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# First X-Ray Structural Characterisation of Host-Guest Interactions in Tetra-Tetrazole Macrocycles

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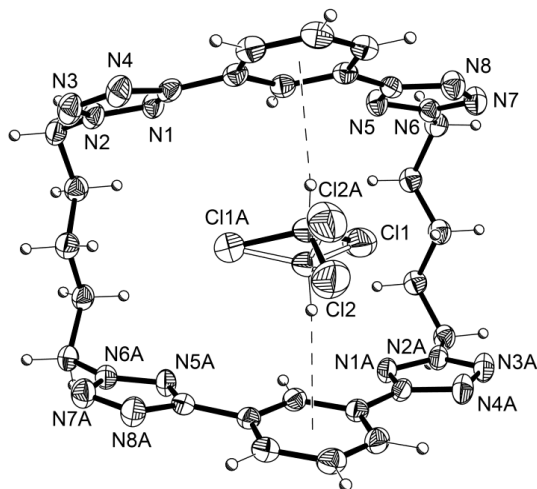
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**Authors**

Fintan Kelleher, Andrew Bond, Adrienne Fleming, Jackie Gaire, John McGinley, and Vickie McKee

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# First X-ray structural characterisation of host-guest interactions in tetra-tetrazole macrocycles

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## Abstract

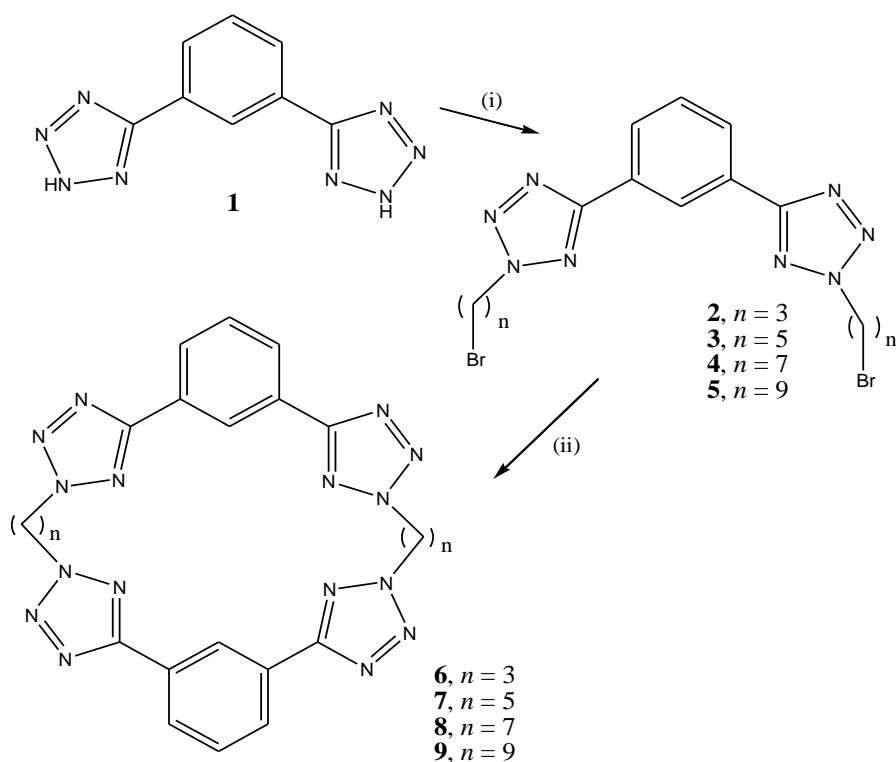
The syntheses of tetra-tetrazole macrocycles, containing two 1,3-bis(tetrazole)benzene units linked by a variety of *n*-alkyl (*n* = 3, 5, 7 or 9 carbon atoms) chain lengths, are described. The crystal structures of two 1,3-bis(tetrazole)benzenes containing pendant bromoalkyl chains (*n* = 3 or 5) are reported. A tetra-tetrazole macrocycle has also been structurally characterised and contains an unexpected “host-guest” interaction through binding of a chloroform solvent molecule. The resulting deviation of the macrocycle from planarity results from a combination of the “host-guest” interaction and strong intermolecular interactions between adjacent tetrazole and phenylene rings.

## Keywords

Tetrazole, macrocycles, host-guest, synthesis, X-ray crystal structure, NMR.

