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1                   **Synthesis of degradable cationic carbosilane dendrimers based**  
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5                                   **on Si-O or ester bonds**  
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1       **Abstract**  
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3       Several cationic carbosilane dendritic molecules have been synthesized containing two different types  
4 of degradable bonds: Si-O and ester bonds. The first type of systems was prepared by reacting carbosilane  
5 dendrimers containing peripheral Si-Cl bonds with first generation dendrons presenting a –OH function at  
6 the focal point and amine peripheral functions. The second type of systems was prepared by esterification  
7 between a dendrimer containing acid groups and an alcohol amine. The stability in water of both types of  
8 cationic systems was evaluated.  
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10       **Keywords:** biodegradable dendrimers, carbosilane dendrimers, ester bonds, stability.  
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## 1. Introduction

Non-viral gene carriers are synthetic systems designed to deliver plasmids, nucleic acids (DNA and RNA) or oligonucleotides to cells with the aim to treat diseases.<sup>1</sup> Several systems have been designed following controlled procedures for this purpose.<sup>2-9</sup> These carriers interact with nucleic acids, usually electrostatically, compacting them and preventing their degradation. Therefore, cationic macromolecules have been widely explored as nucleic acid vectors.<sup>10</sup> However, the intrinsic toxicity of cationic macromolecules is a major drawback and the search of degradable derivatives is a key target of this research area, since degradation of the cationic macromolecule will lead to smaller systems, favoring also their clearance from the body.

One type of non-viral systems widely studied are dendrimers, which are spherical macromolecules with well-defined size and structure, monodisperse, flexible, and with a multivalent molecular surface.<sup>11-13</sup> The controlled synthetic procedure minimizes structural defects and allows establishing structure-activity relationships more easily than for polymeric materials. Cationic dendrimers containing different skeletons have been explored for gene therapy, based on the multicationic charge on dendrimers surface.<sup>8,14-19</sup> Consequently, the development of dendrimers with biodegradable structures leading to less toxic fragments is in the center of attention.<sup>20</sup> The main type of degradable systems contains aliphatic polyester moieties,<sup>20-23</sup> which usually also gives hydrophilicity to the dendrimer scaffold. It is assumed that ester bonds will be degraded in biological environment due to action of enzymes or well by the pH conditions of some body or cell regions. In fact, several studies indicate that hydrolysis is mainly produced at pH ranging from 7 to 9<sup>24,25</sup> and is accelerated in the presence of esterases.<sup>26</sup>

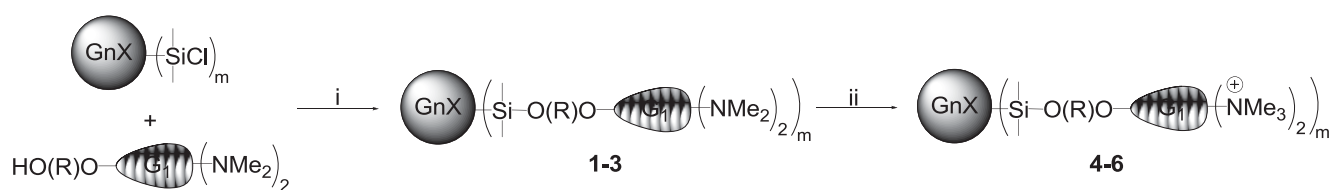
A different approach has been the preparation of carbosilane dendrimers with unstable peripheral Si-O bonds close to the cationic charge, which were prepared by alcoholysis of Si-Cl bonds.<sup>27-29</sup> These water-soluble derivatives bind oligonucleotides and siRNA, protect them from degradation and transport them to the interior of a range of cell types.<sup>27,28,30-33</sup> The hydrophobic framework of these macromolecules, formed by C-C and Si-C bonds, is important for this application, making easier the trespassing of cell membranes and also being able to surpass the blood brain barrier.<sup>34,35</sup> However, this outer Si-O bond is easily

degraded by water and therefore, these dendrimers have limited applications beyond *in vitro* assays. Other type of degradable carbosilane dendrimers, also very unstable in protic environment, has been described containing an acyloxysilane framework.<sup>36</sup>

With the aim to avoid the problem of fast hydrolysis in degradable carbosilane dendrimers, we have designed new cationic systems through two different strategies: with inner Si-O bonds or with peripheral ester bonds. The first type of dendrimers has been prepared by coupling carbosilane dendrons with carbosilane dendrimers. The dendrons present amine peripheral functions and a hydroxyl moiety at the focal point whereas dendrimers are decorated with Si-Cl bonds. For the second type of systems, dendrimers with acid groups have been synthesized followed by and acid-alcohol esterification. The characterization and water stability of these new dendritic macromolecules are also here discussed.

