

Supporting Information

Single-molecule force spectroscopy of supramolecular heterodimeric capsules

Tobias Schröder,^{a,b} Thomas Geisler,^a Volker Walhorn,^b Björn Schnatwinkel,^a Dario Anselmetti^b and Jochen Mattay^a

^aOrganic Chemistry, Chemistry Faculty,

E-mail: oc1jm@uni-bielefeld.de

Homepage: www.uni-bielefeld.de/chemie/oc1/JM/mattay.html

^bExperimental Biophysics & Applied Nanoscience, Physics Faculty

Email: dario.anselmetti@physik.uni-bielefeld.de

Homepage: <http://www.physik.uni-bielefeld.de/biophysik/>

Universitätsstraße 25, D-33615 Bielefeld, Germany

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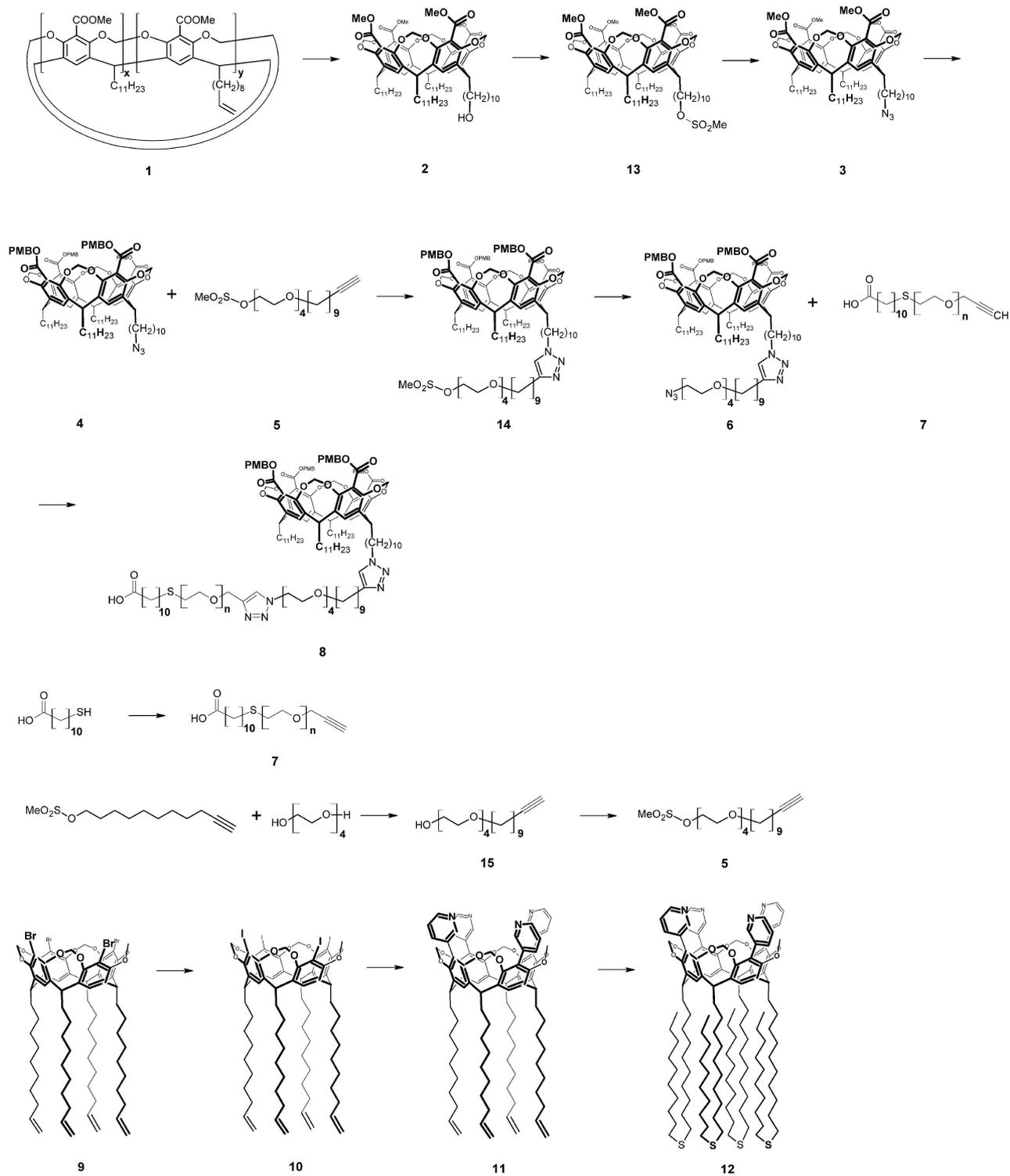
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Synthetic Procedures

General

Undec-10-ynyl methanesulfonate, tris-(benzyltriazolylmethyl)amine (TBTA) and $[\text{Pd}(\text{PPh}_3)_4]$ was prepared as described in the literature.¹⁻³ Tetrahydrofuran and toluene were distilled over potassium and sodium, respectively. Cavitands **3** and **9** were dried by azeotropic distillation of dry tetrahydrofuran and toluene from the substances as described in the literature.⁴ Ethylene oxide was condensed into a Schlenk flask, dried by addition of *n*-BuLi (1.6 M in hexanes) and condensed into a second Schlenk flask.⁵ Transferring the ethylene oxide into the reaction mixture was performed using a pre-cooled syringe. Ultra dry iodine was purchased from ABCR. All other reagents were purchased from Aldrich and used without further purification. Reaction mixtures were cooled to 0 °C and -5 °C using an ice bath and to -90 °C using ethanol cooled down with liquid nitrogen. Gel permeation chromatography (GPC) and HPLC was carried out using a PL gel column (Polymer Laboratorys, Amherst, USA) and Nucleosil 100-7 column (CS Chromatographie Service, Langerwehe, Germany), respectively. For column chromatography silica gel (MN 60, 0.063-0.2 mm, Macherey-Nagel, Düren, Germany) was used.

¹H NMR and ¹³C NMR spectra were recorded on a Bruker DRX 500 spectrometer. ¹H NMR and ¹³C NMR chemical shifts were referenced to residual CHCl₃ at $\delta = 7.27$ ppm and $\delta = 77.2$ ppm, respectively. ESI mass spectra and high resolution mass spectra (HRMS) were recorded using a Fourier Transform Ion Cyclotron Resonance (FT-ICR) mass spectrometer APEX III (Bruker Daltonik GmbH, Bremen, Germany) equipped with a 7.0 T, 160 mm bore superconducting magnet (Bruker Analytik GmbH – Magnetica, Karlsruhe, Germany), infinity cell, and interfaced to an external (nano)ESI ion source. Nitrogen served both as the nebulizer gas and the dry gas for ESI. Nitrogen was generated by a Bruker nitrogen generator NGM 11. Scan accumulation and fourier transformation were performed with XMASS NT (7.08) on a PC Workstation, for further data processing DataAnalysis™ 3.4 was used. MALDI ToF spectra were recorded at a Voyager DE mass spectrometer (Applied Biosystems, Foster City, California, USA).



Tetra(carboxyl)cavitand monofunctionalized at the *lower rim*

The tetra(carboxyl)cavitand with one PEG-linker at the *lower rim* was synthesized starting with a mixture of cavitands with 0-4 terminal double bonds at the *lower rim*, which was prepared following well established procedures.^{6,7} For the cyclisation of resorcin a mixture of undec-10-enal and lauric aldehyde (molar ratio 1:3) was used. The statistical mixture of cyclic tetramers with different numbers of double bonds at the *lower rim* was brominated, the double bonds restored by debromination, the hydroxyl groups reacted with bromochloromethane and the cavitand lithiated and reacted with methyl chloroformate.⁷

Alcohol **2**

To a solution of mixture of cavitands **1** with double bonds at the *lower rim* (72.3 g) in dry THF (500 ml) 9-BBN (0.5 M in THF, 100 mL, 50 mmol) added under argon. After stirring the reaction mixture 24 h at room temperature it was cooled to 0 °C and sodium acetate (3 M in water, 90 mL) and hydrogen peroxide (30 % w/w in water, 55 mL) was added slowly. The solution was stirred at room temperature for 18 h and sodium bisulfite (40 % w/w in water, 200 mL) and ethyl acetate (200 mL) was added. The aqueous phase was extracted two times with ethyl acetate (400 mL) and the combined organic phases dried over MgSO₄. Purification (column chromatography, silica gel, 45 % ethyl acetate/ cyclohexane) yielded the product **2** (7.5 g) as a white solid.

¹H-NMR (500.1 MHz, CDCl₃, 300 K) δ = 7.16 (s, 4 H, ArH), 5.66 (d, *J* = 7.5 Hz, 4 H, OCHHO), 4.75 (dd, *J* = 8.0, 8.0 Hz, 4 H, Ar₂CH), 4.57 (d, *J* = 7.5 Hz, 4 H, OCHHO), 3.85 (s, 12 H, COOCH₃), 3.64 (t, *J* = 6.5 Hz, 2 H, CH₂OH), 2.20 (m, 8 H, Ar₂CH-CH₂), 1.57 (m, 2 H, CH₂CH₂OH), 1.41 (m, 8 H), 1.36-1.25 (m, 60 H), 0.89 (t, *J* = 7.0 Hz, 9 H, CH₃) ppm. ¹³C-NMR (125.8 MHz, CDCl₃, 300 K) δ = 165.7, 151.5, 138.4, 138.4, 123.6, 121.7, 99.8, 63.2, 52.8, 36.3, 36.2, 32.9, 32.1, 29.9, 29.8, 29.8, 29.7, 29.7, 29.6, 29.5, 27.9, 27.8, 25.9, 22.8, 14.3 ppm. *m/z* (HRMS ESI) found: 1404.87340; calcd for [C₈₃H₁₂₂NO₁₇]⁺: 1404.87073; found: 1409.82911; calcd for [C₈₃H₁₁₈O₁₇Na]⁺: 1409.82612.

Methanesulfonate **13**

To a solution of alcohol **2** (7.4 g, 5.3 mmol) and triethylamine (1.8 mL, 1.3 g, 13 mmol) in dry dichloromethane (50 mL) methanesulfonyl chloride (1.0 mL, 1.5 g, 13 mmol) was added at 0 °C and the reaction mixture stirred under argon at room temperature for 22 h. The solvent was removed under reduced pressure and the residue purified by column chromatography (silica gel, 70 % ethyl acetate/ cyclohexane). The product **13** (7.3 g, 93 %) was obtained as a colorless oil.