## Introduction

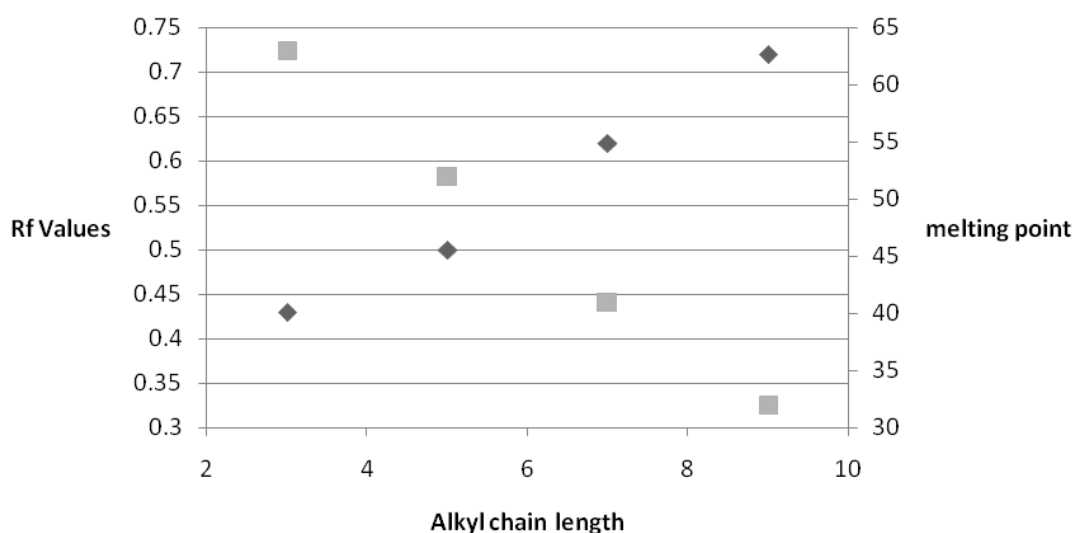
Macrocyclic and macroacyclic compounds have attracted much attention over the past number of years due to their role in understanding molecular processes that occur, for example, in biochemistry, catalysis and material science. The reviews by Vigato *et al.* describe the recent publications relating to these compounds.<sup>1-3</sup> The basis for the design of dinucleating or polynucleating ligands is the ability of ligands to bind different metal ions. Numerous macrocyclic systems exist which contain nitrogen donor atoms, either as a pyridine, imidazole or pyrrole group, or as an amine group.<sup>1-8</sup> However, it is somewhat surprising the relative paucity of macrocycles containing tetrazole groups,<sup>9</sup> considering that there are many articles and reviews on tetrazoles in the literature, including their use as the carboxylic acid bioisosteres in drug discovery.<sup>10-12</sup> The development of “click” chemistry methodology, as described by Sharpless and co-workers,<sup>13,14</sup> has resulted in a recent increase in tetrazole structures, which suggests that molecular recognition studies of tetrazoles will become increasingly important.<sup>15-21</sup> Our interest in tetrazoles concerns their use as precursors for the formation of new functionalised polytetrazole macrocycles, which can find application, for example, as sensors or in molecular recognition. We have previously reported the addition of pendant short-chain alkyl halides and vinyl arms to various bistetrazoles, as well as the synthesis and structural characterisation of tetra-tetrazole macrocycles from 1,2-, 1,3- and 1,4-dicyanobenzene derivatives, using short four-carbon, medium six-carbon and long eight-carbon alkyl linkers.<sup>22-25</sup> This paper focuses on the synthesis and characterisation of bis-tetrazoles, from 1,3-dicyanobenzene, having pendant *n*-alkyl halide arms (where *n* = 3, 5, 7 or 9), and their resulting tetra-tetrazole macrocycles (Scheme 1). The X-ray crystal structures of the 1,3-benzene derivatives with 3- and 5-carbon chain linkers are described, as is the first example of a host-guest interaction between a tetra-tetrazole macrocycle and a solvent molecule.



**Scheme 1.** Reaction conditions: i) 1,*n*-dibromoalkane ( $n = 3, 5, 7$  or  $9$ ), triethylamine, methanol,  $\Delta$ , 24 h; ii) **1**, potassium carbonate, dimethylformamide,  $75^\circ$ , 24 h.

## Results and Discussion

The reactions of 1,3-bis[tetrazol-5-yl]benzene (**1**) with triethylamine and 1,*n*-dibromoalkanes ( $n = 3, 5, 7$  or  $9$ ) were carried out in a manner similar to that previously reported.<sup>24</sup> An excess of the dibromoalkane and base was used in order to eliminate any mono-alkyl halide by-products which may have been formed. The symmetric 2-*N*,2-*N'*-bistetrazole was the major product in all cases. The other products in the reactions were not isolated due to the small quantities involved. The  $^1\text{H}$  and  $^{13}\text{C}$  NMR spectra of the unpurified reaction materials showed that the symmetric 2-*N*,2-*N'*-bistetrazole predominated over the asymmetric 1-*N*,2-*N'*-bistetrazole in an 85:15 ratio. The mass balance of the reaction was the starting bistetrazole (**1**) which accounted for approximately 60% in all cases. Two trends were observed for all the 1,3-bistetrazoles with pendant alkyl halide arms, namely an increase in  $R_f$  value as the chain length increased and a decrease in melting point as the chain length increased (see Figure 1). We have noticed this decrease in melting point for the bistetrazole compounds containing even chain length pendant alkyl halide arms (ethyl – octyl), although the even cases are slightly higher.<sup>26,27</sup>

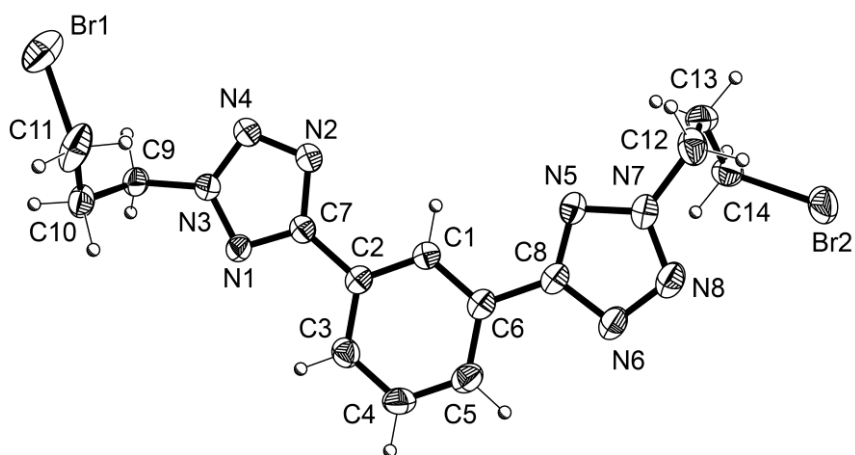


**Figure 1.** Graph showing increase in  $R_f$  value in 70:30 petroleum ether:ethyl acetate (◆) and decrease in melting point (■) with increasing alkyl chain length. Best-fit lines through the two sets of points give:  $R_f = (0.0495 \times \text{no. C atoms}) + 0.2705$ ;  $M.p. = (-5.15 \times \text{no. C atoms}) + 77.9$ .

