1,3,5-Triazinenitrolic acids. Synthesis and NO-releasing properties

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Reactions of salts of 1,3,5-triazine dinitromethyl derivatives with nitrogen dioxide that result mainly in 1,3,5-triazinenitrolic acids are investigated. The behavior of nitrolic acid in electroreduction at a mercury drop electrode at various pH was studied; oxygen was shown to accelerate the process. The promoting effect of nitrolic acids on the activity of soluble guanylate cyclase of human platelets was shown. The studied nitrolic acids are active donors of nitric oxide, a universal and important regulator of cell metabolism functions. NO-releasing properties of furoxans are investigated.

Key words: nitrolic acids, 1,3,5-triazine, furoxan, nitration, NO-donors.

At present it is reliably established that nitric oxide (NO) is an intra- and intercellular second messenger (neurotransmitter). It plays a key role in regulation of the major biological processes of cardiovascular, gastroenteric, urinogenital, respiratory, central and peripheral nervous systems. Chemical, biochemical, and pharmaceutical aspects of action of nitric oxide donors are considered in detail in recent reviews.[1—8]

It is known that the formation of NO in an organism in insufficient quantities leads to a number of serious consequences. In this connection, one of the most actively developing now directions[1—6] is the search for various compounds that can serve as NO generators, *i.e.*, xenobiotics, that are transformed with its formation. At present a number of drugs the activity of which is reasonably connected with their ability to liberate NO *in vivo* is employed in medical practice.

The substances containing *S*-, *O*-, *N*-, and *C*-nitroso- and nitro groups, *viz.*, diazeniumdiolates, furoxans, *NO*-metal complexes, *etc.*,[6] are related to the compounds showing properties of nitric oxide donors. Among the found NO-donors, high efficiency of some oximes[4,6] is noted.

Nitrolic acids, $RC(=NOH)NO_2$, containing the oxime and nitro groups at the same carbon atom, are interesting class of potential prodrugs. Antithrombotic and hypotensive activity[9] was shown for some nitrolic acids. Ophthalmologic effects of imidazolenitrolic acids were recently described.[10,11] On the basis of a structure of the nitrolic acids it is logical to suppose that they are capable to generate nitric oxide. It is established, for example, that some nitrolic acids decompose with formation of HNO even at room temperature. [5]

The basic analytical methods that allow identification of NO are described in detail in a review.[7] The colorimetric method that quantifies the nitrite ion, a marker of NO formation, is one of the most common methods (see Ref. 8). It is this method that is employed in the present work.

A review[12] on development of the synthesis methods and the reactivity of mono-, di-, and trinitromethyl derivatives of 1,3,5-triazines has recently been published.

Published in Russian in *Izvestiya Akademii Nauk. Seriya Khimicheskaya,* No. 9, pp. 1900—1910, September, 2009.

In continuation of our investigations[13–17] in this field of chemistry, we published a preliminary report on possible preparation of model nitrolic acid of the 1,3,5-triazine series.[18]

In the present work, a synthetic scheme that allows designing 1,3,5-triazinenitrolic acids is described in detail, and data on NO release (detected as the nitrite anion) upon transformations of these compounds at different pH are also presented. Furthermore, a question of the NO-donor activity of furoxan derivatives obtained in the present work is considered

Results and Discussion

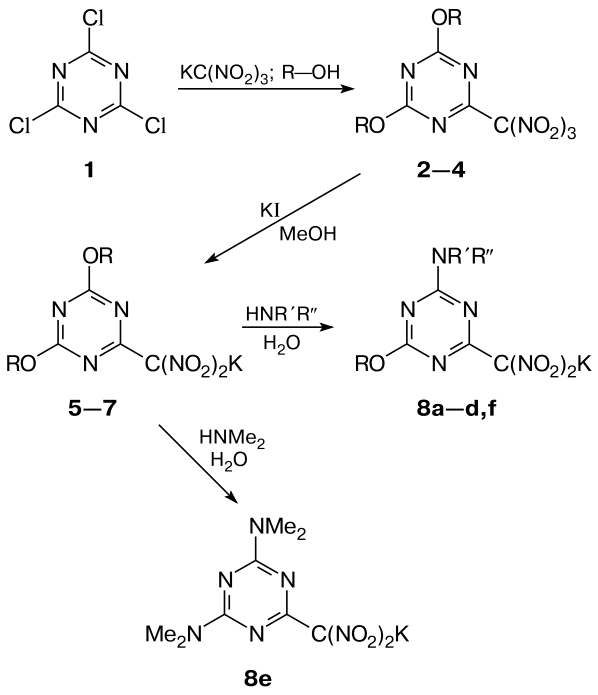
Nitrolic acids are important building blocks for synthesis as well as intermediates in nitration—nitrosation processes.[19] Compounds containing nitromethyl groups serve most often as the starting substances for the synthesis of nitrolic acids. 1,3,5-Triazines with these groups are very scarce.[12] 1,3,5-Triazine-2,4,6-tris(nitrolic) acid was synthesized by destructive nitration of the corresponding tris(hydroxyiminoacetic) acid,[20] which is accessible with difficulty. Therefore, in the present work the readily available di- and trinitromethyl derivatives of alkoxy(dialkylamino)-1,3,5-triazine were chosen as the starting compounds.

For the first time, the reaction of aryldinitromethane salts with N_2O_4 in CCl_4 at −12 °C, resulting in aryltrinitromethanes, was carried out in the 1950s.[21] Later, Russian scientists have studied the reactions of salts of various dinitromethyl compounds with N_2O_4 in inert organic solvents, which resulted in the corresponding trinitromethyl derivatives and/or nitrolic acids, nitrile oxides, furoxans, nitriles.[17,22–27] The first step of this process is nitrosation of the dinitromethane anion resulting in α,α-dinitro-α-nitrosomethyl intermediate,[25,26] which can be converted in different products depending on the reaction conditions. Probably, salts of α,α-dinitromethyl compounds containing the hydroxyimino group in the β-position that are also involved in this reaction[28–30] react with N_2O_4 according to a similar mechanism. Simple and effective reaction of salts of dinitromethyl compounds with N_2O_4 seemed rather attractive for our purposes.

In the reaction of trinitromethane potassium salt with the commercially available 2,4,6-trichloro-1,3,5-triazine (cyanuric chloride) (**1**) in the presence of methanol, n-propanol, or *p*-nitrophenol as described earlier, [31] one trinitromethyl group and two alkoxyl or aryloxide groups were introduced into the molecule of 1,3,5-triazine with formation of products **2—4** in yields 60—75% (Scheme 1).

The trinitromethyl group of compounds **2—4** undergoes denitration on treatment with potassium iodide in methanol,[32] which results in potassium salts **5—7**.

Scheme 1



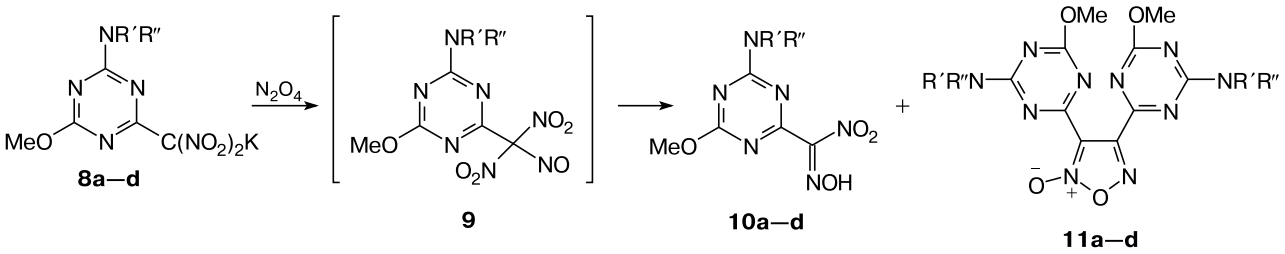
R = Me (**2**, **5**, **8a—d**), Pr^n (**3**, **6**), *p*-$OC_6H_4NO_2$ (**4**, **7**, **8f**)
R′ = R″ = Me (**8a,f**), R′—R″ = $(CH_2)_4$ (**b**), $(CH_2)_5$ (**c**), $(CH_2CH_2)_2O$ (**d**)

The treatment of aqueous suspension of the dimethoxy derivative salt **5** with a small excess of secondary amines at room temperature results in nucleophilic substitution of one methoxy group. The yields of the reaction products **8a—d** were 82—93%. The *p*-nitrophenoxy group in compound **7** is substituted analogously. The substitution of the propoxy group in compound **6** is less straightforward, a mixture of products is formed, and the starting compound remains unconsumed. Bis(dimethylamino) derivative **8e** is formed under the action of Me_2NH (2.5 equiv.).