¹H-NMR (500.1 MHz, CDCl₃, 300 K) δ = 7.16 (s, 4 H, ArH), 5.66 (d, *J* = 7.5 Hz, 4 H, OCHHO), 4.77-4.74 (m, 4 H, Ar₂CH), 4.57 (d, *J* = 7.5 Hz, 4 H, OCHHO), 4.23 (t, *J* = 6.5 Hz, 2 H, CH₂OSO₂CH₃), 3.85 (s, 12 H, COOCH₃), 3.01 (s, 3 H, SO₂CH₃), 2.20 (m, 8 H, Ar₂CHCH₂), 1.75 (m, 2 H), 1.41 (m, 8 H), 1.34-1.24 (m, 60 H), 0.89 (t, *J* = 7.0 Hz, 9 H, CH₃) ppm. ¹³C-NMR (125.8 MHz, CDCl₃, 300 K) δ = 165.7, 165.7, 151.5, 138.4, 138.4, 138.4, 123.6, 121.7, 99.7, 70.3, 52.8, 37.5, 36.3, 36.2, 32.1, 29.9, 29.8, 29.7, 29.7, 29.6, 29.5, 29.3, 29.2, 27.9, 27.8, 25.6, 22.8, 14.3 ppm. *m/z* (HRMS ESI) found: 1487.80437; calcd for [C₈₄H₁₂₀O₁₉SNa]⁺: 1487.80367; found: 1482.84901; calcd for [C₈₄H₁₂₄NO₁₉S]⁺: 1482.84828.

Azide **3**

A solution of cavitand **13** (7.2 g, 4.9 mmol) and sodium azide (3.5 g, 54 mmol) in DMPU (50 mL) was stirred for 16 h at 60 °C. The solvent was evaporated under reduced pressure and the residue dissolved in dichloromethane (100 mL) and water (100 mL). The aqueous phase was extracted three times with dichloromethane (300 mL), the combined organic phases dried over MgSO₄ and the solvent evaporated. Column chromatography (silica gel, 2 % methanol/ chloroform) and GPC (chloroform) yielded **3** (4.4 g, 63 %) as a white solid.

¹H-NMR (500.1 MHz, CDCl₃, 300 K) δ = 7.16 (s, 4 H, ArH), 5.66 (d, *J* = 7.5 Hz, 4 H, OCHHO), 4.76 (t, *J* = 8.0 Hz, 4 H, Ar₂CH), 4.58 (d, *J* = 7.5 Hz, 4 H, OCHHO), 3.85 (s, 12 H, COOCH₃), 3.27 (t, *J* = 7.0 Hz, 2 H, CH₂N₃), 2.20 (m, 8 H, Ar₂CHCH₂), 1.61 (m, 2 H), 1.41 (m, 8 H), 1.35-1.25 (m, 60 H), 0.89 (t, *J* = 7.0 Hz, 9 H, CH₃) ppm. ¹³C-NMR (125.8 MHz, CDCl₃, 300 K) δ = 165.7, 151.5, 138.4, 138.4, 123.6, 121.7, 99.8, 52.8, 51.6, 36.3, 36.2, 33.9, 32.1, 29.9, 29.8, 29.7, 29.6, 29.5, 29.3, 29.1, 29.0, 27.9, 27.8, 26.9, 22.8, 14.3 ppm. *m/z* (HRMS ESI) found: 1434.83219; calcd for [C₈₃H₁₁₇N₃O₁₆Na]⁺: 1434.83261; found: 1429.87791; calcd for [C₈₃H₁₂₁N₄O₁₆]⁺: 1429.87721.

p-Methoxybenzyl ester **4**

A mixture of dry methyl ester **3** (64 mg, 0.045 mmol), sodium *tert*-butoxide (64 mg, 0.67 mmol), 4-*tert*-butylphenol (64 mg, 0.43 mmol) and *p*-methoxybenzyl acetate (500 μL, 2.51 mmol) was stirred 5 h under vacuum (< 0.1 mbar) at room temperature. The viscous reaction mixture was filtrated through silica gel using ethyl acetate as solvent and the crude product purified by column chromatography (silica gel suspended in 35 % ethyl acetate/ cyclohexane, elution with 5 % methanol/ chloroform) and GPC (chloroform). The *p*-methoxybenzyl ester **4** (68 mg, 82 %) was obtained as white solid.

¹H-NMR (500.1 MHz, CDCl₃, 300 K) δ = 7.34 (d, *J* = 8.5 Hz, 8 H, Ar_{PMB}H), 7.08 (s, 4 H, ArH), 6.92 (d, *J* = 8.5 Hz, 8 H, Ar_{PMB}H), 5.23 (d, *J* = 7.5 Hz, 4 H, OCHHO), 5.20 (s, 8 H, COOCH₂Ar), 4.68 (t, *J* = 8.0 Hz, 4 H, OCHHO), 4.38 (d, *J* = 7.5 Hz, 4 H, OCHHO), 3.82 (s, 12 H, OCH₃), 3.26 (t, *J* = 7.0 Hz, 2 H, CH₂N₃), 2.14 (m, 8 H, Ar₂CHCH₂), 1.60 (m, 2 H), 1.37 (m, 8 H), 1.32-1.24 (m, 60 H), 0.89 (t, *J* = 7.0 Hz, 9 H, CH₃) ppm. ¹³C-NMR (125.8 MHz, CDCl₃, 300 K) δ = 165.0, 160.0, 151.6, 138.3, 138.3, 130.7, 127.7, 123.4, 121.6, 114.1, 99.7, 67.2, 55.4, 51.6, 36.3, 36.2, 32.1, 29.9, 29.9, 29.8, 29.6, 29.5, 29.3, 29.0, 27.9, 27.8, 26.8, 22.8, 14.3 ppm. *m/z* (HRMS ESI) found: 1859.00390; calcd for [C₁₁₁H₁₄₁N₃O₂₀Na]⁺: 1859.00007.

O-(Undec-10-ynyl)-tetra(ethylene glycol) **15**

To a solution of tetra(ethylene glycol) (530 μL, 596 mg, 3.07 mmol) in dry THF (10 mL) sodium hydride (60 % dispersion in mineral oil, 106 mg, 4.40 mmol) was added in portions at 0 °C under argon. A solution of undec-10-ynyl methanesulfonate (530 mg, 2.15 mmol) in dry THF (20 mL) was dropped to the stirred mixture at 90 °C during the course of 2 h using a syringe pump. After stirring for 16 h at 90 °C the solution was cooled to room temperature and filtered through silica gel (using a mixture of 2 % methanol/ chloroform as eluent). The solvent was evaporated and the crude product purified by column chromatography (silica gel, gradient elution: chloroform to 2 % methanol/ chloroform) to give **15** (420 mg, 57 %) as a colorless oil.

¹H-NMR (500.1 MHz, CDCl₃, 300 K) δ = 3.70 (t, *J* = 4.5 Hz, 2 H), 3.64 (m, 8 H), 3.61 (m, 2 H), 3.58 (m, 2 H), 3.56 (m, 2 H), 3.42 (t, *J* = 7.0 Hz, 2 H), 2.88 (br s, 1 H, OH), 2.15 (dt, *J* = 7.0, 2.5 Hz, 2 H, CH₂-C≡CH), 1.92 (t, *J* = 2.5 Hz, 1 H, C≡CH), 1.56 (m, 2 H), 1.49 (m, 2H), 1.36 (m, 2 H), 1.27 (br s, 8 H) ppm. ¹³C-NMR (125.8 MHz, CDCl₃, 300 K) δ = 84.8, 72.8, 71.6, 70.7, 70.6, 70.6, 70.3, 70.1, 68.1, 61.7, 29.6, 29.5, 29.4, 29.1, 28.8, 28.5, 26.1, 18.4 ppm. *m/z* (HRMS ESI) found: 367.24512; calcd for [C₁₉H₃₆O₅Na]⁺: 367.24550.

O-(Undec-10-ynyl)-tetra(ethylene glycol) methanesulfonate **5**

To a solution of *O*-(undec-10-ynyl)-tetra(ethylene glycol) **15** (394 mg, 1.14 mmol) and triethylamine (250 μ L, 176 mg, 1.74 mmol) in dry dichloromethane (8 mL) methanesulfonyl chloride (135 μ L, 200 mg, 1.74 mmol) was added at 0 °C and the reaction mixture stirred under argon at room temperature for 22 h. The solvent was removed under reduced pressure and the residue purified by column chromatography (silica gel, 70 % ethyl acetate/ cyclohexane). The product **5** (433 mg, 88 %) was obtained as a colorless oil.

$^1\text{H-NMR}$ (500.1 MHz, CDCl_3 , 300 K) δ = 4.37 (m, 2 H, $\text{CH}_2\text{-SO}_2\text{Me}$), 3.75 (m, 2 H), 3.66-3.61 (m, 10 H, $\text{O-CH}_2\text{CH}_2\text{-O}$), 3.56 (m, 2 H), 3.43 (t, J = 7.0 Hz, 2 H), 3.07 (s, 3 H, $\text{SO}_2\text{-CH}_3$), 2.16 (dt, J = 7.0, 2.5 Hz, 2 H, $\text{CH}_2\text{-C}\equiv\text{CH}$), 1.93 (t, J = 2.5 Hz, 1 H, $\text{C}\equiv\text{CH}$), 1.56 (m, 2 H), 1.50 (m, 2 H), 1.37 (m, 2 H), 1.28 (m, 8 H) ppm. $^{13}\text{C-NMR}$ (125.8 MHz, CDCl_3 , 300 K) δ = 84.8, 71.6, 70.7, 70.7, 70.7, 70.6, 70.1, 69.4, 69.1, 68.2, 37.8 (SO_2CH_3), 29.7, 29.5, 29.5, 29.1, 28.8, 28.5, 26.1, 18.5 ppm. m/z (HRMS ESI) found: 445.22274 ; calcd for $[\text{C}_{20}\text{H}_{38}\text{O}_7\text{SNa}]^+$: 445.22305, found: 440.26735; calcd for $[\text{C}_{20}\text{H}_{42}\text{O}_7\text{SN}]^+$: 440.26765.

Methanesulfonate **14**

A solution of **4** (66 mg, 0.036 mmol), *O*-(undec-10-ynyl)-tetra(ethylene glycol) methanesulfonate (**5**) (17 mg, 0.040 mmol), sodium ascorbate (65 mg, 0.33 mmol) and copper sulfate (4.5 mg, 0.028 mmol) in a degassed mixture (6 mL) of THF, ethanol and water (2:2:1) (0.6 mL) was stirred 15 h under argon at 80 °C. The solvent was evaporated and the residue purified by column chromatography (silica gel, gradient elution 50 % ethyl acetate/ cyclohexane to 100 % ethyl acetate). The product **14** (44 mg, 54 %) was obtained as a white solid.

