Generation of oxodiazonium ions
4.* Nitramine *O*-alkyl derivatives in the synthesis of benzotetrazine-1,3-dioxides

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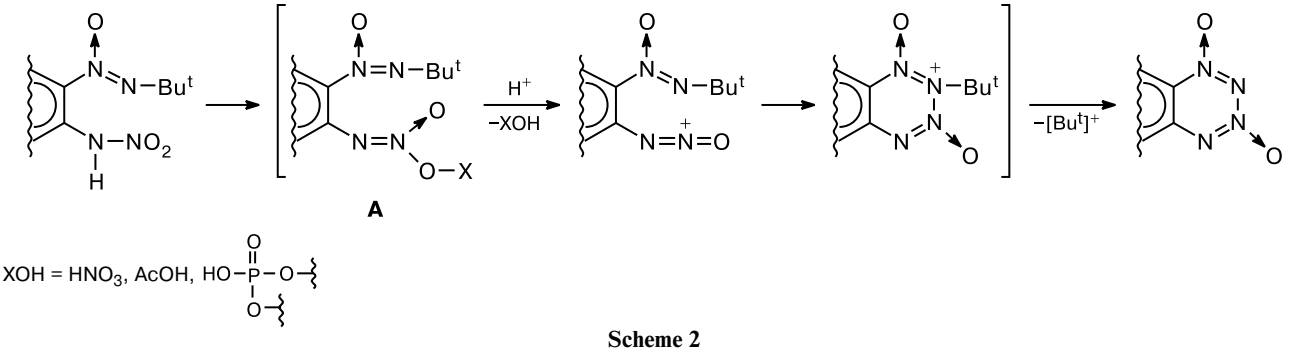
A new method for the synthesis of benzotetrazine-1,3-dioxides was developed from the 2-(*tert*-butyl-*NNO*-azoxy)-*N*-nitroaniline *O*-alkyl derivatives upon the action of strong acids (H_2SO_4, $MeSO_3H$, CF_3CO_2H) or $BF_3 \cdot Et_2O$. A mechanism suggested for these reactions includes transformation of the N=N(O)OR group (R = Me, Pr^i) to the oxodiazonium ion $(N{=}N{=}O)^+$, which intramolecularly reacts with the neighboring *tert*-butyl-*NNO*-azoxy group, furnishing the tetrazine-1,3-dioxide ring.

Key words: 1,2,3,4-tetrazine-1,3-dioxides, azoxy compounds, nitramines, oxodiazonium ion, ^1H, ^{13}C, ^{14}N NMR spectroscopy.

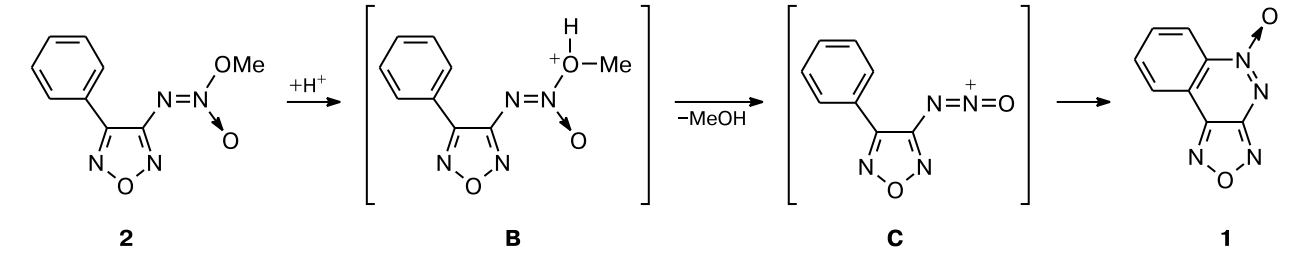
Earlier, we have developed approaches to the synthesis of benzotetrazine-1,3-dioxides (BTDO) by the reaction of 2-(*tert*-butyl-*NNO*-azoxy)-*N*-nitroanilines with nitrating[2,3] (N_2O_5, NO_2BF_4), phosphorylating[4] (P_4O_{10}, PCl_5), or acylating[5] (Ac_2O/H_2SO_4) agents. A mechanism suggested for these processes includes formation of the intermediates **A** by the reaction of the nitramine group with the nitrating, phosphorylating, or acylating agents, transformation of these intermediates to oxodiazonium ion, and the reaction of the latter with the neighboring azoxy group (Scheme 1). The intermediates **A** are extremely reactive and attempts to detect them failed.

Recently,[6] we have developed a method for the preparation of furazanocinnolin-5-oxide **1** by the reaction of 3-[methoxy(oxido)diazenyl]-4-phenylfurazane (**2**) with acids or $BF_3 \cdot Et_2O$ (Scheme 2). These reactions presum-

Scheme 1



Scheme 2



* For part 3, see Ref. 1.