Earlier, we have shown[17] that potassium salts of 2,4-dialkoxy-6-dinitromethyl-1,3,5-triazine are converted into furoxans with yields of 60—85% when treated with N_2O_4 in an inert solvent (for example, toluene or dichloroethane) at room temperature. The reaction of 1,3,5-triazines with a dialkylamino group instead of an alkoxy group as a substituent, follows another pathway.[18]

The reactions of potassium salts **8a—f** with N_2O_4 at room temperature in anhydrous nonpolar solvents (chloroorganic solvents, toluene, *etc.*) leads mainly to triazinenitrolic acids **10a—f** (~60%), furoxans **11a—f** (20—30%) being found only as byproducts (Scheme 2). A mixture of a solution of N_2O_4 in an organic solvent (initially brown) and colorless salts **8a—f** acquired a bright blue-green color for short time, which suggests the formation of nitroso-intermediate **9** (see Refs 25, 26). The blue-green color

Scheme 2

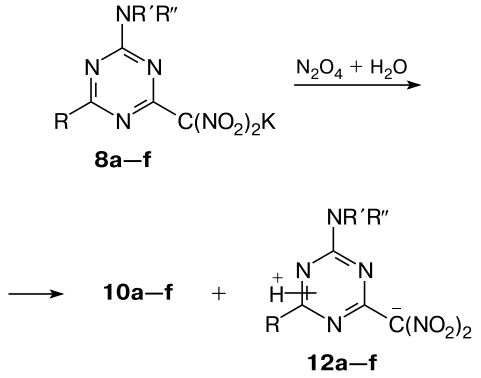


8—11: R′ = R″ = Me (**a**), R′—R″ = $(CH_2)_4$ (**b**), $(CH_2)_5$ (**c**), $(CH_2CH_2)_2O$ (**d**)

soon disappeared, and the reaction mixture became pale yellow.

We observed an interesting and unusual fact of the effect of water on the studied reaction. It was found that if nitrosation of salts **5—7**, **8a—f** was carried out in the presence of water (1—2 mol), the formation of furoxans **11** is completely suppressed. The reactions appear to proceed in a similar manner (the dissolution of the initial salts, formation of a new precipitate, and change in the color of the reaction mixture), but the yields of nitrolic acids **10** increase by 15—25%. The zwitterionic[33] dinitromethyl derivetives **12a—f** are formed as by-products in the case of dialkylamino derivatives **8a—f** (Scheme 3). Dinitromethyl derivitives **13g—i** are formed as by-products from compounds **5** and **6** (Scheme 4).

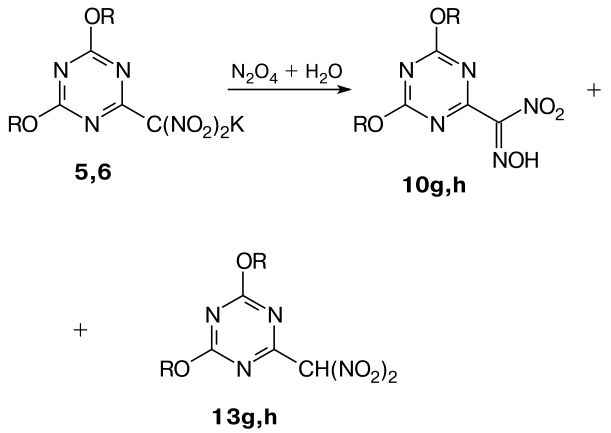
Scheme 3



R = OMe, R′ = R″ = Me (**a**), R′—R″ = $(CH_2)_4$ (**b**), $(CH_2)_5$ (**c**), $(CH_2CH_2)_2O$ (**d**),
R = NMe_2, R′ = R″ = Me (**e**), R = $OC_6H_4NO_2$-*p*, R′ = R″ = Me (**f**)

Probably, the formation of dinitromethyl derivatives **12** and **13** is the result of concurrent reactions of salts **5—8** with nitric acid emerging in the reaction mixture upon the reaction of nitrogen dioxide with water. On the one hand, water is required for the formation of nitrolic acids from intermediate **9**, but, on the other hand, it competes with the dinitromethyl anion in the reaction

Scheme 4



R = OMe (**g**), Pr (**h**)

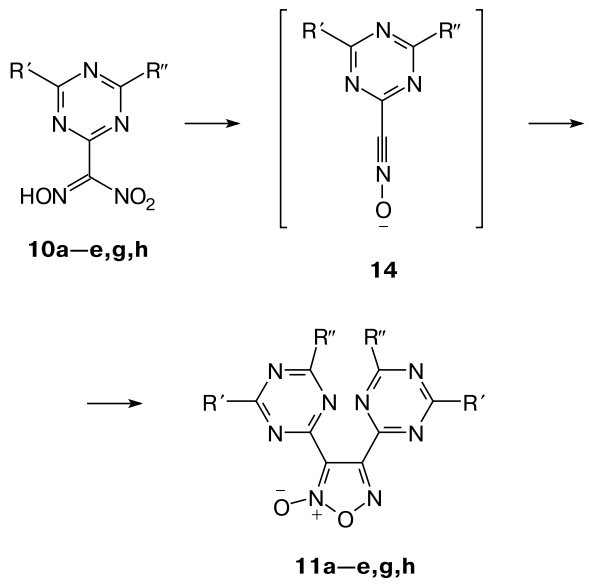
with nitrogen dioxide. Actually, the yields of nitrolic acids decrease with increasing amount of water.

The nitrolic acids **10** exist in the form of one stereoisomer (one set of signals in the NMR spectra), which, probably, has *E*-configuration. In the ^1H NMR spectra of acids **10,** the protons of the hydroxyimino groups appear in the range of δ 14. The presence of signals at δ 151 and −12.8 (nitrogen atom of the NO_2 group) in the ^{13}C and ^{14}N NMR spectra is characteristic of α-nitro-α-hydroxyiminomethyl group, which agrees with the literature data.[26]

The resulting nitrolic acids **10** are stable at room temperature; insignificant signs of decomposition are recorded after 2—3 months. They can be kept for a long time at 0—5 °C. Fast decomposition with nitrous acid release is observed on heating of acids **10a—h** in toluene at 90—110 °C (Scheme 5), and the nitrile oxides **14** formed undergo dimerization resulting in the corresponding furoxans **11a—e,g,h** (up to 95%).

The presence in ^{13}C NMR spectra of signals in the region δ 111—112, for the C(3) atom adjacent to the *N*-oxide function, and signals in the region δ 153—154 corresponding to the carbon atom C(4) remote from the

Scheme 5



N-oxide function is characteristic of the furoxan ring (see Ref. 19). The difference in chemical shifts of the carbon atoms of the furoxan ring in the investigated series is 41.9±0.4 ppm and almost invariable.

