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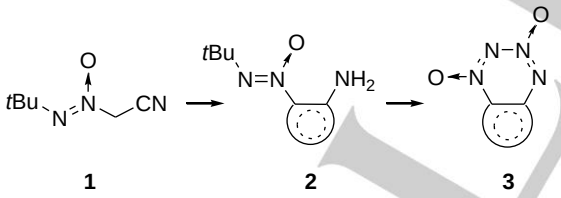
Intramolecular Reaction of *tert*-Butyl-*NNO*-azoxy and Cyano Groups. Novel Synthesis of Pyridazine, 1,2,3-Triazepine and Furan rings

Oleg V. Anikin,[a] Michael S. Klenov,*[a] Aleksandr M. Churakov,*[a] Alexey A. Guskov,[a] Yurii A. Strelenko,[a] Konstantin A. Lyssenko[b] and Vladimir A. Tartakovsky[a]

Abstract: A reaction of (*tert*-butyl-*NNO*-azoxy)acetonitrile with *N,N*-dimethylacetamide dimethylacetal afforded 2,4-bis(*tert*-butyl-*NNO*-azoxy)-3-methylpent-2-enedinitrile **9** as a main product. This compound cyclized on silica gel surface with the loss of isobutylene to give 6-amino-5-(*tert*-butyl-*NNO*-azoxy)-4-methylpyridazine-3-carbonitrile 2-oxide **10**. Contrary, the cyclization of dinitrile **9** in protic solvents resulted in quite different products, furan, 1,2,3-triazepine and pyridazine derivatives were among them. These reactions are the first examples of intramolecular reactions of (*tert*-butyl-*NNO*-azoxy) and cyano groups. The structures of products under investigation were confirmed by X-ray diffraction analysis.

Introduction

Unsaturated cyclic high nitrogen *N*-oxide systems show considerable promise as a new generation of high energy density materials (HEDM)[1] and 1,2,3,4-tetrazine 1,3-dioxides (TDOs) are among them.[2,3] A general synthetic approach to TDOs **3** includes a cyclization of aromatic compounds **2** bearing adjacent amino and (*tert*-butyl-*NNO*-azoxy) groups (Scheme 1).

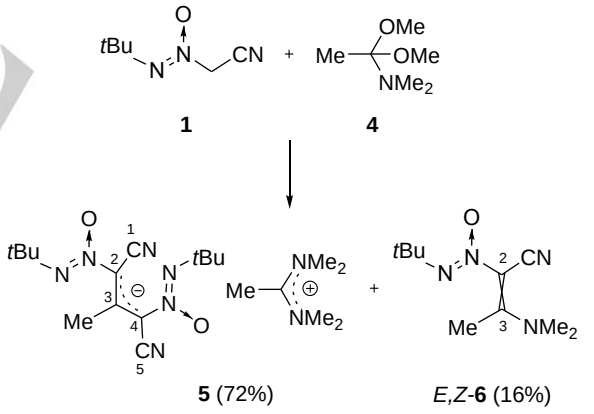


Scheme 1. Nitrile **1** as a precursor for heteroannulated 1,2,3,4-tetrazine 1,3-dioxides **3**.

In the benzene series, the synthesis of these compounds is well developed,[4-7] while for heterocycles it is of challenge and difficulty. Recently obtained (*tert*-butyl-*NNO*-azoxy)acetonitrile (**1**)[8] opened new perspectives for the synthesis of compounds **2**. Aryl substituted 4-amino-5-(*tert*-butyl-*NNO*-azoxy)-1,2,3-triazoles[9] have been already obtained starting from nitrile **1**. Now we report a new synthetic application of this reagent.

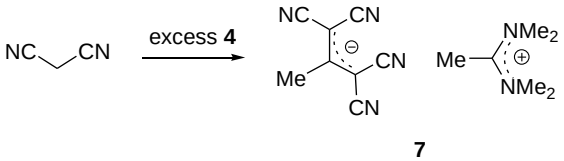
Results and Discussion

In the course of our search for methods of synthesis of heterocyclic compounds **2**, the reaction of nitrile **1** (1 equiv.) with *N,N*-dimethylacetamide dimethylacetal (**4**) (1 equiv.) was investigated. When this reaction was carried out without solvent, salt **5** was the main product (72%) along with an equilibrium mixture of isomeric enamines **6** (16%) (Scheme 2).



Scheme 2. Reaction of nitrile **1** with *N,N*-dimethylacetamide dimethylacetal (**4**).

The reaction investigated is similar to the published synthesis of salt **7** from malononitrile and excess acetal **4** (Scheme 3).[10]



Scheme 3. Reaction of malononitrile with *N,N*-dimethylacetamide dimethylacetal (**4**).[10]

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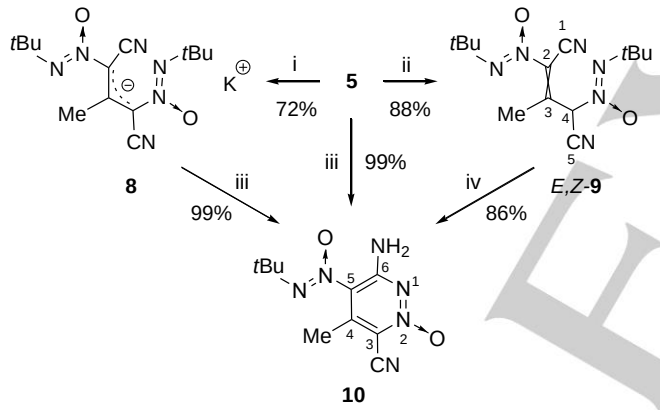
The treatment of salt **5** with cation-exchange resin Amberlyst-15 in K^+ form provided K-salt **8**. Both of these salts are stable in solid state and in acetone solutions. Dinitrile **9** was obtained after careful acidification of salt **5** with 1 N HCl to pH 5 followed by extraction with pentane and removing the solvent in vacuo at room temperature. The ^1H and ^{13}C NMR spectra show that in $CDCl_3$ solutions this compound exists as an equilibrium mixture of *E*/*Z* isomers in 4 : 1 ratio (see below for details).