## 2. Results and Discussion

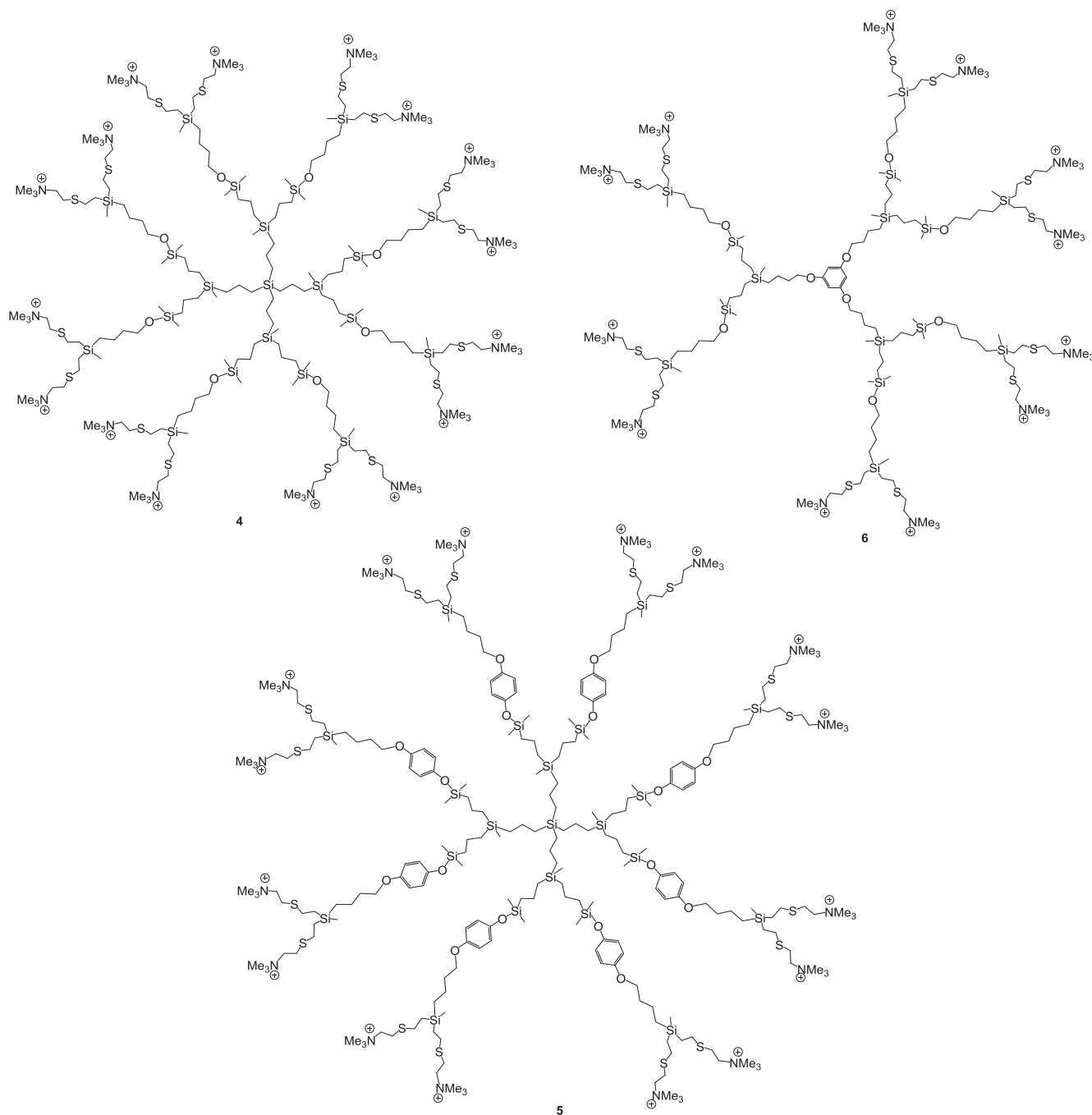
For the synthesis of dendrimers with a hydrolysable Si-O bond we have employed dendrimer cores derived from a Si atom (eight Si-Cl bonds)<sup>37</sup> or from a polyphenoxo group (six Si-Cl bonds),<sup>38</sup> and a first generation carbosilane dendron (two amine -NMe<sub>2</sub> functions, named as HOROG<sub>1</sub>(NMe<sub>2</sub>)<sub>2</sub>, R = (CH<sub>2</sub>)<sub>2</sub>, C<sub>6</sub>H<sub>4</sub>) with a hydroxyl moiety at the focal point, coming from ethyleneglycol (R = (CH<sub>2</sub>)<sub>2</sub>) or hydroquinone (R = C<sub>6</sub>H<sub>4</sub>) fragments.<sup>39</sup>



**Scheme 1.** Synthesis of cationic dendrons with Si-O bonds (R = C<sub>2</sub>H<sub>4</sub>, C<sub>6</sub>H<sub>4</sub>). i) NEt<sub>3</sub>; ii) MeI.

The reactions of dendrimers with wedges in the presence of NEt<sub>3</sub> afforded the corresponding amine-terminated dendrimers **1** (Si atom core, ethyleneglycol focal point), **2** (Si atom core, hydroquinone focal point), and **3** (polyphenoxo core, ethyleneglycol focal point) (scheme 1, figure S1). Transformation of the Si-Cl bonds into Si-O bonds was clearly detected by means of NMR spectroscopy. Thus, <sup>1</sup>H NMR spectra

1 showed the shifting for the MeSi groups from  $\delta$  ca. 0.3 (MeSiCl) to  $\delta$  ca. 0.0 (MeSiO) and the  $^{29}\text{Si}$  NMR  
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3 spectra also showed this change for the outermost Si atoms from  $\delta$  ca. 30 (MeSiCl) to  $\delta$  ca. 5 (MeSiO).  
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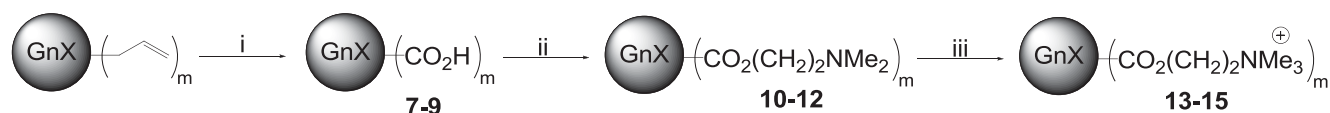
**Figure 1.** Drawing of cationic dendrimers 4-6.