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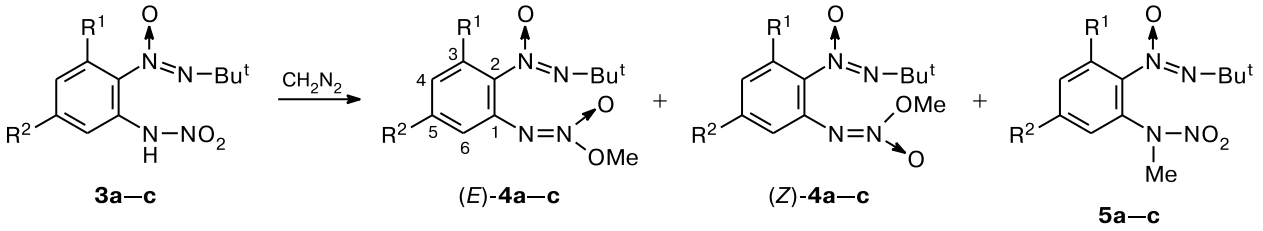
Scheme 3



$R^1 = R^2$ = H (**a**), R^1 = H, R^2 = Br (**b**), $R^1 = R^2$ = Br (**c**)

ably include formation of the intermediate **B** from the N=N(O)OMe group, then converting to the oxodiazonium ion **C**, which is further involved into the intramolecular aromatic electrophilic substitution reaction (S_EAr) with the phenyl group.

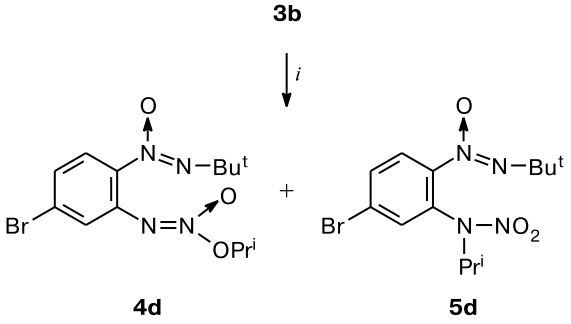
The main goal of the present work is to study a possibility of cyclization of the 2-(*tert*-butyl-*NNO*-azoxy)-*N*-nitroaniline *O*-alkyl derivatives to BTDO upon the action of strong acids or $BF_3 \cdot Et_2O$. *O*-Methyl derivatives of unsubstituted and bromo-substituted 2-(*tert*-butyl-*NNO*-azoxy)-*N*-nitroanilines, as well as *O*-isopropyl derivative of 5-bromo-2-(*tert*-butyl-*NNO*-azoxy)-*N*-nitroaniline, have been chosen as model compounds.

Synthesis of the starting compounds. Methylation of nitramines **3a—c** (see Ref. 5) with diazomethane in diethyl ether at 20 °C leads to the high yields of the mixtures of *O*- and *N*-methyl derivatives **4a—c** and **5a—c** in the ratio close to 1 : 1 (Scheme 3, Table 1), which were separated by preparative TLC. According to the ^{1}H NMR spectroscopic data, the *O*-methyl compounds **4a—c** are mixtures of two geometric isomers at the methoxy(oxido)-diazenyl group (see Table 1). Similarly to the *O*-methylated nitramines,[7] the major isomer of compounds **4a—c** can be assigned the *E*-configuration.

A serious disadvantage in the preparation of the *O*-methyl compounds **4a—c** from nitramines by the reaction with diazomethane is the formation of considerable (to 50%, see Table 1) amounts of the side *N*-methyl compounds **5a—c**. At the same time, it is known that alkylation of the silver salts of nitramines with secondary and tertiary alkyl halides (for example, Pr^iBr, 1-bromoadamantane)[8,9] exclusively leads to the products of *O*-alkylation.

We carried out alkylation of the Ag-salt of nitramine **3b** with isopropyl bromide in MeCN and Et_2O (Scheme 4, Table 2). The reaction with a ten-fold excess of Pr^iBr in MeCN at 20 °C takes 24 days and leads to a mixture of *O*- and *N*-isopropyl compounds **4d** and **5d** in the ratio ~5 : 1, which were separated by preparative TLC. The reaction in Et_2O is slower (35 days), but leads to the formation of only *O*-alkylated product **4d** (the yield was 71%) virtually as a single geometric isomer. Like with *O*-alkylated nitramines,[7] the N=N(O)OPr^i group in compound **4d** can be assigned the *E*-configuration.

Scheme 4



i. 1) $AgNO_3/NH_4OH$; 2) Pr^iBr (10 equiv.)

The structures of 2-(*tert*-butyl-*NNO*-azoxy)-*N*-nitroaniline *O*-alkyl derivatives **4a—c** and *N*-methyl compounds

Table 1. The reaction of nitramines **3a—c** with diazomethane

Nitramine **3**	Ratio[a] **4** : **5** (mol)	Ratio (*E*)-**4** : (*Z*)-**4** (%)	Yield (%)[b]	
			4	**5**
3a	1.1 : 1	96 : 4	48	47
3b	1 : 1	93 : 7	35	48
3c	1 : 1	97 : 3	42	51

[a] The molar ratios of products **4a—c** and **5a—c** were determined from the ^{1}H NMR spectra.

