Triply Bridged Polyoxapolyaza-heterophanes derived from 2,4,6-Trichloro-*s*-triazine. A New Strategy in the Synthesis of Possible Receptors of Charged and/or Neutral Species

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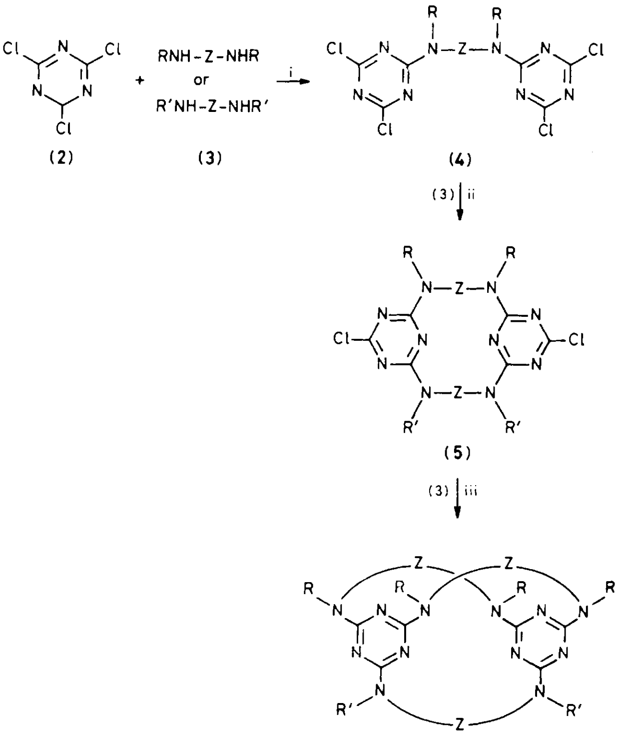
A new series of triply bridged polyoxapolyaza-triazinophanes, potentially capable of molecular recognition, has been synthesized by using the differing reactivity of the three chlorine atoms of 2,4,6-trichloro-*s*-triazine towards nucleophiles.

Recently there has been a rapid growth of interest in the study of host molecules capable of molecular recognition. In addition to the well known coronands and cryptands,[1] new and more complex structures, such as cylindranes[2–4] and spherands,[2,3] have become available. In an effort to extend this exciting field of research, we have now synthesized triazinophanes (**1**) triply bridged by polyheteroatomic alkyl chains using 2,4,6-trichloro-*s*-triazine (**2**) as a building block. 2,4,6-Trichloro-*s*-triazine is peculiar in that the three chlorines may be replaced in a stepwise manner by nucleophiles;[5] this makes possible a new, simple synthesis of macropolycyclic ligands.†



a; Z = $(CH_2CH_2O)_2CH_2CH_2$, R = H, R' = n-C_8H_{17}
b; Z = $(CH_2CH_2O)_2CH_2CH_2$, R = R' = Bu^n
c; Z = $CH_2CH_2OCH_2CH_2$, R = R' = Bu^n

Scheme 1. i, 0—5 °C, 3 h, acetone–H_2O; ii, 50—70 °C, 20 h, tetrahydrofuran–H_2O, KOH; iii, 160—180 °C, 20 h, DMSO–H_2O, KOH.

The synthesis of compound (**1a**)‡ was carried out as follows (Scheme 1). Attachment of the first chain was carried out at 0—5 °C (3 h), with (**2**) suspended in aqueous acetone, in the presence of 1 mol. equiv. of (**3**; R = H) and 2.2 mol. equiv. of KOH. The bridged derivative (**4a**) (74%, m.p. 127—129 °C from acetonitrile) was formed and the second chain was added to this in aqueous tetrahydrofuran (THF) at 65 °C (20 h), to give coronand (**5a**) (43%, m.p. 127—128 °C from acetonitrile). Attachment of the third chain to give triazinophane (**1a**) (28%, glass after column chromatography, silica, 60:39:1 MeCN–EtOH–Et_3N) was achieved in aqueous dimethyl sulphoxide (DMSO) at 160—180 °C (20 h). The second and the third step required high dilution conditions and also the simultaneous addition of substrate

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† Cyclophanes triply bridged with polyoxyethylene chains have previously been synthesized from phloroglucinol (ref. 6) and from 1,3,5-tris(hydroxymethyl)benzene (ref. 7). However, the identity of the three points of attack of the subunits used makes the synthesis of these cyclophanes very tedious and extremely low yielding.

‡ 1,10-Dioctyl-4,7,20,23,36,39-hexaoxa-1,10,17,26,33,42-hexaaza[10.10.10](2,4,6)triazinophane.

(**4a**) or (**5a**) together with a solution of 1 mol. equiv. of diamine (**3**; $R' = n\text{-}C_8H_{17}$ or $R = H$, respectively) and aqueous KOH (2.2 mol. equiv.), the amount of water being enough to maintain homogeneous conditions.

The C, H, N elemental analysis, mass spectrum (*m/z* 818, M^+; *m/2z* 409), and ^1H n.m.r. spectrum [$CDCl_3$: δ 0.80 (t, 6H, CH_3), 1.24 (m, 20H, CH_2), 1.52 (m, 4H, CH_2CH_2N), and 2.90—4.10 (m, 44H, CH_2O, CH_2N, NH)] were in agreement with the assigned structure (**1a**). The ^{13}C n.m.r. spectrum at 75.46 MHz, recorded at +50 °C ($CDCl_3$), shows one, easily attributable signal for each chemically non-equivalent carbon present in the molecule.§ At room temperature some of the lines are broader than others and therefore appear to have lower intensities; this is particularly evident for the signals belonging to the bridging chains. If the temperature was lowered further (CHF_2Cl, −70 °C), additional lines with different relative intensities appeared in the spectrum. This indicates either that the molecular exists in a single non-symmetric conformation up to *ca.* room temperature or, more likely, that there are two, or more, differently populated conformations separated by a high interconversion barrier. Similar temperature-dependent behaviour is shown by coronand (**5a**).

Following the same method, coronands (**5b**) (m.p. 89—90 °C from methanol) and (**5c**) (m.p. 90—92 °C from methanol) and triazinophanes (**1b**) (glass) and (**1c**) (m.p. 88—90 °C from methanol) were synthesized. Heteroatoms in the bridges and alkyl chains have an important effect on the physical properties (solubility, m.p., *etc.*) of compounds (**1**), (**4**), and (**5**). For example, (**4**; $Z = CH_2CH_2$, $R = H$)[8] and coronand [**5**; $Z = (CH_2CH_2O)_2CH_2CH_2$, $R = R' = H$] have m.p. >300 °C and are almost insoluble in most organic solvents, whereas coronands (**5a—c**) and triazinophanes (**1a—c**) have lower m.p.s and good liposolubility.

Triazinophane (**1a**) may be used as phase-transfer catalyst. Preliminary results based on catalytic activity as a function of cation indicate that alkali metal cations are complexed by (**1a**) in the order $Na^+ > K^+ > Cs^+ \gg Li^+$.

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§ δ 166.0 (C_{ar}–NH), 165.3 (C_{ar}–N–C_8H_{17}), 70.7, 70.6, 70.4, and 69.2 (CH_2–O), 47.7 and 46.7 (CH_2-N), 40.7 (CH_2–NH), 31.9, 29.5, 29.4, 28.1, 27.2, and 22.6 (CH_2) and 14.0 p.p.m. (CH_3): L. Lunazzi, University of Bologna, personal communication; spectra recorded at the high field n.m.r. service centre of the C.N.R., Bologna.