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SYNTHESIS, CHARACTERIZATION AND ANTIBACTERIAL BEHAVIOR OF WATER-SOLUBLE CARBOSILANE DENDRONS CONTAINING FERROCENE AT THE FOCAL POINT

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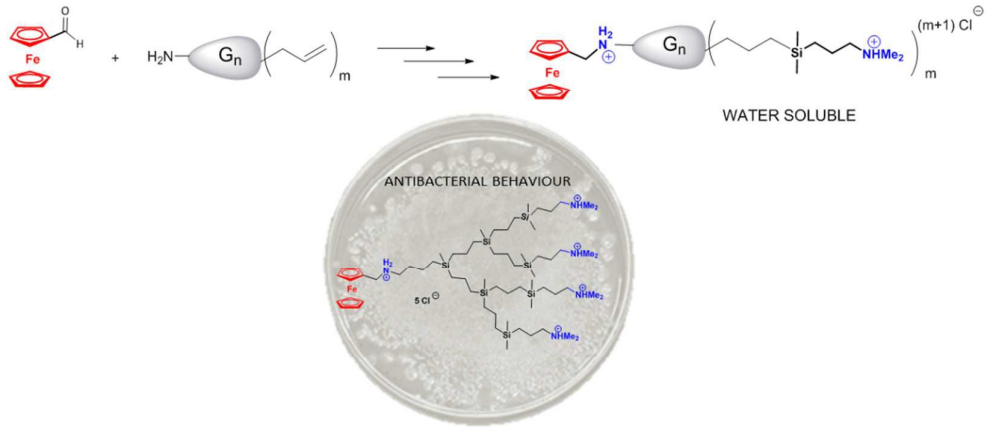
GRAPHIC ABSTRACT:



ABSTRACT

A series of novel water-soluble ammonium-terminated carbosilane dendrons containing a ferrocene unit at the focal point were synthesized, in order to combine the unique redox activity of ferrocene and the precisely designed structure of the dendrons with the aim to evaluate them as a new class of potential organometallic-based antibacterial compounds. The synthetic route is based on the initial amination of ferrocenecarboxaldehyde with carbosilane dendrons that contains allyl groups on the surface followed by reduction of the *in situ* prepared imine product, and the subsequent functionalization of the periphery with terminal amine groups by hydrosilylation reactions. Systems quaternized with HCl are soluble and stable in water or other protic solvents. The obtained compounds were spectrally and electrochemically (cyclic voltammetry) characterized, as well as diffusion-ordered spectroscopy experiments were conducted to determine the size of the dendritic wedges in solution. The antibacterial activity of these compounds was evaluated using Gram-positive bacteria (*Staphylococcus aureus*) and Gram-negative bacteria (*Escherichia coli*), which shows that the first and second generations of cationic dendrons are broad spectrum antibacterial agents, *i.e.* selective and effective in both bacteria strains.

INTRODUCTION

Ferrocenes are known to exhibit a wide range of biological activity and have also attracted special attention since it is a neutral, chemically stable and non-toxic molecule. Incorporation of a ferrocene fragment into an organic molecule often gives rise to unexpected biological activities. The use of ferrocene-based compounds for medicinal applications is an active research area.[1, 2] Ferrocene, compared to other organometallic compounds, has many advantages for biological applications, such as chemical modification capacity, low toxicity and stability under thermal, aqueous and aerobic conditions, together with a small size and a relative lipophilicity.[3] Indeed, ferrocene derivatives undergo fast one-electron oxidation to the ferrocenium form, which is positively charged; such oxidation is frequently fully reversible. The organometallic ferrocenyl compounds are promising candidates for conjugation with biomolecules due to their stability and favorable electrochemical properties.[4] Conjugates of ferrocene with well-known antibiotics such as penicillins and cephalosporins have been reported[5] and different compounds with ferrocene moieties have been evaluated as antimalarial,[6, 7] anticancer,[8] antifungal,[9] antiviral,[10] anti-inflammatory,[11] and anti-tuberculosis[12] agents. However, poor water solubility for many drugs remains a major obstacle to their development and clinical application.[13] To overcome this problem, several strategies and formulations have been employed to increase the solubility and bioavailability in water among

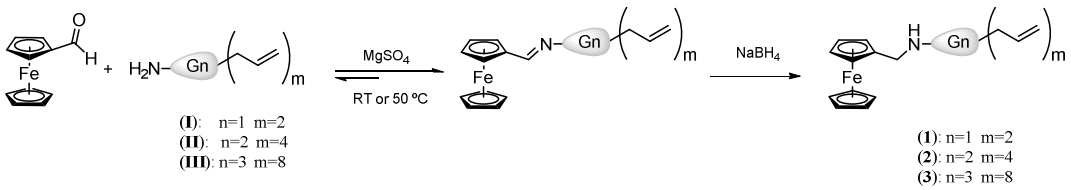
them, complexing drugs with cyclodextrins,[14] salt formation of ionizable drugs and the use of co-solvent,[15] or conjugation to dendrimers.[16]

Dendrimers and dendrons (wedge-shaped dendrimer sections, also known as dendritic wedges) are a class of macromolecular materials with a highly branched three-dimensional structure. They are unique polymers due to their low polydispersity and hyperbranched structure, which provides a multivalent periphery.[17, 18] In recent years, dendrimer-based nanotechnology has emerged as a powerful tool for biomedical applications.[19, 20] Ferrocene has been decorated on the surface of spherical dendrimers of different nature looking for multivalent effects.[21-24] However, just a few examples have been reported concerning its link to the focal point of dendrons,[25-28] in which the ferrocene moiety are linked to poly(arylether) or poly(amido amine) dendrons and study their anti-cancer activity against AGS cell line in the latter case. Carbosilane dendrimers have shown to be effective scaffolds for therapeutic usefulness.[29-31] This type of dendrimers seems to be attractive systems for manufacturing a therapeutic reagent, due to their own characteristic such as: i) simplicity of the synthetic process to extend the generation; ii) the presence of a hydrophobic scaffold in contrast to more hydrophilic polyamine-type dendrimers; iii) chemical and biochemical stability; and iv) biological inertness.[32-35] Carbosilane dendrimers that contain cationic groups on the surface have shown to act as carriers of nucleic acids for transfection purposes[31, 36-38] or antibacterial agents,[39-41] as well as facilitating water solubility to all these systems. However, there are not examples in the literature of carbosilane dendrons functionalized with ferrocene at the focal point, so far. This work entails the incorporation of ferrocene into cationic carbosilane dendrons in order to combine the unique redox activity of ferrocene and the precisely designed structure of the dendrons with the aim to evaluate them as a new class of potential organometallic-based antibacterial compounds.

RESULTS AND DISCUSSION

Synthesis and characterization of carbosilane dendrons containing ferrocene at the focal point. Reductive amination of carbonyl compounds is a powerful reaction in organic chemistry, able to deliver in high yield primary, secondary, and tertiary amines with a great variety of substituents.[42] Therefore, the strategy to prepare a new family of carbosilane dendrons containing ferrocene at the focal point involves the initial amination of ferrocenecarboxaldehyde with $NH_2(CH_2)_4[G_n\text{-}(Allyl)_m]$ prepared elsewhere[43] followed by reduction of the *in situ* prepared imine products with $NaBH_4$ to afford carbosilane dendritic wedges with ferrocene at the focal point and allyl groups on the surface $FcCH_2NH(CH_2)_4[G_n(Allyl)_m]$ (n=1, m=2 (**1**); n=2, m=4 (**2**); n=3, m=8 (**3**)), where Fc denotes a ferrocenyl fragment (see Scheme 1). The formation of intermediate imine derivatives $\{FcCH=N(CH_2)_4[G_n(Allyl)_m]\}$, *in situ* prepared, is confirmed in the ^1H NMR spectra by the presence of a singlet at 8.09 ppm attributed to the imine hydrogen

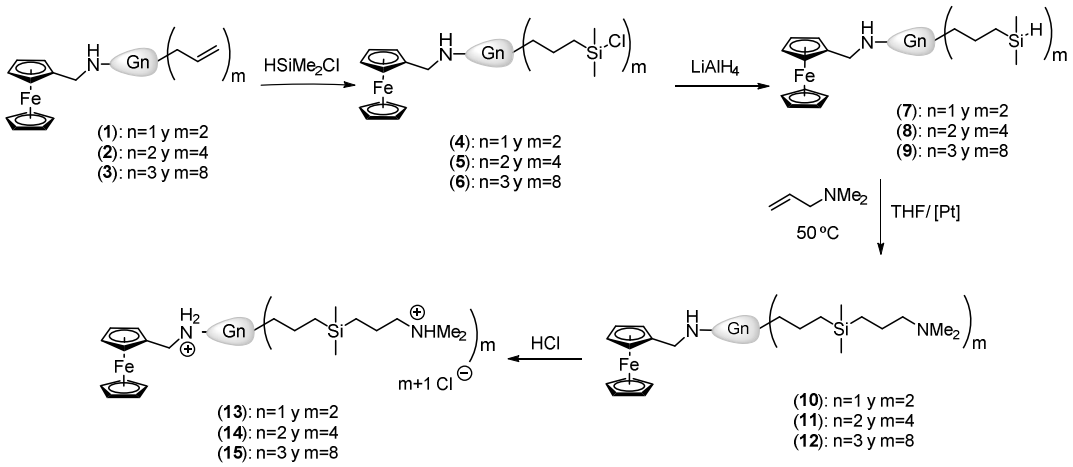
and a multiplet located at 3.43 ppm for the methylene group bonded to nitrogen atom. In these systems, the ferrocene moiety showed two signals at 4.33 and 4.61 ppm for the *meta*- and *ortho*-hydrogen atoms on the substituted Cp ring and a singlet at 4.15 ppm for the unsubstituted Cp ring. The NMR characterization of the isolated amines **1-3** confirmed their purity and supported their structure through the presence of two signals around 3.48 (s) and 2.60 (t) ppm corresponding to the methylene groups CpCH_2N- and -N$CH_2CH_2CH_2CH_2$Si- respectively. Respecting the ferrocenyl fragment, now only one broad signal was observed around 4.05-4.15 ppm. For the characteristic signals of the allyl group, a doublet about 1.50 ppm attributed to the methylene group (-SiCH_2CH=CH_2), and two multiplets about 4.83 (-CH=CH_2) and 5.77 (-C*H*=CH_2) ppm for the olefinic protons, were observed. The ^{13}C {^1H} NMR spectra show four signals for Cp rings, three of them corresponding to the *meta*-, *ortho*- and C_{ipso} carbons atoms on the substituted Cp at 67.7, 68.4 and 86.9 ppm respectively and other one at 68.3 ppm for the unsubstituted Cp ring. Finally, ^1H-^{15}N HMBC experiment shows one resonance at -332.7 ppm attributed to the nitrogen of the amino group.



