Supporting Information

Examination of Structure-Activity Relationship of Viologen-Based Dendrimers as CXCR4 Antagonists and Gene Carriers

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Experimental details corresponding to the synthesis and analytical data of compounds **VGD1** to **VGD1**3. The synthesis of compounds: **VGD1** to **VGD13** are known described in literature.[1-10]

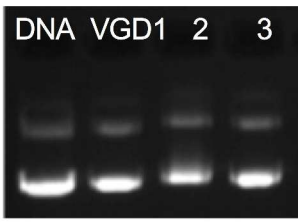


Figure S1. Agarose gel electrophoresis of VGD/DNA polyplexes prepared at N/P 20.

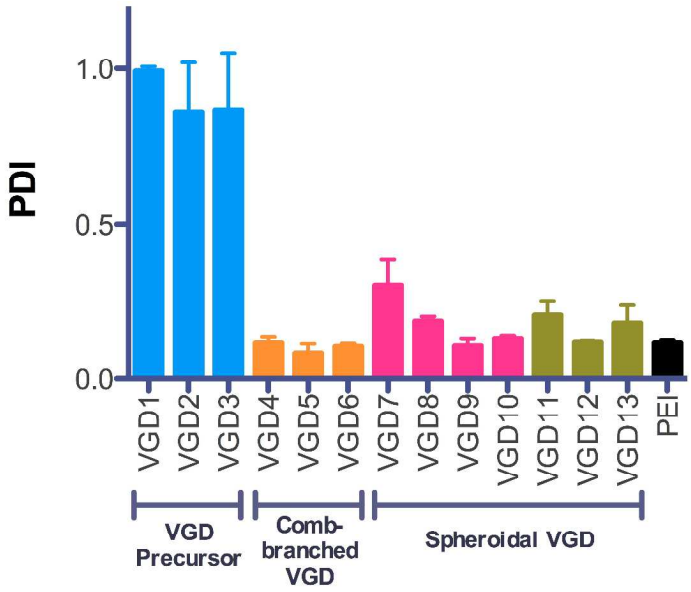


Figure S2. PDI of hydrodynamic size of VGD/DNA polyplexes prepared at N/P 4.

Experimental details for to the synthesis and analytical data of compounds VGD1 to VGD13

Unless otherwise mentioned, the chemicals were analytical grade from Aldrich, Merck or Fluka and used as received. Ethyl acetate, diethyl ether, THF, methanol and petrol ether were distilled before use. Organic solutions were dried over anhydrous Na_2SO_4 or $MgSO_4 \cdot 2H_2O$ and concentrated with a Heidolph rotary evaporator at reduced pressure. Yields are of purified products and were not optimized. All reactions were routinely monitored by thin-layer chromatography (TLC) on silica gel $60F_{254}$ (Merck) plated and visualized by using UV erasing. Flash column chromatographic separations were carried out on silica gel Baker 60 (mesh 30-60) or Sephadex LH-20, Fluka (25-100 μm).^{1}**H**-NMR and ^{13}**C** NMR spectra were recorded in CD_3CN (δ = 1.93), Me_2SO-d_6 (δ = 2.50), CD_3OD-d_6 (δ = 4.87) with Me_4Si as internal standard. ^{1}**H**-NMR at 500.13 MHz and 250 MHz; ^{13}**C**-NMR at 125.7 MHz and 63 MHz (Bruker Avance DPX-250 and Bruker AMX-500). Chemical shifts are given in ppm (δ) and the spectral data are consistent with the assigned structures. IR spectra were recorded with a Bruker Vector 22 FTIR Spektralphotometer. Elemental analyses were performed on a *vario Micro cube* analyzer and the maximum deviation data for C, H, and N is 4.75% of the theoretical values. This is according to requested purity of the compounds.

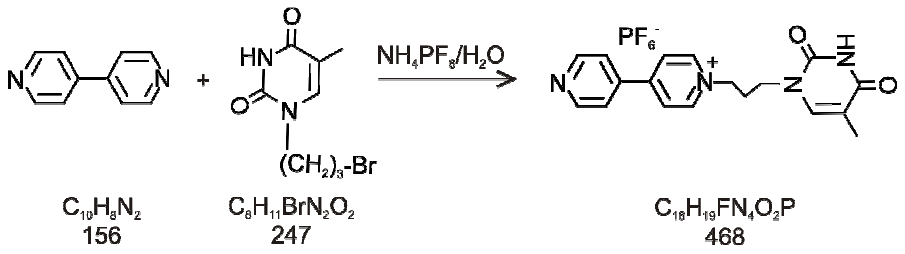
Synthesis of Dendrons:

Synthesis of 1-(3-Bromopropyl)-5-methylpyrimidine-2,4(1H,3H)-dione was performed according to the method by *Baret* et al.[1, 2]

To a solution of thymine (2.24 g, 17.6 mmol) in hexamethyldisilazane (HMDS, 11.4 ml, 54 mmol) under argon was added a catalytic amount of trimethylchlorsilane (1.08 ml, 8.54 mmol), and the mixture was stirred for 21 h under reflux. Excess HMDS was then removed under reduced pressure to afford crude O-silylated thymine. The crude material was taken up in DMF (10 ml), 1,3-dibromopropane (4.6 ml) was added, and the mixture was stirred at 80 °C for 24 h. Water (150 ml) was then added and, after stirring for 10 min, the mixture was filtered, and the aqueous filtrate was extracted with CH_2Cl_2. The combined extracts were dried over $MgSO_4$, filtered, and concentrated under reduced pressure. After crystallization of the residue from abs. EtOH and dried *in* vacuum (r.t., 24h), gave white crystals of *1-(3-bromopropyl)-5-methylpyrimidine-2,4(1H,3H)-dione*; 1.5 g (6.07 mmol, 34.4%). M.p. 140 °C. ^{1}**H**-NMR (500 MHz, DMSO – d_6, δ): 11.17 (*s*, 1H), 7.48 (*s*, 1H), 3.73 (*t*, ^3J(H,H) = 7.0, 2H), 3.51 (*t*, ^3J (H,H) = 6.5, 2H), 2.13 (*qu*, ^3J (H,H) = 6.7 , 2H), 1.74 (*s*, 3H); ^{13}**C**-NMR (125 MHz, DMSO - d_6, δ): 164, 151.1, 140.3, 110.4, 47.2 , 31.2, 29.7, 12.6. Anal. calc. for $C_8H_{11}BrN_2O_2$ (247.09): C 38.89, H 4.49, N 11.34; found: C 39.32, H 4.73, N 11.47.

