Electronic Supplementary Material (ESI) for ChemComm.
This journal is © The Royal Society of Chemistry 2020

Supporting Information

Synthesis of functionalized copillar[4+1]arenes and rotaxane as heteromultivalent scaffolds

Wenzhang Chen, Tharwat Mohy EI Dine, Stéphane P. Vincent*

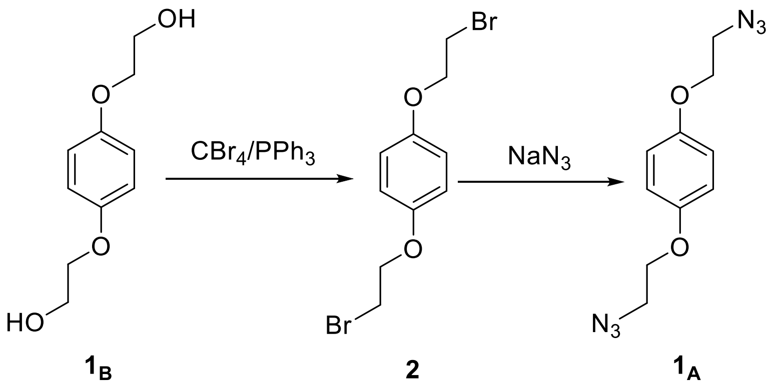
*Corresponding author: stephane.vincent@unamur.be

Table of Contents

S1. General Information

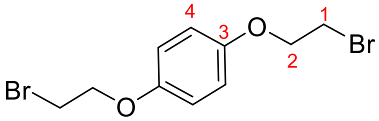
General methods and materials: The solvents used for chromatography were purchased in industrial grade and further distilled before their use. Dry dichloromethane was refluxed over calcium hydride (CaH_2). Reagents and chemicals were purchased from Sigma-Aldrich or Acros at ACS grade and were used without purification. All reactions were monitored by thin-layer chromatography (TLC) carried out on Merck aluminum roll silica gel 60-F_{254} using UV light and a phosphomolybdic acid solution as revelator. Merck silica gel (60, particle size 40-63 µm) was employed for flash column chromatography. IR spectra (cm^{-1}) were measured on a PerkinElmer Series FI-IR instrument. NMR spectra were recorded on a JEOL ECX 400 or 500 with solvent peaks as reference. All compounds were characterized by ^1H and ^{13}C NMR and Dept 135 as well as by ^1H-^1H, ^1H-^{13}C and 1D-NOESY correlation experiments when necessary. The abbreviations used to define the multiplicities are: s = singlet, d = doublet, t = triplet, q = quadruplet, m = multiplet and br = broad. Chemical shifts (δ) are reported in ppm and referenced indirectly to residual solvent signals. High resolution mass spectra (HRMS) were carried out on a Bruker MicroTOF-Q II XL spectrometer and MALDI-TOF-LD+ were recorded using Waters QTOF1 spectrometer. Fluorescence spectrophotometers were measured on an Agilent Cary Eclipse and excited at 380 nm.

S2. General synthetic procedures



Scheme S1. Synthesis of building blocks **1$_A$** and **2**

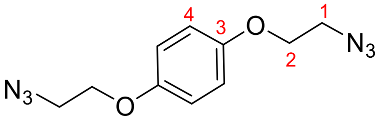
1,4-bis(2-bromoethoxy)benzene (**2**)



To a vigorously stirred mixture of 1.4-bis(2-hydroxyethoxy)benzene **1B** (3.96 g, 20 mmol, 1 equiv.) and PPh_3 (11.5 g, 44 mmol, 2.2 equiv.) in dry acetone (80 mL) was slowly added CBr_4 (14.6 g, 44 mmol, 2.2 equiv.) at the 0°C under argon atmosphere. After stirring for 4 h at room temperature, H_2O (60 mL) was added to the reaction mixture. The crude was filtered and washed with methanol/water (3:2, 150 mL) giving the desired compound **2** as a white solid (6.1 g, 18.83 mmol, 91%).

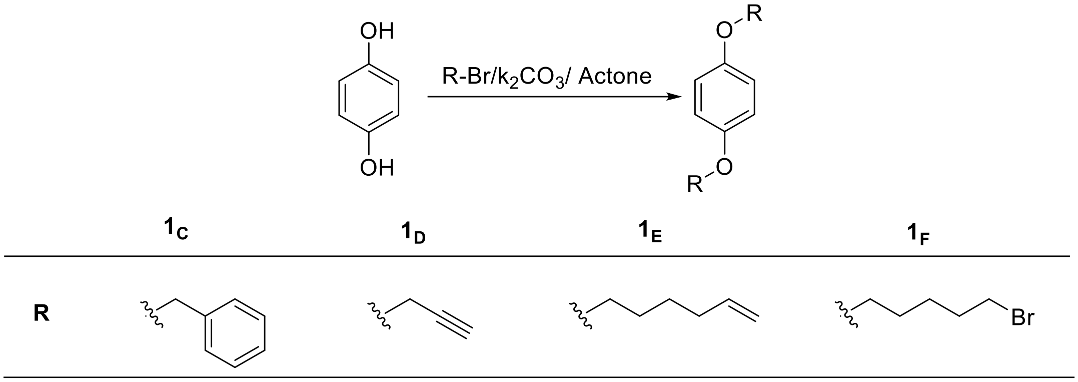
^1H NMR (400 MHz, $CDCl_3$) δ 6.85 (d, J = 0.6 Hz, 4H, 4 x H-4), 4.24 (t, J = 6.3 Hz, 4H, 2 x H-2), 3.61 (t, J = 6.3 Hz, 4H, 2 x H-1). ^{13}C NMR (100 MHz, $CDCl_3$) δ 152.9 (C-3), 116.2 (C-4), 68.8 (C-2), 29.4 (C-1). The data were in accordance with those described in the literature.[1]

1,4-bis(2-azidoethoxy)benzene (**1A**)



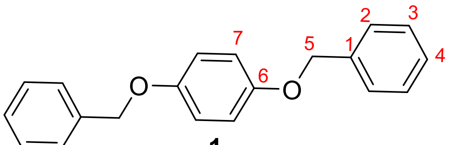
To a solution of 1,4-bis(2-bromoethoxy)benzene **2** (3.24 g, 10 mmol, 1 equiv.) in dry DMF (60 mL) was added NaN_3 (1.95 g, 30 mmol, 3 equiv.) and stirred overnight at room temperature. The reaction solution was then evaporated under vacuum. Afterwards, CH_2Cl_2 (40 mL) and H_2O (40 mL) were added, the organic phase was separated and washed with brine (40 ml), dried over $MgSO_4$ and filtered. The filtrate was evaporated to dryness to give the desired compound **1A** as a white solid (2.35 g, 9.45 mmol, 95%).

^1H NMR (400 MHz, $CDCl_3$) δ 6.87 (s, 4H, 4 x H-4), 4.11 (t, J = 5.0 Hz, 4H, 2 x H-2), 3.58 (t, J = 5.0 Hz, 4H, 4H, 2 x H-1). ^{13}C NMR 100 MHz, $CDCl_3$) δ 153.0 (C-3), 115.9 (C-4), 67.8 (C-2), 50.4 (C-1). The NMR data were in accordance with those described in the literature.[2]



Scheme S2. Synthesis of building blocks of $\mathbf{1_C}$-$\mathbf{1_F}$

1,4-bis(benzyloxy)benzene ($\mathbf{1_C}$)

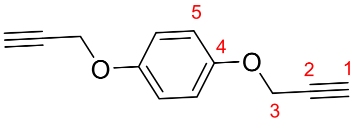


$\mathbf{1_C}$

To a solution of hydroquinone (440 mg, 4.0 mmol, 1 equiv.) in dry acetone (10 mL) was added KI (166 mg, 1.0 mmol, 0.25 equiv.) under argon atmosphere. The mixture was stirred for 0.3 h at 0°C, then BnBr (1.2 mL, 10 mmol, 2.5 equiv.) was added dropwise and stirred for another 36 h at room temperature. The resulting mixture was filtered, the solid was washed with CH_2Cl_2 (2 x10 mL). The combined solution were evaporated to dryness. Recrystallization from ethanol (10 mL) gave the compound $\mathbf{1_C}$ as a flaky crystal (844 mg, 2.9 mmol, 73%).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.44–7.26 (m, 10H, 4 x H-2, 4 x H-3, 2 x H-4), 6.9 (s, 4H, 4 x H-7), 5.0 (s, 4H, 2 x H-5). ^{13}C NMR (100 MHz, $CDCl_3$) δ 153.3 (C-6), 137.4 (C-1), 128.7 (C-3), 128.0 (C-4), 127.6 (C-2), 115.9 (C-7), 70.8 (C-5). The NMR data were in accordance with those described in the literature. [3]

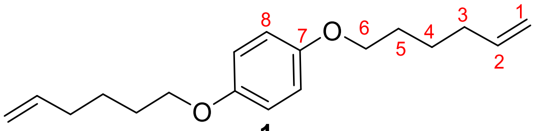
1,4-bis(propargyloxy)benzene (**1**$_D$)



To a solution of hydroquinone (4.4 g, 40 mmol, 1 equiv.) in dry acetone (100 mL) was added anhydrous K_2CO_3 (27.6 g, 200 mmol, 5 equiv.) and the reaction mixture was refluxed for 0.5 h. Then, propargyl bromide (10 mL, 120 mmol, 3 equiv.) was added dropwise over 2 h to the above reaction mixture. The resulting mixture was refluxed for 48 h before cooling down, followed by filtration. The filtrate was evaporated. The residue was purified by column chromatography on silica gel using Cy/EtOAc (20:1) as eluent to give compound **1**$_D$ as a white solid (6.4 g, 34.3 mmol, 86%).

^{1}H NMR (400 MHz, $CDCl_3$) δ 6.94 (s, 4H, 4 x H-5), 4.64 (d, *J* = 2.4 Hz, 4H, 2 x H-3), 2.50 (t, *J* = 2.4 Hz, 2H, 2 x H-1). ^{13}C NMR (100 MHz, $CDCl_3$) δ 152.6 (C-4), 116.2 (C-5), 78.9 (C-2), 75.5 (C-1), 56.7 (C-3). The NMR data were in accordance with those described in the literature. [4]

1,4-bis(5-hexenyloxy)benzene (**1**$_E$)

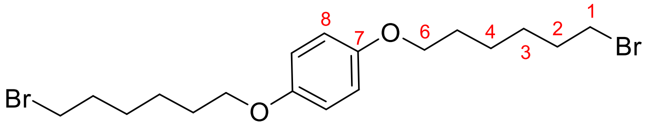


1$_E$

To a solution of the hydroquinone (1.1 g, 10 mmol, 1 equiv.) in dry acetone (40 mL) was added anhydrous K_2CO_3 (6.2 g, 45 mmol, 4.5 equiv.) and KI (0.17 g, 1 mmol, 0.1 equiv.) under argon atmosphere. Then 6-bromo-1-hexene (3.1 mL, 22 mmol, 2.2 equiv.) was added dropwise over 1 h to the above reaction mixture. The resulting mixture was refluxed for 48 h before cooling down, followed by filtration and the filtrate was evaporated. The residue was dissolved in CH_2Cl_2 (50 mL) and the solution was washed with water (3 x 20 mL) and saturated brine (40 mL). The organic layer was dried over anhydrous $MgSO_4$ and then concentrated under vacuum. The residue was purified by column chromatography on silica gel using Cy/EtOAc (10:1) as eluent to give compound **1$_E$** as a white solid (2.1 g, 7.7 mmol, 77%).

^{1}H NMR (400 MHz, CDCl$_3$) δ 6.82 (s, 4H, 4 x H-8), 5.84 (ddt, *J* = 16.9, 10.2, 6.6 Hz, 2H, 2 x H-2), 5.07–4.96 (m, 4H, 2 x H-1), 3.92 (t, *J* = 6.5 Hz, 4H, 2 x H-6), 2.16–2.10 (m, 4H, 2 x H-3), 1.82–1.75 (m, 4H, 2 x H-5), 1.61–1.54 (m, 4H, 2 x H-4). ^{13}C NMR (100 MHz, CDCl$_3$) δ 153.3 (C-7), 138.7 (C-2), 115.5 (C-8), 114.8 (C-1), 68.5 (C-6), 33.6 (C-3), 29.0 (C-5), 25.5 (C-4). The NMR data were in accordance with those described in the literature.[5]

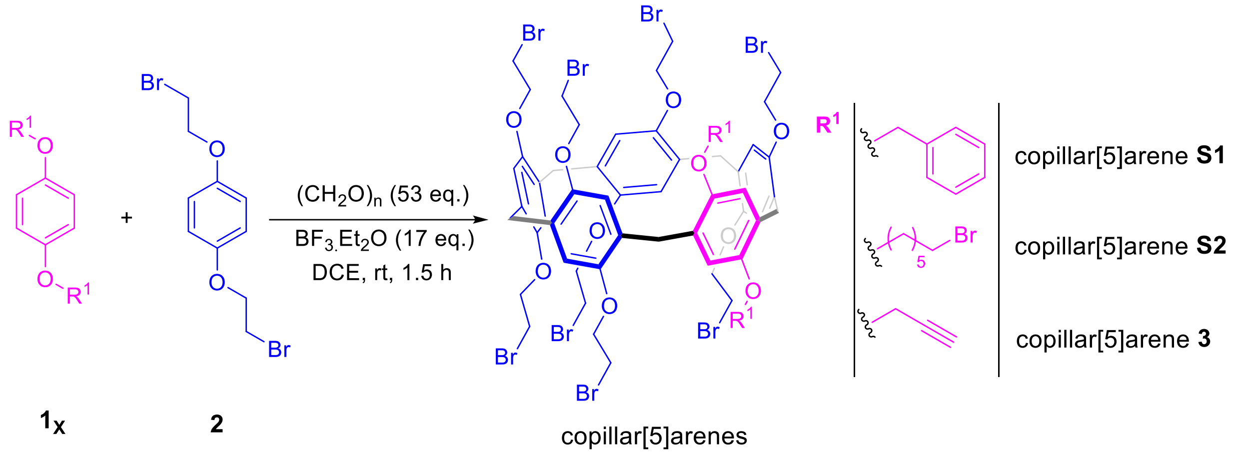
1,4-bis[(6-bromohexyl)oxy]benzene (1$_F$)



To a solution of 1,6-dibromohexane (3.6 mL, 22 mmol, 2.2 equiv.) in dry acetone (40 mL) was added K_2CO_3 (6.9 g, 50 mmol, 5 equiv.) under argon atmosphere. After heating the solution to reflux for 5 min a solution of hydroquinone (1.1g, 10 mmol) in dry acetone (10 mL) was added dropwise over 1 h. The resulting mixture was refluxed for 48 h and allowed to cool down to room temperature, filtered. The filtrate was evaporated to dryness. The residue was purified by column chromatography on silica gel using Cy/DCM (2:1) as eluent to afford compound **1$_F$** as a white solid (1.4 g, 3.2 mmol, 32 %).

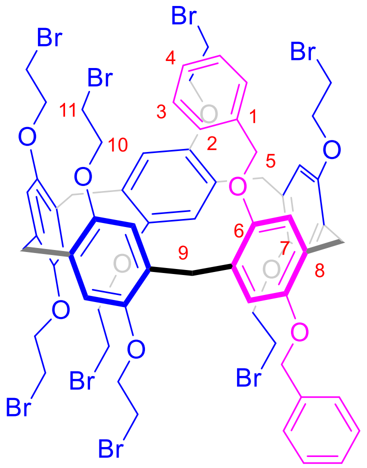
^{1}H NMR (400 MHz, CDCl$_3$) δ 6.82 (s, 4H, 4 x H-8), 3.90 (t, *J* = 6.4 Hz, 4H, 2 x H-6), 3.42 (t, *J* = 6.4 Hz, 4H, 2 x H-1), 1.93–1.86 (m, 4H, 2 x H-2), 1.80–1.74 (m, 4H, 2 x H-5), 1.51–1.47 (m, 8H, 2 x H-3, 2 x H-4). ^{13}C NMR (100 MHz, CDCl$_3$) δ 153.3 (C-7), 115.5 (C-8), 68.5 (C-6), 34.0 (C-1), 32.8 (C-2), 29.3 (C-5), 28.1 (C-3 or C-4) , 25.4 (C-3 or C-4). The NMR data were in accordance with those described in the literature.[6]

S3. Co-oligmerization of bisalkoxybenzene **1**$_x$ with **2**



Scheme S3. Co-oligomerization of **1**$_x$ with **2**

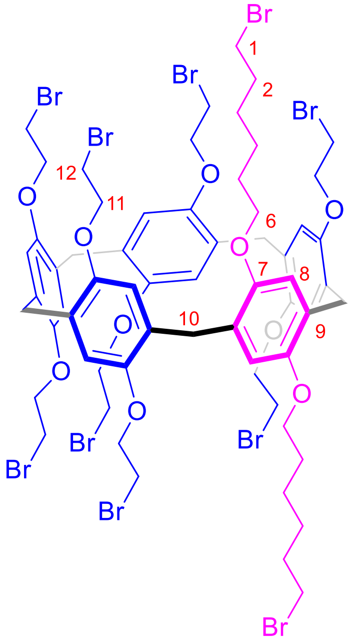
Copillar[5]arene S1:



To a solution of 1,4-bis(benzyloxy)benzene **1**$_C$ (87 mg, 0.3 mmol, 1 equiv.) and 1,4-bis(2-bromoethoxy)benzene **2** (1.56 g, 4.8 mmol, 16 equiv.) in DCE (20 mL) was added paraformaldehyde (525 mg, 37.1 mmol, 53 equiv.) under argon atmosphere. Then, $BF_3.Et_2O$ (0.63 mL, 5.1 mmol, 17 equiv.) was added dropwise. After stirring for 1.5 h at room temperature, the solution was concentrated, CH_2Cl_2 (10 mL) was added and the reaction mixture was filtered. The filtrate was evaporated and the residue was purified by column chromatography on silica gel using DCM/Cy (1:4) as eluent and isolated copillar[5]arene **S1** as a white solid (54 mg, 0.03 mmol, 11%).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.54–7.52 (m, 4H, Bn), 7.43–7.33 (m, 6H, Bn), 7.05 (s, 2H, 2 x H-7), 6.94 (s, 2H, 2 x H-7), 6.88 (s, 2H, 2 x H-7), 6.85 (s, 2H, 2 x H-7), 6.72 (s, 2H, 2 x H-7), 5.07–5.00 (m, 4H, 2 x H-5), 4.33–4.26 (m, 6H, 3 x H-10), 4.19–4.07 (m, 6H, 3 x H-10), 3.93–3.82 (m, 10H, 5 x H-9), 3.66–3.53 (m, 16H, 2 x H-10, 6 x H-11), 3.47–3.33 (m, 4H, 2 x H-11). ^{13}C NMR (100 MHz, $CDCl_3$) δ 150.1, 150.0, 2 x 149.6, 149.5 (Cq, C-6), 138.14 (Cq, C-1), 129.6, 129.1, 128.9, 128.8 (Cq, C-8), 128.7 (Bn), 128.5 (Cq, C-8), 2 x 127.8 (Bn), 116.5, 116.2, 115.4, 115.1 (CH_{Ar}, C-7), 70.4 (OCH_2, C-5), 2 x 69.2, 69.0, 67.9 (OCH_2, C-10), 31.1, 2 x 30.8, 30.7 (CH_2Br, C-11), 30.3, 29.9, 28.8 (CH_2, C-9). HRMS (ESI$^+$-MS, m/z): calculated for $C_{65}H_{70}Br_8NO_{10}$ $[M+NH_4]^+$ 1655.8461; found 1655.8378.

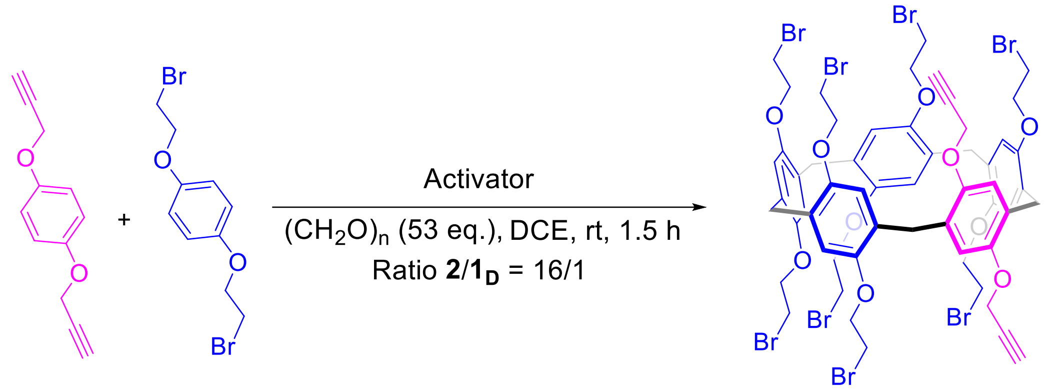
Copillar[5]arene S2:



To a solution of 1,4-bis(6-bromohexyl)oxy)benzene **1$_F$** (109 mg, 0.25 mmol, 1 equiv.) and 1,4-bis(2-bromoethoxy)benzene **2** (1.30 g, 4.0 mmol, 16 equiv.) in DCE (20 mL) was added paraformaldehyde (438 mg, 13.3 mmol, 53 equiv.) under argon atmosphere. Then, $BF_3.Et_2O$ (0.52 mL, 4.25 mmol, 17 equiv.) was added dropwise. After stirring for 1.5 h at room temperature, H_2O (20 mL) was added, separated the organic phase, washed with saturated brine (15 mL), dried over $MgSO_4$, filtered and concentrated under vacuum. The residue was purified by column chromatography on silica gel using DCM/Cy (2:3) as eluent and isolated copillar[5]arene **S2** as a white solid (125 mg, 0.07 mmol, 28%).

^{1}H NMR (400 MHz, CDCl$_3$) δ 6.92–6.90 (m, 6H, 6 x H-8), 6.84–6.81 (m, 4H, 4 x H-8), 4.23–4.14 (m, 14H, H-6, 6 x H-11), 4.06–4.04 (m, 4H, H-6, H-11), 3.93–3.81 (m, 12H, H-11, 5 x H-10), 3.64–3.60 (m, 12H, 6 x H-12), 3.46–3.41 (m, 4H, 2 x H-12), 3.25 (t, *J* = 6.8 Hz, 4H, 2 x H-1), 1.83–1.76 (m, 4H, 2 x H-5), 1.73–1.66 (m, 4H, 2 x H-2), 1.47–1.38 (m, 8H, 2 x H-3, 2 x H-4).^{13}C NMR (100 MHz, CDCl$_3$) δ 152.9, 150.0, 149.9, 149.8 (Cq, C-7), 129.6, 129.3, 129.2, 128.9, 128.4 (Cq, C-9), 116.4, 116.2, 115.9, 115.9 (CH$_{Ar}$, C-8), 69.2, 69.1, 68.9, 68.7, 68.7 (OCH$_2$, C-6), 33.9 (CH$_2$Br, C-1), 32.7 (CH$_2$, C-2), 30.7, 30.6, 30.5, 29.8, 29.68, 29.2 (CH$_2$, C-5, C-10, C-12), 28.2 (CH$_2$, C-3 or C-4), 25.4 (C-3 or C-4). HRMS (ESI$^+$-MS, m/z): calculated for $C_{63}H_{80}Br_{10}NO_{10}$ [M+NH$_4$]$^+$ 1799.7610; found 1799.7610.

S4. Optimization of the co-oligomerization conditions of 1$_D$ with 2



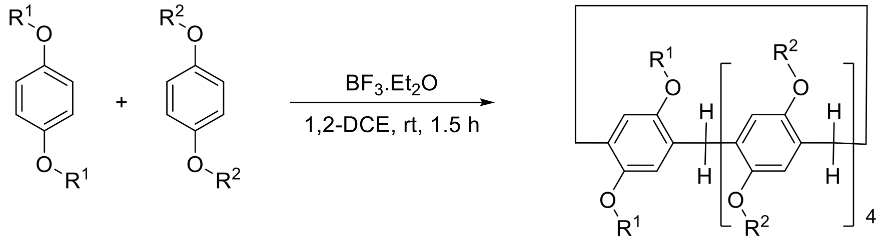
1$_D$ **2** Copillar[5]arene **3**

Table S1. Different optimization conditions

Entry	Conc. of **2** (mM)	Activator (Eq.)	Eq. of **2** (**1$_D$**=1eq.)	Yield (%)[a]
1	0.25	$BF_3.Et_2O$ (17)	16	26
2[ref 16a]	0.05	$FeCl_3$ (2.56)	16	17
3[ref 21]	0.125	CH_3SO_3H (50)	16	16
4[b]	0.125	$BF_3.Et_2O$ (17)	16	15
5	0.125	$BF_3.Et_2O$ (17)	16	37
6	0.0625	$BF_3.Et_2O$ (17)	16	25
7	0.125	$BF_3.Et_2O$ (17)	32	36
8	0.125	$BF_3.Et_2O$ (17)	8	31
9	0.125	$BF_3.Et_2O$ (17)	4	24
10	0.125	$BF_3.Et_2O$ (25.5)	16	40
11	0.125[c]	$BF_3.Et_2O$ (25.5)	0.0625[d]	40[e]

(a) Isolated yield. (b) CH_2Cl_2 was used as the solvent. (c) Conc. of **1$_D$**. (d) Ratio **1$_D$**/**2** = 1/16. (e) Yield of the copillar[5]arene **4** (structure in **Scheme S4** below).

S5. General procedure A for the synthesis of copilllar[5]arenes 3 and 4



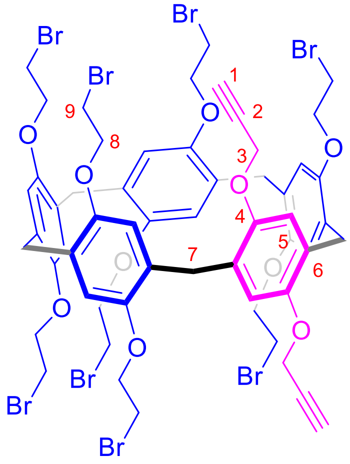
Co-pillar[5]arene **3** R^2 = CH_2CH_2Br R^1 = CH_2CCH

Co-pillar[5]arene **4** R^1 = CH_2CH_2Br R^2 = CH_2CCH

Scheme S4. Synthesis of copillar[5]arene **3** and **4**

To a solution of R^1 substituted 1,4-dialkyloxybenzene (0.125 mmol, 1 equiv.) and R^2 substituted 1,4-dialkyloxybenzene (2.0 mmol, 16 equiv. 0.125 M) in DCE (16 mL) paraformaldehyde (6.6 mmol, 198 mg, 53 equiv.) was added under argon atmosphere. Then, $BF_3.Et_2O$ (0.39 mL, 3.19 mmol, 25.5 equiv.) was added dropwise to the reaction mixture. After stirring for 1.5 h at room temperature, the reaction was quenched by adding MeOH (10 mL) and stirred for another 5 min before being concentrated under vacuum. Afterwards, CH_2Cl_2 (10 mL) was added to the residue and filtered. The crude was concentrated under vacuum and the residue was purified by column chromatography on silica gel.

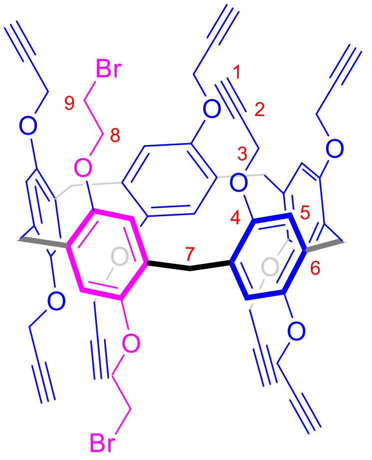
Copillar[5]arene 3:



The title compound was prepared according to the general procedure, purified using DCM/Cy (1:1) as eluent and isolated as a white solid (78 mg, 0.051 mmol, 40%). When the reaction was scaled up 10 times the yield is 38%.

^{1}H NMR (400 MHz, CDCl$_3$) δ 6.93 (s, 2H, 2 x H-5), 6.88 (s, 6H, 6 x H-5), 6.77 (s, 2H, 2 x H-5), 4.60 (s, 4H, 2 x H-3), 4.23–4.14 (m, 16H, 8 x H-8), 3.87 (m, 10H, 5 x H-7), 3.65–3.58 (m, 16H, 8 x H-9), 2.21 (s, 2H, 2 x H-1). ^{13}C NMR (100 MHz, CDCl$_3$) δ 2 x 149.9, 149.8, 149.5 (Cq, C-4), 129.6, 129.3, 129.2, 129.1, 129.0 (Cq, C-6), 116.4, 116.3, 116.1, 116.0, 115.9 (CH$_{Ar}$, C-5), 79.3 (C-2), 75.0 (C-1), 69.3, 69.2, 69.1, 68.9 (CH$_2$, C-8), 56.7 (CH$_2$, C-3), 30.8, 30.7, 30.6 (CH$_2$, C-9), 29.9, 29.8, 29.5 (CH$_2$, C-7). IR (cm^{-1}): 3292 (C*CH*). HRMS (ESI$^+$-MS, m/z): calculated for C$_{57}$H$_{59}$Br$_8$O$_{10}$ [M+H]$^+$ 1534.7570; found 1534.7569.

Copillar[5]arene 4:

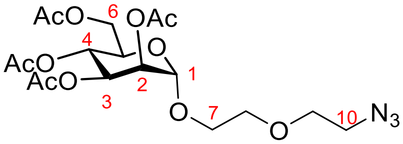


The title compound was prepared according to the general procedure, purified using DCM/Cy (3:2) as eluent and isolated as a white solid (57 mg, 0.050 mmol, 40%). When the reaction was scaled up 16 times the yield is 37%.

^{1}H NMR (400 MHz, CDCl$_3$) δ 6.84–6.82 (m, 8H, 8 x H-5), 6.77 (s, 2H, 2 x H-5), 4.52–4.46 (m, 16H, 8 x H-3), 4.15 (t, *J* = 6.1 Hz, 4H, 2 x H-8), 3.82 (m, 10H, 5 x H-7), 3.57 (t, *J* = 6.1 Hz, 4H, 2 x H-9), 2.29–2.24 (m, 8H, 8 x H-1). ^{13}C NMR (100 MHz, CDCl$_3$) δ 149.8, 2 x 149.5 (Cq, C-4), 129.2, 129.1, 129.0, 128.9 (Cq, C-6), 116.0, 115.8, 115.7, 115.6 (CH$_{Ar}$, C-5), 2 x 79.4, 79.3 (C-2), 2 x 75.1, 75.0, 74.98 (C-1), 68.9 (CH$_2$, C-8), 56.9, 56.8, 56.7, 56.6 (CH$_2$, C-3), 30.3 (CH$_2$Br, C-9), 30.0, 29.99, 29.7 (CH$_2$, C-7). IR (cm^{-1}): 3285, 2126 (*C*CH). HRMS (ESI$^+$-MS, m/z): calculated for $C_{63}H_{53}Br_2O_{10}$ [M+H]$^+$ 1127.2000; found 1127.1999.

S6. Synthesis of clickable functional ligands 5, 11, 7a-h, 9, 13 and 14

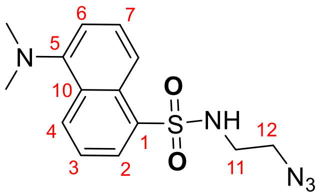
5-Azido-3-oxapentyl 2,3,4,6-tetra-*O*-acetyl-α-D-mannopyranoside (5)



The title compound was prepared following a literature procedure,[7] purified using EtOAc/Cy (1:4) as eluent and isolated as a white solid (2.3 g, 4.99 mmol, 49%).

^{1}H NMR (400 MHz, CDCl$_3$) δ 5.38–5.35 (m, 1H, H-3), 5.31–5.29 (m, 1H, H-4), 5.29–5.27 (m, 1H, H-2), 4.88 (d, *J* = 1.7 Hz, 1H, H-1), 4.29 (dd, *J* = 12.0, 4.9 Hz, 1H, H-6a), 4.12–4.06 (m, 1H, H-6b, H-5), 3.86–3.81 (m, 1H, H-7a), 3.69–3.66 (m, 5H, H-7b, H-8, H-9), 3.39 (t, *J* = 5 Hz, 2H, H-10), 2.15 (s, 3H, OCOCH$_3$), 2.10 (s, 3H, OCOCH$_3$), 2.04 (s, 3H, OCOCH$_3$), 1.99 (s, 3H, OCOCH$_3$). ^{13}C NMR (100 MHz, CDCl$_3$) δ 170.9, 170.2, 170.1, 169.9 (Cq, C=O$_{\text{acetyl}}$), 97.9 (C-1), 70.3 (C-8), 70.2 (C-9), 69.6 (C-2), 69.2 (C-3), 68.5 (C-5), 67.4 (C-7), 66.2 (C-4), 62.6 (C-6), 50.9 (C-10), 21.1, 2 x 20.9 (OCOCH$_3$). The NMR data were in accordance with those described in the literature. [7]

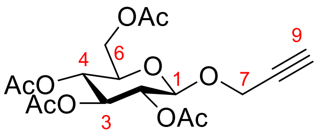
_N_-(2-Azidoethyl)-5-(dimethylamino)naphthalene-1-sulfonamide (**11**)



To a solution of dansyl chloride (540 mg, 2.0 mmol, 1 equiv.) and 2-bromoethylamine hydrobromide (410 mg, 2.0 mmol, 1 equiv.) in CH$_2$Cl$_2$ (10 mL) was slowly added Et$_3$N (4.0 mmol, 0.56 mL, 2 equiv.). After stirring at room temperature for 4 h, the solvent was evaporated and acetonitrile (10 ml), NaN$_3$ (0.36 g, 5 mmol, 2.5 equiv.) were added. The reaction mixture was allowed to reflux overnight before being cooled down. The solvent was evaporated and the crude was purified by column chromatography on silica gel using EtOAc/Cy (5:1) as eluent to give the desired product as a greenish yellow oil (588 mg, 1.84 mmol, 92%).

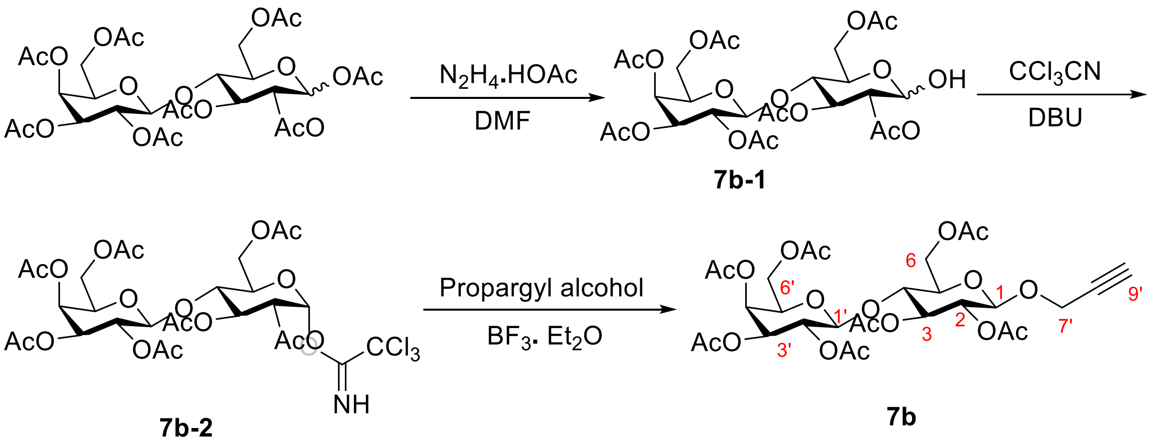
^{1}H NMR (400 MHz, CDCl$_3$) δ 8.56 (d, *J* = 8.5 Hz, 1H, H-2), 8.29 (d, *J* = 8.6 Hz, 1H, H-8), 8.25 (dd, *J* = 7.3, 1.2 Hz, 1H, H-4), 7.58–7.54 (m, 1H, H-3), 7.51 (dd, *J* = 8.5, 7.4 Hz, 1H, H-7), 7.19 (d, *J* = 7.6 Hz, 1H, H-6), 5.42–5.39 (m, 1H, NH), 3.28 (t, *J* = 5.8 Hz, 2H, H-12), 3.05 (dd, *J* = 12.0, 5.9 Hz, 2H, H-11), 2.88 (s, 6H, 2 x NCH$_3$). ^{13}C NMR (100 MHz, CDCl$_3$) δ 152.1 (Cq, C-1), 134.6 (Cq, C-5), 130.8 (C-2), 130.0 (C-4), 129.6 (Cq, C-9), 129.6 (Cq, C-10), 128.7 (C-3), 123.2 (C-7), 118.7 (C-8), 115.5 (C-6), 50.9 (C-12), 45.5 (NCH$_3$), 42.4 (C-11). The NMR data were in accordance with those described in the literature. [8]

2-Propynyl 2,3,4,6-tetra-*O*-acetyl-β-D-glucopyranoside (7a)



In an ice-water cooled solution of D-glucose pentaacetate (772 mg, 2.0 mmol, 1 equiv.) and propargyl alcohol (0.17 mL, 3.0 mmol, 1.5 equiv.) in dry acetonitrile (10 mL) was added $BF_3.Et_2O$ (72 µL, 3.0 mmol, 1.5 equiv.) and TMSOTf (0.38 mL, 0.4 mmol, 0.2 equiv.) dropwise under argon atmosphere. After stirring overnight at room temperature, the reaction was quenched with solution of saturated $NaHCO_3$ (10 mL), extracted with EtOAc (2 x 15 mL). The combined organic layers were washed with H_2O (30 ml), brine (30 mL) and dried over $MgSO_4$, filtered and concentrated under reduced pressure. The crude was purified by column chromatography on silica gel using EtOAc/Cyc (1:5) as eluent and isolated **7a** as a white solid (324 mg, 0.84 mmol, 42%).

^{1}H NMR (400 MHz, $CDCl_3$) δ 5.23 (dd, *J* = 9.5 Hz, 1H, H-3), 5.08 (t, *J* = 9.7 Hz, 1H, H-4), 5.00 (dd, *J* = 9.6, 8.0 Hz, 1H, H-2), 4.76 (d, *J* = 8.0 Hz, 1H, H-1), 4.36 (d, *J* = 2.4 Hz, 2H, H-7), 4.26 (dd, *J* = 12.4, 4.6 Hz, 1H, H-6a), 4.13 (dd, *J* = 12.4, 2.4 Hz, 1H, H-6b), 3.72 (ddd, *J* = 10.0, 4.6, 2.4 Hz, 1H, H-5), 2.46 (t, *J* = 2.4 Hz, 1H, H-9), 2.07 (s, 3H, $OCOCH_3$), 2.04 (m, 3H, CH_3, $OCOCH_3$), 2.01 (s, 3H, $OCOCH_3$), 1.99 (s, 3H, $OCOCH_3$). ^{13}C NMR (100 MHz, $CDCl_3$) δ 170.7, 170.3, 2 x 169.5 (Cq, $C{=}O_{acetyl}$), 98.2 (C-1), 78.2 (C-8), 75.6 (C-9), 72.8 (C-3), 72.0 (C-5), 71.0 (C-2), 68.4 (C-4), 61.8 (C-6), 56.0 (C-7), 20.8, 20.7, 2 x 20.6 ($OCOCH_3$). The NMR data were in accordance with those described in the literature.[9]



Scheme S5. Synthesis of **7b**

2,3,4,6-Tetra-*O*-acetyl-β-D-galactopyranosyl-(1→4)-2,3,6-tri-*O*-acetyl-α/β-D-gluco-pyranose (**7b-1**): Hydrazine acetate (0.3 g, 3.25 mmol, 1.1 equiv.) was added portionwise to a solution of lactose octaacetate (2.0 g, 2.95 mmol, 1 equiv.) in dry DMF (8 mL) under argon and stirred at room temperature overnight. Then Et_2O (30 mL) was added and washed with HCl (20 mL, 1N), H_2O (20 mL), brine (2 x 30 mL), dried over $MgSO_4$, filtered and concentrated under reduced pressure. The crude was purified by column chromatography on silica gel using EtOAc/Cy (1:4) as eluent to obtain compound **7b-1** as a white solid (1.5 g, 2.36 mmol, 80%).

^{1}H NMR (400 MHz, $CDCl_3$) δ 5.44–5.40 (m, 1H, H-3), 5.26–5.25 (m, 2H, H-4’), 5.03–4.99 (m, 1H, H-2’), 4.90–4.86 (m, 1H, H-3’), 4.75–4.62 (m, 2H, H-2, H-1’), 4.45–4.39 (m, 2H, H-6), 4.11–3.97 (m, 3H, H-5, H-6’), 3.85–3.80 (m, 1H, H-5’), 3.76–3.67 (m, 1 H, H-4), 2.07 (s, 3H, $OCOCH_3$), 2.03–2.04 (m, 3H, $OCOCH_3$), 1.99–1.96 (m, 12H, 4 x $OCOCH_3$), 1.88 (s, 3H, $OCOCH_3$). ^{13}C NMR (100 MHz, $CDCl_3$) δ 170.6, 170.4, 170.3, 170.2, 170.1, 169.7, 169.0 (Cq, $C=O_{acetyl}$), 100.9 (C-1´), 90.0 (C-1), 76.3 (C-4), 71.3 (C-3´), 71.0 (C-5), 70.5 (C-5´), 69.5 (C-2), 69.0 (C-2´), 68.0 (C-3), 66.6 (C-4´), 61.88 (C-6), 60.8 (C-6´), 2 x 20.8, 20.70, 20.6 20.5 ($OCOCH_3$). The NMR data were in accordance with those described in the literature. [10]

2,3,4,6-Tetra-*O*-acetyl-*β*-D-galactopyranosyl-(1→4)-2,3,6-tri-*O*-acetyl-*α*-D-gluco-pyranose trichloracetimidate (**7b-2**): The anomeric free lactoside **7b-1** (665 mg, 1.05 mmol, 1 equiv.) and trichloroacetonitrile (1.12 mL, 11.02 mmol, 10 equiv.) were dissolved in dry CH_2Cl_2 (2 mL) and DBU (20 µL, 0.112 mmol, 0.1 equiv.) was added. The reaction solution was stirred at room temperature overnight and purified by column chromatography on silica gel using EtOAc/Cy (1:4) as eluent to give compound **7b-2** as a white solid (640 mg, 0.82 mmol, 78%).

