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Synthesis of Designed Hetero-Polytopic Cryptands Through Schiff Base Condensation

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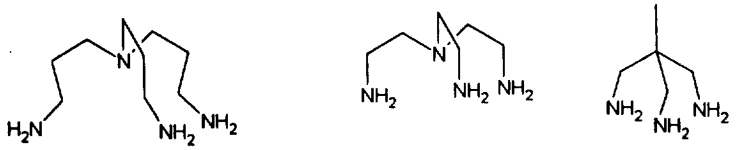
Abstract : Low-temperature synthesis of a number of hetero-polytopic cryptands have been achieved in good yields without employing any templating metal ion. The cryptands are designed to hold more than one metal ion in its cavity.

We are involved in the synthesis of macrobicyclic cryptands to design smart molecules.[1] We are also interested to use the cryptands as ligands to enforce unusual coordination geometry onto transition metal ions. Cryptates are formed when a metal ion enters the cavity forming inclusion complexes. The number of metal ions that can enter the cavity is dependent not only on the size of the cavity itself but also on the number of donor atoms present in the ligand superstructure. Nature of the donor atoms impart specificity to metal binding abilities of the cavity. We are interested in having cryptands with cavities of different topology and rigidity. Some of these cryptands have been shown to be useful as potential molecular photonic devices,[2] cryptand based amphiphiles,[3] homogeneous catalysis[4] besides use as ligands for transition metal ions.[5] In the present paper, we have described a number of new cryptands (tricyclic as well as bicyclic) with different cavity shapes and sizes.

RESULTS AND DISCUSSION

The synthetic procedure adopted for the cryptands and their chemical structures are illustrated in Schemes 1 and 2. While the cryptands **7** and **8** are reported recently,[6] all other cryptands are new. Our earlier method was to use an alkali metal ion as the template at ~ 40 °C for both [1+1] and [2 + 3] Schiff base condensation reactions. Subsequently, we[5] and others[7] have found that if the reactants are allowed to react at low temperature (~5 °C), no templating metal ion is necessary apparently because of decreased degrees of movement of the reacting arms. When the trialdehyde **1** is allowed to react with tris(2-aminoethyl)amine (tren), surprisingly, it undergoes [2+2] Schiff base condensation unlike the expected [1+1] condensation reaction. This result tempted us to synthesize some more cryptands to investigate the cause of such a result. Initially, we assumed that either (i) there was a size mismatch between **1** and tren or (ii) the trialdehyde prefered a



