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Synthesis of Dithiacyclophanes with Large Molecular Cavity

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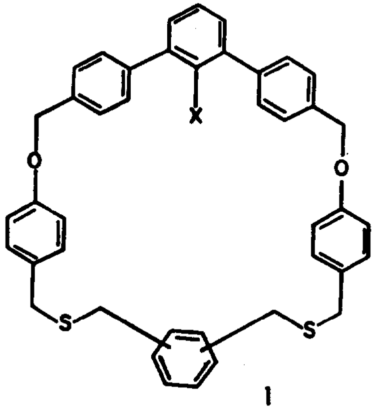
Abstract : Coupling of the dichlorides 9 & 10 with xylenedithiols and m-terphenyldithiol under high dilution technique in presence of KOH in benzene-ethanol afforded the cyclophanes of the class 1 & 2.

Molecules with large cavities in supramolecular chemistry have gained additional impetus during recent times[1]. From simple [2.2]metacyclophane[2] to the new class of macrocycles called cuppedophanes and cappedophanes[3,4], they are synthetically useful molecules in guest host complexation chemistry. We wish to report here the synthesis of macrocyclic host molecule 1 & 2 which on functionalisation can be effectively used as a chelating reagent for trapping small guest molecules or metal ions.



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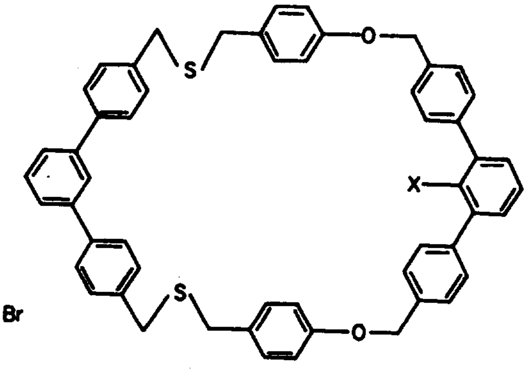

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X = H, Br

Structures 1 & 2 are based on m-terphenyl frame work, that can be obtained by the known[5] tandem aryne sequence. Addtion of three equivalents of p-tolylmagnesiumbromide to 2,6-dichloroiodobenzene followed by quenching with either dilute acid or Br_2 resulted in the formation of 4,4"-dimethyl-1,1':3',1"-terphenyl(3) or2'-bromo-4,4"-dimethyl-1,1':3',1"-terphenyl(4) in excellent yields. Two fold radical bromination of 3 & 4 with NBS in CCl_4 gave 4,4"bis(bromomethyl)-1,1':3',1"-terphenyl 5 and 2'-bromo4,4"bis(bromomethyl)-1,1':3',1"-terphenyl 6 in 80% & 75% yields respectively. Bisalkylation of the dibromides 5 & 6 with p-hydroxymethylbenzoate in presence of K_2CO_3/DMF afforded the diester 7 (mp 184°C;85%) and 8 (mp 185°C;75%). LAH reduction of the diester 7 & 8 followed by treatment with $SOCl_2$ in presence of pyridine in CH_2Cl_2 yielded the dichlorides[6] 9 (mp 164°C) & 10 (mp 166°C) quantitatively.

Coupling of the dichlorides 9 & 10 with o-xylene-α-α'-dithiol under high dilution technique in presence of KOH in benzene-ethanol afforded the cyclophanes 1a (mp 206°C;70%) & 1b (mp 202°C;60%) respectively. The ^{1}H NMR spectrum of 1a showed three singlets each for four protons at δ 3.60, 3.65 & 5.25 for -CH_2S-, -SCH_2- & -OCH_2-respectively. In the aromatic region two pairs of AB quartet each for eight protons were observed at δ 6.80, 7.15 & 7.40, 7.55. Further the o-xylene protons appeared as multiplet at δ 7.10 to 7.21 in addition to a three proton multiplet at δ 7.56 to 7.59. The $C_{2'}$-H of the m-terphenyl framework appeared as a one proton triplet at δ 7.67 (J=1.87Hz). The fact that the chemical shift of the $C_{2'}$-H of the m-terphenyl unit is not affected apparently indicates that the hydrogen is not in the π-cloud vicinity of o-xylene unit. ^{13}C NMR[7] & mass spectrum further supported the structure.