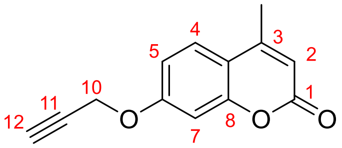
^{1}H NMR (400 MHz, $CDCl_3$) δ 8.65 (s, 1H, NH), 6.47 (d, *J* = 3.8 Hz, 1H, H-1), 5.53 (d, *J* = 10.0 Hz, 1H, H-3), 5.34 (d, *J* = 3.4 Hz, 1H, H-4'), 5.14–5.03 (m, 2H, H-2, H-2'), 4.96–4.93 (m, 1H, H-3), 4.52–4.16 (m, 2H, H-1', H-6a), 4.17–4.05 (m, 4H, H-5, H-6b, H-6'), 3.89–3.84 (m, 2H, H-4, H-5'), 2.15 (s, 3H), 2.10 (s, 3H, 2 x), 2.06 (s, 6H, 2 x $OCOCH_3$), 2.03 (s, 3H, $OCOCH_3$), 2.00 (s, 3H, $OCOCH_3$), 1.96 (s, 3H, $OCOCH_3$).^{13}C NMR (100 MHz, $CDCl_3$) δ 170.4, 170.2, 170.1, 170.0, 169.3, 169.1 (Cq, $C=O_{acetyl}$), 160.8 (Cq, C=NH), 101.12 (C-1´), 92.8 (C-1), 90.6 (CCl_3), 75.8 (C-4), 71.0 (C-3´), 70.9 (C-5), 70.7 (C-5´), 69.9 (C-2), 69.2 (C-3), 69.1 (C-2´), 66.6 (C-4´), 61.5 (C-6), 60.7 (C-6´), 20.8, 20.7, 20.6, 2 x 20.4 ($OCOCH_3$). The NMR data were in accordance with those described in the literature.[10]

2-Propynyl 2,3,4,6,2',3',6'-hepta-*O*-acetyl-β-D-lactopyranoside (**7b**): To an ice-water cooled solution of **7b-1** (120 mg, 0.15 mmol, equiv.) and propargyl alcohol (17 µL, 0.3 mmol, 2 equiv.) in dry CH_2Cl_2 (2 mL) was slowly added BF3.Et_2O (0.15 mmol, 19 µL, 1 equiv.) under argon atmosphere. After stirring overnight, saturated $NaHCO_3$ (8 mL) was added and the aqueous phase was extracted with CH_2Cl_2 (2 x 10 mL). The organic layer was combined, washed with H_2O (20 mL), brine (20 mL) and dried over $MgSO_4$, then filtered and concentrated under reduced pressure. The residue was purified by column chromatography on silica gel using EtOAc/Cy (3:7) as eluent to give the desired compound **7b** as a white solid (64 mg, 0.095 mmol, 63%).

^{1}H NMR (500 MHz, $CDCl_3$) δ 5.35–5.28 (m, 1H, H-4'), 5.28–5.18 (m, 1H, H-3), 5.10–5.06 (m, 1H, H-2'), 4.94–4.87 (m, 2H, H-2, H-3'), 4.73–4.70 (m, 1H, H-1), 4.49–4.45 (m, 2H, H-1', H-6 or H-6'), 4.31 (dd, *J* = 4.2, 2.5 Hz, 2H, H-7'), 4.12–4.03 (m, 3H, H-6, H-6'), 3.85 (t, *J* = 6.8 Hz, 1H, H-5'), 3.81–3.77 (m, 1H, H-4), 3.63–3.60 (m, 1H, H-5), 2.44 (td, *J* = 2.0, 0.9 Hz, 1H, H-9'), 2.15–2.12 (m, 3H, $OCOCH_3$), 2.10–2.09 (m, 3H, $OCOCH_3$), 2.04–2.02 (m, 12H, 4 x $OCOCH_3$), 1.94–1.93 (m, 3H, $OCOCH_3$). ^{13}C NMR (125 MHz,

$CDCl_3$) δ 170.4, 2 x 170.2, 2 x 169.8 (Cq, C=O$_{acetyl}$), 101.1 (C-1'), 97.9 (CH, C-1), 78.1 (Cq, C-8'), 76.2 (C-9'), 75.6 (C-4), 72.8, 72.7 (C-5, C-5'), 71.3, 71.0, 70.7, 69.1 (C-2, C-2', C-3, C-3'), 66.7 (C-4'), 61.9, 60.9 (C-6, C-6'), 56.0 (C-7'), 21.0, 20.9, 20.8, 2 x 20.7, 20.6 ($OCOCH_3$). The NMR data were in accordance with those described in the literature. [11]

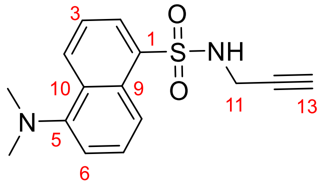
4-Methyl-7-(propargyloxy)coumarin (**7c**)



To a solution of 7-hydroxy-4-methylumbelliferone (528 mg, 3.0 mmol, 1 equiv.) and propargyl bromide (0.34 mL, 3.6 mmol, 1.2 equiv.) in dry DMF (6 mL) was added anhydrous K_2CO_3 (1.67 g, 12.0 mmol, 4 equiv.) under argon atmosphere. The reaction mixture was allowed to stir at 50°C for 5 h prior to dilution with CH_2Cl_2 (20 mL) and filtered at room temperature. The filtrate was evaporated under reduced pressure. The residue was purified by column chromatography on silica gel using EtOAc/Cy (1:2) as eluent to obtain the product **7c** as a white solid (572 mg, 2.67 mmol, 89%).

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.52 (dd, *J* = 7.8, 1.3 Hz, 1H, H-4), 6.94–6.92 (m, 2H, H-5, H-7), 6.16 (q, *J* = 1.5 Hz, 1H, H-2), 4.76 (d, *J* = 2.4 Hz, 2H, H-10), 2.57 (t, *J* = 2.4 Hz, 1H, H-12), 2.40 (d, *J* = 1.2 Hz, 3H, CH_3). ^{13}C NMR (125 MHz, $CDCl_3$) δ 161.2 (Cq, C-1), 160.5 (Cq, C-6), 155.1 (Cq, C-8), 152.6 (Cq, C-3), 125.7 (C-4), 114.4 (Cq, C-9), 112.8 (C-5), 112.5 (C-2), 102.3 (C-7), 77.5 (C-11), 76.6 (C-12), 56.3 (CH_2, C-10), 18.8 (CH_3). The NMR data were in accordance with those described in the literature. [12]

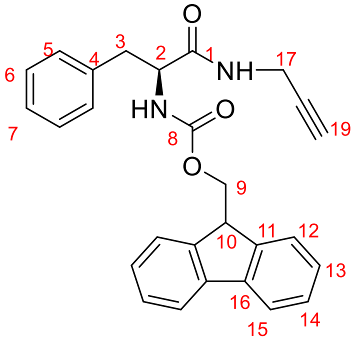
***N*-Propargyl-5-(dimethylamino)naphthalene-1-sulfonamide** (**7d**):



A solution of dansyl chloride (135 mg, 0.5 mmol, 1 equiv.), propargylamine (64 µL, 1 mmol, 2 equiv.) and Et_3N (0.1 mL, 0.75 mmol, 1.5 equiv.) in CH_2Cl_2 (3 mL) was stirred at room temperature for 1 h. The solvent was evaporated under reduced pressure and the residue was purified by column chromatography on silica gel using EtOAc/Cyc (1:2) as eluent to afford a yellow powder (140 mg, 0.49 mmol, 97%).

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.56 (dd, *J* = 8.5, 0.9 Hz, 1H, H-2), 8.27 (d, *J* = 1.1 Hz, 1H, H-8), 8.26–8.24 (m, 1H, H-4), 7.59–7.53 (m, 1H, H-3), 7.51 (ddd, *J* = 8.5, 7.4, 1.0 Hz, 1H, H-7), 7.18 (d, *J* = 7.6 Hz, 1H, H-6), 5.07 (s, *J* = 5.3 Hz, 1H, NH), 3.78–3.76 (m, 2H, H-11), 2.88 (s, 6H, 2 x NCH_3), 1.91–1.90 (m, 1H, H-13). ^{13}C NMR (100 MHz, $CDCl_3$) δ 152.0 (Cq, C-1), 134.4 (Cq, C-5), 130.8 (C-2), 129.9 (C-4), 129.9 (Cq, C-9), 129.8 (Cq, C-10), 128.6 (C-3), 123.3 (C-7), 118.7 C-8), 115.3 (, C-6), 77.9 (C-12), 72.7 (C-13), 45.5 (NCH_3), 33.0 (C-11). The NMR data were in accordance with those described in the literature.[13]

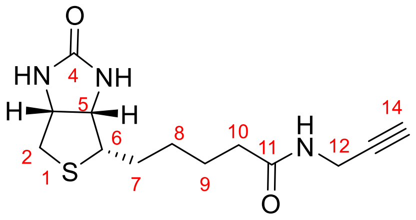
4-[(2S)-2-({[(9H-fluoren-9-yl)methoxy]carbonyl}amino)-3-phenylpropanamido]-1-propyne (7e)



To a solution of the Fmoc-L-phenylalanine (425 mg, 1.10 mmol, 1 equiv.) in dry DMF (10 mL), HBTU (501 mg, 1.32 mmol, 1.2 equiv.) and DIPEA (0.23 mL, 1.32 mmol, 1.2 equiv.) were added under argon atmosphere. After stirring for 0.5 h propargylamine (70 µL, 1.32 mmol, 1.2 equiv.) in dry DMF (2 mL) was added and stirred at room temperature for 48 h. Then, H_2O (50 mL) was added, filtered, and extracted with CH_2Cl_2 (3 x 50 mL). The organic layers were combined, washed with brine (2 x 50 mL), dried over $MgSO_4$, filtered and concentrated under reduced pressure. The residue was purified by column chromatography on silica gel using EtOAc/Cyc/DCM (4:5:5) as eluent to give a white solid (373 mg, 0.88 mmol, 80%).

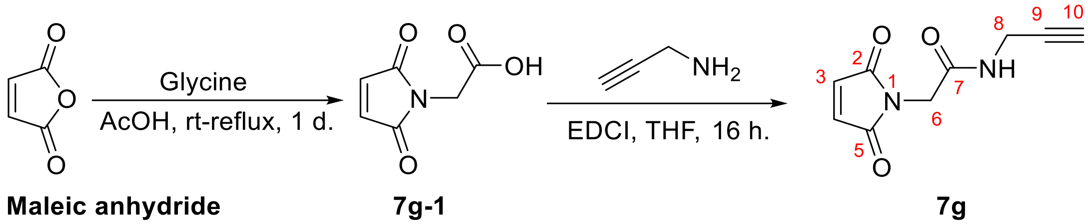
^{1}H NMR (400 MHz, DMSO-d$_6$) δ 8.53 (t, *J* = 5.3 Hz, 1H, N*H*-CH$_2$), 7.88 (d, *J* = 7.6 Hz, 2H, 2 x H-12), 7.75–7.58 (m, 3H, 2 x H-13, N*H*), 7.41 (td, *J* = 7.5, 3.7 Hz, 2H, 2 x H-14 or 2 x H-15), 7.34–7.24 (m, 6H, 2 x H-5, 2 x H-6, 2 x H-14 or 2 x H-15), 7.18–7.17 (m, 1H, H-7), 4.25–4.02 (m, 4H, H-2, H-9, H-10), 3.91–3.88 (m, 2H, H-17), 3.15 (t, *J* = 2.5 Hz, 1H, H-3a), 2.97 (dd, *J* = 13.6, 4.1 Hz, 1H, H-3b), 2.82–2.76 (m, 1H, H-19). ^{13}C NMR (125 MHz, DMSO-d$_6$) δ 171.3 (Cq, C-1), 155.8 (Cq, C-8), 143.8, 143.7 (Cq, C-11), 140.6 (Cq, C-16), 138.1 (Cq, C-4), 129.2 (C-6), 128.0, 127.6 (C-14, C-15), 127.0 (C-5), 126.3 (C-7), 125.4, 125.3 (C-13), 120.1 (C-12), 80.9 (C-18), 73.2 (C-19), 65.6 (C-9), 56.1 (C-2), 46.5 (C-10), 37.4 (C-3), 28.0 (C-17). The NMR data were in accordance with those described in the literature. [14]

3-(D-Biotinylamido)-1-propyne (7f)



A solution of D-biotin (80 mg, 0.327 mmol, equiv.) and propargylamine (26 µL, 0.392 mmol, 1.2 equiv.) in CH$_3$CN/MeOH (3:1, 4 mL) was stirred at room temperature for 6.5 h. Then the reaction was concentrated under reduced pressure. MeOH was added to the crude residue and the solution was filtered through a pad of celite. The filtrate was evaporated and the residue was purified by column chromatography on silica gel using DCM/MeOH (10:1) as eluent and isolated as a white solid (0.263 mmol, 74 mg, 80%).

^{1}H NMR (400 MHz, CD$_3$OD) δ 7.90 (s, 1H, N*H*), 4.49 (ddd, *J* = 7.9, 4.9, 0.8 Hz, 1H, H-3), 4.31 (dd, *J* = 7.9, 4.4 Hz, 1H, H-5), 3.95 (d, *J* = 2.6 Hz, 2H, H-12), 3.28–3.13 (m, 1H, H-6), 2.93 (dd, *J* = 12.8, 5.0 Hz, 1H, H-2a), 2.71 (d, *J* = 12.7 Hz, 1H, H-2b), 2.58 (t, *J* = 2.6 Hz, 1H, H-14), 2.22 (dd, *J* = 11.0, 4.1 Hz, 2H, H-10), 1.79–1.54 (m, 4H, H-7, H-9), 1.48–1.42 (m, 2H, H-8). ^{13}C NMR (100 MHz, CD$_3$OD) δ 175.6 (Cq, C-11), 166.1 (Cq, C-4), 80.7 (C-13), 72.1 (C-14), 63.3 (C-5), 61.6 (C-3), 56.9 (C-6), 41.0 (C-2), 36.5 (C-10), 29.7, 29.4, 29.4, 26.7 (C-7, C-8, C-9, C-12). The NMR data were in accordance with those described in the literature. [15]



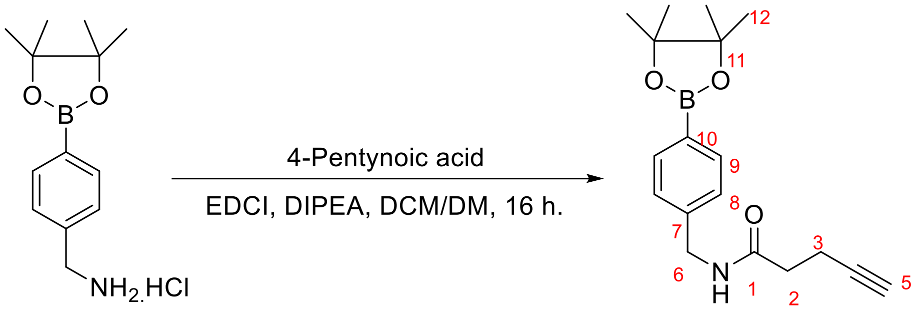
Scheme S6. Synthetic route for **7g**

Maleimidoacetic acid (**7g-1**): To a solution of Maleic anhydride (2.5 g, 25.5 mmol, 1 equiv.) in acetic acid (30 mL) was added to a suspension of glycine (1.91 g, 25.5 mmol, 1 equiv.) in acetic acid (15 mL) and vigorously stirred for 7 h at room temperature. Afterwards, the reaction mixture was heated to reflux overnight, then cooled down before removal of the solvent under vacuum. The crude was then purified by column chromatography on silica gel using DCM/MeOH/AcOH (200:10:1) as eluent to yield product **7g-1** as a white solid (2.6 g, 16.8 mmol, 66%).

^{1}H NMR (500 MHz, CDCl$_3$) δ 6.80 (s, 2H, H-3, H-4), 4.33 (s, 2H, H-6). ^{13}C NMR (125 MHz, CDCl$_3$) δ 172.9 (Cq, C-2, C-5), 169.7 (Cq, C-7), 134.7 (C-3, C-4), 38.4 (C-6). The NMR data were in accordance with those described in the literature. [16]

2-(2,5-Dioxo-2,5-dihydro-pyrrol-1-yl)-*N*-(prop-2-yn-1-yl)acetamide (**7g**): Propargylamine (139 µL, 2.35 mmol, 0.9 equiv.) was slowly added to a solution of **7g-1** (267 mg, 2.37 mmol, 1 equiv.) and EDCI (500 mg, 1.65 mmol, 1.1 equiv.) in dry THF/DMF (3:1, 8 mL) at 0°C. Then the reaction was allowed to warm to room temperature and stirred overnight. Afterwards, the crude was concentrated under reduced pressure and the resulting residue was purified by column chromatography on silica gel using DCM/MeOH (200:1) as eluent to obtain the desired product **7g** as a white solid (91 mg, 0.474 mmol, 20%).

^{1}H NMR (500 MHz, CDCl$_3$) δ 6.80 (s, 2H, H-3, H-4), 4.19 (s, 2H, H-6), 4.07 (dd, J = 5.2, 2.6 Hz, 2H, H-8), 2.26 (t, J = 2.6 Hz, 1H, H-10). ^{13}C NMR (125 MHz, CDCl$_3$) δ 170.2 (Cq, C-2, C-5), 165.7 (Cq, C-7), 134.7 (CH, C-3, C-4), 78.8 (C-9), 72.4 (C-10), 40.5 (CH$_2$, C-6), 29.7 (CH$_2$, C-8). HRMS (ESI$^+$-MS, m/z): calculated for $C_9H_9N_2O_3$ $[M+H]^+$ 193.0607; found 193.0607.

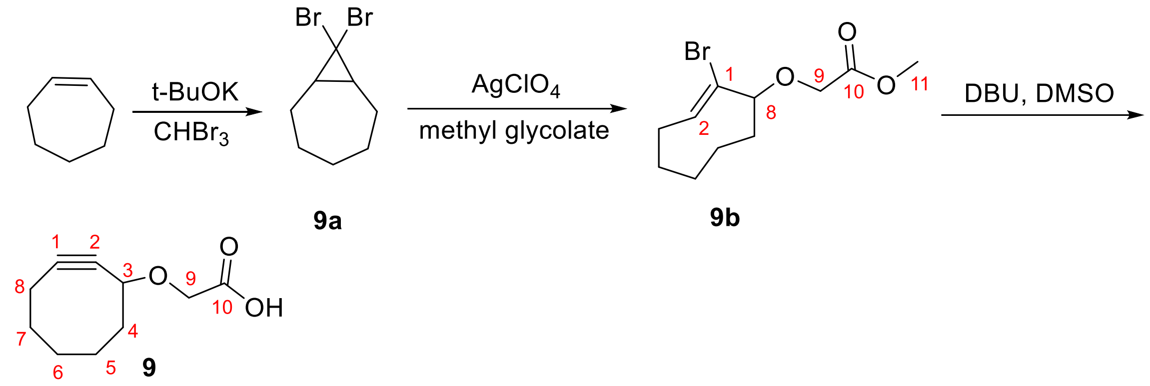


7h

Scheme S7. Synthesis of **7h**

***N*-(4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)benzyl)pent-4-ynamide** (**7h**): To a solution of 4-(aminomethyl)phenylboronic acid pinacol ester hydrochloride (50 mg, 0.185 mmol, 1 equiv.) and 4-pentynoic acid (22 mg, 0.222 mmol, 1.2 equiv.) in dry DCM/DMF (10:1, 2.2 mL) was added EDCI (43 mg, 0.222 mmol, 1.2 equiv.). After stirring at room temperature for 4h, the solution was concentrated under reduced pressure and the resulting residue was purified by column chromatography on silica gel using Cy/EtOAc (4:1) as eluent to yield the desired product as a white solid (54 mg, 0.173 mmol, 93%).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.73 (dd, *J* = 8.1, 2.0 Hz, 2H, 2 x H-9), 7.24 (dd, *J* = 4.4, 3.8 Hz, 2H, 2 x H-8), 4.41–4.38 (m, 2H, H-6), 2.56–2.46 (m, 2H, H-2), 2.38 (td, *J* = 6.0, 1.6 Hz, 2H, H-3), 1.96 (td, *J* = 2.6, 1.4 Hz, 1H, H-5), 1.31 (s, 12H, 4 x H-12). ^{13}C NMR (100 MHz, $CDCl_3$) δ 171.1 (Cq, C-1), 141.3 (Cq, C-7), 135.2 (CH_{Ar}, C-9), 127.1 (CH_{Ar}, C-8), 83.9 (Cq, C-11), 83.0 (C-4), 69.5 (C-5), 43.7 (CH_2, C-6), 35.3 (CH_2, C-2), 24.9 (CH_2, C-12), 15.0 (CH_2, C-3). HRMS (ESI$^+$-MS, m/z): calculated for $C_{18}H_{25}BNO_3$ $[M+H]^+$ 314.1925; found 314.1923.



Scheme S7. Synthesis of **9**

8,8-Dibromobicyclo[5.1.0]octane (9a): A mixture of cycloheptene (1.41 mL, 12 mmol, 1 equiv.) and potassium tert-butoxide (24 mmol, 672 mg, 2 equiv.) in pentane (9 mL) was cooled to -10ºC. $CHBr_3$ (1.6 mL, 18 mmol, 1.5 equiv.) was added dropwise over 0.3 h and allowed it to stir at room temperature overnight. Then, H_2O (15 mL) was added, acidified using HCl (1N) and extracted with pentane (2 x 20 mL), the combined organic layers were washed with brine (30 mL), dried over $MgSO_4$, filtered and concentrated under reduced pressure. The crude was purified by column chromatography on silica gel using Cy as eluent to yield the desired compound **9a** as a colorless oil (1.52 g, 5.67 mmol, 47%).

^{1}H NMR (400 MHz, $CDCl_3$) δ 2.29–2.22 (m, 2H, H-2a, H-6a), 1.91–1.79 (m, 3H, H-3a, H-4a, H-5a), 1.43–1.38 (m, 2H, H-1, H-7), 1.22–1.11 (m, 3H, H-2b, H-4b, H-6b). ^{13}C NMR (100 MHz, $CDCl_3$) δ 40.9 (C-8), 34.8 (C-1, C-7), 32.3 (C-4), 29.0 (C-2, C-6), 28.1 (C-3, C-5). The NMR data were in accordance with those described in the literature.[17]

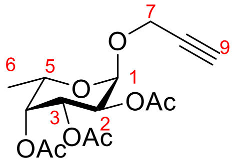
[(Z)-2-Bromo-2-cycloocten-1-yloxy]acetic acid methyl ester (9b): To a vigorously stirred solution of **9a** (536 mg, 2.0 mmol, 1 equiv.) and methyl glycolate (0.93 mL, 12 mmol, 6 equiv.) in dry toluene was added $AgClO_4$ (7.5 mg, 3.4 mmol, 1.7 equiv.) portion-wise under argon atmosphere. The reaction vessel was protected from light by the use of aluminum foil. After stirring for 1.5 h at room temperature, the silver salts were removed by filtration and the residue was purified by column chromatography on silica gel using EtOAc/Cy (1:20) as eluent and isolated **9b** a pale yellow oil (200 mg, 0.72 mmol, 36%).

^{1}H NMR (400 MHz, $CDCl_3$) δ 6.22 (dd, J = 11.7, 4.2 Hz, 1H, H-2), 4.25 (d, J = 16.4 Hz, 1H, H-9a), 4.13 (dd, J = 10.3, 5.1 Hz, 1H, H-8), 3.98 (d, J = 16.5 Hz, 1H, H-9b), 3.74 (s, 3H, H-11), 2.79–2.69 (m, 1H, H-3a), 2.32–2.27 (m, 1H, H-3b), 2.11–1.25 (m, 7H, H-4, H-5, H-6a, H-7), 0.85–0.76 (m, 1H, H-6b). ^{13}C NMR (100 MHz, $CDCl_3$) δ 170.9 (Cq, C=O), 133.1 (C-2), 131.6 (C-1), 85.0 (CH, C-8), 65.6 (C-9), 52.0 (CH_3, C-11), 39.5, 36.7, 33.5, 28.2, 26.4 (C-4, C-5, C-6, C-7, C-8).

(2-Cyclooctyn-1-yloxy)acetic acid (**9**): To a solution of compound **9b** (166 mg, 0.6 mmol, 1 equiv.) in dry DMSO (0.5 ml) was added DBU (0.56 mL, 3.6 mmol, 6 equiv.) under argon atmosphere and the solution was allowed to stir at 60°C overnight. Afterwards, H_2O (0.1 mL) was added and stirred for another 4 h before cooling down. Then, the solution was diluted with hydrochloride (10 mL, 1N) and extracted with Et_2O (3 x 15 mL). The combined organic layer was washed with brine (3 x 15 mL), dried over anhydrous $MgSO_4$, filtered and concentrated under reduced pressure to give the product **9** as a pale yellow solid (0. 86 mg, 47 mmol, 79%).

^{1}H NMR (400 MHz, $CDCl_3$) δ 4.38–4.36 (m, 1H, H-3), 4.25 (d, *J* = 16.8 Hz, 1H, H-9a), 4.09 (d, *J* = 16.8 Hz, 1H, H-9b), 2.30–1.44 (m, 10H, 5 x CH_2). ^{13}C NMR (100 MHz, $CDCl_3$) δ 174.9 (Cq, C-10), 102.29 (C-2), 91.1 (C-1), 73.3 (C-3), 65.8 (C-9), 42.3 (C-4), 34.4, 29.7, 26.3 (C-5, C-6, C-7), 20.8 (C-8). The NMR data were in accordance with those described in the literature. [17]

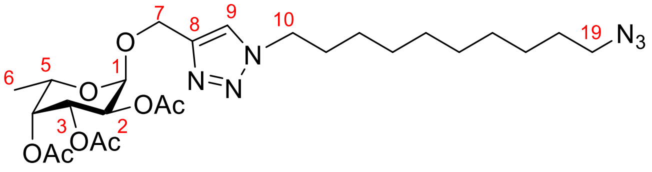
1-*O*-Propargyl-2,3,4-tri-*O*-acetyl-α-L-fucopyranose (13):



The title compound was prepared following a literature procedure,[18] purified using EtOAc/Cy (1:4) as eluent to obtain a white powder (0.74 g, 2.25 mmol, 37%).

^{1}H NMR (500 MHz, $CDCl_3$) δ 5.36 (dd, *J* = 10.9, 3.4 Hz, 1H, H-3), 5.31–5.30 (m, 1H, H-4), 5.25 (d, *J* = 3.8 Hz, 1H, H-1), 5.16 (dd, *J* = 10.9, 3.8 Hz, 1H, H-2), 4.26 (d, *J* = 2.4 Hz, 2H, H-7), 4.20 (dd, *J* = 6.6, 0.6 Hz, 1H, H-5), 2.43 (t, *J* = 2.4 Hz, 1H, H-9), 2.17 (s, 3H, $OCOCH_3$), 2.08 (s, 3H, $OCOCH_3$), 1.98 (s, 3H, $OCOCH_3$), 1.14 (d, *J* = 6.6 Hz, 3H, CH_3). ^{13}C NMR (100 MHz, $CDCl_3$) δ 170.7, 170.6, 170.1 (Cq, $C{=}O_{acetyl}$), 95.2 (C-1), 78.7 (C-8), 75.0 (C-9), 71.2 (C-2), 67.9, 67.9 (C-4, C-3), 65.1 (C-5), 55.3 (C-7), 21.0, 20.8, 20.8 ($OCOCH_3$), 15.9 (C-6). The NMR data were in accordance with those described in the literature. [18]

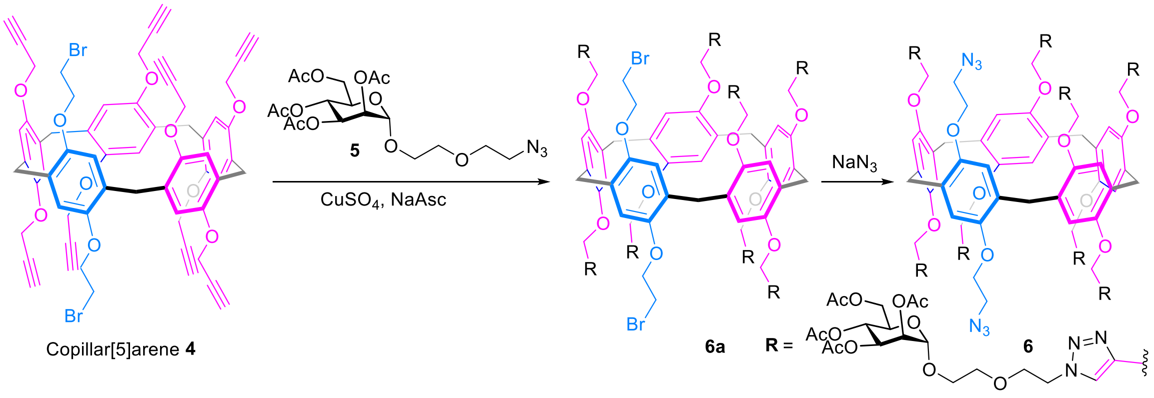
α-L-Galactopyranoside, [1-(10-azidodecyl)-1H-1,2,3-triazol-4-yl]methyl 6-deoxy-2,3,4-triacetate (14):



The title compound was prepared following a literature procedure,[19] purified using EtOAc/Cy (1:2) as eluent and isolated as a colorless oil (372 mg, 0.67 mmol, 74%).

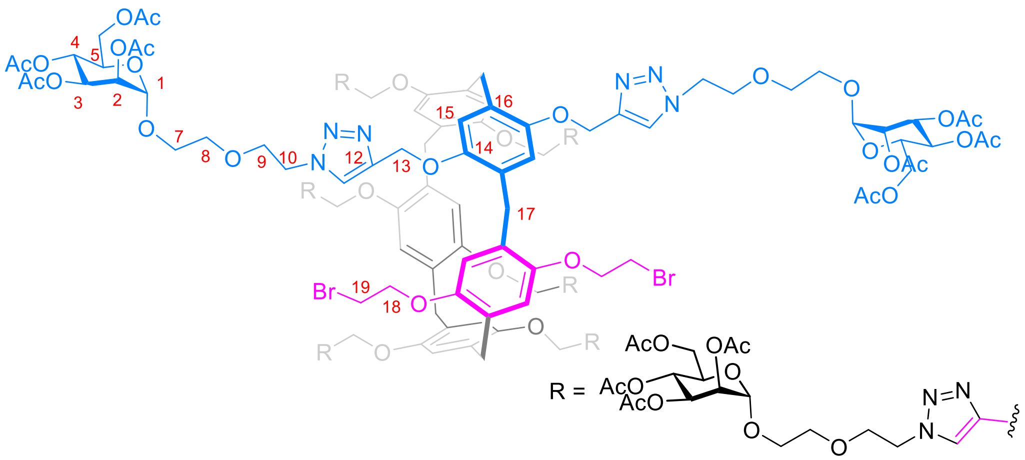
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.50 (s, 1H, H-9), 5.36 (dd, J = 3.2 Hz, J = 10.8 Hz, 1H, H-3), 5.29 (d, J = 3.4 Hz, 1H, H-4), 5.18 (d, J = 3.7 Hz, 1H, H-1), 5.14 (dd, J = 3.7 Hz, J = 10.8 Hz, 1H, H-2), 4.84 (AB, J = 12.4 Hz, 1H, H-7a), 4.66 (AB, J = 12.6 Hz, 1H, H-7b), 4.35 (t, J = 7.3 Hz, 2H, H-10), 4.20 (q, J = 6.6 Hz, 1H, H-5), 3.26 (t, J = 7.1 Hz, 2H, H-19), 2.17 (s, 3H, $OCOCH_3$), 2.04 (s, 3H, $OCOCH_3$), 1.98 (s, 3H, $OCOCH_3$), 1.91 (t, J = 6.8 Hz, 2H, CH_2), 1.57 (tt, J = 6.9 Hz, J = 7.1 Hz, 2H, 6 x CH_2), 1.34–1.25 (m, 12H, CH_2), 1.14 (d, J = 6.6 Hz, 3H, H-6). ^{13}C NMR (100 MHz, $CDCl_3$) δ 170.6, 170.4, 170.1 (Cq, $C{=}O_{acetyl}$), 143.9 (C-8), 122.5 (C-9), 95.7 (C-1), 71.1 (C-2), 2 x 68.0 (C-3, C-4), 64.7 (C-5), 61.4 (C-7), 51.5 (C-10), 50.4 (C-19), 30.4, 29.3, 29.3, 29.1, 29.0, 28.8, 26.7, 26.5 (CH_2), 20.8, 20.7, 20.7 ($OCOCH_3$), 15.9 (C-6). The ^{1}H and ^{13}C NMR data were in accordance with those described in the literature.[19]

S7. Synthesis of the intermediate 6



Scheme S8. Synthesis of **6**

Compound 6a:



To a vigorously stirred solution of copillar[5]arene **4** (448 mg, 0.4 mmol, 1 equiv.) and **5** (2.196 g, 4.76 mmol, 12 equiv) in CH_2Cl_2 (6 mL) under argon atmosphere was added a freshly prepared solution of $CuSO_4$ (23 mg, 0.08 mmol, 0.2 equiv.) and NaAsc (52 mg, 0.264 mmol, 0.66 equiv.) in H_2O (6 mL). The reaction mixture was further vigorously stirred overnight at room temperature. Then, CH_2Cl_2 (20 mL) and H_2O (20 mL) were added, the organic layer was separated, and the aqueous layer was extracted with CH_2Cl_2 (2 x 20 mL). The combined organic phases, washed with brine, dried over anhydrous $MgSO_4$ and concentrated. The obtained residue was purified by column chromatography on silica gel. The resulting crude was purified using DCM/MeOH (30:1) as eluent to give a white solid (1.78 g, 0.37 mmol, 93%).

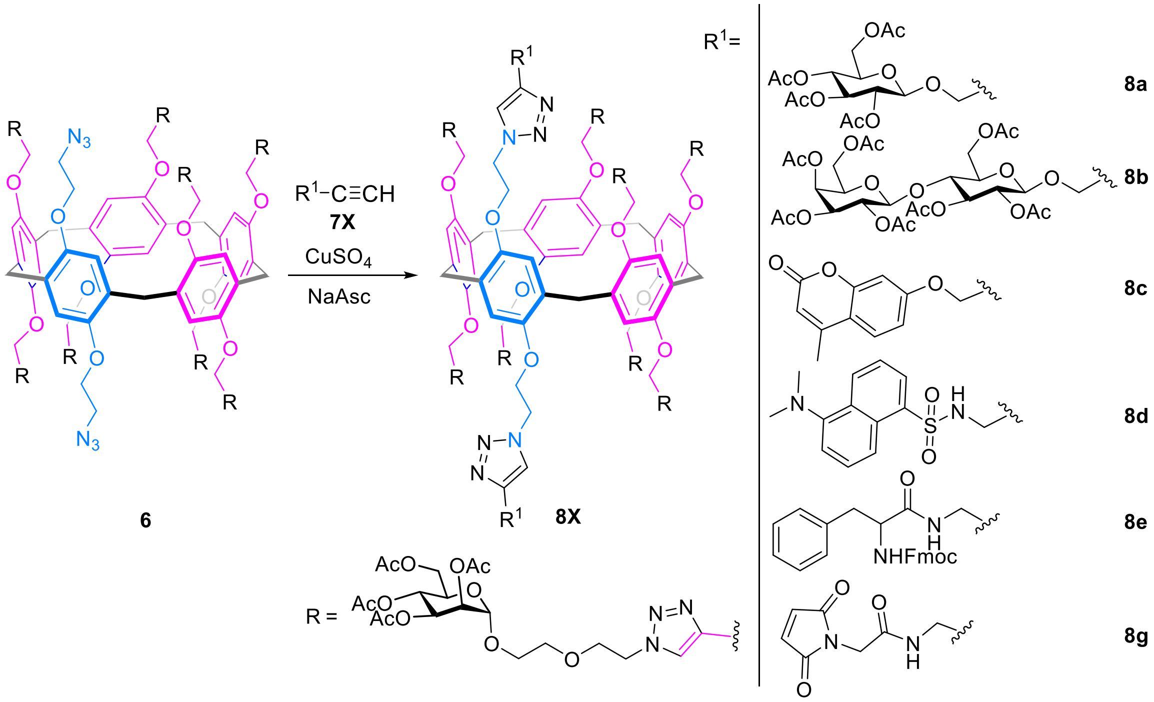
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.90 (m, 4H, 4 x H-11), 7.86 (m, 2H, 2 x H-11), 7.78 (s, 2H, 2 x H-11), 7.01 (s, 2H, 2 x H-15), 6.94–6.90 (m, 6H, 6 x H-15), 6.76 (m, 2H, 2 x H-15), 5.34–5.23 (m, 24H, 8 x H-2, 8 x H-3, 8 x H-4), 5.17 (dd, *J* = 11.5, 3.3 Hz, 2H, H-13), 5.04 (d, *J* = 11.6 Hz, 2H, H-13), 4.93–4.81 (m, 20H, 6 x H-13, 8 x H-1), 4.59–4.49 (m, 16H, 8 x H-10), 4.30–4.25 (m, 8H, 8 x H-6a), 4.10–4.04 (m, 10H, 8 x H-6b, H-18), 4.02–3.96 (m, 8H, 8 x H-5), 3.94–3.86 (m, 18H, 8 x H-9, H-18), 3.79–3.74 (m, 18H, 5 x H-17, 4 x H-7a), 3.64–3.60 (m, 24H, 4 x H-7b, 8 x H-8), 3.55 (t, *J* = 5.4 Hz, 4H, 2 x H-19), 2.14–2.13 (m, 24H, 8 x $OCOCH_3$), 2.08–2.07 (m, 24H, 8 x $OCOCH_3$), 2.04–2.02 (m, 24H, 8 x $OCOCH_3$), 1.97–1.94 (m, 24H, 8 x $OCOCH_3$). ^{13}C NMR (100 MHz, $CDCl_3$) δ 170.4, 2 x 169.8, 2 x

169.7, 169.6, 169.5 (Cq, C=O$_{acetyl}$), 149.6, 2 x 149.5, 149.4 (Cq, C-14), 144.2, 144.1, 144.0 (Cq$_{triazole}$, C-12), 2 x 128.6, 128.4, 128.3, 2 x 128.2, 128.1 (Cq, C-16), 2 x 123.8, 123.7 (CH$_{triazole}$, C-11), 115.8, 115.2 (Cq$_{Ar}$, C-15), 97.5 (CH, C-1), 2 x 69.8, 69.7 (CH$_2$, C-8), 69.4 (CH$_2$, C-9), 69.2 (CH, C-3), 68.9, 68.8 (CH, C-2), 68.5 (CH$_2$, C-18), 68.3 (CH, C-5), 2 x 67.0 (CH$_2$, C-7), 65.8 (CH, C-4), 62.4 (CH$_2$, C-13), 62.2 (CH$_2$, C-6), 61.9 (CH$_2$, C-13), 49.9, 49.8 (CH$_2$, C-10), 31.0 (C-19), 29.5, 29.2, 28.9 (C-17), 2 x 20.7, 20.6, 3 x 20.5 (OCOCH$_3$). Mass (MAlDI-TOF-MS, m/z): calculated for $C_{207}H_{268}Br_2N_{24}O_{98}Na$ [M+Na]$^+$ 4843.29; found 4843.58.

Compound 6: To a solution of **6a** (1.75 g, 0.36 mmol, 1 equiv.) in dry DMF (5 mL) was added NaN_3 (94 mg, 1.44 mmol, 4 equiv.). The mixture was stirred at room temperature overnight before evaporating to dryness under vacuum. Then, the crude slurry was diluted with CH_2Cl_2 (50 mL), washed with H_2O (2 x 40 mL), brine (40 mL), dried over anhydrous $MgSO_4$, filtered and concentrated under reduced pressure to afford the desired as a pale yellow solid (1.62 g, 0.34 mmol, 95%).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.90–7.89 (m, 4H, 4 x H-11), 7.84 (m, 2H, 2 x H-11), 7.78 (s, 2H, 2 x H-11), 6.95–6.93 (m, 4H, 4 x H-15), 6.90 (s, 4H, 4 x H-15), 6.76–6.75 (m, 2H, 2 x H-15), 5.32–5.23 (m, 24H, 8 x H-4, 8 x H-3, 8 x H-2), 5.15 (dd, *J* = 11.7, 4.2 Hz, 2H, H-13), 5.03 (d, *J* = 11.6 Hz, 2H, H-13), 4.91–4.82 (m, 20H, 6 x H-13, 8 x H-1), 4.57–4.53 (m, 16H, 8 x H-10), 4.30–4.23 (m, 8H, 4 x H-6), 4.09–4.05 (m, 8H, 4 x H-6), 4.01–3.96 (m, 8H, 8 x H-5), 3.91–3.84 (m, 18H, 8 x H-9, H-18), 3.79–3.73 (m, 20H, 4 x H-7, 5 x H-17, H-18), 3.64–3.55 (m, 26H, 4 x H-7, 8 x H-8, H-19), 3.47–3.43 (m, 2H, H-19), 2.14–2.13 (m, 24H, 8 x OCOCH$_3$), 2.07 (s, 24H, 8 x OCOCH$_3$), 2.03 (m, 24H, 8 x OCOCH$_3$), 1.97 (s, 24H, 8 x OCOCH$_3$). ^{13}C NMR (100 MHz, $CDCl_3$) δ 170.4, 169.8, 169.6 (Cq, C=O$_{acetyl}$), 149.7, 149.6, 149.4 (Cq, C-14), 144.2, 144.1 (Cq$_{triazole}$, C-12), 128.5, 128.2 (Cq, C-16), 123.8 (CH$_{triazole}$, C-11), 115.3, 115.0 (CHAr, C-15), 97.5 (CH, C-1), 69.8 (CH$_2$, C-8), 69.4 (CH$_2$, C-9), 69.3 (CH, C-3), 68.9 (CH, C-2), 68.3 (CH, C-5), 67.1 (CH$_2$, C-7, C-18), 65.9 (CH, C-4), 62.3 (CH$_2$, C-6), 62.0 (CH$_2$, C-13), 50.7 (CH$_2$, C-19), 49.9 (CH$_2$, C-10), 29.7, 29.2, 29.1 (CH$_2$, C-17), 2 x 20.7, 20.5 (OCOCH$_3$). HRMS (TOF-MS-ESI$^+$, m/z): calculated for $C_{207}H_{268}N_{30}O_{98}Na$ [M+Na]$^+$ 4767.52; found 4767.77.

