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A Synthesis of 1-Hydroxybenzo-1,2,3-triazole 3-Oxide

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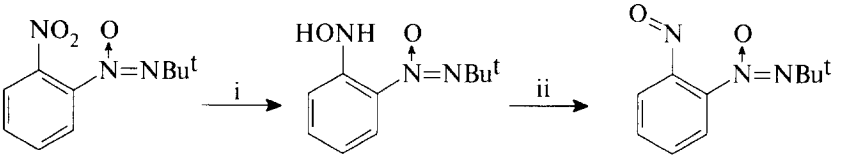
Abstract: The intramolecular reaction of the nitroso group with the azoxy side-chain in 2-(*tert*-butyl)-1-(2-nitrosophenyl)diazene 1-*N*-oxide provides the key step in a synthesis of the previously unknown 1-hydroxybenzo-1,2,3-triazole 3-oxide.

Recently it was disclosed[1] that *tert*-butyl group in a *tert*-butyl-*NNO*-azoxy moiety can be replaced by electrophiles. In present communication we took advantage of this reaction for synthesis of the hitherto unknown 1-hydroxybenzo-1,2,3-triazole 3-oxide[2].

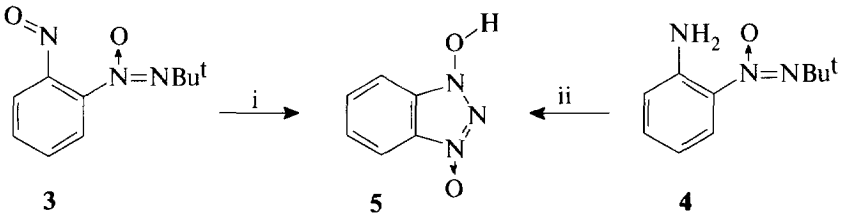
The key intermediate in this synthetic route was the nitroso compound **3**, which was obtained by the reduction of nitro compound **1** with zinc dust to give hydroxylamine derivative **2** and the oxidation of the latter with yellow mercuric oxide in CH_2Cl_2 solution.



1 **2** **3**

Scheme 1. i: Zn/NH_4Cl, H_2O, EtOH; (53%); ii: HgO, CH_2Cl_2; (96%).

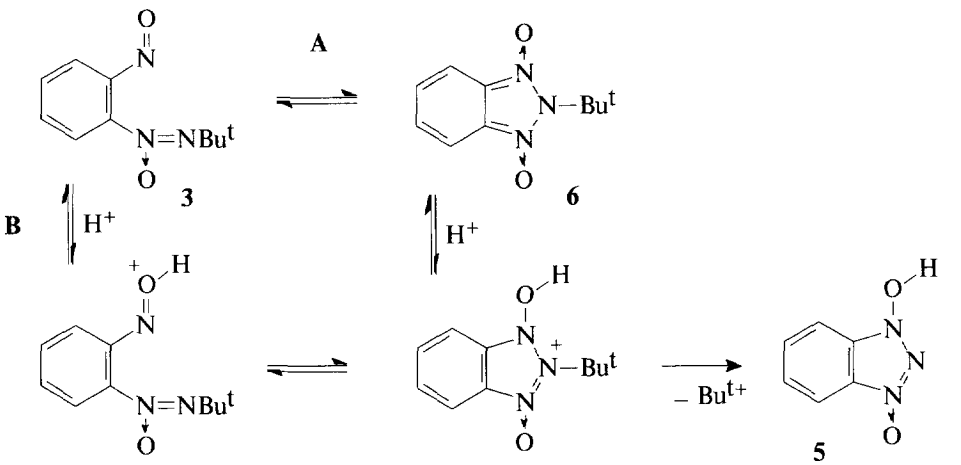
Nitroso compound **3** was stable at room temperature when a small amount of pyridine was present, the color of the solution being green. However, when the base is absent, the solution turned brown in a few hours with 1-hydroxybenzo-1,2,3-triazole 3-oxide (**5**) precipitating (Scheme 2). The rate of cyclization considerably increased when proton donors (e. g. trifluoroacetic acid or methanol) were added.



Scheme 2. i: CF_3CO_2H, CH_2Cl_2; (89%); ii: $PhCO_3H$, CH_2Cl_2; (79%).