4 5 6

Figure 1

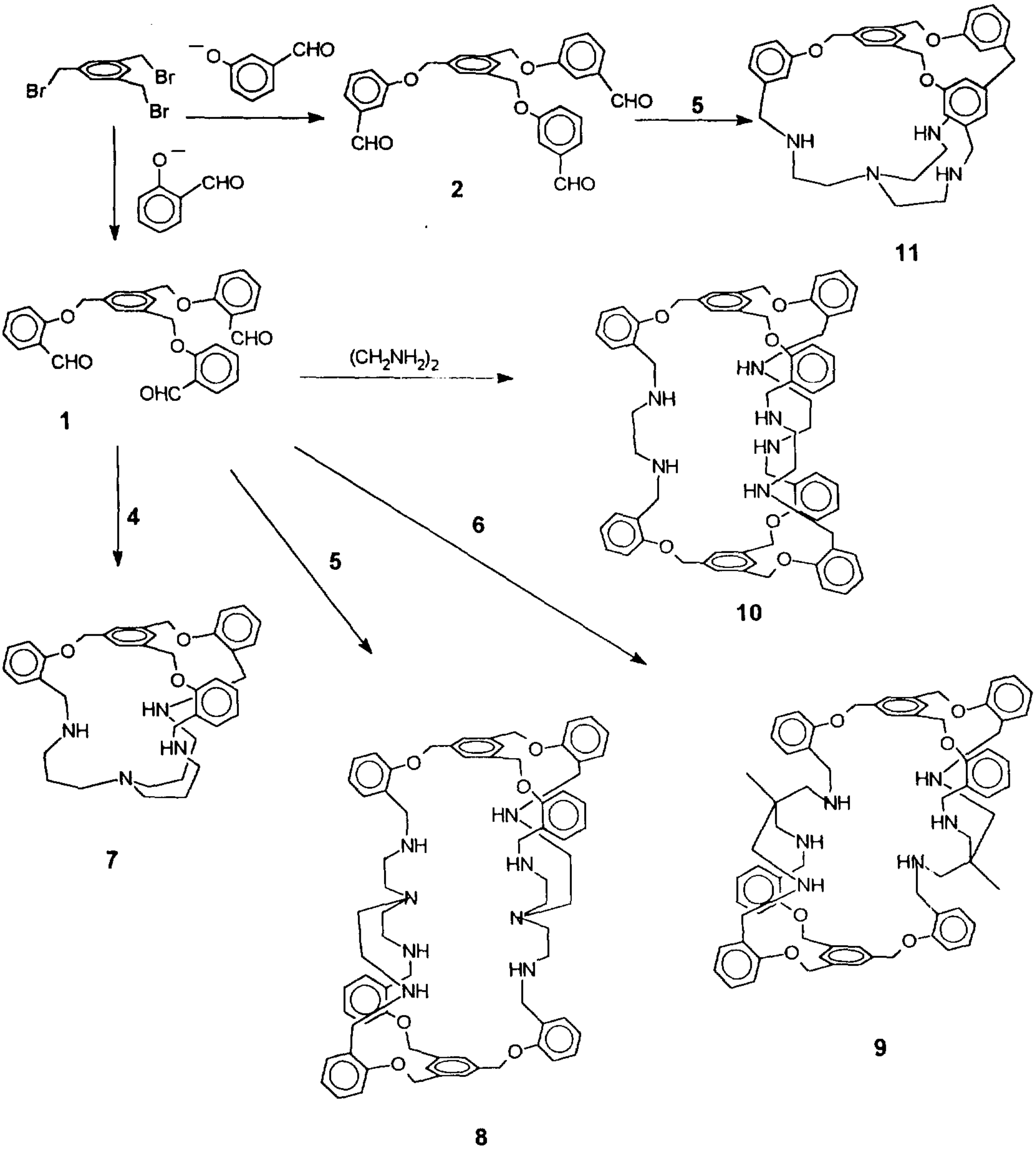
conformation where one arm moved away from the other two. The logic behind (i) and (ii) support the assumption that after two arms of both of the reactants are condensed they dimerise to the tricyclic product. It is now well documented[7,8] that a trialdehyde undergoes [2+3] condensation with a linear diamine. Thus, if **1** has a conformation as mentioned in (ii), then it should favour a [4+6] condensation product with ethylenediamine. However, the reaction affords solely the [2+3] condensation product. To test (i), we fixed the trialdehyde and varied the chain lengths of the amine for the cyclization reactions. When a bigger amine, tris(3-aminopropyl)amine (trpn) is allowed to react with **1**, only the bicyclic product **7** is isolated. But the use of 1,1,1tris(aminomethyl)ethane leads to the tricyclic product **9**. With the trialdehyde **3**, whose size is expected to be smaller than **1** as it can squeeze in, the amines **4** and **5** undergo [1+1] condensation exclusively. The above findings suggest that when there is a size mismatch between two tripods they condense in a [2+2] manner preferably. Finally, we decided to expand the size of trialdehyde compared to **1** and prepared **2**. The new trialdehyde on reaction with tren, affords only the [1+1] condensation product.

CONCLUSION

It is, therefore, concluded that only size mismatch is not the deciding factor and there must be some other factor(s) controlling the reactivity patterns of **1** like rigidity, steric repulsion etc. In case of tripodal amines with smaller than a particular size (i.e. **5**), this behavior of tricyclic cryptand formation is observed. Hence, a rigid tripodal unit having functional groups at close proximity to each other and another tripod of comparatively smaller size may lead to [2+2] condensation.

EXPERIMENTAL

Proton and carbon-13 NMR spectra were obtained at 80 MHz and 20.1 MHz respectively on a Bruker WP-80 FT instrument. The FAB mass spectra were recorded on a JEOL SX 102/DA-6000 mass spectrometer/data system using Xenon as the FAB gas. Reagent grade chemicals were used as received while all the solvents were purified prior to use following standard procedures. 1,3,5-trisbromomethyl benzene,[9] 1,3,5-tris [3-(bromomethyl)phenyl]benzene[10] were synthesized following published procedures.



Cyclisation reactions are followed by *insitu* $NaBH_4$ reduction

Scheme 1

General synthesis of the tripodal trialdehydes, **1-3**

A general method of synthesis was adopted for all the tripodal trialdehydes. Synthesis of the trialdehyde **1** was reported earlier[6] by us. Compound **2** was synthesized from 1,3,5-tris(bromomethyl)benzene and sodium salt of *m*-hydroxybenzaldehyde while compound **3** was obtained from 1,3,5-tris[3-(bromomethyl)phenyl] benzene and sodium salt of *o*-hydroxybenzaldehyde following our previous method[6]. As an example, synthesis of **2** is described here. Sodium salt of *m*-hydroxybenzaldehyde was prepared by adding NaOH (3 mmol) to a solution of *m*-hydroxybenzaldehyde (3 mmol) in 50 mL of ethanol and stirring at RT for 1/2 h. To this solution was added 1,3,5-tris(bromomethyl)benzene (1 mmol) and refluxed for 3 h. The reaction mixture was cooled to RT and the white solid collected by filtration, washed with cold ethanol and finally air-dried.

