

# Synthesis, Electrochemistry, and Interactions with $\beta$ -Cyclodextrin of Dendrimers Containing a Single Ferrocene Subunit Located “Off-Center”

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Two series of dendrimers containing a single ferrocene unit located in the focal point of these macromolecules have been synthesized and characterized. The first series of dendrimers has considerable lipophilic character, with *tert*-butyl ester groups located in their peripheral regions. In contrast, the second series of dendrimers was obtained by the hydrolysis of these peripheral ester groups, yielding water-soluble dendrimers with carboxylic acid groups in their surfaces. The electrochemical properties of these macromolecules were strongly affected by the dendritic groups attached to the ferrocene subunits. Host–guest interactions between the water-soluble dendrimers and the well-known receptor  $\beta$ -cyclodextrin were also investigated. The dendritic groups were found to hamper markedly the formation of inclusion complexes between the cyclodextrin receptor and the dendrimer's ferrocene unit.

## Introduction

The covalent incorporation of redox-active groups into dendrimers<sup>1</sup> is a very active area of chemical research. Numerous reports on dendrimers functionalized with peripheral<sup>2</sup> or core<sup>3</sup> redox groups have been published in the past few years. All these reports focus on essentially symmetric macromolecular structures. For instance, peripheral redox groups are normally attached to every branch<sup>2</sup> of the dendrimer structure. Core redox

groups are usually located at<sup>3</sup> or very near<sup>3b</sup> the center of the dendrimer. In some cases, more than one inner redox group is incorporated inside the dendrimer,<sup>3g,n</sup> but in such a way that the structure maintains its overall branching symmetry.

The molecular weight and size of dendrimers has elicited comparisons to proteins.<sup>3i</sup> Therefore, redox-active dendrimers may be measured up, at least formally, to redox proteins. The former have a clear advantage over the latter; that is, dendrimers are robust molecules that do not denature, unlike proteins, in response to certain environmental conditions. On the other hand, although some heme-containing dendrimers exhibit oxygen and carbon monoxide binding affinities that compare favorably to those of hemoglobin and myoglobin,<sup>4</sup> many redox proteins have properties that current dendrimers do not match, such as directional reactivity and selectivity in their electron-transfer reactions.<sup>5</sup> We reasoned that these

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(1) For recent reviews on the fast developing chemistry of dendrimers, see: (a) Zeng, F.; Zimmerman, S. C. *Chem. Rev.* **1997**, *97*, 1681. (b) Fischer, M.; Vögtle, F. *Angew. Chem., Int. Ed. Engl.* **1999**, *38*, 884. (c) Bosman, A. W.; Janssen, H. M.; Meijer, E. W. *Chem. Rev.* **1999**, *99*, 1665. (d) Newkome, G. R.; He, E.; Moorefield, C. N. *Chem. Rev.* **1999**, *99*, 1689.

(2) (a) Moulines, F.; Djakovitch, L.; Boese, R.; Glaguen, B.; Thiel, W.; Fillaut, J.-L.; Delville, M.-H.; Astruc, D. *Angew. Chem., Int. Ed. Engl.* **1993**, *32*, 1075. (b) Alonso, B.; Cuadrado, I.; Morán, M.; Losada, J. J. *Chem. Soc., Chem. Commun.* **1994**, 2575. (c) Bryce, M. R.; Devonport, W.; Moore, A. J. *Angew. Chem., Int. Ed. Engl.* **1994**, *33*, 1761. (d) Fillaut, J.-L.; Linares, J.; Astruc, D. *Angew. Chem., Int. Ed. Engl.* **1994**, *33*, 2460. (e) Alonso, B.; Morán, M.; Casado, C. M.; Lobete, F.; Losada, J.; Cuadrado, I. *Chem. Mater.* **1995**, *7*, 1440. (f) Cuadrado, I.; Morán, M.; Casado, C. M.; Alonso, B.; Lobete, F.; García, B.; Ibsate, M.; Losada, J. *Organometallics* **1996**, *15*, 5278. (g) Lange, P.; Schier, A.; Schmidbaur, H. *Inorg. Chem.* **1996**, *35*, 637. (h) Haga, M.-A.; Ali, M.-M.; Arakawa, R. *Angew. Chem., Int. Ed. Engl.* **1996**, *35*, 76. (i) Valerio, C.; Fillaut, J.-L.; Ruiz, J.; Guittard, J.; Blais, J.-C.; Astruc, D. *J. Am. Chem. Soc.* **1997**, *119*, 2588. (j) Cuadrado, I.; Casado, C. M.; Alonso, B.; Morán, M.; Losada, J. *J. Am. Chem. Soc.* **1997**, *119*, 7613. (k) Bodige, S.; Torres, A. S.; Maloney, D. J.; Tate, D.; Kinsel, G. R.; Walker, A. K.; MacDonnell, F. M. *J. Am. Chem. Soc.* **1997**, *119*, 10364. (l) Takada, K.; Diaz, D. J.; Abruña, H. D.; Cuadrado, I.; Casado, C. M.; Alonso, B.; Morán, M.; Losada, J. *J. Am. Chem. Soc.* **1997**, *119*, 10763. (m) Serroni, S.; Juris, A.; Venturi, M.; Campagna, S.; Resino, R. I.; Denti, G.; Credi, A.; Balzani, V. *J. Am. Chem. Soc.* **1997**, *119*, 1227. (n) Newkome, G. R.; He, E. *J. Mater. Chem.* **1997**, *7*, 1237. (o) Wang, C.; Bryce, A.; Batsanov, A. S.; Goldenberg, L. M.; Howard, J. A. K. *J. Mater. Chem.* **1997**, *7*, 11189. (p) González, B.; Casado, C. M.; Alonso, B.; Cuadrado, I.; Morán, M.; Wang, Y.; Kaifer, A. E. *Chem. Commun.* **1998**, 2569. (q) Storrer, G.; Takada, K.; Abruña, H. D. *Langmuir* **1999**, *15*, 872.

(3) (a) Dandliker, P. J.; Diederich, F.; Gross, M.; Knobler, C. B.; Louati, A.; Sadford, E. M. *Angew. Chem., Int. Ed. Engl.* **1994**, *33*, 1739. (b) Newkome, G. R.; Guthrie, R.; Moorefield, C. N.; Cardullo, F.; Echegoyen, L.; Perez-Cordero, E.; Luftmann, H. *Angew. Chem., Int. Ed. Engl.* **1995**, *34*, 2023. (c) Dandliker, P. J.; Diederich, F.; Gisselbrecht, J.-P.; Louati, A.; Gross, M. *Angew. Chem., Int. Ed. Engl.* **1995**, *34*, 2725. (d) Chow, H.-F.; Chan, I. Y.-K.; Chan, D. T. W.; Kwok, R. W. M. *Chem. Eur. J.* **1996**, *2*, 1085. (e) Sadamoto, R.; Tomioka, N.; Aida, T. *J. Am. Chem. Soc.* **1996**, *118*, 3978. (f) Bhyrappa, P.; Young, J. K.; Moore, J. S.; Suslick, K. S. *J. Am. Chem. Soc.* **1996**, *118*, 5708. (g) Narayanan, V. V.; Newkome, G. R.; Echegoyen, L. A.; Pérez-Cordero, E. *Polymer Preprints* **1996**, *37*, 419. (h) Gorman, C. B.; Parkhurst, B. L.; Su, W. Y.; Chen, K.-Y. *J. Am. Chem. Soc.* **1997**, *119*, 1141. (i) Dandliker, P. J.; Diederich, F.; Zingg, A.; Gisselbrecht, J. P.; Gross, M.; Louati, A.; Sanford, E. *Helv. Chim. Acta* **1997**, *80*, 173. (j) Balzani, V.; Campagna, S.; Denti, G.; Juris, A.; Serroni, S.; Venturi, M. *Acc. Chem. Res.* **1998**, *31*, 26. (k) Selby, T. D.; Blacstock, S. C. *J. Am. Chem. Soc.* **1998**, *120*, 12155. (l) Pollak, K. W.; Leon, J. W.; Fréchet, J. M. J.; Maskos, M.; Abruña, H. D. *Chem. Mater.* **1998**, *10*, 30. (m) Vögtle, F.; Plevovets, M.; Nieger, M.; Azzellini, G. C.; Credi, A.; De Cola, L.; De Marchis, V.; Venturi, M.; Balzani, V. *J. Am. Chem. Soc.* **1999**, *121*, 6290. (n) Newkome, G. R.; Patri, A. K.; Godínez, L. A. *Chem. Eur. J.* **1999**, *5*, 1445. (o) Gorman, C. B.; Smith, J. C.; Hager, M. W.; Parkhurst, B. L.; Sierzputowska-Gracz, H.; Haney, C. A. *J. Am. Chem. Soc.* **1999**, *121*, 9958.