The respective cationic derivatives 4 (Si atom core, ethyleneglycol focal point), 5 (Si atom core, hydroquinone focal point), and 6 (polyphenoxo core, ethyleneglycol focal point) were easily obtained after reaction of compounds 1-3 with excess MeI. Dendrimers 4-6 were obtained as yellowish solids soluble in

1 very polar solvents as DMSO. Quaternization of the nitrogen atoms was mainly identified by the  
2  
3 resonances in the  $^1\text{H}$  NMR spectra at about  $\delta$  3.0 for the methyl groups bound to this atom, shifted from  $\delta$   
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5 *ca.* 2.2 in the neutral compounds.  
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8 The stability of the Si-O bonds of compounds 4-6 were tested by addition of one eq. of  $\text{H}_2\text{O}$  *per* Si-O  
9 bond to  $\text{DMSO-}D_6$  solutions of these compounds and their evolutions were followed by  $^1\text{H-}^{29}\text{Si}$  HMBC  
10 NMR spectroscopy. These processes showed the hydrolysis of the Si-O-C bonds by means of the  
11 disappearance of the cross-peak belonging to the silicon atom of these bonds ( $\delta$  *ca.* 18) and the appearing  
12 of a new resonance at  $\delta$  *ca.* 10 corresponding to Si-OH systems, which further evolved to Si-O-Si bonds ( $\delta$   
13 *ca.* 5). The rate of hydrolysis of Si-OR bonds is clearly dependent of pendant R groups. In the case of  
14 compounds 4 and 6 (R =  $\text{O}(\text{CH}_2)_2\text{O}$ ), obtained from dendrons with ethyleneglycol at the focal point, the  
15 breakup of this bond is produced immediately. The same procedure for dendrimer 5 (R =  $\text{OC}_6\text{H}_4\text{O}$ ) kept  
16 the system unchanged, being necessary 20 fold excess  $\text{H}_2\text{O}$  to produce the complete hydrolysis. Hence, the  
17 hydrolysis of cationic dendrimers 4-6 would give first generation cationic dendrons of the type  
18  $\text{HOROG}_1(\text{NMe}_3^+)_2$  and also silicone-type polymers. Due to the small size of dendrons they present very  
19 low toxicity and they would be easily clearance from the body.<sup>40</sup>  
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37 To afford the second type of dendrimers with degradable ester bonds, we have followed the next  
38 synthetic procedure (Scheme 2): thiol-ene addition of mercaptopropionic acid to allyl-decorated  
39 dendrimers, coupling of the previous acid dendrimers with *N,N*-dimethylamineethanol and finally addition  
40 of MeI. As in previous dendrimers, two different cores have been employed, Si atom and trisubstituted  
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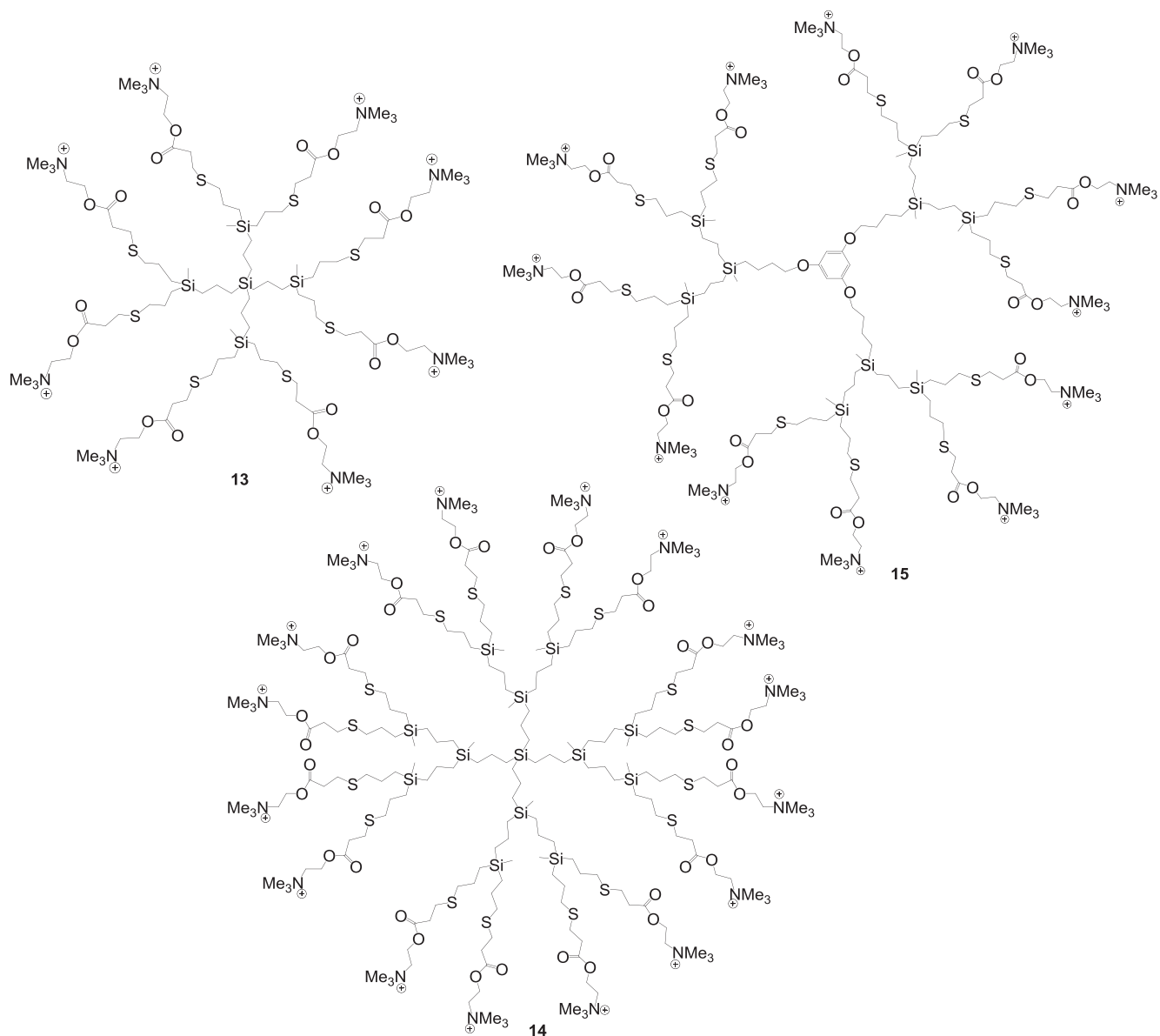
**Scheme 2.** Synthesis of cationic dendrimers with ester bonds. i)  $\text{HS}(\text{CH}_2)_2\text{CO}_2\text{H}$ , DMPA,  $h\nu$ ; ii)  $\text{HO}(\text{CH}_2)_2\text{NMe}_2$ , EDCI, DMAP; iii) MeI.

