Synthesis of macrocyclic systems from 4,4′-diamino-3,3′-bi-1,2,5-oxadiazole and 3(4)-amino-4(3)-(4-amino-1,2,5-oxadiazol-3-yl)-1,2,5-oxadiazole 2-oxides

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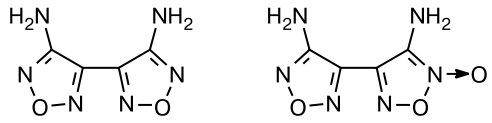
Oxidative cyclocondensation of 4,4′-diamino-3,3′-bi-1,2,5-oxadiazole and isomeric 3(4)-amino-4(3)-(4-amino-1,2,5-oxadiazol-3-yl)-1,2,5-oxadiazole 2-oxides under the action of dibromoisocyanurate gave 12- and 18-membered macrocyclic systems containing two or three bifurazanyl or furazanylfuroxanyl moieties linked by azo bridges. The latter were oxidized into azoxy groups with Caro′s acid in 20% oleum.

Key words: 4,4′-diamino-3,3′-bi-1,2,5-oxadiazole, 3(4)-amino-4(3)-(4-amino-1,2,5-oxadiazol-3-yl)-1,2,5-oxadiazole 2-oxides, dibromoisocyanurate, azo- and azoxybifurazanyl macrocycles, azo- and azoxyfurazanylfuroxanyl macrocycles, oxidative cyclocondensation, oxidation, azo derivatives, azoxy derivatives.

Conjugated macrocyclic systems containing nitrogen heterocycles are well known. For instance, natural macrocyclic compounds such as porphyrins and corrins are found in hemoglobin, vitamin B_{12}, and many enzymes and coenzymes. Macrocyclic phthalocyanines are widely used in the synthesis of organic dyes and dye intermediates. That is why the progress in the chemistry of such structures containing various heterocycles in the macrocyclic system is of considerable interest for organic, coordination, analytical, and biological chemists.

Our laboratory has been investigating for many years 1,2,5-oxadiazoles (furazans) and their 2-oxides (furoxans).[1—3] Earlier, we have synthesized macrocyclic systems containing alternating azo- or azoxyfurazanyl fragments[4—8] and furazan-containing aza crown compounds.[9,10] These compounds have been mostly synthesized *via* various versions of oxidative macrocyclization of diaminofurazan or amino(hydroxyalkyl)furazans. Analogous macrocyclic systems containing the furoxan (furazan 2-oxide) ring have not been documented. The goal of the present work was to study the possibility of oxidative macrocyclization of diamino derivatives containing ensembles of two 1,2,5-oxadiazole rings: 4,4′-diamino-3,3′-bi-1,2,5-oxadiazole (**1**) and isomeric 3(4)-amino-4(3)-(4-amino-1,2,5-oxadiazol-3-yl)-1,2,5-oxadiazole 2-oxides (**2** and **3**).

4,4′-Diamino-3,3′-bi-1,2,5-oxadiazole (**1**) has been obtained earlier,[11,12] although its yield did not exceed 18—20%. Isomeric diaminofurazanylfuroxans **2** and **3** have not been documented. For this reason, we initially



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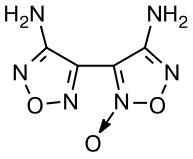

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developed a method for their synthesis from accessible 4-aminofurazan-3-carbohydroximamide,[13] which was converted with $NaNO_2$ in HCl into the corresponding acid chloride **4** according to a known procedure[14] and further, with KCN, into nitrile **5**. Treatment of the latter with hydroxylamine hydrochloride in the presence of $NaHCO_3$ in boiling aqueous methanol gave a mixture of *syn*- and *anti*-isomers of 1-amino-2-(4-aminofurazan-3-yl)glyoxime **6**. Starting from compound **6**, we obtained (1) 4,4′-diamino-3,3′-bi-1,2,5-oxadiazole (**1**) by dehydration of the vicinal oxime groups in boiling aqueous alkali and (2) 3-amino-4-(4-amino-1,2,5-oxadiazol-3-yl)-1,2,5-oxadiazole 2-oxide (**2**) by oxidative cyclization of the glyoxime fragment into a furoxan ring with bromine or $K_3Fe(CN)_6$. Diamine **2** was almost completely isomerized into diamine **3** in boiling dioxane (Scheme 1).