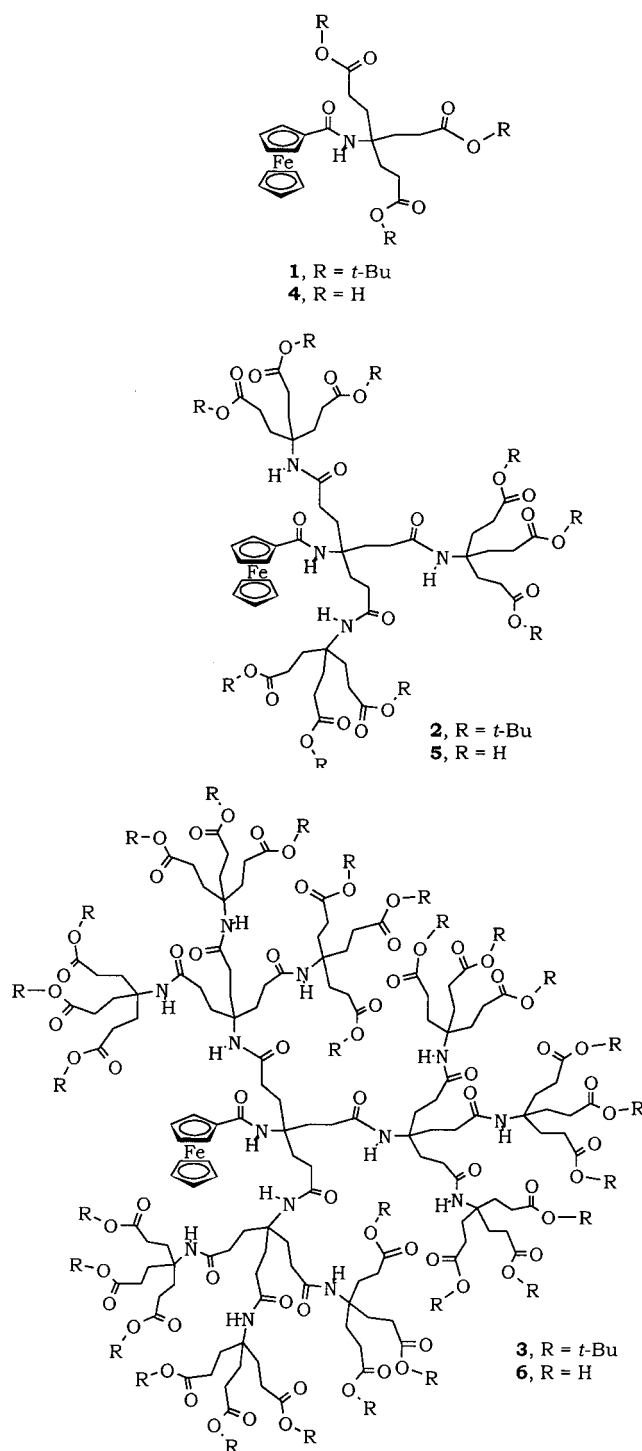
(4) Collman, J. P.; Fu, L.; Zingg, A.; Diederich, F. *Chem. Commun.* **1997**, 193.

desirable properties would be more easily expressed in unsymmetric redox dendrimers, that is, dendrimers that contain a single redox-active group unsymmetrically located in their structures. By positioning the redox subunit "off center", the overall structure loses symmetry, and this lack of symmetry should naturally lead to more directional electron transfer reactivity. In this paper, as a first step in this direction, we describe the synthesis, characterization, and electrochemistry of two new series of unsymmetric dendrimers containing a single ferrocene group covalently attached "off center". The first series of dendrimers (compounds **1–3**) is hydrophobic,<sup>6</sup> while the second one is hydrophilic (**4–6**). For the second series of dendrimers, we also report data on their binding interactions in aqueous solution with  $\beta$ -cyclodextrin ( $\beta$ -CD), a well-established molecular receptor for ferrocene derivatives.<sup>7</sup>

## Results and Discussion

**Synthesis.** The first generation dendrimer **1** was prepared by direct coupling between chlorocarbonylferrocene and Behera's amine.<sup>8</sup> Although **2** and **3** can be prepared from **1** using Newkome's divergent approach,<sup>8</sup> we elected to prepare second- and third-generation building block analogues of Behera's amine and react them directly with chlorocarbonylferrocene to yield **2** and **3**. The preparation of the second-generation building block amine **10** is shown in Scheme 1. Briefly, hydrolysis of the nitrotriester **7**, which is the precursor of Behera's amine and has also been described by Newkome and co-workers,<sup>8</sup> leads to the nitrotriacid **8**. Treatment of this compound with 3 equiv of Behera's amine yields the nitrononaester **9**, which can be reduced with Raney Ni to produce the desired aminononaester **10**. The third-generation building block amine **11** was prepared using a similar procedure, that is, reaction of nitrotriacid **8** with 3 equiv of **10** followed by reduction to give **11** in 77% yield. In all cases, ferrocene was introduced at the end by coupling the corresponding dendritic amine with chlorocarbonylferrocene to produce the *tert*-butyl ester dendrimers **1–3** in moderate yields. Hydrolysis of the peripheral esters in dendrimers **1–3** led to the corresponding carboxylic acid dendrimers **4–6**. All these compounds were characterized by <sup>1</sup>H and <sup>13</sup>C NMR, UV-vis and FT-IR spectroscopy, and MALDI-TOF mass spectrometry.

The purity and degree of monodispersity of the ferrocenyl-functionalized dendrimers depends primarily on the purity and monodispersity of the amine building blocks. The MALDI-TOF spectrum of dendrimer **3** (recorded in an anthracene matrix) is shown in Figure 1 (top) as an illustrative example. Notice that the molecular peak ( $M^+$ ) is the only significant spectral feature for  $m/z$  values up to 12 000. The molecular ion is probably formed by an electron-transfer mechanism.<sup>9</sup> For comparison, the



MALDI-TOF spectrum of the hydrolyzed analogue **6** is shown in Figure 1 (middle). In this case, 2,5-dihydroxybenzoic acid (DHB) was selected as the matrix because the greater polar character of this dendrimer precluded the use of anthracene. The main spectral feature observed is again the molecular peak ( $M + H$ )<sup>+</sup>. The only sign of incomplete hydrolysis of the *tert*-butyl esters of **3** is a tiny peak at  $m/z$  3267 that could correspond to the dendrimer with one residual *tert*-butyl ester. There is no spectral indication of any other hydrolytic failure sequences. There is also a series of peaks at lower  $m/z$  values that may correspond to sequential losses of water from ( $M + H$ )<sup>+</sup> and a cluster of small peaks between  $m/z$  2964 and 3030, which correspond to loss of the ferrocene