$^1\text{H-NMR}$ (500.1 MHz, CDCl_3 , 300 K) δ = 7.34 (d, J = 8.5 Hz, 8 H, $\text{Ar}_{\text{PMB}}\text{H}$), 7.24 (s, 1 H, $=\text{CH}$), 7.08 (s, 4 H, ArH), 6.92 (d, J = 8.5 Hz, 8 H, $\text{Ar}_{\text{PMB}}\text{H}$), 5.23 (d, J = 7.5 Hz, 4 H, OCHHO), 5.20 (s, 8 H, COOCH_2Ar), 4.68 (t, J = 8.0 Hz, 4 H, Ar_2CH), 4.40-4.37 (m, 6 H, OCHHO and CH_2), 4.29 (t, J = 7.5 Hz, 2 H), 3.82 (s, 12 H, OCH_3), 3.78 (m, 2 H), 3.69-3.63 (m, 10 H, $\text{O-CH}_2\text{CH}_2\text{-O}$), 3.59-3.57 (m, 2 H), 3.45 (t, J = 6.5 Hz, 2 H), 3.09 (s, 3 H, SO_2CH_3), 2.71 (t, J = 8.0 Hz, 2 H), 2.14 (m, 8 H, Ar_2CHCH_2), 1.87 (m, 2 H), 1.66 (m, 2 H), 1.57 (m, 2 H), 1.40-1.20 (m, 78 H), 0.88 (t, J = 7.0 Hz, 9 H, CH_3) ppm. $^{13}\text{C-NMR}$ (125.8 MHz, CDCl_3 , 300 K) δ = 165.0, 160.0, 151.5, 148.4, 138.3, 138.3, 138.2, 130.6, 127.7, 123.4, 121.6, 120.5, 114.1, 99.7, 71.7, 70.8, 70.7, 70.6, 70.2, 69.4, 69.2, 67.2, 55.4, 50.3, 37.9, 36.3, 36.2, 33.9, 32.1, 30.5, 29.9, 29.8, 29.7, 29.6, 29.6, 29.5, 29.5, 29.4, 29.2, 27.9, 26.7, 26.2, 25.8, 22.8, 14.3 ppm. m/z (HRMS ESI) found: 1152.11350; calcd for $[\text{C}_{131}\text{H}_{179}\text{N}_3\text{O}_{27}\text{SNa}_2]^{2+}$: 1152.11156; found: 2281.24009; calcd for $[\text{C}_{131}\text{H}_{179}\text{N}_3\text{O}_{27}\text{SNa}]^+$: 2281.23389.

Azide **6**

Cavitand **14** (43 mg, 0.019 mmol) and sodium azide (12 mg, 0.19 mmol) were dissolved in DMPU (3 mL) and the solution stirred 16 h at 60 °C. The solvent was evaporated under reduced pressure and the residue dissolved in dichloromethane (2 mL) and water (10 mL). The aqueous phase was extracted three times with dichloromethane (30 mL), the combined organic phases dried over MgSO₄ and the solvent evaporated. Column chromatography (silica gel, 2 % methanol/ chloroform) yielded **6** (28 mg, 67 %) as a white solid.

¹H-NMR (500.1 MHz, CDCl₃, 300 K) δ = 7.34 (d, *J* = 8.5 Hz, 8 H, Ar_{PMB}H), 7.24 (s, 1 H, =CH), 7.08 (s, 4 H, ArH), 6.91 (d, *J* = 8.5 Hz, 8 H, Ar_{PMB}H), 5.23 (d, *J* = 7.5 Hz, 4 H, OCHHO), 5.20 (s, 8 H, COOCH₂Ar), 4.68 (t, *J* = 8.0 Hz, 4 H, Ar₂CH), 4.38 (d, *J* = 7.5 Hz, 4 H, OCHHO), 4.29 (t, *J* = 7.5 Hz, 2 H), 3.82 (s, 12 H, OCH₃), 3.69-3.64 (m, 12 H, O-CH₂CH₂-O), 3.59-3.58 (m, 2 H), 3.47-3.43 (m, 2 H), 3.40 (t, *J* = 5.0 Hz, 2 H), 2.70 (t, *J* = 8.0 Hz, 2 H), 2.14 (m, 8 H, Ar₂CHCH₂), 1.87 (m, 2 H), 1.66 (m, 2 H), 1.58 (m, 2 H), 1.40-1.22 (m, 78 H), 0.88 (t, *J* = 7.0 Hz, 9 H, CH₃) ppm. ¹³C-NMR (125.8 MHz, CDCl₃, 300 K) δ = 165.0, 160.0, 151.5, 148.5, 138.3, 138.3, 138.2, 130.6, 127.7, 123.4, 121.6, 120.4, 114.1, 99.7, 71.7, 70.8, 70.8, 70.7, 70.2, 67.2, 55.4, 50.8, 50.3, 36.3, 36.2, 32.1, 30.5, 29.9, 29.8, 29.7, 29.7, 29.6, 29.6, 29.5, 29.5, 29.4, 29.2, 29.2, 28.9, 28.6, 27.9, 27.8, 26.7, 26.2, 25.9, 22.8, 14.3 ppm *m/z* (HRMS ESI) found: 2228.26682; calcd for [C₁₃₀H₁₇₆N₆O₂₄Na]⁺: 2228.26282; found: 1114.63575; calcd for [C₁₃₀H₁₇₆N₆O₂₄NaH]²⁺: 1114.63505.

O-(2-(10-carboxydecylthio)ethyl)-*O*'-propargylpoly(ethylene glycol) **7**⁵

To a solution of 11-mercaptoundecanoic acid (200 mg, 0.916 mmol) in dry THF (50 mL) potassium-naphthalene (0.90 mL, 2 M in THF, 1.8 mmol) was added, until a pale green color appeared. The reaction mixture was cooled to -5 °C and dry ethylene oxide (5.0 mL, 4.4 g, 0.10 mol) was added via a cooled syringe. The reactor was sealed and the solution stirred 1 h at 40 °C. After stirring at room temperature for three days, the mixture was cooled to -5 °C and a second portion of dry ethylene oxide (7.0 mL, 6.2 g, 0.14 mol) was added. The solution was stirred 3 h at 40 °C and 16 h at room temperature. To the vigorously stirred reaction mixture a solution of propargyl bromide (99 μL, 80 % in toluene, 0.91 mmol) in dry toluene (20 mL) was added at room temperature during the course of 1.5 h using a syringe pump. The solution was stirred for 1 h at room temperature and poured into diethyl ether (200 mL). The suspension was centrifuged and the precipitate was dissolved in dichloromethane (30 mL). After centrifugation the solvent was removed from the solution to yield **7** (4.3 g) as a colorless solid.

¹H-NMR (500.1 MHz, CDCl₃, 300 K) δ = 4.17 (d, *J* = 2.5 Hz, 2 H, O-CH₂-C≡CH), 3.73 (t, *J* = 5.0 Hz, 2 H), 3.61 (br s, 740 H, O-CH₂CH₂-O) 3.49 (t, *J* = 5.0 Hz, 2 H), 2.67 (dd, *J* = 7.0 Hz, 2 H), 2.50 (t, *J* = 7.5 Hz, 2 H), 2.42 (t, *J* = 2.5 Hz, 1 H, C≡CH), 2.26 (t, *J* = 7.5 Hz, 1H), 1.60-1.51 (m, 4 H), 1.34-1.24 (m, 12 H) ppm.

MALDI-ToF-MS: See mass spectrum below.

PEGylated cavitand **8**

A solution of cavitand **6** (40 mg, 0.018 mmol), *O*-(2-(10-carboxydecylthio)ethyl)-*O'*-propargylpoly(ethylene glycol) (**7**) (318 mg), sodium ascorbate (513 mg, 2.59 mmol), copper sulfate (67 mg, 0.42 mmol) and TBTA (93 mg, 0.17 mmol) in a degassed mixture (16 mL) of THF, ethanol and water (2:2:1) was stirred 16 h under argon at 70 °C. The solvent was evaporated, the residue suspended in a small amount of a mixture of methanol (10 %) and chloroform and purified by column chromatography (silica gel, 10 % methanol/ chloroform) and GPC (chloroform). The product **8** (55 mg) was obtained as a pale yellow solid.

¹H-NMR (500.1 MHz, CDCl₃, 300 K) δ = 7.74 (s, 1 H, =CH), 7.33 (d, *J* = 8.5 Hz, 8 H, Ar_{PMB}H), 7.23 (s, 1 H, =CH), 7.07 (s, 4 H, ArH), 6.90 (d, *J* = 8.5 Hz, 8 H, Ar_{PMB}H), 5.22 (d, *J* = 7.5 Hz, 4 H, OCHHO), 5.19 (s, 8 H, COOCH₂Ar), 4.68-4.65 (m, 6 H, Ar₂CH and CH₂), 4.53 (t, *J* = 5.0 Hz, 2 H), 4.37 (d, *J* = 7.5 Hz, OCHHO), 4.28 (t, *J* = 7.5 Hz, 2 H), 3.87 (t, *J* = 5.0 Hz, 2 H), 3.81 (s, 12 H, OCH₃), 3.76 (t, *J* = 5.0 Hz, 2 H), 3.70-3.61 (m, 474 H, O-CH₂CH₂-O), 3.57-3.56 (m, 2 H), 3.53-3.51 (m, 2 H), 3.43 (t, *J* = 7.0 Hz, 2 H), 2.71-2.68 (m, 4 H), 2.54 (t, *J* = 7.5 Hz, 2 H), 2.31 (t, *J* = 7.5 Hz, 2 H), 2.13 (m, 8 H, Ar₂CHCH₂), 1.86 (m, 2 H), 1.67-1.54 (m, 8 H), 1.40-1.22 (m, x H), 0.87 (t, *J* = 7.0 Hz, 9 H, CH₃) ppm.

MALDI-ToF-MS: See mass spectrum below.

Tetra(iodo)cavitand **10**

A solution of dry tetra(bromo)cavitand **9**⁶ (1.73 g, 1.23 mmol) in dry THF (100 mL) was cooled to -90 °C and *n*-butyllithium (1.6 M in hexane, 8.0 mL, 13 mol) was added under argon. The reaction mixture was stirred at -90 °C for 1 h, dry iodine (6.4 g, 25 mmol) was added and the solution allowed to reach room temperature during the course of 16 h. In a separatory funnel the reaction mixture was washed with sodium bisulfite (40 % in water, 50 mL) and water (30 mL) and the aqueous phase was extracted with ethyl acetate (300 mL). The combined organic phases were dried with MgSO₄ and the crude product purified by column chromatography (silica gel, 60 % chloroform/ cyclohexane) to yield the tetra(iodo)cavitand **10** (538 mg, 27 %) as a white solid.

¹H-NMR (500.1 MHz, CDCl₃, 300 K) δ = 7.06 (s, 4 H, ArH), 5.98 (d, *J* = 7.5 Hz, 4 H, OCHHO), 5.82 (ddt, *J* = 17.0, 10.0, 6.5 Hz, 4 H, -CH₂CH=CH₂), 5.01 (dd, *J* = 17.0, 1.5 Hz, 4 H, CH=CH_{cis}H_{trans}), 4.95 (dd, *J* = 10.0, 1.0 Hz, 4 H, CH=CH_{cis}H_{trans}), 4.86 (t, *J* = 8.0 Hz, 4 H, Ar₂CH), 4.33 (d, *J* = 7.5 Hz, 4 H, OCHHO), 2.20 (m, 8 H, Ar₂CHCH₂), 2.05 (m, 8 H, CH₂CH=CH₂), 1.45-1.29 (m, 48 H) ppm. ¹³C-NMR (125.8 MHz, CDCl₃, 300 K) δ = 155.0, 139.2, 138.8, 120.8, 114.3, 98.8, 93.2, 38.0, 33.9, 31.1, 30.2, 29.8, 29.6, 29.3, 29.1, 27.8 ppm *m/z* (HRMS ESI) found: 1610.33030; calcd for [C₇₂H₉₆I₄O₈N]⁺: 1610.33092; found: 1615.28546; calcd for [C₇₂H₉₂I₄O₈Na]⁺: 1615.28631.

