Supporting Information:

Ultrasound-Promoted Copper-Catalyzed Azide-Alkyne Cycloaddition

Giancarlo Cravotto,[†] Valery V. Fokin,[‡] Davide Garella,[†] Arianna Binello,[†] Luisa Boffa,[†] Alessandro Barge.[†]*

Dipartimento di Scienza e Tecnologia del Farmaco, Università di Torino, Via Giuria 9, 10125 Torino, Italy and Department of Chemistry, The Scripps Research Institute, 10550 North Torrey Pines Road, La Jolla, California 92037.

giancarlo.cravotto@unito.it

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1. Experimental details

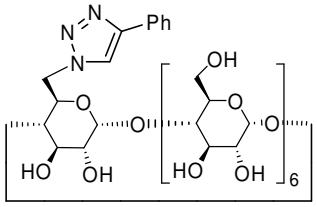
Commercially available reagents and solvents were used without further purification unless otherwise stated. β-CD was kindly provided by Wacker Chemie (Germany). Reactions were monitored by TLC on Merck 60 F254 (0.25 mm) plates, which were visualized by UV inspection and/or by heating after a spray of 5% H_2SO_4 in ethanol or phosphomolybdic acid. The purification was performed by flash-chromatography (CombiFlash Rf® Teledyne ISCO) on appropriate columns (silica gel or RP18). All the sonochemical apparatuses were developed in our laboratory in collaboration with Danacamerini sas (Torino, Italy), *viz.* a model with an immersion titanium horn (21.4 kHz) and a non-metallic horn made in pyrex® to be inserted in a MicroSYNTH-Milestone (Italy) professional oven for simultaneous irradiation. IR spectra were recorded with a Shimadzu FT-IR 8001 spectrophotometer. NMR spectra were recorded on a Bruker Avance 300 (300 MHz and 75 MHz for ^{1}H and ^{13}C, respectively) at 25°C. Low-resolution mass spectra were recorded on a Finnigan-MAT TSQ70 in chemical ionization mode (CI) using isobutane as reactant gas; ESI-mass spectra were recorded on a Waters Micromass ZQ equipped with ESI source. Cu content was determined using inductively coupled plasma mass spectrometry (ICP-MS, Element-2, Thermo-Finnigan, Rodano (MI) Italy). Sample digestion was performed with 2 ml of concentrated HNO_3 (70%) under microwave heating (Milestone MicroSYNTH Microwave labstation equipped with a fibre optic temperature controller and HPR-1000/6M six position high pressure reactor, Bergamo, Italy). After digestion the volume of each sample was brought to 2 ml with ultrapure water, and the sample was analyzed by ICP-MS. Three replicates of each sample solution were analyzed.

2. General procedures

2.1. Synthesis of β-CD derivatives

All reactions were carried out in a 50 ml heavy walled pear-shaped two-neck flask with non-standard taper outer joint. In all cases the temperature was strictly monitored by two measurement systems: an IR pyrometer + a thermocouple (under US) or an IR pyrometer + an optical-fiber thermometer (under MW). The fine turnings of metallic copper (50 mol%, 100 mol%, for entries **27**-**34** respectively) were suspended in DMF (10 ml). The azido compound (1 mmol) and the acetylenic derivative (5.0 mmol) were added and the mixture was heated and/or irradiated with MW or MW/US as indicated in the tables. The reaction outcome was monitored by TLC. Copper was filtered off on paper filter, then solvent was evaporated under vacuum and crude product was purified by flash-chromatography.

2.2. 6-monodeoxy-6-mono(4-phenyl-1,2,3-triazol-1-yl)-β-cyclodextrin.



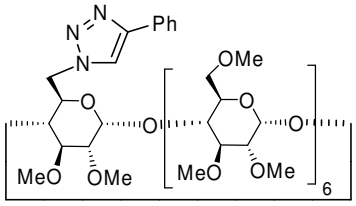
Analytical data consistent with literature.[1] A more detailed characterization is reported below.

TLC: silica gel plates, *i*-PrOH/H_2O/AcOEt/NH_3 5/3/1/1, R_f=0.51.

Flash-Chromatography on RediSep column 26g C18. Solvents: A = water ; B = MeOH, gradient: Time/B%: 1.2/0, 5.9/10, 5.9/10, 5.9/20, 11.7/20, 11.7/50, 5.9/100, 4/100. Flow 22 ml/min.

MW: 1262.13. White powder, Mp = >235°C (dec.). IR: 3420, 2926, 2104 (N_3), 1655, 1458, 1367, 1333, 1157, 1097, 1028, 947, 756. ^{1}H NMR (DMSO, 300MHz): δ 8.51 (s, 1H, H-5 *triaz*), 7.78 (d, *J*=6.9 Hz, 2H, H-2,6 *Ph*), 7.41 (dd, *J*=7.2, 6.9 Hz, 2H, H-3,5 *Ph*), 7.31 (t, *J*=7.2 Hz, 1H, H-4 *Ph*), 6.00-5.50 (overlapped signals, 14H, 2,3-OH), 5.05 (d, *J*=3.3 Hz, 1H, H-1), 4.92 (m, 1H, H-6'a), 4.80-4.70 (m, 6H, H-1), 4.60 (m, 1H, H-6'b), 4.70-4.41 (overlapped signals, 5H, 6-OH,), 4.25 (t, *J*=6.3 Hz, 1H, 6-OH), 4.13 (m, 1H, H-5'), 3.70-3.48 (overlapped signals, 23H, H-3,5,6), 3.48-3.10 (overlapped signals, 14H, H-2,4), 2.90 (br, 2H, H-6). ^{13}C NMR (DMSO, 75 MHz): δ 130.7 (C1 *Ph*), 129.0 (C3,5 *Ph*), 127.8 (C4 *Ph*), 125.1 (C2,6 *Ph*), 122.0 (C5 *Triaz*), 102.0 (C1), 81.5 (C4), 74-71 (C2,3,5), 70 (C5'), 60-58 (C6), 50.8 (C6'). ESI-MS: Calculated for $C_{50}H_{75}N_3NaO_{34}$ $[M + Na]^+$ 1284.41, found 1284.30. For $C_{50}H_{75}N_3O_{34}$ (1262.13) calculated: 47.58% C, 5.99% H, 3.33% N; found: 47.79% C, 5.72% H, 3.40% N.