[b] The yields were calculated on the isolated product. The conversion of **3a—c** was quantitative.

Table 2. The synthesis of *O*- and *N*-isopropyl compounds **4d** and **5d** from nitramine **3b**

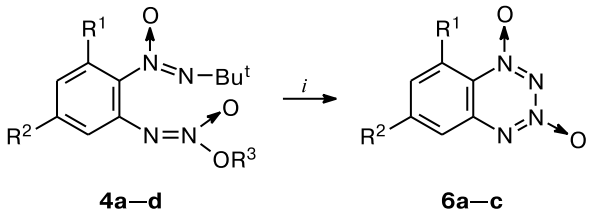
Entry	Solvent	Reaction time/days	Yield (%)*	
			4d	**5d**
1	MeCN	24	64	12
2	Et_2O	35	71	—

* The yields were calculated on the isolated product.

5a—c were confirmed by the ^1H, ^{13}C, and ^{14}N NMR spectra. The full assignment of signals in the ^{13}C NMR spectra of these compounds was performed using the $^1H—^{13}C$ two-dimensional NMR spectra (HMBC and HSQC).

Synthesis of BTDO 6a—c by the reaction of *O*-alkyl compounds 4a—c with acids or $BF_3 \cdot Et_2O$. It was found that *O*-methyl compounds **4a—c** in the solutions of concentrated acids are transformed into BTDO **6a—c** in virtually quantitative yields (Scheme 5, Table 3). The rate of cyclization strongly depends on the acid strengths. Thus, in H_2SO_4 ($H_o = -11.94$[10]), compound **4a** is completely consumed within 5 min (the TLC data), in the weaker $MeSO_3H$ ($H_o = -7.74$[11]), within 10 min, whereas in CF_3COOH ($H_o = -2.71$[12]), the reaction reaches completion within 2 h. Similar tendency is observed in the case of the ring closure in compounds **4b,c** with the cyclization being the slowest in the case of dibromo-substituted compound **4c**, which can be explained by the steric effect of the Br atom in the *ortho*-position to the *tert*-butyl-*NNO*-azoxy group.

Scheme 5



4a—d **6a—c**

i. H^+ or $BF_3 \cdot OEt$

$R^1 = R^2 = H$, $R^3 = Me$ (**a**); $R^1 = H$, $R^2 = Br$, $R^3 = Me$ (**b**); $R^1 = R^2 = Br$, $R^3 = Me$ (**c**); $R^1 = H$, $R^2 = Br$, $R^3 = Pr^i$ (**d**)

In contrast to *O*-methyl derivatives **4a—c**, the *O*-isopropyl compound **4d** upon the action of H_2SO_4 and $MeSO_3H$ leads to BTDO **6b** in only 6—10% yield (the ^1H NMR spectroscopic data), with the reaction mixture containing several unidentified products (the TLC and ^1H NMR spectroscopic data). Apparently, this is caused by involvement of the isopropyl group into the reaction. At the same time, the *O*-isopropyl compound **4d** is quantitatively converted to the corresponding tetrazine-1,3-dioxide **6b** in the solution of weaker CF_3COOH, with the rate of the reaction in this case being higher than that in the case of *O*-methyl derivatives **4a—c** (see Table 3).

A Lewis acid, for example $BF_3 \cdot OEt_2$, can also be used for the transformation of *O*-alkyl compounds **4a—d** into BTDO **6a—c** (see Scheme 5 and Table 3). For compounds **4a**,**b** and **4d**, the cyclization reaction in the solution of $BF_3 \cdot OEt_2$ takes approximately the same time (45—50 min) and leads to BTDO **6a**,**b** in quantitative yields. However, for the sterically hindered **4c** the process comes to completion only for 7 h, and the target product **6c** was obtained in 83% yield.

Suggested scheme for the generation of the oxodiazonium ion from *O*-alkyl compounds 4a—d upon the action of acids or $BF_3 \cdot Et_2O$. Earlier,[6] we have carried out quantum chemical calculations for the reaction of 3-[methoxy(oxido)diazenyl]-4-phenylfurazane **2** with H_2SO_4 (see Scheme 2), which showed that in the course of the reaction, formation of the complex **B** takes place with its further unactivated decomposition to the oxodiazonium ion **C**

