Pentaerythritol-based metallodendrimers

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Two new pentaerythritol-functionalised 2,2′ : 6′,2″-terpyridine (tpy) derivatives have been prepared. One contains four tpy metal-binding domains, whereas the other contains one tpy domain and three pendant CH_2OH groups. The combination of these components with ruthenium-containing building blocks has allowed the specific and stepwise synthesis of tetranuclear and hexadecanuclear metallodendrimers.

There has been an explosion of interest in dendritic systems over the past two decades.[1–5] Although initially regarded as little more than chemical curiosities, dendrimers have developed at the core of new technologies that require nanostructured but molecularly mono-dispersed species as components of molecular or supramolecular machines.[6–10] Dendrimers offer the promise of single, fully characterised and highly spatially defined, molecular species containing a large, but known and controllable, number of identical, repeated, functionalities. Furthermore, the unique surface of the dendrimer offers the possibility of introducing additional surface-generation functionalities to tailor the properties to specific applications or to the targeting of specific molecular or biomolecular species. We are particularly interested in the latter aspect and have developed surface-functionalised metallodendrimers bearing multiple carbaboranyl functionalities.[11–14] In this paper, we describe some key structural units for the development of new metallodendrimers.

Experimental

Materials and techniques

^1H and ^{13}C NMR spectra were recorded on Varian Gemini 300 or Bruker AC250 spectrometers; electron impact (EI) mass spectra were recorded on a VG 70-250 spectrometer and 3-nitrobenzyl alcohol was used as the matrix for the FAB experiments. Laser desorption time-of-flight mass spectra were recorded on a PerSeptive Biosystems Voyager-RP Biospectrometry Workstation using 2,5-dihydroxybenzoic acid as a matrix. IR spectra were recorded on a Genesis Series FTIR spectrophotometer with the samples in compressed KBr discs. Electrochemical measurements were performed using an Eco Chemie Autolab PGSTAT 20 potentiostat. A conventional three-electrode configuration was used, with platinum bead working and auxiliary electrodes and an Ag-AgCl reference. Acetonitrile, freshly distilled from P_4O_{10}, was used as solvent in all cases. The base electrolyte was 0.1 M $[Bu^n{}_4N][BF_4]$, recrystallised twice from ethanol–water and thoroughly dried *in vacuo* over P_4O_{10}. Potentials are quoted *vs.* the ferrocene/ferrocenium couple ($Fc/Fc^+ = 0.0$ V), and all potentials were referenced to internal ferrocene added at the end of each experiment. Ruthenium trichloride trihydrate (Oxchem) was used as supplied; 4′-chloro-2,2′ : 6′,2″-terpyridine was prepared as described earlier.[15]

Synthesis and characterisation

Tetrakis(2,2′ : 6′,2″-terpyridinyl-4′-oxymethyl)methane, 3. Pentaerythritol (38 mg, 0.28 mmol) was added to a suspension of finely powdered potassium hydroxide (370 mg) in DMSO (6 cm^3) and the mixture stirred for 10 min at room temperature. After this period, 4′-chloro-2,2′ : 6′,2″-terpyridine (300 mg, 1.12 mmol) was added and the reaction mixture was heated to 60 °C and stirred at this temperature for 36 h. The resulting suspension was then cooled and treated with water (70 cm^3) to give a white precipitate, which was washed with cold methanol and dried *in vacuo* to give tetrakis(2,2′ : 6′,2″-terpyridinyl-4′-oxymethyl)methane. Yield 223 mg (75%); mp 307–312 °C. Mass spectrum (EI): *m/z* 1062 $[M]^+$, 829 $[M - tpy]^+$, 813 $[M - Otpy]^+$. ^1H NMR ($CDCl_3$): δ 4.76 (8H, s, CH_2), 7.28 (8H, ddd, H^5), 7.78 (8H, dd, H^4), 8.07 (8H, s, $H^{3'}$), 8.53 (8H, d, H^3), 8.64 (8H, d, H^6); (D_2O, DCl): 4.07 (8H, s, CH_2), 7.10 (8H, ddd, H^5), 7.28 (8H, s, $H^{3'}$), 7.64 (8H, 4, H^4), 7.77 (8H, d, H^3), 7.86 (8H, d, H^6). IR: 1581 s, 1561 s, 1467 m, 1441 m, 1402 m, 1357 m, 1252 m, 1204 s, 1092 m, 1033 m, 996 m, 946 w, 863 m, 792 s, 744 m, 658 w cm^{-1}. Anal. calcd (%) for $C_{65}H_{48}N_{12}O_4 \cdot 1.5H_2O$: C 71.7, H 4.7, N 15.4; found C 71.7, H 4.9, N 15.2.

4′-[1,1,1-Tris(hydroxymethyl)methoxy]-2,2′ : 6′,2″-terpyridine, 4. Pentaerythritol (1.50 g, 11 mmol) was added to a suspension of finely powdered potassium hydroxide (3.00 g) in DMSO (20 cm^3) and the mixture stirred for 10 min at room temperature. After this period, 4′-chloro-2,2′ : 6′,2″-terpyridine (2.14 g, 8 mmol) was added and the reaction mixture was heated to 50 °C and stirred at this temperature for 40 h. The resulting suspension was then cooled and treated with water (70 cm^3) to give a white precipitate, which was recrystallised from methanol–THF–H_2O (1 : 1 : 0.25) and dried *in vacuo* to give 4′-[1,1,1-tris(hydroxymethyl)methoxy]-2,2′ : 6′,2″-terpyridine as a white crystalline solid. Yield 1.82 g (62%); mp 204–208 °C. Mass spectrum (EI): *m/z* 368 $[M]^+$. ^1H NMR ($CDCl_3$): δ 3.89 (6H, s, CH_2OH), 4.29 (2H, s, CH_2Otpy), 7.34 (2H, ddd, H^5), 7.85 (2H, dd, H^4), 8.03 (2H, s, $H^{3'}$), 8.60 (2H, d, H^3), 8.68 (2H, d, H^6). IR: 13 229 br s, 1604 m, 1586 s, 1570 s, 1470 s, 1446 s, 1408 s, 1368 m, 1328 m, 1208 s, 1063 s, 1029 s, 866 w, 789 s, 745 m, 628 m cm^{-1}. Anal. calcd (%) for $C_{20}H_{21}N_3O_4 \cdot H_2O$: C 62.3, H 6.0, N 10.9; found C 62.6, H 6.3, N 10.4.