2.3. Heptakis(2,3-di-O-methyl)-hexakis(6-O-methyl)-6-monodeoxy-6-mono(4-phenyl-1,2,3-triazol-1-yl)-β-cyclodextrin.



TLC: silica gel plates, $CHCl_3$/MeOH 95/5, R_f=0.46.

Flash-Chromatography: RediSep column 4g Silica. Solvents: A = CH_2Cl_2 ; B = MeOH, gradient: Time/B%: 2/0, 2/2, 3/2, 2/5, 3/5% B, 1/10, 2/10, 2.5/50, 1.5/50. Flow 18 ml/min.

MW: 1542.66. White powder, Mp = 116°C. ^{1}H NMR ($CDCl_3$, 300MHz): δ 7.88 (s, 1H, H-5 *triaz*), 7.83 (d, *J*=6.9 Hz, 2H, H-2,6 *Ph*), 7.44 (dd, *J*=7.2, 6.9 Hz, 2H, H-3,5 *Ph*), 7.31 (t, *J*=7.2 Hz, 1H, H-

[1] Cintas, P.; Martina, K.; Robaldo, B.; Garella, D.; Boffa, L.; Cravotto, G. *Collect. Czech. Chem. Commun.* **2007**, *72*, 1014-1024.

4 *Ph*), 5.27 (d, *J*=3.6 Hz, 1H, H-1), 5.20-5.05 (overlapped signals, 7H, H-1,6'a), 4.57 (dd, *J*=7.8, 7.5 Hz, 1H, H-6'b), 4.19 (m, 1H, H-5'), 4.02-3.75 (overlapped signals, 10H, H-5,6), 3.70-3.40 (overlapped signals, 62H, H-3,4,6, CH_3O-2,3), 3.40-3.00 (overlapped signals 25H, H-2, CH_3O-6), 3.10 (br, 2H, H-6). ^{13}C NMR ($CDCl_3$, 75 MHz): δ 130.7 (C1 *Ph*), 129.0 (C3,5 *Ph*), 128.3 (C4 *Ph*), 125.7 (C2,6 *Ph*), 122.0 (C5 *Triaz*), 99.7-98.5 (C1), 83.5-81.3 (C2,3), 80.5-79.8 (C4), 71.6-71.4,70.6 (C6), 71.2-70.6 (C5), 61.9-61.4 (3-OCH_3), 59.3-58.7 (2,6-OCH_3), 51.8 (C6'). MS ESI (m/z): Calculated for $C_{70}H_{115}N_3NaO_{34}$ $[M + Na]^+$ 1564.72, found 1564.70 $[M + Na]^+$. For $C_{70}H_{115}N_3O_{34}$ (1542.66) calculated: 54.50% C, 7.51% H, 2.72% N; found: 54.62% C, 7.42% H, 2.83% N.