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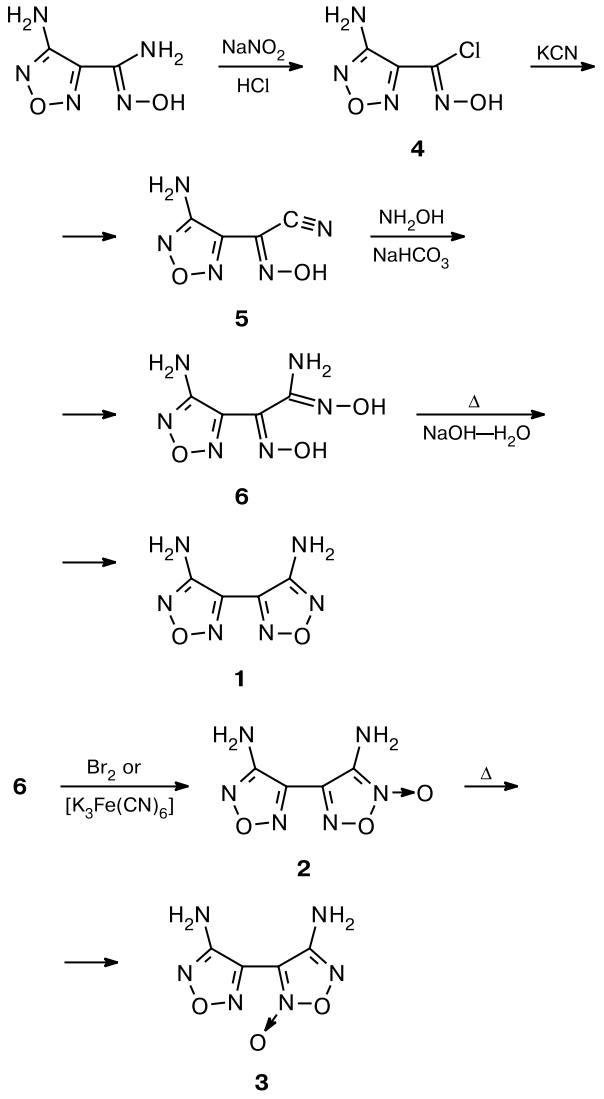
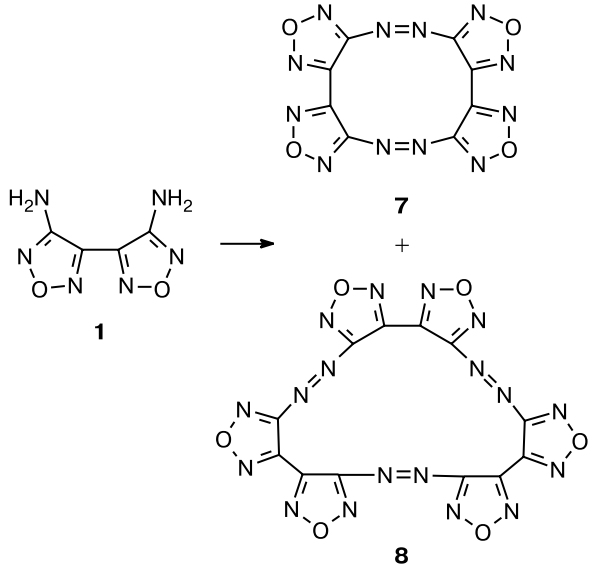
Scheme 1



Prior to the synthesis of macrocyclic compounds, we studied the oxidative macrocyclization of 4,4′-diamino-3,3′-bi-1,2,5-oxadiazole **1** with dibromoisocyanurate (DBI) as an oxidant. The reaction was carried out in acetonitrile at room temperature. The complete conversion of the starting diamine **1** was reached in 48 h (monitoring by TLC). The reaction afforded a mixture of two macrocyclic compounds **7** and **8** containing two and three azobifurazanyl fragments, respectively (Scheme 2). The products were separated by preparative column chromatography on silica gel in close yields (~30%, each). (Preliminary reports on the synthesis of compounds **7** and **8** and X-ray diffraction data for compound **7** have been published earlier.[15,16]) Apparently, this reaction also gives larger macrocycles, which is evident from ^{13}C NMR spectra of the third fraction separated by chromatography from the other reaction products: the spectra show signals for the C atoms in the same region as for compounds **7** and **8**.

Scheme 2



Reagents and conditions: DBI—MeCN, 20 °C.

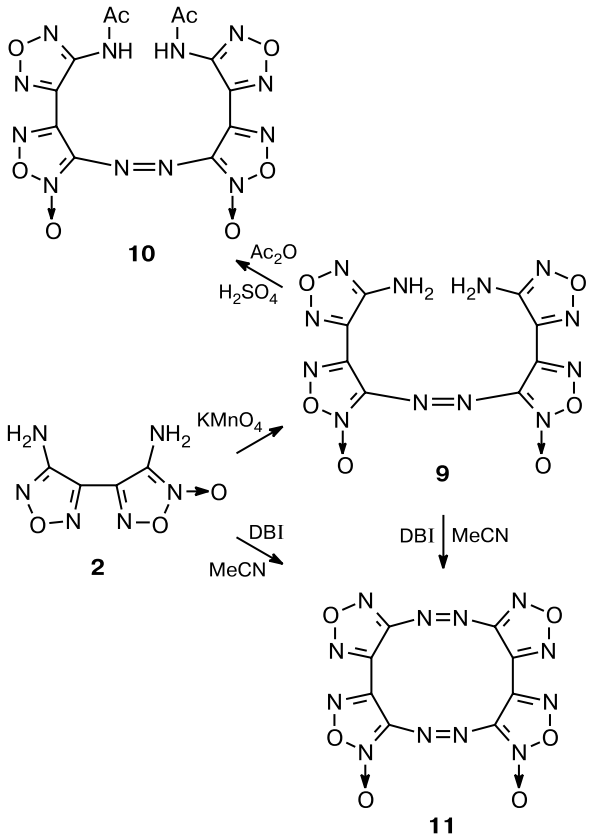
According to X-ray diffraction data,[16] the bifurazanyl fragments in compound **7** are *trans* with respect to the azo groups. By analogy, as well as from X-ray diffraction data for the known azo- and azoxyfurazanyl macrocycles,[4—10] one can assume that the bifurazanyl and furazanylfuroxanyl fragments in compound **8** and the other macrocyclic compounds obtained will also be *trans* with respect to the azo- and azoxy groups. The structural formulas shown in the schemes are conventional because they do not reflect the real spatial structures of these macrocycles.

