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Synthesis of L-ascorbic acid derivatives as potential bone remodeling agents taking advantage of the Mitsunobu reaction

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Abstract—The synthesis of ascorbic acid derivatives **7a–d** is described. Starting from alkenylacetates **1a–d** subjected to a hydrosilylation reaction, the resulting hydroxy chloro silanes **3a–d** were obtained in high yield. The latter compounds were reacted with potassium phthalimide followed with hydrazine hydrate to give the amino silanols **5a–d**. Ascorbic acid was then alkylated on its 3-hydroxy position to give **7a–d** by means of a Mitsunobu reaction.

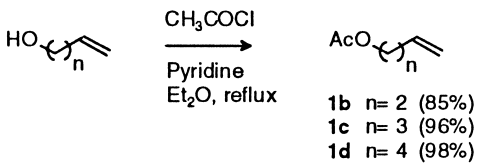
1. Introduction

Treatment of severe bone fractures or bone diseases may need the use of a bone graft.[1] In the autograft procedure, bone fragments are taken from the patient's own body, however, the human body does not posses much spare bone which limits the usefulness of this method, especially for important bone losses. As an alternative, allograft uses bone taken from a deceased donor, but the risk of rejection or of infectious diseases may arise. Presently, the use of synthetic material to replace lost bone is becoming a better choice as new biomaterials continue to come onto the market.[2] The ideal bone substitute must be biocompatible and osteoinductive.[3] To favor both processes, we investigated the possibility of synthesizing molecules that once covalently linked to a suitable biomaterial, might behave as osteoblasts 'concentrators' on biomaterial surfaces through their specific interaction with membrane components. Then, osteoblasts could synthesize extracellular matrix and, afterwards, colonization could favor bone regeneration and growth. Membrane proteins represent one of the most attractive molecular targets as they are cell specific. Among them, carriers seem the most promising one since, unlike receptors, they do not induce cellular response. Furthermore, interactions between carriers and a more or less plane biomaterial would leave enough free carriers on cells to ensure sufficient transport of required metabolites. We took into account two of them: nucleic bases,[4] and ascorbic acid. The latter is an inexpensive carbohydrate used as a vitamin, a drug or in the food industry as antioxidant. It also plays an important role in biology. Actually, it is essential for the formation of bone, and necessary for the in vitro differentiation of osteoblastic cells.[5] Furthermore, it favors bone mineralization.[6] Therefore, we have synthesized four ascorbic acid derivatives including a silyl alkyl chain of variable length, ended by a masked amino group to eventually form an amide linkage with a suitable biomaterial.

2. Results and discussion

The key steps of the synthesis are (1) a hydrosilylation reaction and (2) a Mitsunobu reaction involving ascorbic acid and an appropriate silyl alcohol. The latter compound also possesses a masked amino group to allow its further linkage to a suitable biomaterial by means of an amide bond. The acetoxy compounds **1b–d** were obtained in nearly quantitative yield from the parent alcohols with acylchloride in pyridine/diethylether (Scheme 1), whereas allylacetate **1a** is commercially available.

The hydrosilylation reaction is a versatile reaction commonly used in organosilicon chemistry with no equivalent in carbon chemistry.[7] Anyway, as already noted in a previous work,[8] molecules subjected to hydrosilylation in the presence of chloroplatinic acid as a catalyst, cannot hold acidic protons (e.g. NH, NH_2 or OH groups) and must be protected first, hence the choice for the acetoxy group to mask the unsaturated starting alcohols. Therefore, acetates



Scheme 1.

Keywords: ascorbic acid derivatives; silicon; Mitsunobu reaction; bone.

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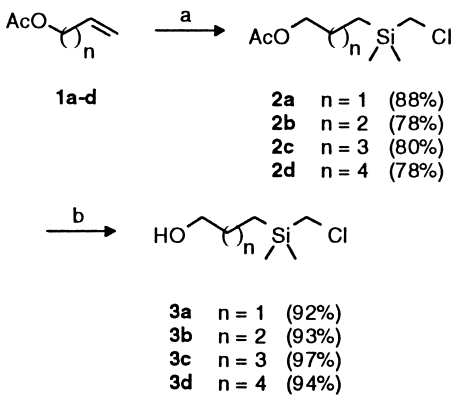
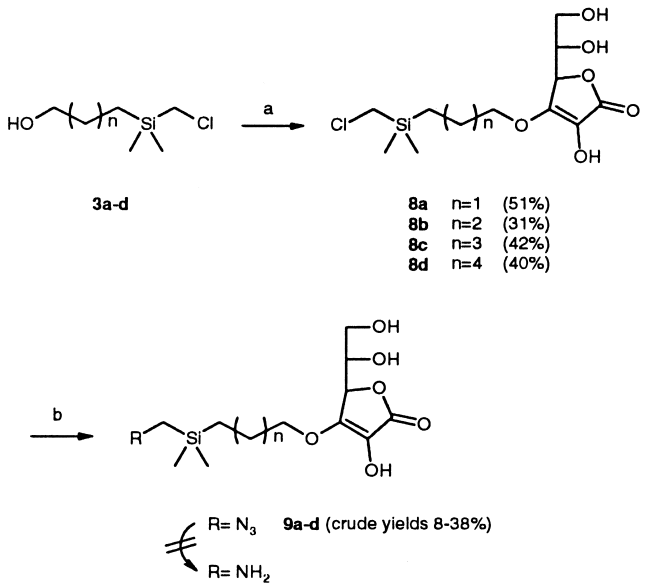


Scheme 2. (a) $ClCH_2Si(H)Me_2$, H_2PtCl_6, THF; (b) MeOH, PTSA.

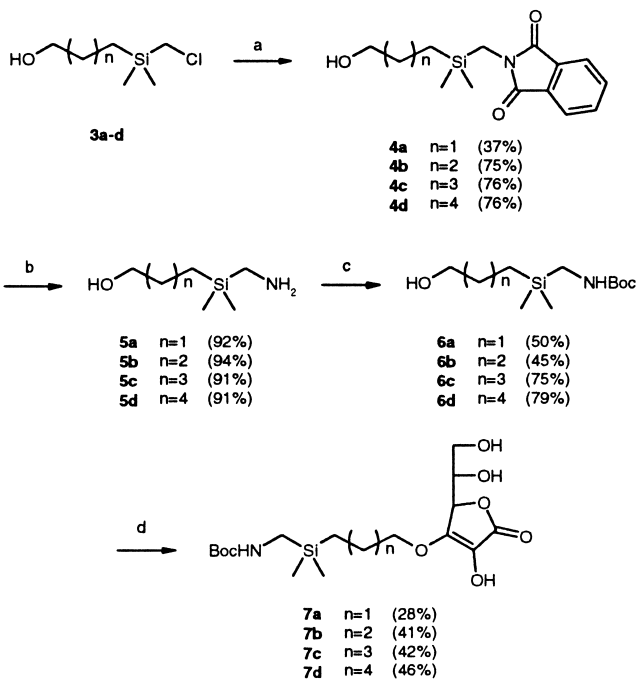
1a–d reacted with chloromethyldimethylsilane and H_2PtCl_6 in anhydrous THF to yield the desired acetoxy silyl derivatives **2a–d** (Scheme 2, step a).

A transesterification of the latter compounds catalyzed with *p*-toluenesulphonic acid in methanol, gave the various silyl alcohols **3a–d** in excellent yield (Scheme 2, step b). From this step, two strategies could be considered depending on whether the amino moiety was introduced early or later during the synthesis.