Oxidation of 2-(*tert*-butylazoxy)aniline (**4**) with perbenzoic acid in CH_2Cl_2 proved to be a more convenient method of synthesis of compound **5** (Scheme 2). The reagents were kept for 3 hours at room temperature and the precipitate of **5** was filtered off. Green color appeared in the course of the reaction; thus, we suggest the reaction to proceed *via* intermediate nitroso compound **3**, which quickly turned into **5** in the presence of an acid.

A priori **5** could be formed by route **A** or **B** (Scheme 3). According to route **A,** nitroso compound **3** is supposed to be in equilibrium with cyclic 2-*tert*-butylbenzotriazole 1,3-dioxide (**6**). After protonation the latter could eliminates *tert*-butyl cation, forming **5**. According to route **B,** the protonation of nitroso compound **3** takes place first, making the cyclization to proceed easily.



Scheme 3.

To elucidate this question, we have carried out the NMR studies (Tables 1 and 2). Preliminary measurements were made for model 2-nitronitrosobenzene (**10**) and 1-phenyl-2-*tert*-butyldiazene 1-oxide (**11**). To calculate ^{13}C chemical shifts of the benzene ring atoms of compounds under investigation, the substituent chemical shifts (SCS) of -N(O)=NBu^t fragment were determined from the ^{13}C NMR spectra of **11**. Fragment -N(O)=N(O)- (nitroso dimer) was approximated by -N(O)=NPh fragment[3]. SCS of nitroso group was taken from the paper of Al-Tahou and Gowenlock[4].

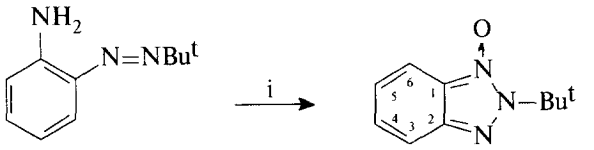
As expected[5], the signal of the proton adjacent to the nitroso group in **10** underwent a strong upfield shift. The ^{13}C NMR spectra of **10** exhibited a similar upfield shift (as compared with the calculated value) for C(2) atom, which was in the *ortho*-position to the nitroso group. Both the indications may make good use of the reliable identification of monomer in *ortho*-substituted nitroso compounds, and the integral intensity of hydrogen signals may be used for the quantitative determination of the monomer in the investigated pattern. The ^{14}N and ^{15}N NMR spectra demonstrate that the monomers of nitroso compounds have characteristic low field signals ca. 500 ppm (very broad in ^{14}N NMR spectra). This is one more indication for these compounds.

The NMR spectra of model **10** showed an equilibrium of the monomer and one of the geometrical isomers of the dimer (the second isomer was not detected). Nitroso compound **3** proved to exist as an equilibrium of three compounds. One of them was a monomer **3a**, identified as described above. At −30°C, the monomer quantity did not exceed 10%, whereas at 30°C its proportion increased to 50% (determined by integral measurements of ^{1}H and ^{15}N signals (INEPT, signal =N−Bu^t)). A special experiment demonstrated the changes in equilibrium to be reversible. Two other compounds **3b** and **3c** were geometrical isomers of nitroso dimer. None of them was cyclic triazole **6**, because otherwise the number of the CH signals of benzene ring in the ^{13}C NMR spectra would be reduced from 12 to 10 on account of the symmetry of **6**.

The absence of NMR signals of cyclic compound **6** made mechanism B more probable.

Because of the poor solubility of compound **5** in water and organic solvents, the NMR spectra were measured for its potassium salt **9**. ^{1}H and ^{13}C NMR spectra confirmed the symmetrical structure of the salt. The structure of **5** was also confirmed by microanalyses and MS. It cannot be excluded that proton in compound **5** is connected not with O-atom, but with N-atom, although H−O-structure seems to be more real. To solve this question we plan to use X-ray crystallography.