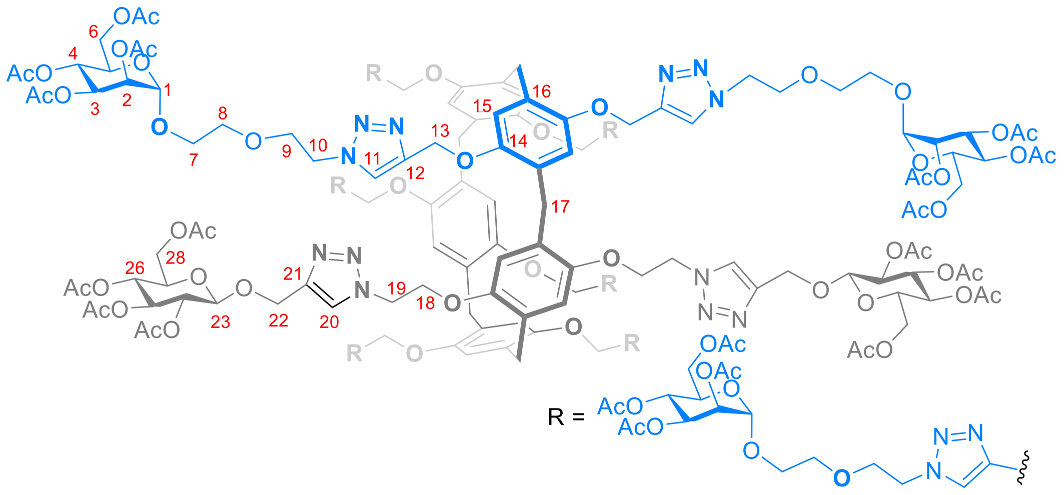
S8. General procedure B for the synthesis of compounds 8a-e and 8g



Scheme S9. Synthesis of compounds **8a-e** and **8g**

To a vigorously stirred solution of compound **6** (1 equiv.) and one of the alkyne functionalized ligands **7x** (3.2 equiv.) in CH_2Cl_2 (v mL), the same volume (v mL) of a freshly prepared solution of $CuSO_4$ (0.2 equiv. × n) and NaAsc (0.66 equiv. × n) in distilled water (v mL × n) was taken and added under argon atmosphere. After stirring at room temperature for 20 h, H_2O (20 mL) and CH_2Cl_2 (20 mL) were added and separated. The organic layer was washed with brine, dried over $MgSO_4$ and concentrated under reduced pressure. The residue was purified by column chromatography on silica gel.

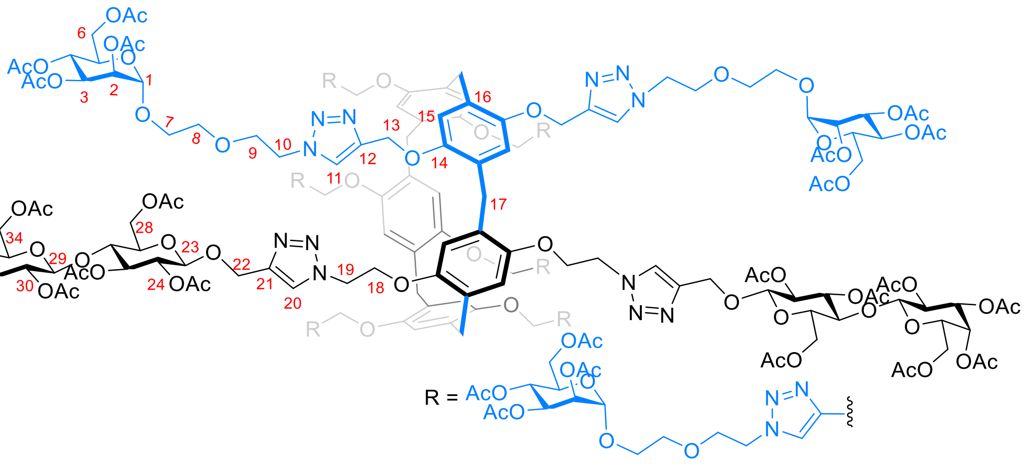
Compound 8a:



The title compound was prepared following the general procedure **B** using **6** (110 mg, 0.023 mmol), **7a** (29 mg, 0.074 mmol), CH_2Cl_2 (1.5 mL), $CuSO_4$ (5.9 mg, 0.037 mmol) and NaAsc (21.3 mg, 0.121 mmol,) [n = 8], purified by using EtOAc/Cy (2:1) as eluent to remove excess **7a**, then DCM/MeOH (30:1) as eluent and isolated as a white solid (116 mg, 0.021 mmol, 91%).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.95–7.83 (m, 10H, 8 x H-11, 2 x H-20), 6.99–6.90 (m, 8H, 8 x H-15), 6.75 (br, 2H, 2 x H-15), 5.32–5.23 (m, 24H, 8 x H-2, 8 x H-3, 8 x H-4), 5.15–5.02 (m, 10H, 2 x H-13, 2 x H-22a, 2 x H-25, 2 x H-26), 4.96–4.84 (m, 24H, 8 x H-1, 5 x H-13, 2 x H-19a, 2 x H-22b, 2 x H-24), 4.76–4.72 (m, 4H, H-13, 2 x H-19b), 4.69 (d, *J* = 7.9 Hz, 2H, 2 x H-23), 4.59–4.54 (m, 16H, 8 x H-10), 4.28–4.20 (m, 12H, 8 x H-6a, H-18, 2x H-28a), 4.10–4.06 (m, 10H, 8 x H-6b, 2 x H-28b), 4.10–3.86 (m, 28H, 8 x H-5, 8 x H-9, H-18, 2 x H-27), 3.79–3.70 (m, 16H, 5 x H-17, 3 x H-7), 3.65–3.61 (m, 24H, 4 x H-7, 8 x H-8), 3.42–3.49 (m, 2H, H-7), 2.14–2.12 (m, 24H, 8 x $OCOCH_3$), 2.07–2.06 (m, 24H, 8 x $OCOCH_3$), 2.04–2.01 (m, 30H, 10 x $OCOCH_3$), 1.99 (m, 6H, 2 x $OCOCH_3$), 1.96 (m, 30H, 10 x $OCOCH_3$), 1.82–1.80 (m, 6H, 2 x $OCOCH_3$). ^{13}C NMR (100 MHz, $CDCl_3$) δ 170.6, 2 x 170.1, 169.91, 169.7, 169.4, 169.3 (Cq, $C{=}O_{acetyl}$), 149.8, 2 x 149.7, 2 x 149.3 (Cq, C-14), 144.3, 144.2 ($Cq_{triazole}$, C-12), 143.6, 143.5 ($Cq_{triazole}$, C-21), 128.7, 128.6, 128.5, 128.4, 2 x 128.0 (Cq, C-16), 124.2, 124.1, 124.0, 123.9 ($CH_{triazole}$, C-11, C-20), 115.6, 115.4, 115.1, 114.9 (CH_{Ar}, C-15), 99.4, 99.3 (CH, C-23), 97.6 (CH, C-1), 72.8, 72.8 (CH, C-25), 2 x 71.7 (CH, C-27), 71.1 (CH, C-24), 69.9 (CH_2, C-8), 69.6 (CH_2, C-9), 69.4 (CH, C-3), 69.0 (CH, C-2), 68.5 (CH, C-5), 68.3 (CH, C-26), 67.2 (CH_2, C-7), 66.8, 66.7 (CH_2, C-18), 66.0 (CH, C-4), 62.5 (CH_2, C-13, C-22), 62.4 (CH_2, C-6), 62.1 (CH_2, C-13), 61.7 (CH_2, C-28), 50.1 (CH_2, C-10, C-19), 29.7, 29.1 (CH_2, C-17), 20.8, 2 x 20.7, 2 x 20.6 ($OCOCH_3$). HRMS (ESI$^+$-MS, m/z): calculated for $C_{241}H_{316}N_{30}O_{118}$ $[M+4H]^{4+}$ 1380.2430; found 1380.2436.

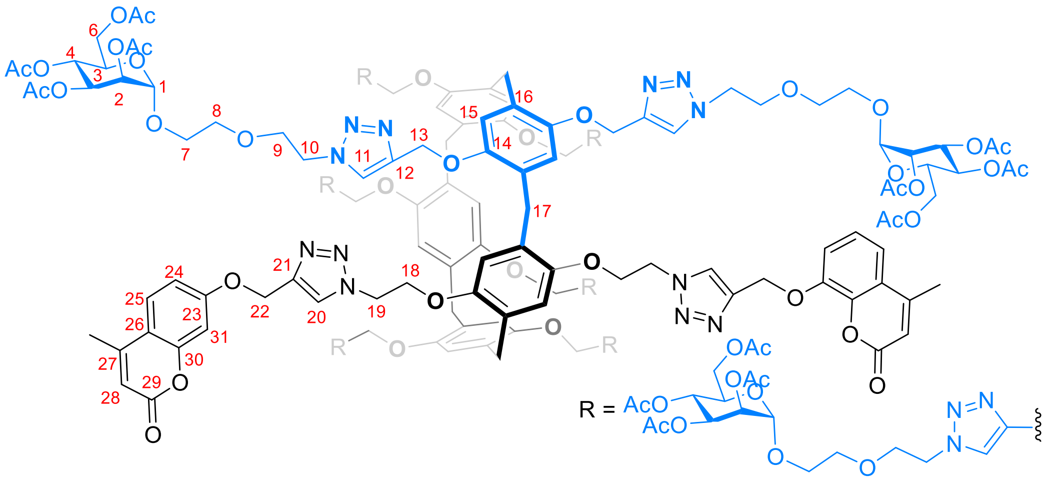
Compound 8b:



The title compound was prepared following the general procedure **B** using **6** (100 mg, 0.021 mmol), **7b** (45 mg, 0.11 mmol), CH_2Cl_2 (1.5 mL), $CuSO_4$ (3.3 mg, 0.021 mmol, 0.2 equiv.) and NaAsc (12.2 mg, 0.069 mmol,) [n = 5], purified by using EtOAc/Cy (2:1) as eluent to remove excess **7b**, then DCM/MeOH (30:1) as eluent and isolated a white solid (119 mg, 0.0195 mmol, 93%).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.88–7.80 (m, 10H, 8 x H-11, 2 x H-20), 6.95–6.87 (m, 8H, 8 x H-15), 6.72 (br, 2H, 2 x H-15), 5.30–5.20 (m, 28H, 8 x H-2, 8 x H-3, 8 x H-4, 2 x H-25, 2 x H-32), 5.13–5.02 (m, 8H, 2 x H-13, 2 x H-30, 2 x H-24), 4.93–4.81 (m, 26H, 8 x H-1, 6 x H-13, 2 x H-22, 2 x H-31), 4.71–4.44 (m, 26H, 8 x H-10, 2 x H-19, 2 x H-23, 2 x H-29, 2 x H-28α), 4.27–4.10 (m, 12H, 8 x H-6a, 2 x H-18), 4.07–4.01 (m, 14H, 8 x H-6b, 2 x H-28b, 2 x H-34), 3.96–3.83 (m, 26H, 8 x H-5, 8 x H-9, 2 x H-33), 3.78–3.71 (m, 18H, 5 x H-17, 6 x H-7a, 2 x H-26), 3.62–3.58 (m, 24H, 8 x H-7b, 8 x H-8), 3.40–3.36 (m, 2H, H-7a), 2.11–2.10 (m, 30H, 10 x $OCOCH_3$), 2.04 (m, 30H, 10 x $OCOCH_3$), 2.06–2.03 (m, 30H, 10 x $OCOCH_3$), 2.01–1.97 (m, 42H, 14 x $OCOCH_3$), 1.81–1.78 (m, 6H, 2 x $OCOCH_3$). ^{13}C NMR (100 MHz, $CDCl_3$) δ 170.6, 170.4, 170.3, 170.2, 170.1, 170.0, 169.8, 2 x 169.7, 169.1 (Cq, C=O_{acetyl}), 149.9, 149.8, 2 x 149.4 (Cq, C-14), 144.4, 2 x 144.3, 143.8, 143.7 ($Cq_{triazole}$, C-12, C-21), 128.8, 128.6, 128.5, 128.2, 128.1 (Cq, C-16), 124.2, 124.1, 124.01 ($CH_{triazole}$, C-11, C-20), 115.8, 115.2 (CH_{Ar}, C-15), 101.1 (CH, C-29), 99.5, 99.3 (CH, C-23), 97.7 (CH, C-1), 76.3 (CH, C-26), 72.9 (CH, C-27), 72.7 (CH, C-30), 71.6, 71.1 (CH, C-24, C-30), 70.7 (CH, C-25), 2 x 70.0 (CH_2, C-8), 69.7 (CH_2, C-9), 69.5 (CH_2, C-3, C-33), 69.1 (CH, C-2), 68.6 (CH, C-5), 67.3 (CH_2, C-7), 66.8 (CH_2, C-21), 66.7 (CH, C-32), 66.2 (CH, C-4), 62.6 (CH_2 or CH, C-13 or C-22), 62.5 (CH_2, C-6), 62.2 (CH_2, C-13 or C-22), 62.0 (CH_2, C-28 or C-34), 61.9 (CH_2, C-13 or C-22), 60.8 (CH_2, C-28 or C-34), 50.1 (CH_2, C-10, C-19), 29.8, 29.3 (CH_2, C-17), 20.9, 2 x 20.8, 3 x 20.7, 2 x 20.6, 20.5 ($OCOCH_3$). HRMS (ESI^+-MS, m/z): calculated for $C_{265}H_{348}N_{30}O_{134}$ $[M+4H]^{4+}$ 1524.2852; found 1524.2868.

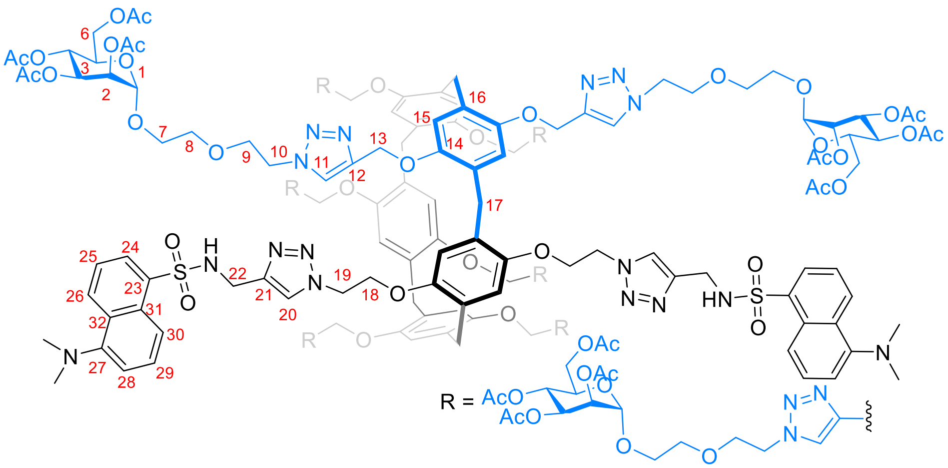
Compound 8c:



The title compound was prepared following the general procedure **B** using **6** (100 mg, 0.021 mmol), **7c** (23 mg, 0.105 mmol, 5 equiv.), CH_2Cl_2 (1.5 mL), $CuSO_4$ (5.3 mg, 0.034 mmol) and NaAsc (19.5 mg, 0.111 mmol) [n = 8], purified by using EtOAc/Cy (2:1) as eluent to remove excess **7c**, then DCM/MeOH (30:1) as eluent and isolated a yellow solid (107 mg, 0.0207 mmol, 98%).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.90–7.85 (m, 10H, 8 x H-11, 2 x H-20), 7.37 (d, *J* = 6.1 Hz, 2H, 2 x H-25), 6.98–6.62 (m, 14H, 10 x H-15, 2 x H-24, 2 x H-31), 6.02 (s, 2H, 2 x H-28), 5.32–5.20 (m, 24H, 8 x H-2, 8 x H-3, 8 x H-4), 5.03–4.71 (m, 30H, 8 x H-1, 8 x H-13, H-19, 2 x H-22), 4.58–4.52 (m, 18H, 8 x H-10, H-19), 4.28–4.24 (m, 8H, 8 x H-6a), 4.16 (br, 2H, H-18), 4.08–3.87 (m, 34H, 8 x H-5, 8 x H-6b, 8 x H-9, H-18), 3.79–3.71 (m, 16H, 6 x H-7a, 5 x H-17) 3.64–3.60 (m, 26H, 8 x H-7b, 2 x H-7a, 8 x H-8), 2.28 (s, 6H, 2 x CH_3), 2.12–2.11 (m, 24H, 8 x $OCOCH_3$), 2.02–2.00 (m, 24H, 8 x $OCOCH_3$), 2.02–2.00 (m, 24H, 8 x $OCOCH_3$), 1.96–1.95 (m, 24H, 8 x $OCOCH_3$). ^{13}C NMR (100 MHz, $CDCl_3$) δ 170.6, 170.0, 169.7 (Cq, $C{=}O_{acetyl}$), 161.1 (CH_{Ar}, C-23, C-29), 154.9 (Cq, C-30), 152.7 (Cq, C-27), 149.7, 149.5, 149.1 (Cq, C-14), 144.3 ($Cq_{triazole}$, C-12), 142.7 (Cq, C-14), 128.7, 128.5, 128.2, 127.9 (Cq, C-16), 125.7 (CH_{Ar}, C-25), 124.8 ($CH_{triazole}$, C-20), 124.2, 123.9 ($CH_{triazole}$, C-11), 115.7, 115.2, 114.8 (CH_{Ar}, C-15), 113.8 (Cq, C-26), 112.2 (CH_{Ar}, C-24), 111.9 (CH_{Ar}, C-28), 102.3 (CH_{Ar}, C-31), 97.7 (CH, C-1), 69.9 (CH_2, C-8), 69.5 (CH_2 and CH, C-9, C-3), 69.1 (CH, C-2), 68.5 (CH, C-5), 67.2 (CH_2, C-7), 66.7 (CH_2, C-21), 66.1 (CH_2, C-6), 62.4, 61.9, 61.6 (CH_2, C-13, C-22), 50.1 (CH_2, C-10, C-19), 29.9, 29.7, 29.0 (CH_2, C-17), 20.8, 20.7, 20.7 ($OCOCH_3$), 18.6 (CH_3). HRMS (ESI^+-MS, m/z): calculated for $C_{233}H_{292}N_{30}O_{104}$ $[M+4H]^{4+}$ 1293.9631; found 1293.9659.

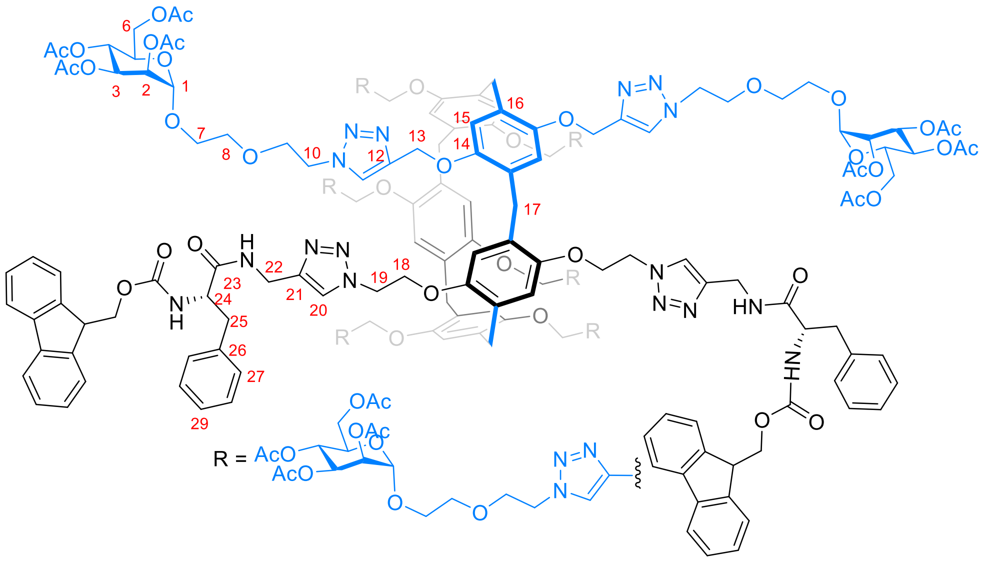
Compound 8d:



The title compound was prepared following the general procedure **B** using **6** (110 mg, 0.023 mmol), **7d** (33 mg, 0.11 mmol, 5 equiv.), CH_2Cl_2 (1.5 mL), NaAsc (21.3 mg, 0.121 mmol) [n = 8], purified by using EtOAc as eluent to remove excess **7d**, then DCM/MeOH (20:1) as eluent and isolated a yellow solid (118 mg, 0.221 mmol, 96%).

^{1}H NMR (400 MHz, CDCl$_3$) δ 8.55 (br, 2H, 2 x H-24), 8.30 (br, 2H, 2 x H-30), 8.23 (d, *J* = 7.2 Hz, 2H, 2 x H-26), 7.98–7.80 (m, 10H, 8 x H-11, 2 x H-20), 7.52–7.48 (m, 2H, 2 x H-25), 7.44–7.39 (m, 2H, 2 x H-29), 7.17 (br, 2H, 2 x H-28), 6.98–6.74 (m, 10H, 10 x H-15), 5.33–5.23 (m, 26H, 8 x H-2, 8 x H-3, 8 x H-4, 2 x NH), 5.10–5.02 (m, 4H, 2 x H-13), 4.92–4.81 (m, 20H, 6 x H-13, 8 x H-1), 4.65–4.64 (m, 4H, 2 x H-19), 4.58–4.47 (m, 16H, 8 x H-10), 4.28–4.23 (m, 8H, 8 x H-6a), 4.19–4.18 (m, 4H, 2 x H-22), 4.09–4.07 (m, 12H, 8 x H-6b, 2 x H-18), 3.99 (br, 8H, 8 x H-5), 3.91–3.83 (m, 16H, 8 x H-9), 3.76 (br, 16H, 6 x H-7α, 5 x H-17), 3.61–3.57 (m, 24H, 8 x H-7b, 8 x H-8), 3.6–3.46 (m, 2H, 2 x H-7a), 2.89 (s, 12H, 4 x NCH$_3$), 2.13–2.11 (m, 24H, 8 x OCOCH$_3$), 2.07–2.05 (m, 24H, 8 x OCOCH$_3$), 2.03–2.01 (m, 24H, 8 x OCOCH$_3$), 1.97–1.95 (m, 24H, 8 x OCOCH$_3$). ^{13}C NMR (100 MHz, CDCl$_3$) δ 170.6, 170.0, 169.9, 169.7 (Cq, C=O$_{\text{acetyl}}$), 151.8 (Cq, C-23), 150.0, 149.8, 149.7, 149.5 (Cq, C-14), 144.4, 144.3, 144.2, 144.1 (Cq$_{\text{triazole}}$, C-12, C-21), 135.0 (Cq, C-27), 130.3 (CH$_{\text{Ar}}$, C-24), 129.8, 129.7 (Cq, C-31, C-32), 129.4 (CH$_{\text{Ar}}$, C-26), 128.9, 128.9, 128.8, 128.5, 128.4 (Cq, C-16), 128.2 (C-25), 124.3, 2 x 124.0, 123.6 (CH$_{\text{triazole}}$, C-11, C-20), 123.3 (CH$_{\text{Ar}}$, C-29), 119.1 (CH$_{\text{Ar}}$, C-30), 115.7, 115.3, 115.2 (CH$_{\text{Ar}}$, C-15, C-28), 97.7 (CH, C-1), 69.9 (CH$_2$, C-8), 69.5 (CH and CH$_2$, C-2, C-9), 69.1 (CH, C-3), 68.6 (CH, C-5), 67.2 (CH$_2$, C-7), 66.9 (CH$_2$, C-18), 66.1 (CH, C-4), 62.5 (CH$_2$, C-6), 62.2, 61.9 (CH$_2$, C-13), 50.2 (CH$_2$, C-10), 50.0 (CH$_2$, C-19), 45.4 (NCH$_3$), 38.9 (CH$_2$, C-22), 30.2, 29.6, 29.3 (CH$_2$, C-17), 20.9, 2 x 20.7 (OCOCH$_3$). HRMS (ESI$^+$-MS, m/z): calculated for $C_{237}H_{304}N_{34}O_{102}S_2$ [M+4H]$^{4+}$ 1330.9781; found 1330.9803.

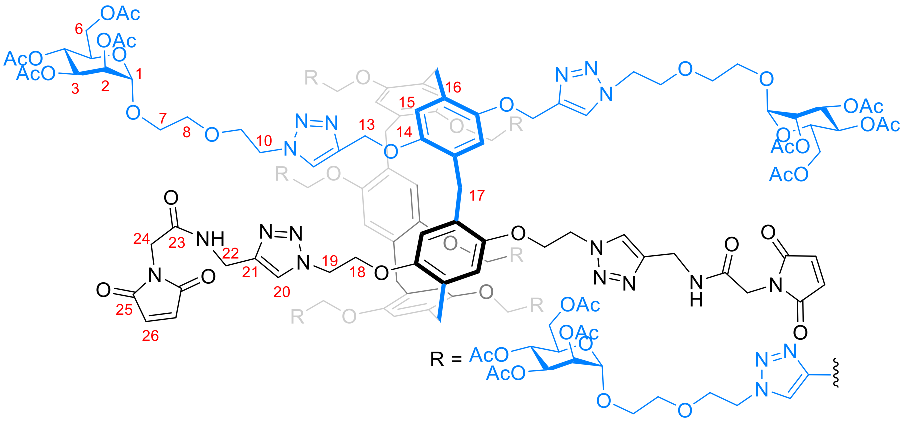
Compound 8e:



The title compound was prepared following the general procedure **B** using **6** (100 mg, 0.021 mmol), **7e** (47 mg, 0.11 mmol,), CH_2Cl_2 (1.5 mL), $CuSO_4$ (5.3 mg, 0.034 mmol) and NaAsc (19.5 mg, 0.111 mmol) [n = 8], purified by using EtOAc/Cy (2:1) as eluent to remove excess **7e**, then DCM/MeOH (25:1) as eluent and isolated a white solid (108 mg, 0.019 mmol, 92%).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.93–7.71 (m, 14H, 8 x H-11, 2 x H-20, 4 x H_{Ar}-Fmoc), 7.52–7.44 (m, 4H, 4 x H_{Ar}-Fmoc), 7.38–7.34 (m, 4H, 4 x H_{Ar}-Fmoc), 7.27–7.23(m, 4H, 2 x H-Ph, 2 x H_{Ar}-Fmoc), 7.14–6.71 (m, 20H, 10 x H-15, 8 x H-Ph, 2 x H_{Ar}-Fmoc), 5.90–5.80 (m, 2H, 2 x NH), 5.33–5.24 (m, 24H, 8 x H-2, 8 x H-3, 8 x H-4), 5.11–5.00 (m, 4H, 2 x H-13), 4.90–4.70 (m, 24H, 8 x H-1, 6 x H-13, 2 x H-19), 4.50–4.43 (m, 20H, 8 x H-10, H-22, 2 x H-24), 4.33–4.16 (m, 16H, 8 x H-6a, H-18, 2 x CH_2-Fmoc, H-22), 4.09–4.04 (m, 10H, 8 x H-6b, 2 x CH-Fmoc), 4.0–3.95 (m, 10H, 8 x H-5, H-18), 3.85–3.71 (m, 32H, 6 x H-7a, 8 x H-9, 5 x H-17), 3.57–3.48 (m, 26H, 2 x H-7a, 8 x H-7b, 8 x H-8), 3.05 (br, 2H, 2 x H-25a), 2.95 (br, 2H, 2 x H-25b), 2.10–2.08 (m, 24H, 8 x $OCOCH_3$), 2.05 (br, 24H, 8 x $OCOCH_3$), 2.00–1.97 (m, 24H, 8 x $OCOCH_3$), 1.93–1.92 (m, 24H, 8 x $OCOCH_3$). ^{13}C NMR (100 MHz, $CDCl_3$) δ 171.0 (Cq, C-23), 170.6, 170.1, 169.9, 169.7 (Cq, C=O_{acetyl}), 155.8 (NHCOO), 149.8, 149.7, 149.5 (Cq, C-14), 144.6, 144.4 ($Cq_{triazole}$, C-12, C-21), 144.3 (Cq, C_{Ar}-Fmoc), 143.9 (Cq, C_{Ar}-Fmoc), 141.3 (CH_{Ar}-Fmoc), 136.7 (Cq, C-26), 129.4 (CH-Ph), 128.8 (Cq, C-16), 128.4 (CH_{Ar}-Fmoc), 128.2 (Cq, C-16), 127.7 (CH_{Ar}-Fmoc), 127.1, 126.8 (CH_{Ar}-Ph), 125.1 (CH_{Ar}-Fmoc), 124.3, 124.0, 123.1 ($CH_{triazole}$, C-11 or C-20), 119.9 (CH_{Ar}-Fmoc), 115.7, 115.4 (CH_{Ar}, C-15), 97.7 (CH, C-1), 70.0 (CH_2, C-8), 69.6 (CH_2, C-9), 69.5 (CH, C-3), 69.1 (CH, C-2), 68.6 (CH, C-5), 67.3 (CH_2, C-7), 66.9 (CH_2, C-18), 66.1 (CH, C-4), 62.5 (CH_2, C-6), 62.1, 61.9 (CH_2, C-13), 56.0 (CH, C-24), 50.2, 50.1 (CH_2, C-10, C-19), 47.1 (CH-Fmoc), 38.7 (CH_2, C-25), 35.1 (CH_2, C-22), 29.9, 29.7, 29.4, 29.1 (CH_2, C-17), 20.9, 2 x 20.7 ($OCOCH_3$). HRMS (ESI^+-MS, m/z): calculated for $C_{261}H_{320}N_{34}O_{104}$ $[M+4H]^{4+}$ 1398.7701; found 1398.7730.

Compound 8g:

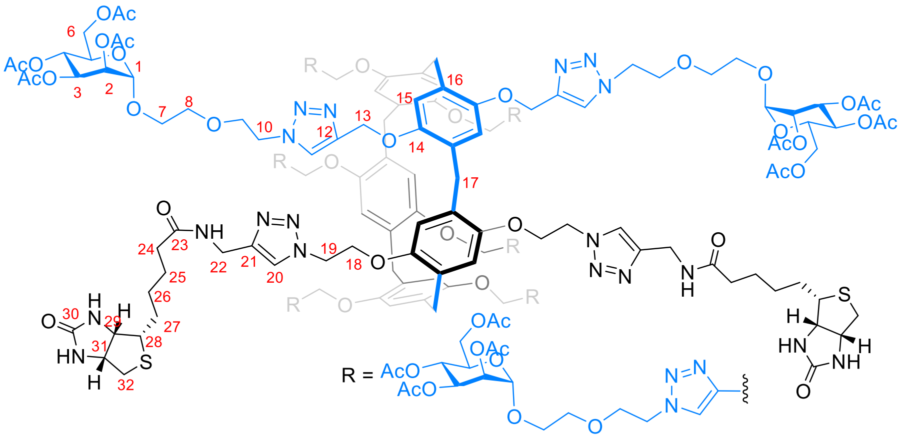


The title compound was prepared following the general procedure **B** using **6** (77 mg, 0.015 mmol), **7g** (17 mg, 0.09 mmol, 6 equiv.), CH_2Cl_2 (1.5 mL), $CuSO_4$ (4.8 mg, 0.03 mmol,) and NaAsc (17.4 mg, 0.099 mmol) [n = 10], purified using EtOAc/Cy (1:1) as eluent to remove excess **7g**, then DCM/MeOH (25:1) as eluent and isolated a pale yellow solid (40 mg, 0.08 mmol, 53%).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.93–7.21 (m, 10H, 8 x H-11, 2 x H-20), 7.05–6.70 (m, 10H, 10 x H-15), 6.63 (s, 4H, 4 x H-26), 5.32–5.23 (m, 24H, 8 x H-2, 8 x H-3, 8 x H-4), 5.04–4.96 (m, 4H, 2 x H-13), 4.91–4.43 (m, 42H, 8 x H-1, 8 x H-10, 6 x H-13, 2 x H-19, 2 x H-22a), 4.38–4.33 (m, 2H, 2 x H-22b), 4.28–4.24 (m, 8H, 8 x H-6a), 4.21–4.13 (m, 6H, 2 x H-18a, 2 x H-24), 4.10–4.06 (m, 8H, 8 x H-6b), 4.01–3.84 (m, 26H, 8 x H-5, 8 x H-9, 2 x H-18b), 3.78–3.73 (m, 14H, 2 x H-7, 5 x H-17), 3.62–3.52 (m, 28H, 6 x H-7, 8 x H-8), 2.16–2.12 (m, 24H, 8 x OCH_3), 2.09–2.06 (m, 24H, 8 x $OCOCH_3$), 2.03–2.02 (m, 24H, 8 x $OCOCH_3$), 1.96 (m, 24H, 8 x $OCOCH_3$). ^{13}C NMR (100 MHz, $CDCl_3$) δ 170.7, 170.3, 170.1, 170.0, 169.8 (Cq, $C{=}O_{acetyl}$), 166.5 (Cq, C-23), 149.8, 149.6 (Cq, C-14), 144.6, 144.3

($Cq_{triazole}$, C-12 or C-21), 134.4 (C-26), 129.0, 128.5, (Cq, C-16), 124.4, 124.0, 123.2 ($CH_{triazole}$, C-11 or C-20), 115.6, 115.3 (CH_{Ar}, C-15), 97.8 (CH, C-1), 70.0 (CH_2, C-8), 69.5 (CH and CH_2, C-9, C-3), 69.2 (CH, C-2), 68.6 (CH, C-5), 67.3 (CH_2, C-7, C-18), 66.2 (CH, C-4), 62.7 (CH_2, C-13), 62.5 (CH_2, C-6), 62.2, 62.1 (CH_2, C-13), 50.1 (CH_2, C-10, C-19), 40.3 (CH_2, C-24), 35.3 (CH_2, C-22), 30.0, 29.8, 29.4 (CH_2, C-17), 21.0, 20.8 ($OCOCH_3$). HRMS (ESI^+-MS, m/z): calculated for $C_{225}H_{288}N_{34}O_{104}$ $[M+4H]^{4+}$ 1282.4568; found 1282.4615.

Compound 8f:

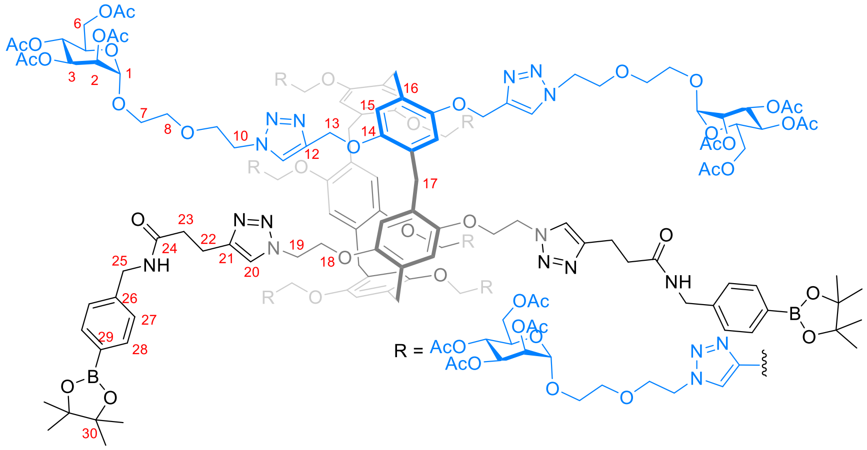


Firstly, a solution of CuI (2.8 mg, 0.0147 mmol) in dry DMF (4 mL) was prepared. Afterwards, 0.5 mL this solution was taken and added to a mixture of **6** (44 mg, 0.00927 mmol), **7f** (11 mg, 0.037 mmol) Et_3N (5 µL, 0.037 mmol) under argon atmosphere. The reaction mixture was stirred overnight at room temperature. Then, it was diluted with CH_2Cl_2 (25 mL), washed with H_2O (25 mL) and brine (25 mL), dried over $MgSO_4$ and concentrated under reduced pressure. The residue was purified by column chromatography on silica gel using DCM/MeOH (12:1) as eluent to afford **8f** as a white solid (0.0049 mmol, 26 mg, 53%).

^1H NMR (500 MHz, $CDCl_3$) δ 8.02–7.77 (m, 10H, 8 x H-11, 2 x H-20), 7.19–6.59 (m, 10H, 10 x H-15), 5.24–5.13 (m, 26H, 8 x H-2, 8 x H-3, 8 x H-4, H-13), 5.08–4.9 (m, 2H, H-13), 4.85–4.76 (m, 20H, 8 x H-1, 6 x H-13), 4.64–4.49 (m, 20H, 8 x H-10, 2 x H-22), 4.36–4.33 (m, 2H, H-19), 4.23–4.14 (m, 10H, 8 x H-6a, H-19), 4.05–3.84 (m, 36H, 8 x H-5, 8 x H-6b, 8 x H-9, 2 x H-18), 3.72–3.68 (m, 14H, 5 x H-17, 2 x H-7), 3.60–3.32 (m, 28H, 6 x H-

7, 8 x H-8), 2.94–2.40 (m, 6H, 2 x H-28, 2 x H-32), 2.21–2.07 (m, 22H, 2 x H-24, 6 x $OCOCH_3$), 2.02–2.01 (m, 24H, 8 x $OCOCH_3$), 1.98–1.97 (m, 24H, 8 x $OCOCH_3$), 1.91 (s, 24H, 8 x $OCOCH_3$), 1.86 (s, 6H, 2 x $OCOCH_3$), 1.45 (br, 8H, 2 x H-25, 2 x H-27), 1.19 (br, 4H, 2 x H-26). ^{13}C NMR (125 MHz, $CDCl_3$) δ 173.6 (Cq, C-23), 170.1, 2 x 170.0, 169.8 (Cq, $C=O_{acetyl}$), 164.1, 163.8 (C-30), 149.8, 149.7, 149.5, 149.4 (Cq, C-14), 144.4, 2 x 144.3, 144.1, 143.9 ($Cq_{triazole}$, C-12, C-21), 131.2, 128.8, 128.7 (Cq, C-16), 124.7, 124.5, 124.1, 124.0, 123.8 ($CH_{triazole}$, C-11, C-20), 115.9, 115.4 (CH_{Ar}, C-15), 97.7, 97.7 (CH, C-1), 70.0, 69.9 (CH_2, C-8), 69.6 (CH_2, C-9), 69.5 (CH, C-3), 69.10 (CH, C-2), 68.6, 68.5 (CH, C-5), 67.3 (CH, C-7, C-18), 2 x 66.1 (CH, C-4), 62.5 (CH_2, C-6), 62.0 (CH, C-29), 61.8 , 61.2 (CH_2, C-13), 60.0 (CH, C-31), 55.5 (CH, C-28), 50.1 (CH_2, C-10), 49.6 (CH_2, C-19), 40.4 (CH_2, C-32), 35.5, 35.0 (CH_2, C-22, C-24), 29.7, 29.2, 28.1, 27.5, 25.1 (CH_2, C-17, C-25, C-26, C-27), 2 x 20.9, 2 x 20.8, 20.7 ($OCOCH_3$). HRMS (ESI^+-MS, m/z): calculated for $C_{233}H_{306}N_{36}O_{102}S_2$ $[M+4H]^{4+}$ 1326.9899; found 1326.9922.

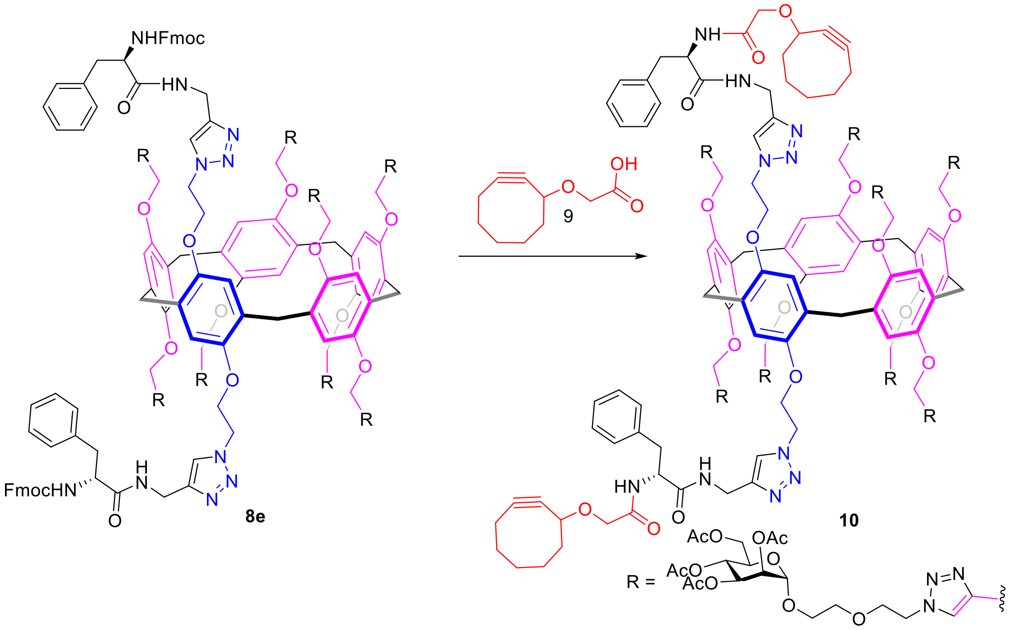
Compound 8h:



Firstly, a well-stirred solution of CuI (3.7 mg, 0.0194 mmol, 2 equiv.) and TBTA (5.2 mg, 0.0097 mmol, 1 equiv.) was prepared in dry DMSO (10 mL). Afterwards, 1 mL this solution was taken and added to a mixture of **6** (46 mg, 0.0097 mmol, 1 equiv.) and **7h** (10 mg, 0.031 mmol, 3.2 equiv.) under argon atmosphere. The reaction mixture was stirred overnight at room temperature. Then, distilled H_2O (20 mL) was added and the mixture was extracted with CH_2Cl_2 (3 x 15 mL), washed with brine (40 mL), dried over $MgSO_4$ and concentrated. The residue was purified by column chromatography on silica gel by using EtOAc/Cy (2:1) as eluent to quickly remove excess **7h**, followed DCM/MeOH (25:1) as eluent to afford the desired product **8h** as a colorless solid (45 mg, 0.0084 mmol, 86%).

