Synthesis and structures of pyridoannelated 1,2,3,4-tetrazine 1,3-dioxides

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Treatment of 2- and 4-amino-3-(*tert*-butyl-*NNO*-azoxy)pyridines with nitrating agents (N_2O_5 or NO_2BF_4) afforded the first representatives of pyridoannelated 1,2,3,4-tetrazine di-*N*-oxides, *viz.*, pyrido[2,3-*e*][1,2,3,4]tetrazine 1,3-dioxide (**9**), 7-nitropyrido[2,3-*e*][1,2,3,4]tetrazine 1,3-dioxide (**10**), and pyrido[3,4-*e*][1,2,3,4]tetrazine 2,4-dioxide (**11**). These compounds were studied by ^1H, ^{13}C, and ^{14}N NMR spectroscopy. The 1 : 1 complex of compound **10** with benzene was studied by X-ray diffraction analysis.

Key words: nitrogen heterocycles, pyridines, 1,2,3,4-tetrazines, *N*-oxides of heterocycles, ^1H, ^{13}C, ^{14}N, and ^{15}N NMR spectroscopy, X-ray diffraction analysis.

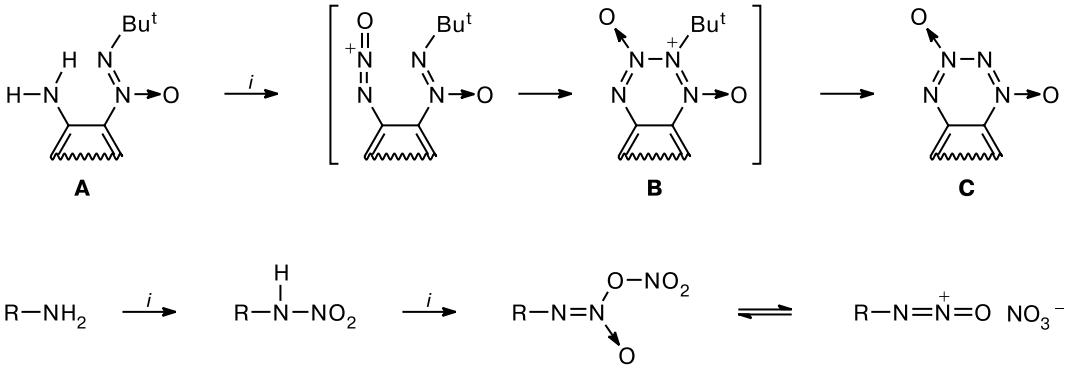
Earlier,[1,2] we have developed a procedure for the synthesis of annelated 1,2,3,4-tetrazine 1,3-dioxides (Scheme 1). This procedure involves treatment of aromatic amino compounds **A**, which contain the (*tert*-butyl)-*NNO*-azoxy group in the adjacent position, with nitrating agents. In the first step of nitration, the amino group is transformed into *N*-nitroamine, which is, presumably, nitrated at the oxygen atom followed by dissociation into the oxodiazonium cation and the nitrate anion. The electrophilic attack of the oxodiazonium cation at the terminal nitrogen atom of the azoxy group gives rise to cyclic intermediate **B**, which readily loses the *tert*-butyl cation to form the tetrazine dioxide ring. This approach was used for the synthesis of benzoannelated and furazanoannelated tetrazine 1,3-dioxides.[1]

Recently, it has been found[3] that some benzotetrazine 1,3-dioxides exhibit biological activity* associated with the ability of these compounds to generate nitrogen oxide in the course of reduction.[4]** Nitro-substituted benzo-

* Nitrobenzotetrazine 1,3-dioxides serve as guanylate cyclase activators[3b] and thrombocyte aggregation inhibitors;[3c] bromobenzotetrazine 1,3-dioxides serve as H,K-adenosine triphosphatase inhibitors.[3d]

** It was demonstrated[4] that reduction of the benzotetrazine 1,3-dioxide ring gives rise to nitrosating species, which can serve as an NO source in biological systems.

Scheme 1



i. Nitration.

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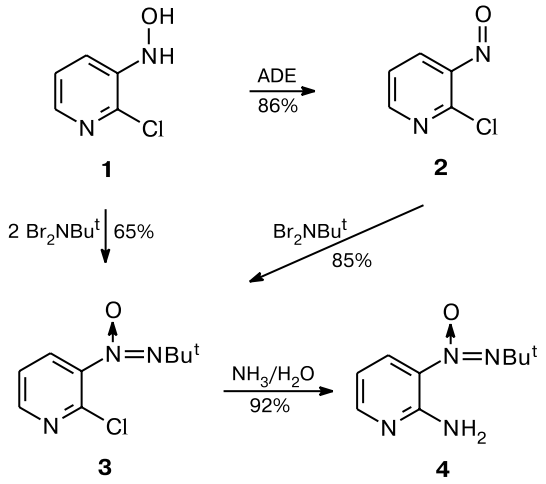
tetrazine 1,3-dioxides are most active. There are reasons to suppose that the activity of benzotetrazine 1,3-dioxides depends, in particular, on the redox potential, which is determined by the substituents in the benzene moiety.* In this connection, it was of interest to synthesize tetrazine 1,3-dioxides annelated to the pyridine moiety. Since these compounds have a redox potential similar to that of nitrobenzotetrazine 1,3-dioxides, they would be an efficient class of NO donors.

