Thermolysis of furoxans annulated with five-membered carbocycles in the presence of dipolarophiles*

*A. S. Kulikov, M. A. Epishina, I. V. Ovchinnikov, and N. N. Makhova**

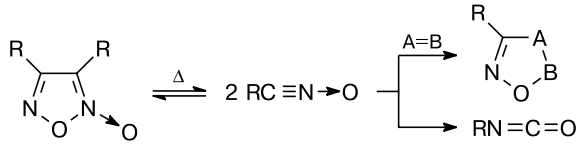
N. D. Zelinsky Institute of Organic Chemistry, Russian Academy of Sciences,
47 Leninsky prosp., 119991 Moscow, Russian Federation.
Fax: +7 (499) 135 5328. E-mail: mnn@ioc.ac.ru

The conditions for the thermolysis of furoxans annulated with differently strained five-membered carbocycles (cyclopentafuroxan **1**, norbornenofuroxan **2**, and acenaphthofuroxan **3**) to bis(nitrile oxides) in the presence of various dipolarophiles (diethyl acetylenedicarboxylate, benzoylformonitrile, and ethoxycarbonylformonitrile) were optimized. It was found that the reactivities of the above furoxans as sources of bis(nitrile oxides) decrease in the order **2** > **1** > **3**. Among the furoxans studied, only norbornenofuroxan **2** can be recommended as a possible cross-linking reagent for polymers. The formation of di-*N*-oxides of 3,4-bis(cyanopropyl)-, 3,4-bis(cyanocyclopentyl)-, and 3,4-bis(cyanonaphthyl)furoxans was detected. They resulted from intermolecular cyclodimerization of bis(nitrile oxides) initially formed in the thermolysis of furoxans **1**—**3**.

Key words: furoxans annulated with five-membered carbocycles, thermolysis, bis(nitrile oxides), dipolarophiles, 1,3-cycloaddition, cross-linking.

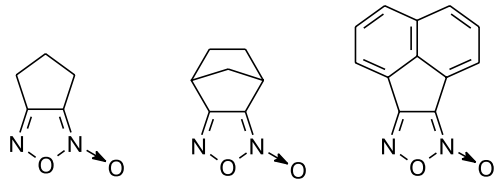
The furoxan (1,2,5-oxadiazole 2-oxide) ring is known for its unique tendency toward thermal opening along two C(3)—C(4) and O(1)—N(2) bonds to give two nitrile oxide fragments. This ring opening depends on the type of the substituents at the ring C atoms and occurs in the temperature range from 20 °C for 3,4-dinitrofuroxan[1] to 250 °C for 3,4-diphenylfuroxan.[2] At the same time, cyclodimerization of nitrile oxides is a common route to furoxans.[3] Therefore, the synthesis and thermolysis of furoxans can be considered to be an equilibrium process shifted in the forward or reverse direction, depending on the reaction conditions. Thermolysis of furoxans in the presence of dipolarophiles yields 1,3-dipolar cycloadducts.[4] In addition, nitrile oxides can isomerize *in situ* into isocyanates[5] (Scheme 1).

Scheme 1



Compounds containing the furoxan ring annulated with other rings can serve as sources of intermediates combining two nitrile oxide or two isocyanate groups in the molecule. Furoxans annulated with five-membered carbocycles (strained furoxans) are especially attractive for access to such intermediates since their thermal opening begins at a sufficiently low temperature (100 °C and below).[6] For thermolysis of furoxans annulated with saturated carbocycles containing more methylene units, higher temperatures are required.[7]

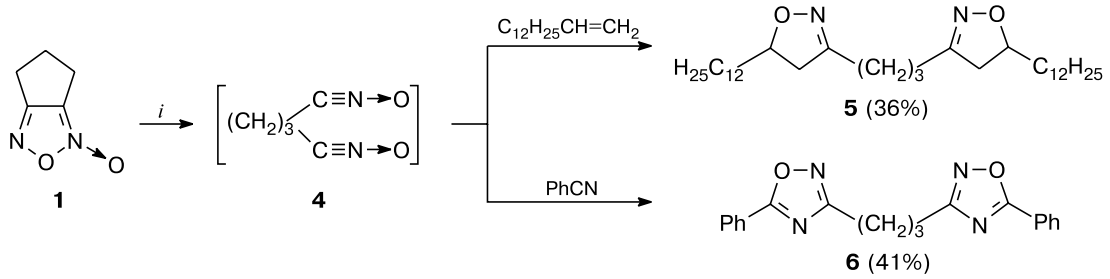
The number of known furoxan derivatives annulated with five-membered carbocycles is limited and they can be structurally classified into three groups. The first group includes furoxans annulated with cyclopentane derivatives, the second group includes furoxans annulated with norbornene derivatives, and the third group includes furoxans annulated with acenaphthene. Below are the most common representatives of each group: 5,6-dihydro-4*H*-cyclopenta[*c*]-1,2,5-oxadiazole 1-oxide (cyclopentafuroxan (**1**)), 4,5,6,7-tetrahydro-4,7-methano-2,1,3-benzoxadiazole 1-oxide (norbornenofuroxan (**2**)), and acenaphtho[1,2-*c*]-1,2,5-oxadiazole 7-oxide (acenaphthofuroxan (**3**)).