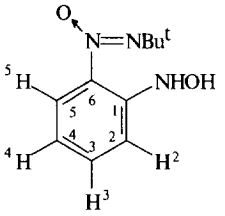
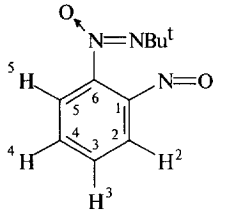
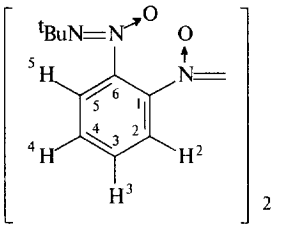
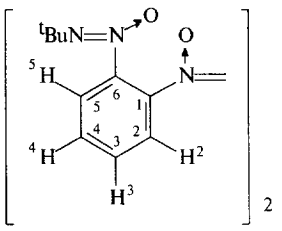
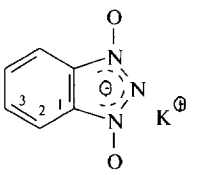
It should be noted, that 2-*tert*-butylbenzotriazole 1-oxide (**8**) exists only in cyclic form and does not eliminate *tert*-butyl group spontaneously. This compound was obtained by oxidation of *tert*-butylazoaniline (**7**) with perbenzoic acid (Scheme 4).

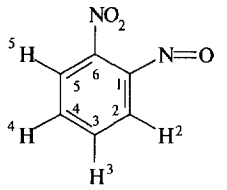
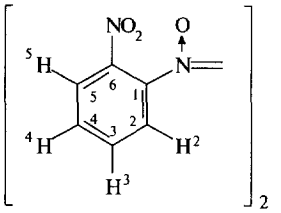
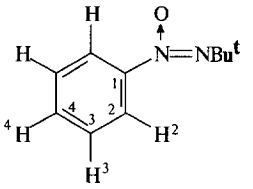


7 **8**

Scheme 4. i: $PhCO_3H$, CH_2Cl_2; (95%).

Table 1. ^{1}H NMR Data of Compounds **2**, **3**, **9** and Model Compounds.

Structure	Comp.[a]	δ (ppm)				
		H^2	H^3	H^4	H^5	$C(CH_3)_3$
1	2	3	4	5	6	7
	**2**[b]	7.07	7.21	6.84	7.85	1.49
	**3a**[c]	6.52	7.48	7.81	7.88	1.50
	**3b**[d]	7.90 or 7.95	7.32 or 7.55	7.55 or 7.32	7.95 or 7.90	1.49
	**3c**[e]	7.87 or 7.98	7.62 or 7.68	7.68 or 7.62	7.98 or 7.87	1.44
	**9**[f]	7.04	6.83	—	—	—

1	2	3	4	5	6	7
	**10a**[g]	6.50	7.68	7.86	8.09	—
	**10b**[h]	7.85	7.98	7.81	8.30	—
	**11**[i]	8.12	7.30	7.30	—	1.44

[a] The solvent for compounds **2**, **10** and **11** was $CDCl_3$, for **3** — CH_2Cl_2, for **9** — D_2O.
[b] The multiplicity of H(2)—H(5) signals were used for assignment of spectrum with proposing that lowest field doublet is a H(5) signal. Two widen lines at 7.20 ppm (NH) and 8.87 ppm (OH) were observed.
[c] In equilibrium with **3b** and **3c**, all signals were determined by comparison of two spectra registrated at 30°C and −30°C. The H(2)—H(5) assignment was made as for **10** and with 2D-COSY.
[d] The dominant isomer, signal assignment was made keeping in mind the integral intensities.
[e] The minor isomer, **3a**:**3b**:**3c** = 2.5:1.8:1.0 at 30°C and 0.4:3.0:1.0 at −30°C.
[f] The H(2) and H(3) signal assignment was made using ^{13}C NMR data (see footnotes in table 2).
[g] In equilibrium mixture with **10b**, H(2) signal assignment was made accordingly with Ref. 4, other protons were recognized in two-dimensional ^1H—^1H COSY spectrum.
[h] The relation of **10b**/**10a** is *ca* 1:2, H(2)—H(5) proton signals assignment was made by 2D-COSY; the lowest field signal was proposed H(5).
[i] H(2) was assumed to be a lowest field signal. Compound **11** was obtained by Kovacic method.[6]

Table 2. ^{13}C NMR Data of Compounds **2**, **3**, **9** and Model Compounds.

