Supporting Information

Facile synthesis and self-assembly behavior of pH-responsive degradable polyacetal dendrimers

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Experimental Section

Materials

Allyl vinyl ether (95%, Alfa Aesar), *N*-(2-hydroxyethyl) acrylamide (98%, TCI), pyridinium *p*-toluenesulfonate (PPTS, 98%, Energy Chemical), tris(2-aminoethyl)amine (TAEA, 97%, Strem Chemicals), cysteamine hydrochloride (99%, Energy Chemical), 2,2-dimethoxy-2-phenylacetophenone (DMPA, 99%, J&K), *N*-(3-(dimethylamino)propyl) acrylamide (98%, J&K), 1,3-propanesultone (99%, J&K) were used as received. Octaamine polyhedral oligomeric silsesquioxane (POSS-[NH₃Cl]₈) and thiol-polyethylene glycol (PEG-SH) were synthesized according to methods given in our previous literatures.^{1,2} Tetrahydrofuran (THF), *N*,*N'*-dimethyl formamide (DMF), chloroform (CHCl₃), dichloromethane (DCM) and triethylamine (TEA) (reagent grade, Beijing Chemical Works) were purified by stirring over calcium hydride for 24 h followed by distillation. Other solvents and compounds were purchased from Beijing Chemical Works and used without further purification.

Characterizations

Nuclear magnetic resonance (NMR) spectra were recorded on a Bruker 400 MHz spectrometer. Matrix-assisted laser desorption ionization-time of flight mass spectrometry (MALDI-TOF MS) measurements were carried out using a Bruker BIFLEX III equipped with a 337 nm nitrogen laser. Gel permeation chromatography (GPC) measurements were performed at 50 °C using an SSI pump fitted with a Wyatt DAWN EOS multiangle laser light scattering (MALLS) detector coupled with Wyatt Optilab DSP refractive index detector with 0.02 M LiBr in DMF as the eluent at a flow rate of 1.0 mL min⁻¹. The dn/dc values of polyacetal dendrimer determined in DMF was 0.174. The molecular weight (MW) and polydispersity (PDI) were calculated from the MALLS signal by Astra software using the dn/dc value. Transmission electron microscopy (TEM) images were obtained on a JEM-2200FS microscope (JEOL, Japan) after the samples were negative stained by sodium phosphotungstate. Generally, a 3 µL droplet of nanoparticles solution was dropped onto a copper grid (300 mesh) coated with a carbon film, then the excess liquid was wicked off and the grids were immediately placed onto individual droplets of freshly prepared and filtered, 2 wt% aqueous sodium phosphotungstate. After 2 minutes excess stain was removed and the grids were allowed to dry thoroughly. Size distribution and zeta potentials of the nanoparticles were characterized by dynamic light scattering (DLS) using a zetasizer (Nano-ZS, Malvern, UK) with a 632.8 nm laser light set at a scattering angle of 173°.

Synthesis of *N*-(2-(1-(allyloxy)ethoxy)ethyl)acrylamide (AEEAA). *N*-(2-hydroxyethyl) acrylamide (27.6 g, 0.24 mol) and PPTS (0.5 g, 0.02 mol) were dissolved in 200 mL of dry DCM at 0 °C under nitrogen. Allyl vinyl ether (16.8 g, 0.2 mol) in 50 mL of dry DCM was added dropwise. It was stirred at room temperature overnight, then K_2CO_3 was added to quench the reaction. The mixture was filtered through a pad of celite and the filtrate was evaporated under reduced pressure to obtain crude product, which was purified by silica gel chromatography using hexane/ethyl acetate (v/v=8/1) containing 1% (v/v) TEA as eluent to obtain the acetal monomer AEEAA as a pale yellow liquid with 79% yield. ¹H NMR (Acetone-d₆, 400 MHz, ppm) δ