Dinitrile **9** is not quite stable. When kept in diluted $CHCl_3$ solution (3 g/L) at room temperature for 28 h, it afforded pyridazine oxide **10** in 86% yield (Scheme 4, Table 1). When this reaction was monitored by ^1H NMR spectroscopy in $CDCl_3$ as a solvent (30 g/L), isobutylene was observed [δ = 1.73 (s, 6 H, Me), 4.66 (s, 2 H, CH_2) ppm]. Volatile components were removed in vacuo and condensed in a cooled trap (–196 °C). Isobutylene was identified by comparison with authentic sample (^1H NMR).

A simple procedure for the preparation of pyridazine oxide **10** was found. Silica gel was added to a solution of salts **5** or **8** in MeOH, the solvent was evaporated, the residue was kept at room temperature for 1 hour and then the product was eluted from silica gel. The yield of pyridazine oxide **10** was almost quantitive.



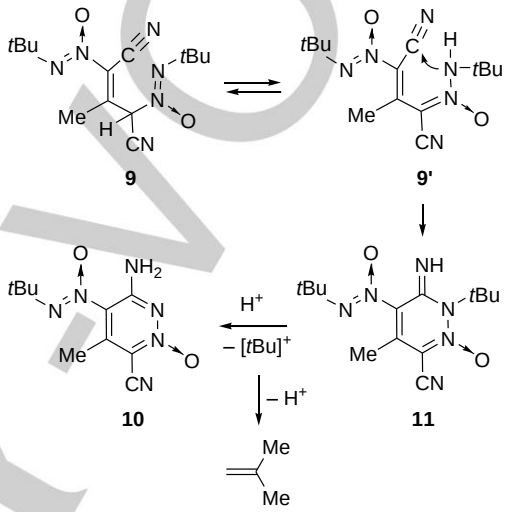
Scheme 4. Reactions of salt **5**. Reagents and conditions: (i) Amberlyst 15 (K^+ form), MeOH; (ii) 1 N HCl, H_2O, 0–5 °C; (iii) Silica gel, 25 °C, 1 h; (iv) $CHCl_3$, 25 °C, 28 h.

Table 1. Solvolysis of dinitrile **9** (see Schemes 4 and 6).

Entry	Solvent	Conc. of **9**, g/L	T, h	Yield, %			
				10	**12**	**13**	**14**
1	$CHCl_3$	3	28	86	2	2	2
2	$CDCl_3$	30	24	49	12	10	10
3	MeOH	3	0.25	1	55	18	22
4	MeCN	30	24	12	24	18	26
5	MeCN/ Me_2NH[a]	30	48	46	0	0	0

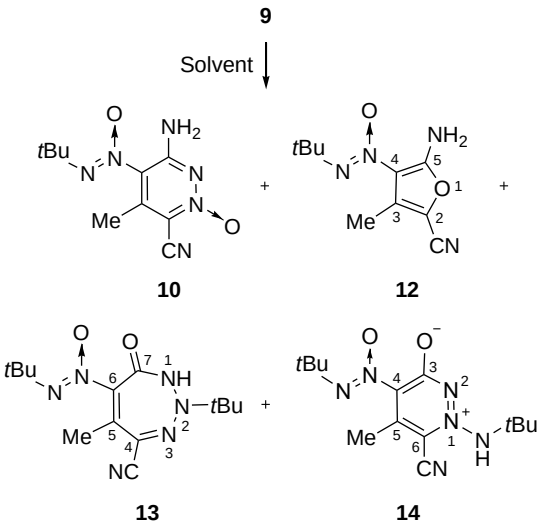
[a] The reaction afforded pyridazinimine **15** (15%) and unidentified products.

Presumably dinitrile **9** could exist in its tautomeric form **9'** to some extent. A plausible mechanism of formation of pyridazine oxide **10** (Scheme 5) involves cyclization of tautomer **9'** to afford intermediate **11**, its protonation and following loss of *tert*-butyl cation. The latter should give isobutylene after deprotonation. We failed to observe intermediate **11** when monitoring the reaction by ^1H NMR spectroscopy. Thus the loss of *tert*-butyl cation was a rather fast process. For trapping intermediate **11** by its reaction with Me_2NH see below (Scheme 8).



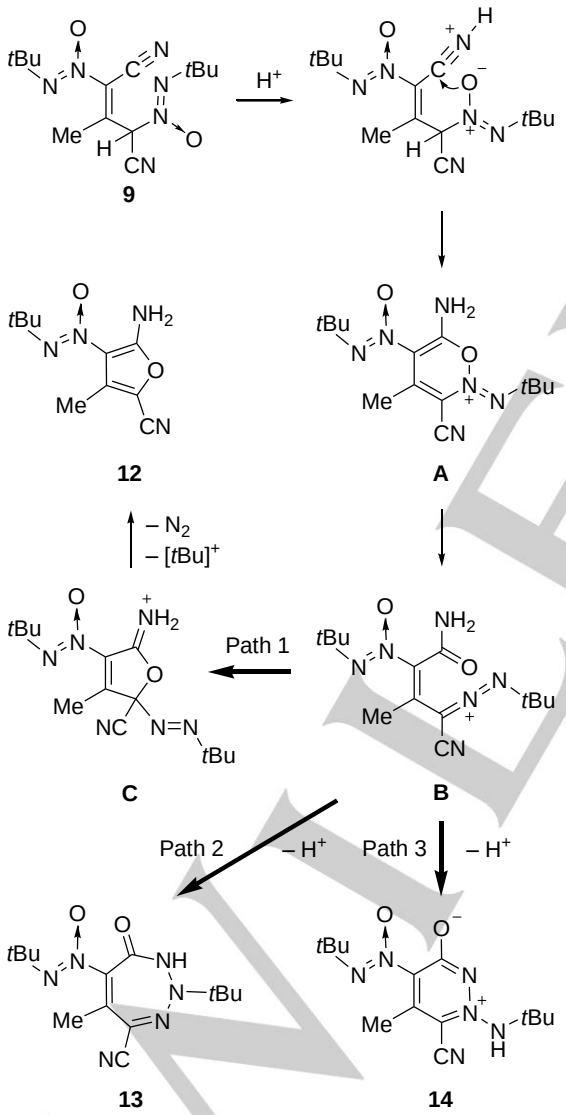
Scheme 5. Plausible mechanism for the formation of pyridazine oxide **10**.