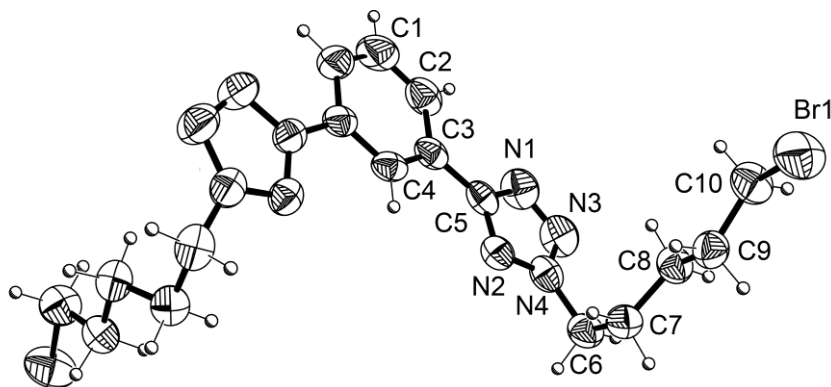
Butler and co-workers have described the synthesis of tetra-tetrazole macrocycles, based on either 1,2- or 1,3-bis(tetrazol-5-yl)benzenes, with alkyl chains having either six or eight carbon chain linkers.<sup>28-30</sup> We have extended this class of compounds by preparing macrocycles with four-carbon chain linkers, and also new macrocycles based on 1,4-bis(tetrazol-5-yl)benzene,<sup>22</sup> by reacting 1,*x*-[bis(2-(*y*-bromoalkyl)tetrazol-5-yl)]benzene ( $x = 2, 3$  or  $4$ ;  $y = 4, 6$  or  $8$ ; alkyl = *n*-butyl, *n*-hexyl or *n*-octyl) with 1,*n*-bis(tetrazol-5-yl)benzene ( $n = 2, 3$  or  $4$ ) in dimethylformamide, using  $K_2CO_3$  as base. The tetra-tetrazole molecule synthesised from 1,3-[bis(2-(6-bromohexyl)tetrazol-5-yl)]benzene and 1,3-bis(tetrazol-5-yl)benzene (**1**) resulted in a macrocycle containing an internal cavity size of  $10.8 \times 9.4$  Å. We have now reacted 1,3-[bis(2-(*n*-bromoalkyl)tetrazol-5-yl)]benzene ( $n = 3, 5, 7$  and  $9$ ) and 1,3-bis(tetrazol-5-yl)benzene in a similar manner. The yields for the cyclisation reactions were in the range 18-50%, with the highest yield obtained for the macrocycle containing the short *n*-propyl chain. As the chain length increased, the resulting yield decreased, as expected, since the entropy of activation is responsible for the difficulty in closing rings larger than six-membered.<sup>31</sup> The cyclisation reaction, in all cases, formed predominantly the symmetric product, where the alkyl chains are joined to the tetrazole moieties at the 2-*N* position, with very little asymmetry being observed. In the  $^1H$  NMR spectra of all the cyclisation products, the signal for the  $CH_2Br$  at  $\sim 3.5$  ppm disappeared, and the accompanying loss of the  $CH_2Br$  signal in the  $^{13}C$  NMR spectra confirmed that cyclisation had occurred. The simplicity of all the spectra indicated in all cases that only a symmetric cyclisation product was obtained, as additional signals would have been expected if any asymmetric product had been formed.

## X-Ray Crystal Structures

Crystals of compounds **2** and **3**, suitable for an X-Ray diffraction study, were obtained from chloroform solution and the structures confirmed the presence of the pendant bromoalkyl groups at the 2-*N*, 2-*N'*-positions for **2** and **3** (Figures 2 and 3). We have previously published the crystal structure of 1,3-bis[(2-bromoethyl)tetrazol-5-yl]benzene (**10**),<sup>24</sup> and a second polymorph of that compound has also been published (denoted **10a**).<sup>32</sup>



**Figure 2.** Molecular structure of **2** with displacement ellipsoids at the 50% probability level for non-H atoms. The N3–C9 and N7–C12 bonds form an obtuse angle.

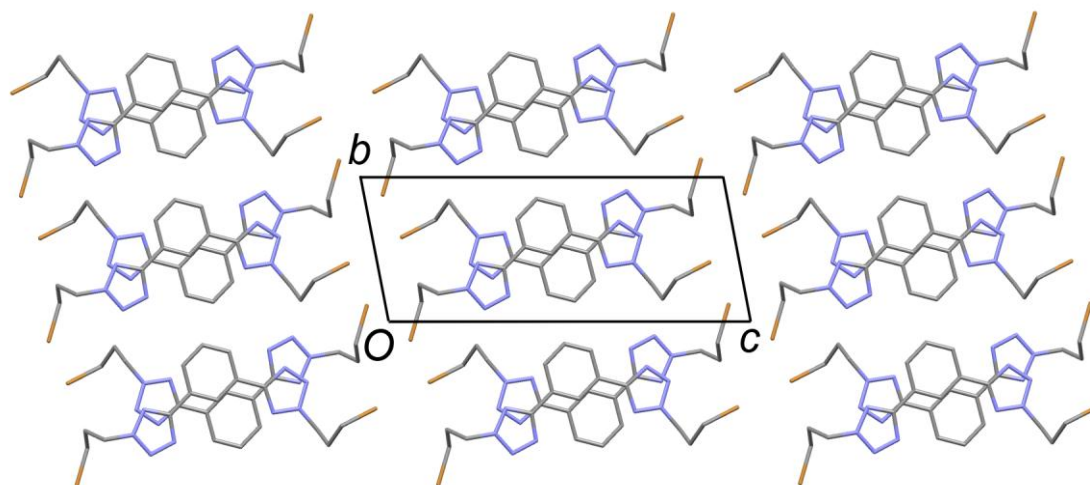


**Figure 3.** Molecular structure of **3** with displacement ellipsoids at the 50% probability level for non-H atoms. A crystallographic 2-fold axis passes through atoms C1 and C4. The N3–C9 and N7–C12 bonds form an acute angle.