Scheme 1. Synthesis of allyl-terminated dendrons with ferrocene at the focal point **1-3**.

The functionalization with ammonium groups on the surface involves a sequence of reactions based on hydrosilylation, reduction and hydrosilylation. Thus, starting from **1-3** dendrons and employing $HSiClMe_2$, in the presence of Karstedt Pt catalyst,[44] the dendritic wedges $FcCH_2NH(CH_2)_4[G_n(SiMe_2Cl)_m]$ (n=1, m=2 (**4**); n=2, m=4 (**5**); n=3, m=8 (**6**)) were obtained as orange oils that were stored under argon. The subsequence reaction of **4-6** with $LiAlH_4$ afforded the corresponding derivatives with Si-H bonds at the periphery $FcCH_2NH(CH_2)_4[G_n(SiMe_2H)_m]$ (n=1, m=2 (**7**); n=2, m=4 (**8**); n=3, m=8 (**9**)). These compounds reacted with allyldimethylamine in ampoules with J. Young valves using THF as a solvent and the Karstedt´s catalyst during 24 h at 50ºC to obtain $FcCH_2NH(CH_2)_4[G_n(SiMe_2(CH_2)_3NMe_2)_m]$ (n=1 m=2 (**10**); n=2 m=4 (**11**); n=3 m=8 (**12**)) as orange oils, soluble in chlorinated solvents and aromatic and aliphatic hydrocarbons but insoluble in water (see Scheme 2). Finally, the ammonium derivatives $FcCH_2NH_2Cl(CH_2)_4[G_n(SiMe_2(CH_2)_3NHMe_2Cl)_m]$ (n=1, m=2 (**13**); n=2, m=4 (**14**); n=3, m=8 (**15**)) were obtained by addition of hydrogen chloride solution over diethyl ether solutions of the neutral dendrons **10-12** in good yields as a brown oily solids, and soluble in protic solvents. A

description of the structures of cationic dendrons with ferrocene at the focal point is depicted in Figure 1.



Scheme 2. Different functionalization of allyl-terminated dendrons with ferrocene at the focal point to afford dendrons **4-15**.

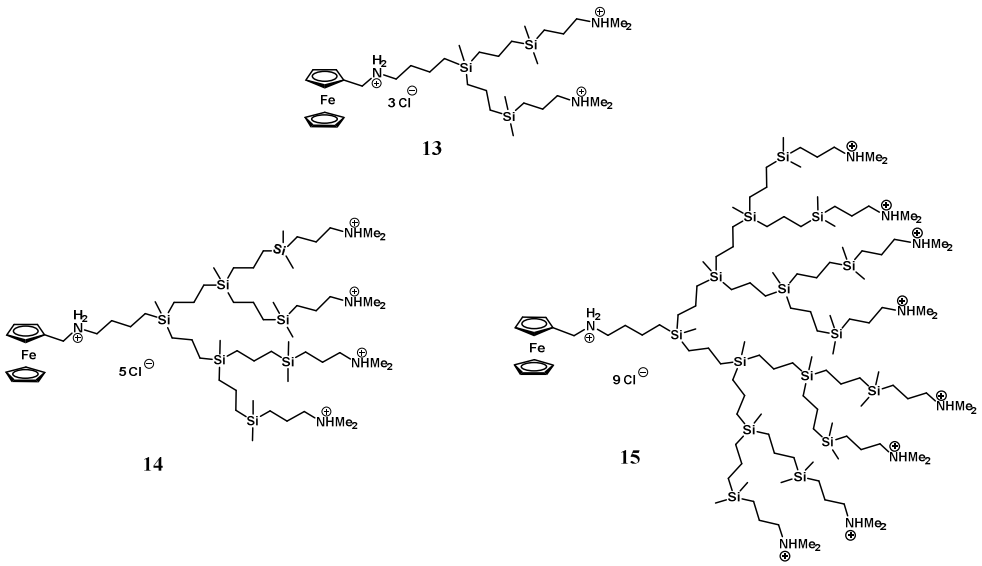


Figure 1. Structures of cationic dendrons G_1-G_3 (**13-15**) with ferrocene at the focal point.

All these compounds (**4-15**) were characterized by multinuclear NMR spectroscopy (^{1}H, ^{13}C, ^{15}N, ^{29}Si), elemental analysis and mass spectrometry. Formation of the chloro-terminated derivatives **4-6** was confirmed in the ^{1}H NMR spectra by one singlet at 0.38 ppm attributed to the -$SiMe_2Cl$ methyl group and also by disappearance of the resonances belonging to the allyl moiety. In the ^{13}C NMR spectra of these compounds, the resonance of the peripheral -$SiMe_2Cl$ methyl groups was observed about 1.7 ppm. ^{1}H NMR spectra of the hydride terminal dendrons **7-9** showed one multiplet at about 3.82 ppm corresponding to the Si-H proton and one doublet

at about - 0.04 ppm for the -$SiMe_2H$ methyl groups. In the ^{13}C NMR spectra, the Me_2Si group afforded a resonance *c.a.* -4.3 ppm. The presence of the -$SiMe_2Cl$ groups was also confirmed in the ^{1}H-^{29}Si HMBC spectra by one cross peak about 31.0 ppm for such Si atoms, whereas the -$SiMe_2H$ groups gave a resonance clearly a lower frequency at -14.1 ppm. Finally, with respect to the outers groups in compounds **10-12** and **13-15**, in the case of neutral derivatives, the signal for the methylene groups bonded to nitrogen atoms and the methyl protons of the dimethylamine fragments overlapped at 2.19 ppm in ^{1}H NMR while in ^{13}C NMR appeared at 45.5 and 63.5 ppm respectively. For cationic systems, the NMR spectra were recorded in DMSO-d_6 or D_2O at room temperature, although in the last solvent the line widths of these spectra tended to be broader. The ^{1}H and ^{13}C NMR spectra (see Figure 2) show that the carbosilane framework is insignificantly affected by the quaternization reaction. For the external fragments in derivatives **13-15**, the quaternization of the amine groups resulted in a deshielding of the chemical shift of the -CH_2N- and -N*Me*$_2$HCl groups in the ^{1}H NMR consistent with the presence of positive charges on the nitrogen atoms. Analogous shifts are observed for the carbon atoms in their ^{13}C NMR spectra.

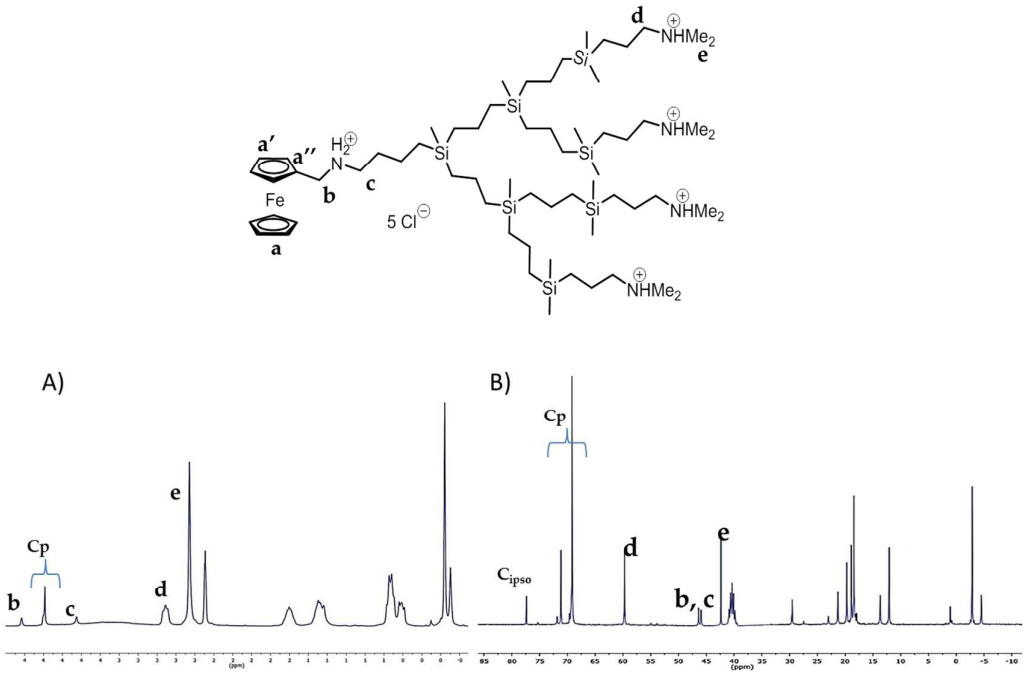


Figure 2. (**A**) ^{1}H- and (**B**) ^{13}C-NMR spectra of ammonium-terminated second generation dendron **14** with ferrocene at the focal point in DMSO-d_6.