7.33 (s, 1H), 6.23 (ddd, J = 19.4, 17.0, 6.2 Hz, 2H), 5.99 – 5.80 (m, 1H), 5.54 (dd, J = 10.0, 2.4 Hz, 1H), 5.24 (dd, J = 17.2, 1.8 Hz, 1H), 5.08 (dd, J = 10.5, 1.8 Hz, 1H), 4.73 (q, J = 5.3 Hz, 1H), 4.12 – 3.94 (m, 2H), 3.66 – 3.48 (m, 2H), 3.42 (m, 2H), 1.23 (d, J = 5.3 Hz, 3H). ¹³C NMR (Acetone-d₆, 400 MHz, ppm) δ 164.69, 135.42, 131.80, 124.41, 115.15, 99.21, 66.01, 63.61, 39.17, 19.20.

Synthesis of polyacetal dendrimers with a TAEA core

Synthesis of G1-[ene]₆. TAEA (292 mg, 2 mmol) and AEEAA (2.99 g, 15 mmol) were dissolved in 10 mL of methanol/water (v/v=7/3) and stirred at 70 °C for 48 hours. The mixture was then diluted by 50 mL of DCM and dried with MgSO₄. After being concentrated to a few milliliter, it was precipitated in diethyl ether/hexane (v/v=1:2) for three times. The precipitate was dried under vacuum to give the product G1-[ene]₆ as a pale yellow oil with 78% yield. ¹H NMR (Acetone-d₆, 400 MHz, ppm) δ 7.75 (d, *J* = 5.5 Hz, 6H), 6.00 – 5.81 (m, 6H), 5.27 (dd, *J* = 17.2, 1.6 Hz, 6H), 5.11 (d, *J* = 10.4 Hz, 6H), 4.76 (q, *J* = 5.2 Hz, 6H), 4.06 (ddd, *J* = 47.7, 13.2, 5.2 Hz, 12H), 3.66 – 3.45 (m, 12H), 3.45 – 3.28 (m, 12H), 2.77 (dd, *J* = 19.3, 12.9 Hz, 21H), 2.55 (s, 15H), 2.35 (t, *J* = 6.1 Hz, 12H), 1.25 (dd, *J* = 10.4, 5.3 Hz, 18H). MS (MALDI-TOF, m/z) Calc. for C₆₆H₁₂₀N₁₀O₁₈: 1341.74 found: 1342.1 (M+H⁺), 1363.8 (M+Na⁺). GPC: *M*_n=1470, *M*_w=1530, PDI=1.04.

Synthesis of G1'-[NH₃Cl]₆. G1-[ene]₆ (2.01 g, 1.5 mmol), cysteamine hydrochloride (3.06 g, 27 mmol), and DMPA (346 mg, 1.35 mmol) were dissolved in methanol. The mixture was purged with argon for 10 minutes and then irradiated under a 365 nm UV lamp at room temperature for 3 hours. It was precipitated in diethyl ether for three times. The precipitate was dissolved in methanol and then THF was added until precipitate appeared. This procedure was repeated three times and the precipitate was dried under vacuum to give the product G1'-[NH₃Cl]₆ as a viscous yellow oil with 28% yield. ¹H NMR (MeOD, 400 MHz, ppm) δ 8.27 (d, *J* = 8.3 Hz, 5H), 4.73 (d, *J* = 5.2 Hz, 6H), 3.87 – 3.46 (m, 68H), 3.23 – 2.96 (m, 30H), 2.94 – 2.75 (m, 31H), 2.68 (s, 12H), 1.95 – 1.74 (m, 12H), 1.29 (d, *J* = 5.1 Hz, 19H).