The solvolysis of dinitrile **9** in MeOH as a solvent practically did not afford pyridazine oxide **10**. Its yield did not exceed 1%. The main product was furan **12** (55%). The other two products were triazepine **13** (18%) and zwitter-ionic cycle **14** (22%) (Scheme 6, Table 1).



Scheme 6. Solvolysis of dinitrile **9** (see Table 1).

The following tentative mechanism is proposed to explain the formation of these unexpected products (Scheme 7). Protonation of the cyano group of dinitrile **9** followed by attack of this group by an oxygen atom of the azoxy group would afford cyclic cation **A**. Ring opening of the latter could give cation **B**, which bears carboxamide group and $[C=N=N\textit{t}Bu]^+$ cation. This cation could undergo recyclization in three reaction pathways. Pathway 1: oxygen atom of the carboxamide group attacks carbon atom of the $[C=N=N\textit{t}Bu]^+$ moiety to give intermediate **C**, which eliminates the N_2 molecule and *tert*-butyl cation to furnish furan **12**. Pathway 2: nitrogen atom of the carboxamide group attacks the terminal N atom in the $[C=N=N\textit{t}Bu]^+$ moiety to yield triazepine **13**. Pathway 3: Nitrogen atom of the carboxamide group attacks the central N atom in the $[C=N=N\textit{t}Bu]^+$ moiety to give zwitter-ionic cycle **14**.



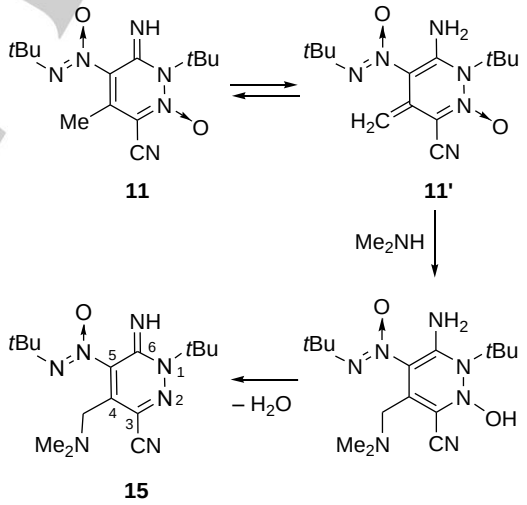
Scheme 7. Plausible mechanism for solvolysis of dinitrile **9**.

Most likely, this mechanism also takes place to some extent in concentrated solutions of dinitrile **9** in the $CDCl_3$ solutions (30 g/L) due to intramolecular protonation. Dinitril **9** as a strong CH-acid can play the role of proton donor. The yield of pyridazine oxide **10** decreased to 49% as compared with the reaction in diluted solutions (3 g/L) and the yields of compounds **12**, **13** and **14** increased (see Table 1).

When the solvolysis of dinitrile **9** was carried out in a polar aprotic solvent such as MeCN, the yield of pyridazine oxide **10** dropped to 12% and the yields of compounds **12**, **13** and **14** increased significantly (see Table 1).

When the solvolysis of dinitrile **9** in MeCN was carried out in presence of 1 equiv. of Me_2NH, compounds **12**, **13** and **14** were not observed at all. The main reaction products were pyridazine oxide **10** (46%) and pyridazinimine **15** (15%) (Scheme 8). In this reaction conditions the most part of dinitrile **9** exist as the dimethylammonium salt. The concentration of the H-form of dinitrile **9** is very low and its intermolecular protonation is practically excluded. This experiment demonstrated the important role of acidic protons in the formation of compounds **12**, **13** and **1**4 (see Scheme 7 above).

The plausible mechanism for the formation of pyridazinimine **15** (Scheme 8) involves rearrangement of compound **11** to its tautomer **11'**, the Michael addition of dimethyl amine and elimination of H_2O. In fact, we trapped intermediate **11** by its reaction with Me_2NH (see Scheme 5 above).



Scheme 8. Plausible mechanism for the formation of pyridazinimine **15** from intermediate **11** and Me_2NH.

We did not find the examples of an intramolecular reaction of the azoxy and cyano groups in literature. At the same time, the nitro group is isoelectronic to the azoxy group and could demonstrate similar reactivity. Actually, the closely related intramolecular reactions of the nitro and the cyano groups were described.[11,12] These reactions involve the transfer of oxygen atom from the nitro group to the cyano group with formation of the carboxamide moiety followed by cyclization reactions.

Besides that, the intramolecular reaction of the *N*-nitro and the cyano groups is known, which affords 4-hydroxy-1,2,3-triazine 2-oxides.[13,14] In the course of this reaction, the cyano group is also transformed to carboxamide group followed by cyclization.

The structures of salt **5**, pyridazine oxide **10**, furan **12**, triazepine **13**, zwitter-ionic cycle **14** and pyridazinimine **15** were confirmed by X-ray diffraction (XRD) of suitable single crystals (Figures 1-6).

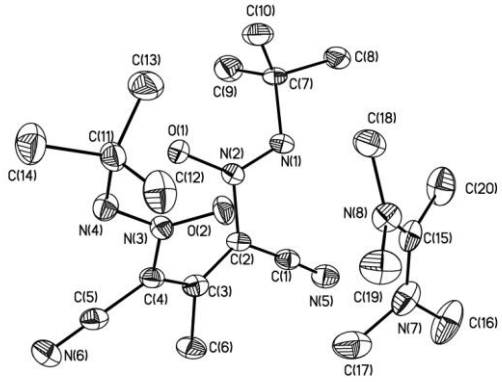


Figure 1. General view of salt **5** in a crystal in representation of non-hydrogen atoms by probability ellipsoids of atomic displacements (p=50%). The hydrogen atoms of methyl groups are omitted for clarity.