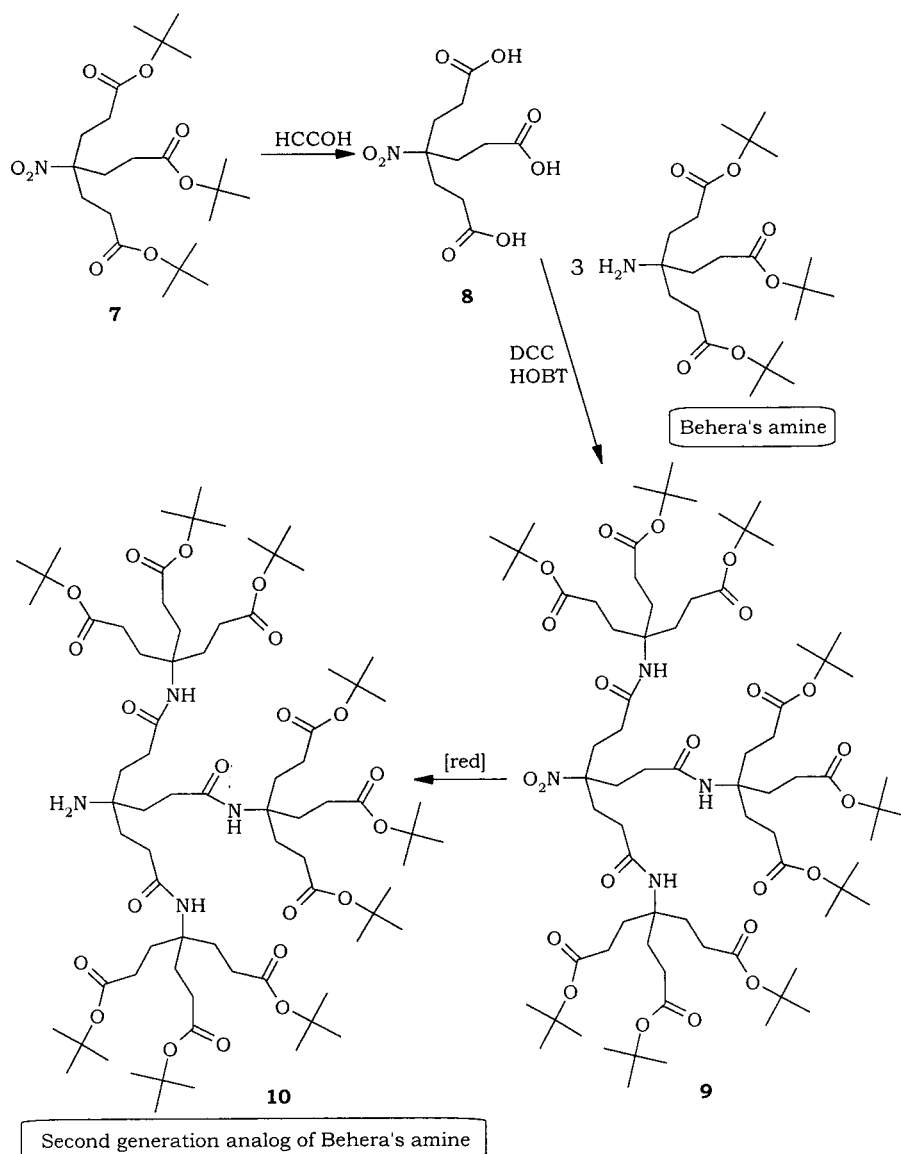
(5) We have recently reported strong molecular orientation effects on the electrochemistry of some of the dendrimers described in this work using gold electrodes covered with cystamine monolayers: Wang, Y.; Cardona, C. M.; Kaifer, A. E. *J. Am. Chem. Soc.* **1999**, *121*, 9756.

(6) For a preliminary report on this series of compounds, see: Cardona, C. M.; Kaifer, A. E. *J. Am. Chem. Soc.* **1998**, *120*, 4023.

(7) Kaifer, A. E. *Acc. Chem. Res.* **1999**, *32*, 62 and references cited therein.

(8) Newkome, G. R.; Behera, R. K.; Moorefield, C. N.; Baker, G. R. *J. Org. Chem.* **1991**, *26*, 7162.

(9) McCarley, T. D.; McCarley, R. L.; Limbach, P. A. *Anal. Chem.* **1998**, *70*, 4376.

**Scheme 1. Synthesis of the Second-Generation Building Block Amine**

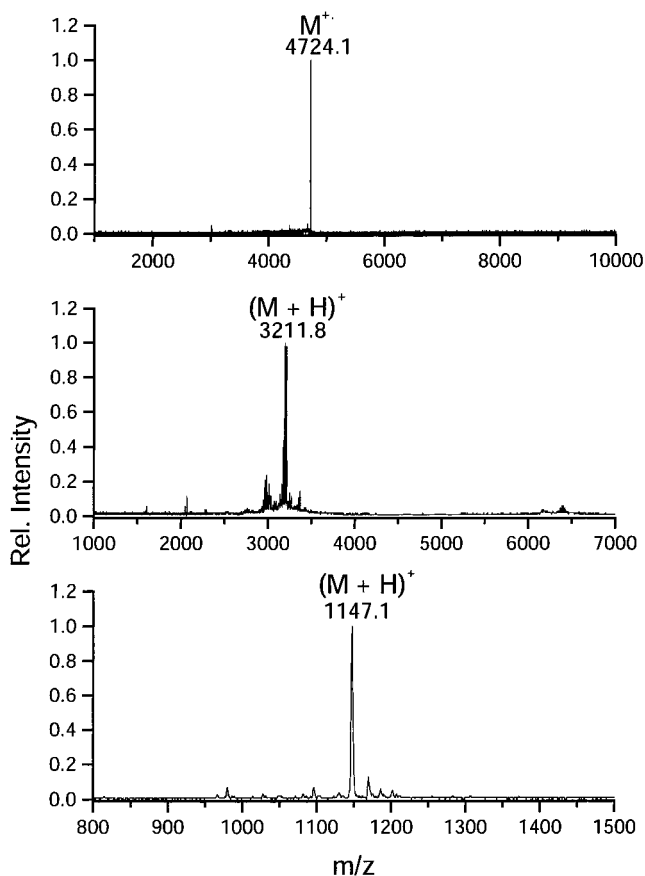
group. These peaks seem to result from fragmentation and not from impurities, as peaks for the building block amine **11** were not detected in the spectrum of the precursor dendrimer **3**.<sup>10</sup> The spectrum of **6** also shows a small peak corresponding to the  $m/z$  value expected for a dimer, which forms in the gas phase probably due to hydrogen bonding between the carboxylic acid "faces" of this dendrimer. The spectrum of the nonaacid, second-generation dendrimer **5** (DHB matrix, Figure 1 (bottom)) is again clearly dominated by the molecular peak.

The synthetic methodology described here affords a series of three dendritic amine building blocks (Behera's amine plus **10** and **11**) that can be utilized to prepare in straightforward one-step reactions a variety of unsymmetrically functionalized dendrimers (Scheme 2). In this work, as represented in the scheme, the attachment of the functional group to the dendrimer structure is done via condensation reactions of the amines with acid chloride functions. However, the highly reactive character

of amines should make the coupling scheme work equally well with a number of other functional groups, such as activated acids, aldehydes, isocyanides, and coordinately unsaturated metal centers. These amine dendrons may thus find a number of applications for the preparation of dendrimer systems containing a single functional group.

**Electrochemistry.** The voltammetric behavior of the ferrocene-containing dendrimers was investigated in  $\text{CH}_2\text{Cl}_2/0.2 \text{ M TBAPF}_6$  (compounds **1–3**) and in  $0.1 \text{ M NaCl}$  aqueous solution (compounds **4–6**) buffered at pH 7 with  $0.05 \text{ M Tris}$ . As anticipated, the electrochemistry of the dendrimers was dominated by the one-electron, reversible oxidation of the ferrocene nucleus. The experimental cyclic voltammograms were fitted to digital simulated ones (see Figure 2 for an example) in order to obtain the voltammetric parameters that describe the electrochemical behavior of each dendrimer. The results are given in Table 1. Representative voltammograms for the **4–6** series are also shown in Figure 3. In both series of dendrimers, the diffusion coefficients ( $D_0$ ) and the standard rate constants for heterogeneous electron transfer ( $k^0$ ) decrease with dendrimer generation. Qualita-

(10) Amine **11** gives a well-defined molecular peak when analyzed in an anthracene matrix. If unreacted or residual **11** were present in our samples of **3**, we should see peaks from this compound in the MALDI-TOF spectra recorded in anthracene matrix.



**Figure 1.** Representative MALDI-TOF mass spectra. (Top) dendrimer **3**, anthracene matrix. (Middle) dendrimer **6**, 2,5-dihydroxybenzoic acid matrix. (Bottom) dendrimer **5**, 2,5-dihydroxybenzoic acid matrix.

tively, these findings agree with other reports on the electrochemical behavior of dendrimers having an electroactive core.<sup>3</sup> The diffusion coefficients decrease with generation due to the anticipated increase in the dendrimer molecular weights and radii. The trend observed with the  $k^{\circ}$  values probably results from the *increasing isolation of the electroactive core from the outer surface* as the dendrimer grows. The higher the generation of the dendrimer, the further away the dendritic bulk keeps the ferrocene subunit from the electrode surface. As the average ferrocene-electrode distance of maximum approach increases with generation, the observed electron-transfer rate decreases. Notice that the  $k^{\circ}$  values are similar for dendrimers of the same generation in the two different media surveyed. For instance, the proximity of the  $k^{\circ}$  values for the pairs **1** and **4**, **2** and **5**, and **3** and **6**, respectively, is noticeable. Since the electron-transfer rate constants are determined by the average ferrocene-electrode distance, a reasonable interpretation for this experimental finding is that the additional steric bulk introduced by the *tert*-butyl groups in the periphery of **1**, **2**, and **3** may be compensated by a more extended, open structure (driven by the solvation of the carboxylates by the water molecules) in **4**, **5**, and **6**. Overall, our data clearly indicate that dendrimer growth extending from one of the cyclopentadienyl rings of the electroactive ferrocene core tends to hinder kinetically the heterogeneous electron-transfer reactions of these dendrimers with the electrode.