Synthesis of 9-(2-bromoethyl)-9H-purin-6-amine. To a solution of 9 H-purin-6-amine (2.21g, 16.35 mmol) dissolved in 110 ml of DMF, 15 g (6.8 ml) of 1,2-Dibromoethane and 6g of K_2CO_3 was added. The reaction mixture was stirred at room temperature for 48 h under nitrogen. After 48 h the reaction mixture was filtered and the mother liquor was evaporated to dryness. The crude orange material was washed with water and filtered. The filter cake was dried and then recrystallized from EtOH. After dried *in* vacuum (r.t., 24h) 2 g (8.26 mmol, 50% yield) of 9-(2-bromoethyl)-9*H*-purin-6-amine was obtained. ^{1}H-NMR (500 MHz, CD_3CN, δ): 8.15 (s, 1H), 8.14 (s, 1H) 7.19 (s, 2H), 4.56 (t, 2H, ^{3}J[H-H] = 6.2 Hz), 3.93 (t, 2H, ^{3}J[H-H] = 6.0 Hz). ^{13}C-NMR (125 MHz, CD_3CN, δ): 155.8, 152.3, 149.4, 140.9, 118.6, 44.6, 31.4. Anal. calc. for $C_7H_8BrN_5$ (242): C 34.73, H 3.33, N 28.93; found: C 34.99, H 3.40, N 28.87.

Synthesis of 1-[3-(5-methyl-2,4-dioxo-3,4-dihydropyrimidin-1(2H)-yl)propyl]-4-(pyridin-4-yl)pyridinium hexafluorophosphate



1.5 g (6.07 mmol) of 1-(3-bromopropyl)-5-methylpyrimidine-2,4(1*H*,3*H*)-dione and 1 g (6.41 mmol) of 4,4'-Bipyridine were dissolved in 20 ml of nitrobenzene and stirred at 110 °C for 1 hour. At the beginning the solution was clear yellow and after few minutes a yellowish precipitate was obtained. The yellow suspension was filtered, washed four times with MeCN (80 ml) and dried in HV for 12 h to obtain 1.475 g (3.64 mmol, 60%

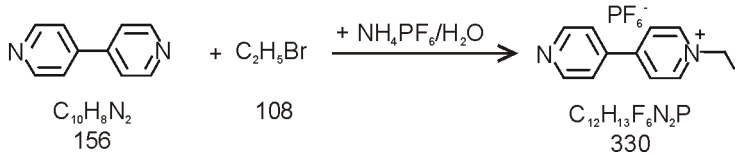
yield as bromide salt). The bromide salt (1.400 mg, 3.46 mmol) was dissolved in 25 ml of warm water and precipitated with 10% aq.NH_4PF_6 solution. The white precipitate was filtered, washed with water and dried in vacuum for 12 h to obtain 1.117 mg (2.38 mmol, 68% yields). **^{1}H**-NMR (500 MHz, CD_3CN, δ): 9.17 (s, 1H), 8.87-8.83 (m, 4H), 8.33 (d, 2H, ^{3}J[H-H] = 6.5 Hz), 7.80 (d, 2H, ^{3}J[H-H] = 6.0 Hz), 7.23 (s, 1H), 4.61 (t, 2H, ^{3}J[H-H] = 7.2 Hz), 3.80 (t, 2H, ^{3}J[H-H] = 6.2 Hz), 2.39 (t, 2H, ^{3}J[H-H] = 6.5 Hz), 1.85 (s, 3H). **^{13}C**-NMR (125 MHz, CD_3CN, δ): 165.19, 155.47, 152.29, 146.22, 142.28, 141.72, 127.12, 122.89, 111.49, 59.79, 45.36, 31.39, 12.41. Anal. calc. for $C_{17}H_{16}F_6N_7P$ (468.3): C 46.16, H 4.09, N 11.96; found: C 45.88, H 4.68, N 12.34.

Synthesis of 1-[2-(6-amino-9H-purin-9-yl)ethyl]-4-(pyridin-4-yl)pyridinium hexa-fluorophosphate

400 mg (1.65 mmol) of 9-(2-bromoethyl)-9*H*-purin-6-amine was dissolved in 30 ml of nitrobenzene and 330 mg (6.4 mmol) of 4,4'-bipyridine was added. The mixture was stirred at 100 °C for 24h. After reaction the cold mixture was filtered, washed 4 times with nitrobenzene and MeCN. After dried in vacuum (r.t., 12h), 362 mg (0.9 mmol, 55% yield) product was obtain as bromide salt. The bromide salt (362 mg, 0.9 mmol) was dissolved in 10 ml of warm water and precipitated with 10% aq. NH_4PF_6 solution. The white precipitate was filtered, washed with water and dried *in* vacuum (r.t., 12h) to obtain 327 mg (0.70 mmol, 78 % yields). **^{1}H**-NMR (500 MHz, CD_3CN, δ): 8.83 (d, 2H, ^{3}J[H-H] = 6.0 Hz, 8.53 (d, 2H, ^{3}J[H-H] = 7.0 Hz), 8.16 (d, 2H, ^{3}J[H-H] = 6.5 Hz), 7.90 (s, 1H), 7.85 (s, 1H), 7.71 (d, 2H, ^{3}J[H-H] = 6.0 Hz), 5.99 (s, 1H), 5.00 (t, 2H, ^{3}J[H-H] = 5.2 Hz), 4.77 (t, 2H, ^{3}J[H-H] = 5.2 Hz); **^{13}C**-NMR (125 MHz, CD_3CN, δ): 157.1, 156.3,

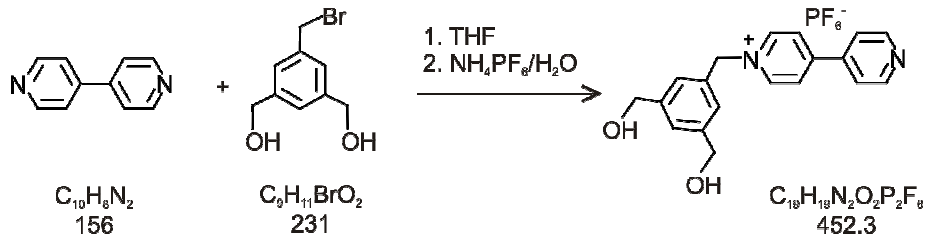
154.0, 152.5, 151.6, 146.8, 142.2, 127.5, 123.1, 62.1, 45.2. Anal. calc. for $C_{17}H_{16}F_6N_7P$ (463.3): C 44.07, H 4.48, N 21.16; found: C 43.62, H 3.39, N 21.47.

