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# Dendrimers based on multiple 1,4,7-triazacyclononane derivatives

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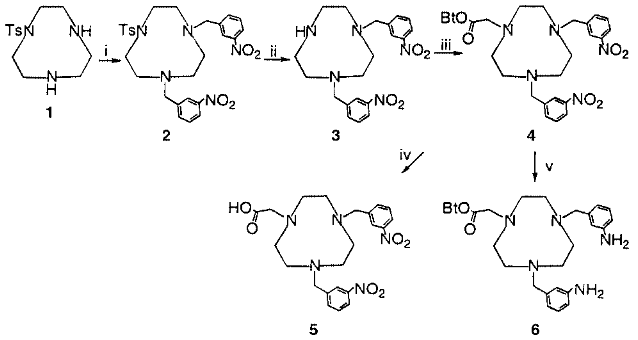
**New first and second generation dendritic poly-1,4,7-triazacyclononane molecules have been prepared and shown to coordinate multiple Cu(II) and Ni(II) metal cations.**

The last decade has witnessed an enormous growth in the field of dendrimer chemistry with current interest being stimulated by the discovery of specific functions and novel properties that are a direct consequence of the dendritic architecture.[1] Metallodendrimers[2] in particular have been shown to exhibit novel electrochemical and photophysical properties. With a view to creating new efficient extraction and membrane transporting reagents for transition metals[3] and for the preparation of metal nanoclusters[4,7] we report here, the first examples of dendrimers containing the well established transition metal coordinating ligand, 1,4,7-triazacyclononane.[5]

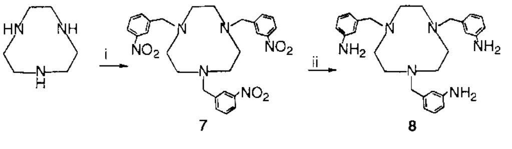
The new key asymmetric functionalised triazacyclononane branching synthons **5** and **6** required for convergent and divergent syntheses of the target dendritic macrocyclic molecules were prepared as shown in Scheme 1. The reaction of **1**[5] with 2 equiv. of 3-nitrobenzyl chloride in the presence of $K_2CO_3$ in MeCN solution gave **2** in 90% yield. Detosylation of **2** using sulfuric acid produced **3** in 50% yield. Refluxing **3** with 1 equiv. of butyl bromoacetate in the presence of $K_2CO_3$ afforded **4** as a pale yellow solid in 82% yield. Hydrolysis of **4** with formic acid gave **5** in 80% yield and reduction of **4** using hydrogen and Raney Ni produced the diamine **6** quantitatively (Scheme 1).



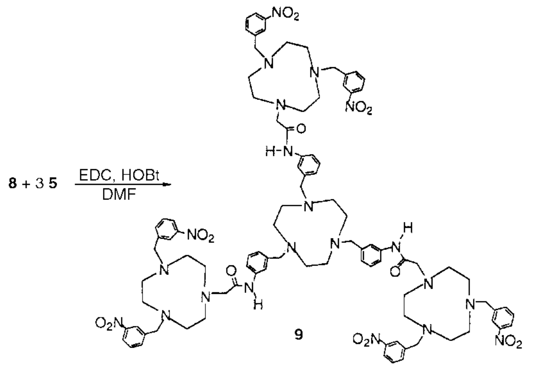
**Scheme 1** *Reagents and conditions*: i, 2 equiv. 3-nitrobenzyl chloride, $K_2CO_3$, MeCN, reflux; ii, conc. $H_2SO_4$, 150 °C; iii, butyl bromoacetate, $K_2CO_3$, MeCN, reflux; iv, formic acid, reflux; v, $H_2$, Raney Ni, MeOH–THF, 55 °C.

The dendritic core triazacyclononane derivative **8** was synthesised *via* reaction of 1,4,7-triazacyclononane with 3 equiv. of 3-nitrobenzyl chloride to give **7** followed by reduction with Raney Ni and $H_2$ (Scheme 2).