Table 3. The synthesis of BTDO **6a—c** from *O*-alkyl compounds **4a—d**

Entry	*O*-Alkyl compound	Acid (concentration (%))	T/°C[a]	Reaction time	BTDO	Yield of BTDO (%)[b]
1	**4a**	H_2SO_4 (93)	0→20	5 min	**6a**	99
2	**4a**	CH_3SO_3H (100)	20	10 min	**6a**	99
3	**4a**	CF_3COOH (100)	20	2h	**6a**	99
4	**4a**	$BF_3 \cdot Et_2O$ (100)	20	50 min	**6a**	99
5	**4b**	H_2SO_4 (93)	0→20	10 min	**6b**	98
6	**4b**	CH_3SO_3H (100)	20	30 min	**6b**	96
7	**4b**	CF_3COOH (100)	20	1.5 h	**6b**	99
8	**4b**	$BF_3 \cdot Et_2O$ (100)	20	45 min	**6b**	97
9	**4c**	H_2SO_4 (93)	0→20	10 min	**6c**	97
10	**4c**	CH_3SO_3H (100)	20	1 h	**6c**	89
11	**4c**	CF_3COOH (100)	20	2 days	**6c**	98
12	**4c**	$BF_3 \cdot Et_2O$ (100)	20	7 h	**6c**	83
13	**4d**	H_2SO_4 (93)	20	5 min	**6b**	10[c]
14	**4d**	CH_3SO_3H (100)	20	10 min	**6b**	6[c]
15	**4d**	CF_3COOH (100)	20	30 min	**6b**	98
16	**4d**	$BF_3 \cdot Et_2O$ (100)	20	50 min	**6b**	98

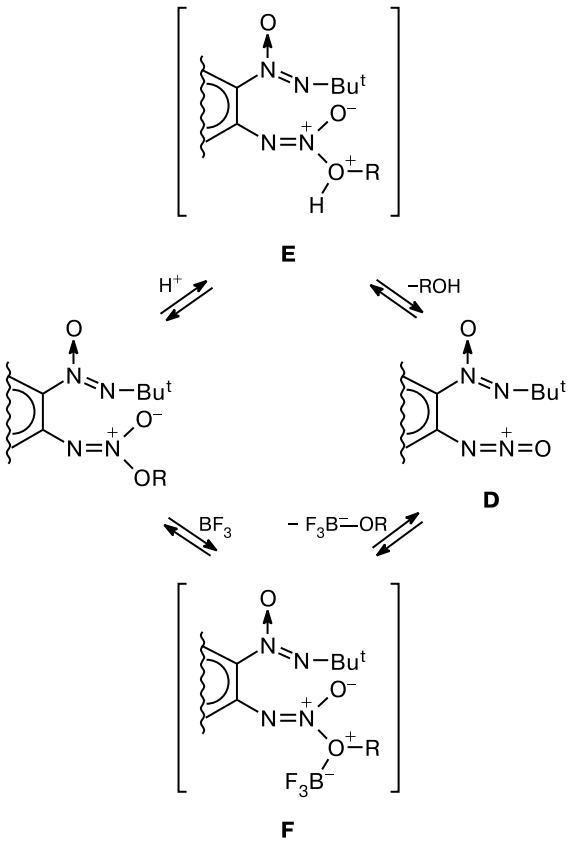
[a] The reaction temperature.

[b] The yields of BTDO **6a—c** were determined from the ^1H NMR spectra. The conversion of compounds **4a—c** was quantitative.

[c] The yields of BTDO **6b** were determined from the ^1H NMR spectra. The conversion of compound **4d** was quantitative. Unidentified products were additionally found in the mixture with BTDO **6b**.

and the molecule of methanol. Formation of the oxodiazonium ion **D** from compounds **4a—d** can occur according to the similar mechanism, which includes protonation with the formation of the kinetically unstable intermediate **E** and its dissociation (Scheme 6).

Scheme 6



Generation of the cation **D** from the *O*-alkyl compound upon the action of $BF_3 \cdot Et_2O$ can occur similarly *via* formation of the intermediate complex **F** (see Scheme 6).

In conclusion, in the present work we developed a new method for the synthesis of benzotetrazine-1,3-dioxides from *O*-alkyl derivatives of 2-(*tert*-butyl-*NNO*-azoxy)-*N*-nitroanilines upon the action of acids or $BF_3 \cdot Et_2O$.

Experimental

^{1}H NMR spectra were recorded on Bruker AM-300 and Bruker DRX 500 spectrometers (300.13 and 500.13 MHz, respectively). ^{13}C and ^{14}N NMR spectra were recorded on a Bruker DRX 500 spectrometer (125.76 and 36.14 MHz, respectively)). Chemical shifts are given relatively Me_4Si (^{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 in KBr pellets or for neat layers on clear NaCl plates. 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 with electrospray ionization (ESI).[13] For the fragments containing bromine atoms, only peaks of ions containing ^{79}Br isotopes are given. Reaction progress and purity of compounds were monitored by thin-layer chromatography (Silufol UV-254 and Merck 60 F_{254}). Silica gel was used for preparative thin-layer chromatography. 2-(*tert*-Butyl-*NNO*-azoxy)-*N*-nitroaniline,[5] 2-(*tert*-butyl-*NNO*-azoxy)-5-bromo-*N*-nitroaniline,[5] 2-(*tert*-butyl-*NNO*-azoxy)-3,5-dibromo-*N*-nitroaniline,[5] and solution of diazomethane in diethyl ether[14] were obtained according to the known procedures.