Synthesis of 1-ethyl-4-pyridin-4-ylpyridinium hexafluorophosphate



The synthesis was performed according to a literature procedure.[3] A suspension of 6 g (73.4 mmol) of 4, 4'-bipyridyl with 50 g (459 mmol) of ethyl bromide was stirred at 34°C for 50 h under reflux. After 30 min a brown precipitate was obtained. After 7 hours a further portion of 5 g ethyl bromide in diethyl ether (30 ml) was added dropwise. The resulting precipitate was filtered and thoroughly washed with dry diethyl ether and toluene. The crystallization of the product proceeded slowly (48 h at 4 °C) from ethanol-ether-toluene. The resulting yellowish powder was dried for 24 h in HV (22 mmol, 30% yield). 1-Ethyl-4-pyridin-4-yl-pyridinium salt (4 g, 15 mmol) was dissolved in 80 ml of water, and 10 ml of a 10 % aq. NH_4PF_6 solution was added dropwise. The resulting solid was filtered off, washed with cold water and dried for 24 h in HV (3.9 g 12.1 mmol, 80% yield). ^{1}**H**-NMR: (500 MHz, DMSO-d_6, δ): 9.25 (d,^{3}J[H,H] = 12.5 Hz, 2H), 8.92 (d, ^{3}J[H,H] = 4.8 Hz, 2H), 8.64 (d, ^{3}J[H,H] = 6.5 Hz, 2H), 8.12 (d, ^{3}J[H,H] = 4.1 Hz, 2H), 4.68 (q, ^{3}J[H,H] = 7.3 Hz, 1H), 1.60 (t, ^{2}J[H,H] = 7.3 Hz, 3H). ^{13}C-NMR (125 MHz, DMSO-d_6, δ): 150.6, 147.2, 138.8, 134.9, 132., 115.2, 55.6, 13.8. Anal. calc. for $C_{12}H_{13}F_6N_2P$ (330): C 43.65, H 3.97, N 8.48; found: C 41.27, H 4.34, N 8.02.

Synthesis of N-(3,5-di(hydroxymethyl)-benzyl)-4,4'-bipyridinium-hexafluoro-phosphate



The synthesis was performed according to a literature procedure.[4] 1g (6.40 mmol) 4, 4'-bipyridine and 1 g (4.32 mmol) 3, 5-di (hydroxymethyl)-benzylbromide were dissolved in 40 mL of anhydrous THF. The reaction mixture was then refluxed for 24 hours under nitrogen. During that time the product precipitated as a pale yellow solid which was filtered, washed with CH_2Cl_2 and dried under vacuum to yield 1.5 g (3.8 mmol, 60%) of N-(3,5-di(hydroxymethyl)-benzyl)-4,4'-bipyridinium as bromide salt. The bromide salt (1.5 g, 3.8 mmol) was dissolved in 25 mL of water, and 6 mL of a 10 % aq. NH_4PF_6 solution was added dropwise. The resulting solid was filtered off, washed with cold water, and dried for 24 h in HV (yield: 1.6 g, 3.53 mmol, 92%). ^{1}**H**-NMR (250 MHz, CD_3CN, δ): 8.86-8.82 (m, 4H), 8.31 (d, J[H,H] = 6.7 Hz, 2H), 7.77 (d, J[H,H] = 6.2 Hz, 2H), 7.39 (s, 1H), 7.35 (s, 2H), 5.47 (s, 2H), 4.59 (d, J[H,H] = 4.4 Hz, 4H), 3.36 (b, 2H). ^{13}**C**-NMR (125 MHz, CD_3CN, δ): 155.1, 152.3, 144.6, 134.2, 126.7, 126.5, 122.1, 64.3, 63.8.

Synthesis of VGD precursors: VGD1, VGD2, and VGD3

Synthesis of 1,1'-bis[2-(6-amino-9H-purin-9-yl)ethyl]-4-(pyridin-4-yl) pyridinium dihexafluorophosphate (VGD1). 200 mg (0.43 mmol) of 1-[2-(6-amino-9*H*-purin-9-yl)

ethyl]-4-(pyridin-4-yl) pyridinium hexafluorophosphate and 1g (4.01 mmol) of 9-(2-bromoethyl)-9*H*-purin-6-amine was dissolved in 15 ml of DMF. The mixture was stirred at 90 °C for 10 days. The mixture was filtered, the solid washed with DMF and MeCN several times to remove the excesses of 9-(2-bromoethyl)-9*H*-purin-6-amine. After drying *in* vacuum (r.t., 24h), 25 mg (0.04 mmol, 9.3%) 1,1'-bis[2-(6-amino-9*H*-purin-9-yl)ethyl]-4,4'-bipyridinium dibromide was obtained as yellow powder. The product as a bromide salt was dissolved in water and precipitated with 10% aq.NH_4PF_6 solution. The precipitate was filtered, washed with water and dried in HV for 12 h to obtain 30 mg of 1,1'-bis[2-(6-amino-9*H*-purin-9-yl)ethyl]-4,4'-bipyridinium dihexafluorophosphate (0.038 mmol, 95% yields). **^{1}H** NMR (250 MHz, DMSO-d_6, δ): 9.19 (d, J=6.91 Hz, 4H), 8.63 (d, J=6.91 Hz, 4H), 8.11 (s, 2H), 7.78 (s, 2H), 7.26 (br. s., 4H), 5.14 (t, J=5.30 Hz, 4H), 4.85 (t, J=4.10 Hz, 4H); **^{13}C**-NMR (125 MHz, D_2O, δ): 155.82, 152.75, 150.69, 149.19, 146.21, 142.02, 127.34, 118.19, 61.52, 44.09. Anal. calc. for VGD1 as PF_6^- salt $C_{24}H_{24}F_{12}N_{12}P_2$ + 0.8 H_2O (770,46 + 14.4): C 37.41, H 3.14, N 21.82; found: C 36.73, H 3.29, N 21.41.

Synthesis of 1-[2-(6-amino-9H-purin-9-yl)ethyl]-1'-[3-(5-methyl-2,4-dioxo-3,4-dihydropyrimidin -1(2H)-yl)propyl]-4-(pyridin-4-yl) pyridinium dihexafluoro-phosphate (VGD2). 200 mg (0.44 mmol) of 1-[2-(6-amino-9*H*-purin-9-yl) ethyl]-4-(pyridin-4-yl)pyridinium hexafluorophosphate and 180 mg (0.72 mmol) of 1-(3-bromopropyl)-5-methylpyrimidine-2,4(1*H*,3*H*)-dione were dissolved in 30 ml of warm MeCN and stirred under reflux for 4 days. The resulting precipitate was filtered, washed four times with MeCN (40 ml) and one time with ether (10 ml). After drying in vacuum (r.t., 12h) 1-[2-(6-amino-9H-purin-9-yl)ethyl]-1'-[3-(5-methyl-2,4-dioxo-3,4dihydropyrimidin - 1(2*H*)-