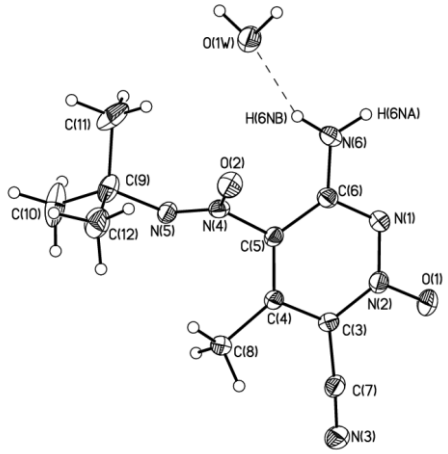


Figure 2. General view of pyridazine oxide **10** in a crystal in representation of non-hydrogen atoms by probability ellipsoids of atomic displacements (p=50%).

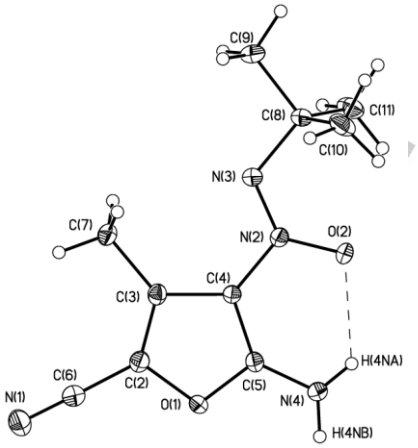


Figure 3. General view of furan **12** in a crystal in representation of non-hydrogen atoms by probability ellipsoids of atomic displacements (p=50%).

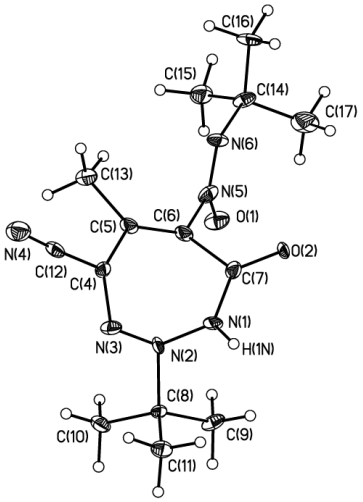


Figure 4. General view of triazepine **13** in a crystal in representation of non-hydrogen atoms by probability ellipsoids of atomic displacements (p=50%).

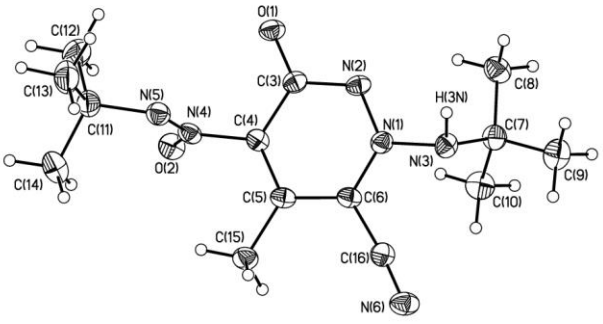


Figure 5. General view of zwitter-ionic cycle **14** in a crystal in representation of non-hydrogen atoms by probability ellipsoids of atomic displacements (p=50%).

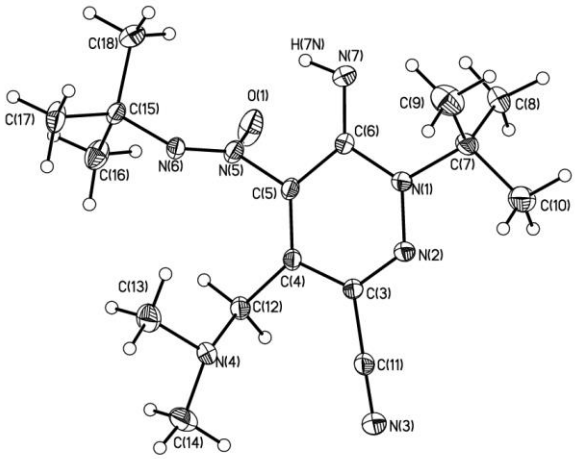


Figure 6. General view of pyridazinimine **15** in a crystal in representation of non-hydrogen atoms by probability ellipsoids of atomic displacements (p=50%).

Signals in the ^{1}H and ^{13}C NMR spectra of the synthesized compounds were attributed by using 2D correlation experiments (^{1}H–^{13}C HSQC and HMBC). The assignments in the ^{13}C NMR spectra were performed taking into account a significant broadening of the signal from the C atom directly bonded to the *N*-oxide fragment of the pyridazine 2-oxide cycle or *tert*-butyl-*NNO*-azoxy group resulting from the spin-spin coupling of the ^{13}C and ^{14}N nuclei in particular.

^{14}N NMR spectroscopy is especially useful for identifying positively charged nitrogen atoms in *tert*-butyl-*NNO*-azoxy group. The ^{14}N NMR spectra of compounds **5-6** and **8-15** bearing the *tert*-butyl-*NNO*-azoxy group showed signals at δ = –45 to –62 ppm [*N*(O)=N*t*Bu, $\Delta\nu_{1/2}$ = 110–620 Hz]. The IR spectrum of these compounds showed strong absorption bands at 1541 to 1595 cm^{-1} that corresponded to stretching vibrations of the *tert*-butyl-*NNO*-azoxy group. The HRMS spectra of compounds **6**, **10**, **12-15** showed peaks of molecular ions.

