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A second generation dendrimer incorporating nine S_2N_2-donor macrocycles and its palladium(II) complex

Ian M. Atkinson,[a] Jy D. Chartres,[a] Andrew M. Groth,[a] Leonard F. Lindoy,*[b] Mark P. Lowe[b] and George V. Meehan*[a]

[a] *School of Pharmacy and Molecular Sciences, James Cook University, Townsville, Qld. 4811, Australia. E-mail: george.meehan@jcu.edu.au*

[b] *Centre for Heavy Metals Research, School of Chemistry F11, University of Sydney, Sydney, N.S.W. 2006, Australia. E-mail: lindoy@chem.usyd.edu.au*

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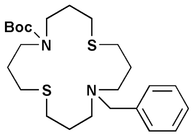
A new second generation dendrimer incorporating nine S_2N_2-donor macrocyclic units that bind nine Pd(II) cations is reported.

Interest in the potential applications of nanoscopic structures has fuelled rapid progress in the chemistry of dendrimers and hyperbranched polymers.[1] While less studied than purely organic systems, the inclusion of transition metals into such structures is of particular interest as the resulting materials may, for example, display novel magnetic, electronic and/or catalytic properties.[2,3] Dendritic structures incorporating macrocyclic ligand units have received less attention.[4–7]

Recently, we have reported metal binding studies[8,9] involving the tri-linked N_2S_2-donor macrocyclic ligands derived from the common precursor **1**.[10] We now report an extension of these studies in which the linking of nine such rings in a dendritic architecture has been achieved.



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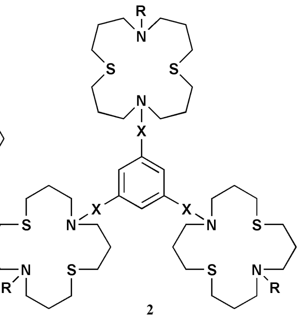

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At the outset it was decided to employ the linked macrocyclic ′trimer′ **2** (X = OCH_2CH_2, R = H), as the core in a ′double-stage convergent′[11] strategy for forming the dendrimer. In principle, this should simplify the synthesis by reducing the number of simultaneous reactions that need to occur at the individual stages of the stepwise process. The commercial availability of 3,5-dihydroxybenzaldehyde suggested a readily accessible route to the preparation of an appropriate bifurcating dendron for use in such an approach. This substituted benzaldehyde possesses the necessary bifurcation capacity, and by appropriate manipulations of the aldehyde functionality should provide a dendron capable of alkylating the core **2** (X = OCH_2CH_2, R = H). Through this approach, the macrocyclic ring substitution pattern in the second generation dendrimer would be similar to that in the previously prepared trimer **2** (X = OCH_2CH_2, R = benzyl)[10]—a desirable feature in the present context since it would facilitate a planned comparative investigation of the difference in metal ion binding between the dendritically linked macrocyclic product and its discrete ring monomeric counterpart.[9]

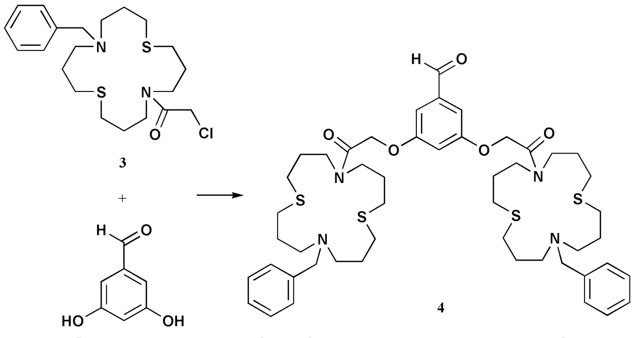
Macrocyclic chloroamide **3** was prepared from **1** as previously described,[10] and used to bis-alkylate 3,5-dihydroxybenzaldehyde in 94% yield (Scheme 1). The aldehyde group of the resulting bis-macrocycle **4** was then reduced with sodium borohydride to give the corresponding alcohol **5** in 97% yield. In a separate reaction, the amide groups of **5** were reduced with borane–dimethyl sulfide complex to give the substituted benzyl alcohol **6** in 89% yield (Scheme 2). This two-step sequence was much more efficient (overall yield 86%) than direct reduction of **4** with borane–dimethyl sulfide complex which produced **6** in very low yield.