* Dedicated to Academician V. A. Tartakovsky on the occasion of his 75th birthday.

Published in Russian in *Izvestiya Akademii Nauk. Seriya Khimicheskaya,* No. 8, pp. 1521—1528, August, 2007.

Scheme 2



i. 195—200 °C, 40 min.

Formation of glutarodinitrile di-*N*-oxide **4** upon the thermolysis of cyclopentafuroxan **1** has been illustrated with the synthesis of biscycloadducts **5** and **6** from tetradec-1-ene[8] and benzonitrile[9] as dipolarophiles (Scheme 2).

Data on the thermolysis of norbornenofuroxan **2** in the presence of such dipolarophiles as phenylacetylene and adipodinitrile are available from the patent literature[9,10] (Scheme 3). A reaction of intermediate cyclopentane-1,3-bis(nitrile oxide) **7** with phenylacetylene gives bisisoxazole **8** and heating of compound **2** with adipodinitrile yields a resinous product identified as polyoxadiazole **9**. However, compound **8** and polymer **9** have been characterized only by melting points (and elemental analysis data for **8**).[9,10] Thermolysis of acenaphthofuroxan **3** in the presence of dipolarophiles has not been studied hitherto.

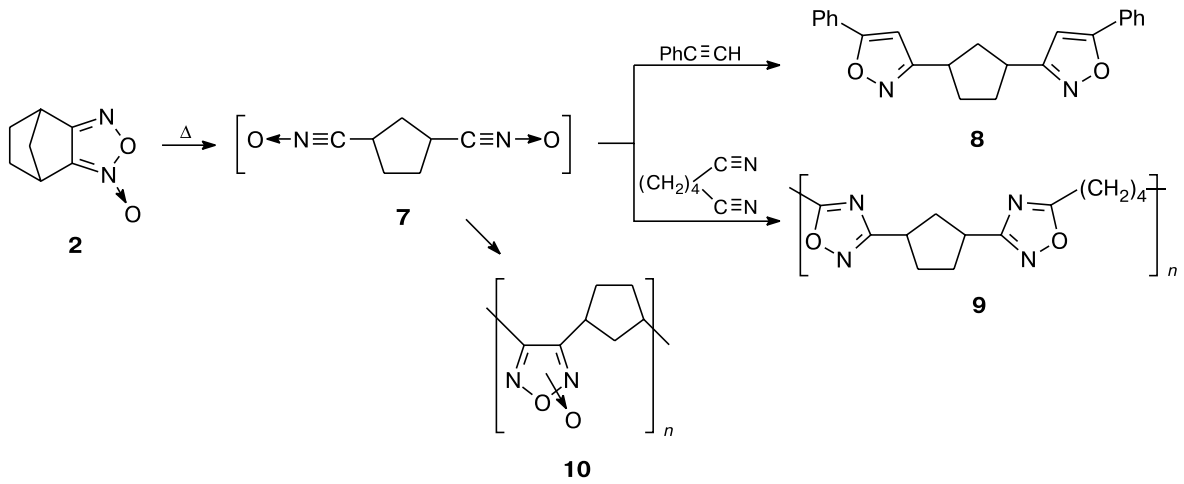
Compounds of the types **1**—**3** can also be used as cross-linking reagents for polymers. Relevant investigations have been described only in the patent literature[9,10] containing no data on the structures of the polymers obtained. It has been reported[5] that bis(nitrile oxide) **7** generated in the thermolysis of norbornenofuroxan **2** can form polymeric product **10** (Scheme 3). However, its structure has not been proved.

Thus, our survey of literature data shows that furoxans of the types **1**—**3** can actually undergo heat-induced opening to the corresponding bis(nitrile oxides) capable of reacting with various dipolarophiles under the thermolysis conditions. However, the reaction conditions have not been optimized for each structural type and the structures of the final adducts mostly have not been proved. At the same time, compounds **1**—**3** are of considerable interest as cross-linking reagents for polymers because of heat-induced generation of the corresponding bis(nitrile oxides) capable of cross-linking oligomers and polymers.

The goal of the present work was to compare furoxan derivatives **1**—**3** (annulated with differently strained five-membered carbocycles) as sources of bis(nitrile oxides) in their thermolysis in the presence of dipolarophiles and test them for potential cross-linking ability.

