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A route to *meta*-benzenocyclophanes containing four tetrazole rings in the macrocycle is described.

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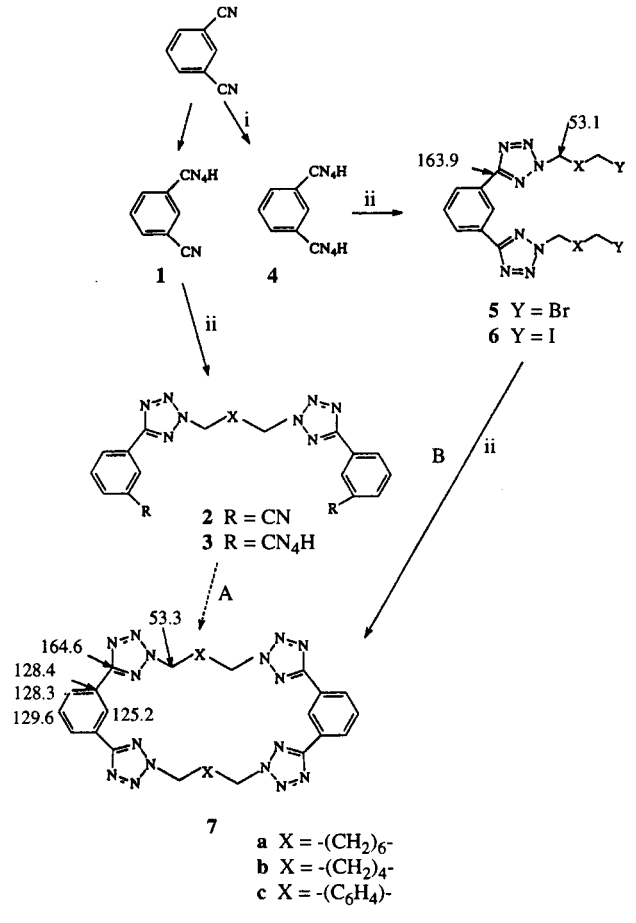
Recent interest in macrocycles containing sub-higher-azole rings has led to macrocyclic structures containing pyrazole [1], triazole [2] and oxadiazole [3] rings as subunits. There are only a few reports of macrocycles based on the tetrazole ring as the subazole moiety. These include one structure with one sp^2 carbon atom between the adjacent tetrazoles [4] and a few systems with two such carbons between the tetrazole units [5-7]. Herein we describe the first *meta*-benzeno based tetratetrazolophanes, **7**, which have three conjugated carbons linking the contigous tetrazole rings at the 5-C-atoms and aliphatic and *para*-xyleno chains linking the tetrazoles at the 2-N-atoms.

Results and Discussion.

Two synthetic routes were examined as possible entries to *meta*-benzenotetratetrazolophanes (Scheme 1). Treatment of *m*-bis(tetrazol-5-yl)benzene, **4**, with α,ω-dibromo- and -diiodoalkanes under basic conditions gave quantities of the symmetrical 1,3-bis[2-(halogenoalkyl)tetrazol-5-yl]benzenes **5** and **6** (Table) as well as some of the corresponding unsymmetrical 1-*N*-, 2-*N*-tetrazole isomers. Compounds **5** and **6** opened a route to the *m*-benzenotetratetrazolophanes **7** by treatment with **4** using potassium carbonate as the base. The use of other bases such as triethylamine were not successful and potassium ions appeared to favour the macrocyclisation possibly by providing some template assistance. Only symmetrical macrocycles, containing all four tetrazole rings substituted at N-2 were encountered (Table). The reactions were difficult and extensive chromatographic separation was required to isolate the macrocycles from intractable polymeric material. The isolated yields were in the range 20-30% but this is not unreasonable for macrocycles of this type and it allows for the preparation of working quantities of the new compounds. The potential second route to the macrocycles **7** was by path A, *via* 5-(*m*-cyanophenyl)tetrazole **1**. However, this faltered at structure **2** when all known methods of converting the cyano groups into tetrazole rings to give **3**, inexplicably failed. This was a surprising result since no difficulty is experienced in converting compound **1** into compound **4**. It was initially thought that steric effects arising from the long chains in the molecules **2** might be preventing azide attack at the nitrile groups. However, when the proton on the tetrazole ring of compound **1** was replaced by a 2-methyl substituent the same phenomenon was encountered and the cyano group could not be converted to a tetrazole. Hence, the effect appears to be electronic in nature but it is difficult to explain why the cyano group should be so unreactive to azide ion. Energy minimised models of the macrocycle **7c** using the computer programme Nemesis (V.1.1. Oxford Molecular Ltd. 1992) showed a rigid structure along the *p*-xylene units with buckling of the 1,3-ditetrazolobenzeno moieties and both ends giving overall a distorted chair-type structure.