Trialdehyde **1**. ^{1}H-NMR δ : 5.3 (s, 6H), 7.5 (m, 15H), 10.7 (s, 3H). Yield 85%, mp 135-137 °C. Anal. Calcd. for $C_{30}H_{24}O_6$: C, 74.98; H, 5.03. Found : C, 74.83; H, 5.14.

Trialdehyde **2**. ^{1}H-NMR δ: 5.3 (s, 6H), 7.5 (m, 15H), 10.0 (s, 3H). Yield 73%, mp 114 °C. Anal. Calcd. for $C_{30}H_{24}O_6$: C, 74.98; H, 5.03. Found : C, 75.14; H, 4.96.

Trialdehyde **3**. ^{1}H-NMR δ : 5.3 (s, 6H), 7.5 (m, 15H), 10.7 (s, 15H). Yield 75%, mp 170 °C. Anal. Calcd. for $C_{48}H_{36}O_6$: C, 81.33; H, 5.12. Found : C, 81.24; H, 5.19.

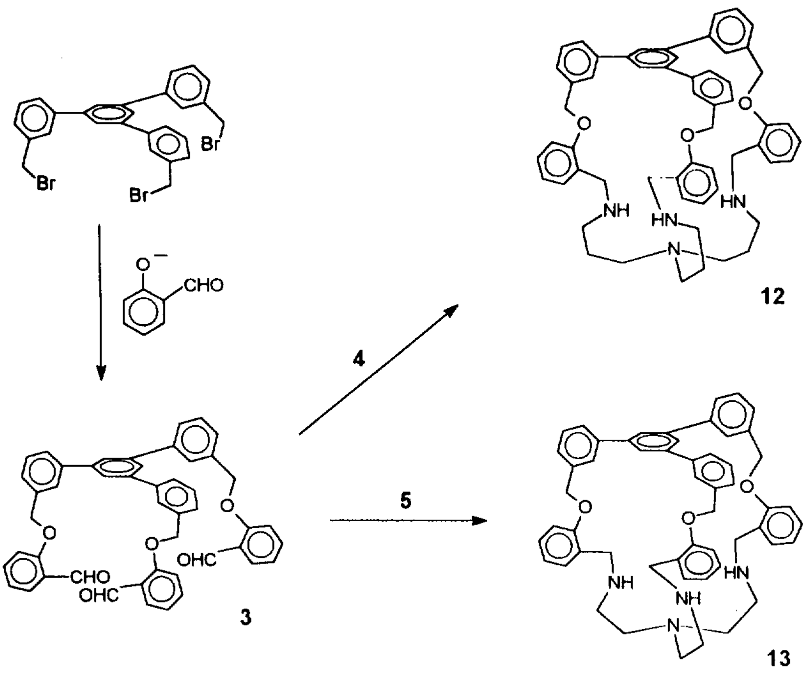
Synthesis of the tripodal amines, **4-6** (structures shown in Figure 1)

While the amines tris(3-aminopropyl)amine **4** and tris(2-aminoethyl)amine **5** were obtained from commercial sources, 1,1,1-tris(aminomethyl)ethane **6** was prepared following a literature procedure.[11]

General synthesis of the cryptands, **7-13**

General method for the synthesis of the cryptands is as follows. The tripodal trialdehyde (1 mmol) was dissolved in 100 mL of the solvent system 1:1 MeOH:THF and cooled to ~5 °C in an ice bath. To this solution was added a solution of the triamine (1 mmol) (in case of the synthesis of cryptand **10**, 1.5 mmol of ethylenediamine was taken) in 100 mL of the solvent system MeOH:THF (1:1 v/v) over a period of 3 h while stirring continuously and maintaining the temperature at ~5 °C. After the addition was complete, the reaction mixture was allowed to warm upto RT and kept for another 12 h with constant stirring. The Schiff base so formed was hydrogenated *in situ* with excess of $NaBH_4$ at RT for 2 h followed by refluxing for another 1 h. The solvent was evaporated to almost dryness and the residue was shaken with 20 mL of cold water. The desired cryptand was extracted from the aqueous medium with $CHCl_3$. The $CHCl_3$ layer was dried over anhydrous Na_2SO_4 and evaporated to obtain a yellow solid/semisolid. The cryptands were characterised by ^{1}H-NMR, ^{13}C-NMR and FAB-mass spectroscopy. Elemental analyses were obtained on solid samples.

