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REVIEW ARTICLE

Synthesis of macrocycles containing tetrazole units—potential metal complexation sites

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Abstract The ability of ligands to bind different metal ions is the basis for the design of dinucleating or polynucleating ligands. Indeed, macrocyclic and macroacyclic compounds have attracted much attention in recent years due to their role in understanding molecular processes that occur in biochemistry, catalysis and material science. For example, much effort has been expended on the construction of coordination polymers and on complexes with double or triple helicate structures. In this review, our recent studies into macrocycles containing tetrazole functional groups are summarised.

Keywords Macrocycles · Tetrazoles · Synthesis · X-ray crystal structures

Introduction

Macrocyclic and macroacyclic compounds have attracted much attention in recent years due to their role in understanding molecular processes that occur in biochemistry, catalysis and material science to name but a few, and the review by Vigato and Tamburini describes the recent publications relating to these compounds [1]. The ability of ligands to bind different metal ions is the basis for the design of dinucleating or polynucleating ligands. In particular, most attention was devoted to their correlation with the active sites of metallo-enzymes and proteins containing dinuclear metallo-entities [2–8]. These types of compounds are currently receiving much attention as a result of their ability to position two metal ions with a distance of 3–6 Å from each other, with the subsequent result that they are being proposed as essential components in the preparation of devices based on molecular assembly. Starting from simple dinucleating ligands, complex three-dimensional systems have been prepared using self assembling processes, molecular recognition processes and the template effect. Furthermore, this type of ligand has also been used in the design of complexes with specific spectroscopic and magnetic properties.

Recently, much effort has been expended on the construction of coordination polymers and on complexes with double or triple helicate structures [9, 10]. In recent years, the construction of coordination polymers is one of the most active areas of coordination chemistry research and is driven by their potential applications and network topologies [9]. Rigid ligands are often employed to design coordination complexes with predictable topologies [11], while flexible ligands can adopt different coordination modes and geometries, according to the geometrical requirements of the metal ion, which can lead to interesting properties and topologies [12]. The field of coordination complexes with helical structures has been of interest to chemists for many years and remains popular because of the development of new research areas involving helical structures, such as control of helical twist, control of helical structure through cation and/or anion binding, to mention but a few [13].

Numerous macrocyclic systems exist which contain nitrogen donor atoms, either as a pyridine, imidazole or pyrrole group, or as an amine group [14]. In many cases, these are present in conjunction with other donor atoms,

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such as oxygen, sulfur or phosphorus. Somewhat surprising is the relative paucity of macrocycles containing tetrazole groups [15–24]. We found this particularly strange, since there are many articles and reviews [25] on tetrazoles in the literature, including their use as the carboxylic acid bioisosteres in drug discovery [26]. Therefore, we decided to look at these macrocycles again, with a view to obtaining metal ion complexation with same. This article looks at macrocycles containing the tetrazole functional group which have been previously reported, our success in the synthesis of such macrocycles as well as some new reaction pathways we have attempted to generate macrocycles containing tetrazoles.

Known macrocycles containing two tetrazole rings

Macrocycles containing two tetrazole rings tend to fall into the class of compounds known as cyclophanes. The term "cyclophane" applies to cyclic systems consisting of ring(s) or ring system(s) having the maximum number of noncumulative double bonds connected by saturated and/or unsaturated chains [27]. The wide interest in macrocycles containing heterocyclic rings, having one or more nitrogen atoms, has led to a range of polyazole macrocycles including pyrazole and triazole rings as sub-units, as well as groupings with other five- and six-membered rings [28]. However, there are only a few examples of macrocycles containing two tetrazole units. Ried and co-workers published a number of papers on the reactions of symmetric or asymmetric 2,3-bis(5-tetrazolyl)pyrazines [15–17] with α,ω-dibromoalkanes in the presence of triethylamine (Et_3N) to give cyclophanes, as shown in Fig. 1.

The cyclisation of 2,3-pyrazinedicarbonitrile with sodium azide in the presence of lithium chloride and ammonium chloride in dimethylformamide (DMF) gave the pyrazine(bis-tetrazoles) in good yield, which on cyclocondensation with α,ω-dibromoalkanes yielded the symmetric and asymmetric macrocycles **1** and **2**. The macrocycles were separated by column chromatography and the X-ray crystal structures of both symmetric and asymmetric macrocycles were obtained. In these papers, Ried also reported the reactions of 1,2-dicyanobenzene leading to the macrocycle as well. Further work by Ried and co-workers involved the methylation of 2*H*-1,2,3-triazole-4,5-dicarbonitrile to give 2-methyl-1,2,3-triazole-4,5-dicarbonitrile [18]. The double cycloaddition reaction of this substituted triazole with ammonium azide gave the corresponding 4,5-bis(tetrazol-5-yl)-1,2,3-triazole, which underwent reactions with α,ω-dibromoalkanes to give symmetric macrocycles (**3**), shown in Fig. 2.

The 1-*N*,1-*N*′-ethylene bridged macrocycle (**4**) (where 1-N denotes the nitrogen of the tetrazole ring to which the substituent is attached) was synthesised by Molloy and co-workers [22], when the alkylation reaction of 1,2-bis[2-(tributylstannyl)tetrazol-5-yl]benzene was carried out with a 10-fold excess of 1,2-dibromoethane in methanol (see Fig. 3). 1,2-Bis[2-(tributylstannyl)tetrazol-5-yl]benzene is synthesised from the reaction of 1,2-dicyanobenzene with two equivalents of tributyltin azide [29]. The ethylene bridge in **4** is the shortest bridge yet incorporated into this family of heterocyclic macrocycles and is also the first structurally characterised example of 1-*N*,1-*N*′-bridging.

Ostrovskii and co-workers have expanded the family of macrocyclic ligands capable of binding metal ions by studying crown-like tetrazole-containing macrocyclic ethers [23]. They used the well-established synthetic route involving the alkylation of bifunctional substrates by electrophiles to achieve their crown-like products [25a]. They used 1,5-bis(tetrazol-5-yl)-3-oxapentane as the bifunctional substrate and 2,2′-dichloroethyl ether as the electrophile, as shown in Fig. 4.

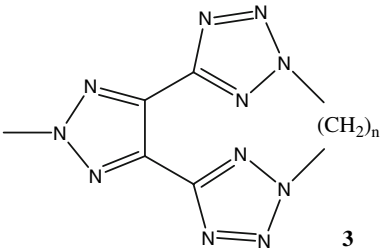

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Fig. 2 Macrocycle containing triazole subunit

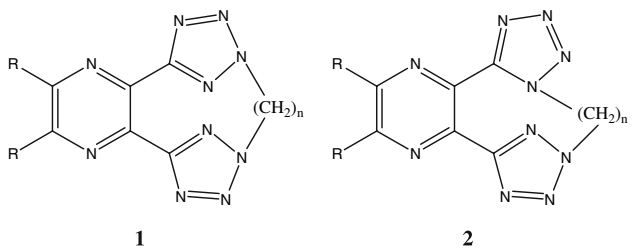

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Fig. 1 Symmetric and asymmetric macrocycles [15–17]

