Synthesis of trisfurazanylamine derivatives

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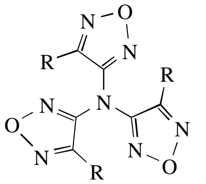
The reactions of the 4*H*,8*H*-bisfurazano[3,4-*b*;3′,4′-*e*]pyrazine dianion with fluorofurazans 6 and 9 yielded tris(4-R-furazanyl)-amine derivatives; a macrocycle incorporating the tertiary amine moiety was synthesised by oxidative cyclization of a linear precursor with terminal amino groups by dibromoisocyanurate.

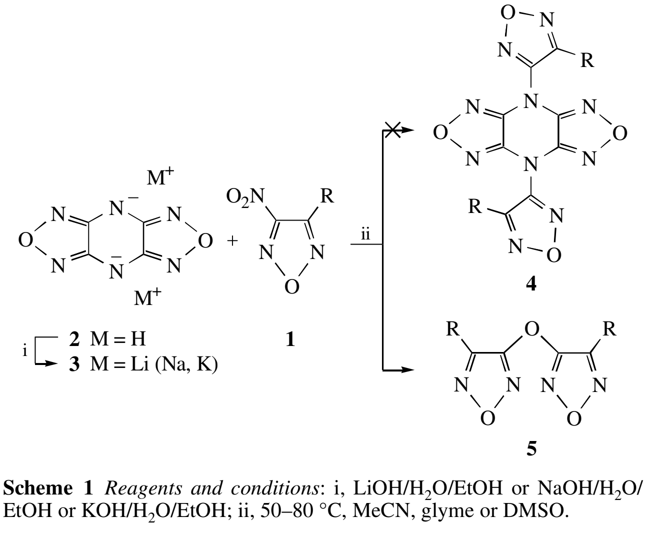
The unique azole containing tertiary amine, tris(4,5-dicyano-1-methylimidazol-2-yl)amine, has been reported.[1] Symmetrical[2,3] and unsymmertical[4] azine-containing trishetaryl amines are also known.

In the context of the synthesis of compounds incorporating furazan rings bonded by various bridging units,[5–9] we are interested in developing a methodology for the construction of tris-(4-R-furazan-3-yl)amine derivatives.



Recently, we described the reactions of 3-nitro-4-R-furazans with various primary and secondary amines to form corresponding 3-amino-4-R-furazans.[10] The reaction involved a nucleophilic displacement of the nitro group.[11,12] We examined the reaction of 3-nitro-4-R-furazans **1** with a compound containing a bis(3-R-furazan-4-yl)amine moiety. Available 4*H*,8*H*-bisfurazano[3,4-*b*;3′,4′-*e*]pyrazine **2**[13–15] was selected as a starting compound for the synthesis. The electron-withdrawing furazan rings are responsible for the acidic properties of piperazine **2**, (pK_a: first, 6.9; second, 10.1).[15] Dianion **3** was generated from **2**, and it reacted with substituted **1** [R = NO_2, N_3 or N(O)=NNO_2] in a polar solvent (Scheme 1). However, the reaction of **3** under these conditions gave no desired tertiary amine **4**, giving instead difurazanyl ether derivatives **5** (up to 87%) as the major product. The transformation is similar to that reported earlier.[6–8,16] The treatment of 3-chloro-4-nitrofurazan[9] with **3** also afforded no tertiary amine; only intractable product mixtures were observed.

We found that fluorofurazans underwent smooth fluorine displacement with anion **3** to give tertiary amine derivatives in good yields (Scheme 2). Thus, the di-N-heterarylation of **3** with 2.5 equiv. of fluorofurazan **6** in acetonitrile at 70–80 °C for 3 h in the presence of tetraalkylammonium fluoride gave target compound **7**† in 73% yield. Under the same conditions, amine **8** was obtained in 85% yield. In the absence of tetraalkylammonium fluoride, the product of mono-N-heterarylation was also observed. For example, when salt **3** was allowed to react with 2.5 equiv. of fluorofurazan **9** in acetonitrile, an easily separable mixture of amine **8** (52%) and a water-soluble mono-substitution product **10** (37%) was obtained. Our attempts to synthesise tertiary amines from salt **3** by a reaction with 4,4-difluoroazofurazan were unsuccessful; inseparable product mixtures were obtained.



