

Macrotricyclic Host Molecules with Basket Shaped Cavities

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Abstract. The syntheses of several macrotricyclic hexalactams (1–3) and of a corresponding hexalactone (4) are described in detail for the first time. The molecules have a basket shaped skeleton and contain a non-collapsible cavity, the size and shape of which is varied by use of spacer groups. Compounds 1–3 selectively form crystalline adducts with ethanol as guest; the macrotricyclic hexaester 4 does not. Evidence for an interaction of 1 with ethanol was obtained by exchange experiments with perdeuteroethanol. Complexation experiments in solution did not show significant host/guest interactions with the guest chosen.

Key words. Cavity, complex formation, ethanol adduct, ethanol inclusion, host/guest chemistry, inclusion compounds, lactam, lactone, macrotricyclic compounds, perdeuteroethanol, spacer groups.

1. Introduction

Future aims of host/guest chemistry include the production of catalytically active cavities and of chiral host compounds of this type [1]. Though there has been some progress in these directions, much fundamental work remains to be done to aim at the synthesis of a specific and effective organic catalyst for a given reaction. It is difficult even today to design general and practically successful strategies for the tailor-shaping of large molecular cavities even if they do not bear catalytically active side arms or chiral units. To improve the situation, standard methods and standard procedures will have to be developed to enable chemists to produce certain cavity sizes and shapes in a short time, e.g. a basket, weir-basket, tube shaped cavity or appropriate niches. It will be necessary to develop functionalized building blocks which can be easily obtained and combined to give cavities of different size and shape without much research effort. If the problems connected with this first step of design and synthesis are solved, the next steps, e.g. fixing side arms and functional groups to the binding sites, will hopefully be easier.

In this study we tried to solve the strategic and synthetic problems encountered in the production of basket shaped molecular cavities [2]. They were selected, because on the one hand macroscopic baskets are well suited for the uptake of macroscopic objects of all kinds, and, on the other hand, they could show similarities with regard to the conically shaped cavities of the cyclodextrins. The new molecular cavities should be synthesized from easily available building blocks and the strategy should allow the use of different building blocks with equal functional groups in order to obtain a variety of smaller and larger basket shaped host molecules.

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2. Experimental Section

5-Hydroxyisophthalic acid (6): To a mixture of 38.0 g (0.20 mol) 5-aminoisophthalic acid-hemihydrate (**5**) and 40 mL of conc. sulphuric acid in 700 mL of water, 14.0 g (0.20 mol) of sodium nitrite dissolved in 200 mL of water, were added at -5°C . The mixture was stirred at room temperature for an additional 30 min and then heated to reflux for 2 hr. The product precipitated after cooling was recrystallized from water and dried *in vacuo*: 33.1 g (91%) yield, m.p. $294\text{--}297^{\circ}\text{C}$ [ref. [3]: 299°C].

5-Hydroxyisophthalic acid dimethyl ester (7): 31.0 g (0.17 mol) of hydroxyisophthalic acid (**6**), 5.00 g of toluene sulphonic acid monohydrate and 50 mL of trimethylorthoformate were dissolved in 500 mL of dry methanol and heated to reflux for 24 hr. The solvent was distilled off, the residue treated with NaHCO_3 solution, dried and recrystallized from xylene after the addition of a small amount of silica gel: 31.8 g (89%), m.p. 164°C [ref. [4]: $163\text{--}165^{\circ}\text{C}$].

1,3,5-Tris(bromomethyl)benzene (10): 60.0 g (0.50 mol) of mesitylene (**9**) and 285 g (1.60 mol) of NBS were refluxed in 1 L of CCl_4 . After addition of 200 mg of azobis (isobutyronitrile) heating was continued for an additional 6 hr. After cooling the succinimide was filtered off and the filtrate evaporated *in vacuo*. The residue was dissolved in toluene, filtered and the solvent removed. The bromide was recrystallized several times from chloroform/petroleum ether ($60\text{--}95^{\circ}\text{C}$). Yield: 40 g (23%), m.p. $90\text{--}93^{\circ}\text{C}$ [ref. [5]: 94°C].

5,5',5''-[1,3,5-Benzenetriyltris(methanediyoxy)]tris(benzene-1,3-dicarboxylic acid dimethyl ester) (11a): 20.66 g (89.0 mmol) of sodium-3,5-bis(carboxylic acid methyl ester) phenolate [prepared from 4.81 g (89.0 mmol) of sodium methanolate, 18.71 g (89.0 mmol) of 5-hydroxyisophthalic acid dimethyl ester (**7**) and 9.64 g (27.0 mmol) of 1,3,5-tris(bromomethyl)benzene (**10**)] were heated to 80°C in 200 mL of DMF under stirring for 2 hr. The solution was stirred for an additional 24 hr at room temperature, then heated to 100°C for a short time and then poured into 3 L of water. The hexaester precipitated was filtered, washed several times with water, dried *in vacuo* and recrystallized from benzene. Yield: 15.3 g (76%), m.p. 173°C . $^1\text{H-NMR}$ (90 MHz, $\text{CDCl}_3/\text{TMS}_{\text{int.}}$): $\delta = 3.92$ (s, 18H, OCH_3), 5.18 (s, 6H, Ar-CH_2), 7.49 (s, 3H, Ar-H), 7.82 (d, $J = 1.5$ Hz, 6H, Ar-H), 8.30 (t, $J = 1.5$ Hz, 3H, Ar-H) ppm. $\text{C}_{39}\text{H}_{36}\text{O}_{15}$ (744.7): Calcd. C 62.90% H 4.87%; Found C 63.09% H 4.75%. MS: $m/z = 744$ (M^{\oplus}).

5,5',5''-[1,3,5-Benzenetriyltris(methanediyoxy)]tris(benzene-1,3-dicarboxylic acid) (11b): 5.10 g (6.80 mmol) of the hexaester **11a** and 2.00 g (50.0 mmol) of sodium hydroxide were heated under reflux in 100 mL of methanol for 15 hr. The solvent was evaporated, the residue taken up in water and the solution acidified with diluted hydrochloric acid. For further purification the filtered hexacarboxylic acid was dissolved in NaHCO_3 solution, again precipitated with hydrochloric acid, filtered and dried. Yield: 4 g (88%), m.p. $283\text{--}287^{\circ}\text{C}$ (dec.). $^1\text{H-NMR}$ (60 MHz, DMSO-d_6): $\delta = 5.30$ (s, 6H, Ar-CH_2), 7.60 (s, 3H, Ar-H), 7.77 (d, $J = 1.5$ Hz, 6H, Ar-H), 8.10 (t, $J = 1.5$ Hz, 3H, Ar-H), 12.17 (s, 6H, COOH) ppm. $\text{C}_{33}\text{H}_{24}\text{O}_{15}$ (660.5). MS: $m/z = 660$ (M^{\oplus}).