Nitrolic acids containing nitro- and hydroxyimino groups, can potentially be NO donors.[6,34] The transformations of the nitrolic acids under hydrolytic conditions result in the nitrite ion, polarography being the most suitable for monitoring these transformations.[35,36]

The polarographic study showed that the height of the first wave of reduction of the nitro group of compounds **10a—d** in alkaline solutions decreases to its full disappearance. The process is dependent, its rate increases with increasing pH. This suggests hydrolysis of the compounds under study with abstraction of the nitro groups in the form of the nitrite anion. The formation of this anion in both the phosphate buffer (pH 8), and 0.01 *M* NaOH is confirmed by the Griess reaction.[37]

The electron-withdrawing character of the 1,3,5-triazine ring is possibly responsible for the behavior of nitrolic acids **10a—d** in media with different pH. Thus they rapidly decompose in alkaline and neutral solutions and are stable only in strong acids (1 *M* $HClO_4$). It should be noted that alkanenitrolic acids are also relatively stable in weakly alkaline solutions. Earlier,[35] it has been shown that the polarographic waves for alkanenitrolic acids in acidic and alkaline solutions relate to reduction of the nitro groups.

The elimination of the nitro group from compounds **10** in the presence of oxygen (when using the Griess reaction for the detection of the nitrite anion) proceeds faster than in the absence of oxygen (the similar effect was observed in another case[38]). In solutions of nitrolic acids **10a—d** in ethanol in the presence of oxygen, 10—15% of the nitrite anion is detected in 15—20 min, and 20%, in 24 h. In ethanol in the absence of oxygen, the amount of the nitrite ion detected after 20 h decreases to 10 %.

In deaerated 10 % ethanol in the presence of AcOH upon contact with air for 2.5 h the nitrite anion (2—6 %) is formed. In 0.1 *M* HCl in 10 % ethanol, no formation of the nitrite anion is observed. In a buffer with pH 10, which is not oxygen-free, 80—90 % of the nitrite anion is released from nitrolic acids **10a—d** even in 1 h.

Thus, the presence of oxygen in an alkaline solution is important for increasing the rate of the nitrite ion generation from nitrolic acids. In general, alkaline hydrolysis in the presence of oxygen causes efficient NO formation from the nitrolic acids **10a—d**.

The activation of soluble guanylate cyclase is a characteristic effect of nitric oxide. All investigated compounds activate this enzyme (Table 1).

The ability of nitrolic acids to activate the soluble guanylate cyclase is caused, apparently, by generation of exogenous NO. For the nitrolic acids studied earlier, a correlation between the amount of NO formed and the degree of activation of guanylate cyclase [6,38] has been established.

Several alternative pathways of NO generation (more exactly, the molecules that are NO precursors) from nitrolic acids are feasible. Thus, it is known that thermolysis of or action of bases on the nitrolic acids brings about elimination of nitrous acid and conversion to nitrile oxides, which undergo either dimerization into furoxans, as is presented in Scheme 5 (see Refs 19, 39), or hydrolysis with formation of the corresponding carboxylic acids, RCOOH (see Refs 40—45).

Table 1. Influence of nitrolic acids **10a—d** on activity of soluble guanylate cyclase of human platelets

Compound	C/mol L^{-1}	a^a	$K_\infty{}^b$
SNP[c]	10^{-4}	533	12.4
10a	10^{-7}	76	1.8
	10^{-6}	104	2.4
	10^{-5}	198	4.6
10b	10^{-7}	86	2.0
	10^{-6}	93	2.2
	10^{-5}	109	2.5
10c	10^{-7}	42	1.0
	10^{-6}	108	2.5
	10^{-5}	187	4.3
10d	10^{-7}	65	1.5
	10^{-6}	106	2.5
	10^{-5}	181	4.2

[a] Activity of soluble guanylate cyclase/pmol cGMP • mg^{-1} • min^{-1}. Base activity is 43±5 pmol cGMP • mg^{-1} • min^{-1}. [b] Enzyme activation coefficient . [c] SNP — sodium nitroprusside (strongest NO donor).

At the same time, it should be noted once again that in acidic media no nitrite anion is determined in the system under consideration and, hence, no formation of nitric oxide occurs, whereas in solution with pH ≥ 8 its formation is dramatically activated. Thus, the preliminary formation of an anion from nitrolic acids is necessary for the process to proceed. It is logical to assume (Scheme 6) that anion **A** is further oxidized by atmospheric oxygen to carbonyl nitro compounds **B** and nitroxyl (HNO) in several steps. It is well known[1,6] that nitroxyl can be oxidized to NO or undergo dimerization in an organism. However, in a chemical experiment the nitroxyl is not oxidised to NO, *i.e.*, only transformation products of the nitro group are detected. Triazinecarboxylic acid **C** is a final product of the given process (see Scheme 6) (it was also obtained by an independent method, see Experimental), which has been found in the reaction mixture.

The main pathway by which the nitrite anions obtained is the transformation of the nitro group of the starting nitrolic acid (see Scheme 6). In spite of the fact that the oxime group can also serve as an NO precursor in biological systems, this pathway seems to be secondary one according to the results of chemical studies, because in this case the amount of the detected nitrite anion corresponds to the transformation of one nitrogen-containing group.

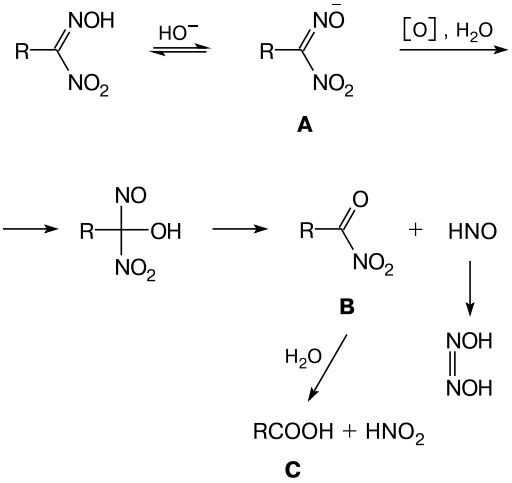
Thus, several pathways of NO generation are feasible, which, most likely, will depend on both the decomposition conditions and the nature of the fragment R linked with the nitrolic group, R—C(=NOH)NO_2.

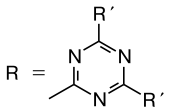
As follows from Scheme 5, furoxans **11** can arise upon dimerization of intermediate nitrile oxides formed from nitrolic acids **10**. Therefore, triazinylfuroxans **11** became yet another subject of the research of NO-donor activity.

It should be pointed out that the fact of NO generation from furoxans is well known.[1,6,46,47] It is established that the ability to generate NO by the reductive mechanism in the presence of thiols[1] is characteristic of furoxans. Furthermore, it is known that furoxan derivatives can be photochemically decomposed with liberation of NO.[48]

A study of the polarographic behavior of furoxans **11** was carried out in 0.1 *M* solutions of sodium perchlorate in DMSO. Thus, for example, $E_{1/2}$ values for compounds **11c** and **11d**, were −0.11 and −0.14 V, respectively, relative to the saturated calomel electrode. These data are important for quantitation of furoxans in a solution under their degradation.

Scheme 6





We have found yet another pathway of NO generation from furoxans that is based not on reductive but on oxidative cleavage of this heterocycle. The oxidation of furoxans in weakly alkaline media leads to the nitrite anions. The data for the yield of NO_2^- formed from furoxans **11c,d** upon oxidation are listed in Table 2. Note that no nitrite anion is formed from furoxans under acidic conditions (pH <4).