2-Amino- and 4-amino-3-(*tert*-butyl-*NNO*-azoxy)pyridines were used as the starting compounds for the synthesis of pyridotetrazine 1,3-dioxides. Hydroxylamine **1** was oxidized with ethyl azodicarboxylate (ADE) to nitroso compound **2**, which was transformed into 3-(*tert*-butyl-*NNO*-azoxy)-2-chloropyridine (**3**) by the reaction with *N*,*N*-dibromo-(*tert*-butyl)amine. Then the chlorine atom was replaced with the amino group by treating compound **3** with aqueous ammonia in an autoclave at 150—180 °C to prepare 2-amino derivative **4**. Compound **3** can also be prepared directly by treating hydroxylamine **1** with two equivalents of *N*,*N*-dibromo-*tert*-butylamine (Scheme 2).

Scheme 2

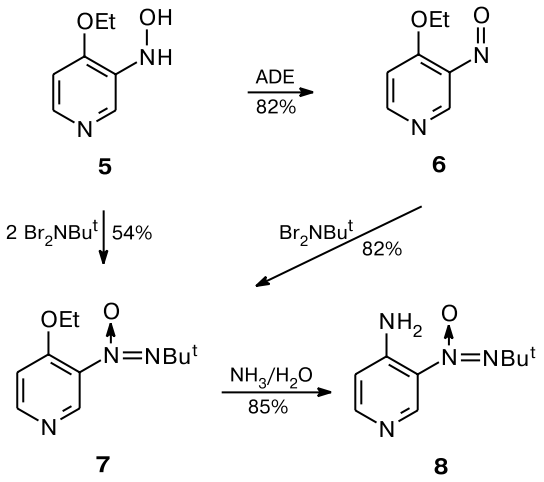


Analogously, 4-amino derivative **8** was synthesized from hydroxylamine **5** (Scheme 3).

Compounds **1**—**8** were characterized by ^{1}H NMR spectroscopy and, in part, by ^{14}N NMR spectroscopy. The complete assignment of the signals in the ^{13}C NMR spectra of compounds **3**, **4**, and **8** was made (for **3**, see the Experimental section; for aminoazoxy compounds **4** and **8**, see Tables 1 and 2). Only the ^{1}H NMR spectra of nitroso compounds **2** and **6** deserve detailed comments. At 25 °C, compound **2** in methanol-d_6 or $CDCl_3$ exists completely in the monomeric form (as evidenced by the

* Apparently, for annelated tetrazine 1,3-dioxides to exhibit NO-donor properties, the reduction rate of these compounds in biological systems should fall within a rather narrow range.

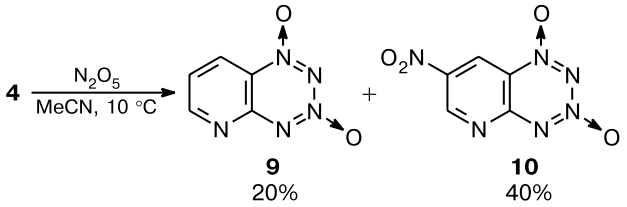
Scheme 3



characteristic upfield shift of the signal for the H(4) proton in the *ortho* position with respect to the nitroso group, $\delta = 6.55$), whereas, under these conditions, the dimeric and monomeric forms of compound **6** are present in solutions in comparable amounts (the dimer/monomer ratio is 1 : 1.7 in a 2% methanolic solution and 1 : 1 in a 8% methanolic solution). At −70 °C, only the dimeric form of compound **6** was observed in solution.

Treatment of 2-amino derivative **4** with nitric anhydride afforded compounds **9** and **10** in a ratio of 1 : 2 (Scheme 4). The latter compound contains the nitro group in the pyridine ring. In this case, an attempt to use nitronium tetrafluoroborate failed. Treatment of 2-amino derivative **4** with this reagent afforded a mixture of products containing only insignificant amounts of compounds **9** and **10**.

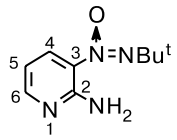
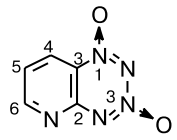
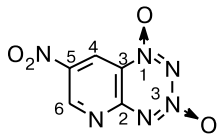
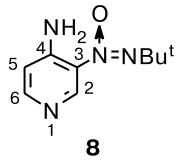
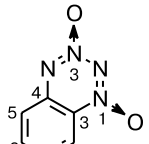
Scheme 4



Treatment of 4-amino derivative **8** with nitric anhydride did not give compound **11**. By contrast, this compound was prepared in good yield by the reaction with nitronium tetrafluoroborate (Scheme 5).