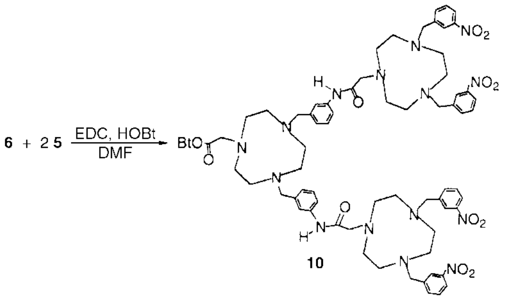
Using a divergent synthetic procedure the first generation dendrimer compound **9** was synthesised *via* a condensation reaction of **8** with 3 equiv. of **5** in DMF in the presence of 1-(3-dimethylaminopropyl)-3-ethylcarbodiimide hydrochloride (EDC) and 1-hydroxybenzotriazole hydrate (HOBt) (Scheme 3). After column chromatography using alumina and $CH_2Cl_2$, **9** was isolated as a yellow solid in 90% yield. The convergent preparative approach is illustrated with the synthesis of **10** from **6** and 2 equiv. of **5** using a similar condensation reaction (Scheme 4).



**Scheme 2** *Reagents and conditions*: i, 3 equiv. 3-nitrobenzyl chloride, $K_2CO_3$, MeCN, reflux; ii, $H_2$, Raney Ni, MeOH–THF, 55 °C.



**Scheme 3** *Reagents and conditions*: EDC, HOBt, DMF, room temp.



**Scheme 4** *Reagents and conditions*: EDC, HOBt, DMF, room temp.

Raney Ni/$H_2$ reduction of **9** and reaction of the corresponding amine **11** with 6 equiv. of **5** in DMF gave the second generation dendrimer **12** in 60% yield (Scheme 5).†

Preliminary transition metal coordination investigations of dendrimers **9** and **12** with Cu(II) and Ni(II) metal cations have been undertaken using UV–VIS spectrophotometric titration experiments. In the absence of dendrimer, MeCN and DMF solutions of copper(II) acetate exhibit a broad d–d absorption at 710 nm. The addition of dendrimers **9** or **12** causes $\lambda_{max}$ to undergo a blue shift to 646 nm which is characteristic of Cu(II) being bound by amine ligands.[5] The spectrophotometric titration curves (Fig. 1) suggest **9** binds four, and **12** ten Cu(II) metal cations, one Cu is coordinates to each triazacyclononane macrocyclic ligand of the respective dendrimer, suggesting the transition metal is complexed at the core, branches and surface dendritic recognition sites.‡ This result contrasts with PAMAM dendrimers which are thought to bind most Cu cations at the outermost tertiary amine donor sites of the dendrimer structure.[7] With Ni(II) preliminary spectrophotometric titration results with the first generation dendrimer **9** indicate as with Cu(II), each

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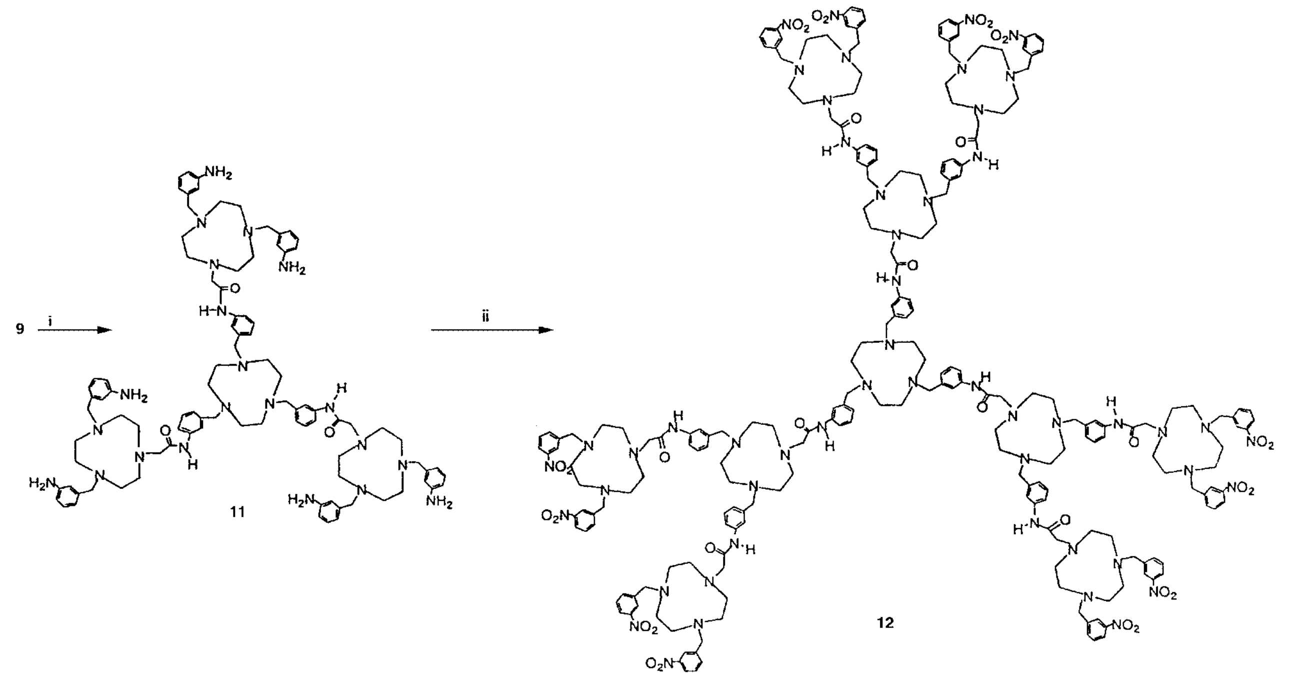