Cryptand 7. (obtained from **1** and **4**) ^{1}H-NMR δ : 1.4 (q, 6H), 2.2 (t, 6H), 2.5 (t, 6H), 3.8 (s, 6H), 5.2 (s, 6H), 7.4 (m, 15H); ^{13}C-NMR δ : 25.99, 47.69, 50.15, 52.09, 70.48, 112.26, 121.48, 127.09, 128.87, 131.27, 138.26, 157.49; FAB-mass m/z (%) 621 (90) (7^+). Yield 45%, mp 45-47 °C. Anal. Calcd. for $C_{39}H_{48}N_4O_3$: C, 75.45; H, 7.79; N, 9.02. Found : C, 75.76 ; H, 7.59; N, 9.21.



Cyclisation reaction are followed by *insitu* $NaBH_4$ reduction

Scheme 2

Cryptand **8**. (obtained from **1** and **5**) ^{1}H-NMR δ : 2.5 (s, 24H), 3.8 (s, 12H), 5.0 (s, 12H), 7.2 (m, 30H); ^{13}C-NMR δ : 47.57, 49.40, 54.67, 70.30, 112.09, 121.14, 125.89, 128.47, 129.15, 130.64, 138.37, 157.03; FAB-mass m/z (%) 1157 (80) (**8**$^+$). Yield 50%, mp 85-86 ^{o}C. Anal. Calcd. for $C_{72}H_{84}N_8O_6$: C, 74.71; H, 7.31; N, 9.68. Found : C, 74.32; H, 7.61; N, 9.84.

Cryptand **9**. (obtained from **1** and **6**) ^{1}H-NMR δ : 0.75 (s, 6H), 2.5 (s, 12H), 3.8 (s, 12H), 5.1 (s, 12H), 7.2 (m, 30H); ^{13}C-NMR δ : 20.85, 25.53, 50.78, 57.45, 70.30, 111.69, 121.14, 125.03, 128.58, 129.38, 130.81, 138.43, 157.04; FAB-mass m/z (%) 1099 (25) (**9**$^+$). Yield 40%, mp 61-62 ^{o}C. Anal. Calcd. for $C_{70}H_{78}N_6O_6$: C, 76.44; H, 7.14; N, 7.67. Found : C, 76.38; H, 7.45; N, 7.90.

Cryptand **10**. (obtained from **1** and ethylenediamine) ^{1}H-NMR δ : 2.7 (s, 12H), 3.8 (s, 12H), 5.2 (s, 12H), 7.2 (m, 30H); ^{13}C-NMR δ : 49.07, 50.39, 69.28, 111.59, 120.92, 125.22, 128.65, 131.17, 138.26, 156.99; FAB-mass m/z (%) 1045 (30) (**10**$^+$). Yield 38% (semisolid).

Cryptand **11**. (obtained from **2** and **5**) ^{1}H-NMR δ : 2.5 (s, 12H), 3.6 (s, 6H), 5.0 (s, 6H), 7.0 (m, 15H); ^{13}C-NMR δ : 54.85, 47.92, 53.71, 69.80, 113.54, 119.66, 121.15, 125.96, 129.74, 138.21, 159.17; FAB-mass m/z (%) 579 (30) (**11**$^+$). Yield 25% (semisolid).

Cryptand **12**. (obtained from **3** and **4**) ^{1}H-NMR δ : 1.4 (q, 6H), 2.2 (t, 6H), 2.5 (t, 6H), 3.8 (s, 6H), 5.2 (s, 6H), 7.4 (m, 27H); ^{13}C-NMR δ : 25.83, 47.66, 49.53, 51.88, 70.37, 112.05, 121.38, 127.28, 128.68, 128.98, 129.45, 131.74, 137.93, 157.28; FAB-mass m/z (%) 849 (100) (**12**$^+$). Yield 37%, mp 55 °C. Anal. Calcd. for $C_{57}H_{60}N_4O_3$: C, 80.62; H, 7.12; N, 6.59. Found : C, 80.91; H, 7.39; N, 6.23.

Cryptand **13**. (obtained from **3** and **5**) ^{1}H-NMR δ : 2.5 (s, 12H), 3.8 (s, 6H), 5.2 (s, 6H), 7.4 (m, 27H); ^{13}C-NMR δ : 46.90, 48.35, 53.59, 70.32, 111.99, 121.32, 125.45, 125.96, 127.22, 128.94, 129.45, 137.87, 156.83; FAB-mass m/z (%) 807 (45) (**13**$^+$). Yield 42%, mp 99 °C. Anal. Calcd. for $C_{54}H_{54}N_4O_3$: C, 80.36; H, 6.74; N, 6.94. Found : C, 80.03; H, 6.86; N, 6.47.

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