5,5',5''-[1,3,5-Benzenetriyltris(methanediyoxy)]tris(benzene-1,3-dicarboxylic acid dichloride) (11c): 4.00 g (6.00 mmol) of hexacarboxylic acid **11b** were heated to reflux in 150 mL of thionylchloride containing a few drops of pyridine. The acid chloride which precipitated

upon cooling was filtered by suction and again recrystallized from thionylchloride. Yield: 3.2 g (69%), m.p. 215–216°C. –¹H-NMR (60 MHz, DMSO-*d*₆): δ = 5.33 (s, 6H, Ar—CH₂), 7.62 (s, 3H, Ar—H), 7.78 (d, *J* = 1.15 Hz, 6H, Ar—H), 8.10 (t, *J* = 1.5 Hz, 3H, Ar—H) ppm. C₃₃H₁₈Cl₆O₉ (771.2): Calcd. C 51.39% H 2.35%; found C 51.63% H 2.66%. Ms: *m/z* = 768 (M[⊕]).

4,4,17,17,30,30-Hexamethyl-1,7,14,20,27,33-hexaoxo-2,6,15,19,28,32-hexaaza [7.7.7](1,3)benzenophane-10,23,36-trioltri [1,3,5-benzenetriyltris(methanediyl)]ether (1)[2]: Using precision funnels 0.53 g (0.69 mmol) of hexacarboxylic acid dichloride **11c** and 0.42 g (4.10 mmol) of 1,3-diamino-2,2-dimethylpropane (each dissolved in 250 mL of chlorobenzene) were dropped into 14% dry chlorobenzene during a 2 day period under reflux and with stirring. The solvent was evaporated, the residue extracted with acetone and chromatographed on silica gel (eluent: acetone). The hexalactam **1** crystallized from ethanol as a 1:1 adduct. Yield: 316 mg (51%), m.p. 347–350°C (dec.), *R_F* 0.4 (CHCl₃/ethanol 10:1). –¹H-NMR (200 MHz, DMSO-*d*₆): δ = 0.85 (s, 9H, CH₃), 0.95 (s, 9H, CH₃), 1.06 (t, *J* = 7 Hz, 3H, CH₃), 3.12 (dd, *J_a* = 14 Hz, *J_b* = 6 Hz, 6H, NCH₂), 3.26 (dd, *J_a* = 14 Hz, *J_b* = 6 Hz, 6H, NCH₂), 3.43 (q, *J* = 7 Hz, 2H, CH₂), 4.37 (t, *J* = 5 Hz, 1H, OH), 5.34 (s, 6H, Ar—CH₂), 7.45 (s, 6H, Ar—H), 7.51 (s, 6H, Ar—H), 8.26 (t, *J* = 6 Hz, 6H, NH) ppm. C₄₈H₅₄N₆O₉ (859.0). Calcd. C 66.35% H 6.68% N 9.29% (1-EtOH); found C 66.26% H 6.36% N 9.55%. MS: *m/z* = 858 (M[⊕]).

Tris(4-methylphenyl)chloromethane (14): 2 mL of iodomethane and 126.6 g 1.00 mol) of 4-chlorotoluene (**12**) in 250 mL of dry THF were dropped under N₂ onto 24.3 g (1.00 mol) of magnesium during a 1 hr period. Additional heating under reflux was continued for 3.5 hr. After 1.5 hr, 29.5 g (0.33 mol) of diethylcarbonate in 100 mL of dry THF were added. After cooling, the mixture was poured on to a ice/hydrochloric acid mixture and extracted three times with diethyl ether. The combined organic phases were dried, the solvent evaporated and the carbinol **13** heated to boiling with 500 mL of acetyl chloride for 20 min. After evaporation and drying *in vacuo* the material was recrystallized from petroleum ether (60–95°C). Yield: 59.3 g (56%), m.p. 169–171°C [ref. [7]: 173°C].

1,1,1-Tris(4-methylphenyl)ethane (15): To 19.5 g (0.11 mol) of methyl magnesium iodide [prepared from 16.7 g (0.12 mol) of iodomethane and 2.80 g (0.11 mol) of magnesium], dissolved in 100 mL of dry diethyl ether, a solution of 19.9 g (0.06 mol) of tris(4-methylphenyl) chloromethane (**14**) in 250 mL of dry toluene was slowly added dropwise under N₂. After heating for 2 hr under reflux the mixture was poured on to ice, decolorized with sodium disulfite and acidified with conc. hydrochloric acid. The aqueous phase was separated and extracted with diethyl ether. The dried organic phases were evaporated *in vacuo* and the residue was recrystallized from ethyl acetate. Yield: 12.7 g (71%), m.p. 166–168°C [ref.[7]: 168–170°C].

1,1,1-Tris(4-bromomethylphenyl)ethane (16): 30.0 g (0.10 mol) of 1,1,1-tris(4-methylphenyl)ethane (**15**), 59.4 g (0.33 mol) of NBS and 50 mg of azobis(isobutyronitrile) were heated to reflux in 400 mL of dry CCl₄ under irradiation using a 300 W bulb. When the reaction slowed down, heating was continued for a further 3 hr. The succinimide was filtered by suction of the hot solution and the solvent evaporated after cooling. The residue was recrystallized from ethyl acetate and then several times from toluene/cyclohexane with the addition of small amounts of alumina. Yield: 16.6 g (31%), m.p. 194–196°C [ref. [7]: 199–200°C].