Conversion of the benzyl alcohol **6** to the corresponding chloride **7** (in 95% yield) using triphenylphosphine in refluxing carbon tetrachloride, provided the required dendron for the peripheral section of the target second generation dendrimer. Thus, the peripheral amino groups of macrocyclic trimer **2** (X = OCH_2CH_2, R = H) were alkylated by **7** (3 equiv.) in refluxing THF containing approximately 10 equiv. of hexamethylphosphorous triamide (HMPA) and sodium carbonate as base. The desired dendrimer **8** was obtained as a viscous oil in 69% yield after purification by column chromatography (Scheme 3).

Dendrimer **8** has a similar substitution pattern on all nine of its constituent macrocyclic rings. In the ^{1}H NMR spectrum dendrimer **8** exhibits both the characteristic doublet–triplet combination (δ 6.46 and 6.34) for the protons of the unsymmetrical aromatic ring linking the first and second generations, and the expected singlet (δ 6.05) indicating the symmetry of the central core.

Dendrimer **8** (M_r > 3600 amu), like its precursors, was found to tenaciously retain solvent even after prolonged evacuation. As a consequence, mass spectrometry was the method of choice for determining molecular composition. The FTICR electrospray mass spectrum of **8** shows a prominent $[M + 2H]^{2+}$ peak at m/z 1813.988 ($C_{195}H_{314}N_{18}O_9S_{18}$ requires $[M + 2H]^{2+}$, 1813.982), with this composition being supported by a close coincidence of the predicted and observed isotopic envelopes for this ion (Fig. 1).

Attempts to prepare Pd(II) complexes from either $Pd(CH_3CN)_2Cl_2$ [formed *in situ* from palladium(II) chloride and acetonitrile] in the presence of excess hexafluorophosphate, or from palladium(II) acetate followed by addition of excess ammonium hexafluorophosphate, resulted in yellow solids whose microanalysis suggested that they were highly (and variously) solvated. Frustratingly, the Pd(II) complex of **8** resisted mass spectral characterisation using a variety of



Scheme 1 *Reagents and conditions:* Cs_2CO_3, DMF, rt, 12 h.

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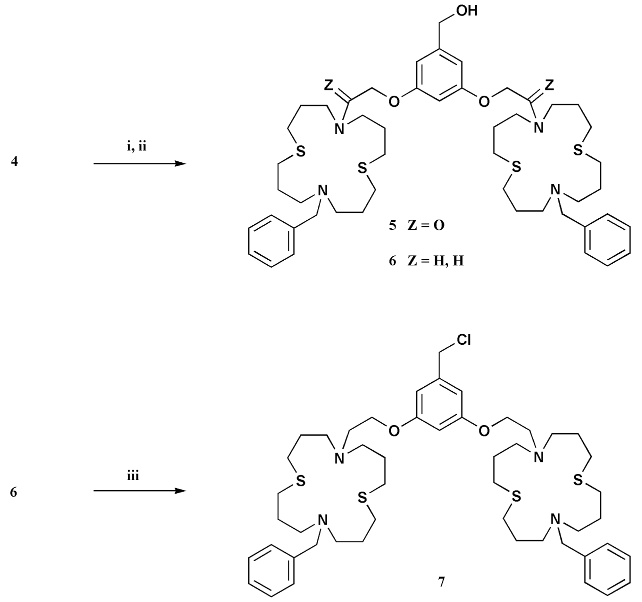
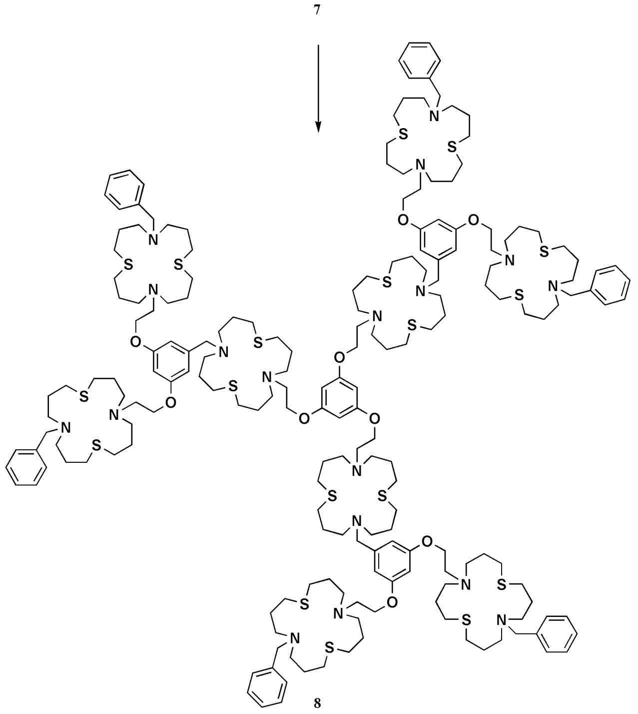