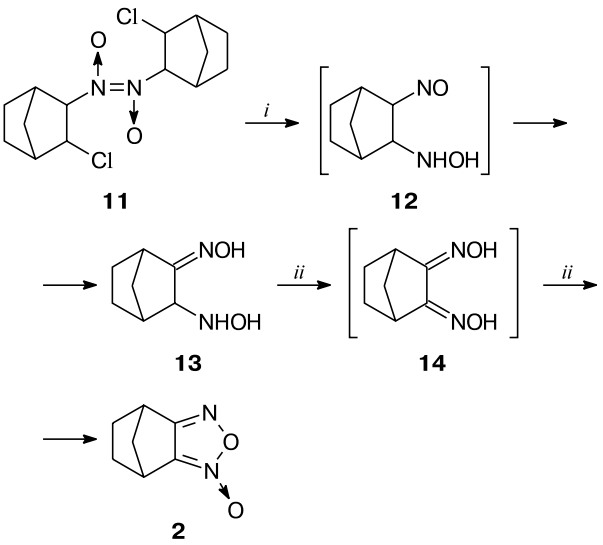
Compounds **1** and **3** were synthesized as described earlier.[11,12] The first step of a known route to norbornenofuroxan **2** involves a reaction of norbornene

Scheme 3



with N_2O_3, which is prepared by mixing NO with air in a precise molar ratio.[13,14] Since this is rather inconvenient under laboratory conditions, we developed an alternative method starting from chloronitrosonorbornane dimer **11** (see Ref. 15) (Scheme 4). Reflux of compound **11** with hydroxylamine in aqueous dioxane resulted in its dedimerization and nucleophilic displacement of the Cl atom by the hydroxylamino group, giving intermediate **12**. Subsequent isomerization of the nitroso group into a hydroxyimino group led to derivative **13**. This derivative was too unstable to be isolated in the analytically pure state (this is characteristic of such compounds[16]) and was characterized only by ^{1}H NMR spectroscopic data. Compound **13** was oxidized into norbornenofuroxan **2** with NaOCl in an aqueous alkali, probably through intermediate dioxime **14**.

Scheme 4



i. NH_2OH, H_2O/dioxane. *ii*. NaOCl.

To study the comparative reactivities of furoxans **1**—**3** under thermolysis conditions, we employed diethyl acetylenedicarboxylate (**15**), benzoylformonitrile (**16**), and ethoxycarbonylformonitrile (**17**) as dipolarophiles. The nitriles served as model compounds because the cyano group is part of many practically important polymers.

Reactions of furoxans **1**—**3** with dipolarophiles were carried out in boiling CCl_4 or $CHCl_3$ or with the use of neat reagents. In some cases, thermolysis was conducted in sealed tubes. We always used an excess of the dipolarophile (2 or 5 mol per mole of furoxan). First, we studied the reactivities of furoxans **1**—**3** in 1,3-dipolar cycloaddition reactions with one of the most reactive dipolarophiles, *viz.*, diethyl acetylenedicarboxylate **15**, under the thermolysis conditions.

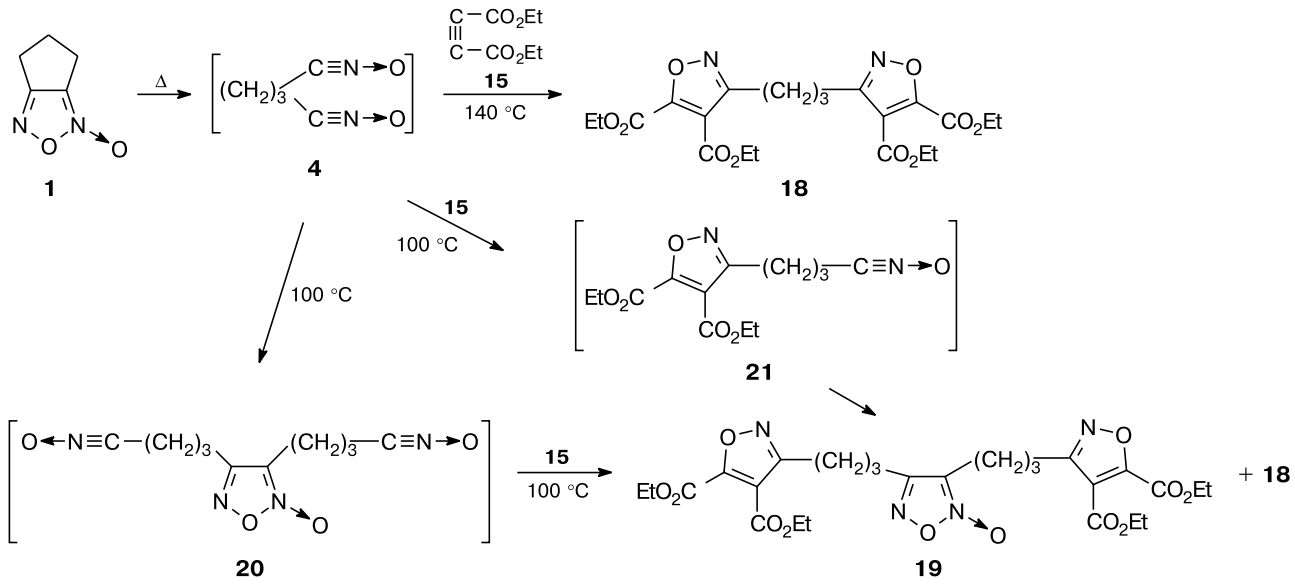
Heating in a sealed tube of a mixture of cyclopentafuroxan **1** and diethyl acetylenedicarboxylate **15** in the molar ratio 1 : 2 in CCl_4 at 100 °C for 30 h gave a mixture of bisisoxazole **18** and furoxan **19** in the ratio 2 : 3 (^{1}H NMR data) (Scheme 5). Individual derivative **18** was obtained in 33% yield when the reaction was carried out at 140 °C for 7 h for the same molar ratio (1 : 2) of neat reagents. The same results were obtained at a ratio of 1 : 5. Compound **19** was not isolated in the individual state; its structure was proposed from a comparison of its ^{1}H NMR spectrum with the spectrum of compound **18**. Both spectra contain signals for the ethoxy groups and the fragment $—(CH_2)_3—$. However, the integral intensity of the signals in these spectra indicates the presence of four ethoxy groups and one fragment $—(CH_2)_3—$ in compound **18** and the presence of four ethoxy groups and two fragments $—(CH_2)_3—$ in compound **19**. Thus, cyclopentafuroxan **1** is not highly reactive as a source of bis(nitrile oxide) **4** in 1,3-dipolar cycloaddition reactions under the thermolysis conditions. Even with such a reactive dipolarophile as diethyl acetylenedicarboxylate **15**, it reacts under sufficiently drastic conditions.

