 °C for the time indicated in Table 1. Disappearance of the starting compound **1** was monitored by TLC.

Treatment of the reaction mixture in the case of R = Ph. Water (100 mL) was added to the reaction mixture without elevation of the temperature, then it was extracted with CH_2Cl_2 (2×30 mL), AcOEt (2×30 mL). The organic extracts were combined, washed with water (2×30 mL) and brine (30 mL), dried with $MgSO_4$, and concentrated *in vacuo*. Residual PhCN was evaporated *in vacuo* (1 Torr). The residue was dissolved in $CHCl_3$ (4 mL), the solution was cooled to −20 °C. The crystals that formed were filtered off, washed with AcOEt (4 mL), dried in air. 2,4,6-Triphenyl-1,3,5-triazine (**5**) (29 mg) was obtained as colorless needle-like crystals, m.p. 239—240 °C (from $CHCl_3$; Ref. 7: m.p. 239—240 °C); the sample was identical to the earlier obtained product[8] (^{1}H NMR spectrum). The mother liquor was concentrated, the residue was separated by preparative TLC on silica gel (eluent: $CHCl_3$—light petroleum (1 : 1), then $CHCl_3$). 5-Nitro-2-phenyl-1,3-benzoxazole (**4a**) (26 mg, 43%) was obtained as yellowish crystals, m.p. 169—171 °C (from EtOH; Ref. 9: m.p. 169—172 °C (from EtOH)), which was identical to the earlier obtained product[10] (IR and ^{1}H NMR spectra). Triazine **5** (32 mg) was additionally obtained, as well.

Treatment of the reaction mixture in the case of R = Et, Me. Water (40 mL) was added to the reaction mixture without elevation of the temperature and it was extracted with CH_2Cl_2 (4×20 mL). The extracts were combined, washed with brine (10 mL), dried with $MgSO_4$, and concentrated *in vacuo*. The products **4b—c** were purified by preparative TLC on silica gel (eluent: $CHCl_3$—AcOEt (16 : 1)).

2-Ethyl-5-nitro-1,3-benzoxazole (4b). The yield was 25 mg (52%), m.p. 83—85 °C (from hexane). IR (KBr), ν/cm^{-1}: 1236 w, 1260 w, 1344 s, 1424 w, 1436 w, 1456 m, 1520 s, 1572 w, 1616 m. ^{1}H NMR ($CDCl_3$), δ: 1.49 (t, 3 H, Me, J = 7.6 Hz); 3.03 (q, 2 H, CH_2, J = 7.6 Hz); 7.59 (d, 1 H, H(7), J = 8.9 Hz); 8.28 (dd, 1 H, H(6), J = 8.9 Hz, J = 2.3 Hz); 8.56 (d, 1 H, H(4), J = 2.3 Hz). ^{13}C NMR ($CDCl_3$), δ: 10.6 (Me), 22.2 (CH_2), 110.4 (C(7)); 115.9 (C(4)); 120.7 (C(6)); 141.8 (C(3a)); 145.1 (br.s, C(5)); 154.4 (C(7a)); 171.3 (C(2)). The HSQC and HMBC experiments were used for assignment of signals in the spectrum. ^{14}N NMR ($CDCl_3$), δ: −12 (NO_2, $\Delta\nu_{1/2}$ = 150 Hz), −140 (N(3), $\Delta\nu_{1/2}$ = 750 Hz). MS (EI, 70 eV), m/z: 192 $[M]^+$, 146 $[M - NO_2]^+$. HRMS (ESI): Found m/z: 193.0603 $[M + H]^+$. $C_9H_8N_2O_3$. Calculated m/z: 193.0608 $[M + H]^+$.

2-Methyl-5-nitro-1,3-benzoxazole (4c). The yield was 19 mg (43%), m.p. 151—153 °C (Ref. 11: m.p. 155 °C); the product was identical to the earlier obtained compound[12] (IR and ^{1}H NMR spectra).

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