Synthesis of G2-[ene]₁₂. G1'-[NH₃Cl]₆ (707 mg, 0.35 mmol), AEEAA (1.99 g, 10 mmol) and TEA (318 mg, 3.15 mmol) were dissolved in methanol/water (v/v=7/3) and stirred at 70 °C for 48 hours. The mixture was diluted by DCM followed by washing three times with brine. The organic layer was dried with MgSO₄ and concentrated to a few milliliter, which was then precipitated in diethyl ether/hexane (v/v=1/2) for three times. The precipitate was dried under vacuum to give the product G2-[ene]₁₂ as a viscous yellow oil with 82% yield. ¹H NMR (Acetone-d₆, 400 MHz, ppm) δ 7.66 (s, 18H), 6.09 – 5.76 (m, 12H), 5.27 (d, *J* = 17.1 Hz, 13H), 5.11 (d, *J* = 10.5 Hz, 12H), 4.76 (d, *J* = 5.3 Hz, 18H), 4.06 (ddd, *J* = 18.6, 13.1, 5.1 Hz, 28H), 3.49 (ddd, *J* = 46.1, 21.4, 7.5 Hz, 124H), 2.88 – 2.56 (m, 106H), 2.37 (dd, *J* = 17.8, 11.8 Hz, 47H), 1.93 – 1.72 (m, 12H), 1.26 (d, *J* = 5.1 Hz, 49H). MS (MALDI-TOF, m/z) Calc. for C₁₉₈H₃₆₆N₂₈O₅₄S₆: 4190.61 found: 4191.4 (M+H⁺), 4213.7 (M+Na⁺). GPC: *M*_n=4020, *M*_w=4260, PDI=1.06.

Synthesis of G2'-[NH₃Cl]₁₂. G2-[ene]₁₂ (1.05 g, 0.25 mmol), cysteamine hydrochloride (1.02 g, 9 mmol), and DMPA (115 mg, 0.45 mmol) were reacted following the same procedure in synthesis of G1'-[NH₃Cl]₆ to obtain G2'-[NH₃Cl]₁₂ as a viscous yellow oil with 43% yield. ¹H NMR (MeOD, 400 MHz, ppm) δ 4.73 (d, J

= 3.5 Hz, 12H), 3.82 – 3.36 (m, 122H), 3.13 (dd, J = 13.5, 6.9 Hz, 26H), 3.07 – 2.96 (m, 27H), 2.82 (dd, J = 16.4, 9.8 Hz, 39H), 2.69 (dd, J = 15.2, 7.1 Hz, 25H), 2.53 (dd, J = 12.3, 7.0 Hz, 22H), 1.85 (dd, J = 13.2, 6.5 Hz, 34H), 1.35 – 1.20 (m, 37H).

Synthesis of G3-[ene]₂₄. G2'-[NH₃Cl]₁₂ (555 mg, 0.1 mmol), AEEAA (2.09 g, 10.5 mmol) and TEA (182 mg, 1.8 mmol) were reacted following the same procedure in synthesis of G2-[ene]₁₂ to obtain G3-[ene]₂₄ as a viscous yellow oil with 87% yield. ¹H NMR (Acetone, 400 MHz, ppm) δ 7.65 (s, 41H), 5.91 (dd, J = 11.5, 5.6 Hz, 24H), 5.27 (d, J = 17.3 Hz, 27H), 5.10 (d, J = 10.3 Hz, 25H), 4.75 (d, J = 5.1 Hz, 42H), 4.05 (d, J = 34.5 Hz, 70H), 3.76 – 3.46 (m, 168H), 3.46 – 3.24 (m, 159H), 3.14 – 2.56 (m, 569H), 2.37 (d, J = 5.0 Hz, 86H), 1.83 (s, 39H), 1.28 (dd, J = 16.3, 7.9 Hz, 160H). GPC: *M*_n=10100, *M*_w=11010, PDI=1.09.