In the latter case (Scheme 3), the versatility of the Mitsunobu reaction allowed the intermolecular dehydration to take place under mild conditions, resulting in the ether linkage in compounds **8a–d**. In this way, we avoided the use of alkoxide alkylation (Williamson reaction) unsuitable for a base sensitive molecule like ascorbic acid. It is known that intermolecular coupling of alcohols with DEAD/PPh_3 usually does not occur with the exception of alkyl aryl, enol and cyclic dialkyl ether formation,[9] or—more recently—fluoro ethers.[10] Usual alcohols may be too weakly acidic for good results in the Mitsunobu reaction.[11] Taking advantage of this difference in reactivity of the Mitsunobu reaction, ethers **8a–d** were obtained from OH-3′ of ascorbic acid in a



Scheme 3. Mitsunobu reaction from **3a–d** (a) ascorbic acid, PPh_3/DEAD, THF; (b) NaN_3/DMSO.



Scheme 4. (a) Potassium phthalimide/DMF; (b) N_2H_4/EtOH, crude yields indicated; (c) $BOC_2O/Et_3N/CH_2Cl_2$; (d) ascorbic acid/PPh_3/DEAD.

30–50% yield range, despite the absence of any protecting group on the other hydroxyles. In the hope of still improving this yield, a search in the litterature indicated that new redox systems like 1,1′-(azodicarboxyl)-dipiperidine-tributyl-phosphine (ADDP-TBP), *N*,*N*,*N*′,*N*′-tetramethylazodicar-boxylate-tributylphosphine (TMAD-TBP) or *N*,*N*,*N*′,*N*′-tetraisopropylazodicarboxylate-tributylphosphine (TIPA-TBP) act as better reagents than the traditionnal DEAD/PPh_3 in the case of high pKa nucleophiles.[12] Unfortunately, the use of the commercially available TMAD-TBP proved to be unsuccessful in our hands.

In order to obtain the final compounds, the azido precursors **9a–d** were synthesized with sodium azide in DMSO,[13] although in moderate crude yields (8–38%). Afterwards, every attemp made to generate the amino moiety did not succeed: LAH reduction, tributyltin hydride reduction in AIBN,[14] or catalytic hydrogenation (H_2/Pd). Displacement of the chlorine atom with potassium phthalimide failed equally. Another possibility was to synthesize the amino precursor before the Mitsunobu reaction takes place. Therefore, chlorosilanols **3a–d** treated with potassium phthalimide gave the N-protected derivatives **4a–d** in good yield (Scheme 4, step a). Unfortunately, the direct use of these compounds with DEAD/PPh_3/ascorbic acid gave only very poor yield of the desired Mitsunobu product along with most of unreacted **4**.

From this result, we inferred that the phthalimido moiety was incompatible with the Mitsunobu reaction conditions, and another *N*-protective group was the obvious solution. For this purpose, the *t*-butoxycarbonyl group is widely used in organic chemistry (especially in peptide synthesis). From the phthalimido derivatives **4a–d** reacted with hydrazine hydrate, the free amino silanols **5a–d** were obtained in nearly quantitative yield (Scheme 4, step b). A purification

Table 1. ^{13}C NMR (δ, ppm, in DMSO-d_6) of ascorbic acid and compound **8a**

	Ascorbic acid	Compound **8a**
C-1′	170.6	170.6
C-2′	117.9	118.9
C-3′	152.9	150.7
C-4′	74.6	74.4
C-5′	68.4	68.6
C-6′	61.9	61.8

of compound **5a** on a chromatography column (silica gel) resulted in numerous degradation products. Therefore, all the amino silanols were used in the next step without further purification. The amino protection of **5a–d** was conducted with di-*tert*-butyl dicarbonate at room temperature to give the more stable **6a–d** compounds. Eventually, the presence of a residual labile proton on the nitrogen atom, did not prevent the Mitsunobu reaction with ascorbic acid to take place, to give **7a–d** in rather good yields.

Throughout this work, it was hypothesized that the Mitsunobu reaction proceeds with the more acidic OH-3′ of ascorbic acid as depicted in Schemes 3 and 4. However, one may ask whether or not the OH-2′ or even the primary OH-6′ are good candidates to form an ether bond? In a ^{13}C NMR comparative study of ascorbic acid and compound **8a**, we did not notice any chemical shift change clear enough to prove our first hypothesis (Table 1).

Therefore, a detailed NMR study using hetero multiple bond coherence (HMBC) was conducted on the model compound **8a**, showing cross correlations from the γ-methylene protons (relative to Si) to the C-3′ carbon of ascorbic acid. This clearly indicates that the etherification step occurred at position 3′ of ascorbic acid.

3. Conclusion

We have described the synthesis of four new compounds **7a–d**, using an unusual application of the Mitsunobu reaction. The latter compounds can be seen as ascorbic acid derivatives. We expect from deprotected **7** to bind to a suitable biomaterial via a peptidic bond and to act in vivo as an potential donnor of vitamin C if needed by osteoblatic cells, favoring the formation of new bone tissue.

4. Experimental

4.1. General

^1H and ^{13}C NMR spectra were recorded with a Bruker AC 200 spectrometer (200 and 50 MHz, resp.); chemical shifts are given in ppm values referenced to the residual solvent peak from tetramethylsilane (δ_H=7.24 ppm and δ_C= 77.7 ppm for $CDCl_3$). 2D NMR experiments were recorded with a Bruker AMX 500 spectrometer. Infrared spectra were measured using neat samples on NaCl plates on a Bruker IFS-25 spectrometer; wave numbers are given in cm^{-1}. Mass spectra (LSIMS-HRMS) were recorded on a AutoSpec-Q Fisons-Instruments spectrometer. Thin layer chromatography was performed on Merck precoated silica gel $60F_{254}$ 0.25 mm plates and visualized under UV light or by staining with $KMnO_4$ (1% solution). Column and flash chromatography were performed using SDS silica gel (70–200 and 230–400 mesh, respectively).

4.2. General procedure for the preparation of alkenyl acetates 1b–d

A solution of unsaturated alcohol in pyridine and anhydrous diethyl ether (15 mL) was boiled under reflux, and acetyl chloride was added dropwise over 60–90 min. The resulting mixture was heated another 1 h, then filtered and the filtrate concentrated under reduced pressure to give the corresponding acetates used in the next step without further purification.

4.2.1. 3-Buten-1-yl acetate (1b). It was obtained from 3-buten-1-ol (5.0 g, 69.0 mmol), pyridine (5.47 g, 69 mmol) and acetyl chloride (5.43 g, 69 mmol); colorless oil (6.75 g, 85%). ^1H NMR ($CDCl_3$): δ=1.80 (s, 3H, CH_3C=O), 2.15 (q, J=6.9 Hz, 2H, CH_2CH_2OAc), 3.88 (t, J=6.9 Hz, 2H, CH_2OAc), 4.85 (m, 2H, CH=CH_2), 5.53 (m, 1H, CH=CH_2). ^{13}C NMR ($CDCl_3$): δ=20.46 (CH_3C=O), 32.82 (CH_2CH_2OAc), 63.11 (CH_2OAc), 116.78 (CH_2=CH), 133.8 (CH=CH_2), 170.44 (C=O). IR (film): 1742 (C=O), 1640 (C=C).