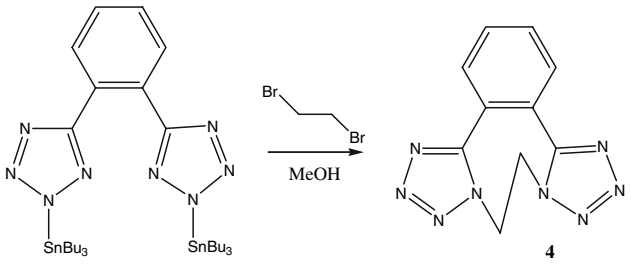

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Fig. 3 Synthesis of 1-*N*,1-*N*′-ethylene bridged macrocycle [22]

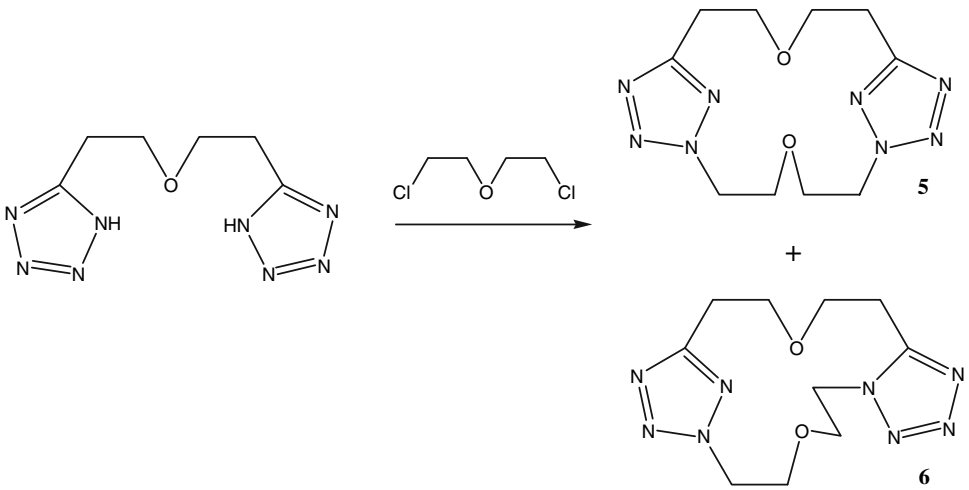


Fig. 4 Synthetic route to crown-like macrocycles [23]

From the crude product mixture, they were able to isolate two macrocycles in low yield, by column chromatography. These were the isomers 4,13-dioxa-1,7,8,9,17,18,19,20-octaazatricyclo[14.2.1.17,10]icosa-8,10(20),16(19),17-tetraene (**5**) and 4,14-dioxa-1,7,8,9,10,18,19,20-octaazatricyclo[15.2.1.07,10]icosa-8,10,17(20),18-tetraene (**6**). A further isomer, which was the 1-*N*,1-*N*′-macrocycle, was observed by ^{1}H NMR spectroscopy in the crude product but was not isolated due to its low yield.

Known macrocycles containing four tetrazole rings

Butler and co-workers have published several papers containing macrocycles with four tetrazole groups [19–21, 24]. The first tetratetrazole macrocycle (**7**) was reported in 1992 by Butler et al. [19] and was based on a hydrazone backbone which contained four tetrazole rings, as shown in Fig. 5.

This macrocycle contained a 1,1-ditetrazol-5-yl hydrazone unit with one planar sp^2 carbon between the tetrazole ring pairs. This contained the potential for variation in both cavity size and further macrocyclic development. There is considerable conformational flexibility in these macrocycles, due to rotation of the bonds from the tetrazole C-5 and N-2. A form with all the tetrazole azo –N=N– units facing in the one direction allows for the possibility of metal ion complexation in the macrocycle with two such metal coordination sites being generated. However, all complexes formed by the reaction of **7** with either $Ni(NCS)_2$ or $Zn(NCS)_2$ in methanol resulted in 1:1 complexes being formed, even though there is the possibility of two metal ions being held in the cavity. This is also the first example of metal ion complexation with macrocycles containing tetrazole rings.

In a subsequent paper, Butler and Ní Bhrádaigh published a route to the synthesis of macrocycles containing four tetrazole rings, namely the *ortho*-benzenotetratetrazolophanes [20]. This route involved the reaction of 1,2-bis(tetrazol-5-yl)benzene with 1,2-[bis(2-(halogenoalkyl)tetrazol-5-yl)]benzenes, formed by the reaction of 1,2-bis(tetrazol-5-yl)benzene with α,ω-diiodoalkanes, under basic conditions to give the macrocycles shown in Fig. 6. Two macrocyclic structures (**8** and **9**) were isolated, one containing all four tetrazole rings substituted at N-2, and the other containing three rings substituted at N-2 and the other one substituted at N-1. One of the macrocycles (**9**) reacted with $Zn(NCS)_2$ in methanol to give a 1:1 metal:-ligand complex, but no structural data was given for the metal complex.

The X-ray crystal structure of the macrocycle **8**, with m = 6, was subsequently published and revealed a lack of

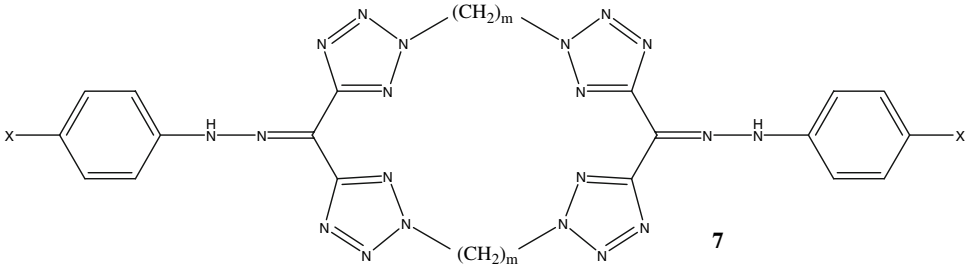


Fig. 5 First tetratetrazole macrocycle [19]

X = Cl, Me; m = 3, 4, 6

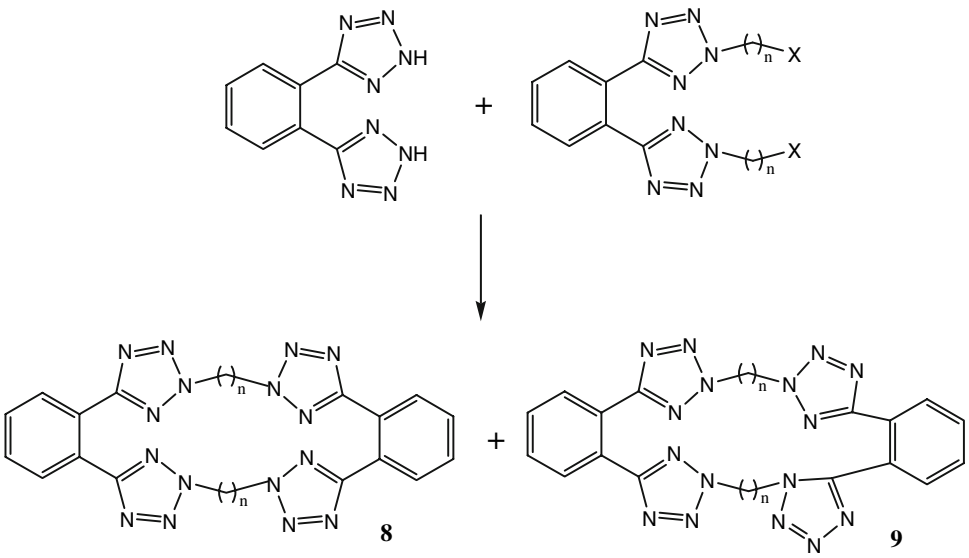


Fig. 6 Synthetic route to tetratetrazole macrocycle **8** and **9** [20]

a cavity between the four tetrazole rings [24]. This precluded any metal ion complexation within the macrocycle.