Compound[a]	δ, ppm, calculated δ in parentheses							
	C(1)	C(2)	C(3)	C(4)	C(5)	C(6)	$\underline{C}(CH_3)_3$	$C(\underline{C}H_3)_3$
2[b]	143.65 (145.0)	115.1 (111.9)	131.8 (131.5)	119.8 (118.8)	123.7 (122.7)	134.2 b (132.3)	59.61	25.93
3a[c]	156.5 (159.5)	110.4 (120.7)	130.3 (131.7)	136.3 (135.4)	124.0 (122.9)	150.1 b (141.1)	60.69	25.93
3b[c]	136.2 (137.7)	125.0 or 125.5 (125.3)	131.4 or 132.4 (131.0)	132.4 or 131.4 (139.3)	125.5 or 125.0 (122.2)	142,7 (145.7)	60.63 25,69	25.69
3c[c]	134.4 (137.7)	124.9 or 125.9 (125.3)	132.1 or 132.2 (131.0)	132.2 or 132.1 (129.3)	135.9 or 124.9 (122.2)	143.0 (145.7)	60.14	25,44
9[d]	126.46	111.36	125.94	—	—	—	—	—
10a[e]	156.0 (158.3)	110.90 (122.0)	133.73 (135.9(	136.02 (136.7)	124.65 (124.4)	(140.9)	—	—
10b[f]	150.5 (139.2)	137.2 (123.7)	132.7 (130.4)	136.3 (134.7)	125.7 (126.4)	(145.4)	—	—
11[g]	148.77	122.15	128.39	131.09	—	—	58.60	25.76

[a] The conditions of measurement were as in Table 1.
[b] SCS for $NH-NH_2$ was used instead of unknown SCS for NHOH group.
[c] The assignment of signals to dimers **3b** and **3c** and monomer **3a** was made by comparison of two spectra at 30°C and −30°C. We assume that *trans*-isomer of dimer was predominant. The C(1)—C(6) signal assignment was made from selective proton decoupling, proton coupled spectra and using calculated chemical shift values.
[d] C(1) signal was identified from proton coupling spectrum; C(2) and C(3) assignment was made assuming a possible diamagnetic increment of triazole ring and using coupling constants $^1J_{H\text{-}C(2)}$=176.7 Hz, $^1J_{H\text{-}C(3)}$=165.5 Hz.
[e] Selective decoupling of H(2)—H(5) protons was used for assignment of C(2)—C(5) signals. The C(6) signal was not found as it was very broad owing to $^{13}C-^{14}N$ coupling.
[f] C(5) signal was identified by selective decoupling of H(5) proton. C(3) and C(4) signals assignment was made accordingly with calculated values of chemical shifts using SCS of N(O)=NPh[3] as approximation for unknown SCS of −N(O)=N(O)− group. The C(6) signal is not observable due to broadening by $^{13}C-^{14}N$ coupling.
[g] The C(2) signal has been recognized by selective decoupling of H(2) proton, C(3) and C(4) signals have different intensities.

Table 3. ^{14}N and ^{15}N NMR Data

Compound	δ(^{14}N), ppm, line width in parentheses, Hz				δ(^{15}N), ppm
	—N=O	$=\overset{\downarrow}{N}\rightarrow O$	$—NO_2$	$=N—Bu^t$	$=N—Bu^t$
2	—	−49.3±0.5 (100)	—	—	−12.01[a]
3a	532±10 (>1000)	−54±2 (100)	—	5±10 (>1000)	4.04
3b	—	−54±2 (100)	—	—	−3.98 −4.17 at −30°C
3c	—	−54±2 (100)	—	—	−6.18 −6.48 at −30°C
10a	522±3 (700)	—	−12.9±0.5 (50)	—	—
10b	—	−85±20 (>1000)	−17.6±1 (150)	—	—
11	—	−52.4±0.5 (150)	—	−12±10 (>1000)	—

[a] NH, δ=−245.80 ppm, $^1J_{^1H-^{15}N}$=86.0 Hz;

EXPERIMENTAL

NMR spectra were recorded on AM 300 Bruker instrument. The chemical shifts were measured relative to internal TMS (^1H, ^{13}C) or CH_3NO_2 (^{14}N, ^{15}N) external reference (δ=0.0 ppm). The INEPT and SPT pulse sequences were used for ^{15}N signal observation[7]. Assignment of ^{13}C and ^1H signals were made by two-dimensioned C—H and H—H correlation spectroscopy and by selective proton decoupling.