4.2.2. 4-Penten-1-yl acetate (1c). It was obtained from 4-penten-1-ol (5.0 g, 58.0 mmol), pyridine (4.59 g, 58 mmol) and acetyl chloride (4.54 g, 58 mmol); colorless oil (6.89 g, 92%). ^1H NMR ($CDCl_3$): δ=1.58 (m, 2H, $CH_2CH_2CH_2$), 1.89 (s, 3H, CH_3C=O), 1.98 (m, 2H, =CH–CH_2), 3.93 (t, J=6.5 Hz, 2H, CH_2OAc), 4.85 (m, 2H, CH=CH_2), 5.53 (m, 1H, CH=CH_2). ^{13}C NMR ($CDCl_3$): δ=20.46 (CH_3C=O), 27.46 (CH_2CH_2OAc), 29.69 (CH_2CH=), 63.43 (CH_2O), 114.85 (CH_2=CH), 137.08 (CH=CH_2), 170.44 (C=O). IR (film): 1742 (C=O), 1640 (C=C), 1244 (Si–C def.), 842 (Si–C strech.).

4.2.3. 5-Hexen-1-yl acetate (1d). It was obtained from 5-hexen-1-ol (5.0 g, 50.0 mmol), pyridine (3.95 g, 50 mmol) and acetyl chloride (3.90 g, 50 mmol); colorless oil (6.98 g, 98%). ^1H NMR ($CDCl_3$): δ=1.26 (m, 2H, $CH_2CH_2CH_2O$), 1.46 (m, 2H, $CH_2CH_2CH_2O$), 1.84 (s, 3H, CH_3C=O), 1.89 (m, 2H, =CH–CH_2), 3.87 (t, J=6.8 Hz, 2H, CH_2OAc), 4.80 (m, 2H, CH=CH_2), 5.65 (m, 1H, CH=CH_2). ^{13}C NMR ($CDCl_3$): δ=19.90 (CH_3C=O), 24.32 (CH_2CH_2OAc), 27.18 (CH_2CH=), 32.42 (CH_2=CH–CH_2), 63.38 (CH_2O), 113.35 (CH_2=CH), 137.35 (CH=CH_2), 170.44 (C=O). IR (film): 1742 (C=O), 1640 (C=C), 842 (Si–C strech.).

4.3. General procedure for the preparation of (chloromethyldimethylsilanyl)alkyl ethanoates 2a–d

To a solution of unsaturated acetate and chloromethyldimethylsilane in boiling THF, was added chloroplatinic acid (0.1 mL of a 0.1N sol. in *i*PrOH). The solution turned brown within a few minutes and was stirred for 2 h. A small quantity of charcoal powder was then added and reflux continued for half an hour. The reaction mixture was cooled

to rt, filtered and concentrated under reduced pressure to give the corresponding silyl esters used in the next step without further purification.

4.3.1. 3-(Chloromethyldimethylsilanyl)propyl ethanoate (2a). It was obtained from commercial allyl acetate (3.00 g, 23 mmol) and chloromethyldimethylsilane (**2**) (2.71 g, 25 mmol); colorless oil (4.26 g, 88%). Bp (0.9 mm Hg)=85°C. ^{1}H NMR ($CDCl_3$): δ=0.05 (s, 6H, $Si(CH_3)_2$), 0.59 (m, 3H, CH_3Si), 1.58 (m, 2H, $SiCH_2CH_2$), 1.97 (s, 3H, CH_3CO), 2.72 (s, 2H, CH_2Cl), 3.95 (t, J=7.5 Hz, 2H, CH_2OAc). ^{13}C NMR ($CDCl_3$): δ=−4.80 ($Si(CH_3)_2$), 49.57 ($SiCH_2$), 20.83 (CH_3CO), 22.79 ($SiCH_2CH_2$), 29.85 (CH_2Cl), 66.60 (CH_2OAc), 170.9 (C=O). IR (film): 1742 (C=O), 1252 (Si−C def.), 842 (Si−C strech.).

4.3.2. 4-(Chloromethyldimethylsilanyl)butyl ethanoate (2b). It was obtained from (**1b**) (7.0 g, 61 mmol) and chloromethyldimethylsilane (**2**) (7.0 g, 65 mmol); colorless oil (10.68 g, 78%). Bp (0.9 mm Hg)=98°C. ^{1}H NMR ($CDCl_3$): δ=0.06 (s, 6H, $Si(CH_3)_2$), 0.61 (m, 2H, $SiCH_2$), 1.35 (m, 2H, $SiCH_2CH_2CH_2$), 1.61 (m, 2H, $SiCH_2CH_2$), 1.99 (s, 3H, CH_3C=O), 2.73 (s, 2H, CH_2Cl), 4.01 (t, J=7.4 Hz, 2H, CH_2O). ^{13}C NMR ($CDCl_3$): δ=−4.18 ($Si(CH_3)_2$), 13.28 ($SiCH_2$), 19.93 ($SiCH_2CH_2$), 19.98 (CH_3C=O), 30.10 (CH_2Cl), 32.09 (CH_2CH_2OAc), 63.09 (CH_2O), 171.11 (C=O). IR (film): 1730 (C=O), 1256 (Si−C def.), 846 (Si−C strech.).

4.3.3. 5-(Chloromethyldimethylsilanyl)pentyl ethanoate (2c). It was obtained from (**1c**) (3.20 g, 25 mmol) and chloromethyldimethylsilane (**2**) (2.71 g, 25 mmol); colorless oil (4.72 g, 80%). Bp (0.9 mm Hg)=108°C. ^{1}H NMR ($CDCl_3$): δ=0.06 (s, 6H, $Si(CH_3)_2$), 0.61 (m, 2H, $SiCH_2$), 1.30−1.38 (m, 4H, $CH_2CH_2CH_2O$), 1.60 (m, 2H, $SiCH_2CH_2$), 2.01 (s, 3H, CH_3C=O), 2.74 (s, 2H, CH_2Cl), 4.02 (t, J=6.5 Hz, 2H, CH_2O). ^{13}C NMR ($CDCl_3$): δ=−4.65 ($Si(CH_3)_2$), 13.53 ($SiCH_2$), 20.96 (CH_3C=O), 23.18 ($SiCH_2CH_2$), 28.19 ($SiCH_2CH_2CH_2$), 29.61 (CH_2Cl), 30.25 (CH_2CH_2OAc), 64.45 (CH_2O), 171.25 (C=O). IR (film): 1742 (C=O), 1256 (Si−C def.), 846 (Si−C strech.).

4.3.4. 6-(Chloromethyldimethylsilanyl)hexyl ethanoate (2d). It was obtained from (**1d**) (6.72 g, 47 mmol) and chloromethyldimethylsilane (**2**) (5.10 g, 47 mmol); colorless oil (9.27 g, 78%). Bp (0.9 mm Hg)=125°C. ^{1}H NMR ($CDCl_3$): δ=0.05 (s, 6H, $Si(CH_3)_2$), 0.61 (m, 2H, $SiCH_2$), 1.30 (m, 6H, $CH_2CH_2CH_2CH_2OAc$), 1.54 (m, 2H, $SiCH_2CH_2$), 2.00 (s, 3H, CH_3C=O), 2.73 (s, 2H, CH_2Cl), 4.00 (t, J=6.8 Hz, 2H, CH_2OAc). ^{13}C NMR ($CDCl_3$): δ=−4.63 ($Si(CH_3)_2$), 13.55 ($SiCH_2$), 23.39 ($SiCH_2CH_2$), 25.51 ($SiCH_2CH_2CH_2$), 28.48 ($SiCH_2CH_2CH_2CH_2$), 30.33 (CH_2Cl), 33.00 (CH_2CH_2OAc), 64.56 (CH_2OAc), 170.5 (CH_3C=O). IR (film): 1738 (C=O), 1248 (Si−C def.), 846 (Si−C strech.).