3. NMR analysis

3.1. NMR spectra of 6-monodeoxy-6-mono(4-phenyl-1,2,3-triazol-1-yl)-β-CD.

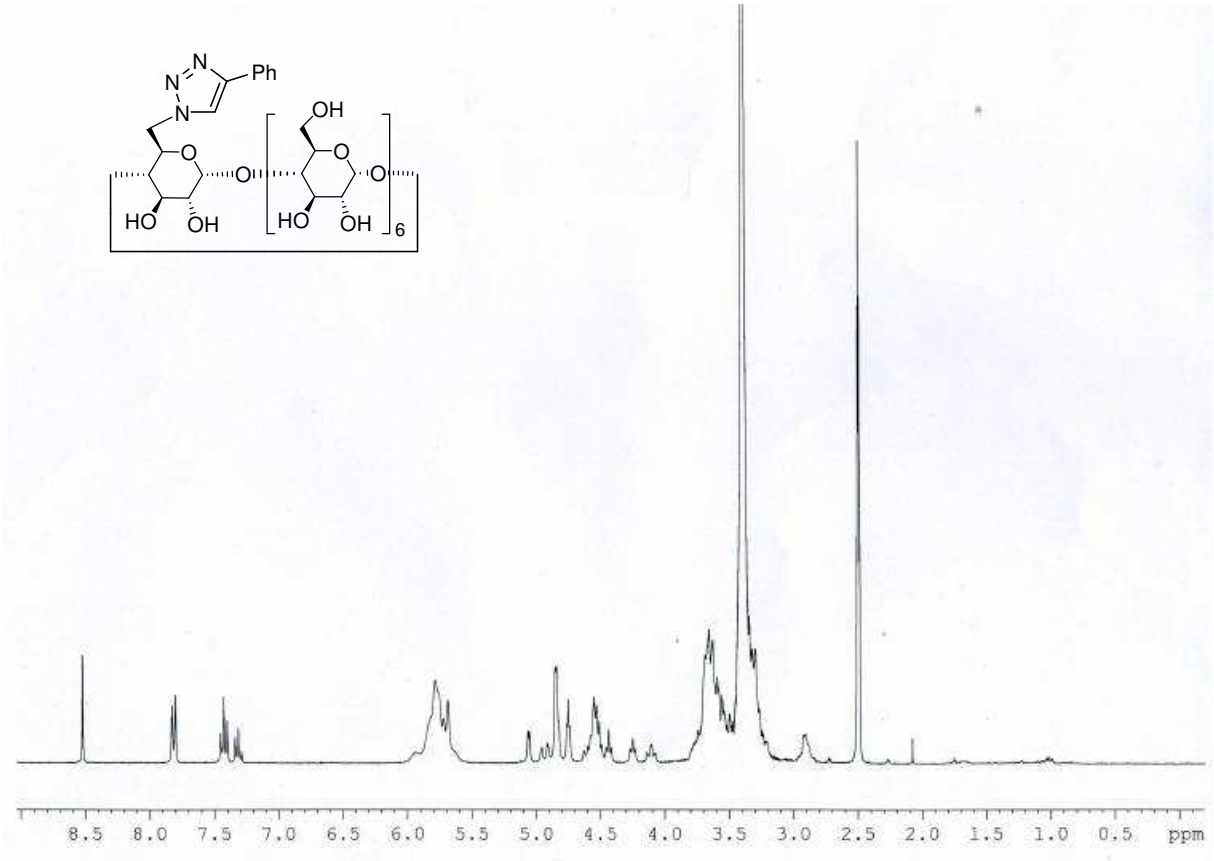


Figure S 1. ^1H NMR spectrum (300 MHz, $CDCl_3$) of 6-monodeoxy-6-mono(4-phenyl-1,2,3-triazol-1-yl)-β-CD.

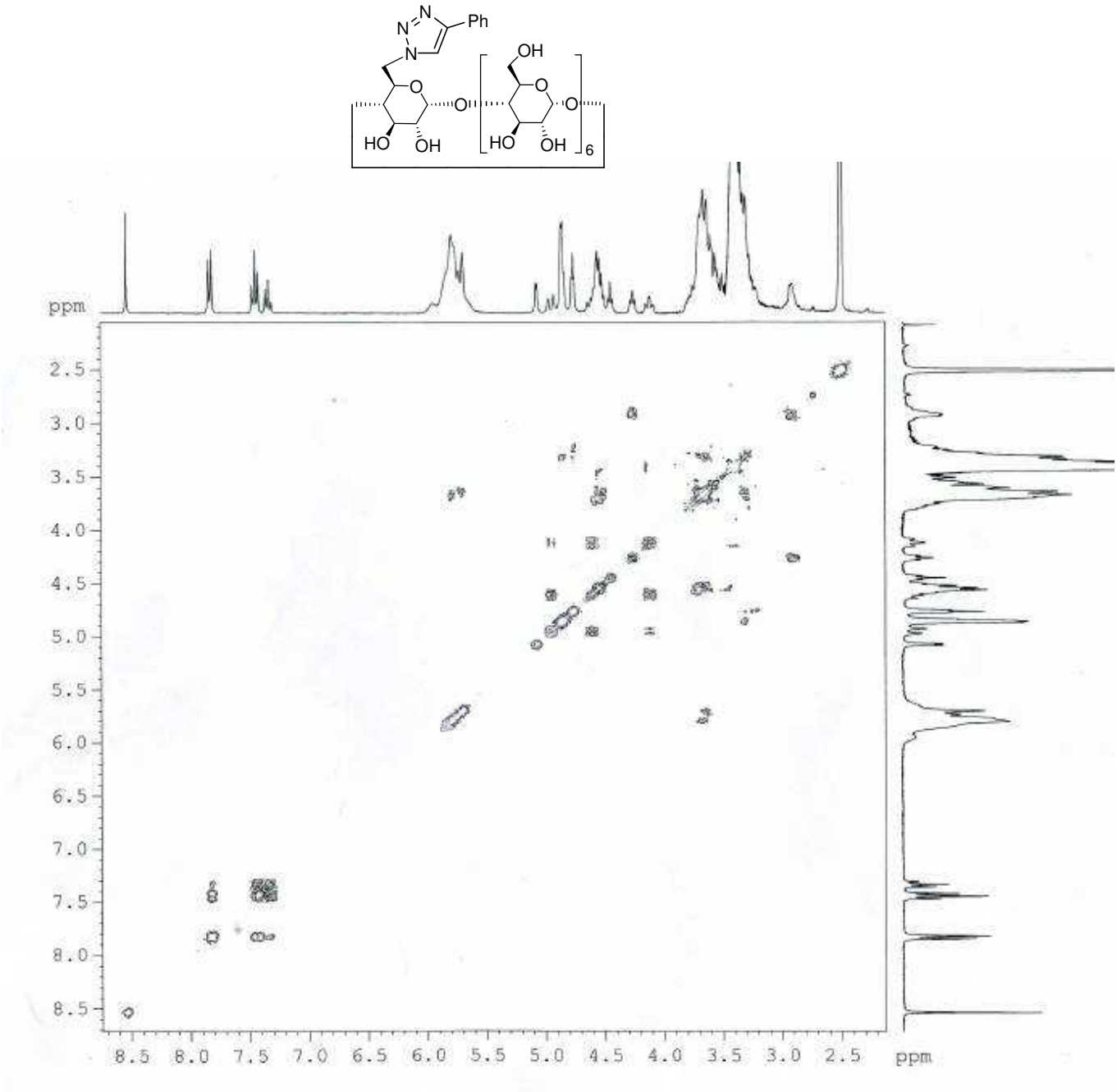


Figure S 2. COSY spectrum (300 MHz, $CDCl_3$) of 6-monodeoxy-6-mono(4-phenyl-1,2,3-triazol-1-yl)-β-CD.