Macrocyclic compounds could be obtained from diamines **2** and **3** (1) *via* macrocyclization of presynthesized linear intermediates containing the azo-bridged fragments of these diamines or (2) *via* their direct macrocyclization (Scheme 3). We tried to synthesize linear structures by oxidizing diamines **2** and **3** with $KMnO_4$. However, the target linear azo derivative was obtained only from diamine **2**; the reaction regiospecifically gave compound **9** in 71% yield out of other possible azofurazanylfuroxan isomers (*i.e.*, only the amino groups in position 3 of the furoxan ring were involved in the reaction). Such a selectivity of the oxidation is probably due to the increased electron density at the above amino groups because of the electron-releasing effect of the *N*-oxide fragment in structure **2** compared to the electron density at the amino groups in the furazan ring and in position 4 of the furoxan ring. The *N*-oxide fragments in compound **9** were located from the signal at δ 128.64 in its ^{13}C NMR spectrum. This region (δ 123.2—125.7) is characteristic

of signals for the C atom in position 3 of the furoxan ring bound to the azo group.[17,18] The mass spectrum of compound **9** was not recorded because of its insufficient volatility. Using acetic anhydride, we converted compound **9** into *N*,*N*´-diacetyl derivative **10** and recorded its mass spectrum. Although the spectrum contained no molecular ion peak (M^+ = 448), the fragmentation ions corresponded to the furazanylfuroxanyl fragment (238) containing the N=N and NHCOMe groups and to the same fragment without the N=N group (210). These data provided additional evidence for the proposed structure.

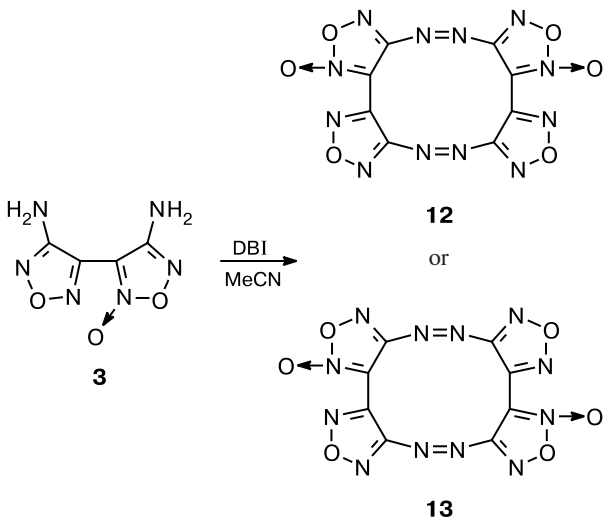
For the macrocyclization of diamines **2** and **9**, we used the same oxidant (DBI) as with 4,4´-diamino-3,3´-bi-1,2,5-oxadiazole (**1**). In both cases, the room-temperature reaction in acetonitrile gave macrocyclic compound **11** as the sole product. The identical products obtained in the macrocyclization of diamines **9** and **2** additionally confirmed the structure of macrocycle **11** (Scheme 3).

Scheme 3



Diamine **3** formed no azo derivatives under the action of $KMnO_4$ in either water or its mixtures with various organic solvents. Apparently, this is due to its very low solubility in the reaction medium. Oxidation of diamine **3** with DBI in acetonitrile gave macrocyclic compound **12**. Unfortunately, spectroscopic data for the reaction product are insufficient for unambiguous assignment of its structure to one of two possible isomers **12** and **13** (head-to-head or head-to-tail cyclization of two starting molecules) (Scheme 4).

Scheme 4



Thus, the direct oxidation of the starting diamines **2** and **3** afforded both the target macrocyclic compounds **11** and **12** (or **13**), although in low yields. Apparently, their low yields in this macrocyclization reaction are due to the formation of linear oligomers and larger macrocycles that were detected at the start line in the thin-layer chromatography of the final mixture. The yields of macrocyclic compounds **11** and **12** (or **13**) were not increased even by high dilution of the reaction mixture to a gram of the starting amine per 100 mL of the solvent.