Butler and Fleming published the reactions of 1,3-bis (tetrazol-5-yl)benzene with α,ω-dibromoalkanes and α,ω-diiodoalkanes to give the corresponding 1,3-[bis(2-(halogenoalkyl)tetrazol-5-yl)]benzenes [21]. These compounds opened a route to the *meta*-benzenotetratetrazolophanes, by treatment with 1,3-bis(tetrazol-5-yl)benzene using potassium carbonate as base. The yields isolated for all these macrocycles were in the range 15–30% with extensive chromatography being required to separate the macrocycles from intractable polymeric material.

Molloy and co-workers have investigated the synthesis of tetrazoles from the cycloaddition reaction between nitriles and either organotin azides or organothallium azides [22, 29–34]. They have made a number of bis(tetrazole) compounds containing either an aromatic ring (**10**) or an alkyl chain (**11**) between the tetrazole rings, as shown in Fig. 7.

They have further introduced nitrile-terminated substituents, which can be further functionalised into additional tetazole groups (Scheme 1) [22]. They reacted **10** with an excess of 1-bromo-3-cyanopropane to give 1,3-bis[2-(3-cyanopropyl)tetrazol-5-yl]benzene (**12**), which was subsequently converted to the tetratetrazole compound (**13**) by the cycloaddition reaction with Bu_3SnN_3. This can be isolated in a non-metallated (N-H) form (**14**) by the reaction of **13** with HCl. Compound **13** can be further reacted with 1-bromo-3-cyanopropane to give **15**, which is the

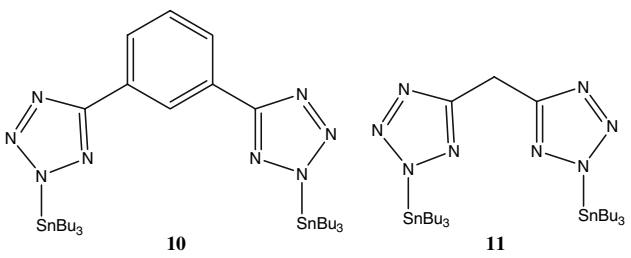
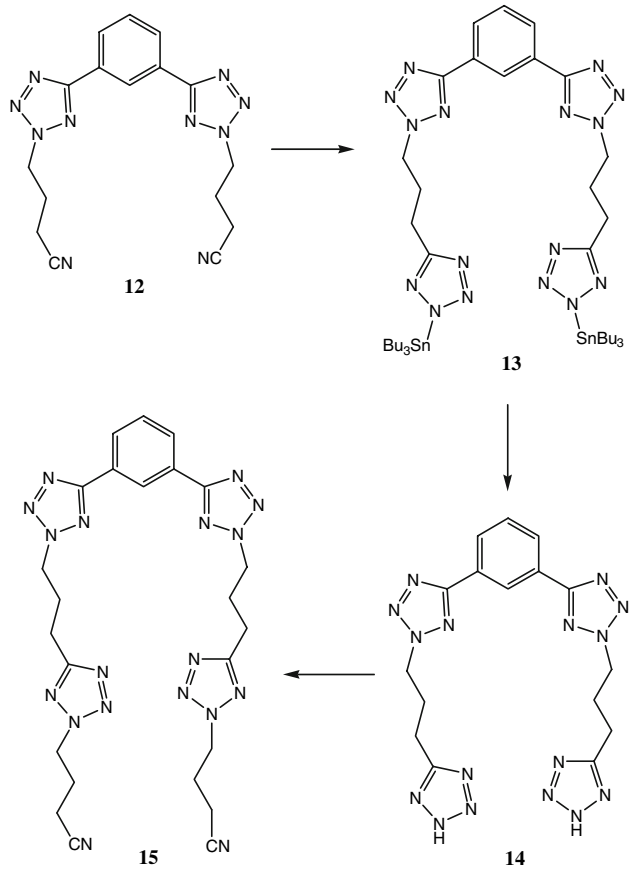


Fig. 7 Examples of some bis(tetrazole) molecules



Scheme 1 Synthetic route to tetrazole molecule **15**

tetratetrazole molecule with pendant alkylnitrile arms. However, no evidence for the formation of a tetratetrazole macrocycle was reported, although such a reaction should have been feasible from the reaction of 13 or 14 with an α,ω-dihaloalkane.

Our approach to macrocycles containing tetrazole groups

Our work focussed on developing the work of Butler to include alkyl chains of varying length (Y = $(CH_2)_n$, n = 0–6) as well as varying the positions of the tetrazole groups on the aromatic ring (X = 1,2-, 1,3- or 1,4-benzene) as shown in Fig. 8. Our strategy was to use both the approaches of Butler and Molloy, that is, the use of both 1,*n*-bis(tetrazol-5-yl)benzene and 1,*n*-bis[2-(tributylstannyl)tetrazol-5-yl]benzene, to obtain sufficient quantities of the 2-*N*, 2-*N*′-isomer of various bis(bromoalkyltetrazol-yl)benzenes with a view to subsequently generating derivatised tetra-tetrazole macrocycles.

When the reactions of 1,*n*-bis(tetrazol-5-yl)benzene (n = 2, 3, 4) with either 1,4-dibromobutane, 1,6-dibromohexane or 1,8-dibromooctane, in the presence of triethylamine in methanol with heating to reflux for 24 h were carried out, the recovered material, after work-up, contained mainly starting bis-tetrazoles, with approx. 30% of products obtained [35, 36]. Extensive separations by column chromatography were required to isolate the products. However, when similar reactions of 1,*n*-bis[2-(tributylstannyl)tetrazol-5-yl]benzene (n = 2, 3, 4) with either 1,4-dibromobutane, 1,6-dibromohexane or 1,8-dibromooctane were heated as neat suspensions, two products were obtained, in relatively high yields (60–90%), in all the reactions, as well as some recovered starting material [35, 36]. The two major products formed were the symmetrical 2-*N*,2-*N*′-bis(bromoalkyl)-derivative and the unsymmetrical 1-*N*,2-*N*′-bis(bromoalkyl)-derivative, with the formation of the symmetrical product being more favoured, suggesting that the organotin route was the better method for the synthesis of this particular type of material. It should be pointed out that neither the cyclophane product nor any products containing additions on one ring only were obtained.