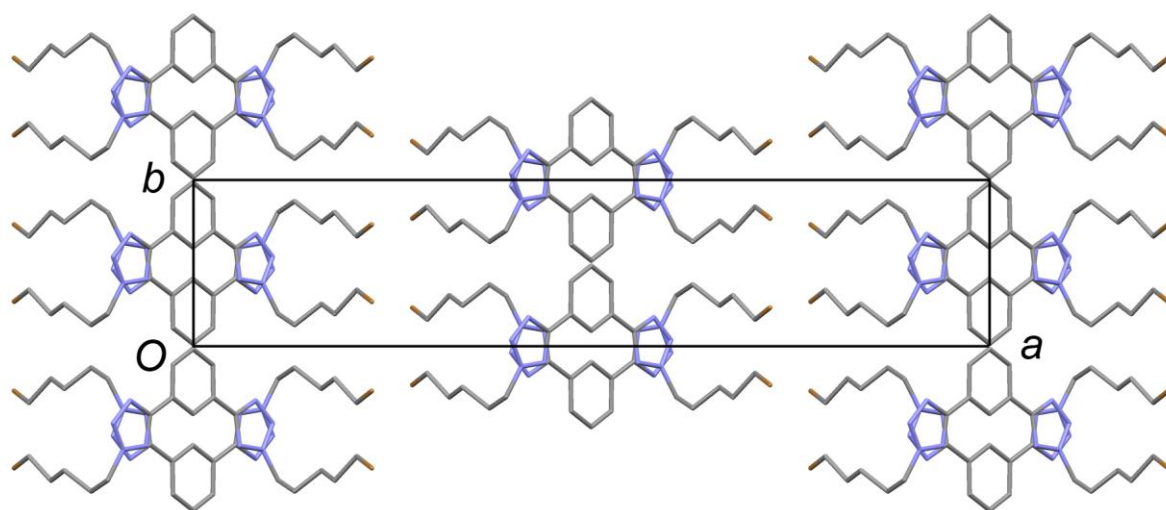


In **2** and **3**, the tetrazole rings are close to coplanar with the benzene ring to which they are attached, and the bromoalkyl groups project to either side of this plane. This feature of the molecular conformation is similar to **10a**, while the bromoalkyl groups project to the same side of the molecular plane in the polymorph **10**. In **3**, **10** and **10a**, the substituted 2-*N* atoms point in the same direction so that the two N-CH<sub>2</sub> bond vectors form an acute angle (see Figure 3). The conformation of **2** is distinct in that one tetrazole ring is flipped over with respect to the molecular plane so that the two N-CH<sub>2</sub> bond vectors form an acute angle (see Figure 2). In **3** and **10a**, the molecules lie on crystallographic 2-fold axes, while in **10** they display approximate (non-crystallographic) mirror symmetry.

The structures of **2** and **3** contain similar 2-D layers (Figures 4 and 5). The central sections of the molecules approach each other in a side-on manner, forming 1-D motifs along the *b* direction. Thus, the length of the *b* axis is closely comparable in the two crystal structures. In both cases, the 1-D motifs are arranged in an anti-parallel manner, with adjacent molecules forming slipped  $\pi$ -stacked arrangements. The perpendicular distance between molecular planes is 3.37(1) Å in **2** and 3.21(1) Å in **3**, and the centroid-centroid distances for interacting phenylene rings are 4.684 and 6.013 Å in **2**, and 5.409 and 6.104 Å in **3**.



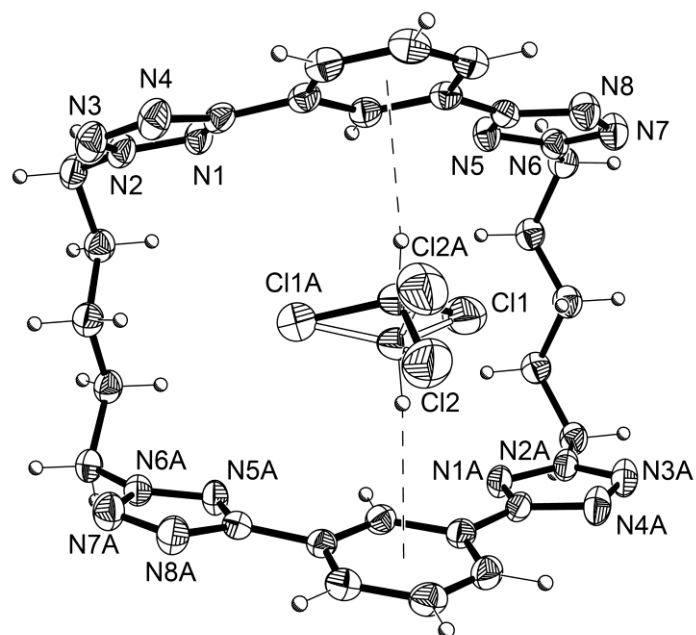
**Figure 4.** Projection of the crystal structure of **2** along the *a* axis, showing the layered structure with “Type II” Br $\cdots$ Br contacts between layers. H atoms are omitted.