yl)propyl]-4-(pyridin-4-yl) pyridinium dibromide 104 mg (0.16 mmol, 36% yield) was obtained. The bromide salt (100 mg, 0.15 mmol) was dissolved in 10 ml of warm water and precipitated with 10% aq.NH_4PF_6 solution. The precipitate was filtered, washed with water and dried in vacuum (r.t., 12h) (93 mg, 0.12 mmol, 80% yield). **^{1}H** NMR (250 MHz, CD_3CN, δ): 9.78 (br. s, 1H), 8.94 (d, J=6.91 Hz, 2H), 8.67 (d, J=6.91 Hz, 2H), 8.34 (d, J=6.91 Hz, 2H), 8.23 (d, J=6.59 Hz, 2H), 7.94 (s, 1H), 7.79 (s, 1H), 7.23 (s, 1H), 6.22 (br. s., 2H), 5.07 (t, J=5.70 Hz, 2H), 4.80 (t, J=5.00 Hz, 2H), 4.67 (t, J=7.06 Hz, 2H), 3.79 (t, J=6.12 Hz, 2H), 2.40 (quin, J=1.00 Hz, 2H), 1.85 (s, 3H); **^{13}C**-NMR (125 MHz, CD_3CN, δ): 165.78, 157.43, 154.05, 152.90, 151.96(s), 151.70, 151.20, 147.69, 147.37, 142.32(d), 142.08, 128.65, 128.54, 120.26, 111.93, 63.02, 60.93, 45.43, 45.40, 31.86, 12.73. Anal. calc. for VGD2 as PF_6^- salt $C_{25}H_{27}F_{12}N_9O_2P_2$ + 0.1 H_2O (775.48 + 1.8): C 38.72, H 3.51, N 16.26; found: C 38.63, H 3.53, N 16.22.

*Synthesis of 1,1'-bis[3-(5-methyl-2,4-dioxo-3,4-dihydropyrimidin -1(2H)-yl)propyl]-4-(pyridin-4-yl) pyridinium dihexafluorophosphate (*VGD3*).* 1.756 g (7.1 mmol, 2.3 eqv.) of 1-(3-Bromopropyl)-5-methylpyrimidine-2,4(1H,3H)-dione and 0.240 g (1.54 mmol) of 4,4'-bipyridine were dissolved in 60 ml dry DMF and stirred at 80°C for 4 days. Resulted light-yellow precipitate was filtered, washed with 20 ml DMF, 20 ml Et_2O and dry in ultra high vacuum at 45°C to afford 760 mg of **VGD-3** as bromide salt (1.16 mmol, 76%). **^{1}H NMR** (500 MHz, D_2O, δ): 9.26 (d, J=6.62 Hz, 4H), 8.66 (d, J=6.30 Hz, 4H), 7.60 (s, 2H), 4.93 (t, J=7.25 Hz, 4H), 4.05 (t, J=6.62 Hz, 4H), 2.65 (quin, J=6.70 Hz, 4H), 1.96 (s, 6H); **^{13}C NMR** (125 MHz, D_2O, δ): 166.87, 152.31, 150.31, 145.76, 142.49, 127.16, 111.47, 59.43, 45.25, 29.53, 11.33. Anal. calc. for **VGD3** as PF_6^- salt $C_{26}H_{30}F_{12}N_6O_4P_2$ (780.48): C 40.0, H: 3.87, N 10.77; found C 39.69, H 3.60, N 10.71.

Synthesis of comb-branched VGD: VGD4, VGD5, and VGD6

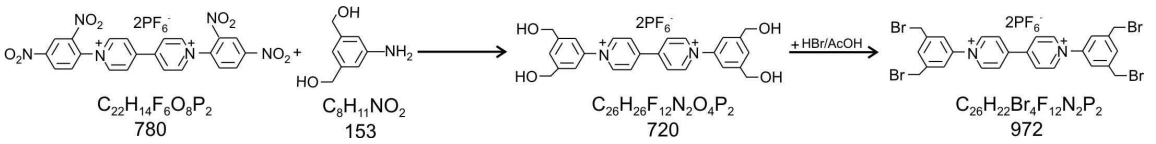
Synthese of 1,1'-Bis[3,5-bis(bromomethyl)phenyl]-4,4'bipyridinium dihexafluoro-phosphate (4-fold nucleophilic core)

1,1'-Bis(2,4-dinitrophenyl)-4,4'-bipyridinium dichloride: the synthesis follows a known procedure.[5] 4 g (25.6 mmol) of 4,4'-bipyridine and 26 g (89,6 mmol) of 2,4-dinitro-chlorobenzene in MeCN (150 ml) was stirred at 90^{o}C for 24 h under reflux. At the beginning, the solution was clear brown, after 4 h first yellow crystals were obtained. The yellow suspension was filtered. The filtrate was washed once with MeCN (50 ml) and four times with diethyl ether (40 ml). After drying *in* vacuum for 16 h, 10.6 g as chloride (yield 18,9 mmol, 74%) of 1,1'-Bis(2,4-dinitrophenyl)-4,4'-bipyridinium dichloride was obtained. ^{1}H-NMR (250 MHz, CD_3OH, δ): 9.67 (d, J[H,H] = 7.0 Hz, 4H), 8.99 (d, J[H,H] = 7,0 Hz, 4H), 8.44 (d, J[H,H] = 7.5 Hz, 4H), 8.07 (d, J[H,H] = 7.5 Hz, 4H).

3,5-Bis-(hydroxymethyl)aniline was synthesized in two steps from 5- aminoisophthalic acid according to previously reported procedures.[6-7] $LiAlH_4$ 2 g (52.7 mmol) was suspended in 300 mL of diethylether. 5-amino-isophtalsäuredimethylester 5 g (23.9 mmol) was extracted with refluxing ether for 1 week at 50 ^{o}C. During that time there was a hydrogen evolution, and the color of the reaction mixture turned to orange. After cooling to ^{o}0, the reaction mixture was quenched by addition of 200 mL of water and neutralized with 10 % of H_2SO_4. The ether phase was evaporated, and the aqueous phase was extracted in a *Ludwig*-extractor with ethyl acetate for 3 days. After this period ethyl acetate was removed *in* vacuum, and the residue was crystallized from MeOH/Et_2O to

yield 1.20 g (7.65 mmol, 32%) of yellow crystals. ^{1}H-NMR (250 MHz, DMSO-d_6, δ): 6.50 (s, 1H), 6,45 8s, 2H), 4.93 (t, J[H,H] = 5.8Hz, 4H), 4.32 (d, J[H,H] = 5.3 Hz, 4H).