The syntheses of tetratetrazole macrocycles, containing two bis-tetrazole units linked by a variety of alkyl chain lengths from four to eight carbons, were carried out and the X-ray crystal structures of three macrocyclic derivatives were reported [36]. The syntheses were carried out in a manner similar to that described [19–21], by reacting 1,*n*-[bis(2-(*m*-bromoalkyl)tetrazol-5-yl]benzene (*n* = 2, 3 or 4; *m* = 4, 6 or 8; alkyl = butyl, hexyl or octyl) with 1,*n*-bis(tetrazol-5-yl)benzene (*n* = 2, 3 or 4) in dimethylformamide, using K_2CO_3 as base. Figure 9 shows the X-ray crystal structure of two macrocycles. The macrocycle conformation is influenced by the length of the alkyl chain linker, the relative orientation of the tetrazole rings on the benzene ring, and by intermolecular interactions. In the macrocycles based on 1,2-bis(tetrazole)benzene, the adjacent tetrazole rings on the benzene ring are prevented from becoming co-planar on intramolecular (steric) grounds. This agrees with the structure published by Butler and

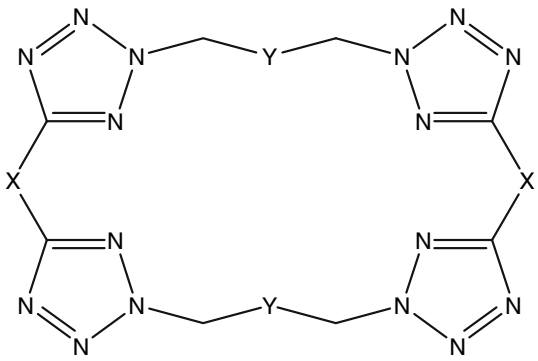
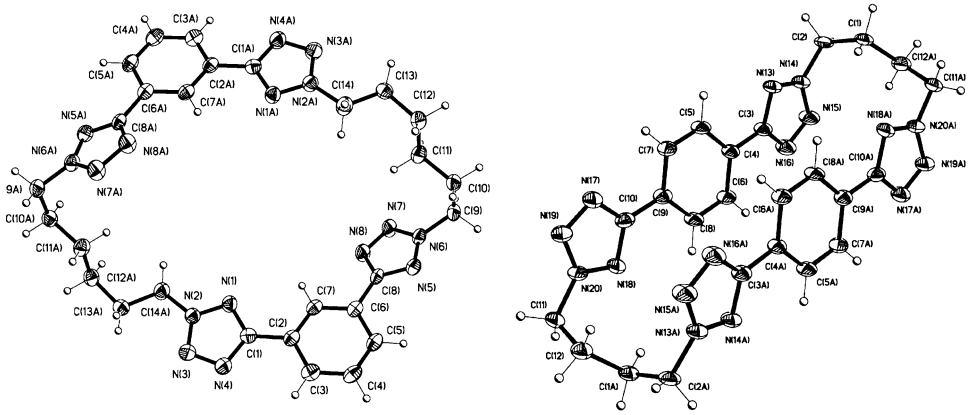


Fig. 8 General formula of tetratetrazole macrocycles



16 **17**

Fig. 9 X-ray structures of two macrocycles [36]

co-workers [24]. In the 1,3- and 1,4-bis(tetrazole)benzene derivatives (**16** and **17**), there is no such impediment, and a co-planar arrangement is observed where intra- and/or intermolecular stacking interactions exist. Deviations from co-planarity are associated with optimisation of intermolecular interactions between the tetrazole rings and adjacent alkyl chains. In the macrocycle based on 1,4-bis(tetrazole)benzene with four-carbon linkers (**17**), an intramolecular stacking interaction exists, which precludes the presence of any cavity. In the macrocycle based on 1,3-bis(tetrazole)benzene with six-carbon linkers (**16**), a cavity of 10.8 × 9.4 Å is observed for each molecule in the solid state. We tried some metal ion complexation reactions with **16** and found that, in the case of $Ni(NCS)_2$, $Cu(NCS)_2$ and $Zn(NCS)_2$, solid material precipitated from solution almost immediately. The IR spectra of these solids showed a shift in the NCS signal compared to the starting metal salts, indicating that complexation had occurred. However, when the solids were dissolved in various solvents in an effort to get crystals which were suitable for an X-ray crystallography study, the complexes broke up, in solution, to give the tetratetrazole macrocycle and the metal salt on their own. Apart from the early work of Butler and co-workers [19, 20], no other complexation studies have been undertaken. The X-ray crystallographic evidence of the majority of the tetratetrazole macrocycles we have described [36] would indicate that complexation will be difficult due to the lack of a cavity with the macrocyclic ring. We are currently investigating other 1,3-bis(tetrazole)benzene with various linkers to try and improve the binding properties of these macrocycles.

The reactions of 1,*n*-bis(tetrazol-5-yl)benzene (n = 2, 3, 4) or 1,*n*-bis[2-(tributylstannyl)tetrazol-5-yl]benzene (n = 2, 3, 4) with 1,2-dibromoethane were carried out in order to synthesise pendant alkyl halide derivatives of the parent bis-tetrazoles [37]. This led to the formation of several alkyl halide derivatives, substituted at either N1 and N2 on the tetrazole ring, as well as the surprising formation of several vinyl derivatives. The three major products formed were the symmetrical 2-*N*, 2-*N*′-bis(vinyl)-derivative, the unsymmetrical 1-*N*, 2-*N*′-bis(vinyl)-derivative and the 2-*N*, 2-*N*′-vinyl-bromoethyl-derivative (see Fig. 10). All products showed the distinct signal pattern for the presence of vinyl groups, while in the case of **20**, the presence of a bromoalkyl group was also observed. The X-ray crystal structure of **19** confirmed that the pendant vinyl groups were attached to the tetrazole ring at N-1 and N-2 positions (see Fig. 11). The formation of the vinyl group must be due to the presence of unreacted triethylamine abstracting HBr from the initially formed alkylbromo-compound in all cases, although no sign of this initial bis-alkylbromotetrazole derivative was observed by TLC. Further evidence

