Supporting Information for:

Controlled self-assembly of stomatosomes by use of single-component fluorinated dendritic amphiphiles

H. v. Berlepsch[1,3], B. N. S. Thota[2], M. Wyszogrodzka[2], S. de Carlo[4], R. Haag[2]* and C. Böttcher[1]*

[1] Forschungszentrum für Elektronenmikroskopie, Institut für Chemie und Biochemie, Freie Universität Berlin, Fabeckstraße 36a, 14195 Berlin, Germany

[2] Institut für Chemie und Biochemie, Freie Universität Berlin, Takustraße 3, 14195 Berlin, Germany

[3] Core Facility BioSupraMol, Institut für Chemie und Biochemie, Freie Universität Berlin, Fabeckstraße 36a, 14195 Berlin, Germany

[4] Thermo Fisher Scientific, Achtseweg Noord 5, 5651 GG Eindhoven, The Netherlands

Content:

1) Additional graphics

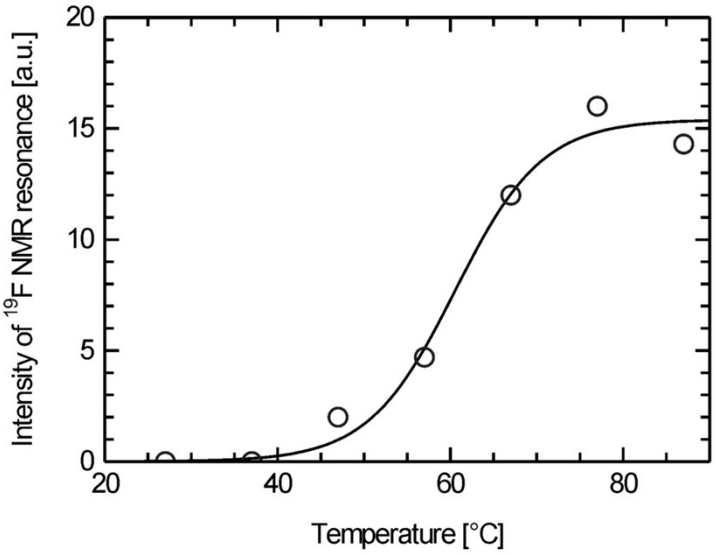


Figure S1: Plot of the intensity of the ^{19}F resonance at -83.7 ppm for amphiphile **8** (**[**G2**]-**(C_6-R_f)$_2$) as a function of temperature. The curve reveals that chain melting occurred over a broad temperature range between 50 and 70°C.

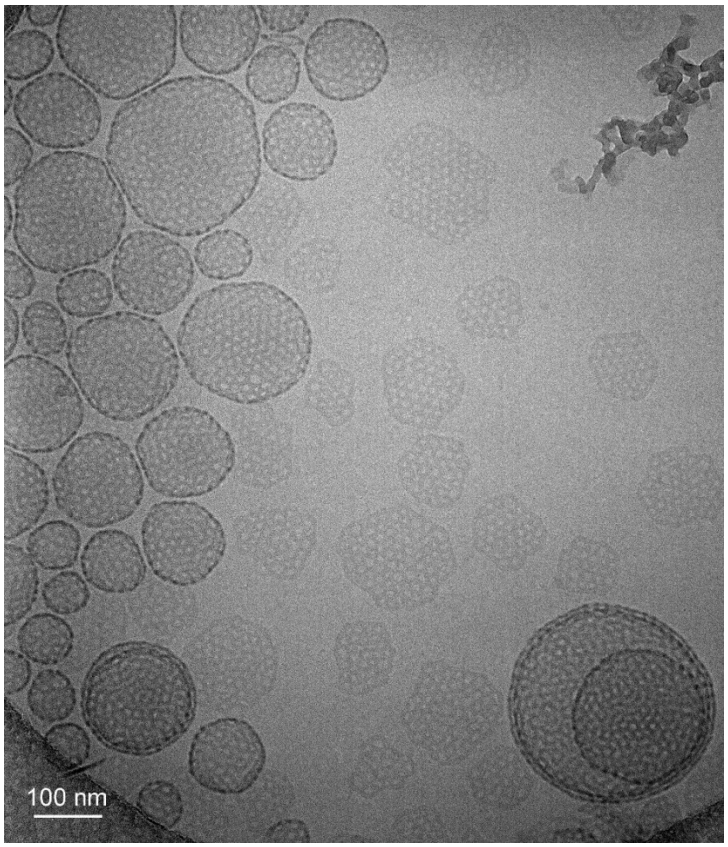


Figure S2: Cryo-TEM image of compound **7** ([G2]-(C_3-R_f)$_2$) after standard preparation. Typical stomatosomes and perforated layers are visible. Sample was vitrificated at 20 °C.

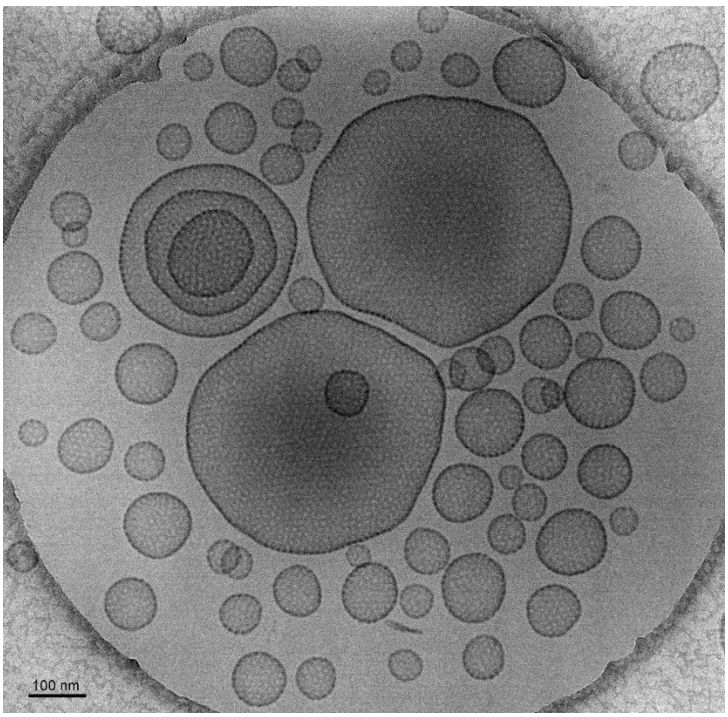


Figure S3: Cryo-TEM micrograph of the same sample as shown in Figure S2 (amphiphile **7** ([G2]-(C_3-R_f)$_2$)), but here vitrificated at 70 °C. A decreased size of perforations as compared to the state at room temperature is clearly visible.

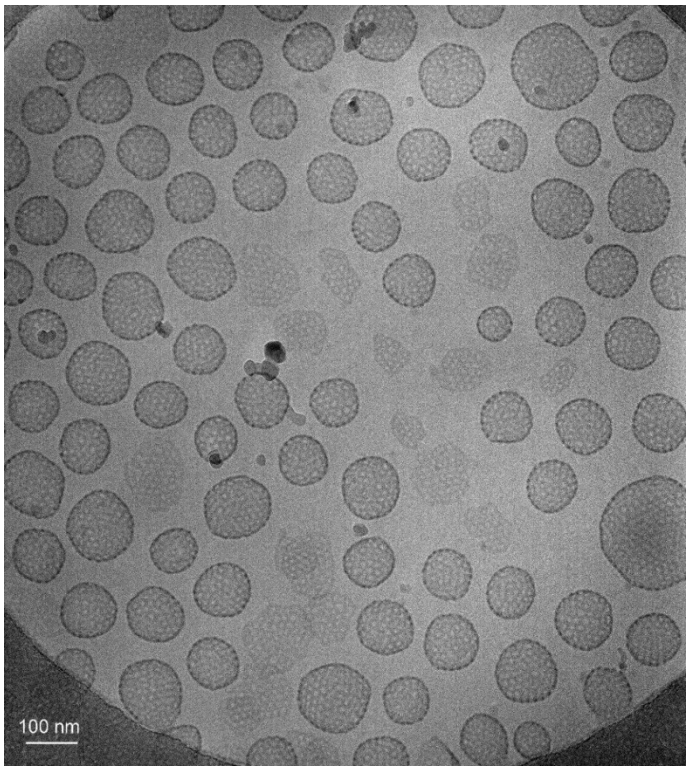


Figure S4: Cryo-TEM image of compound **7** ([G2]-(C_3-R_f)$_2$) after standard preparation. Typical stomatosomes and perforated layers are visible.

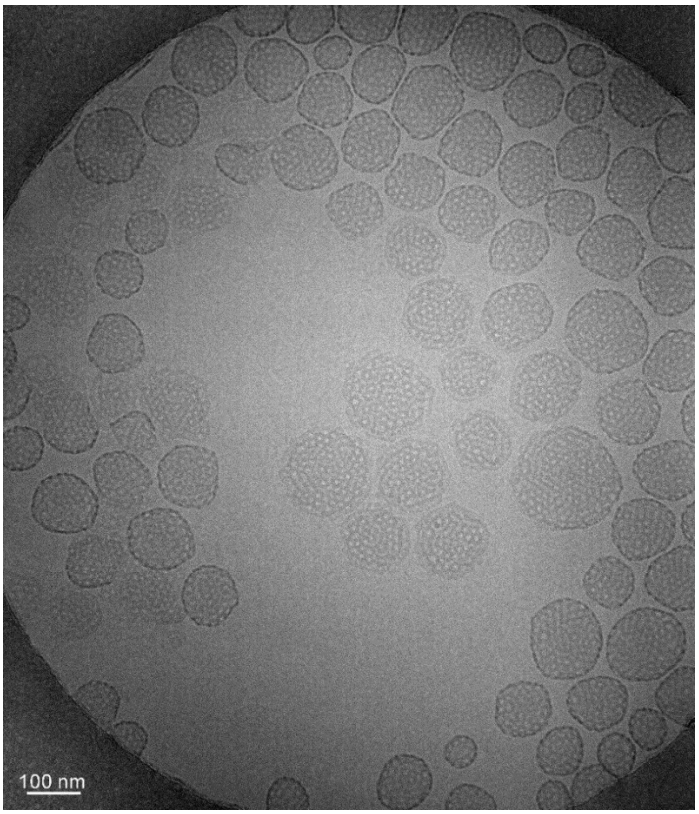


Figure S5: Cryo-TEM micrograph of amphiphile **7** ([G2]-(C_3-R_f)$_2$) after annealing for two hours at 60 °C. During annealing several stomatosomes lost their contrast-rich seem (objects in the center) or developed an asymmetric density profile.

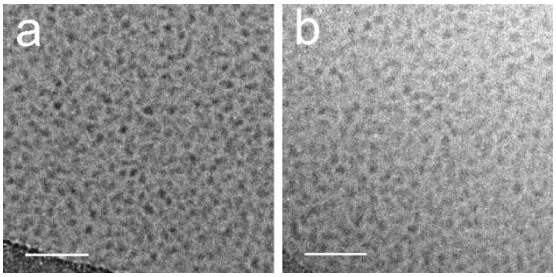


Figure S6: Cryo-TEM images of compounds **9** and **10** showing spherical micelles of ~ 5.5 nm (a) and ~ 7 nm (b) diameter, respectively. Scale bars are 50 nm.

2) Experimental Details

2.1. Analytic methods

DLS measurements were performed on a Malvern Zetasizer Nano ZS (Malvern Instruments Ltd.). Disposable BRAND UV-Cuvettes micro were used. NMR spectra were recorded on JOEL ECX400, JOEL ECP500 and BRUKER AV500 spectrometers. Flash chromatography was performed on silica gel 60 (230-400 mesh) using head pressure by means of compressed air. HPLC was carried out on a Knauer HPLC (pump K-1800) using a Knauer RI-detector K-2401 and a Nucleosil 50-5 (32 x 240) column. Mass analyses were performed on an Agilent 6210 ESI-TOF, Agilent Technologies, Santa Clara, CA, USA. Surface tension measurements were performed on a contact angle measuring and contour analysis system Dataphysics OCA 20 (DataPhysics Instruments GmbH, Filderstadt, Germany).

2.2. Sample preparation protocol

As described in the manuscript, the single-tailed and the **[**G3.0**]** molecules are much better soluble in water than the double-chained perfluorinated molecules with **[**G2.0**]** heads. Hence, different sample preparation protocols had to be adapted for their solubilization. The single-tailed and the **[**G3.0**]** amphiphiles did not show any considerable difference in self-assembly behavior depending on the sample preparation procedure. The **[**G2.0**]** amphiphiles with two perfluoroalkyl chains, however, have shown some differences in the particle morphology depending on sample preparation. For the preparation of solutions Milli-Q water was used, which was obtained from a Merck Millipore Milli-Q Integral System.

Standard sample preparation protocol:

The samples were prepared by thin film hydration method. A thin film was prepared by dissolving the compound in an organic solvent such as methanol, whereby the solvent was evopared under Argon flow. The samples were dried under high vacuum for 1-2h, and the required amount of Milli-Q water was added to the samples. The vials were sonicated for 1 minute, and the samples were heated at 60-70 °C for 1-2 hours. All the samples were filtered through 0.45 μm RC membrane filters before studying by DLS and cryo-TEM.

Harsher sample preparation protocol:

The required amount of the sample was taken in a vial, and Milli-Q water was added. The vials were sonicated for 45-60 minutes to obtain homogeneous dispersions. Furthermore, these samples were heated at 65-70 °C for 2-3 h. The samples were cooled down to room temperature and filtered through 0.45 μm RC membrane filters before they were studied further by DLS and cryo-TEM.

2.3. Critical micelle concentration (*cmc*) measurements using the pendant drop method

The pendant drop method was used to measure the surface tension of the amphiphile solutions at different concentration in Milli-Q water. These measurements were performed on a commercially available contact angle measuring and contour analysis system OCA 20. Calculation of surface tension was done by using the Young-Laplace equation. The surface tension was measured trice per minute and was stopped when the value did not change by more than 0.1 mN/m over 5 minutes. The samples were carefully equilibrated before the surface tension measurements. At lower concentrations (as compared to the *cmc*) we waited 60-90 minutes, while a period of 15-30 minutes was sufficient at higher concentrations. The samples were prepared in Milli-Q water 24 hours before the measurement using a two-fold serial dilution

method in which a concentrated solution of the compound was diluted to half of its actual concentration in the next sample. All measurements were performed at 25 ± 0.5 °C.

2.4. Dynamic light scattering measurements

The dynamic light scattering studies were conducted using a Malvern Zetasizer Nano ZS. All the samples were prepared by weighing the required amount of the compound into a vial and adding in Milli-Q water to maintain the concentration at 0.5-1 wt%. The samples were prepared as described above in the section "sample preparation protocol". Before the DLS measurements all samples were filtered through 0.45 μm RC membrane filters.

2.5. Cryogenic transmission electron microscopy

Preparation of samples:

The samples for cryogenic transmission electron microscopy (cryo-TEM) were prepared at room temperature by placing a droplet (6 μL) of the solution on a hydrophilized perforated carbon filmed Quantifoil grid (60 s Plasma treatment at 8 W using a BALTEC MED 020 device). The excess fluid was blotted off to create an ultrathin layer (typical thickness of 100 nm) of the solution spanning the holes of the carbon film. The grids were immediately vitrified in liquid ethane at its freezing point (-184 °C) using a standard plunging device. Ultra-fast cooling is necessary for an artifact-free thermal fixation (vitrification) of the aqueous solution avoiding crystallization of the solvent or rearrangement of the assemblies.