1 Hence, the first step is the reaction of allyl derivatives  $G_nXA_m$  ( $X = \text{Si}$ ,  $n = 1$ ,  $m = 8$ ;  $X = \text{Si}$ ,  $n = 2$ ,  $m =$   
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3 16;  $X = \text{C}_6\text{H}_3\text{O}_3$ ,  $n = 2$ ,  $m = 12$ ) with mercaptopropionic acid under UV irradiation, obtaining the  
4  
5 respective acid dendrimers  $G_nX(\text{S-CO}_2\text{H})_m$  ( $X = \text{Si}$ ,  $n = 1$ ,  $m = 8$  (**7**);  $X = \text{Si}$ ,  $n = 2$ ,  $m = 16$  (**8**);  $X =$   
6  
7  $\text{C}_6\text{H}_3\text{O}_3$ ,  $n = 2$ ,  $m = 12$  (**9**)) in high yields (> 85%). NMR spectroscopy clearly showed this transformation  
8  
9 with the disappearance of the resonances belonging to the allyl groups and the presence of the resonances  
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11 belonging to the new alkyl chain formed ( $\text{Si}(\text{CH}_2)_3\text{S}$ ) and to the new chain introduced ( $\text{S}(\text{CH}_2)_2\text{CO}$ ),  
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13 both in the  $^1\text{H}$  NMR and in the  $^{13}\text{C}$  NMR.  
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18 Next, reaction of esterification between dendrimers **7-9** and the alcohol-amine  $\text{HO}(\text{CH}_2)_2\text{NMe}_2$ , in the  
19  
20 presence of coupling agents, led to the corresponding ester dendrimers  $G_nX(\text{S-CO}_2(\text{CH}_2)_2\text{NMe}_2)_m$  ( $X = \text{Si}$ ,  
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22  $n = 1$ ,  $m = 8$  (**10**);  $X = \text{Si}$ ,  $n = 2$ ,  $m = 16$  (**11**);  $X = \text{C}_6\text{H}_3\text{O}_3$ ,  $n = 2$ ,  $m = 12$  (**12**)) in high yields (> 80%). The  
23  
24 presence of the ester bond was confirmed in the  $^1\text{H}$  NMR spectrum by the resonance around  $\delta$  ca. 4.20 for  
25  
26 the  $\text{CH}_2\text{O}$  group and in the  $^{13}\text{C}$  NMR spectrum by the resonance at about  $\delta$  ca. 170 for the carbon atom of  
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28 the carbonyl group. Moreover, the resonances for the outer chain  $(\text{CH}_2)_2\text{NMe}_2$  were also observed.  
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32 Finally, quaternization of the amine groups with excess MeI allowed obtaining the goal cationic  
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34 dendrimers  $G_nX(\text{S-CO}_2(\text{CH}_2)_2\text{NMe}_3^+)_m$  ( $X = \text{Si}$ ,  $n = 1$ ,  $m = 8$  (**13**);  $X = \text{Si}$ ,  $n = 2$ ,  $m = 16$  (**14**);  $X =$   
35  
36  $\text{C}_6\text{H}_3\text{O}_3$ ,  $n = 2$ ,  $m = 12$  (**15**), Figure 2) in high yields (> 90%). Clearly, the  $^1\text{H}$  NMR spectra showed the  
37  
38 shifting of the methyl groups bound to the nitrogen atom from ca.  $\delta$  ca. 2.20 to  $\delta$  ca. 3.20, whilst both  $^1\text{H}$   
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40 and  $^{13}\text{C}$  NMR spectra also showed the presence of the ester linkage. The stability of these derivatives was  
41  
42 checked by  $^1\text{H}$  NMR spectroscopy. Cationic dendrimers kept unaltered in  $\text{D}_2\text{O}$  solutions even after heating  
43  
44 at 40 °C. It is important to note that the breaking off of the ester bond would lead to acid or carboxylate  
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46 dendrimers, which are clearly less toxic.<sup>41</sup>  
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**Figure 2.** Drawing of cationic dendrimers **13-15**.

### 3. Conclusions

Cationic carbosilane dendrimers with degradable bonds can be prepared following two different approaches: 1) by reacting dendrimers with Si-Cl peripheral bonds with amine dendrons containing a hydroxyl group at the focal point; 2) by reacting dendrimers with acid peripheral groups with an alcohol-amine; and finally by quaternization of neutral compounds by adding MeI.