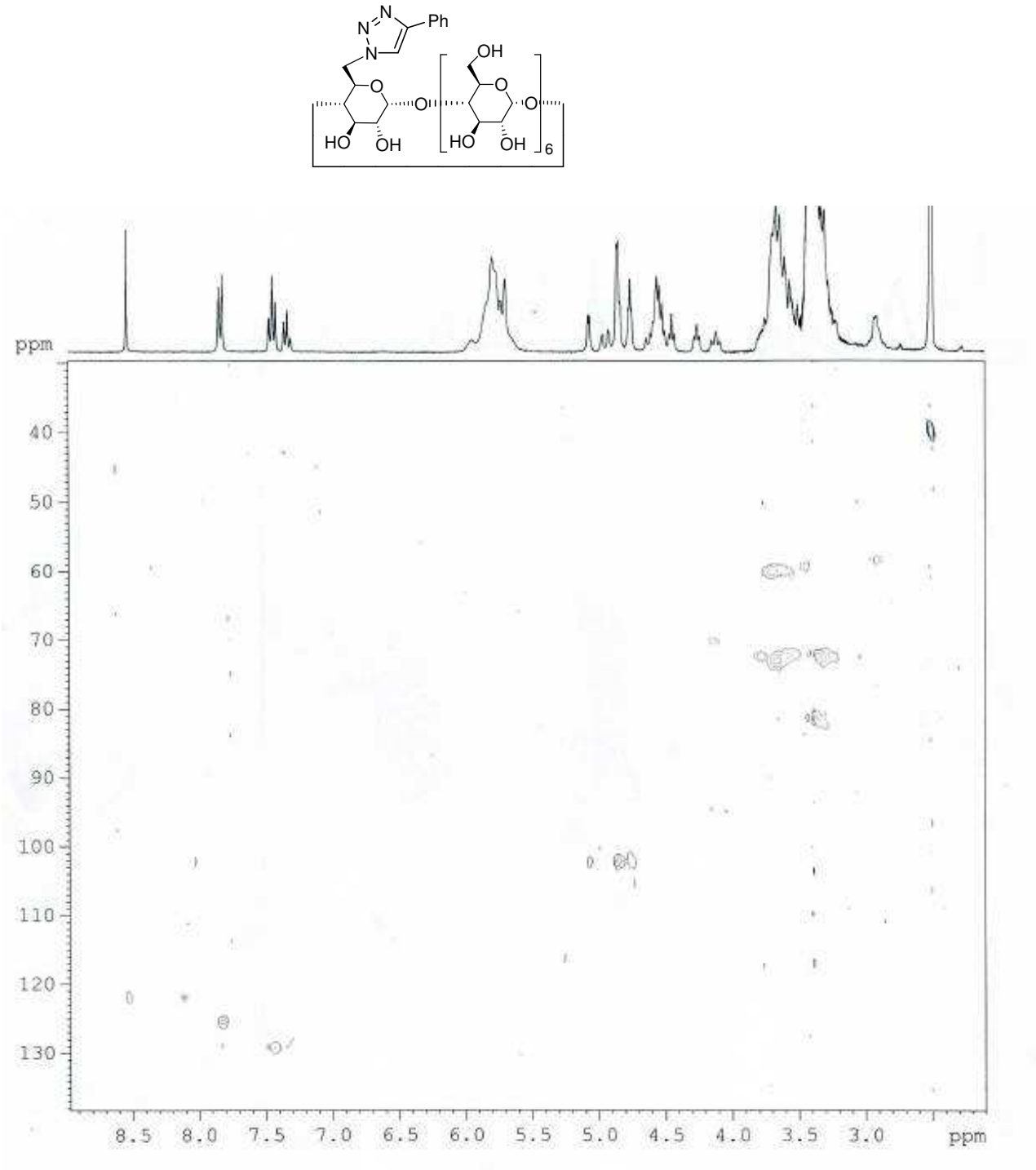


Figure S 3. HSQC spectrum (300 MHz, $CDCl_3$) of 6-monodeoxy-6-mono(4-phenyl-1,2,3-triazol-1-yl)-β-CD.

