Electronic Supplementary Material (ESI) for Organic & Biomolecular Chemistry.

Electronic Supplementary Information accompanying:

Synthesis and evaluation of a desymmetrised synthetic lectin: An approach to carbohydrate receptors with improved versatility.

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1. Synthesis and characterisation of receptors

The synthetic route to the receptors is summarised in

Figure **S1**. The structures of the receptors are shown in
Figure **S2** with the labelling system used for NMR analysis. Note that the product from O-deprotection of hydroperoxide **17** is shown as **A**, based on the supposition that the hydroperoxide would survive the deprotections conditions. However, this assignment could not be confirmed by MS[1] and is therefore tentative. A structure in which the –O-OH group is replaced by OH is a possible alternative.

All commercially available chemicals were purchased from Sigma-Aldrich, Alfa-Aesar, Acros Organics, ABCR or Carbosynth Ltd., and used without further purification unless stated otherwise. Solvents were utilized as supplied unless otherwise stated. 4-(Azidomethyl)benzeneboronic acid pinacol ester (**8**),[2] 3,5-Bis[(*N*-*tert*-butyloxycarbonyl)aminomethyl]-iodobenzene (**9**),[3] benzene-1,3-pentafluorophenoxycarbonyl -5-[tris-(2-amido-[tris-(2-methoxycarbonylethyl)methane]-ethyl)amidomethane] (**11**),[4] and 2-amino-methyl-6,8-bis[(*N*-*tert*-butyloxycarbonyl)amino-methyl]pyrene (**12**),[5] and benzene-1,3-pentafluorophen-oxycarbonyl-5-[tris-(2-amido-[tris-(2-tert-butoxycarbonylethyl)methane]-ethyl)amidomethane] (**13**),[5] were prepared according to literature procedures. Anhydrous solvents (e.g. THF or CH_2Cl_2) were dried by passing through a modified Grubbs system[6] manufactured by Anhydrous Engineering. Anhydrous DMF and DMSO were dried by vacuum distillation from P_2O_5 and CaH_2, respectively[7]. Flash column chromatography was carried out using chromatography grade silica 60Å (Sigma-Aldrich, particle size 35-70 micron). TLC analysis was performed using precoated silica gel TLC plates (Merck silica gel 60 F254). Spots were visualised by means of UV light (254 or 365 nm) or using solutions of phosphomolybdic acid, alizarin, potassium permanganate, or ninhydrin. HPLC was performed using a Waters 600 controller with

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[1] We have previously found that mass spectroscopy of water-soluble polycarboxylate receptors is challenging, and usually unsuccessful.

[2] J. R. White, G. J. Price, S. Schiffers, P. R. Raithby, P. K. Plucinski, C. G. Frost, *Tetrahedron Letters*, *Vol. 51,* **30**, 3913-3917 (2010).

[3] B. Sookcharoenpinyo, E. Klein, Y. Ferrand, D. B. Walker, P. R. Brotherhood, C. Ke, M. P. Crump, A. P. Davis, *Angewandte Chemie International Edition*, **51**, 4186-4590 (2012).

[4] H. Destecroix, C. M. Renney, T. J. Mooibroek, T. S. Carter, P. F. N. Stewart, M. P. Crump, A. P. Davis, *Angewandte Chemie International Edition*, **54**, 2057-2061 (2015).

[5] T. J. Mooibroek, J. M. Casas-Solvas, R. L. Harniman, T. S. Carter, C. Renney, M. P. Crump, A. P. Davis, *Nature Chemistry*, Accepted (2015).

[6] Pangborn, A. B., Giardello, M. A., Grubbs, R. H., Rosen, R. K. & Timmers, F. J. Safe and convenient procedure for solvent purification. *Organometallics* **15**, 1518-1520 (1996).

[7] Armarego, W. F. & Chai, C. L. L. *Purification of Laboratory Chemicals* (Elsevier, Oxford, 2009).

a Waters 2998 photodiode array detector. For analytical runs an XSELECT CSH C_{18} 5 μm (4.6 × 150 mm), or ACE 5 C_{18}-PFP (4.6 × 250 mm, 40 mL/min) column was used, and for preparative runs a XSELECT CSH Prep C_{18} 5 μm OBD (19 × 250 mm, 17 mL/min), or ACE 5 C_{18}-PFP (250 × 30.0 mm, 40 mL/min) column was utilised.

^{1}H-, ^{13}C-, ^{19}F-, ^{31}P-, and 2D-NMR spectra were acquired at 298 K (unless otherwise specified) at 400, 500, or 600 MHz using the following spectrometers: Jeol ECS 400, Varian 400-MR, Varian VNMRS-500 equipped with either a triple resonance or broadband probe and a Varian VNMRS-600 equipped with a 5mm cryogenically cooled triple resonance probe (Wellcome Trust grant WT082352MA). Chemical shifts (δ) are reported in parts per million (ppm). Residual solvent resonances were used as internal reference for δ-values in ^{1}H-, and ^{13}C-NMR,[8] while ^{19}F- and ^{31}P-NMR spectra were externally referenced to CF_3COOH (–76.55 ppm) and H_3PO_4 (0 ppm) respectively. IR spectra were measured on a Perkin-Elmer Spectrum One FT-IR. Low resolution mass spectra were recorded on a VG Analytical Quattro or Bruker ESQUIRE 300 for ESI and Nanospray, or an Applied Biosystems 4700 spectrometer for MALDI. High resolution mass spectra were recorded on a Bruker Apex 4e 7.0T FT-MS. Elemental analyses were provided by the Microanalytical laboratory of the University of Bristol.

[8] Fulmer, G. R. *et al.* NMR chemical shifts of trace impurities: common laboratory solvents, organics, and gases in deuterated solvents relevant to the organometallic chemist. *Organometallics* **29**, 2176-2179 (2010).

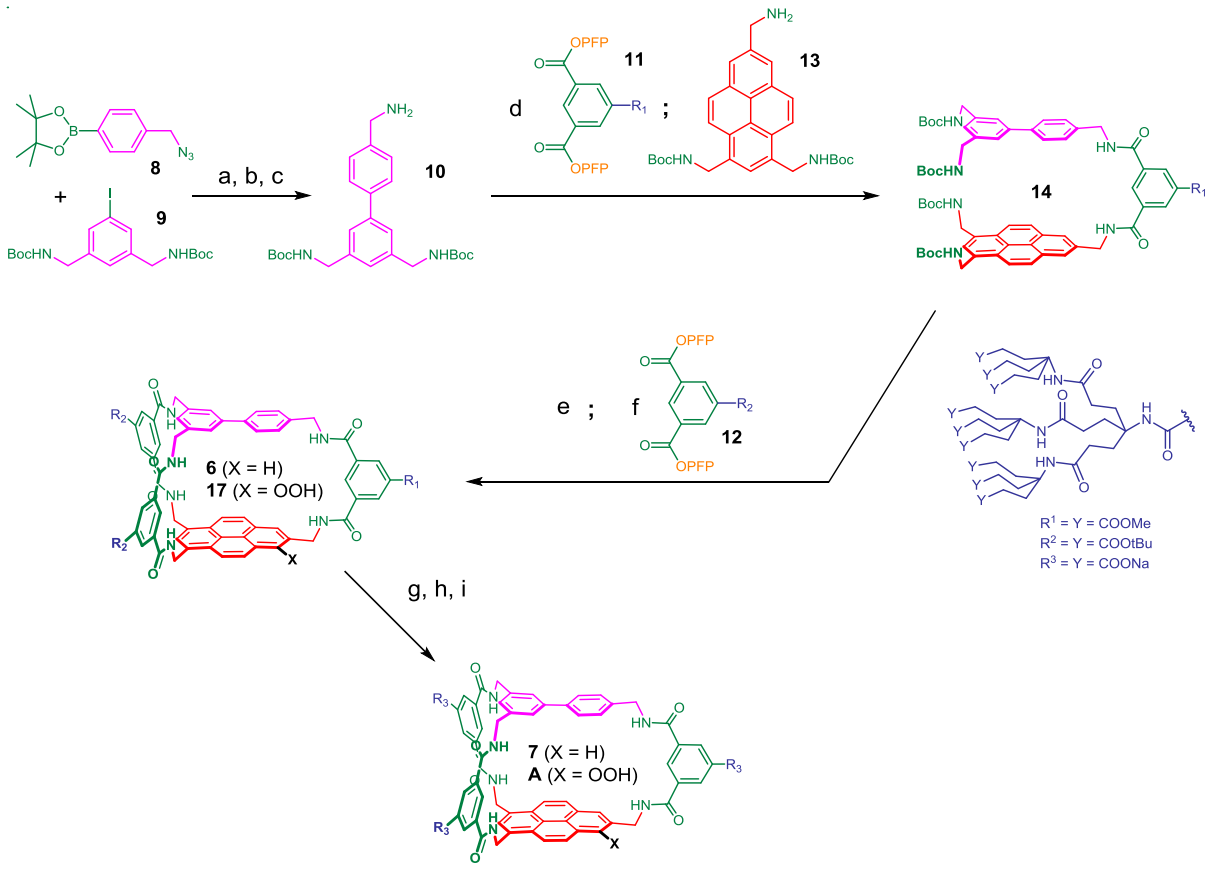


Figure S1. Synthesis scheme for receptor **7** and the oxidised analogue (shown as **A**; see discussion on page S2). a) Excess K_2CO_3 and $Pd(PPh_3)_4$ (5.5 mole %) in THF/H_2O, heated for 12 h at 60 °C; b) PMe_3 (2.5 eq.) in THF heated for 2 h at 60 °C; c) excess H_2O in THF, heated for 12 h at 60 °C; 33% yield over steps a-c ; d) DIPEA (33 eq.) in THF, at RT for 1 h; 55%; e) $HSiEt_3$ (21 eq.) in DCM at 0 °C; dropwise addition of TFA to 1:1 ($^v/_v$) then warming to RT; f) DIPEA (50 eq.) in THF at RT for 120 h; 5.1% for protected receptor **6** and 5.6% for protected receptor **17** over steps e-f; g) DCM, 0 °C, dropwise addition of TFA to 1:1 ($^v/_v$) then warming to RT; h) treatment with NaOH aq.); i) Desalting with Amberlist resin H-form to pH < 3, then neutralization with NaOH to pH 7.1; 100% over steps g-I for both **7** and **A**. Boc = *tert*-butyloxycarbonyl; PFP = pentafluorophenyl; THF = tetrahydrofuran; DIPEA = diisopropylethylamine; RT = room temperature (~ 25°C); TFA = trifluoroacetic acid.

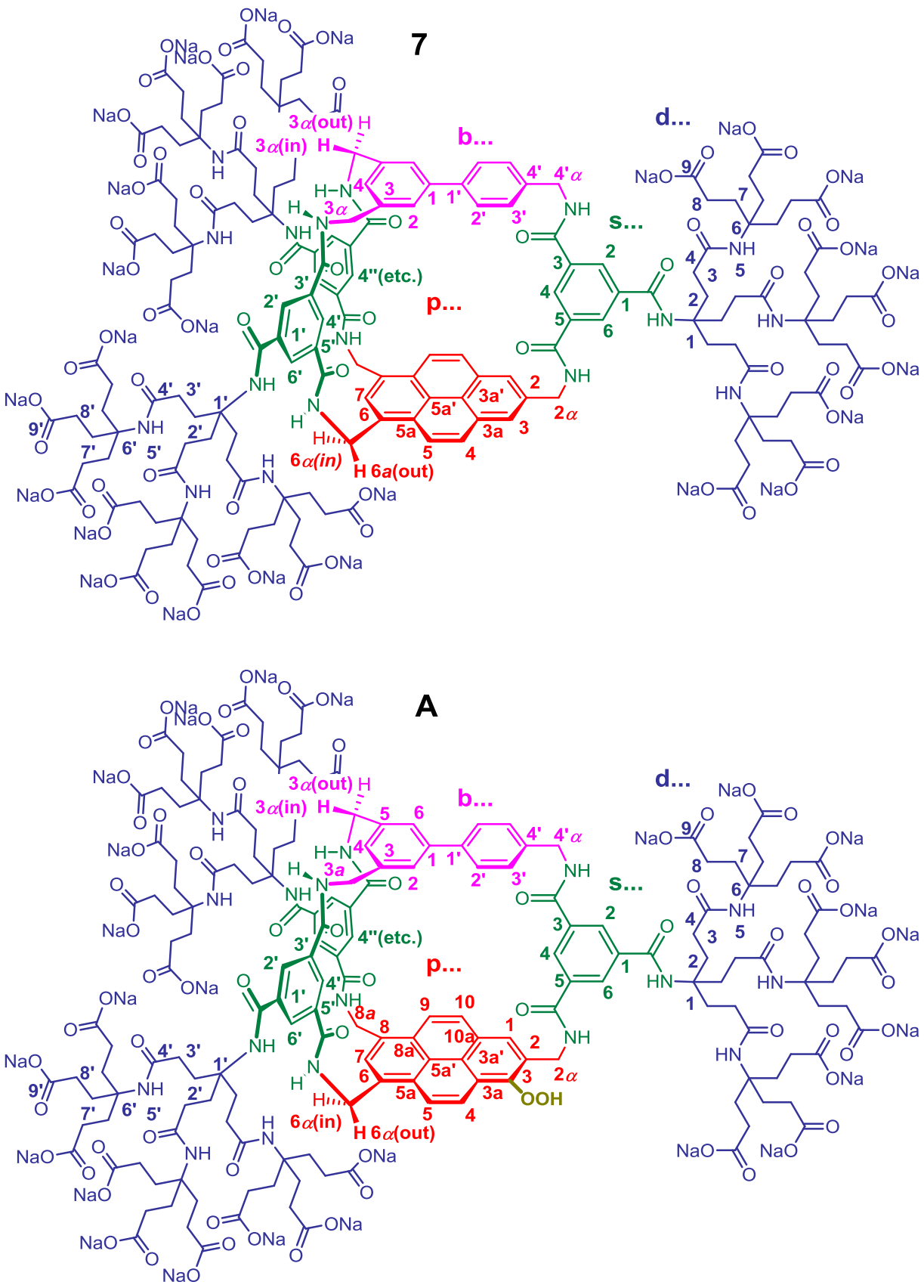
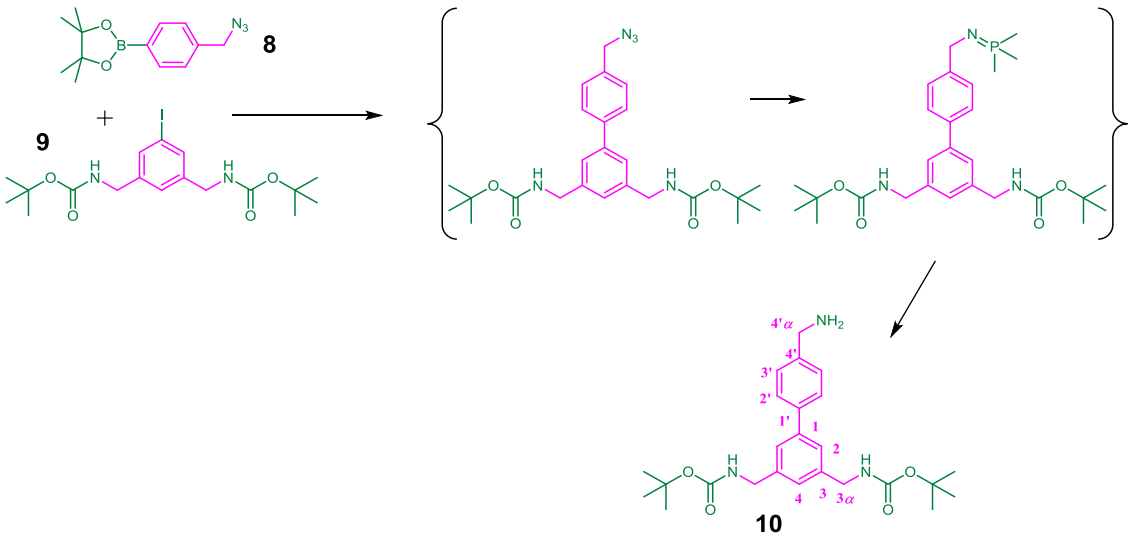


Figure S2. Complete numbering schemes for **7** and **A** as used in the main text and ESI.



1,1'-biphenyl-3,5-bis[3-(*N*-*tert*-butyloxycarbonyl)aminomethyl]-4'-aminomethyl (10).

To a stirred solution of 3,5-Bis[(*N*-*tert*-butyloxycarbonyl)aminomethyl]-iodobenzene **9** (0.295 g, 0.64 mmol) and of 4-(azidomethyl)benzeneboronic acid pinacol ester **8** (0.220 g, 0.85 mmol) in N_2 saturated THF (12 mL) were added K_2CO_3 aq. (2 M, 3 mL) (also N_2 saturated), followed by $Pd(PPh_3)_4$ (41.2 mg, 0.035 mmol). The resulting yellow biphasic system was heated at 60 °C for 12 h, evaporated to dryness and purified by silica column chromatography (EtOAc/Hexane 1:1; R_f = 0.68) to give a 1:1 mixture (^{1}H-NMR) of unreacted iodo starting material and 1,1'-biphenyl-3,5-bis[3-(*N*-*tert*-butyloxycarbonyl)aminomethyl]-4'-azidomethyl (0.281 g, 0.32 mmol of both). This solid was dissolved in N_2 saturated THF (50 mL) and trimethylphosphane was added (1.51 mmol). After stirring for two hours at 60 °C, N_2 saturated water was added, and the resulting mixture stirred for additional 2 h at 60 °C. The solvent was evaporated and the crude was purified by column chromatography to yield 1,1'-biphenyl-3,5-bis[3-(*N*-*tert*-butyloxycarbonyl)aminomethyl]-4'-aminomethyl **10** (0.100 g, 0.214 mmol, 33% over three steps) as a yellow solid. R_f = 0.26 (NH_3OH(aq.)/MeOH/DCM 1:9:90). ^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.48 (d, 2H, ^3J = 8.0 Hz, H-2'), 7.36 (d, 2H, ^3J = 8.0 Hz, H-3'), 7.34 (s, 2H, H-2), 7.14 (s, 1H, H-4), 5.04 (s, 2H, C(O)N*H*), 4.31 (d, 4H, ^3J = 5.5 Hz, H-3α), 3.90 (s, 2H, H-4'α), 2.78 (s, 2H, NH_2) and 1.45 (s, 18H, C(CH_3)$_3$) ppm; {^{1}H-^{13}C} HSQC: δ = 127.8 (C-3'), 127.3 (C-2'), 125.2 (C-4), 125.1 (C-2), 45.6 (C-4'α), 44.6 (C-3α), 28.5 (C(*C*H$_3$)$_3$) ppm; {^{1}H-^{13}C} HMBC: 181.7 (*C*O), 156.0 (C-3), 141.2 (C-1'), 139.9 (C-1), 139.4 (C-4'), 130.2 (*C*(CH$_3$)$_3$), 127.8 (C-3'), 127.3 (C-2'), 125.2 (C-4), 125.1 (C-2), 45.6 (C-4'α), 44.6 (C-3α), 28.5 (C(*C*H$_3$)$_3$) ppm (see Figure S3 and Figure **S4** for spectra); HRMS (ESI$^+$): *m/z* calculated for $C_{25}H_{36}N_3O_4$ [M + H]$^+$: 442.2700, found 442.2714.

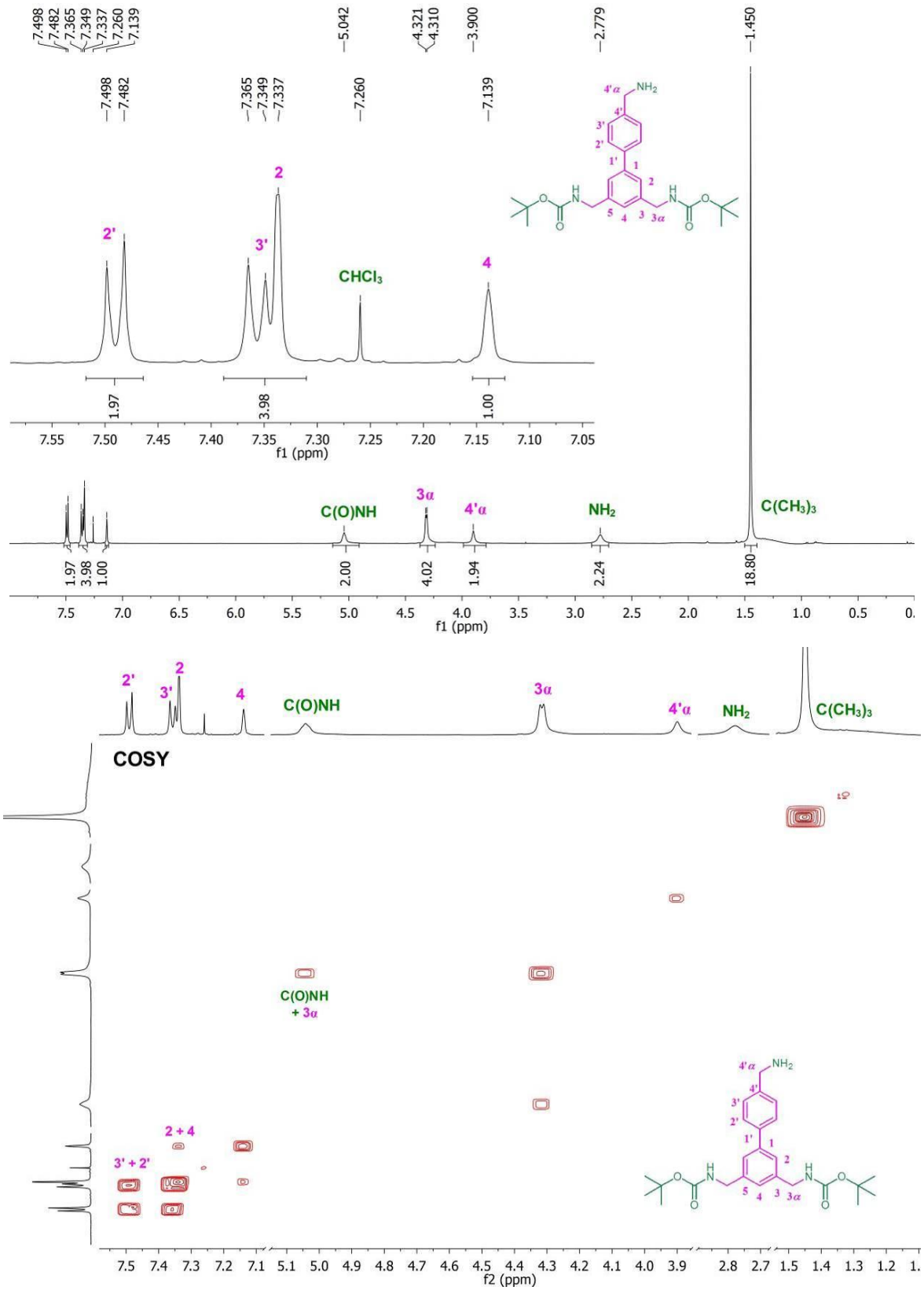


Figure S3. ^{1}H-NMR (top) and {^{1}H-^{1}H}-COSY (bottom) spectra of 1,1'-biphenyl-3,5-bis[3-(N-tert-butyloxycarbonyl)aminomethyl]-4'-aminomethyl **10**, with assignments. The spectra were recorded at 500 MHz in $CDCl_3$.

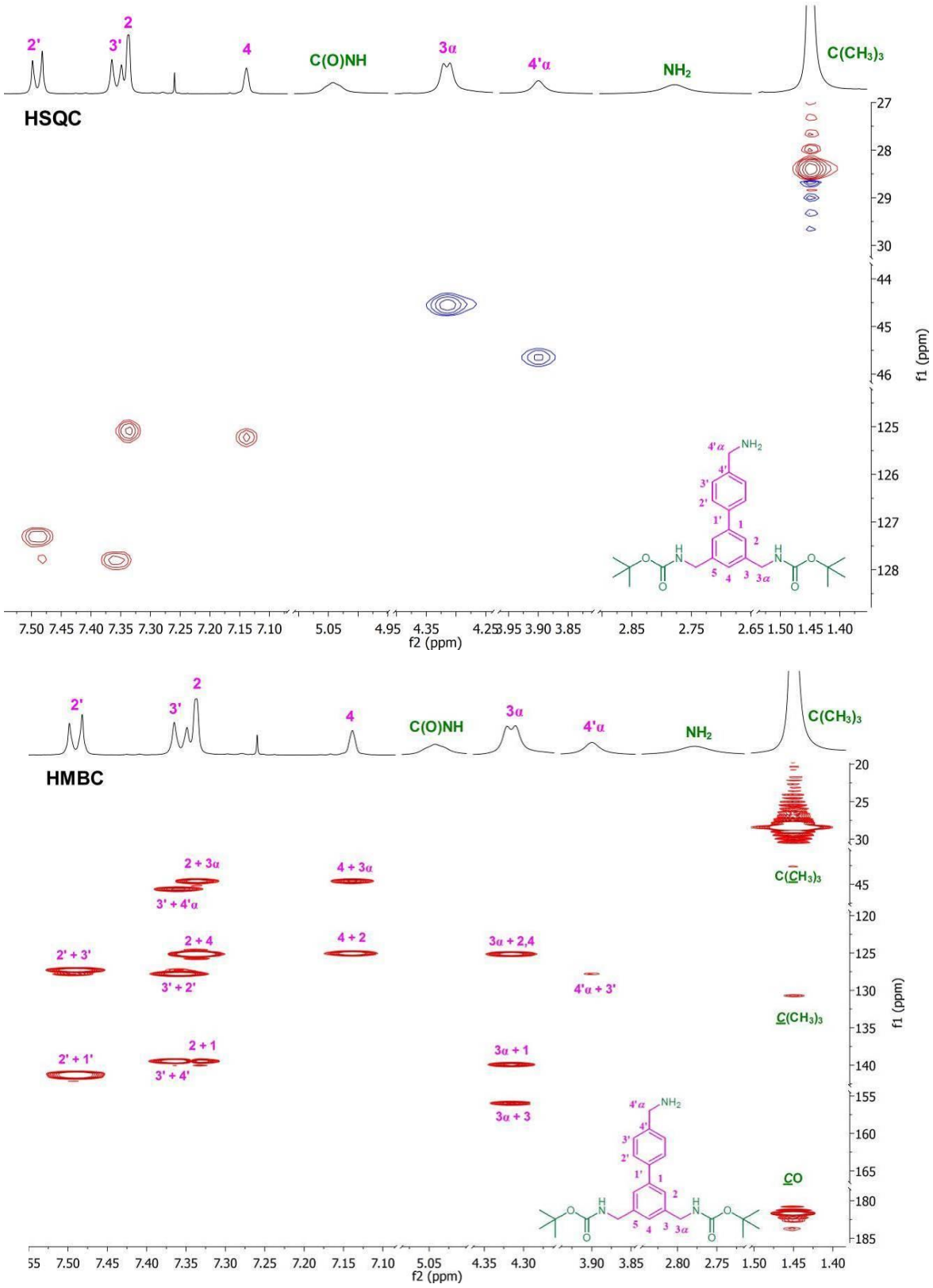
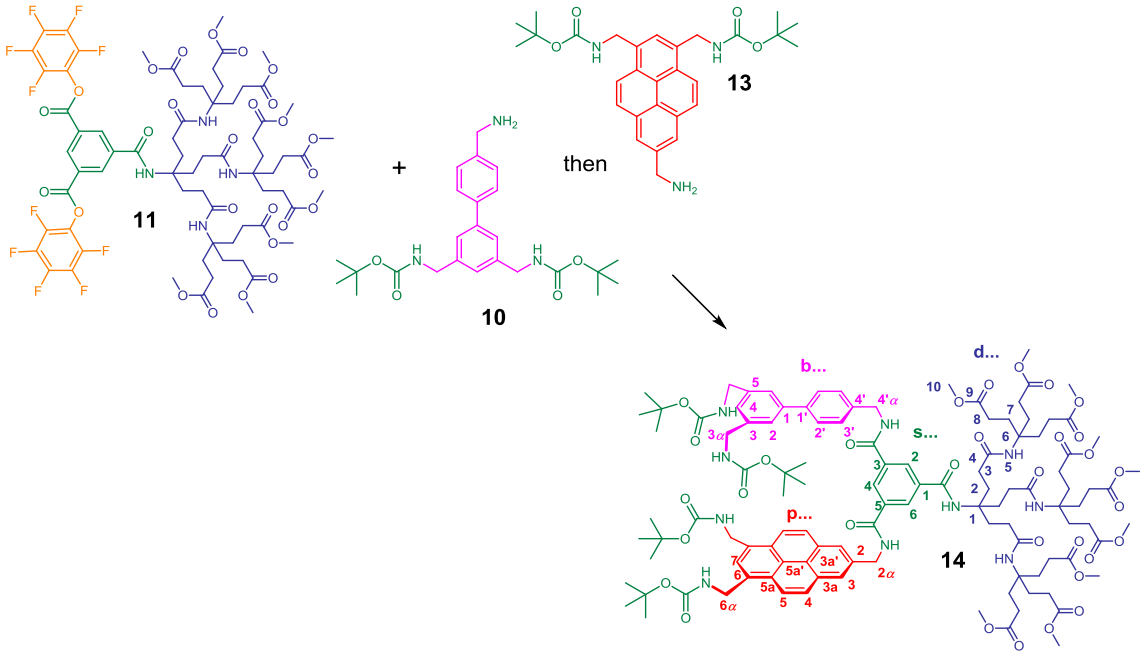


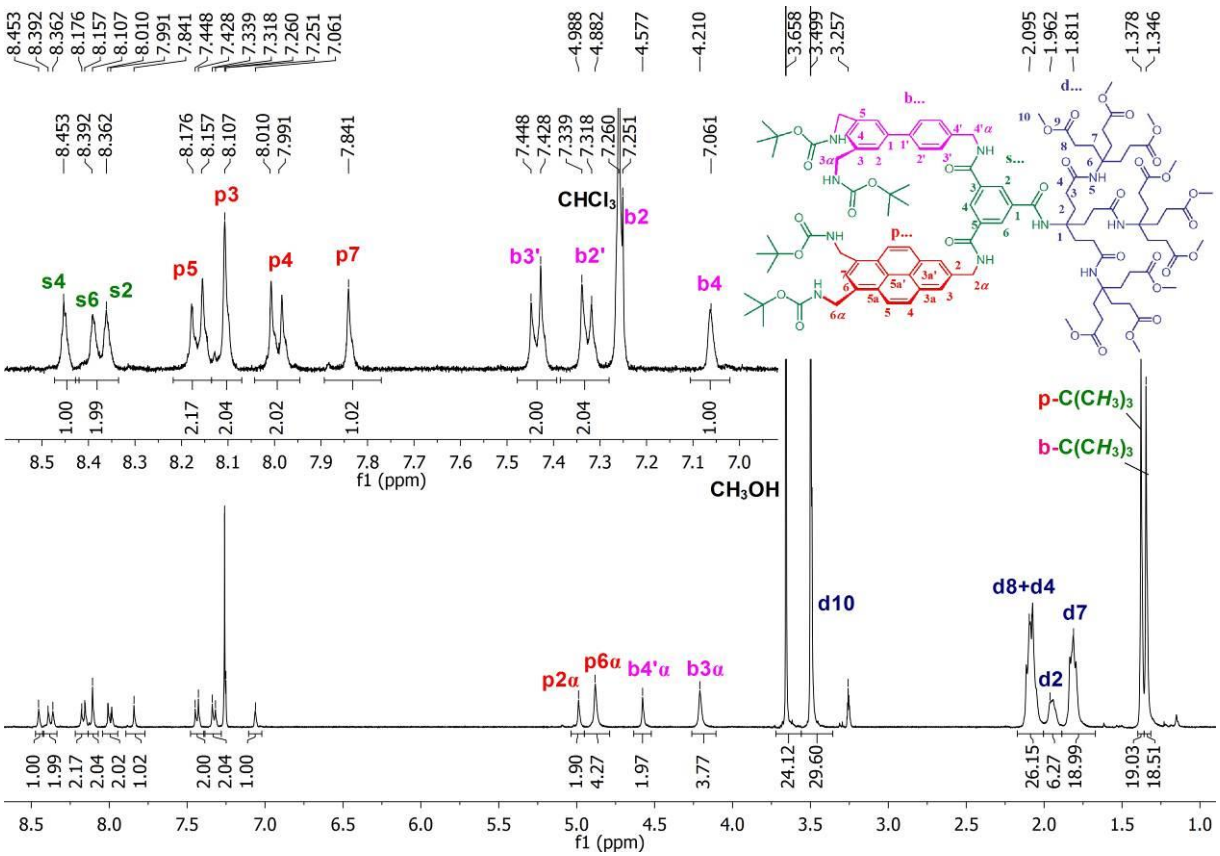
Figure S4. {^{1}H-^{13}C}-HSQC (top) and HMBC (bottom) spectra of 1,1'-biphenyl-3,5-bis[3-(N-tert-butyloxycarbonyl)aminomethyl]-4'-aminomethyl **10**, with assignments. The spectra were recorded at 500 MHz in $CDCl_3$.



Boc-protected pyrene-biphenyl tetraamine 14

A solution of methylaminobiphenyl **10** (50 mg, 0.107 mmol) in dry THF (2 mL) was slowly added to a stirred solution of bis-pentafluorophenylester **11** (0.461 g, 0.291 mmol) in dry THF (10 mL). After adding DIPEA (0.1 mL, 0.57 mmol) and stirring for two hours, TLC analysis (MeOH/DCM 1:9) indicated the absence of starting methylaminobiphenyl. Methylaminopyrene **13** (0.123 g, 0.252 mmol) was then added, together with an additional 0.2 mL DIPEA (1.2 mmol). After stirring for two hours, the solvents were removed and the crude was purified by HPLC using a C_{18} stationary phase and eluting with acetone in water (30 min. at 50% then to 60% in 60 min. and kept at 60% for 30 min.). Boc-protected pyrene-biphenyl tetraamine **14** (126 mg, 59 μmol, 55%) eluted at t = 80-90 minutes and was isolated as a light yellow solid.[9] ^{1}H NMR (500 MHz, $CDCl_3$): δ = 8.45 (s, 1H, H-S4), 8.39 (s, 1H, H-26), 8.36 (s, 1H, H-s2), 8.17 (d, 2H, ^3J = 4.8 Hz, H-p5), 8.11 (s, 2H, H-p3), 8.00 (d, 2H, ^3J = 4.8 Hz, H-p4), 7.84 (s, 1H, H-p7), 7.44 (d, 2H, ^3J = 5.0 Hz, H-b3'), 7.33 (d, 2H, ^3J = 5.3 Hz, H-b2') 7.25 (s, 2H, H-b2), 7.06 (s, 1H, H-b4), 4.99 (s, 2H, H-p2α), 4.88 (s, 4H, H-p6α), 4.58 (s, sH, H-4'α), 4.21 (s, 4H, H-3α), 3.50 (s, 27H, H-d10), 2.10 (m, 24H, H-d4+H-d8), 1.96 (m, 6H, H-d2), 1.81 (t, 18H, ^3J = 8.0 Hz, H-d7), 1.38 (s, 18H, p-C(CH_3)$_3$), 1.35 (s, 18H, b-C(CH_3)$_3$) ppm; {^{1}H-^{13}C} HSQC: δ = 128.7 (C-s2), 128.4 (C-s2), 128.0 (C-s6), 127.8 (C-b2'), 127.1 (C-p4), 126.9 (C-b3'), 126.7 (C-p7), 124.9 (C-b4), 124.6 (C-b2), 124.4 (C-p3), 122.7 (C-p5), 52.0 (C-d10), 44.6 (C-b3α), 44.5 (C-p2α), 43.8 (C-b4'α), 42.7 (C-p6α), 31.2 (C-d2; C-d4), 29.1 (C-d7), 28.2 (p-C(CH_3)$_3$; b-C(CH_3)$_3$), 28.1 (C-d8) ppm. (see Figure S5 for spectra); HRMS (ESI$^+$): m/z calculated for $C_{112}H_{150}N_{10}O_{32}Na$ [M + Na]$^+$: 2170.0314, found 2170.0335.

[9] Boc-protected dipyrene tetraamine (54 mg, 25 μmol) eluted at t = 90-100 minutes.


s4
s6
s2
p5
p3
p4
p7
b3'
b2'
CHCl3
b2
b4
p-C(CH3)3
b-C(CH3)3
CH3OH
d10
d8+d4
d7
d2
p2α
p6α
b4'α
b3α
f1 (ppm)

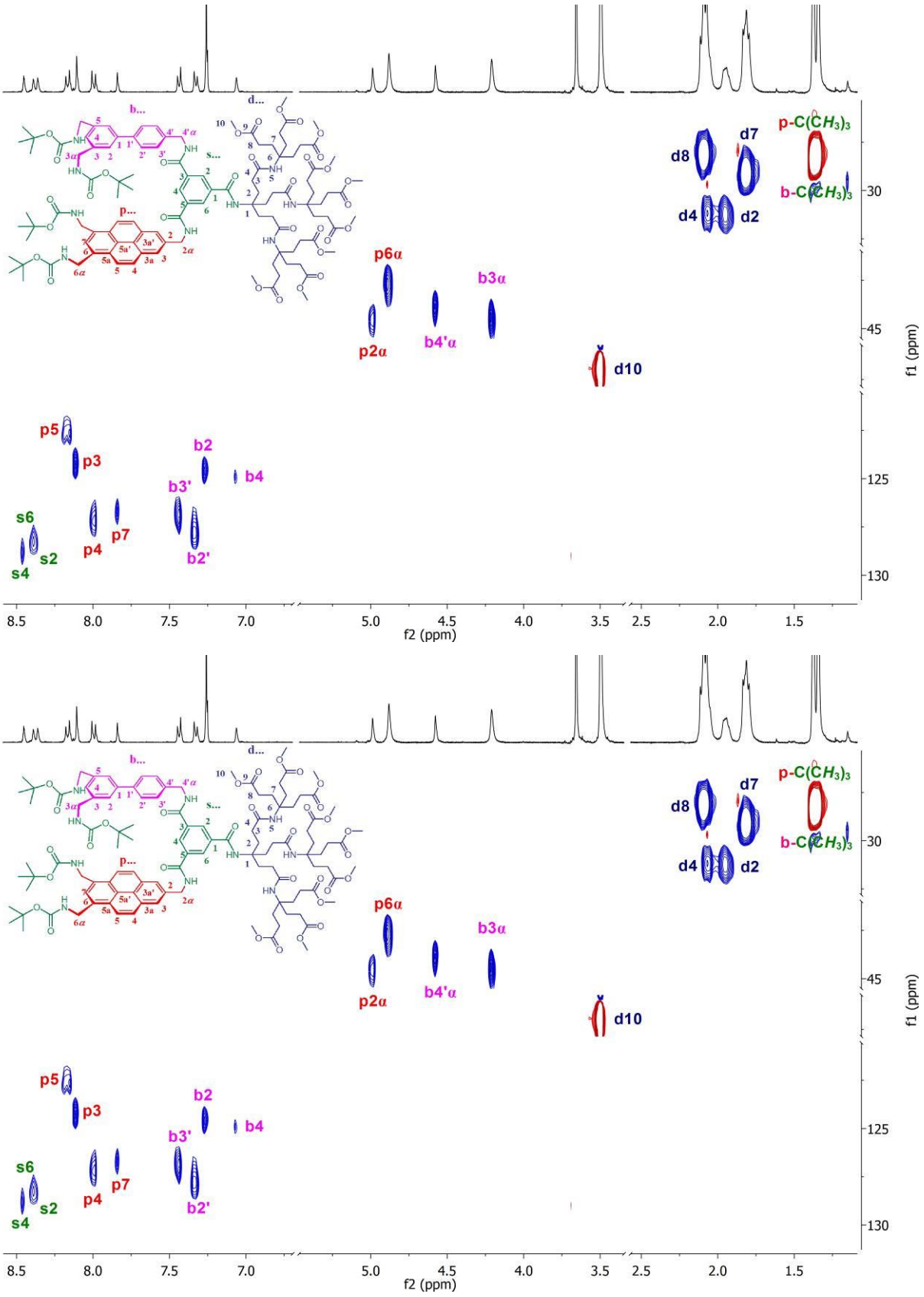
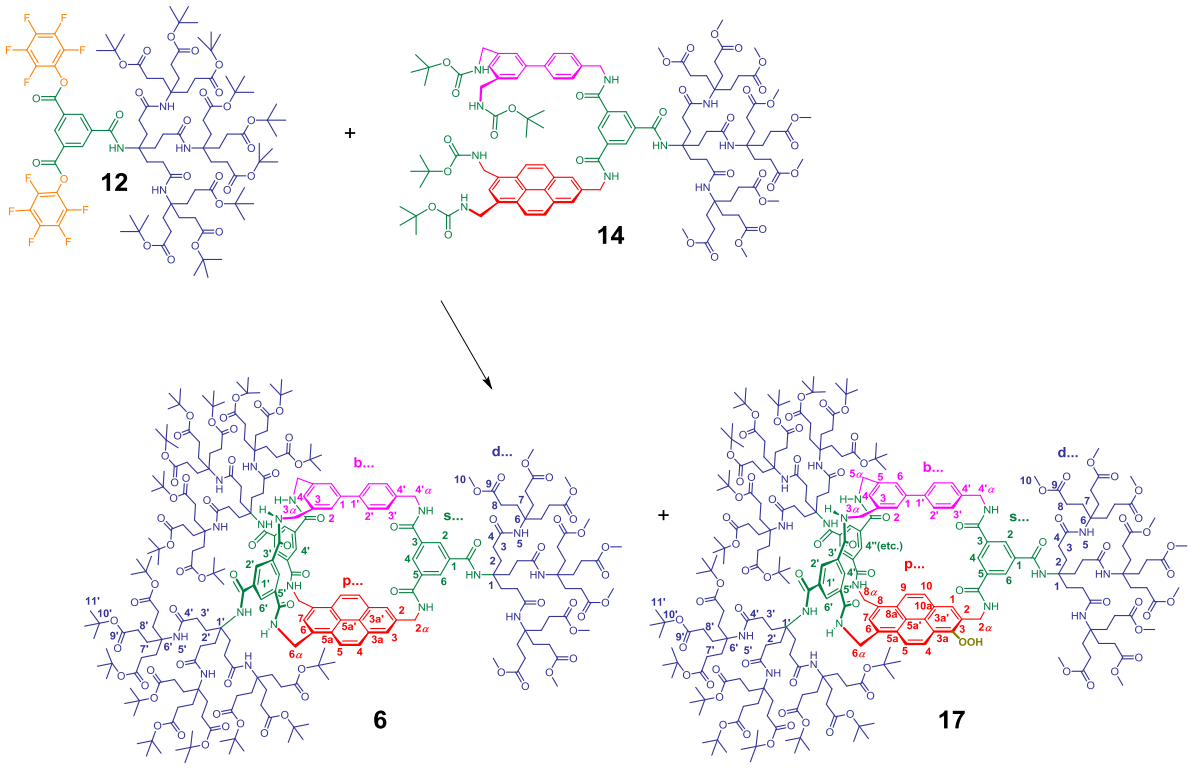


Figure S5. ^{1}H-NMR (top) and {^{1}H-^{13}C}-HSQC (bottom) spectra of Boc-protected pyrene-biphenyl tetraamine **14**, with assignments. The spectra were recorded at 500 MHz in $CD_3OD/CDCl_3$ 1:4.



Protected receptors 6 and 17

To a stirred solution of Boc-protected tetraamine **14** starting material (126 mg, 59 μmol) and $HSiEt_3$ (200 μL, 1.25 mmol) in DCM (5 mL) at 0 °C, was added TFA (5 mL) in a drop wise manner. The resulting solution was stirred for 16 h, after which the volatiles were removed by passing a stream of N_2 over the stirred mixture. After thorough drying *in vacuo*, the remaining solid was dissolved in dry and degassed THF (600 mL) and DIPEA (0.51 mL, 2.9 mmol) was added. To this stirred solution was added a solution of bispentafluorophenyl ester **12** (0.25 g, 127 μmol) in THF (20 mL) over the course of 48 h. After the addition was complete, the reaction mixture was stirred for an additional 72 h. The solvent was removed *in vacuo* and the resulting oil dissolved in CH_2Cl_2 (25 mL). This solution was washed with saturated NH_4Cl aq. (25 mL), water (25 mL), and dried with $MgSO_4$. After removal of the solvent, the crude was dissolved in an acetone/water 8:2 mixture (15 mL) and purified by preparative HPLC (Waters CSH C18 5 μm 19×250 mm) by injecting 3 ml portions and eluting with acetone in water (from 80% to 92% in 18 min., then to 100% in 2 min., then back to 80% in 5 min.). The material eluting as one peak in between 12 and 14 minutes was isolated (see Figure S6, top) and found to be a mixture of macrobicycles **6** and **17**. Separation (see Figure S6, bottom) was achieved using an ACE 5 C_{18}-PFP column eluting with acetone in water (60 min. at 70%, then to 77% over 44 min., kept at 77% for 33 min., then to 100% in 10 min.), giving protected receptor **6** (R_f = 167.5 min., 14.9 mg, 3.01 μmol, 5.1%) and protected receptor **17** (R_f = 171.5 min., 16.4 mg, 3.30 μmol,