Scheme 1 *Reagents and conditions*: i, LiOH/H_2O/EtOH or NaOH/H_2O/EtOH or KOH/H_2O/EtOH; ii, 50–80 °C, MeCN, glyme or DMSO.

Compounds **7**, **8**, and **10** are amorphous powders unsuitable for X-ray diffraction study. In contrast, the oxidative cyclization of diamine **8** with dibromoisocyanurate (DBI) afforded macrocycle **11** (Scheme 3) as red-orange crystals in 52% yield. Solvent-including crystals for X-ray analysis were obtained from DMSO (Figure 1).‡

The asymmetric part of a unit cell contains macrocyclic **11**, two DMSO molecules, and a water molecule occupying a position on crystallographic axis 2. The macrocycle cavity may be

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† All new compounds gave satisfactory spectroscopic and analytical results.

For **7**: mp 252–255 °C. Found (%): C, 27.73; N, 53.81. Calc. for $C_{12}N_{20}O_6$ (%): C, 27.70; N, 53.84. MS, *m/z*: 520 (M^+), 492 ($M^+ - N_2$), 462 ($M^+ - N_2 - NO$).

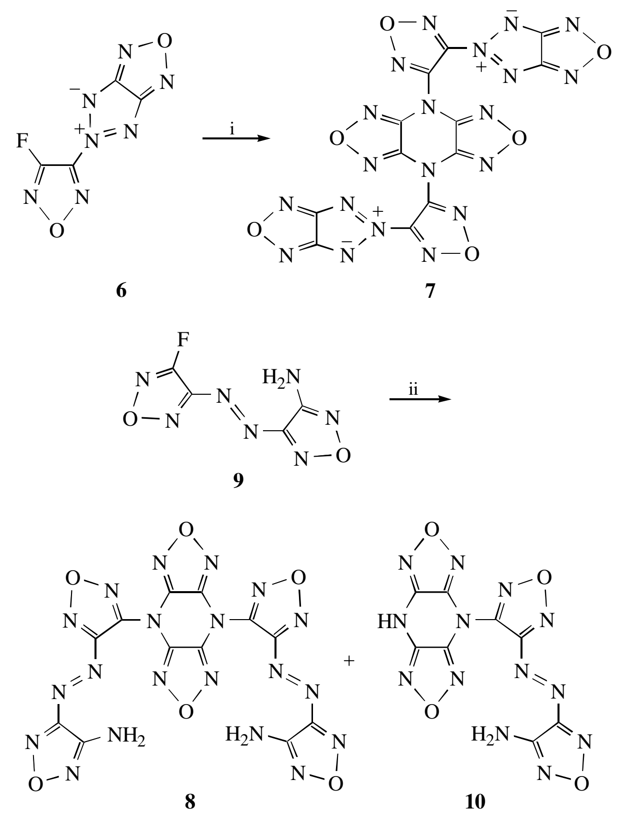
For **8**: mp 325–329 °C (decomp.). IR (KBr, ν/cm^{-1}): 3480, 3340 (NH_2). Found (%): C, 27.50; H, 0.76; N, 53.45. Calc. for $C_{12}H_4N_{20}O_6$ (%): C, 27.49; H, 0.77; N, 53.43.

For **10**: mp > 360 °C (decomp.). Found (%): C, 27.89; H, 0.91; N, 52.74. Calc. for $C_8H_3N_{13}O_4$ (%): C, 27.84; H, 0.88; N, 52.75.

For **11**: mp 295–298 °C (decomp.). Found (%): C, 27.72; N, 53.87. Calc. for $C_{12}N_{20}O_6$ (%): C, 27.70; N, 53.84. MS, *m/z*: 520 (M^+), 490 ($M^+ - NO$), 460 ($M^+ - 2NO$), 430 ($M^+ - 3NO$).

