Electronic Supplementary Material (ESI) for Chemical Communications

Sweet switches: Azobenzene glycoconjugates by click chemistry

Supporting Information

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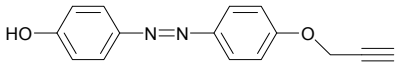
1. General methods

Thin layer chromatography was performed on silica gel plates (GF 254, Merck). Detection was effected by UV and subsequent charring with 10% sulphuric acid in EtOH followed by heat treatment at ~180 °C. Flash chromatography was performed on silica gel 60 (Merck, 230-400 mesh, particle size 0.040-0.063 mm) using distilled solvents. Optical rotations were measured with a Perkin-Elmer 241 polarimeter (sodium D-line: 589 nm, length of cell: 1 dm) in the solvents indicated. ^{1}H and ^{13}C NMR spectra were recorded on Bruker DRX-500 and AV-600 spectrometers at 300 K. Chemical shifts are reported relative to internal tetramethylsilane (δ = 0.00 ppm) or D_2O (δ = 4.76 ppm). Full assignment of the peaks was achieved with the aid of 2D NMR techniques (^{1}H-^{1}H COSY and ^{1}H-^{13}C HSQC). IR spectra were measured with a Perkin Elmer FT-IR Paragon 1000 (ATR) spectrometer. ESI mass spectra were recorded on a Esquire-LC instrument from Bruker Daltonics. MALDI-TOF mass spectra were recorded on a Bruker Biflex III instrument with 19 kV acceleration voltage. 2,5-Dihydroxybenzoic acid (DHB) was used as a matrix. Air/moisture sensitive reactions were carried out under nitrogen in dry glassware. UV-Vis absorption spectra were performed on Perkin-Elmer Lambda-241 and Varian Cary-5000 at a temperature of 18 $\pm$ 1 °C. Photoirradiaton was carried out with a high pressure mercury lamp UV-P 250C from Panacol-Elosol. The bandpass filters were obtained from "Laser" components.

2. Synthetic procedures

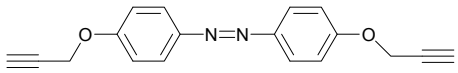
4-Hydroxy-4'-propargyloxy azobenzene (2):



A mixture of *p,p'*-dihydroxyazobenzene (**1**, 1.00 g, 4.67 mmol) and propagyl bromide (611 mg, 5.14 mmol, 1.1 equiv.) was added to acetone (50 mL) and stirred under nitrogen at room temperature for 30 min. K_2CO_3 (322 mg, 2.34 mmol, 0.5 equiv.) was added and then the reaction mixtue was refluxed for 12 h. TLC (cyclohexane/ethyl acetate, 4:1) showed a mixture of 3 spots corresponding to compounds **1**, **2**, and **3**. After the solvent was evaporated under reduced pressure, the residue was dissolved in ethyl acetate (50 mL) and washed with water (50 mL),

dried over $MgSO_4$, filtered and concentrated under reduced pressure. Purification by column chromatography on silica gel (cyclohexane/ethyl acetate, 4:1) gave the mono-substituted product **2** as a ocher solid (410 mg, 1.63 mmol, 35%) along with the disubstituted product **3** (100 mg, 0.34 mmol, 7%) and recovered **1** (420 mg, 1.96 mmol, 42%). R_f 0.20 (cyclohexane/ethyl acetate, 4:1); m.p. 134 °C; ^{1}H NMR (500 MHz, CD_3OD, 300 K, TMS): δ = 7.83 (d, *J* = 9.1 Hz, 2 aryl-H), 7.77 (d, *J* = 8.9 Hz, 2 aryl-H), 7.10 (d, *J* = 9.1 Hz, 2 aryl-H), 6.90 (d, *J* = 8.9 Hz, 2 aryl-H), 4.81 (d, *J* = 2.4 Hz, 2H, H-C≡C-C<u>H</u>$_2$), 2.98 (t, *J* = 2.4 Hz, 1H, <u>H</u>-C≡C-CH$_2$) ppm; ^{13}C NMR (125 MHz, CD_3OD, 300 K, TMS): δ = 161.6 (C_q, aryl-C), 160.9 (C_q, aryl-C), 148.8 (aryl-C), 147.5 (aryl-C), 125.6 (aryl-C), 124.9 (aryl-C), 116.7 (aryl-C), 116.3 (aryl-C), 79.5 (H-C≡<u>C</u>-CH$_2$), 77.1 (H-<u>C</u>≡C-CH$_2$), 56.9 (H-C≡C-<u>C</u>H$_2$),ppm; ESI MS calcd for $C_{15}H_{12}N_2O_2$: *m/z* 253.0898 $[M+1]^+$; found: *m/z* 253.0966 $[M+1]^+$; IR (ATR) 3264 (C≡C), 1588, 1504, 1270, 1024, 826, 676 cm^{-1}.

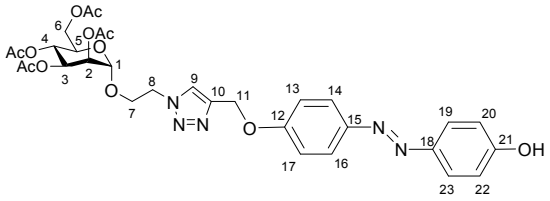
4,4'-Di-propargyloxy azobenzene (3):[1]



A mixture of *p,p'*-dihydroxyazobenzene (**1**, 100 mg, 0.467 mmol) and propagyl bromide (278 mg, 2.34 mmol, 5.0 equiv.) was added to acetone (5 mL) and the reaction mixture stirred under nitrogen at room temperature for 30 min. Then, K_2CO_3 (322 mg, 2.34 mmol, 5 equiv.) was added and the reaction mixture was refluxed for 16 h. TLC (cyclohexane/ethyl acetate, 4:1) showed a spot-to-spot conversion of product **3**. After the solvent was evaporated under reduced pressure, the residue was dissolved in ethyl acetate (30 mL) and washed with water (10 mL), dried over $MgSO_4$, filtered and concentrated under reduced pressure. Purification by column chromatography on silica gel (cyclohexane/ethyl acetate, 4:1) gave the disubstituted product **3** (123 mg, 0.42 mmol, 91%) as a yellow solid. R_f 0.45 (cyclohexane/ethyl acetate, 4:1); m.p. 191 °C; ^{1}H NMR (500 MHz, $CDCl_3$, 300 K, TMS): δ = 8.22 (d, *J* = 9.2 Hz, 4 aryl-H), 7.05 (d, *J* = 9.2 Hz, 4 aryl-H), 4.79 (d, *J* = 2.4 Hz, 4H, 2 H-C≡C-C<u>H</u>$_2$), 2.58 (d, *J* = 2.4 Hz, 2H, 2 <u>H</u>-C≡C-CH$_2$) ppm; ^{13}C NMR (125 MHz, $CDCl_3$, 300 K, TMS): δ = 162.3 (C_q, aryl-C), 142.2 (C_q, aryl-C), 125.8, 115.0 (aryl-C), 77.3 (H-C≡<u>C</u>-CH$_2$), 76.8 (H-<u>C</u>≡C-CH$_2$), 56.3 (H-C≡C-<u>C</u>H$_2$) ppm; ESI

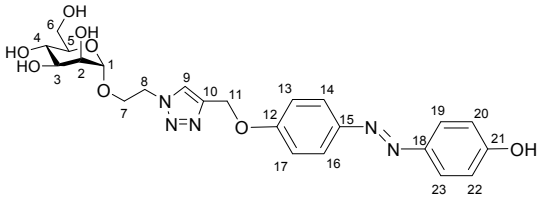
MS calcd for $C_{18}H_{14}N_2O_2$: *m/z* 290.1055 $[M+1]^+$; found: *m/z* 291.1055 $[M+1]^+$; IR (ATR): 3260 (C≡CH), 1587, 1493, 1245, 1020, 844, 663 cm^{-1}.

Click reaction: Acetylated monoglycosylated azobenzene glycoconjugate 5 (Man-a z o [OAc]$_4$):



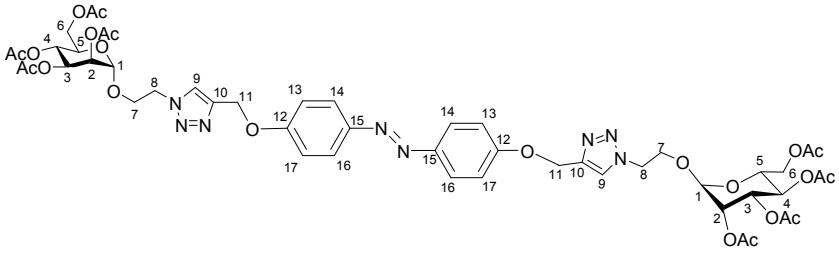
A mixture of *tert*-butanol and water (1:1, 3 mL) was added to a mixture of the azobenzene alcohol **2** (50 mg, 0.19 mmol, 1.0 equiv.), the mannoside **4**[2] (99.3 mg, 0.24 mmol, 1.2 equiv.). $CuSO_4$ x $5H_2O$ (3 mg) and Cu powder (30 mg). The reaction mixture was stirred at room temperature for 30 h. Then, TLC (cyclohexane/ethyl acetate, 1:4) showed complete consumption of **2**. Ethyl acetate (30 mL) was added, Cu removed by filteration over celite, and the filtrate was dried over $MgSO_4$. It was filtered and the filtrate concentrated under reduced pressure. Purification of crude product by column chromatography on silica gel (cyclohexane/ethyl acetate, 1:4) gave mannoside **5** as a reddish brown low melting solid (118 mg, 0.18 mmol, 89%). R_f 0.22 (cyclohexane/ethyl acetate, 1:4); $[\alpha]_D^{22} = +23$ ($c = 0.64$, CH_2Cl_2); m.p. 70-72 °C; ^{1}H NMR (500 MHz, $CDCl_3$, 300 K, TMS): δ = 7.83-7.81 (m, 3H, H-16, H-14, H-9), 7.78 (d, *J* = 8.7 Hz, 2H, H-19, H-23), 7.06 (d, *J* = 8.9 Hz, 2H, H-13, H-17), 6.94 (d, *J* = 8.7 Hz, 2H, H-20, H-22), 5.27 (s, 2H, H-11), 5.25-5.23 (m, 2H, H-3, H-4), 5.21 (m, 1H, H-2), 4.80 (d, *J* = 1.4 Hz, 1H, H-1), 4.63 (t, *J* = 5.1 Hz, 2H, H-8a, H-8b), 4.20 (dd, *J* = 12.3, 5.3 Hz, 1H, H-6a), 4.15 (m_c, 1H, H-7a), 4.06 (dd, *J* = 12.34, 2.4 Hz, 1H, H-6b), 3.89 (m_c, 1H, H-7b), 3.55 (ddd, *J* = 9.4, 5.3, 2.3 Hz, 1H, H-5), 2.14, 2.09, 2.00, 1.98 (each s, each 3H, 4 C(O)CH_3) ppm; ^{13}C NMR (125 MHz, $CDCl_3$, 300 K, TMS): δ = 170.7, 170.1, 170.0, 169.7 (4 $\underline{C}OCH_3$), 160.1 (C-12), 158.4 (C-21), 147. 4 (C-15), 146.9 (C-18), 144.0 (C-10), 124.6 (C-19, C-23), 124.3 (C-10, C-14, C-9), 115.8 (C-20, C-22), 115.0 (C-13, C-17), 97.5 (C-1), 69.2 (C-5, C-2), 68.9 (C-3), 66.2 (C-7), 65.7 (C-4), 62.3 (C-6), 61.9 (C-11), 49.9 (C-8), 20.8, 20.7, 20.7, 20.6 (4 CO$\underline{C}H_3$) ppm; ESI MS calcd for $C_{31}H_{35}N_5O_{12}$: *m/z* 692.228 $[M+Na]^+$; found: *m/z* 692.219 $[M+Na]^+$; IR (ATR) 3144, 1750, 1580, 1498, 1221, 1147, 850, 554 cm^{-1}.