Conclusions

2,4-Bis(*tert*-butyl-*NNO*-azoxy)-3-methylpent-2-enedinitrile (**9**) was synthesized and its cyclization reactions were investigated. The key stage of these cyclizations is a novel intramolecular reaction of *tert*-butyl-*NNO*-azoxy and cyano groups. Dinitrile **9** absorbed on silica gel cyclized with the loss of isobutylene to give 6-amino-5-(*tert*-butyl-*NNO*-azoxy)-4-methylpyridazine-3-carbonitrile 2-oxide (**10**). Contrary, in MeOH cyclization, resulted in furan, 1,2,3-triazepine and pyridazine derivatives. This reaction provided a new synthetic route to heterocycles bearing adjacent amino and (*tert*-butyl-*NNO*-azoxy) groups. Two of them, i.e., pyridazine oxide **10** and furan **12**, were isolated. Their cyclization to 1,2,3,4-tetrazine 1,3-dioxides is under investigation.

Experimental Section

General Remarks: ^{1}H, ^{13}C and ^{14}N NMR spectra were recorded with Bruker DRX-500 (500.1, 125.8, 36.1 MHz, respectively) and Bruker AV600 (600.1, 150.9, 43.4, respectively) spectrometers. *Chemical shifts* are reported in delta (*δ*) *units*, parts per million (ppm) downfield from internal TMS (^{1}H, ^{13}C) or external CH_3NO_2 (^{14}N, negative values of δ_N correspond to upfield shifts). The IR spectra were recorded with a Bruker ALPHA-T spectrometer in the range 400–4000 cm^{-1} (resolution 2 cm^{-1}) as pellets with KBr or as a thin layer. Low-resolution mass spectra were recorded with a Varian MAT-311A instrument (EI, 70 eV). High-resolution ESI mass spectra (HRMS) were recorded with a Bruker micrOTOF II instrument. Melting points were determined with a Kofler melting point apparatus and are uncorrected. Silica gel 60 Merck (15–40 μm) was used for preparative column chromatography. Silica gel «Silpearl UV 254» was used for preparative thin-layer chromatography. Analytical thin-layer chromatography (TLC) was carried out on Merck silica gel 60 F254. All reagents were purchased from Acros and Sigma-Aldrich. *Solvents were purified* before use, according to standard procedures. All other reagents were used without further purification. (*tert*-Butyl-*NNO*-azoxy)acetonitrile (**1**) was prepared according to the reported procedure.[8]

The crystal data and structure-refinement parameters for compounds **5**, **10** and **12-15** can be found in the Supporting Information, Table S1. Structures were deposited to Cambridge Structural Database, CCDC 1845524 (for **5**), 1572578 (for **10**), 1845523 (for **12**), 1845525 (for **13**), 184552 (for **14**) and 1572579 (for 1**5**) contain the supplementary crystallographic data for this paper. These data can be obtained free of charge viahttp://www.ccdc.cam.ac.uk/data_request/cif, or by e-mailing data_request@ccdc.cam.ac.uk, or by contacting The Cambridge Crystallographic Data Centre, 12 Union Road, Cambridge CB2 1EZ, UK; fax: +44(0)1223-336033.

Reaction of (*tert*-Butyl-*NNO*-azoxy)acetonitrile (1) with Dimethylacetamide Dimethyl Acetal (4); Synthesis of *N*-[1-(Dimethylamino)ethylidene]-*N*-methylmethanaminium Salt of 2,4-Bis(*tert*-butyl-*NNO*-azoxy)-3-methylpent-2-enedinitrile (5) and 2-(*tert*-Butyl-*NNO*-azoxy)-3-(dimethylamino)but-2-enenitrile (6): *N*,*N*-Dimethylacetamide dimethyl acetal (**4**) (90% by weight) (576 mg, 3.9 mmol) was added to a stirred (*tert*-butyl-*NNO*-azoxy)acetonitrile (**1**) (423 mg, 3.0 mmol) at 0–5 °C. The reaction mixture was stirred for 10 min at 0–5 °C, then was warmed to 20 °C for 15 min and Et_2O (5 mL) was added. The resulting mixture was stirred for 5 min and precipitate was formed. The precipitate was then filtered off, washed with Et_2O (2 × 5 mL) and air-dried to give salt **5** (454 mg, 72%) as a yellow solid. The combined filtrates were concentrated under reduced pressure and the residue was purified by preparative thin-layer chromatography (petroleum ether/ethyl acetate, 2:1) to give enamine **6** (101 mg, 16%) as a white solid.

***N*-[1-(Dimethylamino)ethylidene]-*N*-methylmethanaminium Salt of 2,4-Bis(*tert*-butyl-*NNO*-azoxy)-3-methylpent-2-enedinitrile (5):** Yellow crystals (recrystallization from *t*BuOMe); m.p. 115–117 °C. ^{1}H NMR (500.1 MHz, $CDCl_3$): *δ* = 1.31 (s, 9 H, CMe_3), 2.22 (s, 3 H, Me), 2.45 [s, 3 H, Me (amidinium)], 3.27 (s, 12 H, both NMe_2) ppm. ^{13}C NMR (125.8 MHz, $CDCl_3$): *δ* = 18.9 [Me (amidinium)], 21.0 (br., Me), 26.8 (CMe_3), 43.5 (NMe_2), 57.8 (CMe_3), 100.2 (br., C-2 and C-4), 120.9 (CN), 142.3 (br., C-3), 171.5 (C=NMe_2) ppm. ^{14}N NMR (36.1 MHz, $CDCl_3$): *δ* = –45 [*N*(O)=N*t*Bu, $\Delta\nu_{1/2}$ = 620 Hz], –286 (NMe_2, $\Delta\nu_{1/2}$ = 2500 Hz) ppm. IR (KBr): ν = 2965 (m), 2926 (w), 2360 (m), 2342 (w), 2171 (s), 1629 (s), 1542 (s), 1427 (m), 1297 (m), 1218 (m) cm^{-1}. Elemental analysis: calcd. for $C_{20}H_{36}N_8O_2$: C, 57.12; H, 8.63; N, 26.64; found C, 57.01; H, 8.68; N, 26.24

(*E,Z*)-2-(*tert*-Butyl-*NNO*-azoxy)-3-(dimethylamino)but-2-enenitrile (6): Colorless crystals (recrystallization from cyclohexane); m.p. 65–67 °C. NMR spectra of enamine **6** show two *E*/*Z* isomers with respect to the C=N bond. The (*E*)-**6** : (*Z*)-**6** isomer ratio was 1.8 : 1 in $CDCl_3$.