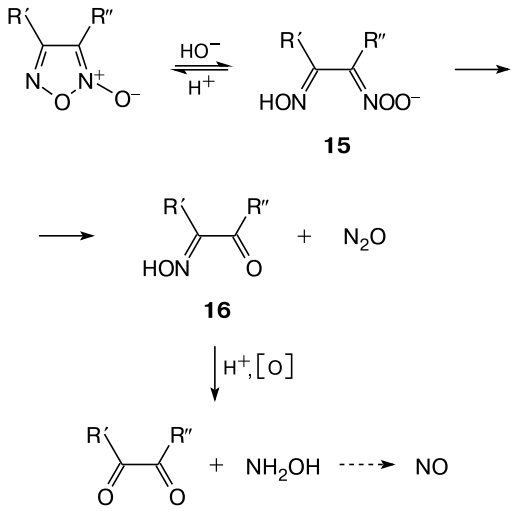
In alkaline media, the furoxan ring is unstable and undergoes ring opening with conversion into α-nitrooxime **15** (see Ref. 49). Depending on the type of substitutents, nitrooximes **15** can undergo either cyclization to the initial furoxans or (if R is an electron-withdrawing group) the Nef reaction[50] (Scheme 7), *i.e.*, hydrolytic abstraction of the nitro group (with formation of N_2O) resulting in diketone monoxime **16**. At the same time, the deoximation[51] proceeds easily under the oxidation conditions, and compounds **15** and **16** can be involved in this process. Thus, both the nitro group and the oxime group of the intermediate **15** can be a source of NO *in vivo* (see Ref. 6).

Table 2. Formation of the nitrite anion upon oxidation of furoxans **11c,d**

Conditions					NO_2^- (%)	
Oxidant	Solvent	Media	τ/h	*T*/°C	**11c**	**11d**
O_2[a]	DMSO—2% H_2O	0.1 *M* ammonia buffer (pH 9.5)	72	18	3.1	0.6
O_2[a]	DMSO—25% H_2O	0.08 *M* Bu_4NOH	24	18	4.7	2.6
H_2O_2[b]	DMSO—22% H_2O	0.1 *M* NaOH	2	80	28	12

[a] Atmospheric oxigen. [b] 0.01 *M* H_2O_2 (10-fold excess).

Scheme 7



This research has designated new aspects of the behavior of furoxans that should be taken into account in further studying their biological action.

Certain furoxans obtained in the present work were investigated in relation to ability to activate the soluble guanylate cyclase[52] (Table 3).

A comparison of the results presented in Tables 1 and 3 suggests that furoxan derivatives are less active than nitrolic acids with the same substituents in the triazine ring. Nevertheless, it should be taken into account that furoxans can be formed in the process of NO generation from nitrolic acids. The net result of their action can be rather efficient.

In conclusion, we note that both nitrolic acids and furoxans of the 1,3,5-triazine series are generators of nitric oxide, a universal and necessary regulator of functions of a cellular metabolism. Altogether, this shows that compounds of this type are doubtless of interest for further biological studies and search for new efficient drugs. Design and studies of new compounds incorporating a fragment of nitrolic acid can lead to disclosure of original derivatives possessing specific physiological activity.

Table 3. Influence of furoxans **11c,d** on activity of soluble guanylate cyclase of human platelets

Compound	C/mol L^{-1}	a^a	$K_\infty{}^b$
SNP[c]	10^{-4}	561±39	11.0
11c	10^{-8}	41±3	0.8
	10^{-7}	306±21	6.0
	10^{-6}	112±8	2.2
11d	10^{-8}	77±7	1.5
	10^{-7}	107±6	2.1
	10^{-6}	46±3	0.9
	10^{-5}	122±8	2.2

[a] Activity of soluble guanylate cyclase/pmol cGMP • mg^{-1} • min^{-1}. Base activity is 51±3 pmol cGMP • mg^{-1} • min^{-1}. [b] Enzyme activation coefficient . [c] SNP (100 μmol) — sodium nitroprusside (strongest NO donor).

Experimental

Attention! Polynitrocompounds are potential explosives and are sensitive to shock, friction, and heating. Operations with such compounds require great care.

Melting points were determined in a Gallenkamp melting block and are uncorrected. ^{1}H, ^{13}C and ^{14}N NMR spectra with the natural content of isotopes were recorded on a Bruker AM-300 spectrometer with the working frequencies 300.13, 75.7, and 21.5 MHz, respectively. Chemical shifts in the ^{14}N NMR spectra were measured in the δ scale with nitromethane as the internal standard. Spin-spin coupling constants $^1J_{^{15}N,^1H}$ were measured using the INEPT technique. Mass spectra were recorded on Varian MAT CH-6 and Varian MAT CH-111 (70 eV) instruments. IR spectra were recorded on a Perkin-Elmer Model 577 spectrometer (in pellets with KBr for solids, and in thin layer for liquids). The course of the reactions and the purity of the products were monitored by TLC on Silufol UV-254 plates; silica gel SiO_2 40/100 was used for preparative chromatography. Compounds **2—4** (see Ref. 31) and **5—7** (see Ref. 32) were obtained according to the published procedures. Solvents were purified by conventional methods.

Polarography. A universal polarograph PU-1 (Byelorussia) and a two-coordinate recorder LKD4-0.03 (Russia) were used for research. Polarograms were recorded by means of a three-electrode scheme. The working electrode was a mercury dropping electrode with parameters m = 1 mg • s^{-1}, τ = 2.0 s, the auxiliary electrode was a platinum wire, the reference electrode was a saturated calomel or silver electrode. The measurements were performed in a cell at 25 °C. Solutions in cell were purged with argon for removal of dissolved oxygen. Solutions of unstable compounds were prepared directly in the polarographic cell for recording polarograms. For this purpose, the exactly weighted sample of a compound under study was dissolved in the cell, with the background electrolyte previously purged with argon.

Determination of the nitrite anion according to the Griess reaction. Sulfanilic acid was used as the diazo component and *N*-(α-naphthyl)ethylenediamine as the azo component. The reaction was carried out at pH 1 (0.1 *M* HCl). The content of the nitrite anion was determined by the addition technique.[37]

Activity of guanylate cyclase. Human platelets were used as the source of soluble guanylate cyclase. Platelets were isolated from blood of healthy donors as described earlier.[52] A suspension of washed platelets in a 50 mM Tris-HCl buffer (pH 7.6) containing 0.2 mM dithiothreitol was disintegrated in an ultrasonic disintegrator MSE 5-78 (Great Britain) for 20 s and centrifuged for 1 h at 105 000 *g*. The supernatant obtained from 40 mL of blood of one donor was used as a source of soluble guanylate cyclase in one experiment.

The activity of guanylate cyclase was quantified as described.[53] The samples (total volume 150 μL) contained a 50 mM Tris-HCl buffer (pH 7.6), 1 mM guanosine 5-triphosphate, 4 mM $MgCl_2$, 4 mM creatine phosphate, 20 μg creatine phosphokinase, 10 mM theophyilline, 105 000 g supernatant (20 μg of protein), and optionally other additives. The influence

of the used compounds on the basal activity of soluble guanylate cyclase and activation of the enzyme by sodium nitroprusside were investigated at concentrations of 10 μmol • L^{-1}. First, all the components mentioned were incubated with the enzyme (10 min at 2 °C), then the NO-donor under study was added. Due to low solubility of the compounds in the buffer, they were previously dissolved in DMSO with subsequent dilution of solution with the 50 mM Tris-HCl buffer (pH 7.6) to desired concentration. Control samples contained the same amount of DMSO. The amount of cGMP formed in 15 min at 37 °C was determined by ELISA. The protein was determined by the Bradford method.[54] Guanosine 5′-triphosphate sodium salt was from Fluka (Switzerland), other chemicals were from Sigma (USA).

Preparation of 2-dimethylamino-4-dinitromethyl-6-methoxy-1,3,5-triazine potassium salt (8a). A 33% aqueous solution of dimethylamine (1.8 mL, 0.012 mol) was added with stirring at 20—25 °C to a suspension of salt **5** (2.83 g, 0.01 mol) (see Ref. 32) in water (25 mL). The reaction mixture was stirred for 24 h at 20—25 °C (TLC). The precipitated product was filtered off and washed with cold water (5 mL) and crystallized from 50% aqueous methanol. The yield was 85%. m.p. 240—241 °C (decomp.). IR, ν/cm^{-1}: 3020, 2932, 2870, 1602, 1570, 1500, 1479, 1460, 1400, 1387, 1360, 1230, 1125, 1075, 1015, 785. ^{1}H NMR (DMSO-d_6, δ): 3.08 (s, 6 H, NCH_3), 3.82 (s, 3 H, OCH_3). Found (%): C, 28.30; H, 3.12; N, 28.49. $C_7H_9N_6O_5K$. Calculated (%): C, 28.38; H, 3.06; N, 28.37.