Standard cryo-TEM investigations:

For standard cryo-TEM investigations we used a Philips CM12 transmission electron microscope. The vitrified samples were transferred under liquid nitrogen into the microscope using the Gatan cryoholder and -stage (Model 626). Microscopy was carried out at -175 °C

sample temperature using the microscopes low dose mode at a primary magnification of 58300×. Accelerating voltage was 100 kV and the defocus was chosen to be 1.2 µm.

Cryo-electron tomography:

1. Vitrified samples were transferred under liquid nitrogen into a Tecnai F20 TEM (FEI company, Hillsboro; USA) using the Gatan cryoholder and -stage (Model 626) and operated at 160kV accelerating voltage. A tomographic tilt series was performed using the FEI Tomography software in the tilt range of -65°/65° in 2° increments. The image stack alignment and 3D reconstruction was performed in the context of the FEI Inspect 3D software. Visualization was done with AMIRA software Version 6.0.0 (Thermo Fisher Scientific, Hillsboro, Oregon; USA).

2. Vitrified samples were transferred under liquid nitrogen into a Titan Krios (FEI company, Hillsboro; USA) operated at 200kV accelerating voltage and by use of the FEI Volta phase plate inserted in the back focal plane of the objective lens. A tomographic tilt series was performed using the FEI Tomography software in the tilt range of -65°/65° in 2° increments and a primary magnification of 22 500x. Images were recorded at full size (4096 by 4096 pixel) using a FEI Falcon II camera with an exposure time of 1 s per image. A total dose of 180 e/Å^2 was accumulated on the specimen. The image stack alignment and 3D reconstruction was performed in the context of the FEI Inspect 3D software V4.1. Visualization was done with AMIRA software Version 6.0.0 (Thermo Fisher Scientific, Hillsboro, Oregon; USA).

3) Synthesis and characterization of compounds

3.1. General synthetic and analytic methods

All commercially available compounds were used as received without further purification. NMR spectra were recorded on JOEL ECX400, JOEL ECP500 and BRUKER AV500 spectrometers. ^{1}H NMR data are reported as follows: chemical shift, multiplicity (s = singlet, br s = broad singlet, d = doublet, t = triplet, q = quartet, hept = heptet, dd = doublet of doublets, ddd = doublet of doublet of doublets, dq = doublet of quartets, m = multiplet, m_{broad} = broad multiplet), coupling constants (Hz), and integration. Flash chromatography was performed on silica gel 60 (230-400 mesh) using head pressure by means of compressed air. HPLC was carried out on a Knauer HPLC (pump K-1800) using a Knauer RI-detector K-2401 and a Nucleosil 50-5 (32 x 240) column. Mass analyses were performed on an Agilent 6210 ESI-TOF, Agilent Technologies, Santa Clara, CA, USA. Elemental analyses were performed on a Perkin-Elmer EA 240.

Acetalprotected glycerol dendrons [Gn] were synthesized according to the previously published procedure.[1]

List of Abbreviations

AIBN = azobisisobutyronitrile
15-C-5 – 15-Crown-5
18-C-6 – 18-Crown-6
DCM = dichloromethane
DMSO = dimethylsulfoxide
DIPEA = diisopropylethyl amine
DMF = N,N-dimethylformamide
EtOAc = ethyl acetate
MsCl = Methanesulfonyl chloride

[1] M. Wyszogrodzka, R. Haag *Chem.−Eur. J.* **2008**, *14*, 9202-9214.

TEA = triethylamine

THF = tetrahydrofuran

R_f = $C_8F_{17}CH_2CH_2S$-

3.2. General synthesis procedures

General procedure A: Ether formation.

Procedure A1. To the anhydrous DMSO freshly powdered KOH (4.0 equiv.) was added. After stirring for 5 min an alcohol R-OH was added to the solution and allowed to stir for additional 5 min. Finally respective bromoalkene (1.05-2.0 equiv. per OH group) was added to the reaction mixture and stirred for 30-45 min. Reaction was quenched by addition of water, followed by extraction with CH_2Cl_2. The combined organic layers were dried over Na_2SO_4, filtered and concentrated under reduced pressure. Purification of the residue by column chromatography gives the desired compounds in high yield.

Procedure A2. [G*n*]-OH (1.0 equiv.), NaH (60% in mineral oil, 2.5 - 5.0 equiv. per OH group), cat. amount of 15-C-5 and freshly distilled anhydrous THF were placed in a dry two necked round bottomed flask under inert gas atmosphere. After 2-3 h stirring at 40 °C with respective bromoalkene (2.0 equiv. per OH), cat. amount of KI and 18-C-6 were added to the solution. The mixture was stirred under reflux for 12 – 24 h. After cooling to room temp., the reaction was quenched with distilled water and extracted with CH_2Cl_2. The organic layer then was dried over Na_2SO_4 and solvent was removed under vacuum. Purification of the residue was performed by silica gel column chromatography giving the desired product in high yield.

General Procedure B: Thiol coupling

Procedure B1. Attachment of perfluoro segment to the "OH" funtionality.

MsCl (1.1 – 1.5 equiv. per OH) and Et_3N (1.4 equiv. per OH) were added to a solution of R-OH (1.0 equiv.) in abs. toluene being cooled to 0 °C. The mixture was stirred for 4-12h. The reaction progress was monitored by TLC. The precipitate was removed by filtration and the product was dried under vacuum and used for next step without further purification. The mesylate was dissolved in dioxane and Cs_2CO_3 (2.7 equiv. per OMs) and $C_8F_{17}CH_2CH_2SH$ (2.6-2.7 equiv. per OMs) were added. The mixture was stirred for 18-20h at 60 °C. The reaction mixture was quenched with water and extracted with DCM. The organic layer was dried over Na_2SO_4, and the solvent was removed. The product was purified via column chromatography yielding a title compound.

Procedure B2. Attachment of perfluoro segment to the "ene" funtionality.

Mixture of "ene" compound (1.0 equiv.) and $C_8F_{17}CH_2CH_2SH$ (4.0 equiv. per "ene" group) was degassed by freeze pump thaw procedure and bubbling Argon through the solution to remove oxygen. After heating to 80 °C, cat. amount (a spatula-tip) of AIBN was added under an atmosphere of argon, and the reaction mixture was stirred for 2 h. After further addition of the same amount of AIBN, the mixture was stirred for another 24 h at 80 °C, and the solvent was then evaporated. The further purification was achieved by column chromatography.

General Procedure C: "Click" coupling.

To the [G*n*]-Propagyl (1.0equiv.) and respective azide (1.1 equiv.) dissolved in THF a 15 mol% of DIPEA was added. After stirring for 5 min sodium ascorbate (30 mol%) was added, followed by $CuSO_4 \cdot 5H_2O$ (15 mol%). (A stock solution of sodium ascorbate and $CuSO_4 \cdot 5H_2O$ in water was prepared in concentration 100 mg/mL) THF/H_2O ratio must be 1/1 (v/v). The

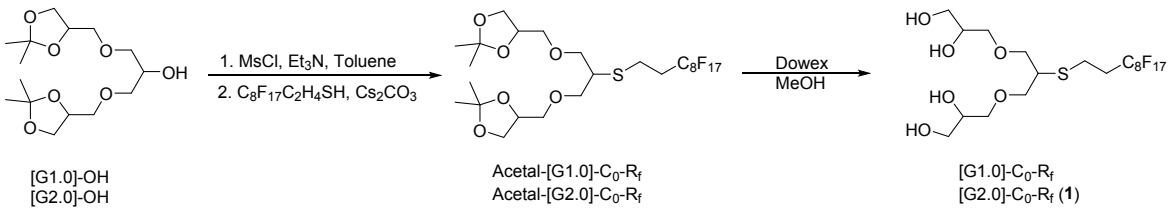
heterogeneous mixture was stirred vigorously until TLC analysis indicated complete consumption of the starting material. The reaction mixture was diluted with water, extracted three times with DCM. The combined organic layers were washed with a small amount of saturated solution of EDTA, dried with Na_2SO_4 and concentrated in vacuo. Purification by column chromatography gives the desired product.

General Procedure D: Deprotection of the alcohol functionality.

To a solution of acetal-protected compound (1.0 equiv.) in a solvent mixture of DCM/MeOH Dowex® 50W as a H^+ ion exchange resin (1.0-2.0 equiv. per weight) was added and the reaction mixture was stirred over night at room temperature or refluxed for 3-4 hours. Reaction progress was monitored via TLC or NMR. After completion of reaction, the resin was filtered off and washed with a 5% solution of Et_3N in MeOH. Concentration of the residue under reduced pressure yielded desired product. Final purification was done by reverse-phase column chromatography.

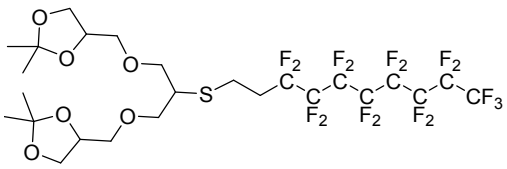
3.3. Synthesis of single-tail amphiphiles

3.3.1. Synthesis of [G*n*]-C_0-R_f

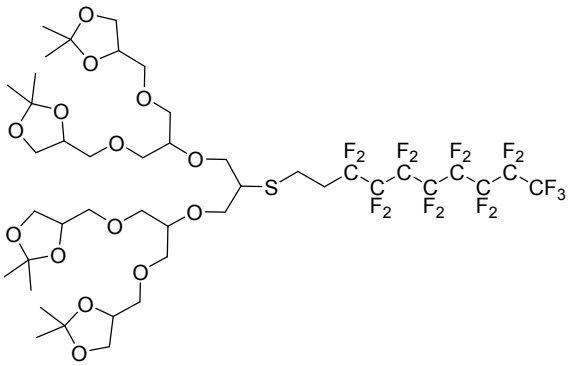


Scheme 1: Synthesis pathway for [G*n*]-C_0-R_f, where n = 1, 2 (shown here [G1.0]-C_0-R_f)

Acetal-[G*n*]-C_0-R_f



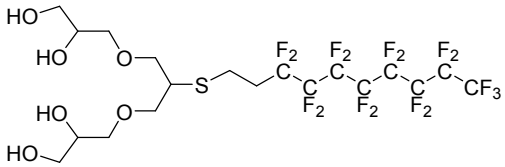
Acetal-[G1.0]-C_0-R_f: was synthesized according to the general procedure **B1**, with [G1.0]-OH (1.82 g, 5.7 mmol, 1.0 equiv.), Et_3N (0.65 g, 6.4 mmol, 1.1 equiv.) and MsCl (0.6 g, 5.3 mmol, 1.1 equiv.) in dry toluene (15 mL) resulting a crude **Acetal-[G1.0]-OMs** (1.5 g, 72%). To the mesylate solution in dioxane (20 mL) Cs_2CO_3 (3.3 g, 10 mmol, 2.7 equiv.) and $C_8F_{17}CH_2CH_2SH$ (4.8 g, 10 mmol, 2.7 equiv.) were added. Purification by column chromatography (10% EtOAc/hexane) lead to the title compound (2.2 g, yield 49%) as a colorless gummy material. **^{1}H NMR** (500 MHz, MeOD-d_4) δ 4.27 – 4.21 (m, 2H), 4.04 (dd, J = 8.2, 6.5 Hz, 2H), 3.75 – 3.66 (m, 5H), 3.64 (d, J = 5.4 Hz, 1H), 3.54 – 3.48 (m, 4H), 3.03 (p, J = 5.8 Hz, 1H), 2.91 – 2.86 (m, 2H), 2.50 (tt, J = 18.0, 8.0 Hz, 2H), 1.38 (s, 6H), 1.32 (s, 6H). **^{13}C NMR** (125 MHz, MeOD-d_4): δ 110.6, 76.2, 76.1, 73.4, 73.2, 73.1, 67.5, 67.5, 47.0, 33.6, 27.1, 25.6, 25.5, 23.3.



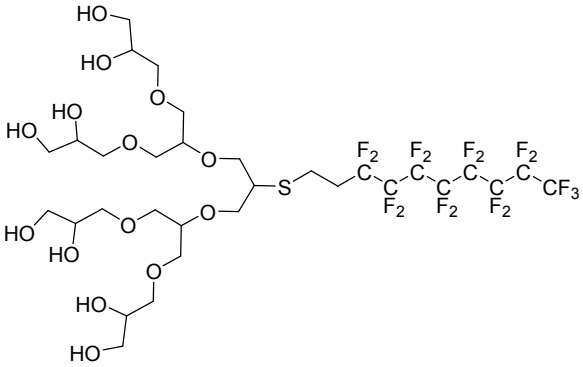
Acetal-[G2.0]-C_0-R_f: was synthesized according to the general procedure **B1**, with [G2.0]-OH (2.66 g, 3.8 mmol, 1.0 equiv.), MsCl (0.48 g, 4.2 mmol, 1.1 equiv.) and Et_3N (0.55 g, 5.4 mmol, 1.4 equiv.) in abs. toluene (20 mL) resulting a crude **Acetal-[G2.0]-OMs.** The mesylate was dissolved in dioxane (30 mL) and Cs_2CO_3 (3.3 g, 10.0 mmol, 2.7 equiv.) and $C_8F_{17}CH_2CH_2SH$ (4.96 g, 10 mmol, 2.7 equiv.) were added. Purification of the product via column chromatography (1:19 isopropanol/hexane) yielding a title compound (1.77 g, 40%). **^{1}H NMR** (500 MHz, MeOH-d_4): δ 4.26 – 4.20 (2x q, J = 6.0 Hz, 4H), 4.05 – 4.02 (dd, J = 7.5 Hz, 4H), 3.83 – 3.78 (m, 2H), 3.77 – 3.71 (m, 4H), 3.69 – 3.63 (m, 4H), 3.61 – 3.48 (m$_{broad}$, 15H), 3.03 – 2.98 (m, 1H), 2.91 – 2.88 (m, 2H), 2.56 – 2.43 (m, 2H), 1.38 (s, 12H), 1.32 (s, 12H). **^{13}C NMR** (126 MHz, MeOH-d_4): δ 109.2, 74.8,

72.1, 71.1, 66.3, 25.8, 24.3 ppm. **Elemental analysis:** Calcd. (%) for $C_{43}H_{63}F_{17}O_{14}S$ (1158.37): C 44.56, S 2.77, H 5.48; found: C 44.62, S 3.07, H 5.48.

[G*n*]-C_0-R_f

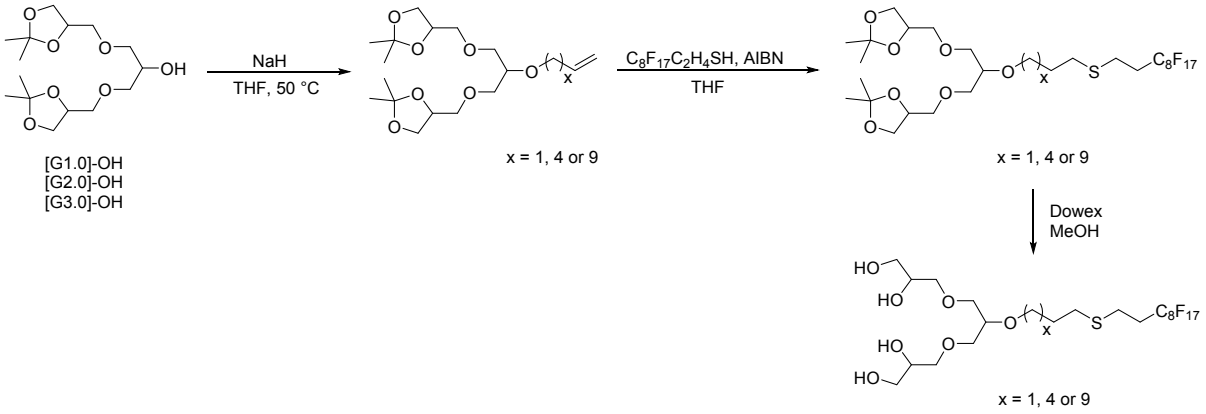


[G1.0]-C_0-R_f: was synthesized according to the general procedure D, with **Acetal-[G1.0]-C_0-R_f** (2.2 g, 2.8 mmol), DOWEX® 50 WX8-100 (4.8 g) in MeOH (20 mL). Purification via reverse phase HPLC (eluent: 90% MeOH/water to 100% MeOH) gave a title compound (1.44 g, 75%). **^{1}H NMR** (500 MHz, MeOD-d_4) δ 3.75 (p, J = 5.5 Hz, 2H), 3.71 – 3.63 (m, 4H), 3.62 – 3.50 (m, 6H), 3.50 – 3.44 (m, 2H), 3.05 (p, J = 5.9 Hz, 1H), 2.91 – 2.86 (m, 2H), 2.49 (tt, J = 17.8, 8.5 Hz, 2H). **^{13}C NMR** (126 MHz, MeOD-d_4) δ 73.7, 73.1, 72.2, 64.4, 46.9, 46.9, 33.7, 33.5, 23.2. **HRMS** calcd. for $C_{19}H_{23}F_{17}NaO_6S$ [M + Na] (725.0842); found: 725.0837.