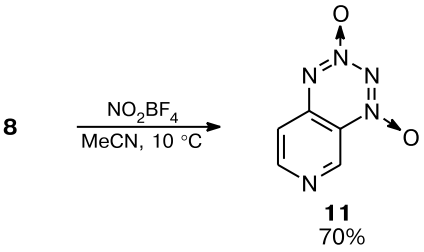
To understand the factors responsible for the difference in the behavior of 2- and 4-aminopyridines, it is necessary to perform additional investigations. It should be noted that one of the evident differences between these compounds is a higher basicity of 4-aminopyridines.

Table 1. ^{1}H, ^{14}N, and ^{15}N/INEPT NMR spectra

Compound	Solvent for ^{1}H and ^{14}N NMR	^{1}H NMR, δ (*J*/Hz)	^{14}N NMR, δ ($\Delta\nu_{1/2}$/Hz)	^{15}N/INEPT NMR,* δ
 **4**	$CDCl_3$	1.46 (s, 9 H, 3 Me); 6.6 (br.s, 2 H, NH_2); 6.70 (dd, 1 H, H(5), *J* = 8.1, *J* = 4.6); 8.17 (dd, 1 H, H(6), *J* = 4.6, *J* = 1.6); 8.36 (dd, 1 H, H(4), *J* = 8.1, *J* = 1.6)	−51 (40) (N→O)	−16.0 (NBu^t); −49.7 (N→O); −300.0 (NH_2, $^{1}J_{N,H}$ = 94.3)
 **9**	Acetone-d_6	7.93 (dd, 1 H, H(5), *J* = 8.5, *J* = 4.4); 8.77 (dd, 1 H, H(4), *J* = 8.5, *J* = 1.7); 9.31 (dd, 1 H, H(6), *J* = 4.4, *J* = 1.7)	−39 (20) (N(1)); −44 (30) (N(3))	—
 **10**	Acetone-d_6	9.40 (dd, 1 H, H(4), *J* = 2.5); 9.94 (dd, 1 H, H(6), *J* = 2.5)	−21 (85) (NO_2), −39 (30) (N(1)), −42 (45) (N(3))	—
 **8**	DMSO-d_6	1.45 (s, 9 H, 3 Me); 6.87 (d, 1 H, H(2), *J* = 5.8); 7.3 (br.s, 2 H, NH_2); 8.10 (d, 1 H, H(6) *J* = 5.8); 8.85 (s, 1 H, H(5))	−50 (350) (N→O)	−16.1 (NBu^t); −49.1 (N→O); −305.0 (NH_2, $^{1}J_{N,H}$ = 90.8)
 **11**	Acetone-d_6	7.83 (dd, 1 H, H(5), ^{3}J = 5.8, ^{5}J = 0.8); 9.08 (d, 1 H, H(6), ^{3}J = 5.8); 9.58 (d, 1 H, H(2), ^{5}J = 0.8)	−39 (30) (N(1)); −43 (40) (N(3))	—

* In DMSO-d_6.

Scheme 5



Pyridoannelated 1,2,3,4-tetrazine 1,3-dioxides **9**—**11** are stable yellow compounds, which melt without decomposition (**9**, m.p. 228—229 °C; **10**, m.p. 189—190 °C; **11**, m.p. 179—180 °C).

Pyridotetrazine 1,3-dioxides were studied by NMR spectroscopy. The assignments of the signals in the ^{1}H and ^{13}C NMR spectra of these compounds are given in Tables 1 and 2. For comparison, these tables include also the data for the starting aminoazoxy compounds. It should be noted that the signals for the C(2), C(3), and C(4) atoms in amino derivatives **4** and **8** differ only slightly from the corresponding signals in the spectra of compounds **9** and **11**. To explain this factor, one should take into account, among other things, the electron-releasing effect of the *N*-oxide oxygen atom responsible for shielding of the corresponding carbon atom.