1,1'-bis[3,5-bis(hydroxymethyl)phenyl]4,4'-bipyridinium dihexafluorophosphate[8]



A mixture of 1 g (1.28 mmol) of 1,1'-Bis(2,4-dinitrophenyl)-4,4'-bipyridinium dichloride and 460 mg (3.1 mmol) of *2,4-Bis-(hydroxymethyl)aniline* in 50 ml MeOH was stirred at 70^{o}C for 23 h under reflux. The cold mixture was poured into 100 ml of brined diethyl ether. The brown precipitate was filtered off and washed three times with ether and dried in HV. The resulted brown powder was dissolved in 80 ml H_2O and 10 ml of a 10% NH_4PF_6 solution was added dropwise. After drying *in* vacuum for 6 h, 813 mg (1.14 mmol, 89 % yield) of 1,1'-bis[3,5-bis(hydroxymethyl)phenyl]4,4'-bipyridinium dihexafluorophosphate was obtained. ^{1}H-NMR: (250 MHz, DMSO-d_6, δ): 9.68 (d, ^{3}J[H,H] = 6.1 Hz, 4H), 9.03 (d, ^{3}J[H,H] = 6.2 Hz, 4H), 7.74 (s, 4H), 7.68 (s, 2H), 5.58 (b, 4H), 4.70 (s, 8H).

1,1'-bis[3,5-bis(bromomethyl)phenyl]-4,4'bipyridinium hexafluorophosphate

The synthesis was performed according to a literature procedure.[4] 1,1'-Bis[3,5-bis[hydroxymethyl)phenyl]-4,4'-bipyridinium salt (630 mg, 0.875 mmol) was dissolved in 150 ml of HBr/acetic acid under argon and stirred for 4 d. at r.t. The reaction mixture

was evaporated, and the residue was dissolved in 2 ml of water and 3 ml of a 10% aq. NH_4PF_6 solution was added. The brown precipitate was filtered, washed with water and dried in HV. The resulting brown powder was dissolved in $MeNO_2$ and 5 ml of 10% aq. NH_4PF_6 was added dropwise. The organic phase was filtered, and the light brown precipitate was washed with $CHCl_3$, ether and water. A light brown powder was isolated and dried for 24 h in HV (0.501 mmol, 57% yields). **^{1}H**-NMR: (250 MHz, CD_3CN, δ): 9.21 (d, ^{3}J[H,H] = 7.1 Hz, 4H), 8.64 (d, ^{3}J[H,H] = 7.1Hz, 4H), 7.93 (s, 2H), 7.80 (s, 4H), 4.71 (s, 8H), 4.69 (s, 8H). **^{13}C**-NMR (63 MHz, CD_3CN, δ): 150,7, 146.3, 143.01, 142.5, 133.6, 128.0, 125.6, 31.5. Anal. calc. for $C_{26}H_{22}Br_4F_6N_2P_2$ (972): C 32.13, H 2.28, N 2.88; found: C 31.54, H 2.44, N 2.83.

Synthesis of ***VGD5***[9]

80 mg (0.082 mmol) tetrabromide precursor and 230 mg (0.49 mmol) of 1-[3-(5-methyl-2,4-dioxo-3,4-dihydropyrimidin-1(2H)-yl)propyl]-4-(pyridin-4-yl)pyridinium hexafluoro-phosphate were dissolved in 20 mL of MeCN. The mixture was refluxed at 70 °C for 5 days. The cooled reaction mixture was filtered, washed with MeCN (10 mL) and ether, respectively, and dried. The mother liquor was evaporated, and the residue was dried. The residue was dissolved in 7 mL of nitromethane and extracted with 3 mL of a NH_4PF_6 solution (10 % in water). The organic phase was washed one more time with water and evaporated to dryness. The residue was put in water, filtered, washed several times with water and dried in a vacuum for 12 h. The product was purified by chromatography (Sephadex LH-20, column 2.5 × 25 cm, MeCN : MeOH,1:1 as eluent) the product 160 mg dendrimer **VGD-5** (0.051 mmol, 62% yields), after dried in a *vacuum* at 40^{o}C for 24

h. **^{1}H**-NMR (500 MHz, CD_3CN, δ): 9.10 (d, 4H, ^{3}J[H-H] = 6.5 Hz), 8.98 (d, 8H, ^{3}J[H-H] = 5.5 Hz), 8.94 (d, 8H, ^{3}J[H-H] = 6.0 Hz), 8.63 (d, 4H, ^{3}J[H-H] = 4.0 Hz), 8.41 (d, 8H, ^{3}J[H-H] = 5.5 Hz, 8.37 (d, 8H, ^{3}J[H-H] = 5.5 Hz, 7.97 (s, 2H), 7.90 (s, 4H), 7.20 (s, 4H), 5.98 (s, 8H). 4.65 (t, 6H, ^{3}J[H-H] = 7.2 Hz), 3.77 (t, 8H, ^{3}J[H-H] = 6.2 Hz), 2.36 (t, 8H, ^{3}J[H-H] = 6.7 Hz), 1.82 (s, 12H). **^{13}C**-NMR (125 MHz, CD_3CN, δ): 165.2, 152.6, 152.0, 151.0, 147.1, 147.0, 146.8, 144.5, 141.7, 137.3, 135.0, 128.7, 128.3, 128.1, 111.6, 64.2, 60.4, 45.3, 31.4, 12.4. IR (cm^{-1}): 3650.5, 3073.0, 2977.6, 1674.8, 1637.4, 1452.4, 1366.1, 1223.2, 820.1, 552.9. UV-Vis (MeCN, partial reduced): V^{++} λ_{max}: 264 (64465), 422 (4352); $V^{\cdot+}$ at -0.5 V λ_{max}: 402 (70253), 608 (27740). Anal. calc. for $C_{98}H_{98}F_{60}N_{18}O_8P_{10}$ (3105.5): C 37.90, H 3.18, N 8.12; found: C 37.10, H 4.71, N 7.87.