To oxidize the azo groups of the macrocyclic systems obtained into azoxy groups, we studied various oxidative mixtures based on hydrogen peroxide, sulfuric acid or oleum, and sodium tungstate. We found that the oxidation of macrocycles **7** and **8** requires sufficiently drastic conditions (Caro´s acid in 20% oleum). Clearly, this is because the diazene fragments of these macrocycles are electron-deficient due to the strong electron-withdrawing effect of the 1,2,5-oxadiazole rings. It turned out that the oxidation under these conditions affects all the azo groups in macrocycles **7** and **8**, although being a nonselective process leading to a mixture of isomers. The oxidation of macrocycle **7** gave two isomers with distal or proximal arrangement of the *N*-oxide oxygen atoms (compounds **14** and **15**). The formation of the mixture of isomers was confirmed by spectroscopic data: the ^{13}C NMR spectrum contained eight signals and the ^{14}N NMR spectrum contained two signals for the azoxy groups at δ −66.66 and −64.41. The oxidation of macrocycle **8** yielded a more complex mixture of isomeric azoxy deriv-

atives represented by structure **16**; this was confirmed by the increased number of signals in its ^{13}C NMR spectrum (about 30 signals). However, the presence of a molecular ion peak in the mass spectrum of the oxidized product provided evidence for the oxidation of all azo groups. It is worth noting that the starting macrocyclic compounds **7** and **8** are colored deep red and orange, respectively, owing to their conjugated double bonds, while the oxidized products are colorless because the oxidation of the azo groups into the azoxy groups breaks the conjugation.

In attempted oxidation of the azo groups in macrocycle **12** or **13**, we obtained a complex mixture of inseparable products. Compound **17** was isolated in the individual state only in the oxidation of macrocycle **11**, although in a low yield (Scheme 4). The complete conversion of macrocycle **11** was reached under the action of 85% H_2O_2 in 20% oleum in the presence of $Na_2WO_4 \cdot 2H_2O$ at 50 °C for 3 h. According to the mass spectrum of the product obtained, only one N=N group is oxidized. The number of signals in the ^{13}C NMR spectrum of compound **17** is eight (double that of the starting compound). The chemical shifts of the C atom in position 3 of the furoxan ring bound to the N=N group change only slightly (from δ 128.89 to 128.82 and 128.90) and one of the signals for the C atom in position 4 of the furazan ring also bound to the N=N group is shifted upfield by approximately 3 ppm (from δ 163.19 to 160.30). This is evidence for the oxidation of the azo group bridging the furazan rings (Scheme 5).

The yields and selected physicochemical characteristics of the compounds obtained are given in Table 1; their spectroscopic characteristics are presented in Table 2.

To sum up, we synthesized for the first time macrocyclic systems containing alternating azo- and azoxybifurazanyl and -furazanylfuroxanyl fragments. We found that the oxidation of 3-amino-4-(4-amino-1,2,5-oxadiazol-3-yl)-1,2,5-oxadiazole 2-oxide (**2**) into azo derivative **9** is a regioselective reaction involving only the NH_2 group in position 3 of the furoxan ring.