Coordination of 3 with iron(II) chloride. $FeCl_2 \cdot 4H_2O$ (37 mg, 0.189 mmol) was added to a solution of **3** (50 mg, 0.047 mmol) in MeOH–$CHCl_3$ (2 : 1, 25 cm^3) and the mixture stirred at room temperature for 1 h. After this period a clear solution containing a purple solid had been obtained. The solid was collected by filtration and dried to give a solid of constitution $(\mathbf{3})Fe_{4.5}Cl_9 \cdot 18H_2O$. Yield 70%. Mass spectrum (FAB): *m/z* 1135 $[Fe(\mathbf{3})(H_2O)]^+$, 1117 $[Fe(\mathbf{3})]$. IR: 3400 vs br, 1613 s, 1560 m, 1474 s, 1422 m, 1364 s, 1214 m, 1162 w, 1059 w, 1023 m, 792 s, 668 w cm^{-1}. Anal. calcd (%) for

$C_{65}H_{84}N_{12}O_{22}Fe_{4.5}Cl_9$: C 39.9, H 4.3, N 8.6; found C 39.3, H 4.3, N 8.5.

$[\{(tpy)Ru\}_4(3)][PF_6]_8$. $[Ru(tpy)Cl_3]$ (90 mg, 0.2 mmol) was added to a solution of **3** (50 mg, 0.05 mmol) and *N*-ethylmorpholine (2 drops) in ethane-1,2-diol (20 cm^3) and the mixture heated to 120 °C for 18 h. The resulting deep red solution was concentrated to 5 cm^3 volume *in vacuo*, cooled to room temperature and treated with water (15 cm^3). The red solution was filtered and the filtrate treated with ammonium hexafluorophosphate to give a deep red solid, which was purified by chromatography over silica using acetonitrile–saturated aqueous potassium nitrate–water (7 : 1 : 0.5) as eluent. The major red fraction was collected and the solvent removed *in vacuo* to give a red solid, which was dissolved in water and the salt $[\{(tpy)Ru\}_4(\mathbf{3})][PF_6]_8$ by the addition of ammonium hexafluorophosphate. Yield 50 mg (30%). Mass spectrum (MALDI TOF): *m/z* 2852 $[(\mathbf{3})Ru_4(tpy)_4(PF_6)_3F]^+$, 2928 $[(\mathbf{3})Ru_4(tpy)_4(PF_6)_3F_5]^+$, 3016 $[(\mathbf{3})Ru_4(tpy)_4(PF_6)_4F_2]^+$.

$[Ru(4)Cl_3]$. A solution of **4** (0.20 g, 0.54 mmol) and $RuCl_3 \cdot 3H_2O$ (0.15 g, 0.54 mmol) in ethanol (50 cm^3) was heated to reflux for 1 h after which period the reaction mixture was cooled to room temperature and the dark brown solid collected by filtration, washed well with ethanol and water and dried *in vacuo* to give $[Ru(\mathbf{4})Cl_3]$. Yield 0.19 g (61%). Mass spectrum (MALDI TOF): *m/z* 598 $[Ru(\mathbf{4})Cl_3 + Na]^+$.

$[\{(4)Ru\}_4(3)][PF_6]_8$. A mixture of $[Ru(\mathbf{4})Cl_3]$ (0.16 g, 0.27 mmol) and **3** (0.071 g, 0.068 mmol) in ethane-1,2-diol (20 cm^3) was treated with two drops of *N*-ethylmorpholine and the mixture heated to 120 °C for 12 h after which period a deep red solution had been obtained. This solution was cooled and the bulk of the solvent removed *in vacuo* to give a red oily residue. This was dissolved in water (15 cm^3) and treated with ammonium hexafluorophosphate to give the desired $[\{(\mathbf{4})Ru\}_4(\mathbf{3})][PF_6]_8$ as a deep red solid. Yield 0.22 g (80%). Mass spectrum (MALDI TOF): *m/z* 3950 $[[\{(\mathbf{4})Ru\}_4(\mathbf{3})][PF_6]_7]^+$.

$[\{[(tpy)Ru(3)]_3(3)Ru\}_4(3)][PF_6]_{32}$. $[\{(\mathbf{4})Ru\}_4(\mathbf{3})][PF_6]_8$ (0.245 g, 0.06 mmol) was added to a suspension of potassium hydroxide (0.25 g) in DMSO (20 cm^3) and the mixture stirred for 10 min at room temperature. After this time, $[Ru(\mathbf{2})(tpy)][PF_6]_2$ (0.63 g, 0.71 mmol) was added and the mixture stirred at 60 °C for 36 h to give a deep red solution. This was then concentrated to ≈ 5 cm^3 volume by distillation of the solvent under reduced pressure, cooled and dissolved in water (15 cm^3). The red solution was filtered and an excess of ammonium hexafluorophosphate added. The solid was collected by filtration and purified by chromatography over silica using acetonitrile–saturated aqueous KNO_3 solution–water (7 : 1 : 0.5) containing 1% triethylamine as the mobile phase. The major fraction was collected and the solvent removed under reduced pressure. Finally, the red solid so obtained was dissolved in water to give a red solution from which the salt $[\{[(tpy)Ru(\mathbf{3})]_3(\mathbf{3})Ru\}_4(\mathbf{3})][PF_6]_{32}$ was precipitated. Yield 0.22 g (25.5%). Mass spectrum (MALDI TOF): *m/z* 9717 ± 3 $[\{[(tpy)Ru(\mathbf{3})]_3(\mathbf{3})Ru\}_4(\mathbf{3})]^+$.