Electrochemical behavior. The oxidation of ferrocenyl moiety, $[Fe(C_5H_5)(C_5H_4R)]$, to the ferrocenium cation, $[Fe(C_5H_5)(C_5H_4R)]^{+}$ was examined by cyclic voltammetry (CV) for the

neutral compound **10** in dichloromethane/Bu_4NBF_4 and for the ionic derivatives **13-15** in MeOH/$LiClO_4$ (Figure 3). The peak potentials measured at scan rate of 100mV/s (summarized in Table 1) are quoted with respect to the Ag/Ag^+(sat) reference electrode. All the complexes display the chemically reversible ferrocene/ferrocenium couple. In the case of the neutral compound **10** was possible to observe a second oxidative process, corresponding to the secondary amine oxidation to a cation radical, which overlaps the oxidative peak of the ferrocene unit. The former process can afford the decomposition of the molecule via imine intermediate reducing the formation of the ferrocene/ferrocenium couple within the molecule. Concerning the cyclic voltammetry of the quaternary salts, and due to the only oxidation of the ferrocene unit, the value of E_{pa} is easily measured, eliminating such potential decomposition.

Table 1. Peak potentials E (V, vs Ag/Ag+).Scan rate: 100 mV/s.

Substrate	E_{pa1}	E_{pc1}	***SSE***
Ferrocene	+0.45	+0.37	MeOH/$LiClO_4$
10	+0.85	+0.45	CH_2Cl_2/ Bu_4NBF_4
13	+0.56	+0.50	MeOH/$LiClO_4$
14	+0.55	+0.49	MeOH/$LiClO_4$
15	+0.54	+0.48	MeOH/$LiClO_4$

In general, the values of the halfwave potentials for the oxidation of the ferrocene into dendritic wedges were slightly more positives than the ferrocene alone. This is consistent with the withdrawal of electronic density produced by the presence of a positive charge near to the cyclopentadienyl ring but also to the presence of a non-polar microenvironment for the ferrocene moiety. No significant differences were observed on dendron growth suggesting that ferrocene centers at the focal point were not influenced by the ammonium groups located on the surface of the dendritic wedge. This means that the ferrocene remains predominantly in a non-polar microenvironment probably helped for the carbosilane architectural flexibility. Similar behaviours were observed by Kaifer *et al.* in the use of ferrocene attached to non-polar Fréchet dendrons.[25]

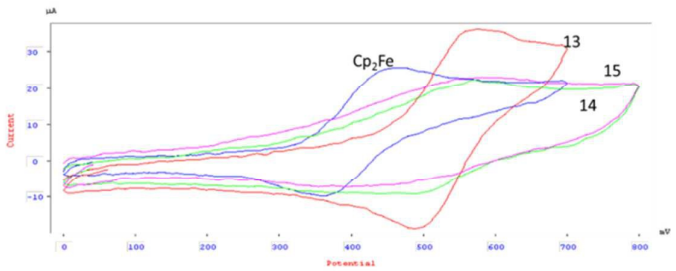


Figure 3. Cyclic voltammetry of cationic ferrocenyl dendrons measured in MeOH/$LiClO_4$

It is well noting that although the halfwave potentials remain constant, the kinetic seems decay (slow electron transfer process to ferrocene side) when the molecule became larger as expected due to the different diffusion process (see Figure 3).

DOSY NMR (diffusion-ordered spectroscopy). The experiments were conducted for the dendrimers **10-15** in different solvents. The main goal of these experiments was to determine the size of the dendrimers in solution, through the measurement of their hydrodynamic radii (r_H). The diffusion of a species is directly related to their molecular size and the nature of the solvent. This is modeled using the Stokes−Einstein equation, which in the stick boundary condition has the form, $r_H = kT/6\pi\eta D$, where k is the Boltzmann constant, η is the solvent viscosity, T is the temperature, and r_H is the hydrodynamic (or Stokes) radius and D is the diffusion coefficient.[45] This method was very useful for a clear comparison between the dendron generations, providing evidences for the formation of distinct ionic assemblies. In general, dendritic radius increases on increasing the generation (along with molecular weight). However, different factors such as hydrogen-bonding, ionic strength, counter ion composition, pH and temperature may affect to the hydrodynamic radius. Table 2 contains the experimental data on hydrodynamic radii of samples obtained by DOSY NMR measurement in $CDCl_3$ and MeOH-d_4 for neutral dendrons while cationic dendrons were studied in MeOH-d_4 and D_2O.

Table 2. Experimental diffusion coefficients (D)[a], hydrodynamic radius (r_H)[b] and hydrodynamic volumes (V_H)[c] in different solvents for **10-15.**

	$CDCl_3$		MeOD-d_6			D_2O			
dendron	r_H	D[a]	r_H	D	V_H	r_H	D	V_H	N[f]
10	0.75	5.23	0.81	5.05	--	--	--	--	--
11	0.94	4.23	0.81	5.03	--	--		--	--
12	---[d]	---[d]	0.96	4.21	--	--	--	--	--
13			0.85	4.71	2.57	1.98	1.15	6.37	2.5
14			1.24	3.03	7.99	2.69	0.89	81.53	10
15			1.50-1.64[e]	---	14.14-18.48[e]	3.46	0.71	173.51	10[e]

[a] Diffusion coefficient D ($x10^{-10}cm^2s^{-1}$); [b] hydrodynamic radius r_H (nm). [c] V_H (nm^3). [d] **12** was not soluble in $CDCl_3$; [e] estimated values due to **15** was not soluble in MeOD-d_4, [f] N denotes aggregation number, calculated on the basis of monomer formation in methanol for **13-15**.

For the neutral dendrons **10-12**, the calculated hydrodynamic radii were similar in $CDCl_3$ and MeOD-d_4 with a slightly tendency to increase when the generation increases. For cationic dendrons **13-15**, the r_H data obtained in MeOD-d_4 were slightly higher than those of neutral precursors. However, the experimental r_H values measured in deuterated water were

significantly higher and generation-dependent. These differences correlate well with the presence of self-aggregation processes in water due to their amphiphilic nature, being not relevant in methanol. To determine more clearly the influence of the dendritic framework on the tendency of such compounds to form aggregates, hydrodynamics volumes (V_H) and the aggregation number (N) were calculated on the basis of monomer formation in methanol. For dendron **15**, the r_H was estimated for comparison with analogous dendrimers.[46, 47] The apparent hydrodynamic volume of compound **13** affords a low aggregation number compared to dendrons **14** and **15**. This observation is consistent with the notion that ferrocene units are less expose to the aqueous medium and therefore less accessible on increasing the generation.

Antibacterial activity. To date, the contribution of ferrocene to antibacterial, antifungal and other biological properties of ferrocene-containing compounds, remains uncertain. Some authors proposed a more ''active'' role for ferrocene, namely as a source of ferrocenium (Fe^{3+})[48] or reactive oxygen species (ROS) formation that may have a direct influence on activity.[49] In addition, carbosilane dendrimers that contain cationic groups on the periphery have proven to be active as antibacterial agents.[40, 41] For these reasons, the possible cooperative effect of both systems by covalent inclusion of ferrocene to the carbosilane dendron has been studied. The antibacterial activity of water-soluble dendrons **13**, **14** and **15** has been tested on *Staphylococcus aureus* (Gram-positive) and *Escherichia coli* (Gram-negative) along with the dendritic wedge $(ClNH_3)(CH_2)_4[G_1(SiMe_2(CH_2)_3NHMe_2Cl)_2]$ (**16**) (see Experimental Section) for comparison purposes and the results showed in Table 3.

The results of the antibacterial tests show the high activity against both Gram-positive and Gram-negative bacteria of **13**, **14** and **16** but not for the third generation dendron **15**. The generation dependence of dendrimer biocides showed that the first generation dendron is slightly more potent than the second one, mainly in the case of the Gram-negative bacteria, while poorly acting as biocide in the case of the third generation. This discrepancy has been also shown by other authors[50] in the case of dendrimers, and has been ascribed to the different size and molecular weight of the dendrimer and its capacity to cross the membrane of the bacteria. A possible explanation of this behavior can be inferred from the aggregation and size data obtained by DOSY NMR experiments. G_1 (**13**) does not suffer aggregation leaving ferrocene exposed to the aqueous medium and prone to act. In this case, the small size and possible cooperative effect between ferrocene, probably through ROS formation mechanism, and ammonium groups could be responsible of its high activity. A fact that corroborates this assumption is that dendron **13** is slightly more active than the analogous first generation dendron **16** without containing ferrocene at the focal point, mainly in Gram + bacteria. However, for G_3 (**15**), the observed aggregation affords a large apparent size and hydrodynamic volume which can diminish the interaction with the bacterial membrane and also allowing ferrocene units to be less exposed and therefore less accessible. In the case of G_2 (**14**), where

aggregation is also observed, the antibacterial activity may be attributed to a balance between the increased number of positive charges which may favor the interaction with the bacterial membranes and the large size respecting to **13** that disfavor such interaction. In addition, **13** is more active than the analogous linear system $FcCH_2NH_2(Cl)(CH_2)_4Si(Me_2)(CH_2)NMe_2HCl$ (see S.I.) containing two positives charges with MIC and MBC values of 16 mg/L in both types of bacteria. This difference could be ascribed to the presence of three positive charges on dendron **13**, but also a contribution of the dendritic structure cannot be ruled out.

In general, the minimum inhibitory concentration (MIC) and minimum bactericidal concentration (MBC) data for active dendrons **13**, **14** and **16**, are equal for Gram-positive and Gram-negative bacteria. This fact would mean that these systems could be considered as antibacterial agents of broad spectrum despite of the well-known differences in the cell wall structure in both types of bacteria, opposite what it is observed in most common antibiotics. For instance, antibacterial activity of ferrocene-containing bioorganometallic compounds inspired by antibiotic Platensimycin has shown to be active against Gram-positive bacteria like *S. aureus* with a MIC of 128 mg/L and no active in Gram-negative bacteria like *E. coli.*[51] Analogously, inhibitory properties of ferrocene-substitutes chalcones and aurones on Gram-positive and -negative bacteria afforded MIC values > 32 mg/L.[52] Other examples are found in ferrocene-containing penicillins and cephalosporins tested towards both types of bacterial strains, showing equal o higher activity respecting the control sample employed on Gram-positive bacteria and no activity on Gram-negative bacteria.[5]

Table 3. Antibacterial activity (mg/L) of water-soluble compounds **13**, **14**, **15** and **16**.