The similar variation of the  $D_0$  and  $k^{\circ}$  values observed for the two series of dendrimers (soluble in  $\text{CH}_2\text{Cl}_2$  and

$\text{H}_2\text{O}$ , respectively) contrasts with the differing trends seen in the half-wave potentials ( $E_{1/2}$ , see Table 1). While the  $E_{1/2}$  value for ferrocene oxidation decreases with increasing dendrimer generation in the **1–3** series (in  $\text{CH}_2\text{Cl}_2/0.2$  M TBAPF<sub>6</sub>), the trend is exactly the opposite in the water-soluble series **4–6** (in 0.1 M NaCl buffered at pH 7 with 0.05 M Tris). The potential variation in the latter series is likely to be determined by the relative ease of hydration of the oxidized form of the redox couple, the positively charged ferrocenium. Dendrimer growth appears to interfere with ferrocenium solvation by water molecules, probably because the dendrimer branches start to surround the ferrocene group in the second and in the third generation compounds (**5** and **6**). This interference or hindrance on hydration processes is responsible for the shift to more positive values, which is observed in the half-wave potentials. However, the magnitude of this shift is rather modest, as the total potential change from compound **4** to **6** is +30 mV. In contrast to this, the observed potential shifts are in the opposite direction and larger in magnitude for the series of hydrophobic, *tert*-butyl ester dendrimers; the total potential shift from compound **1** to **3** is –90 mV. This finding means that the generation of positive charge is thermodynamically favored in this dendrimer series by the growth of the dendron covalently attached to one of the cyclopentadienyl rings of the ferrocene residue, a result that cannot be described as intuitive. Other groups have observed comparable potential trends in dendrimers with electroactive cores. The most relevant example is the porphyrin-containing dendrimers, prepared by Diederich and co-workers, that possess similar dendritic structures.<sup>3a,i</sup> A clear rationalization of this potential trend in dendrimers **1–3** is not yet available.

We have also performed some isolated electrochemical measurements with ultramicroelectrodes in order to verify the quality of the parameters given in Table 1. For instance, we used platinum ultramicroelectrodes (4- $\mu\text{m}$  radius) to record current–potential curves corresponding to the electrochemical oxidation of dendrimers **1** and **2** in  $\text{CH}_2\text{Cl}_2/0.2$  M TBAPF<sub>6</sub> solution. The results were analyzed according to the convenient method described by Mirkin and Bard,<sup>11</sup> yielding values of  $0.20 \pm 0.05$  cm/s for **1** and  $0.023 \pm 0.007$  cm/s for **2**. These  $k^{\circ}$  values are in reasonable agreement with those given in Table 1. We could not extend these measurements to the remaining systems as we found highly irreproducible behavior and/or problems associated with adsorptive behavior in some ultramicroelectrode experiments.

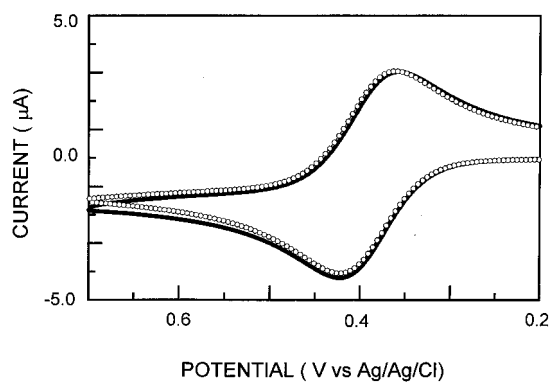
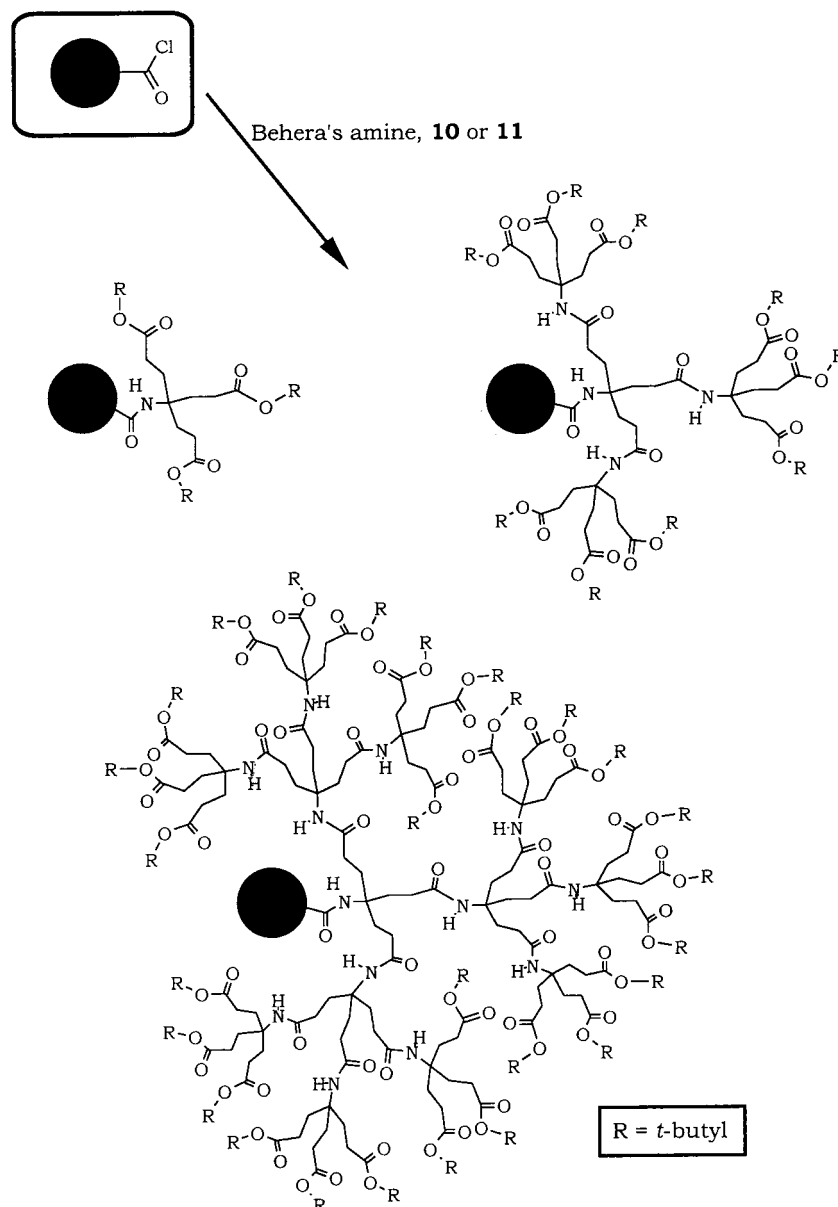
**Binding Interactions with  $\beta$ -CD.** Ferrocene is a well-known guest for binding inside the cavity of the  $\beta$ -CD host.<sup>7</sup> Therefore, we decided to investigate the binding interactions between the ferrocene containing dendrimers described here and  $\beta$ -CD (see Scheme 3). This investigation was constrained to dendrimers **4–6**, since compounds **1–3** are not water-soluble. The host–guest interactions can be conveniently monitored by voltammetric techniques taking advantage of the electroactive character of the ferrocene nucleus. Similar methodology has been utilized in the past by our group<sup>12</sup> and others<sup>13</sup> with simpler CD inclusion complexes. Figure 4A shows

(11) Mirkin, M. V.; Bard, A. J. *Anal. Chem.* **1992**, *64*, 2293.

(12) (a) Mirzozian, A.; Kaifer, A. E. *Chem. Eur. J.* **1997**, *3*, 1052. (b) Wang, Y.; Mendoza, S.; Kaifer, A. E. *Inorg. Chem.* **1998**, *37*, 317.