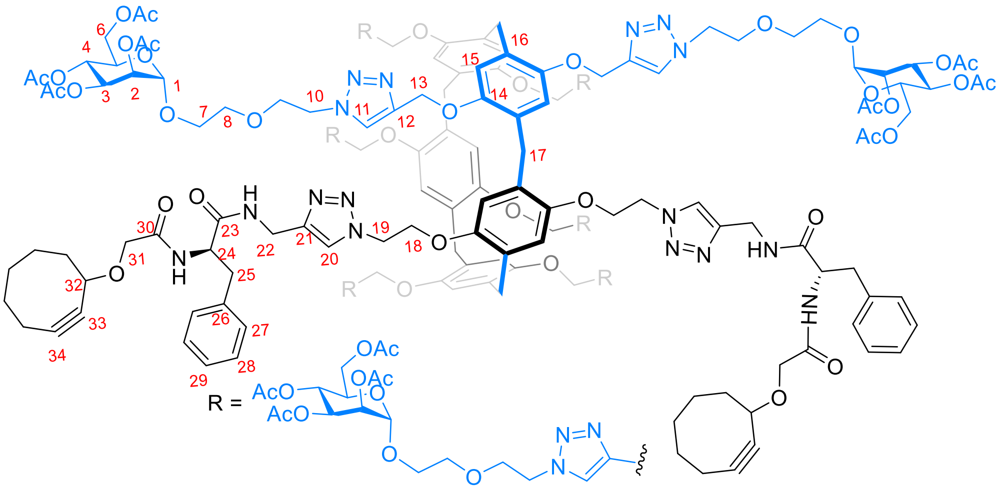
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.95–7.70 (m, 12H, 8 x H-11, 2 x H-20, 2 x H-28), 7.33–7.19 (m, 4H, 2 x H-27), 7.03–6.73 (m, 10H, 10 x H-15), 5.53–3.45 (m, 158H, 8 x H-1, 8 x H-2, 8 x H-3, 8 x H-4, 8 x H-5, 8 x H-6, 8 x H-7, 8 x H-8, 8 x H-9, 8 x H-10, 8 x H-13, 5 x H-17, 2 x H-18, 2 x H-19, 2 x H-25), 3.01–2.98 (br, 4H, 2 x H-23), 2.58 (br, 4H, 2 x H-22), 2.12–1.96 (m, 96H, 24 x $OCOCH_3$), 1.34–1.25 (m, 24H, 8 x CH_3). ^{13}C NMR (100 MHz, $CDCl_3$) δ 172.2, 170.8, 170.7, 170.2, 170.0, 169.8 (Cq, C=O_{acetyl}, C-24), 149.8, 149.5 (Cq, C-14), 144.4, 143.9 ($Cq_{triazole}$, C-12), 142.0 (Cq, C-26), 135.1 (C-28), 134.6 134.5 ($Cq_{triazole}$, C-21), 129.2, 128.9, 128.1 (Cq, C-16), 127.0 (CH_{Ar}, C-27), 124.4, 124.1 ($CH_{triazole}$, C-11), 122.6 ($CH_{triazole}$, C-20), 115.6, 115.3, 115.2 (CH_{Ar}, C-15), 97.8 (CH, C-1), 83.9 (C-30), 70.0 (CH_2, C-8), 69.6 (CH_2 and CH, C-3, C-9), 69.2 (CH, C-2), 68.6 (CH, C-5), 67.3 (CH_2, C-7), 67.1 (CH_2, C-18), 66.2 (CH, C-4), 62.8 (CH_2, C-13), 62.5 (CH_2, C-6), 62.2 (CH_2, C-13), 61.9 (CH_2, C-13), 50.2 (CH_2, C-10), 46.9 (CH_2, C-19), 43.4 (CH_2, C-25), 35.7 (CH_2, C-23), 31.0 (CH_2, C-22), 29.8, 29.4 (CH_2, C-17), 24.9 (CH_3), 21.0, 20.8 ($OCOCH_3$). HRMS (ESI$^+$-MS, m/z): calculated for $C_{243}H_{319}B_2N_{32}O_{104}$ $[M+3H]^{3+}$ 1790.3625; found 1790.3653.

S9. Synthesis of clickable compound 10



Scheme S10. Synthesis of **10**

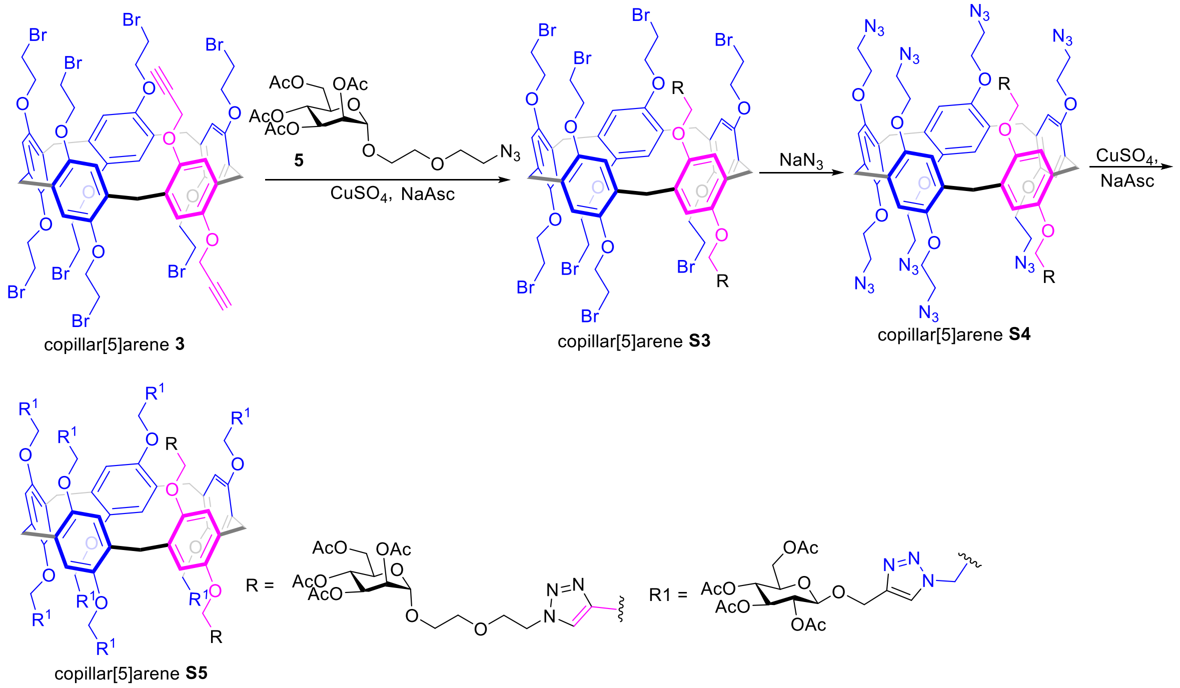
Compound 10



To a solution of **8e** (82 mg, 0.0147 mmol, 1 equiv.) in dry CH_2Cl_2 (2 mL) was added DBU (5 µL, 0.0334 mmol, 2.2 equiv.) under argon atmosphere and the mixture was stirred at room temperature for 40 min. After concentrating the crude under vacuum, dry CH_2Cl_2 (2 mL), EDCI (8.4 mg, 0.044 mmol, 3 equiv.) and **9** (8 mg, 0.044 mmol, 3 equiv.) were added and stirred overnight. Then, CH_2Cl_2 was evaporated and the residue was purified by column chromatography on silica gel using DCM/MeOH (30:1) as eluent to afford **10** as a pale-yellow solid (48 mg, 0.0088 mmol, 60%).

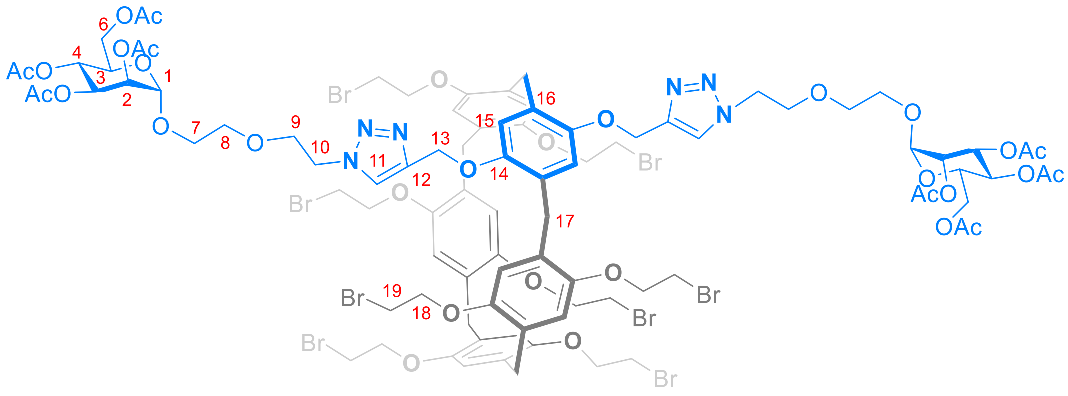
^{1}H NMR (500 MHz, $CDCl_3$) δ 7.90–7.86 (m, 6H, 6 x H-11), 7.79–7.73 (m, 4H, 2 x H-11, 2 x H-20), 7.17–6.98 (m, 12H, 2 x H-15, 4 x H-27, 4 x H-28, 2 x H-29), 6.9–6.71 (m, 8H, 8 x H-15), 5.31–5.22 (m, 24H, 8 x H-2, 8 x H-3, 8 x H-4), 5.11–5.00 (m, 4H, 2 x H-13), 4.89–4.65 (m, 26H, 8 x H-1, 6 x H-13, 2 x H-19, 2 x H-24), 4.56–4.32 (m, 20H, 8 x H-10, H-22, 2 x H-32), 4.26–4.05 (m, 20H, 8 x H-6, H-22, H-18), 3.98 (br, 10H, 8 x H-5, H-18), 3.93–3.86 (m, 20H, 8 x H-9, 2 x H-31), 3.77–3.73 (m, 16H, 5 x H-17, 3 x H-7a), 3.61–3.59 (br, 24H, 8 x H-7b, 8 x H-8), 3.48–3.43 (m, 2H, 2 x H-7a), 3.02–3.01 (m, 4H, 2 x H-25), 2.25–2.14 (m, 6H, 3 x $CH_{2cyclooctyne}$), 2.12–2.11 (m, 24H, 8 x $OCOCH_3$), 2.06–2.05 (m, 24H, 8 x $OCOCH_3$), 2.00–2.05 (m, 26H, 8 x $OCOCH_3$, $CH_{2cyclooctyne}$), 1.95 (m, 24H, 8 x $OCOCH_3$, $CH_{2cyclooctyne}$), 1.88–1.61 (m, 10H, 5 x $CH_{2cyclooctyne}$), 1.47–1.32 (m, 2H, $CH_{2Cyclooctyne}$). ^{13}C NMR (125 MHz, $CDCl_3$) δ 3 x 170.6, 2 x 170.0, 3 x 169.9, 2 x 169.7, 169.6, 169.5, 169.4, 169.3 (Cq, $C{=}O_{acetyl}$, CONH), 149.8, 149.7, 2 x 149.6, 2 x 149.4 (Cq, C-14), 144.5, 3 x 144.3, 144.2 ($Cq_{triazole}$, C-12, C-21), 136.5, 2 x 136.4 (Cq, C-26), 2 x 129.3 (CH_{Ar}, C-28), 128.8, 128.7 (Cq, C-16), 128.6, 128.4 (CH_{Ar}, C-27), 128.4, 2 x 128.2 (Cq, C-16), 126.8 (CH_{Ar}, C-29), 2 x 124.2, 124.0, 123.9, 123.0 ($CH_{triazole}$, C-11 or C-20), 115.7, 115.6, 115.4, 115.3, 115.2 (CH_{Ar}, C-15), 101.8, 101.6 (Cq_{alkyne}, C-33), 97.7, 97.6 (CH, C-1), 91.4, 91.3 (Cq_{alkyne}, C-34), 73.3, 73.0 (CH, C-32), 2 x 69.9 (CH_2, C-8), 69.6, 69.5 (CH_2, C-9), 69.4 (CH, C-3), 69.0 (CH, C-2), 68.5 (CH, C-5), 68.3, 68.1 (CH_2, C-18), 67.2 (CH_2, C-7), 67.0, 66.9 (C-31), 66.1 (CH, C-4), 62.4 (CH_2, C-6), 62.1, 62.9, 61.8 (CH_2, C-13), 53.6, 2 x 53.6, 53.5 (CH, C-24), 50.1, 50.0 (CH_2, C-10 or C-19), 42.1 ($CH_{2cyclooctyne}$), 38.4, 38.3, 38.2, 38.1 (CH_2, C-25), 35.1 (CH_2, C-23), 34.2, 34.1 ($CH_{2cyclooctyne}$), 29.9, 29.8, 2 x 29.6, 29.5, 29.3 (CH_2, C-17, $CH_{2cyclooctyne}$), 26.2, 26.1 ($CH_{2Cyclooctyne}$), 20.8, 2 x 20.7, 3 x 20.6 ($OCOCH_3$, $CH_{2cyclooctyne}$). HRMS (ESI$^+$-MS, m/z): calculated for $C_{251}H_{324}N_{34}O_{104}$ $[M+4H]^{4+}$ 1369.5272; found 1369.5294.

S10. Synthesis of copillar[5]arene S5 with an inverse azide:alkyne ration (8:2)



Scheme S11. Synthesis of copillar[5]arene **S5**

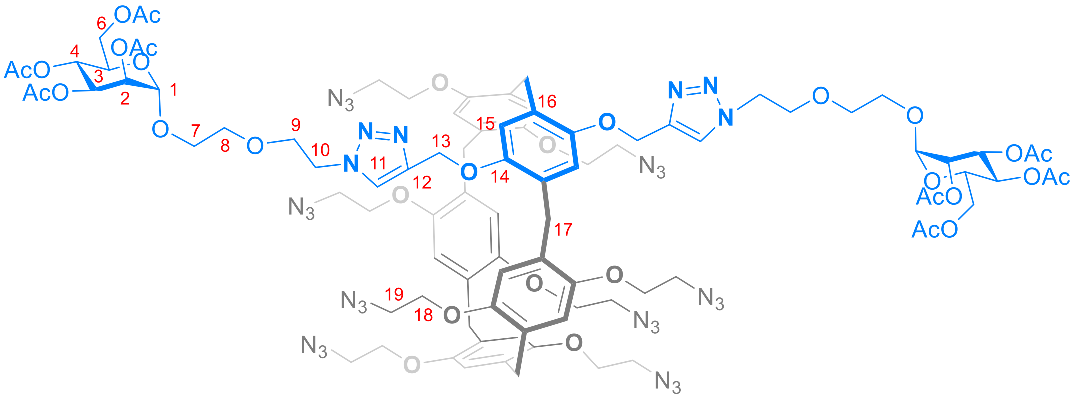
Compillar[5]arene S3:



The title compound was prepared following the synthetic procedure of compound **6a** using copillar[5]arene **3** (100 mg, 0.065 mmol, 1equiv.), **5** (90 mg, 0.194 mmol, 3 equiv.), $CuSO_4$ (2.0 mg, 0.013 mmol, 0.2 equiv.), NaAsc (7.6 mg, 0.043 mmol, 0.66 equiv.), CH_2Cl_2 (1 mL) and H_2O (1 mL). The resulting crude was by purified using EtOAc/Cy (1:1) as eluent to remove **5**, then DCM/MeOH (300:1) as eluent to isolate as a white solid (145 mg, 0.059 mmol, 90%).

^{1}H NMR (400 MHz, CDCl$_3$) δ 7.70 (s, 2H, 2 x H-11), 7.04 (s, 2H, 2 x H-15), 6.93–6.83 (m, 6H, 6 x H-15), 6.80–6.78 (m, 2H, 2 x H-15), 5.35–5.24 (m, 6H, 2 x H-2, 2 x H-3, 2 x H-4), 5.16–5.03 (m, 4H, 2 x H-13), 4.84 (s, 2H, 2 x H-1), 4.51 (br, 4H, 2 x H-10), 4.28–4.25 (m, 8H, 3 x H-18, 2 x H-6a), 4.14–4.08 (m, 10H, 4 x H-18, 2 x H-6b), 3.97 (m, 4H, 2 x H-5, H-18), 3.84–3.57 (m, 38H, 2 x H-7, 2 x H-8, 2 x H-9, 5 x H-17, 8 x H-19), 2.14 (s, 6H, 2 x OCOCH$_3$), 2.08 (s, 6H, 2 x OCOCH$_3$), 2.04–2.03 (m, 6H, 2 x OCOCH$_3$), 1.97 (s, 6H, 2 x OCOCH$_3$). ^{13}C NMR (100 MHz, CDCl$_3$) δ 2 x 170.6, 170.1, 169.9, 169.7 (Cq, C=O$_{\text{acetyl}}$), 149.9, 2 x 149.8, 2 x 149.5 (Cq, C-14), 144.2 (Cq$_{\text{triazole}}$, C-12), 129.3, 129.2, 129.1, 129.0, 128.9, 128.8 (Cq, C-16), 123.9 (CH$_{\text{triazole}}$, C-11), 116.4, 116.3, 115.7 (CH$_{\text{Ar}}$, C-15), 97.7 (CH, C-1), 70.0 (CH$_2$, C-8), 69.6 (C-9, C-2), 69.2, 2 x 69.1 (CH$_2$, C-18), 69.0 (CH, C-3), 68.6 (CH, C-5), 67.2 (CH$_2$, C-7), 66.2 (CH, C-4), 62.5 (CH$_2$, C-13), 62.5 (CH$_2$, C-6), 50.2 (CH$_2$, C-10), 31.3, 2 x 30.7 (CH$_2$, C-19), 29.7, 29.4, 29.3 (CH$_2$, C-17), 20.9, 20.8, 2 x 20.7 (OCOCH$_3$). HRMS (ESI$^+$-MS, m/z): calculated for $C_{93}H_{113}Br_8N_6O_{32}$ [M+H]$^+$ 2465.0810; found 2465.0781.

Compillar[5]arene S4:

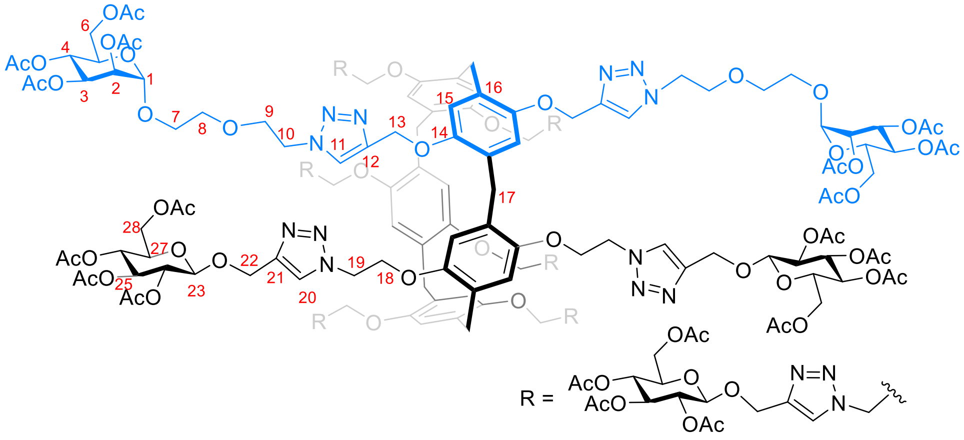


The title compound was prepared following the synthetic procedure of **7** using **S3** (132 mg, 0.053 mmol, 1 equiv.), NaN$_3$ (56 mg, 0.857 mmol, 16 equiv.) and dry DMF (1.5 mL) and isolated as a pale yellow solid (106 mg, 0.049 mmol, 92%).

^{1}H NMR (400 MHz, CDCl$_3$) δ 7.75 (br, 2H, 2 x H-11), 6.99 (s, 2H, 2 x H-15), 6.83–6.79 (m, 8H, 8 x H-15), 5.36–5.25 (m, 6H, 2 x H-2, 2 x H-3, 2 x H-4), 5.13–4.94 (m, 4H, 2 x H-

13), 4.86 (s, 2H, 2 x H-1), 4.54 (br, 4H, 2 x H-10), 4.27 (dd, *J* = 12.2, 5.1 Hz, 2H, 2 x H-6a), 4.12–3.74 (m, 36H, 2 x H-5, 2 x H-6b, 8 x H-18, 2 x H-7a, 2 x H-9, 5 x H-17), 3.69–3.54 (m, 22H, 8 x H-19, 2 x H-7b, 2 x H-8), 2.15–1.98 (m, 24H, 3 x $OCOCH_3$). ^{13}C NMR (100 MHz, $CDCl_3$) δ 170.4, 169.9, 2 x 169.8, 169.5 (Cq, C=O$_{acetyl}$), 149.9, 149.7, 149.4, 149.3 (Cq, C-14), 144.0 (Cq$_{triazole}$, C-12), 128.9, 2 x 128.7, 128.5, 128.4, 128.3 (Cq, C-16), 123.8 (CH$_{triazole}$, C-11), 115.7, 115.3, 115.2, 115.0 (CH$_{Ar}$, C-15), 97.5 (CH, C-1), 69.7 (CH_2, C-8, C-9), 69.3 (CH, C-2), 68.8 (CH, C-3), 68.4 (CH, C-5), 67.4, 67.2, 67.0, 66.9 (CH_2, C-7, C-18), 65.9 (CH, C-4), 62.3 (CH_2, C-6), 62.2 (CH_2, C-13), 50.7 (CH_2, C-19), 50.0 (CH_2, C-10), 29.8, 3 x 29.4 (CH_2, C-17), 20.6, 2 x 20.5, 20.4 ($OCOCH_3$). HRMS (ESI$^+$-MS, m/z): calculated for $C_{93}H_{113}N_{30}O_{32}$ $[M+2H]^{2+}$ 1081.9119; found: 1081.9116.

Compillar[5]arene S5:

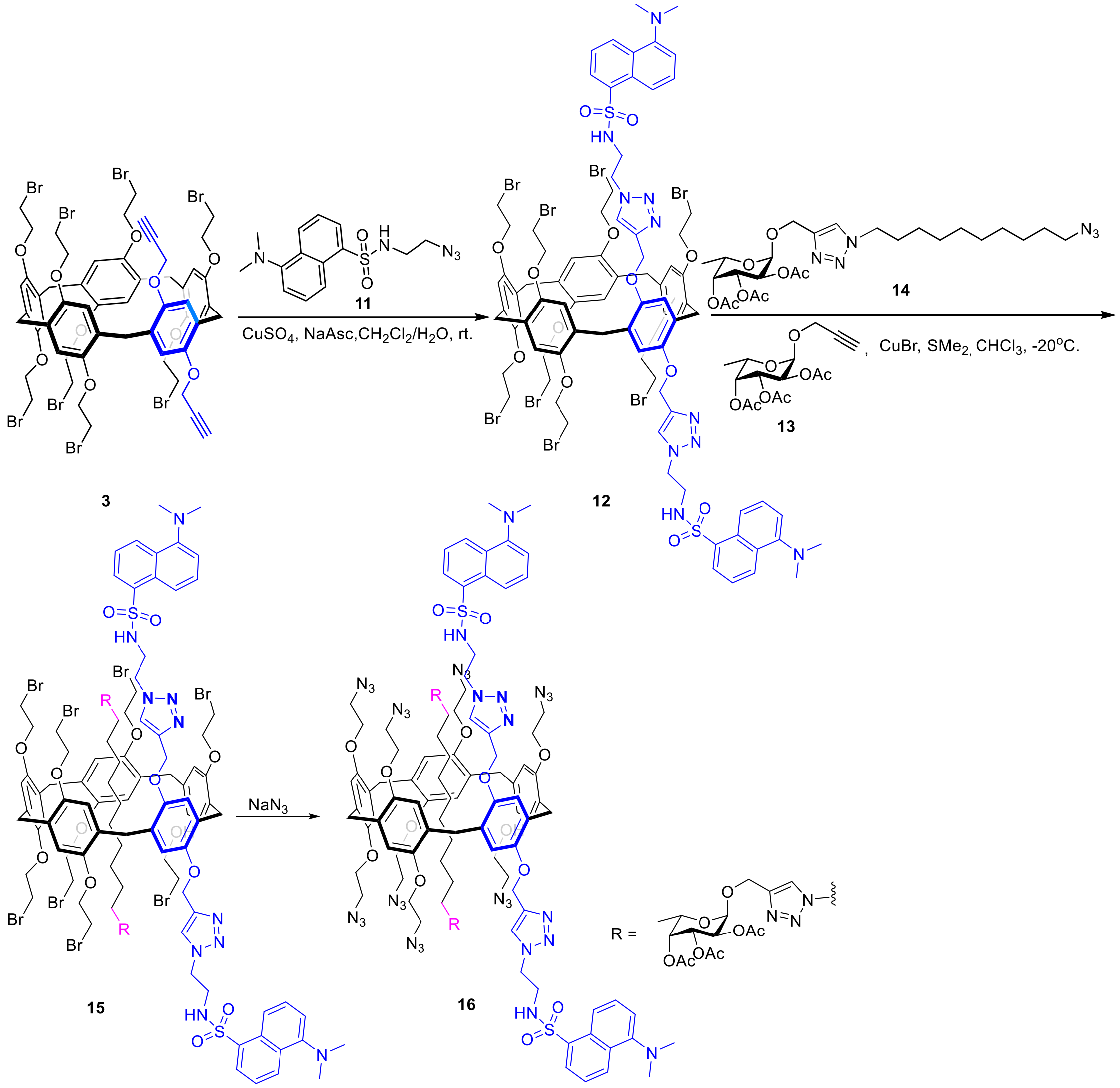


The title compound was prepared following general procedure B using **S4** (54 mg, 0.025 mmol, 1 equiv.), **7a** (96 mg, 0.250 mmol, 10 equiv.), CH_2Cl_2 (2 mL), $CuSO_4$ (0.2 equiv.) and NaAsc (0.66 equiv.) [n = 6], purified using EtOAc/Cy (2:1) as eluent to remove excess **7a**, then DCM/MeOH (30:1) as eluent and isolated as a pale yellow solid (118 mg, 0.0225 mmol, 90%).

^1H NMR (400 MHz, $CDCl_3$) δ 7.88–7.87 (m, 2H, 2 x H-11), 7.83–7.77 (m, 8H, 8 x H-20), 6.82–6.78 (m, 4H, 4 x H-15), 6.62–6.55 (m, 4H, 4 x H-15), 6.48–6.44 (m, 2H, 2 x H-15), 5.29–4.57 (m, 80H, 2 x H-1, 2 x H-2, 2 x H-3, 2 x H-4, 2 x H-10, 2 x H-13, 8 x H-18, 8 x H-22, 8 x H-23, 8 x H-24, 8 x H-25, 8 x H-26), 4.27–4.07 (m, 34H, 2 x H-6a, 8 x H-19, 8 x H-28), 3.99–3.89 (m, 8H, 2 x H-5, 2 x H-6b, 2 x H-9), 3.78–3.58 (m, 20H, 2 x H-7, 2 x

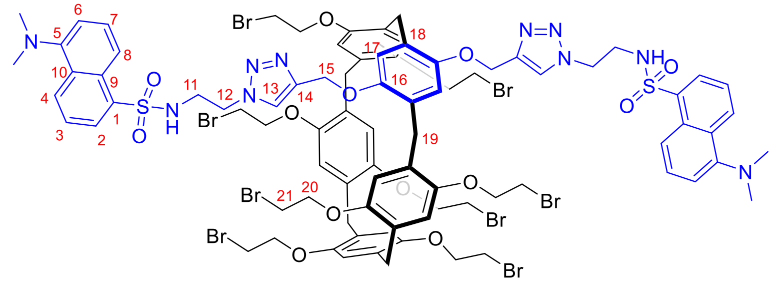
H-8, 2 x H-17, 8 x H-27), 3.35–3.27 (m, 6H, 3 x H-17), 2.12–2.10 (m, 6H, 2 x $OCOCH_3$), 2.05–1.93 (m, 90H, 30 x $OCOCH_3$), 1.90–1.84 (m, 24H, 8 x $OCOCH_3$). ^{13}C NMR (100 MHz, $CDCl_3$) δ 170.6, 170.1, 170.0, 169.7, 2 x 169.4 (Cq, $C{=}O_{acetyl}$), 149.8, 149.5, 149.4, 149.2 (Cq, C-14), 144.2, 144.0 ($Cq_{triazole}$, C-12, C-21), 129.0, 128.9, 128.5, 128.2 (Cq, C-16), 124.5, 123.7 ($CH_{triazole}$, C-11, C-20), 116.4, 115.7, 115.5, 115.1 (CH_{Ar}, C-15), 99.9, 2 x 99.7, 99.6 (CH, C-23), 97.7 (CH, C-1), 72.8 (CH, C-25), 71.9 (CH, C-27), 71.2 (CH, C-24), 70.0 (CH_2, C-8), 69.6 (CH_2, C-9), 69.5 (CH, C-2), 69.0 (CH, C-3), 68.6 (CH, C-5), 68.3 (CH, C-26), 67.5, 67.3, 67.0 (CH_2, C-7, C-18), 66.1 (CH, C-4), 62.8, 62.5, 62.0 (CH_2, C-6, C-22, C-28), 61.8 (CH_2, C-28), 50.2 (CH_2, C-10, C-19), 29.3, 29.1, 28.9, 20.9 (CH_2, C-17), 2 x 20.7, 20.6 ($OCOCH_3$). HRMS (ESI$^+$-MS, m/z): calculated for $C_{229}H_{289}N_{30}O_{112}$ $[M+H]^+$ 5250.7835; found $[M+H]^+$ 5250.7858

S11. Synthesis of fluorescent rotaxane 16



Scheme S12. Synthesis of **16**

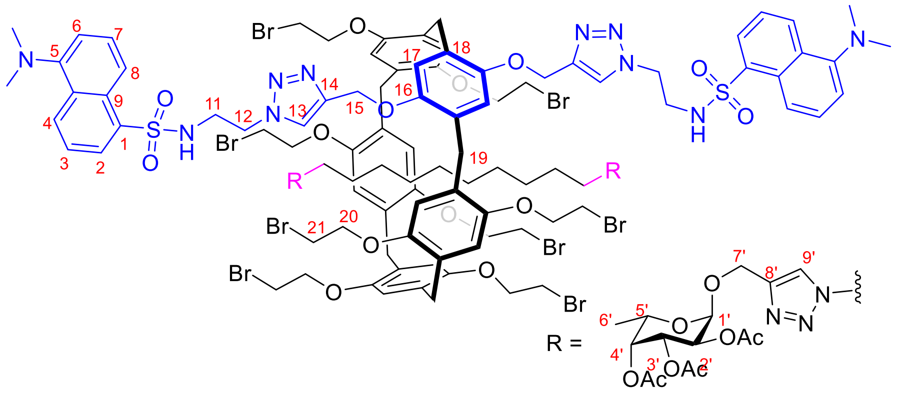
Compound 12:



To a vigorously stirred solution of copillar[5]arene **3** (583 mg, 0.378 mmol, 1 equiv.) and **11** (290 mg, 0.908 mmol, 2.4 equiv.) in CH_2Cl_2 (8 mL) under argon atmosphere, was added a freshly prepared solution of $CuSO_4$ (0.075 mmol, 12 mg, 0.2 equiv.) and NaAsc (49 mg, 0.249 mmol, 0.66 equiv.) in distilled H_2O (8 mL). After stirring for 12h, distilled H_2O (50 mL) and CH_2Cl_2 (50 mL) were added and the organic layer was separated and dried over $MgSO_4$, the solvent was concentrated and the residue was purified by column chromatography on silica gel using DCM/MeOH (150:1) as eluent to yield **12** as a yellow solid (774 mg, 0.355 mmol, 94%).

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.56 (d, *J* = 8.5 Hz, 2H, 2 x H-2), 8.23–8.21 (m, 4H, 2 x H-8, 2 x H-4), 7.53 (dd, *J* = 16.1, 8.4 Hz, 6H, 2 x H-3, 2 x H-7, 2 x H-13), 7.17 (d, *J* = 7.6 Hz, 2H, 2 x H-6), 6.98 (s, 2H, 2 x H-17), 6.94 (s, 2H, 2 x H-17), 6.87 (s, 4H, 4 x H-17), 6.78 (s, 2H, 2 x H-17), 6.01 (s, 2H, 2 x NH), 5.16 (m, 4H, 2 x H-15), 4.32–4.26 (m, 8H, 2 x H-12, 2 x H-20), 4.14–4.08 (m, 8H, 4 x H-20), 4.03–3.96 (m, 4H, 2 x H-20), 3.86–3.82 (m, 10H, 5 x H-19) 3.60 (t, *J* = 5.5 Hz, 8H, 4 x H-21), 3.54 (t, *J* = 5.5 Hz, 8H, 4 x H-21), 3.39 (m, 4H, 2 x H-11), 2.88 (s, 12H, 4 x NCH_3). ^{13}C NMR (100 MHz, $CDCl_3$) δ 152.1 (C-1), 149.8, 2 x 149.7 (Cq, C-16), 144.3 ($Cq_{triazole}$, C-14), 134.5 (Cq, C-5), 130.8 (CH_{Ar}, C-2), 130.0, 129.5 (Cq, C-18), 129.4 (CH_{Ar}, C-4), 129.3, 3 x 129.2 (Cq, C-18, C-9, C-10), 128.7 (CH_{Ar}, C-3), 124.1 ($CH_{triazole}$, C-13), 123.28 (CH_{Ar}, C-7), 118.7 (CH_{Ar}, C-8), 116.7, 116.4, 116.3, 116.1, 116.0 (CH_{Ar}, C-17, C-17), 115.5 (CH_{Ar}, C-6), 69.3 (CH_2, C-20), 62.8 (CH_2, C-15), 50.3 (CH_2, C-12), 45.5 (NCH_3), 42.9 (CH_2, C-11), 31.2, 31.0, 30.9, 30.7 (CH_2Br, C-21), 2 x 29.8, 29.3 (CH_2, C-19). HRMS (ESI$^+$-MS, m/z): calculated for $C_{85}H_{93}Br_8N_{10}O_{14}S_2$ $[M+H]^+$ 2172.9776; found $[M+H]^+$ 2172.9758.

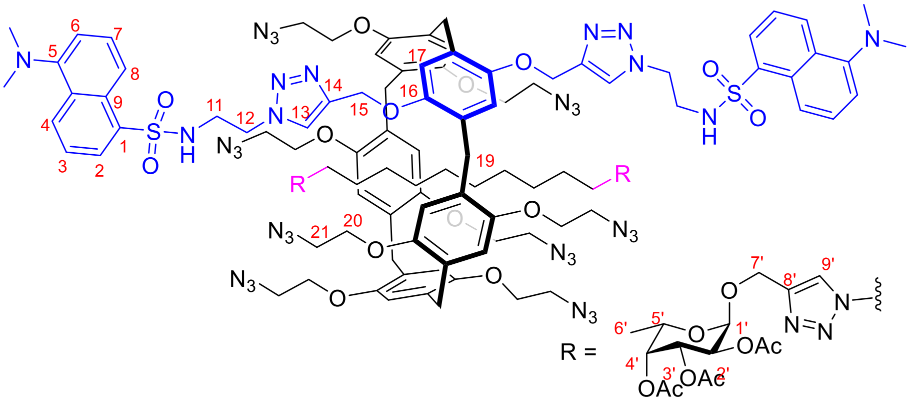
Rotaxane 15:



A solution of **12** (200 mg, 0.092 mmol, 4 equiv.) and **14** (12.7 mg, 0.023 mmol, 1 equiv.) in dry $CHCl_3$ (0.3 mL) was stirred at room temperature for 5h. Afterwards, **13** (9.1 mg, 0.0276 mmol, 1.2 equiv.) was added and the solution was cooled to - 20 °C using an ice-acetone bath, then $CuBr.SMe_2$ (9.5 mg, 0.046 mmol, 2 equiv.) was added. The mixture was stirred for 12 h while warming slowly to room temperature. Then, $CHCl_3$ was evaporated and the residue was re-dissolved in CH_2Cl_2 (4 mL) and washed with H_2O (2 x 2 mL) and NH_4Cl (2 x 2 mL). The aqueous phase was extracted with CH_2Cl_2 (2 x 4 mL) and the organic layer was dried over $MgSO_4$, filtered and concentrated under reduced pressure. The residue was purified by column chromatography on silica gel using DCM/MeOH (9.95/0.05 to 9.9/0.1 then 9.8/0.2) as eluent to furnish the desired product **15** as a yellow solid (30 mg, 0.011 mmol, 48%).

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.66 (s, 2H, 2 x H-2), 8.36 (s, 2H, 2 x H-8), 8.29–8.27 (m, 2H, 2 x H-4), 7.70–7.55 (m, 8H, 2 x H-3, 2 x H-7, 2 x H-13, 2 x H-9’), 7.30 (s, 2H, 2 x H-6), 7.09–7.00 (m, 8H, 8 x H-17), 6.94–6.93 (m, 2H, 2 x H-17), 6.83 (s, 1H, N*H*), 5.39–5.16 (m, 8H, 2 x H-1’, 2 x H-2’, 2 x H-3’, 2 x H-4’), 5.01–4.85 (m, 6H, 2 x H-15, H-7’), 4.70–4.64 (m, 2H, H-7’), 4.55–4.48 (m, 4H, 2 x H-12), 4.36–4.23 (m, 10H, 4 x H-20, 2 x H-5’), 4.19–4.10 (m, 6H, 3 x H-20), 4.03–3.98 (m, 2H, H-20), 3.82 (br, 8H, 4 x H-19), 3.76–3.59 (m, 22H, H-19, 8 x H-21, 2 x C-10’), 3.47 (s, 4H), 3.51–3.47 (m, 4H, 2 x H-11), 2.99–2.95 (m, 12H, 4 x NCH_3), 2.17 (s, 6H, 2 x $OCOCH_3$), 2.07 (s, 3H, $OCOCH_3$), 2.05 (s, 3H, $OCOCH_3$), 1.97–1.92 (m, 6H, 2 x $OCOCH_3$), 1.16–1.10 (m, 6H, 2 x H-6’), 0.75 (br, 4H, 2 x CH_{2axle}), 0.22 (br, 4H, 2 x CH_{2axle}), -0.14 – -0.2 (m, 8H, 4 x CH_{2axle}). ^{13}C NMR (100 MHz, $CDCl_3$) δ 2 x 170.8, 170.6, 170.4, 170.3 (Cq, C=O$_{acetyl}$), 151.4 (Cq, C-1), 150.0, 149.9, 149.8, 2 x 149.6 (C-16), 143.8, 143.5 ($Cq_{triazole}$, C-14, C-8’), 134.9 (Cq, C-5), 130.6 (CH_{Ar}, C-2), 129.7 (CH_{Ar}, C-4), 2 x 129.5, 129.3, 129.1 (Cq, C-9, C-10, C-18), 128.5 (CH_{Ar}, C-3), 124.5 ($CH_{triazole}$, C-13), 123.7 (CH_{Ar}, C-7), 123.0 ($CH_{triazole}$, C-9’), 119.5 (CH_{Ar}, C-8), 116.4, 116.1, 116.0, 115.8, 115.7, 115.2 (CH_{Ar}, C-6, C-17), 96.1, 96.0 (CH, C-1’), 71.4, 71.3 (CH, C-2’), 69.6, 69.4, 69.3, 69.0 (CH_2, C-20), 68.4, 68.2 (CH, C-4’), 68.0 (CH, C-3’), 2 x 64.9 (CH, C-5’), 62.4 (CH_2, C-15), 2 x 61.4 (CH_2, C-7’), 50.4 (CH_2, C-12, C-10’), 45.7 (NCH_3), 43.0 (CH_2, C-11), 32.0, 31.9, 31.2, 31.2, 31.0 (C-19, C-21), 30.3 (CH_{2axle}), 29.8 (CH_{2axle}), 29.3 (CH_{2axle}), 29.1, 26.13 (CH_{2axle}), 2 x 21.1, 20.9, 20.8 ($OCOCH_3$), 16.0 (CH_3, C-6’). HRMS (ESI^+-MS, m/z): calculated for $C_{125}H_{154}Br_8N_{16}O_{30}S_2$ $[M+2H]^+$ 1532.1934; found 1532.1940.

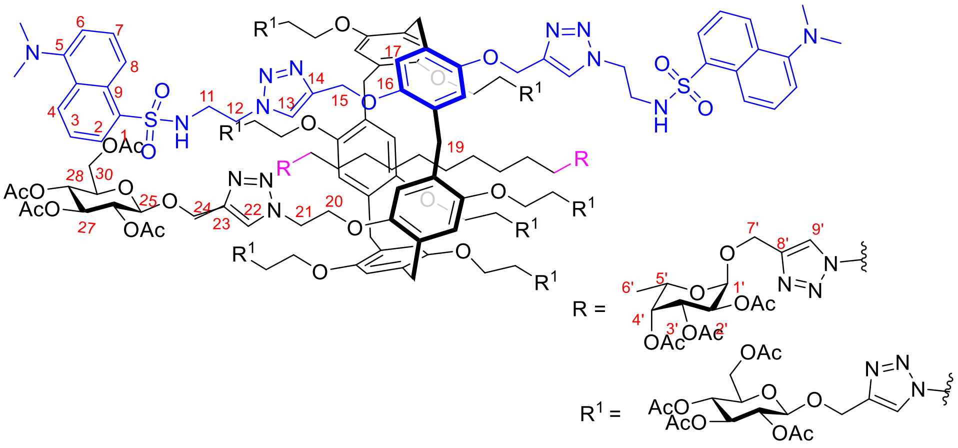
Rotaxane 16:



The title compound was prepared following the synthetic procedure of **7** using rotaxane **15** (25 mg, 0.0081 mmol, 1 equiv.), NaN_3 (9 mg, 0.13 mmol, 10 equiv.) and dry DMF (1 mL), and isolated as a yellow solid (22 mg, 00786 mmol, 97%).