4.4. General procedure for the preparation of chloromethyldimethylsilanyl alcohols 3a–d

Chloromethyldimethylsilanyl alkyl ethanoate was added under nitrogen to a solution of *p*-toluenesulphonic acid in methyl alcohol. After stirring for 24 h at room temperature, the solution was concentrated under reduced pressure, rinsed with water, and extracted with dichloromethane; the extracts were combined, washed with water, dried on magnesium sulfate, and evaporated to give the crude product used in the next step without further purification.

4.4.1. 3-(Chloromethyldimethylsilanyl)propan-1-ol (3a). It was obtained from **2a** (4 g, 19 mmol) and PTSA (0.76 g, 4 mmol) in absolute methyl alcohol (150 mL); colorless oil (2.92 g, 92%). ^{1}H NMR ($CDCl_3$): δ=0.06 (s, 6H, $Si(CH_3)_2$), 0.63 (m, 2H, $SiCH_2$), 1.57 (m, 2H, $SiCH_2CH_2$), 2.77 (s, 2H, CH_2Cl), 3.58 (t, J=6.7 Hz, 2H, CH_2OH). ^{13}C NMR ($CDCl_3$): δ=−3.97 ($Si(CH_3)_2$), 10.06 ($SiCH_2$), 27.40 ($SiCH_2CH_2$), 30.85 (CH_2Cl), 66.15 (CH_2OH). IR (film): 3356 (OH), 1252 (Si−C def.), 842 (Si−C strech.).

4.4.2. 4-(Chloromethyldimethylsilanyl)butan-1-ol (3b). It was obtained from **2b** (10.6 g, 47 mmol) and PTSA (1.78 g, 9.4 mmol) in absolute methyl alcohol (300 mL); colorless oil (7.95 g, 93%). ^{1}H NMR ($CDCl_3$): δ=0.05 (s, 6H, $Si(CH_3)_2$), 0.59 (m, 2H, $SiCH_2$), 1.43 (m, 2H, $SiCH_2CH_2CH_2$), 1.52 (m, 2H, $SiCH_2CH_2$), 2.73 (s, 2H, CH_2Cl), 3.56 (t, J=6.8 Hz, 2H, CH_2OH). ^{13}C NMR ($CDCl_3$): δ=−4.71 ($Si(CH_3)_2$), 13.38 ($SiCH_2$), 19.75 ($SiCH_2CH_2$), 30.21 (CH_2Cl), 36.28 ($SiCH_2CH_2CH_2$), 62.17 (CH_2OH). IR (film): 3356 (OH), 1256 (Si−C def.), 846 (Si−C strech.).

4.4.3. 5-(Chloromethyldimethylsilanyl)pentan-1-ol (3c). It was obtained from **2c** (5.3 g, 22 mmol) and PTSA (0.85 g, 4.4 mmol) in absolute methyl alcohol (200 mL); colorless oil (4.19 g, 97%). ^{1}H NMR ($CDCl_3$): δ=0.03 (s, 6H, $Si(CH_3)_2$), 0.61 (m, 2H, $SiCH_2$), 1.40 (m, 4H, $Si(CH_2)_2CH_2CH_2$), 1.50 (m, 2H, $SiCH_2CH_2$), 2.73 (s, 2H, CH_2Cl), 3.56 (t, J=7.0 Hz, 2H, CH_2OH). ^{13}C NMR ($CDCl_3$): δ=−4.76 ($Si(CH_3)_2$), 13.59 ($SiCH_2$), 23.33 ($SiCH_2CH_2$), 29.48 ($SiCH_2CH_2CH_2$), 30.30 (CH_2Cl), 32.30 (CH_2CH_2OH), 62.69 (CH_2OH). IR (film): 3356 (OH), 1256 (Si−C def.), 842 (Si−C strech.).

4.4.4. 6-(Chloromethyldimethylsilanyl)hexan-1-ol (3d). It was obtained from **2d** (9.27 g, 37 mmol) and PTSA (1.4 g, 7.4 mmol) in absolute methyl alcohol (350 mL); colorless oil (7.81 g, 94%). ^{1}H NMR ($CDCl_3$): δ=0.06 (s, 6H, $Si(CH_3)_2$), 0.60 (m, 2H, $SiCH_2$), 1.31 (m, 6H, $Si(CH_2)_2CH_2CH_2CH_2$), 1.54 (m, 2H, $SiCH_2CH_2$), 2.74 (s, 2H, CH_2Cl), 3.60 (t, J=7.5 Hz, 2H, CH_2OH). ^{13}C NMR ($CDCl_3$): δ=−4.65 ($Si(CH_3)_2$), 13.54 ($SiCH_2$), 23.43 ($SiCH_2CH_2$), 25.30 ($SiCH_2CH_2CH_2$), 30.36 (CH_2Cl), 32.30 ($CH_2CH_2CH_2OH$), 33.14 (CH_2CH_2OH), 62.95 (CH_2OH). IR (film): 3334 (OH), 1252 (Si−C def.), 848 (Si−C strech.).

4.5. General procedure for the preparation of phtalimidomethyldimethylsilanyl alcohols 4a–d

A mixture of chloromethyldimethylsilanyl alcohol, potassium phthalimide, anhydrous DMF and ca. 10 mg of crown ether (18-C-6) was stirred for 24 h under nitrogen at 120°C. The mixture was cooled, then filtered, and the filtrate evaporated under reduced pressure. The remaining residue was poured into water and extracted with dichloromethane; the organic extracts were washed with water, dried over magnesium sulphate, concentrated, then chromatographed on silica gel with hexane/ethyl acetate (6:4) as eluant.

4.5.1. 3-(Phthalimidomethyldimethylsilanyl)propan-1-ol (4a). It was obtained from **3a** (2 g, 12 mmol), potassium phthalimide (2.22 g, 12 mmol), 18-C-6, and DMF (40 mL); pale yellow oil (1.26 g, 37%). ^{1}H NMR ($CDCl_3$): δ=0.05 (s, 6H, $Si(CH_3)_2$), 0.55–0.63 (m, 2H, $SiCH_2$), 1.50–1.65 (m, 2H, $SiCH_2CH_2$), 1.94 (broad s, 1H, OH), 3.16 (s, 2H, CH_2N), 3.56 (t, J=6.5 Hz, 2H, CH_2OH), 7.61–7.78 (m, 5H, Pht.). ^{13}C NMR ($CDCl_3$): δ=−3.74 ($Si(CH_3)_2$), 10.37 ($SiCH_2$), 26.69 ($SiCH_2CH_2$), 27.96 (CH_2N), 65.29 (CH_2O), 122.88 (CH Pht.), 132.17 (Pht. quat. C), 133.64 (CH Pht.), 168.50 (C=O). IR (film): 3472 (OH), 1708 (C=O), 1248 (Si–C def.), 836 (Si–C strech.).

4.5.2. 4-(Phthalimidomethyldimethylsilanyl)butan-1-ol (4b). It was obtained from **3b** (3 g, 16 mmol), potassium phthalimide (3 g, 16.2 mmol), 18-C-6, and DMF (50 mL); pale yellow oil (3.53 g, 75%). ^{1}H NMR ($CDCl_3$): δ=0.07 (s, 6H, $Si(CH_3)_2$), 0.57–0.65 (m, 2H, $SiCH_2$), 1.34–1.65 (m, 4H, $SiCH_2CH_2CH_2$), 3.18 (s, 2H, CH_2N), 3.62 (t, J=5.7 Hz, 2H, CH_2OH), 7.63–7.80 (m, 4H, Pht.). ^{13}C NMR ($CDCl_3$): δ=−3.69 ($Si(CH_3)_2$), 14.26 ($SiCH_2$), 19.58 ($SiCH_2CH_2$), 27.97 ($SiCH_2CH_2CH_2$), 36.19 (CH_2N), 62.03 (CH_2OH), 122.85 (CH Pht.), 132.15 (quat. C Pht.), 133.62 (CH Pht.), 168.50 (C=O). IR (film): 3460 (OH), 1704 (C=O), 1252 (Si–C def.), 836 (Si–C strech.).