*Synthesis of dendrimer **VGD6**[9]*

100 mg (0.028 mmol) octabromide precursor and 150 mg (0.31 mmol) of 1-[3-(5-methyl-2,4-dioxo-3,4-dihydropyrimidin-1(2H)-yl)propyl]-4-(pyridin-4-yl)pyridinium hexafluoro-phosphate were dissolved in 20 ml of MeCN. The mixture, protected from light was refluxed at 75 °C for 1 week. The cooled reaction mixture was filtered and washed with ether, respectively, and dried. The mother liquor was evaporated, and the residue was dried. The residue was dissolved in 7 mL of nitromethane and extracted with 3 mL of a NH_4PF_6 solution (10 % in water). The organic phase was washed one more time with water and evaporated to dryness. The residue was put in water, filtered, washed several times with water and dried in a vacuum for 12 h. The product was purified by chromatography (Sephadex LH-20, column 2.5 × 25 cm, MeCN : MeOH,1:1 as eluent) the product 140 mg **VGD-6** (0.017 mmol, 60% yields) after dried in vacuum at 40^{o}C for

24 h. ^{1}**H**-NMR (500 MHz, CD_3CN, δ): 9.16 (*s*, 4H), 8.97-8.92 (*m*, 48H), 8.68 (*s*, 4H), 8.44-8.37 (*m*, 48H), 8.01 (*s*, 4H), 7.68 (*s*, 12H), 7.66 (*s*, 2H), 7.23 (*s*, 8H), 5.98 (*s*, 8H), 5.84 (*s*, 24H), 4.67 (*t*, 16H, ^{3}J[H-H] = 7.2 Hz), 3.79 (*t*, 16H, ^{3}J[H-H] = 6.0 Hz), 2.38 (*qu*, 16H, ^{3}J[H-H] = 6.6 Hz), 1.83 (*s*, 24H). ^{13}**C**-NMR (125 MHz, CD_3CN, δ): 165.3, 152.7, 151.7, 151.1, 147.1, 146.9, 146.8, 141.8, 137.4, 137.2, 128.6, 128.5, 128.3, 111.6, 64.8, 64.2, 45.3, 31.4, 12.4. IR (cm^{-1}): 3650.0, 3071.9, 2977.7, 1674.0, 1636.9, 1451.6, 1367.3, 1223.1, 1172.2, 811.8, 551.3. UV-Vis (MeCN, partial reduced): V^{++} λ_{max}: 269 (250850), 424 (16487); $V^{\cdot+}$ at -0.5 V λ_{max}: 402 (206665), 608 (78825). Anal. calc. for $C_{246}H_{242}F_{156}N_{42}O_{16}P_{26}$ (7811.8): C 37.82, H 3.12, N 7.53; found: C 36.66, H 4.71, N 7.30.

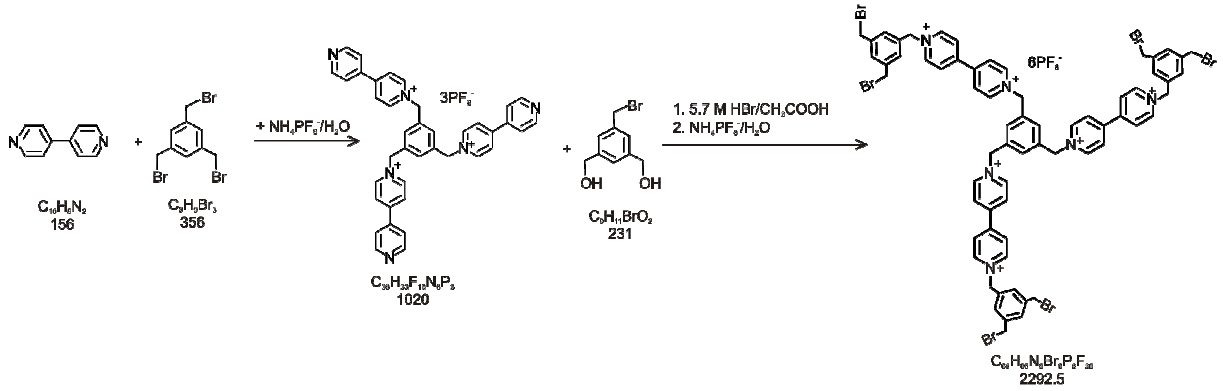
Synthesis of spheroidal VGD: VGD7-13 [9]

1,1'-1''-[benzene-1,3,5-triyl-tris(methylene)]-tris-[1'-1-(3-propyl)-5-methyl-pyrimidine-2,4(1H,3H)-dione]-4,4'-bipyridinium hexafluorophosphate – VGD8 [2]

A solution of 214 mg (0.20 mmol) of 1,1',1''-[benzene-1,3,5-triyl-tris(methylene)tris](4-pyridin-4-ylpyridinium trihexafluorophosphate in 10 ml of MeCN were added to a stirred solution of 1,570 g (6.33 mmol) of 1-(3-bromopropyl)-5-methyl -*1H*- pyrimidine -2,4-dione in 45 ml of MeCN. The whole mixture was refluxed for four days at 85 °C. The cooled reaction mixture was added dropwise to 30 ml of a stirred tetrabutylammonium chloride solution (5 % in MeCN). The yellowish precipitate was filtered off and washed three times with 10 ml of MeCN and three times with 10 ml of CH_2Cl_2. After drying for 24 hours in vacuum the powder was dissolved in 20 ml of water and precipitated with NH_4PF_6 solution(10 % in water).The residue was washed several times with water and

dried in vacuum for 24 hours to obtain 285 mg (0.14 mmol, 70 %)of **VGD-8**- thymine. **^{1}H**-NMR (500 MHz, CD_3CN, δ): 9.34 (s, 3H), 8.98 (d, ^{3}J [H,H] = 6.5 Hz,6H), 8.93 (d, ^{3}J [H,H] = 7.0 Hz, 6H), 8,43-8,34 (m, 12H), 7,68 (s, 3H), 7.24 (s, 3H), 5.86(s, 6H), 4.68 (t, ^{3}J [H,H] = 7.2 Hz, 6H), 3.80 (t, ^{3}J[H,H] = 6.2 Hz, 6H),2.39 (qu, ^{3}J [H,H] = 6.7 Hz, 6H), 1.85 (s, 9H). **^{13}C**-NMR (125 MHz, CD_3CN, δ): 165.4, 152.7, 151.7, 151.1, 146.8, 141.7, 136.1, 132.8, 128.5, 111,6, 64.8, 60.4, 45.3 , 31.4, 12.4. Anal. calc. for $C_{63}H_{66}F_{36}N_{12}O_6P_6$ (1957): C 38.66, H 3.39, N 8.58; found: C 38.37, H 3.65, N 7.60.