Scheme 5

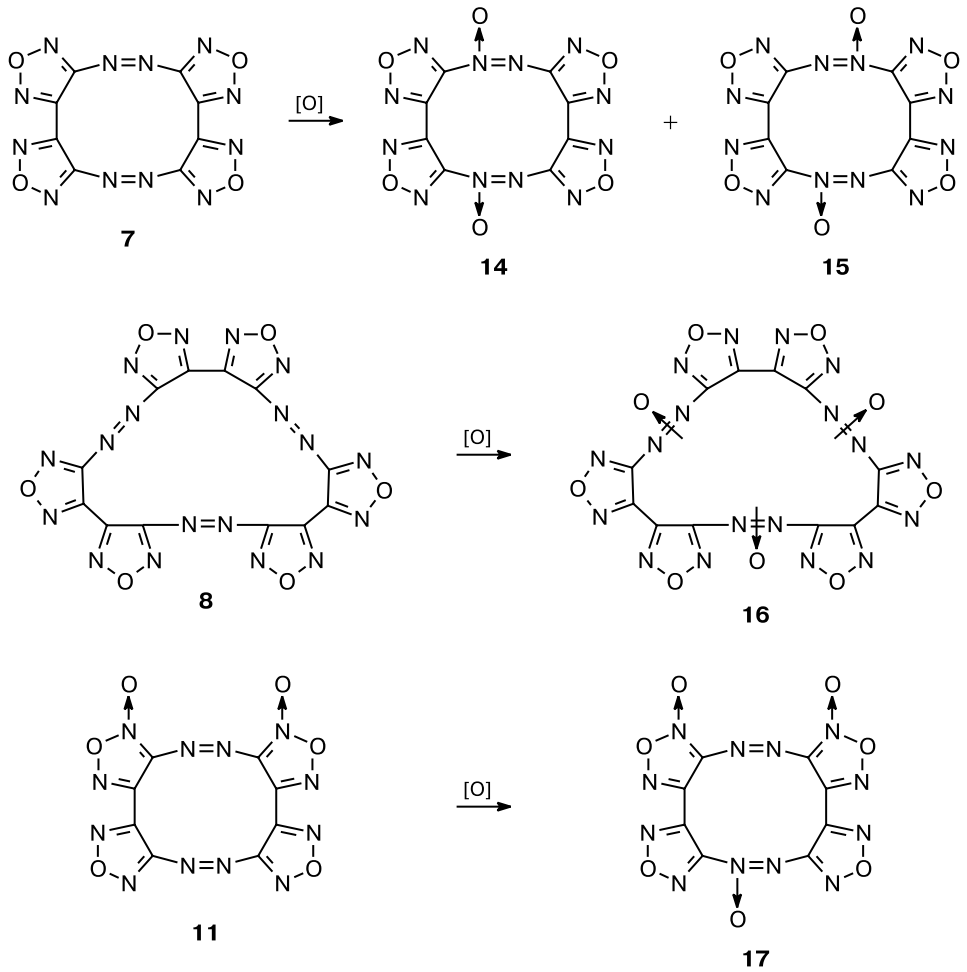


Table 1. Yields and selected physicochemical characteristics of the compounds obtained

Compound	Yield (%) (Method)	M.p./°C	R_f (eluent)*	Found / Calculated (%)			Molecular formula
				C	H	N	
2	30 (*A*) 66 (*B*)	164—165	0.50 (A)	25.98 26.09	2.24 2.19	45.42 45.65	$C_4H_4N_6O_3$
3	83	197—198	0.58 (A)	26.18 26.09	2.27 2.19	45.51 45.65	$C_4H_4N_6O_3$
5	55	195—198	0.32 (A)	31.52 31.38	2.03 1.96	45.56 45.74	$C_4H_3N_5O_2$
6	71	180—185 (a mixture of isomers)	0.20 (A)	25.74 25.81	3.14 3.25	45.30 45.15	$C_4H_6N_6O_3$
7	32	220—222	0.52 (B)	29.00 29.27	—	51.41 51.22	$C_8N_{12}O_4$
8	28	300—303	0.47 (B)	29.81 29.27	—	50.88 51.22	$C_{12}N_{18}O_6$
9	71	250—252	0.50 (B)	26.55 26.38	1.20 1.11	46.19 46.15	$C_8H_4N_{12}O_6$
10	41	199—200	0.77 (B)	32.22 32.14	1.78 1.80	37.68 37.50	$C_{12}H_8N_{12}O_8$
11	11 (*A*) 11 (*B*)	189—191	0.28 (B)	26.47 26.66	—	46.72 46.68	$C_8N_{12}O_6$
12 or **13**	12	158—160	0.33 (B)	26.55 26.66	—	46.58 46.68	$C_8N_{12}O_6$
14 and **15**	60	137—140	0.37 (B)	26.51 26.66	—	46.53 46.68	$C_8N_{12}O_6$
16	47	172—175	0.36 (B)	26.60 26.66	—	46.77 46.68	$C_{12}N_{18}O_9$
17	5	198—200	0.24 (B)	25.62 25.54	—	46.63 44.68	$C_8N_{12}O_7$

* The eluents are $CHCl_3$—Me_2CO (1 : 1) (*A*) and CH_2Cl_2—CCl_4 (1 : 5) (*B*).

Table 2. ^1H and ^{13}C NMR (DMSO-d_6), IR, and mass spectra of the compounds obtained

Compound	IR, ν/cm^{-1}	^{13}C NMR* δ	^1H NMR, δ [MS, *m/z* (*I* (%)]
2	3470, 3340, 1680, 1640, 1610, 1570, 1500, 1460, 1420, 1295, 1070, 1020, 980, 920, 890, 860, 750, 680	122.23 (C(3) furox. ring); 137.09 (C(4) furox. ring); 141.50 (C(3) furaz. ring); 155.12 (C(4) furaz. ring)	6.20 (s, 2 H, NH_2); 6.49 (s, 2 H, NH_2);
3	3480, 3450. 3300, 1620, 1520, 1480, 1405, 1205, 1120, 1080, 1020, 960, 880	100.83 (C(3) furox. ring); 133.18 (C(4) furox. ring); 154.60, 155,30 (C(3) и C(4) furaz. ring)	6.41 (s, 2 H, NH_2); 6.51 (s, 2 H, NH_2)
5	3480, 3340, 3280, 2250, 1620, 1600, 1540, 1420, 1350, 1080, 1050, 980, 920	108.20 (CN); 122.51 (C=NOH); 140.51 (C(3) furaz. ring); 154.41 (C(4) furaz. ring)	6.28 (s, 2 H, NH_2); 14.80 (br.s, 1 H, 2 NOH)
6	3480, 3380, 3350, 3280, 1680, 1660, 1620, 1610, 1580, 1520, 1410, 1380, 1300, 1120, 1070, 960, 920		5.93, 6.17, 6.25, 6.40 (all s, 4 H, NH_2); 7.82, 8.08, 9.77, 12.70 (all s, 2 H, 2 NOH) (a mixture of *syn*- and *anti*-isomers)
7	1500, 1400, 1370, 1270, 1230, 1110, 1030, 1000, 930, 915, 860	138,82 (C(4) furaz. ring); 163.24 (C(3) furaz. ring)	[328 [M^+], 270 (30), 232 (28), 202 (100), 198 (80), 188 (69), 185 (96)]
8	1450, 1400, 1370, 1230, 1100, 1040, 1000, 915	138,28 (C(4) furaz. ring); 163.28 (C(3) furaz. ring)	[492 [M^+] (100), 434 (15), 300 (19), 288 (15), 276 (27), 275 (85), 268 (27)]