5,5',5''-[1,1,1-Ethanetriyltris(4,1-phenylenemethanediylloxy)]tris(benzene-1,3,-dicarboxylic acid dimethyl ester) (17a): A solution of 2.10 g (10.0 mmol) of 5-hydroxyisophthalic acid dimethyl ester (**7**) and 0.54 g (10.0 mmol) of sodium methanolate in 50 mL of dry methanol was evaporated *in vacuo*. To a suspension of the sodium phenolate **8** in 100 mL of dry diglyme 1.82 g (3.40 mmol) of 1,1,1-tris(4-bromomethylphenyl)ethane (**16**) in 80 mL of diglyme were added dropwise during a 1 hr period while the mixture was boiled. After the addition the mixture was refluxed for an additional 2 hr. The solvent was evaporated *in vacuo*, the residue washed several times with water, dried and recrystallized from chloroform/methanol. Yield: 2.76 g (90%). m.p. 115–118°C. $^1\text{H-NMR}$ (90 MHz, $\text{CDCl}_3/\text{TMS}_{\text{int.}}$): δ 2,23 (s, 3H, CH_3), 3.93 (s, 18H, OCH_3), 5.12 (s, 6H, Ar-CH_2), 7.10, 7.37 (AA'BB', $J = 8$ Hz, 12H, Ar-H), 7.80 (d, $J = 1.5$ Hz, 6H, Ar-H), 8.27 (t, $J = 1.5$ Hz, 3H, Ar-H) ppm. $\text{C}_{53}\text{H}_{48}\text{O}_{15}$ (925.0): Calcd. C 68.92% H 5.23%. Found C 68.64% H 5.21%.

5,5',5''-[1,1,1-Ethanetriyltris(4,1-phenylenemethanediylloxy)]tris(benzene-1,3,-dicarboxylic acid) (17b): 2.00 g (2.16 mmol) of the hexaester **17a** and 2.00 g (50.0 mmol) of sodium hydroxide were heated under reflux in 200 mL of ethanol for 24 hr. After cooling the precipitated sodium salt was filtered by suction, washed with ethanol and dissolved in water. The hexacarboxylic acid was precipitated with hydrochloric acid, dried and recrystallized from methanol/chloroform. Yield: 1.34 g (74%). m.p. 215°C. $^1\text{H-NMR}$ (90 MHz, $\text{DMSO}-d_6$): $\delta = 2.19$ (s, 3H, CH_3), 5.08 (s, 6H, Ar-CH_2), 7.12, 7.45 (AA'BB', $J = 6$ Hz, 12H, Ar-H), 7.79 (d, $J = 1$ Hz, 6H, Ar-H), 8.16 (t, $J = 1$ Hz, 3H, Ar-H) ppm $\text{C}_{47}\text{H}_{36}\text{O}_{15}$ (840.8)

5,5',5''-[1,1,1-Ethanetriyltris(4,1-phenylenemethanediylloxy)]tris(benzene,1,3,-dicarboxylic acid dichloride) (17c): 1.24 g (1.47 mmol) of hexacarboxylic acid **17b** and 1.84 g (8.84 mmol) of PCl_5 were heated for 1 hr in 120 mL of phosphoryl chloride. A stream of N_2 was bubbled through the solution. After the reaction had been completed, the solvent was distilled off, the residue recrystallized from methylcyclohexane and chromatographed on silica gel (eluent: dichloromethane). Yield: 1.22 g (88%), m.p. 54–56°C. $^1\text{H-NMR}$ (90 MHz, $\text{CDCl}_3/\text{TMS}_{\text{int.}}$): $\delta = 2.17$ (s, 3H, CH_3), 5.14 (s, 6H, Ar-CH_2), 7.08, 7.31 (AA'BB', $J = 6$ Hz, 12H, Ar-H), 7.91 (d, $J = 1$ Hz, 6H, Ar-H), 8.45 (t, $J = 1$ Hz, 3H, Ar-H) ppm. $\text{C}_{47}\text{H}_{30}\text{Cl}_6\text{O}_9$ (951.5): Calcd. C 59.33% H 3.18%. Found C 59.19% H 3.68%.

4,4,17,17,30,30-Hexamethyl-1,7,14,20,27,33-hexaoxo-,1,6,15,19,28,32-hexaaza [7,7,7](1,3) benzenophane-10,23,36-trioltrifethanetriyltris(4,1-phenylenemethanediyl)ether (2): 1.20 g (1.26 mmol) of hexacid chloride **17c** and 0.79 g (7.73 mmol) of 1,3-diamino-2,2-dimethylpropane (each dissolved in 250 mL of dry dioxane) were added dropwise during a 2 day period simultaneously into 1 L of boiling dry dioxane from precision dropping funnels. The solvent then was distilled off *in vacuo*, the residue chromatographed on silica gel (eluent: acetone) and then recrystallized several times from ethanol/water. Yield: 8 mg (0.6%), m.p. 347–350°C (dec.), R_F : 0.4 ($\text{CHCl}_3/\text{ethanol}$ 10:1). $^1\text{H-NMR}$ (400 MHz, $\text{DMSO}-d_6$): $\delta = 0.92$ (s, 9H, CH_3), 0.98 (s, 9H, CH_3), 2.05 (s, 3H, CH_3), 3.00 (dd, $J_a = 14$ Hz, $J_b = 5.5$ Hz, 6H, NCH_2), 3.29 (dd, $J_a = 14$ Hz, $J_b = 5.5$ Hz, 6H, NCH_2), 5.38 (s, 6H, Ar-CH_2), 6.60, 7.09 (AA'BB', $J = 9$ Hz, 12H, Ar-H), 7.24 (s, 6H, Ar-H), 7.25 (s, 3H, Ar-H), 8.13 (t, $J = 5.5$ Hz, 6H, NH) ppm $\text{C}_{62}\text{H}_{66}\text{N}_6\text{O}_9$ (1039.2) [6]. FAB-MS: $m/z = 1039$ [$\text{M}^{\oplus} + \text{H}$], 1038 (M^{\oplus}).

1,3,5-Tris(4-methylphenyl)benzene (19): A solution of 500 g (3.73 mmol) of 4-methylacetophenone (**18**) and 485 g (4.57 mol) of trimethylorthoformate in 1 L of chloroform was saturated under cooling with hydrogen chloride gas. The mixture was stirred overnight, the solvent then removed under suction and the residue was recrystallized from toluene/acetic acid (5 : 7, v/v). Yield: 248 g (57%), m.p. 174°C [ref.[4]: 174°C].