The structures of the final products suggest that intermediate bis(nitrile oxide) **4** could undergo cyclodimerization into 3,4-bis(3-cyanopropyl)furoxan di-*N*-oxide **20**, which reacts with compound **15** to give furoxan **19**. The detection of oligomeric compounds provides evidence for this mechanism of the formation of furoxan **19** (see Refs 9, 10). Alternatively, compound **19** could be formed *via* a two-step process involving addition of diethyl acetylenedicarboxylate **15** to one nitrile oxide fragment of intermediate **4** followed by cyclodimerization of product **21**.

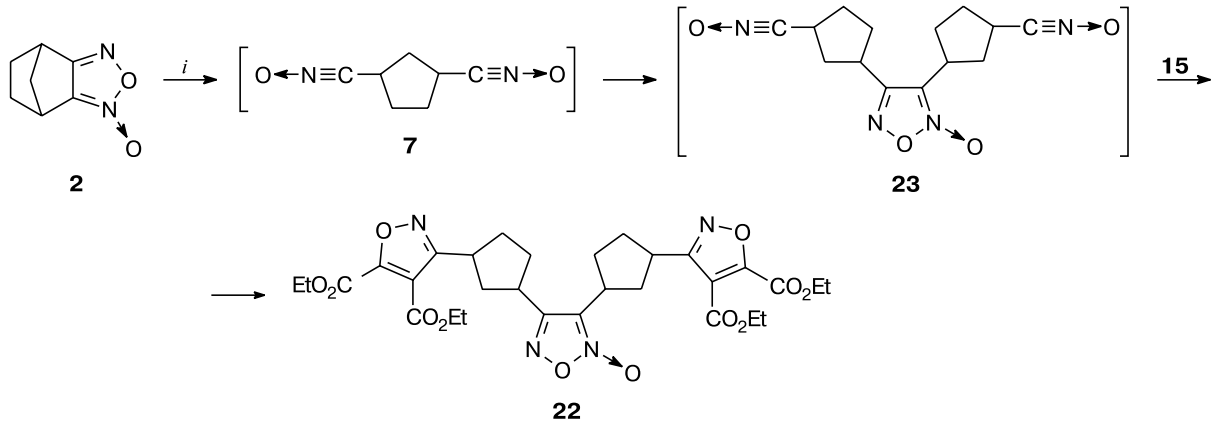
Norbornenofuroxan **2** was substantially more reactive toward compound **15** than was cyclopentafuroxan **1**. The reaction of compound **2** with diethyl acetylenedicarboxylate **15** in the molar ratio 1 : 2 was completed over 1 and 1.5 h in boiling CCl_4 and $CHCl_3$, respectively (monitoring by TLC). In both cases, the major product was furoxan **22**. Under more drastic conditions (heating of the neat reagents at 100 °C), a complex mixture of products was obtained. Nevertheless, this mixture also contained compound **22** (^{1}H NMR data). Obviously, in this case too, the reaction of bis(nitrile oxide) **7** with dipolarophile **15** proceeds more slowly than its intermolecular dimerization into bis(nitrile oxide) **23**, which reacts with diethyl acetylenedicarboxylate **15** to give final product **22** (Scheme 6).