^1H NMR (500 MHz, $CDCl_3$) δ 8.66 (s, 2H, 2 x H-2), 8.33 (s, 2H, 2 x H-8), 8.21 (s, 2H, 2 x H-4), 7.71–7.63 (m, 4H, 2 x H-13, 2 x H-9’), 7.55–7.49 (m, 4H, 2 x H-3, 2 x H-7), 7.24 (br, 2H, 2 x H-6), 7.01 (s, 2H, 2 x H-17), 6.94 (s, 4H, 4 x H-17), 6.88 (s, 3H, 3 x H-17), 6.85 (s, 1H, H-17), 5.37–5.31 (m, 2H, 2 x H-3’), 5.27–5.26 (m, 1H, H-2’), 5.23–5.12 (m, 5H, 2 x H-1’, H-2’, 2 x H-4’), 5.07 (d, *J* = 10.8 Hz, 1H, H-15), 4.99 (d, *J* = 10.8 Hz, 1H, H-15), 4.92–4.81 (m, 4H, H-15, H-7’), 4.64 (dd, *J* = 22.6, 11.8 Hz, 2H, H-7’), 4.48 (br, 4H, 2 x H-12), 4.28–4.27 (m, 2H, 2 x H-5’), 4.18–4.14 (m, 2H, H-20), 3.99–3.95 (m, 12H, 6 x H-20), 3.78–3.49 (m, 32H, 5 x H-19, H-20, 8 x H-21, 2 x H-10’), 3.43 (br, 4H, 2 x H-11), 2.96–2.94 (m, 4 x NCH$_3$), 2.15 (s, 6H, 2 x OCOCH$_3$), 2.04 (s, 3H, OCOCH$_3$), 2.02 (s, 3H, OCOCH$_3$), 1.95 (s, 2 x OCOCH$_3$), 1.11 (br, 6H, 2 x H-6’), 0.72–0.64 (m, 4H, 2 x CH$_{2\text{axle}}$), 0.31–0.24 (m, 4H, 2 x CH$_{2\text{axle}}$), -0.08 – -0.22 (m, 8H, 4 x CH$_{2\text{axle}}$). ^{13}C NMR (125 MHz, CDCl$_3$) δ 2 x 170.7, 170.6, 170.4, 2 x 170.2 (Cq, C=O$_{\text{acetyl}}$), 149.7, 149.6, 149.4 (Cq, C-1, C-16), 143.6, 143.5, 2 x 143.3 (Cq, Cq$_{\text{triazole}}$, C-14, C-8’), 134.8 (Cq, C-5), 130.1 (CH$_{\text{Ar}}$, C-2), 129.4 (CH$_{\text{Ar}}$, C-4), 129.0, 128.85, 128.73, 128.66 (Cq, C-18, C-9, C-10), 128.2 (CH$_{\text{Ar}}$, C-3), 124.5 (CH$_{\text{triazole}}$, C-13), 123.7 (CH$_{\text{Ar}}$, C-7), 122.9 (CH$_{\text{triazole}}$, C-9’), 116.03 (CH$_{\text{Ar}}$, C-6, C-8), 114.98, 114.83 (CH$_{\text{Ar}}$, C-17), 95.83, 95.70 (CH, C-1’), 2 x 71.2 (CH, C-2’), 68.2, 68.1 (CH, C-4’), 2 x 67.9 (CH, C-3’), 67.3, 67.2, 67.0 (CH$_2$, C-20), 2 x 64.7 (CH, C-5’), 2 x 62.0 (CH$_2$, C-15), 2 x 61.0 (CH$_2$, C-7’), 51.4, 51.3, 51.2 (CH$_2$, C-21), 50.1 (CH$_2$, C-12, C-10’), 45.7 (NCH$_3$), 42.8 (CH$_2$, C-11), 30.2 (CH$_{2\text{axle}}$), 29.5, 29.4, 2 x 29.2, 28.9, 28.8 (CH$_2$, C-19, CH$_{2\text{axle}}$), 26.0 (CH$_{2\text{axle}}$), 20.8, 20.7 (OCOCH$_3$), 15.8 (CH$_3$, C-6’). HRMS (ESI$^+$-MS, m/z): calculated for $C_{125}H_{154}N_{40}O_{30}S_2$ [M+2H]$^{2+}$ 1379.5592; found 1379.5599.

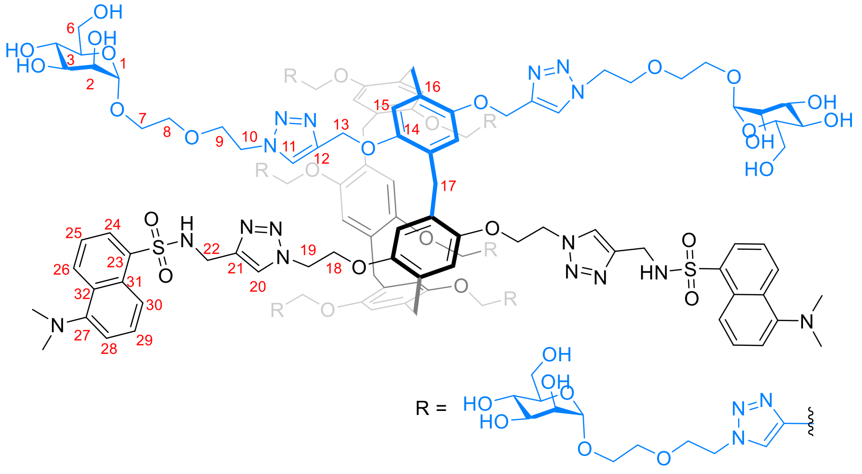
Rotaxane 17:



The title compound was prepared following general procedure B using rotaxane **16** (30 mg, 0.011 mmol, 1 equiv.), **7a** (42 mg, 0.108 mmol, 10 equiv.), CH$_2$Cl$_2$ (0.6 mL), CuSO$_4$ (0.2 equiv.) and NaAsc (0.66 equiv.) [n = 6], purified using EtOAc/Cy (2:1) as eluent to remove excess **7a**, then DCM/MeOH (30:1) as eluent and isolated **17** as orange solid (50 mg, 0.0085 mmol, 79%).

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.53 (s, 2H, 2 x H-2), 8.24–8.19 (m, 4H, 2 x H-4, 2 x H-8), 7.85–7.64 (m, 12H, 2 x H-13, 8 x H-22, 2 x H-9’), 7.54–7.44 (m, 4H, 2 x H-3, 2 x H-7), 7.17 (s, 2H, 2 x H-6), 6.99–6.58 (m, 12H, H-17, 2 x N*H*), 5.23–5.22 (m, 2H, 2 x H-3’), 5.15–4.59 (m, 78H, 2 x H-15, 8 x H-21, 8 x H-24, 8 x H-25, 8 x H-26, 8 x H-27, 8 x H-28, 2 x H-1’, 2 x H-2’, 2 x H-4’, 2 x H-7’), 4.49 (br, 4H, 2 x H-12), 4.38–4.07 (m, 34H, 8 x H-30, 2 x H-5’, 8 x H-20), 3.64–3.51 (m, 10H, H-19, 8 x H-29), 3.38 (br, 8H, 2 x H-11, 2 x H-10’), 3.22–3.13 (m, 8H, 4 x H-19), 2.93–2.85 (m, 12H, 4 x NCH_3), 2.08 (s, 6H, 2 x $OCOCH_3$), 1.99–1.79 (m, 108H, 2 x 36 $OCOCH_3$), 1.04–1.00 (m, 6H, 2 x H-6’), 0.50 (s, 4H, 2 x $CH_{2\text{axle}}$), 0.19 (s, 4H, 2 x $CH_{2\text{axle}}$), 0.01 – -0.49 (m, 8H, 4 x $CH_{2\text{axle}}$). ^{13}C NMR (100 MHz, $CDCl_3$) δ 170.6, 170.1, 169.4, 169.3 (Cq, C=O_{acetyl}), 149.6, 149.4, 149.3, 149.2, 149.0 (Cq, C-1, C-16),144.3, 144.2 (Cq, Cq_{triazole}, C-23), 143.5, 143.3 (Cq, Cq_{triazole}, C-14, C-8’), 134.5 (Cq, C-5), 130.5 (CH_{Ar}, C-2), 129.5 (CH_{Ar}, C-4), 128.8, 128.7, 128.57 (Cq, C-18, C-9, C-10), 128.4 (CH_{Ar}, C-3), 127.9 (Cq, C-18, C-9, C-10), 124.9 (C-13), 123.5, 123.3 (C-7, C-9’, C-22), 115.7, 115.4, 115.0 (CH_{Ar}, C-6, C-8, C-17), 99.8, 99.6 (C-25), 95.9, 95.7 (C-1’), 72.7 (C-27), 71.7 (C-29), 71.1 (C-26, C-2’), 68.2 (C-28, C-4’), 68.1 (C-4’), 67.8, 67.6 (C-3’), 67.0 (C-20), 64.7, 64.7 (C-5’), 62.7 (C-24), 62.2, 62.1 (C-15), 61.7 (C-30), 60.9, 60.8 (C-7’), 50.2, 49.9 (CH_2, C-12, C-10’, C-21), 45.5 (NCH_3), 42.7 (CH_2, C-11), 30.0 ($CH_{2\text{axle}}$), 29.3, 28.8 (CH_2, C-19, $CH_{2\text{axle}}$), 25.9, 25.8 ($CH_{2\text{axle}}$), 20.7, 20.6 ($OCOCH_3$), 15.8 (CH_3, C-6’). HRMS (ESI$^+$-MS, m/z): calculated for $C_{261}H_{331}N_{40}O_{110}S_2$ $[M+3H]^{3+}$ 1949.6987; found 1949.7002.

S12. Synthesis of Compound S6

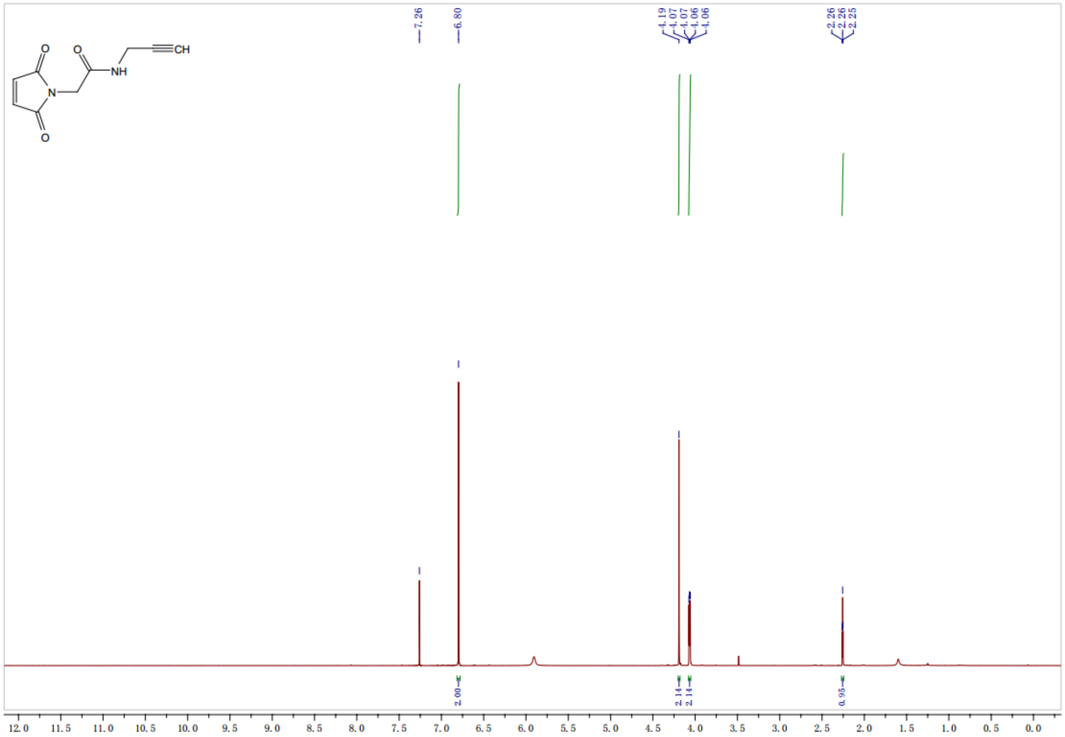


To a solution of **8d** (55 mg, 0.01 mmol) in dry MeOH (1.5 mL) was added NaOMe (5.4 mg, 0.1mmol) at 0^{o}C. Then, the solution was stirred for 1.5 h at room temperature before evaporating to get the salt solid. The salt solid was dissolved in detailed water (3 ml) and added Dowex®50WX2 (H$^+$ resin form) to neutralize the base. Afterwards, The resin was removed by filtration, the filtrate was purified by Sephadex G15 column and the yellow fraction was concentrated under reduced pressure to generate compound **S6** as an orange solid (35 mg, 0.0086 mmol, 86%).

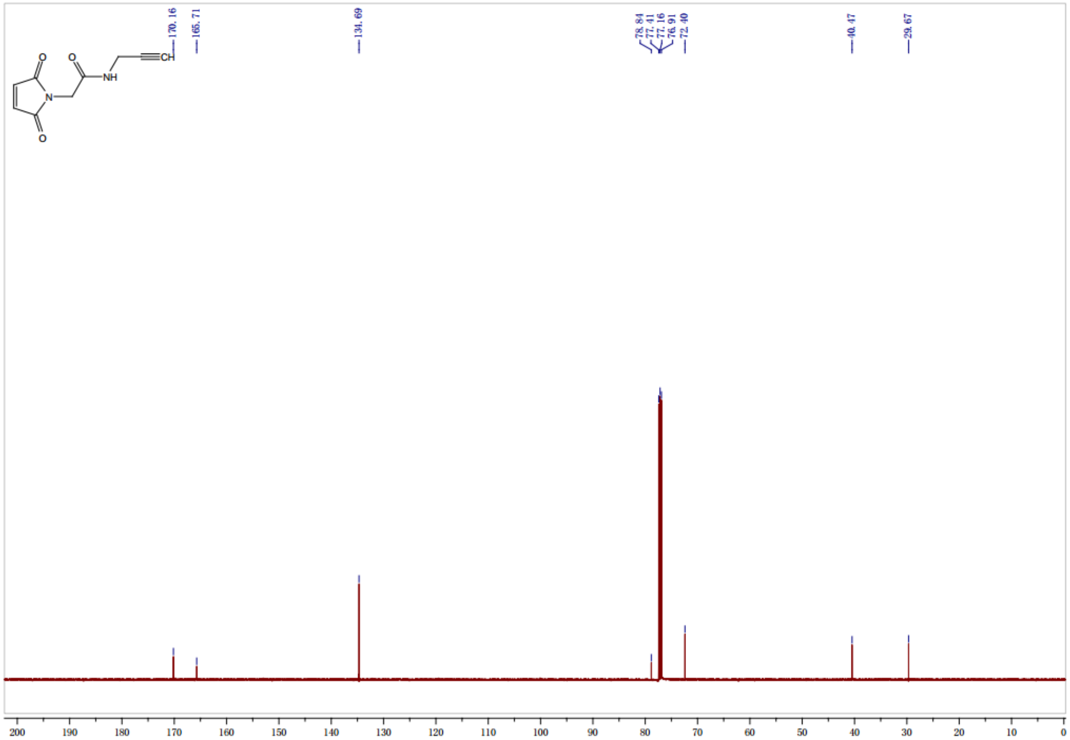
^{1}H NMR (500 MHz, D$_2$O) δ 7.95 (br, 16H, 8 x H-11, 2 x H-20, 2 x H-24, 2 x H-26, 2 x H-30), 7.20–6.71 (m, 16H, 2 x H-25, 2 x H-29, 2 x H-28, 10 x H-15), 4.70 (br, 8H, 4 x H-13), 4.46 (br, 20H, 8 x H-10, 2 x H-19), 3.83–3.49 (m, 118H, 8 x H-1–H-9, 2 x H-22), 2.25 (br, 12H, 4 x NCH$_3$). ^{13}C NMR (125 MHz, D$_2$O) δ 151.0, 149.4 (C-14, C-23), 143.6 (C-21, C-22), 134.60 (C-27), 128.6 (C-16, C-24, C-25, C-26, C-31, C-32), 124.9 (C-11, C-20, C-29), 118.0, 115.8 (C-15, C-28, C-30), 100.0, 99.7 (C-1), 72.8, 72.6, 70.7, 70.5, 70.1, 69.9 (C-2, C-3, C-5), 69.3, 68.8 (C-8, C-9, C-18), 66.5 (C-4), 66.1(C-7), 62.5, 62.2, 62.05, 61.7 (C-13), 60.7 (C-6), 49.8 (C-10, C-19), 44.4 (NCH$_3$), 37.2 (C-22), 29.4 (C-17). HRMS (ESI$^+$-MS, m/z): calculated for $C_{173}H_{236}N_{34}Na_3O_{70}S_2$ [M+3Na]$^{3+}$ 1347.5024; found 1347.4968.

S13. ^{1}H- and ^{13}C NMR Spectra of new compounds

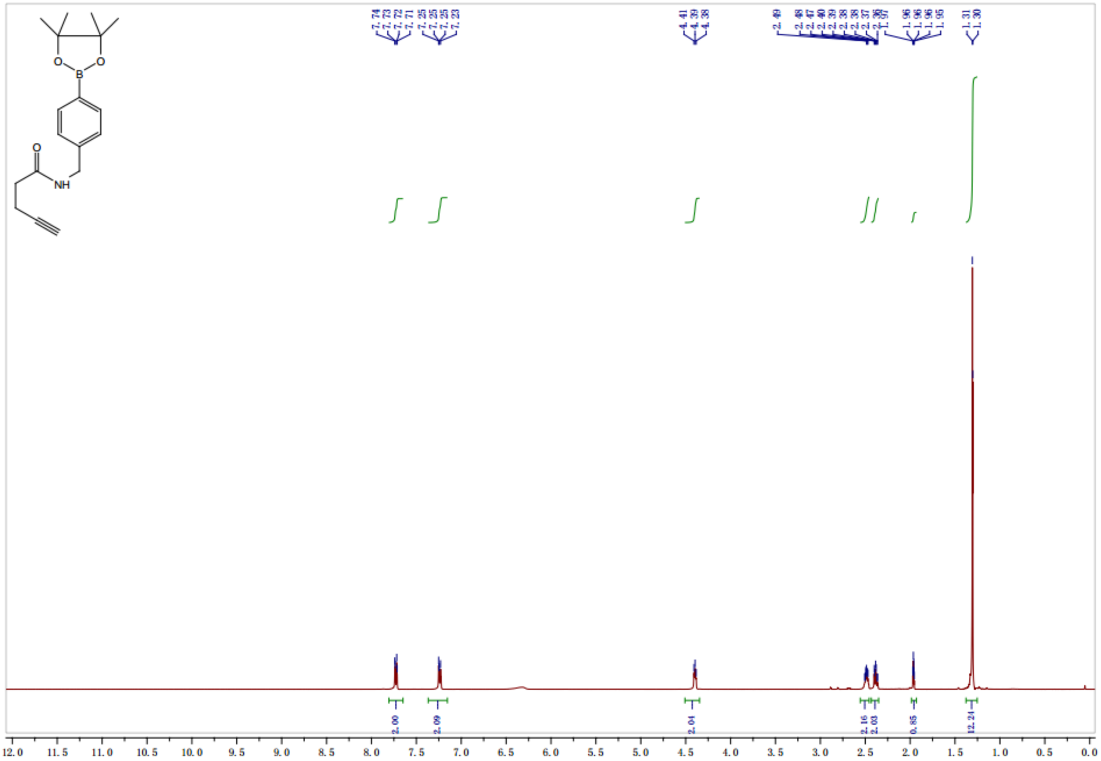
^{1}H NMR spectrum of **7g**



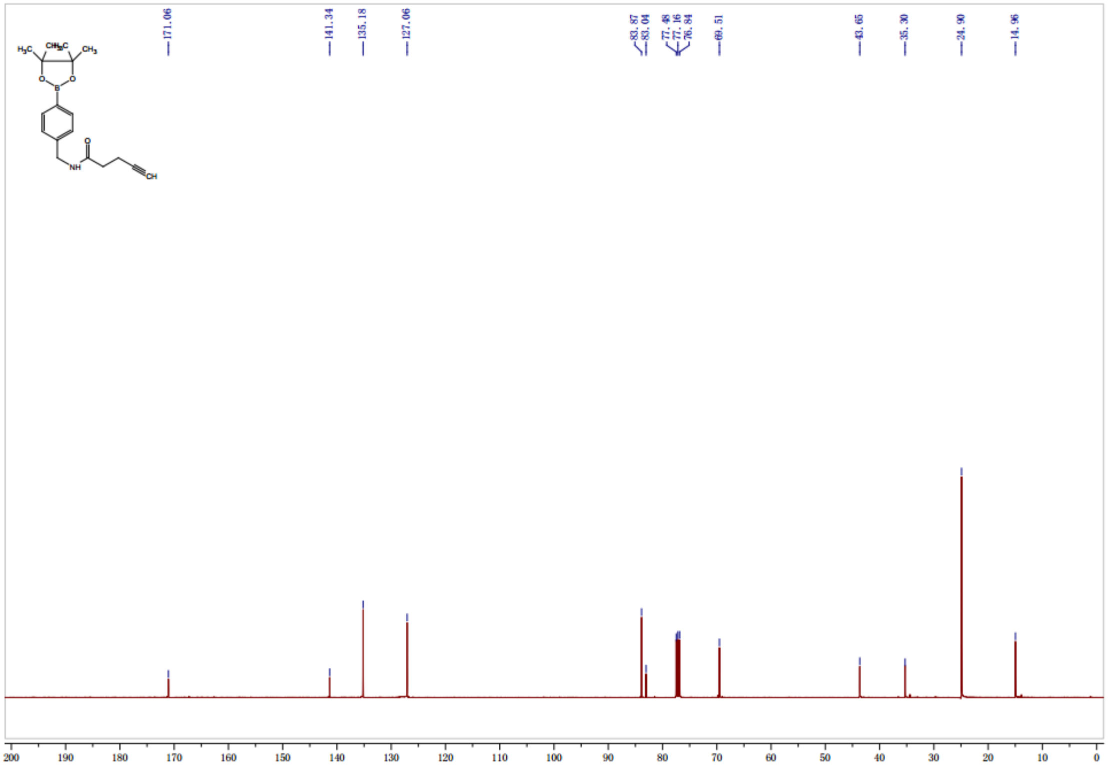
^{13}C NMR spectrum of **7g**



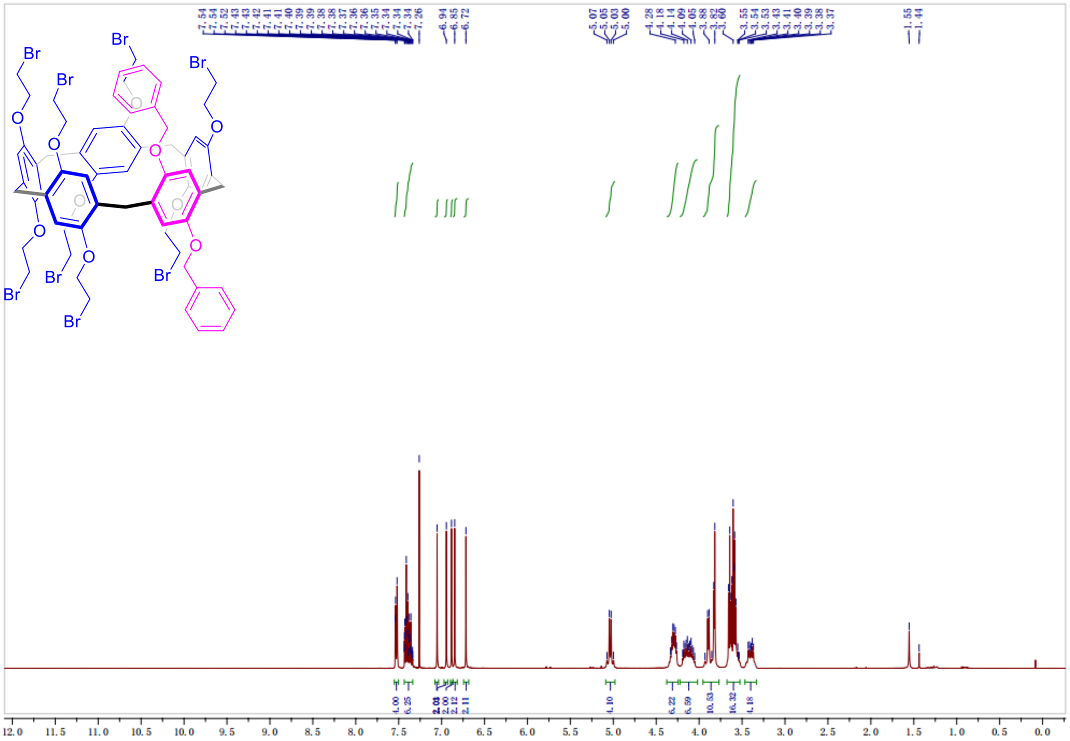
^{1}H NMR spectrum of **7h**



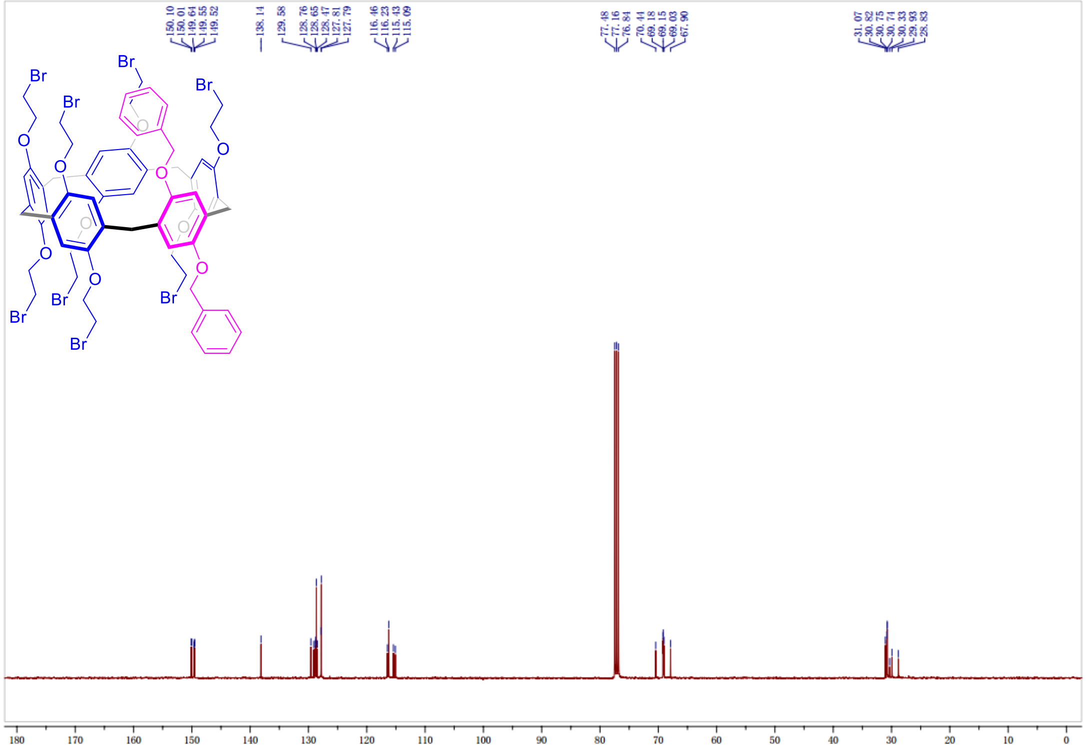
^{13}C NMR spectrum of **7h**



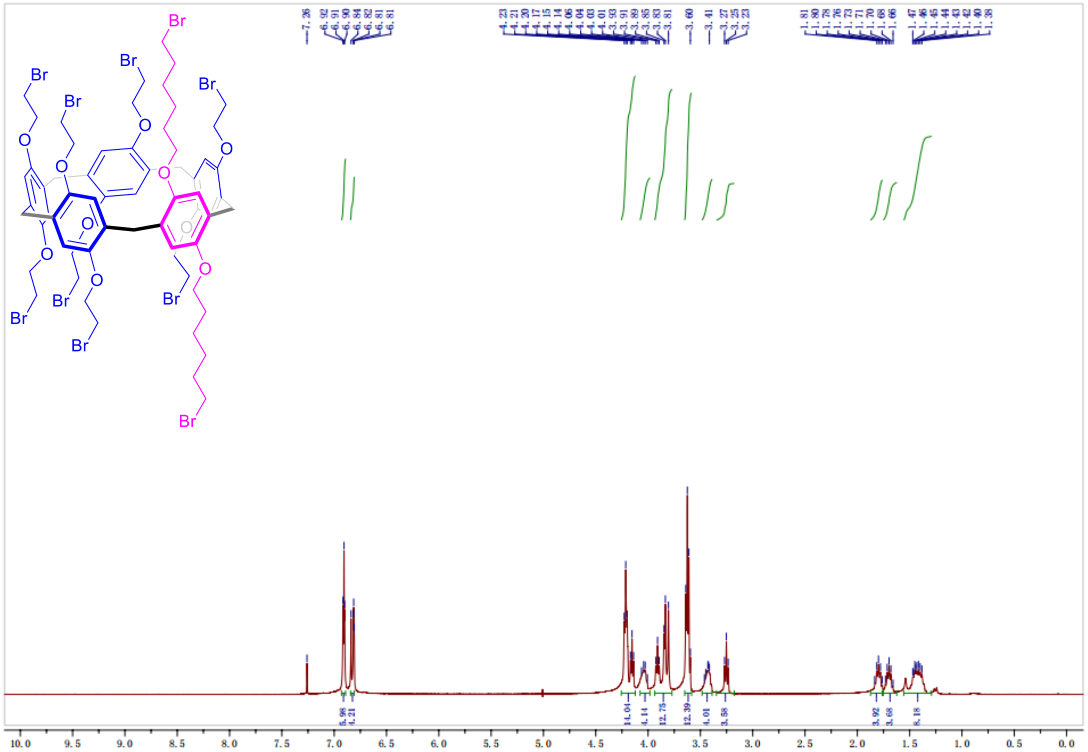
^{1}H NMR spectrum of copillar[5]arene **S1**



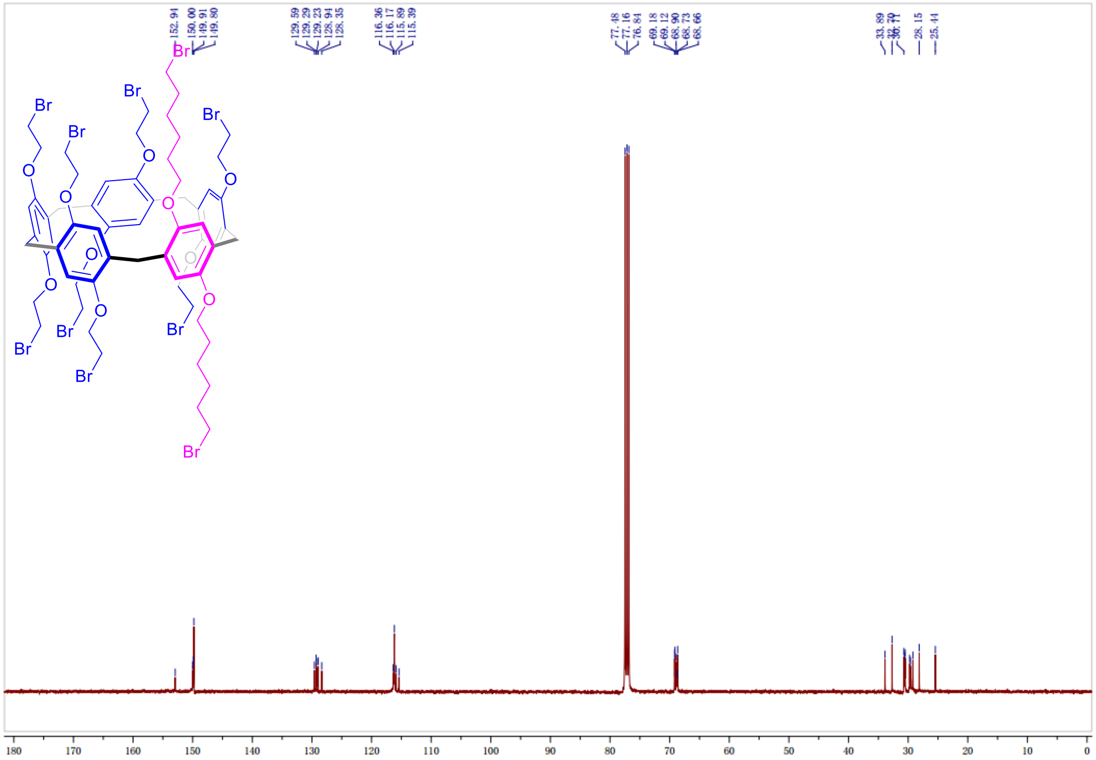
^{13}C NMR spectrum of copillar[5]arene S**1**



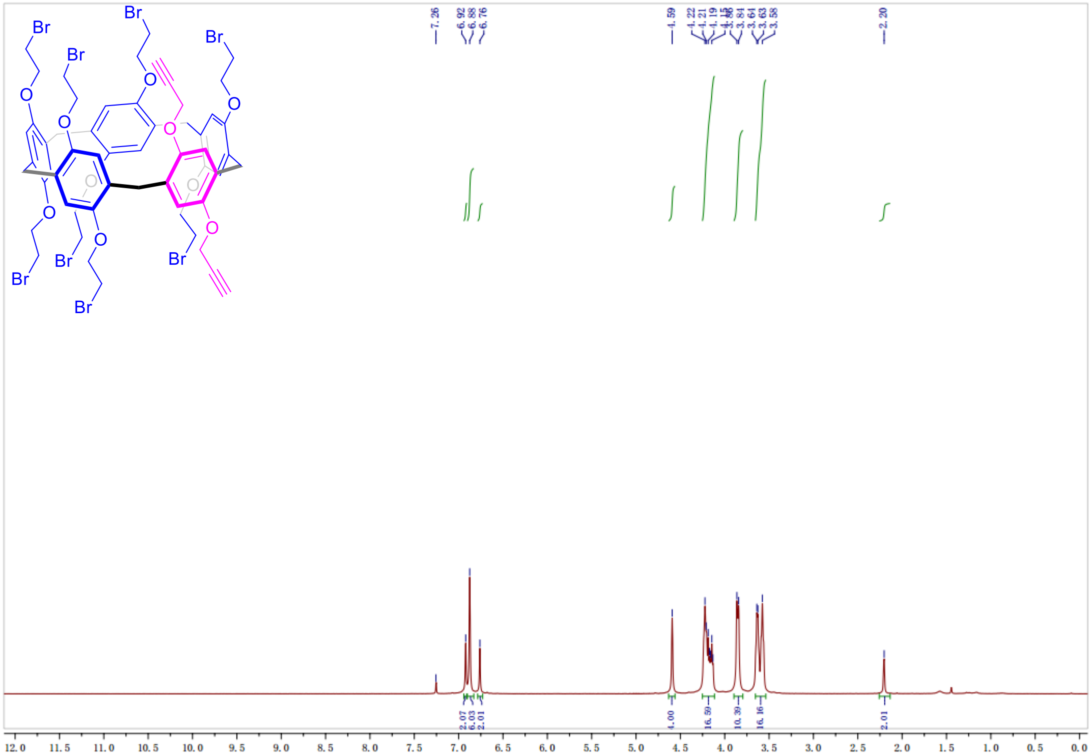
^{1}H NMR spectrum of copillar[5]arene **S2**



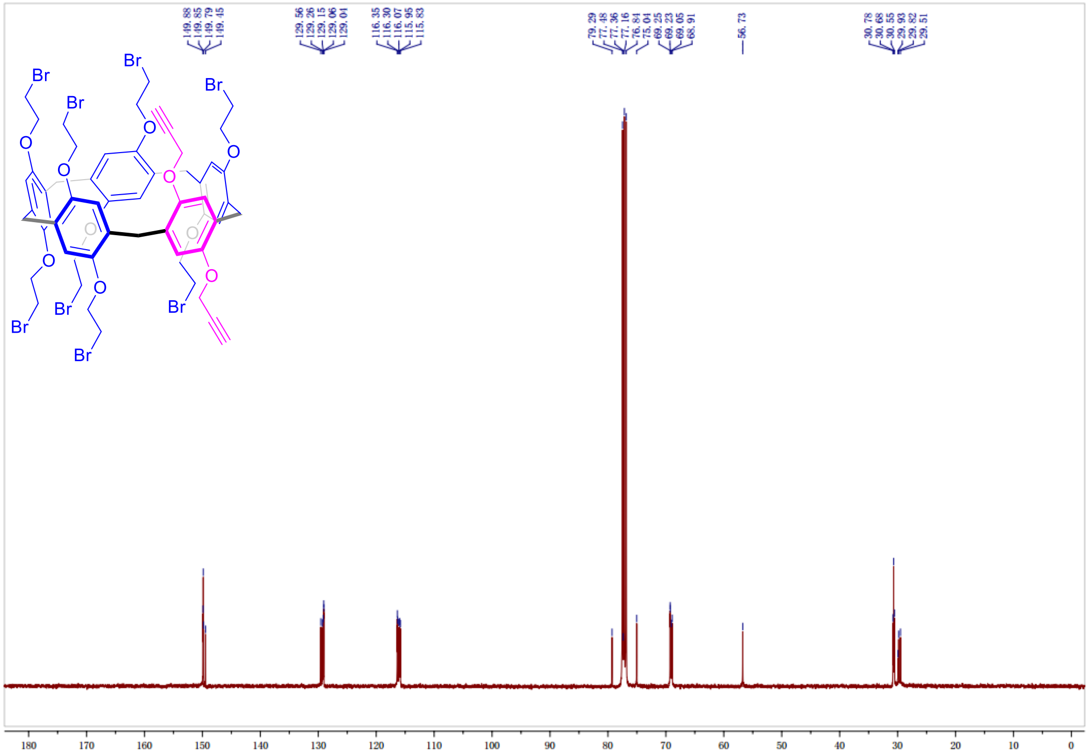
^{13}C NMR spectrum of copillar[5]arene S**2**



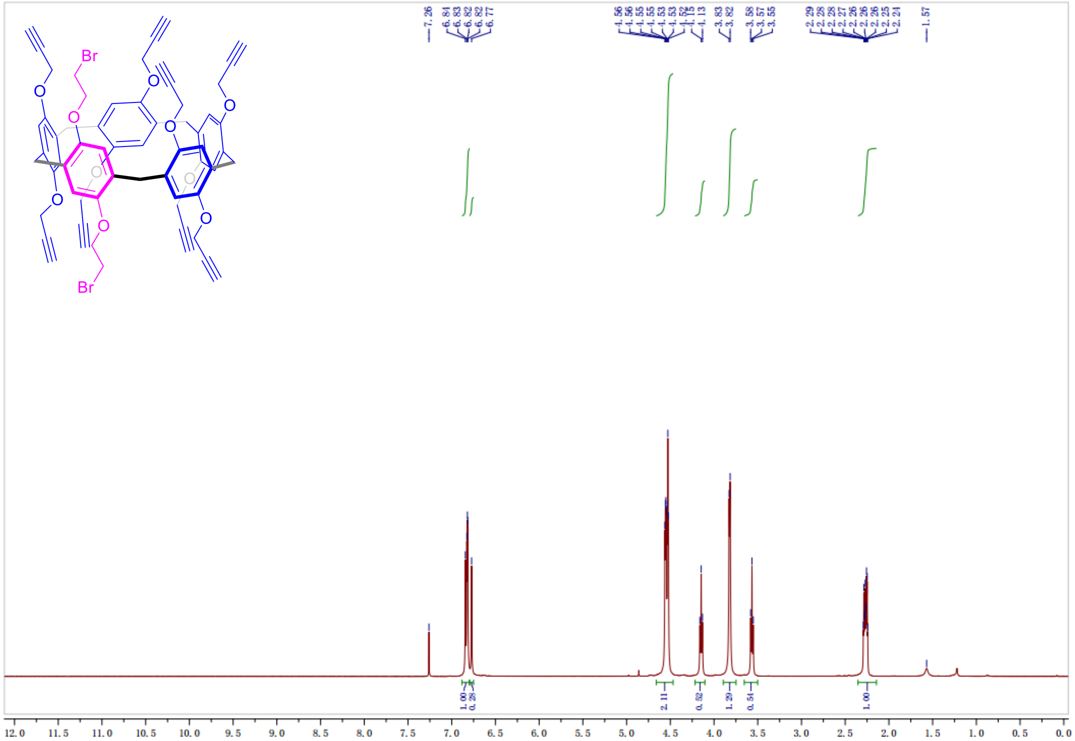
^{1}H NMR spectrum of copillar[5]arene **3**



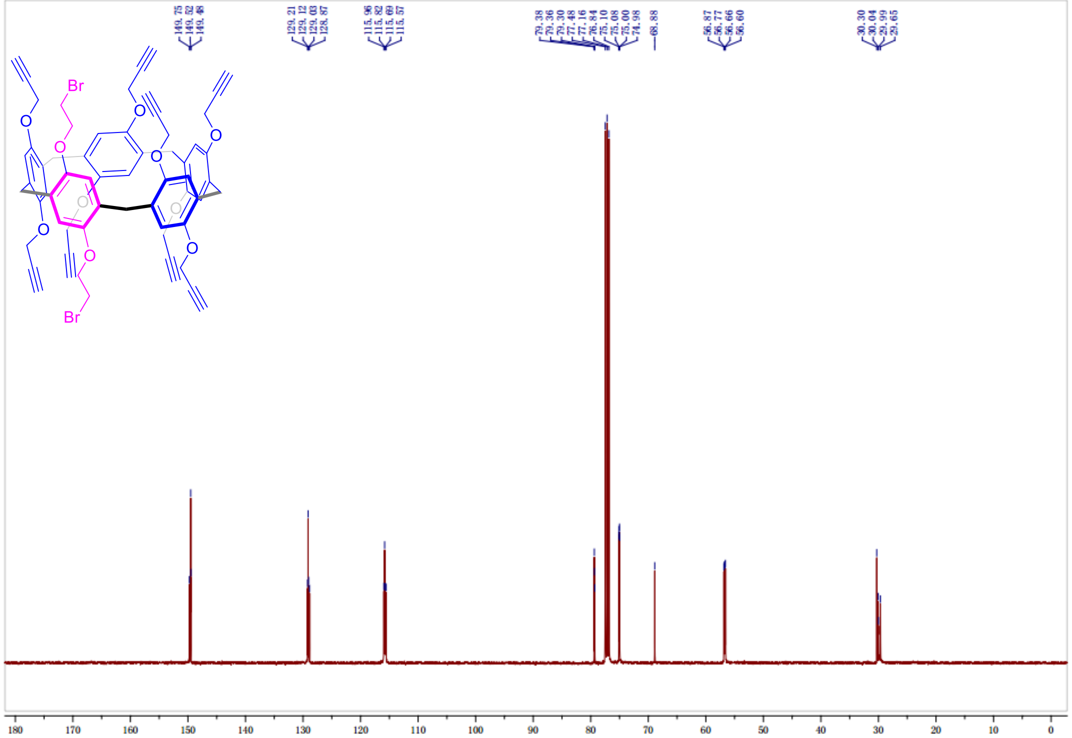
^{13}C NMR spectrum of copillar[5]arene **3**



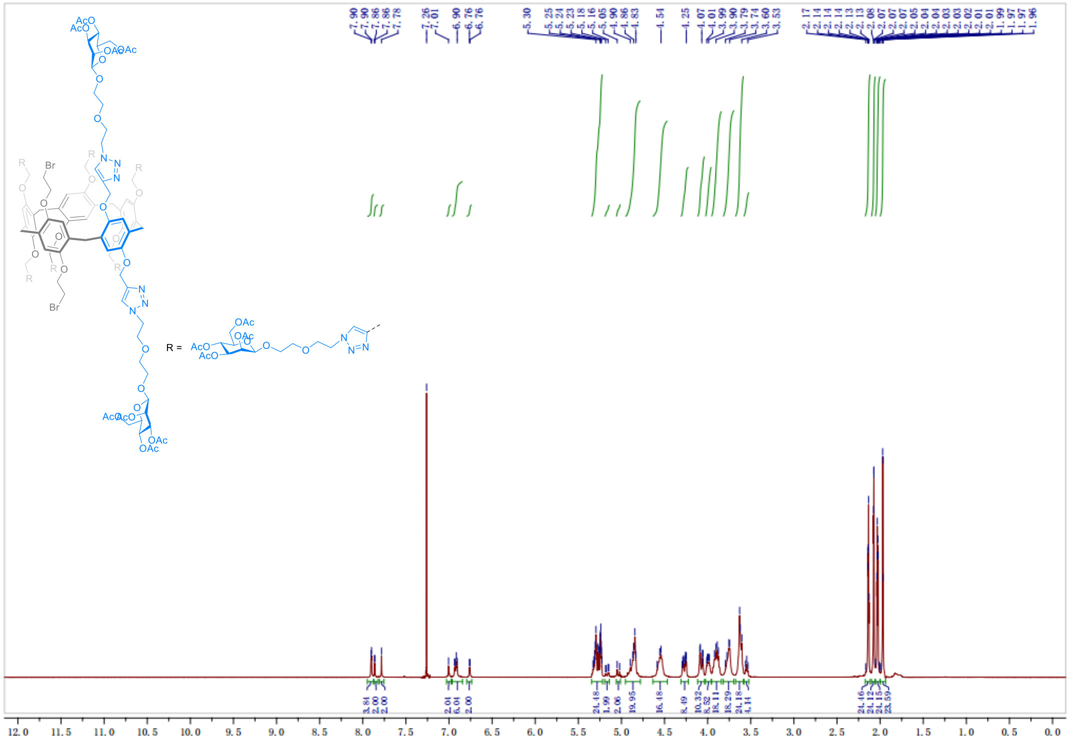
^{1}H NMR spectrum of copillar[5]arene **4**



