Approaches towards specifically functionalized cascade macromolecules: dendrimers with incorporated metal binding sites and their palladium(ii) and copper(ii) complexes

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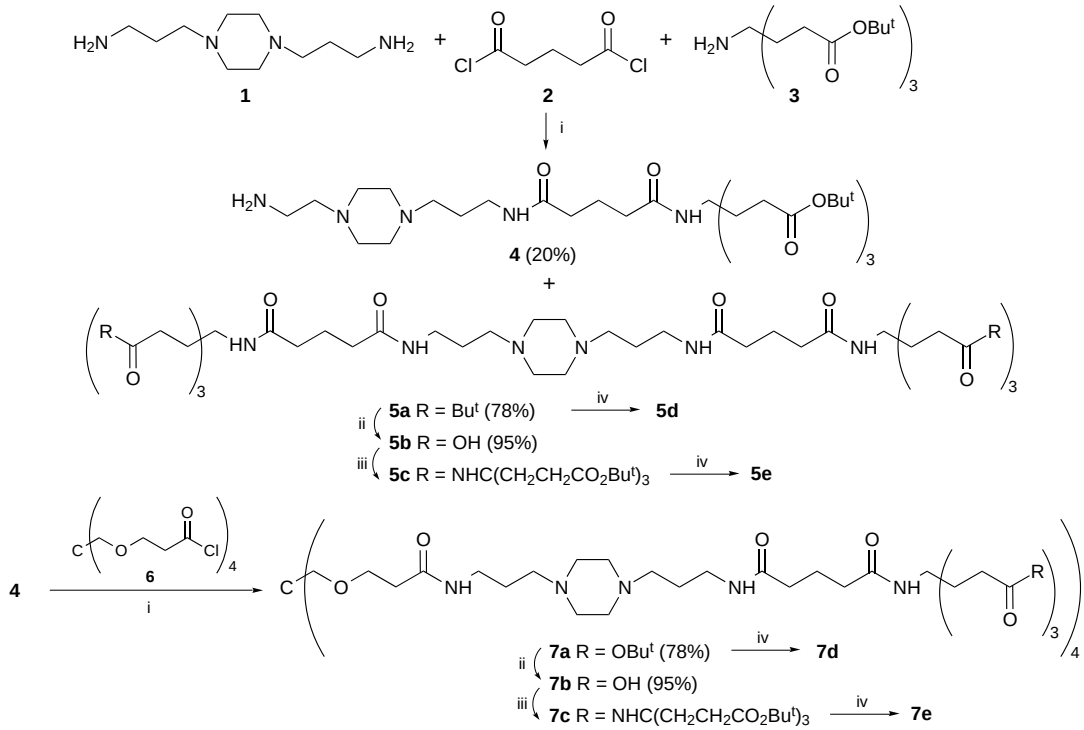
Construction of ligand functionalized branched building blocks has afforded entrance to a series of dendrimers possessing multiple, internally incorporated piperazine moieties, which readily form Pd^{II} and Cu^{II} complexes.

Metallodendrimer coordination spheres,[1–6] which are not completely filled, are of particular interest with regard to utilitarian aspects. We herein report the synthesis of related two- (**5a**,**c**) and four-directional (**7a**,**c**) dendrimers possessing specifically localized piperazine subunits and their complexation to afford Cu^{II} and Pd^{II} complexes.

N,*N*′-Bis(3-aminopropyl)piperazine **1**, as the metal binding site,[7] and the tris(*tert*-butyl ester)[8] **3** are readily linked in a one-pot reaction with glutaric acid dichloride **2** to form the extended building block **4**† and the colourless, two-directional dendrimer **5a**† in moderate yields (20 and 30%, respectively; Scheme 1). Amidation of **4** with the tetrakis(acyl halide) **6**, prepared from the corresponding tetraacid,[9] afforded (78%) the related four-directional dodecaester dendrimer **7a**† as a colourless solid. Hydrolysis of the *tert*-butyl esters **5a** and **7a** using formic acid generated (> 95%) the corresponding 6- (**5b**)† and 12-acid (**7b**).† Reaction of these polyacids with building block **3** under typical peptide coupling conditions (DCC, 1-BHT)[10] transformed each to the corresponding next higher 18- (**5c**)† and 36-ester (**7c**)† homologues.

Stable, orange microcrystalline Pd^{II} complexes (**5d**,**e**) were formed upon stirring solutions of the 6- (**5a**) and 12-ester (**5c**) in MeCN at 25 °C with added $Pd(MeCN)_2Cl_2$. ^{13}C NMR Spectra (Fig. 1) provide direct evidence of a successful complexation at the piperazine binding loci due to the appearance of a new set of signals; titration of the free ligands by controlled addition of the metal salt can be conveniently followed by the observation of these absorptions. Evidence for complexation is provided by significant downfield shifts (3 and 1.2 ppm) for the C1 and C2 piperazine carbon atoms; however, the upfield shift (1.8 and 0.2 ppm) for C4 and C5, respectively, as well as the shift ($\Delta\delta$ = 0.6 ppm) for the innermost amido carbonyls support a further contribution to the coordination sphere. It is postulated that for metal chelation, the piperazine ring adopts the boat conformation[11] facilitating an overall compression of the molecular framework (Fig. 2).