Compound (*E*)-6: ^{1}H NMR (500.1 MHz, $CDCl_3$): δ = 1.37 (s, 9 H, CMe_3), 2.27 (s, 3 H, Me), 3.03 (s, 6 H, NMe_2) ppm. ^{13}C NMR (125.8 MHz, $CDCl_3$): δ = 20.3 (Me), 25.7 (C*Me*$_3$), 42.2 (NMe_2), 58.9 (*C*Me_3), 100.1 (br., C-2), 118.8 (CN), 156.8 (C-3) ppm.

Compound (*Z*)-6: ^{1}H NMR (500.1 MHz, $CDCl_3$): δ = 1.37 (s, 9 H, CMe_3), 2.23 (s, 3 H, Me), 3.22 (s, 6 H, NMe_2) ppm. ^{13}C NMR (125.8 MHz, $CDCl_3$): δ = 18.3 (Me), 25.7 (C*Me*$_3$), 42.9 (NMe_2), 59.3 (*C*Me_3), 102.0 (br., C-2), 117.3 (CN), 162.5 (C-3) ppm. ^{14}N NMR (36.1 MHz, $CDCl_3$): δ = –51 [*N*(O)=N*t*Bu, $\Delta\nu_{1/2}$ = 140 Hz] ppm. IR (KBr): ν = 2977 (m), 2936 (w), 2191 (s), 1589 (s), 1432 (s), 1373 (m), 1357 (s), 1293 (s), 1232 (m) cm^{-1}. HRMS (ESI): *m/z* calcd for $C_{10}H_{18}N_4O$ $[M + H]^+$ 211.1553, found 211.1554.

Potassium Salt of 2,4-Bis(*tert*-butyl-*NNO*-azoxy)-3-methylpent-2-enedinitrile (8): A solution of salt **5** (630 mg, 1.5 mmol) in MeOH (4 mL) was put on a column packed with Amberlyst 15 (K^+ form), (20.0 g) and absorbed material was eluted with MeOH (200 mL) until potassium salt **8** disappeared in the eluate (TLC control). The eluate was concentrated under reduced pressure, the residue was washed with CH_2Cl_2 (50 mL) and air-dried to give potassium salt **8** (375 mg, 72%) as a yellow solid, m.p. 231–233 °C (decomp.). ^{1}H NMR (600.1 MHz, [D_4]methanol): δ = 1.32 (s, 9 H, CMe_3), 2.22 (s, 3 H, Me) ppm. ^{13}C NMR (150.8 MHz, [D_4]methanol): δ = 21.1 (Me), 27.2 (C*Me*$_3$), 59.0 (*C*Me_3), 101.3 (br., C-2 and C-4), 121.3 (CN), 143.1 (br., C-3) ppm. ^{14}N NMR (43.4 MHz, [D_4]methanol): δ = –46 [*N*(O)=N*t*Bu, $\Delta\nu_{1/2}$ = 260 Hz] ppm. IR (KBr): ν = 2973 (m), 2924 (w), 2205 (m), 2178 (s), 1541 (s), 1438 (s), 1360 (w), 1305 (w), 1275 (m), 1225 (m) cm^{-1}. Elemental analysis: calcd. for $C_{14}H_{21}N_8O_2K$: C, 48.82; H, 6.15; N, 24.40; found C, 48.73; H, 6.19; N, 23.91.

2,4-Bis(*tert*-butyl-*NNO*-azoxy)-3-methylpent-2-enedinitrile (9): A solution of salt **5** (420 mg, 1 mmol) in H_2O (35 mL) was acidified to pH ≈ 5 with aqueous 1 N HCl at 0–5 °C and then extracted with pentane (3 × 10 mL). The combined organic extracts were dried (Na_2SO_4) at 0–5 °C for 15 min and concentrated under reduced pressure at 20 °C to give dinitrile **9** (270 mg, 88%) as yellow viscous oil. Two E/Z isomers with respect to the C=C bond [the isomer ratio (*E*)-**9**/(*Z*)-**9** = 4:1 (in $CDCl_3$)].

Compound (*E*)-**9:** ^{1}H NMR (600.1 MHz, $CDCl_3$): δ = 1.35 (s, 9 H, CMe_3), 1.42 (s, 9 H, CMe_3), 2.43 (s, 3 H, Me), 7.30 (s, 1 H, H-4) ppm. ^{13}C NMR (150.9 MHz, $CDCl_3$): δ = 18.5 (Me), 25.1 (C*Me*$_3$), 25.3 (C*Me*$_3$), 61.0 (*C*Me_3), 61.4 (*C*Me_3), 68.7 (br., C-4), 110.7 (CN), 110.9 (CN), 128.0 (br., C-2), 141.3 (C-3) ppm.

Compound (*Z*)-**9:** ^{1}H NMR (600.1 MHz, $CDCl_3$): δ = 1.38 (s, 9 H, CMe_3), 1.42 (s, 9 H, CMe_3), 2.30 (s, 3 H, Me), 6.10 (s, 1 H, H-4) ppm. ^{13}C NMR (150.9 MHz, $CDCl_3$): δ = 14.9 (Me), 25.1 (C*Me*$_3$), 25.3 (C*Me*$_3$), 61.2 (*C*Me_3), 61.3 (*C*Me_3), 73.3 (br., C-4), 110.1 (CN), 110.4 (CN), 128.4 (br., C-2), 141.8 (C-3) ppm. ^{14}N NMR (43.4 MHz, $CDCl_3$): δ = –62 [*N*(O)=N*t*Bu, $\Delta\nu_{1/2}$ = 140 Hz] ppm.