Tetra(pyridyl)cavitand **11**

To cavitand **10** (160 mg, 0.100 mmol), 3-pyridineboronic acid pinacol ester (310 mg, 1.51 mmol), tetrakis(triphenylphosphine)palladium (23 mg, 0.020 mmol), potassium hydroxide (186 mg, 3.31 mmol) and tetrabutylammonium bromide (16 mg, 0.050 mmol) degassed toluene (4 mL) and degassed water (1 mL) was added under argon. The reaction mixture was stirred 16 h at 90 °C and toluene (20 mL) was added. The organic phase was separated, the aqueous phase extracted with toluene (30 mL) and the combined organic phases dried with MgSO₄. The solvent was removed under reduced pressure and the crude product purified by GPC (chloroform) and HPLC (gradient elution with ethyl acetate and up to 10 % ethanol/ 85 % ethyl acetate/ 5 % triethylamine). The product **11** (81 mg, 58 %) was obtained as a pale yellow solid.

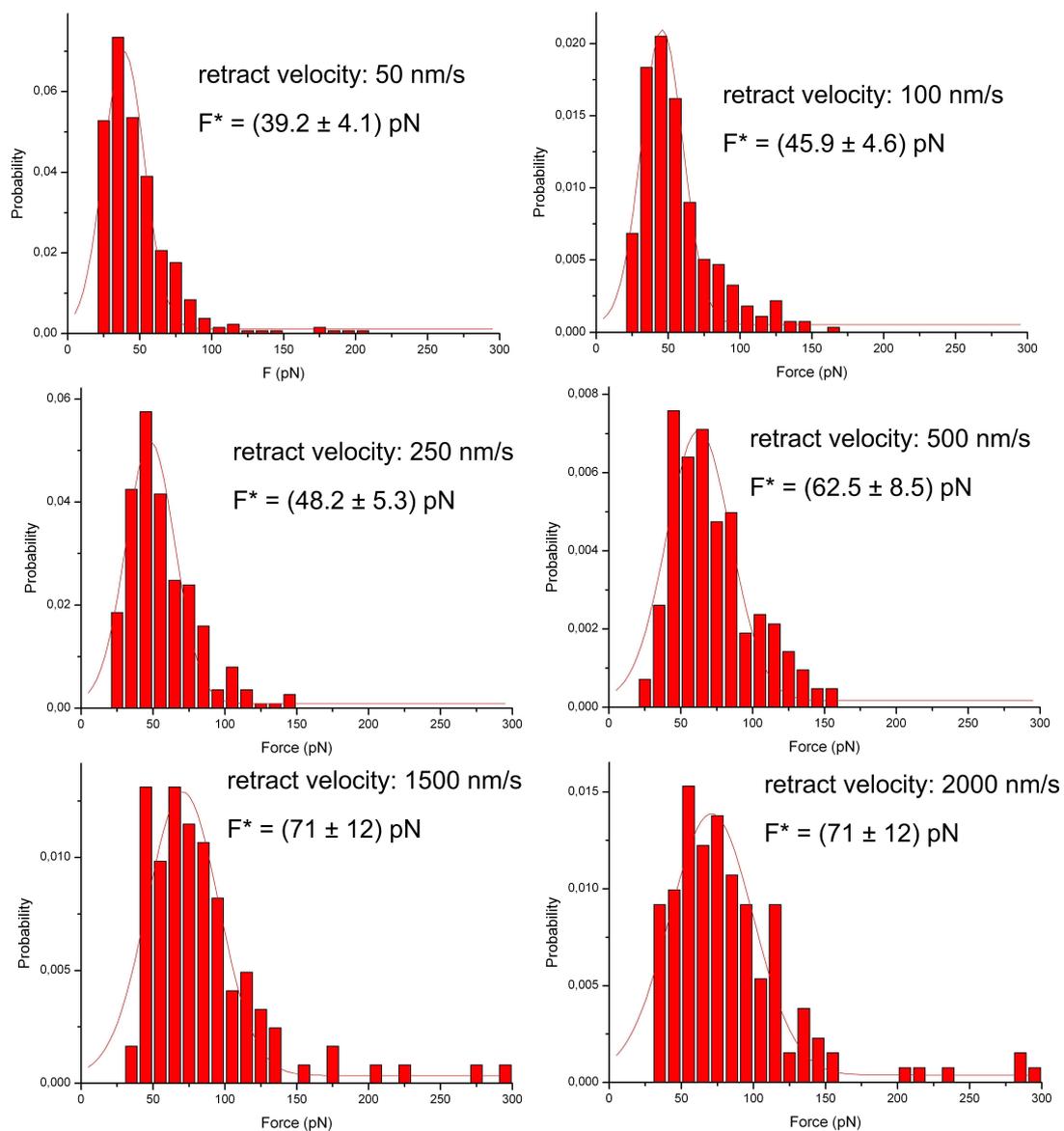
¹H-NMR (500.1 MHz, CDCl₃, 300 K) δ = 8.54 (br s, 4 H, PyrH), 8.37 (s, 4 H, PyrH), 7.58 (br s, 4 H, PyrH), 7.39 (s, 4 H, ArH), 7.24 (br s, 4 H, PyrH), 5.83 (ddt, *J* = 17.0, 10.0, 6.5 Hz, 4 H, CH=CH₂), 5.32 (br s, 4 H, OCHHO), 5.01 (dd, *J* = 17.0, 1.5 Hz, 4 H, CH=CH_{cis}H_{trans}), 4.95 (br d, *J* = 10.0 Hz, 4 H, CH=CH_{cis}H_{trans}), 4.86 (t, *J* = 8.0 Hz, 4 H, Ar₂CH), 4.30 (br s, 4 H, OCHHO), 2.36 (m, 8 H, Ar₂CHCH₂), 2.07 (m, 8 H, CH₂CH=CH₂), 1.54-1.32 (m, 48 H) ppm. ¹³C-NMR (125.8 MHz, CDCl₃, 300 K) δ = 152.8, 150.0, 148.1, 139.2, 138.7, 138.2, 129.9, 125.9, 123.2, 120.9, 114.4, 100.6, 37.2, 34.0, 30.5, 30.0, 29.8, 29.7, 29.3, 29.1, 28.1 ppm. *m/z* (HRMS ESI) found: 1397.82464; calcd for [C₉₂H₁₀₉N₄O₈]⁺: 1397.82399; found: 699.41570; calcd for [C₉₂H₁₁₀N₄O₈]²⁺: 699.41563.

Thioether-substituted tetra(pyridyl)cavitand **12**

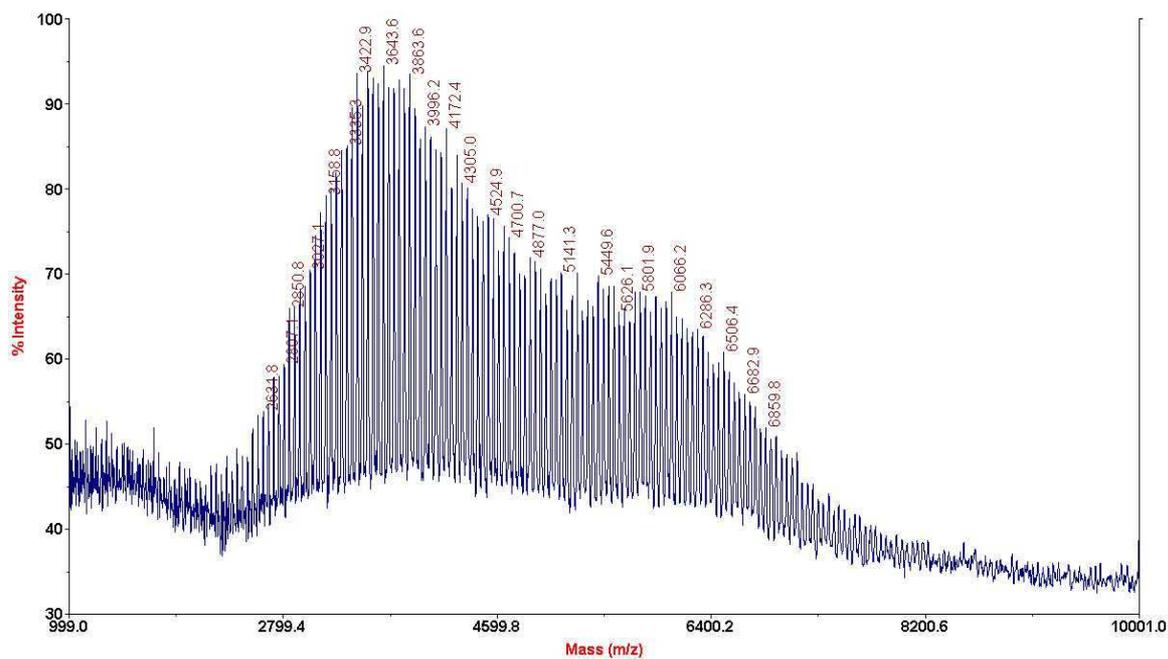
A solution of cavitand **11** (45 mg, 0.029 mmol) in dry THF (1 mL) was cooled to 0 °C and 1-decanethiol (270 μL, 229 mg, 1.31 mmol) and 9-BBN (0.5 M in THF, 0.25 mL, 0.13 mmol) was added. The reaction mixture was allowed to reach room temperature during the course of 16 h. The solvent was removed under reduced pressure and methylene chloride (20 mL) and water (5 mL) was added. The aqueous phase was extracted two times with methylene chloride (40 mL) and the combined organic phases dried over MgSO₄. The solvent was removed and the crude product purified by GPC (chloroform) and HPLC (silica gel, gradient elution with ethyl acetate and up to 10 % ethanol/ 85 % ethyl acetate/ 5 % triethylamine) to yield **12** (30 mg, 44 %) as a pale yellow solid.