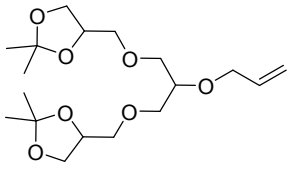
[G2.0]-C_0-R_f: was synthesized according to the general procedure D, with **Acetal-[G2.0]-C_0-R_f** (1.77 g, 1.5 mmol), DOWEX® (3.8 g) in MeOH (15 mL). Purification by HPLC which gave title compound as colourless solid (1.21 g, 81%). **^{1}H NMR** (400 MHz, MeOH-d_4): δ 3.86 – 3.80 (m, 2H), 3.77 – 3.73 (m, 4H), 3.71 – 3.67 (m, 4H), 3.63 – 3.52 (brm, 18 H), 3.50 – 3.46 (m, 4H), 3.05 – 2.99 (m, 1H), 2.91 – 2.87 (m, 2H), 2.55 – 2.45 (m, 2H). **^{13}C NMR** (126 MHz, MeOH-d_4): δ 78.5, 72.6, 71.6, 71.0, 70.9, 63.2, 63.1. **Elemental analysis:** Calcd. (%) for $C_{31}H_{47}F_{17}O_{14}S$ (998.24): C 37.28, S 3.21, H 4.74; found: C 36.47, S 3.36, H 4.88.

3.3.2. Synthesis of [G*n*]-C_x-R_f, where n = 1, 2, 3 and x = 3, 6, 11

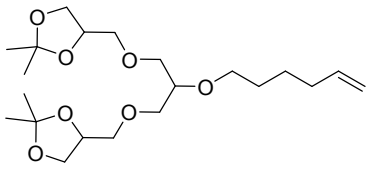


Scheme 2: Synthesis pathway for [G*n*]-C_x-R_f, where n = 1, 2, 3 and x = 1, 4, 9, (shown: [G1.0]-C_3-R_f)

<u>Acetal-[G*n*]-C_x-ene</u>

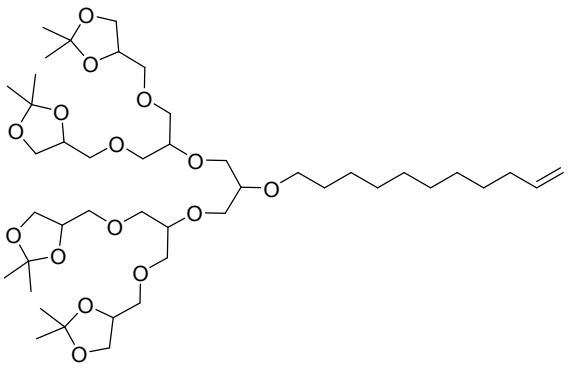


Acetal-[G1.0]-C_3-ene was synthesized according to the general procedure A2, with [G1.0]-OH (1.95 g, 6.086 mmol, 1.0 equiv.), NaH (60% in mineral oil, 0.82 g, 24.35 mmol, 4.0 equiv.), allyl bromide (1.05 mL, 12.17 mmol, 2.0 equiv.). Purification by flash column chromatography (*n*-hexane:EtOAc (4:1, v/v)) gives a title compound (1.70 g, 78%). **^{1}H NMR** (400 MHz, MeOD-d_4) δ 5.92 (ddq, *J* = 15.9, 10.6, 5.3 Hz, 1H), 5.28 (d, *J* = 17.1 Hz, 1H), 5.15 (t, *J* = 9.1 Hz, 1H), 4.24 (sext., *J* = 5.7 Hz, 2H), 4.17 – 3.97 (m, 4H), 3.81 – 3.61 (m, 4H), 3.63 – 3.48 (m, 8H), 1.38 (s, 6H), 1.33 (s, 6H). **^{13}C NMR** (101 MHz, MeOD-d_4) δ 136.5, 136.1, 117.1, 117.0, 110.5, 79.9, 78.5, 76.2, 76.15 73.4, 73.3, 72.4, 72.3, 72.2, 71.1, 67.7, 67.5, 27.1, 25.7. **HRMS** calcd. for $C_{18}H_{32}NaO_7$ [M + Na] (383.2046); found 383.2045.

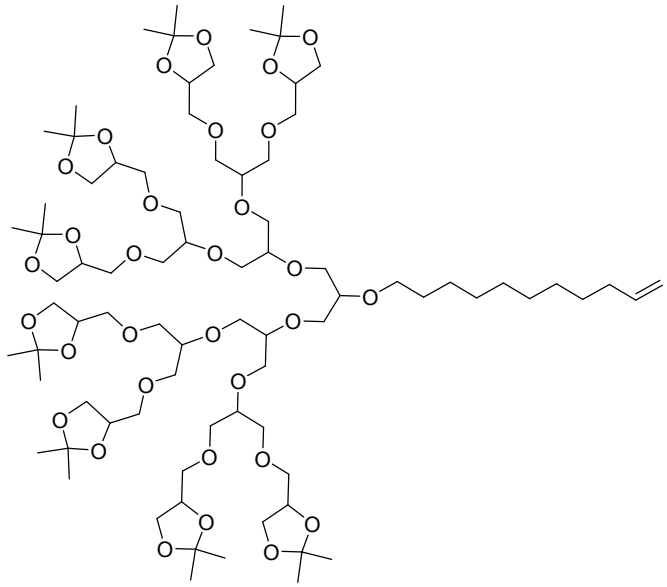


Acetal-[G1.0]-C_6-ene: was synthesized according to the general procedure A1 with [G1]-OH (1.00 g, 3.121 mmol, 1.0 equiv.) KOH (1.1 g, 19.6 mmol, 6.3 equiv.) in DMSO (20 mL), followed by addition of 6-bromo-1-hexene (1.05 g, 6.44 mmol, 2.06 equiv.) and 18-crown-6

(300 mg, 1.13 mmol, 0.36 equiv.). Purification by flash column chromatography (15% EtOAc:*n*-hexane) gives a title compound (1.10 g, 88%). **^{1}H NMR** (500 MHz, CD_2Cl_2): δ 5.86 – 5.71 (m, 1H), 4.95 (d, J = 17.0 Hz, 1H), 4.93 (d, J = 12.0 Hz, 1H), 4.23 – 4.17 (m, 2H), 4.02 – 3.99 (m, 2H), 3.69 –3 .39 (m, 15H), 2.08–2.03 (m, 2H), 1.55 – 1.49 (m, 2H), 1.46 – 1.39 (m, 2H), 1.36 (s, 6H), 1.32 (s, 6H). **^{13}C NMR** (125 MHz, CD_2Cl_2): δ 138.9, 138.8, 114.1, 109.1 78.6, 77.8, 74.9, 74.7, 72.4, 71.4, 71.4, 71.2, 70.5, 70.2, 70.1, 70.1, 66.7, 66.6, 53.3, 33.5, 29.6, 29.1, 26.6, 26.5, 25.4, 25.2, 25.1. **HRMS:** calcd. for $C_{21}H_{38}NaO_7$ [M + Na] (425.2515); found: 425.2522.

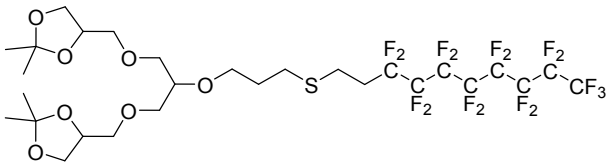


Acetal-[G2.0]-C_{11}-ene: The title compound was prepared using Procedure A2 with [G2.0]-OH (4.0 g, 5.74 mmol, 1.0 equiv.), 11-bromoundecene (1.87 mL, 8.61 mmol, 1.5 equiv.) and NaH (1.15 g, 28.7 mmol, 5.0 equiv.) in THF (50 mL). Purification by flash chromatography on silica gel (*n*-hexane:EtOAc (1:1, v/v)) to gives a tile compound as a colorless oil (2.02 g, 50 %). **^{1}H NMR** (250 MHz, $CDCl_3$): δ 5.76 (tdd, J = 16.9, 10.1, 6.6 Hz, 1H), 4.97 – 4.85 (m, 2H), 4.19 (p, J = 5.9 Hz, 4H), 4.01 (m, 4H), 3.69 (m, 4H), 3.65 – 3.40 (br m, 25H, CH_2CHO backbone), 2.00 (q, 2 H, J = 6.6 Hz), 1.63 – 1.42 (m, 4H), 1.38 (s, 12H), 1.32 (s, 12H), 1.24 (br s, 10H) ppm. **^{13}C NMR** (67.5 MHz, $CDCl_3$, 25 °C): δ 139.1, 114.05, 109.25, 78.6, 78.4, 78.2, 77.9, 74.7, 74.5, 72.4, 71.4, 71.3, 70.4, 70.3, 66.9, 66.7, 33.7, 30.1, 29.5, 29.4, 29.4, 29.0, 28.8, 26.7, 26.0, 25.3 ppm. **ESI-TOF MS** calcd. for $C_{44}H_{80}O_{15}$ (848.5497); found 849.5573 $[M + H]^+$, 871.5395 $[M + Na]^+$, 887.5133 $[M + K]^+$. **Anal. Calcd** for $C_{44}H_{80}O_{15}$: C, 62.24; H, 9.50. Found: C, 62.54; H, 9.11.



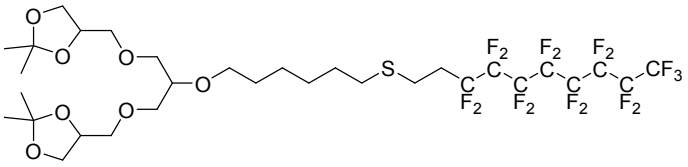
Acetal-[G3.0]-C_{11}-ene: The title compound was synthesized according to the general procedure Procedure A2 with [G3.0]-OH (2.0 g, 1.38 mmol, 1.0 equiv.), NaH (0.275 g, 6.9 mmol, 5.0 equiv.), 11-bromoundecene (0.45 mL, 2.07 mmol, 1.5 equiv.) in THF (50 mL). Purification by flash chromatography on silica gel (25% isopropanol in *n*-hexane) gives a title compound as a colorless oil (1.0 g, 66%). **^{1}H NMR** (400 MHz, $CDCl_3$): δ 5.80 – 5.70 (m, 1H), 4.95 – 4.91 (m, 1H), 4.88 – 4.86 (m, 1H), 4.21 – 4.15 (m, 8H), 4.00 – 3.96 (m, 8H), 3.70 – 3.62 (m, 8H), 3.62 – 3.38 (m_{broad}, 54H, C*H*$_2$C*H*O backbone), 2.00 (m, 2H), 1.47 (m, 2H), 1.36 (s, 24H), 1.30 (s, 24H), 1.22 (br s, 12H) ppm. **^{13}C NMR** (100 MHz, $CDCl_3$): δ 139.2, 114.2, 109.4, 78.7, 78.4, 74.8, 74.7, 72.6, 71.7, 71.5, 71.3, 70.7, 70.2, 67.0, 66.9, 66.9, 33.9, 30.3, 29.7, 29.6, 29.2, 29.1, 29.0, 26.9, 26.3, 25.5 ppm. **ESI-TOF MS** calcd. for $C_{80}H_{144}O_{31}$ (1600.9692); found 1619.0037 $[M + NH_4]^+$, 1623.9595 $[M + Na]^+$.

<u>Acetal-[G*n*]-C_x-R_f, where n = 1, 2, 3 and x = 3, 6, 11</u>

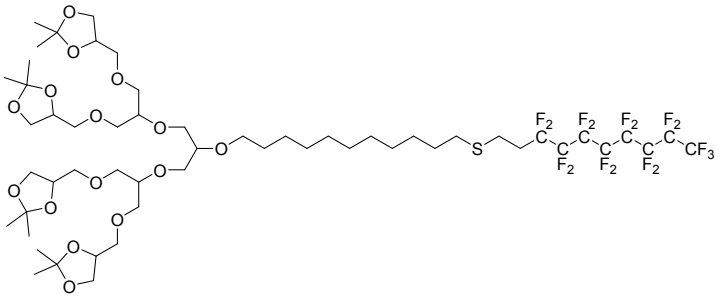


Acetal-[G1.0]-C_3-R_f: The title compound was synthesized according to the general procedure B2, with **Acetal-[G1.0]-C_3-ene** (1.3 g, 3.61 mmol, 1.0 equiv.), $C_8F_{17}CH_2CH_2SH$ (5.4 g, 11.25 mmol, 3.1 equiv.) and cat. amount AIBN. Purification by flash column (*n*-hexane:EtOAc (9:1 to 4:1, v/v)) gives title compound (2.6 g, 85%). **^{1}H NMR** (500 MHz, MeOD-d_4) δ 4.26 (h, *J* = 7.2, 6.7 Hz, 2H), 4.06 (dd, *J* = 8.2, 6.5 Hz, 2H), 3.79 – 3.67 (dtt, 4H), 3.66 – 3.48 (m, 9H), 2.79 (dd, *J* = 9.3, 6.8 Hz,

2H), 2.70 (q, J = 7.1 Hz, 2H), 2.50 (tt, J = 18.0, 8.1 Hz, 2H), 1.86 (h, J = 6.6 Hz, 2H), 1.40 (s, 6H), 1.34 (s, 6H). **^{13}C NMR** (125 MHz, MeOD-d_4) δ 110.5, 79.9, 79.3, 76.2, 73.4, 72.4, 71.8, 70.6, 69.5, 67.8, 67.6, 33.1, 31.0, 30.6, 29.6, 29.5, 27.1, 25.6, 23.4. **HRMS** calcd. for $C_{28}H_{37}F_{17}NaO_7S$ [M + Na] (863.1886); found: 863.1909.