4.5.3. 5-(Phthalimidomethyldimethylsilanyl)pentan-1-ol (4c). It was obtained from **3c** (2.39 g, 12.2 mmol), potassium phthalimide (2.27 g, 12.2 mmol), 18-C-6 and DMF (40 mL); pale yellow oil (2.84 g, 76%). ^{1}H NMR ($CDCl_3$): δ=0.04 (s, 6H, $Si(CH_3)_2$), 0.54–0.62 (m, 2H, $SiCH_2$), 1.29–1.37 (m, 4H, $Si(CH_2)_2CH_2CH_2$), 1.52 (m, 2H, $SiCH_2CH_2$), 3.15 (s, 2H, CH_2N), 3.58 (t, J=6.4 Hz, 2H, CH_2OH), 7.61–7.78 (m, 4H, Pht). ^{13}C NMR ($CDCl_3$): δ=−3.59 ($Si(CH_3)_2$), 14.66 ($SiCH_2$), 23.27 ($SiCH_2CH_2$), 28.06 ($Si(CH_2)_2CH_2$), 29.46 ($Si(CH_2)_3CH_2$), 32.33 (CH_2N), 62.75 (CH_2OH), 122.86 (CH pht.), 132.22 (Pht. quat. C), 133.59 (CH pht.), 168.48 (C=O). IR (film): 3460 (OH), 1712 (C=O), 1244 (Si–C def.), 840 (Si–C strech.).

4.5.4. 6-(Phthalimidomethyldimethylsilanyl)hexan-1-ol (4d). It was obtained from **3d** (2.5 g, 12 mmol), potassium phthalimide (2.4 g, 13 mmol), 18-C-6, and DMF (30 mL); pale yellow oil (2.94 g, 76%). ^{1}H NMR ($CDCl_3$): δ=0.04 (s, 6H, $Si(CH_3)_2$), 0.54–0.62 (m, 2H, $SiCH_2$), 1.30–1.60 (m, 8H, $SiCH_2(CH_2)_4$), 3.14 (s, 2H, CH_2N), 3.57 (t, J=6.5 Hz, 2H, CH_2OH), 7.60–7.80 (m, 4H, Pht.). ^{13}C NMR ($CDCl_3$): δ=−3.71 ($Si(CH_3)_2$), 14.42 ($SiCH_2$), 23.28 ($SiCH_2CH_2$), 25.24 ($Si(CH_2)_2CH_2$), 27.88 (CH_2N), 32.40 ($Si(CH_2)_3CH_2$), 33.05 ($Si(CH_2)_4CH_2$), 62.30 (CH_2OH), 122.67 (CH Pht.), 131.97 (Pht. quat. C), 133.49 (CH Pht.), 168.25 (C=O). IR (film): 3440 (OH), 1704 (C=O), 1252 (Si–C def.), 840 (Si–C strech.).

4.6. General procedure for the preparation of aminomethyldimethylsilyl alcohols 5a–d

A solution of (phthalimidomethyldimethylsilanyl)alkanol and hydrazine hydrate in absolute ethyl alcohol, was stirred for 24 h at reflux under nitrogen. The resulting mixture was cooled, filtered, and the filtrate evaporated under reduced pressure. The remaining residue was washed with dichloromethane, filtered again, and the filtrate concentrated to give the crude product used in the next step without further purification.

4.6.1. 3-(Aminomethyldimethylsilanyl)propan-1-ol (5a). It was obtained from **4a** (0.65 g, 2.35 mmol), hydrazine hydrate (0.3 mL, 9.4 mmol) and absolute ethanol (20 mL); faint yellow oil (0.32 g, 92%). ^{1}H NMR ($CDCl_3$): δ=0.02 (s, 6H, $Si(CH_3)_2$), 0.57–0.65 (m, 2H, $SiCH_2$), 1.50–1.65 (m, 2H, $SiCH_2CH_2$), 2.19 (s, 2H, CH_2N), 2.60 (broad s, 3H, OH, NH_2), 3.56 (t, J=6.2 Hz, 2H, CH_2OH). ^{13}C NMR ($CDCl_3$): δ=−4.53 ($Si(CH_3)_2$), 9.53 ($SiCH_2$), 26.87 ($SiCH_2CH_2$), 30.30 (CH_2N), 64.57 (CH_2OH). IR (film): 3272 (NH_2, OH), 1252 (Si–C def.), 840 (Si–C def.).

4.6.2. 4-(Aminomethyldimethylsilanyl)butan-1-ol (5b). It was obtained from **4b** (2 g, 6.8 mmol), hydrazine hydrate (1.3 mL, 27.4 mmol) and absolute ethanol (90 mL); yellow oil (1.05 g, 94%). ^{1}H NMR ($CDCl_3$): δ=−0.02 (s, 6H, $Si(CH_3)_2$), 0.50–0.58 (m, 2H, $SiCH_2$), 1.29–1.59 (m, 4H, $SiCH_2CH_2CH_2$), 2.16 (s, 2H, CH_2N), 2.68 (broad s, 3H, NH_2, OH), 3.56 (t, J=6 Hz, 2H, CH_2OH). ^{13}C NMR ($CDCl_3$): δ=−4.71 ($Si(CH_3)_2$), 13.05 ($SiCH_2$), 19.71 ($SiCH_2CH_2$), 29.75 ($Si(CH_2)_2CH_2$), 36.04 (CH_2NH_2), 61.51 (CH_2OH). IR (film): 3356 (NH_2, OH), 1252 (Si–C def.), 836 (Si–C def.).

4.6.3. 5-(Aminomethyldimethylsilanyl)pentan-1-ol (5c). It was obtained from **4c** (1.55 g, 5 mmol), hydrazine hydrate (1 g, 0.02 mol) and absolute ethanol (50 mL); yellow oil (0.8 g, 91%). ^{1}H NMR ($CDCl_3$): δ=0.01 (s, 6H, $Si(CH_3)_2$), 0.51–0.59 (m, 2H, $SiCH_2$), 1.27–1.33 (m, 4H, $Si(CH_2)_2CH_2CH_2$), 1.43–1.53 (m, 2H, $SiCH_2CH_2$), 2.17 (s, 2H, CH_2N), 3.12 (broad s, 3H, OH, NH_2), 3.54 (t, J=6.4 Hz, 2H, CH_2OH). ^{13}C NMR ($CDCl_3$): δ=−4.62 ($Si(CH_3)_2$), 13.72 ($SiCH_2$), 23.39 ($SiCH_2CH_2$), 29.51 ($Si(CH_2)_2CH_2CH_2$), 32.28 (CH_2N), 62.26 (CH_2OH). IR (film): 3356 and 3272 (NH_2, OH), 1252 (Si–C def.), 840 (Si–C strech.).