(13) Matsue, T.; Evans, D. H.; Osa, T.; Kobayashi, N. *J. Am. Chem. Soc.* **1985**, *107*, 3411.

## Scheme 2. One-Step Synthesis of Unsymmetrically Functionalized Dendrimers



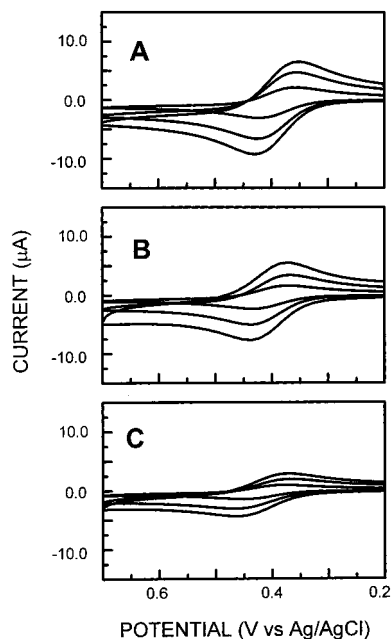
**Figure 2.** Cyclic voltammetric response (continuous line) on glassy carbon (0.018 cm<sup>2</sup>) of a 1.0 mM solution of **4** in 0.1 M NaCl buffered at pH 7 with 0.05 M Tris. Scan rate: 0.2 V/s. The circles represent a simulated voltammogram obtained with the parameters given in Table 1.

the changes observed in the cyclic voltammetric response of the first generation dendrimer **4** upon addition of 7 equiv of  $\beta$ -CD. The presence of the host shifts the

**Table 1.** Structural and Electrochemical Parameters for the Ferrocene-Containing Dendrimers 1–6 at 25 °C

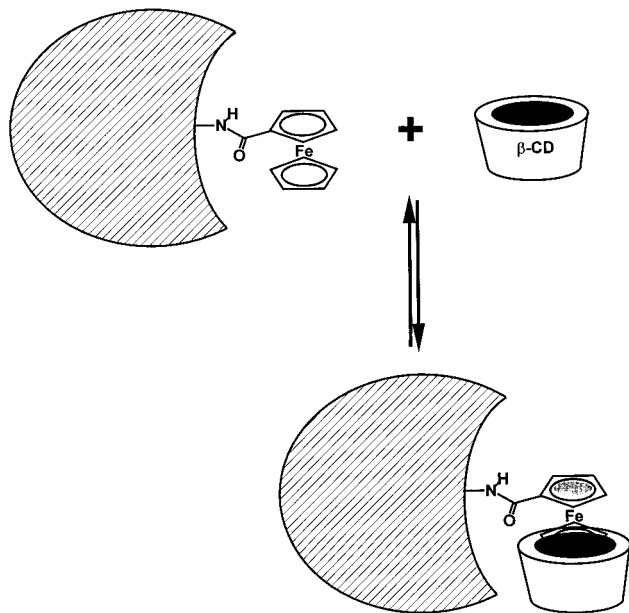
	MW (amu)	medium	$E_{1/2}$ (V vs Ag/AgCl)	$D_0$ ( $10^6 \times$ cm <sup>2</sup> ·s <sup>-1</sup> )	$\alpha$	$k^0$ ( $10^3 \times$ cm·s <sup>-1</sup> )
<b>1</b>	627.6	CH <sub>2</sub> Cl <sub>2</sub>	0.63	9.5 ± 1.0	0.5	80 ± 20
<b>2</b>	1652.0	CH <sub>2</sub> Cl <sub>2</sub>	0.60	4.0 ± 0.5	0.5	17 ± 3
<b>3</b>	4725.0	CH <sub>2</sub> Cl <sub>2</sub>	0.54	2.3 ± 0.3	0.4	5 ± 1
<b>4</b>	459.3	H <sub>2</sub> O (pH 7)	0.39	3.5 ± 0.4	0.5	70 ± 30
<b>5</b>	1147.0	H <sub>2</sub> O (pH 7)	0.41	2.2 ± 0.2	0.5	20 ± 4
<b>6</b>	3210.1	H <sub>2</sub> O (pH 7)	0.42	0.8 ± 0.1	0.5	6 ± 1

apparent half-wave potential to more positive values and causes a considerable decrease on the currents associated with the ferrocene/ferrocenium wave. Both effects clearly reveal the formation of an inclusion complex between  $\beta$ -CD and the ferrocene nucleus. The shift of the  $E_{1/2}$  value in the positive direction reflects the more pronounced CD-induced stabilization of ferrocene compared to that experienced by ferrocenium. The current decrease results from the lower diffusion coefficient of the inclusion complex relative to that of the uncomplexed ferrocene derivative. Similar results have been obtained with many

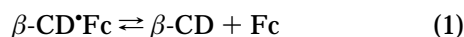


**Figure 3.** Cyclic voltammetric responses on glassy carbon (0.018 cm<sup>2</sup>) of 1.0 mM solutions of (A) **4**, (B) **5**, and (C) **6** in 0.1 M NaCl buffered at pH 7 with 0.05 M Tris. Scan rates: 0.1, 0.5, and 1.0 V/s.

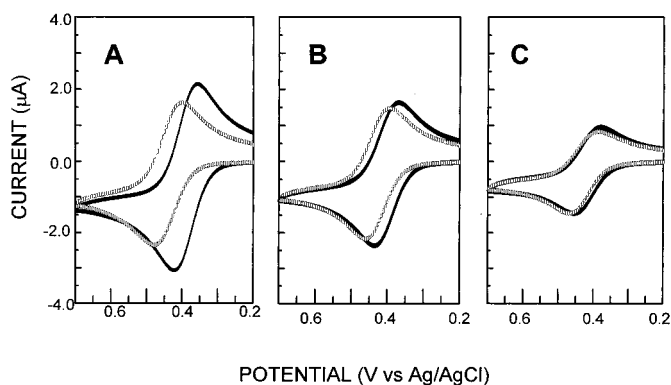
**Scheme 3. Association Equilibrium between Ferrocene-Containing Dendrimer and  $\beta$ -CD**



other ferrocene derivatives.<sup>13,14</sup> The electrochemical oxidation of ferrocene derivatives in the presence of  $\beta$ -CD is widely accepted to proceed through a mechanism of the type



In electrochemical terms, this is a CE mechanism (electron-transfer preceded by a chemical step). Notice that the adoption of this mechanism carries along the



**Figure 4.** Cyclic voltammetric responses on glassy carbon (0.018 cm<sup>2</sup>) of 1.0 mM solutions of (A) **4**, (B) **5**, and (C) **6** in 0.1 M NaCl buffered at pH 7 with 0.05 M Tris. The voltammograms were recorded in the absence (continuous line) and in the presence (open circles) of 7.0 mM  $\beta$ -CD. Scan rate: 0.1 V/s.

**Table 2. Parameters for the Association of Ferrocene-Containing Dendrimers and the  $\beta$ -CD Host at 25 °C in Aqueous Solution**

dendrimer	$D_c$ ( $10^6 \times \text{cm}^2 \cdot \text{s}^{-1}$ )	$K$ ( $\text{L} \cdot \text{mol}^{-1}$ )
<b>4</b>	$2.0 \pm 0.2$	$950 \pm 140$
<b>5</b>	$1.8 \pm 0.2$	$250 \pm 50$
<b>6</b>	$0.2 \pm 0.1$	$50 \pm 10$

implicit recognition that electron transfer does not take place from the inclusion complex; that is, the complex must first dissociate before the electrochemical oxidation reaction.<sup>12–14</sup>

Figure 4B,C shows the corresponding  $\beta$ -CD-induced changes observed with the second and third generation compounds (**5** and **6**). The voltammetric responses in the presence of  $\beta$ -CD can also be simulated using the CE mechanism proposed above. From the optimization of the fit between the simulated and experimental voltammograms, the equilibrium binding constant ( $K$ ) for the complexation process, and the diffusion coefficient of the complex ( $D_c$ ) can be estimated. The resulting values are given in Table 2. As anticipated from the simple inspection of the voltammetric results of Figure 4, the equilibrium binding constant between the dendrimer and  $\beta$ -CD quickly decreases as the dendrimer grows. The first-generation compound exhibits a  $K$  value that is in the low end of the normal range for  $\beta$ -CD complexes of ferrocene derivatives. The  $K$  value is substantially lower for the second-generation compound, while the binding becomes very weak for the third-generation dendrimer. These results strongly suggest that the growth of the dendrimer interferes with the approach to the ferrocene residue and inclusion by the CD host. This finding is in excellent agreement with the variation of  $E_{1/2}$  values observed in this series of dendrimers, which reveals that the ferrocene subunit is at least partially surrounded by the growing dendron in compounds **5** and **6**. It is this steric crowding effect that is responsible for the low stability of the corresponding  $\beta$ -CD inclusion complexes.