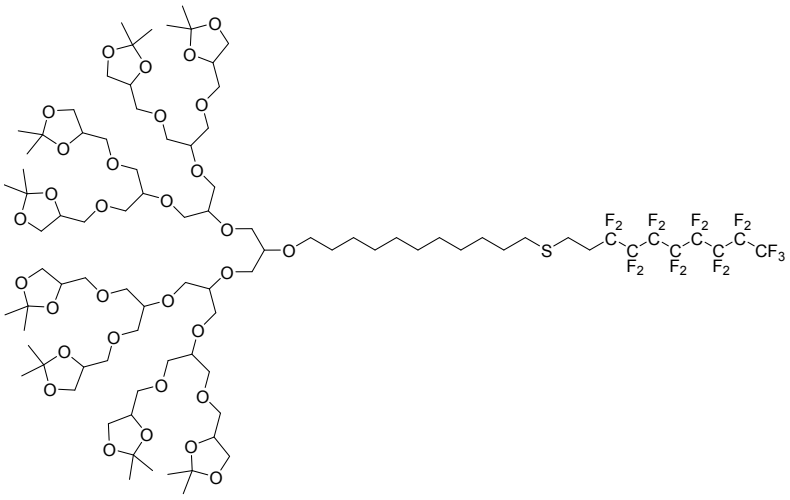


Acetal-[G1.0]-C_6-R_f: The title compound was synthesized according to the general procedure B2, with **Acetal-[G1.0]-C_6-ene** (0.75 g, 1.86 mmol, 1.0 equiv.), $C_8F_{17}CH_2CH_2SH$ (3.5 g, 7.29 mmol, 3.9 equiv.) and cat. amount AIBN. Purification by flash column chromatography gives a desired product (1.10 g, 68%). **^{1}H NMR** (400 MHz, Methylene Chloride-d_2) δ 4.23 – 4.14 (m, 2H), 3.99 (dd, J = 8.1, 6.5 Hz, 2H), 3.69 – 3.63 (m, 2H), 3.63 – 3.35 (m_{broad}, 11H), 2.74 – 2.68 (m, 2H), 2.53 (dd, J = 7.9, 6.9 Hz, 2H), 2.38 (tt, J = 17.9, 8.6 Hz, 2H), 1.64 – 1.46 (m, 5H), 1.41 – 1.24 (m, 3H), 1.35 (s, 6H), 1.30 (s, 6H). **^{13}C NMR** (101 MHz, CD_2Cl_2) δ 109.8, 79.2, 78.4, 75.5, 75.3, 73.1, 72.0, 71.9, 70.8, 67.4, 67.3, 54.00, 32.7, 30.6, 30.2, 30.0, 29.2, 27.1, 26.3, 25.8, 23.0. **HRMS** calcd. for $C_{31}H_{43}F_{17}NaO_7S$ $[M + Na]^+$ (905.2356); found: 905.2355.



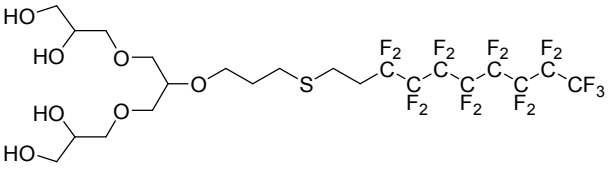
Acetal-[G2.0]-C_{11}-R_f: The title compound was synthesized according to the general procedure B2, with **Acetal-[G2.0]-C_{11}-ene** (1.5 g, 1.74 mmol, 1.0 equiv.), $C_8F_{17}CH_2CH_2SH$ (3.33 g, 6.94 mmol, 4.0 equiv.) and cat. amount AIBN. Purification by flash column (petroleum ether (40-60°C)/CH_2Cl_2 (7:1, v/v) and (*n*-hexane:EtOAc (4:1, v/v) gives a desired product (2.3 g, 98%). **^{1}H NMR** (400 MHz, $CDCl_3$): δ 4.25 – 4.19 (m, 4H), 4.05 – 4.00 (m, 4H), 3.75–3.68 (m, 5H), 3.66 – 3.43 (m_{broad}, 25H, CH_2CHO backbone), 2.76 – 2.65 (m,

2H), 2.57 – 2.49 (m, 2H), 2.42–2.29 (m, 2H), 1.61 – 1.44 (m, 5H), 1.39 (s, 12H), 1.33 (s, 12H), 1.25 (br s, 12H) ppm. **^{13}C NMR** (100 MHz, $CDCl_3$): δ 109.5, 78.6, 74.9, 74.7, 72.6, 71.6, 71.5, 70.7, 70.45, 67.1, 66.9, 32.4, 30.3, 29.75, 29.6, 29.3, 28.9, 26.9, 26.3, 25.5, 22.7 ppm. **^{19}F NMR** (376 MHz, $CDCl_3$): δ -80.8 (t, J = 10.3 Hz), -114.3, -121.7, -121.9, -122.7, -123.3, -126.1 ppm. **ESI-TOF MS** calcd. for $C_{54}H_{85}F_{17}O_{15}S$ (1328.5338); found 1351.5253 $[M + Na]^+$, 1367.5055 $[M + K]^+$.

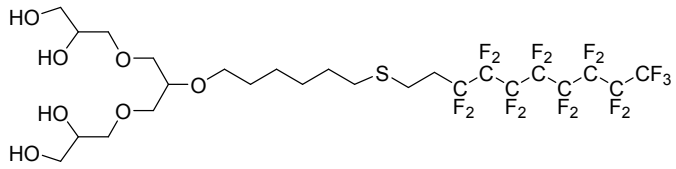


Acetal-[G3.0]-C_{11}-R_f: The title compound was synthesized according to the general procedure B2, with **Acetal-[G3.0]-C_{11}-ene** (2.0 g, 1.248 mmol, 1.0 equiv.), $C_8F_{17}CH_2CH_2SH$ (2.4 g, 4.994 mmol, 4.0 equiv.) and cat. amount AIBN. Purification by flash column (petroleum ether (40-60 °C)/CH_2Cl_2 (7:1, v/v)) and (*n*-hexane:EtOAc (4:1, v/v)) gives a desired product (1.81 g, 70%). **^{1}H NMR** (400 MHz, $CDCl_3$): δ 4.26 – 4.18 (m, 8H), 4.02 (dd, J = 8.2, 6.4 Hz, 8H), 3.75 – 3.67 (m, 8H), 3.66 – 3.42 (m_{broad}, 55H, C*H*$_2$C*H*O backbone), 2.73 – 2.68 (m, 2H), 2.55 – 2.51 (m, 2H), 2.42 – 2.29 (m, 2H), 1.61 – 1.44 (m, 4H), 1.39 (s, 24H), 1.33 (s, 24H), 1.26 (br s, 12H) ppm. **^{13}C NMR** (100 MHz, $CDCl_3$): δ 109.4, 78.8, 78.6, 78.5, 74.9, 74.7, 72.6, 71.7, 71.6, 71.4, 70.7, 70.3, 67.2, 66.9, 32.4, 30.4, 29.8, 29.7, 29.5, 29.4, 29.0, 26.9, 26.3, 25.5, 22.7 ppm. **^{19}F NMR** (376 MHz, $CDCl_3$) δ -80.7, -114.2, -121.6, -121.8, -122.6, -123.3, -126.0 ppm. **ESI-TOF MS** calcd. for $C_{90}H_{149}F_{17}O_{31}S$ (2080.9532); found 2081.9605 $[M + H]^+$, 2098.9870 $[M+NH_4]^+$, 2103.9424 $[M + Na]^+$, 2119.9164 $[M + K]^+$.

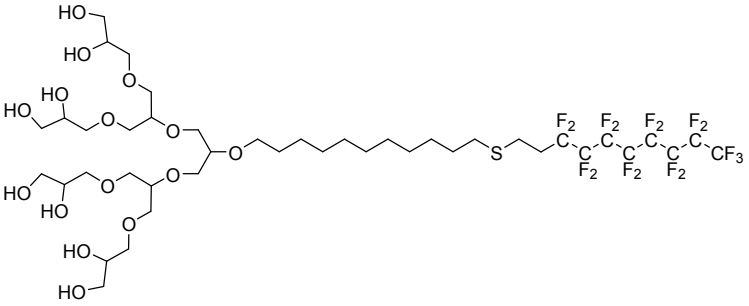
[G*n*]-C_x-R_f, where n = 1, 2, 3 and x = 3, 6, 11.



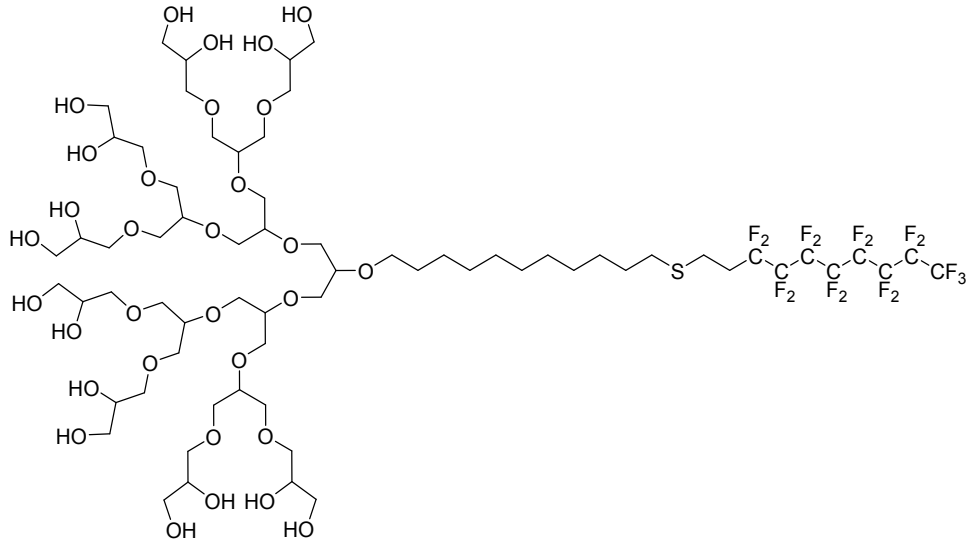
[G1.0]-C_3-R_f: The title compound was synthesized according to the general procedure D with **Acetal-[G1.0]-C_3-R_f** (1.8 g, 2.14 mmol, 1.0 equiv.). Evaporation of the solvent gives desired product (1.20 g, 74%). **^{1}H NMR** (500 MHz, MeOD-d_4): δ 3.81 – 3.73 (m, 3H), 3.71 – 3.56 (m, 2H), 3.65 – 3.43 (m_{broad}, 12H), 3.24 – 3.14 (m, 1H), 3.08 – 2.86 (m, 3H), 2.79 – 2.57 (m, 2H), 2.11 – 1.97 (m, 2H). **^{13}C NMR** (125 MHz, MeOD-d_4): δ 79.8, 79.4, 74.0, 72.9, 72.4, 72.2, 71.8, 70.6, 69.5, 64.4, 25.5, 24.6, 24.2. **^{19}F NMR** (471 MHz, MeOD-d_4) δ -82.29 (t, J = 10.0 Hz), -122.54, -122.80, -123.66, -124.06, -127.22. **HRMS** calcd. for $C_{22}H_{29}F_{17}NaO_7S$ $[M + Na]^+$ (783.1255); found: 783.1283.



[G1.0]-C_6-R_f: The title compound was synthesized according to the general procedure D with **Acetal-[G1.0]-C_6-R_f** (0.7 g, 0.79 mmol, 1.0 equiv.). Evaporation of the solvent gives title compound (0.5 g, 79%). **^{1}H NMR** (500 MHz, MeOD-d_4) δ 3.77 – 3.72 (m, 2H), 3.71 – 3.64 (m, 1H), 3.64 – 3.43 (m_{broad}, 14H), 2.79 – 2.69 (m, 2H), 2.59 (t, J = 7.3 Hz, 2H), 2.45 (tt, J = 17.8, 8.0 Hz, 2H), 1.64 – 1.54 (m, 4H), 1.50 – 1.33 (m, 4H). **^{13}C NMR** (126 MHz, MeOD-d_4): δ 79.9, 79.2, 74.0, 73.9, 73.0, 72.5, 72.4, 72.2, 72.2, 71.4, 64.5, 33.1, 32.9, 31.0, 30.6, 30.4, 29.6, 26.8, 26.8, 23.3. **^{19}F NMR** (471 MHz, MeOD-d_4) δ -82.3 (t, J = 10.0 Hz), -122.6, -122.8, -123.6, -124.2, -127.2. **HRMS** calcd. for $C_{25}H_{35}F_{17}NaO_7S$ $[M + Na]^+$ (825.1724); found: 825.1741.



[G2.0]-C_{11}-R_f: The title compound was synthesized according to the general procedure D with **Acetal-[G2.0]-C_{11}-R_f** (1.5 g, 1.128 mmol, 1.0 equiv.) in MeOH. Evaporation of the solvent gives desired product (1.3 g, 98%). **^{1}H NMR** (400 MHz, MeOD-d_4) δ 3.80 – 3.73 (m, 5H), 3.70 – 3.62 (m, 4H), 3.62 – 3.42 (m, 28H, CH_2CHO backbone), 2.77 – 2.69 (m, 2H), 2.57 (t, J = 7.3 Hz, 2H), 2.53 – 2.34 (m, 2H), 1.64 – 1.49 (m, 4H), 1.42 – 1.36 (m, 2H), 1.30 (br s, 12H). **^{13}C NMR** (175 MHz, MeOD–d_4) δ 161.8, 161.6, 161.5, 119.5, 117.9, 116.4, 116.3, 111.2, 111.0, 110.8, 109.9, 78.5, 78.5, 78.3, 78.0, 72.6, 72.5, 71.5, 71.0, 70.9, 70.8, 70.0, 69.6, 63.1, 31.8, 31.7, 31.5, 29.8, 29.4, 29.3, 29.3, 29.1, 28.9, 28.4, 25.9, 21.9. **^{19}F NMR** (376 MHz, MeOD-d_4) δ-82.2 (t, J = 10.6 Hz), -115.2 (quint, J = 16.4 Hz), -122.6, -122.8, -123.6, -124.3, -127.2. **ESI-TOF MS** calcd. for $C_{42}H_{69}F_{17}O_{15}S$ (1168.4086); found 1191.3971 $[M + Na]^+$.

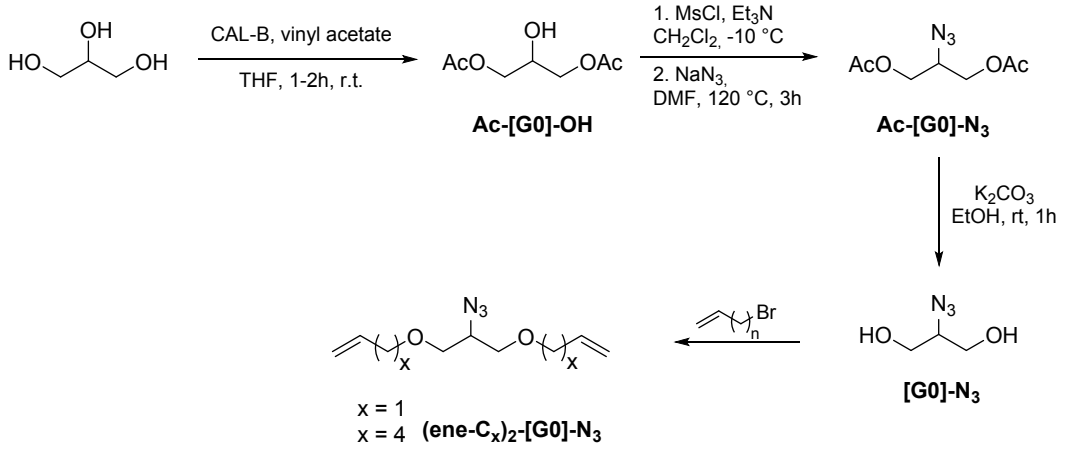


[G3.0]-C_{11}-R_f: The title compound was synthesized according to the general procedure D with **Acetal-[G3.0]-C_{11}-R_f** (0.9 g, 0.432 mmol, 1.0 equiv.). Evaporation of the solvent gives title compound (0.72 g, 95%). **^{1}H NMR** (400 MHz, MeOD-d_4) δ 3.77 (br s, 10H), 3.73 (br s, 12H), 3.66 – 3.47 (m_{broad}, 55H, CH_2CHO backbone), 2.76 – 2.73 (m, 2H), 2.60 – 2.57 (m, 2H), 2.50 – 2.39 (m, 2H), 1.62

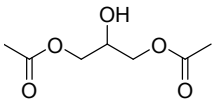
– 1.52 (m, 4H), 1.41 – 1.32 (m_{broad}, 14H). **^{13}C NMR** (100 MHz, MeOD-d_4) δ 80.3, 80.0, 79.8, 79.7, 74.0, 73.9, 72.9, 72.4, 72.4, 72.3, 72.2, 71.5, 71.0, 64.5, 64.4, 33.3, 33.1, 32.9, 31.2, 30.8, 30.7, 30.5, 30.3, 29.8, 27.3, 23.3. **^{19}F NMR** (376 MHz, MeOD-d_4) δ –82.2 (t, J = 10.5 Hz), –115.1 (q, J = 15.4 Hz), –122.6, –122.7, –123.6, –124.2, –127.1. **ESI-TOF MS** calcd. for $C_{66}H_{117}F_{17}O_{31}S$ (1760.7028); found 1783.6890 $[M + Na]^+$.