	13		**14**		**15**		**16**	
	MIC	MBC	MIC	MBC	MIC	MBC	MIC	MBC
E. Coli (Gram -)	2	2	8	8	>512	>512	4	4
S. Aureus (Gram +)	2	2	4	4	32	64	4	8

CONCLUSIONS

In summary, a simple and efficient method for the synthesis of cationic carbosilane dendrons with ferrocene at the focal point has been developed. It involves the initial amination of ferrocenecarboxaldehyde with $NH_2(CH_2)_4[G_n\text{-}(Allyl)_m]$ followed by reduction of the *in situ* prepared imine products with $NaBH_4$. The functionalization with ammonium groups on the surface involves a sequence of orthogonal reactions based on hydrosilylation, reduction and hydrosilylation along with final quaternization with HCl. The electrochemical behavior of

dendrons showed that ferrocenyl moieties in the focal point of the dendrons were not influenced by the ammonium groups located on the surface and no significant differences were observed for the length of the aliphatic chain on increasing the dendritic generation. Protonation of the amino group close to the cyclopentadienyl ring seems to be important in order to avoid partial decomposition of the system by oxidation reactions, holding the optimal formation of ferrocenium to ensure the generation of reactive oxygen species. The cationic dendrons **13**-**15** gave rise to different behavior towards aggregation in water. The aggregation number in generation 1 was very low, opposite what happened for higher generations, probably as consequence to the hydrophilic/lipophilic balance imposed in these amphiphilic systems. These systems have been tested as antibacterial agents against both Gram-positive and Gram-negative bacteria showing high activity for dendrons **13** and **14**, but not for the third generation dendron **15**. The different activity could be explained in terms of size where the aggregation process can be considered an important feature to take into consideration. Dendron **13** was slightly more active than the analogue ferrocene-free dendron **16** mainly in Gram-positive bacteria. This observation is consistent with a cooperative effect between the ferrocene unit and the ammonium groups located at the dendritic surface. The fact that dendrons **13**, **14** and also **16** were very active against both Gram-positive and -negative bacteria, would mean that these systems could be considered as antibacterial agents of broad spectrum.

EXPERIMENTAL SECCION

4.1 General Considerations. All reactions were carried out under an inert atmosphere, and solvents were purified from appropriate drying agents when necessary.

NMR spectra were recorded on a Varian Unity VXR-300 (300.13 (1H), 75.47 MHz (13C)) or on a Bruker AV400 instrument (400.13 (^{1}H), 100.60 (^{13}C), 40.56 MHz (^{15}N), and 79.49 MHz (^{29}Si)). Chemical shifts (δ) are given in ppm. ^{1}H and ^{13}C resonances were measured relative to solvent peaks considering TMS at 0 ppm; meanwhile ^{15}N and ^{29}Si resonances were measured relative to external MeNO and TMS, respectively. When necessary, assignment of resonances was done from HSQC, HMBC, COSY, TOCSY, and NOESY NMR experiments.

Elemental analyses were performed on a LECO CHNS-932 instrument.

Mass spectra were obtained from a Bruker Ultraflex III instrument for MALDI-TOF in dithranol, an Agilent 6210 TOF LC/MS instrument for ESI-TOF in MeOH/H_2O with $(NH_4)(HCO_2)$, and an AB Sciex QSTAR instrument for ESIPOS in H_2O/MeOH.

Voltammetric curves with IR compensation were obtained with a polarographic Analyzer POL150 Tracelab Radiometer in a MDE150 Polarographic Stand Voltalab in a three electrode cell. As working and counter electrode a Platinum wire was employed. The electrochemical properties of compounds have been studied by cyclic voltammetry (CV) in dichloromethane

(DCM)/ tetrabutylammonium tetrafluorborate or MeOH/LiClO4 respectively as SSE (solvent-supporting electrolyte systems). Before the voltammetric experiments, the solutions were deaerated by bubbling of N_2 (99.98% purity, purchased by Air Liquide) for 5 minutes.

Antimicrobial activity assay, the minimal inhibitory concentration (MIC) of the products were done in 96-well tray microplates using the international standard methods ISO 20776-1 by microdilutions trays preparations.57 The assays were done in duplicate microplates with three different wells for each concentration analyzed in the microplate. The bacteria used in the analysis were Escherichia coli (CECT 515) (Gram-negative) and Staphylococcus aureus (CECT 240) (Gram-positive). Both strains were obtained from the "Coleccion Española de cultivos tipo" (CECT). A stock solution of the products was obtained dissolving 0.01024 g of the compound with 10 mL of distillated water. After that, distilled water was added to obtain the desired concentration. The microplates were incubated at 37ºC using an ultra-microplate reader ELX808iu (Bio-Tek Instruments). The minimal bactericidal concentration (MBC) was calculated inoculating 3 mL of the samples used to calculate the MIC in Petri dish with Mueller-Hinton agar (Ref. 02-136, Scharlau). The samples were put it on a drop in the plates. After 48 h of incubation at 37ºC the presence of colonies was tested. The MBC was the minimal concentration where not growth was detected.

4.2. Synthesis of Compounds.

4.2.1. $FcCH_2NH(CH_2)_4$ [$G_1(Allyl)_2$] (1). To a THF solution of ferrocenecarboxaldehyde (0.82 g, 3.81 mmol) was added 0.75 g of carbosilane dendron $NH_2(CH_2)_4$ [$G_1(Allyl)_2$] (3.81 mmol) and anhydrous $MgSO_4$. The mixture was stirred at room temperature for 24 h. The orange solution was then filtered to a Schlenk flask and $NaBH_4$ (0.16 g, 4.19 mmol) and MeOH (2mL) was added slowly at 0 °C. 24 h later, the solvent was removed *in vacuo* and the residue was suspended in Et_2O. The aqueous layer was washed three times with Et_2O and dried over $MgSO_4$. The orange solution was then evaporated to dryness under reduced pressure and the resulting residues was sublimated at 100 °C for 48 h. **1** was obtained as an orange oil. Yield: 1.25 g (83%). ^{1}H-RMN ($CDCl_3$): δ -0.04 (s, Si*Me*), 0.54 (t, $NCH_2CH_2CH_2CH_2Si$), 1.32 (t, $NCH_2CH_2CH_2CH_2Si$), 1.51 (d, $SiCH_2CH{=}CH_2$), 1.54 (t, $NCH_2CH_2CH_2CH_2Si$), 2.60 (t, $NCH_2CH_2CH_2CH_2Si$), 3.48 (s, $FcCH_2NH$), 4.06-4.16 (s, FcC_5H_5 y FcC_5H_4), 4.75 (m, $CH{=}CH_2$), 5.75 (m, $CH{=}CH_2$). ^{13}C{^{1}H}-RMN ($CDCl_3$): δ -5.9 (Si*Me*), 12.9 ($NCH_2CH_2CH_2CH_2Si$), 21.3 ($SiCH_2CH{=}CH_2$), 21.4 (t, $NCH_2CH_2CH_2CH_2Si$), 33.9 $NCH_2CH_2CH_2CH_2Si$), 49.1 ($NCH_2CH_2CH_2CH_2Si$), 49.3 ($FcCH_2NH$), 67.7-68.4(FcC_5H_5 y FcC_5H_4), 86.9 (C_{ipso}) 113.1 ($CH{=}CH_2$), 134.7 ($CH{=}CH_2$). ^{1}H-^{29}Si-HMBC (DMSO-d_6): δ = 0.87 (*Si*Me) ^{1}H-^{15}N-HMBC ($CDCl_3$): δ -332.7 ($FcCH_2NH$). Anal. Calcd for $C_{22}H_{33}FeNSi$ (395.43 g mol^{-1}): C, 66.82; H, 8.41; N, 3.54 %. Found: C, 66.12; H, 8.23; N, 3.50 %. MS: $[M + H]^+$ 396.12 uma (Calcd 396.18 uma).

4.2.2. $FcCH_2NH(CH_2)_4[G_2(Allyl)_4]$ (2). The preparation of **2** is similar to that of 1 above ferrocenecarboxaldehyde (0.81 g, 3.80 mmol), carbosilane dendron $NH_2(CH_2)_4[G_2(Allyl)_4]$ (1.71 g, 3.80 mmol) and $NaBH_4$ (0.16 g, 4.18 mmol). In this case the solution was heated at 50 °C. **2** was obtained as orange oil. Yield: 2.02 g (82%). ^{1}H-RMN ($CDCl_3$): δ -0.10 (s, Si*Me*), -0.07 (s, Si*Me*$CH_2CH{=}CH_2$), 0.46-0.62 (m, $NCH_2CH_2CH_2CH_2Si$, $SiCH_2CH_2CH_2Si$), 1.25-1.30 (m, $SiCH_2CH_2CH_2Si$, $NCH_2CH_2CH_2CH_2Si$), 1.51 (d, $SiCH_2CHCH_2$), 2.60 (t, $NCH_2CH_2CH_2CH_2Si$), 3.49 (s, $FcCH_2NH$), 4.08-4.16 (s, FcC_5H_5 y FcC_5H_4), 4.83 (m, $CH{=}CH_2$), 5.75 (m, $CH{=}CH_2$). ^{13}C{^{1}H}-RMN ($CDCl_3$): δ -5.7 (s, Si*Me*), -5.1 (s, Si*Me*CH_2CHCH_2), 13.9 ($NCH_2CH_2CH_2CH_2Si$), 17.9-21.4 ($SiCH_2CH_2CH_2Si$), 21.3 ($SiCH_2CHCH_2$), 21.8 ($NCH_2CH_2CH_2CH_2Si$), 34.0 ($NCH_2CH_2CH_2CH_2Si$), 49.0 ($NCH_2CH_2CH_2CH_2Si$), 49.3 ($FcCH_2NH$), 67.7-68.4 (FcC_5H_5 y FcC_5H_4), 86.6 (C_{ipso}), 113.0 ($CH{=}CH_2$), 134.9 ($CH{=}CH_2$). ^{1}H-^{29}Si-HMBC (DMSO-d_6): δ = 0.2 (*Si*CH_2CHCH_2), 1.6 (*Si*Me) ^{1}H-^{15}N-HMBC ($CDCl_3$): δ -332.4 ($FcCH_2NH$). Anal. Calcd for $C_{36}H_{61}FeNSi_3$ (647.98 g mol^{-1}): C, 66.73; H, 9.49; N, 2.16 %. Found: C, 65.84; H, 9.90; N, 2.54 %. MS: $[M + H]^+$ 648.25 uma (Calcd 648.35 uma).