Scheme 1



Reagents: i, NaN_3, NH_4Cl, HCl, DMF; ii, Et_3N, Y-CH_2-X-CH_2-Y (X = $(CH_2)_6$, -$(CH_2)_4$-, -C_6H_4-); iii, K_2CO_3, DMF, **4**. (Some key ^{13}C nmr shifts for **5a** and **7a** are shown).

Table
Products

Compounds	Mp(T/°C)	Yield(%) [b]	*Anal.* C	Found H	(Calcd.) % N	M (a.m.u.)
2a	129-131 [a]	29	63.35 (63.7)	5.75 (5.35)	30.6 (30.95)	-
5a	48-50 [a]	35 [c]	48.25 (48.35)	6.1 (6.05)	18.7 (18.8)	-
5b	60-62 [a]	15 [c]	45.0 (44.45)	5.0 (5.2)	20.75 (20.75)	-
5c	169-171 [a]	10	50.1 (49.7)	3.1 (3.45)	19.35 (19.3)	-
6a	62-64 [a]	45 [d]	41.95 (41.75)	4.9 (5.25)	15.9 (16.25)	-
6b	oil	27 [c]	37.9 (37.9)	4.1 (4.45)	17.55 (17.7)	-
7a	144-146 [a]	32	59.65 (59.3)	6.2 (6.15)	34.9 (35.0)	638 (648)
7b	150-152 [a]	22	56.4 (56.75)	5.25 (5.4)	37.4 (37.8)	620 (592)
7c	158-160 [a]	20	60.9 (60.6)	4.1 (4.1)	35.35 (35.3)	618 (634)

[a] From ethanol. [b] After separation from complicated mixtures. [c] The tetrazole N-1, N-2 substituted isomers were isolated as oils in yields of 3-6%. [d] The N-1, N-2 isomer of **6a** was isolated (2%) as a white solid, mp 64-66° (ethanol).

Models of the compounds **7a** and **7b** gave a planar picture with small twisting of the tetrazoles and some conformational flexibility along the methylene chains.

The structures of the products were established by ^1H and ^{13}C nmr spectra which showed all of the expected signals. The macrocycles were distinguished from possible polymeric alternatives by molecular-weight measurements using the isopiestic method with a Perkin Elmer 115 Molecular Weight machine (Table). Tetrazole rings substituted in the 2,5-pattern showed C-5 shifts at 162-164.6 ppm while those substituted in the 1,5-pattern showed C-5 shifts at 153-155 ppm. The methylene groups bonded at the tetrazole N-2 showed carbon shifts at 52.5-53.5 ppm and proton shifts at 4.4-4.7 ppm while those bonded at N-1 gave shifts at 47.0-48.5 and 4.0-4.3 respectively in accordance with shielding trends which we have established previously [8].

EXPERIMENTAL

Melting points were measured on an Electrothermal apparatus. The ir spectra were measured for Nujol mulls with a Perkin-Elmer 983 G spectrophotometer. The nmr spectra were measured on a JEOL JNM-GX-270 instrument with tetramethylsilane as the internal reference and deuteriochloroform or hexadeuteriodimethyl sulphoxide as solvents. Elemental analyses were performed on Perkin-Elmer model 240 CHN analyser.

Typical Examples:

Synthesis of **7a** from **4**.

(i) A mixture of 1,3-bis(tetrazol-5-yl)benzene **4** [mp 268-270° (lit [9] 260°) (1.0 g, 5 mmoles) and triethylamine (1.4 ml, 10 mmoles) and dry dichloromethane (50 ml) was heated to give a clear solution, treated with 1,8-dibromooctane (1.84 ml, 10 mmoles) and stirred at 40° for 24 hours. After removal of insoluble salts the solution was evaporated under reduced pressure and the oily residue taken up in chloroform, placed on a column of silica gel (Merck 230-400 mesh ASTM) and carefully eluted with hexane and gradient mixtures of hexane-ethyl acetate (95:5 to 50:50 v/v) to give products in the following order:

(a) 1,3-bis[2-(8-Bromooctyl)-2*H*-tetrazol-5-yl]benzene **5a**.