6-Amino-5-(*tert*-butyl-*NNO*-azoxy)-4-methylpyridazine-3-carbonitrile 2-oxide (10): Silica gel 60 (Merck; 40–63 µm; 10.0 g) was added to a solution of salt **5** (420 mg, 1 mmol) in MeOH (20 mL), and the solvent was removed under reduced pressure. The residue was kept at 25 °C for 1 h, then it was transferred onto a Schott filter, and eluted with MeOH (100 mL). The eluate was concentrated under reduced pressure to give pyridazine oxide **10** (247 mg, 99%) as colorless crystals. An analytical sample of pyridazine oxide **10** was obtained by recrystallization from EtOH as colorless crystals, m.p. 214–215 °C. ^{1}H NMR (500.1 MHz, [D_6]acetone): δ = 1.49 (s, 9 H, CMe_3), 2.41 (s, 3 H, Me), 6.95 (br., 2 H, NH_2) ppm. ^{13}C NMR (125.8 MHz, [D_6]acetone): δ = 15.6 (Me), 25.8 (C*Me*$_3$), 61.4 (*C*Me_3), 111.9 (CN), 114.5 (br., C-3 or C-5), 125.2 (br., C-5 or C-3), 143.4 (C-4), 154.5 (C-6) ppm. ^{14}N NMR (36.1 MHz, [D_6]acetone): δ = –56 (N→O, $\Delta\nu_{1/2}$ = 75 Hz), –59 (N→O, $\Delta\nu_{1/2}$ = 90 Hz), –310 (NH_2, $\Delta\nu_{1/2}$ = 750 Hz) ppm. IR (KBr): ν = 3476 (w), 3303 (s), 2230 (w), 1615 (s), 1553 (s), 1464 (s), 1413 (w), 1377 (m), 1304 (m), 1234 (w), 1205 (m) cm^{-1}. MS (EI, 70 eV): *m/z* = 250 [M^+]. HRMS (ESI): *m/z* calcd for $C_{10}H_{14}N_6O_2$ $[M + H]^+$ 251.1251; found 251.1250.

Solvolysis of 2,4-Bis(*tert*-butyl-*NNO*-azoxy)-3-methylpent-2-enedinitrile (9) in $CDCl_3$; Isobutylene Trapping: A solution of dinitrile **9** (30 mg, 0.1 mmol) in $CDCl_3$ (1 mL) was kept at 25 °C for 24 h. Then the volatile components were removed in vacuo and condensed in a cooled trap (–196 °C). ^{1}H NMR spectrum of the distillate showed characteristic signals of isobutylene [δ = 1.73 (s, 6 H, Me), 4.66 (s, 2 H, CH_2) ppm]. Isobutylene was identified by comparison with authentic sample (^{1}H NMR).

Solvolysis of 2,4-Bis(*tert*-butyl-*NNO*-azoxy)-3-methylpent-2-enedinitrile (9) in Organic Solvents (General Procedure): A solution of dinitrile **9** (200 mg, 0.66 mmol) in appropriate solvent was kept at 25 °C until the starting material disappeared (TLC control). The yields and reaction conditions are shown in Table 1. The reaction mixture was concentrated under reduced pressure. The residue was purified by preparative thin-layer chromatography (petroleum ether/ethyl acetate, 4:1) to give pyridazine oxide **10**, furan **12**, triazepine **13** and zwitter-ionic cycle **14**. The pyridazine oxide **10** obtained was identical (m.p., TLC, ^{1}H NMR) to compound **10** prepared by the procedure described above.

5-Amino-4-(*tert*-butyl-*NNO*-azoxy)-3-methyl-2-furonitrile (12): Colorless crystals; m.p. 173–174 °C. ^{1}H NMR (500.1 MHz, $CDCl_3$): δ = 1.42 (s, 9 H, CMe_3), 2.38 (s, 3 H, Me), 6.21 (br., 2 H, NH_2) ppm. ^{13}C NMR (125.8 MHz, $CDCl_3$): δ = 11.6 (Me), 26.2 (C*Me*$_3$), 58.7 (*C*Me_3), 111.8 (br., C-4), 112.1 (CN), 113.4 (C-3 or C-2), 132.7 (C-2 or C-3), 155.4 (C-5) ppm. ^{14}N NMR (36.1 MHz, $CDCl_3$): δ = –56 [*N*(O)=N*t*Bu, $\Delta\nu_{1/2}$ = 110 Hz], –318 (NH_2, $\Delta\nu_{1/2}$ = 650 Hz) ppm. IR (KBr): ν = 3436 (s), 3296 (s), 2971 (w), 2975 (w), 2214 (s), 1655 (s), 1593 (m), 1449 (s), 1386 (w), 1346 (w), 1305 (w), 1228 (m) cm^{-1}. HRMS (ESI): *m/z* calcd for $C_{10}H_{14}N_4O_2$ $[M + H]^+$ 223.1190; found 223.1191.

2-*tert*-Butyl-6-(*tert*-butyl-*NNO*-azoxy)-5-methyl-7-oxo-2,7-dihydro-1H-1,2,3-triazepine-4-carbonitrile (13): Yellow crystals; m.p. 194–196 °C (decomp.). ^{1}H NMR (500.1 MHz, $CDCl_3$): δ = 1.32 (s, 9 H, CMe_3), 1.45 [s, 9 H, N(O)=NCMe_3], 2.23 (s, 3 H, Me), 8.83 (br., 1 H, NH) ppm. ^{13}C NMR (125.8 MHz, $CDCl_3$): δ = 16.8 (Me), 25.5 [N(O)=NC*Me*$_3$], 25.8 (C*Me*$_3$), 60.7 [N(O)=N*C*Me_3], 62.4 (*C*Me_3), 113.7 (CN), 129.7 (C-4 or C-5 or C-6), 138.2 (C-4 or C-5 or C-6), 147.0 (C-4 or C-5 or C-6), 163.9 (C-7) ppm. ^{14}N NMR (36.1 MHz, $CDCl_3$): δ = –57 [*N*(O)=N*t*Bu, $\Delta\nu_{1/2}$ = 230 Hz] ppm. IR (KBr): ν = 3425 (s), 3190 (w), 3091 (m), 2971 (w), 1699 (s), 1627 (w), 1495 (m), 1450 (w), 1368 (w), 1311 (m), 1212 (m) cm^{-1}. HRMS (ESI): *m/z* calcd for $C_{14}H_{22}N_6O_2$ $[M + H]^+$ 307.1877; found 307.1876.