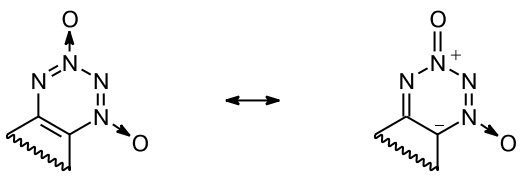
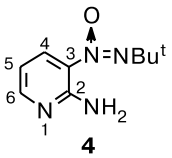
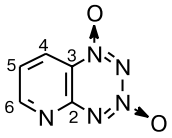
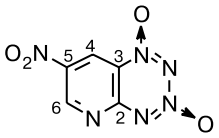
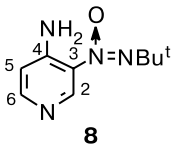
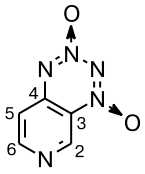


Table 2. ^{13}C NMR spectra*

Compound	Solvent	δ					
		C(2)	C(3)	C(4)	C(5)	C(6)	Other signals
 **4**	DMSO-d_6	152.4	127.8	132.5 (ddd, J = 166, J = 6.7, J = 2.1)	111.9 (dd, J = 169, $J_{H(6)}$ = 8.1)	151.1 (ddd, J = 180, J = 8.5, J = 3.5)	25.6 (Me); 58.8 (CMe_3)
 **9**	DMSO-d_6	153.1	126.2	128.6 (ddd, J = 177, J = 6.3, J = 1.6)	127.0 (dd, J = 173, $J_{H(6)}$ = 8.9)	160.9 (ddd, J = 185, J = 8.2, J = 3.6)	—
 **10**	Acetone-d_6	156.4 (dd, J = 14.7, J = 4.5)	125.9	126.0 (dd, J = 182, J = 4.0)	145.5	155.8 (dd, J = 196, J = 4.9)	—
 **8**	DMSO-d_6	145.6 (dd, J = 182, J = 11.9)	129.0	147.6 (dd, ^3J = 8.1, ^3J = 5.0)	111.6 (m, J = 164)	149.9 (ddd, J = 177, ^3J = 13.3, ^2J = 1.8)	25.7 (Me); 58.8 (CMe_3)
 **11**	Acetone-d_6	144.5 (dd, J = 195, J = 12.0)	125.4	148.5 (ddd, J = 8.8, J = 4.1, J = 1.3)	117.1 (ddd, J = 170, J = 8.6, J = 1.6)	156.2 (ddd, J = 185, J = 12.9, J = 2.0)	—

* The assignment of the signals was made based on $^1H—^{13}C$ correlations, accumulation of ^{13}C NMR signals with selective proton decoupling and without proton decoupling.

The ^{14}N NMR spectra of pyridotetrazine 1,3-dioxides show two narrow signals corresponding to the N(1) and N(3) atoms of the 1,2,3,4-tetrazine 1,3-dioxide ring. The narrower low-field signal (δ = −39, $\Delta\nu_{1/2}$ = 20—30 Hz, in acetone-d_6), like that in the spectra of benzoannelated 1,2,3,4-tetrazine 1,3-dioxides,[1] is assigned to N(1) bound to the C atom of the pyridine ring, whereas the broader high-field signal (δ from −43 to −45, $\Delta\nu_{1/2}$ = 30—45 Hz, in acetone-d_6) belongs to N(3). The assignment of the signals for the nitrogen atoms was made based on the ^{13}C NMR spectra measured with $^{13}C—^{14}N$ decoupling.

Compound **10** can form stable complexes with aromatic solvents. For example, crystallization from benzene afforded the 1 : 1 complex, which loses benzene *in vacuo* or upon heating above 50 °C. This complex was studied by X-ray diffraction analysis (Tables 3—5). In the crystal, molecule **10** is located parallel to the benzene solvate molecule, the benzene ring being projected onto the pyridine ring of molecule **10** (Fig. 1). The C(12) atom of the benzene ring is located above the C(2) atom bound to the nitro group. The C(12)...C(2) distance (3.329 Å) is somewhat smaller than twice the van der Waals radius of the carbon atom (3.4 Å). Such geometric parameters are typical of interactions in charge-transfer complexes.

Molecule **10** is virtually planar (the N(5)—N(6)—N(7)—N(8) torsion angle is 4.7°). The endocyclic bond angles at the N(8) and N(6) atoms (114.4° and 115.0°, respectively) are somewhat smaller, whereas the angles at the N(7) and N(5) atoms bound to the oxygen atom (128.1° and 122.4°, respectively) are

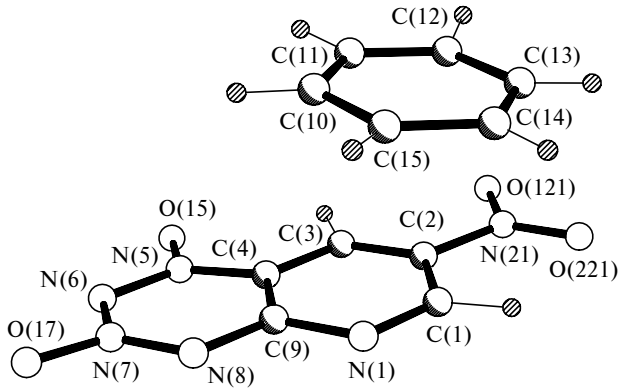


Fig. 1. Three-dimensional structure of the molecular complex of 7-nitropyrido[2,3-*e*]tetrazine 1,3-dioxide with benzene.