Deprotection: Monoglycosylated azobenzene glycoconjugate 6 (Man-a z o):



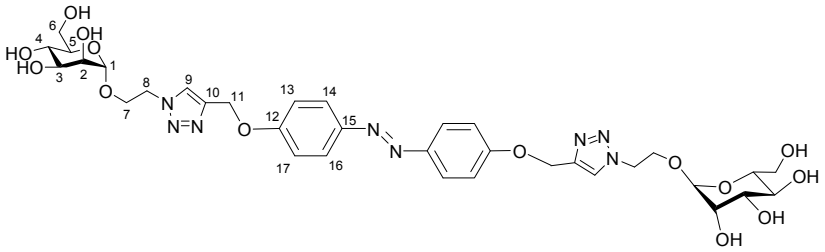
The acetyl-protected monovalent azobenzene glycoconjugate **5** (100 mg, 0.14 mmol) was dissolved in anhydrous methanol (5 mL) and a catalytic amount of solid NaOMe was added. The reaction mixture was stirred at room temperature overnight. Then, it was neutralized with Amberlite IR 120 ion exchange resin and filtered. The filtrate was evaporated to yield **6** as a dark orange syrup compound (71.8 mg, 0.143 mmol, 92%). R_f 0.28 (CH_2Cl_2 / MeOH, 4:1); $[\alpha]_D^{22}$ = + 15.6 (*c* = 1.03, DMSO); ^{1}H NMR (500 MHz, CD_3OD, 300 K, TMS): δ = 8.13 (s, 1H, H-9), 7.84 (d, *J* = 8.9 Hz, 2H, H-14, H-16), 7.77 (d, *J* = 8.9 Hz, 2H, H-19, H-23), 7.16 (d, *J* = 9.0 Hz, 2H, H-13, H-17), 6.90 (d, *J* = 8.9 Hz, 2H, H-20, H-22), 5.26 (s, 2H, H-11a, H-11b), 4.74 (d, *J* = 1.5 Hz, 1H, H-1), 4.66 (ddd, *J* = 10.5, 7.2, 3.9 Hz, 2H, H-8a, H-8b), 4.14 (ddd, *J* = 10.5, 6.5, 3.8 Hz, 1H, H-7a), 3.90 (ddd, *J* = 10.6, 6.5, 3.3 Hz, 1H, H-7b), 3.78 (dd, *J* = 11.8, 2.3 Hz, 1H, H-6a), 3.75 (dd, *J* = 2.8, 1.8 Hz, 1H, H-2), 3.66 (dd, *J* = 11.8, 5.9 Hz, 1H, H-6b), 3.61-3.56 (m, 2H, H-3, H-4), 3.23-3.24 (ddd~m_c, 1H, H-5) ppm; ^{13}C NMR (125 MHz, $CDCl_3$, 300 K, TMS): δ = 160.8 (C-21), 160.5 (C-12), 146.9 (C-15), 145.7 (C-18), 142.7 (C-10), 125.5 (C-9), 124.9 (C-20, C-22), 124.4 (C-13, C-17), 116.3 (C-19, C-23), 115.7 (C-14, C-16), 100.3 (C-1), 74.7 (C-5), 71.3 (C-3), 70.5 (C-2), 67.3 (C-4), 65.4 (C-7), 61.9 (C-11), 61.6 (C-6), 49.9 (C-8) ppm; UV/Vis (DMSO) λ_{max} = 364 nm; ε = 25804 ± 1109 L x mol^{-1} x cm^{-1}; MALDI-TOF MS calcd for $C_{23}H_{27}N_5O_8$: *m/*z 524.185 $[M+Na]^+$; found: *m/z* 524.176 $[M+Na]^+$.

Click reaction: Acetylated bisglycosylated azobenzene glycoconjugate 7 (Man-a z o-Man [OAc]$_8$):



To a mixture of the azobenzene **3** (200 mg, 0.689 mmol), the mannoside **4**[2] (633 mg, 1.52 mmol, 2.2 equiv.), $CuSO_4$ x $5H_2O$ (12 mg) and Cu powder (100 mg) *tert*-butanol and water (1:1, 10 mL) were added. The reaction mixture was stirred at room temperature for 48 h. Then, TLC (CH_2Cl_2/MeOH, 4:1) showed complete consumption of **3**. The reaction was diluted with ethyl acetate (100 mL), Cu removed by filteration using celite, and the filtrate was dried over $MgSO_4$. It was filtered and the filtrate concentrated under reduced pressure. Purification of the crude by column chromatography on silica gel (CH_2Cl_2/MeOH, 4:1) gave product **7** as a crystalline pale yellow solid (643 mg, 0.572 mmol, 83%). R_f 0.24 (cyclohexane/ethyl acetate, 1:1); $[\alpha]_D^{22} = +29.6$ (c = 1.01, CH_2Cl_2); m.p. 99-103 °C; ^{1}H NMR (500 MHz, $CDCl_3$, 300 K, TMS): δ = 7.87 (d, J = 9.0 Hz, 4H, aryl-H), 7.79 (s, 2H, 2 H-9), 7.11 (d, J = 9.1 Hz, 4H, aryl-H), 5.30 (s, 4H, 2 H-11a, 2 H-11b), 5.24- 5.22 (m_c, 4H, 2 H-4, 2 H-3), 5.20-5.19 (m_c, 2H, 2 H-2), 4.80 (d, J = 1.5 Hz, 2H, 2 H-1), 4.62 (t, J = 5.2 Hz, 4H, 2 H-8a, 2 H-8b), 4.20 (dd, J = 12.3, 5.4 Hz, 2H, 2 H-6a), 4.14 (td, J = 10.9, 5.4 Hz, 2H, 2 H-7a), 4.04 (dd, J = 12.3, 2.4 Hz, 2H, 2 H-6b), 3.91-3.87 (m, 2H, 2 H-7b), 3.53 (ddd, J = 9.7, 5.2, 2.4 Hz, 2H, 2 H-5), 2.14, 2.09, 1.99, 1.98 (each s, each 6H, 8 C(O)$\underline{CH_3}$) ppm; ^{13}C NMR (125 MHz, $CDCl_3$, 300 K, TMS): δ = 170.6, 169.9, 169.9, 169.6 (8 $\underline{C}OCH_3$), 160.3 (2 C-12), 147.4 (2 C-15), 144.0 (2 C-10), 124.4 (2 C-14, 2 C-16), 124.3 (2 C-10, 2 C-14, 2 C-9), 115.1 (2 C-13, 2 C-17), 97.5 (2 C-1), 69.2 (2 C-5, 2 C-3), 68.8 (2 C-2), 66.2 (2 C-7), 65.7 (2 C-4), 62.2 (2 C-6), 62.1 (2 C-11), 49.8 (2 C-8), 20.8, 20.7, 20.7, 20.6 (8 CO$\underline{CH_3}$) ppm; ESI MS calcd for $C_{50}H_{60}N_8O_{22}$: *m/*z 1147.382 $[M+Na]^+$; found: *m/z* 1147.373 $[M+Na]^+$; IR (ATR) 2933, 1739, 1597, 1367, 1214, 1041, 841, 599 cm^{-1}.

Deprotection: Bisglycoslyated azobenzene glycoconjugate 8 (Man-a z o-Man):



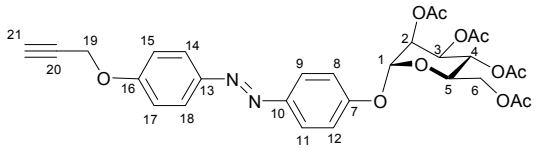
The acetyl-protected azobenzene glycoconjugate **7** (100 mg, 0.09 mmol) was dissolved in anhydrous methanol (3 mL) and a catalytic amount of solid NaOMe was added. The reaction mixture was stirred at room temperature overnight. Then, it was neutralized with Amberlite IR 120 ion exchange resin and filtered. The filtrate was evaporated to yield **8** (67 mg, 0.085 mmol, 96%) as a reddish brown solid. R_f 0.28 (CH_2Cl_2/ MeOH, 3:7); $[\alpha]_D^{22} = +22$ ($c = 0.96$, DMSO); m.p. 170-171 °C; ^{1}H NMR (600 MHz, DMSO-d_6, 300 K, TMS): δ = 8.20 (s, 2H, 2 H-9), 7.82 (d, J = 8.9 Hz, 4H, 2 H-14, 2 H-16), 7.20 (d, J = 9.0 Hz, 4H, 2 H-13, 2 H-17), 5.22 (s, 4H, 2 H-11a, 2 H-11b), 4.61 (d, J = 1.2 Hz, 2H, 2 H-1), 4.58 (dd, J = 4.0, 6.3 Hz, 4H, 2 H-8a, 2 H-8b), 4.53 (dd, J = 6.6, 4.0 Hz, 2H, 2 H-7a), 3.94 (ddd, J = 10.7, 6.4, 4.0 Hz, 2H, 2 H-7b), 3.78 (dd, J = 11.6, 1.9 Hz, 2H, 2 H-6a), 3.56-3.53 (m, 2H, 2 H-2), 3.40 (dd, J = 11.7, 6.3 Hz, 2H, 2 H-6b), 3.39-3.32 (m, 4H, 2 H-4, 2 H-3), 3.14-3.11 (m_c, 2H, 2 H-5) ppm; ^{13}C NMR (150 MHz, DMSO-d_6, 300 K, TMS): δ = 160.6 (2 C-12), 146.6 (2 C-15), 142.5 (2 C-10), 125.3 (2 C-9), 124.4 (2 C-14, 2 C-16), 115.6 (2 C-13, 2 C-17), 100.0 (2 C-1), 74.2 (2 C-5), 70.9 (2 C-3), 70.2 (2 C-2), 66.8 (2 C-4), 65.1 (2 C-7), 61.6 (2 C-11), 61.2 (2 C-6), 49.7 (2 C-8) ppm; UV/Vis (DMSO) λ_{max} = 363 nm; ε = 27858 ± 902 L x mol^{-1} x cm^{-1}; MALDI-TOF MS calcd for $C_{34}H_{44}N_8O_{14}$: *m/z* 811.297 $[M+Na]^+$; found: *m/z* 811.249 $[M+Na]^+$; IR (ATR) 2933, 1739, 1597, 1367, 1214, 1041, 841, 599 cm^{-1}.

After irradiation: *Z*-8:

^{1}H NMR (600 MHz, DMSO-d_6, 300 K, TMS): δ = 8.18 (s, 2H, 2 H-9′), 7.00 (d, J = 8.9 Hz, 4H, 2 H-13, 2 H-17), 6.87 (d, J = 8.9 Hz, 4H, 2 H-14, 2 H-16), 5.11 (s, 4H, 2 H-11a, 2 H-11b), 4.62 (bs, 2H, 2 H-1), 4.56-4.52 (m, 4H, 2 H-8a, 2 H-8b), 3.95 (ddd, J = 10.7, 6.3, 4.1 Hz, 2H, 2 H-7a), 3.79 (ddd, J = 10.9, 6.7, 4.0 Hz, 2H, 2 H-7b), 3.61 (dd, J = 9.9, 5.7 Hz, 2H, 2 H-6a), 3.53 (bs, 2H, 2 H-2), 3.43-3.30 (m, 6H, 2 H-6b, 2 H-4, 2 H-3), 3.16-3.12 (m, 2H, 2 H-5) ppm; ^{13}C NMR

(150 MHz, DMSO-d_6, 300 K, TMS): δ = 157.1 (2 C-12), 146.9 (2 C-15), 142.3 (2 C-10), 125.0 (2 C-9), 122.2 (2 C-14, 2 C-16), 114.8 (2 C-13, 2 C-17), 99.9 (2 C-1), 74.2 (2 C-5), 70.8 (2 C-3), 70.1 (2 C-2), 66.8 (2 C-4), 64.9 (2 C-7), 61.3 (2 C-11), 61.2 (2 C-6), 49.4 (2 C-8) ppm; UV/Vis (DMSO) λ_{max} = 448 nm; ε = 2466 ± 782 L x mol^{-1} x cm^{-1}.

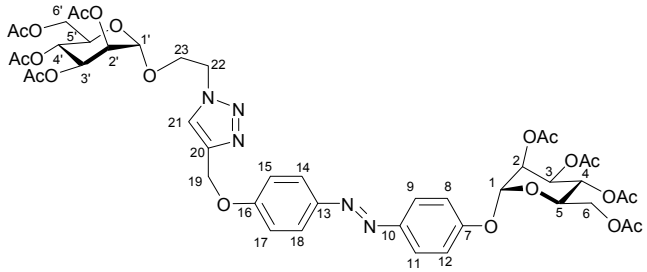
Glycosylation: Acetylated monoglycosylated azobenzene glycoconjugate 10 (a z o-Man [OAc]$_4$):



A mixture of azobenzene alcohol **2** (100 mg, 0.397 mmol, 1 equiv.) and the glycosyl donor **9**[3,4] (293 mg, 0.595 mmol, 1.5 equiv.) were dried under vacuum for about 15 mintues, then added of dry CH_2Cl_2 (6 mL) was added and the reaction mixture cooled to 0 °C. The Lewis acid BF_3 x Et_2O (75 µL, 0.595 mmol, 1.5 equiv.) was added and the reaction mixture stirred at room temperature for overnight. Then, TLC showed complete consumption of **2**. Solid $NaHCO_3$ was added and CH_2Cl_2 (30 mL). It was washed with water (10 mL) and the organic layer dried over $MgSO_4$. It was filtered and the filtrate concentrated under reduced pressure. Purification of the crude product by column chromatography on silica gel (cyclohexane/ethyl acetate, 7:3) gave the title compound as a pale yellow low melting solid (203 mg, 0.348 mmol, 88%). R_f 0.29 (cyclohexane/ethyl acetate, 7:3); $[\alpha]_D^{22}$ = + 72.7 (c = 0.81, CH_2Cl_2); m.p.: 54 °C; ^{1}H NMR (500 MHz, $CDCl_3$, 300 K, TMS): δ = 7.90 (d, J = 9.0 Hz, 2H, H-14, H-18), 7.88 (d, J = 8.9 Hz, 2H, H-9, H-11), 7.21 (d, J = 9.0 Hz, 2H, H-8, H-12), 7.09 (d, J = 9.0 Hz, 2H, H-25, H-17), 5.61 (d, J = 1.7 Hz, 1H, H-1), 5.58 (dd, J = 10.0, 3.5 Hz, 1H, H-3), 5.48 (dd, J = 3.5, 1.9 Hz, 1H, H-2), 5.38 (dd~t, J = 10.1 Hz, 1H, H-4), 4.78 (d, J = 2.4 Hz, 2H, H-19a, H-19b), 4.29 (dd, J = 12.2, 5.5 Hz, 1H, H-6a), 4.12-4.08 (m, 2H, H-5, H-6b), 2.56 (t, J = 2.38 Hz, 1H, H-21), 2.22, 2.06, 2.05, 2.03 (each s, each 3H, 4 C(O)CH_3) ppm; ^{13}C NMR (150 MHz, $CDCl_3$, 300 K, TMS): δ = 170.5, 169.9, 169.9, 169.7 (4 C(O)CH_3), 159.7 (C-16), 157.2 (C-7), 148.5 (C-10), 147.5 (C-13), 124.5 (C-14, C-18), 124.3 (C-9, C-11), 116.7 (C-8, C-12), 115.2 (C-15, C-17), 97.1 (C-1), 78.1 (C-20), 75.9 (C-21), 69.4 (C-5), 69.3 (C-2), 68.8 (C-3), 65.8 (C-4), 62.1 (C-6), 56.0 (C-19),

20.8, 20.8, 20.7, 20.7 (4 C(O)$\underline{C}H_3$) ppm; ESI MS calcd for $C_{29}H_{30}N_2O_{11}$: *m/z* 605.184 $[M+Na]^+$; found: *m/z* 605.173 $[M+Na]^+$; IR (ATR) 3287, 2955, 1743, 1597, 1496, 1209, 1025, 840, 599 cm^{-1}.

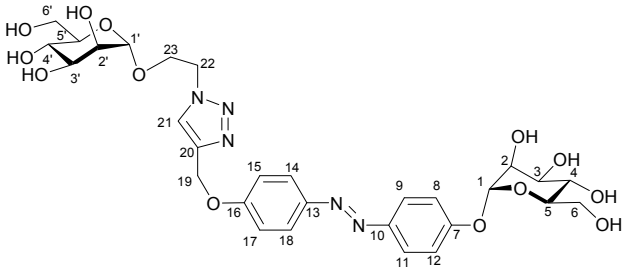
Click reaction: Acetylated bisglycosylated azobenzene glycoconjugate 11 (Man-a z o-Man [OAc]$_8$):



To a mixture of the alkyne **10** (100 mg, 0.172 mmol, 1.0 equiv.), the mannoside **4**[2] (86 mg, 0.206 mmol, 1.2 equiv.), $CuSO_4$ x $5H_2O$ (6 mg) and Cu powder (60 mg) a mixture of *tert*-butanol, THF and water (1:1:1, 6 mL) was added. The reaction mixture was heated at 70 °C for 16 h. Then, TLC showed complete consumption of starting material **10**. The reaction mixture was diluted with ethyl acetate (30 mL), Cu was removed by filteration using celite, and the filtrate was dried over $MgSO_4$. It was filtered and the filtrate concentrated under reduced pressure. Purification of crude product by column chromatography on silica gel using 1% MeOH in CH_2Cl_2 gave the required product **11** as a pale yellow solid (122 mg, 0.122 mmol, 82%). R_f 0.33 (cyclohexane/ethyl acetate; 2:3); $[\alpha]_D^{22} = +66.8$ (c = 1.05, CH_2Cl_2); m.p. 72-75 °C; ^{1}H NMR (500 MHz, $CDCl_3$, 300 K, TMS): δ = 7.89-7.86 (m, 4H, aryl-H), 7.79 (s, 1H, H-21), 7.20 (d, *J* = 9.0 Hz, 2H, aryl-H), 7.12 (d, *J* = 9.0 Hz, 2H, aryl-H), 5.61 (d, *J* = 1.7 Hz, 1H, H-1), 5.58 (dd, *J* = 10.0, 3.6 Hz, 1H, H-3), 5.48 (dd, *J* = 3.5, 1.8 Hz, 1H, H-2), 5.38 (dd~t, *J* = 10.2 Hz, 1H, H-4), 5.31 (s, 2H, H-11), 5.24-5.23 (m, 2H, H-4', H-3'), 5.21 (m_c, 1H, H-2'), 4.80 (d, *J* = 1.4, 1H, H-1'), 4.63 (t, *J* = 5.1 Hz, 2H, H-8), 4.29 (dd, *J* = 12.3, 5.5 Hz, 1H, H-6'a), 4.20 (dd, *J* = 12.3, 5.4 Hz, 1H, H-6'b), 4.16-4.07 (m, 3H, H-23a, H-5, H-6a), 4.04 (dd, *J* = 12.3, 2.4 Hz, 1H, H-6b), 3.89 (m_c, 2H, H-7), 3.54 (ddd, *J* = 9.5, 5.3, 2.3 Hz, H-5'), 2.22, 2.14, 2.09, 2.06, 2.05, 2.03, 2.00, 1.93 (each s, each 3H, 8 C(O)CH_3) ppm; ^{13}C NMR (125 MHz, $CDCl_3$, 300 K, TMS): δ = 170.5, 170.5, 170.5, 169.9, 169.8 169.7, 169.7, 169.6 (8 $\underline{C}OCH_3$), 160.5 (C-16), 157.2 (C-7),

148.5 (C-10), 147.3 (C-13), 143.9 (C-20), 124.6 (C-14, C-18), 124.3 (C-9, C-11), 124.1 (C-21), 116.7 (C-8, C-12), 115.1 (C-15, C-17), 97.5 (C-1'), 95.7 (C-1), 69.3 (C-5, C-5′), 69.2 (C-2, C-2′), 68.8 (C-3, C-3′), 66.2 (C-23), 65.9 (C-4'), 65.7 (C-4), 62.2 (C-6, C-6′), 62.1 (C-19), 49.8 (C-22), 20.9, 20.8, 20.8, 20.7, 20.7, 20.6, 20.6, 20.6 (8 $CO\underline{C}H_3$) ppm; ESI MS calcd for $C_{43}H_{53}N_5O_{21}$: *m/*z 1022.323 $[M+Na]^+$; found: *m/z* 1022.290 $[M+Na]^+$; IR (ATR) 2932, 1739, 1598, 1367, 1211, 1032, 843, 599 cm^{-1}.

Deprotection: Bisglycosylated azobenzene glycoconjugate 12 (Man-a z o-Man):



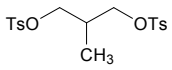
The acetyl-protected biglycosylated azobenzene glycoconjugate **11** (50 mg, 0.05 mmol) was dissolved in anhydrous methanol (2 mL) and a catalytic amount of solid NaOMe was added. The reaction mixture was stirred at room temperature for 5 h. Then, TLC control indicated that the starting material had fully disappeared. It was neutralized with Amberlite IR 120 ion exchange resin and filtered. The filtrate was evaporated to yield **12** as a yellow solid (30.8 mg, 0.047 mmol, 93%). R_f 0.31 (CH_2Cl_2 / MeOH, 7:3); $[\alpha]_D^{22} = +31.2$ ($c = 0.91$, MeOH); ^{1}H NMR (600 MHz, DMSO-d_6, 300 K, TMS): δ = 8.22 (s, 1H, H-21), 7.85 (d, J = 8.9 Hz, 2H, aryl-H), 7.82 (d, J = 8.9 Hz, 2H, aryl-H), 7.24 (d, J = 9.0 Hz, 2H, aryl-H), 7.22 (d, J = 9.1 Hz, 2H, H-15, H-17), 5.50 (d, J = 1.6 Hz, 1H, H-1), 5.24 (s, 2H, H-19a, H-19b), 4.63 (d, J = 1.5 Hz, 1H, H-1'), 4.59 (dd, J = 6.3, 4.2 Hz, 1H, H-22a), 4.56 (dd, J = 6.6, 4.0 Hz, 1H, H-22b), 3.96 (ddd, J = 10.7, 6.5, 4.1 Hz, 1H, H-23a), 3.86 (dd, J = 3.3, 1.9 Hz, 1H, H-2), 3.80 (ddd, J = 10.8, 6.5, 4.0 Hz, 1H, H-23b), 3.70 (dd, J = 9.2, 3.5 Hz, 1H, H-3), 3.56-3.36 (m, 9H, H-6'a, H-6a, H-2', H-4', H-6'b, H-6b, H-4, H-3', H-5'), 3.14 (dd, J = 11.1, 4.6 Hz, 1H, H-5) ppm; ^{13}C NMR (150 MHz, DMSO-d_6, 300 K, TMS): δ = 160.8 (C-16), 158.8 (C-7), 147.4 (C-10), 146.8 (C-13), 142.7 (C-20), 125.5 (C-21), 124.7 (C-9, C-11), 124.4 (C-14, C-18), 117.5 (C-8, C-12), 115.8 (C-15, C-17), 100.2 (C-1'), 99.0 (C-1), 75.5 (C-5'), 74.4 (C-5), 71.03 (C-3'), 70.84 (C-3), 70.3 (C-2'), 70.2 (C-2), 67.0

(C-4'), 66.9 (C-4), 65.3 (C-23), 61.8 (C-19), 61.4 (C-6'), 61.2 (C-6), 49.9 (C-22) ppm; UV/Vis (DMSO) λ_{max} = 360 nm; ε = 25562 $\pm$ 865 L x mol^{-1} x cm^{-1}; MALDI-TOF MS calcd for $C_{29}H_{37}N_5O_{13}$: *m/z* 686.283 $[M+Na]^+$; found: *m/z* 686.131 $[M+Na]^+$.

After irradiation: *Z*-12:

^{1}H NMR (600 MHz, DMSO-d_6, 300 K, TMS): δ = 8.16 (s, 1H, H-21), 7.02 (d, *J* = 8.6 Hz, 2H, H-8, H-12), 6.97 (d, *J* = 8.8 Hz, 2H, H-16, H-17), 6.85 (d, *J* = 8.8 Hz, 2H, H-14, H-18), 6.82 (d, *J* = 8.7 Hz, 2H, H-9, H-11), 5.35 (bs, 1H, H-1), 5.09 (2, 2H, H-19a, H-19b), 4.61 (bs, 1H, H-1'), 4.57 (dd, *J* = 8.9, 4.1 Hz, 1H, H-22a), 4.53 (dd, *J* = 9.8, 4.2 Hz, 1H, H-22b), 3.93 (dd, *J* = 10.2, 4.4 Hz, 1H, H-23a), 3.79 (m, 2H, H-2, H-23b), 3.57-3.34 (m, 10H, H-2', H-3, H-4', H-6'a, H-6a, H-4, H-3', H-5', H-6'b, H-6b), 3.12 (m_c, 1H, H-5) ppm; ^{13}C NMR (125 MHz, DMSO-d_6, 300 K, TMS): δ = 157.6 (C-16), 155.6 (C-7), 148.2 (C-10), 147.2 (C-13), 142.7 (C-20), 125.5 (C-21), 122.8 (C-9, C-11), 122.2 (C-14, C-18), 117.5 (C-8, C-12), 115.3 (C-15, C-17), 100.2 (C-1'), 99.2 (C-1), 75.3 (C-5'), 74.4 (C-5), 71.0 (C-3'), 70.8 (C-3), 70.3 (C-2'), 70.2 (C-2), 67.0 (C-4'), 66.9 (C-4), 65.3 (C-23), 61.6 (C-19), 61.4 (C-6'), 61.2 (C-6), 49.9 (C-22) ppm; UV/Vis (DMSO) λ_{max} = 448 nm; nm ε = 2316 $\pm$ 61 L x mol^{-1} x cm^{-1}.

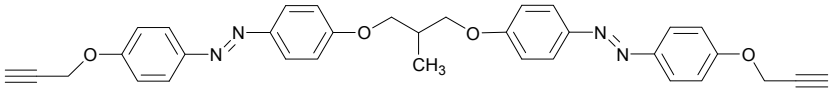
1,3-Dihydroxy-2-methyl-1,3-di-*O*-tosyl-propane 14[5]



According to the literature, a mixture of the diol **13** (1.0 g, 0.011 mmol, 1.0 equiv.) in pyridine (20 mL) was treated with tosyl chloride (6.30 g, 0.033 mmol, 3 equiv.) and the reaction mixture was stirred at room temperature for 14 h. Then, TLC showed complete consumption of the starting material. Aqueous 6N HCl (100 mL) was added and the aqueous phase extracted with ethyl acetate (2 x 50 mL). The combined organic layers were washed with water and brine and dried over $MgSO_4$. It was filtered and concentrated under reduced pressure. Purification of the crude product by column chromatography on silica gel (cyclohexane/ethylacetate, 4:1) gave the ditosylate **14** as a white solid (3.67 g, 0.01 mmol, 83%). R_f 0.27 (cyclohexane/ethyl acetate); m.p.: 71 °C; ^{1}H NMR (200 MHz, $CDCl_3$, 300 K, TMS): δ = 7.74 (d, *J* = 8.4 Hz, 4H, aryl-H), 7.34 (d, *J* = 8.5 Hz, 4H, aryl-H), 3.90 (dd, *J* = 5.7 Hz, 1.5 Hz, 4H, 2 CH_2-O), 2.45 (s, 6H, Ts-

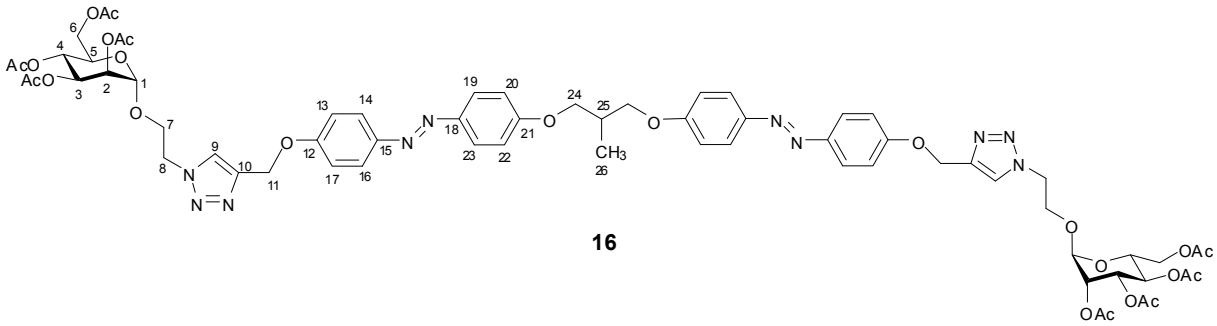
CH_3), 2.14 (tt, *J* = 14.4 Hz, 7.1 Hz, 1H, C<u>H</u>(CH_3)), 0.91 (d, *J* = 6.9 Hz, 3H, CH(C<u>H</u>$_3$) ppm; ^{13}C NMR (125 MHz, $CDCl_3$, 300 K, TMS): δ = 145.1 (C_q, aryl-C), 132.6 (C_q, aryl-C), 129.9, 127.8 (aryl-C), 70.3 (2 CH_2), 33.0 (CH), 21.6 (Ts-CH_3), 12.9 (CH-<u>C</u>H_3) ppm; ESI MS calcd for $C_{18}H_{22}O_6S_2$: *m/z* 421.085 $[M+Na]^+$; found: *m/z* 421.077 $[M+Na]^+$; IR (ATR) 2973, 1597, 1355, 1174, 1095, 936, 848, 667 cm^{-1}.

Bivalent azobenzene dialkyne 15:



A solution of the alcohol **2** (82.3 mg, 0.327 mmol, 2.6 equiv.) and K_2CO_3 (52 mg, 0.377 mmol, 3 equiv.) in DMF (2 mL) was stirred at room temperature for ~30 min, then added the ditosylate **14** (50 mg, 0.125 mmol, 1.0 equiv.) was added. the reaction mixture was heated at 100 ºC for 16 h until TLC showed complete absence of **14**. After the solvent was evaporated under reduced pressure, the residue was dissolved in ethyl acetate (30 mL) and washed with water (2 x 25 mL). The organic phase was dried over $MgSO_4$, its was filtered and concentrated under reduced pressure. Purification by column chromatography on silica gel (cyclohexane/ethylacetate, 4:1) gave product **15** as a pale yellow liquid (52 mg, 0.09 mmol, 74%); m.p.: 164-166 °C; ^{1}H NMR (500 MHz, $CDCl_3$, 300 K, TMS): δ = 7.89 (d, *J* = 9.0 Hz, 4H), 7.88 (d, *J* = 8.9 Hz, 4H), 7.09 (d, *J* = 9.1 Hz, 4H), 7.03 (d, *J* = 9.0 Hz, 4H), 4.77 (d, *J* = 2.4 Hz, 4H), 4.15 (dd, *J* = 9.2 Hz, 6.2 Hz, 2H), 4.09 (dd, *J* = 9.2 Hz, 5.8 Hz, 2H), 2.56 (t, *J* = 2.4 Hz, 2H), 2.54-2.53 (m, 1H), 1.25 (d, *J* = 6.9 Hz, 3H) ppm; ^{13}C NMR (125 MHz, $CDCl_3$, 300 K, TMS): δ = 161.1 (C_q, aryl-C), 159.4 (C_q, aryl-C), 147.6 (C_q, aryl-C), 147.1 (C_q, aryl-C), 124.5 (aryl-C), 124.3 (aryl-C), 115.1 (aryl-C), 114.7 (aryl-C), 78.2 (H-C≡<u>C</u>-CH_2), 75.9, (H-<u>C</u>≡C-CH_2) 69.9 (2 <u>C</u>H_2), 56.0 (H-C≡C-<u>C</u>H_2), 33.8 (H<u>C</u>-CH_3), 14.1 (HC-<u>C</u>H_3) ppm; ESI MS calcd for $C_{34}H_{30}N_4O_4$: *m/z* 559.226 $[M+Na]^+$; found: *m/z* 559.241 $[M+Na]^+$; IR (ATR) 3275, 2916, 1596, 1579, 1495, 1232, 1146, 1013, 841, 666 cm^{-1}.

Click reaction: Acetylated bivalent azobenzene glycoconjugate 16 (Man-a z o-a z o-Man [OAc]$_8$):

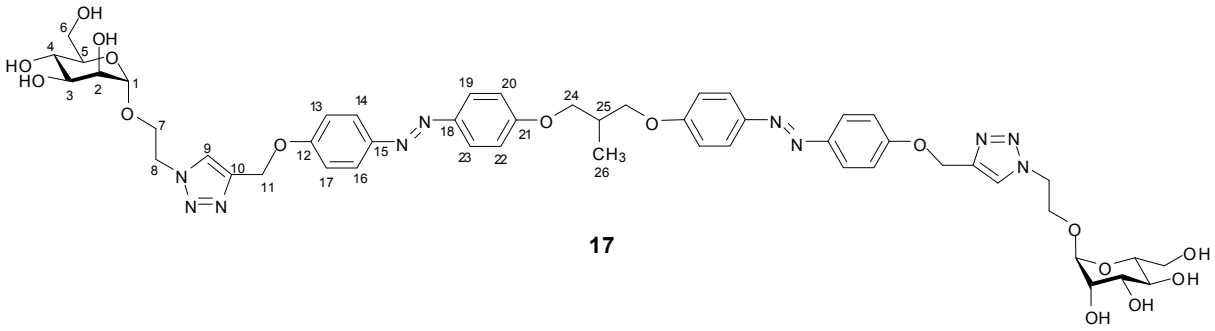


16

To a mixture of the dialkyne **15** (50 mg, 0.089 mmol, 1.0 equiv.), the mannoside **4** (89.7 mg, 0.215 mmol, 2.4 equiv.). $CuSO_4$ x $5H_2O$ (6 mg) and Cu powder (60 mg) was added to a mixture of *tert*-butanol and water (1:1, 5 mL). The reaction mixture was stirred at 70 °C for 48 h. Then, TLC showed complete absence of **15**. The reaction mixture was diluted with ethyl acetate (30 mL), Cu was removed by filteration using celite, and the filtrate was dried over $MgSO_4$. It was filtered and the filtrate concentrated under reduced pressure. Purification of crude product by column chromatography on silica gel (3% MeOH in CH_2Cl_2) gave the required product **16** as a pale yellow solid (101 mg, 0.01 mmol, 81%); R_f: 0.28 (3% MeOH in Dichloromethane); $[\alpha]_D^{22} = +21.1$ (c = 0.94, CH_2Cl_2); m.p. 85 °C (decompos.); ^{1}H NMR (600 MHz, $CDCl_3$, 300 K, TMS): δ = 7.88-7.86 (m, 8H, 2 H-14, 2 H-16, 2 H-19, 2 H-23), 7.79 (s, 2H, 2 H-9), 7.11 (d, *J* = 9.0 Hz, 4H, 2 H-13, 2 H-17), 7.02 (d, *J* = 9.0 Hz, 4H, 2 H-20, 2 H-22), 5.29 (bs, 4H, 2 H-11), 5.24- 5.23 (m, 4H, 2 H-4, 2 H-3), 5.20 (dd, *J* = 2.9, 1.6 Hz, 2H, 2 H-2), 4.79 (d, *J* = 1.4 Hz, 2H, 2 H-1), 4.62 (t, *J* = 5.2 Hz, 4H, 2 H-8), 4.19 (dd, *J* = 12.3, 5.3 Hz, 2H, 2 H-6a), 4.14 (dd, *J* = 9.6, 5.9 Hz, 4H, 2 H-24a, 2 H-7a), 4.07 (dd, *J* = 9.2, 5.6 Hz, 2H, 2 H-24b), 4.04 (dd, *J* = 12.3, 2.3 Hz, 2H, 2 H-6b), 3.90-3.87 (m, 2H, 2 H-7b), 3.53 (ddd, *J* = 9.5, 5.2, 2.2 Hz, 2H, 2 H-5), 2.54 (tt, *J* = 12.5, 6.3 Hz, 1H, H-25), 2.14, 2.09, 2.00, 1.98 (s, 3H, C(O)CH_3 x 2), 1.24 (d, *J* = 6.92 Hz, 3H, H-26) ppm; ^{13}C NMR (150 MHz, $CDCl_3$, 300 K, TMS): δ = 170.6, 169.9, 169.9, 169.6 (2 $\underline{C}OCH_3$), 161.1 (2 C-21), 160.2 (2 C-12), 147.4 (2 C-15), 147.0 (2 C-18), 144.0 (2 C-10), 124.4 (2 C-14, 2 C-16, 2 C-192, 2 C-23), 124.1 (2 C-9), 115.0 (2 C-13, 2 C-17) 114.7 (2 C-20, 2 C-22), 97.4 (2 C-1), 69.8 (2 C-24), 69.4 (2 C-5), 69.2 (2 C-2), 68.8 (2 C-3), 66.2 (2 C-7), 65.6 (2 C-4), 62.2 (2 C-6), 62.1 (2 C-11), 49.8 (2 C-8), 33.7 (C-25), 20.8, 20.7, 20.7, 20.6 (2 CO$\underline{C}H_3$), 14.1 (C-26) ppm; ESI MS calcd for $C_{66}H_{76}N_{10}O_{24}$: *m/z* 1393.503

$[M+1]^+$; found: *m/z* 1393.550 $[M+1]^+$; IR (ATR) 2928, 1742, 1597, 1498, 1367, 1215, 1041, 840, 553 cm^{-1}.

Deprotection: Bivalent azobenzene glycoconjugate 17 (Man-a z o-a z o-Man):



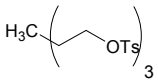
17

The acetyl-protected divalent azobenzene glycoconjugate **16** (90 mg, 0.06 mmol, 1.0 equiv.) was dissolved in anhydrous methanol (3 mL) and a catalytic amount of solid NaOMe was added. The reaction mixture was stirred at room temperature overnight. TLC control (CH_2Cl_2/MeOH, 3:7) indicated that the starting material had fully disappeared. It was neutralized with Amberlite IR 120 ion exchange resin and filtered. The filtrate was evaporated to yield **17** as a yellow solid (62 mg, 0.058 mmol, 91%). R_f 0.24 (CH_2Cl_2 / MeOH, 3:7); $[\alpha]_D^{22}$ = + 17.9 (*c* = 0.43, DMSO); m.p. 148-150 °C; ^{1}H NMR (600 MHz, DMSO-d_6, 300 K, TMS): δ = 8.22 (s, 2H, 2 H-9), 7.83 (m, 8H, 2 H-14, 2 H-16, 2 H-19, 2 H-23′), 7.21 (d, *J* = 8.8 Hz, 4H, 2 H-13, 2 H-17), 7.14 (d, *J* = 8.8 Hz, 4H, 2 H-20, 2 H-22), 5.23 (s, 4H, 2 H-11), 4.62 (bs, 2H, 2 H-1), 4.60 (dd, *J* = 8.9, 4.8 Hz, 2H, 2 H-8), 4.55 (dd, *J* = 9.8, 3.7 Hz, 2H, 2 H-8a), 4.12 (td, J = 14.9, 9.3 Hz, 4H, 2 H-24), 3.91-3.94 (m, 2H, 2 H-7a), 3.82-3.78 (m, 2H, 2 H-7b), 3.64-3.54 (m, 4H, 2 H-6a, 2 H-2), 3.42-3.34 (m, 6H, 2 H-3, 2 H-6b, 2 H-4), 3.15-3.12 (m, 2H, 2 H-5), 2.47-2.44 (m, 1H, H-25), 1.15 (d, *J* = 6.7 Hz, 3H, H-26) ppm; ^{13}C NMR (150 MHz, DMSO-d_6, 300 K, TMS): δ = 161.2 (2 C-21), 160.5 (2 C-12), 146.6 (2 C-15), 146.5 (2 C-18), 142.5 (2 C-10), 125.3 (2 C-9), 124.5 (2 C-13, 2 C-17), 124.4 (2 C-19, 2 C-23), 115.6 (2 C-14, 2 C-16), 115.4 (2 C-20, 2 C-22), 100.0 (2 C-1), 74.2 (2 C-5), 70.1 (2 C-3), 70.2 (2 C-2), 69.9 (2 C-24), 66.8 (2 C-4), 65.2 (2 C-7), 61.7 (2 C-11), 61.2 (2 C-6), 49.7 (2 C-8), 33.3 (C-25), 14.0 (C-26) ppm; MALDI-TOF MS calcd for $C_{50}H_{60}N_{10}O_{16}$: *m/*z 1079.418 $[M+Na]^+$; found: *m/z* 1079.4622 $[M+Na]^+$; UV/Vis (DMSO) λ_{max} = 364 nm; ε = 29063 ± 950 L x mol^{-1} x cm^{-1}.

After irradiation: *Z*-17:

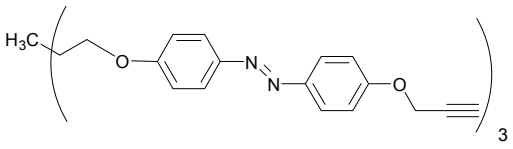
^{1}H NMR (600 MHz, DMSO-d_6, 300 K, TMS): δ = 8.16 (s, 2H, 2 H-9), 6.97 (d, J = 8.3 Hz, 4H, 2 H-20, 2 H-22), 6.92-6.83 (m, 12H, 2 H-13, 2 H-17, 2 H-14, 2 H-16, 2 H-19, 2 H-23′), 5.09 (s, 4H, 2 H-11), 4.61 (s, 2H, H-1), 4.58-4.51 (m, 4H, 2 H-8), 3.95-3.90 (m, 6H, 2 H-7a, 2 H-24), 3.79-3.77 (m, 2H, 2 H-7b), 3.59-3.53 (m, 4H, 2 H-6a, 2 H-2′), 3.41-3.35 (m, 6H, 2 H-4, 2 H-6b′, 2 H-3), 3.15-3.12 (m, 2H, 2 H-5), 2.31 (dd, J = 12.2, 5.7 Hz, 1H, H-25), 1.05 (d, J = 5.7 Hz, 3H, H-26) ppm; ^{13}C NMR (150 MHz, DMSO-d_6, 300 K, TMS): δ = 157.9 (2 C-21), 157.3 (2 C-12), 147.2 (2 C-18), 146.9 (2 C-15), 142.5 (2 C-10), 124.4 (2 C-9), 122.6 (2 C-19, 2 C-23′), 122.4 (2 C-14, 2 C-16), 115.1 (2 C-20, 2 C-22), 114.9 (2 C-13, 2 C-17), 100.0 (2 C-1), 74.2 (2 C-5), 70.9 (2 C-3), 70.2 (2 C-2), 69.6 (2 C-24), 66.8 (2 C-4), 65.2 (2 C-7), 61.5 (2 C-11), 61.2 (2 C-6), 49.7 (2 C-8), 33.2 (C-25), 14.1 (C-26) ppm; UV/Vis (DMSO) λ_{max} = 449 nm; ε = 2544 ± 77 L x mol^{-1} x cm^{-1}.

2,2,2-Tri-[(*O*-tosyl)-2'-hydroxyethyl]ethane 19[6]



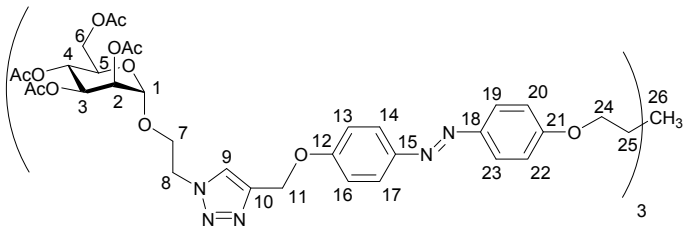
To a solution of the triol **18** (2.0 g, 16.66 mmol, 1.0 equiv.) in pyridine (20 mL) tosyl chloride (12.6 g, 66.66 mmol, 4 equiv.) was added and the reaction mixture stirred at room temperature for 16 h. Then, TLC showed complete absence of **18** Aqueous HCl (6N, 200 mL) was added and then it was extracted with ethyl acetate (2 x 100 mL). The combined organic layers were washed with water and brine, and dried over $MgSO_4$. After filtration, the filtrate was concentrated under reduced pressure to give product **19** as a white solid (10.3 g. 17.69 mmol, quant.). R_f: 0.24 (cyclohexane/ethyl acetate, 7:3); m.p. 132-135 °C; ^{1}H NMR (500 MHz, $CDCl_3$, 300 K, TMS): δ = 7.70 (d, J = 8.3 Hz, 6H), 7.35 (d, J = 7.9 Hz, 6H), 3.76 (s, 6H), 2.46 (s, 9H), 0.88 (s, 3H) ppm; ^{13}C NMR (125 MHz, $CDCl_3$, 300 K, TMS): δ = 145.2 (C_q, aryl-C), 131.9 (C_q, aryl-C), 130.1, 127.9 (aryl-C), 69.8 (3 CH_2), 39.4 (CH_3-C), 21.7 (Ts-CH_3), 14.2 (CH_3-C) ppm; ESI MS calcd for $C_{26}H_{30}O_9S_3$: *m/z* 605.105 $[M+Na]^+$; found: *m/z* 605.013 $[M+Na]^+$; IR (ATR) 1598, 1355, 1174, 1096, 960, 835, 666 cm^{-1}.

Trivalent azobenzene trialkyne 20:



A mixture of the alcohol **2** (156 mg, 0.619 mmol, 3.6 equiv.) and K_2CO_3 (42.6 mg, 0.309 mmol, 1.8 equiv.) in DMF (6 mL) was stirred at room temperature for ~30 min, then the tritosylate **19** (100 mg, 0.172 mmol, 1.0 equiv.) was added and the reaction mixture stirred at 100 ºC for 16 h. Then, TLC showed complete consumption of **19**. After the solvent was evaporated under reduced pressure, the residue was dissolved in ethyl acetate (30 mL) and washed with water (2 x 25 mL). The combined organic phases were dried over $MgSO_4$, it was filtered and the filtrate concentrated under reduced pressure. Purification by column chromatography on silica gel (cyclohexane/ethylacetate, 3:2) gave product **20** as a pale yellow syrup (86.8 mg, 0.110 mmol, 65%). R_f 0.26 (cyclohexane/ethyl acetate, 3:7); ^{1}H NMR (500 MHz, $CDCl_3$, 300 K, TMS): $\delta = 7.88$ (d, $J = 9.1$ Hz, 6H), 7.87 (d, $J = 9.1$ Hz, 6H), 7.08 (d, $J = 9.1$ Hz, 6H), 7.05 (d, $J = 9.0$ Hz, 6H), 4.76 (s, 6H), 2.56 (t, $J = 2.4$ Hz, 3H), 1.48 (s, 3H) ppm; ^{13}C NMR (125 MHz, $CDCl_3$, 300 K, TMS): 159.9, 158.4, 146.6, 146.2, 123.4, 123.3, 114.1, 113.8, 77.1, 74.9, 69.3, 55.0, 39.5, 16.3 ppm; IR (ATR) 3288, 2924, 1595, 1580, 1496, 1214, 1145, 1019, 835, 548 cm^{-1}.

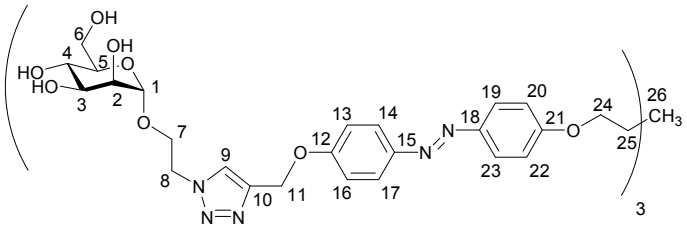
Click reaction: Acetylated trivalent azobenzene glycoconjugate 21 ([Man-a z o(OAc$_{12}$)]$_3$):



To a mixture of the trialkyne **20** (100 mg, 0.128 mmol, 1.0 equiv.), the mannoside **4**[2] (192 mg, 0.462 mmol, 3.6 equiv.). $CuSO_4$. x H_2O (12 mg) and Cu powder (120 mg) was added to a mixture of *tert*-butanol, THF and water (1:1:1, 6 mL). The reaction mixture was refluxed for 16 h until TLC showed absence of starting material **20**. The reaction mixture was diluted with ethyl acetate (30 mL), Cu was removed by filteration using celite, and the filtrate was dried over $MgSO_4$. After filtration it was concentrated under reduced pressure. Purification by column

chromatography on silica gel (2% MeOH in CH_2Cl_2) gave the required product **21** as a pale yellow syrup (209 mg, 0.10 mmol, 79%). R_f 0.29 (3% MeOH in CH_2Cl_2); $[\alpha]_D^{22} = +19.7$ (c = 1.15, CH_2Cl_2); m.p. 103-106 °C; ^{1}H NMR (600 MHz, $CDCl_3$, 300 K, TMS): δ = 7.87 (d, J = 8.8 Hz, 12H, 3 H-14, 3 H-16, 3 H-19, 3 H-23), 7.80 (s, 3H, 3 H-9), 7.11 (d, J = 9.0 Hz, 6H, 3 H-13, 3 H-17), 7.05 (d, J = 9.0 Hz, 6H, 3 H-20, 3 H-22), 5.30 (bs, 6H, 3 H-11a, 3H-11b), 5.25- 5.23 (m, 6H, 3 H-4, 3 H-3), 5.21 (dd, J = 2.9, 1.6 Hz, 3H, 3 H-2), 4.80 (d, J = 1.4 Hz, 3H, 3 H-1), 4.63 (t, J = 5.2 Hz, 6H, 3 H-8a, 3-H-8b), 4.22 (bs, 6H, 3 H-24), 4.21- 4.18 (m, 3H, 3 H-6a), 4.14 (td, J = 10.7, 5.4 Hz, 3H, 3 H-7a), 4.04 (dd, J = 12.3, 2.3 Hz, 3H, 3 H-6b), 3.89 (td, J = 10.7, 10.1, 3H, 3 H-7b), 3.55-3.52 (m, 3H, 3 H-5), 2.14, 2.09, 1.99, 1.98 (each s, each 9H, 12 C(O)CH_3), 1.41 (s, 3H, 3 H-26) ppm; ^{13}C NMR (150 MHz, $CDCl_3$, 300 K, TMS): δ = 170.6, 169.9, 169.9, 169.6 (12 $\underline{C}OCH_3$), 160.9 (3 C-21), 160.2 (3 C-12), 147.4 (3 C-15), 147.2 (3 C-18), 144.0 (3 C-10), 124.4 (3 C-14, 3 C-16, 3 C-19, 3 C-23), 124.1 (3 C-9), 115.0 (3 C-13, 3 C-17) 114.8 (3 C-20, 3 C-22), 97.4 (3 C-1), 70.3 (3 C-24), 69.4 (3 C-5), 68.8 (3 C-2), 68.8 (3 C-3), 66.2 (3 C-7), 65.6 (3 C-4), 62.2 (3 C-6), 62.1 (3 C-11), 49.8 (3 C-8), 40.5 (C-25), 20.8, 20.7, 20.7, 20.6 (12 CO$\underline{C}H_3$), 17.3 (C-26) ppm; MALDI-TOF MS calcd for $C_{98}H_{111}N_{15}O_{36}$: m/z 2074.731 $[M+1]^+$; found: m/z 2074.391 $[M+1]^+$; IR (ATR) 2926, 1742, 1596, 1498, 1367, 1215, 1042, 840, 553 cm^{-1}.

Deprotection: Trivalent azobenzene glycoconjugate 22 ([Man-a z o]$_3$):



The acetyl-protected trivalent azobenzene glycoconjugate **21** (100 mg, 0.048 mmol) was dissolved in anhydrous methanol (3 mL) and a catalytic amount of solid NaOMe was added. The reaction mixture was stirred at room temperature for 16 h until TLC control (CH_2Cl_2 / MeOH, 3:7) indicated that the starting material had fully disappeared. It was neutralized with Amberlite IR 120 ion exchange resin and filtered. The filtrate was evaporated to yield **22** as a yellow solid (78 mg, 0.049 mmol, quantitative). R_f 0.21 (CH_2Cl_2 / MeOH, 3:7); $[\alpha]_D^{22} = +13.7$ (c = 0.92,

DMSO); m.p. 166-167 °C; ^{1}H NMR (600 MHz, DMSO-d_6, 300 K, TMS): δ = 8.21 (s, 3H, 3 H-9), 7.83-7.81 (m, 12H, 3 H-14, 3 H-16, 3 H-19, 3 H-23), 7.20 (d, *J* = 8.6 Hz, 6H, 3 H-13, 3 H-17), 7.17 (d, *J* = 9.0 Hz, 6H, 3 H-20, 3 H-22), 5.22 (s, 6H, 3 H-11a, 3 H-11b), 4.63 (s, 3 H-1), 4.59-4.53 (m, 6H, 3 H-8a, 3-H8b), 4.22 (bs, 6H, 3 H-24a, 3 H-24b), 3.97-3.94 (m, 3H, 3 H-7a), 3.81-3.79 (m, 3H, 3 H-7b), 3.64-3.54 (m, 6H, 3 H-6a, 3 H-2), 3.42 (dd, *J* = 11.6, 6.2 Hz, 3H, 3 H-6b), 3.39-3.34 (m, 6H, 3 H-3, 3 H-4), 3.14-3.13 (m, 3H, 3 H-5), 1.32 (s, 3H, 3 H-26) ppm; ^{13}C NMR (150 MHz, DMSO-d_6, 300 K, TMS): δ = 161.2 (3 C-21), 160.6 (3 C-12), 146.6 (3 C-15, 3 C-18), 142.7 (3 C-10), 125.4 (3 C-9), 124.5 (3 C-14, 3 C-16, 3 C-19, 3 C-23), 115.6 (3 C-20, 3 C-22), 115.5 (3 C-13, 3 C-17), 110.0 (3 C-1), 74.2 (3 C-5), 70.9 (3 C-3), 70.2 (3 C-2), 70.1 (3 C-24), 66.9 (3 C-4), 65.2 (3 C-7), 61.7 (3 C-11), 61.3 (3 C-6), 49.8 (3 C-8), 40.4 (C-25), 17.2 (C-26) ppm; MALDI-TOF MS calcd for $C_{74}H_{87}N_{15}O_{24}$: *m/z* 1592.6048 $[M+Na]^+$; found: *m/z* 1592.6006 $[M+Na]^+$; UV/Vis (DMSO) λ_{max} = 364 nm; ε = 29426 ± 958 L x mol^{-1} x cm^{-1}.

After irradiation: *Z*-22:

^{1}H NMR (600 MHz, DMSO-d_6, 300 K, TMS): δ = 8.15 (s, 3H, 3 H-9), 6.96 (d, *J* = 8.2 Hz, 6H, 3 H-14, 3 H-16), 6.88 (d, *J* = 8.5 Hz, 6H, 3 H-20, 3 H-22), 6.83-6.81 (m, 12H, 3 H-13, 3 H-17, 3 H-19, 3 H-23), 5.08 (s, 6H, 3 H-11a, 3 H11b), 4.61 (s, 3H, 3 H-1), 4.59-4.53 (m, 6H, 3 H-8a, 3 H-8b), 4.23 (bs, 6H, 3 H-24a, 3 H-24b), 3.95 (dd, *J* = 10.6, 6.0 Hz, 3H, 3 H-7a), 3.80 (dd, *J* = 10.8, 6.5 Hz, 3H, 3 H-7b), 3.69-3.53 (m, 6H, 3 H-6a, 3 H-2), 3.41 (dd, *J* = 11.8, 5.8 Hz, 3H, 3 H-6b), 3.39-3.34 (m, 6H, 3 H-3, 3 H-4), 3.14-3.12 (m, 3H, 3 H-5), 1.16 (s, 3H, H-26) ppm; ^{13}C NMR (150 MHz, DMSO-d_6, 300 K, TMS): δ = 157.3 (3 C-21, 3 C-12), 147.2 (3 C-15), 147.0 (3 C-18), 142.6 (3 C-10), 125.4 (3 C-9), 122.6 (3 C-13, 3 C-17), 122.4 (3 C-19, 3 C-23), 115.1 (3 C-14, 3 C-16), 115.0 (3 C-20, 3 C-22), 110.0 (3 C-1), 74.2 (3 C-5), 70.9 (3 C-3), 70.2 (3 C-2), 70.0 (3 C-24), 66.9 (3 C-4), 65.2 (3 C-7), 61.7 (3 C-11), 61.3 (3 C-6), 49.8 (3 C-8), 40.4 (C-25), 17.2 (C-26) ppm; UV/Vis (DMSO): λ_{max} = 449 nm; ε = 2749 ± 101 L x mol^{-1} x cm^{-1}.

3. Photochemistry of azobenzene glycoconjugates

Half life determination: *E*→*Z* photoisomerisation was effected using a high pressure mercury lamp UV-P 250C from Panacol-Elosol (50 µM solution, 30 min at 365 nm). The bandpass filters were obtained from Laser components. All photoisomerization and relaxation experiments were performed in DMSO. Upon irradiation of azobenzene glycosides in the ground state (GS) at 365 nm, the absorption spectra showed an increase in the absorbance in the n-π* transition and simultaneous decrease in the π-π* transition, as expected, indicating the generation of the respective *Z* isomer. The *E*:*Z* ratios in the ground state (GS) as well as in the photostationary state (PSS) were determined by integration of the respective signals in the ^{1}H NMR spectra.

To make sure that in case of the di- and trivalent azobenzene glycoconjugates **17** and **22** PSS was reached after irradiation for 30 min, *E*:*Z* ratios were also determined after 60 and 90 min of irradiation, respectively: no significant change was observed in comparison to 30 min irradiation time.

The kinetics of the *Z*→*E* relaxation process were determined by UV-Vis spectroscopy in the dark employing 50 µM solutions in DMSO at 18 °C. For determination of the rate constants, a graph of $\ln(A_\infty - A_t)$ was plotted as a function of time; where A_∞ is the absorbance of ππ* transition at infinitive time and A_t is the absorbance at time t after start of the relaxation process. The negative slope *k* of the linear plot is the rate constant of the *Z*→*E* relaxation process. The half life $\tau_{1/2}$ was determined as $\tau_{1/2} = \ln 2/k$.

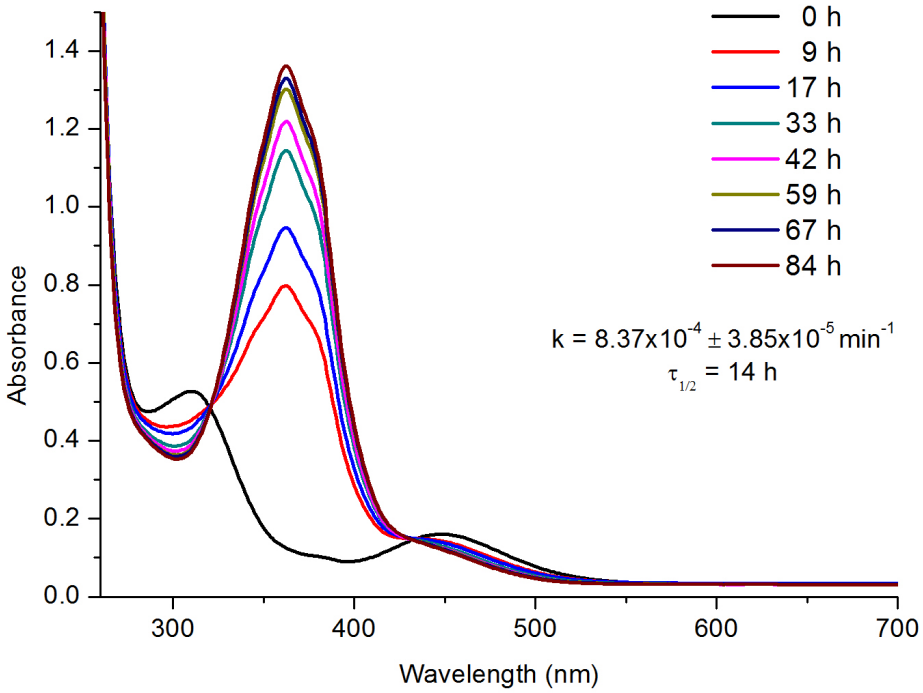


Figure S1. Thermal relaxation of *Z*-**8** to *E*-**8** (Man-a z o-Man) in DMSO; $\tau_{1/2} = 14$ h.

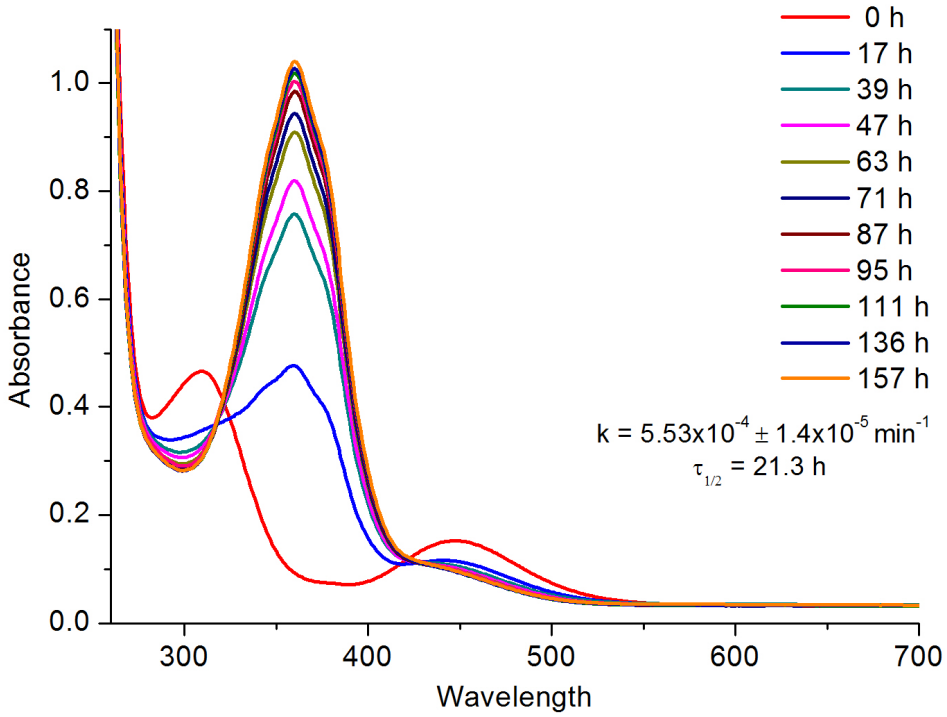


Figure S2. Thermal relaxation of ***Z*-12** to *E*-**12** (Man-a z o-Man) in DMSO; $\tau_{1/2} = 21.3$ h.

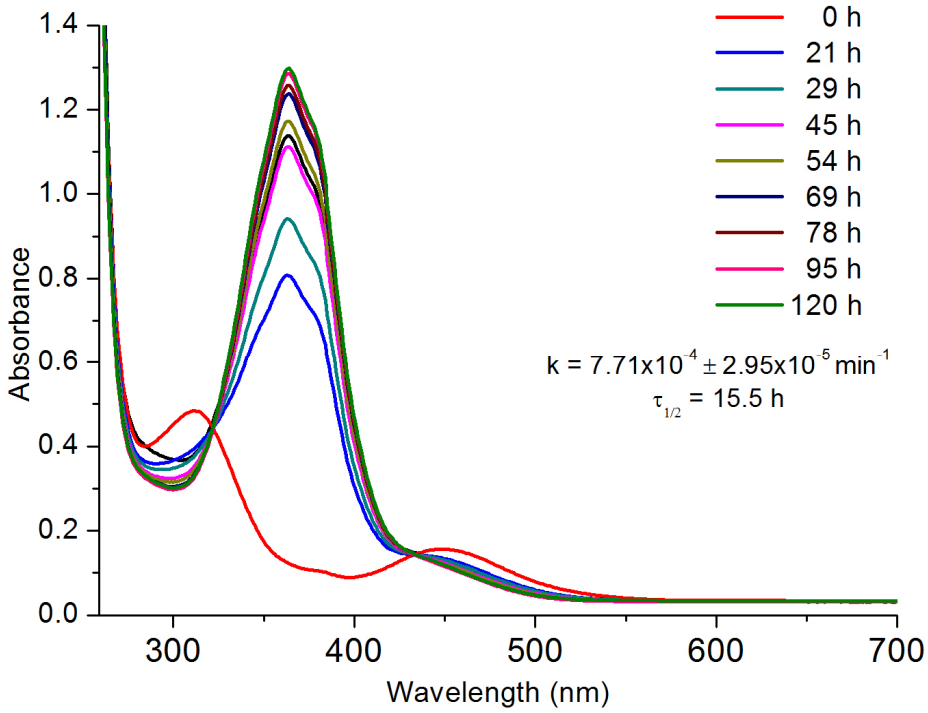


Figure S3. Thermal relaxation of *Z*-**17** to *E*-**17** (Man-a z o-a z o-Man) in DMSO; $\tau_{1/2}$ = 15.5 h.

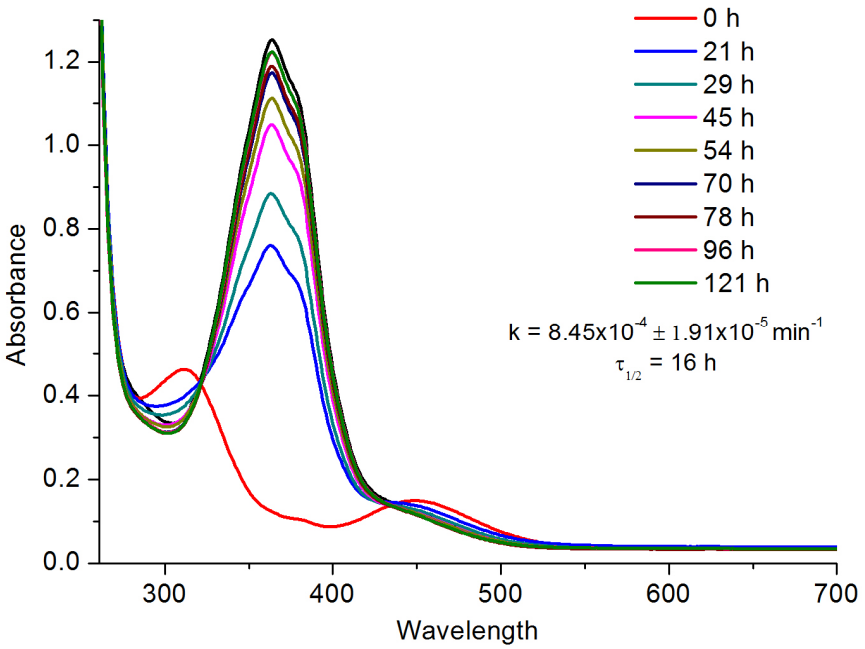


Figure S4. Thermal relaxation of *Z*-**22** to *E*-**22** ([Man-a z o]$_3$) in DMSO; $\tau_{1/2}$ = 16 h.

4. NMR Spectra of azobenzene glycoconjugates

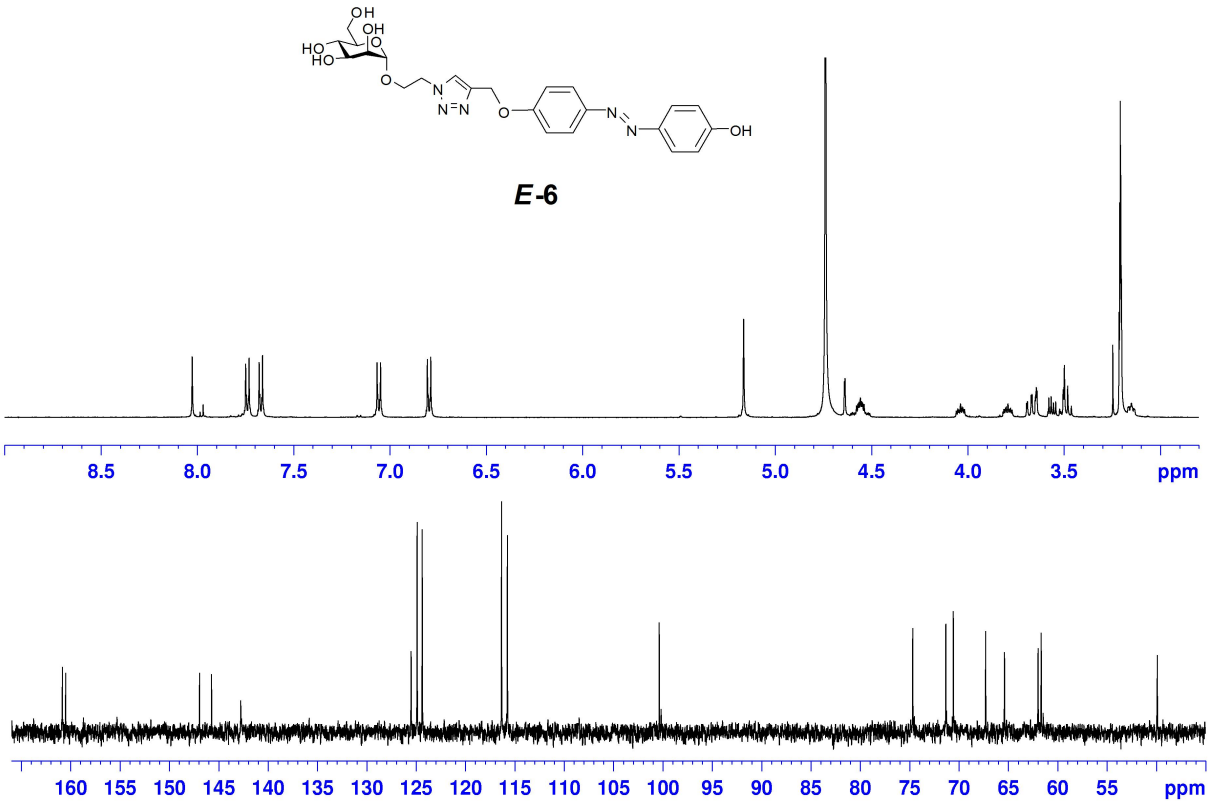


Figure S5. ^{1}H NMR (500 MHz, CD_3OD) and ^{13}C NMR (125 MHz, CD_3OD) of *E*-**6** (Man-a z o).

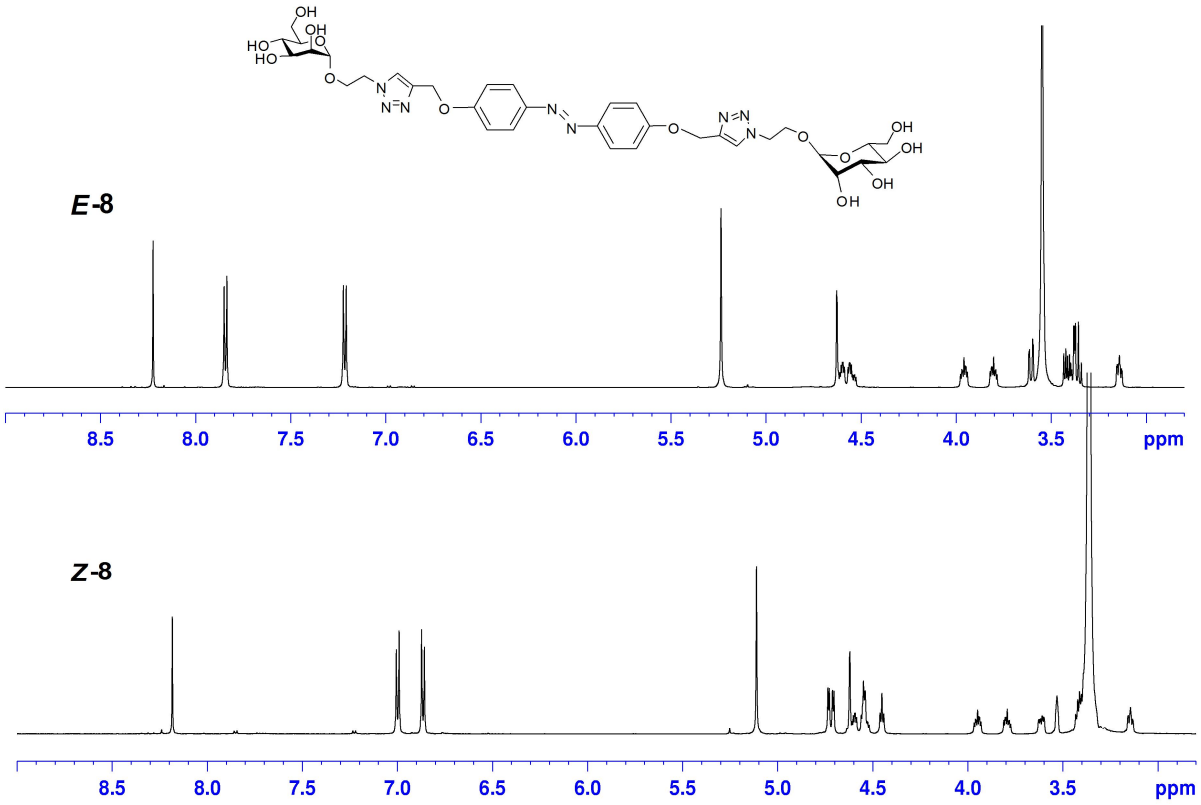


Figure S6. ^{1}H NMR (600 MHz, DMSO-d_6) of *E*-**8** and *Z*-**8** (Man-a z o-Man).

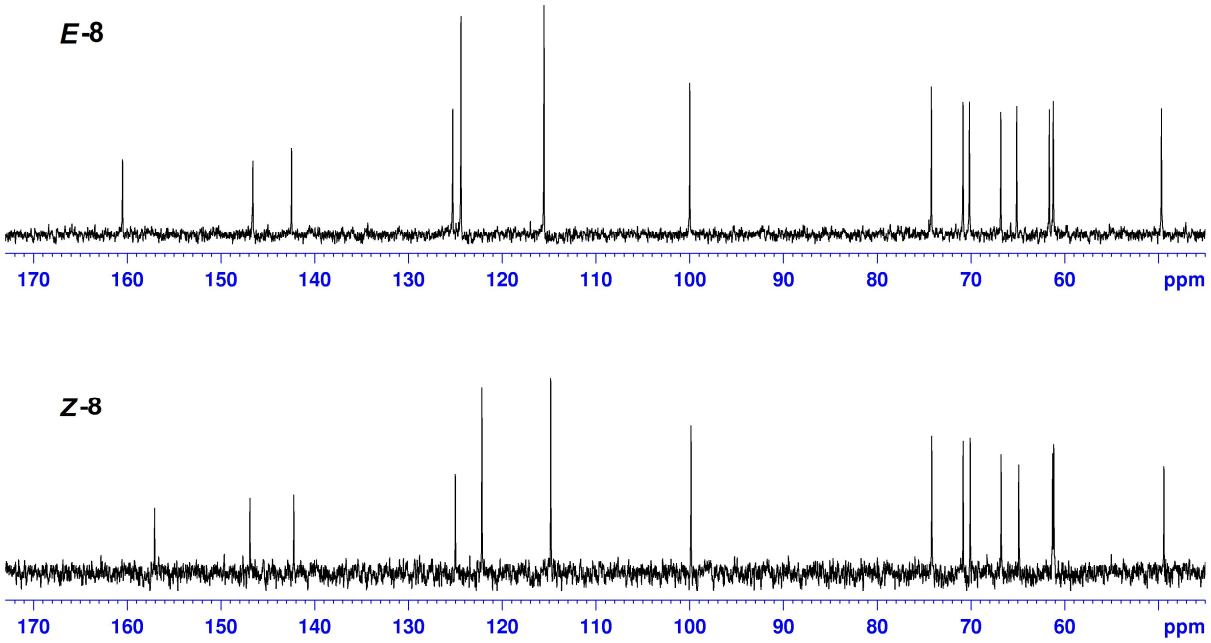


Figure S7. ^{13}C NMR (150 MHz, DMSO-d_6) of *E*-**8** and *Z*-**8** (Man-a z o-Man).

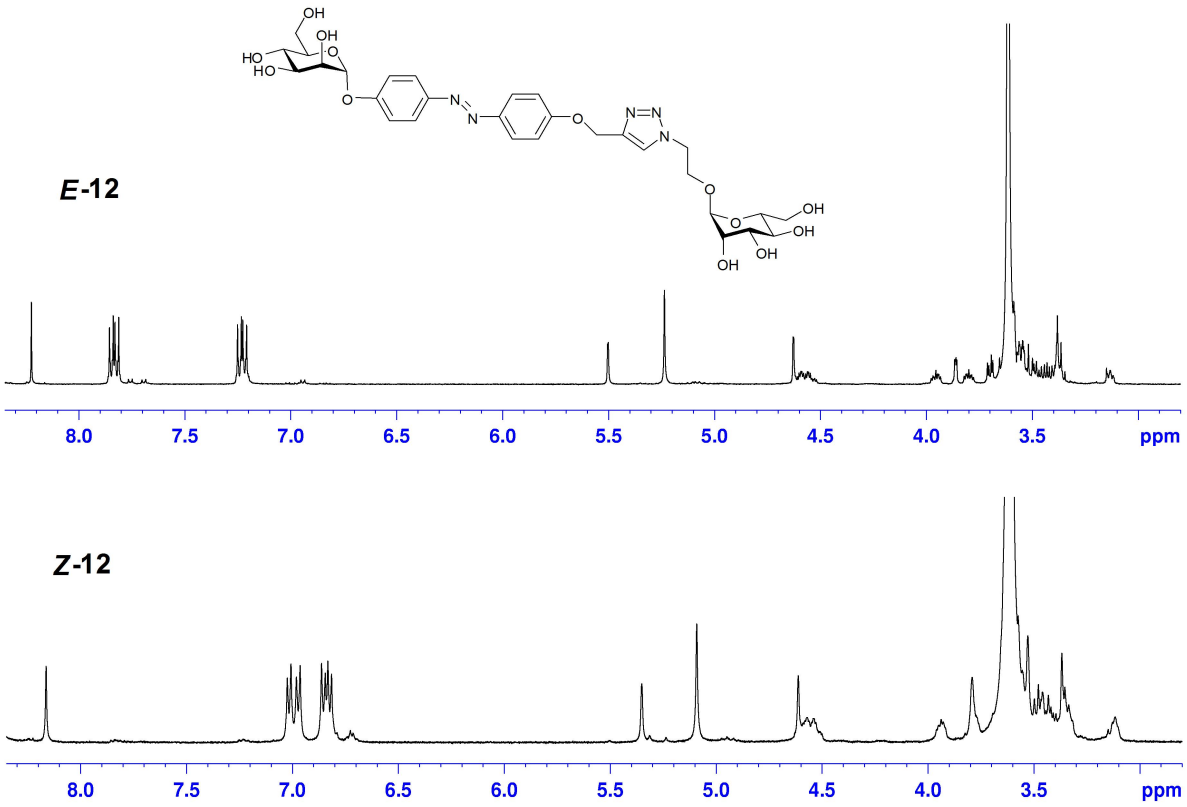


Figure S8. ^{1}H NMR (600 MHz, DMSO-d_6) of *E*-**12** and *Z*-**12** (Man-a z o-Man).

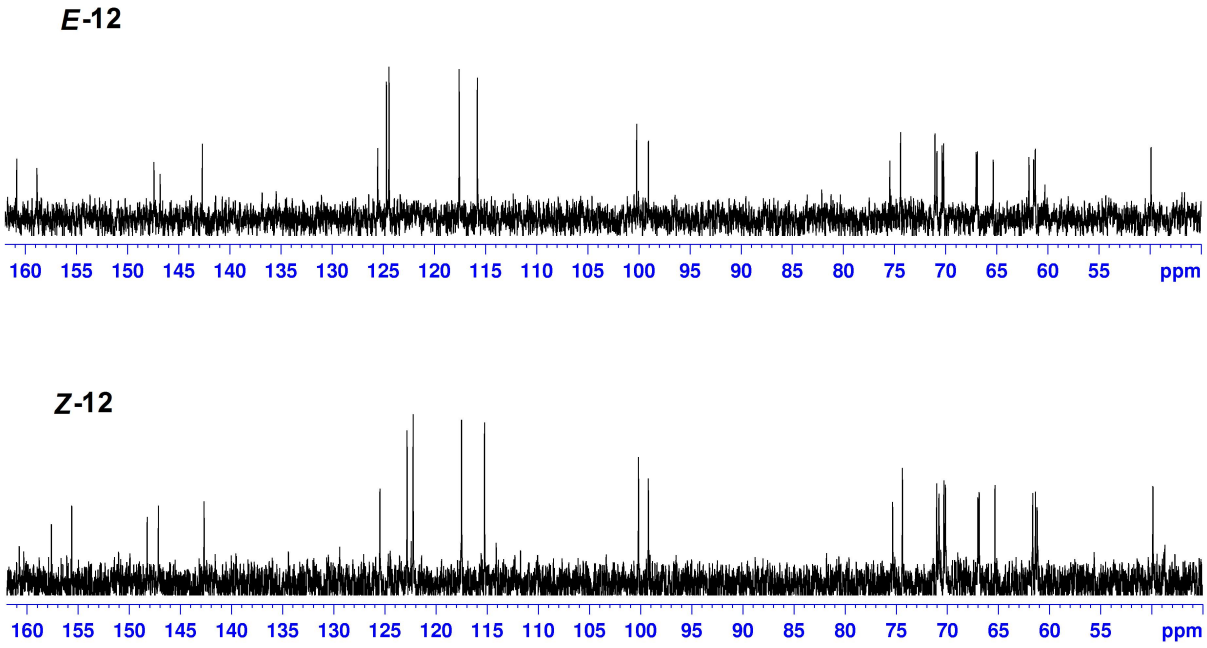


Figure S9. ^{13}C NMR (150 MHz, DMSO-d_6) of *E*-**12** and *Z*-**12** (Man-a z o-Man).

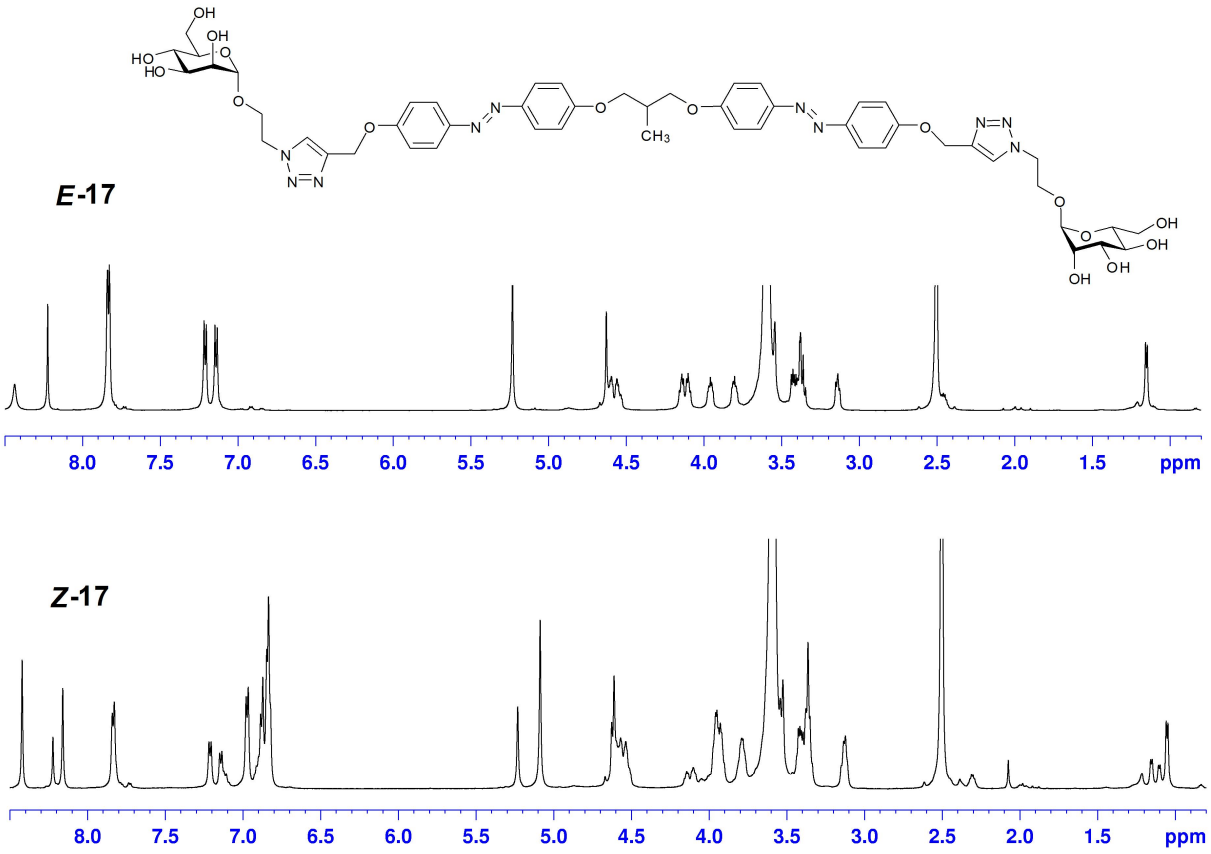


Figure S10. ^{1}H NMR (600 MHz, DMSO-d_6) of *E*-**17** and *Z*-**17** (Man-a z o-a z o-Man).

Note, that there is an equilibrium of *EE*, *EZ*, and *ZZ* isoforms after irradiation ('**Z-17**')as can be seen from the three dubletts for the protons of the methyl group at the focal point of the molecule at 1.0-1.2 ppm.

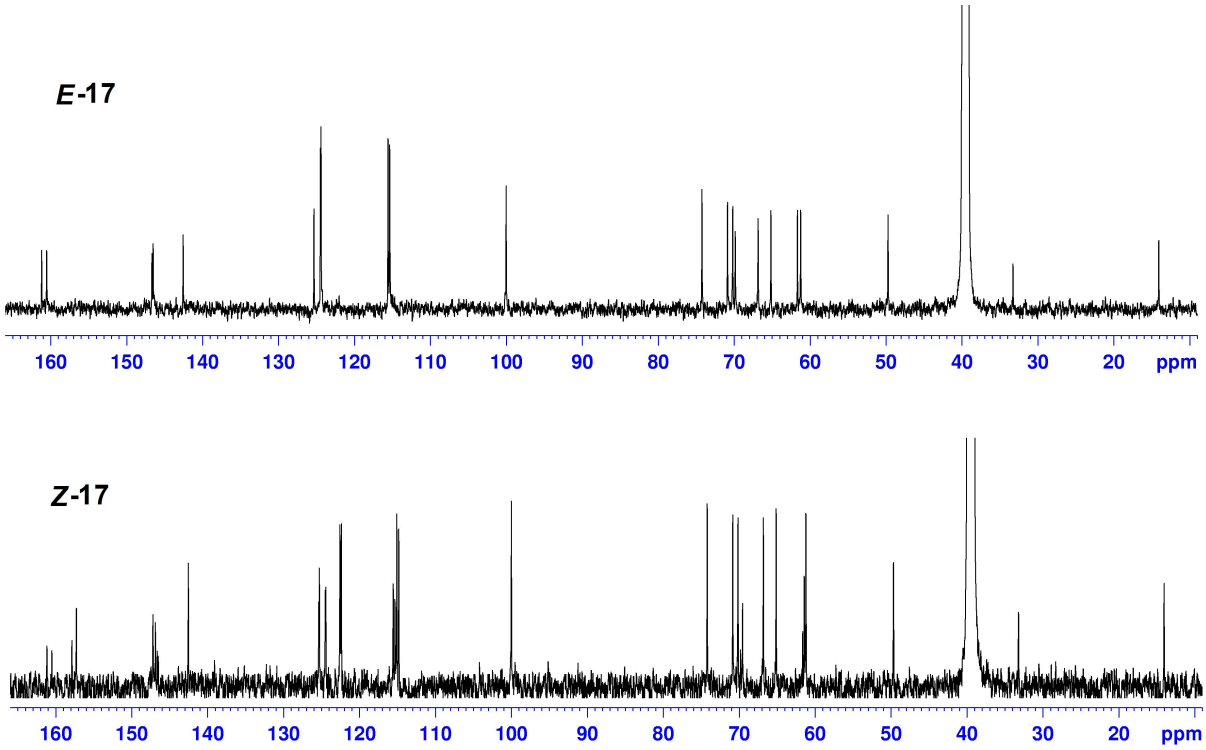


Figure S11. ^{13}C NMR (150 MHz, DMSO-d_6) of *E*-**17** and *Z*-**17** (Man-a z o-a z o-Man).

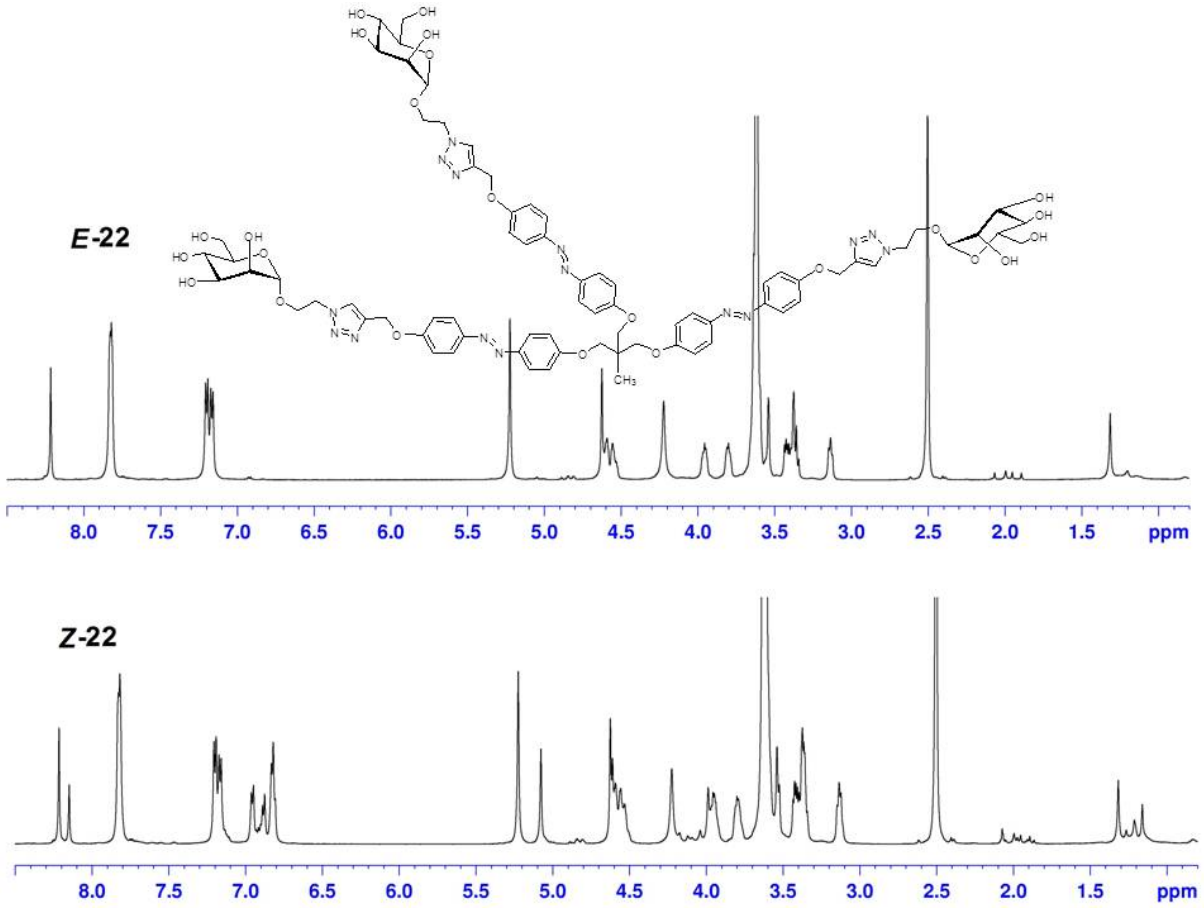


Figure S12. ^{1}H NMR (600 MHz, DMSO-d_6) of *E*-**22** and Z-**22** ([Man-a z o]$_3$).

Note, that there is an equilibrium of *EEE*, *EEZ*, *EZZ*, and *ZZZ* isoforms after irradiation (‘**Z-22**’)as can be seen from the four signals for the protons of the methyl group at the focal point of the molecule. at 1.1-1.4 ppm.

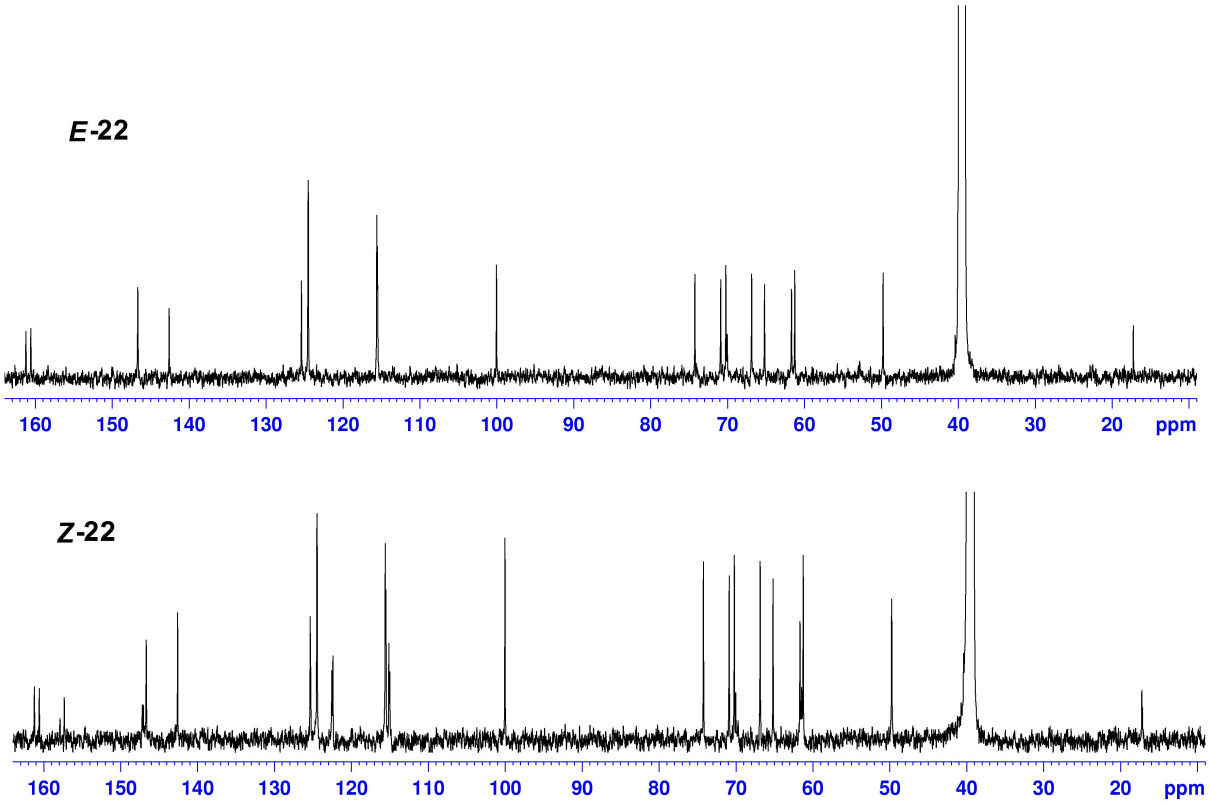


Figure S13. ^{13}C NMR (150 MHz, DMSO-d_6) of *E*-**22** and ***Z*-22** ([Man-a z o]$_3$).

5. References

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