4.2.3. $FcCH_2NH(CH_2)_4[G_3(Allyl)_8]$ (3). The preparation of **3** is similar to that of **2** above ferrocenecarboxaldehyde (0.18 g, 0.86 mmol) and carbosilane dendron $NH_2(CH_2)_4[G_3(Allyl)_8]$ (0.82 g, 0.86 mmol) and $NaBH_4$ (0.04 g, 0.95 mmo). **3** was obtained as orange oil. Yield: 0.80 g (80%)

^{1}H-RMN ($CDCl_3$): δ -0.10 (s, Si*Me*), -0.37 (s, Si*Me*$CH_2CH{=}CH_2$), 0.50-0.63 (m, $NCH_2CH_2CH_2CH_2Si$, $SiCH_2CH_2CH_2Si$), 1.26-1.34 (m, $SiCH_2CH_2CH_2Si$, $NCH_2CH_2CH_2CH_2Si$), 1.52 (d, $SiCH_2CHCH_2$), 2.60 (t, $NCH_2CH_2CH_2CH_2Si$), 3.48 (s, $FcCH_2NH$), 4.07-4.16 (s, FcC_5H_5 y FcC_5H_4), 4.83 (m, $CH{=}CH_2$), 5.75 (m, $CH{=}CH_2$). ^{13}C{^{1}H}-RMN ($CDCl_3$): δ -5.7 (s, Si*Me*), -5.0 (s, Si*Me*CH_2CHCH_2), 14.0 ($NCH_2CH_2CH_2CH_2Si$), 17.9-18.8 ($SiCH_2CH_2CH_2Si$), 21.5 ($SiCH_2CHCH_2$), 21.8 ($NCH_2CH_2CH_2CH_2Si$), 34.2 ($NCH_2CH_2CH_2CH_2Si$), 49.2 ($NCH_2CH_2CH_2CH_2Si$), 49.6 ($FcCH_2NH$), 67.7-68.4 (FcC_5H_5 y FcC_5H_4), 86.7 (C_{ipso}), 113.0 ($CH{=}CH_2$), 134.8 ($CH{=}CH_2$). ^{1}H-^{29}Si-HMBC (DMSO-d_6): δ = 0.2 (*Si*CH_2CHCH_2), 1.6 (*Si*Me) ^{1}H-^{15}N-HMBC ($CDCl_3$): δ -332.3 ($FcCH_2NH$). Anal. Calcd for $C_{64}H_{117}FeNSi_7$ (1153.06 g mol^{-1}): C, 66.66; H, 10.23; N, 1.21 %. Found: C, 65.94; H, 9.39; N, 1.10 %.MS: $[M + H]^+$ 1152.70 uma (Calcd 1152.70 uma).

4.2.4. $FcCH_2NH(CH_2)_4[G_1(SiMe_2Cl)_2]$ (4). In an ampule, 0.52 g (1.31 mmol) of compound **1** and 0.57 mL of chlorodimethylsilane (5.22 mmol) were mixed in presence of Karstedt's catalyst and THF as solvent. The mixture was refluxed at 60 °C for 24 h. The solvent volume and excess of chlorodimethylsilane was then removed in vacuum in order to obtain **4** as orange oil. Yield: 0.69 g (90%). ^{1}H-RMN ($CDCl_3$): δ -0.08 (s, Si*Me*), 0.38 (s, Si*Me*$_2$Cl), 0.57 (m, $NCH_2CH_2CH_2CH_2Si$ y $SiCH_2CH_2CH_2SiMe_2$), 0.86 (m, $SiCH_2CH_2CH_2SiMe_2$), 1.29-1.41 (m, $NCH_2CH_2CH_2CH_2Si$ y $SiCH_2CH_2CH_2SiMe_2$), 2.62 (t, $NCH_2CH_2CH_2CH_2Si$), 3.75 (s,

FcC*H*$_2$NH), 4.07-4.13 (s, FcC$_5$*H*$_5$ y FcC$_5$*H*$_4$). ^{13}C{^{1}H}-RMN ($CDCl_3$): δ -5.2 (Si*Me*), 1.7 (Si*Me*$_2$Cl), 13.7 (NCH$_2$CH$_2$CH$_2$*C*H$_2$Si), 17.6 (Si*C*H$_2$CH$_2$CH$_2$SiMe$_2$), 17.8 (SiCH$_2$*C*H$_2$CH$_2$SiMe$_2$), 21.3 (NCH$_2$CH$_2$*C*H$_2$CH$_2$Si), 21.4 (SiCH$_2$CH$_2$*C*H$_2$SiMe$_2$), 32.5 (NCH$_2$*C*H$_2$CH$_2$CH$_2$Si), 44.7 (N*C*H$_2$CH$_2$CH$_2$CH$_2$Si), 44.9 (Fc*C*H$_2$NH), 67.7-68.4(Fc*C*$_5$H$_5$ y Fc*C*$_5$H$_4$), 85.9 (C$_{ipso}$). ^{1}H-^{29}Si-HMBC (DMSO-d_6): δ 1.7 (*Si*Me), 31.2 (*Si*Me$_2$Cl). ^{1}H,^{15}N-HMBC ($CDCl_3$): δ -332.9 (FcCH$_2$*N*H).

4.2.5. FcCH$_2$NH(CH$_2$)$_4$[G$_2$(SiMe$_2$Cl)$_4$] (5). The compound of second generation was prepared in a similar way to that for **4** starting from 0.65 g (1.01 mmol) of **2** and 0.88 mL (8.09 mmol) of chlorodimethylsilane in presence of Karstedt's catalyst. **5** was obtained as orange oil. Yield: 0.93 g (90%). ^{1}H-RMN ($CDCl_3$): δ -0.10 (s, Si*Me*), -0.07 (*Me*SiC*H*$_2$CH$_2$C*H*$_2$SiMe$_2$), 0.38 (s, Si*Me*$_2$Cl), 0.53-0.60 (m, NCH$_2$CH$_2$CH$_2$C*H*$_2$Si y SiC*H*$_2$CH$_2$C*H*$_2$Si), 0.86 (m, SiCH$_2$CH$_2$C*H*$_2$SiMe$_2$), 1.29-1.41 (m, NCH$_2$C*H*$_2$C*H*$_2$CH$_2$Si, SiCH$_2$C*H*$_2$CH$_2$Si), 2.60 (t, NC*H*$_2$CH$_2$CH$_2$CH$_2$Si), 3.73 (s, FcC*H*$_2$NH), 4.05-4.11 (s, FcC$_5$*H*$_5$ y FcC$_5$*H*$_4$). ^{13}C{^{1}H}-RMN ($CDCl_3$): δ -5.3 (Si*Me*), 1.8 (Si*Me*$_2$Cl), 13.7 (NCH$_2$CH$_2$CH$_2$*C*H$_2$Si), 17.6-20.6 (Si*C*H$_2$*C*H$_2$CH$_2$SiMe$_2$, Si*C*H$_2$*C*H$_2$CH$_2$Si), 21.2 (NCH$_2$CH$_2$*C*H$_2$CH$_2$Si), 21.4 (SiCH$_2$CH$_2$*C*H$_2$SiMe$_2$), 32.7 (NCH$_2$*C*H$_2$CH$_2$CH$_2$Si), 44.8 (N*C*H$_2$CH$_2$CH$_2$CH$_2$Si), 45.0 (Fc*C*H$_2$NH), 67.5-68.2(Fc*C*$_5$H$_5$ y Fc*C*$_5$H$_4$), 86.0 (C$_{ipso}$). ^{1}H-^{29}Si-HMBC (DMSO-d_6): δ 1.1 y 1.6 (Me*Si*CH$_2$CH$_2$CH$_2$*Si*Me), 31.2 (*Si*Me$_2$Cl). ^{1}H-^{15}N-HMBC ($CDCl_3$): δ -332.8 (FcCH$_2$*N*H).