**Conclusions.** We present here a synthetic method for the preparation of dendrimers containing a single ferrocenyl residue positioned “off center” in the dendrimer structure. This method can be easily extended to the preparation of other unsymmetric dendrimers containing different functional groups at their focal points. The dendron attached to the ferrocene residue has a pro-

nounced effect on its electrochemical properties and in its ability to function as an effective guest for inclusion complexation by  $\beta$ -CD. Our data suggests that in the third-generation dendrimers (**3** and **6**) the dendritic growth is enough to wrap around and isolate to some extent the ferrocene group from solvent and environmental effects.

### Experimental Section

All chemicals employed were reagent grade (Aldrich or Across) and were used as received. Solvents, such as THF and DMF, were freshly distilled. Column chromatography was performed with Scientific Adsorbents silica gel (63–200  $\mu$ m).  $^1\text{H}$  and  $^{13}\text{C}$  NMR spectra were recorded on a Varian VXR-400 spectrometer; all the chemical shift ( $\delta$ ) values are reported in ppm. MALDI-TOF mass spectra were recorded at the LSU Mass Spectrometry Facility.

The electrochemical behavior of the dendrimers was studied with a Bioanalytical Systems 100 B/W workstation controlled by a 100 MHz Pentium PC, which was also employed to run the Digi-Sim 2.1 software for the digital simulation work. The voltammetric experiments were performed in a 1.0-mL cell equipped with a glassy carbon electrode (0.0078  $\text{cm}^2$  for the esters and 0.018  $\text{cm}^2$  for the acids), a platinum counter electrode, and a Ag/AgCl reference electrode. The esters were dissolved (0.001 M) in HPLC grade dichloromethane containing tetrabutylammonium hexafluorophosphate (Fluka, >99%) as the supporting electrolyte (0.2 M). Prior to its use, this material had been recrystallized twice from an ethanol/ $\text{H}_2\text{O}$  (80:20) mixture. The acids were dissolved (0.001 M) in Tris (Across Reagent ACS) buffer prepared in 0.1 M NaCl (Strem Chemicals, 99.999%). A nitrogen atmosphere was maintained over the solutions throughout the electrochemical experiments.

Cyclic voltammetry (CV) was the primary technique employed to obtain the reported electrochemical parameters. Typical scan rate values of 0.100, 0.200, 0.500, 1.000, and 2.000 V/s were used. The  $K^0$  and  $D$  values were obtained by fitting digital simulations (Digi-Sim 2.1) to the experimental voltammograms throughout the entire range of scan rates surveyed. IR compensation as implemented in the BAS 100 B/W potentiostat was used throughout the experiments and every effort was made to minimize capacitive currents and uncompensated resistance. Osteryoung Square Wave voltammetry was mainly used to verify the half-wave potential values and the purity of the compounds.

The electrochemical titrations with  $\beta$ -cyclodextrin ( $\beta$ -CD) were monitored only at 0.100 V/s except for the ferrocene triacid **4** that was also followed at 0.500, 1.0, 5.0, and 10.0 V/s. Voltammograms taken at  $\beta$ -CD concentrations of 0.001, 0.003, 0.005, and 0.007 M were fitted by digital simulations (Digi-Sim 2.1) to obtain the corresponding binding parameters (equilibrium association constant,  $K$ , and diffusion coefficient for the complex,  $D$ ).

**9 Cascade/(2-Azaethylidene)/(3-Oxo-2-azapentylidene)/tert-Butyl Propanoate (10).** The nitrotriester **7**, precursor of Behera's amine, was hydrolyzed by stirring in 10 mL of 96% formic acid. The formed triacid **8** (2.5 g, 9.0 mmol) was coupled to Behera's amine (11.2 g, 27.0 mmol) in the presence of DCC (5.60 g, 27.1 mmol) and 1-HOBT (1.2 g, 9.1 mmol). The mixture was stirred in 100 mL of dry THF for 6 days at room temperature. The product was filtered, and after evaporation of the solvent, the residue was purified by column chromatography (2:1  $\text{CH}_2\text{Cl}_2/\text{EtOAc}$ ). A portion (7.1 g) of the isolated product (10.1 g, 76%) was reduced (50 psi  $\text{H}_2$ , 60  $^\circ\text{C}$ ) with 18.0 g of activated Raney nickel. After filtration of the catalyst, the solvent was evaporated and traces of it were chased with hexane to procure the product as a white solid (6.0 g, 86%). FT-IR ( $\text{CH}_2\text{Cl}_2$ ): 1724, 1674 ( $\nu(\text{C}=\text{O})$ )  $\text{cm}^{-1}$ .  $^1\text{H}$  NMR ( $\text{CDCl}_3$ )  $\delta$ : 1.41 (s,  $\text{CH}_3$ , 81H); 1.55–2.15 (m,  $\text{CH}_2\text{CH}_2$ , 12H,  $J = 8.9$  Hz); 1.85–2.20 (m,  $\text{CH}_2\text{CH}_2$ , 36H,  $J = 8$  Hz); 6.05 (sb, NH, 3H).  $^{13}\text{C}$  NMR  $\delta$ : 28.1 ( $\text{CH}_3$ ); 29.9, 30.0 ( $\text{CH}_2\text{CH}_2$ ) gen 2; 31.6, 35.3 ( $\text{CH}_2\text{CH}_2$ ) gen 1; 52.7 ( $\text{C}(\text{CH}_2\text{CH}_2)$ ) gen 1; 57.4 ( $\text{C}(\text{CH}_2\text{CH}_2)$ ) gen 2; 80.7 ( $\text{C}(\text{CH}_3)_3$ ); 172.5 (CONH); 172.7 (COOtBu).

MALDI-TOF MS: 1439.13 (100,  $\text{M}^+$ , calcd 1439.91), 1461.23 ( $\text{M} + \text{Na}^+$ ), 1383.1 ( $\text{MH}^+ - t\text{BuH}$ ).

**27 Cascade/(2-Azaethylidene)/(3-Oxo-2-azapentylidene)/(3-Oxo-2-azapentylidene)/tert-Butyl Propanoate (11).** Triacid **8** (0.25 g, 0.90 mmol) was reacted with the second-generation building block amine **10** (4.04 g, 2.81 mmol) in the presence of DCC (0.79 g, 3.8 mmol) and 1-HOBT (0.19 g, 1.4 mmol). The mixture was stirred in 75 mL of dry THF under  $\text{N}_2$  for 6 days at room temperature. The urea byproduct was filtered off, and after evaporation of the solvent, the residue was purified by column chromatography ( $\text{SiO}_2$ , 5:1  $\text{CH}_2\text{Cl}_2/\text{EtOAc}$ ) followed by EtOAc. The recovered product was reduced in a Parr Hydrogenator, 55 psi  $\text{H}_2$ , 60  $^\circ\text{C}$ , with 23.0 g of activated Raney nickel. The catalyst was filtered, and the solvent was removed under reduced pressure and chased with hexane to procure a white solid in a 77% yield (3.12 g). FT-IR (KBr): 3312.77 ( $\nu(\text{N}-\text{H})$ )  $\text{cm}^{-1}$ ; 1732.13 ( $\nu(\text{C}=\text{O})$ )  $\text{cm}^{-1}$ ; 1652.20 ( $\nu(\text{amide-I}, \text{C}=\text{O})$ )  $\text{cm}^{-1}$ ; 1542.13 ( $\nu(\text{amide II}, \text{N}-\text{H})$ )  $\text{cm}^{-1}$ ; 1154.94 ( $\nu(\text{C}-\text{O})$ )  $\text{cm}^{-1}$ .  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$ : 1.4 (s,  $\text{CH}_3$ , 243 H); 1.7–2.4 (m,  $\text{CH}_2\text{CH}_2$ , 156 H); 6.2 (sb, NH, 9H) gen 3; 6.85 (sb, NH, 3H) gen 2.  $^{13}\text{C}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$ : 28.13 ( $\text{CH}_3$ ); 29.81 ( $\text{CH}_2\text{CH}_2$ ) gen 3; 31.52 ( $\text{CH}_2\text{CH}_2$ ) gen 2; 57.37 ( $\text{C}(\text{CH}_2\text{CH}_2)_3$ ) gen 3; 80.37 ( $\text{C}(\text{CH}_3)_3$ ) gen 3; 172.68 (COOtBu). MALDI-TOF MS: 4513.44 (100,  $\text{M}^+$ , calcd 4512.94).