slightly larger than the standard value. The bond lengths in the tetrazine ring differ only slightly (by 0.002—0.015 Å) from the corresponding bond lengths in benzotetrazine 1,3-dioxide.[5]

Experimental

The ^{1}H, ^{13}C, ^{14}N, and ^{15}N NMR spectra were recorded on a Bruker AM-300 spectrometer (300.13, 75.5, 21.5, and 30.42 MHz, respectively). The chemical shifts were measured relative to Me_4Si (^{1}H and ^{13}C) or $MeNO_2$ (^{14}N and ^{15}N; external standard, upfield chemical shifts are negative). The mass spectra were obtained on a Varian MAT-311A instrument (EI, 70 eV). The course of the reactions was monitored by TLC (Silufol UV-254). Hydroxylaminopyridines **1** and **5** were synthesized according to procedures described earlier.[6]

X-ray diffraction study. Single crystals of the complex of 7-nitropyrido[2,3-*e*][1,2,3,4]tetrazine 1,3-dioxide **10** with benzene were grown from benzene. X-ray diffraction data were

Table 3. Bond lengths (*d*) in the complex of molecule **10** with benzene

Bond	*d*/Å	Bond	*d*/Å
O(15)—N(5)	1.233(3)	N(21)—C(2)	1.454(4)
O(17)—N(7)	1.247(3)	C(1)—C(2)	1.414(4)
O(121)—N(21)	1.239(3)	C(2)—C(3)	1.345(4)
O(221)—N(21)	1.212(3)	C(3)—C(4)	1.393(3)
N(1)—C(1)	1.320(3)	C(4)—C(9)	1.383(4)
N(1)—C(9)	1.352(3)	C(10)—C(11)	1.360(4)
N(5)—N(6)	1.321(3)	C(10)—C(15)	1.360(5)
N(5)—C(4)	1.391(4)	C(11)—C(12)	1.343(4)
N(6)—N(7)	1.382(3)	C(12)—C(13)	1.354(6)
N(7)—N(8)	1.308(3)	C(13)—C(14)	1.391(6)
N(8)—C(9)	1.357(3)	C(14)—C(15)	1.376(7)

Table 4. Bond angles (ω) in the complex of molecule **10** with benzene

Angle	ω/deg	Angle	ω/deg	Angle	ω/deg
C(1)—N(1)—C(9)	116.6(2)	O(121)—N(21)—C(2)	117.1(3)	N(1)—C(9)—N(8)	114.6(2)
O(15)—N(5)—N(6)	116.7(3)	O(221)—N(21)—C(2)	118.8(3)	N(1)—C(9)—C(4)	122.3(2)
O(15)—N(5)—C(4)	120.9(3)	N(1)—C(1)—C(2)	122.7(3)	N(8)—C(9)—C(4)	123.1(2)
N(6)—N(5)—C(4)	122.4(2)	N(21)—C(2)—C(1)	117.6(3)	C(11)—C(10)—C(15)	120.0(3)
N(5)—N(6)—N(7)	115.0(3)	N(21)—C(2)—C(3)	120.7(2)	C(10)—C(11)—C(12)	120.7(3)
O(17)—N(7)—N(6)	112.3(2)	C(1)—C(2)—C(3)	121.7(2)	C(11)—C(12)—C(13)	120.5(4)
O(17)—N(7)—N(8)	119.6(2)	C(2)—C(3)—C(4)	115.2(2)	C(12)—C(13)—C(14)	120.3(4)
N(6)—N(7)—N(8)	128.1(2)	N(5)—C(4)—C(3)	121.8(3)	C(13)—C(14)—C(15)	118.2(3)
N(7)—N(8)—C(9)	114.4(3)	N(5)—C(4)—C(9)	116.7(2)	C(10)—C(15)—C(14)	120.4(4)
O(121)—N(21)—O(221)	124.2(3)	C(3)—C(4)—C(9)	121.5(2)		

Table 5. Torsion angles (φ) in the complex of molecule **10** with benzene

Angle	φ/deg	Angle	φ/deg	Angle	φ/deg
C(9)—N(1)—C(1)—C(2)	−1.21(0.56)	N(6)—N(7)—N(8)—C(9)	3.50(0.52)	C(2)—C(3)—C(4)—C(9)	−0.68(0.51)
C(1)—N(1)—C(9)—N(8)	−177.26(0.33)	N(7)—N(8)—C(9)—N(1)	−179.09(0.31)	N(5)—C(4)—C(9)—N(1)	176.04(0.32)
C(1)—N(1)—C(9)—C(4)	2.23(0.53)	N(7)—N(8)—C(9)—C(4)	1.43(0.50)	N(5)—C(4)—C(9)—N(8)	−4.52(0.50)
O(15)—N(5)—N(6)—N(7)	−178.74(0.30)	O(121)—N(21)—C(2)—C(1)	−178.45(0.36)	C(3)—C(4)—C(9)—N(1)	−1.33(0.54)
C(4)—N(5)—N(6)—N(7)	1.02(0.47)	O(121)—N(21)—C(2)—C(3)	0.89(0.55)	C(3)—C(4)—C(9)—N(8)	178.12(0.33)
O(15)—N(5)—C(4)—C(3)	0.24(0.51)	O(221)—N(21)—C(2)—C(3)	1.31(0.55)	C(15)—C(10)—C(11)—C(12)	0.56(0.69)
O(15)—N(5)—C(4)—C(9)	−177.11(0.32)	C(221)—N(21)—C(2)—C(3)	−179.35(0.38)	C(11)—C(10)—C(15)—C(14)	0.33(0.70)
N(6)—N(5)—C(4)—C(3)	−179.51(0.32)	N(1)—C(1)—C(2)—N(21)	178.55(0.35)	C(10)—C(11)—C(12)—C(13)	−1.23(0.71)
N(6)—N(5)—C(4)—C(9)	3.13(0.48)	N(1)—C(1)—C(2)—C(3)	−0.79(0.60)	C(11)—C(12)—C(13)—C(14)	1.02(0.77)
N(5)—N(6)—N(7)—O(17)	176.18(0.30)	N(21)—C(2)—C(3)—C(4)	−177.63(0.32)	C(12)—C(13)—C(14)—C(15)	−0.14(0.79)
N(5)—N(6)—N(7)—N(8)	−4.75(0.51)	C(1)—C(2)—C(3)—C(4)	1.68(0.54)	C(13)—C(14)—C(15)—C(16)	−0.52(0.73)
O(17)—N(7)—N(8)—C(9)	−177.50(0.32)	C(2)—C(3)—C(4)—N(5)	−177.91(0.33)		

collected on an automated Enraf-Nonius CAD-4 diffractometer (MoKα radiation, graphite monochromator, θ/2θ scanning technique, $2\theta \leq 52.0°$). A total of 1088 reflections with $I \geq 2\sigma$ were measured. The structure was solved by direct methods using the SHELX program package[7] and refined anisotropically (isotropically for hydrogen atoms) to the reliability factor $R = 0.046$. The accuracy of the determination of the bond lengths and bond angles is ±0.003—0.007 Å and ±0.2—0.4°, respectively. The crystallographic data: $C_5H_2N_6O_4 \cdot C_6H_6$, M = 228, orthorhombic crystals, space group $P2_1P2_1P2_1$, a = 5.798(5), b = 7.594(2), c = 28.328(9) Å, V = 1247.3(6) Å^3, calculated density d = 1.535 g cm^{-3}, Z =4, μ_{Mo} = 0.208 mm^{-1}.

2-Chloro-3-nitrosopyridine (2). Ethyl azodicarboxylate (17.4 g, 0.1 mol) was added with stirring to a suspension of hydroxylaminopyridine **1** (14.4 g, 0.1 mol) in dry CH_2Cl_2 (400 mL) at −10 °C for 15 min. The reaction mixture was stirred for 30 min and filtered through a short silica gel layer, a green fraction being collected. The solution was concentrated *in vacuo* (the bath temperature was ≤ 25 °C). The product was purified by column chromatography (silica gel, CH_2Cl_2 as the eluent), and a blue fraction was collected. Nitrosopyridine **2** was obtained in a yield of 12.3 g (86%), m.p. 85—89 °C. After recrystallization from EtOH, m.p. 90—90.5 °C. Found (%): C, 41.80; H, 2.24; N, 19.50. $C_5H_3ClN_2O$. Calculated (%): C, 42.13; H, 2.12; N, 19.65. ^{1}H NMR (monomer) (298 K, $CDCl_3$), δ: 6.55 (dd, 1 H, H(4), J = 7.9 Hz, J = 1.9 Hz); 7.36 (dd, 1 H, H(5), J = 7.9 Hz, J = 4.6 Hz); 8.78 (dd, 1 H, H(6), J = 4.6 Hz, J = 1.9 Hz).

4-Ethoxy-3-nitrosopyridine (6). Nitrosopyridine **6** was prepared according to an analogous procedure from hydroxylaminopyridine **5** (16.0 g, 0.1 mol). The yield was 13.6 g (82%), m.p. 96—96.5 °C. Found (%): C, 50.03; H, 5.43; N, 18.19. $C_7H_8N_2O_2$. Calculated (%): C, 55.26; H, 5.30; N 18.41. ^{1}H NMR (monomer) (298 K, methanol-d_4), δ: 1.50 (t, 3 H, Me); 4.23 (q, 2 H, CH_2); 7.53 (d, 1 H, H(5), J = 4.9 Hz); 7.65 (s, 1 H, H(2)); 8.53 (d, 1 H, H(6), J = 4.9 Hz). ^{1}H NMR (dimer) (203 K, methanol-d_4), δ: 1.50 (t, 3 H, CH_3); 4.17 (q, 2 H, CH_2); 7.16 (d, 1 H, H(5), J = 4.5 Hz); 8.47 (d, 1 H, H(6), J = 4.9 Hz); 8.80 (s, 1 H, H(2)).