4.2.6. FcCH$_2$NH(CH$_2$)$_4$[G$_3$(SiMe$_2$Cl)$_8$] (6). The compound of second generation was prepared in a similar way to that for **4** starting from 0.19 g (0.17 mmol) of **3** and 0.29 mL (2.67 mmol) of chlorodimethylsilane in presence of Karstedt's catalyst. **6** was obtained as orange oil. Yield: 0.28 g (90%). ^{1}H-RMN ($CDCl_3$): δ -0.10 (s, Si*Me*), -0.07 (*Me*SiC*H*$_2$CH$_2$C*H*$_2$SiMe$_2$), 0.38 (s, Si*Me*$_2$Cl), 0.40-0.60 (m, NCH$_2$CH$_2$CH$_2$C*H*$_2$Si y SiC*H*$_2$CH$_2$C*H*$_2$Si), 0.86 (m, SiCH$_2$CH$_2$C*H*$_2$SiMe$_2$), 1.29-1.41 (m, NCH$_2$C*H*$_2$C*H*$_2$CH$_2$Si, SiCH$_2$C*H*$_2$CH$_2$Si), 2.62 (t, NC*H*$_2$CH$_2$CH$_2$CH$_2$Si), 3.75 (s, FcC*H*$_2$NH), 4.07-4.11 (s, FcC$_5$*H*$_5$ y FcC$_5$*H*$_4$). ^{13}C{^{1}H}-RMN ($CDCl_3$): δ -5.3 (Si*Me*), 1.8 (Si*Me*$_2$Cl), 13.7 (NCH$_2$CH$_2$CH$_2$*C*H$_2$Si), 17.5-20.8 (Si*C*H$_2$*C*H$_2$CH$_2$SiMe$_2$, Si*C*H$_2$*C*H$_2$CH$_2$Si), 21.3 (NCH$_2$CH$_2$*C*H$_2$CH$_2$Si), 21.6 (SiCH$_2$CH$_2$*C*H$_2$SiMe$_2$), 32.7 (NCH$_2$*C*H$_2$CH$_2$CH$_2$Si), 44.8 (N*C*H$_2$CH$_2$CH$_2$CH$_2$Si), 45.0 (Fc*C*H$_2$NH), 67.4-68.2(Fc*C*$_5$H$_5$ y Fc*C*$_5$H$_4$), 86.1 (C$_{ipso}$). ^{1}H-^{29}Si-HMBC (DMSO-d_6): δ 1.1 y 1.6 (Me*Si*CH$_2$CH$_2$CH$_2$*Si*Me), 31.2 (*Si*Me$_2$Cl). ^{1}H-^{15}N-HMBC ($CDCl_3$): δ -332.8 (FcCH$_2$*N*H).

4.2.7. FcCH$_2$NH(CH$_2$)$_4$[G$_1$(SiMe$_2$H)$_2$] (7). An Et_2O solution of **4** (0.76 g, 1.31 mmol) was added dropwise to a stirred cooled solution of $LiAlH_4$ (1.30 mL, 2.61 mmol) in the same solvent and was kept stirring overnight at room temperature. Afterward, the mixture was added over a saturated water solution of $NaCO_3$ and the aqueous layer was then washed three times with Et_2O and dried over $MgSO_4$. The solvent was removed under vacuum yielding **7** as orange oil. Yield: 0.55 g (81%). ^{1}H-RMN ($CDCl_3$): δ -0.10 (s, Si*Me*), -0.04 (d, HSi*Me*$_2$), 0.53 (m, NCH$_2$CH$_2$CH$_2$C*H*$_2$Si y SiC*H*$_2$CH$_2$C*H*$_2$SiMe$_2$), 1.25-1.40 (m, NCH$_2$C*H*$_2$C*H*$_2$CH$_2$Si y

SiCH$_2$C*H*$_2$CH$_2$Si), 2.60 (t, NC*H*$_2$CH$_2$CH$_2$CH$_2$Si), 3.49 (s, FcC*H*$_2$NH), 3.82 (m, *H*SiMe$_2$) 4.07-4.13 (s, FcC$_5$*H*$_5$ y FcC$_5$*H*$_4$). ^{13}C{^{1}H}-RMN (CDCl$_3$): δ -5.1 (Si*Me*), -4.3 (HSi*Me*$_2$), 13.9 (NCH$_2$CH$_2$CH$_2$*C*H$_2$Si), 18.1-19.0 (Si*C*H$_2$*C*H$_2$*C*H$_2$SiMe$_2$), 21.8 (NCH$_2$CH$_2$*C*H$_2$CH$_2$Si), 34.1 (NCH$_2$*C*H$_2$CH$_2$CH$_2$Si), 49.1 (N*C*H$_2$CH$_2$CH$_2$CH$_2$Si), 49.4 (Fc*C*H$_2$NH), 67.7-68.4(Fc*C*$_5$H$_5$ y Fc*C*$_5$H$_4$), 86.9 (C$_{ipso}$). ^{1}H-^{29}Si-HMBC (DMSO-*d*$_6$): δ -14.1 (H*Si*Me$_2$), 1.8 (*Si*Me). ^{1}H-^{15}N-HMBC (CDCl$_3$): δ -332.8 (FcCH$_2$*N*H). Anal. Calcd for C$_{26}$H$_{49}$FeNSi$_3$ (515.78 g mol^{-1}): C, 60.55; H, 9.58; N, 2.72. Found: C, 59.89; H, 9.39; N, 3.01. MS: [M + H]$^+$ 516.22 uma (Calcd 516.25 uma).

4.2.8. FcCH$_2$NH(CH$_2$)$_4$[G$_2$(SiMe$_2$H)$_4$] (8). Following the procedure described for compound **7**, compound **8** was obtained as orange oil from the reaction of **5** (1.10 g, 1.06mmol) and LiAlH$_4$ (2 mL, 4.24 mmol). Yield: 0.80 g (85%). ^{1}H-RMN (CDCl$_3$): δ -0.10 (s, Si*Me*), -0.04 (d, HSi*Me*$_2$), 0.53 (m, NCH$_2$CH$_2$CH$_2$C*H*$_2$Si, SiC*H*$_2$CH$_2$C*H*$_2$Si, SiC*H*$_2$CH$_2$C*H*$_2$SiH), 1.25-1.40 (m, NCH$_2$C*H*$_2$C*H*$_2$CH$_2$Si, SiCH$_2$C*H*$_2$CH$_2$Si, SiCH$_2$C*H*$_2$CH$_2$SiH), 2.60 (t, NC*H*$_2$CH$_2$CH$_2$CH$_2$Si), 3.49 (s, FcC*H*$_2$NH), 3.81 (m, *H*SiMe$_2$) 4.07- 4.15 (s, FcC$_5$*H*$_5$ y FcC$_5$*H*$_4$). ^{13}C{^{1}H}-RMN (CDCl$_3$): δ -5.1 (Si*Me*), -4.3 (HSi*Me*$_2$), 14.0 (NCH$_2$CH$_2$CH$_2$*C*H$_2$Si), 18.1-19.0 (Si*C*H$_2$*C*H$_2$*C*H$_2$Si y Si*C*H$_2$*C*H$_2$*C*H$_2$SiH), 21.8 (NCH$_2$CH$_2$*C*H$_2$CH$_2$Si), 34.1 (NCH$_2$*C*H$_2$CH$_2$CH$_2$Si), 49.1 (N*C*H$_2$CH$_2$CH$_2$CH$_2$Si), 49.5 (Fc*C*H$_2$NH), 67.7-68.4(Fc*C*$_5$H$_5$ y Fc*C*$_5$H$_4$), 86.9 (C$_{ipso}$). ^{1}H-^{29}Si-HMBC (DMSO-*d*$_6$): δ -14.1 (H*Si*Me$_2$), 1.1 y 1.8 (Me*Si*CH$_2$CH$_2$CH$_2$*Si*Me). ^{1}H-^{15}N-HMBC (CDCl$_3$): δ -332.7 (FcCH$_2$*N*H). Anal. Calcd for C$_{44}$H$_{93}$FeNSi$_7$ (888.66 g mol^{-1}): C, 59.47; H, 10.55; N, 1.58. Found: C, 58.50; H, 10.14; N, 1.70. MS: [M + H]$^+$ 888.44 uma (Calcd 888.51 uma).

4.2.9. FcCH$_2$NH(CH$_2$)$_4$[G$_3$(SiMe$_2$H)$_8$] (9). Following the procedure described for compound **7**, compound **9** was obtained as orange oil from the reaction of **6** (0.28 g, 0.15 mmol) and LiAlH$_4$ (0.60 mL, 1.19 mmol). Yield: 0.20 g (83%). ^{1}H-RMN (CDCl$_3$): δ -0.10 (s, Si*Me*), 0.04 (d, HSi*Me*$_2$), 0.52-0.65 (m, NCH$_2$CH$_2$CH$_2$C*H*$_2$Si, SiC*H*$_2$CH$_2$C*H*$_2$Si, SiC*H*$_2$CH$_2$C*H*$_2$SiH), 1.25-1.40 (m, NCH$_2$C*H*$_2$C*H*$_2$CH$_2$Si, SiCH$_2$C*H*$_2$CH$_2$Si, SiCH$_2$C*H*$_2$CH$_2$SiH), 2.61 (t, NC*H*$_2$CH$_2$CH$_2$CH$_2$Si), 3.52 (s, FcC*H*$_2$NH), 3.83 (m, *H*SiMe$_2$) 4.07- 4.15 (s, FcC$_5$*H*$_5$ y FcC$_5$*H*$_4$). ^{13}C{^{1}H}-RMN (CDCl$_3$): δ -5.2 (Si*Me*), -4.4 (HSi*Me*$_2$), 13.9 (NCH$_2$CH$_2$CH$_2$*C*H$_2$Si), 18.3-19.0 (Si*C*H$_2$*C*H$_2$*C*H$_2$Si y Si*C*H$_2$*C*H$_2$*C*H$_2$SiH), 21.6 (NCH$_2$CH$_2$*C*H$_2$CH$_2$Si), 34.3 (NCH$_2$*C*H$_2$CH$_2$CH$_2$Si), 49.2 (N*C*H$_2$CH$_2$CH$_2$CH$_2$Si), 49.5 (Fc*C*H$_2$NH), 67.6-68.7(Fc*C*$_5$H$_5$ y Fc*C*$_5$H$_4$), 86.9 (C$_{ipso}$). ^{1}H-^{29}Si-HMBC (DMSO-*d*$_6$): δ -14.0 (H*Si*Me$_2$), 1.1 y 1.7 (Me*Si*CH$_2$CH$_2$CH$_2$*Si*Me). ^{1}H-^{15}N-HMBC (CDCl$_3$): δ -332.4 (FcCH$_2$*N*H). Anal. Calcd (found) for C$_{80}$H$_{9181}$FeNSi$_{15}$ (1634.43 g mol^{-1}): C, 59.79; H, 11.16; N, 0.86. Found: C, 58.64; H, 10.98; N, 1.06. MS: [M + H]$^+$ 686.31 uma (Calcd 686.44 uma).