3.4. Synthesis of double-tail amphiphiles

3.4.1. Synthesis of (ene-C_x)$_2$-[G0]-N_3

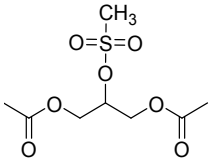


Scheme 3: Synthesis of two-tail linker (ene-C_x)$_2$-[G0]-N_3.

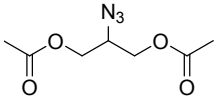


2-hydroxypropane-1,3-diyl diacetate (Ac-[G0]-OH): Glycerin (5.0 g, 54.28 mmol, 1.0 equiv.), 1.5 g of CAL-B and vinyl acetate (12.15 g, 141.17 mmol, 2.6 equiv.) were dissolved in 200 mL THF and stirred for 1 h at room temp. After the completion of the reaction, CAL-B was filtered off and washed 3 times with MeOH. Solvents were removed under reduced pressure, the residue was purified *via* flash chromatography using EtOAc:MeOH (1:4.5 → 3:2, v/v) as an eluent giving title compound (9.54 g, 99 %) as an colorless liquid. **^{1}H NMR** (400 MHz, $CDCl_3$): δ 4.13–4.00 (m, 5H), 3.01

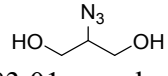
(br s, 1H, –OH), 2.03 (s, 6H).**^{13}C NMR** (100 MHz, $CDCl_3$): δ 171.0, 67.7, 65.0, 20.6. **ESI-TOF MS** calcd. for $C_7H_{12}O_5$ (176.0685); found 199.0528 $[M + Na]^+$.



Ac-[G0]-OMs: MsCl (13.5 mL, 174.8 mmol, 2.0 equiv.) was added to a solution of Ac-[G0]-OH (15.4 g, 87.4 mmol, 1.0 equiv.) and Et_3N (24.3 mL, 174.8 mmol, 2.0 equiv.) in CH_2Cl_2 (160 mL), cooled to -10 °C in an ice bath. Progress of the reaction was monitored by TLC. After completion, the precipitate was filtered and the mixture concentrated under vacuum to give an oil as a final product. The product was used for the next reaction step without purification. **^{1}H NMR** (400 MHz, $CDCl_3$): δ 4.99 (tt, J = 6.5, 3.8 Hz, 1H) 4.26 (ddd, J = 18.9, 12.3, 5.2 Hz, 4H), 3.06 (s, 3H), 2.08 (s, 6H).**^{13}C NMR** (100 MHz, $CDCl_3$): δ 170.1, 76.4, 62.2, 38.4, 20.4.

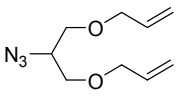


Ac-[G0]-N_3: Sodium azide (14.2 g 218.5 mmol, 2.5 eqiuv.) was added to a solution of the Ac-[G0]-OMs (22.2 g 87.0 mmol, 1.0 equiv.) in dry DMF (150 mL). After the mixture had been stirred at 120 °C under argon for 3 h, the excess of NaN_3 was filtered off, and DMF was removed under high vacuum by cryodistillation. The crude product was purified by filtration through a thin layer of silica gel (ethyl acetate/hexane, 3:2). The title compound was obtained as a light yellow, viscous oil in (16.7 g, 95% yield over two steps. **^{1}H NMR** (250 MHz, $CDCl_3$): δ 4.10 (dq, J = 11.6, 5.7 Hz, 4H), 3.83 (m, 1H), 2.04 (s, 6H). **^{13}C NMR** (62.9 MHz, $CDCl_3$): δ 170.1, 62.9, 58.2, 20.3. **ESI-TOF MS** calcd. for $C_9H_{15}N_3O_2$ (201.0750); found 224.0648 $[M + Na]^+$.

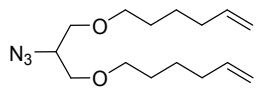


HO-[G0]-N_3 (2-azidoglycerin): To the solution of **Ac-[G0]-N_3** (16.7 g, 83.01 mmol, 1.0 equiv.) in ethanol (167 mL, 1 g/10 mL ethanol) were K_2CO_3 (28.68 g, 0.207 mol, 2.5 equiv.) added and stirred over night at room temperature. The K_2CO_3 was filtered off, washed with ethanol. Removal of the solvent under reduced pressure gives title

compound (9.52 g, 98%). **^{1}H NMR** (250 MHz, MeOD-d_4) δ 3.64 – 3.48 (m, 5H). **^{13}C NMR** (67.5 MHz, MeOD-d_4) δ 68.9, 65.1.

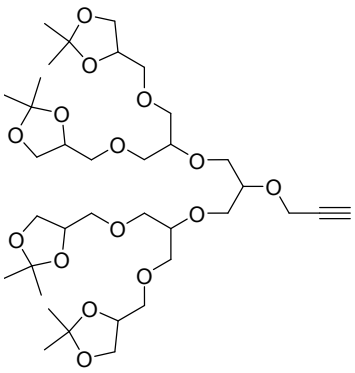


(ene-C_3)$_2$-[G0]-N_3: Allyl bromide (13.2 mL, 152.0 mmol, 5.0 equiv.) was added to a solution of **2-azidoglycerin** (3.6 g, 30.4 mmol, 1.0 equiv.) and TBAI (1.12 g, 3.04 mmol, 10 mol%) as phase-transfer catalyst in 50% w/v aqueous NaOH (12.17 g, 152.0 mmol, 5.0 equiv.). The reaction mixture was stirred for 24 h at 40 °C. After addition of *n*-hexane and sat. NH_4Cl, the organic phase was separated, washed with water, dried over Na_2SO_4 and concentrated under vacuum. The crude product was purified by column chromatography on silica gel (12:1 *n*-hexane/EtOAc) to give product as colorless oil (5.4 g, 90%). **^{1}H NMR** (400 MHz, $CDCl_3$): δ 5.87 (ddt, J = 17.2, 10.6, 5.6 Hz, 2H), 5.26 (qd, J = 17.2, 1.6 Hz, 2 H), 5.17 (ddd, J = 10.4, 2.9, 1.3 Hz, 2H), 3.99 (td, J = 5.6, 1.4 Hz, 4H), 3.70 (tt, J = 6.5, 4.6 Hz, 1H), 3.53 (ddd, J = 16.6, 10.0, 5.6 Hz, 4H). **^{13}C NMR** (100 MHz, $CDCl_3$): δ 134.3, 117.4, 72.4, 69.8, 60.8 ppm. **ESI-TOF MS** calcd. for $C_9H_{15}N_3O_2$ (197.1164); found 198.1253 $[M + H]^+$.

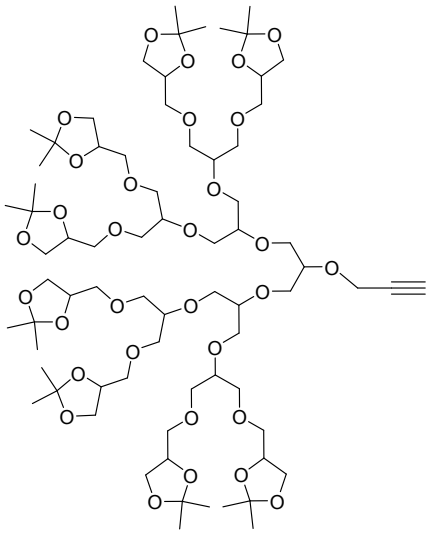


(ene-C_6)$_2$-[G0]-N_3: The reaction was carried out according to the Procedure A with **2-azidoglycerin** (1.87 g, 15.98 mmol, 1.0 equiv.), KOH-powder (7.17 g, 128 mmol, 4.0 equiv.) and 6-bromohex-1-ene **(x)** (10.0 g, 61 mmol, 1.9 equiv. per OH) in 50 mL DMSO. Extraction with DCM (3 x 100 mL) and purification by column chromatography (4%→5% EtOAc/n-hexane) yielded title compound as a colourless fluid (4.05 g, 90%). **^{1}H NMR** (400 MHz, $CDCl_3$): δ 5.79 (tdd, J = 16.9, 10.2, 6.7 Hz, 2H), 4.99 (ddt, J = 17.1, 2.0, 1.6 Hz, 2H), 4.94 (ddt, J = 10.2, 2.4, 1.2 Hz, 2H), 3.66 (tt, J = 6.3, 4.6 Hz, 1H), 3.56 – 3.46 (m, 4H), 3.45 (td, J = 6.5, 1.5 Hz, 4H), 2.10 – 2.02 (m, 4H), 1.64 – 1.54 (m, 4H), 1.49 – 1.40 (m, 4H). **^{13}C NMR** (400 MHz, $CDCl_3$): δ 138.6, 114.5, 71.4, 70.3, 60.6, 33.4, 29.0, 25.2. **ESI-TOF MS:** calcd. for $C_{15}H_{27}N_3O_2$ (281.2103);found 304.2001 $[M + Na]^+$.

3.4.2. Synthesis of Acetal-[G*n*]-yne, where n = 2, 3



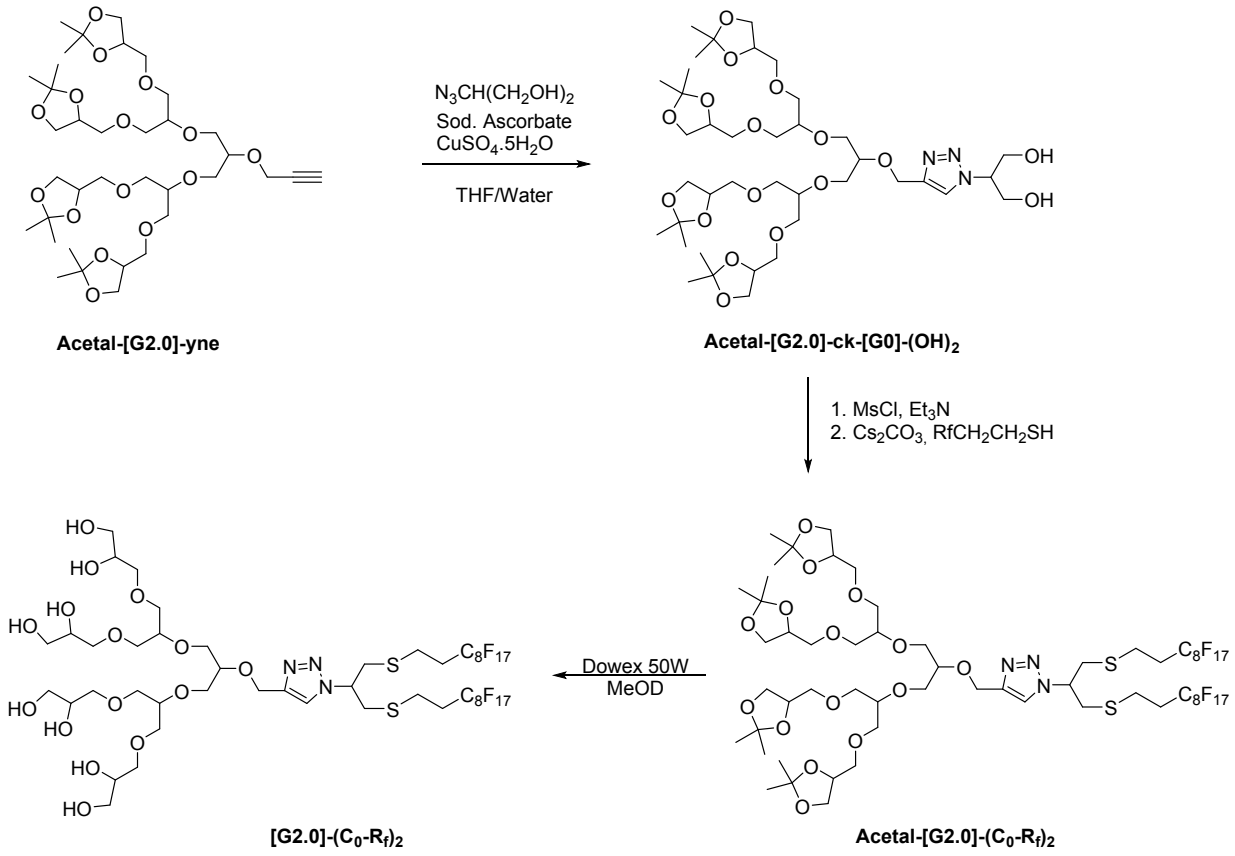
Acetal-[G2.0]-yne: The title compound was synthesized according to the general procedure A2, with [G2.0]-OH (10.0 g, 14.35 mmol, 1.0 equiv.), NaH (60% in mineral oil) (1.45 g, 43.05 mmol, 3.0 equiv.), propargyl bromide (80% in toluene) (3.70 mL, 28.70 mmol, 2.0 equiv.), cat. amount KI, 15-C-5 and 18-C-6 in THF (100 mL). Purification of the residue by silica gel column chromatography with EtOAc/*n*-hexane (3:1→6:1, v/v) providing title compound (10.02 g, 95%) as a colourless oil. **^{1}H NMR** (250 MHz, $CDCl_3$): δ 4.23 (dd, J = 2.4, 1.3 Hz, 2H), 4.21 – 4.09 (m, 4H), 3.95 (dd, J = 8.2, 6.4 Hz, 4H), 3.77– 3.68 (m, 1H), 3.63 (dd, J = 8.2, 6.4 Hz, 4H), 3.60–3.37 (m_{broad}, 23H), 2.36 (p, J = 2.5 Hz, 1H), 1.32 (s, 12H, CH_3), 1.26 (s, 12H, CH_3). **^{13}C NMR** (67.5 MHz, $CDCl_3$): δ 109.3, 78.4, 78.3, 74.5, 72.4, 71.9, 71.7, 71.6, 69.7, 66.7, 57.4, 26.6, 25.3. **ESI-TOF MS** calcd. for $C_{36}H_{62}O_{15}$ (734.4089); found 757.3994 [M + Na]$^{+}$.