4.6.4. 6-(Aminomethyldimethylsilanyl)hexan-1-ol (5d). It was obtained from **4d** (2.73 g, 8.5 mmol), hydrazine hydrate (1.6 mL, 34 mmol) and absolute ethanol (60 mL); yellow oil (1.48 g, 91%). ^{1}H NMR ($CDCl_3$): δ=−0.01 (s, 6H, $Si(CH_3)_2$), 0.48–0.56 (m, 2H, $SiCH_2$), 1.28 (m, 6H, $HOCH_2(CH_2)_3$), 1.45–1.52 (m, 2H, $SiCH_2CH_2$), 2.15 (s, 2H, CH_2NH_2), 2.60 (large s, 3H, NH_2, OH), 3.54 (t, J=6.5 Hz, 2H, CH_2OH). ^{13}C NMR ($CDCl_3$): δ=−4.73 ($Si(CH_3)_2$), 13.60 ($SiCH_2$), 25.33 ($SiCH_2CH_2$), 29.68 (CH_2N), 32.61 ($Si(CH_2)_3CH_2$), 33.15 ($Si(CH_2)_4CH_2$), 62.45 (CH_2OH). IR (film): 3356 and 3272 (NH_2, OH), 1252 (Si–C def.), 840 (Si–C strech.).

4.7. General procedure for the preparation of *tert*-butylaminomethyldimethylsilanyl alcohols 6a–d

To a solution of aminomethyldimethylsilanyl alcohol and triethylamine in dichloromethane or chloroform, was added $(Boc)_2O$ under inert atmosphere. After stirring at rt for 24 h, the solution was washed with acidic water ($NaHSO_4$, 3×30 mL, pH 3), then with water, the organic layer separated, dried ($MgSO_4$), filtrated and concentrated under reduced pressure. The residue was applied to a column of silica gel eluted with dichloromethane/methyl alcohol (95:5) to give the pure compound.

4.7.1. 3-(*tert*-Butylaminomethyldimethylsilanyl)-propan-1-ol (6a). It was obtained from **5a** (0.6 g, 40 mmol), $(Boc)_2O$ (0.87 g, 40 mmol) and triethylamine (0.40 g, 40 mmol) in chloroform (40 mL); colorless oil (0.50 g, 50%). ^1H NMR ($CDCl_3$): δ=0.03 (s, 6H, $Si(CH_3)_2$), 0.53–0.61 (m, 2H, $SiCH_2$), 1.41 (s, 9H, $C(CH_3)_3$), 1.52–1.63 (m, 2H, $SiCH_2CH_2$), 2.60 (d, J=5.6 Hz, 2H, CH_2NH), 3.58 (t, J=6.4 Hz, 2H, CH_2OH). ^{13}C NMR ($CDCl_3$): δ=−4.53 ($Si(CH_3)_2$), 9.64 ($SiCH_2$), 26.07 ($SiCH_2CH_2$), 28.37 ($C(CH_3)_3$), 29.21 (CH_2N), 65.20 (CH_2OH), 79.06 ($C(CH_3)_3$), 156.89 (C=O). IR (film): 3356 (NH, OH), 1692 (C=O), 1252 (Si–C def.), 1172 (COO), 840 (Si–C strech.).

4.7.2. 4-(*tert*-Butylaminomethyldimethylsilanyl)-butan-1-ol (6b). It was obtained from **5b** (1 g, 62 mmol), $(Boc)_2O$ (1.35 g, 62 mmol) and triethylamine (0.62 g, 62 mmol) in dichloromethane (40 mL); colorless oil (0.74 g, 45%). ^1H NMR ($CDCl_3$): δ=0.02 (s, 6H, $Si(CH_3)_2$), 0.52–0.60 (m, 2H, $SiCH_2$), 1.41 (s, 9H, $C(CH_3)_3$), 1.46–1.61 (m, 4H, $SiCH_2(CH_2)_2$), 2.58 (d, J=5.7 Hz, 2H, CH_2NH), 3.62 (t, J=6.2 Hz, 2H, CH_2OH). ^{13}C NMR ($CDCl_3$): δ=−4.51 ($Si(CH_3)_2$), 13.56 ($SiCH_2$), 19.69 ($SiCH_2CH_2$), 28.39 ($C(CH_3)_3$), 29.18 ($Si(CH_2)_2CH_2$), 36.22 (CH_2N), 62.20 (CH_2OH), 79.04 ($C(CH_3)_3$), 164.50 (C=O). IR (film): 3356 (NH, OH), 1692 (C=O), 1252 (Si–C def.), 1172 (COO), 840 (Si–C strech.).

4.7.3. 5-(*tert*-Butylaminomethyl-dimethylsilanyl)-pentan-1-ol (6c). It was obtained from **5c** (0.8 g, 45.6 mmol), $(Boc)_2O$ (1 g, 45.6 mmol) and triethylamine (0.46 g, 45.6 mmol) in dichloromethane (40 mL); colorless oil (0.90 g, 75%). ^1H NMR ($CDCl_3$): δ=0.01 (s, 6H, $Si(CH_3)_2$), 0.50–0.58 (m, 2H, $SiCH_2$), 1.29–1.37 (m, 4H, $Si(CH_2)_2CH_2CH_2$), 1.41 (s, 9H, $C(CH_3)_3$), 1.53–1.57 (m, 2H, $SiCH_2CH_2$), 2.57 (d, J=5.5 Hz, 2H, CH_2NH), 3.60 (t, J=6.4 Hz, 2H, CH_2OH). ^{13}C NMR ($CDCl_3$): δ=−4.49 ($Si(CH_3)_2$), 13.93 ($SiCH_2$), 23.38 ($SiCH_2CH_2$), 28.39 ($C(CH_3)_3$), 29.19 (CH_2N), 29.48 ($Si(CH_2)_2CH_2$), 32.33 ($Si(CH_2)_3CH_2$), 62.75 (CH_2OH), 79.00 ($C(CH_3)_3$), 156.87 (C=O). IR (film): 3356 (NH, OH), 1692 (C=O), 1252 (Si–C def.), 1172 (COO), 840 (Si–C strech.).

4.7.4. 6-(*tert*-Butylaminomethyldimethylsilanyl)hexan-1-ol (6d). It was obtained from **5d** (3.48 g, 18 mmol), $(Boc)_2O$ (3.93 g, 18 mmol) and triethylamine (1.82 g, 18 mmol) in chloroform (120 mL); colorless oil (4.16 g, 79%). ^1H NMR ($CDCl_3$): δ=0.01 (s, 6H, $Si(CH_3)_3$), 0.50–0.58 (m, 2H, $SiCH_2$), 1.27–1.37 (m, 6H, $Si(CH_2)_2$-$CH_2CH_2CH_2$), 1.41 (s, 9H, $C(CH_3)_3$), 1.47–1.56 (m, 4H, $SiCH_2CH_2$), 2.58 (d, J=5.5 Hz, 2H, CH_2NH), 3.60 (t, J=6.4 Hz, 2H, CH_2OH). ^{13}C NMR ($CDCl_3$): δ=−4.53 ($Si(CH_3)_2$), 13.83 ($SiCH_2$), 23.45 ($SiCH_2CH_2$), 25.29 ($SiCH_2CH_2$), 27.33 ($Si(CH_2)_2$-CH_2), 28.36 ($C(CH_3)_3$), 29.21 (CH_2N), 32.55 ($Si(CH_2)_3$-CH_2), 33.12 ($Si(CH_2)_4$-CH_2), 62.71 (CH_2OH), 78.94 ($C(CH_3)_3$), 156.88 (C=O). IR (film): 3356 (NH, OH), 1692 (C=O), 1252 (Si–C def.), 1172 (COO), 840 (Si–C strech.).