4.2.10. FcCH$_2$NH(CH$_2$)$_4$[G$_1$(SiMe$_2$(CH$_2$)$_3$NMe$_2$)$_2$] (10). Compound **7** (0.44 g, 0.80 mmol) was dissolved in THF, *N,N*-dimethylallylamine (0.38 g, 3.21 mmol) was added under inert atmosphere and the resulting solution was heated at 50 °C for 24 h. Afterwards, the volatiles

was removed under vacuum, obtaining **10** as orange oil. Yield: 0.52 g (89%) ^{1}H-RMN ($CDCl_3$): δ -0.12 (s, Si*Me*), -0.07 (s, Si*Me*$_2$), 0.43-0.54 (m, $NCH_2CH_2CH_2CH_2Si$, $SiCH_2CH_2CH_2SiMe_2$, $SiCH_2CH_2CH_2NMe_2$), 1.26-1.42 (m, $NCH_2CH_2CH_2CH_2Si$, $SiCH_2CH_2CH_2SiMe_2$, $SiCH_2CH_2CH_2NMe_2$), 2.19 (s, N*Me*$_2$), 2.19 (m, $SiCH_2CH_2CH_2NMe_2$), 2.60 (t, $NCH_2CH_2CH_2CH_2Si$), 3.48 (s, $FcCH_2NH$), 4.06-4.16 (s, FcC_5H_5 y FcC_5H_4). ^{13}C{^{1}H}-RMN ($CDCl_3$): δ -5.0 (Si*Me*), -3.3 (Si*Me*$_2$), 12.9 ($SiCH_2CH_2CH_2NMe_2$), 14.0 ($NCH_2CH_2CH_2CH_2Si$), 18.1-19.0 ($SiCH_2CH_2CH_2SiMe_2$), 21.7 ($NCH_2CH_2CH_2CH_2Si$), 22.0 ($SiCH_2CH_2CH_2NMe_2$), 34.2 ($NCH_2CH_2CH_2CH_2Si$), 45.5 (N*Me*$_2$), 49.2 ($NCH_2CH_2CH_2CH_2Si$), 49.5 ($FcCH_2NH$), 63.5 ($SiCH_2CH_2CH_2NMe_2$), 67.7-68.5 (FcC_5H_5 y FcC_5H_4), 86.9 (C_{ipso}). ^{1}H-^{29}Si-HMBC (DMSO-*d*$_6$): δ 1.6 (*Si*Me), 2.0 (*Si*Me$_2$). ^{1}H-^{15}N-HMBC ($CDCl_3$): δ -353.2 (*N*Me$_2$), -332.8 ($FcCH_2NH$). Anal. Calcd for $C_{36}H_{71}FeN_3Si_3$ (686.07 g mol^{-1}): C, 63.02; H, 10.43; N, 6.12. Found: C, 62.68; H, 10.12; N, 5.98. MS: $[M + H]^+$ 686.31 uma (Calcd 686.44 uma).

4.2.11. $FcCH_2NH(CH_2)_4[G_2(SiMe_2(CH_2)_3NMe_2)_4]$ (11). Following the procedure described for compound **10**, compound **11** was obtained as orange oil from the reaction of **8** (0.36 g, 0.40 mmol) and N,N-dimethylallylamine (0.40 mL, 3.21 mmol). Yield: 0.44 g (90%). ^{1}H-RMN ($CDCl_3$): δ -0.10 (s, Si*Me*), -0.06 (s, Si*Me*$_2$), 0.53 (m, $NCH_2CH_2CH_2CH_2Si$, $SiCH_2CH_2CH_2Si$, $SiCH_2CH_2CH_2SiH$, $SiCH_2CH_2CH_2NMe_2$), 1.25-1.42 (m, $NCH_2CH_2CH_2CH_2Si$, $SiCH_2CH_2CH_2Si$, $SiCH_2CH_2CH_2SiH$, $SiCH_2CH_2CH_2NMe_2$), 2.19 (s, N*Me*$_2$), 2.19 (m, $SiCH_2CH_2CH_2NMe_2$), 2.59 (t, $NCH_2CH_2CH_2CH_2Si$), 3.49 (s, $FcCH_2NH$), 4.07- 4.15 (s, FcC_5H_5 y FcC_5H_4). ^{13}C{^{1}H}-RMN ($CDCl_3$): δ -5.0 (Si*Me*), -3.3 (Si*Me*$_2$), 12.9 ($SiCH_2CH_2CH_2NMe_2$), 13.9 ($NCH_2CH_2CH_2CH_2Si$), 18.1-19.0 ($SiCH_2CH_2CH_2Si$), 21.8 ($NCH_2CH_2CH_2CH_2Si$), 22.1 ($SiCH_2CH_2CH_2NMe_2$), 34.1 ($NCH_2CH_2CH_2CH_2Si$), 45.5 (N*Me*$_2$), 49.1 ($NCH_2CH_2CH_2CH_2Si$), 49.5 ($FcCH_2NH$), 63.4 ($SiCH_2CH_2CH_2NMe_2$), 67.7-68.4(FcC_5H_5, FcC_5H_4), 86.9 (C_{ipso}). ^{1}H-^{29}Si-HMBC (DMSO-*d*$_6$): δ 1.1 (*Si*$CH_2CH_2CH_2$*Si*), 1.9 (*Si*Me$_2$). ^{1}H-^{15}N-HMBC ($CDCl_3$): δ -352.90 (*N*Me$_2$), -332.7 ($FcCH_2NH$). Anal. Calcd. for $C_{64}H_{137}FeN_5Si_7$ (1229.25 g mol^{-1}): C, 62.53; H, 11.23; N, 5.70. Found: C, 61.87; H, 10.94; N, 5.35. MS: $[M + H]^+$ 1228.81 uma (Calcd 1228.87 uma).

4.2.12. $FcCH_2NH(CH_2)_4[G_3(SiMe_2(CH_2)_3NMe_2)_8]$ (12). Following the procedure described for compound **10**, compound **12** was obtained as orange oil from the reaction of **9** (0.23 g, 0.14 mmol) and *N,N*-dimethylallylamine (0.28 mL, 2.22 mmol). Yield: 0.29 g (90%). ^{1}H-RMN ($CDCl_3$): δ -0.12 (s, Si*Me*), -0.07 (s, Si*Me*$_2$), 0.48-0.57 (m, $NCH_2CH_2CH_2CH_2Si$, $SiCH_2CH_2CH_2Si$, $SiCH_2CH_2CH_2SiH$, $SiCH_2CH_2CH_2NMe_2$), 1.25-1.47 (m, $NCH_2CH_2CH_2CH_2Si$, $SiCH_2CH_2CH_2Si$, $SiCH_2CH_2CH_2SiH$, $SiCH_2CH_2CH_2NMe_2$), 2.18 (s, N*Me*$_2$), 2.20 (m, $SiCH_2CH_2CH_2NMe_2$), 2.59 (t, $NCH_2CH_2CH_2CH_2Si$), 3.47 (s, $FcCH_2NH$), 4.07-4.15 (s, FcC_5H_5 y FcC_5H_4). ^{13}C{^{1}H}-RMN ($CDCl_3$): δ -5.0 (Si*Me*), -3.3 (Si*Me*$_2$), 12.9 ($SiCH_2CH_2CH_2NMe_2$), 14.0 ($NCH_2CH_2CH_2CH_2Si$), 18.1-19.0 ($SiCH_2CH_2CH_2Si$), 21.9 ($NCH_2CH_2CH_2CH_2Si$), 22.2 ($SiCH_2CH_2CH_2NMe_2$), 34.3 ($NCH_2CH_2CH_2CH_2Si$), 45.5 (N*Me*$_2$),

49.2 (N*C*$H_2CH_2CH_2CH_2Si$), 49.6 (Fc*C*H_2NH), 63.4 ($SiCH_2CH_2CH_2NMe_2$), 67.5-68.6(FcC_5H_5, FcC_5H_4), 87.1 (C_{ipso}). ^{1}H-^{29}Si-HMBC (DMSO-d_6): δ 1.1 (*Si*$CH_2CH_2CH_2Si$), 1.9 (*Si*Me_2). ^{1}H-^{15}N-HMBC ($CDCl_3$): δ -352.9 (*N*Me_2), -333.1 ($FcCH_2NH$). Anal. Calcd. for $C_{120}H_{269}FeN_9Si_{15}$ (2315.61 g mol^{-1}): C, 62.24; H, 11.71; N, 5.44. Found: C, 61.03; H, 10.66; N, 4.97. MS: [M + H]$^+$ 2314.70 uma (Calcd 2314.72 uma).