¹H-NMR (500.1 MHz, CDCl₃, 300 K) δ 8.48 (br s, 4 H), 8.30 (s, 4H), 7.48 (br d, *J* = 5.0 Hz, 4 H, ArH), 7.38 (s, 4 H, ArH), 7.29 (br s, 4H, ArH), 5.28 (br d, *J* = 4.8 Hz, 4 H, OCH₂O), 4.86 (t, *J* = 8.0 Hz, 4 H, Ar₂CH), 4.28 (br d, *J* = 5.5 Hz, 4 H, OCH₂O), 2.51 (m, 16 H, CH₂SCH₂), 2.36 (m, 8 H, Ar₂CH-CH₂), 1.58 (m, 16 H, CH₂), 1.50–1.20 (m, 112 H, CH₂), 0.88 (t, *J* = 6.0 Hz, 12 H, CH₃) ppm; ¹³C-NMR (125.8 MHz, CDCl₃, 300 K) δ = 152.8, 150.0, 148.2, 138.6, 137.99, 129.8, 126.2, 123.0, 120.8, 100.4, 37.1, 32.3, 32.3, 32.0, 30.5, 29.9, 29.9, 29.9, 29.8, 29.7, 29.7, 29.7, 29.5, 29.4, 29.4, 29.1, 29.1, 28.1, 22.8, 14.3 ppm; *m/z* (HRMS ESI) found: 2094.39898; calcd for [C₁₃₂H₁₉₇N₄O₈S₄]⁺: 2094.40088; found: 1047.70443; calcd for [C₁₃₂H₁₉₈N₄O₈S₄]²⁺: 1047.70408.

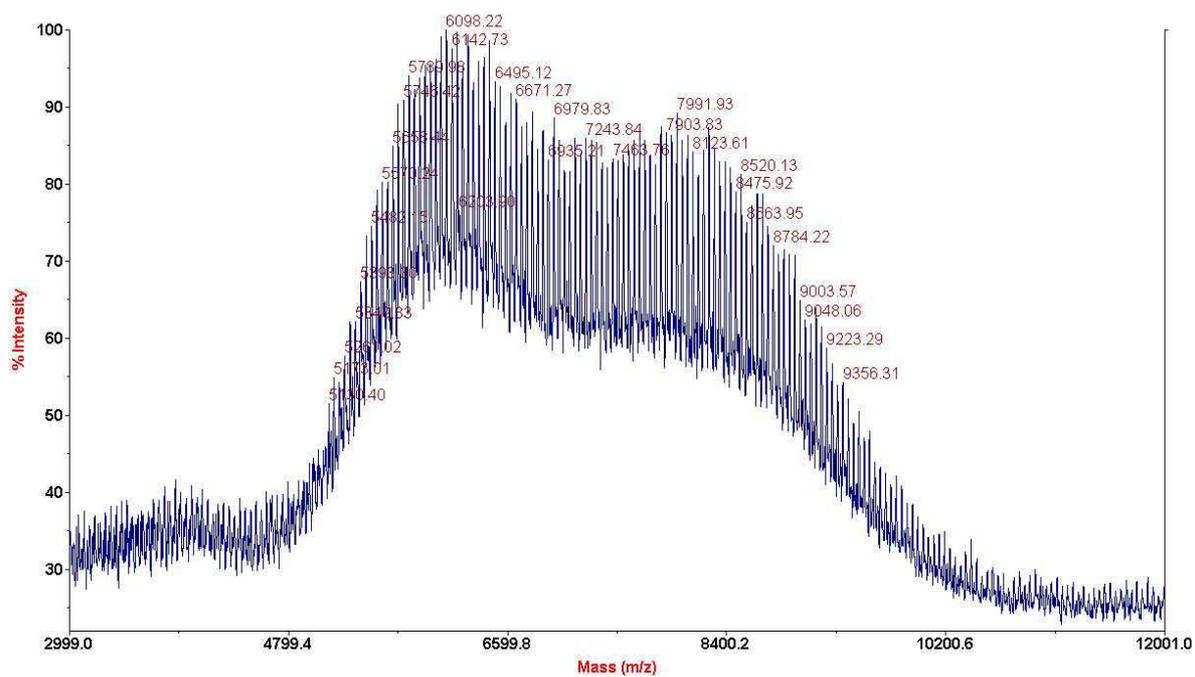
Histograms obtained for different loading rates