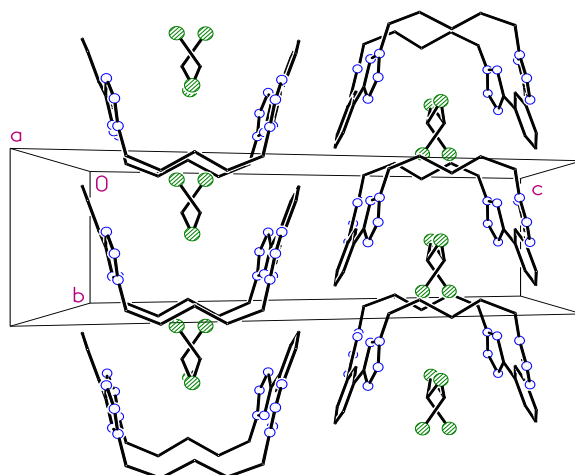
**Figure 5.** Projection of **3** along the *c* axis, showing the layered structure with “Type I” Br⋯Br contacts between layers. H atoms are omitted.

In **3**, adjacent 2-D layers meet so as to bring the terminal CH<sub>2</sub>—Br bonds into an offset co-linear alignment (Figure 5), forming “Type I” Br⋯Br interactions, as classified previously by Desiraju *et al.*<sup>33</sup> The intermolecular Br⋯Br distance is 3.489(2) Å, which is considerably shorter than twice the bromine van der Waals radius (3.90 Å) and within the range of those values previously reported, 3.415–3.691 Å.<sup>23,34-36</sup> In **2**, the Br⋯Br interactions resemble side-on “Type II” interactions, with a shortest distance of 3.771(3) Å.

Crystals of **7** were obtained from chloroform solution, and the crystal structure confirms the expected tetra-tetrazole macrocyclic structure, with each tetrazole ring substituted at the 2-*N* position, as suggested by <sup>13</sup>C NMR spectroscopy. The structure also reveals an unexpected “host-guest” interaction between the macrocycle and a molecule of chloroform solvent (Figure 6). The molecule lies on a crystallographic 2-fold rotation axis, and the CHCl<sub>3</sub> molecule is disordered equally over two orientations about this axis, forming C—H⋯π interactions in which the H atom lies 2.50 Å above the mean plane of the phenylene ring. The interaction and encapsulation of the CHCl<sub>3</sub> molecule is facilitated by a bowl-shaped conformation of the tetra-tetrazole macrocycle, which is distinctly different from the essentially flat structure that we have reported for a similar six-carbon linked macrocycle for which no solvent is present.<sup>22</sup> The molecules of **7** are stacked in columns parallel to the *b* axis (see Figure 7) with π–π stacking interactions between neighbouring tetrazole and phenylene rings (centroid-centroid distance 3.694 Å. Similar interactions have been observed in other tetrazole structures.<sup>22-25</sup>



**Figure 6.** Molecular structure of **7** with displacement ellipsoids at the 50% probability level for non-H atoms. The  $\text{CHCl}_3$  molecule is disordered about a crystallographic 2-fold rotation axis; atoms with suffix A are generated by the symmetry operator  $-x, y, \frac{1}{2}-z$ . Dashed lines represent  $\text{C-H}\cdots\pi$  interactions.



**Figure 7.** Partial packing diagram of **7** showing the bowl-shaped macrocycles stacked in columns along the  $b$  axis. Both orientations of the disordered  $\text{CHCl}_3$  molecule are shown. H atoms are omitted.

## Conclusions

In this paper, we have reported on the syntheses and characterisation of bromo-alkyl derivatives of 1,3-bis(tetrazole)benzene, where the alkyl chain contains either 3, 5, 7 or 9 carbons atoms. Interestingly, the predominant compound formed in all these reactions is the symmetric 2-*N*,2-*N'*-bistetrazole isomer, whereas the same reactions carried out with even *n*-alkyl chains have previously yielded both symmetric 2-*N*,2-*N'*-bistetrazole and asymmetric 1-*N*,2-*N'*-bistetrazole derivatives. Four new macrocycles containing four tetrazole rings were synthesised and the X-ray crystal structure of **7** showed a bowl-shaped conformation with an interesting host-guest interaction with an encapsulated solvent chloroform molecule.

## Experimental

<sup>1</sup>H and <sup>13</sup>C NMR ( $\delta$  ppm; *J* Hz) spectra were recorded on a JEOL JNM-LA300 FT-NMR spectrometer using saturated CDCl<sub>3</sub> solutions with Me<sub>4</sub>Si reference, unless indicated otherwise, with resolutions of 0.18 Hz and 0.01 ppm, respectively. Infrared spectra (cm<sup>-1</sup>) were recorded as KBr discs or liquid films between KBr plates using a Nicolet Impact 410 FT-IR. Melting point analysis was carried out using a Stewart Scientific SMP 1 melting point apparatus and are uncorrected. Mass spectra were obtained from the CSCB Mass Spectrometry Centre, School of Chemistry and Chemical Biology, University College Dublin using a Micromass/Waters Corp. Liquid chromatography time-of-flight (LCT) mass spectrometer equipped with an electrospray source. Microanalysis was carried out at the Microanalytical Laboratory of University College, Dublin. Standard Schlenk techniques were used throughout. Starting materials were commercially obtained and used without further purification. The synthesis of compound **1** has been described in the literature previously.<sup>24</sup>

### *General Syntheses of 1,n-bis(bromoalkyltetrazolyl)benzenes*

Compound **1** (1.0 g, 0.47 mmol) was dissolved in methanol (30 ml) and, to the stirred solution, was added triethylamine (3.0 ml, 2.8 mmol). The resulting solution was heated to reflux for 30 min, and to the hot solution was added 1,*n*-dibromoalkane (1.4 mmol). The reaction mixture was then heated to reflux for a further 24 hours. After cooling, the solvent was removed under reduced pressure to afford an oil which was then purified by column chromatography on silica gel (initially at the ratio of petroleum ether:ethyl acetate 80:20, followed by the ratio 60:40).