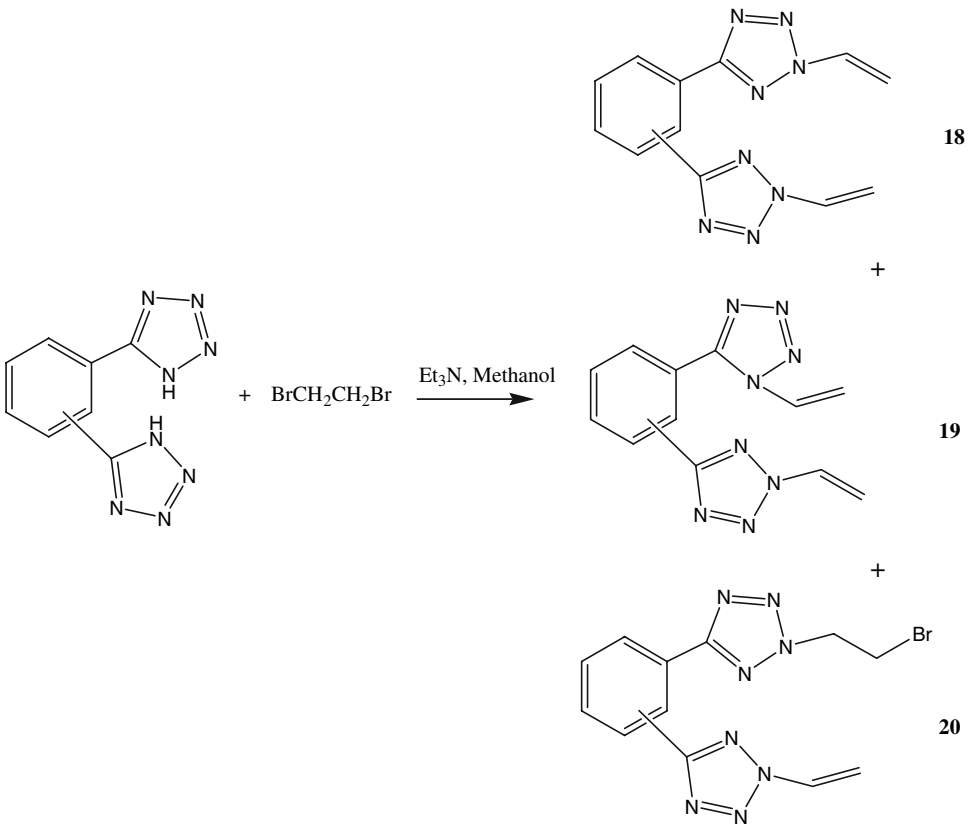


Fig. 10 Products from reaction involving dibromoethane

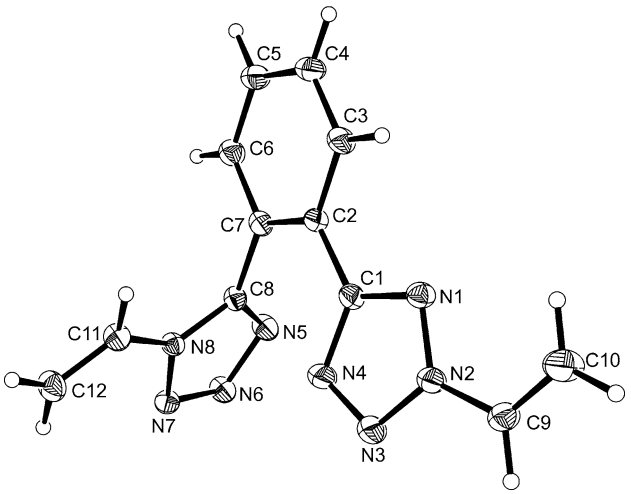


Fig. 11 X-ray crystal structure of 1,2-bis[(2-vinyl)tetrazol-5-yl)]benzene (1-*N*′,2-*N*) (**19**) [37]

to back up this assumption came from the macrocyclic reaction of 1,3-bis(tetrazol-5-yl)benzene (1-*N*,1-*N*′) with 1,3-bis[(2-bromoethyl)tetrazol-5-yl]benzene (2-*N*,2-*N*′) to give a tetratetrazole macrocycle (as shown in Fig. 12), but which instead gave a bis(tetrazole) compound with pendant vinyl arms [38].

In an effort to overcome the synthetic challenges which we have encountered to date (low yield, several isomers, little control of reaction pathway), we turned our attention to the formation of macrocycles containing four amide functionalities, so that each amide could be converted into a tetrazole group, resulting in a macrocycle with four tetrazole units. Jurczak and co-workers have recently reported the formation of macrocycles containing polylactam functionalities, formed from the reactions of dimethyl pyridine-2,6-dicarboxylate with an appropriate α,ω-diamine in methanol [39, 40]. Furthermore, Duncia and co-workers reported, in 1991, a one-step reaction for the conversion of an amide to a tetrazole [41]. Focusing our attention on the work of Jurczak and Duncia on poly-lactam containing macrocycles and the conversion of amides into tetrazoles prompted the development of an alternate route for synthesising the tetratetrazole macrocycles.

To develop poly-lactam macrocycles, we chose phthaloyl dichloride or isophthaloyl dichloride and 1,8-diaminooctane as starting materials, because of their commercial availability. The poly-lactam macrocycle (**21** and **22**), as shown in Fig. 13, was synthesised using a similar cyclisation reaction to that described by Jurczak et al. [39, 40]. While the macrocycles were synthesized [42], they were in

Fig. 12 Attempted macrocycle formation

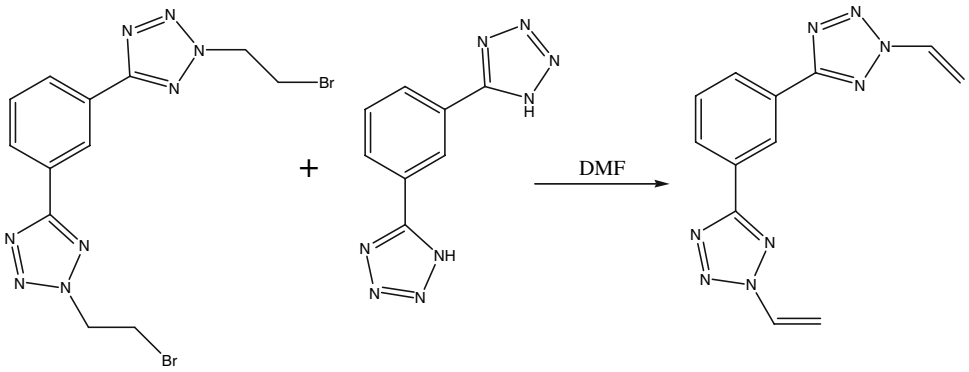
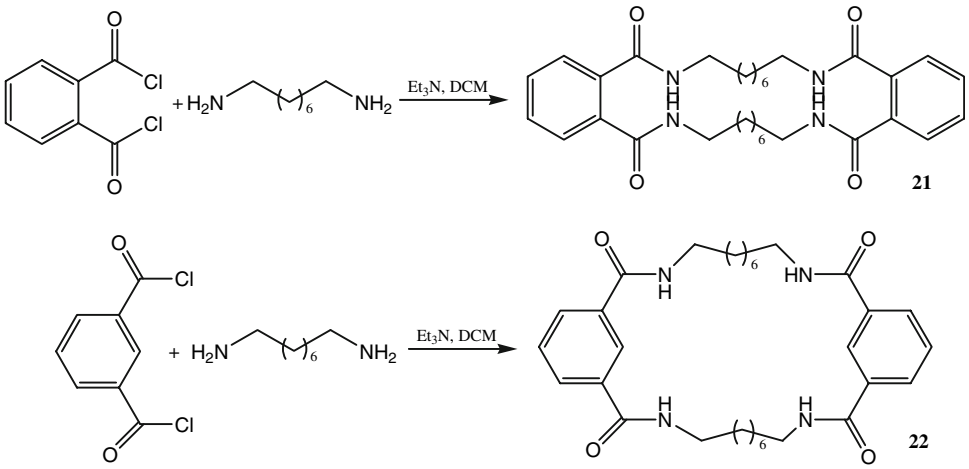


Fig. 13 Synthesis of poly-lactam macrocycles



low yield (14%) with starting material (35%) and polymeric material (40%) accounting for the majority of the reaction product. It necessitated extensive column chromatography to isolate the low yields of the desired products from the complicated mixtures. The products were characterised by IR, ^{1}H and ^{13}C NMR spectroscopy. The disappearance of the IR bands due to υ(COCl) at $\sim$1770 cm^{-1} and the appearance of a new band at $\sim$1635 cm^{-1}, due to an aromatic secondary amine, was used to monitor the reaction. The ^{13}C NMR spectrum showed four signals for the eight carbon linker between the amide pairs, which suggested that the compound was symmetric.