Synthesis of the polyacetal dendrimers with a POSS core

Synthesis of G1-[ene]₁₆. POSS-[NH₃Cl]₈ (308 mg, 0.2 mmol), AEEAA (1.27 g, 6.4 mmol) and TEA (242 mg, 2.4 mmol) were dissolved in methanol/water (v/v=7/3) and stirred at 70 °C for 48 hours. The mixture was diluted by DCM followed by washing three times with brine. The organic layer was dried with MgSO₄ and concentrated to a few milliliter, which was then precipitated in diethyl ether/hexane (v/v=1/2) for three times. The precipitate was dried under vacuum to give the product G1-[ene]₁₆ as a viscous yellow oil with 88% yield. ¹H NMR (MeOD, 400 MHz, ppm) δ 6.03 – 5.80 (m, 15H), 5.29 (d, *J* = 17.2 Hz, 15H), 5.15 (d, *J* = 10.4 Hz, 16H), 4.77 (d, *J* = 5.2 Hz, 16H), 4.07 (dd, *J* = 29.5, 5.3 Hz, 32H), 3.69 – 3.48 (m, 32H), 3.36 (d, *J* = 9.7 Hz, 33H), 2.76 (d, *J* = 40.6 Hz, 100H), 2.39 (s, 33H), 1.31 (d, *J* = 5.2 Hz, 50H), 1.08 (s, 16H). ¹³C NMR (MeOD, 400 MHz, ppm) δ 174.75, 136.31, 116.98, 100.98, 67.78, 65.04, 51.23, 46.33, 40.71, 34.75, 30.85, 27.62, 20.46, 15.81. MS (MALDI-TOF, m/z) Calc. for C₁₉₂H₃₅₂N₂₄O₆₀S₈Si₈: 4438.2 found: 3992.0-5042.6. GPC: *M*_n=4530, *M*_w=4720, PDI=1.04.

Synthesis of G1'-[NH₃Cl]₁₆. G1-[ene]₁₆ (709 mg, 0.16 mmol), cysteamine hydrochloride (872 mg, 7.68 mmol), and DMPA (97 mg, 0.38 mmol) were dissolved in methanol. The mixture was purged with argon for 10 minutes and then irradiated under a 365 nm UV lamp at room temperature for 3 hours. It was precipitated in diethyl ether for three times. The precipitate was dissolved in methanol and then THF was added until precipitate appeared. This procedure was repeated three times and the precipitate was dried under vacuum to give the product G1'-[NH₃Cl]₁₆ as a pale yellow solid with 79% yield. ¹H NMR (MeOD, 400 MHz, ppm) δ 4.76 (s, 16H), 3.64 (m, 160H), 3.18 (s, 34H), 2.87 (s, 79H), 2.70 (s, 29H), 1.87 (dd, *J* = 8.2, 4.9 Hz, 46H), 1.31 (s, 49H), 1.16 (s, 16H). ¹³C NMR (MeOD, 400 MHz, ppm) δ 172.06, 101.55, 89.84, 68.90, 65.18, 65.02, 49.90, 49.33, 40.89, 40.11, 39.31, 34.94, 30.86, 29.77, 29.25, 26.53, 20.44, 15.76.

Synthesis of G2-[ene]₃₂. G1'-[NH₃Cl]₁₆ (750 mg, 0.12 mmol), AEEAA (3.06 g, 15.36 mmol) and TEA (291 mg, 2.88 mmol) were reacted following the same procedure in synthesis of G1-[ene]₁₆ to obtain G2-[ene]₃₂ as a pale yellow solid with 87% yield. ¹H NMR (MeOD, 400 MHz, ppm) δ 5.91 (dd, *J* = 11.2, 5.6 Hz, 31H), 5.28 (d, *J* = 17.2 Hz, 30H), 5.15 (d, *J* = 10.3 Hz, 31H), 4.78 – 4.68 (m, 48H), 4.25 – 3.91 (m, 75H), 3.74 – 3.59 (m, 76H), 3.53 (s, 68H), 3.35 (d, *J* = 7.7 Hz, 139H), 2.96 – 2.58 (m, 295H), 2.38 (d, *J* = 6.3 Hz, 101H), 1.84 (d, *J* = 5.9 Hz, 33H), 1.30 (d, *J* = 3.2 Hz, 149H), 1.07 (s, 17H). ¹³C NMR (MeOD, 400 MHz, ppm) δ

174.91, 136.26, 116.94, 100.93, 67.74, 64.94, 50.81, 46.28, 40.65, 36.22, 34.51, 32.22, 31.23, 30.50, 29.86, 29.44, 20.51, 20.36. GPC: *M*_p=13700, *M*_w=14700, PDI=1.07.