1 Dendrimers with internalized Si-O bonds were very water unstable, although the presence of aryl  
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3 groups attached to the oxygen atom of Si-OR fragment notably reduces hydrolysis rate with respect to  
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5 compounds with an alkyl chain attached to this atom. Thus, these compounds would be rejected for future  
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7 biomedical assays. On the other hand, dendrimers with ester bonds show stability in water media and  
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9 could be adequate candidates to study their capability as carriers for drug or gene delivery.  
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## 15 4. Experimental Section

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17 **4.1. General Considerations.** All reactions were carried out under inert atmosphere and solvents were  
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19 purified from appropriate drying agents when necessary. NMR spectra were recorded on a Varian Unity  
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21 VXR-300 (300.13 ( $^1\text{H}$ ), 75.47 ( $^{13}\text{C}$ ) MHz) or on a Bruker AV400 (400.13 (1H), 100.60 ( $^{13}\text{C}$ ), 40.56 ( $^{15}\text{N}$ ),  
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23 79.49 ( $^{29}\text{Si}$ ) MHz). Chemical shifts ( $\delta$ ) are given in ppm.  $^1\text{H}$  and  $^{13}\text{C}$  resonances were measured relative to  
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25 internal deuterated solvent peaks considering TMS = 0 ppm, meanwhile  $^{15}\text{N}$  and  $^{29}\text{Si}$  resonances were  
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27 measured relative to external MeNO and TMS, respectively. When necessary, assignment of resonances  
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29 was done from HSQC, HMBC, COSY, TOCSY and NOESY NMR experiments. Elemental analyses were  
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31 performed on a LECO CHNS-932. Mass Spectra were obtained from a Thermo Scientific and an Agilent  
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33 6210. Thiol-ene reactions were carried out employing a HPK 125 W mercury lamp from Heraeus  
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35 Noblelight with maximum energy at 365 nm, in normal glassware under an inert atmosphere. Compounds  
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37  $\text{NEt}_3$ , MeI,  $\text{HS}(\text{CH}_2)_2\text{CO}_2\text{H}$ , 2,2'-dimethoxy-2-phenylacetophenone (DMPA), N,N-dimethylaminopyridine  
38  
39 (DMAP),  $\text{HO}(\text{CH}_2)_2\text{NMe}_2$ , and *N*-(3-dimethylaminopropyl)-*N'*-ethylcarbodiimide hydrochloride (EDCI)  
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41 were obtained from commercial sources. Compounds  $[\text{G}_1\text{Si}(\text{Cl})_8]$ ,<sup>37</sup>  $[\text{G}_1\text{O}_3(\text{Cl})_6]$ ,<sup>38</sup>  $[\text{HOROG}_1(\text{S-NMe}_2)_2]$   
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43 ( $\text{R} = (\text{CH}_2)_2, \text{C}_6\text{H}_4$ ),<sup>42</sup>  $[\text{G}_1\text{SiA}_8]$ ,  $[\text{G}_2\text{SiA}_{16}]$ , and  $[\text{G}_2\text{O}_3\text{A}_{12}]$ <sup>38</sup> were synthesized as published.  
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## 52 4.2. Synthesis of selected compounds.

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54 The synthesis of all compounds is described in Supporting Information, collecting here a selection.  
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57 **Dendrimer 1.** To a solution of  $[\text{G}_1\text{Si}(\text{Cl})_8]$  (0.150 mg, 0.103 mmol) in THF (50 ml) was added  $\text{NEt}_3$   
58  
59 (1.65 mmol) and  $[\text{HOROG}_1(\text{S-NMe}_2)_2]$  ( $\text{R} = (\text{CH}_2)_2$ ) (0.350 g, 0.825 mmol) and the reaction was stirred  
60  
61 for 16 h. Afterward, the volatiles were removed under vacuum until ca. 15 ml, hexane was added (ca. 15  
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1 ml), the solution was filtered and volatiles were removed under vacuum, obtaining **1** as a yellowish oil  
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3 (0.32 g, 74 %). Data for **1**:  $^1\text{H}$  NMR ( $\text{CDCl}_3$ ): -0.09 (s, 24H,  $\text{Si}(\text{CH}_3)_2$ ); 0.01 (s, 12H,  $\text{Si}(\text{CH}_3)\text{CH}_2\text{CH}_2\text{S}$ );  
4  
5 0.08 (s, 24H,  $\text{Si}(\text{CH}_3)_2\text{O}$ ); 0.54 (m, 32H,  $\text{CH}_2\text{Si}$ ); 0.64 (m, 8H,  $\text{OCH}_2\text{CH}_2\text{CH}_2\text{CH}_2\text{Si}$ ); 0.89 (t, 16H,  
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7  $\text{SiCH}_2\text{CH}_2\text{S}$ ); 1.34 (m, 24H,  $\text{CH}_2\text{CH}_2\text{Si}$ ); 1.58 (m, 8H,  $\text{OCH}_2\text{CH}_2\text{CH}_2\text{CH}_2\text{Si}$ ); 2.24 (s, 48H,  $\text{N}(\text{CH}_3)_2$ );  
8  
9 2.48 (t, 16H,  $\text{SiCH}_2\text{CH}_2\text{S}$ ); 2.53 (t, 16H,  $\text{SCH}_2\text{CH}_2\text{N}$ ); 2.61 (t, 16H,  $\text{SCH}_2\text{CH}_2\text{N}$ ); 3.45 (m, 16H,  
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11  $\text{OCH}_2\text{CH}_2\text{O}$ ); 3.70 (t, 8H,  $\text{OCH}_2\text{CH}_2\text{CH}_2\text{CH}_2\text{Si}$ );  $^{13}\text{C}$  NMR ( $\text{CDCl}_3$ ): -5.3,-4.9, -1.8 ( $\text{SiCH}_3$ ); 13.5, 17.8,  
12  
13 17.9, 18.6, 19.1, 19.9, 20.4, 21.1 ( $\text{CH}_2\text{Si}$  and  $\text{CH}_2\text{CH}_2\text{Si}$ ); 14.5 ( $\text{SiCH}_2\text{CH}_2\text{S}$ ); 27.6 ( $\text{SiCH}_2\text{CH}_2\text{S}$ ); 29.7  
14  
15 ( $\text{SCH}_2\text{CH}_2\text{N}$ ); 33.6 ( $\text{OCH}_2\text{CH}_2\text{CH}_2\text{CH}_2\text{Si}$ ); 45.4 ( $\text{N}(\text{CH}_3)_2$ ); 59.3 ( $\text{SiCH}_2\text{CH}_2\text{S}$ ); 62.0  
16  
17 ( $\text{OCH}_2\text{CH}_2\text{CH}_2\text{CH}_2\text{Si}$ ); 71.0, 72.1 ( $\text{OCH}_2\text{CH}_2\text{O}$ );  $^{15}\text{N}$  NMR ( $\text{CDCl}_3$ ): 27.5;  $^{29}\text{Si}$  NMR ( $\text{CDCl}_3$ ): 2.8  
18  
19 ( $\text{SiMe}$ ), 18.0 ( $\text{SiMe}_2\text{O}$ ). Elemental analysis ( $\text{C}_{192}\text{H}_{444}\text{N}_{16}\text{O}_8\text{S}_{16}\text{Si}_{21}$ , FW = 4208.52 g mol $^{-1}$ ): C, 54.79; H,  
20  
21 10.63; N, 5.33; S, 12.19; Exp.: C, 53.10; H, 11.46; N, 5.36; S, 11.94.