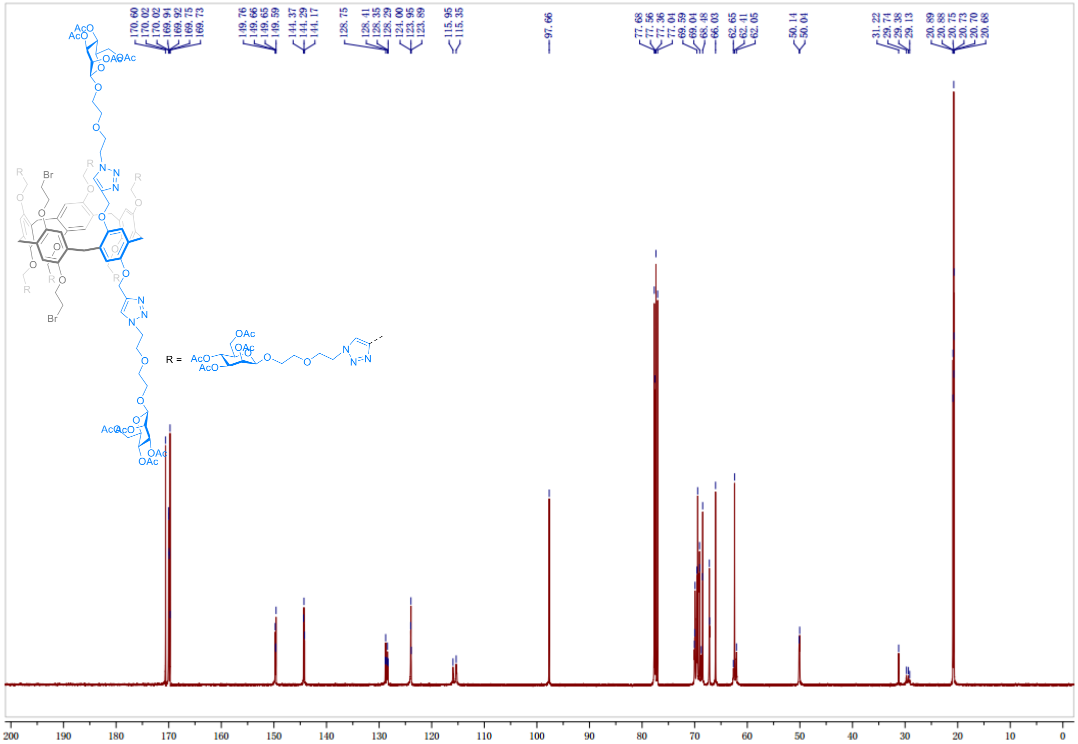
^{13}C NMR spectrum of copillar[5]arene **4**