1,3,5-Tris(4-bromomethylphenyl)benzene (20): 174 g (0.50 mol) of 1,3,5-tris(4-methylphenyl)benzene (**19**), 280 g (1.57 mol) of NBS and 100 mg of azobis(isobutyronitrile) were heated to reflux in 1 L of CCl₄ for 2 hr. The succinimide was filtered off by suction of the hot mixture. The bromide **20** precipitated on cooling and was recrystallized from CCl₄ and several times from toluene/ethyl acetate (4 : 3, v/v). Yield: 77 g (13%), m.p. 194–196°C [ref. [7]: 196–197°C].

5,5',5''-[1,3,5-Benzenetriyltris(4,1-phenylenemethanediyoxy)]tris(benzene-1,3,-dicarboxylic acid dimethyl ester) (21a): 26.7 g (115 mmol) of sodium-3,5-bis(carboxylic acid methyl ester)phenolate (**8**) [prepared from 24.17 g (115 mmol) of 5-hydroxyisophthalic acid dimethyl ester, 6.21 g (115 mmol) of sodium methanolate] and 22.4 g (38.3 mmol) of 1,3,5-tris(4-bromomethylphenyl)benzene (**20**) were heated to 60–70°C for 24 hr under stirring in 250 mL of DMSO. The mixture was poured into 3 L of water, then stirred for 3 hr. The precipitate was filtered by suction and washed several times with water. After drying *in vacuo* the product was recrystallized from toluene under addition of some silica gel. Yield: 34.4 g (92%), m.p. 224–225°C. – ¹H-NMR (90 MHz, CDCl₃/TMS_{int.}): δ = 3.95 (s, 18H, OCH₃), 5.21 (s, 6H, Ar—CH₂), 7.54, 7.73 (AA'BB', *J* = 8 Hz, 12H, Ar—H), 7.79 (s, 3H, Ar—H), 7.84 (d, *J* = 1 Hz, 6H, Ar—H), 8.31 (t, *J* = 1 Hz, 3H, Ar—H) ppm. C₅₇H₄₈O₁₅ (973.0): Calcd. C 70.36% H 4.97%. Found C 70.48% H 5.25%. MS: *m/z* = 972 (M[⊕]).

5,5',5''-[1,3,5-Benzenetriyltris(4,1-phenylenemethanediyoxy)]-tris(benzene-1,3,-dicarboxylic acid) (21b): 7.78 g (8.00 mmol) of the hexaester **21a** and 3.80 g (57.6 mmol) of potassium hydroxide (85%) were heated to reflux in 150 mL of ethylene-glycol, whereby the methanol formed was distilled off. After the boiling temperature of the glycol had been reached, the mixture was allowed to cool, then diluted with 1.5 L of water and acidified with formic acid. The hexaacid was filtered by suction, washed neutral with water, heated to reflux for 1 hr in dimethoxyethane and then filtered. Yield: 5.32 g (75%), m.p. 255°C (dec.). – ¹H-NMR (90 MHz, DMSO-*d*₆): δ = 5.33 (s, 6H, Ar—CH₂), 7.59, 7.90 (AA'BB', *J* = 8 Hz, 12H, Ar—H), 7.72 (d, *J* = 1.5 Hz, 6H, Ar—H), 7.90 (s, 3H, Ar—H), 8.07 (t, *J* = 1.5 Hz, 3H, Ar—H) ppm. C₅₁H₃₆O₁₅ (888.8).

5,5',5''-[1,3,5-Benzenetriyltris(4,1-phenylenemethanediyoxy)]tris(benzene-(1,3-dicarboxylic acid dichloride) (21c): 5.00 g (5.63 mmol) of hexacarboxylic acid **21b** were heated to reflux with 10.0 g (48.0 mmol) of PCl₅ in 150 mL of phosphoryl chloride for 1 hr. The mixture was evaporated *in vacuo*, washed with pentane and chromatographed on silica gel (eluent: dichloromethane). Yield: 3.95 g (70%), m.p. 298–301°C. – ¹H-NMR (90 MHz, CDCl₃/TMS_{int.}): δ 5.23 (s, 6H, Ar—CH₂), 7.55, 7.75 (AA'BB', *J* = 9 Hz, 12H, Ar—H), 7.97 (d, *J* = 2 Hz, 6H, Ar—H), 8.47 (t, *J* = 2 Hz, 3H, Ar—H) ppm. C₅₁H₃₀Cl₆O₉ (999.5): Calcd. C 61.29% H 3.03%. Found C 61.72% H 3.39%. MS: *m/z* = 996 (M[⊕]).

4,4,17,17,30,30-Hexamethyl-1,7,14,20,27,33-hexaoxo-2,6,15,19,28,32-hexaaza[7,7,7](1,3)-benzenophane-10,23,36-trioltri[1,3,5-benzenetriyltris(4,1-phenylenemethanediyl)]ether (3): In a 2C-VP apparatus [8] 3.95 g (3.95 mmol) of hexaacid chloride **21c** and 1.94 g (18.97 mmol) of 1,3-diamino-2,2-dimethylpropane (each dissolved in 250 mL of dioxane) were dropped simultaneously during a 14 hr period on to 1 L of dry boiling dioxane. After the addition the solution was boiled for an additional 2 hr, then filtered by suction and the solution stirred with 20 g of basic Al₂O₃ for 2 hr at room temperature. Then the mixture was filtered by suction, the solution evaporated *in vacuo* and the residue chromatographed on silica gel (eluent: dichloromethane/ethanol 15:1, v/v; *R_F*: 0.4). Yield: 18 mg (0.4%), m.p. > 350°C (dec.). - ¹H-NMR (90 MHz, DMSO-*d*₆): δ = 0.64 (s, 9H, CH₃), 0.95 (s, 9H, CH₃), 3.02 (m, 6H, NCH₂), 3.30 (m, 6H, NCH₂), 5.42 (s, 6H, Ar-CH₃), 7.36–7.54 (m, 15H, Ar-H), 7.82–8.09 (m, 9H, Ar-H), 8.41 (s, 6H, NH) ppm. C₆₆H₆₆N₆O₉ (1087.3) [6].