Synthesis of G2'-[NH₃Cl]₃₂. G2-[ene]₃₂ (1.2 g, 0.1 mmol), cysteamine hydrochloride (1.09 g, 9.6 mmol), and DMPA (123 mg, 0.48 mmol) were reacted following the same procedure in synthesis of G1'-[NH₃Cl]₁₆ to obtain G2'-[NH₃Cl]₃₂ as a pale yellow solid with 76% yield. ¹H NMR (MeOD, 400 MHz, ppm) δ 4.74 (s, 48H), 3.83 – 3.63 (m, 137H), 3.61 – 3.33 (m, 337H), 3.17 (s, 62H), 2.76 (dd, *J* = 49.1, 16.1 Hz, 269H), 1.88 (d, *J* = 3.1 Hz, 98H), 1.30 (s, 151H), 1.14 (s, 16H). ¹³C NMR (MeOD, 400 MHz, ppm) δ 172.39, 101.51, 68.89, 65.11, 64.96, 51.22, 45.22, 40.79, 40.03, 39.32, 34.93, 30.81, 29.75, 29.55, 29.20, 28.37, 27.14, 26.52, 20.31.

Synthesis of G3-[ene]₆₄. G2'-[NH₃Cl]₃₂ (940 mg, 0.06 mmol), AEEAA (4.58 g, 23 mmol) and TEA (291 mg, 2.88 mmol) were reacted following the same procedure in synthesis of G1-[ene]₁₆ to obtain G3-[ene]₆₄ as a viscous yellow oil with 88% yield. ¹H NMR (MeOD, 400 MHz, ppm) δ 5.93 (ddd, *J* = 22.2, 10.5, 5.3 Hz, 62H), 5.29 (d, *J* = 17.2 Hz, 63H), 5.15 (d, *J* = 10.4 Hz, 64H), 4.77 – 4.70 (m, 112H), 4.07 (ddd, *J* = 42.6, 12.9, 5.1 Hz, 147H), 3.66 (dd, *J* = 9.9, 5.8 Hz, 214H), 3.53 (d, *J* = 4.3 Hz, 210H), 3.37 (d, *J* = 4.8 Hz, 259H), 2.98 – 2.56 (m, 763H), 2.38 (s, 258H), 1.95 – 1.76 (m, 119H), 1.30 (d, *J* = 5.0 Hz, 347H), 1.08 (s, 17H). ¹³C NMR (MeOD, 400 MHz, ppm) δ 174.90, 136.28, 116.94, 101.45, 100.98, 67.78, 65.28, 65.11, 65.00, 50.86, 46.32, 40.67, 36.34, 34.58, 32.36, 31.25, 30.59, 29.91, 29.50, 20.39. GPC: *M*_n=25400, *M*_w=27900, PDI=1.10.

Synthesis of G3'-[NH₃Cl]₆₄. G3-[ene]₆₄ (545 mg, 0.02 mmol), cysteamine hydrochloride (436 mg, 3.84 mmol), and DMPA (49 mg, 0.19 mmol) were reacted following the same procedure in synthesis of G1'-[NH₃Cl]₁₆ to obtain G3'-[NH₃Cl]₆₄ as a pale yellow solid with 78% yield. ¹H NMR (MeOD, 400 MHz, ppm) δ 4.74 (d, *J* = 5.0 Hz, 112H), 3.71 (ddd, *J* = 17.3, 11.8, 7.7 Hz, 262H), 3.61 – 3.34 (m, 674H), 3.16 (s, 96H), 2.96 (s, 161H), 2.90 – 2.66 (m, 501H), 1.88 (dd, *J* = 6.4, 2.9 Hz, 223H), 1.29 (s, 341H), 1.14 (s, 18H). ¹³C NMR (MeOD, 400 MHz, ppm) δ 172.56, 101.58, 68.91, 65.18, 65.04, 51.30, 45.25, 40.82, 40.09, 35.03, 30.86, 29.84, 29.64, 29.30, 28.46, 27.38, 26.54, 20.33.