**Scheme 5** *Reagents and conditions*: i, $H_2$, Raney Ni, MeOH–THF, 55 °C; ii, 6 equiv. **5**, EDC, HOBt, DMF, room temp.

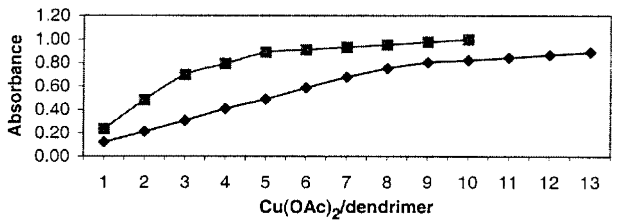

**Fig. 1** Spectrophotometric titration of **8** (■) (3 mM) with $Cu(OAc)_2$ in acetonitrile, absorbance at 646 nm and of **12** (◆) (0.5 mM) with $Cu(OAc)_2$ in DMF, absorbance at 600 nm.

triazacyclononane ligand complexes one Ni(II) cation resulting in 4 $Ni^{2+}$: **9** solution stoichiometry.

Further transition metal coordination chemistry investigations with these novel dendritic poly-triazacyclononane-molecules are in progress.

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## Notes and references

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† All new compounds were characterised by $^1H$ NMR, mass spectrometry and elemental analysis.

*Selected data*: **9**: $^1H$ NMR ($CDCl_3$) $\delta$ 2.76 (16H, s, $CH_2CH_2$, ring), 2.85 (32H, s, $CH_2CH_2$, ring), 3.27 (6H, s, $CH_2$), 3.54 (6H, s, $CH_2$), 3.78 (12H, s, $CH_2$), 7.06–8.18 (36H, m, aromatics), 9.96 (3H, s, amide). $C_{99}H_{111}N_{21}O_{15}$ requires C, 63.36; H, 6.35; N, 16.68. Found: C, 62.95; H, 6.41; N, 16.37%. FAB MS: *m/z* 1764 (M + H).

**10**: $^1H$ NMR ($CDCl_3$) $\delta$ 1.43 (9H, s, $CH_3$), 1.59–2.86 (36H, m, $CH_2CH_2$, ring), 3.27 (2H, s, $CH_2$), 3.52 (4H, s, $CH_2$), 3.60 (4H, s, $CH_2$), 3.78 (8H, s, $CH_2$), 6.46–8.20 (24H, m, aromatics), 9.96 (2H, s, amide). $C_{70}H_{89}N_{15}O_{12}$. FAB MS: *m/z* 1332 (M + H).

**12**: $^1H$ NMR ($CDCl_3$) $\delta$ 2.60–2.86 (120H, m, $CH_2CH_2$, ring), 3.20 (6H, s, $CH_2$), 3.32 (6H, s, $CH_2$), 3.50 (12H, s, $CH_2$), 3.64 (12H, s, $CH_2$), 3.76 (24H, s, $CH_2$), 6.95–8.20 (84H, m, aromatics), 9.96 (9H, s, amide). $C_{225}H_{273}N_{51}O_{33}$. ES MS: *m/z* $(2109.87)^{2+}$, $(1406.9)^{3+}$.

‡ This assumes the absorption coefficients are additive. Also the error in estimating the stoichiometry of metal uptake from the titration data is ±1 or 2.

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