**3 Cascade/Ferrocene[1]/(3-Oxo-2-azapropylidene)/tert-Butyl Propanoate (1).** Ferrocene carboxylic acid (0.372 g, 1.62 mmol) was dissolved in 8.1 mL of 0.2 N NaOH and filtered, and the water was removed under vacuum to complete dryness. The residue was mixed with 5 mL of oxalyl chloride and 20 mL of dry benzene and stirred for 1 h under  $\text{N}_2$ . After removal of the solvent in vacuo, the residue was mixed with Behera's amine (0.687 g, 1.65 mmol) and  $\text{Et}_3\text{N}$  (1.65 mmol, 0.230 mL) in 25 mL of THF. The reaction mixture was stirred at room temperature for 3 days under  $\text{N}_2$ . Removal of the solvent under vacuum procured a brown residue that was dissolved in 75 mL of  $\text{CHCl}_3$ . The organic layer was then extracted with 0.2 N NaOH, 10% HCl, and brine and dried over  $\text{Na}_2\text{SO}_4$ . Purification was accomplished by column chromatography ( $\text{SiO}_2$ ,  $\text{CHCl}_3$ ), and yellow crystals were obtained (0.363 g, 36%) after recrystallization from  $\text{CHCl}_3$ /hexane mixture. FT-IR ( $\text{CH}_2\text{Cl}_2$ ): 1727, 1654 ( $\nu(\text{C}=\text{O})$ )  $\text{cm}^{-1}$ .  $^1\text{H}$  NMR ( $\text{CDCl}_3$ )  $\delta$ : 1.42 (s,  $\text{CH}_3$ , 27H); 2.0–2.3 (m,  $\text{CH}_2$ , 12H,  $J = 7.9$  Hz); 4.2 (s, Fc  $\text{C}_5\text{H}_5$ , 5H); 4.3–4.7 (m, Fc CH, 4H,  $J = 1.7$  Hz); 6.2 (bs, NH, 1H).  $^{13}\text{C}$  NMR  $\delta$ : 28.1 ( $\text{CH}_3$ ); 30.0, 30.4 ( $\text{CH}_2\text{CH}_2$ ); 57.5 ( $\text{C}(\text{CH}_2\text{CH}_2)_3$ ); 68.1, 70.2 (Fc CHCH); 69.6 (Fc  $\text{C}_5\text{H}_5$ ); Fc C-quaternary is under the solvent signal,  $\text{CDCl}_3$ ; 80.6 ( $\text{C}(\text{CH}_3)_3$ ); 169.6 (CONH); 173.1 (COOtBu). UV-vis [ $\lambda_{\text{max}}$ , nm ( $\epsilon$ ,  $\text{M}^{-1}\text{cm}^{-1}$ ),  $\text{CH}_2\text{Cl}_2$ ]: 303 (1002.1); 337 (shoulder); 445 (202.9). MALDI-TOF MS: 627.433 (100,  $\text{M}^+$ , calcd 627.60), 650.441 ( $\text{M} + \text{Na}^+$ ), 666.431 ( $\text{M} + \text{K}^+$ ).

**9 Cascade/Ferrocene[1]/(3-Oxo-2-azapropylidene)/(3-Oxo-2-azapentylidene)/tert-Butyl Propanoate (2).** Starting with ferrocene carboxylic acid (0.164 g, 0.710 mmol), the acid chloride was prepared as described in the procedure above. Then, it was mixed with the second-generation building block amine **10** (1.02 g, 0.706 mmol) and  $\text{Et}_3\text{N}$  (0.72 mmol, 0.10 mL) in 20 mL of THF and stirred for 4 days at room temperature under  $\text{N}_2$ . After evaporation of the solvent, the residue was dissolved in 75 mL of  $\text{CHCl}_3$  and extracted with 0.2 N NaOH, 10% HCl, and brine. The organic layer was then dried over  $\text{Na}_2\text{SO}_4$ . After removal of the solvent, purification was accomplished by column chromatography ( $\text{SiO}_2$ , 3:1  $\text{CHCl}_3/\text{EtOAc}$ ) and an orange foam was obtained (0.36 g, 31%). FT-IR ( $\text{CH}_2\text{Cl}_2$ ): 1726, 1663 ( $\nu(\text{C}=\text{O})$ )  $\text{cm}^{-1}$ .  $^1\text{H}$  NMR ( $\text{CDCl}_3$ )  $\delta$ : 1.4 (s,  $\text{CH}_3$ , 81H); 1.9–2.2 (m,  $\text{CH}_2$ , 36H,  $J = 8$  Hz); 2.0–2.3 (m,  $\text{CH}_2$ , 12H,  $J = 7.3$  Hz); 4.2 (s, Fc  $\text{C}_5\text{H}_5$ , 5H); 4.3–4.8 (m, Fc CH, 4H,  $J = 1.7$  Hz); 6.1 (bs, NH, 3H); 8.2 (bs, NH, 1H).  $^{13}\text{C}$  NMR  $\delta$ : 28.1 ( $\text{CH}_3$ ); 29.9, 30.1 ( $\text{CH}_2\text{CH}_2$ ) gen 2; 32.1, 32.7 ( $\text{CH}_2\text{CH}_2$ ) gen 1; 57.5 ( $\text{C}(\text{CH}_2\text{CH}_2)_3$ ) gen 2; 57.9 ( $\text{C}(\text{CH}_2\text{CH}_2)_3$ ) gen 1; 68.5, 70.4 (Fc CHCH); 69.6 (Fc  $\text{C}_5\text{H}_5$ ); Fc C-quaternary is under the solvent signal,  $\text{CDCl}_3$ ; 80.6 ( $\text{C}(\text{CH}_3)_3$ ); 171.1 (CONH) gen 1; 172.7 (CO<sub>2</sub>tBu); 173.1 (CONH) gen 2. UV-vis [ $\lambda_{\text{max}}$ , nm ( $\epsilon$ ,  $\text{M}^{-1}\text{cm}^{-1}$ ),  $\text{CH}_2\text{Cl}_2$ ]: 304 (1059.1); 335 (shoulder); 444 (216.6). MALDI-TOF MS: 1652.74 (100,  $\text{M}^+$ , calcd 1651.95).

**(27 Cascade/Ferrocene[1]/(3-Oxo-2-azapropylidyne)/(3-Oxo-2-azapentylidyne)(3-Oxo-2-azapentylidyne)/tert-Butyl Propanoate (3).** Ferrocene acyl chloride (prepared from ferrocenecarboxylic acid, 0.060 g, 0.26 mmol) was combined with the third generation building block amine **11** (1.0 g, 0.22 mmol) in the presence of Et<sub>3</sub>N (0.28 mmol, 0.040 mL) in 5 mL of dry THF. The reactants are stirred for 4 days under N<sub>2</sub> at room temperature. The resulting mixture was filtered. The filtrate was chromatographed (SiO<sub>2</sub>, CH<sub>2</sub>Cl<sub>2</sub> followed by 1:1 CH<sub>2</sub>Cl<sub>2</sub>/EtOAc) to procure an orange foam after evaporation of all the solvent and drying under vacuum (0.60 g, 49%). FT-IR (KBr): 3365.63 ( $\nu(\text{N-H})$ ) cm<sup>-1</sup>; 1732.77 ( $\nu(\text{C=O})$ ) cm<sup>-1</sup>; 1653.82 ( $\nu(\text{amide-I, C=O})$ ) cm<sup>-1</sup>; 1540.83 ( $\nu(\text{amide II, N-H})$ ) cm<sup>-1</sup>; 1154.59 ( $\nu(\text{C-O})$ ) cm<sup>-1</sup>. <sup>1</sup>H NMR (CDCl<sub>3</sub>)  $\delta$ : 1.4 (s, CH<sub>3</sub>, 243); 1.9–2.2 (m, CH<sub>2</sub>, 156H, *J* = 7.8 Hz); 4.2 (s, Fc C<sub>5</sub>H<sub>5</sub>, 5H); 4.3–4.9 (m, Fc CH, 4H, *J* = 1.7 Hz); 6.3 (bs, NH, 9H); 6.8 (bs, NH, 3H); 8.0 (bs, NH, 1H). <sup>13</sup>C NMR  $\delta$ : 28.15 (CH<sub>3</sub>); 29.8 (CH<sub>2</sub>CH<sub>2</sub>) gen 3; 31.6 (CH<sub>2</sub>CH<sub>2</sub>) gen 2; 57.4 (C(CH<sub>2</sub>CH<sub>2</sub>)<sub>3</sub>) gen 3; 69.8 (Fc C<sub>5</sub>H<sub>5</sub>); 80.4 (C(CH<sub>3</sub>)<sub>3</sub>); 172.7 (CO<sub>2</sub>tBu). UV-vis [ $\lambda_{\text{max}}$ , nm ( $\epsilon$ , M<sup>-1</sup> cm<sup>-1</sup>), CH<sub>2</sub>Cl<sub>2</sub>]: 300 (shoulder), 335 (shoulder), 439 (231.2). MALDI-TOF MS: 4726.29 (100, M<sup>+</sup>, calcd 4724.98).