This compound was a white solid, mp 48-50° (35%); ir (Nujol): ν_{max}/cm^{-1} 1611 (>C=N); ^1H nmr: (deuteriochloroform): δ 8.9 (s, 1H, Ph), 8.2 (d, 2H, Ph), 7.61-7.66 (m, 1H, Ph), 4.7 (t, 4H, tetrazole two 2-N-CH_2), 3.4 (t, 4H, two CH_2Br), 1.2-2.1 (m, 24H, two -$(CH_2)_6$-); ^{13}C nmr (deuteriochloroform): 163.4 (2,5-tetrazole 5-C), 125.1, 129.4, 128.4, 128.1 (phenyl C's), 53.1 (tetrazole N-2-CH_2), 33.8 (CH_2Br), 32.6, 28.2, 28.6, 28.4, 27.9, 26.2 (-$(CH_2)_6$-); molecule shows plane of symmetry.

(b) 1-[1-(8-Bromooctyl)-1*H*-tetrazol-5-yl]-3-[2-(8-bromooctyl)-2*H*-tetrazol-5-yl]benzene, the (N-2, N-1) Isomer of **5a**.

This compound was a yellow oil (5.5%); ir (Nujol): ν_{max}/cm^{-1} 1610 (>C=N); ^1H nmr: (deuteriochloroform): δ 8.5 (s, 1H, Ph), 8.37 (d, 1H, Ph), 7.80 (d, 1H, Ph), 7.70 (m, 1H, Ph), 4.45 (t, 2H, tetrazole 2-N-CH_2), 4.00 (t, 2H, tetrazole-1-N-CH_2), 3.30 (m, 4H, two CH_2-Br), 1.2-2.08 (m, 24H, two -$(CH_2)_6$-); ^{13}C nmr: (deuteriochloroform): δ 163.9 (2,5-tetrazole 5-C), 154.1 (1,5-tetrazole 5-C), 131.2, 130.2, 129.4, 128.1 (phenyl C's), 126.2 (phenyl C), 125.2 (phenyl C), 53.1 (tetrazole N-2 CH_2), 48.1

(tetrazole N-1-CH_2), 33.9, 32.5 (CH_2Br), 30.0, 29.8, 29.3, 28.9, 28.3, 26.3 (-CH_2-)$_6$ (overlap of methylene carbon signals).

*Anal.*Calcd. for $C_{24}H_{36}N_8Br_2$: C, 48.35; H, 6.05; N, 18.8. Found: C, 48.8; H, 6.1; N, 18.7.

(ii) A mixture of **4** (240 mg, 1.1 mmoles) and potassium carbonate (1.5 g, 11 mmoles) in dimethylformamide (60 ml) was stirred at 75° under an atmosphere of nitrogen and treated with **5a** (660 mg, 1.1 mmoles) and stirred at 75° for 24 hours. Insoluble salts, removed from the cooled mixture were washed with ethyl acetate and the combined washings and mother liquor were evaporated under reduced pressure. The oily residue was chromatographed on a Merck silica gel column (230-400 ASTM) using as eluant, hexane and gradient mixtures of hexane-ethyl acetate (95:5 to 50:50 v/v) to give the following products:

(a) Di-*meta*benzenotetra(5',2'-tetrazolo)[5'-(3)-2'-(8)]cyclophane, **7a**.

Compound **7a** was obtained as a white solid, mp 144-146° (32% from ethanol); ^{1}H nmr: (deuteriochloroform): δ 8.83 (s, 2H), 8.25 (d, 4H), 7.60 (t, 2H), 4.64 (t, 8H, tetrazole four N-2-CH_2), 2.03 (m, 8H, four -$(CH_2)_2$-), 1.32 (m, 16H, two -$(CH_2)_4$-); ^{13}C nmr (deuteriochloroform): 164.6 (2,5-tetrazole 5-C), 128.4, 125.2, 129.6, 128.3 (Phenyl C's), 53.3 (tetrazole 2-N-CH_2), 29.3, 28.7, 26.1 (-$(CH_2)_6$-). The molecule shows plane of symmetry.

(b) Compound **5a** was also recovered (35%) from the column along with some intractable resins.

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