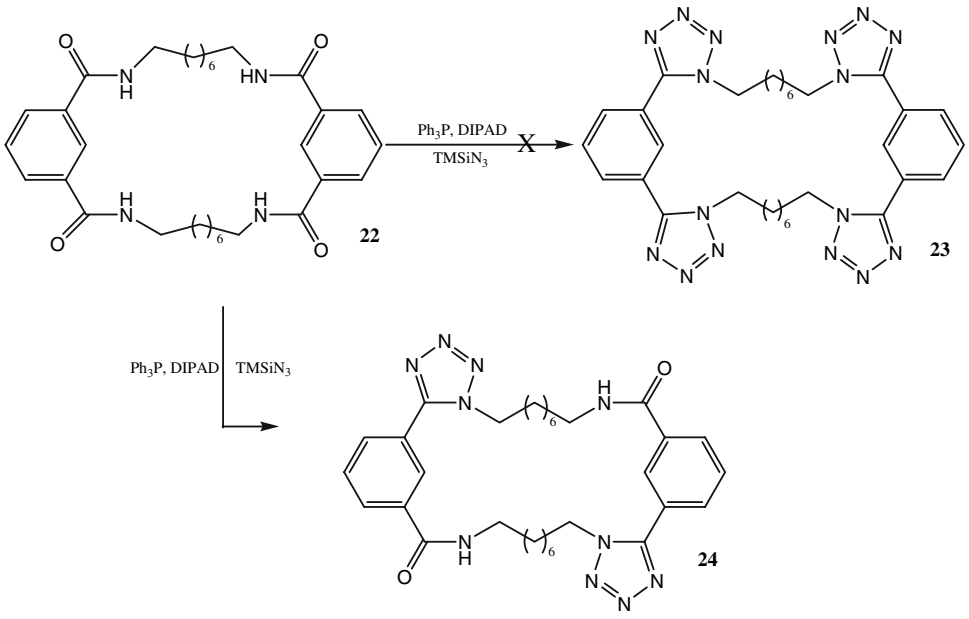
As mentioned above, Dunica and co-workers introduced a mild one-step method for the conversion of amides to tetrazoles [41]. He employed triphenylphosphine and diethylazodicarboxylate (DEAD) to activate the amide towards reaction with trimethylsilyl azide that yielded tetrazoles. We repeated the reaction using compound **21** and diisopropylazodicarboxylate (DIAD) instead of DEAD, but no reaction occurred despite increasing reaction time and the number of equivalents of reagents. We believe that the failure of the reaction may have been due to the presence of the sterically hindered amide group.

On repeating the reaction with **22**, instead of **21**, we obtained a material, in 5% yield, which contained tetrazole functional groups. The majority of the reaction product ($\sim$85%) contained a polymeric material, insoluble in most common solvents, which we are still trying to analyse. However, we did not obtain the tetratetrazole system **23**, as shown in Scheme 2, but instead obtained a product which contained only two tetrazole rings (**24**) [43]. The fact that the macrocycle did not contain four tetrazole groups could have been due to some steric effects. Compound **24** may have three isomeric forms, only one of which is shown in Scheme 2 and all of which are indistinguishable by either ^{1}H or ^{13}C NMR spectroscopy. The three isomers could have the two tetrazole groups on opposite sides of the ring (that is, attached to a different alkyl chain), on the same side of the ring (that is, attached to the same alkyl chain) or attached to the same benzene ring. Only an X-ray crystal structure can tell exactly what isomer is present, and despite several efforts, no suitable crystals have been grown so far. The low yield is not surprising, since Dunica and co-workers [41] have reported that as steric hindrance around the carboxamide increases, the yields of the tetrazole product steadily decrease.

Conclusions and future work

In the solid state, the conformation of the tetratetrazole macrocycle is influenced by the orientation of the tetrazole rings on the benzene ring, by the length of the alkyl-chain linkers and by intermolecular interactions. In the macrocycles based on 1,2-bis(tetrazole)benzene, the adjacent tetrazole substituents on the benzene ring are prevented from becoming co-planar on steric grounds. In the macrocycles based on 1,3- and 1,4-bis(tetrazole)benzene, there is no intramolecular impediment to co-planarity of the tetrazole rings with the benzene ring, and co-planarity is observed where stacking interactions are present.

Our current focus is on the synthesis of a tetratetrazole macrocycle from a tetra-lactam macrocycle. But this is resulting in low yielding reactions. The latter reaction for the conversion of the amide group into a



Scheme 2 Proposed synthetic route to tetratetrazole molecules

tetrazole group may be increased by using trifluoromethanesulfonic anhydride and sodium azide, as reported by Thomas [44].