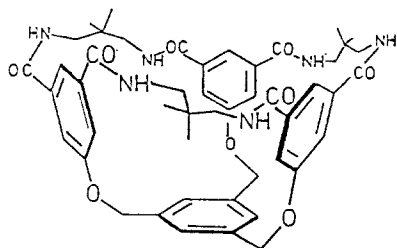
4,4,17,17,30,30-Hexamethyl-1,7,14,20,27,33-hexaoxo-2,6,15,19,28,32-hexaoxa[7.7.7](1,3)-benzeneophane-10,23,36-trioltri[1,3,5-benzenetriyltris(methanediyl)]ether (4): To a boiling mixture of 1 L of dry chlorobenzene and 40 mL of pyridine 0.53 g (0.687 mmol) of hexaacid chloride **11c** (dissolved in 250 mL of chlorobenzene) and 0.22 g (2.11 mmol) of 2,2-dimethylpropane-1,3-diol (dissolved in 250 mL of dioxane) were added dropwise and simultaneously from two precision dropping funnels over a period of 13 hr. After complete addition the mixture was refluxed for an additional 6 hr, then the solvent was evaporated, the residue chromatographed on silica gel (MPLC, 10 bar, eluent: dichloromethane) and recrystallized from cyclohexane. Yield: 166 mg (28%), m.p. 299–301°C, *R_F*: 0.7 (CHCl₃/ethanol 10:1). - ¹H-NMR (60 MHz, CDCl₃/TMS_{int.}): δ = 0.92 (s, 9H, CH₃), 1.16 (s, 9H, CH₃), 3.88, 4.39 (AB, *J* = 11 Hz, 12H, OCH₂), 5.16 (s, 6H, Ar-CH₂), 7.06 (s, 3H, Ar-H), 7.28 (d, *J* = 1,5 Hz, 6H, Ar-H), 7.87 (t, *J* = 1.5 Hz, 3H, Ar-H) ppm. C₄₈H₄₈O₁₅ (864.9): Calcd. C 66.66% H 5.59%. Found C 66.79% H 5.55%. MS: *m/z* = 864 (M⁺).

4,4,17,17,30,30-Hexamethyl-1,7,14,20,27,33-hexaoxo-2,6,15,19,28,32-hexaaza[7,7,7](1,3)-benzeneophane 10,23,36-triol (22): To a suspension of 120 mg (0.14 mmol) of the hexalactam **1** in 50 mL of dry dichloromethane 2 mL of boron tribromide in 20 mL of dichloromethane were slowly added dropwise at -10°C. The mixture was stirred overnight at room temperature, then hydrolyzed with water and the pH adjusted to 8–9 using NaOH. The aqueous phase was separated, acidified with hydrochloric acid and evaporated *in vacuo*. The product was chromatographed on silica gel (eluent: ethanol). Yield: 67 mg (64%), m.p. > 300°C (dec.), *R_F*: 0.8 (ethanol). - ¹H-NMR (60 MHz, DMSO-*d*₆): δ = 0.97 (s, 18H, CH₃), 3.20 (d, *J* = 5 Hz, 12H, NCH₂), 7.35 (s, 6H, Ar-H), 7.67 (s, 3H, Ar-H), 8.53 (t, *J* = 5 Hz, 6H, NH), 9.03 (s, 3H, OH) ppm. C₃₉H₄₈N₆O₉ (744.8).

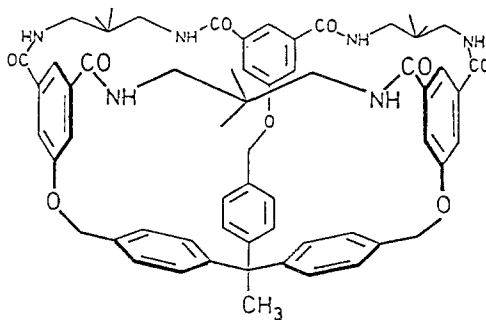
3. Results and Discussion

3.1. SYNTHESSES

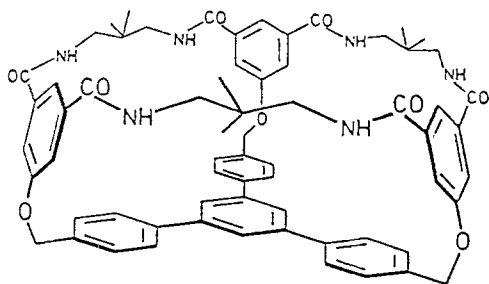
For the syntheses of the basket shaped host molecules, the lactams **1–3** and the lactone **4**, the tris(bromomethyl) compounds **10**, **16** and **20** were used as intermediates.



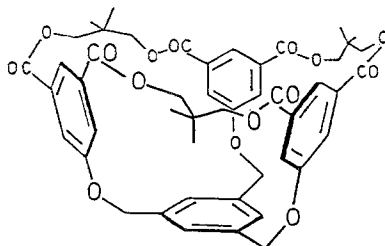
1



2



3



4

They were each treated with the sodium phenolate **8** to yield the tris(benzyl)ethers **11**, **17** and **21**.