1,3-Bis[(3-bromopropyl)tetrazol-5-yl]benzene (2-*N*, 2-*N'*) (**2**)

White solid. Analysis: Found: C, 37.12; H, 3.58; N, 24.41. Calc. For  $C_{14}H_{16}N_8Br_2$ : C, 36.86; H, 3.54; N, 24.57; Yield: 0.32 g, 16 %, 0.70 mmol;  $R_f$  0.43 (70:30 petroleum ether:ethyl acetate); M.p. 62–64 °C;  $\nu_{max}$  (KBr) 3421, 2919, 2847, 1623, 1521, 1455, 1347, 1276, 1194, 1086, 799, 743  $cm^{-1}$ ;  $\delta_H$ : 2.65 (m, 4 H,  $CH_2$ ), 3.49 (t, 4 H,  $J = 6.8$  Hz,  $CH_2Br$ ), 4.88 (t, 4 H,  $J = 5.6$  Hz, tetrazole N2- $CH_2$ ), 7.64 (t, 1 H,  $J = 7.9$  Hz, Ar-H), 8.29 (dd, 2 H,  $J = 7.6, 1.2$  Hz, Ar-H), 8.92 (s, 1 H, Ar-H);  $\delta_C$ : 29.0, 31.0 ( $CH_2Br$ ), 51.0 (tetrazole N2- $CH_2$ ), 125.2, 128.0, 128.1, 129.0, 164.0 (2,5-tetrazole).

### 1,3-Bis[(5-bromopentyl)tetrazol-5-yl]benzene (2-*N*, 2-*N'*) (**3**)

White solid. Analysis: Found: C, 42.46; H, 4.77; N, 21.74. Calc. For  $C_{18}H_{24}N_8Br_2$ : C, 42.40; H, 4.72; N, 21.88; Yield: 0.32 g, 18 %, 0.62 mmol;  $R_f$  0.50 (70:30 petroleum ether:ethyl acetate); M.p. 51–52 °C;  $\nu_{max}$  (KBr) 3448, 2956, 2922, 2851, 1638, 1513, 1456, 1430, 1385, 1271, 1196, 1048, 904, 799, 740, 689, 638  $cm^{-1}$ ;  $\delta_H$ : 1.55 (m, 4 H,  $CH_2$ ), 1.86 (m, 4 H,  $CH_2$ ), 2.01 (m, 4 H,  $CH_2$ ), 3.41 (t, 4 H,  $J = 6.4$  Hz,  $CH_2Br$ ), 4.70 (t, 4 H,  $J = 7.6$  Hz, tetrazole N2- $CH_2$ ), 7.63 (t, 1 H,  $J = 7.6$  Hz, Ar-H), 8.24 (dd, 2 H,  $J = 7.6, 1.2$  Hz, Ar-H), 8.92 (s, 1 H, Ar-H);  $\delta_C$ : 24.8, 28.3, 31.7, 32.9 ( $CH_2Br$ ), 52.8 (tetrazole N2- $CH_2$ ), 125.0, 128.3, 128.5, 129.4, 164.0 (2,5-tetrazole).

### 1,3-Bis[(7-bromoheptyl)tetrazol-5-yl]benzene (2-*N*, 2-*N'*) (**4**)

White solid. Analysis: Found: C, 46.38; H, 5.69; N, 19.45. Calc. For  $C_{22}H_{32}N_8Br_2$ : C, 46.49; H, 5.67; N, 19.72; Yield: 0.32 g, 12 %, 0.56 mmol;  $R_f$  0.62 (70:30 petroleum ether:ethyl acetate); M.p. 41–42 °C;  $\nu_{max}$  (KBr) 3430, 3016, 2934, 2858, 1625, 1521, 1455, 1347, 1214, 1040, 932, 800, 753, 671  $cm^{-1}$ ;  $\delta_H$ : 1.55 (m, 12 H,  $CH_2$ ), 1.88 (m, 4 H,  $CH_2$ ), 2.09 (m, 4 H,  $CH_2$ ), 3.38 (t, 4 H,  $J = 5.9$  Hz,  $CH_2Br$ ), 4.68 (t, 4 H,  $J = 5.9$  Hz, tetrazole N2- $CH_2$ ), 7.63 (t, 1 H,  $J = 8.1$  Hz, Ar-H), 8.27 (dd, 2 H,  $J = 7.6, 1.2$  Hz, Ar-H), 8.93 (s, 1 H, Ar-H);  $\delta_C$ : 26.1, 27.7, 29.1, 32.5, 33.7 ( $CH_2Br$ ), 53.1 (tetrazole N2- $CH_2$ ), 125.1, 128.2, 128.4, 129.4, 164.0 (2,5-tetrazole).

### 1,3-Bis[(9-bromononyl)tetrazol-5-yl]benzene (2-*N*, 2-*N'*) (**5**)

White solid. Analysis: Found: C, 50.18; H, 6.46; N, 16.91. Calc. For  $C_{26}H_{40}N_8Br_2$ : C, 50.01; H, 6.46; N, 17.94; Yield: 0.61 g, 21.3 %, 0.98 mmol;  $R_f$  0.72 (70:30 petroleum ether:ethyl acetate); M.p. 31–33 °C;  $\nu_{max}$  (KBr) 3442, 2919, 2849, 1654, 1526, 1455, 1347, 1256, 1191, 1082, 788, 742, 723, 683, 648  $cm^{-1}$ ;  $\delta_H$ : 1.37 (m, 20 H,  $CH_2$ ), 1.84 (m, 4 H,  $CH_2$ ), 2.08 (m, 4 H,  $CH_2$ ), 3.39 (t, 4 H,

$J = 6.3$  Hz, CH<sub>2</sub>Br), 4.67 (t, 4 H,  $J = 5.9$  Hz, tetrazole N<sub>2</sub>-CH<sub>2</sub>), 7.63 (t, 1 H,  $J = 7.9$  Hz, Ar-H), 8.27 (dd, 2 H,  $J = 7.6, 1.2$  Hz, Ar-H), 8.94 (s, 1 H, Ar-H);  $\delta_C$  : 26.2, 28.1, 28.5, 28.7, 29.1, 29.3, 32.2, 34.0 (CH<sub>2</sub>Br), 53.2 (tetrazole N<sub>2</sub>-CH<sub>2</sub>), 125.1, 128.2, 128.4, 129.4, 164.0 (2,5-tetrazole).