**Dendrimer 4.** Compound **1** (0.110 g, 0.026 mmol) was solved in THF (50 mL) and MeI (0.83 mmol  
28  
29 (excess 32 fold)) was added. The solution was stirred for 16 h. Next, volatiles were removed under  
30  
31 vacuum to 25 mL and Et<sub>2</sub>O was added (25 mL). The solution was filtered off and **4** was obtained as  
32  
33 yellow powder (0.154 g, 91 %). Data for **4**:  $^1\text{H}$  NMR ( $\text{DMSO-d}_6$ ): -0.09 (s, 24H,  $\text{Si}(\text{CH}_3)_2$ ); -0.07 (s, 12H,  
34  
35  $\text{Si}(\text{CH}_3)\text{CH}_2\text{CH}_2\text{S}$ ); 0.03 (s, 24H,  $\text{Si}(\text{CH}_3)_2\text{O}$ ); 0.56 (m, 40H,  $\text{CH}_2\text{Si}$ ); 0.86 (t, 16H,  $\text{SiCH}_2\text{CH}_2\text{S}$ ); 1.32 (m,  
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37 8H,  $\text{OCH}_2\text{CH}_2\text{CH}_2\text{CH}_2\text{Si}$ ); 1.42 (m, 8H,  $\text{CH}_2\text{CH}_2\text{Si}$ ); 1.51 (m, 16H,  $\text{CH}_2\text{CH}_2\text{Si}$ ); 1.67 (m, 8H,  
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39  $\text{OCH}_2\text{CH}_2\text{CH}_2\text{CH}_2\text{Si}$ ); 2.62 (t, 16H,  $\text{SiCH}_2\text{CH}_2\text{S}$ ); 2.89 (t, 16H,  $\text{SCH}_2\text{CH}_2\text{N}$ ); 3.08 (s, 72H,  $\text{N}(\text{CH}_3)_3$ );  
40  
41 3.36 (m, 16H,  $\text{OCH}_2\text{CH}_2\text{O}$ ); 3.50 (m, 16H,  $\text{SCH}_2\text{CH}_2\text{N}$ ); 3.87 (m, 8H,  $\text{OCH}_2\text{CH}_2\text{CH}_2\text{CH}_2\text{Si}$ );  $^{13}\text{C}$  NMR  
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43 ( $\text{DMSO-d}_6$ ): -5.8 ( $\text{Si}(\text{CH}_3)$ ); 12.2, 12.9, 17.8, 17.9, 18.6, 19.1, 19.4, 20.4 ( $\text{CH}_2\text{Si}$  and  $\text{CH}_2\text{CH}_2\text{Si}$ ); 13.5  
44  
45 ( $\text{SiCH}_2\text{CH}_2\text{S}$ ); 23.0 ( $\text{SiCH}_2\text{CH}_2\text{S}$ ); 26.2 ( $\text{SCH}_2\text{CH}_2\text{N}$ ); 32.5 ( $\text{OCH}_2\text{CH}_2\text{CH}_2\text{CH}_2\text{Si}$ ); 51.6 ( $\text{N}(\text{CH}_3)_3$ ); 59.7  
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47 ( $\text{OCH}_2\text{CH}_2\text{CH}_2\text{CH}_2\text{Si}$ ); 63.9 ( $\text{CH}_2\text{N}$ ); 69.3, 71.5 ( $\text{OCH}_2\text{CH}_2\text{O}$ );  $^{15}\text{N}$  NMR ( $\text{DMSO-d}_6$ ): 50.6;  $^{29}\text{Si}$  NMR  
48  
49 ( $\text{DMSO-d}_6$ ): 3.0 ( $\text{SiMe}$ ), 18.0 ( $\text{SiMe}_2\text{O}$ ). Elemental analysis ( $\text{C}_{268}\text{H}_{611}\text{O}_{16}\text{N}_{16}\text{Si}_{29}$ , FW = 6479.54 g mol $^{-1}$ ):  
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51 C, 42.38; H, 8.13; N, 2.77; S, 6.77; Exp.: C, 43.10; H, 7.46; N, 2.36; S, 6.94.