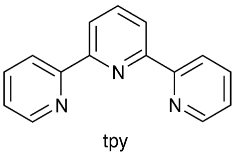
Results and Discussion

Synthetic rationâle—metallodendrimers

The majority of dendritic systems are based upon "carbon" or "organic" chemistry. In effect, this means that the key formation steps in the assembly of the dendrimer rely upon the formation of C—C or C—X bonds. This strategy has many features to recommend it. Once C—C or C—X bonds have been formed, they are usually kinetically stable. Furthermore, the whole range of organic synthetic methodology is available for the preparation of suitable precursor components and the specific formation of the desired C—C or C—X bonds. However, the kinetic stability of the "organic" dendrimers also brings an inherent disadvantage. The principle of microscopic reversibility means that there are likely to be significant kinetic barriers to the formation of the desired C—C or C—X bonds. This is, of course, the origin of the high specificity found in many of the "organic" reactions utilised in dendrimer formation. Unfortunately, the presence of these barriers often leads to long reaction times and very specific and forcing reaction conditions. In addition, the very nature of dendrimers means that the same reaction is repeated many times over within a given generation. In effect, this frequently leads to a "law of diminishing returns" in which reaction within a given generation is not complete. This incomplete growth of a generation provides one of the principal problems associated with both the preparation and the characterisation of dendrimers. In essence, the key questions are "How may I force the key bond formation reactions within a given generation to completion?" and "How can I show that the reaction has gone to completion within a different generation to yield a monodispersed product?".

These problems have led us and others to consider alternatives to "organic" chemistry for the assembly of dendrimers. The rationâle for our approach comes from the observation that ligand replacement reactions at metal centres show an enormous variation in rates. Metal centres may exhibit ligand replacement rates between 10^8 s^{-1} (labile) and 10^{-8} s^{-1} (inert). The factors that control the rates of ligand exchange are particularly well understood for transition metal complexes and may be rationalised in terms of the metal ion electronic configuration and the ligand structure. With this knowledge, we considered that the use of donor–acceptor interactions involving transition metal centres might provide a useful alternative to C—C or C—X bond formation reactions in the assembly of dendrimers. In particular, we considered that rapid reactions involving labile metal centres might allow complete growth of any given generation to give a monodispersed species. Furthermore, judicious choice of labile or inert metal centres should allow control over the reactivity or specificity of the system, although, in practice, specificity in metal complexation processes is effectively controlled by the number, the spatial arrangement and the type of donor atoms involved. We originally introduced the term metallodendrimer to describe a dendrimer in which the key assembly step involved the formation of metal–ligand bonds but we have since extended the term to include those dendrimers in which a metal is incorporated anywhere in the structural framework of the dendrimer.[12,16–21]

When we came to apply this approach to the development of a synthetic strategy for the preparation of metallodendrimers we recognised that the key components were multinucleating ligands that could be linked together by coordination to metal centres. In order to control the overall growth of the dendrimer, we considered that these ligands should be partitioned into individual metal-binding domains, where a metal-binding domain is a group that is readily recognised as a conventional ligand. The synthetic problem then becomes one of preparing organic ligands that contain a number of metal-binding domains covalently linked one to another. The spatial separation of these metal-binding domains should be controlled so as to remove any ambiguity in the coordination



tpy

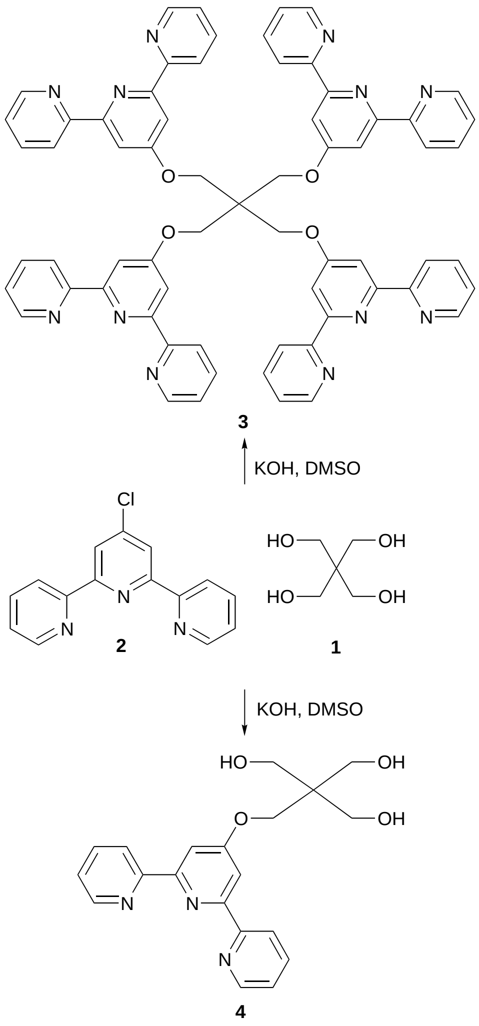
mode. We have chosen to adopt the 2,2′ : 6′,2″-terpyridine (tpy) metal-binding domain as our motif of choice on the basis of its favourable stereogenic properties.[22,23] We note here that other workers have adopted didentate 1,10-phenanthroline,[24] 2,2′-bipyridine,[25–30] porphyrin,[31,32] amine[33,34] or metallocene[35] amongst other domains.

Initial studies of species containing multiple tpy motifs by us[14,22,23,36–48] and others[49–53] concentrated upon the design of ligands in which rigid spacers were introduced between the metal-binding domains and lead to the formation of a series of linear, starburst or closed cyclic structures. More recently we have introduced ligands with a degree of flexibility[12,16–18,54,55] and it is this feature that we wish to develop in this paper.

Ligand design and synthesis

We decided to choose pentaerythritol **1** as our starting point for the metallodendrimers. This provides a convenient and cheap building block bearing four functionalised side-chains distributed about a tetrahedral carbon centre. The pendant hydroxy groups are nucleophilic and reaction with electrophilic reagents should allow the addition of metal-binding domains to these sites. Our electrophile of choice was 4′-chloro-2,2′ : 6′,2″-terpyridine **2**, which we have previously shown to react with a variety of nucleophiles[12–14,17,18,21,22,54] in both the free and coordinated forms. Our initial multi-domain ligand was **3**, in which four tpy metal-binding domains were attached to the pentaerythritol core. We found that an excess of **2** reacted cleanly with **1** in the presence of KOH in DMSO solution to give the desired tetrafunctionalised system as a white solid in 75% isolated yield. The new ligand was fully characterised by conventional methods and exhibited the expected parent ion in its mass spectrum (*m*/*z* 1062). The ^{1}H NMR spectrum of **3** in both $CDCl_3$ and DCl solution fully confirmed the overall high symmetry of the molecule. In both solvents, a single tpy environment was observed and the four methylene groups were seen as a single singlet (δ 4.76 in $CDCl_3$, δ 4.07 in DCl) The differences between the spectra in the two solvents are in accord with the protonation of the pendant tpy domains.

A second ligand **4** was prepared from the same two reactants. The reaction of **2** with an excess of **1** in DMSO in the presence of KOH gave **4** as a white crystalline solid in high yield. The new ligand exhibited a parent ion in its mass spectrum. The ^{1}H NMR spectrum of **4** clearly indicates the structure. A single tpy domain is observed, with chemical shifts almost identical to those of **3**. The most characteristic feature is the observation of two methylene environments in a ratio of 3 : 1 at δ 3.89 and 4.29 corresponding to the CH_2OH and CH_2Otpy methylene groups, respectively. Once again, the methylene groups are observed as singlets. The synthetic details for the preparation of the ligands are presented in Scheme 1.



Scheme 1

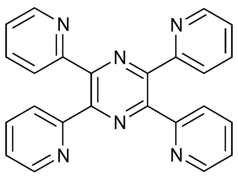
Preliminary coordination studies with 3

These ligands were designed for the assembly of metallodendrimers using kinetically inert metal centres, and we considered that interactions with labile metal centres would be likely to lead to the formation of insoluble polymeric species of variable constitution. However, although our experience with ligands such as **5**[15] and **6**[48] suggested that polymers were to be expected, spectacular examples of the formation of discrete molecular species from the interaction of multi-domain ligands with labile metal centres abound and we felt that we should investigate such possibilities.

The reaction of **3** with a solution of iron(II) chloride in methanol resulted in the immediate precipitation of a purple solid of approximate composition (**3**)$Fe_{4.5}Cl_9 \cdot 18H_2O$. The large amount of water suggests that a very open coordination network has been formed, but we can say little more about this material. The IR spectrum of the compound exhibited the expected absorptions assigned to coordinated tpy domains and a very strong absorption at 3400 cm^{-1} compatible with the presence of large amounts of lattice water. Mass spectrometry showed fragments such as Fe(**3**) but no identifiable larger components. These preliminary results suggested that controlled assembly of dendritic systems with labile metal ions and **3** would not be possible.

Controlled assembly of metallodendrimers with inert metal centres

In view of the results above, we concentrated upon a stepwise assembly methodology using kinetically inert metal centres. In this paper we describe a divergent approach in which each generation is built sequentially. The key to this approach is the use of {Ru(tpy)Cl_3} units. These contain a kinetically inert d^5 ruthenium(III) centre bearing one chelating tridentate and



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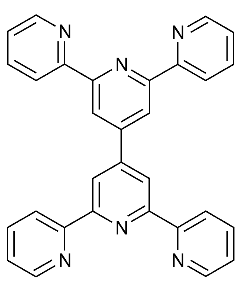

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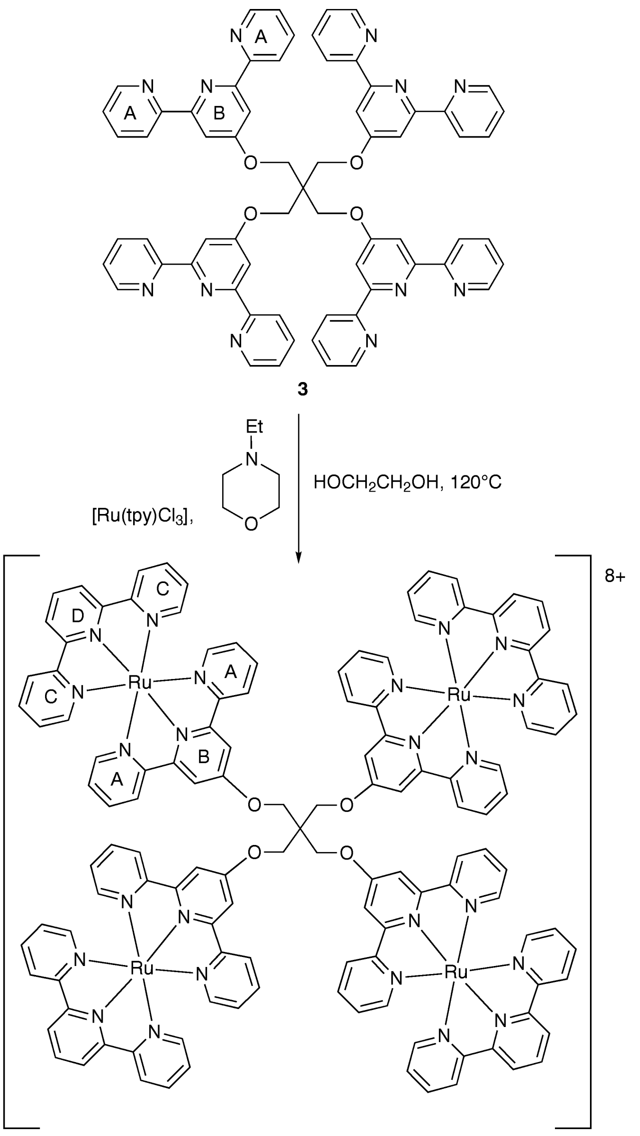
three monodentate ligands. Under forcing conditions, only the monodentate ligands are likely to be replaced. When two tpy domains are coordinated to a ruthenium centre the ligand field is sufficiently strong that a low-spin d^6 ruthenium(II) state is strongly favoured and reduction to ruthenium(II) is the usual consequence of the reaction of a $\{Ru(tpy)Cl_3\}$ unit with a second tpy domain. In order to ensure the formation of the low-spin system, the reactions are often conducted in a reducing solvent or in the presence of a mild reducing agent.

The reaction of one equivalent of **3** with four equivalents of $[Ru(tpy)Cl_3]$ in ethane-1,2-diol in the presence of *N*-ethylmorpholine as a reducing agent resulted in the formation of a deep red solution from which a red hexafluorophosphate salt could be precipitated (Scheme 2). Purification by column chromatography gave $[\{(tpy)Ru\}_4(\mathbf{3})][PF_6]_8$ as a deep red solid in 30% yield. We have previously commented on the problems associated with the conventional microanalysis of ruthenium oligopyridine complexes, which lead to the observation of low carbon values due to the formation of refractory ruthenium carbides and these problems are exacerbated in multinuclear ruthenium species. Microanalytical data for these compounds are consistently between three and five percent too low in the carbon figure. Furthermore, the very nature of the repeated units in dendritic structures means that microanalysis is no longer a good method for the establishment of the purity or the constitution of metallodendrimers. The addition of each subsequent generation has only fractional effects upon the ratios of component atoms.

The MALDI TOF mass spectrum of $[\{(tpy)Ru\}_4(\mathbf{3})][PF_6]_8$ exhibited a series of peaks at *m/z* 2852 $[(\mathbf{3})Ru_4(tpy)_4(PF_6)_3F]^+$ 2928 $[(\mathbf{3})Ru_4(tpy)_4(PF_6)_3F_5]^+$, and 3016 $[(\mathbf{3})Ru_4(tpy)_4(PF_6)_4F_2]^+$. Although no parent ion was observed, all of the observed fragmentation peaks contain four $\{Ru(tpy)\}$ subunits. Orange acetonitrile solutions of $[\{(tpy)Ru\}_4(\mathbf{3})][PF_6]_8$ exhibit a MLCT absorption at 482 nm (ε 60 × 10^{-3}), which may be compared with the mononuclear model compound $[Ru(tpy)(EtOtpy)][PF_6]_2$ (EtOtpy = 4′-ethoxy-2,2′ : 6′,2″-terpyridine) with an absorption at 479 nm (ε 15.2 × 10^{-3}).[57] The equivalence of the four terminal $\{Ru(tpy)_2\}$ domains comes from the observation of a single fully reversible ruthenium(II)/(III) process at + 0.816 V {*cf.* $[Ru(tpy)(EtOtpy)]^{2+}$, +0.834 V,[57] potentials quoted *vs.* Fc/Fc^+}.

The primary evidence for the complete growth of the first metallated generation comes from the ^1H NMR spectrum of a CD_3CN solution of $[\{(tpy)Ru\}_4(\mathbf{3})][PF_6]_8$ (Fig. 1). This immediately indicates the very high symmetry of the product.



Scheme 2

The CH_2 groups appear as a sharp singlet at δ 5.53. No resonances are observed in the δ 4.0–5.0 region where any non-coordinated CH_2Otpy methylene resonances would be expected. Two tpy environments are observed, corresponding