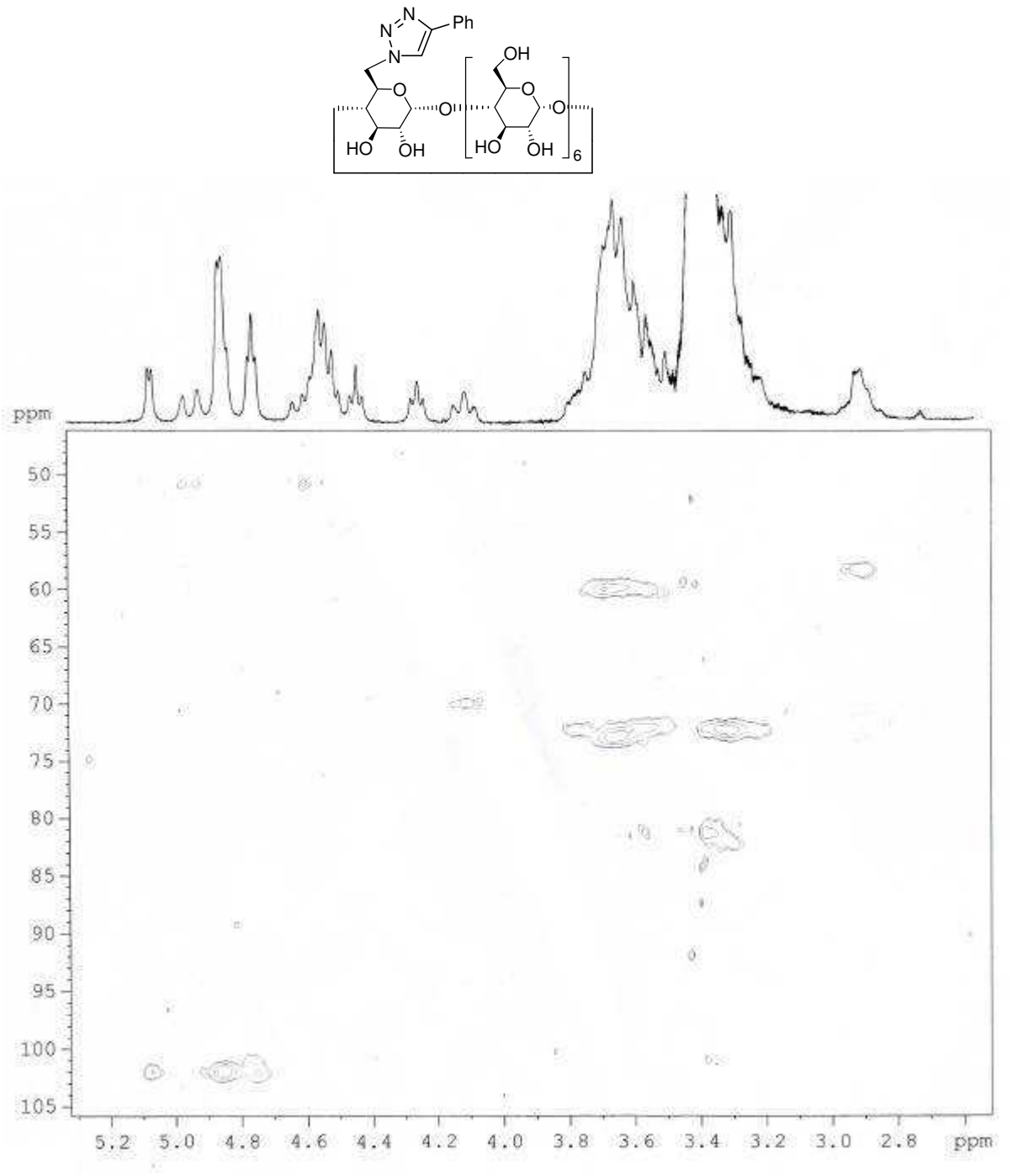


Figure S 4. HSQC spectrum (300 MHz, $CDCl_3$) of 6-monodeoxy-6-mono(4-phenyl-1,2,3-triazol-1-yl)-β-CD.

3.2 NMR spectra of heptakis(2,3-di-O-methyl)-hexakis(6-O-methyl)-6-monodeoxy-6-mono(4-phenyl-1,2,3-triazol-1-yl)-β-CD.

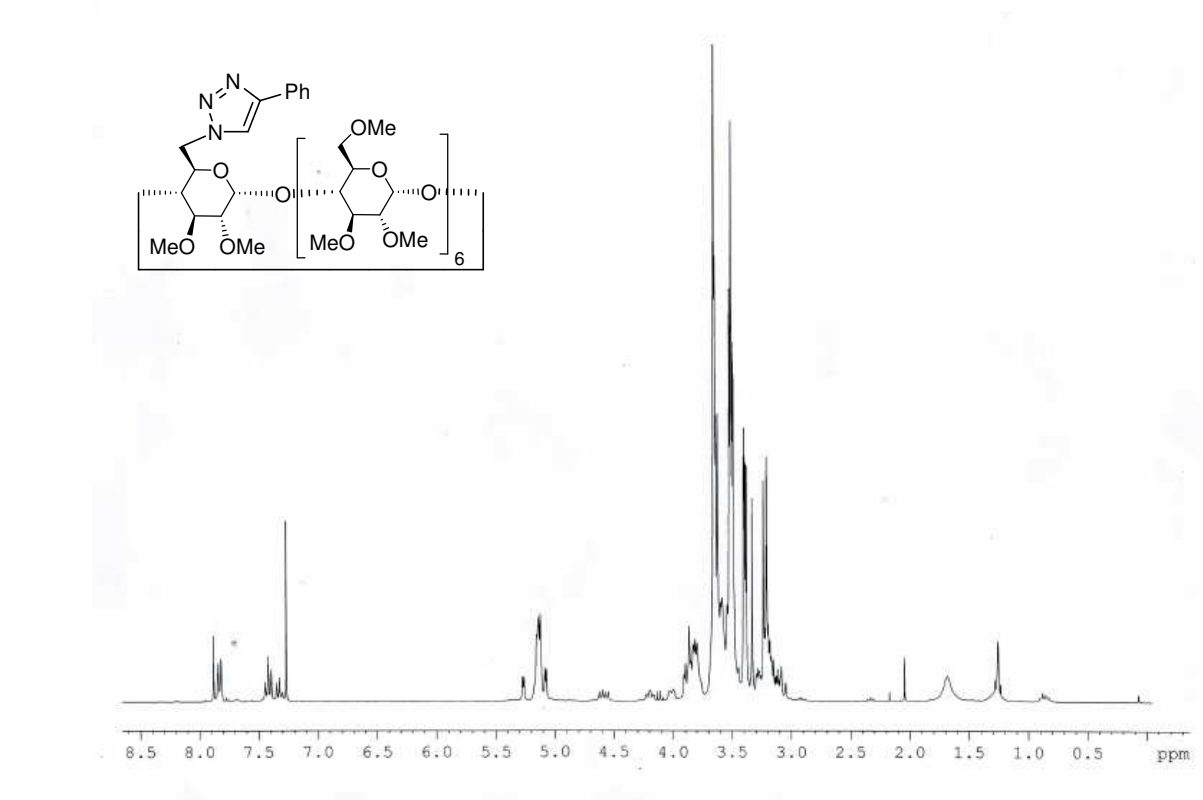


Figure S 5. ^{1}H NMR spectrum (300 MHz, $CDCl_3$) of heptakis(2,3-di-*O*-methyl)-hexakis(6-O-methyl)-6-monodeoxy-6-mono(4-phenyl-1,2,3-triazol-1-yl)-β-CD.