Much more drastic conditions were required for acenaphthofuroxan **3** to react with diethyl acetylenedicarboxylate **15**. Heating of their mixture in the molar ratio 1 : 2 in chloroform at 100 °C for a day in a sealed tube yielded furoxan **24**. Under different reaction conditions, no other cycloaddition products were obtained. The formation of product **24** suggests that in this case too,

Scheme 5



Scheme 6

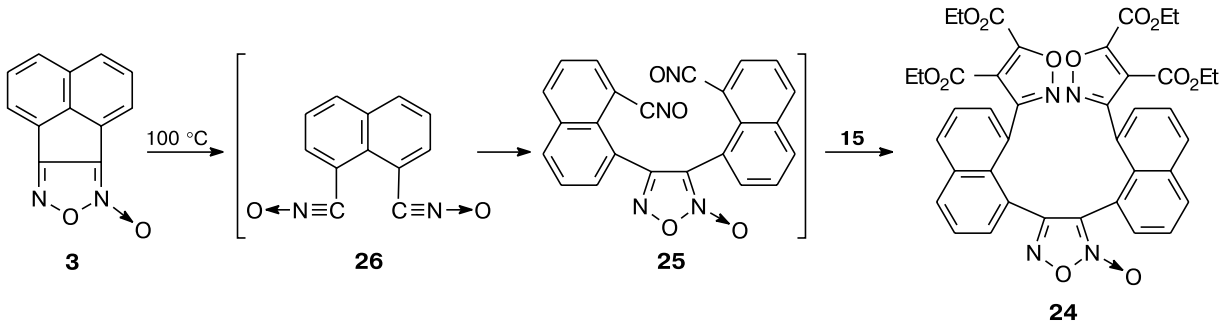


i. Heating.

1,3-dipolar cycloaddition involves bis(nitrile oxide) **25** rather than initially formed 1,8-naphthylenebis(nitrile oxide) **26** (Scheme 7).

The formation of compounds **19**, **22**, and **24** is the first known example of another reaction pathway for furoxans **1**—**3** subjected to thermolysis in the presence of di-

Scheme 7

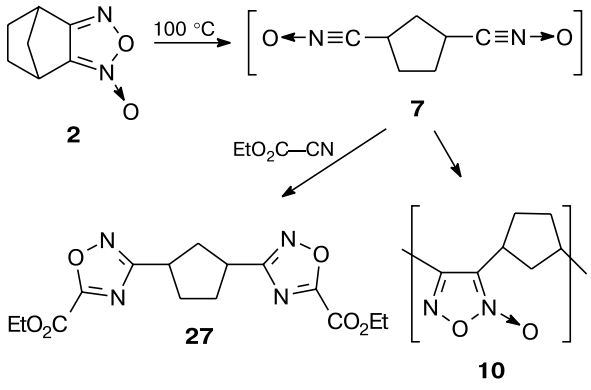


polarophiles: one nitrile oxide fragment of intermediates **4**, **7**, and **26** is involved in intermolecular cyclodimerization leading to new furoxan bis(nitrile oxides) **20**, **23**, and **25**, which then react with appropriate dipolarophiles.

Benzoylformonitrile **16** in reactions with furoxans **1**—**3** was much less reactive than diethyl acetylenedicarboxylate **15**. Cyclopentafuroxan **1** and acenaphthofuroxan **3** did not react with nitrile **16** under different conditions (the reaction temperature and time and the ratio of the reagents were varied); they were recovered from the reaction mixture either unchanged or contaminated with polymeric products of the thermolysis. In a reaction of norbornenofuroxan **2**, which is most reactive among the furoxans studied, with nitrile **16** at 65 to 100 °C, we observed only gradual decomposition of the starting furoxan without detecting any products by chromatography. Only short-time (5—20 min) keeping of the reaction mixture at 150 °C gave several products (TLC data). A product with the most intense TLC spot was isolated by preparative chromatography on silica gel. The ^{1}H NMR spectrum recorded in $CDCl_3$ immediately after its isolation contained signals at δ 7—8 attributable to aromatic protons and signals for aliphatic protons (δ 2—3.5). However, the data obtained were insufficient for rigorous proof of its structure and the product was not isolated in the analytically pure state because of its small amount.

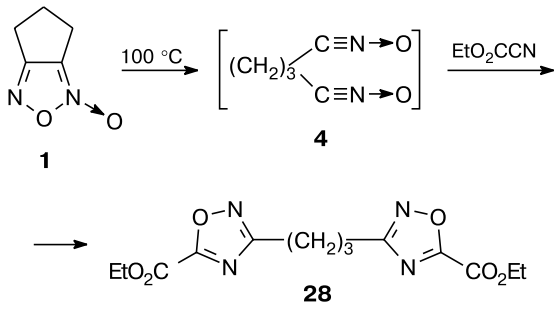
As expected, ethoxycarbonylformonitrile **17** was substantially more reactive than benzoylformonitrile **16**. Heating of its mixture with norbornenofuroxan **2** in the molar ratio 5 : 1 at 100 °C for 1 h gave a mixture of three products with R_f 0.12, 0.34, and 0.69 ($CHCl_3$—EtOAc (20 : 1)). The product with R_f 0.34 (the largest spot) was isolated by preparative TLC on silica gel. According to elemental analysis data and spectroscopic characteristics, this compound was 1,3-bis(5-ethoxycarbonyl-1,2,4-oxadiazol-3-yl)cyclopentane (**27**) (Scheme 8). Analogous results were obtained on heating of the same mixture at 90 °C for 3 h; however, the final mixture was more complex (monitoring by TLC). In all cases, the starting furoxan **2** was partly converted into a polymeric product (probably, similar to polymeric product **10**) (see Scheme 3). Obviously, ethoxycarbonylformonitrile **17** as a dipolarophile is less reactive in polycyclodimerization than initially formed bis(nitrile oxide) **7**.