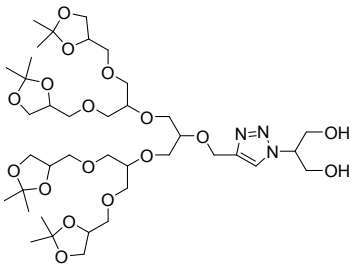
Acetal-[G3.0]-yne: The title compound was synthesized according to the general procedure A2, with [G3.0]-OH (10.0 g, 6.90 mmol, 1.0 equiv.), NaH (60% in mineral oil) (0.69 g, 20.69 mmol, 3.0 equiv.), propargyl bromide (80 % in toluene) (1.97 mL, 13.80 mmol, 2.0 equiv.), cat. amount KI, 15-C-5 and 18-C-6 in THF (100 mL). Purification of the residue by silica gel column chromatography with EtOAc/*n*-hexane (3:1→6:1, v/v) providing title compound (9.85 g, 96 %) as a colourless oil.**^{1}H-NMR** (400 MHz, $CDCl_3$): δ 4.30 (d, J = 2.1 Hz, 2H), 4.25 – 4.16 (m, 8H), 4.01 (dd, J = 8.1, 6.5 Hz, 8H), 3.68 (dd, J = 8.3, 6.2 Hz, 8H), 3.74 – 3.40 (m_{broad},

51H), 2.45 – 2.41 (m, 1H, *J* = 2.5Hz), 1.37 (s, 24H, CH_3), 1.31 (s, 24H, CH_3). **^{13}C-NMR** (100 MHz, $CDCl_3$): δ 109.2, 80.5, 78.8, 78.6, 78.3, 74.7, 74.5, 72.4, 71.9 71.7, 71.6, 69.7, 66.7, 57.4, 26.70, 25.3. **ESI-TOF MS** calcd. for $C_{72}H_{126}O_{31}$ (1486.8283); found 1509.8193 [M + Na]$^+$.

3.4.3. Synthesis of [G2.0]-(C_0-R_f)$_2$.

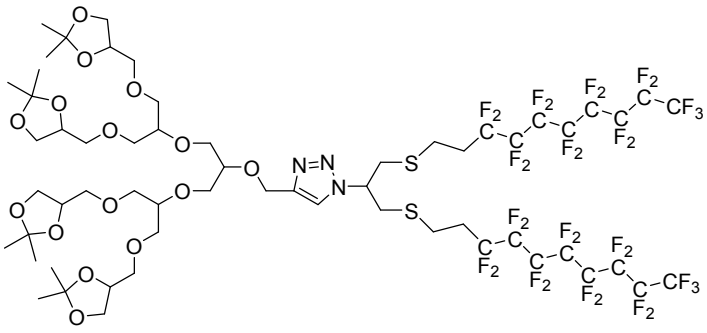


Scheme 4: Synthesis of [G2.0]-(C_0-R_f)$_2$.

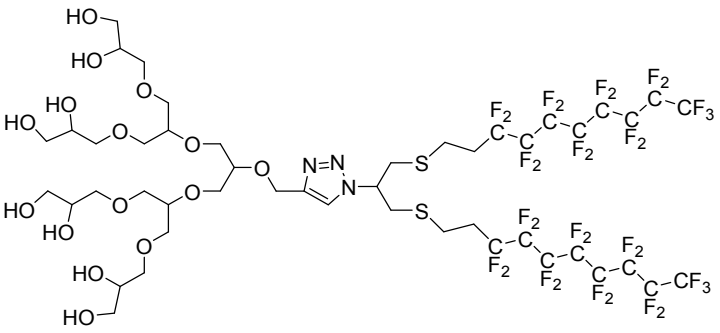


Acetal-[G2.0]-ck-[G0]-(OH)$_2$: The title compound was synthesized according to the general procedure C, with **Acetal-[G2.0]-yne** (2.5 g, 3.4 mmol, 1.0 equiv.), **[G0]-N_3** (0.550 g, 4.696 mmol, 1.4 equiv.), DIPEA (400 µL, 2.4 mmol, 0.69 equiv.), sodium ascorbate (0.277 g, 1.4 mmol, 0.4 equiv.) and copper(II) sulfate

pentahydrate (0.125 g, 0.5 mmol, 0.15 equiv.) in THF/H_2O (27 mL). Purification by column chromatography (10-25% isopropanol/hexane) gives a desired product (2.47 g, 84%). **^{1}H NMR** (500 MHz, MeOD-d_4) δ 8.08 (s, 1H), 4.81 – 4.77 (m, 2H), 4.70 (p, J = 5.8 Hz, 1H), 4.24 (p, J = 5.9 Hz, 4H), 4.05 – 4.00 (m, 4H), 3.99 – 3.95 (m, 3H), 3.94 – 3.89 (m, 1H), 3.78 – 3.63 (m_{broad}, 10H), 3.63 – 3.44 (m_{broad}, 17H), 1.37 (s, 12H), 1.32 (s, 12H). **^{13}C NMR** (125 MHz, MeOD-d_4): δ 110.4, 79.8, 76.2, 76.2, 76.1, 76.1, 73.4, 72.4, 71.3, 67.7, 67.6, 67.6, 66.6, 64.7, 64.4, 62.2, 27.1, 25.7, 25.3. **HRMS** calcd. for $C_{39}H_{69}N_3O_{17}$ (851.4627); found 874.4531 [M + Na]$^+$.

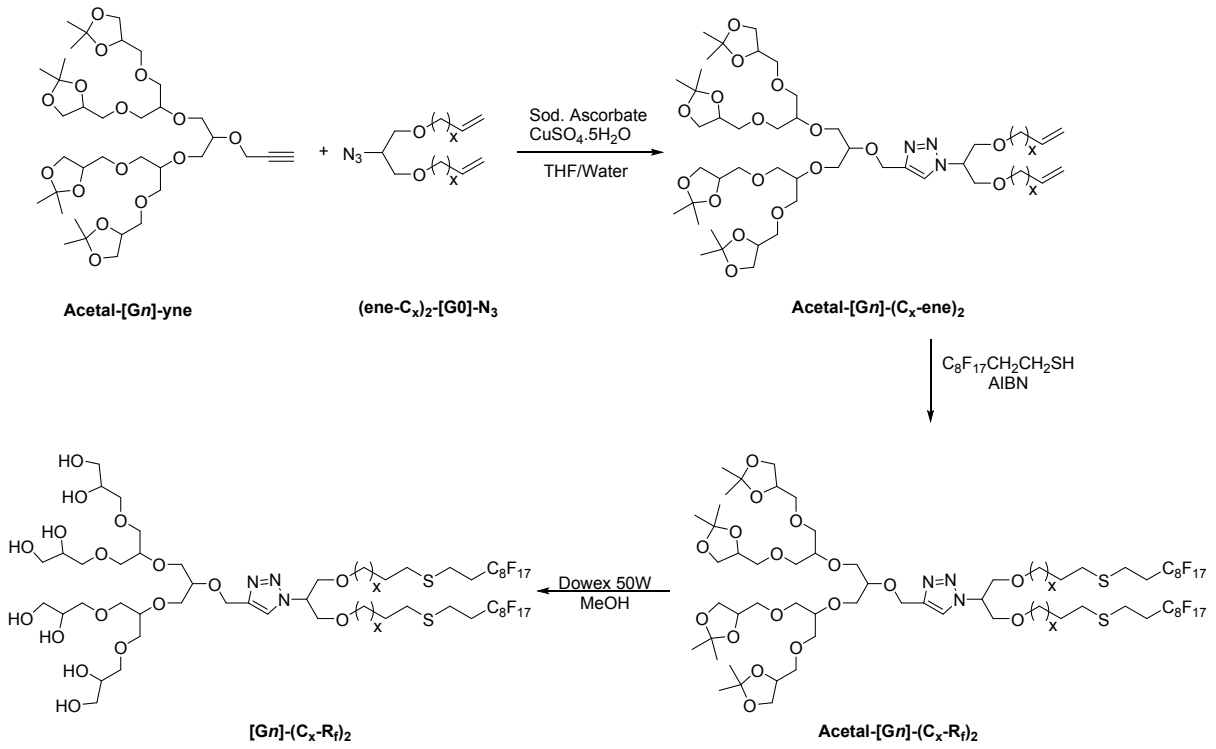


Acetal-[G2.0]-(C_0-R_f)$_2$: The title compound was synthesized according to the general procedure B1, with **Acetal-[G2.0]-ck-[G0]-(OH)$_2$** (1.3 g, 2.74 mmol, 1.0 equiv.) Et_3N (0.68 g, 6.71 mmol, 2.5 equiv.) and MsCl (0.72 g, 6.3 mmol, 2.3 equiv.) in dry toluene (10 mL) resulting a crude **[G2.0]-ck-[G0]-(OMs)$_2$**. To the mesylate solution in dioxane (15 mL) Cs_2CO_3 (4.8 g, 14.73 mmol, 5.4 equiv.) and $C_8F_{17}CH_2CH_2SH$ (6.8 g, 14.16 mmol, 5.2 equiv.) were added. Purification by column chromatography (15-25% isopropanol/hexane) lead to the title compound (540 mg, 11%). **^{1}H NMR** (500 MHz, MeOD-d_4): δ 8.05 (br s, 1H), 4.80 - 4.79 (m, 2H), 4.7 (tt, J= 6.4, 5.3 Hz, 1H), 4.27 - 4.22 (m, 4H), 4.06 - 4.02 (m, 4H), 3.99 (dd, J = 11.0, 6.5 Hz), 3.96 (dd, J = 11.0, 5.0 Hz), 3.75 - 3.48 (m_{broad}, 27H), 1.38 (s, 12H), 1.32 (s, 12H). **^{13}C NMR** (125 MHz, MeOD-d_4): δ 124.9, 110.5, 79.9, 76.3, 76.2, 73.4, 72.4, 71.3, 67.8, 67.6, 67.6, 66.6, 64.4, 62.3, 48.9, 27.2, 27.1, 25.7. **HRMS** calcd. for $C_{59}H_{75}F_{34}N_3O_{15}S_2$ (1775.4097); found 1798.3991 [M + Na]$^+$.



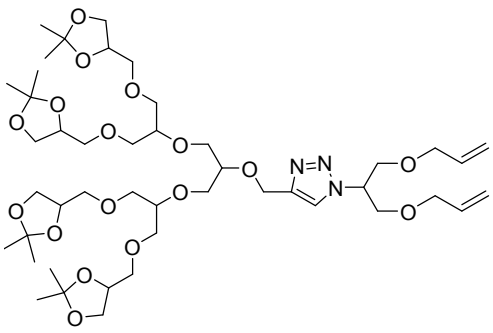
[G2.0]-(C_0-R_f)$_2$: Reaction conditions and workup were as described above according to the deprotection procedure with **Acetal-[G2.0]-(C_0-R_f)$_2$** (200 mg, 0.17 mmol). Evaporation of the solvent gives title compound (0.16 g, 88%). **^{1}H NMR** (500 MHz, MeOD-d_4) δ 8.16 (s, 1H), 4.82 – 4.76 (m, 1H), 4.59 (s, 2H), 3.80 – 3.71 (m, 6H), 3.71 – 3.64 (m, 4H), 3.64 – 3.41 (m$_{broad}$, 25H), 3.32 – 3.25 (m, 2H), 3.18 (dd, J = 14.4, 9.0 Hz, 2H), 2.80 – 2.62 (m, 4H), 2.45 (tt, J = 17.5, 7.9 Hz, 4H). **^{13}C NMR** (125 MHz, MeOD-d_4): δ 125.3, 101.3, 79.9, 78.9, 74.0, 73.9, 72.9, 72.5, 72.3, 72.2, 71.2, 64.5, 64.4, 64.3, 62.8, 49.1, 48.9, 36.9, 32.9, 32.8, 32.6, 23.6. **HRMS** calcd. for $C_{47}H_{59}F_{34}N_3O_{15}S_2$ (1615.2815); found 1638.2685 $[M + Na]^+$.

3.4.4. Synthesis of [G*n*]-(C_x-R_f)$_2$, where n = 2, 3 and x = 3, 6



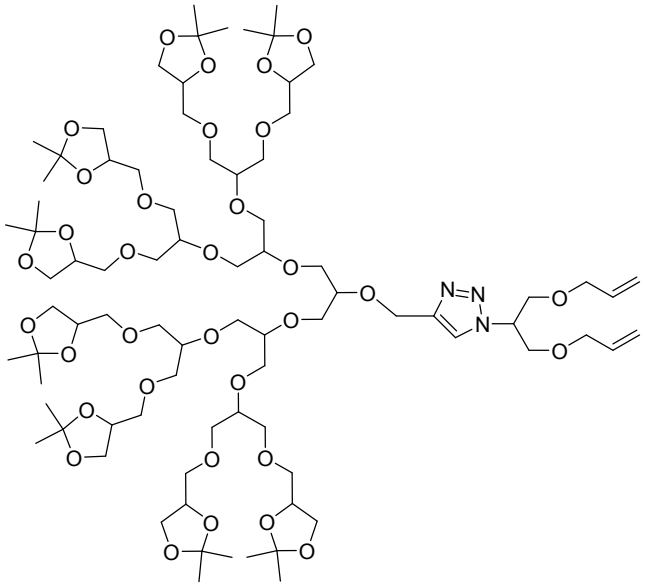
Scheme 5: Synthesis of [G*n*]-(C_x-R_f)$_2$, where n = 2, 3 and x = 3, 6 (shown: [G2.0]-(C_x-R_f)$_2$)

Acetal-[G*n*]-(C_x-ene)$_2$, where n = 2, 3 and x = 3, 6

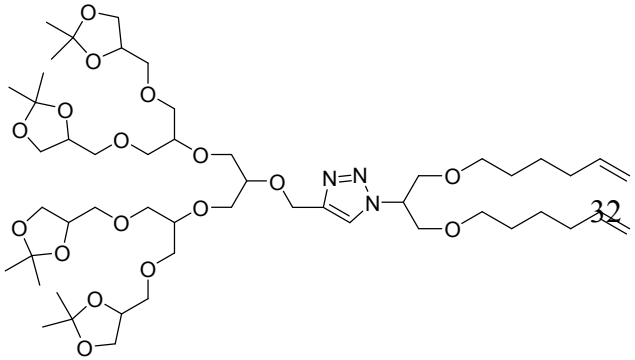


Acetal-[G2.0]-(C_3-ene)$_2$: The title compound was synthesized according to the general procedure C, with **Acetal-[G2.0]-yne** (1.81 g, 2.47 mmol, 1.0 equiv.), **(ene-C_3)$_2$-[G0]-N_3** (0.535 g, 2.71 mmol, 1.1 equiv.), DIPEA (61.2 µL, 0.37 mmol, 0.15 equiv.), sodium ascorbate (0.147 g, 0.74 mmol, 0.3 equiv.) and copper(II) sulfate pentahydrate (92 mg, 0.37 mmol, 0.15 equiv.) in THF/H_2O (6 mL). Purification by column chromatography (15% isopropanol in *n*-hexane and 2% MeOH in DCM) gives title compound (2.15 g, 93 %). **^{1}H NMR** (500 MHz, $CDCl_3$): δ 7.70 (s, 1H), 5.84–5.74 (m, 2H), 5.23–5.11 (m, 4H), 4.85 (q, J = 5.7 Hz, 1H), 4.75 (s, 2H), 4.24–4.15 (m, 4H), 4.03–3.92 (m, 8H), 3.82 (d, J = 5.7 Hz, 4H), 3.75–3.40 (m_{broad}, 27H), 1.36 (s, 12 H), 1.30 (s, 12 H). **^{13}C NMR** (125 MHz, $CDCl_3$): δ 145.0,

133.9, 122.9, 117.5, 109.2, 78.6, 78.3, 72.2, 71.8, 71.2, 72.42, 66.7, 63.9, 60.6, 26.7, 25.3. **ESI-TOF MS:** calcd. for $C_{45}H_{77}N_3O_{17}$ (931.5253); found 954.5142 $[M + Na]^+$.