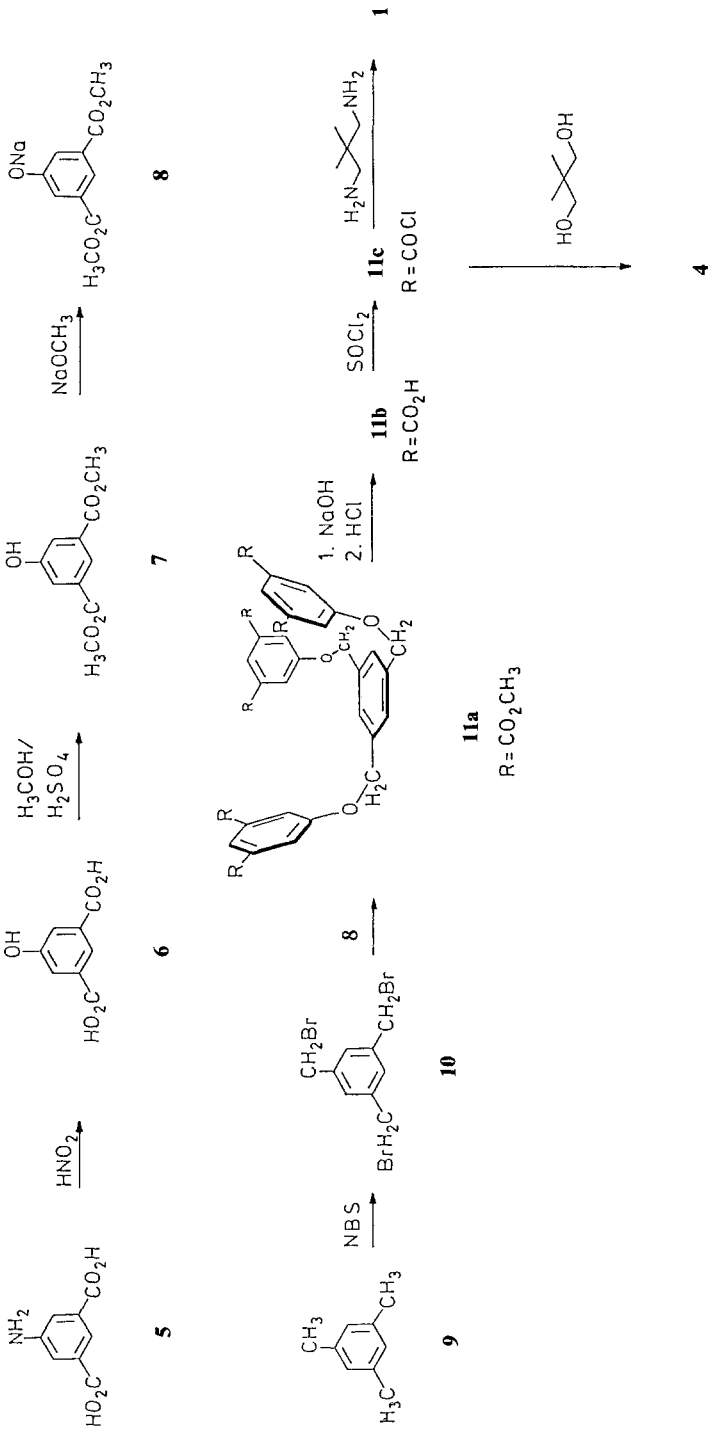
Their isophthalic acid units form the side walls of the preshaped cavities, the width of which has been varied by use of the spacer units of different size (benzene, triphenylethane, triphenylbenzene) functioning as the bases of the molecular baskets.

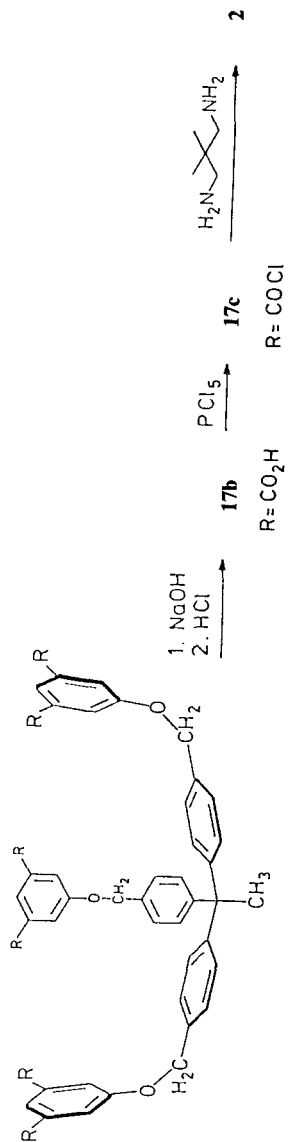
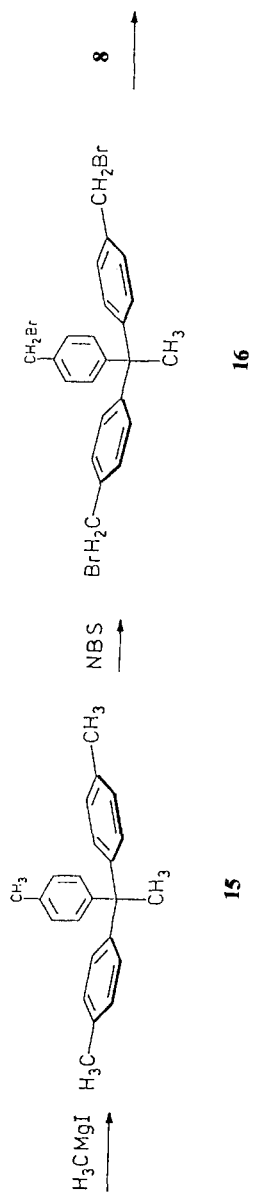
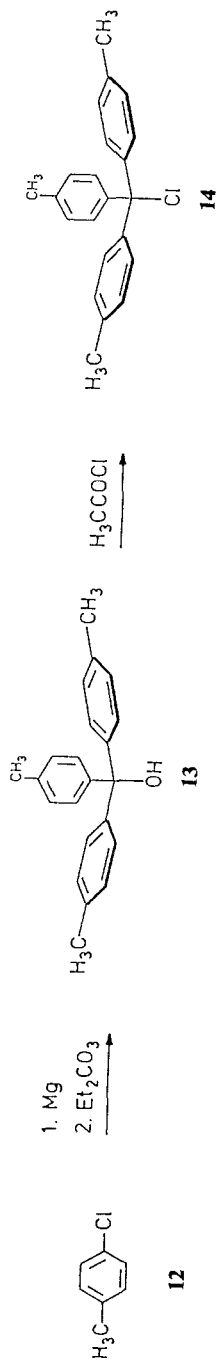
The hexaesters **11a**, **17a** and **21a** formed were transformed into the corresponding acid chlorides **11c**, **17c**, and **21c** and cyclized using the bridging units 1,3-diamino-2,2-dimethylpropane and 2,2-dimethylpropane-1,3-diol, respectively, in a two component high dilution apparatus [8].

For the preparation of the monocyclic comparison compound **22** the hexalactam **1** was reacted with boron tribromide, whereby the benzyl ether bonds are split.

In the reactions of the polyfunctionalized intermediates **17b**, **21a** and **21b** the difficulty arises that on the one hand for a complete reaction rather drastic reaction conditions are necessary, but on the other hand, side reactions should be excluded.