Synthesis of 1,1,'1,''-[(benzene-1,3,5-triyltris(methylene) tris(3,5-di(bromomethyl) benzene- (4,4'-bipyridinium)] hexafluorophosphate



1,1',1''- [benzene-1,3,5-triyltris(methylene)tris](4-pyridin-4-ylpyridinium trihexafluoro-phosphate

The synthesis was performed according to a literature procedure.[4] 4,4'-Bipyridine (14 g, 89 mmol) was dissolved in warm MeCN (80 ml), and 2.1 g (5.8 mmol) of 1,3,5 tris (bromomethyl) benzene was added in 50 ml MeCN within 7 h (1 ml/8,5 minute). The mixture was stirred at 70°C for 30 h under reflux. The cold mixture was filtered and

washed three times with CH_2Cl_2. The filter cake was dissolved in water and extracted four times with CH_2Cl_2. Methanol was added dropwise to initiate the precipitation. A yellow powder was obtained and dried in HV (4.4 mmol, 74% yields as bromide salt). The bromide -salt (3.2 g, 3.88 mmol) was dissolved in 80 ml of water, and 15 ml of a NH_4PF_6 10% was added dropwise. The precipitate was filtered and washed with cold water; a white powder was obtained and dried for 24 h in HV (2.7 mmol, 78% yields). **^{1}H**-NMR: (250 MHz, CD_3CN, δ): 8.87 (d, ^{3}J[H,H] = 6.3 Hz, 6H), 8.82 (d, ^{3}J[H,H] = 7,0 Hz, 6H), 8.38 (d, ^{3}J[H,H] = 7.0 Hz, 6H), 7.83 (d, ^{3}J[H,H] = 6,3 Hz, 6H), 7.59 (s, 3H), 5.81 (s, 6H).

3,5-Di(hydroxymethyl)benzylbromide:

The synthesis follows a known procedure.[4] A solution of 4.4g (26.2 mmol) 1,3,5-tris(hydroxymethyl)benzene and 6.86 g (26.2 mmol) triphenylphosphine in anhydrous THF 220 ml was stirred at room temperature. Drop wise solution of 8.6 g (25.9 mmol) tetrabrommethan in anhydrous THF was added. The reaction occurred for 2.5 hours. The white precipitate of triphenylphosphinoxide was filtered and the mother liquor evaporated. The mixture of 3,5-di(hydroxymethyl) benzylbromide, 3,5-di(bromomeyl)hydroxymethyl benzene and 1,3,5-tris-bromomethyl) benzene was separated by column chromatography (silica gel and ethyl acetate as eluent). The first fraction was 1,3,5-tris(bromomethyl)benzene, the second fraction was 3,5-di(bromomethyl)hydroxymethylbenzene 279 mg (0.95 mmol, 8%) and the third fraction was 3,5-di(hydroxymethyl)benzylbromide 1150 mg (5.4 mmol, 45%). The second fraction was recrystallized from chloroform/petrolether and the third fraction was

recrystallized from dioxane/petrolether. **^{1}H**-NMR: (250 MHz, CD_3CN, δ): 7.29 (s, 2H), 7.25 (s, 1H), 4.60 (s, 2H) 4.57 (d, ^{3}J[H,H] = 5.9 Hz, 4H), 3.30 (t, ^{3}J[H,H] = 5.9 Hz, 2H).

1 g (0.98 mmol) *1,3,5-tris(4,4'-bipyridinium)methyl)benzene-trishexafluorophosphate* was dissolved in MeCN (50 ml) and 0.9 g (3.9 mmol) of 1,3,5-di(hydroxymethyl)benzyl bromide in 5 ml MeCN was added. The mixture was stirred at 95°C for 44 h under reflux. The resulting precipitate was filtered and thoroughly washed with dry diethyl ether and dried in vacuum. The product was isolated as light yellow powder as bromide salt 1.46 g (0.96 mmol, 98% yield). The bromide -salt (1.46 g, 0.96 mmol) was dissolved in 80 ml of water, and 15 ml of a NH_4PF_6 10% was added dropwise. The precipitate was filtered and washed with cold water; a white powder was obtained and dried for 24 h in vacuum, 1.6 g (0,84 mmol, 87% yields) of *1,1,'1,''-[(benzene-1,3,5-triyltris(methylene) tris(3,5-di(hydroxymethyl)benzene- (4,4'-bipyridinium)] hexafluorophosphate* was obtained. **^{1}H**-NMR: (250 MHz, CD_3CN, δ): 8.95 (d,^{3}J[H,H] = 6.5 Hz, 6H), 8.92 (d,^{3}J[H,H] = 6.5 Hz, 6H), 8.40-8.36 (m, 12H), 7.67 (s,3H), 7.44 (s, 3H), 7.40 (s, 6H), 5.82 (s, 12H), 4,63 (d, ^{3}J[H,H] = 5.0 Hz, 12H), 3.42(t, ^{3}J[H,H] = 5.3 Hz, 6H).

1,1,'1,''-[(benzene-1,3,5-triyltris(methylene) tris(3,5-di(brommethyl)benzene- (4,4'-bipyridinium)] hexafluorophosphate

The synthesis was performed according to a literature procedure.[3] *1,1,'1,''-[(benzene-1,3,5-triyltris(methylene) tris(3,5-di(hydroxymethyl)benzene- (4,4'-bipyridinium)] hexafluorophosphate* (1 g, 0.6 mmol) was dissolved in 200 ml of HBr/acetic acid under argon and stirred for 4 d. at r.t. The reaction mixture was evaporated, and the residue was dissolved in 2 ml of water and 3 ml of a 10% aq. NH_4PF_6 solution was added. The brown precipitate was filtered, washed with water and dried in HV. A white powder was isolated

and dried for 24 h in HV (1.20 g, 0.52 mmol, 86 % yields). **^{1}H**-NMR: (250 MHz, CD_3CN, δ): 8.95 (d, ^{3}J[H,H] = 6.5 Hz, 6H), 8.64 (d, ^{3}J[H,H] = 6.5Hz, 6H), 8.39 (d, ^{3}J[H,H] = 6.5 Hz, 12H), 7.69 (s, 3H), 7.60 (s, 3H), 7.47 (s, 6H), 5.82 (s, 6H), 5.80 (s, 6H), 4.58 (s,12H). **^{13}C**-NMR (63 MHz, CD_3CN, δ): 150.7, 146.3, 135.3, 134.0, 132.1, 131.5, 130.1, 128.2, 64.2, 32.5.