Scheme 8



A reaction of a solution of cyclopentafuroxan **1** in CCl_4 with ethoxycarbonylformonitrile **17** in the molar ratio 1 : 2 in a sealed tube at 100°C for 30 h did not yield the expected products. Under these conditions, a considerable part of the starting furoxan remained unchanged. An increase in the molar ratio of the reagents to 1 : 5 under the same conditions had no effect. Only when the reaction was carried out between the neat reagents at 140 °C for 7 h (monitoring by TLC), the 1,3-dipolar cycloadduct 1,3-bis(5-ethoxycarbonyl-1,2,4-oxadiazol-3-yl)propane **28** was obtained in 33% yield (Scheme 9).

Scheme 9



Reactions with acenaphthofuroxan **3** were always carried out in sealed tubes. Its mixture with ethoxycarbonylformonitrile **17** in the molar ratio 1 : 2 or 1 : 5 was heated in CCl_4 at 100—140 °C for 30 h. In all cases, only the starting furoxan slightly contaminated with a polymeric product was recovered from the reaction mixture (TLC and ^{1}H NMR data).

In conclusion, we found that furoxans **1**—**3** annulated with five-membered carbocycles show, as sources of bis(nitrile oxides), a decreasing tendency toward 1,3-dipolar cycloaddition upon the thermolysis in the presence of dipolarophiles and can be arranged in the following order: norbornenofuroxan **2** > cyclopentafuroxan **1** > > acenaphthofuroxan **3**. The synthesis of cycloaddition products was almost always complicated by the formation of polycyclodimerization products from intermediate bis(nitrile oxides). We discovered and chemically detected the formation of 3,4-bis(cyanopropyl)-, 3,4-bis(cyanocyclopentyl)-, and 3,4-bis(cyanonaphthyl)furoxan di-*N*-oxides resulting from intermolecular cyclodimerization of bis(nitrile oxides) initially formed in the thermolysis. Out of the furoxan derivatives **1**—**3** studied, only norbornenofuroxan **2** can be recommended as a potential cross-linking reagent for polymers.

Table 1. Yields, IR spectra, and selected physicochemical characteristics of the compounds obtained

Compound	Yield (%)	M.p. /°C	R_f (eluent)	Found / Calculated (%)			Molecular formula	IR, ν/cm^{-1}
				C	H	N		
18	26	Oil	0.17 ($CHCl_3$)	54.66 / 54.05	5.88 / 5.62	5.57 / 6.01	$C_{21}H_{26}N_2O_{10}$	2984, 2940, 2908, 1732, 1608, 1480, 1448, 1392, 1372, 1304, 1200, 1172, 1104, 1036, 860, 836, 768
22	29	Oil	0.20 ($CHCl_3$)	55.22 / 55.90	5.49 / 5.63	9.11 / 8.70	$C_{30}H_{36}N_4O_{12}$	2984, 2940, 1732, 1640, 1608, 1480, 1448, 1392, 1372, 1304, 1200, 1172, 1104, 1036, 860, 836, 768
24	36	150—151	0.51 ($CHCl_3$)	63.59 / 63.14	4.38 / 4.21	7.12 / 7.37	$C_{40}H_{32}N_4O_{12}$	2984, 1756, 1584, 1492, 1476, 1444, 1372, 1320, 1264, 1216, 1196, 1184, 1152, 1096, 1020, 976, 956, 928, 896, 856, 820, 768, 700
27	15	62—63	0.34 ($CHCl_3$: EtOAc = 20 : 1)	49.32 / 49.98	4.89 / 5.18	16.23 / 16.01	$C_{15}H_{18}N_4O_6$	2980, 2936, 2884, 1756, 1588, 1564, 1512, 1476, 1452, 1378, 1360, 1304, 1204, 1112, 1032, 1004, 880, 844, 736
28	33	42—43	0.60 ($CHCl_3$: EtOAc = 1 : 10)	49.02 / 49.15	4.69 / 4.95	17.49 / 17.28	$C_{13}H_{16}N_4O_6$	3500, 1736, 1720, 1612, 1580, 1552, 1508, 1460, 1440, 1404, 1348, 1296, 1260, 1160, 880

The yields and selected physicochemical characteristics of the compounds obtained are summarized in Table 1. Their ^{1}H and ^{13}C NMR and mass spectra are given in Table 2.

Experimental

IR spectra were recorded on a UR-20 spectrometer (KBr). ^{1}H and ^{13}C NMR spectra were recorded on a Bruker AM-300 instrument (300 and 75.5 MHz, respectively). Chemical shifts are given on the δ scale with reference to Me_4Si. Mass spectra were recorded on a Varian MAT 6 spectrometer (70 eV). Melting points were determined on a GALLENKAMP instrument (Sanyo). Thin-layer chromatography was carried out on Silufol UV-254 plates with spot visualization under UV light. Elemental analysis was carried out on a Hewlett-Packard 185 C,H,N-analyzer.