Alkylamine derivatives **8b—d** and **8f** were prepared according to this procedure.

2-Dinitromethyl-4-methoxy-6-pyrrolidino-1,3,5-triazine potassium salt (8b). The yield was 90%, m.p. 234—235 °C (decomp.). IR, ν/cm^{-1}: 3013, 2972, 2899, 1606, 1581, 1512, 1486, 1471, 1438, 1412, 1398, 1367, 1344, 1263, 1240, 1205, 1142, 1044, 1028, 816, 772, 752. ^{1}H NMR (DMSO-d_6, δ): 1.96 (m, 4 H, CH_2CH_2); 3.38 and 3.50 (both t, 4 H, CH_2NCH_2, J = 6.4 Hz), 3.84 (s, 3 H, OCH_3). Found (%): C, 33.63; H, 3.50; N, 26.10. $C_9H_{11}N_6O_5K$. Calculated (%): C, 33.54; H, 3.44; N, 26.07.

2-Dinitromethyl-4-methoxy-6-piperidino-1,3,5-triazine potassium salt (8c). The yield was 84%, m.p. 202—203 °C (decomp.). IR, ν/cm^{-1}: 3359, 3232, 3006, 2935, 2858, 1591, 1506, 1488, 1411, 1369, 1295, 1249, 1226, 1130, 1091, 1024, 998, 896, 856, 819, 769, 755. ^{1}H NMR (DMSO-d_6, δ): 1.52 and 1.63 (both m, 6 H, CH_2), 3.72 (m, 4 H, CH_2NCH_2), 3.85 (s, 3 H, OCH_3). Found (%): C, 35.80; H, 3.92; N, 24.90. $C_{10}H_{13}N_6O_5K$. Calculated (%): C, 35.61; H, 3.82; N, 24.99.

2-Dinitromethyl-4-methoxy-6-morpholino-1,3,5-triazine potassium salt (8d). The yield was 93%, m.p. 245—246 °C (decomp.). IR, ν/cm^{-1}: 2962, 2928, 2880, 1608, 1587, 1520, 1492, 1466, 1420, 1386, 1316, 1252, 1204, 1173, 1132, 1073, 1043, 1012, 924, 898, 852, 828, 816, 768. 1H NMR (DMSO-d_6, δ): 3.65 (br.s, 4 H, CH_2NCH_2), 3.74 (br.s, 4 H, CH_2OCH_2), 3.87 (s, 3 H, OCH_3). Found (%): C, 31.89; H, 3.38; N, 24.76. $C_9H_{11}N_6O_6K$. Calculated (%): C, 31.95; H, 3.47; N, 24.62.

2-(Dimethylamino)-4-dinitromethyl-6-(*p*-nitrophenoxy)-1,3,5-triazine potassium salt (8f). The yield was 82%, m.p. 190—192 °C (decomp.). IR, ν/cm^{-1}: 3080, 1602, 1580, 1576, 1524, 1514, 1492, 1464, 1432, 1380, 1348, 1272, 1222, 1144, 1114, 1068, 1020, 996, 948, 870, 856, 776, 752, 706. ^{1}H NMR (DMSO-d_6, δ): 3.02 and 3.08 (6 H, NCH_3, Δν = 12.0 Hz); 7.44—7.53 and 8.24—8.33 (4 H, *p*-C_6H_4, J = 1.2 Hz). Found (%): C, 35.60; H, 2.62; N, 24.25. $C_{12}H_{10}N_7O_7K$. Calculated (%): C, 35.74; H, 2.76; N, 24.12.

2,4-Bis(dimethylamino)-6-dinitromethyl-1,3,5-triazine potassium salt (8e). A 33% aqueous solution of dimethylamine (7.6 mL, 0.05 mol) was added with stirring at 20—25 °C to a suspension of salt **5** (2.83 g, 0.01 mol) (see Ref. 32) in water (20 mL). The reaction mixture was stirred for 5 h at 45—50 °C, and cooled to 0—5 °C. The precipitate of the product was filtered off, washed with cold water (5 mL), and crystallized from 50% aqueous methanol. The yield was 78%, m.p. 196—198 °C (decomp.). IR, ν/cm^{-1}: 3002, 2946, 2850, 1600, 1587, 1560, 1520, 1503, 1470, 1410, 1370, 1355, 1320, 1235, 1200, 1115, 1015, 980, 775. ^{1}H NMR (DMSO-d_6, δ): 3.05 (s, 12 H, NCH_3). Found (%): C, 30.95; H, 3.83; N, 31.74. $C_8H_{12}N_7O_4K$. Calculated (%): C, 31.06; H, 3.91; N, 31.70.

The reaction of 2-R′-4-R″-6-dinitromethyl-1,3,5-triazine K-salts with nitrogen dioxide in the presence of water (general procedure). To a stirred suspension of 2-R′-4-R″-6-dinitromethyl-1,3,5-triazine potassium salt **5**, **7**, **8a—f** (0.003 mol) in a mixture of toluene (or dichloroethane) (7 mL) and water (0.11 mL, 0.006 mol), a solution of N_2O_4 (0.24 ml, 0.0039 mol) in the same solvent (3 mL) was poured in one portion at 15—20 °C. The precipitate of the starting salt gradually disappeared and the precipitate of potassium nitrate sedimented; the solution colored blue-green. The color of the reaction mixture changed gradually from blue-green to yellow-green and then to yellow. Nitrolic acids **10a—i** precipitated in 30—60 min. The reaction mixture was cooled to 0 °C, kept for 60 min. The mixture of nitrolic acid and potassium nitrate was filtered off and washed with cold toluene or dichloroethane (2×3 mL). The product was dried in air and then washed with water (10—15 mL) for removing potassium nitrate.

The organic solution was concentrated and an additional amount of nitrolic acids **10a—i** and zwitterionic salts **12a—f** were isolated from the residue by column chromatography (Merck Silica gel 60 (0.063—0.200), dichloroethane—methanol, 4 : 1, as the eluent). Nitrolic acid is eluted first followed by zwitterionic salt.

2-Dimethylamino-4-methoxy-1,3,5-triazine-6-nitrolic acid (10a). The yield was 52 + 20% (hereinafter; the first value denotes the amount of precipitated product, the second one refers to the additional portion isolated by chromatography), m.p. 109—111 °C (decomp.), R_f 0.71 (dichloroethane—methanol, 4 : 1). IR, ν/cm^{-1}: 3145, 3049, 3004, 2933, 2879, 2811, 1608, 1587, 1552, 1511, 1417, 1382, 1268, 1224, 1149, 1074, 1051, 1002, 902, 864, 806, 727, 646. ^{1}H NMR (DMSO-d_6, δ): 3.12 and 3.20 (both s, 6 H, NCH_3, Δν = 16 Hz), 3.96 (s, 3 H, OCH_3), 13.63 (br.s, 1 H, NOH). ^{13}C NMR (DMSO-d_6, δ): 36.4, 36.6 (NCH_3), 55.0 (OCH_3), 151.3 (C(NO_2)=NOH), 163.0 (N=C—C); 166.5 (N=C—N), 171.5 (N=C—OCH_3). ^{14}N NMR (DMSO-d_6, δ): −13.6 (NO_2). Found (%): C, 34.77; H, 4.20; N, 34.64. $C_7H_{10}N_6O_4$. Calculated (%): C, 34.71; H, 4.16; N, 34.70.