(*to be continued*)

Table 2. (*continued*)

Compound	IR, ν/cm^{-1}	^{13}C NMR* δ	^{1}H NMR, δ [MS, m/z (I(%)]
9	3320, 3160, 1620, 1590, 1490, 1470, 1420, 1350, 1220, 1120, 1080, 1050, 1020, 980, 970, 870	128.64 (C(3) furox. ring); 136.89 (C(4) furox. ring); 141.19 (C(3) furaz. ring); 155.52(C(4) furaz. ring)	
10	3280, 3060, 1700, 1610, 1580, 1500, 1450, 1380, 1320, 1310, 1260, 1210, 1070, 1040, 1000, 980, 890, 860		8.82 (s, 2 H, 2 NH); [238 (4), 224 (22), 211 (20), 210 (90), 195 (4), 182 (20), 180 (14), 169 (16), 168 (100), 153 (16), 138 (14)]
11	1600, 1410, 1390, 1180, 1050, 1010, 960	128.89 (C(3) furox. ring); 139.91 (C(4) furox. ring); 141.33 (C(3) furaz. ring); 163.19 (C(4) furaz. ring)	[360 [M^+] (100), 345 (28), 331 (90), 329 (25), 315 (20), 300 (10)]
12 or **13**	1580, 1500, 1480, 1440, 1415, 1360, 1300, 1260, 1180, 1060, 1030, 1000, 920, 910, 890	101.20 (C(3) furox. ring); 137.42 (C(4) furox. ring); 162.91, 163.30 (C(3) и C(4) furaz. ring)	[360 [M^+] (10), 330 (8), 300 (30), 180 (70), 168 (100), 152 (40)]
14 and **15**	1550, 1510, 1500, 1480, 1440, 1415, 1360, 1300, 1260, 1180, 1060, 1030, 1000, 920, 910, 890	138.77, 139.69, 140.52, 140.72 (C(3) furaz. ring); 153.87, 153.98, 159.70, 159.74 (C(4) furaz. ring)	[360 [M^+] (2), 330 (20), 300 (100), 195 (80), 180 (75), 164 (10), 135 (15)]
16	1630, 1620, 1480, 1380, 1180, 1110, 1100, 1080, 1020, 1000, 980, 910	About 30 signals: 138—141 ppm (C(3) furaz. ring), 153—160 ppm (C(4) furaz. ring)	[540 [M^+] (20), 524 (15), 510 (2), 480 (75), 464 (2), 405 (13), 360 (40), 330 (100), 270 (21), 210 (3)]
17	1650, 1640, 1580, 1500, 1280, 1150, 1040, 980	128.82, 128.90, 139.68, 139.92 (C(3) и C(4) furox. ring); 141.21, 141.32, 160.30, 163 (C(3) и C(4) furaz. ring)	[376 [M^+] (23), 360 (100), 346 (18), 344 (12), 330 (53), 300 (35)]

* The signals for the C atoms in the compounds obtained were assigned from the previously derived correlations.[4—10,17,18]

Experimental

IR spectra were recorded on a UR-20 spectrometer (KBr pellets). UV spectra were recorded on a Specord UV-VIS spectrometer in methanol. NMR spectra were recorded on Bruker WM-250 (^1H, 250 MHz) and Bruker AM-300 spectrometers (^{13}C, 75.5 MHz; ^{14}N, 21.5 MHz). ^1H and ^{13}C chemical shifts were measured on the δ scale with Me_4Si as the internal standard; ^{14}N NMR chemical shifts were measured with $MeNO_2$ as the external standard. Mass spectra were recorded on a Varian MAT CH-6 instrument (70 eV). Thin-layer chromatography was carried out on Silufol UV-254 plates (spots were visualized under UV light). *Caution! The macrocyclic compounds obtained are moderately sensitive to mechanical impact and friction and should be handled carefully.*

2-(4-Amino-1,2,5-oxadiazol-3-yl)-2-hydroxyiminoacetonitrile (5). A solution of 4-aminofurazan-3-carbohydroximoyl chloride (**4**) (8.78 g, 54 mmol) in ethyl acetate (500 mL) was added dropwise at 10 °C to a solution of KCN (7 g, 108 mmol) in water (80 mL). The reaction mixture was stirred for 8 h; the organic layer was separated and the aqueous layer was acidified with HCl to pH 7. The product was extracted with ethyl acetate. The combined organic extracts were dried with $MgSO_4$ and concentrated in a rotary evaporator. The yield of compound **5** was 4.52 g.