2-(tert-butyl-NNO-azoxy)hydroxylaminobenzene (2). The solution of NH_4Cl (1 g) in water (25 ml) was added to a stirred solution of 2-(*tert*-butyl-*NNO*-azoxy)nitrobenzene (2 g, 9 mmol) in ethanol (30 ml) at 60°C and then zinc dust (2 g) was added in small portions over a period of 10 min. The stirring was continued for another 10 min. at the same temperature, the mixture was filtered, washed with ethanol, the solvent was partially removed *in vacuo* up to 25 ml. Concentrated hydrochloric acid (15 ml) was added and then the solution was extracted with ether (4 x 50 ml). The extract was washed with water, dried ($MgSO_4$), the solvent was removed *in vacuo*, pentane (10 ml) was added, the solution was cooled to −70°C and the precipitated **2** was removed *via* filtration to give white needles m.p. 49—50°C (1.0 g, 53%). Anal. Calcd for $C_{10}H_{15}N_3O_2$: C, 57.40; H, 7.23; N, 20.08 %. Found: C, 57.50; H, 7.20; N, 19.80 %.

2-(tert-butyl-NNO-azoxy)nitrosobenzene (3). To a solution of **2** (0.45 g, 2.15 mmol) in CCl_4 (10 ml) was added the yellow mercuric oxide (0.5 g, 2.30 mmol). The mixture was stirred at r.t. until **2** disappeared (c.a. 30 min., TLC, 20% ethyl acetate/CH_2Cl_2) and after filtration concentrated up to 2 ml to give the solution of **3**, which was investigated by NMR spectroscopy. The yield of **3** was almost quantitative (determined with internal standard).

1-Hydroxybenzo-1,2,3-triazole 3-oxide (5) from 3. To the above mentioned solution of **3** a few drops of trifluoroacetic acid were added. In 5 min. the precipitate was filtered off and washed with CH_2Cl_2 and pentane to give **5** (0.29 g, 89 %) as a white solid. It began to decompose at 110°C without melting. MS: m/z 151 (M^+) Anal. Calcd for $C_6H_5N_3O_2$: C, 47.68; H, 3.33; N, 27.81%. Found: C, 47.60; H, 3.38; N, 28.07%.

1-Hydroxybenzo-1,2,3-triazole 3-oxide (5) from 4. To the solution of 2-(*tert*-butyl-*NNO*-azoxy)aniline[8] (**4**) (1 g, 5.18 mmol) in CH_2Cl_2 (5 ml) was added the solution of perbenzoic acid (18 mmol) in CH_2Cl_2 (25 ml) at 15°C. After 3 h at r.t. the precipitate was filtered off and washed with CH_2Cl_2 and pentane to give **5** (0.62 g, 79%)

2-tert-butylbenzo-1,2,3-triazole 1-oxide (8). To a solution of 2-(*tert*-butylazo)aniline[8] (**7**) (1 g, 5.18 mmol) in CH_2Cl_2 (25 ml) at 0°C was added the solution of perbenzoic acid (18 mmol) in CH_2Cl_2 (25 ml). The mixture was allowed to stand overnight in a refrigerator. The excess of perbenzoic acid was removed by KI workup followed by treatment with sodium thiosulfate, the organic solution was washed with $NaHCO_3$ solution, dried over $CaCl_2$, the solvent was removed, leaving 0.2 g (95%) of **8**, mp 97—98°C. ^1H NMR ($CDCl_3$): δ 1.93 (s, 9H, *t*-Bu), 7.27—740 (m, 2H, Ar), 7.69—7.74 (m, 2H, Ar); ^{13}C NMR ($CDCl_3$): δ 27.0 (CH_3), 66.5 (C-CH_3), 113.4 (C-6), 119.0 (C-3), 125.7 (C-5), 127.7 (C-1), 128.0 (C-4), 139.4 (C-2); ^{14}N NMR ($CDCl_3$): δ −90.3 (N-1), −116.0 (N-2); ^{15}N NMR ($CDCl_3$): δ −111.3 (INEPT from *t*-Bu, N-2); MS: m/z 191 (M^+). Anal. Calcd for $C_6H_5N_3O_2$: C, 62.83; H, 6.81; N, 21.99%. Found: C, 62.73; H, 6.86; N, 21.85%.

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