Reaction of 2-(*tert*-butyl-*NNO*-azoxy)-*N*-nitroanilines (3a—c) with diazomethane (general procedure). A solution of diazomethane in Et_2O (3 mL), obtained from *N*-methyl-*N*-nitrosourea (0.2 g), was added dropwise to a stirred solution of nitramine **3a—c** (0.33 mmol) in Et_2O (5 mL) at 20 °C until evolution of the gas and pale yellow coloring of the solution stopped. Then, the solvent was evaporated *in vacuo*. The molar ratios of the *O*-alkylated **4a—c** and *N*-alkylated **5a—c** products were determined by ^{1}H NMR spectroscopy. The products **4b** and **5b** were separated by preparative TLC on silica gel (light petroleum—AcOEt (20 : 1, then 10 : 1)). The products **4a** and **5a**, as well as **4c** and **5c**, were separated by preparative TLC on silica gel (light petroleum—AcOEt (20 : 1)). The yields of products **4a—c** and **5a—c** are given in Table 1.

2-(*tert*-Butyl-*NNO*-azoxy)[methoxy(oxido)diazenyl]benzene (4a). A mixture of *E*- and *Z*-isomers at the methoxy(oxido)-diazenyl group in the ratio 96 : 4. Oil. MS (ESI), *m/z*: 253.1298 $[M + H]^+$; calculated for $C_{11}H_{16}N_4O_3$, $[M + H]^+$: *m/z* 253.1295. MS (EI), *m/z*: 191 $[M - MeONO]^+$. IR (KBr), ν/cm^{-1}: 1280 s, 1316 s, 1360 m, 1392 w, 1456 s, 1488 s, 1560 s, 1604 w. ^{14}N NMR ($CDCl_3$) δ: −52 (N→O, $\Delta\nu_{1/2}$ = 130 Hz); −57 (N(O)OMe, $\Delta\nu_{1/2}$ = 250 Hz). ^{1}H NMR of the major isomer (*E*) ($CDCl_3$), δ: 1.46 (s, 9 H, 3 Me); 4.07 (s, 3 H, OMe); 7.37 (dd, 1 H, H(4), *J* = 8.0 Hz, *J* = 7.7 Hz); 7.48 (dd, 1 H, H(5), *J* = 8.0 Hz, *J* = 7.7 Hz); 7.60 (d, 1 H, H(6), *J* = 8.0 Hz); 7.72 (d, 1 H, H(3), *J* = 8.0 Hz). ^{13}C NMR of the major isomer (*E*) ($CDCl_3$), δ: 27.0 ($C\underline{Me}_3$); 59.9 (OMe); 61.1 ($\underline{C}Me_3$); 124.9 (C(6)); 125.7 (C(3)); 129.7 (C(4)); 131.8 (C(5)); 136.7 (C(1)); 145.1 (br.s, C(2)). The HMBC and HSQC experiments were used for the assignment of the signals in the spectrum. ^{1}H NMR of the minor isomer (*Z*) ($CDCl_3$), δ: 1.43 (s, 9 H, 3 Me); 3.88 (s, 3 H, OMe); the other signals overlap with the signals of the *E*-isomer. ^{13}C NMR ($CDCl_3$), δ (there are given some signals, which presumably are related to the minor *Z*-isomer and do not overlap with the signals of the major *E*-isomer): 27.1 ($C\underline{Me}_3$); 125.2 (C(6)); 128.7 (C(4)); 132.1 (C(5)).

2-(*tert*-Butyl-*NNO*-azoxy)-*N*-methyl-*N*-nitroaniline (5a), m.p. 34—36 °C. MS (ESI), *m/z*: 275.1122 $[M + Na]^+$, calculated for $C_{11}H_{16}N_4O_3$, $[M+Na]^+$: *m/z* 275.1115. MS (EI), *m/z*: 176. IR (KBr), ν/cm^{-1}: 1304 s, 1360 w, 1392 w, 1420 w, 1440 w, 1456 w, 1480 m, 1516 s, 1588 w, 1604 w. ^{1}H NMR ($CDCl_3$), δ: 1.43 (s, 9 H, 3 Me); 3.68 (s, 3 H, NMe); 7.35 (dd, 1 H, H(6), *J* = 7.9 Hz, *J* = 1.1 Hz); 7.52—7.57 (m, 2 H, H(4) and H(5)); 7.91 (dd, 1 H, H(3), *J* = 7.7 Hz, *J* = 1.1 Hz). ^{13}C NMR ($CDCl_3$), δ: 26.8 (Me); 42.9 (NMe); 61.4 ($\underline{C}Me_3$); 126.7 (C(3)); 130.1 (C(6)); 131.8 (C(4)); 132.9 (C(5)); 134.3 (C(1)); 146.7 (br.s, C(2)). The HMBC and HSQC experiments were used for the assignment of the signals in the spectrum. ^{14}N NMR ($CDCl_3$), δ: −31 (N—$\underline{N}O_2$, $\Delta\nu_{1/2}$ = 30 Hz); −53 (N→O, $\Delta\nu_{1/2}$ = 70 Hz).