2-(4-Amino-1,2,5-oxadiazol-3-yl)-1,2-di(hydroxyimino)-ethanamine (6). A solution of nitrile **5** (0.72 g, 4.6 mmol) in methanol (20 mL) was added to a solution of $NaHCO_3$ (0.48 g, 5.7 mmol) and $NH_2OH \cdot HCl$ (0.39 g, 5.5 mmol) in water (7 mL). The reaction mixture was refluxed for 3 h, the solvent was removed in a rotary evaporator, and the product was extracted from the aqueous layer with ethyl acetate (3×10 mL). The extracts were dried with $MgSO_4$ and concentrated in a rotary evaporator. The yield of compound **6** was 0.61 g (a mixture of isomers).

3,3′-Bi-1,2,5-oxadiazole-4,4′-diamine (1). A suspension of compound **6** (2.0 g, 10.8 mmol) was refluxed in 2 *M* NaOH (20 mL) for 1.5 h. On cooling, the precipitate that formed was filtered off, washed with cold water, and dried in air. The yield of compound **1** was 1.02 g (56%), m.p. 179—180 °C (*cf.* Ref. 11: m.p. 180 °C).

3-Amino-4-(4-amino-1,2,5-oxadiazol-3-yl)-1,2,5-oxadiazole 2-oxide (2). ***A.*** A solution of $K_3Fe(CN)_6$ (1.32 g, 4 mmol) in water (4 mL) was added at 5—10 °C to a stirred solution of compound **6** (0.37 g, 2 mmol) in a mixture of KOH (0.7 g, 12.5 mmol) and water (3 mL). After 1 h, the precipitate that formed was filtered off, washed with water, and dried in air. The product was isolated by preparative

TLC with $CHCl_3$—acetone (3 : 1) as an eluent. The yield of compound **2** was 0.11 g.

B. A 2 *M* solution of HCl (1.5 mL) was added to a suspension of compound **6** (0.50 g, 2.7 mmol) in water (3 mL). Then a solution of bromine (0.43 g, 2.7 mmol) in conc. HCl (2 mL) was added dropwise at 5—10 °C. After 20 min, the precipitate that formed was filtered off, washed with water, and dried in air. The yield of compound **2** was 0.30 g.

4-Amino-3-(4-amino-1,2,5-oxadiazol-3-yl)-1,2,5-oxadiazole 2-oxide (3). A suspension of compound **2** (0.30 g, 1.6 mmol) was refluxed in dioxane for 5 h. The solvent was removed in a rotary evaporator and the product was isolated by preparative TLC with $CHCl_3$—acetone (3 : 1) as an eluent. The yield of compound **3** was 0.25 g.

4,4´-Bis(4-amino-1,2,5-oxadiazol-3-yl)-3,3´-azo(1,2,5-oxadiazole 2-oxide) (9). Hydrochloric acid (30 mL) was added at 18—20 °C to a suspension of diamine **2** (1.0 g, 5.4 mmol) in acetone (20 mL). Then a solution of $KMnO_4$ (0.87 g, 5.4 mmol) in water (54 mL) was added dropwise at the same temperature. The reaction mixture was stirred for 30 min until it became colorless; the resulting precipitate was filtered off, washed with water, and dried in air. The yield of compound **9** was 0.71 g.

4,4´-Bis(4-acetylamino-1,2,5-oxadiazol-3-yl)-3,3´-azo(1,2,5-oxadiazole 2-oxide) (10). Acetic anhydride (10 mL) was added to compound **9** (1 g, 2.74 mmol). The mixture was stirred for 30 min, acidified with two drops of conc. H_2SO_4, and stirred again for an additional 30 min. The precipitate was filtered off, washed with water, and dried in air. The yield of compound **10** was 0.50 g.

Tetrakis[1.2.5]oxadiazolo[3,4-*c*:3´,4´-*e*:3´´,4´´-*i*:3´´´,4´´´-*k*][1,2,7,8]tetraazacyclododecine (7) and hexakis[1.2.5]oxadiazolo[3,4-*c*:3´,4´-*e*:3´´,4´´-*i*:3´´´,4´´´-*k*:3´´´´,4´´´´-*o*:3´´´´´,4´´´´´-*q*][1,2,7,8,13,14]hexaazacyclooctadecine (8). Dibromoisocyanurate (20 g, 140 mmol) prepared according to a known procedure[19] was added to a stirred suspension of 3,3´-bi-1,2,5-oxadiazole-4,4´-diamine **1** (5.88 g, 35 mmol) in MeCN (500 mL). The reaction mixture was kept for 48 h. The excess DBI was filtered off and the solvent was removed in a rotary evaporator. The products were isolated by preparative column chromatography on silica gel (40/100 μ) with CH_2Cl_2—CCl_4 (1 : 5) as an eluent. The yield of compound **7** was 1.87 g, red crystals. UV, λ_{max}/nm: 227 and 370. The yield of compound **8** was 1.61 g, orange crystals.