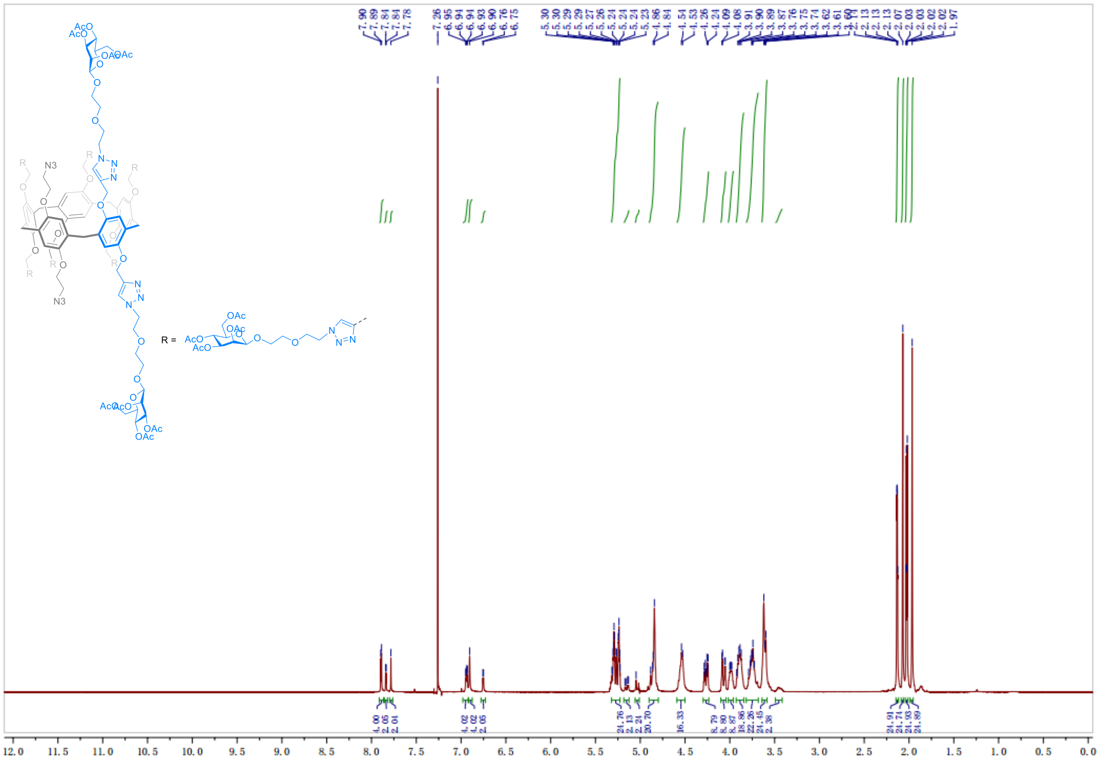
^{1}H NMR spectrum of compound **6a**



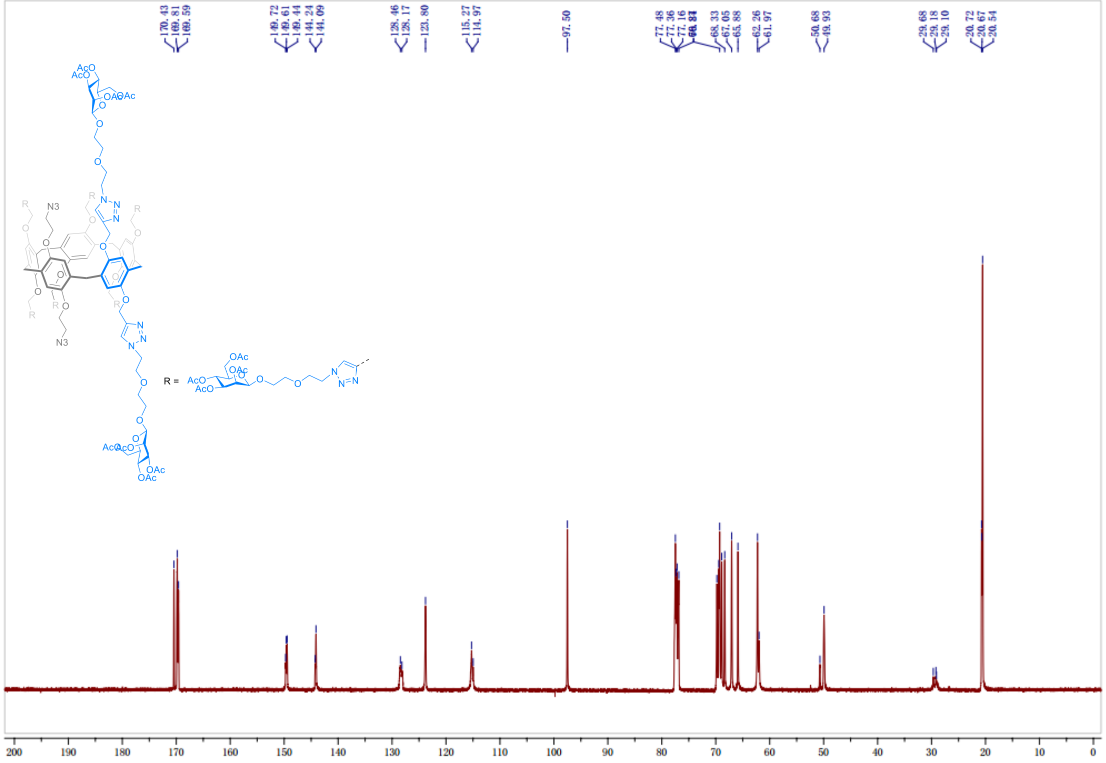
^{13}C NMR spectrum of compound **6a**



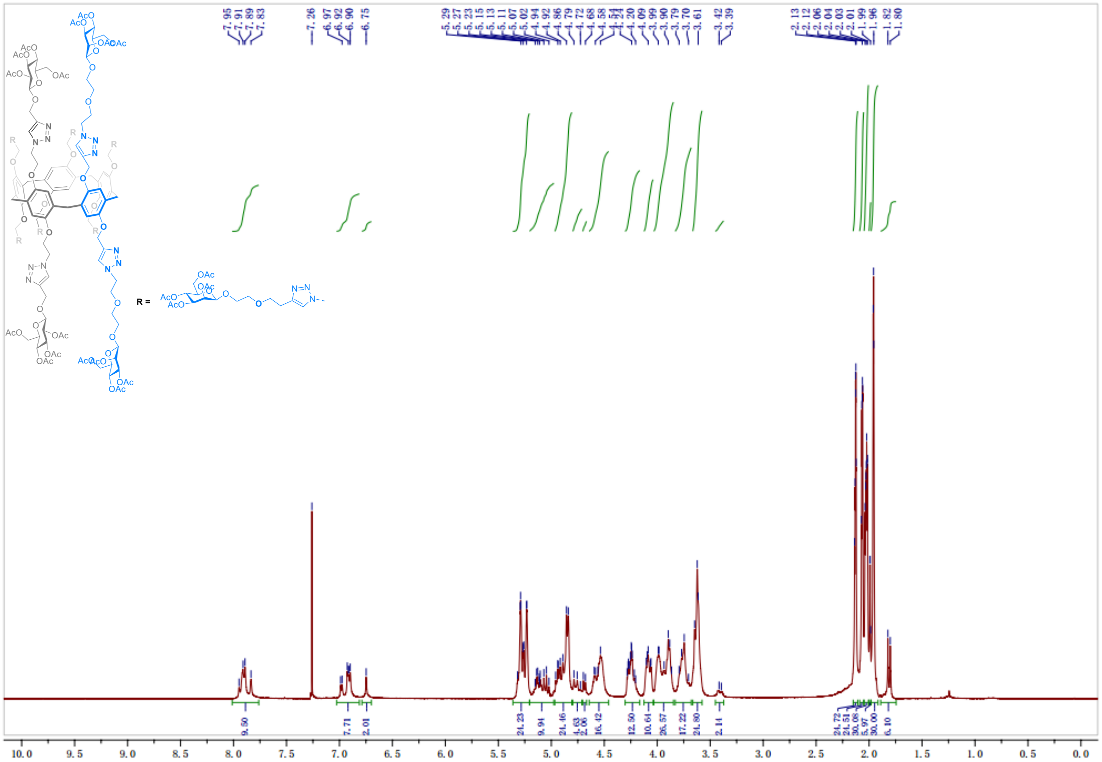
^{1}H NMR spectrum of compound **6**



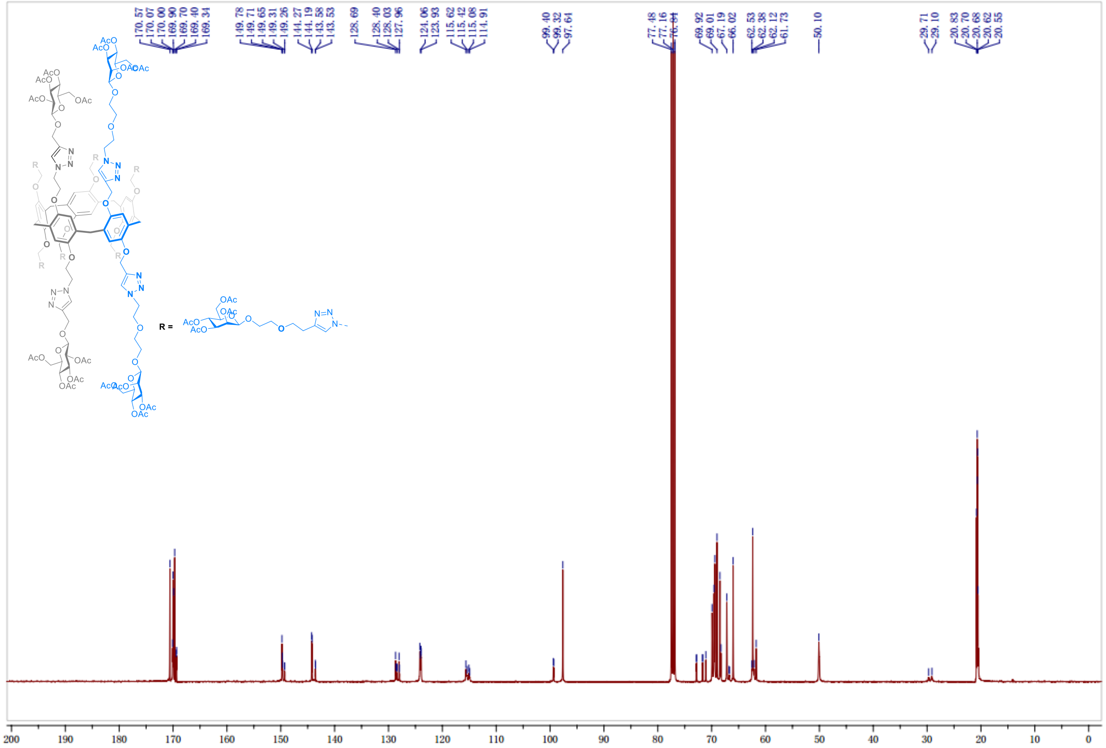
^{13}C NMR spectrum of compound **6**



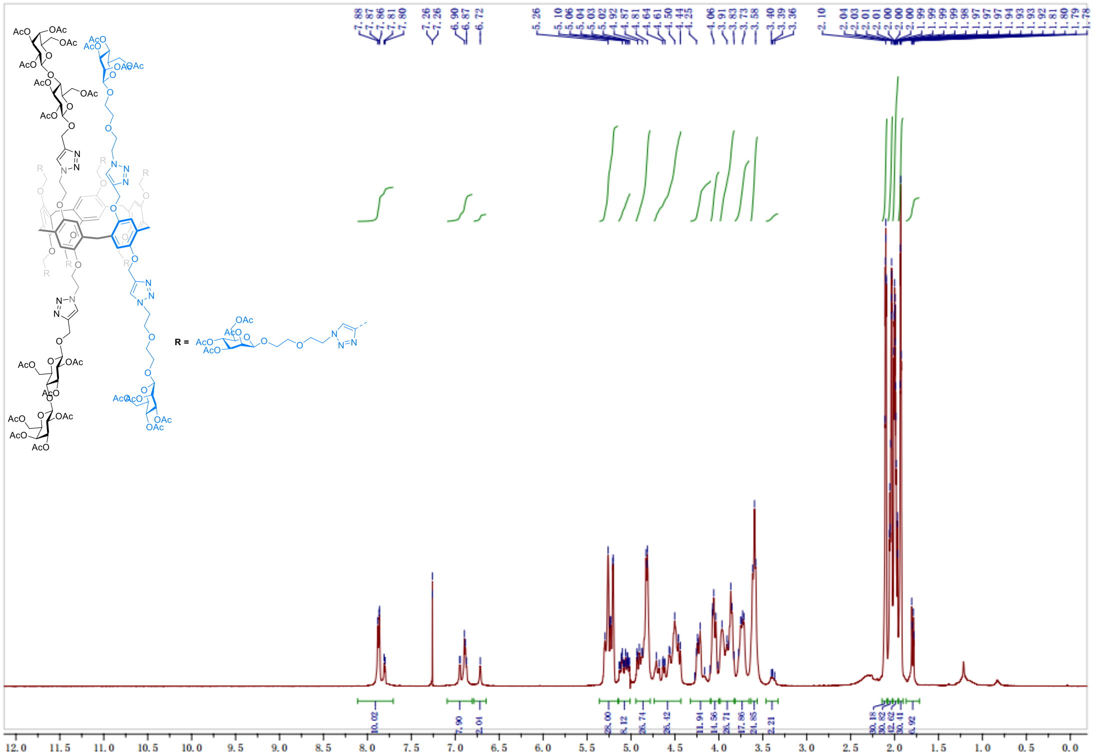
^{1}H NMR spectrum of compound **8a**



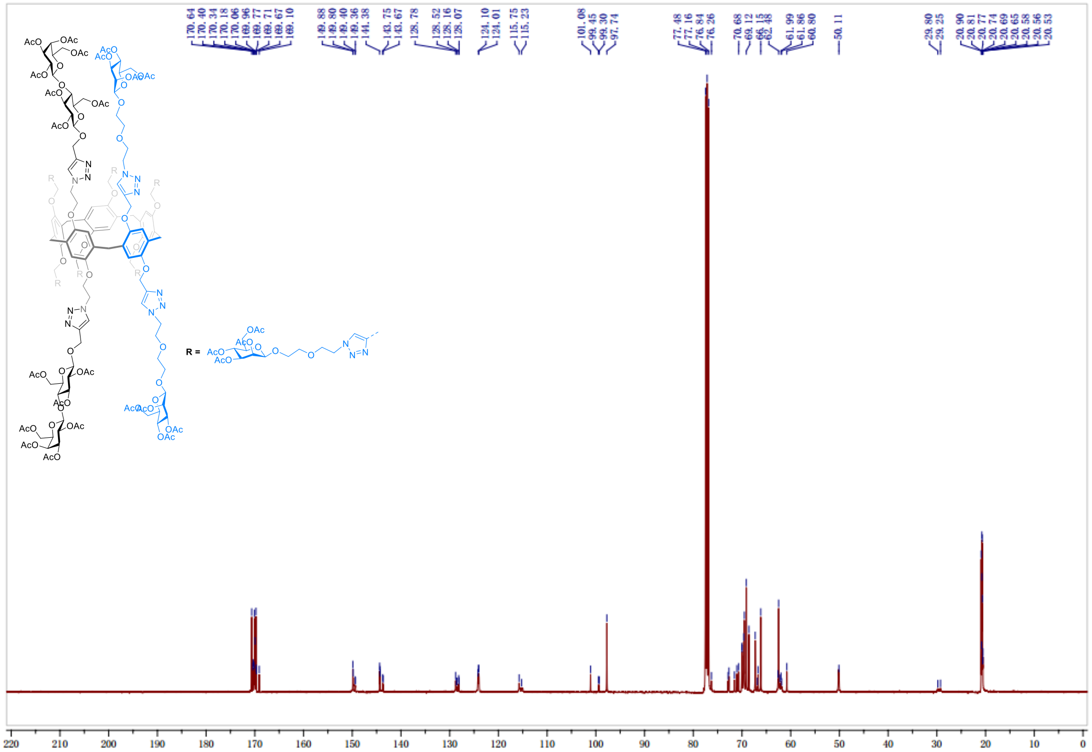
^{13}C NMR spectrum of compound **8a**



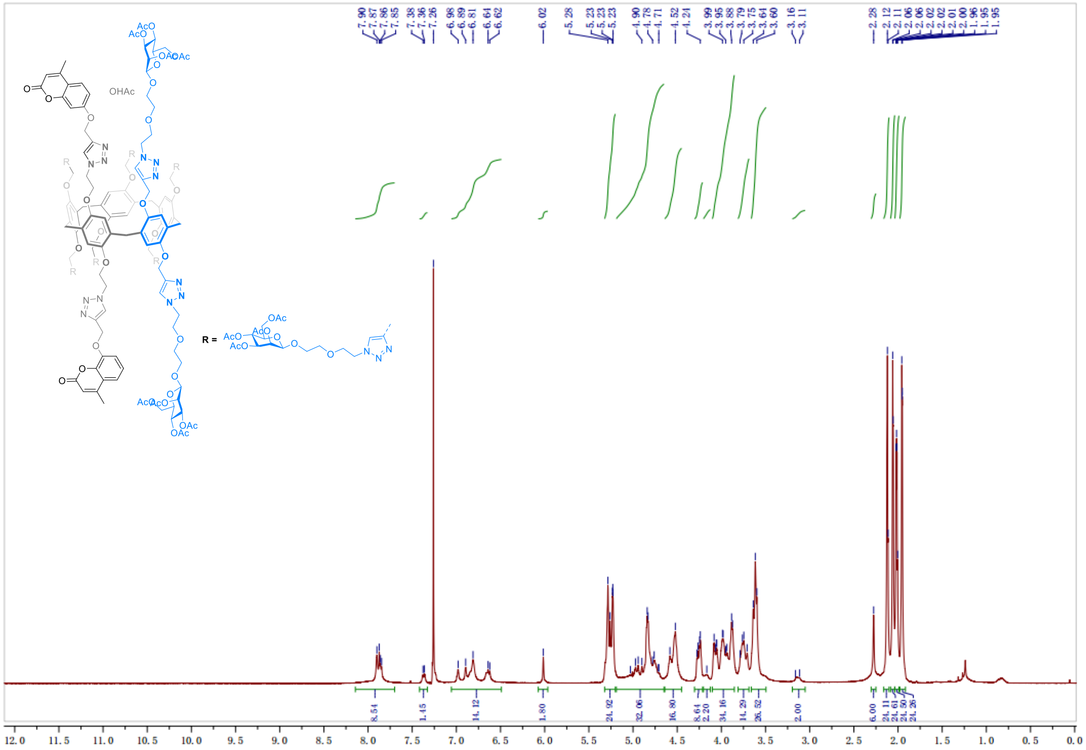
^{1}H NMR spectrum of compound **8b**



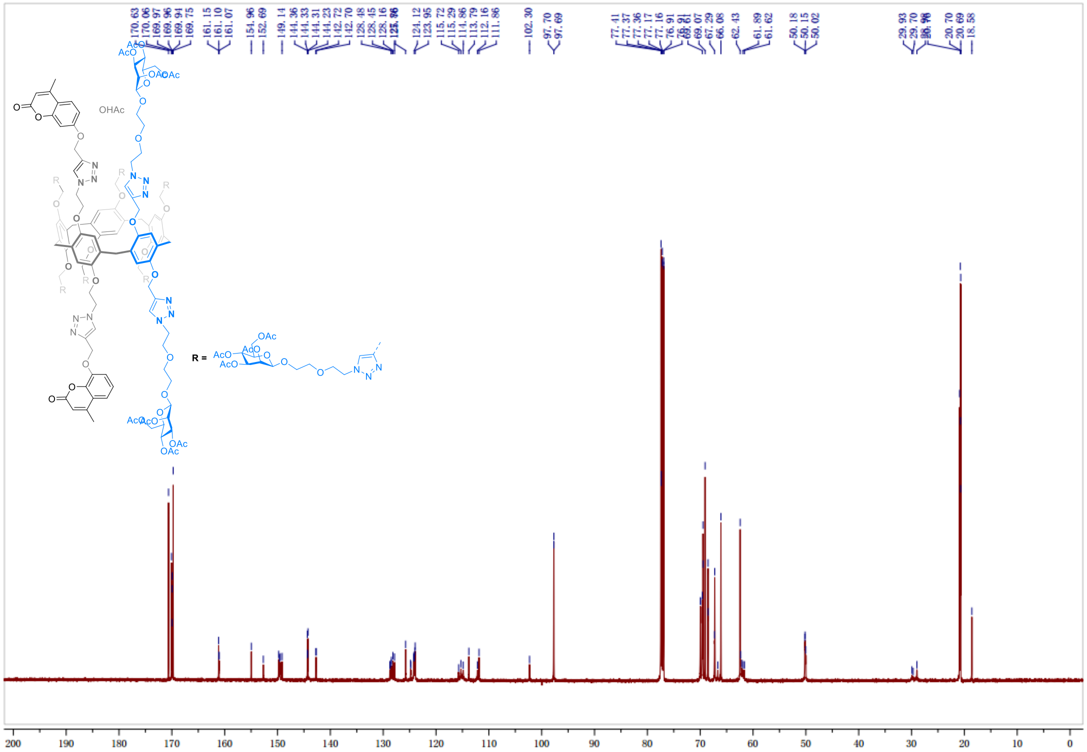
^{13}C NMR spectrum of compound **8b**



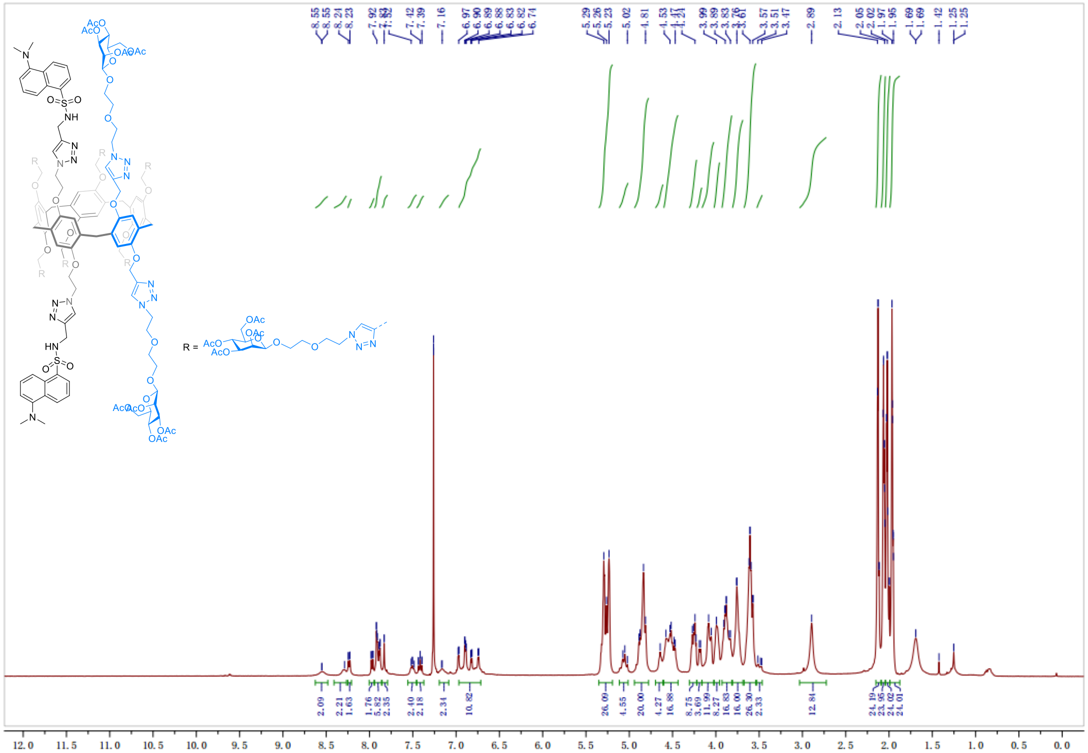
^{1}H NMR spectrum of compound **8c**



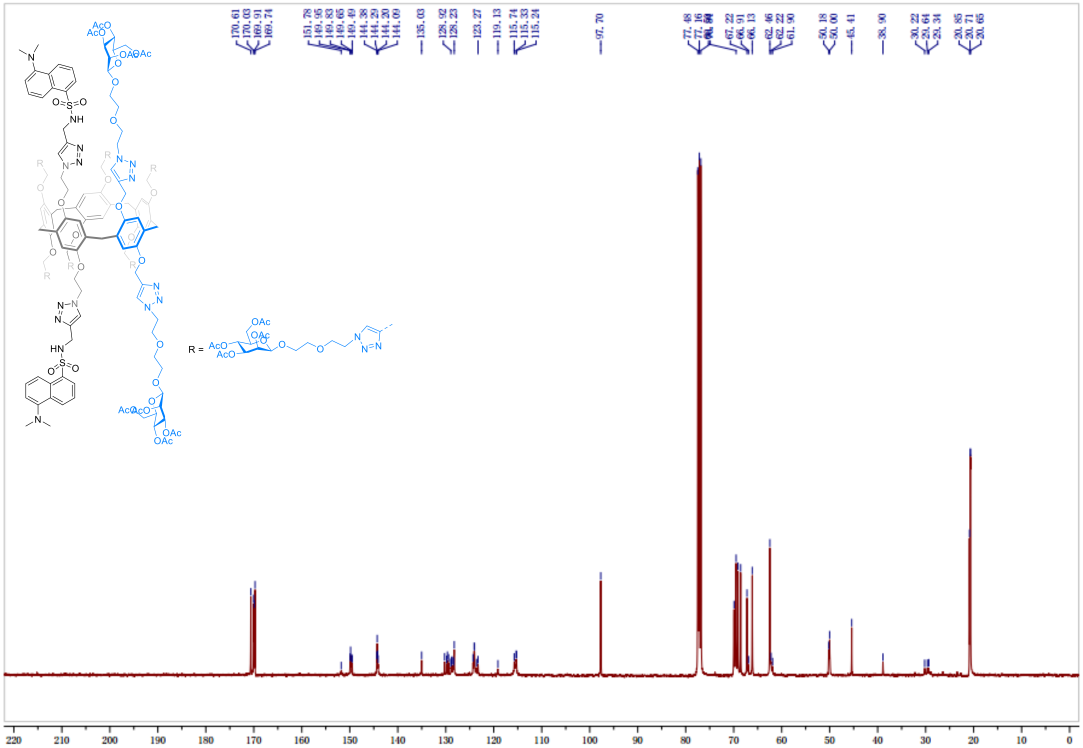
^{13}C NMR spectrum of compound **8c**



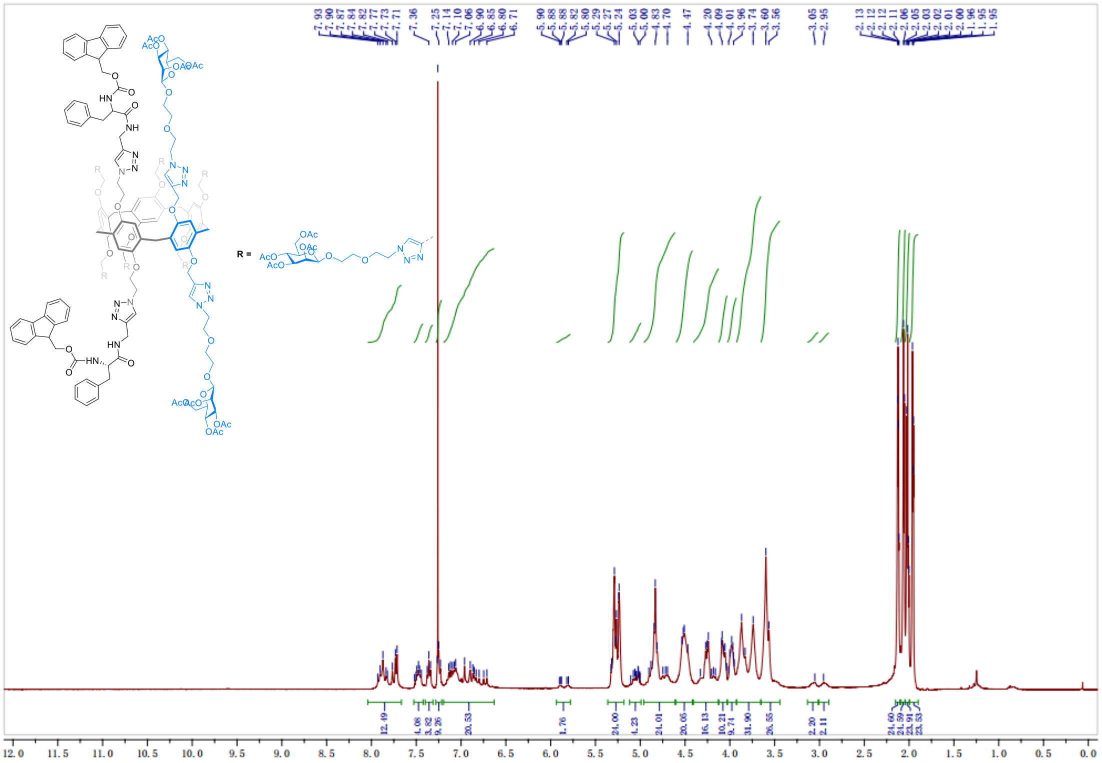
^{1}H NMR spectrum of compound **8d**



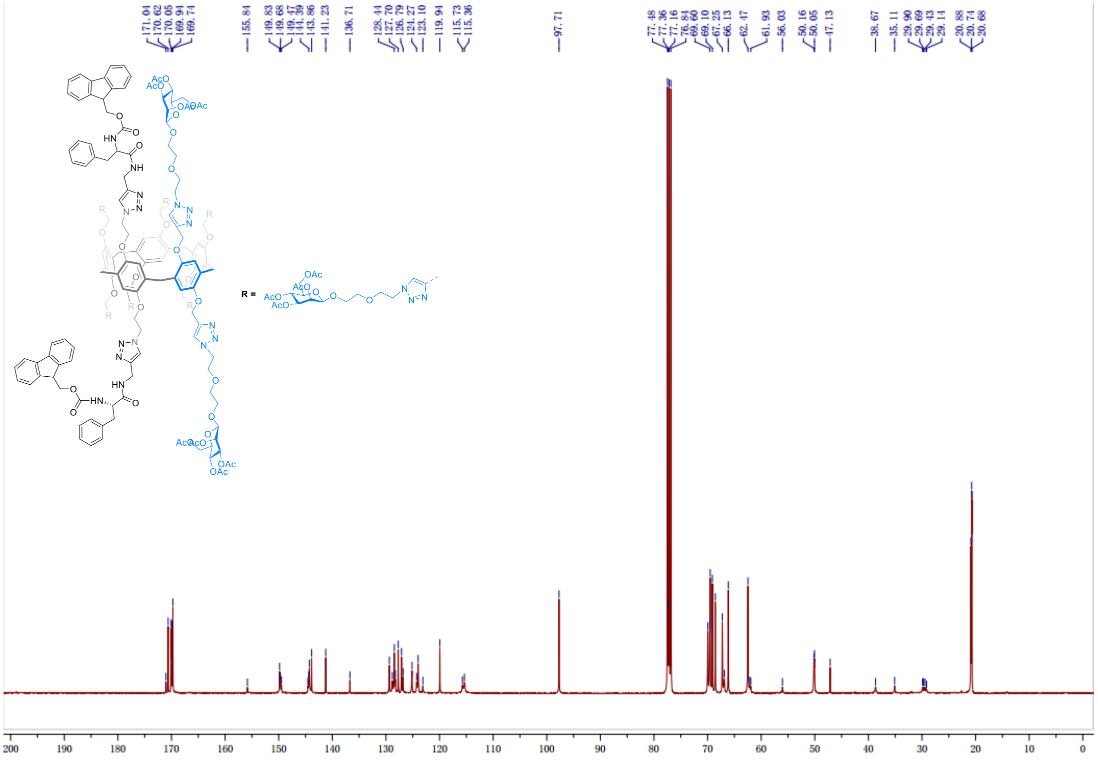
^{13}C NMR spectrum of compound **8d**



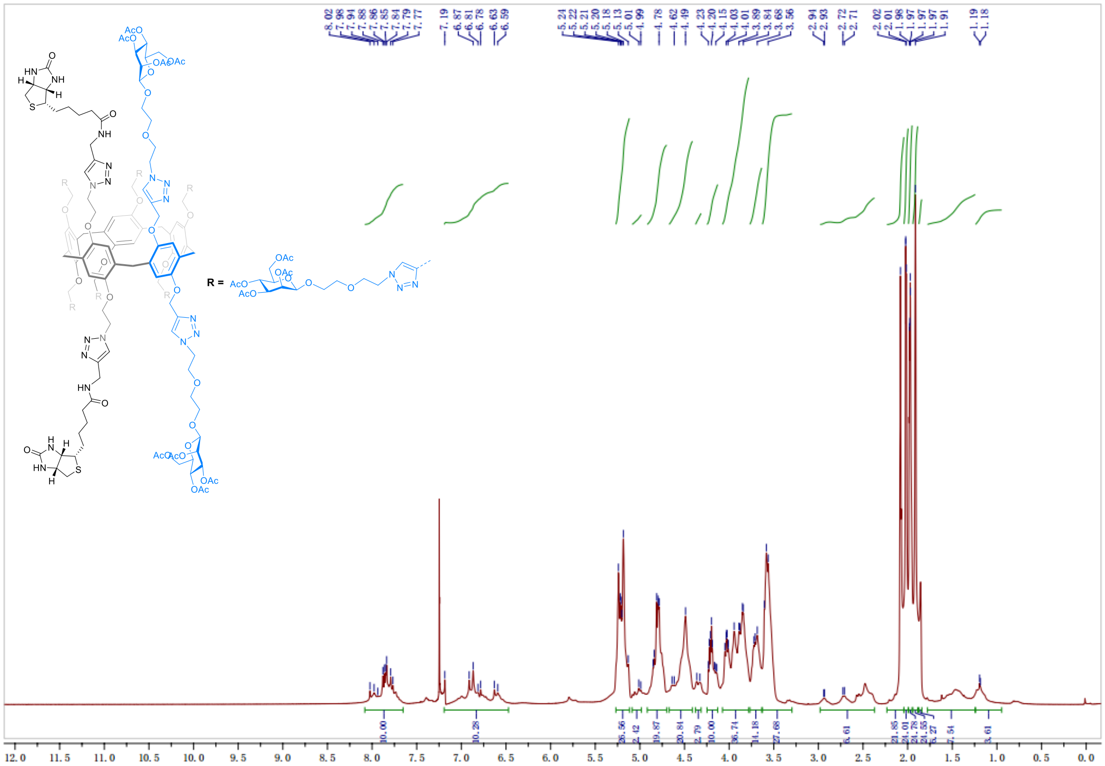
^{1}H NMR spectrum of compound **8e**



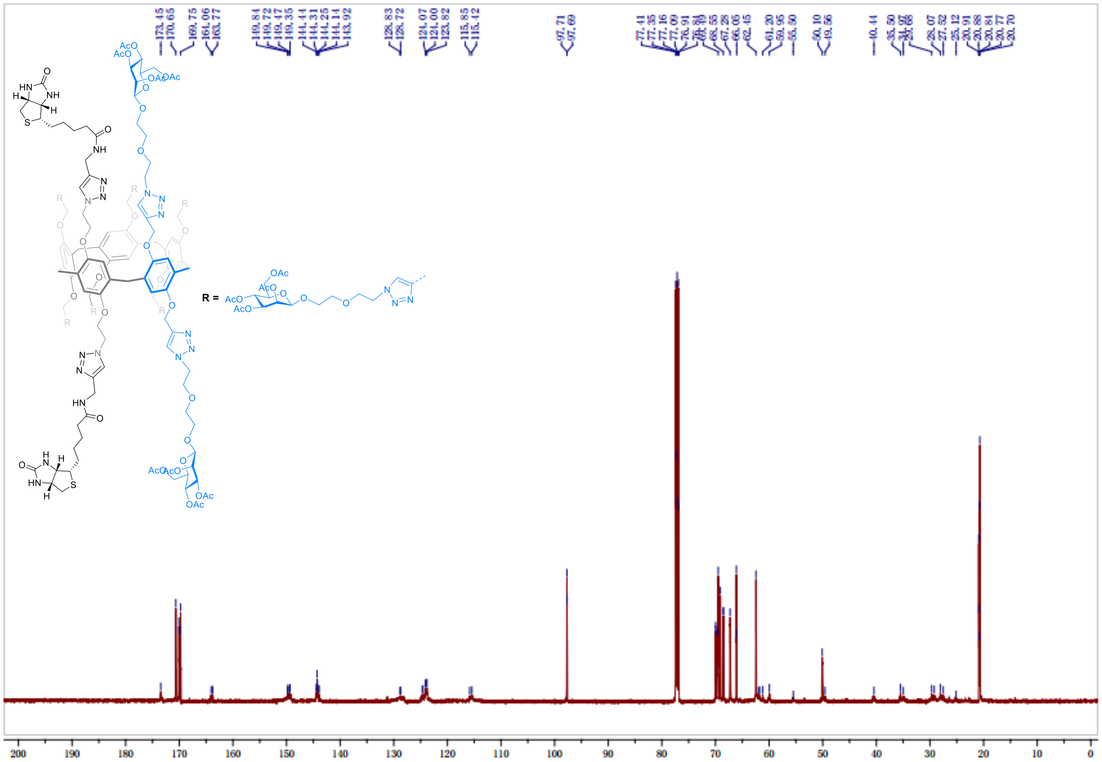
^{13}C NMR spectrum of compound **8e**



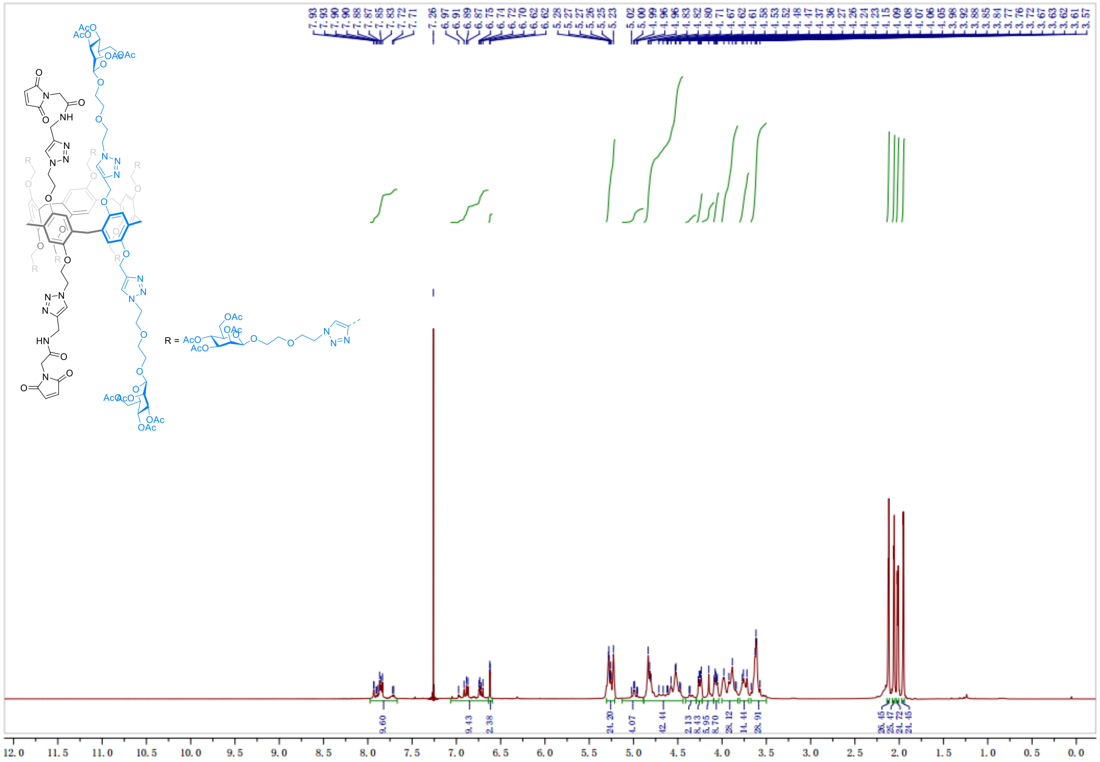
^{1}H NMR spectrum of compound **8f**



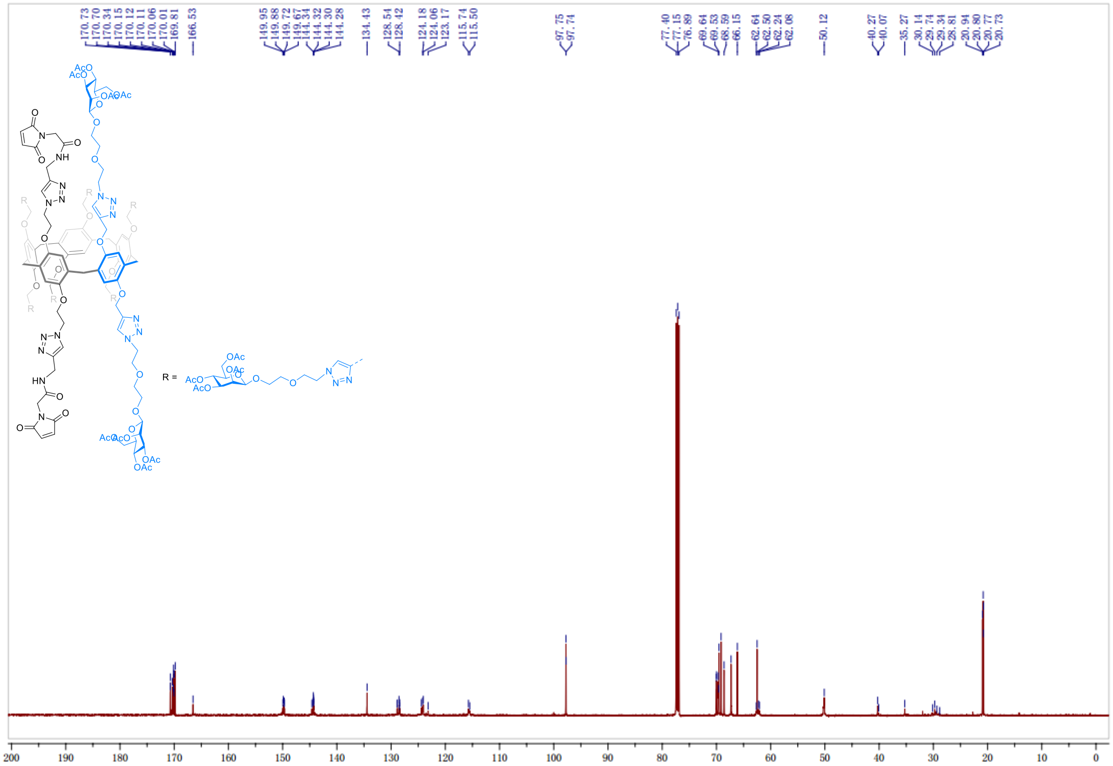
^{13}C NMR spectrum of compound **8f**



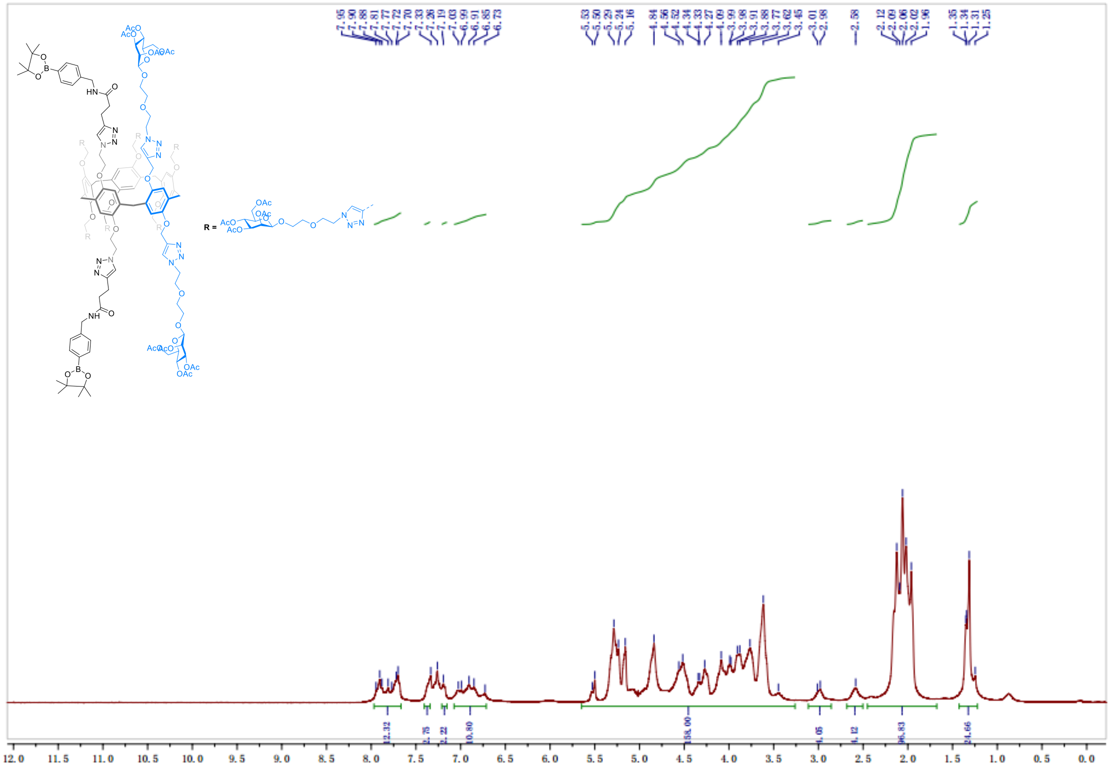
^{1}H NMR spectrum of compound **8g**



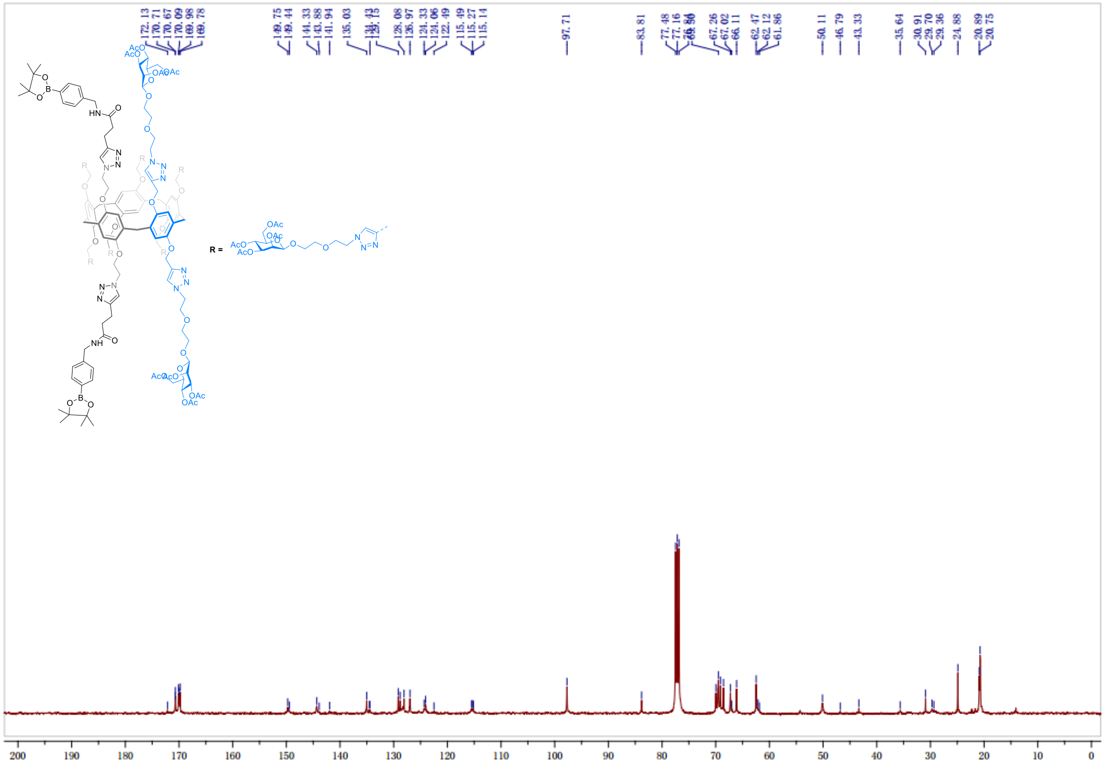
^{13}C NMR spectrum of compound **8g**



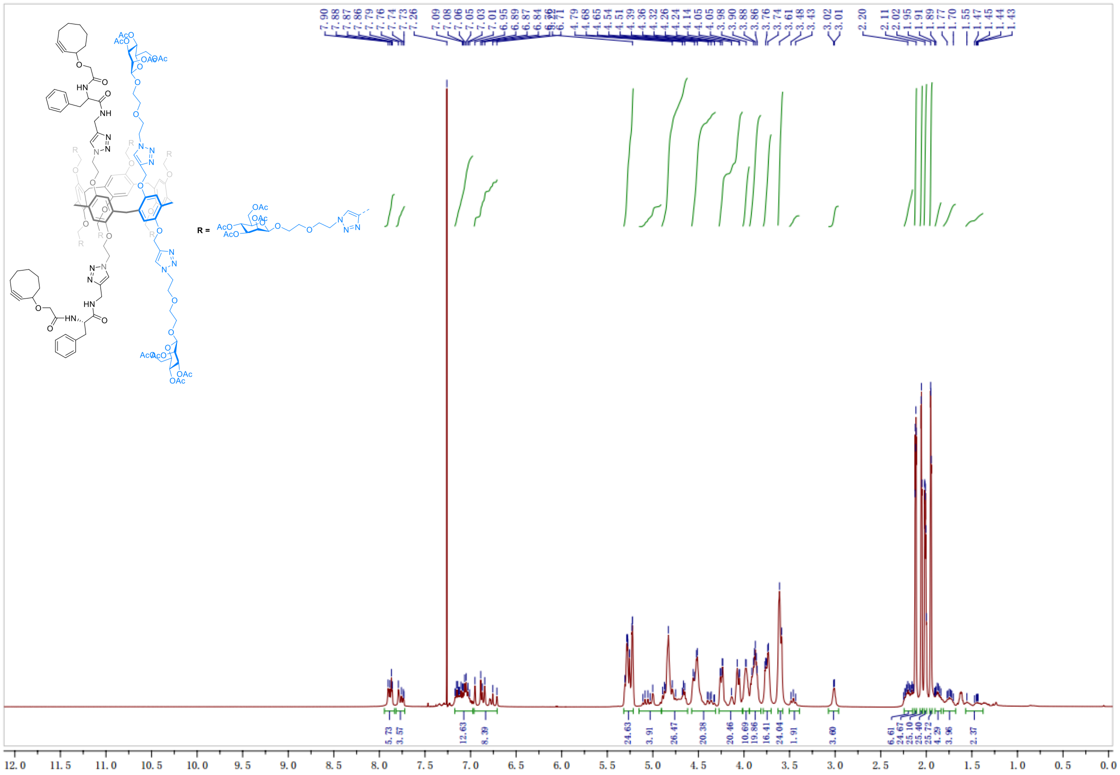
^{1}H NMR spectrum of compound **8h**



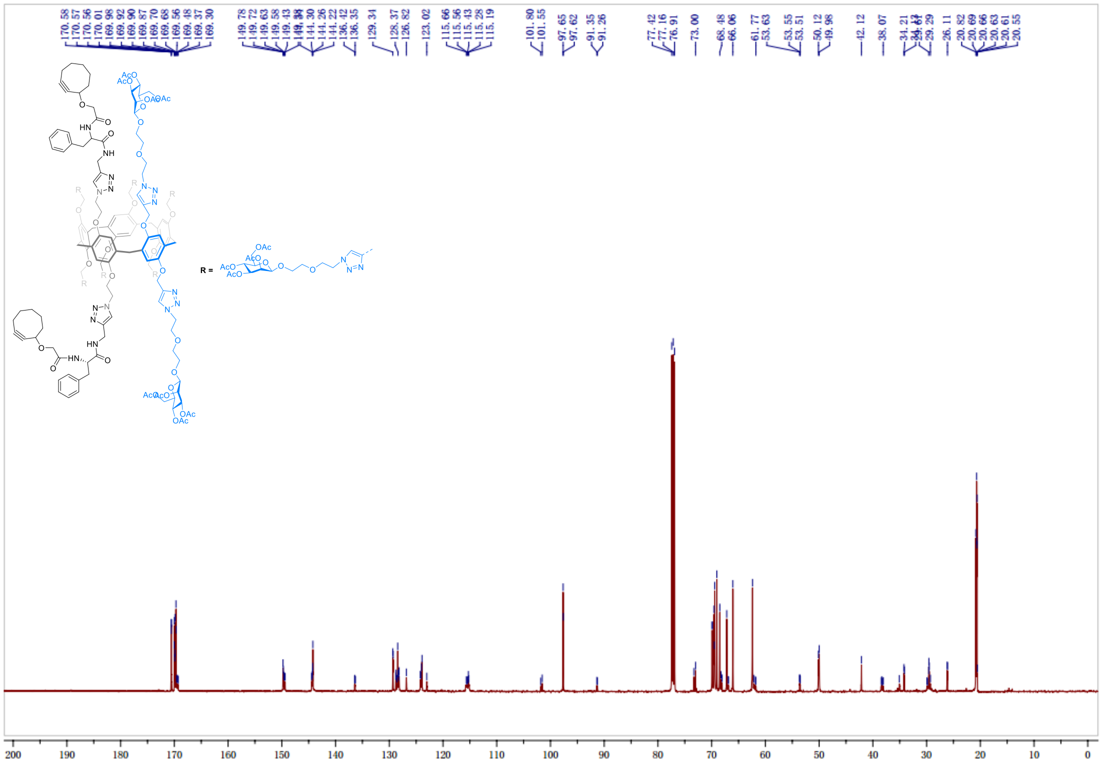
^{13}C NMR spectrum of compound **8h**



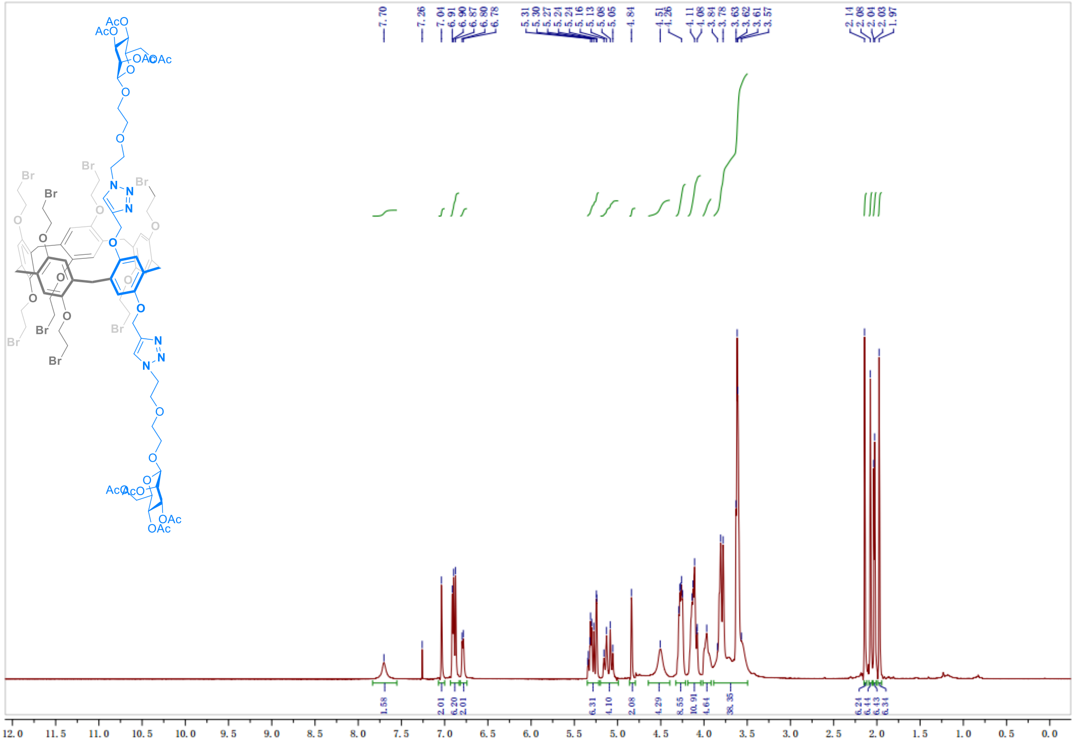
^{1}H NMR spectrum of compound **10**



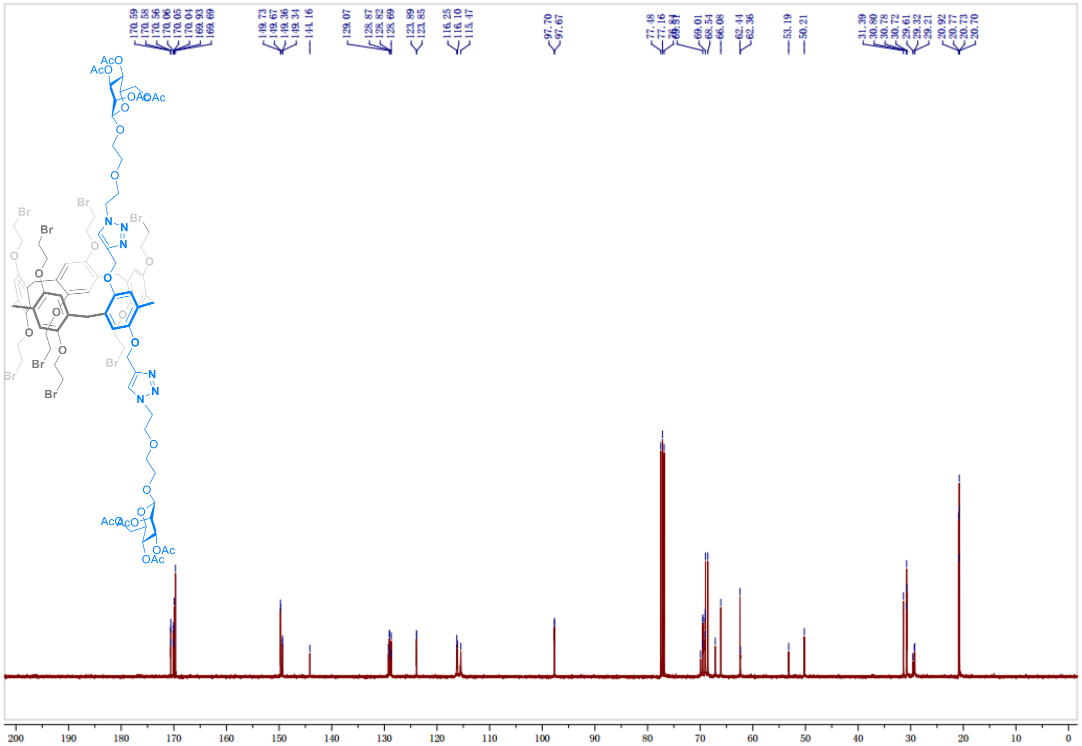
^{13}C NMR spectrum of compound **10**



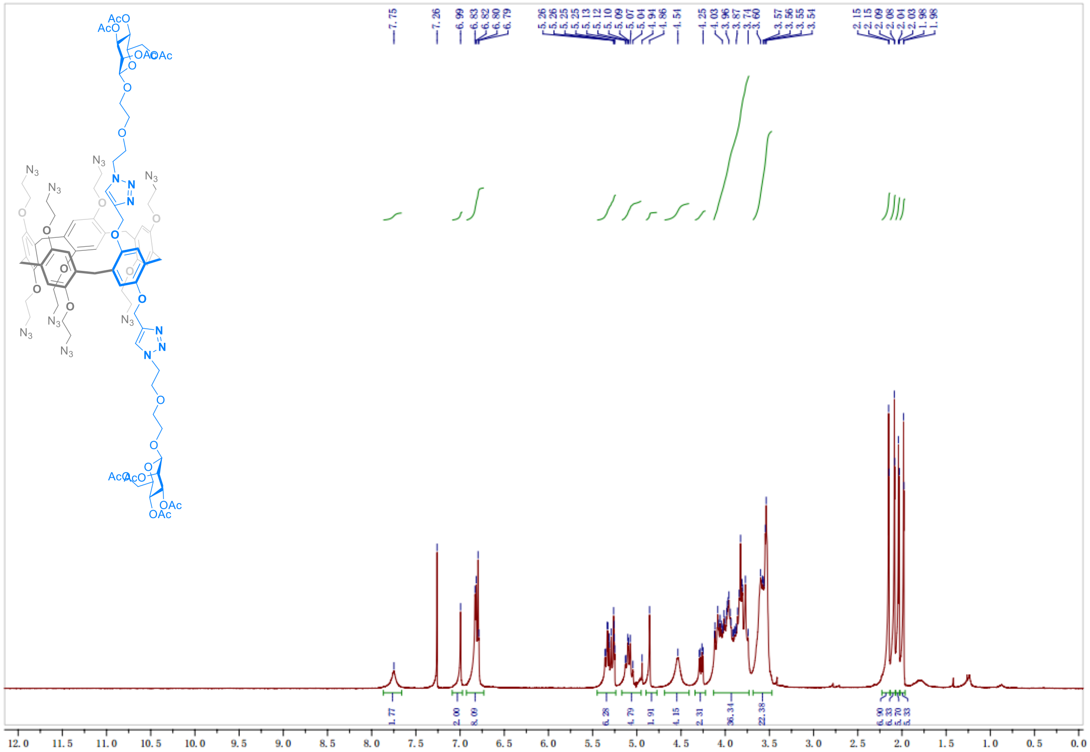
^{1}H NMR spectrum of compound **S3**



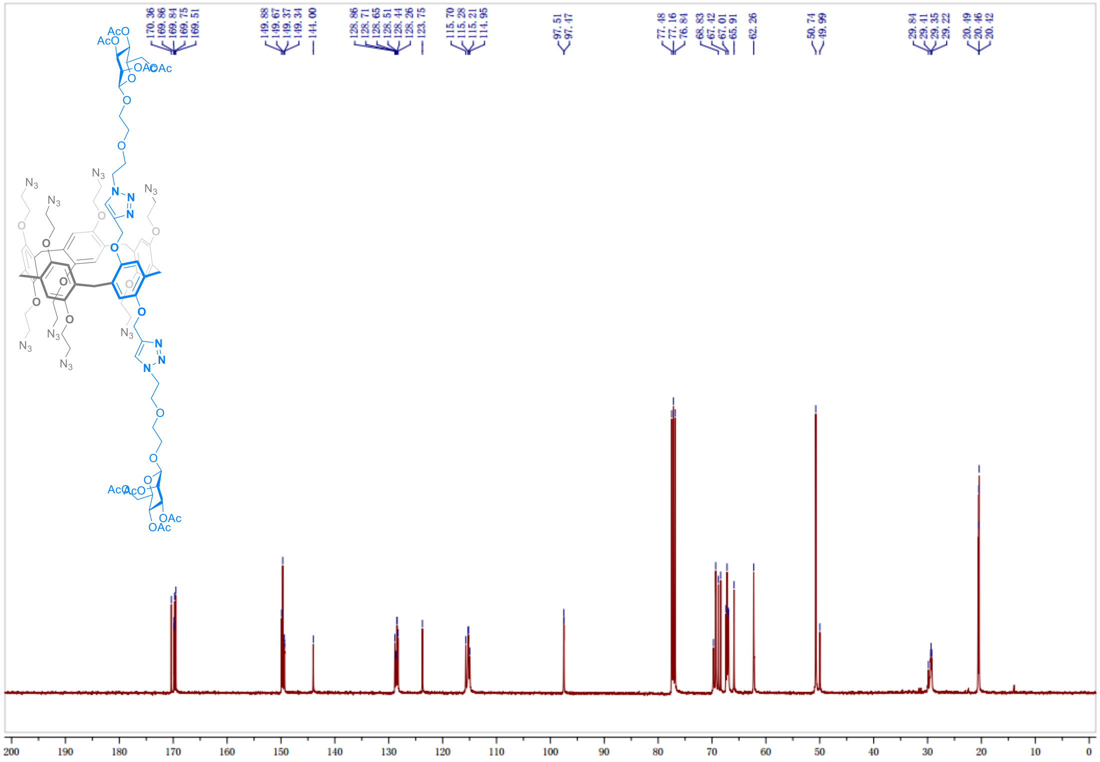
^{13}C NMR spectrum of compound **S3**



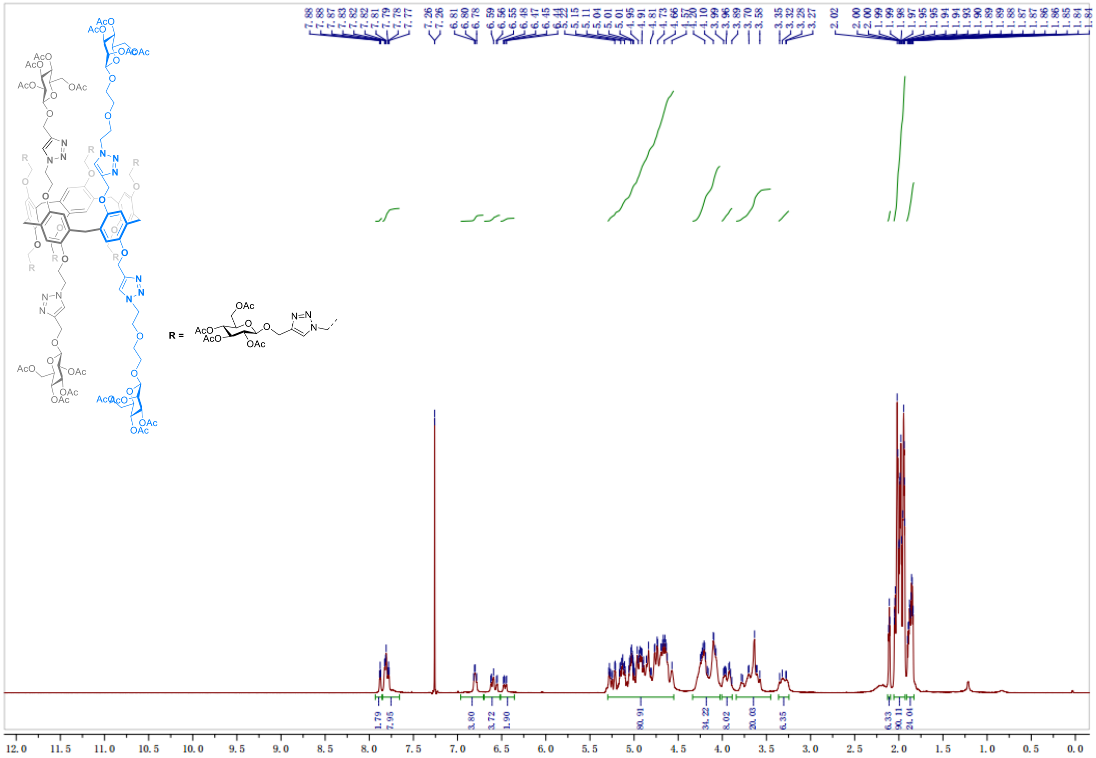
^{1}H NMR spectrum of compound **S4**



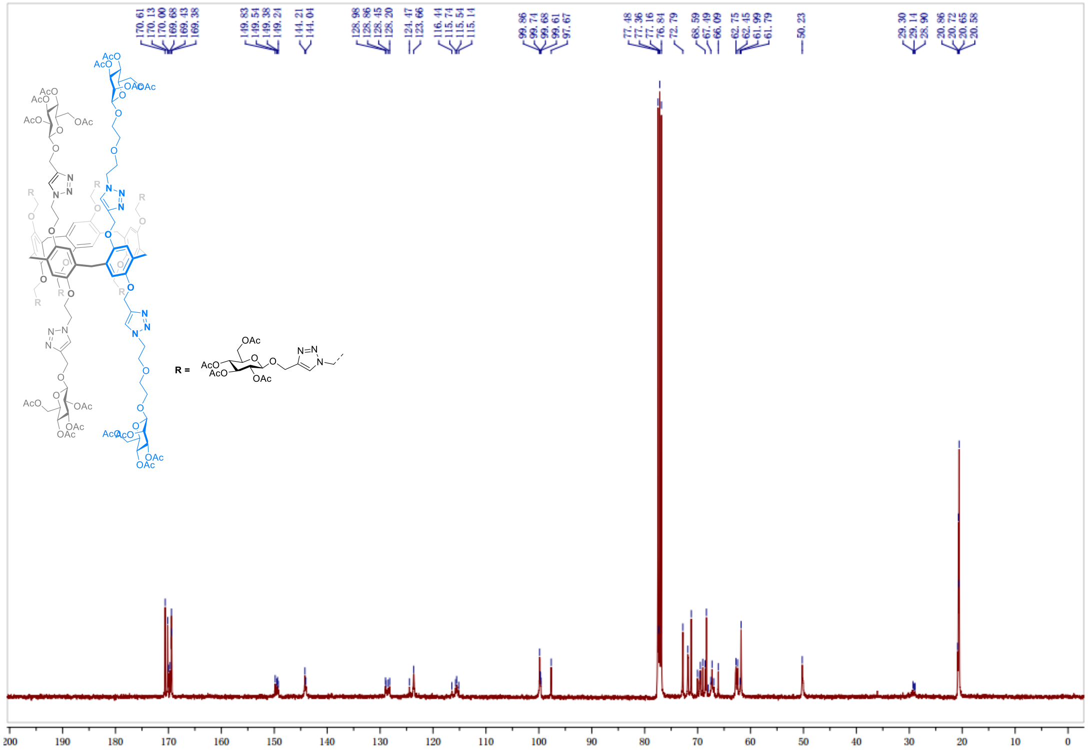
^{13}C NMR spectrum of compound **S4**



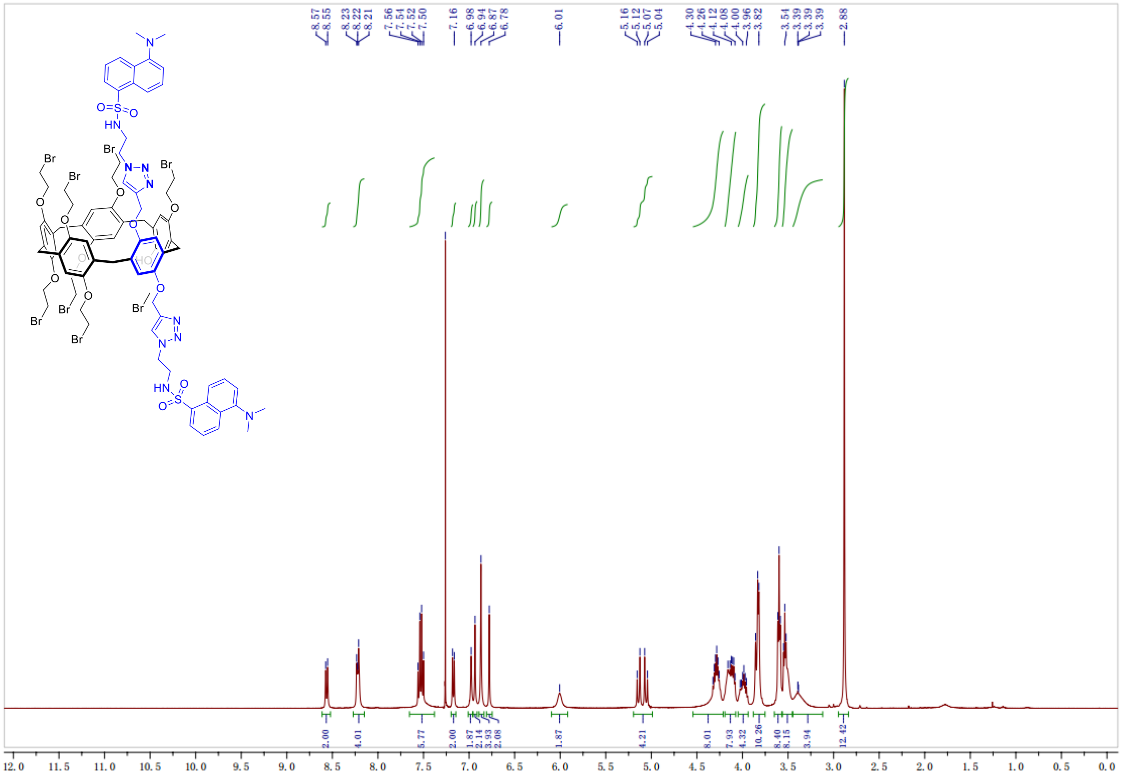
^{1}H NMR spectrum of compound **S5**



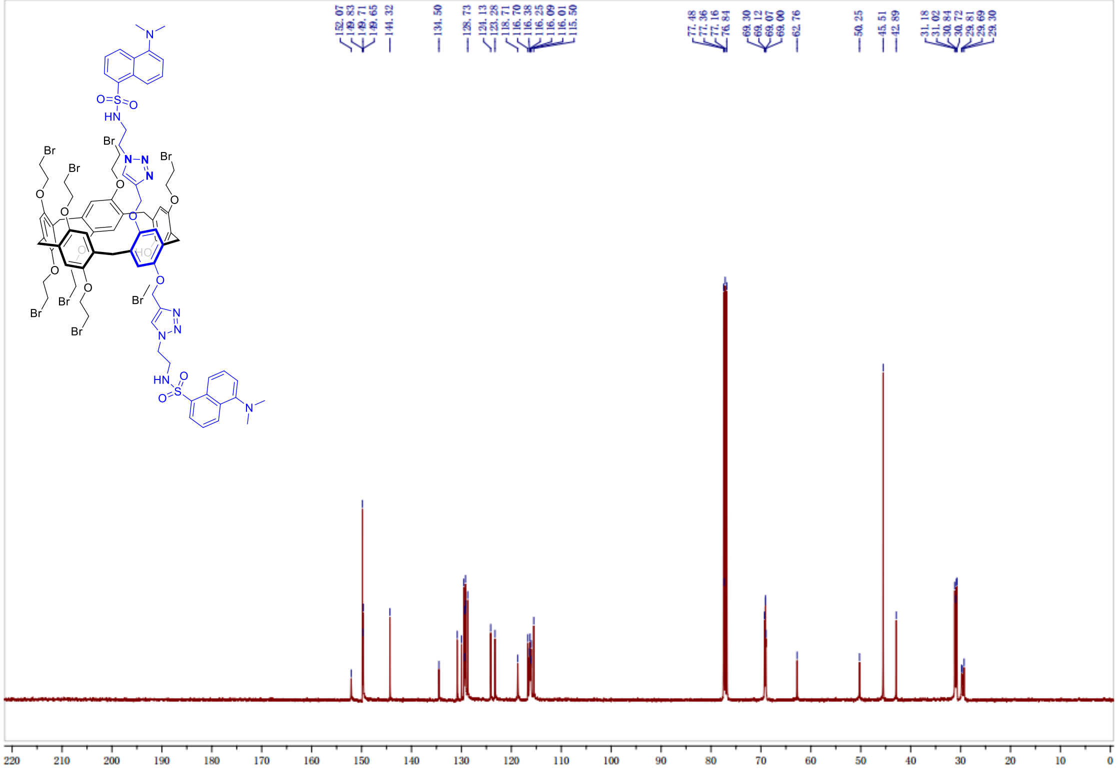
^{13}C NMR spectrum of compound **S5**



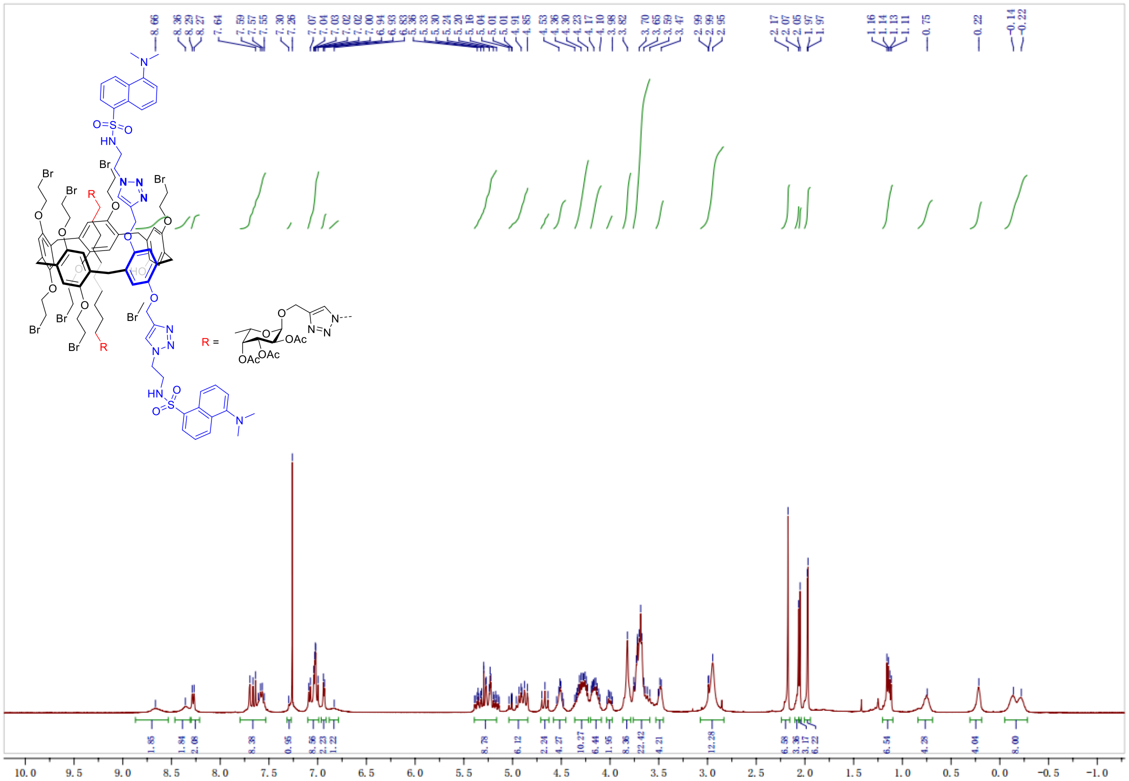
^{1}H NMR spectrum of compound **12**



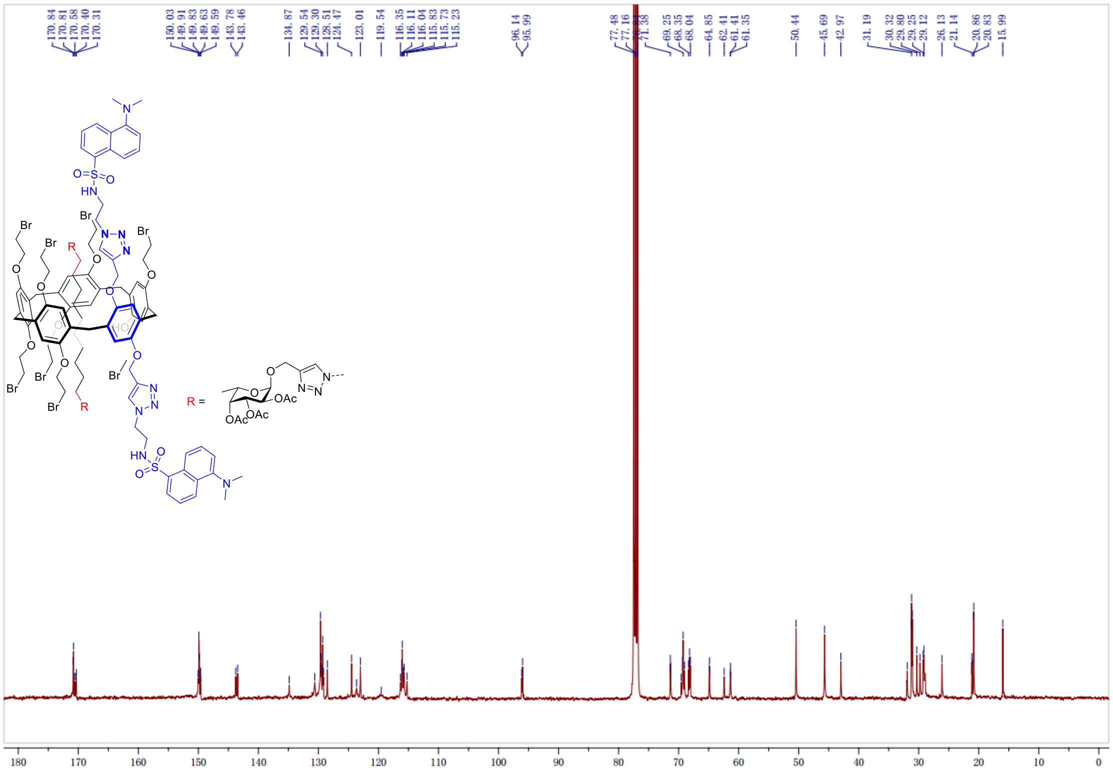
^{13}C NMR spectrum of compound **12**



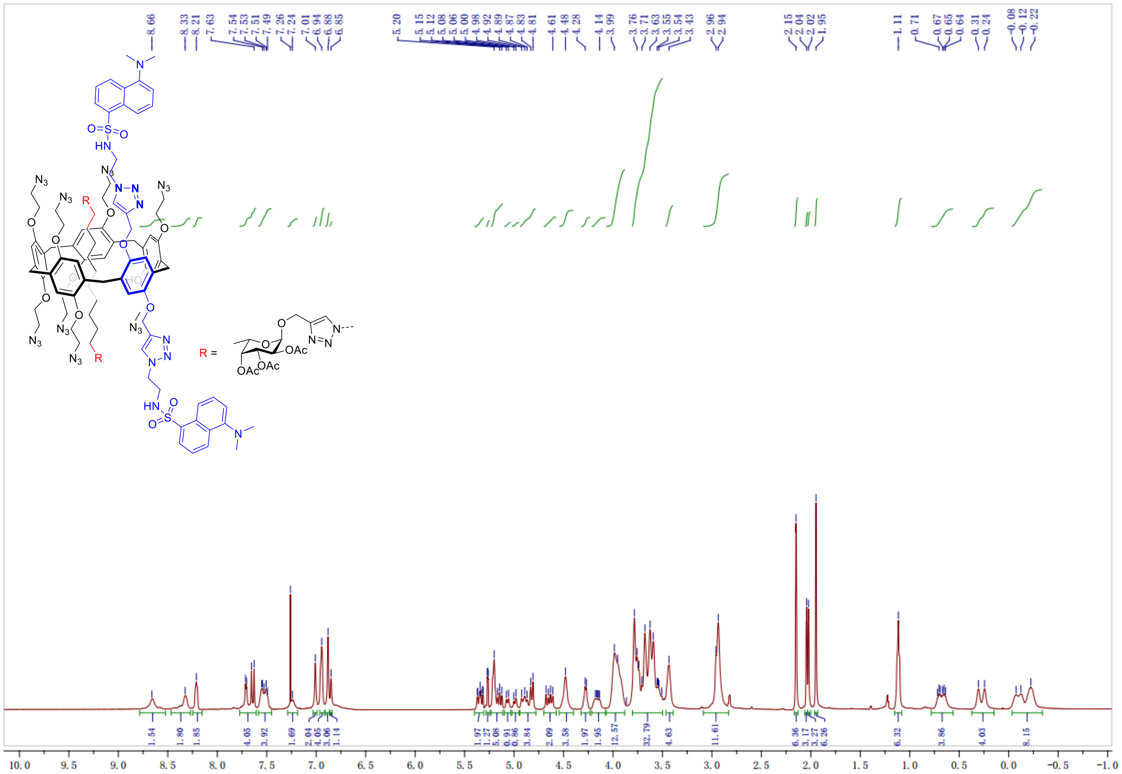
^{1}H NMR spectrum of rotaxane **15**



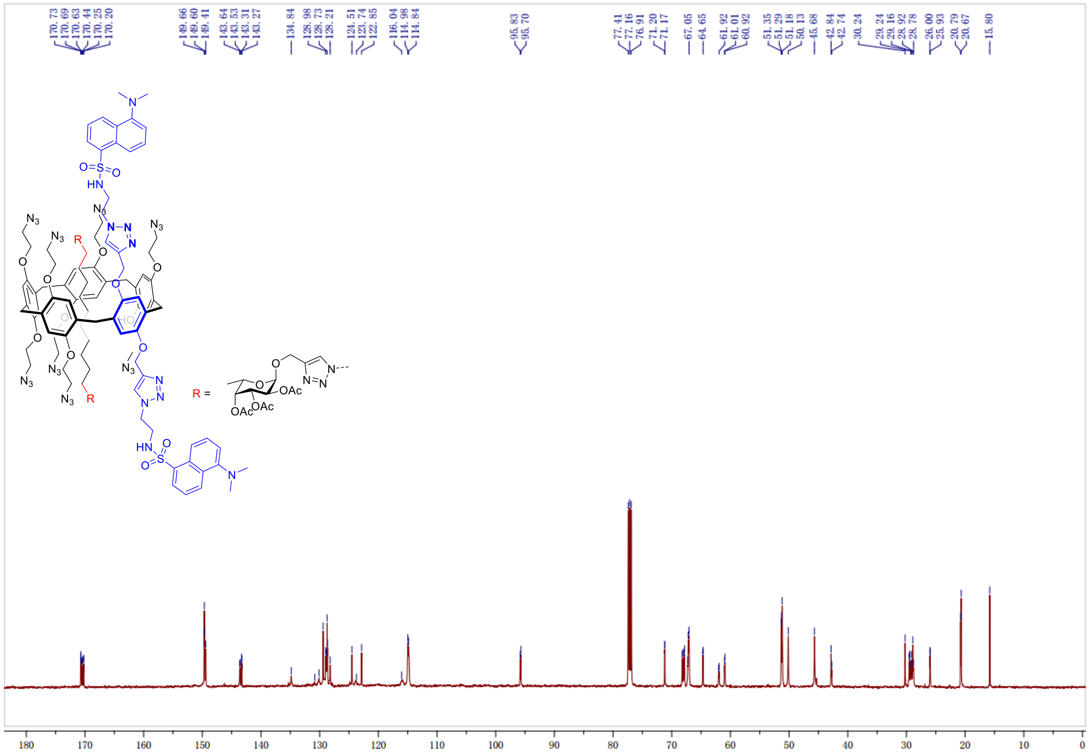
^{13}C NMR spectrum of rotaxane **15**



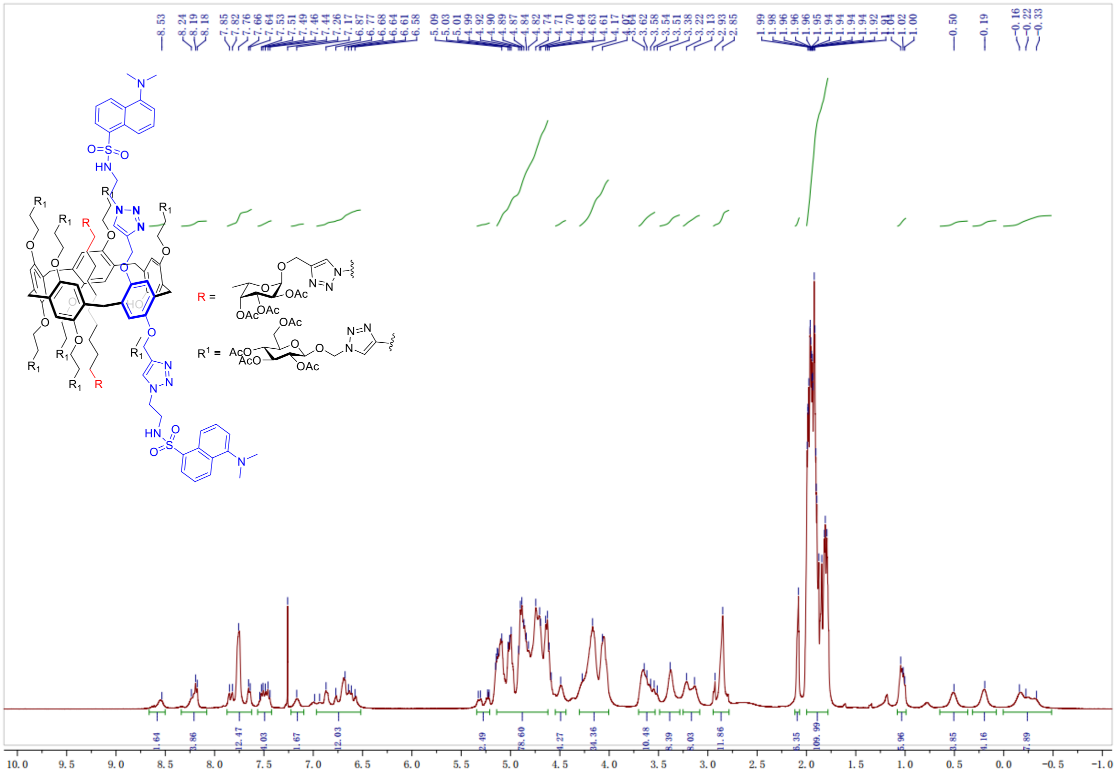
^{1}H NMR spectrum of rotaxane **16**



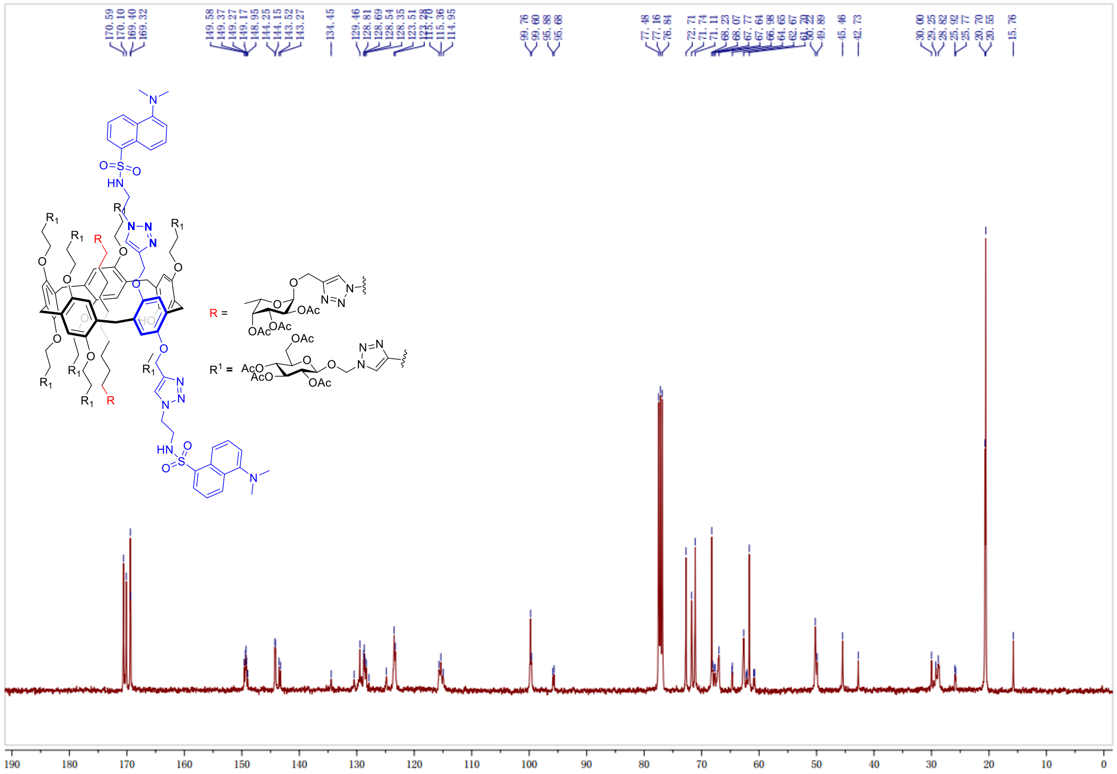
^{13}C NMR spectrum of rotaxane **16**



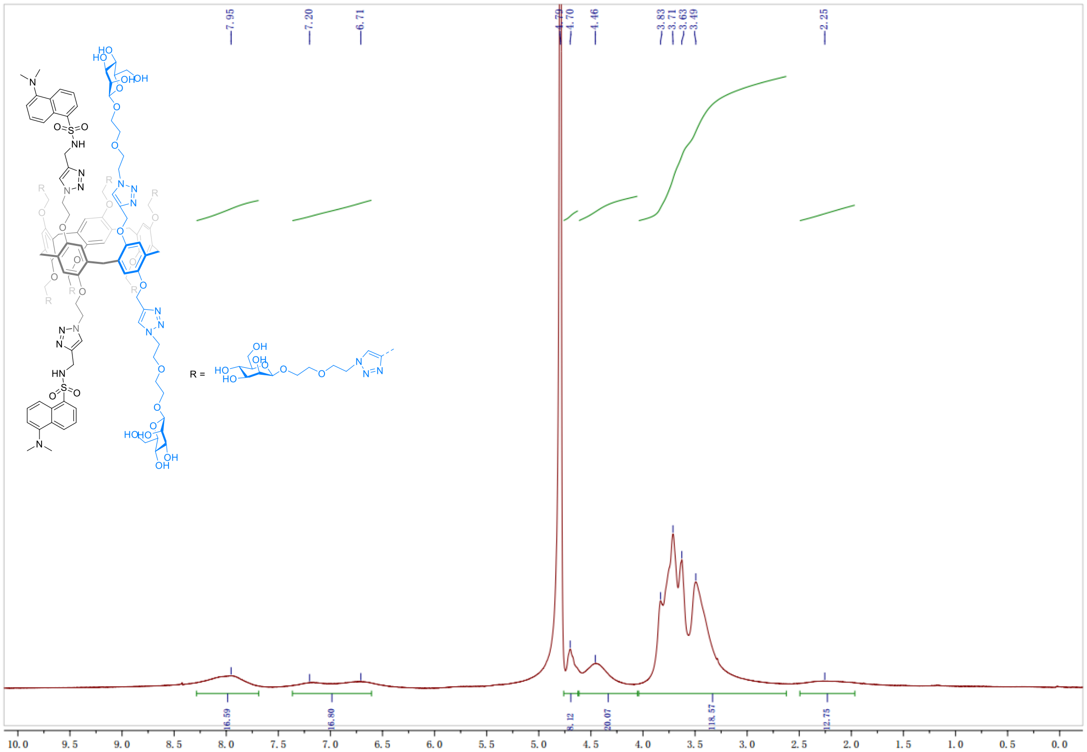
^{1}H NMR spectrum of **17**



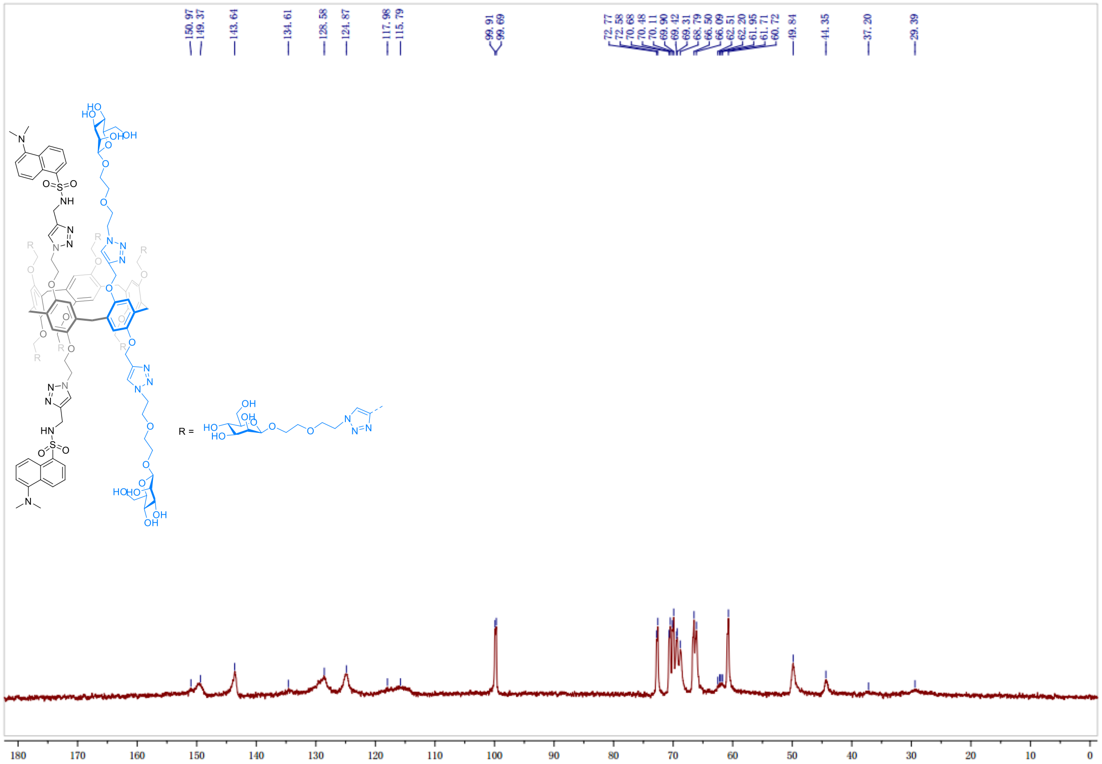
^{13}C NMR spectrum of **17**



^{1}H NMR spectrum of **S6**



^{13}C NMR spectrum of **S6**



S14. Fluorescence spectra of compounds 12, 15,16 and S6

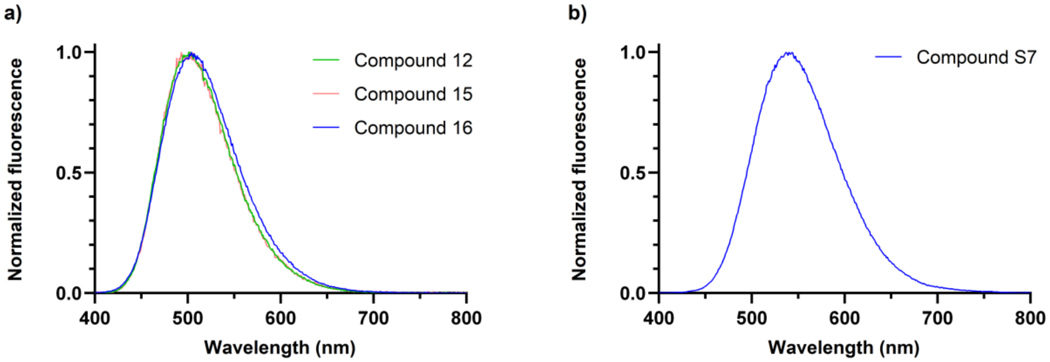


Figure S1: Fluorescence emission spectra of **a**) compounds **12**, **15** and **16** dissolved in chloroform and **b**) compound **S6** dissolved in water (λex = 380 nm)

S15.The ^{1}H NMR spectra of compounds 12, 15, 16 and axle

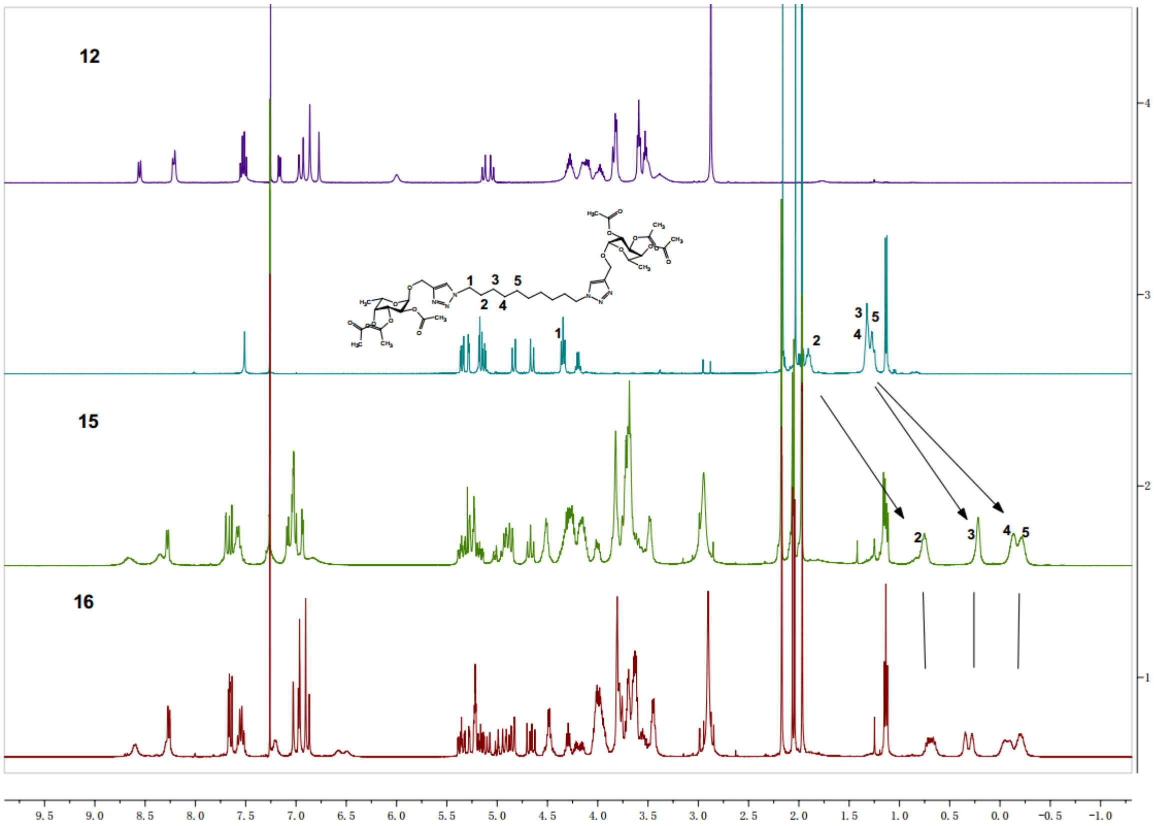
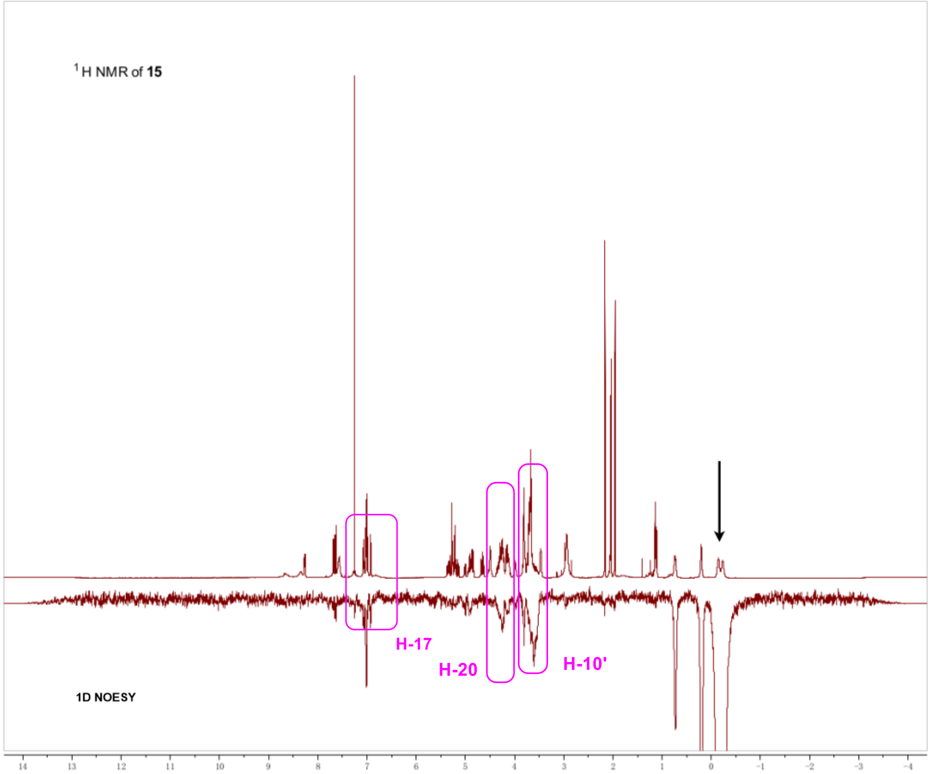