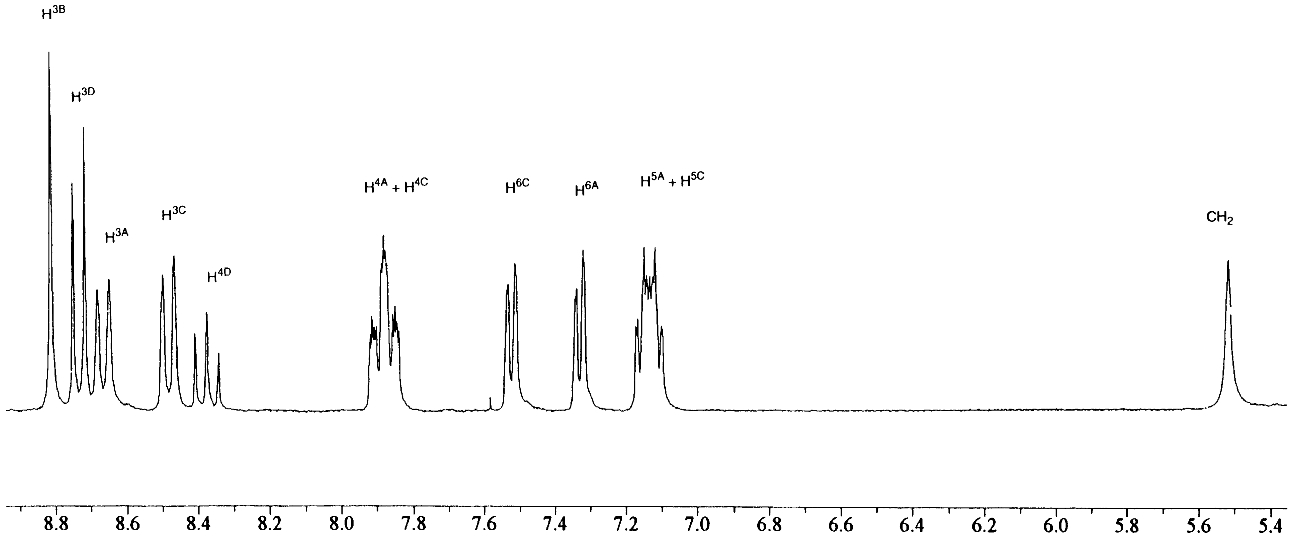
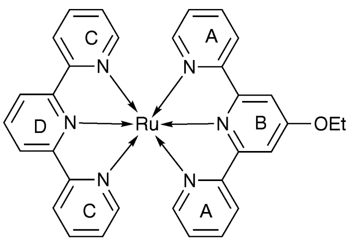


Fig. 1 250 MHz ^1H NMR spectrum of a CD_3CN solution of $[\{(tpy)Ru\}_4(\mathbf{3})][PF_6]_8$ showing the assignments



[Ru(tpy)(EtOtpy)]$^{2+}$

to the terminal tpy ligand and the Otpy groups. These are in a 1 : 1 ratio and the spectrum was fully assigned by means of a COSY spectrum (Fig. 2) and by analogy with the model compound [Ru(tpy)(EtOtpy)][PF$_6$]$_2$.[57] The chemical shifts of the various protons together with the reference compound [Ru(tpy)(EtOtpy)][PF$_6$]$_2$ are presented in Table 1. Worthy of note is the down field shifting of the protons on the "inside" of the dendrimer.

We were now at the stage to extend into the second generation of the metallodendrimer. The reaction of **4** with ruthenium trichloride in ethanol yielded a dark brown precipitate of [Ru(**4**)Cl$_3$], which was not further purified. These adducts of 2,2′ : 6′,2″-terpyridines with ruthenium trichloride are rather poorly characterised species. We merely note here that the MALDI TOF mass spectrum exhibits a parent ion at *m*/*z* 598 corresponding to [Ru(**4**)Cl$_3$ + Na]$^+$. This compound is of importance because it possesses three pendant hydroxy groups for subsequent functionalisation and a metal centre that can coordinate to a second tpy metal-binding domain.

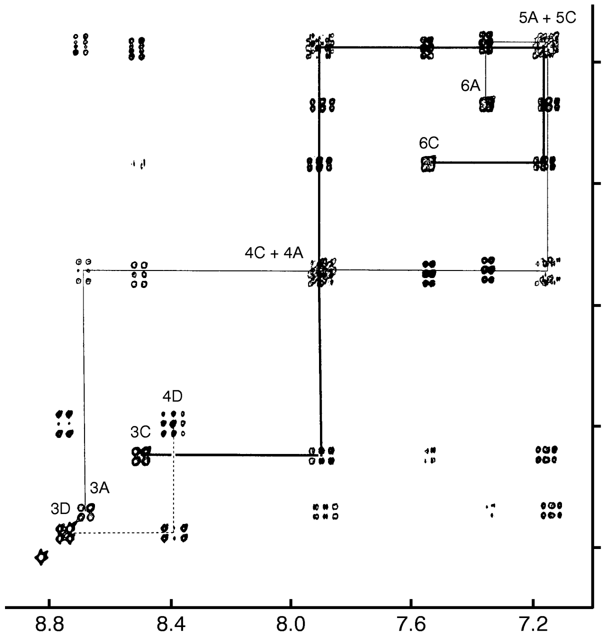
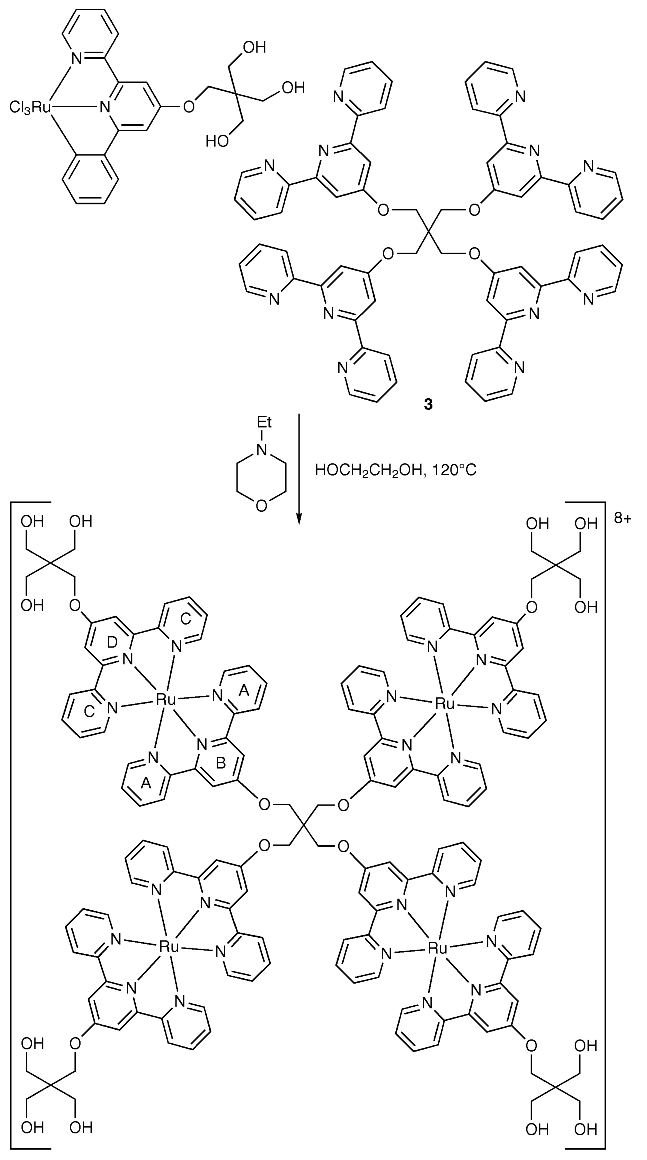