3-(*tert*-Butyl-*NNO*-azoxy)-2-chloropyridine (3). *N*,*N*-dibromo-*tert*-butylamine (26.6 g, 0.15 mol) was added with stirring to a solution of nitrosopyridine **2** (14.3 g, 0.1 mol) in CH_2Cl_2 (360 mL) at ~20 °C. After completion of the reaction (5—6 h, TLC control), the reaction mixture was washed with 5% aqueous ammonia (to decompose an excess of *N*,*N*-dibromo-*tert*-butylamine) and water. The solvent was distilled off *in vacuo*. The residue was dissolved in 15% hydrochloric acid (100 mL), decolorized with activated carbon (1.5 g), and slowly diluted with water (300 mL) on cooling. The crystals that formed were separated, washed with water, and dried *in vacuo*. Azoxypyridine **3** was obtained in a yield of 18.6 g (85%), m.p. 53—54 °C. After recrystallization from EtOH, m.p. 55—55.5 °C. Found (%): C, 51.30; H, 5.20; N, 20.10. $C_9H_{12}ClN_3O$. Calculated (%): C, 50.59; H, 5.66; N, 19.67. ^{1}H NMR ($CDCl_3$), δ: 1.49 (s, 9 H, 3 Me); 7.37 (dd, 1 H, H(5)); 7.81 (dd, 1 H, H(4), J = 7.8 Hz, J = 1.8 Hz); 8.47 (dd, 1 H, H(6), J = 4.7 Hz, J = 1.7 Hz). ^{13}C NMR ($CDCl_3$), δ: 25.4 (Me); 60.5 (CMe_3); 122.9 (dd, C(5), J = 169 Hz, J = 8.6 Hz); 132.7 (ddd, C(4), J = 166 Hz, J = 7.1 Hz, J = 1.8 Hz); 143.4 (ddd, C(2), J = 14.4 Hz, J = 7.6 Hz, J = 1.7 Hz); 144.4 (ddd, C(3), J = 8.4 Hz, J = 2.8 Hz, J = 2.0 Hz); 149.7 (ddd, C(6), J = 185 Hz, J = 8.3 Hz, J = 3.4 Hz). ^{14}N NMR ($CDCl_3$), δ: −54 (N(O), $\Delta\nu_{1/2}$ = 65 Hz).

3-(*tert*-Butyl-*NNO*-azoxy)-4-ethoxypyridine (7). The reaction of nitrosopyridine **6** (15.2 g, 0.1 mol) with *N*,*N*-dibromo-*tert*-butylamine (26.6 g, 0.15 mol) was carried out as described above. The reaction solution was washed with an ammonia solution and water, filtered through a short silica gel layer, and concentrated *in vacuo* to prepare azoxypyridine **7** as a yellowish oil in a yield of 18.3 g (82%). An analytically pure sample was obtained by chromatographic purification (silica gel, CH_2Cl_2 as the eluent). Found (%): C, 59.23; H, 7.53; N, 18.85. $C_{11}H_{17}N_3O_2$. Calculated (%): C, 59.17; H, 7.67; N, 18.82. ^{1}H NMR ($CDCl_3$), δ: 1.44 (t, 3 H, Me); 1.48 (s, 9 H, 3 Me); 4.17 (q, 2 H, CH_2); 6.90 (d, 1 H, H(5), J = 5.87 Hz); 8.46 (d, 1 H, H(6)); 8.55 (s, 1 H, H(2)).

Synthesis of azoxypyridines 3 and 7 from hydroxylaminopyridines (general procedure). *N*,*N*-Dibromo-*tert*-butylamine (5.31 g, 30 mmol) was added in one portion with stirring to a suspension of hydroxylaminopyridine (10 mmol) in CH_2Cl_2 (30 mL) at −10 °C. The reaction mixture was stirred at the same temperature for 1 h, during which hydroxylaminopyridine was dissolved and the nitroso compound precipitated followed by dissolution of the precipitate. Then the solution was kept at ~20 °C for 5—6 h until the reaction was completed (TLC control), the solvent was distilled off *in vacuo*, and the residue was purified by chromatography (silica gel, CH_2Cl_2 as the eluent).

3-(*tert*-Butyl-*NNO*-azoxy)-2-chloropyridine (3) from hydroxylaminopyridine 1. Azoxypyridine **3** was synthesized from hydroxylaminopyridine **1** (1.45 g) in a yield of 1.39 g (65%). The product was identical (m.p. and ^{1}H NMR spectra) to the sample prepared earlier.