2-(*tert*-Butyl-*NNO*-azoxy)-5-bromo[methoxy(oxido)diazenyl]benzene (4b). A mixture of *E*- and *Z*-isomers at the meth-

oxy(oxido)diazenyl group in the ratio 93 : 7 after recrystallization from light petroleum gave a mixture of *E*- and *Z*-isomers in the ratio 98 : 2. M.p. 27—29 °C (from light petroleum). MS (ESI), *m/z*: 331.0392 $[M + H]^+$; calculated for $C_{11}H_{15}N_4O_3Br$, $[M + H]^+$: *m/z* 331.0400. MS (EI), *m/z*: 269 $[M - MeONO]^+$. IR (neat), ν/cm^{-1}: 1275 m, 1313 m, 1361 w, 1392 w, 1454 m, 1476 s, 1553 s, 1595 w. ^{14}N NMR ($CDCl_3$), δ: −54 (N→O and N(O)OMe, $\Delta\nu_{1/2}$ = 140 Hz). ^{1}H NMR of the major isomer (*E*) ($CDCl_3$), δ: 1.44 (s, 9 H, 3 Me); 4.09 (s, 3 H, OMe); 7.51 (dd, 1 H, H(4), *J* = 8.6 Hz, *J* = 2.1 Hz); 7.63 (d, 1 H, H(3), *J* = 8.6 Hz); 7.77 (d, 1 H, H(6), *J* = 2.1 Hz). ^{13}C NMR of the major isomer (*E*) ($CDCl_3$), δ: 25.5 (C<u>Me</u>$_3$); 58.6 (OMe); 59.9 (<u>C</u>Me$_3$); 123.8 (C(5)); 125.6 (C(3)); 126.6 (C(6)); 131.1 (C(4)); 136.3 (C(1)); 142.6 (br.s, C(2)). The HMBC and HSQC experiments and calculations by the additive scheme[15] were used for the assignment of the signals in the spectrum. ^{1}H NMR of the minor isomer (*Z*) ($CDCl_3$), δ: 1.42 (s, 9 H, 3 Me); 3.91 (s, 3 H, OMe); the other signals overlap with the signals of *E*-isomer. ^{13}C NMR ($CDCl_3$), δ (there are given some signals, which presumably are related to the minor *Z*-isomer and do not overlap with the signals of the major *E*-isomer): 25.6 (C<u>Me</u>$_3$); 124.1 (C(5)); 126.7 (C(6)); 130.3 (C(4)).

2-(*tert*-Butyl-*NNO*-azoxy)-5-bromo-*N*-methyl-*N*-nitroaniline (5b), oil. MS (ESI), *m/z*: 331.0399 $[M + H]^+$; calculated for $C_{11}H_{15}N_4O_3Br$, $[M + H]^+$: *m/z* 331.0400. MS (EI), *m/z*: 254. IR (neat), ν/cm^{-1}: 1296 s, 1364 m, 1396 w, 1428 w, 1452 w, 1484 m, 1540 s, 1576 w, 1596 w. ^{1}H NMR ($CDCl_3$), δ: 1.41 (s, 9 H, 3 Me); 3.67 (s, 3 H, NMe); 7.52 (d, 1 H, H(6), *J* = 2.1 Hz); 7.67 (dd, 1 H, H(4), *J* = 8.7 Hz, *J* = 2.1 Hz); 7.84 (d, 1 H, H(3), *J* = 8.7 Hz). ^{13}C NMR ($CDCl_3$), δ: 25.4 (C<u>Me</u>$_3$); 41.4 (NMe); 60.2 (<u>C</u>Me$_3$); 124.6 (C(5)); 126.6 (C(3)); 131.8 (C(6)); 133.3 (C(4)); 133.9 (C(1)); 144.2 (br.s, C(2)). The HMBC and HSQC experiments and calculations by the additive scheme[15] were used for the assignment of the signals in the spectrum. ^{14}N NMR ($CDCl_3$), δ: −32 (N—<u>N</u>O$_2$, $\Delta\nu_{1/2}$ = 30 Hz); −55 (N→O, $\Delta\nu_{1/2}$ = 90 Hz).

2-(*tert*-Butyl-*NNO*-azoxy)-3,5-dibromo[methoxy(oxido)-diazenyl]benzene (4c). A mixture of *E*- and *Z*-isomers at the methoxy(oxido)diazenyl group in the ratio 97 : 3. M.p. 94—97 °C. MS (ESI), *m/z*: 430.9310 $[M + Na]^+$; calculated for $C_{11}H_{14}N_4O_3Br_2$, $[M + Na]^+$: *m/z* 430.9325. MS (EI), *m/z*: 347 $[M - MeONO]^+$. IR (KBr), ν/cm^{-1}: 1320 m, 1364 w, 1388 w, 1436 m, 1468 w, 1500 m, 1548 s, 1580 m. ^{14}N NMR ($CDCl_3$), δ: −57 (N→O and N(O)OMe, $\Delta\nu_{1/2}$ = 240 Hz). ^{1}H NMR of the major isomer (*E*) ($CDCl_3$), δ: 1.50 (s, 9 H, 3 Me); 4.07 (s, 3 H, OMe); 7.74 (d, 1 H, H(4), *J* = 1.9 Hz); 8.36 (d, 1 H, H(6), *J* = 1.9 Hz). ^{13}C NMR of the major isomer (*E*) ($CDCl_3$), δ: 25.6 (C<u>Me</u>$_3$); 58.7 (OMe); 60.7 (<u>C</u>Me$_3$); 116.6 (C(3)); 122.7 (C(5)); 124.4 (C(6)); 135.0 (C(4)); 136.5 (C(1)); 143.3 (br.s, C(2)). The HMBC and HSQC experiments and calculations by the additive scheme[15] were used for the assignment of the signals in the spectrum. ^{1}H NMR of the minor isomer (*Z*) ($CDCl_3$), δ: 1.44 (s, 9 H, 3 Me); 3.96 (s, 3 H, OMe); the rest of the signals overlap with the signals of *E*-isomer. ^{13}C the minor isomer (*Z*) ($CDCl_3$), δ: 25.4 (C<u>Me</u>$_3$); the other signals overlap with the signals of *E*-isomer.