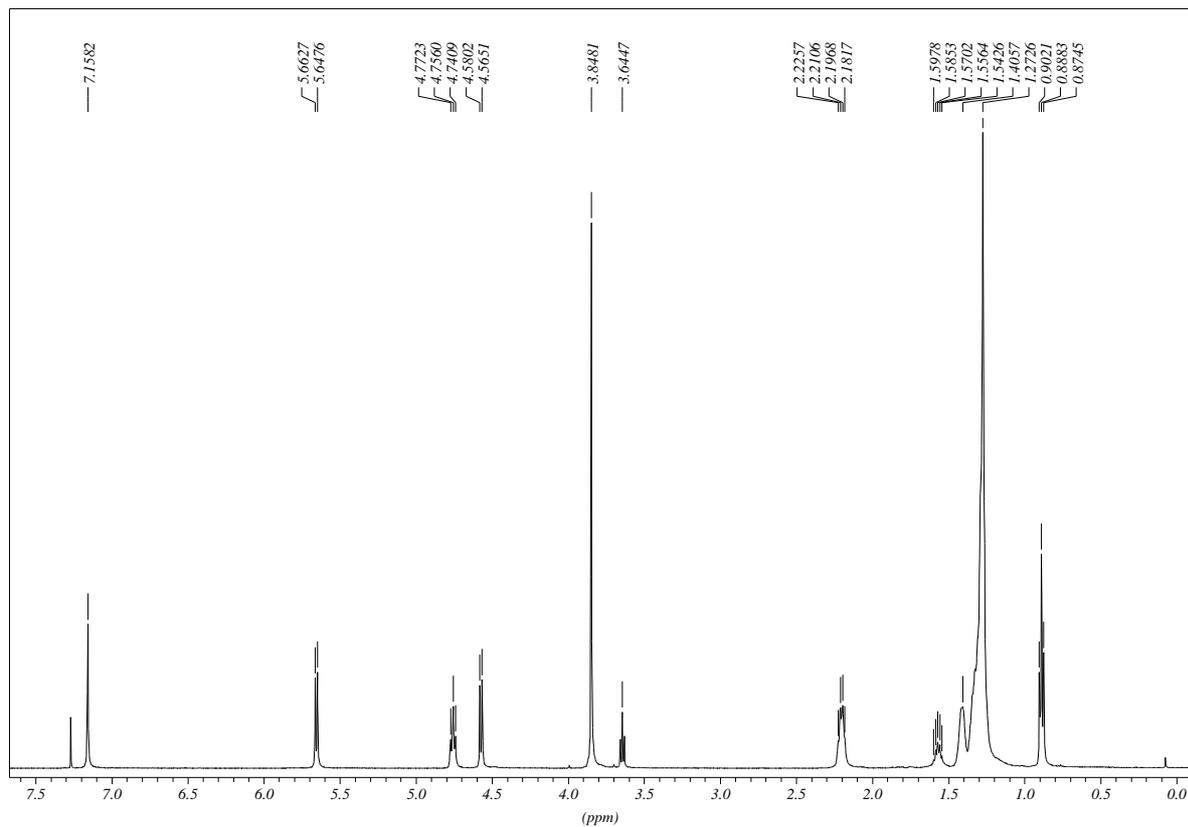
MALDI-ToF-MS of 7



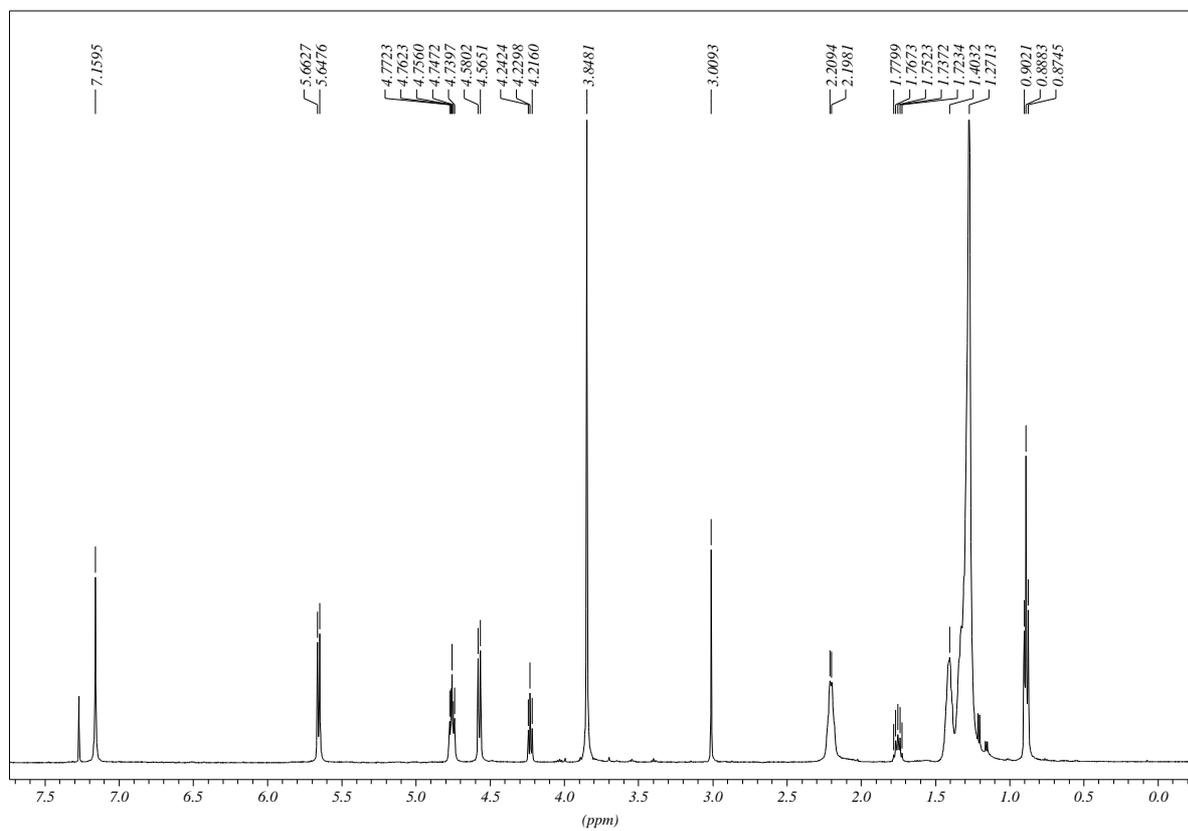
MALDI-ToF-MS of 8



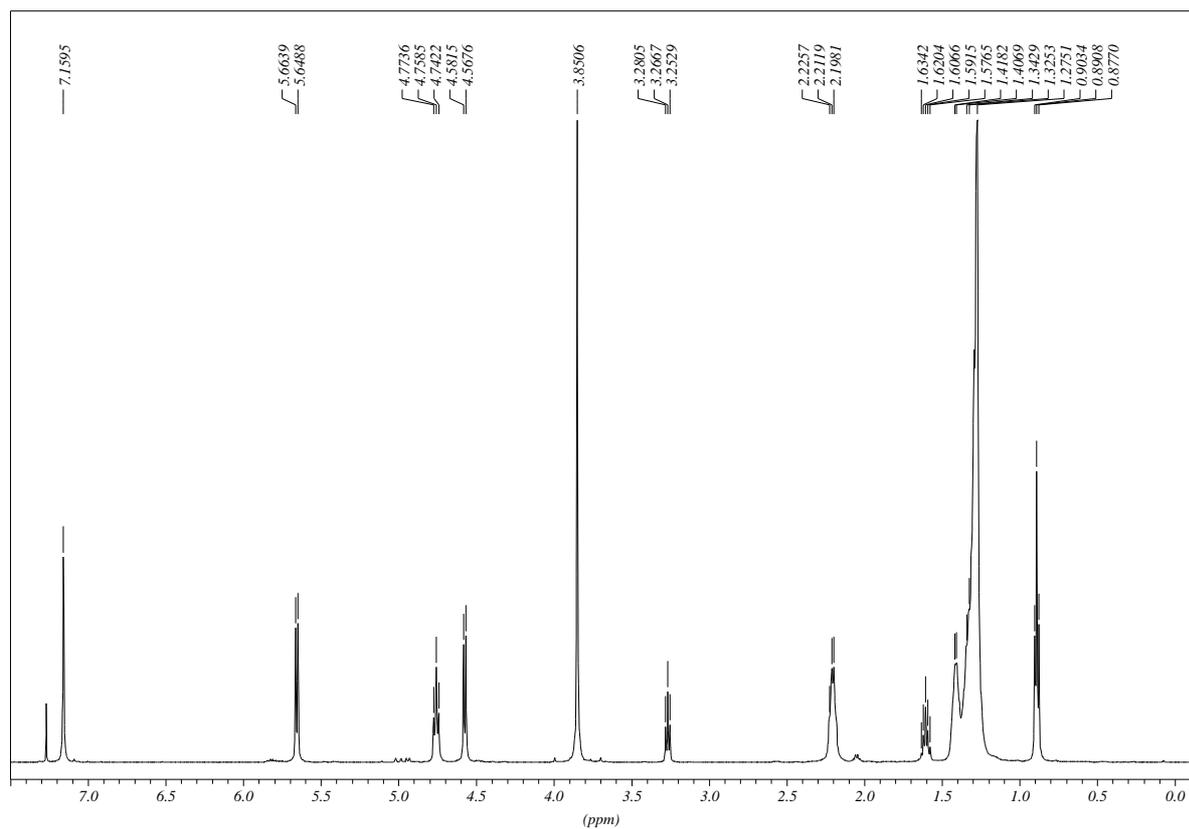
$^1\text{H-NMR}$ of **2**



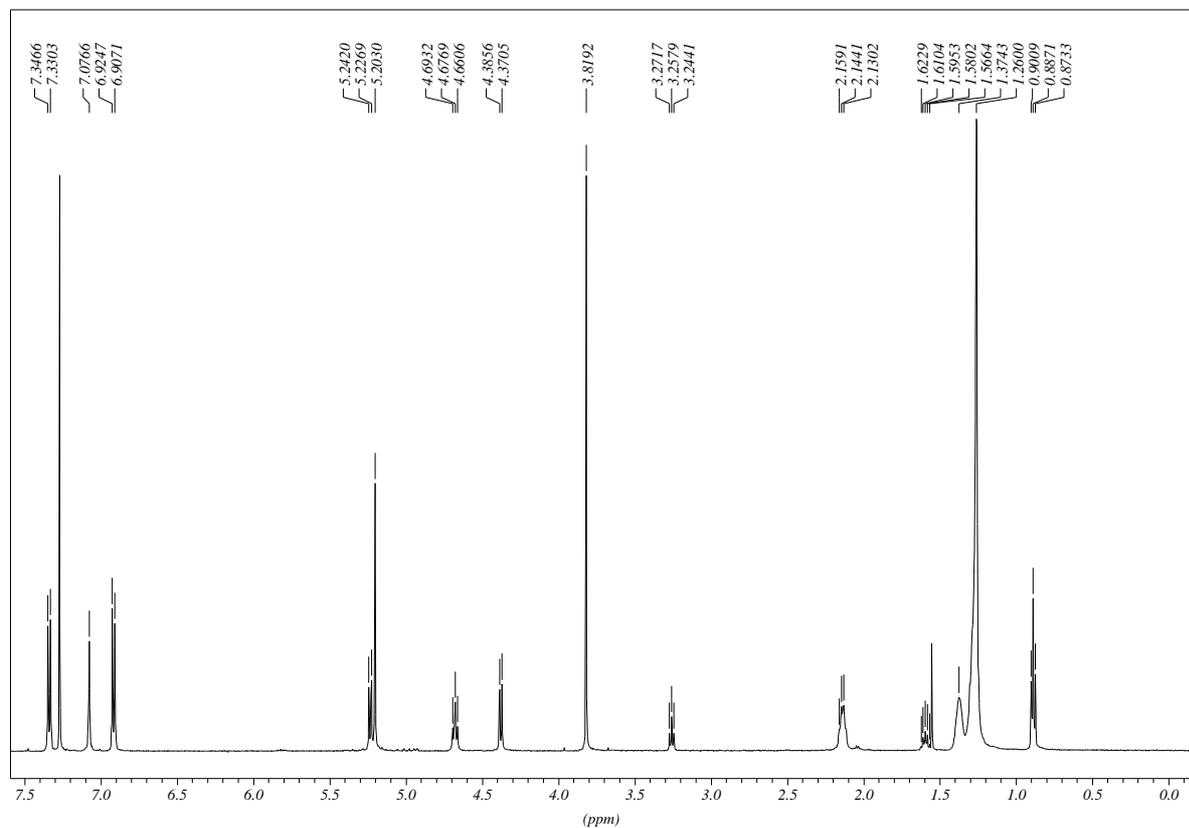
$^1\text{H-NMR}$ of **13**



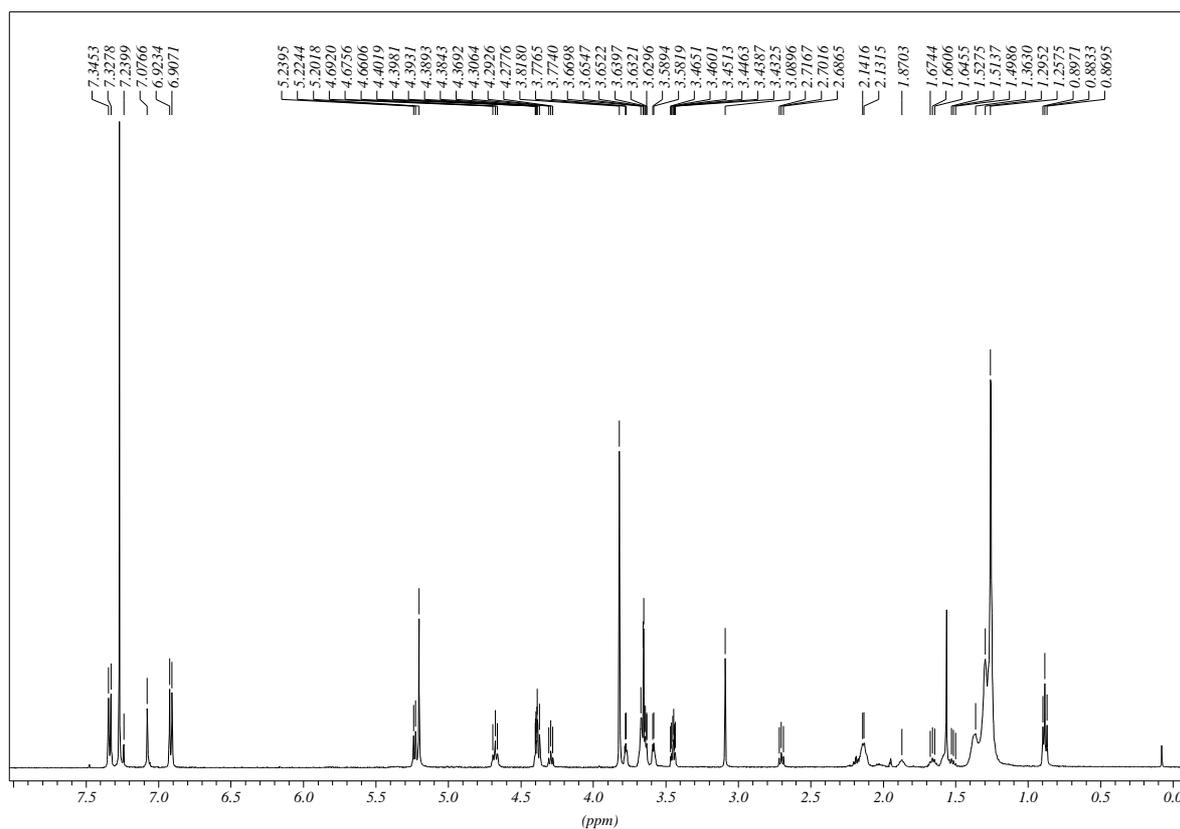
$^1\text{H-NMR}$ of **3**