1-(*tert*-Butylamino)-4-(*tert*-butyl-*NNO*-azoxy)-6-cyano-5-methylpyridazin-1-ium-3-olate (14): Colorless crystals; m.p. 218–222 °C (decomp.). ^{1}H NMR (500.1 MHz, $CDCl_3$): δ = 1.34 (s, 9 H, NHCMe_3), 1.49 [s, 9 H, N(O)=NCMe_3], 2.34 (s, 3 H, Me), 6.56 (br., 1 H, NH) ppm. ^{13}C NMR (125.8 MHz, $CDCl_3$): δ = 13.8 (Me), 25.7 [N(O)=NC*Me*$_3$], 28.1 (NHC*Me*$_3$), 61.2 [N(O)=N*C*Me_3], 61.5 (NH*C*Me_3), 110.4 (CN), 119.3 (C-4 or C-5 or C-6), 135.7 (C-4 or C-5 or C-6), 140.7 (C-4 or C-5 or C-6), 160.9 (C-3) ppm. ^{14}N NMR (36.1 MHz, $CDCl_3$): δ = –61 [*N*(O)=N*t*Bu, $\Delta\nu_{1/2}$

= 250 Hz], –114 (CN, $\Delta\nu_{1/2}$ = 470 Hz) ppm. IR (KBr): ν = 3148 (m), 3045 (m), 2974 (m), 2924 (m), 2236 (w), 1613 (s), 1595 (s), 1499 (m), 1454 (w), 1388 (w), 1369 (w), 1337 (w), 1228 (s), 1208 (m) cm^{-1}. HRMS (ESI): *m/z* calcd for $C_{14}H_{22}N_6O_2$ $[M + H]^+$ 307.1877; found 307.1882.

Reaction of Dinitrile 9 with Dimethylamine; Synthesis of 1-*tert*-Butyl-5-(*tert*-butyl-*NNO*-azoxy)-4-[(dimethylamino)methyl]-6-imino-1,6-dihydropyridazine-3-carbonitrile (15): A solution of dimethylamine (~40%) in pentane (1 mL) was added to a stirred solution of dinitrile **9** (224 mg, 0.73 mmol) in pentane (40 mL) at 25 ºC. A yellow precipitate was formed. The precipitate was filtered off and air-dried to give dimethylammonium salt of dinitrile **9** (257 mg, 100%). The obtained salt was dissolved in MeCN (8 mL) and the resulting solution was kept at 25 ºC for 48 h. Then the reaction mixture was concentrated under reduced pressure. The residue was purified by preparative thin-layer chromatography (petroleum ether/ethyl acetate, 2:1) to give pyridazine oxide **10** (84 mg, 46%) and pyridazinimine **15** (37 mg, 15%). The pyridazine oxide **10** obtained was identical (m.p., TLC, ^{1}H NMR) to compound **10** prepared by the procedure described above.

1-*tert*-Butyl-5-(*tert*-butyl-*NNO*-azoxy)-4-[(dimethylamino)methyl]-6-imino-1,6-dihydropyridazine-3-carbonitrile (15), colorless crystals, m.p. 133–135 °C (from EtOH); ^{1}H NMR (600.1 MHz, $CDCl_3$): δ = 1.48 [s, 9 H, N(O)=NCMe_3], 1.69 (s, 9 H, NCMe_3), 2.28 (s, 6 H, NMe_2), 3.21 (s, 2 H, CH_2), 7.18 (br., 1 H, NH) ppm. ^{13}C NMR (150.9 MHz, $CDCl_3$): δ = 25.6 [N(O)=NC*Me*$_3$], 27.3 (NC*Me*$_3$), 45.8 (NMe_2), 54.8 (CH_2), 61.0 [N(O)=NCMe_3], 69.5 (N*C*Me_3), 114.2 (CN), 118.1 (C-5), 127.3 (C-4), 142.0 (C-3), 149.3 (C=NH) ppm. ^{14}N NMR (43.4 MHz, $CDCl_3$): δ = –61 (N→O, $\Delta\nu_{1/2}$ = 190 Hz) ppm. IR (KBr): ν = 3325 (w), 2984 (m), 2780 (m), 2232 (m), 1655 (s), 1583 (s), 1487 (s), 1454 (s), 1394 (w), 1382 (w), 1365 (s), 1341 (m), 1318 (m), 1268 (m), 1237 (m) cm^{-1}. HRMS (ESI): *m/z* calcd for $C_{16}H_{27}N_7O$ 334.2350 $[M + H]^+$, found 334.2340.

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Keywords: Nitrogen heterocycles • Cyclization • Cyanides • Synthetic methods • Solvent effects

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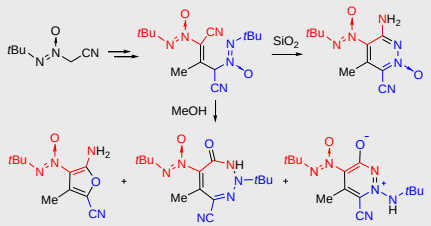

A novel intramolecular reaction of (*tert*-butyl-*NNO*-azoxy) and cyano groups was discovered, which provide a new route to pyridazine, furan and 1,2,3-triazepine systems.

Nitrogen heterocycles*

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Intramolecular Reaction of *tert*-Butyl-*NNO*-azoxy and Cyano Groups. Novel Synthesis of Pyridazine, 1,2,3-Triazepine and Furan rings