2-(*tert*-Butyl-*NNO*-azoxy)-3,5-dibromo-*N*-methyl-*N*-nitroaniline (5c), m.p. 112—115 °C. MS (ESI), *m/z*: 430.9316 $[M + Na]^+$; calculated for $C_{11}H_{14}N_4O_3Br_2$, $[M + Na]^+$: *m/z* 430.9325. MS (EI), *m/z*: 332. IR (KBr), ν/cm^{-1}: 1284 s, 1316 m, 1364 w, 1404 w, 1428 m, 1452 m, 1488 m, 1544 s, 1584 w. ^{1}H NMR ($CDCl_3$), δ: 1.44 (s, 9 H, 3 Me); 3.61 (s, 3 H, NMe); 7.53 (d, 1 H, H(6), *J* = 1.9 Hz); 7.92 (d, 1 H, H(4), *J* = 1.9 Hz). ^{13}C NMR ($CDCl_3$), δ: 25.2 (C<u>Me</u>$_3$); 41.4 (NMe); 60.8 (<u>C</u>Me$_3$); 117.4 (C(3)); 123.1 (C(5)); 131.2 (C(6)); 134.6 (C(1)); 137.7 (C(4)); 145.2 (br.s, C(2)). The HMBC and HSQC experiments and calculations by the additive scheme[15] were used for the assignment of the signals in the spectrum. ^{14}N NMR ($CDCl_3$), δ: −32 (N—<u>N</u>O$_2$, $\Delta\nu_{1/2}$ = 30 Hz); −59 (N→O, $\Delta\nu_{1/2}$ = 170 Hz).

2-(*tert*-Butyl-*NNO*-azoxy)-5-bromo[(*E*)-isopropoxy(oxido)-diazenyl]benzene (4d) and 2-(*tert*-butyl-*NNO*-azoxy)-5-bromo-*N*-isopropyl-*N*-nitroaniline (5d). Concentrated aqueous NH_3 (0.1 mL) was added in one portion to a suspension of nitramine **3b** (0.26 g, 0.82 mmol) in DI water (3 mL), followed by a dropwise addition of a solution of $AgNO_3$ (0.14 g, 0.82 mmol) in DI water (0.5 mL). A white precipitate that formed was filtered off, washed with DI water (3 mL), EtOH (2 mL), dried for 12 h in a vacuum desiccator over P_2O_5 to obtain Ag-salt of nitramine **3b** (260 mg, 75%). The Ag-salt that obtained was further used without additional purification.

A. Isopropyl bromide (0.22 mL, 2.4 mmol) was added in one portion to a solution of Ag-salt of nitramine **3b** (0.1 g, 0.24 mmol) in anhydrous MeCN (3 mL) at 20 °C under argon. The reaction mixture was kept for 3 weeks at 20 °C, a precipitate was filtered off, washed with MeCN (2 mL), the filtrates were combined, the solvent was evaporated *in vacuo*. The residue was separated by preparative TLC (light petroleum—AcOEt (20 : 1)) to obtain *O*-isopropyl compound **4d** (54 mg, 64%) as a light yellow oil and *N*-isopropyl compound **5d** (10 mg, 12%) as a light yellow oil, as well.

B. Isopropyl bromide (0.11 mL, 1.2 mmol) was added in one portion to a suspension of thoroughly powdered Ag-salt of nitramine **3b** (50 mg, 0.12 mmol) in anhydrous Et_2O (2 mL) at 20 °C under argon. The reaction mixture was stirred for 1 month at 20 °C, then applied on the layer of silica gel (*h* = 1 cm, *d* = 2 cm), eluted with the light petroleum—AcOEt solvent mixture (20 : 1, 50 mL), the eluate was concentrated *in vacuo*. The *O*-isopropyl compound **4d** was purified by preparative TLC (light petroleum—AcOEt (20 : 1, then 10 : 1)) to obtained *O*-isopropyl compound **4d** (30 mg, 71%) as a light yellow oil.