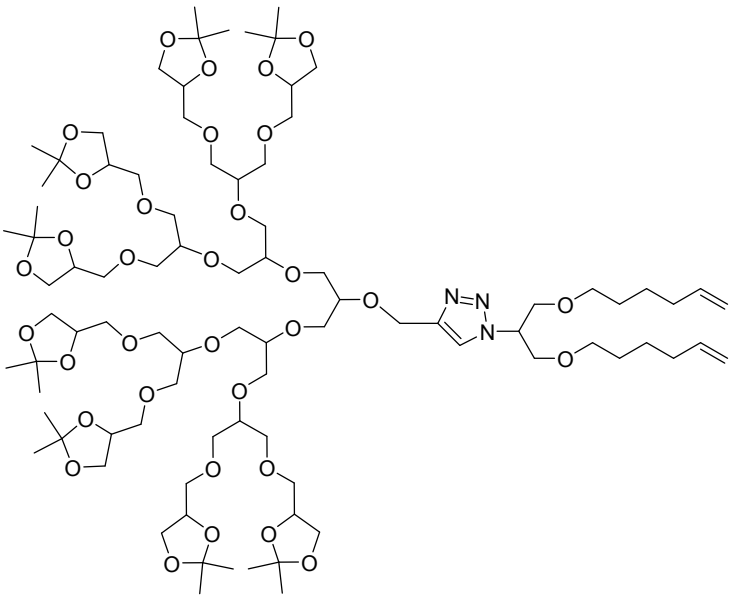


Acetal-[G3.0]-(C_3-ene)$_2$: The title compound was synthesized according to the general procedure C, with **Acetal-[G3.0]-yne** (2.21 g, 1.484 mmol, 1.0 equiv.), **(ene-C_3)$_2$-[G0]-N_3** (0.322 g, 1.632 mmol, 1.1 equiv.), DIPEA (36.8 µL, 0.223 mmol, 0.15 equiv.), sodium ascorbate (0.088 g, 0.445 mmol, 0.3 equiv.) and copper(II) sulfate pentahydrate (0.056 g, 0.223 mmol, 0.15 equiv.) in THF/H_2O (8 mL). Purification by column chromatography (20% isopropanol in *n*-hexane and 3% MeOH in CH_2Cl_2) gives a title compound (2.31 g, 92%). **^{1}H NMR** (500 MHz, $CDCl_3$): δ 7.71 (s, 1H), 5.79 (ddt, J = 17.3, 10.7, 5.6 Hz, 2H), 5.19 (dq, J = 17.3, 1.7 Hz, 2H), 5.15 (dq, J = 10.4, 1.4 Hz,2H), 4.84 (p, J = 5.8 Hz, 1H), 4.76 (s, 2H), 4.21 (m, 8H), 4.02 – 3.98 (m, 8H), 3.94 (dt, J = 5.6, 1.3 Hz, 4H), 3.83 (d, J = 5.7 Hz, 4H), 3.73 – 3.65 (m, 8H), 3.65 – 3.37 (m_{broad}, 51H), 1.36 (s, 24H), 1.30 (s, 24H). **^{13}C NMR** (125 MHz, $CDCl_3$): δ 144.9, 133.9, 122.8, 117.4, 109.2, 78.5, 78.2, 74.6, 74.5, 72.1, 71.8, 71.1, 70.5, 69.9, 68.7, 72.4, 66.6, 63.8, 60.5, 26.7, 25.3. **ESI-TOF MS:** calcd. for $C_{81}H_{141}N_3O_{33}$ (1683.9447); found 864.9635 $[M + Na]^{2+}$, 1706.9375 $[M+Na]^+$.



Acetal-[G2.0]-(C_6-ene)$_2$: The title compound was synthesized according to the general procedure C with **Acetal-**

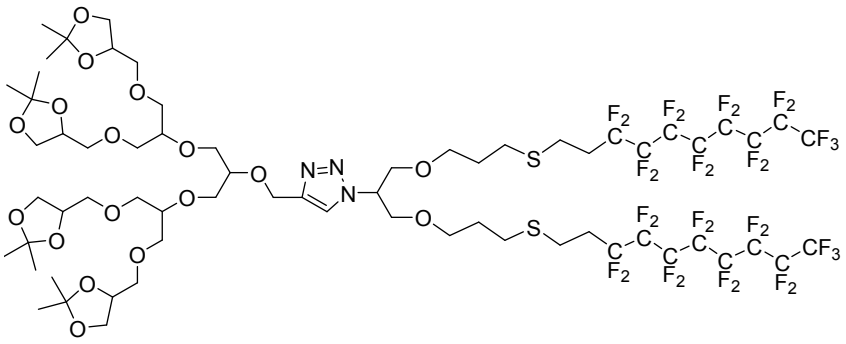
[G2.0]-yne (2.391 g, 3.256 mmol), **(ene-C_6)$_2$-[G0]-N_3** (1.008 g, 3.581 mmol), DIPEA (126 mg, 0.977 mmol), sodium ascorbate (194 mg, 0.977 mmol) and $CuSO_4$ x 5 H_2O (122 mg, 0.488 mmol) in 3 mL THF. Extraction with DCM (3 x 75 mL) and purification by column chromatography over silica gel (EtOAc/*n*-hexane, 1:1, then 6:1) yielded title compound as pale yellow oil (2.53 g, 76%). **^{1}H NMR** (500 MHz, $CDCl_3$): δ 7.68 (s, 1H), 5.75 (tdd, J = 16.9, 10.2, 6.7 Hz, 2H), 4.96 (dq, J = 17.1, 1.6 Hz, 2H), 4.92 (ddt, J = 10.2, 2.0, 1.1 Hz, 2H), 4.85 – 4.80 (m, 1H), 4.75 (s, 2H), 4.21 (ddp, J = 8.6, 5.7, 3.0 Hz, 4H), 4.03 – 3.98 (m, 4H), 3.79 (d, J = 5.7 Hz, 4H), 3.68 - 3.43 (m_{broad}, 27H), 3.40 (tdd, J = 9.4, 6.4, 2.8 Hz, 4H), 2.01 (q, J = 14.3, 7.2 Hz, 4H), 1.56 – 1.49 (m, 4H), 1.35 (m, 4H), 1.37 (s, 12H), 1.32 (s, 12H) ppm. **^{13}C NMR** (400 MHz, $CDCl_3$): δ 144.9, 138.4, 122.7, 114.6, 109.2, 78.4, 78.3, 74.5, 72.4, 71.4, 71.3, 69.3, 66.7, 63.8, 60.4, 33.3, 28.7, 26.7, 25.3, 25.2 ppm. **ESI-TOF MS:** calcd. for $C_{51}H_{89}N_3O_{17}$ (1015.6192); found 1016.6282 $[M + H]^+$.



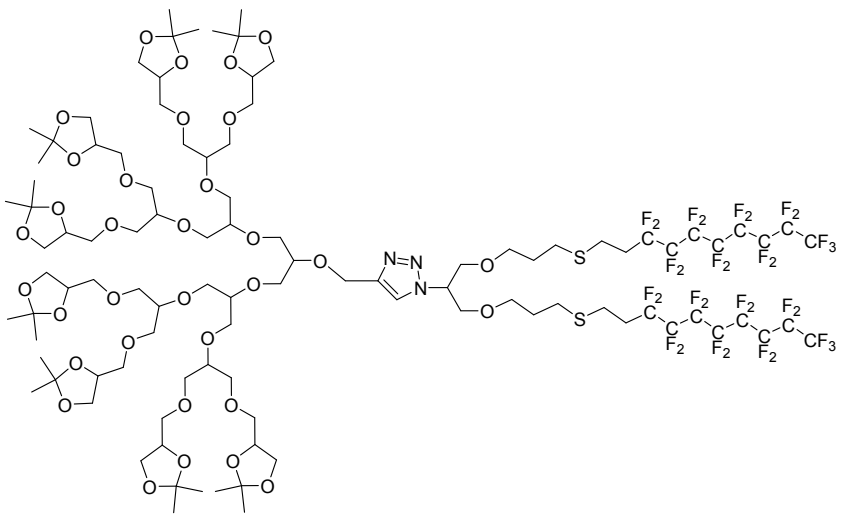
Acetal-[G3.0]-(C_6-ene)$_2$: The title compound was synthesized according to the general procedure C with **Acetal-[G3.0]-yne** (1.536 g, 1.032 mmol), **(ene-C_6)$_2$-[G0]-N_3** (0.32 g, 1.137 mmol), DIPEA (40 mg, 0.310 mmol), sodium ascorbate (61 mg, 0.310 mmol) and $CuSO_4$ x 5H_2O (39 mg, 0.155 mmol) in 3 mL THF. Extraction with DCM (3 x 75 mL) and purification by filtration over silica gel with 5% EtOAc in n-hexane, afterwards 35% *i*-propanol in n-hexane yielded title compound as pale brown oil (1.05 g, 58%). The regio-isomer ratio resulting from

the "click"-coupling is 87:13 (calculated from ^{1}H NMR). **^{1}H NMR** (500 MHz, $CDCl_3$): δ 7.68 (s, 1H), 5.75 (ddt, J = 16.9, 10.2, 6.7 Hz, 2H), 4.97 (dq, J = 17.1, 1.7 Hz, 2H), 4.94 – 4.90 (m, 2H), 4.82 (qd, J = 11.3, 5.5 Hz, 1H), 4.76 (s, 2H), 4.21 (p, J = 5.5 Hz, 8H), 4.07 – 3.95 (m, 8H), 3.79 (dt, J = 6.8, 3.2 Hz, 4H), 3.74 – 3.64 (m, 8H), 3.64 - 3.47 (m_{broad}, 55H), 2.02 (dd, J = 14.4, 7.1 Hz, 4H), 1.53 (td, J = 14.6, 6.6 Hz, 4H), 1.38 (s, 24H), 1.36 (m, 4H), 1.32 (s, 24H) ppm. **^{13}C NMR** (400 MHz, $CDCl_3$): δ 144.9, 138.4, 122.7, 114.6, 109.2, 78.5, 78.3, 74.5, 72.4, 71.4, 71.3, 69.3, 66.7, 63.9, 60.4, 33.3, 28.8, 26.7, 25.3, 25.2 ppm. **ESI-TOF MS**: calcd. for $C_{87}H_{153}N_3O_{33}$ (1768.0386); found: 1791.0324 $[M + Na]^+$.

Acetal-[G*n*]-(C_x-R_f)$_2$, where n = 2, 3 and x = 3, 6

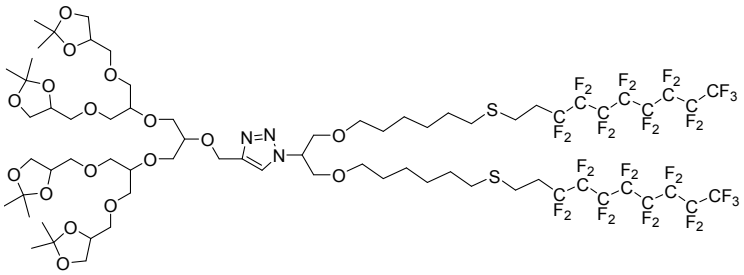


Acetal-[G2.0]-(C_3-R_f)$_2$: The title compound was synthesized according to the general procedure B2, with **Acetal-[G2.0]-(C_3-ene)$_2$** (1.4 g, 1.502 mmol, 1.0 equiv.), $C_8F_{17}CH_2CH_2SH$ (5.77 g, 12.02 mmol, 8.0 equiv.) and cat. amount AIBN. Purification by flash column (petroleum ether (40-60 °C)/CH_2Cl_2 (7:1) and EtOAc/*n*-hexane (3:1)) gives a title compound (2.67 g, 94%). **^{1}H NMR** (500 MHz, $CDCl_3$): δ 7.68 (s, 1H), 4.88 – 4.82 (m, 1H), 4.78 (s, 2H), 4.26 – 4.20 (m, 4H), 4.06 – 3.95 (m, 4H), 3.84 (d, J = 5.8 Hz, 4H), 3.74 – 3.38 (m_{broad}, 31H), 2.76 – 2.68 (m, 4H), 2.57 (t, J = 7.1 Hz, 4H), 2.44 – 2.28 (m, 4H), 1.83 (ddd, J = 13.3, 7.1, 6.1 Hz, 4H), 1.35 (s, 12H), 1.29 (s, 12H). **^{13}C NMR** (125 MHz, $CDCl_3$): δ 145.1, 122.6, 122.0-107.0 (C-F), 109.3, 74.61, 78.6, 78.5, 72.5, 71.5, 71.3, 70.3, 69.5, 66.7, 63.9, 60.4, 32.0, 29.1, 28.7, 26.7, 25.3, 22.6, ppm. **^{19}F NMR** (376 MHz, $CDCl_3$): δ –80.7, –114.2, –121.6, –121.8, –122.6, –123.2, –126.0 ppm. **ESI-TOF MS:** calcd. for $C_{65}H_{87}F_{34}N_3O_{17}S_2$ (1891.4934); found 1914.4870 $[M + Na]^+$.



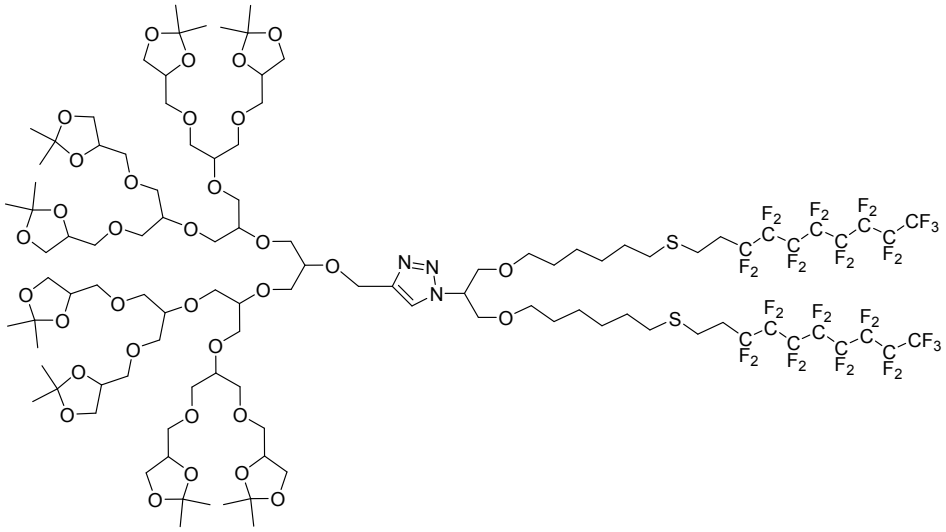
Acetal-[G3.0]-(C_3-R_f)$_2$: The title compound was synthesized according to the general procedure B2, with **Acetal-[G3.0]-(C_3-ene)$_2$** (1.3 g, 0.772 mmol, 1.0 equiv.), $C_8F_{17}CH_2CH_2SH$ (2.966 g, 6.176 mmol, 8.0 equiv.) and cat. amount AIBN. Purification by flash column (petroleum ether (40-60 °C)/CH_2Cl_2 (7:1, v/v) and EtOAc/*n*-hexane (10:1, v/v))

gives title compound (1.48 g, 73%). **^{1}H NMR** (500 MHz, $CDCl_3$): δ 7.67 (s, 1H), 4.88 – 4.76 (m, 1H), 4.76 (s, 2H), 4.24 – 4.16 (m, 8H), 4.04 – 3.98 (m, 8H), 3.87 – 3.76 (m, 4H), 3.73 – 3.65 (m, 12H), 3.64 – 3.40 (m_{broad}, 53H), 2.71 – 2.68 (m, 4H), 2.57 (t, J = 7.1 Hz, 4H), 2.34 (tt, J = 17.5, 8.6 Hz, 4H), 1.82 (p, J = 6.5 Hz, 4H), 1.37 (s, 24H), 1.32 (s, 24H) ppm. **^{13}C NMR** (125 MHz, $CDCl_3$): δ 145.1, 122.6, 122.0-107.0 (C-F), 109.3, 74.6, 78.6, 78.4, 72.5, 71.4, 70.6, 70.1, 69.5, 66.7, 63.8, 60.3, 31.9, 29.1, 28.7, 26.7, 25.3, 22.5 ppm. **^{19}F NMR** (376 MHz, $CDCl_3$): δ –80.7, –114.3, –121.7, –121.8, –122.7, –123.3, –126.1 ppm. **QFT-ESI MS:** calcd. for $C_{101}H_{151}F_{34}N_3O_{33}S_2$ (2643.9128); found 2667.748 $[M + Na]^+$.