Scheme 2 *Reagents and conditions:* i, $NaBH_4$, CH_2Cl_2–MeOH, rt, 2 h; ii, $BH_3{\cdot}Me_2S$, THF, reflux, 12 h; iii, PPh_3, CCl_4, reflux, 12 h.

ionisation methods (EI, FAB, MALDI or electrospray). In each case only uncharacterised low mass fragment ions were observed, perhaps reflecting the 18+ charge that would be associated with a nonanuclear cation of the present type.

Finally, definitive evidence for the complexation of nine Pd(II) ions by **8** *was* obtained *via* spectrophotometric titration. The titration was employed to follow complexation of Pd(II) by the dendritic ligand **8**. The addition of **8** in acetonitrile to $PdCl_2$ in acetonitrile was characterised by the build up of a peak at 300 nm, with an associated decrease of the $PdCl_2$ absorption at 245 nm. The increase in absorbance at 340 nm was used to derive the plot shown in Fig. 2 which shows a sharp ligand to metal end point at 1:9—consistent with the formation of the expected dendritic complex species.



Scheme 3 *Reagents and conditions:* 0.32 equiv. **2** (X = OCH_2CH_2, R = H), Na_2CO_3, HMPA, THF, reflux, 72 h.

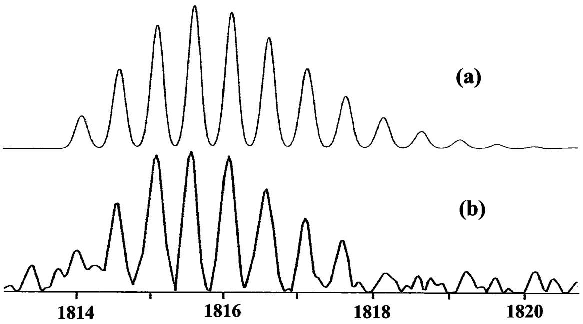


Fig. 1 (a) Predicted isotopic envelope for the $[M + 2H]^{2+}$ ion in the mass spectrum of **8** and (b) observed mass spectral distribution.

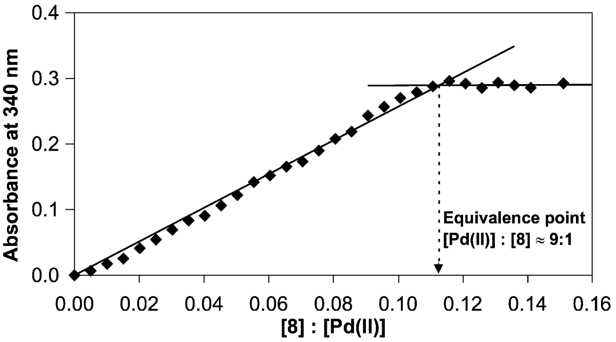


Fig. 2 Spectrophotometric titration curve for the addition of **8** to palladium(II) chloride in acetonitrile.

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