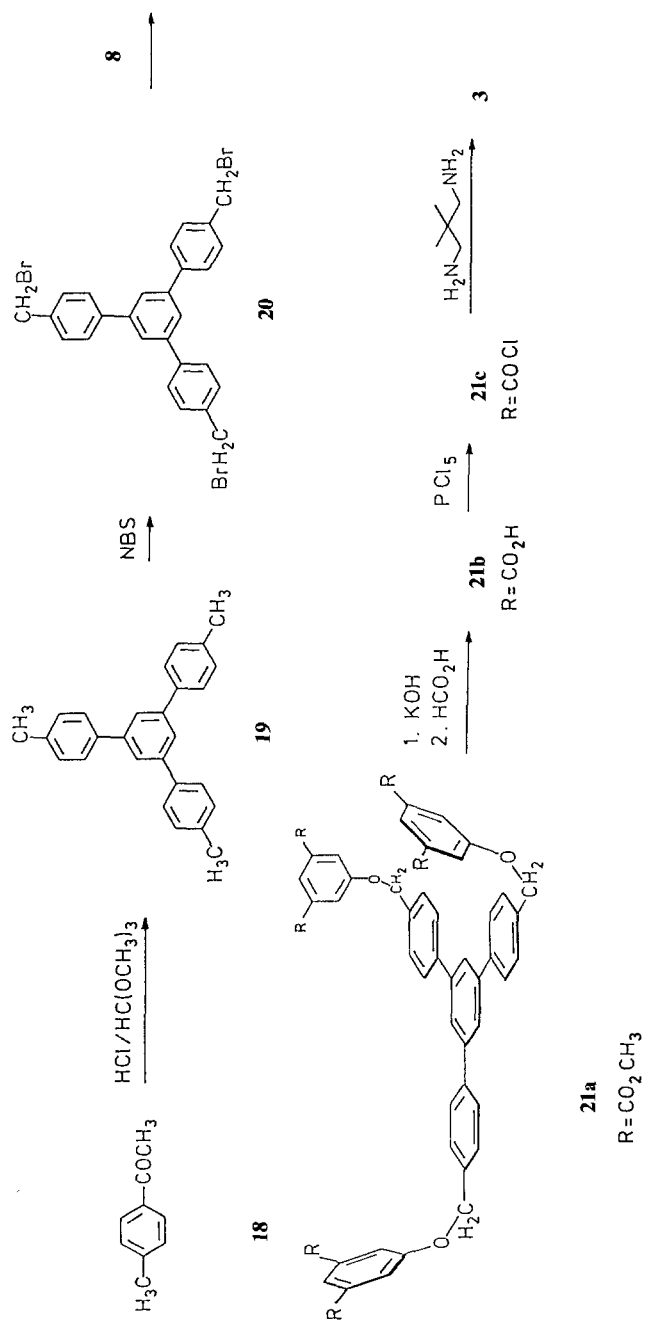
In the cyclization reactions yielding the macrotricyclic molecules **1–4** the yields decrease in this order [9], which means that the yield is lower the larger the bottom plate of the basket is chosen.

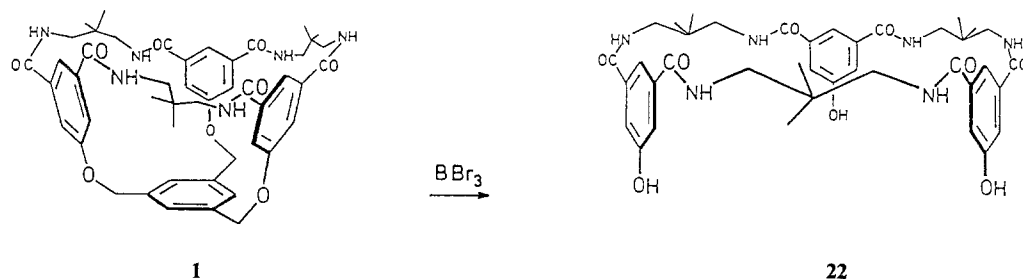




17a

R = CO₂CH₃





3.2. PROPERTIES OF THE BASKET SHAPED MOLECULES

For the lactam **1** and the lactone **4** M^{\oplus} peaks were obtained by EI-MS. The macrotricyclic molecules **2** and **3** were identified by FAB mass spectrometry ($[M + H]^{\oplus}$ peak). All 1H -NMR spectra (Figure 1) are in full agreement with the constitutions shown [10].

As can be seen from Figure 1, the CH_3 and CH_2 groups are magnetically nonequivalent, but two singlets are found e.g. for the geminal methyl groups with a difference in chemical shifts of $\Delta\delta = 0.1$ ppm (for **1**) to 0.31 ppm (for **3**). High temperature NMR measurements up to $130^{\circ}C$ (with **1**) did not lead to the coalescence of these signals. The molecular baskets therefore are rather rigid and the bottom cannot swing through the opening of the 30-membered hexalactam and hexalactone rings, respectively.

3.3. ETHANOL INCLUSION

Recrystallization of **1** from ethanol leads to a crystalline "adduct" with a stoichiometry of 1:1 (determined by 1H -NMR spectroscopy and elemental analysis). The ethanol is not removed even on drying of the solid adduct at $170^{\circ}C/1$ Torr for three days. The 1:1 ratio remains constant under these conditions.

400 MHz 1H -NMR exchange experiments [11] of the ethanol inclusion compound in solution using perdeuterioethanol for competition give hints to the existence of a **1**-ethanol complex also in solution: A sample of the crystalline inclusion compound **1**-ethanol was dissolved in 0.5 mL of perdeuterioethanol and the solution heated to reflux for three minutes. Even under these conditions there is only a very slow exchange of ethanol by perdeuterioethanol. Only after one hour at room temperature *two* quartet and *two* triplet absorptions are observed. We interpret these two ethanol absorptions as corresponding to both free and complexed ethanol. Addition of some ethanol to the perdeuterioethanol solution in agreement with this assumption shows that only one triplet and one quartet (of the free ethanol) is increased in intensity. The chemical shift difference between the two ethanol species is rather small (0.9 Hz). The ethanol bound to the host compound **1** seems to be the one which is shifted to lower field strengths. Only after standing for one week does the spectrum of the sample show the 1H -NMR signals of the non-complexed free ethanol.

Whereas the lactone **22** crystallized without ethanol from ethanolic solutions, the basket shaped molecules **2** and **3** like **1** form crystalline ethanol "adducts", but the ethanol is less strongly bound to these molecular baskets, and there is no simple stoichiometry between host and guest. The amount of ethanol bound to crystalline **2** and **3** also varies depending on the drying conditions of the samples [6]. Also shift differences in solution as observed with the **1**-ethanol complex could not be detected.