Broadened, equatorial and axial ^1H NMR signals of the uncomplexed, rapidly interconverting piperazine ring are enveloped by a triplet assigned to the adjacent aminomethyl moiety (shaded region; Fig. 3). Whereas in the metal-complexed ring, there is a downfield shifted signal attributed to



Scheme 1 *Reagents and conditions*: i, $EtPr^i_2N$, THF, 25 °C, 24 h; ii, HCO_2H, 25 °C, 12 h, then 40–50 °C, 3 h; iii, DCC, 1-HBT, 25 °C, then DMF, amine **3**, 25 °C, 48 h; iv, $Pd(MeCN)_2Cl_2$, MeCN, 25 °C

the equatorial protons ($\Delta\delta$ = 1.4 ppm) with a concomitant upfield shifted signal for the axial protons ($\Delta\delta$ = 0.05 ppm); geminal coupling in each signal suggests a frozen bond configuration in the complex. The triplet assigned to the adjacent methylene moiety is observed to broaden and shift downfield. Further, participation of the more closely juxtaposed amido moiety is evident from an observed upfield shift of the amide proton ($\Delta\delta$ = 0.35 ppm); the more distant amide proton adjacent to the branching centre is only slightly shifted ($\Delta\delta$ = 0.04 ppm downfield) upon complexation.

Similar first order patterns (^{13}C NMR) are found for the metal-free four-directional dendrimers **7a** and **7c**; however, upon complexation, only at early stages of the addition of the Pd salt was the spectral data of interest. Compared to the NMR spectra of the two-directional dendrimers, the signals exhibit enhanced broadening attributed to the presence of four competing adjacent binding sites. As the metal : ligand ratio increases above 1.2 equiv. (4 : 1 maximum), the metal complexes become markedly less soluble in diagnostic solvents further inhibiting NMR complexation monitoring. After addition of 4 equiv. of Pd salt, the resultant bright yellow complex precipitates from MeCN.

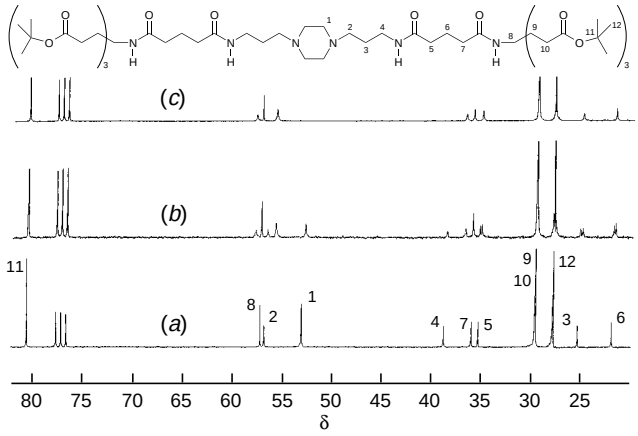


Fig. 1 (*a*) ^{13}C NMR Spectrum of the two-directional ligand **5a**; (*b*) with added 0.5 equiv. $PdCl_2(MeCN)_2$; (*c*) with 1 equiv. of $PdCl_2(MeCN)_2$

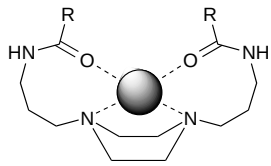


Fig. 2 Pictorial representation of the metal centre depicting the interaction of the juxtaposed amido groups

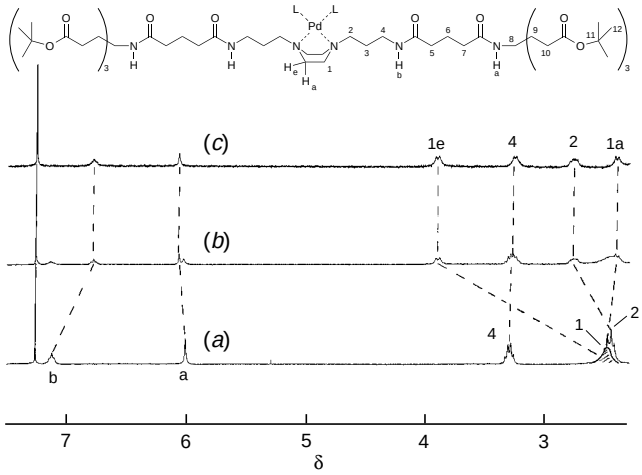


Fig. 3 (*a*) Partial ^{1}H NMR spectrum of ligand **5a** without added metal salt where the shaded region depicts H1 absorption for clarity; (*b*) with 0.7 equiv. of added $PdCl_2(MeCN)_2$; (*c*) with 1 equiv. of added $PdCl_2(MeCN)_2$

The related Cu^{II} complexes were easily obtained by treating absolute EtOH solutions of either **5a,c** or **7a,c** with anhydrous $CuCl_2$ resulting in translucent olive-green solutions that exhibit excellent solubility in common organic solvents (*e.g.* $CHCl_3$). The signals (^{13}C NMR) do not significantly shift in contrast to those of the corresponding Pd complexes but significantly broaden and decrease in intensity due to presence of the new paramagnetic metal centre. For hexaester **5a** containing 1 equiv. of Cu^{II} or dodecaester **7a** containing 4 equiv. of Cu^{II}, all of the internal carbon resonances disappear, while the outer carbon absorptions identifying the branching portion of these macromolecules remain as sharp, first-order patterns.

These specifically localized metal centres afford insight into their use as metallo-unimolecular micelles and metallospheres and superclusters,[12] as well as suggesting the use of dendrimers for ordered networks. Also, similarly constructed bipyridine-based dendrimers are currently under investigation.

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Footnote

† All new compounds gave consistent ^{1}H and ^{13}C NMR spectral and analytical data.

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