Fig. 2 250 MHz ^{1}H NMR COSY spectrum of a CD$_3$CN solution of [{(tpy)Ru}$_4$(**3**)][PF$_6$]$_8$

Table 1 ^{1}H NMR spectroscopic data for CD$_3$CN solutions of [{(tpy)Ru}$_4$(**3**)][PF$_6$]$_8$ and the model compound [Ru(tpy)(EtOtpy)][PF$_6$]$_2$

	Proton			
Compound	6	5	4	3
[{(tpy)Ru}$_4$(**3**)][PF$_6$]$_8$				
Ring A	7.33	7.13	7.88	8.67
Ring B				8.81
Ring C	7.52	7.15	7.88	8.48
Rind D			8.37	8.74
[Ru(tpy)(EtOtpy)][PF$_6$]$_2$				
Ring A	7.37	7.13	7.88	8.48
Ring B				8.27
Ring C	7.33	7.15	7.91	8.48
Ring D			8.40	8.34



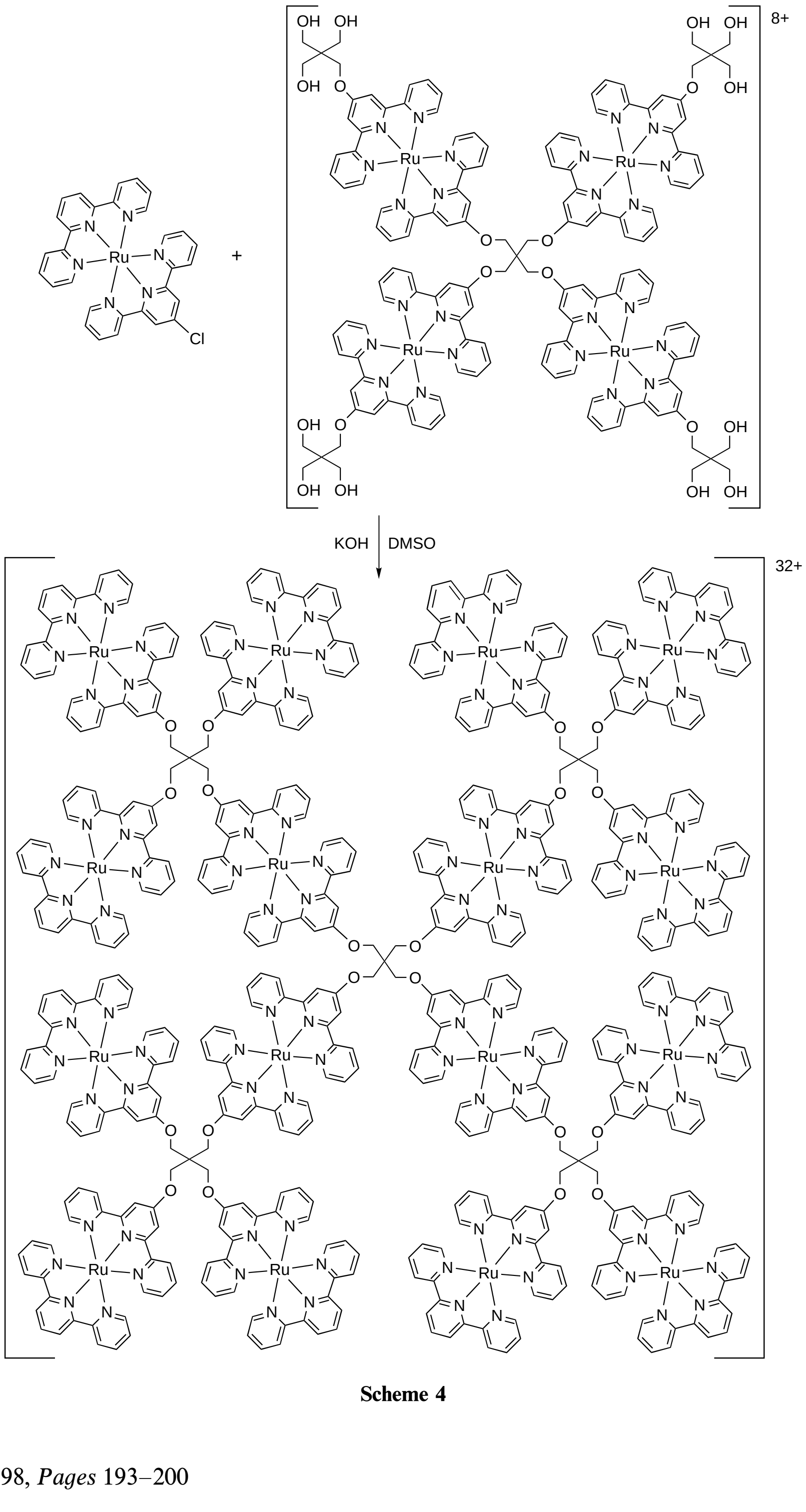
Scheme 3

The combination of [Ru(**4**)Cl$_3$] with **3** provides the crucial growth step that will lead to the second metal-containing generation. The reaction of [Ru(**4**)Cl$_3$] with **3** was conducted under identical conditions to the analogous reaction with [Ru(tpy)Cl$_3$] to give, after work-up, [{(**4**)Ru}$_4$(**3**)][PF$_6$]$_8$ as a deep red solid in 80% yield (Scheme 3). This new complex is structurally closely related to [{(tpy)Ru}$_4$(**3**)][PF$_6$]$_8$ but bears on the surface a total of twelve nucleophilic hydroxy groups.