**(3 Cascade/Ferrocene[1]/(3-Oxo-2-azapropylidyne)/(3-Oxo-2-azapentylidyne)/Propanoic Acid (4).** A solution (0.307 g, 0.489 mmol) of the *tert*-butyl triester dendrimer **1** in formic acid (96%, 5 mL) was stirred at 25 °C for 24 h. The solvent was removed in vacuo, and the remaining formic acid was chased with acetone followed by methylene chloride. The product recovered in 95% yield may be further purified if required by dissolving it in 0.2 N NaOH and reprecipitating with conc HCl. A yellow powder was obtained after drying the product in a vacuum at 80 °C (0.20 g, 90%). FT-IR (KBr): 3300–2500 ( $\nu(\text{O-H})$ ) cm<sup>-1</sup>; 3427.31 ( $\nu(\text{N-H})$ ) cm<sup>-1</sup>; 1714.44 ( $\nu(\text{C=O})$ ) cm<sup>-1</sup>; 1621.93 ( $\nu(\text{amide-I, C=O})$ ) cm<sup>-1</sup>; 1526.91 ( $\nu(\text{amide II, N-H})$ ) cm<sup>-1</sup>; 1293.42 ( $\nu(\text{C-O})$ ) cm<sup>-1</sup>. <sup>1</sup>H NMR (400 MHz, DMSO-*d*<sub>6</sub>)  $\delta$ : 1.9–2.25 (m, CH<sub>2</sub>CH<sub>2</sub>, 12H); 4.15 (s, FcC<sub>5</sub>H<sub>5</sub>, 5H); 4.30–4.85 (m, FcCHCH, 4H); 6.75 (sb, NH, 1H); 12.10 (sb, COOH, 3H). <sup>13</sup>C NMR (400 MHz, DMSO-*d*<sub>6</sub>)  $\delta$ : 28.18, 29.10 (CH<sub>2</sub>CH<sub>2</sub>); 56.98 (C(CH<sub>2</sub>CH<sub>2</sub>)<sub>3</sub>); 68.31, 69.67 (FcCHCH); 69.14 (FcC<sub>5</sub>H<sub>5</sub>); 77.45 (FcCONH); 168.54 (CONH); 174.52 (COOH). MALDI-TOF MS: 460.889 (100, M<sup>+</sup>, calcd 459.28); 482.847 (M + Na<sup>+</sup>).

**9 Cascade/Ferrocene[1]/(3-Oxo-2-azapropylidyne)/(3-Oxo-2-azapentylidyne)/Propanoic Acid (5).** Following the procedure described above, a solution of the *tert*-butyl nano-ester dendrimer **2** (0.303 g, 0.183 mmol) in formic acid (96%,

5 mL) was stirred at 25 °C for 24 h. The solvent was removed in vacuo, and the remaining formic acid was chased with acetone followed by methylene chloride. After the residue was dried under vacuum at 80 °C overnight, an orange powder (0.20 g, 95%) was obtained. FT-IR (KBr): 3300–2500 ( $\nu(\text{O-H})$ ) cm<sup>-1</sup>; 3348.01 ( $\nu(\text{N-H})$ ) cm<sup>-1</sup>; 1716.84 ( $\nu(\text{C=O})$ ) cm<sup>-1</sup>; 1652.2 ( $\nu(\text{amide-I, C=O})$ ) cm<sup>-1</sup>; 1540.49 ( $\nu(\text{amide II, N-H})$ ) cm<sup>-1</sup>; 1291.19 ( $\nu(\text{C-O})$ ) cm<sup>-1</sup>. <sup>1</sup>H NMR (400 MHz, DMSO-*d*<sub>6</sub>)  $\delta$ : 1.6–2.20 (m, CH<sub>2</sub>CH<sub>2</sub>, 48H) gen 1 & 2; 4.15 (s, FcC<sub>5</sub>H<sub>5</sub>, 5H); 4.30–4.80 (m, FcCHCH, 4H); 7.30 (sb, NH, 3H); 7.40 (sb, NH, 1H); 12.10 (sb, COOH, 9H). <sup>13</sup>C NMR (400 MHz, DMSO-*d*<sub>6</sub>)  $\delta$ : 28.07, 29.11 (CH<sub>2</sub>CH<sub>2</sub>) gen 2; 30.26, 30.71 (CH<sub>2</sub>CH<sub>2</sub>) gen 1; 56.28 (C(CH<sub>2</sub>CH<sub>2</sub>)<sub>3</sub>) gen 2; 57.04 (C(CH<sub>2</sub>CH<sub>2</sub>)<sub>3</sub>) gen 1; 68.17, 69.57 (FcCHCH); 69.17 (FcC<sub>5</sub>H<sub>5</sub>); 77.71 (FcCCONH); 168.0 (CONH) gen 1; 172.05 (CONH) gen 2; 174.05 (COOH). MALDI-TOF MS: 1147.76 (100, M<sup>+</sup>, calcd 1146.98); 1170.96 (M + Na<sup>+</sup>).

**(27 Cascade/Ferrocene[1]/(3-Oxo-2-azapropylidyne)/(3-Oxo-2-azapentylidyne)/(3-Oxo-2-azapentylidyne)/Propanoic Acid (6).** As described above, a solution (0.15 g, 0.032 mmol) of the *tert*-butyl ester dendrimer **3** in formic acid (96%, 5 mL) was stirred at 25 °C for 36 h. The solvent was removed in vacuo, and the remaining formic acid was chased with DMF. Some residual DMF could not be removed from the final orange-brown product after drying it under vacuum at 80 °C overnight (0.098 g, 98%). FT-IR (KBr): 3300–2500 ( $\nu(\text{O-H})$ ) cm<sup>-1</sup>; 3349.27 ( $\nu(\text{N-H})$ ) cm<sup>-1</sup>; 1720.12 ( $\nu(\text{C=O})$ ) cm<sup>-1</sup>; 1649.68 ( $\nu(\text{amide-I, C=O})$ ) cm<sup>-1</sup>; 1546.45 ( $\nu(\text{amide II, N-H})$ ) cm<sup>-1</sup>; 1294.49 ( $\nu(\text{C-O})$ ) cm<sup>-1</sup>. <sup>1</sup>H NMR (400 MHz, DMSO-*d*<sub>6</sub>)  $\delta$ : 1.6–2.40 (m, CH<sub>2</sub>CH<sub>2</sub>, 156H) gen 1, 2 & 3; 4.1 (s, FcC<sub>5</sub>H<sub>5</sub>, 5H); 4.30–4.80 (m, FcCHCH, 4H); 7.30 (sb, NH, 13H); 12.10 (sb, COOH, 27H). <sup>13</sup>C NMR (400 MHz, DMSO-*d*<sub>6</sub>)  $\delta$ : 28.27, 29.19 (CH<sub>2</sub>CH<sub>2</sub>) gen 3; 30.26, 30.75 (CH<sub>2</sub>CH<sub>2</sub>) gen 2; 56.29 (C(CH<sub>2</sub>CH<sub>2</sub>)<sub>3</sub>) gen 3; 69.31 (FcC<sub>5</sub>H<sub>5</sub>); 172.18 (CONH) gen 2; 174.66 (COOH). MALDI-TOF MS: 3211.62 (100, M<sup>+</sup>, calcd 3210.07); 6418.1 (dimer).

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