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Zero-Hydrogen Furazan Macrocycles with Oxy and Azo Bridges

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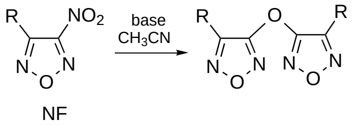
There is current interest in the synthesis of crown ethers and related macrocycles because they are excellent complexing agents.[1] These macrocyclic compounds are expected to interact as electron donors with metal cations and other electron acceptors. A recent development lies in the introduction of a photoresponsive function, namely an azobenzene subunit, into macrocyclic ligands. This functionalization provides chromophoric macrocycles that change binding ability as a result of the photoinduced *cis*−*trans* isomerism of the azobenzene subunit.[1,2]

In the course of our studies of furazan-macrocycles,[3] we became interested in chromophoric derivatives of this series. Earlier work in our laboratory[4] showed that bis(aminofurazanylic) ethers of glycols undergo intramolecular and intermolecular oxidative coupling to form chromophoric azofurazan-containing macrocycles when treated with dibromoisocyanurate. The macrocyclic closure was a result of $N{=}N$ bond formation.

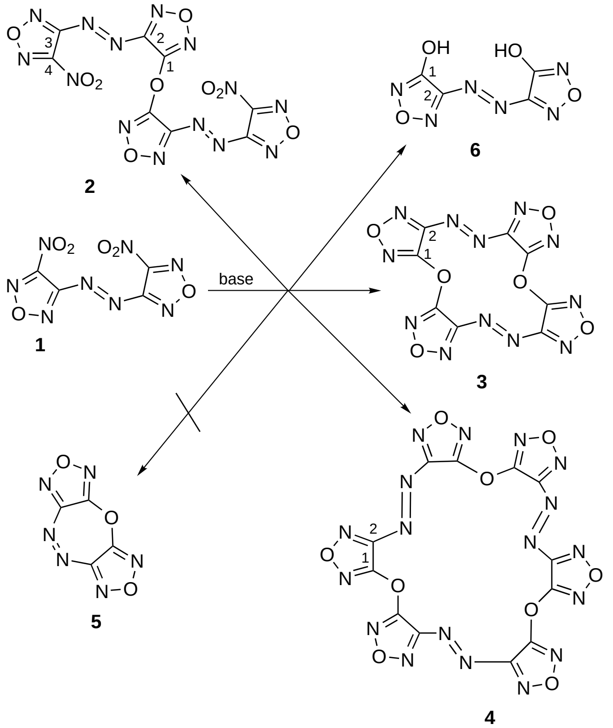
We wish to report a simple procedure for the synthesis of zero-hydrogen furazan macrocycles with oxy and azo bridges. The key step in our approach to these macrocycles consists of ether bond formation. The bond construction is based upon a reaction developed in our laboratories, the synthesis of difurazanyl ethers through base-promoted transformation of 3-nitro-4-R-furazans (NF).[5] The simplicity of this strategy is illustrated in Scheme 1.

The reaction of 4,4′-dinitroazofurazan (**1**) and a series of weak bases was studied. All experiments were run under a dry atmosphere at 70 °C with 1−15 mmol of base in acetonitrile. The progress of the reaction was monitored by TLC. The products were isolated by silica gel chromatography. Precursor **1** was available in two steps and 75% overall yield from diaminofurazan.[6]

Scheme 1



Scheme 2



In the initial experiment, reaction of **1** with Na_2CO_3 produced three major products, **2** (12%), **3** (23%), and **4** (19%), but also an additional product **6** (6%) as well as a linear oligomeric material (Scheme 2). The reaction did not produce any detectable quantities of the intramolecular coupling product **5**. Column chromatography afforded clean macrocycles as highly stable crystals whose orange color is characteristic of this class of compounds.