2-Methoxy-4-pyrrolidino-1,3,5-triazine-6-nitrolic acid (10b). The yield was 43 + 12%, m.p. 119—121 °C (decomp.), R_f 0.72 (dichloroethane—methanol, 4 : 1). IR, ν/cm^{-1}: 3104, 2973, 2887, 2802, 2780, 1596, 1562, 1508, 1477, 1457, 1380, 1340, 1245, 1054, 1008, 970, 806, 727. ^{1}H NMR (DMSO-d_6, δ): 2.46 (m, 4 H, CH_2CH_2), 4.00 (m, 4 H, CH_2NCH_2), 4.39 (m, 3 H, OCH_3); 14.10 (s, 1 H, NOH). ^{13}C NMR (DMSO-d_6, δ): 25.5, 25. 6 (CH_2CH_2), 47.2, 47.4 (CH_2NCH_2), 55.0 (OCH_3), 151.3

($C(NO_2)$=NOH), 162.9 (N=C—C), 164.4 (N=C—N), 171.4 (N=C—OCH_3). ^{14}N NMR (DMSO-d_6, δ): −12.8 (NO_2). Found (%): C, 40.25; H, 4.59; N, 31.40. $C_9H_{12}N_6O_4$. Calculated (%): C, 40.30; H, 4.51; N, 31.33.

2-Methoxy-4-piperidino-1,3,5-triazine-6-nitrolic acid (10c). The yield was 58 + 10%, m.p. 113—114 °C (decomp.), R_f 0.77 (dichloroethane—methanol, 4 : 1). IR, ν/cm^{-1}: 3131, 3043, 3010, 2937, 2861, 2806, 1589, 1560, 1508, 1473, 1450, 1382, 1295, 1234, 1099, 1052, 1016, 993, 889, 856, 831, 808, 786, 721. ^{1}H NMR (DMSO-d_6, δ): 2.04 (m, 6 H, $CH_2CH_2CH_2$), 4.25 (t, 4 H, CH_2NCH_2), 4.37 (s, 3 H, OCH_3), 14.06 (s, 1 H, NOH). ^{13}C NMR (DMSO-d_6, δ): 25.0 (CH_2), 26.2, 26.3 (CH_2), 45.1, 45.5 (CH_2NCH_2), 55.1 (OCH_3), 151.4 ($C(NO_2)$=NOH), 163.5 (N=C—C), 165.7 (N=C—N), 172.0 (N=C—OCH_3). ^{14}N NMR (DMSO-d_6, δ): −12.3 (NO_2). Found (%): C, 42.66; H, 4.97; N, 29.82. $C_{10}H_{14}N_6O_4$. Calculated (%): C, 42.55; H, 5.00; N, 29.77.

2-Methoxy-4-morpholino-1,3,5-triazine-6-nitrolic acid (10d). The yield was 64 + 11%, m.p. 110—111 °C (decomp.), R_f 0.68 (dichloroethane—methanol, 4 : 1). IR, ν/cm^{-1}: 3216, 3012, 2968, 2912, 2860, 2782, 2686, 1600, 1550, 1517, 1473, 1442, 1380, 1305, 1286, 1243, 1157, 1112, 1068, 1029, 998, 896, 840, 813, 800, 725. ^{1}H NMR (DMSO-d_6, δ): 4.12—4.35 (m, 8 H, NCH_2CH_2O), 4.38 (s, 3 H, OCH_3), 14.15 (s, 1 H, NOH). ^{13}C NMR (DMSO-d_6, δ): 44.0, 44.4 (NCH_2), 54.7 (OCH_3), 66.2 (OCH_2), 150.7 ($C(NO_2)$=NOH), 162.9 (N=C—C), 165.6 (N=C—N), 171.3 (N=C—OCH_3). NMR ^{14}N (DMSO-d_6, δ): −12.2 (NO_2). Found (%): C, 38.10; H, 4.20; N, 29.51. $C_9H_{12}N_6O_5$. Calculated (%): C, 38.03; H, 4.26; N, 29.57.

2,4-Bis(dimethylamino)-1,3,5-triazine-6-nitrolic acid (10e). The yield was 45 + 15%, m.p. 88—89 °C (decomp.), R_f 0.66 (dichloroethane—methanol, 4 : 1). IR, ν/cm^{-1}: 3589, 3143, 3043, 3012, 2935, 2879, 2811, 1606, 1585, 1554, 1511, 1479, 1417, 1376, 1272, 1226, 1149, 1070, 1047, 1002, 902, 863, 808, 727, 644. ^{1}H NMR (DMSO-d_6, δ): 3.10 and 3.24 (both s, 6 H, NCH_3, Δν = 24 Hz), 13.10 (s, 1 H, NOH). Found (%): C, 37.54; H, 5.22; N, 38.55. $C_8H_{13}N_7O_3$. Calculated (%): C, 37.65; H, 5.13; N, 38.41.

2-Dimethylamino-4-(*p*-nitrophenoxy)-1,3,5-triazine-6-nitrolic acid (10f). The yield was 47% + 10%, m.p. 114—115 °C (decomp.), R_f 0.7 (dichloroethane—methanol, 4 : 1). IR, ν/cm^{-1}: 3116, 3087, 2935, 2852, 1618, 1554, 1521, 1486, 1419, 1386, 1369, 1344, 1255, 1224, 1166, 1132, 1045, 983, 939, 862, 809. ^{1}H NMR (DMSO-d_6, δ): 3.09 and 3.18 (both s, 6 H, NCH_3, Δν = 18 Hz); 7.62 and 8.34 (both d, 4 H, $OC_6H_4NO_2$-*p*, *J* = 6 Hz); 12.70 (s, 1 H, NOH). Found (%): C, 41.34; H, 3.30; N, 28.00. $C_9H_{12}N_6O_5$. Calculated (%): C, 41.27; H, 3.17; N, 28.07.

2,4-Dimethoxy-1,3,5-triazine-6-nitrolic acid (10g). The yield was 60% + 20%, m.p. 130—131 °C (decomp.), R_f 0.78 (dichloroethane—methanol, 4 : 1). IR, ν/cm^{-1}: 3168, 3141, 3066, 3012, 2964, 2921, 2848, 2690, 2640, 2482, 1587, 1552, 1529, 1490, 1458, 1394, 1373, 1240, 1217, 1166, 1101, 1060, 1012, 871, 823, 727, 661. ^{1}H NMR (DMSO-d_6, δ): 4.10 (s, 6 H, OMe), 13.45 (br.s, 1 H, NOH). Found (%): C, 31.24; H, 3.97; N, 30.26. $C_6H_9N_5O_5$. Calculated (%): C, 31.17; H, 3.92; N, 30.30.

2,4-Di(*n*-propoxy)-1,3,5-triazine-6-nitrolic acid (10i). The yield was 52% + 16%, m.p. 73—75 °C (decomp.), R_f 0.81 (dichloroethane—methanol, 4 : 1). IR, ν/cm^{-1}: 3485, 3203, 3081, 2987, 2966, 2943, 2883, 1579, 1556, 1542, 1496, 1434, 1384, 1355, 1303, 1230, 1149, 1109, 1053, 997, 912, 873, 823, 765, 728. ^{1}H NMR (DMSO-d_6, δ): 1.05 (t, 6 H, CH_3); 1.86 (t, 4 H, CH_2); 4.49 (t, 4 H, OCH_2); 13.07 (br.s, 1 H, NOH). Found (%): C, 41.88; H, 6.02; N, 24.45. $C_{10}H_{17}N_5O_5$. Calculated (%): C, 41.81; H, 5.96; N, 24.38.

2-Dimethylamino-4-dinitromethyl-6-methoxy-1,3,5-triazine zwitterionic salt (12a). The yield was 18%, m.p. 110—112 °C (decomp.), R_f 0.34 (dichloroethane—methanol, 4 : 1). IR, ν/cm^{-1}: 3176, 2942, 2888, 1620, 1564, 1536, 1500, 1476, 1380, 1316, 1244, 1200, 1136, 1048, 1004, 968, 904, 856, 780, 728, 712. ^{1}H NMR (acetone-d_6, δ): 3.12 and 3.19 (both s, 6 H, NCH_3, Δν = 4.2), 3.92 (s, 3 H, OCH_3), 7.98 (s, 1 H, NH). Found (%): C, 32.51; H, 3.94; N, 32.62. $C_7H_{10}N_6O_5$. Calculated (%): C, 32.56; H, 3.90; N, 32.55.