4,5,6,7-Tetrahydro-2,1,3-benzoxadiazole 1-oxide (norbornenofuroxan) (2). A mixture of 3-chloro-2-nitrosobicyclonorbornane dimer **11** (18 g, 0.113 mol) (see Ref. 15), hydroxylamine hydrochloride (19.6 g, 0.28 mol), and sodium acetate trihydrate (35.4 g, 0.26 mol) in dioxane (140 mL) and water (40 mL) was refluxed for 5 h. The mixture was evaporated to dryness *in vacuo* and the residue was treated with a solution of potassium carbonate (18 g, 0.13 mol) in water (80 mL). The product was extracted with chloroform (3×120 mL), dried over $MgSO_4$, and concentrated to give 3-hydroxyimino-2-hydroxylaminonorbornane **13** (15.7 g, 89%) as an oil. ^{1}H NMR (DMSO-d_6), δ: 1—4 (wm), 10.5 and 11.0 (both br.s, OH).

Aqueous alkaline 8% NaOCl (67 mL, 82 mmol) was added dropwise at −5 to 0 °C for 30 min to a stirred suspension of 3-hydroxyimino-2-hydroxylaminonorbornane **13** (5.4 g, 34.6 mmol) in a mixture of CH_2Cl_2 (80 mL) and 10% NaOH (16 mL). Then the reaction mixture was allowed to slowly warm to ambient temperature. The organic layer was separated, washed with cold water (2×20 mL), dried over $MgSO_4$, and concentrated *in vacuo*. The physicochemical and spectroscopic characteristics of the compound obtained agree with literature data.[13]

1,3-Bis(4,5-diethoxycarbonylisoxazol-3-yl)propane (18). A mixture of cyclopentafuroxan **1** (0.50 g, 4 mmol) and diethyl acetylenedicarboxylate **15** (1.36 g, 8 mmol) was refluxed in a sealed tube at 140 °C for 7 h. The product was isolated by preparative TLC with chloroform as an eluent. The yield of compound **18** was 0.48 g (26%), an oil.

3,4-Bis[3-(4,5-diethoxycarbonylisoxazol-3-yl)propyl]furoxan (19). A mixture of the reagents used in the synthesis of compound **18** was heated in a sealed tube in CCl_4 (3 mL) at 100 °C for 30 h and then concentrated. The residue contained compounds **18** and **19** in the ratio 2 : 3 (^{1}H NMR data). Compound **19**. ^{1}H NMR ($CDCl_3$), δ: 1.32 (t, 12 H, 4 Me, ^3J = 8.0 Hz); 2.1 (m, 4 H, $CH_2\underline{CH_2}CH_2$, ^3J = 7.8 Hz), 2.52 (t, 4 H, CH_2 furoxan, ^3J = 7.8 Hz); 2.75 (t, 4 H, CH_2 isoxazole, ^3J = 7.8 Hz).

3,4-Bis[1-(4,5-diethoxycarbonylisoxazol-3-yl)cyclopentan-3-yl]furoxan (22). A mixture of freshly prepared norbornenofuroxan **2** (0.57 g, 3.75 mmol) and diethyl acetylenedicarboxylate **15** (1.28 g, 7.5 mmol) in CCl_4 or $CHCl_3$ (2.5 mL) was refluxed for 1 or 1.5 h, respectively. The solvent was removed in a rotary evaporator and the major product (R_f 0.20) was isolated by preparative TLC with $CHCl_3$ as an eluent. The solvent was removed *in vacuo*. The yield of compound **22** was 0.35 g (29%).

3,4-Bis[8-(4,5-diethoxycarbonylisoxazol-3-yl)-1-naphthyl]furoxan (24). A mixture of acenaphthofuroxan **3** (0.21 g, 1 mmol) and diethyl acetylenedicarboxylate **15** (0.34 g, 2 mmol) in CCl_4 (2 mL) was heated in a sealed tube at 100 °C for 24 h. The solvent was removed in a rotary evaporator and the residue was purified by preparative column chromatography on SiO_2 with $CHCl_3$ as an eluent. The solvent was removed *in vacuo*. The yield of compound **24** was 0.14 g (36%).

1,3-Bis(5-ethoxycarbonyl-1,2,4-oxadiazol-3-yl)cyclopentane (27). A mixture of freshly prepared norbornenofuroxan **2** (2.30 g,

Table 2. ^{1}H and ^{13}C NMR ($CDCl_3$) and mass spectra of the compounds obtained