2-(*tert*-Butyl-*NNO*-azoxy)-5-bromo[(*E*)-isopropoxy(oxido)-diazenyl]benzene (4d). MS (ESI), *m/z*: 359.0719 $[M + H]^+$; calculated for $C_{13}H_{19}N_4O_3Br$, $[M + H]^+$: *m/z* 359.0713. MS (EI), *m/z*: 269 $[M - Pr^iONO]^+$. IR (neat), ν/cm^{-1}: 1272 m, 1316 m, 1360 w, 1388 w, 1448 m, 1476 s, 1540 s, 1596 w. ^{1}H NMR ($CDCl_3$), δ: 1.39 (d, 6 H, OCH<u>Me</u>$_2$, *J* = 6.3 Hz); 1.44 (s, 9 H, C<u>Me</u>$_3$); 5.25 (sept, 1 H, OC<u>H</u>Me$_2$, *J* = 6.3 Hz); 7.49 (dd, 1 H, H(4), *J* = 8.6 Hz, *J* = 2.1 Hz); 7.62 (d, 1 H, H(3), *J* = 8.6 Hz); 7.74 (d, 1 H, H(6), *J* = 2.1 Hz). ^{13}C NMR ($CDCl_3$), δ: 20.4 (OCH<u>Me</u>$_2$); 25.6 (C<u>Me</u>$_3$); 59.8 (<u>C</u>Me$_3$); 76.1 (O<u>C</u>HMe$_2$); 123.8 (C(5)); 125.7 (C(3)); 126.8 (C(6)); 130.9 (C(4)); 136.6 (C(1)); 142.6 (br.s, C(2)). The HMBC and HSQC experiments and calculations by the additive scheme[15] were used for the assignment of the signals in the spectrum. ^{14}N NMR ($CDCl_3$), δ: −53 (N→O and N(O)OPr^i, $\Delta\nu_{1/2}$ = 170 Hz).

2-(*tert*-Butyl-*NNO*-azoxy)-5-bromo-*N*-isopropyl-*N*-nitroaniline (5d). MS (ESI), *m/z*: 397.0287 $[M + K]^+$; calculated for $C_{13}H_{19}N_4O_3Br$, $[M + K]^+$: *m/z* 397.0272. MS (EI), *m/z*: 312 $[M - NO_2]^+$. IR (neat), ν/cm^{-1}: 1256 m, 1280 s, 1300 s, 1364 m, 1388 w, 1452 m, 1484 s, 1540 s, 1572 m, 1592 w. ^{1}H NMR ($CDCl_3$), δ: 1.41 (s, 9 H, C<u>Me</u>$_3$); 1.48 (d, 6 H, NCH<u>Me</u>$_2$, *J* = 6.5 Hz); 4.87 (sept, 1 H, OC<u>H</u>Me$_2$, *J* = 6.5 Hz); 7.41 (d, 1 H,

H(6), J = 2.1 Hz); 7.71 (dd, 1 H, H(4), J = 8.7 Hz, J = 2.1 Hz); 7.87 (d, 1 H, H(3), J = 8.7 Hz). ^{14}N NMR ($CDCl_3$), δ: −33 (N—$\underline{N}O_2$, $\Delta\nu_{1/2}$ = 30 Hz); −55 (N→O, $\Delta\nu_{1/2}$ = 100 Hz).

Synthesis of BTDO 6a—c from *O*-alkyl compounds 4a—d (general procedure). ***A.*** An acid (0.5 mL) (see Table 3) was added in one portion to *O*-alkyl compound **4a—d** (0.015 mmol) with vigorous stirring at 20 °C.* The reaction mixture was kept at 20 °C for the time indicated in Table 3, then poured into water with ice (3 mL),** followed by extraction with CH_2Cl_2 (3×2 mL). The organic extracts were combined, washed with brine (1 mL), dried with $MgSO_4$, and concentrated *in vacuo*. The yields of BTDO **6a—c** were determined from the ^{1}H NMR spectroscopic data (see Table 3).

B. Boron trifluoride diethyl etherate (0.5 mL) was added in one portion to *O*-alkyl compound **4a—d** (0.015 mmol) at 20 °C under dry argon. The reaction mixture was kept at 20 °C for the time indicated in Table 3 and then diluted with CH_2Cl_2 (3 mL) and H_2O (2 mL). The mixture was neutralized with $NaHCO_3$ to pH 7, followed by separation of the organic layer. The aqueous layer was extracted with CH_2Cl_2 (3 mL). The organic extracts were combined, washed with brine (1 mL), dried with $MgSO_4$, and concentrated *in vacuo*. The yield of BTDO **6a—c** were determined by ^{1}H NMR spectroscopy (see Table 3).

Physicochemical and spectral data for compounds **6a—c** agrees with those given in the literature.[3]

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* For the reaction with H_2SO_4, an acid, preliminary cooled to 0 °C, was added to the *O*-alkyl compound **4a—c**, and then the temperature was raised to 20 °C over the time indicated in Table 3.

** For the reaction in CF_3COOH, the reaction mixture was concentrated, and the residue was analyzed by ^{1}H NMR spectroscopy.

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