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References

1. Vigato, P.A., Tamburini, S.: The challenge of cyclic and acyclic schiff bases and related derivatives. Coord. Chem. Rev. **248**, 1717–2128 (2004)
2. Fenton, D.E., Vigato, P.A.: Macrocyclic schiff base complexes of lanthanides and actinides. Chem. Soc. Rev. **17**, 69–90 (1988)
3. Vigato, P.A., Tamburini, S., Fenton, D.E.: The activation of small molecules by dinuclear complexes of copper and other metals. Coord. Chem. Rev. **106**, 25–170 (1990)
4. Menif, R., Martell, A.E., Squattrito, P.J., Clearfield, A.: New hexaaza macrocyclic binucleating ligands. Oxygen insertion with a dicopper(I) schiff base macrocyclic complex. Inorg. Chem. **29**, 4723–4729 (1990)
5. Collinson, S.R., Fenton, D.E.: Metal complexes of bibracchial schiff base macrocycles. Coord. Chem. Rev. **148**, 19–40 (1996)
6. Ōkawa, H., Furutachi, H., Fenton, D.E.: Heterodinuclear metal complexes of phenol-based compartmental macrocycles. Coord. Chem. Rev. **174**, 51–75 (1998)
7. Amendola, V., Fabbrizzi, L., Mangano, C., Pallavicini, P., Poggi, A., Taglietti, A.: Anion recognition by dimetallic cryptates. Coord. Chem. Rev. **219–221**, 821–837 (2001)
8. Brooker, S.: Complexes of thiophenolate-containing schiff-base macrocycles and their amine analogues. Coord. Chem. Rev. **222**, 33–56 (2001)
9. See, for example, Sun, R., Wang, S., Xing, H., Bai, J., Li, Y., Pan, Y., You, X.: Unprecedented $4^2 6^4$ topological 2-D rare-earth coordination polymers from a flexible tripodal acid with additional amide groups. Inorg. Chem. **46**, 8451–8453 (2007) and references therein
10. See, for example, Al-Rasbi, N.K., Adams, H., Harding, L.P., Ward, M.D.: Coordination behaviour of bis-terdentate N-donor ligands: double- and single-stranded helicates, mesocates and cyclic oligomers. Eur. J. Inorg. Chem. 4770–4780 (2007) and references therein
11. See, for example, (a) Huang, X.C., Lin, Y.Y., Zhang, J.P., Chen, X.M.: Ligand-directed strategy for zeolite-type metal-organic frameworks: zinc(II) imidazolates with unusual zeolitic topologies. Angew. Chem. Int. Ed. **45**, 1557–1559 (2006); (b) Sun, J., Weng, L., Zhou, Y., Chen, J., Chen, Z., Liu, Z., Zhao, D.: QMOF-1 and QMOF-2: three-dimensional metal-organic open frameworks with a quartzlike topology. Angew. Chem. Int. Ed. **41**, 4471–4473 (2002); (c) Batten, S.R., Hoskins, B.F., Moubaraki, B., Murray, K.S., Robson, R.: Crystal structures and magnetic properties of the interpenetrating rutile-related compounds $M(tcm)_2$ [M = octahedral, divalent metal: $tcm^- = $ tricyanomethanide, $C(CN)_3^-$] and the sheet structures of $[M(tcm)_2(EtOH)_2]$ (M = Co or Ni). J. Chem. Soc. Dalton Trans. 2977–2986 (1999)
12. Hammes, B.S., Ramos-Maldonado, D., Yap, G.P.A., Rheingold, A.L., Young, V.G. Jr., Borovik, A.S.: The use of C3-symmetric tripodal ligands in crystal engineering. Coord. Chem. Rev. **174**, 241–253 (1998)
13. See, for example, (a) Hannon, M.J., Childs, L.J.: Helices and helicates: beautiful supramolecular motifs with emerging application. Supramol. Chem. **16**, 7–22 (2004); (b) Albrecht, M.: "Let's twist again"—double-stranded, triple-stranded and circular helicates. Chem. Rev. **101**, 3457–3497 (2001); (c) Harding, L.P., Jeffrey, J.C., Riis-Johannessen, T., Rice, C.R., Zeng, Z.: Anion control of ligand self-recognition in a triple helical way. Chem. Commun. 654–655 (2004); (d) Harding, L.P., Jeffrey, J.C., Riis-Johannessen, T., Rice, C.R., Zeng, Z.: Anion control of the formation of geometric isomers in a triple helical way. Dalton Trans. 2396–2397 (2004); (e) Jeffrey, J.C., Riis-Johannessen, T., Anderson, C.J., Adams, C.J., Robinson, A., Argent, S.P., Ward, M.D., Rice, C.R.: Localization and delocalization in a mixed-valence dicopper helicate. Inorg. Chem. **46**, 2417–2426 (2007); (f) Nitschke, J.R.: Construction, substitution, and sorting of metallo-organic structures via subcomponent self-assembly. Acc. Chem. Res. **40**, 103–112 (2007)
14. See, for example, (a) Aly, A.A.M., Vatsadze, S.Z., Chernikov, A.V., Walfort, B., Rueffer, T., Lang, H.: A binuclear silver(I) perchlorate macrocycle based on 2,5-bis[(*E*)-(3-pyridyl)methylene]cyclopentanone: crystal structure and solution behaviour. Polyhedron **26**, 3925–3929 (2007); (b) Spitler, E.L., McClintock, S.P., Haley, M.M.: Dynamic proton-induced emission switching in donor-functionalized dehydrobenzopyrid[15]annulenes. J. Org. Chem. **72**, 6692–6699 (2007); (c) Katayev, E.A., Ustynuk, Y.A., Lynch, V.M., Sessler, J.L.: Mono-palladium(II) complexes of diamidopyridine-dipyrromethane hybrid macrocycles. Chem. Commun. 4682–4684 (2006); (d) Li, F., Delgado, R., Drew, M.G.B., Felix, V.: Dioxadiaza- and trioxadiaza-macrocycles containing one benzofuran unit selective for cadnium. Dalton Trans. 5396–5403 (2006); (e) Vasilescu, I.M., Bray, D.J., Clegg, J.K., Lindoy, L.F., Meehan, G.V., Wei, G.: Rational ligand design for metal ion recognition. Synthesis of a N-benzylated N_2S_3-donor macrocycle for enhanced silver(I) discrimination. Dalton Trans. 5115–5117 (2006); (f) Habermehl, N.C., Mohr, F., Eisler, D.J., Jennings, M.C., Puddephatt, R.J.: Organogold(I) macrocycles and [2]catenanes containing pyridyl and bipyridyl substituents—organometallic catenanes as ligands. Can. J. Chem. **84**, 111–123 (2006); (g) Koschabek, R., Gleiter, R., Rominger, F.: Synthesis and properties of cryptands with a thioether bridge and π-donors—silver(I) and copper(I)-complexes. Eur. J. Org. Chem. 609–620 (2006)
15. Ried, W., Tsiotis, G.: Synthesis of new cyclophanes from pyrazinedicarbonitriles. Chem. Ztg. **112**, 385–386 (1988)
16. Ried, W., Aboul-Fetouh, S.: Synthesis of substituted heterocyclic cyclophanes. Tetrahedron. **44**, 3399–3404 (1988)
17. Ried, W., Lee, C., Bats, J.W.: New heterocyclic phanes from 2,3-bis(5-tetrazolyl)pyrazines and α,ω-dibromoalkanes. Liebigs Ann. Chem. 497–500 (1989)
18. Ried, W., Laoutidis, J.: Synthesis of new, heterocyclic phanes from 1,2,3-triazolo-4,5-dicarbonitrile. Chem. Ztg. **113**, 384–385 (1989)
19. Butler, R.N., Quinn, F., Welke, B.: Tetratetrazole macrocycles. J. Chem. Soc. Chem. Commun. 1481–1482 (1992)
20. Butler, R.N., Ní Bhrádaigh, E.: Tetratetrazolophanes. J. Chem. Res. (S). 148–149 (1994)
21. Butler, R.N., Fleming, A.F.M.: meta-Benzenotetratetrazolophanes. J. Heterocycl. Chem. **34**, 691–693 (1997)
22. Bethel, P.A., Hill, M.S., Mahon, M.F., Molloy, K.C.: Reactions of organotin tetrazoles: synthesis of functionalised poly-tetrazoles. J. Chem. Soc. Perkin Trans. **1**, 3507–3514 (1999)
23. Zubarev, V.Y., Trifonov, R.E., Filichev, V.V., Ostrovskii, V.A., Abell, A.D., Edmonds, M.K.: Synthesis, X-ray and conformational studies of novel tetrazole-containing macrocycles: 4,13-

dioxa-1,7,8,9,17,18,19,20-octaazatricyclo[14.2.1.17,10]icosa-8,10(20),16(19),17-tetraene and 4,14-dioxa-1,7,8,9,10,18,19,20-octaazatricyclo[15.2.1.07,10]icosa-8,10,17(20),18-tetraene. J. Chem. Soc. Perkin Trans. **2**, 417–421 (2001)