4.2.13. $FcCH_2NH_2Cl(CH_2)_4[G_1(SiMe_2(CH_2)_3NHMe_2Cl)_2]$ (13). HCl (2M in Et_2O, 0.50 mL, 0.98 mmol) was added to a stirred solution of **10** (0.30 g, 0.44 mmol) in Et_2O at room temperature for 2 h. The solution is centrifuged and then the precipitate is washed several times with ether and hexane, yielding **13** as dark brown solid. Yield: 0.30 g (86%) ^{1}H-RMN (DMSO-d_6): δ -0.10 (s, Si*Me*), -0.04 (s, SiMe_2), 0.42-0.54 (m, $NCH_2CH_2CH_2CH_2Si$, $SiCH_2CH_2CH_2SiMe_2$, $SiCH_2CH_2CH_2NMe_2$), 1.27(m, $NCH_2CH_2CH_2CH_2Si$, $SiCH_2CH_2CH_2SiMe_2$), 1.59 (m, $SiCH_2CH_2CH_2NMe_2$), 2.68 (s, NHMe_2), 2.94 (m, $SiCH_2CH_2CH_2NHMe_2$), 3.87 (t, $NCH_2CH_2CH_2CH_2Si$), 4.19-4.20 (s, FcC_5H_5 y FcC_5H_4), 4.43 (s, $FcCH_2NH$). ^{13}C{^{1}H}-RMN (DMSO-d_6): δ -5.6 (Si*Me*), 4.0 (SiMe_2), 10.9 ($SiCH_2CH_2CH_2NMe_2$), 12.6 ($NCH_2CH_2CH_2CH_2Si$), 17.0-19.0 ($SiCH_2CH_2CH_2Si$), 18.6 ($NCH_2CH_2CH_2CH_2Si$), 20.2 ($SiCH_2CH_2CH_2NMe_2$), 28.4 ($NCH_2CH_2CH_2CH_2Si$), 41.3 (NHMe_2), 44.8 ($H_2NCH_2CH_2CH_2CH_2Si$), 45.3 ($FcCH_2NH_2$), 58.6 ($SiCH_2CH_2CH_2NHMe_2$), 67.7-68.5 (s, FcC_5H_5 y FcC_5H_4), 76.1 (C_{ipso}). ^{1}H-^{29}Si-HMBC (DMSO-d_6): δ 1.8 (*Si*Me), 2.0 (*Si*Me_2). Anal. Calcd for $C_{36}H_{74}Cl_3FeN_3Si_3$ (795.46g mol^{-1}): C, 54.36; H, 9.38; N, 5.28. Found: C, 53.52; H, 9.45; N, 5.04.

4.2.14. $FcCH_2NH_2Cl(CH_2)_4[G_2(SiMe_2(CH_2)_3NHMe_2Cl)_4]$ (14). Following the procedure described for compound **13**, compound **14** was obtained as dark brown solid from the reaction of **11** (0.15 g, 0.13 mmol) and HCl (2M in Et_2O, 0.26 mL, 0.52 mmol). Yield: 0.15 g (84%). ^{1}H-RMN (DMSO-d_6): δ -0.10 (s, Si*Me*), -0.04 (s, SiMe_2), 0.38-0.53 (m, $H_2NCH_2CH_2CH_2CH_2Si$, $SiCH_2CH_2CH_2Si$, $SiCH_2CH_2CH_2NHMe_2$), 1.25-1.40 (m, $H_2NCH_2CH_2CH_2CH_2Si$, $SiCH_2CH_2CH_2Si$), 1.60 (m, $SiCH_2CH_2CH_2NHMe_2$), 2.68 (s, NHMe_2), 2.91 (m, $SiCH_2CH_2CH_2NHMe_2$), 3.85 (t, $H_2NCH_2CH_2CH_2CH_2Si$), 4.07- 4.15 (s, FcC_5H_5, FcC_5H_4), 4.44 (s, $FcCH_2NH_2$). ^{13}C{^{1}H}-RMN (DMSO-d_6): δ -5.4 (Si*Me*), -4.0 (SiMe_2), 12.9 ($SiCH_2CH_2CH_2NHMe_2$), 13.9 ($H_2NCH_2CH_2CH_2CH_2Si$), 17.4-18.8 ($SiCH_2CH_2CH_2Si$), 20.2 ($H_2NCH_2CH_2CH_2CH_2Si$), 22.7 ($SiCH_2CH_2CH_2NHMe_2$), 28.4 ($H_2NCH_2CH_2CH_2CH_2Si$), 41.3 (NHMe_2), 44.7 ($H_2NCH_2CH_2CH_2CH_2Si$), 45.3 ($FcCH_2NH_2$), 58.7 ($SiCH_2CH_2CH_2NHMe_2$), 67.7-68.4(FcC_5H_5 y FcC_5H_4), 76.5 (C_{ipso}). ^{1}H-^{29}Si-HMBC (DMSO-d_6): δ 1.2 (*Si*$CH_2CH_2CH_2Si$), 2.0 (*Si*Me_2).

Anal. Calcd. for $C_{64}H_{142}Cl_5FeN_5Si_7$ (1411.57 g mol^{-1}): C, 56.46; H, 10.14; N, 4.96. Found: C, 56.02; H, 9.94; N, 4.68.

4.2.15. $FcCH_2NH_2Cl(CH_2)_4[G_3(SiMe_2(CH_2)_3NHMe_2Cl)_8]$ (15). Following the procedure described for compound **13**, compound **15** was obtained as pale yellow solid from the reaction

of **12** (0.15 g, 0.06 mmol) and HCl (2M in Et_2O, 0.27 mL, 0.54 mmol). Yield: 0.15 g (84%). ^{1}H-RMN (DMSO-d_6): δ -0.10 (s, Si*Me*), -0.04 (s, SiMe_2), 0.38-0.52 (m, $H_2NCH_2CH_2CH_2CH_2Si$, $SiCH_2CH_2CH_2Si$, $SiCH_2CH_2CH_2NHMe_2$), 1.30 (m, $H_2NCH_2CH_2CH_2CH_2Si$, $SiCH_2CH_2CH_2Si$), 1.60 (m, $SiCH_2CH_2CH_2NHMe_2$), 2.68 (s, NHMe_2), 2.94 (m, $SiCH_2CH_2CH_2NHMe_2$), 3.86 (t, $H_2NCH_2CH_2CH_2CH_2Si$), 4.19 (s, FcC_5H_5, FcC_5H_4), 4.44 (s, $FcCH_2NH_2$). ^{13}C{^{1}H}-RMN (DMSO-d_6): δ -5.1 (Si*Me*), -4.1 (SiMe_2), 12.9 ($SiCH_2CH_2CH_2NHMe_2$), 13.9 ($H_2NCH_2CH_2CH_2CH_2Si$), 17.3-18.9 ($SiCH_2CH_2CH_2Si$), 20.1 ($H_2NCH_2CH_2CH_2CH_2Si$), 22.8 ($SiCH_2CH_2CH_2NHMe_2$), 28.4 ($H_2NCH_2CH_2CH_2CH_2Si$), 41.3 (NHMe_2), 44.8 ($H_2NCH_2CH_2CH_2CH_2Si$), 45.3 ($FcCH_2NH_2$), 58.5 ($SiCH_2CH_2CH_2NHMe_2$), 67.7-68.4(FcC_5H_5 y FcC_5H_4), 76.5 (C_{ipso}). ^{1}H-^{29}Si-HMBC (DMSO-d_6): δ 1.2 (*Si*$CH_2CH_2CH_2Si$), 2.0 (*Si*Me_2). Anal. Calcd. for $C_{120}H_{269}FeN_9Si_{15}$ (2315,61 g mol^{-1}): C, 62.24; H, 11.71; N, 5.44. Found: C, 61.03; H, 10.66; N, 4.97. Anal. Calcd. for $C_{120}H_{278}Cl_9FeN_9Si_{15}$ (2643.78 g mol^{-1}): C, 54.52; H, 10.60; N, 4.77. Found: C, 54.12; H, 10.36; N, 4.67.

4.2.16. $(ClNH_3)(CH_2)_4[G_1(SiMe_2(CH_2)_3NHMe_2Cl)_2]$ (16).

To a DMF solution (25 mL) of carbosilane dendron BrG_1SiMe_2H[53] (0.20g, 0.52mmol) were added the commercial reagent KPht (0.21 g, 1.14 mmol) and 10% NaI. The reaction mixture was heated to 80 °C for 16 h in a Teflon-valved ampule. Then a Et_2O/H_2O extraction was performed, and after the organic phase was dried over $MgSO_4$ and the volatiles were evaporated, compound $PhtG_1(SiMe_2H)_2$ **I** (Yield: 0.21 g, 0.47 mmol, 90%) was obtained as a yellowish oil. After, Compound **I** (0.13 g, 0.31 mmol) was dissolved in THF, and excess N,N-dimethylallylamine (0.15 mL, 1.20 mmol) was added under inert atmosphere and the resulting solution was heated at 50 °C for 24 h. Afterwards, the volatiles was removed under vacuum, obtaining $PhtG_1(SiMe_2(CH_2)_3NH_2)_2$ **II** (Yield: 0.16 g, 0.26 mmol, 86%) as orange oil. The subsequent reaction between a solution of **II** (0.16 g, 0.26 mmol) in MeOH and N_2H_4 (0.01 mL, 0.32 mmol)) in excess at 80 °C in a sealed ampule overnight led the product $NH_2G_1(SiMe_2(CH_2)_3NH_2)_2$ **III** (Yield: 0.09 g, 0.18 mmol, 70%)**,** that was obtained after remove of solvent and excess N_2H_4 and extracted into CH_2Cl_2. Finally, HCl (2M in Et_2O, 0.20 ml, 0.39 mmol) was added to a stirred solution of **III** (0.09 g, 0.18 mmol) in Et_2O at room temperature for 2 h. The solution is centrifuged and then the precipitate is washed several times with ether and hexane, yielding **16** as white solid. Yield: 0.09 g (85%). ^{1}H NMR (D_2O): δ -0.15 (s, 3H, *Me*Si), -0.11 (s, 12H, SiMe_2), 0.50 (m, 14H, CH_2Si) 1.28 (m, 6H, CH_2CH_2Si), 1.56 (m, 6H, $CH_2CH_2NH_3Cl$), 2.85 (m, 6H, CH_2NH_3Cl). ^{13}C {^{1}H} NMR (D_2O): δ -5.65 (*Me*Si), -4.20 (SiMe_2), 11.19-21.55 ($SiCH_2$), 42.32 and 39.18 (CH_2NH_3Cl).

SUPPORTING INFORMATION

^{1}H and ^{13}C NMR, spectra of all compounds, and the synthesis of selected compounds.

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GRAPHIC ABSTRACT: