

Synthesis and Electrochemical Characterization of 4-Thio Pseudo-Glycolipids as Candidate Tethers for Lipid Bilayer Models.

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Supporting Information 1

- General Synthetic methods
- Analytical data for compound **3–4, 7, 10, 11**
- Figure S1

1. General synthetic methods. ^1H NMR (400.13 or 600.13 MHz) and ^{13}C NMR (100.6 or 150.9 MHz) spectra were recorded in CDCl_3 (internal standard, for ^1H residual CHCl_3 δ 7.24; for ^{13}C CDCl_3 δ 77.0), CD_3OD (internal standard, for ^1H residual CD_3HOD δ 3.31; for ^{13}C CD_3OD δ 49.15), $(\text{CD}_3)_2\text{SO}$ (internal standard, for ^1H residual $(\text{CD}_2\text{H})_2\text{SO}$ δ 2.50; for ^{13}C $(\text{CD}_3)_2\text{SO}$ δ 39.51) or a mixture of CDCl_3 and CD_3OD . Chemical shifts (ppm) and coupling constants (J , Hz) were obtained from a first-order analysis of one-dimensional spectra and assignments of protons and carbon resonances were based on two dimensional ^1H - ^1H homonuclear (COSY) and ^{13}C - ^1H heteronuclear (HSQC) correlation spectra. ^1H NMR data are reported using standard abbreviations: singlet (s), doublet (d), triplet (t), doublet of doublet (dd), quartet (q), multiplet (m) and broad singlet (bs). TLC analysis was performed on aluminum plates pre-coated with Silica Gel 60 (250 μm) containing a fluorescent indicator. The plates were visualized under UV and/or iodine and/or charred with a 10% solution of H_2SO_4 in EtOH. Compounds were purified by flash chromatography with Silica Gel 60 (230-400 mesh) unless otherwise stated. Solvents

were distilled and dried according to standard procedures, and organic solutions were dried over Na₂SO₄ and concentrated under reduced pressure below 50 °C. Optical rotations were measured at 22 °C and are reported as follows: [α]_D (*c* in grams per 100 mL of solvent). Commercial phytol (3,7,11,15-tetramethyl-hexadec-2-en-1-ol) (97%) was purchased as a mixture of isomers and converted in three steps to the 1-azido-3,7,11,15-tetramethyl-hexadecane (**9**) following reported literature procedures.[13-15] Mass spectra were obtained under electrospray ionization (ESI) on a high resolution mass spectrometer equipped with a TOF analyzer.

2. Analytical data for compound 3–4 7, 10, 11

2.1. 2-Propynyl 4-O-(2,3,6-tri-O-acetyl-4-S-acetyl-4-thio- β -D-glucopyranosyl)- 2,3,6-tri-O-acetyl- β -D-glucopyranoside (7). ¹H NMR (400 MHz, CDCl₃): δ 5.19 (t, 1H, *J* = 9.4 Hz, H-3), 5.15 (dd, 1H, *J* = 9.2, 11.1 Hz, H-3'), 4.90 (dd, 1H, *J* = 8.0, 9.6, H-2), 4.86 (dd, 1H, *J* = 8.1, 9.1 Hz, H-2'), 4.70 (d, 1H, *J* = 7.9 Hz, H-1), 4.53 (dd, 1H, *J* = 2.0, 12.0 Hz, H-6a'), 4.47 (d, 1H, *J* = 8.0 Hz, H-1'), 4.40 (dd, 1H, *J* = 4.7, 12.4 Hz, H-6a), 4.30 (d, 2H, *J* = 2.5 Hz, OCH₂), 4.13 (dd, 1H, *J* = 1.9, 12.3 Hz, H-6b), 4.06 (dd, 1H, *J* = 4.8, 12.0 Hz, H-6b'), 3.79 (m, 1H, H-5'), 3.75 (t, 1H, *J* = 9.3 Hz, H-4), 3.60 (t, 1H, *J* = 11.1 Hz, H-4'), 3.59 (m, 1H, H-5), 2.42 (t, 1H, *J* = 2.4 Hz, C \equiv CH), 2.29 (s, 3H, SCOCH₃), 2.10, 2.06, 2.01, 1.98, 1.96 (5s, 18H, 5 \times OCOCH₃). ¹³C NMR (100 MHz, CDCl₃): δ 192.5 (SC=O), 170.6, 170.3, 170.1, 169.8, 169.7, 169.2 (C=O), 100.5 (C-1'), 97.9 (C-1), 78.1 (C \equiv CH), 76.2 (C-4), 75.4 (C \equiv CH), 72.9, 72.82, 72.35 (C-3, C-5, C-2', C-5'), 71.4, 71.23 (C-2, C-3'), 62.9 (C-6'), 61.7 (C-6), 55.9 (OCH₂), 43.7 (C-4'), 30.73 (SCOCH₃) 20.9, 20.7, 20.6, 20.53 (OCOCH₃). HRESIMS (*m/z*): [M + NH₄]⁺ calcd C₂₉H₄₂NO₁₇S 708.2173, found 708.2162.

2.2. 1-(3,7,11,15-tetramethylhexadecane)-4-(4-O-[2,3,6-tri-O-acetyl-4-S-acetyl-4-thio- β -D-glucopyranosyl]-2,3,6-tri-O-acetyl- β -D-glucopyranosyloxymethyl)-[1,2,3]-triazole (10). ¹H

NMR (400 MHz, (CD₃)₂SO): δ 8.07 (s, 1H, =CH), 5.29 (dd, 1H, J = 9.2, 11.1 Hz, H-3'), 5.14 (t, 1H, J = 9.4 Hz, H-3), 4.80 (d, 1H, J = 8.1 Hz, H-1), 4.74 (d, 1H, J = 12.0 Hz, OCHH), 4.71 (d, 1H, J = 8.0 Hz, H-1'), 4.67 (dd, 1H, J = 8.1, 9.7 Hz, H-2), 4.58 (d, 1H, J = 11.9 Hz, OCHH), 4.56 (t, 1H, J = 8.1 Hz, H-2'), 4.40-4.27 (m, 4H, H-6a, H-6a', NCH₂), 4.12-3.95 (m, 3H, H-6b, H-5', H-6b'), 3.86 (m, 1H, H-5), 3.77 (t, 1H, J = 9.7 Hz, H-4), 3.58 (t, 1H, J = 11.0 Hz, H-4') 2.32 (s, 3H, SCOCH₃), 2.01, 1.96, 1.94, 1.93, 1.91, 1.89 (6s, 18H, OCOCH₃), 1.82 (m, 1H, NCH₂CHH), 1.60 (m, 1H, NCH₂CHH), 1.56-0.97 (m, 22H, N(CH₂)₂CH(CH₃)[(CH₂)₃CH(CH₃)]₃CH₃), 0.90-0.77 (3d, 15H, 5 \times CHCH₃). ¹³C NMR (100 MHz, (CD₃)₂SO): δ 193.5 (SCOCH₃), 170.4, 170.1, 170.0, 169.5, 169.4, 169.1 (C=O), 142.8 (C=CH), 124.1 (C=CH) 99.3 (C-1'), 98.4 (C-1), 76.1 (C-4), 72.6 (C-2'), 72.0 (C-3), 71.8 (C-5), 71.6 (C-5'), 71.2 (C-2), 71.0 (C-3'), 62.6 (C-6'), 62.2 (C-6), 61.9 (OCH₂), 47.6 (NCH₂), 42.9 (C-4'), 39.3, 36.9, 36.8, 36.7, 36.6, 36.4 (CH₂ \times 7), 32.1, 32.0 (CH \times 2), 30.1 (SCOCH₃), 27.4 (CH \times 2), 24.2, 23.8, 23.6 (CH₂ \times 3), 22.6, 22.5 (CH₃ \times 2), 20.7, 20.5, 20.4, 20.3, 20.2 (OCHCH₃ \times 6), 19.7, 19.6, 19.5, 19.07, 19.0 (CH₃ \times 5). HRESIMS (m/z): [M + H]⁺ calcd C₄₉H₈₀N₃O₁₇S 1014.5208, found 1014.5173.

2.3. 1-(3,7,11,15-tetramethylhexadecane)-4-(4-O-[2,3,4,6-tetra-O-acetyl- β -D-

galactopyranosyl]-2,3,6-tri-O-acetyl- β -D-glucopyranosyloxymethyl)-[1,2,3]-triazole (11). ¹H

NMR (400 MHz, CD₃OD): δ 7.96 (s, 1H, =CH), 5.35 (bd, 1H, J = 3.5 Hz, H-4'), 5.17 (t, 1H, J = 9.3 Hz, H-3), 5.11 (dd, 1H, J = 3.5, 10.4 Hz, H-3'), 5.01 (dd, 1H, J = 7.8, 10.4 Hz, H-2'), 4.86 (d, 1H, J = 12.5, OCHH), 4.83 (dd, 1H, J = 8.1, 9.5 Hz, H-2), 4.76-4.69 (m, 3H, H-1, H-1', OCHH), 4.56 (dd, 1H, J = 1.9, 12.1 Hz, H-6a), 4.44 (m, 2H, NCH₂), 4.19-4.07 (m, 4H, H-6b, H-5', H-6a', H-6b'), 3.87 (t, 1H, J = 9.8 Hz, H-4), 3.77 (m, 1H, H-5), 2.13, 2.06, 2.04, 2.03, 1.95, 1.93 (7s,

21H, OCOCH₃), 1.94 (m, 1H, NCH₂CHH), 1.71 (m, 1H, NCH₂CHH), 1.60–1.03 (m, 22H, N(CH₂)₂CH(CH₃)[(CH₂)₃CH(CH₃)]₃CH₃), 0.99–0.84 (3d, 15H, 5 × CHCH₃). ¹³C NMR (100 MHz, CD₃OD): δ 172.1, 172.0, 171.8, 171.5, 171.3, 171.2 (C=O), 145.2 (C=CH), 125.5 (C=CH), 102.2 (C-1'), 100.9 (C-1), 77.6 (C-4), 74.5 (C-3), 74.2 (C-5), 73.1 (C-2), 72.6 (C-3'), 71.8 (C-5'), 70.8 (C-2'), 68.7 (C-4'), 63.5 (C-6), 63.3 (C-6'), 62.3 (OCH₂), 49.8 (NCH₂), 40.7, 38.7, 38.6, 38.5, 38.4, 38.2 (CH₂ × 7), 34.1, 34.0, 31.5, 29.3 (CH × 4), 26.1, 25.7, 25.6, 25.5 (CH₂ × 3), 23.3, 23.2 (CH₃ × 2), 21.3, 21.0, 20.9, 20.8, 20.6, 20.4, 20.3, 20.2 (COCH₃ × 6), 19.8, 19.7 (CH₃ × 3). HRESIMS (m/z): [M + H]⁺ calcd C₄₉H₈₀N₃O₁₈ 998.5437, found 998.5394.

2.4. 1-(3,7,11,15-tetramethylhexadecane)-4-[4-O-(4-deoxy-4-thio-β-D-glucopyranosyl)-β-D-glucopyranosyloxymethyl]-[1,2,3]-triazole disulfide (3). ¹H NMR (400 MHz, CD₃OD): δ 8.01 (s, 1H, =CH), 4.96 (d, 1H, *J* = 12.4 Hz, OCHH), 4.77 (d, 1H, *J* = 12.4 Hz, OCHH), 4.49–4.35 (m, 4H, NCH₂, H-1', H-1), 3.99–3.84 (m, 3H, H-6a, H-6b, H-6a'), 3.77 (dd, 1H, *J* = 5.1, 12.1 Hz, H-6b'), 3.57 (t, 1H, *J* = 8.9 Hz, H-4), 3.51 (t, 1H, *J* = 8.8 Hz, H-3), 3.47–3.38 (m, 2H, H-5, H-5'), 3.34–3.19 (m, 3H, H-2, H-2', H-3'), 2.74 (t, 1H, *J* = 10.2 Hz, H-4'), 1.95 (m, 1H, NCH₂CHH), 1.70 (m, 1H, NCH₂CHH), 1.58–1.01 (m, 22H, N(CH₂)₂CH(CH₃)[(CH₂)₃CH(CH₃)]₃CH₃), 0.99–0.81 (3d, 15H, 5 × CHCH₃). ¹³C NMR (100 MHz, CD₃OD): δ 145.7 (C=CH), 125.3 (C=CH), 104.6 (C-1'), 103.5 (C-1), 80.7 (C-4), 79.6 (C-5 or C-5'), 78.9 (C-2 or C-2'), 76.6 (C-5 or C-5'), 76.4 (C-3), 76.1 (C-3'), 74.8 (C-2 or C-2'), 63.2 (C-6'), 63.1 (OCH₂), 61.9 (C-6), 49.7 (NCH₂), 43.3 (C-4'), 40.7, 38.7, 38.6, 38.5, 38.2 (CH₂ × 7), 34.1, 34.0, 31.5, 29.3 (CH × 4), 26.0, 25.6, 25.5 (CH₂ × 3), 23.3, 23.2, 20.4, 20.3, 20.2, 19.8, 19.7 (CH₃ × 5). HRESIMS (m/z): [M + H]⁺ calcd C₇₀H₁₂₉N₆O₂₀S₂ 1437.8703, found 1437.8650.

2.5. 1-(3,7,11,15-tetramethylhexadecane)-4-[4-O-(4-deoxy-4-thio- β -D-glucopyranosyl)- β -D-glucopyranosyloxymethyl]-[1,2,3]-triazole (4). ^1H NMR (400 MHz, CD_3OD): δ 8.01 (s, 1H, =CH), 4.97 (d, 1H, $J = 12.4$ Hz, OCHH), 4.78 (d, 1H, $J = 12.4$ Hz, OCHH), 4.49–4.35 (m, 4H, NCH₂, H-1', H-1), 4.01 (dd, 1H, $J = 2.0, 12.5$ Hz, H-6b'), 3.96–3.83 (m, 3H, H-6a, H-6b, H-6a'), 3.70 (m, 1H, H-5'), 3.65 (dd, 1H, $J = 9.0, 10.6$ Hz, H-3'), 3.61–3.50 (m, 2H, H-3, H-4'), 3.43 (m, 1H, H-5), 3.35–3.27 (m, 2H, H-2, H-2'), 2.74 (t, 1H, $J = 10.7$ Hz, H-4'), 1.95 (m, 1H, NCH₂CHH), 1.70 (m, 1H, NCH₂CHH), 1.58–1.01 (m, 22H, N(CH₂)₂CH(CH₃)[(CH₂)₃CH(CH₃)]₃CH₃), 0.99–0.83 (3d, 15H, 5 \times CHCH₃). ^{13}C NMR (100 MHz, CD_3OD): δ 145.6 (C=CH), 125.1 (C=CH), 104.1, 103.4 (C-1', C-1), 80.7 (C-3 or C-4), 77.5 (C-5'), 76.5, 76.2 (C-2, C-3 or C-4, C-5), 74.7 (C-2'), 73.7 (C-3'), 63.1 (OCH₂), 62.7 (C-6'), 61.8 (C-6), 55.7 (C-4'), 49.7 (NCH₂), 40.6, 38.6, 38.5, 38.4, 38.1 (CH₂ \times 7), 33.9, 31.5, 29.2 (CH \times 4), 26.0, 25.6, 25.4 (CH₂ \times 3), 23.3, 23.2, 20.4, 20.3, 19.8, 19.7 (CH₃ \times 5). HRESIMS (m/z): [M + H]⁺ calcd C₃₅H₆₆N₃O₁₀S 720.4463, found 720.4438.

2.6. Synthesis of 1-(3,7,11,15-tetramethylhexadecane)-4-[4-O-(β -D-galactopyranosyl)- β -D-glucopyranosyloxymethyl]-[1,2,3]-triazole (5). ^1H NMR (400 MHz, CD_3OD): δ 8.02 (s, 1H, =CH), 4.96 (d, 1H, $J = 12.4$ Hz, OCHH), 4.78 (d, 1H, $J = 12.4$ Hz, OCHH), 4.48–4.40 (m, 3H, H-1, NCH₂), 4.37 (d, 1H, $J = 7.7$ Hz, H-1'), 3.94 (dd, 1H, $J = 2.3, 12.2$ Hz, H-6a), 3.86 (dd, 1H, $J = 4.3, 12.1$ Hz, H-6b), 3.82 (bd, 1H, $J = 3.1$ Hz, H-4'), 3.78 (dd, 1H, $J = 7.6, 11.5$ Hz, H-6a'), 3.70 (dd, 1H, $J = 4.6, 11.5$ Hz, H-6b'), 3.62–3.51 (m, 4H, H-3, H-4, H-2', H-5'), 3.49 (dd, 1H, $J = 3.3, 9.7$ Hz, H-3'), 3.45 (m, 1H, H-5), 3.30 (t, 1H, $J = 8.8$ Hz, H-2), 1.93 (m, 1H, NCH₂CHH), 1.72 (m, 1H, NCH₂CHH), 1.56–1.03 (m, 22H, N(CH₂)₂CH(CH₃)[(CH₂)₃CH(CH₃)]₃CH₃), 0.98–

0.83 (3d, 15H, 5 × CHCH₃). ¹³C NMR (100 MHz, CD₃OD): δ 145.7 (C=CH), 125.3 (C=CH), 105.2 (C-1'), 103.5 (C-1), 80.6 (C-4), 77.2 (C-5'), 76.6 (C-5), 76.3 (C-3), 74.9 (C-3'), 74.7 (C-2), 72.6 (C-2'), 70.3 (C-4'), 63.2 (C-6'), 62.6 (C-6), 61.9 (CH₂O), 49.7 (NCH₂), 40.7, 38.7, 38.6, 38.5, 38.2 (CH₂ × 7), 34.1, 34.0, 31.4, 29.3 (CH × 4), 26.0, 25.6, 25.5 (CH₂ × 3), 23.3, 23.2, 20.4, 20.3, 20.2 19.8, 19.7 (CH₃ × 5). HRESIMS (m/z): [M + H]⁺ calcd C₃₅H₆₆N₃O₁₁ 704.4697, found 704.4696.

3. Figure S1

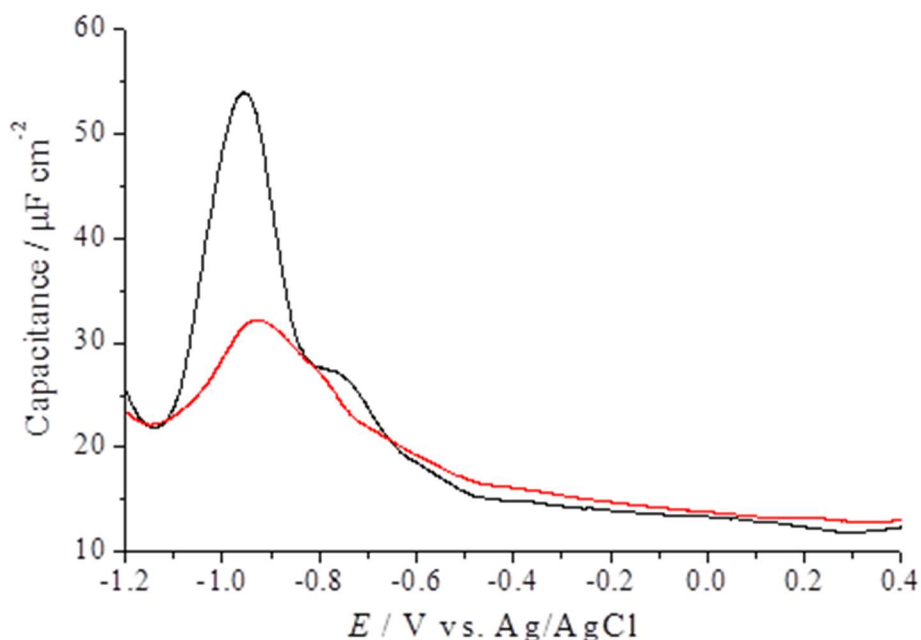


Figure S1. Differential capacitance curves of thiol **4** monolayers self-assembled in ethanol at 20 °C (black) and 40 °C (red), electrolyte: 0.1 M aq KClO₄. Thiol **4** monolayers were stable on gold surface between 0.4 V to -0.5 V and began to detach at E < -0.5 V. The desorption peak is located at -0.94 V. The minimum capacitance was 11.9 μF×cm⁻² for the monolayer self-assembled at 20 °C and 12.8 μF×cm⁻² for the monolayer self-assembled at 40 °C.