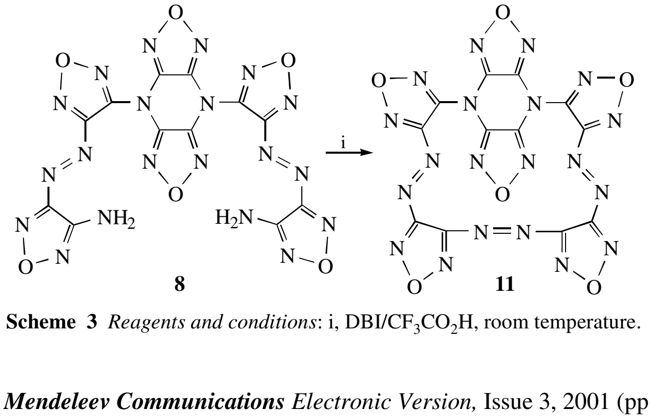
‡ *Crystal data for* $C_{12}N_{20}O_6 \cdot 2SOC_2H_6 \cdot 0.5H_2O$, $M = 693.5$; monoclinic, space group *C*2/*c*; $a = 19.912(9)$, $b = 11.887(8)$, $c = 24.594(9)$ Å; $\beta = 92.58(7)°$; $V = 5815.4$ Å^3, $Z = 8$, $d_{calc} = 1.57$ g cm^{-3}, $R = 0.078$.

All X-ray diffraction data were collected at room temperature on an Enraf-Nonius CAD-4 diffractometer using graphite-monochromated MoKα radiation ($\omega/2\theta$ scan technique, $\theta_{max} = 25°$). 3292 independent reflections were measured, 1350 with $I > 2\sigma(I)$. All calculations were performed using the SHELX program.[24] The structure was solved by a direct method and refined by a full-matrix least-squares method. Refinement was anisotropic for all non-hydrogen atoms. The H atoms of water molecules were localised in a differential synthesis; the H atoms of methyl groups in DMSO were inserted into calculated positions. All hydrogen atoms were included in the refinement with fixed thermal and positional parameters. The structure refinement revealed that one DMSO molecule was disordered among 2 positions (75 and 25%). The position occupations of S, O and C atoms were refined isotropically with fixed thermal parameters. The obtained values were used as fixed in anisotropic refinement. The H atoms of a disordered methyl group were not calculated. Though all atoms in the structure were reliably detected from the electron-density distribution, the determination accuracy of geometrical parameters was low: the mean bond length deviation $\sigma = 0.02$–0.03 Å. Atomic coordinates, bond lengths, bond angles and thermal parameters have been deposited at the Cambridge Crystallographic Data Centre (CCDC). For details, see 'Notice to Authors', *Mendeleev Commun.*, Issue 1, 2001. Any request to the CCDC for data should quote the full literature citation and the reference number 1135/83.



Scheme 2 *Reagents and conditions*: i, **3**/MeCN/NBu_4F, 70–80 °C; ii, **3**/MeCN, 70–80 °C.

described as a tetragon; furazan rings are the vertices of the tetragon; azo bridges and the difurazanopiperazinic frame are the sides of the tetragon. Distances between the opposite tetragon sides [N(10)···N(17) and N(1)···N(14)] are equal to 5.12 and 4.53 Å, respectively. The following short non-bonded contacts were found in the macrocycle: N(2)···N(17) 2.93, N(3)···C(5) 2.95, N(4)···C(12) 2.85, N(5)···C(12) 2.96, N(6)···C(5) 2.88, N(7)···C(1) 2.99, N(9)···N(11) 2.63, N(10)···C(5) 2.88, N(13)···N(15) 2.68, N(14)···C(7) 2.88, N(16)···N(18) 2.76, N(17)···C(12) 2.76 Å. The difurazanopiperazine moiety is approximately coplanar with the root-mean-square deviations from planarity of 0.08 Å, but there are small distortions to a 'butterfly' conformation: the dihedral angle between furazan rings is equal to 11°. The furazan rings B and C are planar (the root-mean-square deviations from planarity are equal to 0.00 and 0.01 Å, respectively) and form the dihedral angles with the tricycle plane A/F_B and A/F_C of 123 and 70°, respectively. Azo bridges at F_B and F_C rings are coplanar to appropriate heterocycles: the torsion angles C(5)–C(6)–N(9)–N(10) and C(12)–C(11)–N(18)–N(17) are equal to –5°. Furazan rings F_D and F_E of the azodifurazan subunit produce the dihedral angles with the azo-bridged plane C(8)–N(13)–N(14)–C(9) equal to 168 and 41°, respectively. Three azodifurazan subunits F_B–N(9)=N(10)–F_D, F_D–N(13)=N(14)–F_E and F_E–N(17)=N(18)–F_C in the macrocycle may be recognised.