pH-responsive degradation of the polyacetal dendrimers

The pH-responsive degradation of the polyacetal dendrimers was studied by dissolving the amine-terminated dendrimers Gn' in deuterated phosphate buffer at pH=5.8, which was prepared using sodium dihydrogen phosphate and disodium hydrogen phosphate. Then ¹H NMR spectra of the dendrimers were recorded at different time intervals and degradation profiles were calculated from the integration of the peaks at 1.31 ppm due to the methyl in the acetal groups.

Functionalization and self-assembly of polyacetal dendrimers

Synthesis of G3-PEG₁₆₀. G3-[ene]₆₄ (172 mg, 6.32 μ mol), PEG₁₆₀-SH (152 mg, 0.81 mmol), and DMPA (26 mg, 0.10 mmol) were dissolved in methanol. The mixture was purged with argon for 10 minutes and then irradiated under a 365 nm UV lamp at room temperature for 3 hours. It was precipitated in diethyl ether for three times and the precipitate was dried under vacuum to give the product G3-PEG₁₆₀ as a viscous yellow

oil with 82% yield. ¹H NMR (MeOD, 400 MHz, ppm) δ 4.73 (s, 112H), 3.81 – 3.44 (m, 614H), 3.37 (s, 243H), 3.03 – 2.53 (m, 678H), 2.39 (s, 200H), 1.84 (s, 144H), 1.30 (s, 355H).

Synthesis of G3-PEG₃₅₀. G3-[ene]₆₄ (144 mg, 5.29 µmol), PEG₃₅₀-SH (372 mg, 1.02 mmol), and DMPA (20 mg, 0.08 mmol) were reacted following the same procedure in synthesis of G3-PEG₁₆₀ to obtain G3-PEG₃₅₀ as a brown solid with 85% yield. ¹H NMR (MeOD, 400 MHz, ppm) δ 4.73 (s, 112H), 3.64 (s, 828H), 3.54 (s, 224H), 2.77 (dd, *J* = 73.6, 28.4 Hz, 612H), 2.40 (s, 124H), 1.84 (s, 136H), 1.30 (s, 345H).

Synthesis of G3-DMA. G2'-[NH₃Cl]₃₂ (130 mg, 8.96 µmol), *N*-(3-(dimethylamino) propyl) acrylamide (448 mg, 2.87 mmol) and TEA (43 mg, 0.43 mmol) were dissolved in methanol/water (v/v=7/3) and stirred at 70 °C for 48 hours. Then the mixture was precipitated in diethyl ether for three times and the precipitate was dried under vacuum to give the product G3-DMA as a viscous yellow oil with 88% yield. ¹H NMR (MeOD, 400 MHz, ppm) δ 4.67 (d, *J* = 5.0 Hz, 48H), 3.62 (dd, *J* = 13.9, 9.3 Hz, 104H), 3.53 – 3.39 (m, 171H), 3.30 (d, *J* = 9.2 Hz, 132H), 3.15 (t, *J* = 6.9 Hz, 112H), 2.91 – 2.48 (m, 535H), 2.43 – 2.26 (m, 315H), 2.20 (s, 342H), 1.86 – 1.73 (m, 85H), 1.72 – 1.54 (m, 117H), 1.23 (d, *J* = 5.0 Hz, 160H).

Synthesis of G3-SB. G3-DMA (170 mg, 6.94 µmol) and 1, 3-propanesultone were dissolved in anhydrous THF and stirred at room temperature for 24 hours. The resulting precipitate was filtered, washed with THF and acetone, and dried under vacuum to obtain the product G3-SB as a pale yellow solid with 93% yield. ¹H NMR (D₂O, 400 MHz, ppm) δ 3.69 (d, *J* = 49.6 Hz, 243H), 3.54 – 3.21 (m, 494H), 3.14 (s, 387H), 3.05 – 2.59 (m, 710H), 2.49 (s, 216H), 2.24 (s, 215H), 2.04 (s, 137H), 1.89 (s, 90H), 1.34 (s, 144H).