24. Butler, R.N., McGinley, J.M.G., Mahon, M.F., Molloy, K.C., Ní Bhrádaigh, E.P.: Diorthobenzenotetra(5′,2′-tetrazolo)[5′-(2)-(2′-(6)]cyclophane. Acta Cryst. **E57**, o195–o197 (2001)
25. See, for example, (a) Butler, R.N.: In: Katritzky, A.R., Rees, C.W., Scriven, E.F.V. (eds) Comprehensive Heterocyclic Chemistry, vol 4, Permagon, Oxford (1996); (b) Herr, R.J.: 5-Substituted-1*H*-tetrazoles as carboxylic acid isosteres: medicinal chemistry and synthetic methods. Bioorg. Med. Chem. **10**, 3379–3393 (2002); (c) Ostrovskii, V.A., Pevzner, M.S., Kofman, T.P., Shcherbinin, M.B., Tselinskii, I.V.: Energetic 1,2,4-triazoles and tetrazoles synthesis, structure and properties. Targets Heterocycl Syst. **3**, 467–526 (1999)
26. Zych, A.J., Herr, R.J.: Tetrazoles as carboxylic acid bioisosteres in drug discovery. PharmaChem. **6**, 21–24 (2007)
27. IUPAC, Commission on Nomenclature of Organic Chemistry: A Guide to IUPAC Nomenclature of Organic Compounds (Recommendations 1993), Blackwell Scientific (1993)
28. See, for example, (a) Kaden, T.A.: Dinuclear metal complexes of bis-macrocycles. Coord. Chem. Rev. **190–192**, 371–389 (1999); (b) Tarrago, T., Marzin, C., Najimi, O., Pellegrin, V.: New tetraheterocyclic macrocycles containing triazole, pyrazole, pyridine, and/or furan subunits. Synthesis and cation binding properties. J. Org. Chem. **55**, 420–425 (1990); (c) Newkome, G.R., Sauer, J.D., Roper, J.M., Hager, D.C.: Construction of synthetic macrocyclic compounds possessing subheterocyclic rings, specifically pyridine, furan and thiophene. Chem. Rev. **77**, 513–597 (1977)
29. Hill. M., Mahon, M.F., McGinley, J., Molloy, K.C.: New supramolecular architectures based on polyfunctional organotin tetrazoles: synthesis and characterisation of phenylene-bridged bis(organotin tetrazoles). J. Chem. Soc. Dalton Trans. 835–845 (1996)
30. Goodger, A., Hill. M., Mahon, M.F., McGinley, J., Molloy, K.C.: Organotin-functionalised poly(tetrazoles), including the supramolecular structure of 1,6-(2-$Bu_3SnN_4C)_2(CH_2)_6$. J. Chem. Soc. Dalton Trans. 847–852 (1996)
31. Hill. M., Mahon, M.F., Molloy, K.C.: Tris(triorganostannyltetrazoles): synthesis and supramolecular structures. J. Chem. Soc. Dalton Trans. 1875–1865 (1996)
32. Bhandari, S., Mahon, M.F., Molloy, K.C.: Synthesis and supramolecular architectures of tetrakis(triorganostannyltetrazoles), including the crystal structure of hydrated 1,2,4,5- tetrakis(triethylstannyltetrazolyl)benzene. J. Chem. Soc. Dalton Trans. 1951–1956 (1999)
33. Bhandari, S., Frost, C.G., Hague, C.E., Mahon, M.F., Molloy, K.C.: Synthesis of functionalised (triorganostannyl)tetrazoles: supramolecular structures of n-[2- (triorganostannyl)tetrazol-5-yl]pyridine (n = 2, 3 or 4). Dalton Trans. 663–669 (2000)
34. Bhandari, S., Mahon, M.F., Molloy, K.C., Palmer, J.S., Sayers, S.F.: Thallium(I)- and organothallium(III)-substituted mono-, bis- and tris-tetrazoles: synthesis and supramolecular structures. Dalton Trans. 1053–1060 (2000)
35. Bond, A.D., Fleming, A., Kelleher, F., McGinley J., Prajapati, V.: Reactions of 1,4-bis(tetrazole)benzenes: formation of long chain alkyl halides. Tetrahedron **62**, 9577–9581 (2006)
36. Bond, A.D., Fleming, A., Kelleher, F., McGinley, J., Prajapati, V., Skovsgaard, S.: Synthesis and characterisation of tetra-tetrazole macrocycles. Tetrahedron **63**, 6835–6842 (2006)
37. Fleming, A., Kelleher, F., Mahon, M.F., McGinley, J., Prajapati, V.: Reactions of bis(tetrazole)phenylenes. Surprising formation of vinyl compounds from alkyl halides. Tetrahedron **61**, 7002–7011 (2005)
38. Prajapati, V.: PhD thesis. Higher Education and Training Awards Council, Ireland (2007)
39. Szumna, A., Jurczak, J.: A new macrocyclic polylactam-type neutral receptor for anions—structural aspects of anion recognition. Eur. J. org. Chem. 4031–4039 (2001)
40. Chmielewski, M., Jurczak, J.: Size complementarity in anion recognition by neutral macrocyclic tetraamides. Tetrahedron Lett. **45**, 6007–6010 (2004)
41. Duncia, J.V., Pierce, M.E., Santella, J.B.: Three synthetic routes to a sterically hindered tetrazole. A new one-step conversion of an amide into a tetrazole. J. Org. Chem. **56**, 2395–2400 (1991)
42. **21**: White solid. Analysis: Found: C, 70.94; H, 8.77; N, 9.58. Calc. For $C_{32}H_{44}N_4O_4$: C, 70.91; H, 8.84; N, 9.45; Yield: 92 mg, 14.0 %, 0.17 mmol; R_f 0.15 (98: 2 DCM: MeOH); M.p. 218–220 °C; ν_{max} (KBr) 3265, 3073, 2925, 2858, 1631, 1577, 1553, 1460, 1397, 1364, 1310, 1264, 668 cm^{-1}; δ_H: 1.35 (m, 16 H, CH_2), 1.56 (m, 8 H, CH_2), 3.46 (m, 8 H, $C\underline{H}_2NH$), 7.11 (br, 4 H, NH), 7.44 (m, 4 H, Ar-H), 7.65 (m, 4 H, Ar-H); δ_C: 22.8, 25.3, 28.0, 38.6, 128.9, 130.1, 134.2, 169.4; HRMS (EI) Calc. 549.3441, Found 549.3461; **22**: White solid. Analysis: Found: C, 70.85; H, 8.66; N, 9.38. Calc. For $C_{32}H_{44}N_4O_4$: C, 70.91; H, 8.84; N, 9.45; Yield: 71 mg, 10.7 %, 0.13 mmol; R_f 0.12 (98: 2 DCM: MeOH); M.p. 244–250 °C; ν_{max} (KBr) 3308, 3018, 2932, 2852, 1634, 1553, 1541, 1462, 1397, 1364, 1307, 1215, 754, 668 cm^{-1}; δ_H: 1.27 (m, 16 H, CH_2), 1.40 (m, 8 H, CH_2), 3.32 (m, 8 H, $C\underline{H}_2NH$), 7.45 (m, 2 H, Ar-H), 7.83 (br, 4 H, NH), 8.00 (m, 4 H, Ar-H), 8.84 (s, 2 H, Ar-H); δ_C: 26.8, 28.8, 29.0, 40.2, 127.5, 129.0, 130.5, 134.3, 166.9; HRMS (EI) Calc. 549.3441, Found 549.3428
43. **24**: White solid. Analysis: Found: C, 64.02; H, 7.17; N, 23.35. Calc. For $C_{32}H_{42}N_{10}O_2$: C, 64.19; H, 7.07; N, 23.39; Yield: 10 mg, 9.2%, 0.02 mmol; R_f 0.43 (5: 95 hexane : ethyl acetate); M.p. 192–194 °C; ν_{max} (KBr) 3261, 3081, 2929, 2860, 1634, 1550, 1466, 1368, 1315, 1115, 902, 820, 717 cm^{-1}; δ_H: 1.27 (m, 4 H, CH_2), 1.59 (m, 4 H, CH_2), 1.84 (m, 4 H, CH_2), 1.96 (m, 4 H, CH_2), 3.57 (m, 4 H, $C\underline{H}_2NH$), 4.18 (m, 4 H, $NC\underline{H}_2$), 7.46 (m, 4 H, Ar-H), 7.56 (br, 4 H, $\underline{NH}$), 7.57 (s, 2 H, Ar-H), 7.68 (m, 4 H, Ar-H), 7.94 (m, 4 H, Ar-H); δ_C: 24.0, 24.9, 26.3, 27.6, 27.7, 28.6, 40.0, 47.9, 122.7, 125.4, 127.5, 130.3, 131.1, 131.9, 136.7, 153.2, 167.6; HRMS (EI) Calc. 593.3074, Found 593.3080
44. Thomas, E.W.: The conversion of secondary amides to tetrazoles with trifluoromethanesulfonic anhydride and sodium azide. Synthesis 767–768 (1993)