3-(*tert*-Butyl-*NNO*-azoxy)-4-ethoxypyridine (7) from hydroxylaminopyridine 5. Azoxypyridine **7** was synthesized from hydroxylaminopyridine **5** (1.54 g) in a yield of 1.20 g (54%). The product was identical (m.p. and ^{1}H NMR spectra) to the sample prepared earlier.

2-Amino-3-(*tert*-butyl-*NNO*-azoxy)pyridine (4). A mixture of azoxypyridine **3** (5 g, 23.4 mmol) and 25% ammonia (100 mL) was heated in an autoclave at 150—180 °C for 10 h. Then the reaction mixture was cooled to 0 °C. The crystals were filtered off, dissolved in 10% hydrochloric acid (50 mL), filtered off from unconsumed compound **3**, decolorized with activated carbon, cooled to 0 °C, and saturated with gaseous ammonia. The crystals that formed were filtered off and dried *in vacuo*. Aminoazoxypyridine **4** was obtained in a yield of 3.9 g (92%), m.p. 104—105 °C. After recrystallization from octane, m.p. 105—106 °C. Found (%): C, 55.80; H, 7.40; N, 28.70. $C_9H_{14}N_4O$. Calculated (%): C, 55.65; H, 7.26; N 28.85.

4-Amino-3-(*tert*-butyl-*NNO*-azoxy)pyridine (8). Aminoazoxypyridine **8** was prepared in a yield of 3.70 g (85%) from azoxypyridine **7** (5.0 g, 22.4 mmol) according to an analogous procedure, m.p. 158—159 °C. Found (%): C, 55.61; H, 7.290; N, 29.13. $C_9H_{14}N_4O$. Calculated (%): C, 55.65; H, 7.26; N, 28.85.

Reaction of 2-amino-3-(*tert*-butyl-*NNO*-azoxy)pyridine (4) with N_2O_5. Dinitrogen pentoxide (8.0 g, 74 mmol) and aminoazoxypyridine **4** (2.0 g, 10.3 mmol) were successively added with stirring to dry acetonitrile (100 mL) at −20 °C. The reaction mixture was stirred at the same temperature for 30 min and then at a temperature from 0 to −5 °C for 1.5 h. Then the mixture was diluted with dichloromethane (100 mL), and ice (30 g) was added. The organic layer was separated and washed with water. The aqueous layer was extracted with dichloromethane

(3×50mL). The combined extracts were washed with a 5% aqueous $NaHCO_3$ solution (20 mL) and dried with $MgSO_4$. The solvent was distilled off *in vacuo*, the residue was washed with Et_2O (10 mL), and the products were separated by chromatography (silica gel, a 1 : 1 EtOAc/$CHCl_3$ mixture as the eluent) to give pyrido[2,3-*e*][1,2,3,4]tetrazine 1,3-dioxide (**9**) and 7-nitropyrido[2,3-*e*][1,2,3,4]tetrazine 1,3-dioxide (**10**) were obtained in yields of 0.357 g (21%) and 0.855 g (39%), respectively.

Pyrido[2,3-*e*][1,2,3,4]tetrazine 1,3-dioxide (9). Yellow crystals, m.p. 228—229 °C (from EtOH). Found (%): C, 36.43; H, 1.92; N, 42.49. $C_5H_3N_5O_2$. Calculated (%): C, 36.37; H, 1.83; N, 42.42. MS, m/z : 165 $[M]^+$.

7-Nitropyrido[2,3-*e*][1,2,3,4]tetrazine 1,3-dioxide (10). Yellow crystals, m.p. 189—190 °C (from EtOH). Found (%): C, 28.63; H, 1.03; N, 40.64. $C_5H_2N_6O_4$. Calculated (%): C, 28.58; H, 0.96; N, 40.00. MS, m/z : 210 $[M]^+$.

Pyrido[3,4-*e*][1,2,3,4]tetrazine 2,4-dioxide (11). Nitronium tetrafluoroborate (7.0 g, 53.6 mmol) was added with stirring to a solution of aminodiazine oxide **8** (2.0 g, 10.3 mmol) in dry MeCN (100 mL) at −20 °C. The reaction mixture was allowed to warm to 20 °C and then stirred for 4 h, after which the mixture was cooled to 0 °C and Et_2O (40 mL) was added. The resulting mixture was washed with a 10% aqueous $KHCO_3$ solution and water and dried with $MgSO_4$. The solvent was distilled off *in vacuo*. Crystallization of the residue from EtOH afforded tetrazine dioxide **11** in a yield of 1.17 g (69%) as yellow crystals, m.p. 179—180 °C. Found (%): C, 36.32; H, 1.90; N, 42.30. $C_5H_3N_5O_2$. Calculated (%): C, 36.37; H, 1.83; N 42.42. MS, m/z : 165 $[M]^+$.

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