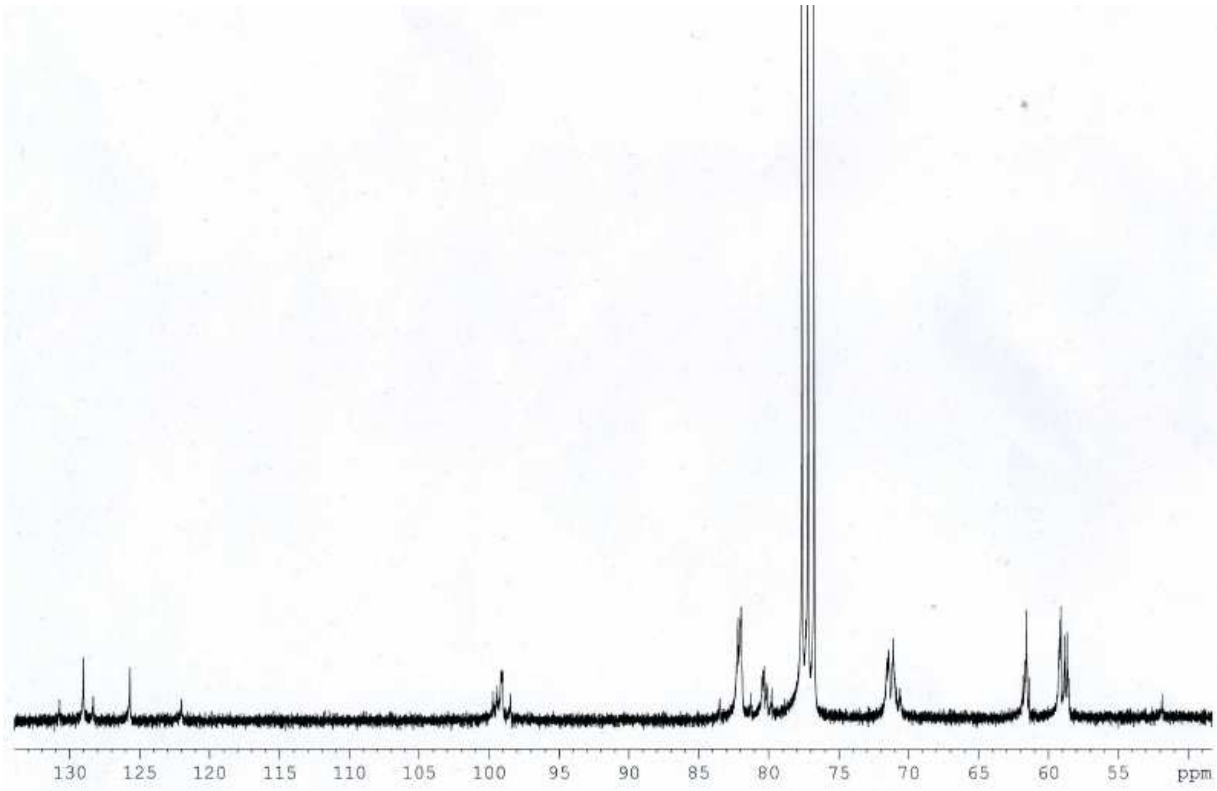
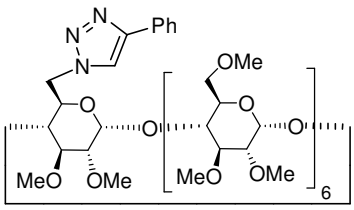


Figure S 6. ^{13}C NMR spectrum (300 MHz, CDCl3) of heptakis(2,3-di-*O*-methyl)-hexakis(6-*O*-methyl)-6-monodeoxy-6-mono(4-phenyl-1,2,3-triazol-1-yl)-β-CD.



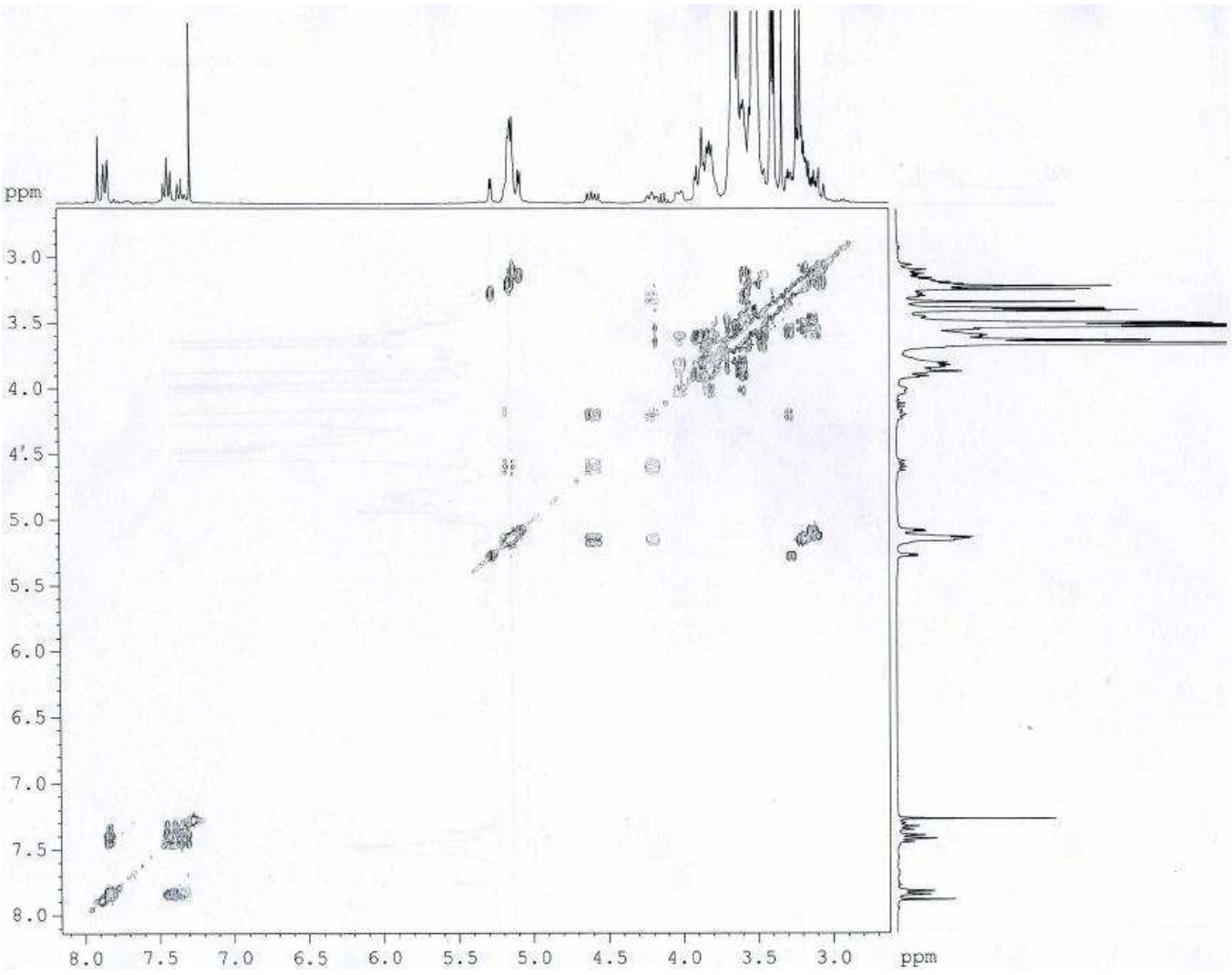


Figure S 7. COSY spectrum (300 MHz, $CDCl_3$) of heptakis(2,3-di-*O*-methyl)-hexakis(6-*O*-methyl)-6-monodeoxy-6-mono(4-phenyl-1,2,3-triazol-1-yl)-β-CD.

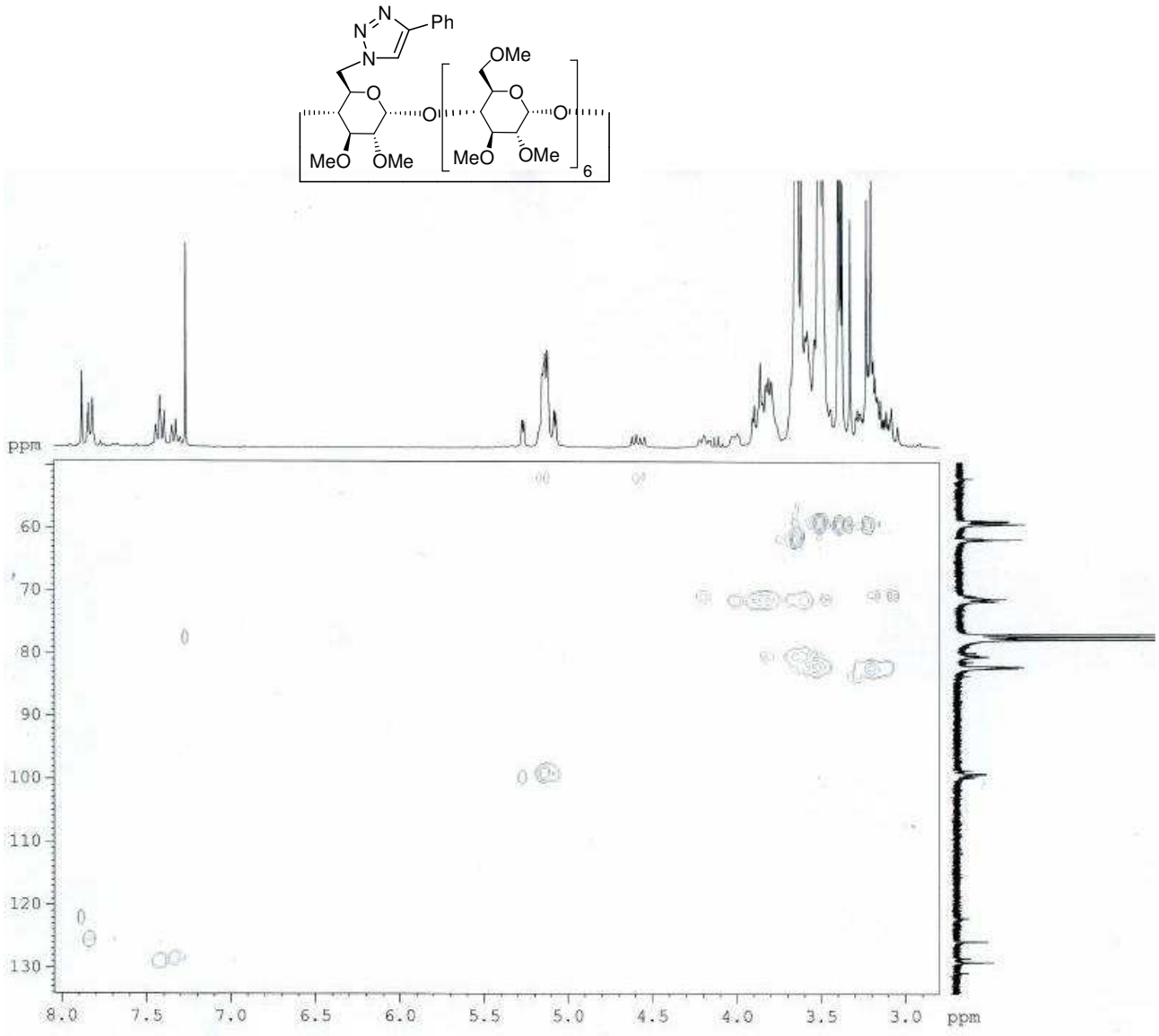


Figure S 8. HSQC spectrum (300 MHz, $CDCl_3$) of heptakis(2,3-di-*O*-methyl)-hexakis(6-*O*-methyl)-6-monodeoxy-6-mono(4-phenyl-1,2,3-triazol-1-yl)-β-CD.

4. Purification

4.1. Flash-chromatography of 6-monodeoxy-6-mono(4-phenyl-1,2,3-triazol-1-yl)-β-cyclodextrin.

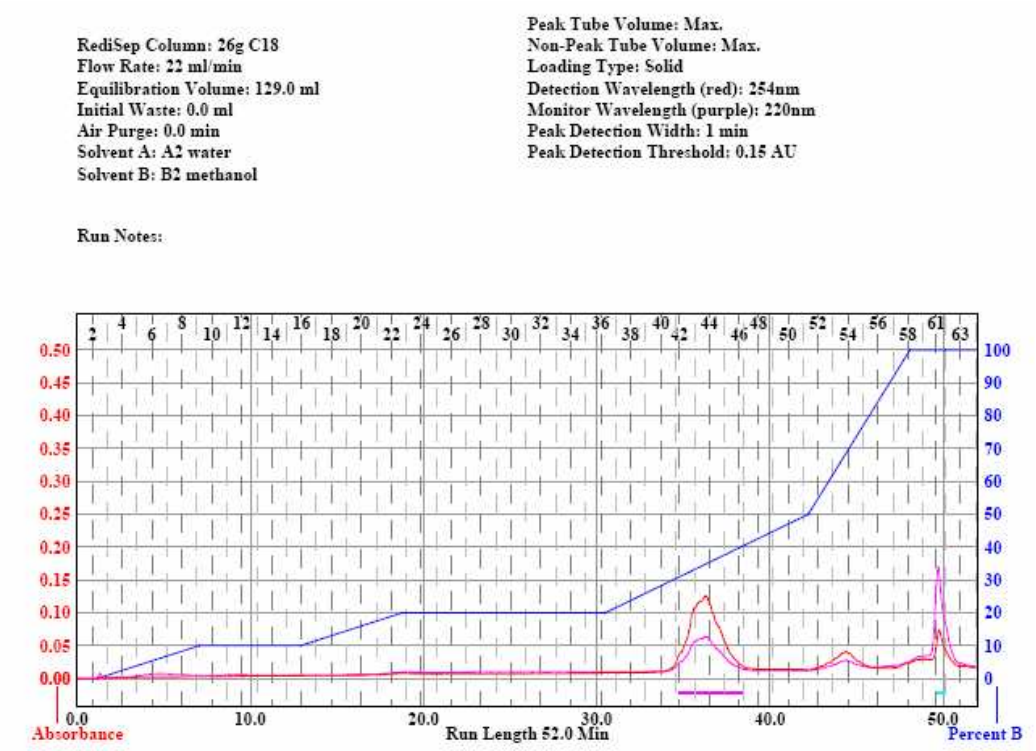


Figure S 9. Flash-chromatography on RP18.

4.2 Flash-chromatography of heptakis(2,3-di-O-methyl)-hexakis(6-O-methyl)-6-monodeoxy-6-mono(4-phenyl-1,2,3-triazol-1-yl)-β-CD.

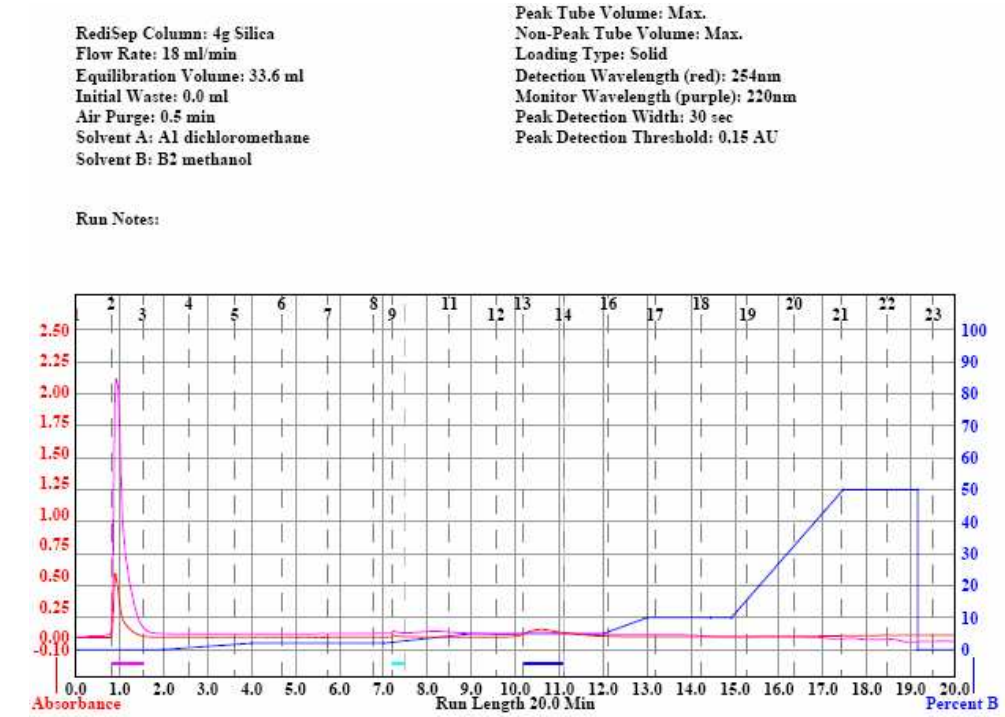


Figure S 10. Flash-chromatography on silica gel.