2-Dinitromethyl-4-methoxy-6-pyrrolidino-1,3,5-triazine zwitterionic salt (12b). The yield was 15%, m.p. 111—112 °C (decomp.), R_f 0.32 (dichloroethane—methanol, 4 : 1). IR, ν/cm^{-1}: 3103, 2987, 2958, 2883, 1635, 1608, 1567, 1540, 1483, 1432, 1392, 1340, 1301, 1257, 1232, 1211, 1182, 1141, 1033, 1002, 966, 894, 856, 833, 777, 752, 729. ^{1}H NMR (acetone-d_6, δ): 1.96—2.04 (m, 4 H, CH_2CH_2), 3.54 and 3.66 (both t, 4 H, NCH_2, *J* = 4.6 Hz), 3.94 (s, 3 H, OCH_3), 7.95 (s, 1 H, NH). Found (%): C, 38.00; H, 4.35; N, 29.54. $C_9H_{12}N_6O_5$. Calculated (%): C, 38.05; H, 4.26; N, 29.57.

2-Dinitromethyl-4-methoxy-6-piperidino-1,3,5-triazine zwitterionic salt (12c). The yield was 16%, m.p. 115—116 °C (decomp.), R_f 0.36 (dichloroethane—methanol, 4 : 1). IR, ν/cm^{-1}: 3174, 3014, 2946, 2927, 2858, 1629, 1592, 1564, 1535, 1488, 1421, 1382, 1311, 1272, 1251, 1201, 1162, 1132, 1047, 1024, 993, 854, 821, 777, 736. ^{1}H NMR (acetone-d_6, δ): 1.62—1.80 (m, 6 H, $CH_2CH_2CH_2$), 3.79 and 3.88 (both t, 4 H, NCH_2, *J* = 4.4 Hz), 3.98 (s, 3 H, OCH_3), 7.96 (s, 1 H, NH). Found (%): C, 40.36; H, 4.78; N, 28.44. $C_{10}H_{14}N_6O_5$. Calculated (%): C, 40.27; H, 4.73; N, 28.28.

2-Dinitromethyl-4-methoxy-6-morpholino-1,3,5-triazine zwitterionic salt (12d). The yield was 20%, m.p. 135—136 °C (decomp.), R_f 0.32 (dichloroethane—methanol, 4 : 1). IR, ν/cm^{-1}: 3212, 2956, 2928, 2890, 1634, 1602, 1566, 1546, 1536, 1500, 1448, 1438, 1392, 1312, 1280, 1268, 1246, 1184, 1156, 1116, 1076, 1038, 1004, 958, 888, 856, 828, 772, 746. ^{1}H NMR (acetone-d_6, δ): 3.69—3.80 (m, 8 H, NCH_2CH_2O), 3.92 (s, 3 H, OCH_3), 7.95 (s, 1 H, NH). Found (%): C, 36.07; H, 4.10; N, 27.90. $C_9H_{12}N_6O_6$. Calculated (%): C, 36.00; H, 4.03; N, 27.99.

2,4-Bis(dimethylamino)-6-dinitromethyl-1,3,5-triazine zwitterionic salt (12e). The yield was 25%, m.p. 124—125 °C (decomp.), R_f 0.46 (dichloroethane—methanol, 4 : 1). IR, ν/cm^{-1}: 3050—2850, 1630, 1600—1555, 1520, 1480, 1455, 1380, 1330, 1295, 1200, 1135—1100, 1080, 1025, 990, 965, 930, 845. ^{1}H NMR (acetone-d_6, δ): 3.02 (s, 3 H, NCH_3), 3.07 (s, 3 H, NCH_3), 3.10 (s, 3 H, NCH_3), 3.15 (s, 3 H, NCH_3), 8.26 (s, 1 H, NH). Found (%): C, 35.35; H, 4.62; N, 36.23. $C_8H_{13}N_7O_4$. Calculated (%): C, 35.42; H, 4.80; N, 36.16.

2-Dimethylamino-4-dinitromethyl-6-(4-nitrophenoxy)-1,3,5-triazine zwitterionic salt (12f). The yield was 12%, m.p. 117—118 °C (decomp.), R_f 0.38 (dichloroethane—methanol, 4 : 1). IR, ν/cm^{-1}: 3116, 3077, 3023, 2962, 2935, 2879, 2852, 1616, 1592, 1571, 1519, 1488, 1380, 1342, 1263, 1243, 1216, 1197, 1133, 1062, 1039, 1010, 977, 946, 914, 856, 809, 779, 755, 700. ^{1}H NMR (acetone-d_6, δ): 3.05 and 3.12 (both s, 6 H, NCH_3, Δν = 14.0 Hz); 7.61 and 8.28 (both d, 4 H, *p*-C_6H_4); 8.71 (br.s, 1 H, NH). Found (%): C, 39.46; H, 3.04; N, 26.84. $C_{12}H_{11}N_7O_7$. Calculated (%): C, 39.34; H, 3.18; N, 26.91.

The reaction of 2-R′-4-R″-6-dinitromethyl-1,3,5-triazine K-salts with nitrogen dioxide under anhydrous conditions (general procedure). To a suspension of potassium salts **8a—e** (0.003 mol) in toluene (or dichloroethane) (7 mL) at 15—20 °C, a solution of N_2O_4 (0.24 mL, 0.0039 mol) in the same solvent (3 mL) was poured in one portion. The precipitate of the starting salt gradually disappeared and the precipitate of potassium nitrate sedimented; the solution turned blue-green. The color of the reaction mixture changed gradually from blue-green to green. Nitrolic acid **10a—e** precipitated in 30—60 min. The reaction mixture was cooled to 0 °C, kept for 60 min, a mixture of nitrolic acid and potassium nitrate was filtered off, and washed with a cold solvent (2×3 mL). The product was dried in air, then washed with water (10—15 mL) to remove potassium nitrate. The yields of **10a, 10b, 10c, 10d, 10e** were 56%, 53%, 59%, 67% and 49% respectivelly.

Filtrates were kept for 24 h at 20—25 °C and the solvent was distilled under reduced pressure. Furoxans **11a—e** were isolated from the residue by silica gel chromatography in dichloroethane—methanol (4 : 1).

3,4-Bis(4-dimethylamino-6-methoxy-1,3,5-triazin-2-yl)-furoxan (11a). The yield was 32%, m.p. 140—142 °C (decomp.), R_f 0.84 (dichloroethane—methanol, 4 : 1). IR, ν/cm^{-1}: 3031, 2964, 2921, 2856, 1627, 1569, 1548, 1481, 1367, 1311, 1230, 1116, 1018, 1004, 931, 819, 779. ^{1}H NMR (acetone-d_6, δ): 3.08 and 3.16 (both s, 6 H, NCH_3, Δν = 24 Hz), 3.92 (s, 3 H, OCH_3). Found (%): C, 43.12; H, 4.59; N, 35.86. $C_{14}H_{18}N_{10}O_4$. Calculated (%): C, 43.08; H, 4.65; N, 35.72.

3,4-Bis(4-methoxy-6-pyrrolidino-1,3,5-triazin-2-yl)furoxan (11b). The yield was 30%, m.p. 132—134 °C (decomp.), R_f 0.82 (dichloroethane—methanol, 4 : 1). IR, ν/cm^{-1}: 2971, 2956, 2877, 1623, 1587, 1569, 1533, 1504, 1457, 1371, 1342, 1315, 1238, 1222, 1012, 998, 968, 912, 858, 817, 767. ^{1}H NMR (acetone-d_6, δ): 1.94 (m, 8 H, CH_2CH_2), 3.38 and 3.52 (t, d, 8 H, CH_2NCH_2), 3.88 (s, 3 H, OCH_3), 3.92 (s, 3 H, OCH_3). Found (%): C, 48.95; H, 5.10; N, 31.73. $C_{18}H_{22}N_{10}O_4$. Calculated (%): C, 48.80; H, 5.01; N, 31.66.