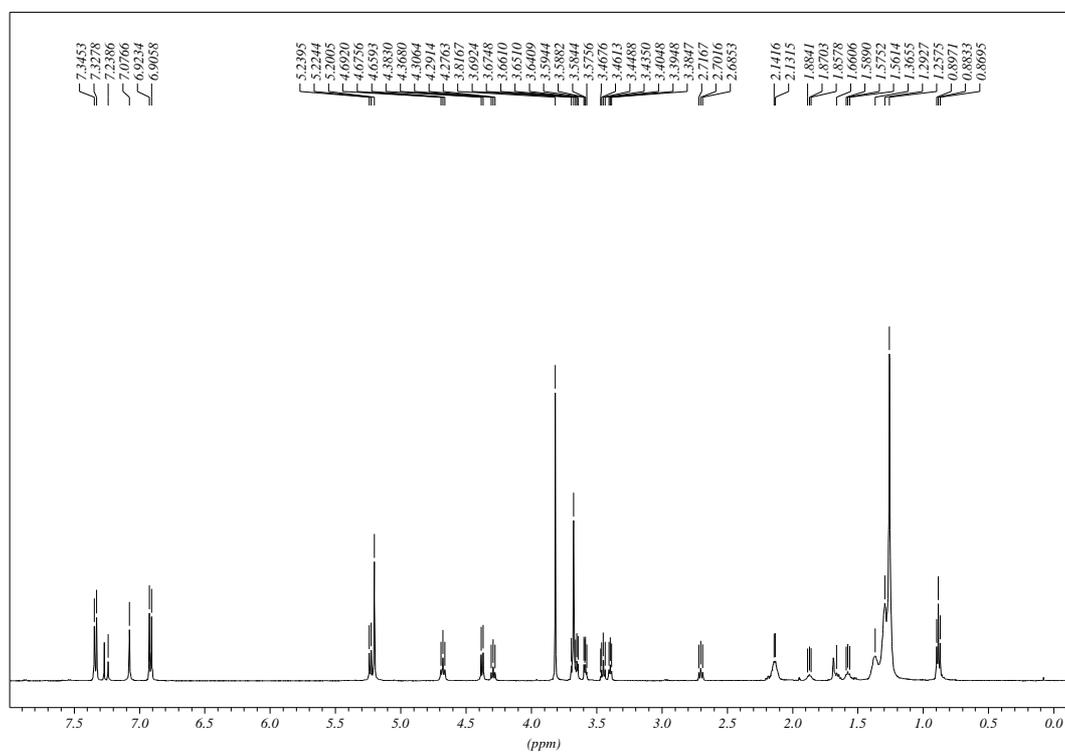
$^1\text{H-NMR}$ of **4**



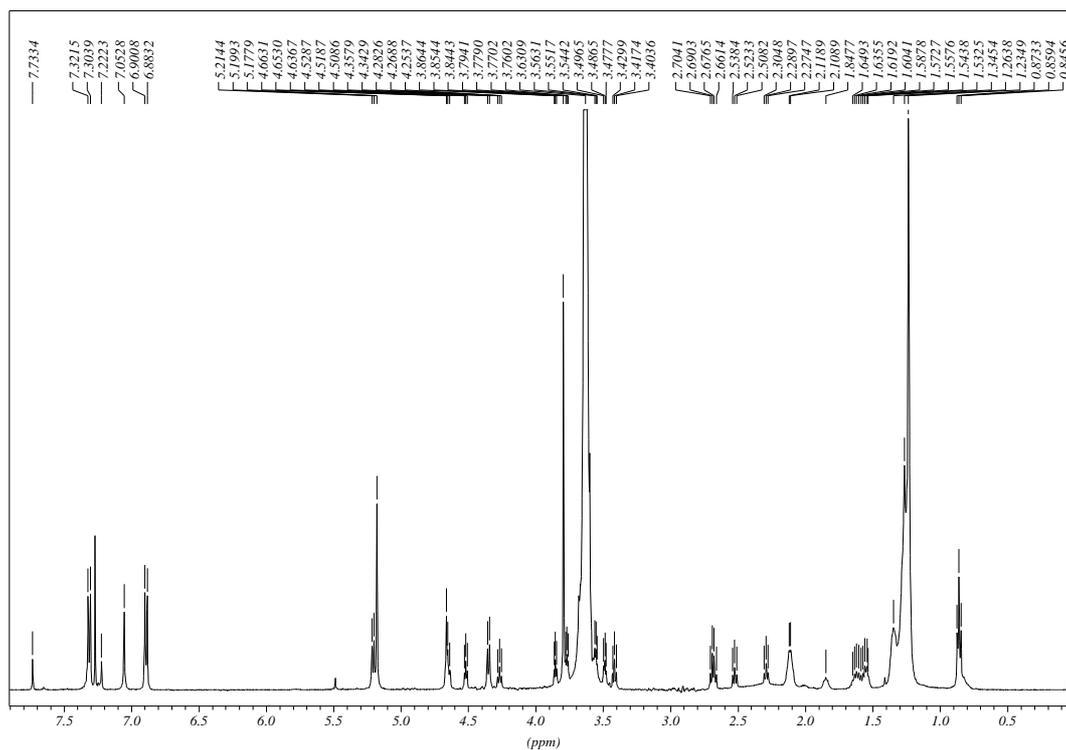
$^1\text{H-NMR}$ of **14**



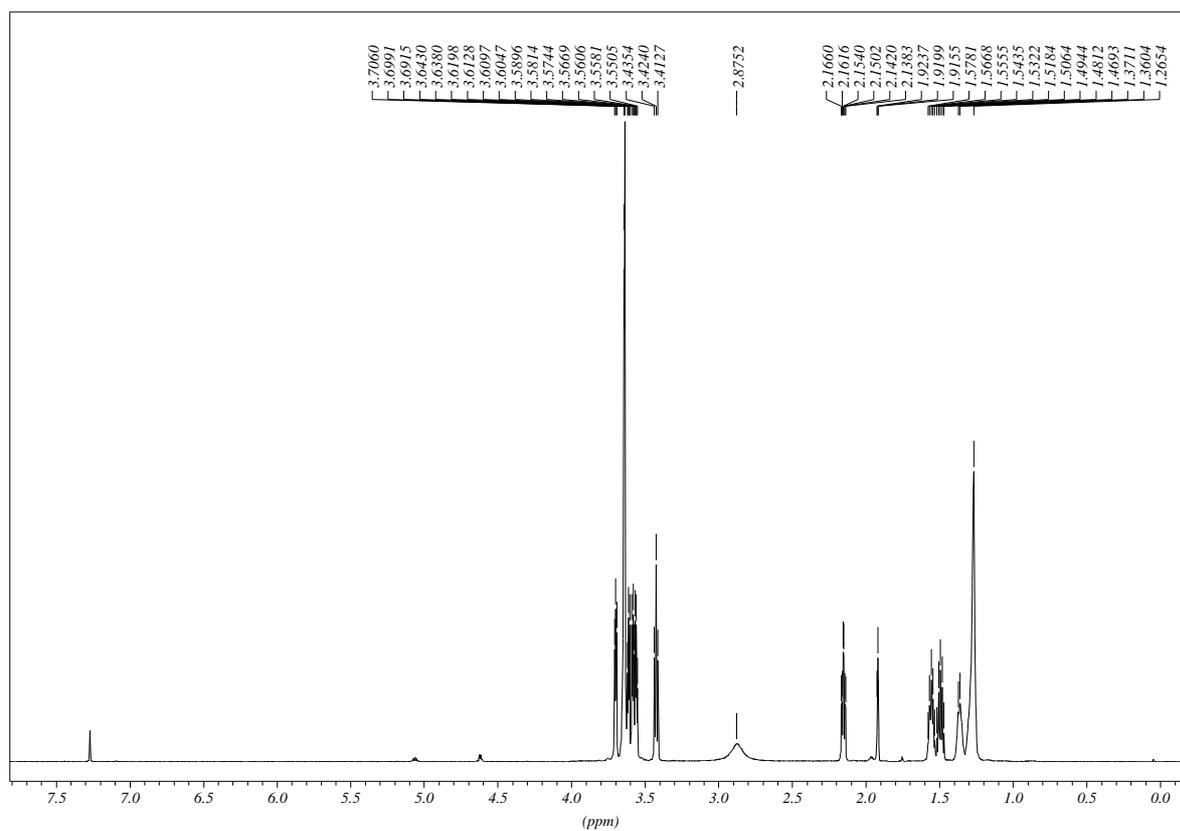
$^1\text{H-NMR}$ of **6**



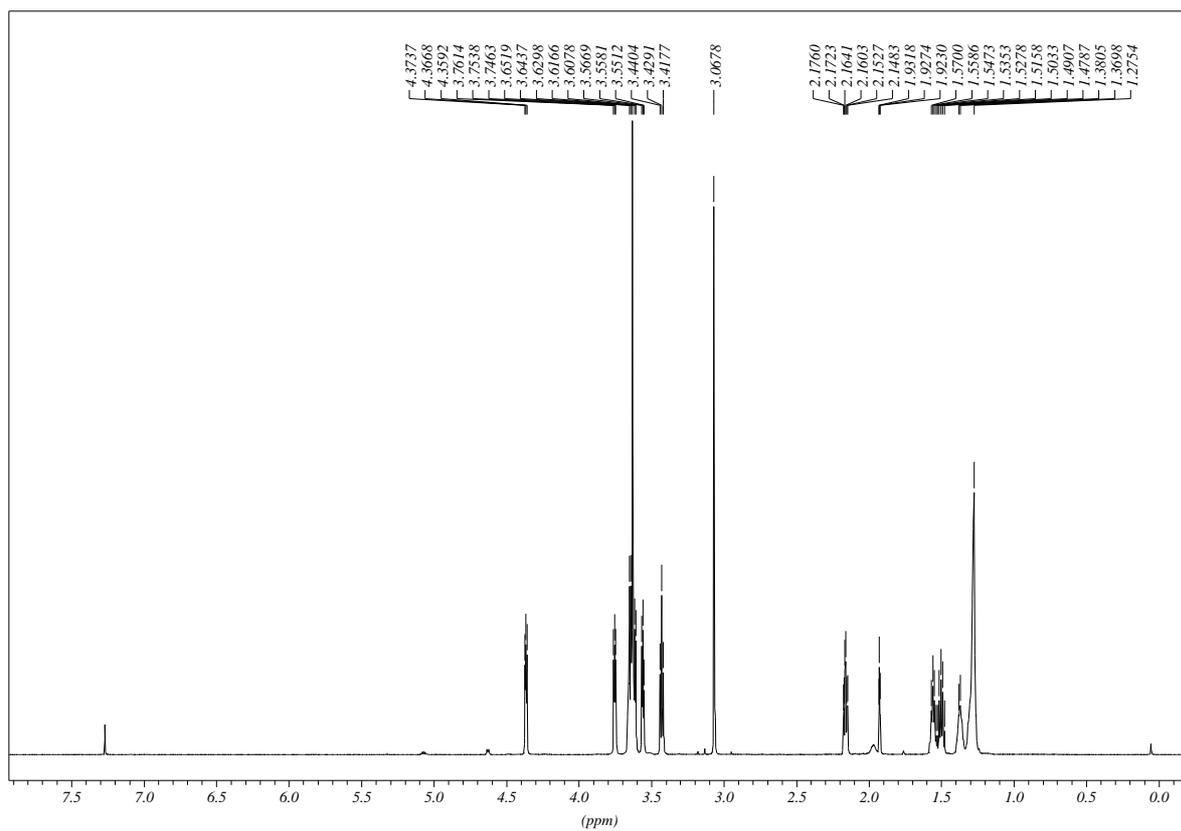
$^1\text{H-NMR}$ of **8**



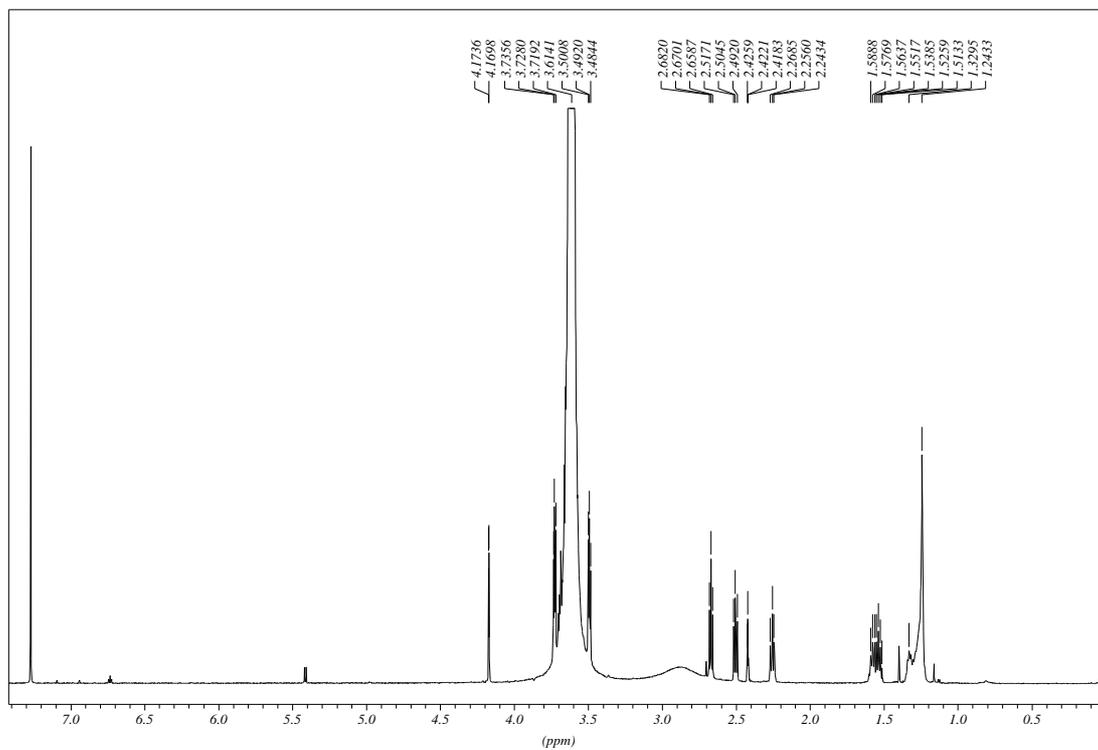
$^1\text{H-NMR}$ of **15**