**Dendrimer 7.** Compound  $\text{G}_1\text{SiA}_8$  (0.150 g, 0.215 mmol),  $\text{HS}(\text{CH}_2)_2\text{CO}_2\text{H}$  (0.183 g, 1.724 mmol) were  
60  
61 solved in a THF/DMF mixture (4 mL, 3.5/0.5), and DMPA was added (2.0 % mol per allyl group). The  
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63

1 mixture was desoxygenated and stirred under UV light for 2 h. Afterward, more DMPA was added (2.0 %  
2 mol per allyl group), and the mixture was again desoxygenated and stirred under UV light for 2 h. more.  
3 Then, volatiles were removed under vacuum and compound **7** was purified by size exclusion  
4 chromatography (acetone) to afford pale yellow oil (0.26 g, 78 %). A similar yield was obtained by  
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Then, volatiles were removed under vacuum and compound **7** was purified by size exclusion chromatography (acetone) to afford pale yellow oil (0.26 g, 78 %). A similar yield was obtained by treating an unpurified MeOH solution of compound **7** with excess NaHCO<sub>3</sub>, then filtering off the solution, resolving the white powder in water and acidifying the solution with HCl to pH below 3 and finally extracting compound **7** with ethyl acetate, drying with Na<sub>2</sub>SO<sub>4</sub> and removing solvent under vacuum. Data for **7**: <sup>1</sup>H NMR (MeOD-d<sub>4</sub>): 0.04 (s, 12 H, SiMe), 0.68 (m, 32 H, CH<sub>2</sub>Si), 1.44 (m, 8 H, SiCH<sub>2</sub>CH<sub>2</sub>CH<sub>2</sub>Si), 1.64 (m, 16 H, CH<sub>2</sub>CH<sub>2</sub>CH<sub>2</sub>S), 2.61 (m, 32 H, CH<sub>2</sub>S), 2.78 (m, 16 H, CH<sub>2</sub>CO); <sup>13</sup>C NMR (MeOD-d<sub>4</sub>): -4.5 (SiMe), 14.4 (CH<sub>2</sub>Si), 18.7 (CH<sub>2</sub>Si), 19.8, 19.9, 25.5 (CH<sub>2</sub>), 27.9 (CH<sub>2</sub>CO), 35.9 and 36.8 (CH<sub>2</sub>S), 175.7 (CO); <sup>29</sup>Si NMR (MeOD-d<sub>4</sub>): 0.7 (Si(CH<sub>2</sub>)<sub>4</sub>), 2.5 (SiMe). Elemental analysis (C<sub>64</sub>H<sub>124</sub>O<sub>16</sub>S<sub>8</sub>Si<sub>5</sub>, MW = 1546.61): C, 49.70; H, 8.08; S, 16.59. Exp.: C, 49.01; H, 7.79; S, 16.13.

**Dendrimer 10.** Compound **7** (0.150 g, 0.105 mmol) was dissolved in DMF (5 mL) and DMAP (0.122 g, 1.00 mmol) and HO(CH<sub>2</sub>)<sub>2</sub>NMe<sub>2</sub> (0.082 g, 0.920 mmol) were added to the solution. This solution was stirred for 15 min. and solid EDCI (0.192 g, 1.00 mmol) was added. The mixture was stirred for 3 d., the solvent was evaporated and the remaining oil was purified by size exclusion chromatography in acetone, yielding **10** as pale yellow oil (0.153 g, 69%). Data for **10**: <sup>1</sup>H NMR (CDCl<sub>3</sub>): -0.09 (s, 12 H, SiMe), 0.53 (m, 32 H, CH<sub>2</sub>Si), 1.22 (m, 8 H, SiCH<sub>2</sub>CH<sub>2</sub>CH<sub>2</sub>Si), 1.50 (m, 16 H, CH<sub>2</sub>CH<sub>2</sub>CH<sub>2</sub>S), 2.30 (s, 48 H, NMe<sub>2</sub>), 2.48 (m, 16 H, CH<sub>2</sub>S), 2.60 (m, 32 H, CH<sub>2</sub>S and CH<sub>2</sub>CO), 2.72 (m, 16 H, CH<sub>2</sub>N), 4.18 (m, 16 H, CH<sub>2</sub>O); <sup>13</sup>C NMR (CDCl<sub>3</sub>): -5.1 (SiMe), 13.5 (CH<sub>2</sub>Si), 17.9 (CH<sub>2</sub>Si), 18.4, 24.1 (CH<sub>2</sub>), 26.8 (CH<sub>2</sub>CO), 34.7 and 35.8 (CH<sub>2</sub>S), 45.3 (NMe<sub>2</sub>), 57.4 (CH<sub>2</sub>N), 61.8 (CH<sub>2</sub>O), 172.2 (CO); <sup>29</sup>Si NMR (CDCl<sub>3</sub>): 0.4 (Si(CH<sub>2</sub>)<sub>4</sub>), 2.4 (SiMe). Elemental analysis (C<sub>96</sub>H<sub>196</sub>N<sub>8</sub>O<sub>16</sub>S<sub>8</sub>Si<sub>5</sub>, MW = 2115.57): C, 54.50; H, 9.34; N, 5.30; S, 12.13. Exp.: C, 55.67; H, 9.79; N, 4.89; S, 15.63.