Synthesis of ***VGD10***[9]

106 mg (0.046 mmol) hexabromide precursor and 230 mg (0.49 mmol) of 1-[3-(5-methyl-2,4-dioxo-3,4-dihydropyrimidin-1(2H)-yl)propyl]-4-(pyridin-4-yl)pyridinium hexafluoro-phosphate were suspended in 20 mL of MeCN. The mixture, protected from light was refluxed at 75 °C for 6 days. The cooled reaction mixture was filtered and washed with ether, respectively, and dried. The mother liquor was evaporated, and the residue was dried. The combined solids were dissolved in 10 mL of nitromethane and extracted with 4 mL of a NH_4PF_6 solution (10 % in water). The organic phase was washed one more time with water and evaporated to dryness. The residue was put in water, filtered, washed several times with water and dried in a vacuum for 12 h. For purification the product was further dissolved in $MeNO_2$ and extracted with water for one week in a Ludwig apparatus. The $MeNO_2$ phase was evaporated and dried in HV for 12 h. The residue was washed with water, filtered and dried in a vacuum to obtain 156 mg **7** (0.028 mmol, 61% yields). **^{1}H**-NMR (500 MHz, DMSO-d_6, δ): δ = 9.29 (s, 6H), 8.98-8.92 (m, 36H), 8.32-8.38 (m, 36H), 7.69 (s, 9H), 7.65 (s, 3H), 7.24 (s, 6H), 5.85 (s, 24H), 4.69 (t, 12H, ^{3}J[H-H] = 7.5 Hz), 3.81 (t, 12H, ^{3}J[H-H] = 8.7 Hz), 2.39 (t, 12H, ^{3}J[H-H] = 6.7 Hz), 1.85 (s, 18H). **^{13}C**-NMR (125 MHz, CD_3CN, δ): 165.6, 153.1, 152.3,

151.7, 147.4, 142.2, 136.5, 136.5, 133.5, 133.4, 129.1, 129.1, 128.8, 112.1, 65.3, 61.0, 45.8, 31.8, 12.0. IR (cm^{-1}): 3651.4, 3072.2, 2977.9, 1674.8, 1637.9, 1450.9, 1362.6, 1223.4, 1167.7, 813.0, 552.3. UV-Vis (MeCN): V^{++} λ_{max}: 268 (159365), 422 (20177); $V^{\cdot+}$ at -0.5 V λ_{max}: 402 (121785), 608 (37488). Anal. calc. for $C_{174}H_{174}F_{108}N_{30}O_{12}P_{18}$ (5486.8): C 38.09, H 3.20, N 7.66; found: C 37.20, H 3.35, N 7.39.

*Synthesis of dendrimer **VGD11***

140 mg (0.022 mmol) dodecabromide precursor and 150 mg (0.32 mmol) of 11-[3-(5-methyl-2,4-dioxo-3,4-dihydropyrimidin-1(2H)-yl)propyl]-4-(pyridin-4-yl)pyridinium hexafluorophosphate were suspended in 20 mL of MeCN. The mixture, protected from light was refluxed at 75 °C for 4 days. The cooled reaction mixture was filtered and washed with ether, respectively, and dried. The mother liquor was evaporated, and the residue was dried. The combined solids were dissolved in 10 mL of nitromethane and extracted with 4 mL of a NH_4PF_6 solution (10 % in water). The organic phase was washed one more time with water and evaporated to dryness. The residue was put in water, filtered, washed several times with water and dried in a vacuum for 12 h. For purification the product was further dissolved in $MeNO_2$ and extracted with water for one week in a Ludwig apparatus. The $MeNO_2$ phase was evaporated and dried in HV for 12 h. The residue was washed with water, filtered and dried in a vacuum at 40 ^oC for 24 h to obtain 140 mg **VGD11** (0.011 mmol, 50% yields). ^{1}**H**-NMR (500 MHz, CD_3CN, δ): 11.24 (s, 12H), 9.37 (s, 84H), 9.14 (m, 84H), 7.79 (b, 30H), 7.49 (s, 12H), 5.92 (s, 60H), 4.74 (s, 24H), 3.78 (s, 24H), 2.35 (s, 24H), 1.77 (s, 36H). ^{13}**C**-NMR (125 MHz, CD_3CN, δ): 164.2, 151.1, 149.1, 148.3, 146.0, 140.8, 135.3, 130.0, 126.8, 126.3, 109.0, 62.7,

58.6, 43.9, 30.2, 11.9. IR (cm^{-1}): 3648.6, 3073.0, 2980.5, 1673.3, 1637.7, 1450.9, 1363.5, 1223.6, 1167.7, 817.0, 553.3. UV-Vis (MeCN): V^{++} λ_{max}: 267 (436080), 422 (20119); $V^{\cdot+}$ at -0.5 V λ_{max}: 402 (358640), 608 (145420). Anal. calc. for $C_{396}H_{390}F_{252}N_{66}O_{24}P_{42}$ (12546.3): C 37.91, H 3.13, N 7.37; found: C 36.59, H 3.39, N 6.81.

*Synthesis of dendrimer **VGD13***

230 mg (0.016 mmol) tetraeicosabromid precursor and 225 mg (0.48 mmol) of 1-[3-(6-hydroxy-5-methyl-2-oxo-1,2,3,6-tetrahydropyridin-3-yl)propyl]-4-(pyridin-4-yl) pyridinium were suspended in 15 mL of MeCN. The mixture was refluxed at 75 °C for one week. The cooled reaction mixture was filtered and washed with ether, respectively, and dried. The mother liquor was evaporated, and the residue was dried. The combined solids were dissolved in 10 mL of nitromethane and extracted with 4 mL of a NH_4PF_6 solution (10 % in water). The organic phase was washed one more time with water and evaporated to dryness. The residue was put in water, filtered, washed several times with water and dried in a vacuum for 12 h. For purification the product was further dissolved in $MeNO_2$ and extracted with water for one week in a Ludwig apparatus. The $MeNO_2$ phase was evaporated and dried in HV for 12 h. The residue was washed with water, filtered and dried in a vacuum at 40°C for 24 h to obtain 270 mg **VGD13** (0.010 mmol, 63% yields). **^{1}H**-NMR (500 MHz, CD_3CN, δ):8.98-8.93 (m, 180H), 8.40-8.39 (m, 180H), 7.68 (b, 66H), 7.25 (s, 24H), 5.86 (s, 132H), 4.68 (t, 48H, ^{3}J[H-H] = 7.0 Hz), 3.80 (t, 48H, ^{3}J[H-H] = 5.5 Hz), 2.39 (t, 48H, ^{3}J[H-H] = 6.0 Hz), 1.84 (s, 72H). **^{13}C**-NMR (125 MHz, CD_3CN, δ)165.1, 152.4, 151.5, 150.8, 146.6, 135.7, 132.6, 128.4, 128.3, 128.3, 111.35, 64.5, 60.1, 45.0, 31.2, 12.1. IR (cm^{-1}): 3650.7, 3138.63, 2977.7, 1676.3, 1638.2,

1451.1, 1380.2, 1165.0, 820.7, 553.7. UV-Vis (MeCN): V^{++} λ_{max}: 268 (517700), 416 (28088); $V^{\cdot+}$ at -0.5 V λ_{max}: 402 (418805), 608 (170175). Anal. calc. for $C_{841}H_{824}F_{540}N_{138}O_{48}P_{90}$ (26679.4): C 37.86, H 3.11, N 7.25; found: C 36.03, H 3.47, N 6.62.

The compound VGD-4, VGD-9, VGD-12, VGD-8 were performed according to a literature procedure.[10, 11]

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