Self-assembly of G3-PEG. Nano-precipitation technique was employed to prepare the self-assembly aggregates of G3-PEG. Typically, G3-PEG (5 mg) was dissolved in 1 ml of DMSO and stirred at room temperature overnight. Then the DMSO solution was added to 2 mL of deionized water under mild stirring through a syringe within 1.5 hours. Subsequently, the solution was dialyzed against deionized water for 24 hours (molecular weight cutoff = 3500 g/mol), during which the water was renewed every 3 hours. The volume of the solution was increased to 5 mL with the addition of deionized water to produce a solution with a concentration of 1 mg/mL for further experiments.

pH-responsive degradation of the self-assembled aggregates. For the self-assembled aggregates of G3-PEG, their pH-responsive degradation was investigated by adding 100 μ L solution to 1.5 mL phosphate buffer with a pH of 5.8 and then recording the size distribution by DLS at different time intervals. The pH-responsive degradation of the G3-SB unimolecular micelles was investigated by dissolving them in phosphate buffer with a pH of 5.8 and then recording the size distribution by DLS at different time intervals. Besides, morphologies of these self-assemble aggregates before and after degradation were examined by TEM.

Charge reversal of G3-SB. Charge reversal of G3-SB was investigated by tracking their zeta potentials at various pH values. A series of buffers with pH values from 3.0 to 8.0 were prepared using citric acid/sodium citrate and sodium dihydrogen phosphate/disodium hydrogen phosphate. Then G3-SB was dissolved in the buffers with a concentration of 1 mg/mL and their zeta potentials were collected.

References

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Scheme S1. Synthesis of the acetal monomer AEEAA



Scheme S2. Synthetic route of the polyacetal dendrimers with a TAEA core





Scheme S3. Synthetic route of the polyacetal dendrimers with a POSS core



Scheme S4. Schematic approach for preparation of (A) G3-PEG and (B) G3-SB



Fig. S1 (A) 1 H NMR and (B) 13 C NMR spectra of the acetal monomer AEEAA.



Fig. S2 ¹H NMR spectra of the polyacetal dendrimers with a TAEA core.



Fig. S3 (A) MALDI-TOF MS spectra and (B) GPC traces of the polyacetal dendrimers with a TAEA core.



Fig. S4 ¹³C NMR spectra of the polyacetal dendrimers with a POSS core.



Fig. S5 ¹H NMR spectrum of the polyacetal dendrimer G3-[ene]₆₄.



Fig. S6 ¹H NMR spectra of (A) G1'-[NH₃Cl]₁₆ and (B) G2'-[NH₃Cl]₃₂ at pH=5.8 for various times.



Fig. S7 1 H NMR spectra of (A) G3-[ene]₆₄, (B) G3-PEG₁₆₀ and (C) G3-PEG₃₅₀.



Fig. S8 1 H NMR spectra of (A) G2'-[NH₃Cl]₃₂, (B) G3-DMA and (C) G3-SB.



Fig. S9 Zeta potentials of G3-SB at various pH values.

Sample		$M_{ m n, \ calc.}$	M _{n, GPC}	M _{w, GPC}	PDI
Polyacetal dendrimers with a TEAE core	G1-[ene] ₆	1340	1470	1530	1.04
	G2-[ene] ₁₂	4190	4020	4260	1.06
	G3-[ene] ₂₄	9890	10100	11010	1.09
Polyacetal dendrimers with a POSS core	G1-[ene] ₁₆	4432	4530	4720	1.04
	G2-[ene] ₃₂	12032	13700	14700	1.07
	G3-[ene] ₆₄	27232	25400	27900	1.10

Table S1. Molecular weights of the polyacetal dendrimers