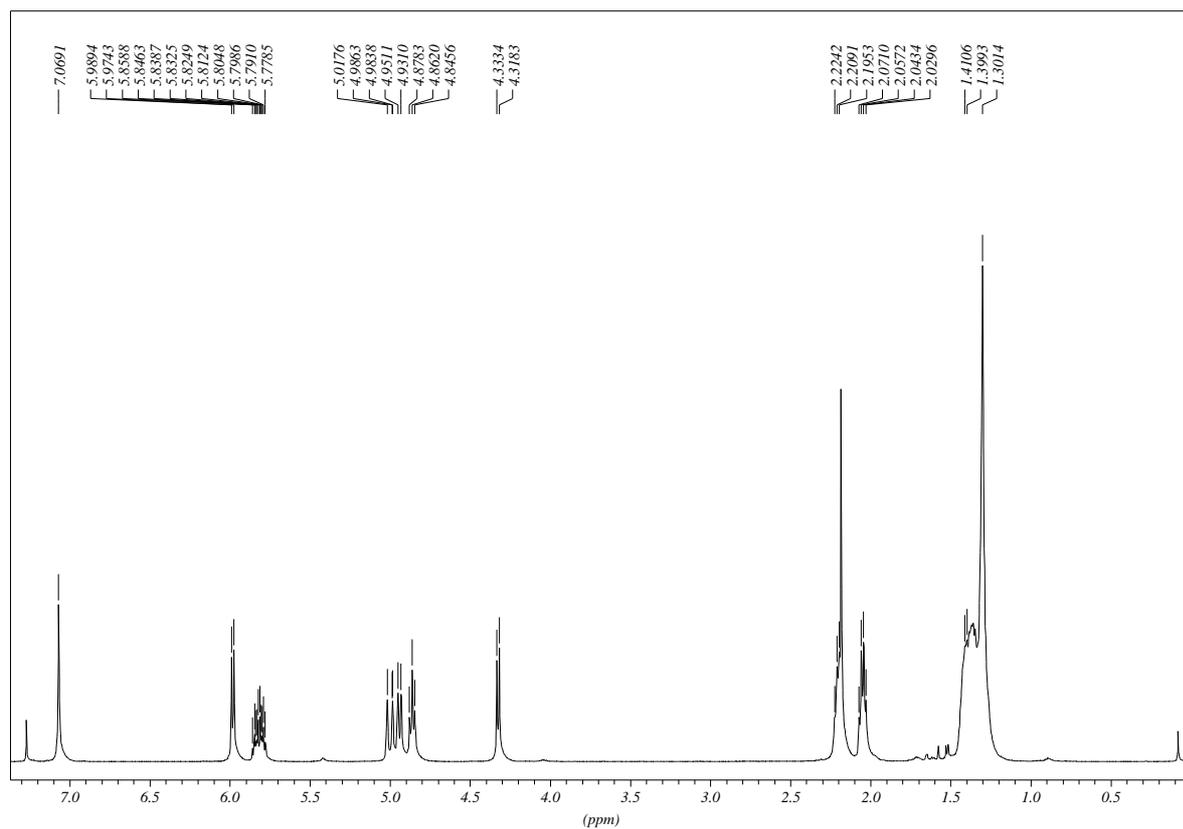
$^1\text{H-NMR}$ of **5**



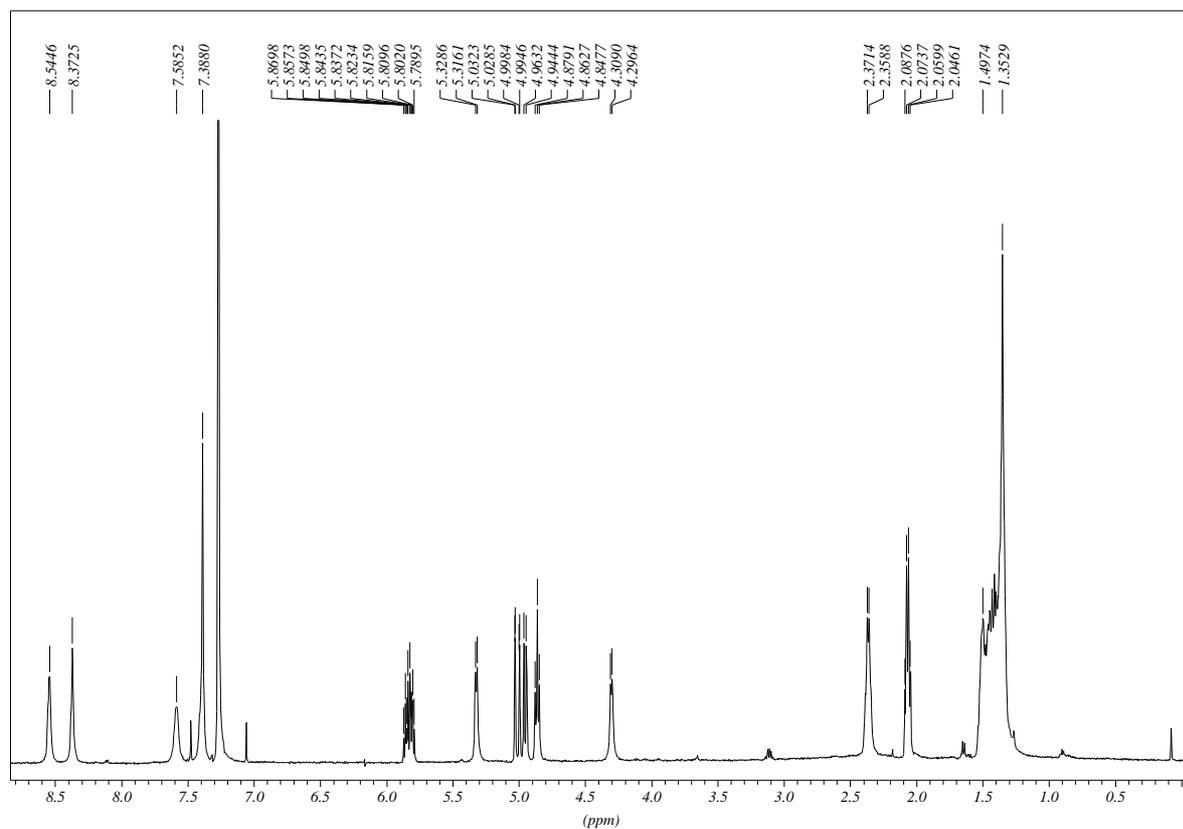
$^1\text{H-NMR}$ of **7**



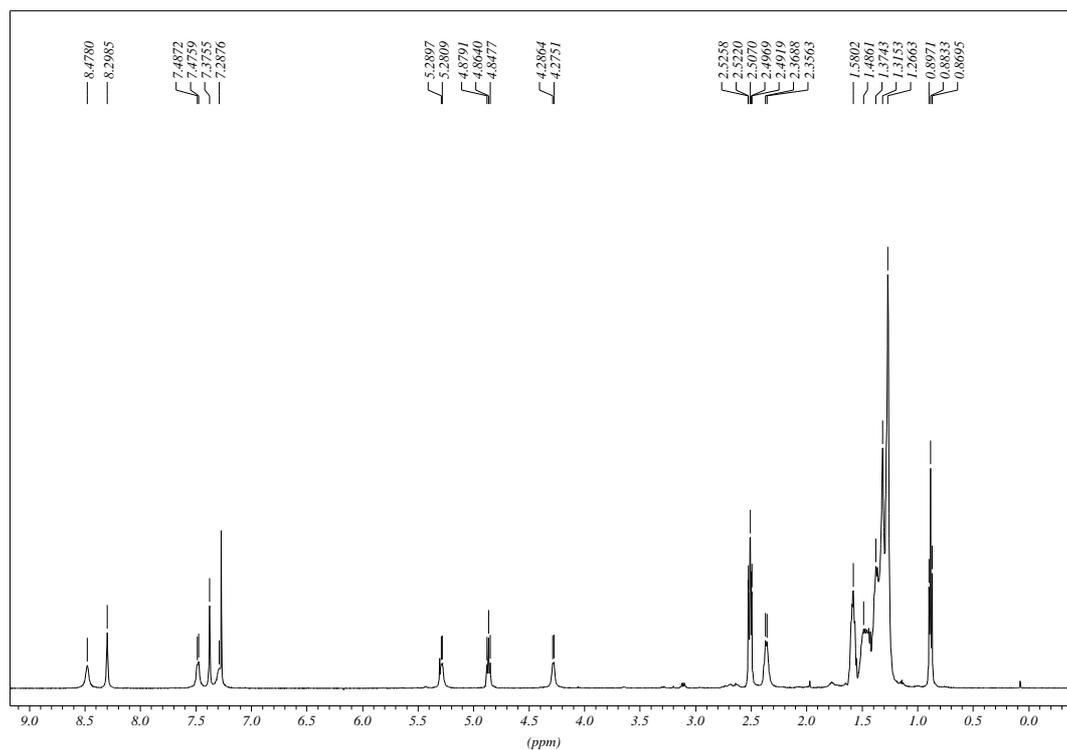
$^1\text{H-NMR}$ of **10**



$^1\text{H-NMR}$ of **11**



$^1\text{H-NMR}$ of **12**



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