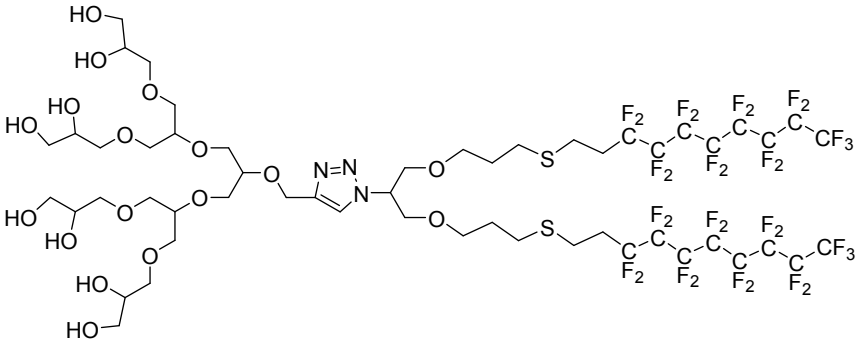
Acetal-[G2.0]-(C_6-R_f)$_2$: The title compound was synthesized according to the general procedure B2 with **Acetal-[G2.0]-(C_6-ene)$_2$** (1.510 g, 1.486 mmol) in $C_8F_{17}CH_2CH_2SH$ (5.70 g, 11.89 mmol). Purification by filtration over silica gel (PE/DCM, 7:1 followed by EtOAc/n-hexane, 5:1) yielded **Acetal-[G2.0]-(C_6-R_f)$_2$** as a colourless oil (2.421 g, 1.224 mmol, 82%), that formed a milky wax after storage in the fridge.

^{1}H NMR (500 MHz, $CDCl_3$): δ 7.69 (s, 1H), 4.85 – 4.80 (m, 1H), 4.76 (s, 2H), 4.25 – 4.19 (m, 4H), 4.03 – 3.99 (m, 4H), 3.80 (d, J = 5.6 Hz, 4H), 3.75 – 3.67 (m, 4H), 3.67 – 3.46 (m_{broad}, 23H), 3.46 – 3.36 (m, 4H), 2.73 – 2.67 (m, 4H), 2.52 (t, J = 7.3 Hz, 4H), 2.40 – 2.28 (m, 4H), 1.59 – 1.49 (m, 8H), 1.38 (s, 12H), 1.35 (m, 4H), 1.32 (s, 12H), 1.29 (m, 4H) ppm. **^{13}C NMR** (400 MHz, $CDCl_3$): δ 144.9, 122.7, 121–107 (m, C-F), 109.3, 78.6, 78.4, 74.6, 72.4, 71.4, 71.3, 69.4, 66.7, 63.9, 60.5, 32.1, 32.1, 29.3, 29.2, 28.5, 26.7, 25.6, 25.3, 22.5 ppm. **^{19}F NMR** (376 MHz, $CDCl_3$): δ -80.7 (t, J = 10.0 Hz), -114.3, -121.7, -121.9, -122.7, -123.3, -126.1 ppm. **ESI-TOF MS**: calcd. for $C_{71}H_{99}F_{34}N_3O_{17}S_2$ (1975.5873); found 1010.7823 $[M + 2\ Na]^{2+}$, 1518.5926 $[(M - RfC_2H_4SH) + Na]^+$, 1998.5762 $[M + Na]^+$.

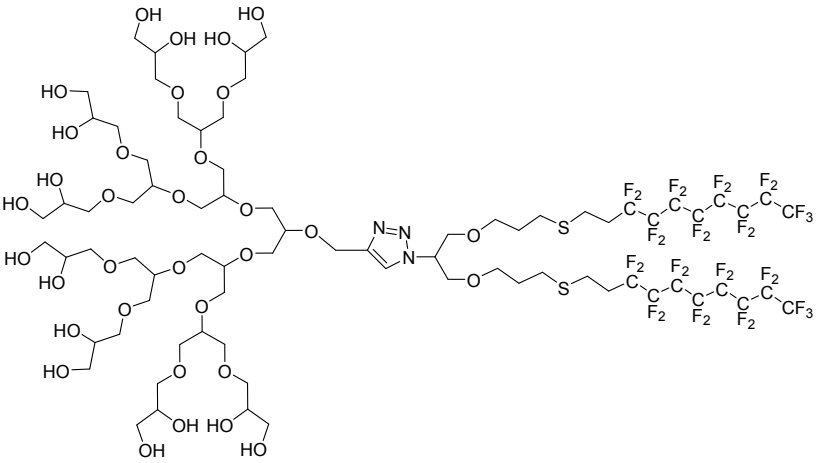


Acetal-[G3.0]-(C_6-R_f)$_2$: The title compound was synthesized according to the general procedure B2 with **Acetal-[G3.0]-(C_6-ene)$_2$** (0.796 g, 0.450 mmol) in $C_8F_{17}CH_2CH_2SH$ (1.70 g, 3.6 mmol). Purification by filtration over silica gel with a mixture of PE/DCM (7:1) followed by 35% isopropanol in n-hexane yielded title compound as a colorless oil (0.615 g, 50%), that formed a milky wax after storage in the fridge. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.68 (s, 1H), 4.85 – 4.78 (m, 1H), 4.76 (s, 2H), 4.21 (p, *J* = 5.1 Hz, 8H), 4.05 – 3.97 (m, 8H), 3.85 – 3.76 (m, 4H), 3.76 – 3.64 (m, 14H), 3.64 – 3.35 (m_{broad}, 51H), 2.70 (dd, *J* = 9.7, 6.7 Hz, 4H), 2.53 (t, *J* = 7.3 Hz, 4H), 2.43 – 2.26 (m, 4H), 1.56 (dp, *J* = 21.4, 7.0 Hz, 8H), 1.38 (s, 24H), 1.32 (s, 24H), 1.29 – 1.21 (m, 6H). **^{13}C NMR** (100 MHz, $CDCl_3$): δ 144.9, 122.7, 121-107 (m, C-F), 109.5, 78.8, 78.6, 74.9, 72.6, 71.5, 67.1, 66.9, 63.9, 60.5, 32.4, 32.0, 29.5, 29.4, 28.7, 26.9, 25.8, 25.5, 22.6. **^{19}F NMR** (376 MHz, $CDCl_3$): *δ* -80.7 (t, *J* = 10.0 Hz), -114.3 (m), -121.6, -121.8, -122.6, -123.2, -126.0. **ESI-TOF MS**: calcd. for $C_{107}H_{163}F_{34}N_3O_{33}S_2$ (2728.0067); found 2750.9805 $[M + Na]^+$.

[G*n*]-(C_x-R_f)$_2$, where n = 2, 3 and x = 3, 6

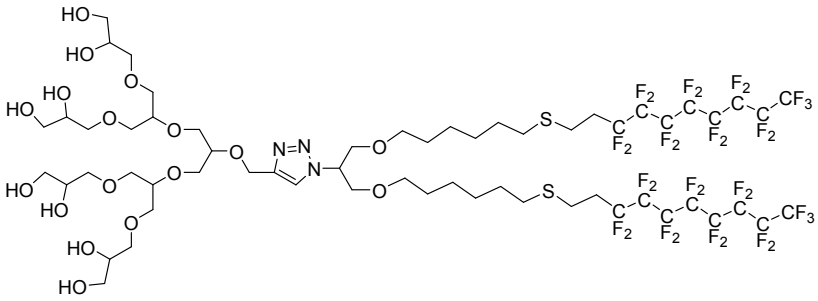


[G2.0]-(C_3-R_f)$_2$: The title compound was synthesized according to the general procedure D. Evaporation of the solvent gives title compound (1.03 g, 95%). **^{1}H NMR** (500 MHz, MeOD-d_4) (500 MHz, $CDCl_3$/MeOD-d_4) δ 7.72 – 7.67 (m, 1H), 4.72 (p, J = 5.6 Hz, 1H), 4.64 – 4.54 (m, 2H), 3.68 (d, J = 5.8 Hz, 4H), 3.64 – 3.55 (m, 6H), 3.55 – 3.48 (m, J = 10.5, 5.2, 4.7 Hz, 5H), 3.45 – 3.28 (m, 28H), 2.53 (dd, J = 9.5, 6.8 Hz, 4H), 2.40 (t, J = 7.1 Hz, 4H), 2.26 – 2.11 (m, 4H), 1.65 (p, J = 6.5 Hz, 4H). **^{13}C NMR** (100 MHz, $CDCl_3$/MeOD-d_4) δ 144.8, 123.8, 122.0-107.0 (C-F),78.8, 77.8, 73.1, 71.3, 71.0, 69.9, 69.7, 63.7, 61.1, 32.4, 32.2, 32.0, 29.3, 28.9, 22.8. **^{19}F NMR** (471 MHz, $CDCl_3$/MeOD-d_4 1:6): δ -81.2 (t, J = 10.7 Hz), -114.6 – -114.8 (m), -122.1, -122.3, -123.1, -123.7, -126.6. **QFT-ESI MS:** calcd. for $C_{53}H_{71}F_{34}N_3O_{17}S_2$ (1731.3682); found 1754.3557 $[M + Na]^+$.

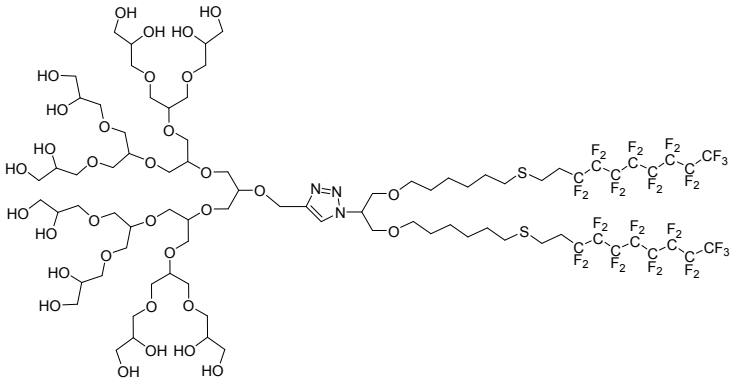


[G3.0]-(C_3-R_f)$_2$: The title compound was synthesized according to the general procedure D. Evaporation of the solvent gives title compound (0.32 g, 96%). **^{1}H NMR** (500 MHz, $CDCl_3$/MeOD-d_4 1:5) δ 7.69 – 7.66 (m, 1H), 4.72 (p, J = 5.6 Hz, 1H), 4.60 (s, 2H), 3.69 (d, J =

5.8 Hz, 4H), 3.66 – 3.58 (m, 10H), 3.58 – 3.47 (m, 16H), 3.48 – 3.27 (m_{broad}, 61H), 3.17 (dt, *J* = 3.3, 1.6 Hz, 2H), 2.58 – 2.52 (m, 4H), 2.43 (t, *J* = 7.1 Hz, 4H), 2.27 – 2.13 (m, 4H), 1.67 (p, *J* = 6.5 Hz, 4H). **^{13}C NMR** (100 MHz, $CDCl_3$/MeOD-d_4 1:5) δ 144.7, 123.2, 117.5, 110.6, 78.7, 78.5, 78.4, 78.0, 72.7, 71.8, 71.2, 71.0, 70.8, 70.7, 69.9, 69.6, 69.5, 69.3, 63.3, 60.5, 49.5, 32.0, 31.8, 31.6, 28.9, 28.6, 22.4. **^{19}F NMR** (471 MHz, $CDCl_3$/MeOD-d_4 6:1) δ -81.2 (t, *J* = 9.8 Hz), -114.5 – -114.7 (m); -121.98, -122.21, -123.03, -123.60, -126.46. **ESI-TOF MS:** calcd. for $C_{77}H_{119}F_{34}N_3O_{33}S_2$ (2323.6624); found 2346.6524 $[M + Na]^+$.



[G2.0]-(C_6-R_f)$_2$: The title compound was synthesized according to the general procedure D with **Acetal-[G2.0]-(C_6-R_f)$_2$** (0.963 g, 0.487 mmol, 1.0 equiv.) Dowex® 50W (2.0 g) in methanol (25 ml) /DCM (10 mL). Removal of the solvent under reduced pressure gives a title compound (0.85 g, 96%). **^{1}H NMR** (500 MHz, MeOD-d_4) δ 8.06 (br s, 1H), 4.99 – 4.93 (m, 1H), 4.82 – 4.77 (m, 2H), 3.87 (qd, *J* = 10.3, 5.9 Hz, 4H), 3.81 – 3.73 (m, 6H), 3.73 – 3.67 (m, 4H), 3.66 – 3.40 (m_{broad}, 29H), 2.79 – 2.71 (m, 4H), 2.59 (t, *J* = 7.3 Hz, 4H), 2.46 (tt, *J* = 17.6, 8.2 Hz, 4H), 1.57 (dp, *J* = 21.0, 6.8 Hz, 8H), 1.41 (dt, *J* = 14.6, 7.0 Hz, 4H), 1.39 – 1.26 (m, 4H). **^{13}C NMR** (125 MHz, MeOD-d_4) δ 125.0, 79.9, 74.0, 74.0, 72.4, 72.3, 72.2, 70.6, 64.4, 32.9, 30.4, 29.5, 26.7, 23.3. **^{19}F NMR** (471 MHz, MeOD-d_4) δ -82.3 (t, *J* = 9.9 Hz), -115.6, -122.5, -122.6, -122.8, -123.6, -124.2, -127.2. **QFT-ESI MS**: calcd. for $C_{59}H_{83}F_{34}N_3O_{17}S_2$ (1815.4621); found 919.6291 [M +H+ Na]$^{2+}$, 935.6084 $[M + NH_4 + Na]^{2+}$.



[G3.0]-(C_6-R_f)$_2$: The title compound was synthesized according to the general procedure D with **Acetal-[G3.0]-(C_6-R_f)$_2$** (0.70 g, 0.256 mmol, 1.0 equiv.) Dowex® 50W (1.4 g) in methanol (20 ml) /DCM (10 mL). Removal of the solvent under reduced pressure gives a title compound (0.57 g, 93%). **^{1}H NMR** (500 MHz, MeOD-d_4) δ 8.04 (s, 1H), 5.00 – 4.88 (m, 1H), 4.82 – 4.79 (m, 2H), 3.91 – 3.84 (m, 4H), 3.81 – 3.70 (m, 12H), 3.73 – 3.66 (m, 12H), 3.66 – 3.41 (m_{broad}, 59H), 2.77 – 2.72 (m, 4H), 2.59 (t, J = 7.3 Hz, 4H), 2.53 – 2.39 (m, 4H), 1.62 – 1.52 (m, 8H), 1.45 – 1.37 (m, 4H), 1.37 – 1.26 (m, 4H). **^{13}C NMR** (101 MHz, MeOD-d_4) δ 145.9, 124.7 (122-107, C-F), 79.6, 78.1, 73.7, 71.9, 70.9, 70.4, 69.3, 64.3, 64.2, 62.1, 32.6, 30.2, 29.3, 25.6, 23.12. **^{19}F NMR** (376 MHz, MeOD-d_4): δ -80.6 (t, J = 10.0 Hz), -114.2, -121.6, -121.8, -122.6, -123.2, -126.0. **ESI-TOF MS**: calcd. for $C_{83}H_{131}F_{34}N_3O_{33}S_2$ (2407.7563); found 2430.7241 $[M + Na]^+$.