**Dendrimer 13.** Dendrimer **10** (0.100 g, 0.047 mmol) was dissolved in DMF/THF (10/30 mL) and MeI was added (0.080 g, 0.546 mmol). The mixture was stirred for 24 h. THF and excess MeI was removed under vacuum, Et<sub>2</sub>O (30 mL) was added to precipitate **13** and the solution was filtered off. The remaining

1 solid was washed again with Et<sub>2</sub>O/THF (20/20 mL) and finally Et<sub>2</sub>O (40 mL) rendering **13** as a yellowish  
2  
3 solid (0.14 g, 91 %). Data for **13**: <sup>1</sup>H NMR (DMSO-d<sub>6</sub>): -0.07 (s, 12 H, SiMe), 0.53 (m, 32 H, CH<sub>2</sub>Si),  
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5 1.28 (m, 8 H, SiCH<sub>2</sub>CH<sub>2</sub>CH<sub>2</sub>Si), 1.48 (m, 16 H, CH<sub>2</sub>CH<sub>2</sub>CH<sub>2</sub>S), 2.49 (CH<sub>2</sub>S), 2.68 (broad m, 32 H, CH<sub>2</sub>S  
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7 and CH<sub>2</sub>CO), 3.14 (s, 72 H, NMe<sub>3</sub><sup>+</sup>), 3.69 (m, 16 H, CH<sub>2</sub>N), 4.18 (m, 16 H, CH<sub>2</sub>O); <sup>13</sup>C NMR (DMSO-  
8  
9 d<sub>6</sub>): -4.2 (SiMe), 13.4 (CH<sub>2</sub>Si), 18.4, 24.2 (CH<sub>2</sub>), 25.7 (CH<sub>2</sub>CO), 34.7 and 35.1 (CH<sub>2</sub>S), 53.1 (NMe<sub>3</sub><sup>+</sup>),  
10  
11 58.0 (CH<sub>2</sub>O), 64.1 (CH<sub>2</sub>N), 170.8 (CO); <sup>29</sup>Si NMR (DMSO-d<sub>6</sub>): 0.4 (Si(CH<sub>2</sub>)<sub>4</sub>), 2.4 (SiMe). Elemental  
12  
13 analysis (C<sub>104</sub>H<sub>220</sub>I<sub>8</sub>N<sub>8</sub>O<sub>16</sub>S<sub>8</sub>Si<sub>5</sub>, MW = 3251.09): C, 38.42; H, 6.82; N, 3.45; S, 7.89. Exp.: C, 38.03; H,  
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15 6.26; N, 4.89; S, 7.23.  
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## 40 6. Supporting Information

41  
42 Full experimental details and selected NMR spectra.  
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1 For Table of Contents:  
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3 **Synthesis of degradable cationic carbosilane dendrimers based**  
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7 **on Si-O or ester bonds**  
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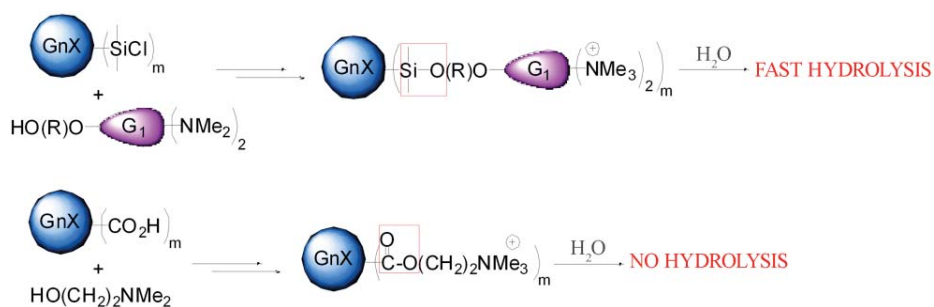
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31 Two types of degradable cationic carbosilane dendrimers have been synthesized, one with internal Si-  
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33 O bonds, which is easily hydrolyzed, and other with ester bonds, which was water resistant.  
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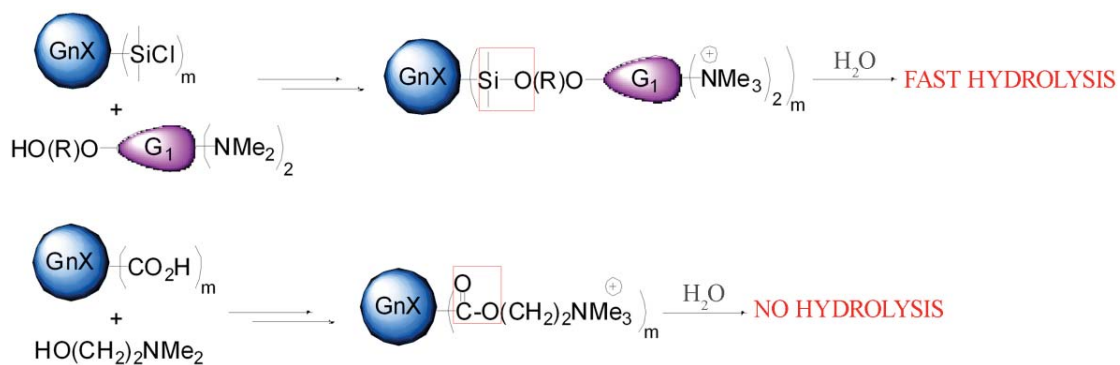




For Graphical Abstract:

## Synthesis of degradable cationic carbosilane dendrimers based on Si-O or ester bonds

Two types of degradable cationic carbosilane dendrimers have been synthesized, one with internal Si-O bonds, which is easily hydrolyzed, and other with ester bonds, which was water resistant.



**Supplementary Material**

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