Tetrakis[1.2.5]oxadiazolo[3,4-*c*:3´,4´-*e*:3´´,4´´-*i*:3´´´,4´´´-*k*]-[1,2,7,8]tetraazacyclododecine 1,14-dioxide (11). ***A.*** Dibromoisocyanurate (8.5 g, 60 mmol) was added to a stirred solution of compound **9** (4.37 g, 12 mmol) in MeCN (500 mL). The reaction mixture was kept for 33 h. The excess DBI was filtered off and the solvent was removed in a rotary evaporator. Dichloromethane (200 mL) was added and DBI was filtered off again. The solvent was removed and the product was isolated by preparative column chromatography on silica gel (40/100 μ) with CH_2Cl_2—CCl_4 (1 : 5) as an eluent. The yield of compound **11** was 0.45 g.

B. Dibromoisocyanurate (8.20 g, 58 mmol) was added to a stirred suspension of compound **2** (2.95 g, 16 mmol) in MeCN (300 mL). The reaction mixture was kept for 72 h. The excess DBI was filtered off and the solvent was removed in a rotary evaporator. Dichloromethane (200 mL) was added and DBI was filtered off again. The solvent was removed and the product was isolated by preparative column chromatography on silica gel (40/100 μ) with CH_2Cl_2—CCl_4 (1 : 5) as an eluent. The yield of compound **11** was 0.32 g.

Tetrakis[1.2.5]oxadiazolo[3,4-*c*:3´,4´-*e*:3´´,4´´-*i*:3´´´,4´´´-*k*]-[1,2,7,8]tetraazacyclododecine 3,12-dioxide (12) or tetrakis-[1.2.5]oxadiazolo[3,4-*c*:3´,4´-*e*:3´´,4´´-*i*:3´´´,4´´´-*k*][1,2,7,8]-tetraazacyclododecine 3,11-dioxide (13). Under the conditions described for the synthesis of compound **11** (method ***B***), compound **12** or **13** (0.34 g) was obtained from diamine **3** (2.95 g, 16 mmol).

Tetrakis[1.2.5]oxadiazolo[3,4-*c*:3´,4´-*e*:3´´,4´´-*i*:3´´´,4´´´-*k*]-[1,2,7,8]tetraazacyclododecine 7,15(16)-dioxides (14 and 15). 20% Oleum (20 mL) was added to tetrakis[1.2.5]oxadiazolo[3,4-*c*:3´,4´-*e*:3´´,4´´-*i*:3´´´,4´´´-*k*][1,2,7,8]tetraazacyclododecine (**7**) (0.98 g, 3 mmol). The reaction mixture was stirred at 50 °C to complete homogenization. On cooling to 30 °C, 85% H_2O_2 (2.5 mL) was added dropwise. Then the reaction mixture was stirred at 80 °C for 1 h, cooled, and poured into water with ice (100 mL). The precipitate was filtered off, washed with water, dried in air, and recrystallized from CCl_4 to give a mixture of compounds **14** and **15** (0.64 g). UV, λ_{max}/nm: 227 and 270. ^{14}N NMR, δ: −66.66 and −64.41.

Hexakis[1.2.5]oxadiazolo[3,4-*c*:3´,4´-*e*:3´´,4´´-*i*:3´´´,4´´´-*k*:3´´´´,4´´´´-*o*:3´´´´´,4´´´´´-*q*][1,2,7,8,13,14]hexaazacyclooctadecine 4(5),12(13),20(21)-trioxide (16). 20% Oleum (20 mL) was added to hexakis[1.2.5]oxadiazolo[3,4-*c*:3´,4´-*e*:3´´,4´´-*i*:3´´´,4´´´-*k*:3´´´´,4´´´´-*o*:3´´´´´,4´´´´´-*q*][1,2,7,8,13,14]hexaazacyclooctadecine (**8**) (0.98 g, 2 mmol). The reaction mixture was stirred at 50 °C to complete homogenization. On cooling to 30 °C, 85% H_2O_2 (3.7 mL) was added dropwise. Then the reaction mixture was stirred at 80 °C for 1 h, cooled to ambient temperature, stirred for 72 h, and poured into water with ice (100 mL). The precipitate was filtered off, washed with water, dried in air, and recrystallized from CCl_4. The yield of compound **16** was 0.51 g.

Tetrakis[1.2.5]oxadiazolo[3,4-*c*:3´,4´-*e*:3´´,4´´-*i*:3´´´,4´´´-*k*]-[1,2,7,8]tetraazacyclododecine 1,7,14-trioxide (17). 20% Oleum (20 mL) was added to tetrakis[1.2.5]oxadiazolo[3,4-*c*:3´,4´-*e*:3´´,4´´-*i*:3´´´,4´´´-*k*][1,2,7,8]tetraazacyclododecine 1,14-dioxide (**10**) (0.97 g, 2.7 mmol). The reaction mixture was stirred at 50 °C to complete homogenization. On cooling to 30 °C, 85% H_2O_2 (3.0 mL) was added dropwise. Then the reaction mixture was heated to 50 °C and $Na_2WO_4 \cdot 2H_2O$ (1.62 g, 5.4 mmol) was carefully added in portions. The reaction mixture was stirred for 3 h, cooled to ambient temperature, and poured into water with ice (100 mL). The precipitate was filtered off, washed with water, and dried in air. The yield of compound **17** was 0.05 g.

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