Scheme 3 *Reagents and conditions*: i, DBI/CF_3CO_2H, room temperature.

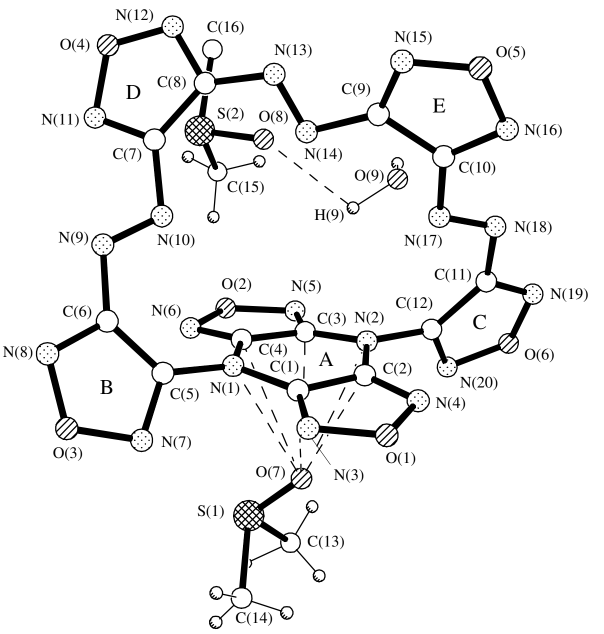


Figure 1 Molecular structure of macrocycle **11**.

According to the Klyne–Prelog nomenclature,[18] azofurazans may be characterised by the *cis*/*trans* positions of furazan rings relative to each other, the *Z*/*E* configurations of heterocycles relative to the azo bridge, and the conformations around the exocyclic C–N bond. In macrocyclic systems, an azofurazan fragment exhibits a significant distortion from coplanarity; furazan rings have *E*-configuration and can be in the *trans* or *cis* position.[19,20] Here, the azofurazan subunits F_B–N(9)=N(10)–F_D, F_D–N(13)=N(14)–F_E and F_E–N(17)=N(18)–F_C have the *cis*-position of the furazan rings with *E*-configuration and *ap-sc*, *ap-sc* and *sp-ap* conformations, respectively. Furazan rings are twisted around N–C bonds: the dihedral angles F_B/F_D, F_D/F_E, F_E/F_C are equal to 139, 128 and 31°, respectively. In the tricyclic fragment of the macromolecule, the mean lengths of the C–C (1.41 Å), C–N (1.38 Å in piperazine and 1.30 Å in furazan), and N–O (1.38 Å) bonds are similar to standard values.[21] The tertiary amine nitrogen atoms in **11** have a planar bond configuration [the sum of valence angles at N(1) and N(2) is equal to 359.6°]. A higher degree of planarity, as compared to tris(4,5-dicyano-1-methylimidazol-2-yl)amine (the sum of the C–N–C bond angles at the amine nitrogen atom is equal to 350.7°),[1] may be explained by the incorporation of the tertiary amine moiety into a piperazine ring. The mean N=N distance in azo bridges (1.24 Å) is consistent with the localised N=N bond length.[22] DMSO molecules have the shape of trigonal pyramids; S=O and S–C distances are similar to those found for DMSO.[22] The ordered DMSO molecule forms a charge-transfer complex with a difurazanopiperazine subunit. The O(7) atom from the ordered DMSO molecule is located approximately above the piperazine ring centre: the distances N(1)···O(7), N(2)···O(7), C(1)···O(7), C(2)···O(7), C(3)···O(7) and C(4)···O(7) are equal to 3.03, 2.94, 2.79, 2.80, 2.84 and 2.93 Å, respectively. The disordered DMSO and H_2O molecules are associated by weak H-bonds [distances O(8)···O(9) and O(8)···H(9) are 2.83 and 1.63 Å, respectively; the angle O(9)–H(9)–O(8) is 139.3°]. Other intermolecular contacts in the crystal structure are at normal van der Waals distances.

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