Figure S2. ^{1}H NMR spectra (400 MHz, $CDCl_3$) of compound **12**, rotaxane **15**, rotaxane **16** and axle. As a result of the ring current effect of the pillar[5]arene aromatic subunits on the -$(CH_2)_{10}$- chain of the axle, the signals of protons H (2-5) are dramatically shielded in rotaxane **15** and rotaxane **16** when compared to the corresponding signals in axle molecular.

S16. ^{1}H NMR and 1D NOESY spectra of compounds 15 and 16



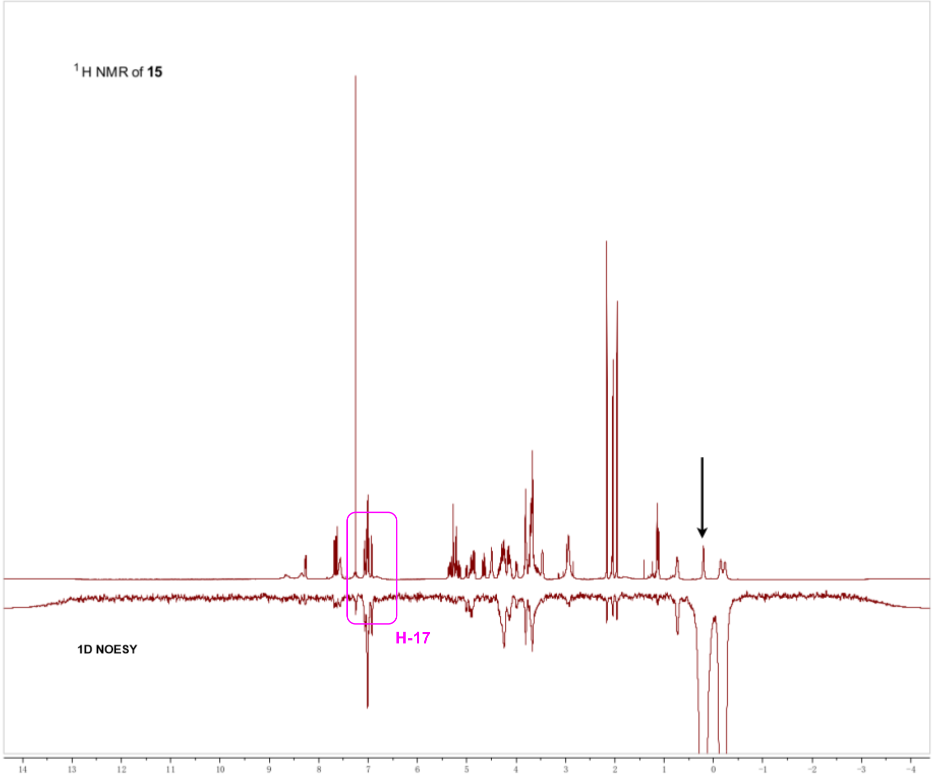


Figure S3. The black arrow indicates the protons that were excited in 1D NOESY of **15**.

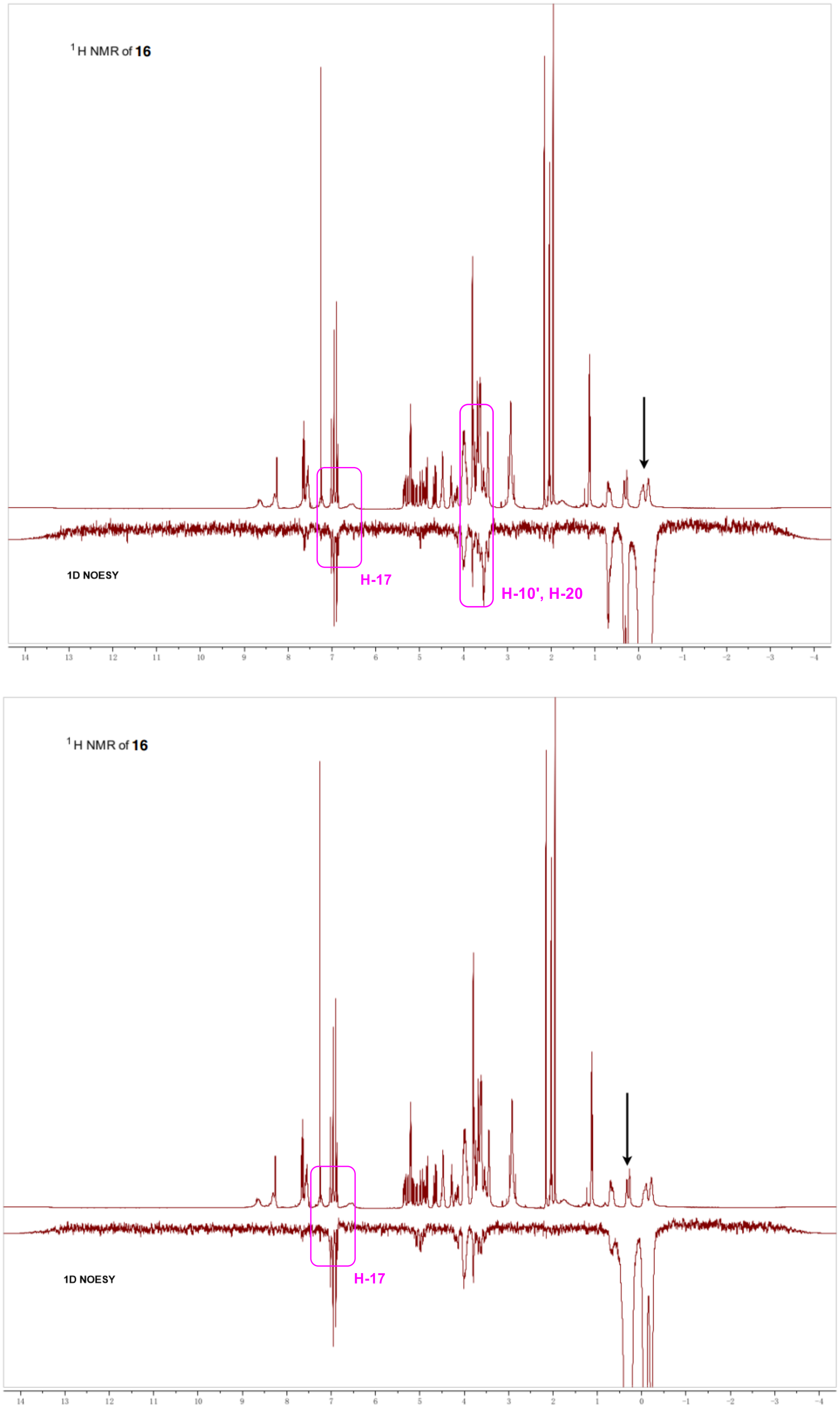
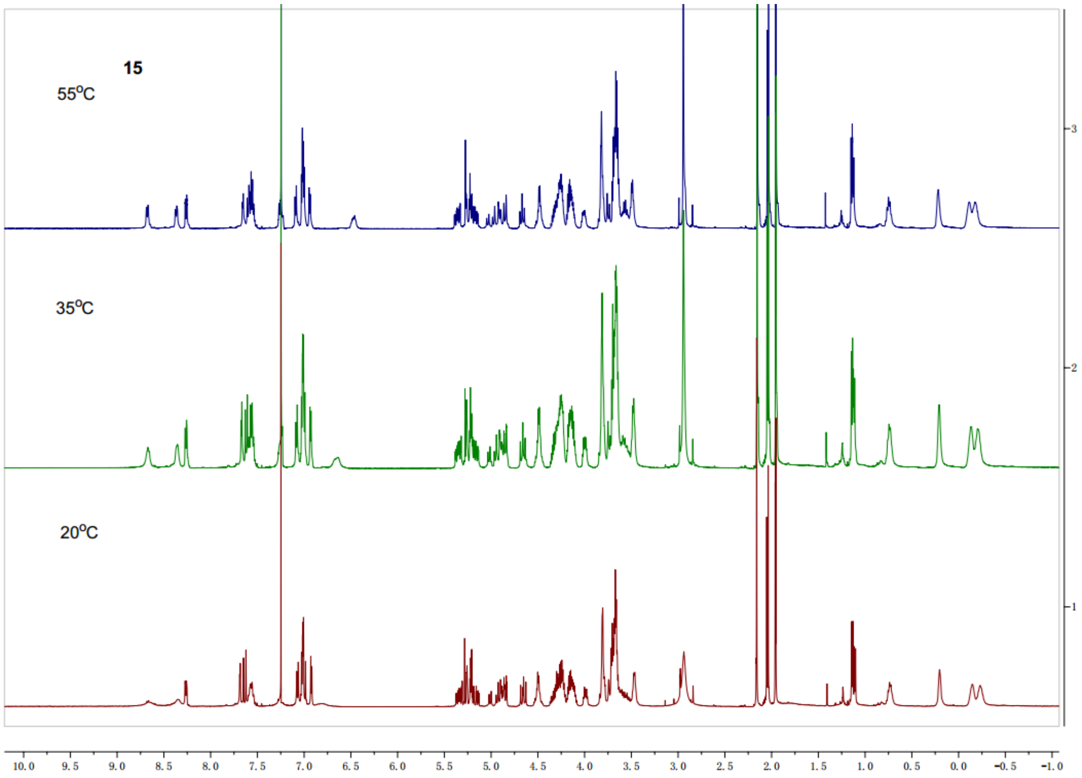
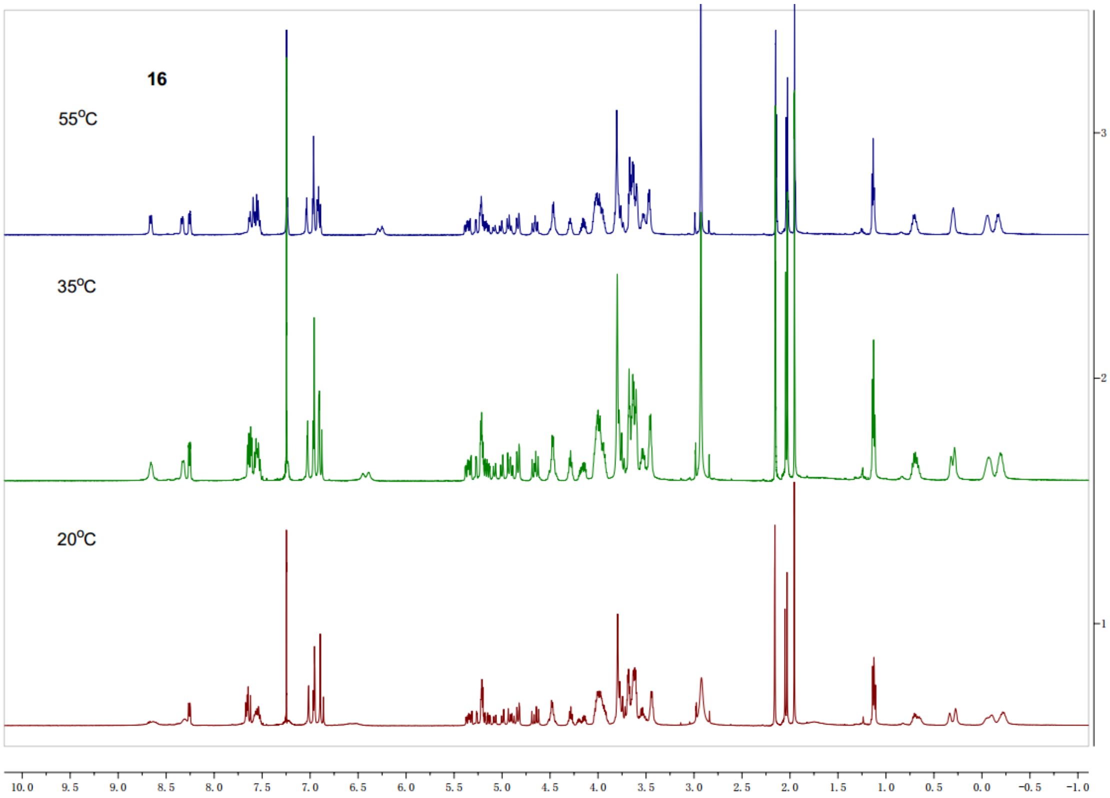


Figure S4. The black arrow indicates the protons that were excited in 1D NOESY of **16**

S17. Temperature dependent ^{1}H NMR spectra of compounds 15, 16 and 8c





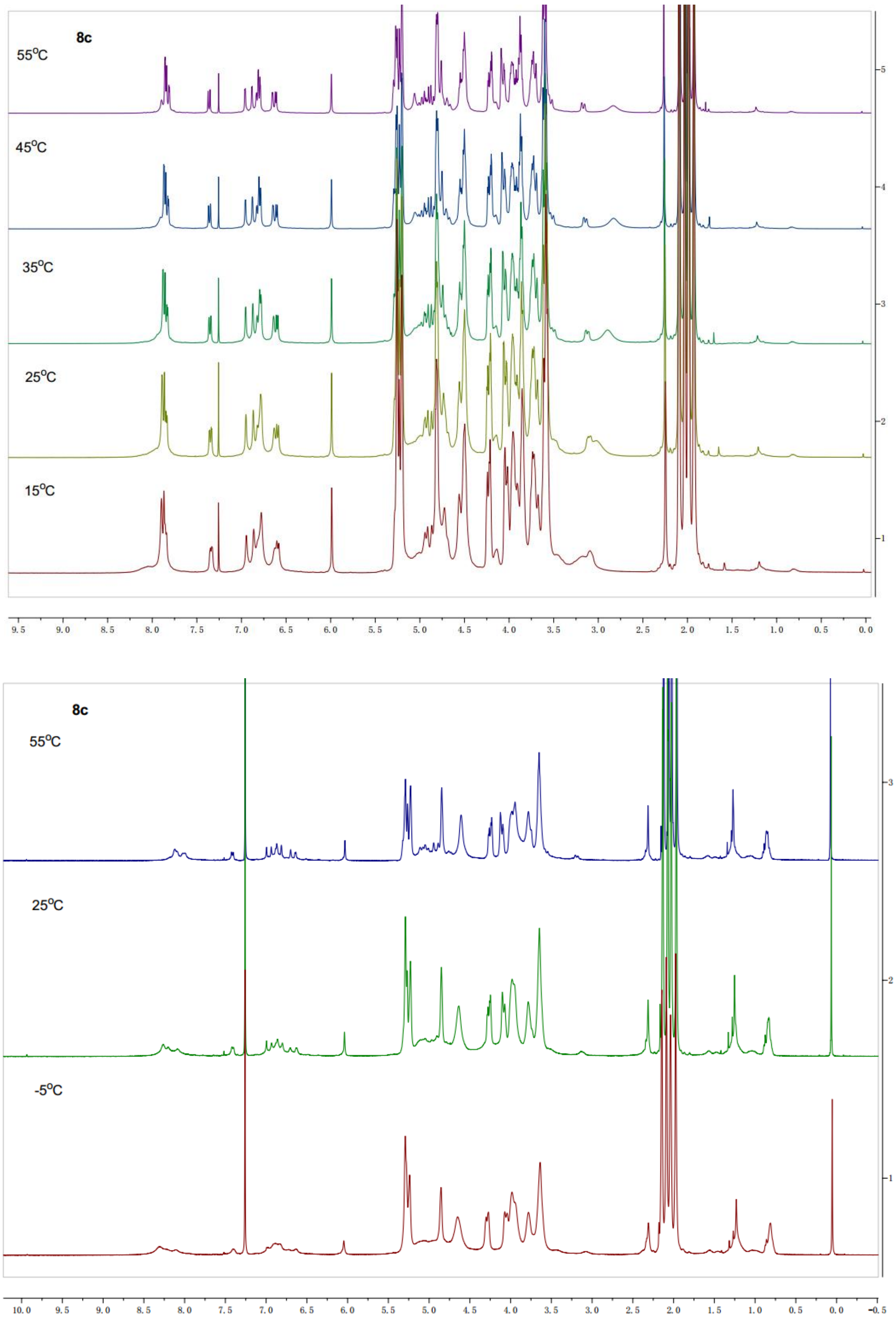


Figure S5. Temperature dependent ^{1}H NMR spectra of **8c**. The upper spectra of **8c** were recorded at higher concentration (0.030 M) and the lower spectra were recorded at a lower concentration (0.004 M). The specific temperatures are indicated in each spectra.

Reference

[1] Y. Yao, M. Xue, X. Chi, Y. Ma, J. He, Z. Abliz and F. Huang, *Chem. Commun.,* **2012**, *48*, 6505-6507.

[2] I. Nierengarten, S. Guerra, M. Holler, J. F. Nierengarten and R. Deschenaux, *Chem. Commun.,* **2012**, *48*, 8072-8074.

[3] D. Pendin, R. Norante, A. De Nadai, G. Gherardi, N. Vajente, E. Basso, N. Kaludercic, C. Mammucari, C. Paradisi, T. Pozzan and A. Mattarei, *Angew. Chem. Int. Ed.,* **2019**, *58*, 9917-9922.

[4] A. Anand, R. J. Naik, H. M. Revankar, M. V. Kulkarni, S. R. Dixit and S. D. Joshi, *Eur. J. Med. Chem.,* **2015**, *105*, 194-207.

[5] T. R. Hoye and Z. J. J. o. t. A. C. S. Ye, *J. Am. Chem. Soc.,* **1996**, *118*, 1801-1802.

[6] Q. Lin, P.-P. Mao, Y.-Q. Fan, L. Liu, J. Liu, Y.-M. Zhang, H. Yao and T.-B. Wei, *Soft Matter,* **2017**, *13*, 7085-7089.

[7] B. J. Timmer, M. A. Flos, L. M. Jorgensen, D. Proverbio, S. Altun, O. Ramstrom, T. Aastrup and S. P. Vincent, *Chem. Commun.,* **2016**, *52*, 12326-12329.

[8] R. Yan, K. Sander, E. Galante, V. Rajkumar, A. Badar, M. Robson, E. El-Emir, M. F. Lythgoe, R. B. Pedley and E. Arstad, *J. Am. Chem. Soc.,* **2013**, *135*, 703-709.

[9] C. D. Spicer and B. G. Davis, *Chem. Commun.,* **2013**, *49*, 2747-2749.

[10] L. F. Tietze, H. J. Schuster, B. Krewer and I. Schuberth, *J. Med. Chem.,* **2009**, *52*, 537-543.

[11] L. F. Tietze and U. Bothe, *Chem. Eur. J.,* **1998**, *4*, 1179-1183.

[12] J. Rull-Barrull, M. d'Halluin, E. Le Grognec and F. X. Felpin, *Angew. Chem. Int. Ed. Engl.,* **2016**, *55*, 13549-13552.

[13] M. Rubinshtein, C. R. James, J. L. Young, Y. J. Ma, Y. Kobayashi, N. C. Gianneschi and J. Yang, *Org. Lett.,* **2010**, *12*, 3560-3563.

[14] M. Patra and N. Metzler-Nolte, *Chem. Commun.,* **2011**, *47*, 11444-11446.

[15] S. Nainar, M. Kubota, C. McNitt, C. Tran, V. V. Popik and R. C. Spitale, *J. Am. Chem. Soc.,* **2017**, *139*, 8090-8093.

[16] X. Li, S. Qiao, L. Zhao, S. Liu, F. Li, F. Yang, Q. Luo, C. Hou, J. Xu and J. Liu, *ACS Nano.,* **2019**, *13*, 1861-1869.

[17] H. L. Evans, R. L. Slade, L. Carroll, G. Smith, Q. D. Nguyen, L. Iddon, N. Kamaly, H. Stockmann, F. J. Leeper, E. O. Aboagye and A. C. Spivey, *Chem. Commun.,* **2012**, *48*, 991-993.

[18] J. F. Nierengarten, J. Iehl, V. Oerthel, M. Holler, B. M. Illescas, A. Munoz, N. Martin, J. Rojo, M. Sanchez-Navarro, S. Cecioni, S. Vidal, K. Buffet, M. Durka and S. P. Vincent, *Chem. Commun.,* **2010**, *46*, 3860-3862.

[19] S. P. Vincent, K. Buffet, I. Nierengarten, A. Imberty and J. F. Nierengarten, *Chem. Eur. J.,* **2016**, *22*, 88-92.