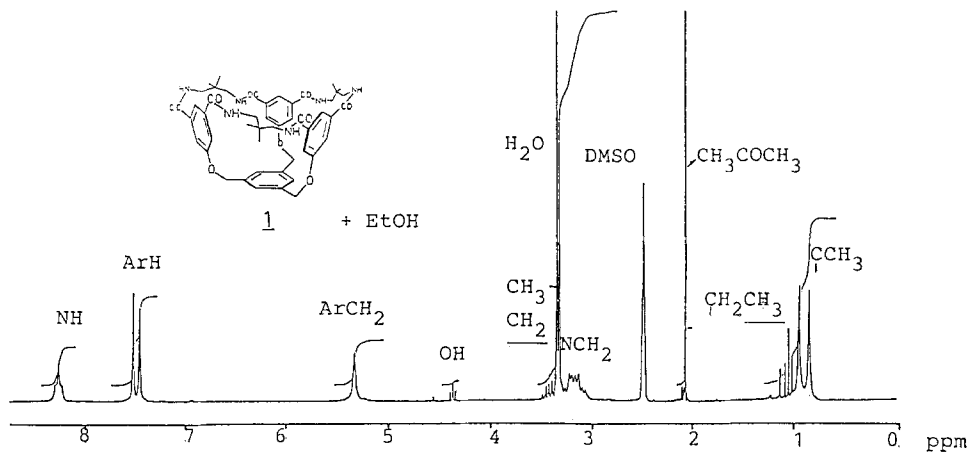


Fig. 1(a).

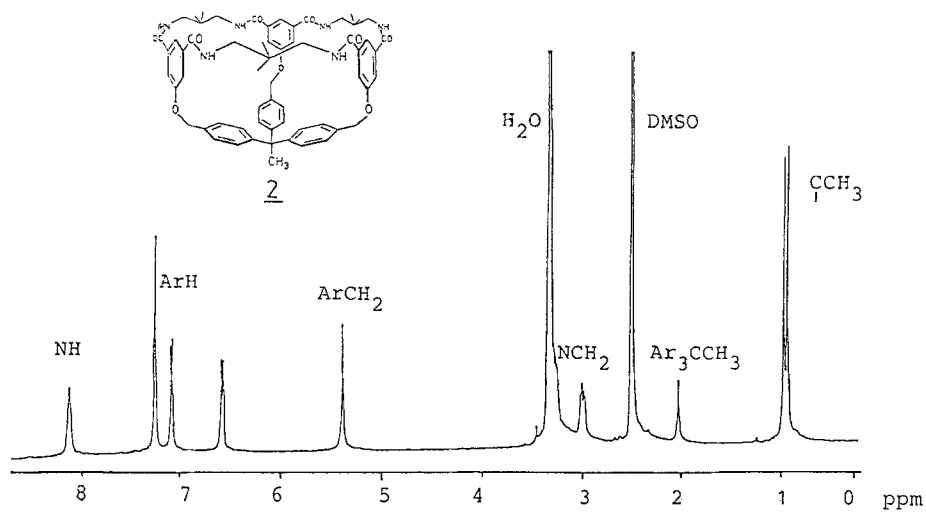


Fig. 1(b).

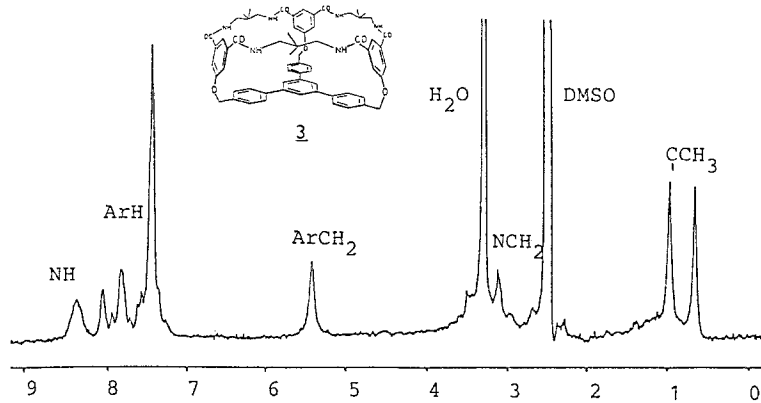


Fig. 1(c).

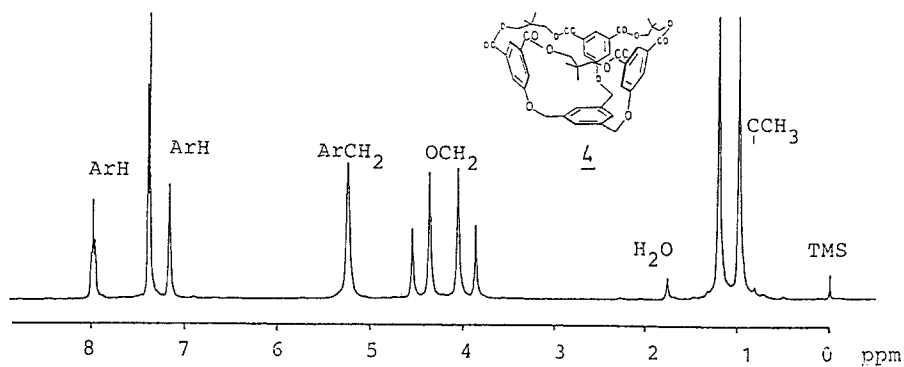


Fig. 1(d).

Larger and smaller alcoholic guest molecules like 1-propanol, 2-propanol, *tert*-butanol and methanol, respectively, are not bound to **1** nor to **2** and **3**. This is in accord with molecular model considerations, which show that the host **1** and the guest ethanol fit well to each other if the guest is embedded into the basket type molecular cavity. From the experiments in solution we conclude that the ethanol inclusion compound of **1** should be regarded as a complex rather than as a clathrate. Further modifications of sizes and shapes of this type of cavities seem to be necessary in order to find better fitting host/guest pairs.

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10. The spectra are given here in detail for comparison and to facilitate the identification of those compounds (**1**–**3**) which do not have sharp melting points, but decompose beyond 350°C.
11. We are grateful to Mr. R. Hartmann for measuring the 400 MHz NMR spectra on a Bruker WM-400.