### *General Syntheses of tetra-tetrazolophanes*

A mixture of **1** (240 mg, 1.1 mmol) and potassium carbonate (1.5 g, 11 mmol) in dimethylformamide (60 ml) was stirred for one hour at 75 °C under a nitrogen atmosphere, and then treated with the appropriate 1,*n*-bis(bromoalkyltetrazolyl)benzene (**2-5**, 1.1 mmol) and stirred at 75 °C for 24 h. Insoluble salts, filtered from the cooled mixture, were washed with ethyl acetate and the combined washings and mother-liquor were evaporated under reduced pressure. The white residue which remained was dissolved in chloroform and chromatographed on silica gel using DCM:MeOH (99.5:0.5 to 99.0:1.0 v/v) as eluent to give the tetra-tetrazolophane macrocycle.

Di-*metabenzenotetra*(5', 2'-tetrazolo)[5'-(2)-2'-(3)]-cyclophane (2-*N*, 2-*N'*, 2-*N''*, 2-*N'''*) (**6**).

White solid. Analysis: Found: C, 51.83; H, 4.01; N, 44.17. Calc. For C<sub>22</sub>H<sub>20</sub>N<sub>16</sub>: C, 51.96; H, 3.96; N, 44.07; Yield: 0.28 g, 50.0 %, 0.55 mmol;  $R_f$  0.14 (40:60 petroleum ether:ethyl acetate); M.p. >300 °C;  $\nu_{\max}$  (KBr) 3439, 2927, 2852, 1637, 1515, 1455, 1432, 1357, 1214, 1088, 1047, 920, 786, 746, 691 cm<sup>-1</sup>;  $\delta_H$  : 2.18 (m, 4 H, CH<sub>2</sub>), 4.68 (t, 8 H,  $J = 6.9$  Hz, NCH<sub>2</sub>), 7.63 (t, 2 H,  $J = 7.9$  Hz, Ar-H), 8.27 (d, 4 H,  $J = 7.9$  Hz, Ar-H), 8.72 (s, 2 H, Ar-H);  $\delta_C$  : 22.9, 29.0, 52.6 (tetrazole N<sub>2</sub>-CH<sub>2</sub>), 126.3, 128.0, 128.5, 129.6, 164.4 (2,5-tetrazole); HRMS (ES) Calc. [M+1] 509.502, Found 509.504.

Di-*metabenzenotetra*(5', 2'-tetrazolo)[5'-(2)-2'-(5)]-cyclophane (2-*N*, 2-*N'*, 2-*N''*, 2-*N'''*) (**7**).

White solid. Analysis: Found: C, 55.65; H, 5.09; N, 39.47. Calc. For C<sub>26</sub>H<sub>28</sub>N<sub>16</sub>: C, 55.31; H, 5.00; N, 39.69; Yield: 0.25 g, 40.0 %, 0.44 mmol;  $R_f$  0.35 (40:60 petroleum ether:ethyl acetate); M.p. >300 °C;  $\nu_{\max}$  (KBr) 3435, 2927, 2852, 1647, 1523, 1455, 1432, 1390, 1357, 1214, 1088, 1047, 820, 786, 746, 690 cm<sup>-1</sup>;  $\delta_H$  : 1.25 (m, 4 H, CH<sub>2</sub>), 2.23 (m, 8 H, CH<sub>2</sub>), 4.69 (t, 8 H,  $J = 6.8$  Hz, NCH<sub>2</sub>), 7.61 (t, 2 H,  $J = 7.9$  Hz, Ar-H), 8.27 (d, 4 H,  $J = 7.9$  Hz, Ar-H), 8.72 (s, 2 H, Ar-H);  $\delta_C$  : 22.9, 28.7, 29.7, 52.6 (tetrazole N<sub>2</sub>-CH<sub>2</sub>), 125.8, 127.9, 128.4, 129.5, 164.6 (2,5-tetrazole); HRMS (ES) Calc. [M+1] 565.608, Found 565.273.

Di-*metabenzenotetra*(5', 2'-tetrazolo)[5'-(2)-2'-(7)]-cyclophane (2-*N*, 2-*N'*, 2-*N''*, 2-*N'''*) (**8**).

White solid. Analysis: Found: C, 58.35; H, 6.11; N, 35.88. Calc. For C<sub>30</sub>H<sub>36</sub>N<sub>16</sub>: C, 58.05; H, 5.85; N, 36.10; Yield: 0.14 g, 20 %, 0.23 mmol; R<sub>f</sub> 0.49 (40:60 petroleum ether:ethyl acetate); M.p. 258-260 °C;  $\nu_{\max}$  (KBr) 3423, 2922, 2853, 1648, 1523, 1452, 1430, 1384, 1357, 1214, 1088, 1045, 912, 781, 746, 692 cm<sup>-1</sup>;  $\delta_{\text{H}}$ : 0.80 (m, 8 H, CH<sub>2</sub>), 1.18 (m, 4 H, CH<sub>2</sub>), 2.02 (m, 8 H, CH<sub>2</sub>), 4.59 (t, 8 H,  $J = 6.6$  Hz, NCH<sub>2</sub>), 7.51 (t, 2 H,  $J = 7.9$  Hz, Ar-H), 8.17 (d, 4 H,  $J = 7.9$  Hz, Ar-H), 8.77 (s, 2 H, Ar-H);  $\delta_{\text{C}}$ : 22.7, 26.0, 29.7, 53.1 (tetrazole N2-CH<sub>2</sub>), 125.7, 128.2, 128.4, 129.5, 164.5 (2,5-tetrazole); HRMS (ES) Calc. [M+1] 621.330, Found 621.332.