4.8. General procedure for the preparation of ascorbic acid derivatives 7a–d and 8a–d

To a mixture of triphenylphosphine in anhydrous THF at −15°C, DEAD was added dropwise over a period of ca. 15 min, followed by ascorbic acid and a solution in THF of *tert*-butylaminomethyldimethylsilyl alcohol (**6a–d**) or chloromethyldimethylsilanyl alcohol (**3a–d**) respectively. The mixture was stirred under nitrogen at this temperature for 24 h. The resulting light brown mixture was filtered, and the filtrate concentrated under reduced pressure. The oily residue was applied to a silicagel column eluted with dichloromethane/methyl alcohol (97:3) to give the pure compound.

4.8.1. Ascorbic acid 3-(3-(*tert*-butylaminomethyl-dimethylsilanyl)propyl) oxide (7a). It was obtained from **6a** (0.5 g, 2.0 mmol), ascorbic acid (0.44 g, 2.5 mmol), triphenylphosphine (0.65 g, 2.5 mmol), DEAD (0.43 g, 2.5 mmol) and THF (15 mL); colorless oil (0.23 g, 28%). ^1H NMR ($CDCl_3$): δ=0.02 (s, 6H, $Si(CH_3)_2$), 0.54–0.63 (m, 2H, $SiCH_2$), 1.39 (s, 9H, $C(CH_3)_3$), 1.62–1.78 (m, 2H, $SiCH_2CH_2$), 2.57 (d, J=5.6 Hz, 2H, $SiCH_2NH$), 3.70–3.73 (m, 2H, CH_2O), 3.90 (m, 1H, H-5′), 4.33–4.43 (m, 2H, H-6′), 4.63 (d, J=1.3 Hz, 1H, H-4′). ^{13}C NMR ($CDCl_3$): δ=−4.58 ($Si(CH_3)_2$), 9.36 ($SiCH_2$), 23.88 ($SiCH_2CH_2$), 28.33 ($C(CH_3)_3$), 28.99 (CH_2N), 63.23 (CH_2O), 69.99 (C-5′), 73.94 (C-6′), 76.21 (C-4′), 79.35 ($C(CH_3)_3$), 119.02 (C-2′), 150.74 (C-3′), 157.12 (C=O Boc), 172.04 (C=O ascorbic ac.). IR (film): 3356 (NH, OH), 1756 (C=O), 1684 (C=C), 1256 (Si–C def.), 1164 (COO), 844 (Si–C strech.). HRMS obsd. m/z 428.17166 $C_{17}H_{31}O_8NSi$ ($M+Na^+$) requires 428.17164.

4.8.2. Ascorbic acid 3-(4-(*tert*-butylaminomethyl-dimethylsilanyl)butyl) oxide (7b). It was obtained from **6b** (0.95 g, 36 mmol), ascorbic acid (0.79 g, 45 mmol), triphenylphosphine (1.18 g, 45 mmol), DEAD (0.78 g, 45 mmol) and THF (15 mL); orange oil (0.62 g, 41%). ^1H NMR ($CDCl_3$): δ=0.03 (s, 6H, $Si(CH_3)_2$), 0.55–0.63 (m, 2H, $SiCH_2$), 1.36–1.50 (m, 2H, $Si(CH_2)_2CH_2$), 1.42 (s, 9H, $C(CH_3)_3$), 1.67–1.80 (m, 2H, $SiCH_2CH_2$), 2.59 (d, J=5.5 Hz, CH_2NH), 3.76–3.80 (m, 2H, CH_2O), 3.96 (m, 1H, H-5′), 4.43–4.51 (m, 2H, H-6′), 4.65 (d, J=2 Hz, 1H, H-4′). ^{13}C NMR ($CDCl_3$): δ=−4.41 ($Si(CH_3)_2$), 13.38 ($SiCH_2$), 19.59 ($SiCH_2CH_2$), 28.39 ($C(CH_3)_3$), 29.03 (CH_2N), 32.96 ($Si(CH_2)_2CH_2$), 63.47 (CH_2O), 70.17 (C-5′), 71.44 (C-6′), 76.34 (C-4′), 79.40 ($C(CH_3)_3$), 118.84 (C-2′), 150.17 (C-3′), 157.17 (C=O Boc), 171.67 (C=O ascorbic ac.). IR (film): 3356 (OH, NH), 1756 (C=O), 1684 (C=C), 1252 (Si–C def.), 1172 (COO), 840 (Si–C strech.). HRMS obsd. m/z 442.18731 $C_{18}H_{33}O_8NSi$ ($M+Na^+$) requires 442.18729.

4.8.3. Ascorbic acid 3-(5-(*tert*-butylaminomethyl-dimethylsilanyl)pentyl) oxide (7c). It was obtained from **6c** (0.90 g, 3.4 mmol), ascorbic acid (0.74 g, 4.2 mmol), triphenylphosphine (1.10 g, 4.2 mmol), DEAD (0.73 g, 4.2 mmol) and THF (15 mL); colorless oil (0.63 g, 42%). ^1H NMR ($CDCl_3$): δ=0.01 (s, 6H, $Si(CH_3)_2$), 0.50–0.58 (m, 2H, $SiCH_2$), 1.28–1.37 (m, 4H, $Si(CH_2)_2CH_2CH_2$), 1.39 (s, 9H, $C(CH_3)_3$), 1.62–1.72 (m, 2H, $SiCH_2CH_2$), 2.56 (d, J=5.5 Hz, 2H, CH_2NH), 3.72–3.76 (m, 2H, CH_2O), 3.88–3.95 (td, $J_{5',6'}$=5.7 Hz, $J_{5',4'}$=2.1 Hz, 1H, H-5′), 4.38–4.49 (m, 2H, H-6′), 4.63 (d, J=2.1 Hz, 1H, H-4′). ^{13}C NMR ($CDCl_3$): δ=−4.47 ($Si(CH_3)_2$), 13.86 ($SiCH_2$), 23.23 ($SiCH_2CH_2$), 28.37 ($C(CH_3)_3$), 29.22 ($Si(CH_2)_2CH_2CH_2$,

CH_2N), 63.29 (CH_2O), 70.12 (C-5′), 71.92 (C-6′), 76.28 (C-4′), 79.19 ($C(CH_3)_3$), 118.98 (C-2′), 150.85 (C-3′), 157.05 (C═O Boc), 172.09 (C═O ascorbic ac.). IR (film): 3336 (NH, OH), 1756 (C═O), 1684 (C═C), 1252 (Si–C def.), 1164 (COO), 840 (Si–C strech.). HRMS obsd. *m/z* 456.20296 $C_{19}H_{35}O_8NSi$ ($M+Na^+$) requires 456.20294.

4.8.4. Ascorbic acid 3-(6-(*tert*-butylaminomethyl-dimethylsilanyl)hexyl) oxide (7d). It was obtained from **6d** (1.16 g, 4 mmol), ascorbic acid (0.88 g, 5 mmol), triphenylphosphine (1.31 g, 5 mmol), DEAD (0.87 g, 5 mmol) and THF (20 mL); faint yellow oil (0.83 g, 46%). ^1H NMR ($CDCl_3$): δ=0.01 (s, 6H, $Si(CH_3)_2$), 0.50–0.58 (m, 2H, $SiCH_2$), 1.25–1.36 (m, 6H, $Si(CH_2)_2CH_2CH_2CH_2$), 1.42 (s, 9H, $C(CH_3)_3$), 1.66–1.72 (m, 2H, $SiCH_2CH_2$), 2.57 (d, *J*=5.5 Hz, 2H, CH_2NH), 3.78 (m, 2H, CH_2O), 3.94 (m, 1H, H-5′), 4.43–4.49 (m, 2H, H-6′), 4.65 (d, *J*=2.2 Hz, 1H, H-4′). ^{13}C NMR ($CDCl_3$): δ=−4.44 ($Si(CH_3)_2$), 13.78 ($SiCH_2$), 23.35 ($SiCH_2CH_2$), 24.96 (C-4), 28.42 ($C(CH_3)_3$), 29.41 ($Si(CH_2)_3CH_2$, CH_2N), 32.76 ($Si(CH_2)_4CH_2$), 63.48 (CH_2O), 70.28 (C-5′), 72.10 (C-6′), 76.47 (C-4′), 79.27 ($C(CH_3)_3$), 118.84 (C-2′), 150.22 (C-3′), 157.08 (C═O Boc), 171.66 (C═O ascorbic ac.). IR (film): 3356 (NH, OH), 1756 (C═O), 1690 (C═C), 1252 (Si–C def.), 1161 (COO), 848 (Si–C strech.). HRMS obsd. *m/z* 470.21861 $C_{20}H_{37}O_8NSi$ ($M+Na^+$) requires 470.21859.