Compound	^{1}H NMR	^{13}C NMR	MS, *m/z*
	δ (*J*/Hz)		
18	1.30 (t, 6 H, 2 Me, ^{3}J = 8.0); 1.38 (t, 6 H, 2 Me, ^{3}J = 8.0); 2.14 (m, 2 H, $CH_2\underline{CH_2}CH_2$); 2.95 (t, 4 H, ($\underline{CH_2}CH_2\underline{CH_2}$), ^{3}J = 7.2); 4.30 (q, 4 H, 2 OCH_2, ^{3}J = 8.0); 4.40 (q, 4 H, 2 OCH_2, ^{3}J = 8.0)	13.97 (Me); 24.96 ($CH_2\underline{CH_2}CH_2$); 25.20 ($\underline{CH_2}CH_2\underline{CH_2}$); 61.44 ($OCH_2$); 62.94 ($OCH_2$); 113.77 (C(4) isoxaz. ring); 156.79 (C(3) isoxaz. ring); 160.36 (C(5) isoxaz. ring); 161.34, 162.40 (2 CO)	467 [M^+ + 1], 393 [$M^+ - CO_2Et$] 365 [$M^+ - CO_2Et - C_2H_4$] 319 [$M^+ - 2\ CO_2Et - 1$] 292 [$M^+ - 2\ CO_2Et - C_2H_4 + 1$] 240, 227, 180, 152
22	1.38, 1.43 (both dt, 12 H, 4 Me, ^{3}J = 8.0); 1.50—1.70, 2.05—2.40, 2.50—2.70 (all m, 12 H, 6 CH_2 in cyclopent. ring); 3.50–3.70 (m, 4 H, 4 CH); 4.45, 4.55 (both q, 8 H, 4 OCH_2, ^{3}J = 8.0)	13.50 (Me); 28.05, 28.17 (C(5) cyclopent. ring); 29.36 (C(4) cyclopent. ring); 38.00 (C(2) cyclopent. ring); 39.38 (C(3) cyclopent. ring); 40.16, 43.10 (C(1) cyclopent. ring); 60.22 (OCH_2); 113.08 (C(3) furox. ring); 117.65 (C(4) isoxaz. ring); 153.18 (C(4) furox. ring); 157.55 (C(3) isoxaz. ring); 161.36 (C(5) isoxaz. ring); 162.54, 164.82 (2 CO)	
24	1.01 (t, 6 H, 2 Me, ^{3}J = 8.0); 1.42 (t, 6 H, 2 Me, ^{3}J = 8.0); 4.04 (q, 4 H, 2 OCH_2, ^{3}J = 8.0); 4.40 (q, 4 H, 2 OCH_2, ^{3}J = 8.0); 7.68 (m, 4 H, Ar); 8.05 (m, 8 H, Ar)	8.32, 8.74 (2 Me); 58.07, 58.45 (2 OCH_2); 110.00 (C(3) furox. ring); 115.08—133.52 (Ar, isoxaz. ring); 148.66 (C(4) furox. ring); 156.54 (CO)	
27	1.35 (t, 6 H, 2 Me, ^{3}J = 8.0); 2.00–2.35, 2.45–2.60 (both m, 6 H, 3 CH_2); 3.35–3.60 (m, 2 H, 2 CH); 4.40 (q, 4 H, 2 OCH_2, ^{3}J = 8.0)	8.73 (2 Me); 25.04 (2 CH_2 oxadiaz. ring); 31.23 (2 CH oxadiaz. ring); 31.41 (CH_2 oxadiaz. ring); 58.57 (2 OCH_2); 148.80 (C(3) oxadiaz. ring); 161.18 (C(5) oxadiaz. ring); 168.53 (CO)	
28	1.45 (t, 6 H, 2 Me, ^{3}J = 8.0); 2.20–2.40 (m, 2 H, $CH_2\underline{CH_2}CH_2$, ^{3}J = 8.5); 2.95 (t, 4 H, ($\underline{CH_2}CH_2\underline{CH_2}$, ^{3}J = 8.5); 4.50 (q, 4 H, 2 OCH_2, ^{3}J = 8.0)	14.05 (2 Me); 23.92 (CH_2); 25.29 (2 CH_2); 63.99 (2 OCH_2); 154.02 (C(5) oxadiaz. ring); 166.52 (C(4) oxadiaz. ring); 170.79 (CO)	324 [M^+], 279 [$M^+ - OEt$], 251 [$M^+ - CO_2Et$], 224 [$M^+ - CO_2Et - C_2H_4 + 1$], 170, 151, 136

15 mmol) and ethoxycarbonylformonitrile **17** (7.42 g, 75 mmol) was refluxed for 1 h. The excess of nitrile **17** was removed in a rotary evaporator. The product with R_f 0.34 was isolated by preparative TLC with $CHCl_3$—EtOAc (20 : 1) as an eluent. The solvent was removed *in vacuo*. The yield of compound **27** was 0.78 g (15%).

1,3-Bis(5-ethoxycarbonyl-1,2,4-oxadiazol-3-yl)propane (28). A mixture of cyclopentafuroxan **1** (0.45 g, 3.6 mmol) and ethoxycarbonylformonitrile **17** (1.76 g, 18 mmol) was heated in a sealed tube at 140 °C for 7 h. The excess of nitrile **17** was removed in a rotary evaporator. The final product was isolated by preparative column chromatography on silica gel with $CHCl_3$ as an eluent. The solvent was removed *in vacuo*. The yield of compound **28** was 0.39 g (33%).

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Received March 28, 2007;
in revised form May 17, 2007