Primary characterisation of the tetranuclear species comes from the MALDI TOF mass spectrum, which exhibits a highest mass peak at *m*/*z* 3950 corresponding to [[{(**4**)Ru}$_4$(**3**)][PF$_6$]$_7$]$^+$. In contrast to that of [{(tpy)Ru}$_4$(**3**)][PF$_6$]$_8$, the ^{1}H NMR spectrum of a CD$_3$CN solution of this complex is slightly broadened, possibly indicative of a complex and dynamic intramolecular hydrogen-bonding process. However, two singlets are clearly observed at δ 8.85 and 8.77, corresponding to the H^3 of rings B and D. Although the remaining aromatics are not sufficiently wellresolved for a full assignment, H^{5A} and H^{5C} are observed overlapping at δ 7.30, H^{6A} and H^{6C} at δ 7.8, H^{4A} and H^{4C} at δ 8.0, whilst H^{3A} and H^{3C} are in the region of δ 8.9. The most characteristic feature is the appearance of the various methylene groups. A total of three different types of methylene groups are expected in [{(**4**)Ru}$_4$(**3**)][PF$_6$]$_8$. The innermost methylene groups of the pentaerythritol core, the CH_2O groups directly attached to the D ring, and the terminal CH_2OH groups are expected in a ratio of 8 : 8 : 24 and such a ratio is indeed observed. The central pentaerythritol methylene protons are observed as a singlet at δ 5.6 and the CH_2O group directly attached to the D ring is observed at δ 5.2, whilst the terminal CH_2OH methylene protons are found as a singlet at δ 4.62. The chemical shift of the central core corresponds well to that observed in the similarly charged complex [{(tpy)Ru}$_4$(**3**)][PF$_6$]$_8$.

To incorporate the next metal-containing generation, it is now necessary to react the surface generation hydroxy groups of [{(**4**)Ru}$_4$(**3**)][PF$_6$]$_8$ with a suitable electrophile. Although the logical propagation step would involve reaction with **2**, we have noted earlier[54] that the conditions necessary for formation of the new C—O bond (KOH, DMSO) lead to competitive cleavage of inner generation ether linkages. Accordingly, we decided to use a metal-activated electrophile to incorporate the metal-containing generation in a single step. We have previously shown that the coordination of 4-halopyridines to transition metal centres dramatically activates the 4-position to attack by nucleophiles.[54,58,59] Accordingly, we decided to react [{(**4**)Ru}$_4$(**3**)][PF$_6$]$_8$ not with **2** but with [Ru(**2**)(tpy)][PF$_6$]$_2$.

The reaction of [{(**4**)Ru}$_4$(**3**)][PF$_6$]$_8$ with [Ru(**2**)(tpy)][PF$_6$]$_2$ in DMSO containing KOH at 60 °C resulted in the formation of a deep red solution from which the hexadecanuclear complex [{[(tpy)Ru(**3**)]$_3$(**3**)Ru}$_4$(**3**)][PF$_6$]$_{32}$ was isolated in 25% yield after chromatographic purification (Scheme 4). The first point to note about this



Scheme 4

species is that, despite that +32 charge on the cation, the complex is soluble in acetonitrile and polar organic solvents. Chromatographic analysis indicates a mono-dispersed species, and the mobile phases that we used (aqueous KNO_3, acetonitrile) are optimised to separate compounds on the basis of their charge. Accordingly, we are confident that the isolated species represents complete functionalisation of the surface generation with the second metal-containing generation.

The ^1H NMR spectrum of the complex $[\{[(tpy)Ru(\mathbf{3})]_3(\mathbf{3})Ru\}_4(\mathbf{3})][PF_6]_{32}$ in acetonitrile solution exhibits a large number of sharp and overlapping resonances in the aromatic region corresponding to the 332 aromatic protons in 21 different environments. We have, as yet, been unable to resolve this spectrum by COSY spectroscopy. Three separate methylene signals are observed, but these are broadened and relaxation effects have prevented us from obtaining reliable integrals. The best characterisation of the complex comes from the MALDI TOF mass spectrum, which exhibits a high mass peak corresponding to $[\{[(tpy)Ru(\mathbf{3})]_3(\mathbf{3})(Ru\}_4(\mathbf{3})]^+$ at m/z 9717 ± 3.

Although all of these complexes are electrochemically active, we have only observed a single ruthenium(II)/(III) process in each case. We are currently investigating this phenomenon; we are presently uncertain whether this represents a multiple electron process in which all of the ruthenium centres undergo electron transfer at the same potential or whether we are observing dramatic differences in the rate of electron transfer to inner generations. The electrochemical behaviour is complicated by adsorption processes and we have been unable to quantify the processes.

Conclusion

We have shown that high nuclearity metallodendrimers may be prepared from pentaerythritol cores functionalised with 2,2′ : 6′,2″-terpyridine metal-binding domains. Extensions to this work will be reported involving the use of alternative cores and the use of protected derivatives of **4** to allow the growth of third and higher metal-containing generations. We are also investigating these nanostructured species by electron microscopy.

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