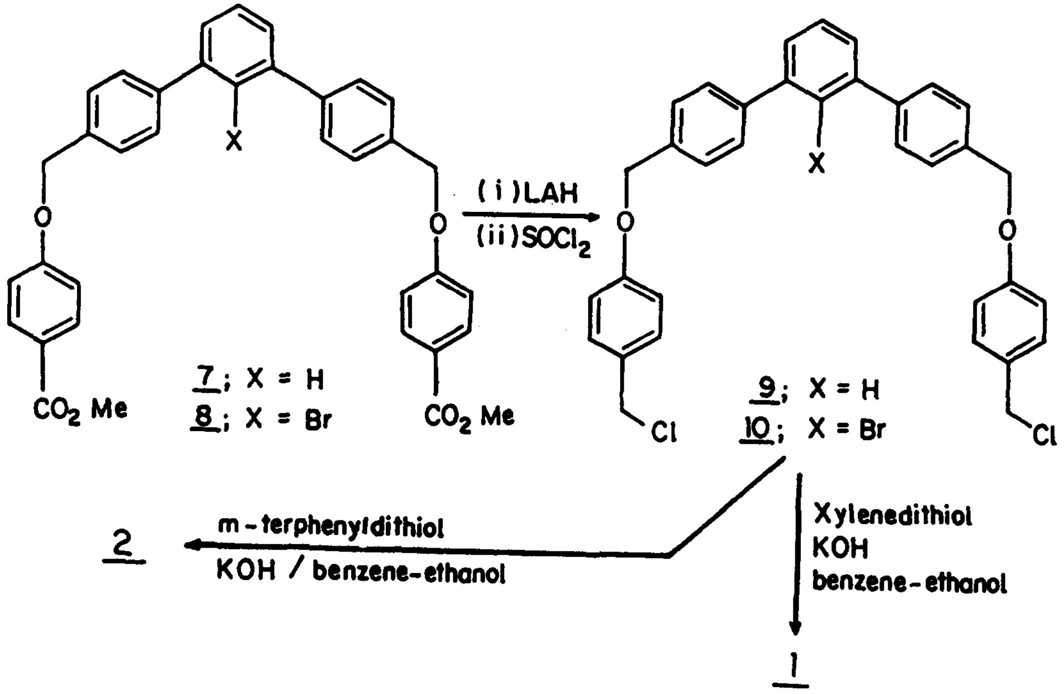
Moreover, coupling of the dichlorides 9 & 10 with p-xylene-α,α'-dithiol under similar condition gave the cyclophanes 1c (mp 155°C;60%) & 1d (mp 153°C;66%) respectively. The ^{1}H NMR of 1c displayed three singlets of four proton each at δ 3.49, 3.55 & 5.25 for -CH_2S-, -SCH_2- & -OCH_2- and two sets of AB quartet for eight protons each at δ 6.75, 7.05 & 7.38, 7.53 respectively. The p-xylene protons appeared as singlet at δ 7.16 and three proton multiplet was observed at δ 7.46 to 7.53 (middle ring of the m-terphenyl unit) in addition to one proton triplet at δ 7.61 for the $C_{2'}$-H of m-terphenyl unit. The p-xylene proton in the bromo substituted cyclophane 1d also appeared as 4H singlet at δ 7.16 indicating that the presence of bromine atom has no influence on the chemical shift of p-xylene protons.

The bromo compounds 1b & 1d when treated with 1 equivalent of BuLi at-78°C followed by quenching with dil HCl afforded quantitatively the cyclophanes 1a & 1c respectively indicating the generation of the Lithium salt and this reaction has the scope of introducing various functionality at $C_{2'}$ position of the m-terphenyl frame work.

With a view to further increase the cage size, the dichlorides 9 & 10 were coupled with 4,4"bis(mercaptomethyl)-1,1':3',1"-terphenyl obtained by the conventional method of KOH hydrolysis of the corresponding thiouronium salt. The coupling afforded the cyclophanes 2a (mp 175°C;30%) & 2b (mp

170°C;25%) as supported by the spectral data and satisfactory elemental analysis[8]. Our attempts to synthesis functionalised macromolecular cavitiy is under further investigation.

The synthetic scheme is as follows,



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References and Notes

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6. ^{1}H NMR ($CDCl_3$, 90MHz) for **9** : δ 4.4(s,4H), δ 4.9(s,4H), δ 6.7-6.8(m, 4H), δ 7.0-7.5(m, 16H), ^{1}H NMR ($CDCl_3$, 90MHz) for **10** : δ 4.4 (s,4H), δ 4,9(s,4H), 6.7-6.8(m,4H), δ 7.1-7.6(m,15H)

7. ^{13}C NMR ($CDCl_3$, 400 MHz) for **1a** 33.193 (-CH_2S-), 35.936(-SCH_2-), 69.016(-OCH_2-), 115.646, 125.527, 126.924, 127.015, 127.744, 128.169, 128.958, 129.671, 129.808, 130.354, 136.335, 136.745, 140.706, 141.678, 156.599(15Ar-C), MS (m/e) 546 (M-$C_6H_5CH_2$), 532, 500, 498, 407, 484, 384, 368, 256 (Base peak). ^{13}C NMR ($CDCl_3$, 400 MHz) for **1c** 35.121 (-CH_2S-), 35.409 (-SCH_2-), 69.669 (-OCH_2-), 115.798, 125.740, 127.091, 127.410, 127.668, 129.034, 129.110, 129.808, 129.990, 136.441, 136.745, 140.676, 141.572, 156.994 (14Ar-C)

8. ^{1}H NMR ($CDCl_3$, 400MHz) for **2a** : δ 3.55 (s,4H,-CH_2S-), δ 3.58(s,4H, -SCH_2-), δ 5.2(s, 4H-OCH_2-), δ 6.74, 7.04 (ABq,8H,J=8Hz), δ 7.15 (d,6H,J=8Hz), δ 7.24-7.27(m,4H), δ 7.40-7.55(m,12H), δ 7.64(t, 1H,J=1.8Hz), δ7.66 (t,1H,J=1.87H$_z$) C_2.-H of the m-terphenyl frame work, ^{13}C NMR ($CDCl_3$, 400 MHz) for **2a** : 34,559 (-CH_2S-), 35.607 (-SCH_2-), 69.790 (-OCH_2-), 115.782, 125.573, 125.770, 126.013, 126.575, 126.878, 127.015, 127.410, 127.637, 129.186, 129.413, 129.717, 129.899, 130.779, 136.821, 139.988, 140.069, 140.904, 141.708, 157.221 (20Ar-C)

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