3,4-Bis(4-methoxy-6-piperidino-1,3,5-triazin-2-yl)furoxan (11c). The yield was 20%, m.p. 139—141 °C (decomp.), R_f 0.83 (dichloroethane—methanol, 4 : 1). IR, ν/cm^{-1}: 3010, 2939, 2858, 1623, 1577, 1535, 1508, 1467, 1448, 1375, 1324, 1294, 1222,1091, 1062, 1020, 985, 898, 854, 819, 748. ^{1}H NMR (DMSO-d_6, δ): 1.36—1.69 (m, 12 H, CH_2), 3.54 and 3.73 (both m, 8 H, NCH_2), 3.92 (s, 6 H, OCH_3). ^{13}C NMR (DMSO-d_6, δ): 23.83, 25.29 (CH_2—CH_2—CH_2), 44.19 (CH_2—N), 54.54, 54.59 (OCH_3), 112.00 (C=N$^+$—O$^-$), 154.07 (C=N—O), 162.55, 163.91 (N—C—C=NO), 164.15 (C—NCH_2), 170.65 (C—OCH_3). Found (%): C, 51.19; H, 5.61; N, 29.65. $C_{20}H_{26}N_{10}O_4$. Calculated (%): C, 51.06; H, 5.57; N, 29.77.

3,4-Bis(4-methoxy-6-morpholino-1,3,5-triazin-2-yl)furoxan (11d). The yield was 24%, m.p. 180—182 °C (decomp.), R_f 0.86 (dichloroethane—methanol, 4 : 1). IR, ν/cm^{-1}: 2968, 2925, 2869, 1631, 1577, 1565, 1529, 1486, 1467, 1444, 1371, 1301, 1284, 1230, 1114, 1068, 1025, 999, 989, 852, 813, 756, 636, 540. ^{1}H NMR (DMSO-d_6, δ): 3.6—3.8 (m, 16 H, NCH_2CH_2O), 3.96 (s, 6 H, OCH_3). NMR ^{13}C (DMSO-d_6, δ): 43.85 (CH_2—N), 54.59 (OCH_3), 65.72 (CH_2—O), 111.73 (C=N$^+$—O$^-$), 153.85 (C=N—O), 162.72, 164.16 (N—C—C=NO), 165.05, 165.15 (C—NCH_2), 170.79, 170.91 (C—OCH_3). Found (%): C, 45.50; H, 4.72; N, 29.37. $C_{18}H_{22}N_{10}O_6$. Calculated (%): C, 45.57; H, 4.67; N, 29.52.

3,4-Bis[4,6-bis(dimethylamino)-1,3,5-triazin-2-yl)furoxan (11e). The yield was 38%, m.p. 210—212 °C, R_f 0.77 (dichloroethane—methanol, 4 : 1). IR, ν/cm^{-1}: 2935, 2871, 1618, 1569, 1523, 1502, 1398, 1330, 1299, 1201, 1049, 979, 970, 846, 813, 746. ^{1}H NMR (DMSO-d_6, δ): 3.06 (s, 12 H, NCH_3), 3.15 (s, 12 H, NCH_3). Found (%): C, 46.02; H, 5.97; N, 40.44. $C_{16}H_{24}N_{12}O_2$. Calculated (%): C, 46.15; H, 5.81; N, 40.36.

Synthesis of furoxans 11a—e,g,h from nitrolic acids 10a—d,e—i (general procedure). Nitrolic acid **10a—d,e—i** (0.03 mol) was heated in toluene (20 ml) at 90—110 °C. The evolution of brown nitrogen oxides was observed beginning from 90 °C. The end of the reaction was monitored by disappearance of the starting compounds (TLC, dichloroethane—methanol, 4 : 1). The resulting solution was cooled to room temperature and passed through a small silica gel layer (1—2 cm). The solvent was removed under residue pressure. The residue was treated with water, the insoluble crystalline product was filtered off and dried in air. The yields of **11a, 11b, 11c, 11d, 11e** were 89%, 92%, 82%, 86% and 84% respectivelly.

3,4-Bis(4,6-dimethoxy-1,3,5-triazin-2-yl)furoxan (11g). The yield was 86%, m.p. 148—150 °C. IR, ν/cm^{-1}: 3022, 2960, 2919, 2885, 2852, 1629, 1591, 1548, 1481, 1367, 1311, 1230, 1201, 1105, 1018, 1004, 931, 819, 779, 759. ^{1}H NMR (DMSO-d_6, δ): 3.84 (s, 6 H, OCH_3), 3.92 (s, 6 H, OCH_3). ^{13}C NMR (DMSO-d_6, δ): 55.97, 56.15 (OCH_3), 111.81 (C=N$^+$—O$^-$), 153.35 (C=N—O), 164.42, 166.09 (N—C—C=NO), 172.43, 172.63 (C—OCH_3). Found (%): C, 39.67; H, 3.41; N, 30.88. $C_{12}H_{12}N_8O_6$. Calculated (%): C, 39.57; H, 3.32; N, 30.76.

3,4-Bis(4,6-di-*n*-propoxy-1,3,5-triazin-2-yl)furoxan (11i). The yield was 85%, pale yellow viscous liquid. IR, ν/cm^{-1}: 2969, 2939, 2879, 1629, 1554, 1484, 1454, 1419, 1355, 1330, 1301, 1218, 1122, 1056, 987, 931, 827, 790, 755. ^{1}H NMR (DMSO-d_6, δ): 1.00 (m, 16 H, CH_3); 1.78 (m, 8 H, CH_2); 4.25 (t, 4 H, OCH_2, J = 6.7 Hz), 4.34 (t, 4 H, OCH_2, J = 6.7 Hz). Found (%): C, 50.35; H, 6.03; N, 23.46. $C_{20}H_{28}N_8O_6$. Calculated (%): C, 50.41; H, 5.92; N, 23.52.

2-Methoxy-4-pyrrolidinyl-1,3,5-triazine-6-carboxylic acid. Sodium nitrite (0.21 g, 0.003 mol) was added with stirring at 20—25 °C to a solution of nitrolic acid **7b** (0.536 g, 0.002 mol) in DMF (5 mL). The reaction mixture was kept at 20—25 °C until the starting compound disappeared (TLC, 1—1.5 h), DMF was evaporated with a flow of air, and the residue was suspended in water (20 mL). Sodium hydroxide (0.12 g) was added and stirred for 1 h. The filtered solution was acidified with 10% HCl to pH 1—2. Water was evaporated with a flow of air, the residue was extracted with methanol (3×5 mL). The combined methanolic extracts were concentrated under reduced pressure, the residue was washed with cold acetone (3 mL) dried in air. The colorless amorphous compound (0.2 g, 45%) was obtained, m.p. 125—126 °C (decomp.). IR, ν/cm^{-1}: 2973, 2933, 2890, 1726, 1600, 1556, 1511, 1459, 1375, 1342, 1241, 1058, 1014, 972, 914, 867, 811, 792. ^{1}H NMR (DMSO-d_6, δ): 2.06 (m, 4 H, CH_2); 3.65 (m, 4 H, NCH_2), 3.96 (s, 3 H, OCH_3), 4.30 (br.s, H_3O^+). Found (%): C, 48.14; H, 5.31; N, 25.10. $C_9H_{12}N_4O_3$. Calculated (%): C, 48.21; H, 5.39; N, 24.99.

The work was partially financially supported by the Russian Foundation for Basic Research (Project Nos 05-04-48577 and 07-03-00403) and the Russian Academy of Sciences (Program of the Presidium of RAS "Basic Research").

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Received October 20, 2008;
in revised form Februare 24, 2009