By contrast, the inclusion of 2−5% water in the acetonitrile reaction medium increased the dominance of the hydroxy compound **6** (87%). When **1** was allowed to react with K_2CO_3, the main products formed were dimeric product **3** and trimeric product **4** in 31 and 26% yields, respectively. The linear ether **2** was also formed in a yield of 3%. If **1** was coupled with Cs_2CO_3, **2** was not detected in the reaction mixture. Other promotion systems were examined in an attempt to displace the reaction to the formation of any single macrocycle (Table 1); however, none proved satisfactory. On the other hand, reaction between **7** and sodium carbonate proceeds selectively to produce a single product, macrocycle **8**, in a quantitative yield (Scheme 3). It should be noted that

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(6) Novikova, T. S.; Mel'nikova, T. M.; Kharitonova, O. V.; Kulagina, V. O.; Aleksandrova, N. S.; Sheremetev, A. B.; Pivina, T. S.; Khmel'nitskii, L. I.; Novikov, S. S. *Mendeleev Commun.* **1994**, 138.

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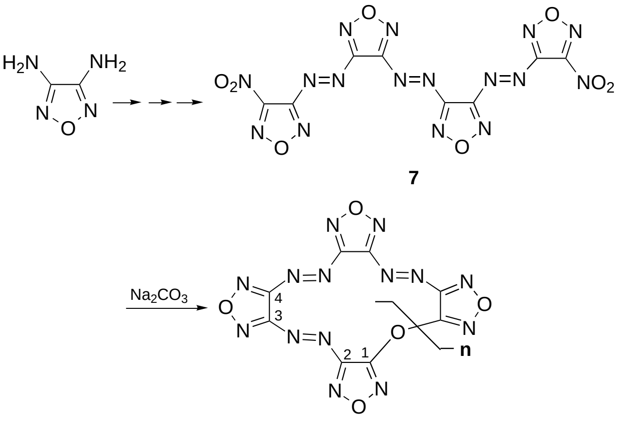
Table 1. Products for the Reaction of 1 with Bases in Acetonitrile at 70 °C

entry	base	product yield (%) 2	3	4	6
1	Li_2CO_3	18	21	15	5
2	Na_2CO_3	12	23	19	6
3	K_2CO_3	3	31	26	29
4	Cs_2CO_3	0	17	22	48
5	NaOAc	11	27	25	14
6	KOAc	3	19	17	33
7	NaF	7	22	18	11
8	KF	1	25	17	27

Scheme 3



7

8, *n* = 1; **9**, *n* = 2

precursor **7**, much longer than **1**, readily closed intramolecularly to give structures related to inaccessible **5**, and vice versa, intermolecular coupling products like **9** were not formed in this case. Compound **7**, 3,3′-azobis[4-[(nitrofurazan-3-yl)azo]furazan], like **1**, was available in three steps from diaminofurazan.[7]

All products were characterized by IR and ^{13}C NMR spectroscopy and elemental analyses. However, the macrocycles **3**, **4**, and **5**, and also macrocycles **8** and **9**, have the same molecular formula and cannot be distinguished by these methods. Mass spectrometry proved highly effective for this task. The molecular ion peak is observed in all of their mass spectra. The fragmentation patterns provided support for this series of structures. The product ion peaks at *m/z* ($M^+ - 30$) confirmed the presence of the furazan unit. The presence of the azo linkage in the product ion peaks at *m/z* ($M^+ - 30 - 28$) was confirmed. The structure of **4** was firmly established by an X-ray crystallographic study.[8]

In conclusion, we have demonstrated that the base-promoted coupling of bis[(nitrofurazanyl)azo] compounds provides a new and versatile approach to the synthesis of chromophoric macrocyclic ethers. Current efforts in this laboratory are focused on further applications of this methodology to the formation of related systems, and we are now exploring the use of the products in redox reactions. The complexing properties of macrocycles possessing an azofurazan subunit will be disclosed when the work is finished.

Experimental Section

CAUTION! Compounds **1** and **7** are potential explosives and may be sensitive to shock and must be handled with appropriate precautions.

Melting points are uncorrected. Elemental analyses and spectral measurements were performed at the N. D. Zelinsky Institute of Organic Chemistry, RAC, Moscow.