4.8.5. Ascorbic acid 3-(3-(chloromethyldimethyl-silanyl)-propyl) oxide (8a). It was obtained from **3a** (2 g, 12 mmol), ascorbic acid (2.64 g, 15 mmol), triphenylphosphine (3.93 g, 15 mmol), DEAD (2.61 g, 15 mmol) and THF (15 mL); dark orange oil (2.00 g, 51%). ^1H NMR ($CDCl_3$): δ=0.11 (s, 6H, $Si(CH_3)_2$), 0.63–0.71 (m, 2H, $SiCH_2$), 1.67–1.79 (m, 2H, $SiCH_2CH_2$), 2.78 (s, 2H, CH_2Cl), 3.74–3.89 (m, 2H, CH_2O), 3.97 (m, 1H, H-5′), 4.38–4.50 (m, 2H, H-6′), 4.65 (d, *J*=1.8 Hz, 1H, H-4′). ^{13}C NMR ($CDCl_3$): δ=−4.75 ($Si(CH_3)_2$), 9.11 ($SiCH_2$), 23.85 ($SiCH_2CH_2$), 29.97 (CH_2Cl), 63.48 (CH_2O), 70.04 (C-5′), 74.24 (C-6′), 76.59 (C-4′), 118.20 (C-2′), 151.50 (C-3′), 172.00 (C═O ascorbic ac.). IR (film): 3356 (OH), 1756 (C═O), 1690 (C═C), 1252 (Si–C def.), 1062 (CH_2Cl), 844 (Si–C strech.).

4.8.6. Ascorbic acid 3-(4-(chloromethyldimethyl-silanyl)butyl) oxide (8b). It was obtained from **3b** (1.64 g, 9.1 mmol), ascorbic acid (2 g, 11.3 mmol), triphenylphosphine (2.97 g, 11.3 mmol), DEAD (1.97 g, 11.3 mmol) and THF (15 mL); dark orange oil (1.21 g, 31%). ^1H NMR ($CDCl_3$): δ=0.09 (s, 6H, $Si(CH_3)_2$), 0.62–0.70 (m, 2H, $SiCH_2$), 1.29–1.50 (m, 2H, $SiCH_2CH_2CH_2CH_2$), 1.68–1.82 (m, 2H, $SiCH_2CH_2CH_2$), 2.77 (s, 2H, CH_2Cl), 3.77–3.83 (m, 2H, CH_2O), 3.94 (m, 1H, H-5′), 4.45–4.55 (m, 2H, H-6′), 4.65 (d, *J*=2 Hz, 1H, H-4′). ^{13}C NMR ($CDCl_3$): δ=−4.64 ($Si(CH_3)_2$), 13.26 ($SiCH_2$), 19.58 ($SiCH_2CH_2$), 30.19 (CH_2Cl), 33.15 ($Si(CH_2)_2CH_2CH_2CH_2$), 63.38 (CH_2O), 70.00 (C-5′), 71.72 (C-6′), 76.99 (C-4′), 118.81 (C-2′), 146.24 (C-3′), 172.09 (C═O ascorbic ac.). IR (film): 3356 (OH), 1750 (C═O), 1690 (C═C), 1252 (Si–C def.), 1068 (CH_2Cl), 842 (Si–C strech.).

4.8.7. Ascorbic acid 3-(5-(chloromethyldimethyl-silanyl)pentyl) oxide (8c). It was obtained from **3c** (2.06 g, 10.5 mmol), ascorbic acid (2.29 g, 13 mmol), triphenylphosphine (3.40 g, 13 mmol), DEAD (2.26 g, 13 mmol) and THF (15 mL); orange oil (1.57 g, 42%). ^1H NMR ($CDCl_3$): δ=0.08 (s, 6H, $Si(CH_3)_2$), 0.58–0.66 (m, 2H, $SiCH_2$), 1.29–1.46 (m, 4H, $Si(CH_2)_2CH_2CH_2CH_2$), 1.64–1.78 (m, 2H, $SiCH_2CH_2CH_2$), 2.75 (s, 2H, CH_2Cl), 3.75–3.83 (m, 2H, CH_2O), 3.93 (m, 1H, H-5′), 4.43–4.56 (m, 2H, H-6′), 4.63 (d, *J*=1.6 Hz, 1H, H-4′). ^{13}C NMR ($CDCl_3$): δ=−4.62 ($Si(CH_3)_2$), 13.56 ($SiCH_2$), 23.27 ($SiCH_2CH_2$), 29.25 ($Si(CH_2)_2CH_2CH_2CH_2$), 30.28 (CH_2Cl), 63.45 (CH_2O), 70.11 (C-5′), 72.09 (C-6′), 76.56 (C-4′), 118.89 (C-2′), 150.95 (C-3′), 172.27 (C═O ascorbic ac.). IR (film): 3356 (OH), 1750 (C═O), 1690 (C═C), 1252 (Si–C def.), 1068 (CH_2Cl), 842 (Si–C strech.).

4.8.8. Ascorbic acid 3-(6-(chloromethyldimethyl-silanyl)-hexyl) oxide (8d). It was obtained from **3d** (0.80 g, 3.83 mmol), ascorbic acid (0.84 g, 4.78 mmol), triphenylphosphine (1.25 g, 4.78 mmol), DEAD (0.83 g, 4.78 mmol) and THF (15 mL); orange oil (0.57 g, 40%). ^1H NMR ($CDCl_3$): δ=0.09 (s, 6H, $Si(CH_3)_2$), 0.60–0.68 (m, 2H, $SiCH_2$), 1.32–1.42 (m, 6H, $SiCH_2CH_2(CH_2)_3$), 1.66–1.79 (m, 2H, $SiCH_2CH_2$), 2.76 (s, 2H, CH_2Cl), 3.80 (m, 2H, CH_2O), 3.91–3.98 (td, *J*=5.5, 2.3 Hz, 1H, H-5′), 4.42–4.53 (m, 2H, H-6′), 4.65 (d, 1H, H-4′). ^{13}C NMR ($CDCl_3$): δ=−4.62 ($Si(CH_3)_2$), 13.56 ($SiCH_2$), 23.39 ($Si(CH_2)_3CH_2$), 30.35 (CH_2Cl), 33.03 ($Si(CH_2)_4CH_2$), 63.44 (CH_2O), 70.06 (C-5′), 72.19 (C-6′), 76.56 (C-4′), 118.81 (C-2′), 150.69 (C-3′), 172.00 (C═O ascorbic ac.). IR (film): 3356 (OH), 1756 (C═O), 1690 (C═C), 1252 (Si–C def.), 1062 (CH_2Cl), 848 (Si–C strech.).

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