Di-*metab*enzenotetra(5', 2'-tetrazolo)[5'-(2)-2'-(9)]-cyclophane (2-*N*, 2-*N'*, 2-*N''*, 2-*N'''*) (**9**).

White solid. Analysis: Found: C, 60.43; H, 6.62; N, 33.15. Calc. For C<sub>34</sub>H<sub>44</sub>N<sub>16</sub>: C, 60.34; H, 6.55; N, 33.11; Yield: 0.14 g, 18 %, 0.21 mmol; R<sub>f</sub> 0.75 (40:60 petroleum ether:ethyl acetate); M.p. 206-209 °C;  $\nu_{\max}$  (KBr) 3423, 2925, 2851, 1637, 1536, 1458, 1432, 1261, 1088, 1045, 810, 743, 688 cm<sup>-1</sup>;  $\delta_{\text{H}}$ : 1.54 (m, 20 H, CH<sub>2</sub>), 2.13 (m, 8 H, CH<sub>2</sub>), 4.72 (t, 8 H,  $J = 6.6$  Hz, NCH<sub>2</sub>), 7.65 (t, 2 H,  $J = 7.9$  Hz, Ar-H), 8.22 (d, 4 H,  $J = 7.9$  Hz, Ar-H), 8.95 (s, 2 H, Ar-H);  $\delta_{\text{C}}$ : 26.7, 27.3, 28.6, 30.1, 52.1 (tetrazole N2-CH<sub>2</sub>), 126.8, 128.1, 128.3, 129.5, 164.0 (2,5-tetrazole); HRMS (ES) Calc. [M+1] 677.393, Found 677.401.

### X-Ray Crystallography

Crystals of **2**, **3** and **7** suitable for X-ray analysis, were obtained by recrystallisation from chloroform solution. Data for **2** and **3** were collected on a Bruker Nonius X8 APEXII diffractometer<sup>37</sup> at 180(2) K and 298(2) K, respectively, and data for **7** were collected at 150(2) K on a Bruker APEXII diffractometer. In each case Mo-K $\alpha$  radiation ( $\lambda = 0.71073$  Å) was used, a multi-scan correction was applied<sup>38</sup> and the structure was refined against  $F^2$  using all data. All non-hydrogen atoms were refined with anisotropic atomic displacement parameters and hydrogen atoms were placed at calculated positions and refined using a riding model.

**Compound 2.** *Crystal data:* C<sub>14</sub>H<sub>16</sub>Br<sub>2</sub>N<sub>8</sub>,  $M = 456.17$ , triclinic,  $a = 7.0009(4)$ ,  $b = 7.1694(4)$ ,  $c = 17.5789(10)$  Å,  $\alpha = 100.518(2)$ ,  $\beta = 92.790(2)$ ,  $\gamma = 92.019(2)^\circ$ ,  $U = 865.60(5)$  Å<sup>3</sup>, space group  $P-1$ ,  $Z = 2$ ,  $\mu = 4.697$  mm<sup>-1</sup>,  $\rho_{\text{calc}} = 1.750$  g cm<sup>-3</sup>. 33334 data (3891 unique,  $R_{\text{int}} = 0.0285$ ) were measured in the range  $3.54 < \theta < 28.34^\circ$ .  $R_1(I > 2\sigma(I)) = 0.0312$  and  $wR_2(\text{all data}) = 0.0863$ . Goodness of fit on  $F^2 = 1.06$ . CCDC No. 725917.

**Compound 3.** *Crystal data:* C<sub>18</sub>H<sub>24</sub>Br<sub>2</sub>N<sub>8</sub>, *M* = 512.27, monoclinic, *a* = 34.3306(7), *b* = 7.0548(1), *c* = 9.0546(2) Å, β = 102.433(1)°, *U* = 2141.55(7) Å<sup>3</sup>, space group C 2/*c*, *Z* = 4, μ = 3.806 mm<sup>-1</sup>, ρ<sub>calc</sub> = 1.589 g cm<sup>-3</sup>. 8687 data (2034 unique, *R*<sub>int</sub> = 0.0232) were measured in the range 3.65 < θ < 25.73°. *R*<sub>1</sub>(*I* > 2σ(*I*)) = 0.0328 and *wR*<sub>2</sub>(all data) = 0.0827. Goodness of fit on *F*<sup>2</sup> = 1.03. CCDC No. 725918.

**Compound 7.** *Crystal data:* C<sub>27</sub>H<sub>29</sub>Cl<sub>3</sub>N<sub>16</sub>, *M* = 684.01, monoclinic, *a* = 24.584(3), *b* = 6.5069(8), *c* = 22.926(3) Å, β = 119.469(2)°, *U* = 3192.9(6) Å<sup>3</sup>, space group C 2/*c*, *Z* = 4, μ = 0.335 mm<sup>-1</sup>, ρ<sub>calc</sub> = 1.423 g cm<sup>-3</sup>. 13630 data (3282 unique, *R*<sub>int</sub> = 0.0472) were measured in the range 1.90 < θ < 26.45°. *R*<sub>1</sub>(*I* > 2σ(*I*)) = 0.0426 and *wR*<sub>2</sub>(all data) = 0.1213. Goodness of fit on *F*<sup>2</sup> = 0.937. CCDC No. 725395.

### Supplementary material

Crystallographic data for **2**, **3** and **7** have been deposited with the Cambridge Crystallographic Data Centre, CCDC Nos. 725917, 725918 and 725395. Copies of this information may be obtained free of charge from deposit@ccdc.cam.ac.uk or [www:http://www.ccdc.cam.ac.uk](http://www.ccdc.cam.ac.uk)

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