General Procedure for Reaction of 4,4′-Dinitroazofurazan (1) with Base. To solution of **1** (2.56 g, 0.01 mol) in CH_3CN (10 mL) was added base (1−15 mmol) under a dry atmosphere at 70 °C. The resulting suspension was stirred 1−10 h at 75 °C. The progress of the reaction was monitored by TLC and on consumption of starting material. The reaction was cooled. After addition of water (100 mL), the resulting mixture was extracted with CH_2Cl_2 (4 × 50 mL). The combined extracts were concentrated by distilling off solvent. The residue was a mixture of **2**−**4**. The products were separated by silica gel flash chromatography using CH_2Cl_2/hexane (4:1) as eluent. The yields are summarized in the Table 1 and the physical data are collected as follows: the first fraction, **3,3′-oxybis[[4-[(nitrofurazan-3-yl)azo]furazan]** (**2**) was obtained as orange oil: MS *m/z* 436 (M^+), 390 ($M^+ - NO_2$), 362 ($M^+ - NO_2 - N_2$), 322, 294; IR 1580, 1540, 1500, 1470, 1440, 1350, 1280, 1180, 1035, 825 cm^{-1}; ^{13}C NMR (acetone-d_6) δ 157.3 (C1), 156.7, 157.4 (C2, C3), 155.2 (C4); ^{14}N NMR (acetone-d_6) δ −37.1 (NO_2). Anal. Calcd for $C_8N_{14}O_9$ (436.18): C, 22.03; N, 44.96. Found: C, 22.22; N, 45.14. The second fraction gave orange crystals of **tetrakisfurazano[3,4-*b*:3′,4′-*f*:3″,4″-*i*:3‴,4‴-*m*][1,8,4,5,11,12]-dioxatetraazacyclotetradecene** (**3**): mp 138−140 °C; MS *m/z* 360 (M^+), 330 ($M^+ - NO$), 302 ($M^+ - NO - N_2$), 274 ($M^+ - NO - 2N_2$), 244 ($M^+ - 2NO - 2N_2$); IR 1580, 1495, 1450, 1410, 1270, 1235, 1040, 925 cm^{-1}; ^{13}C NMR (acetone-d_6) δ 157.1 (C1), 156.6 (C2). Anal. Calcd for $C_8N_{12}O_6$ (360.16): C, 26.68; N, 46.67. Found: C, 26.59; N, 46.75. The third fraction gave orange crystals of **hexakisfurazano[3,4-*b*:3′,4′-*f*:3″,4″-*i*:3‴,4‴-*m*:3⁗,4⁗-*p*:3′′′′′,4′′′′′-*t*][1,8,15,4,5,11,12,18,19]-trioxahexaazacyclohenicosene** (**4**): mp 263−265 °C; MS *m/z* 540 (M^+), 510 ($M^+ - NO$), 482 ($M^+ - NO - N_2$), 480 ($M^+ - 2NO$), 422 ($M^+ - 3NO - N_2$), 414, 368, 318, 234, 206; IR 1570, 1485, 1465, 1405, 1260, 1045, 1030, 905, 880 cm^{-1}; ^{13}C NMR (acetone-d_6) δ 157.2 (C1), 156.6 (C2). Anal. Calcd for $C_{12}N_{18}O_9$ (540.25): C, 26.68; N, 46.67. Found: C, 26.79; N, 46.68.

The aqueous phase was acidified with hydrochloric acid and extracted with Et_2O (3 × 30 mL). The combined organic layers were dried ($MgSO_4$), filtered, and evaporated. Recrystallization of the residue from propanol-2 afforded yellow crystals of **4,4′-dihydroxyazofurazan** (**6**): mp 263−265 °C; MS *m/z* 198 (M^+); IR 3100, 1580, 1250, 970 cm^{-1}; ^{13}C NMR (acetone-d_6) δ 157.9 (C1), 156.6 (C2). Anal. Calcd for $C_4H_2N_6O_4$ (198.10): C, 24.25; H, 1.02; N, 42.42. Found: C, 24.33; H, 1.07; N, 42.34.

Tetrakisfurazano[3,4-*b*:3′,4′-*f*:3″,4″-*j*:3‴,4‴-*n*][1,4,5,8,9,-12,13]oxahexaazacyclopentadecene (**8**). The compound was synthesized according to a general procedure from **7**; yield 95%. Orange crystals: mp 235−236 °C; MS *m/z* 372 (M^+), 256 ($M^+ - 2NO - 2N_2$); IR 1575, 1245, 1050, 910 cm^{-1}; ^{13}C NMR (DMSO-d_6) δ 159.6 (C1), 158.1, 155.8, 155.5 (C2, C3, C4); Anal. Calcd for $C_8N_{14}O_5$ (372.18): C, 25.82; N, 52.69. Found: C, 25.88; N, 52.76.

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