5.6%).[10] A full assignment of both receptors could be made based on ^{1}H, {^{1}H-^{1}H}-COSY, NOESY, TOCSY and {^{1}H-^{13}C}-HSQC. **Data for protected receptor 6** (see also Figure S7-Figure S9): ^{1}H NMR (600 MHz, CD_3OD): δ = 8.64 (s, 2H, H-s6'), 8.58 (s, 1H, H-s6), 8.51 (s, 2H, H-s2'), 8.46 (s, 1H, H-s2), 8.32 (d, 2H, ^{3}J = 9 Hz, H-p5), 8.21 (s, 2H, H-p3), 8.21 (s, 1H, H-p7), 8.10 (s, 1H, H-s4), 8.05 (d, 2H, ^{3}J = 9 Hz, H-p4), 7.99 (s, 2H, H-s4'), 7.36 (s, 2H, H-b2), 7.31 (d, 2H, ^{3}J = 8 Hz, H-b2'), 7.23 (s, 1H, H-b4), 7.22 (d, 2H, ^{3}J = 8 Hz, H-b3'), 5.70 (d, 2H, ^{2}J = 14 Hz, H-p6α(out)), 4.96 (s, 2H, H-p2α), 4.79 (d, 2H, ^{2}J = 14 Hz, H-p6α(in)), 4.55 (d, 2H, ^{2}J = 14 Hz, H-b3α(out)), 4.49 (s, 2H, H-b4'α), 4.39 (d, 2H, ^{2}J = 14 Hz, H-b3α(in)), 3.63 (s, 27H, H-d10), 2.32 (t, 6H, H-d3), 2.3 (t, 18H, H-d8), 2.3 (t, 12H, H-d3'), 2.21 (t, 36H, H-d8'), 2.15 (t, 6H, H-d2), 2.15 (t, 12H, H-d2'), 2.02 (t, 18H, H-d7), 1.98 (t, 36H, H-d7'), 1.41 (s, 162H, H-d11') ppm; {^{1}H-^{13}C} HSQC: δ = 134.22 (C-p3), 132.28 (C-s6'), 132.05 (C-s6), 131.91 (C-s2), 131.85 (C-s2'), 130.84 (C-b3'), 130.54 (C-b4), 130.28 (C-p4), 129.74 (C-s4), 129.68 (C-s4'), 128.97 (C-b2'), 128.25 (C-b2), 128.09 (C-p7), 125.91 (C-p5), 53.54 (C-d10), 46.93 (C-p2α), 46.54 (C-b3α(in)), 46.54 (C-b3α(out)), 45.77 (C-b4'α), 44.94 (C-p6α(in)), 44.94 (C-p6α(out)), 33.53 (C-d2), 33.53 (C-d2'), 33.48 (C-d3), 33.28 (C-d3'), 31.95 (C-d8'), 31.69 (C-d7'), 31.52 (C-d7), 30.38 (C-d8), 29.66 (C-d11') ppm; HRMS (ESI^{+}): *m/z* calculated for $C_{262}H_{386}N_{18}O_{72}Na_3$ $[M + 3Na]^{3+}$: 1668.5591, found 1668.5577. **Data for protected receptor 17** (see also Figure S10-Figure S13): ^{1}H NMR (600 MHz, CD_3OD): δ = 8.66 (s, 1H, H-s6'), 8.66 (s, 1H, H-s6''), 8.58 (s, 1H, H-s6), 8.51 (s, 1H, H-s2'), 8.51 (s, 1H, H-s2''), 8.45-8.47 (m, 3H, H-s2, p4, p5), 8.34 (d, 1H, ^{3}J = 9.3 Hz, H-p9), 8.30 (s, 1H, H-p1), 8.25 (s, 1H, H-p7), 8.09 (s, 1H, H-s4), 8.04 (d, 1H, ^{3}J = 9.35 Hz, H-p10), 8.01 (s, 1H, H-s4'), 7.97 (s, 1H, H-s4''), 7.36 (s, 1H, H-b6), 7.34 (s, 1H, H-b2), 7.29 (d, 2H, ^{3}J = 8.05 Hz, H-b2'), 7.24 (s, 1H, H-b4), 7.21 (d, 2H, ^{3}J = 8.25 Hz, H-b3'), 5.72 (d, 1H, ^{2}J = 14.1 Hz, H-p6α(out)), 5.72 (d, 1H, ^{2}J = 14.1 Hz, H-p8α(out)), 5.31 (d, 1H, ^{2}J = 13.55 Hz, H-p2α→OH), 4.87 (d, 1H, H-p2α→p1), 4.81 (d, 1H, H-p6α(in)), 4.81 (d, 1H, H-p8α(in)), 4.57 (d, 1H, ^{2}J = 13.45 Hz, H-b3α(out)), 4.54 (d, 1H, ^{2}J = 14 Hz, H-b5α(out)), 4.51 (d, 1H, ^{2}J = 11.15 Hz, H-b4'α→OH), 4.45 (d, 1H, ^{2}J = 11.3 Hz, H-b4'α→p1), 4.39 (d, 1H, ^{2}J = 11.3 Hz, H-b5α(in)), 4.37 (d, 1H, ^{2}J = 11.55 Hz, H-b3α(in)), 3.64 (s, 27H, H-d10), 2.32 (t, 6H, H-d3), 2.31 (t, 18H, H-d8), 2.3 (t, 12H, H-d3'), 2.22 (t, 36H, H-d8'), 2.18 (t, 6H, H-d2), 2.16 (t, 12H, H-d2'), 2.02 (t, 18H, H-d7), 1.98 (t, 36H, H-d7'), 1.41 (s, 162H, H-d11') ppm; {^{1}H-^{13}C} HSQC: δ = 135.05 (C-p7), 132.33 (C-s6'), 132.33 (C-s6''), 132.04 (C-s6), 131.92 (C-s2), 131.90 (C-s2'), 131.90 (C-s2''), 130.75 (C-b3'), 130.67 (C-b4), 130.32 (C-p1), 129.95 (C-s4), 129.88 (C-p10), 129.82 (C-s4'), 129.79 (C-s4''), 129.04 (C-b2'), 128.3 (C-b2), 128.3 (C-b6), 127.41 (C-p4), 126.16 (C-p9), 126.01 (C-p5), 53.57 (C-d10), 46.52 (C-b3α(in)), 46.52 (C-b3α(out)), 46.52 (C-b5α(in)), 46.52 (C-b5α(out)), 45.95 (C-p2α→OH), 45.95 (C-p2α→p1), 45.73 (C-b4'α→OH), 45.73 (C-b4'α→p1), 44.98 (C-p6α(in)), 44.98 (C-p6α(out)), 44.98 (C-p8α(in)), 44.98 (C-p8α(out)), 33.62 (C-d2), 33.51 (C-d3), 33.46 (C-d2'), 33.34 (C-d3'), 31.98 (C-d8'), 31.73

[10] 6.7 mg (~ 1.35 μmol) of a mixed fraction eluting at 169-170 minutes was also collected.

(C-d7'), 31.57 (C-d7), 30.41 (C-d8), 29.69 (C-d11') ppm; HRMS (ESI$^+$): *m/z* calculated for $C_{262}H_{386}N_{18}O_{74}Na_3$ $[M + 3Na]^{3+}$: 1679.2224, found 1679.2290.

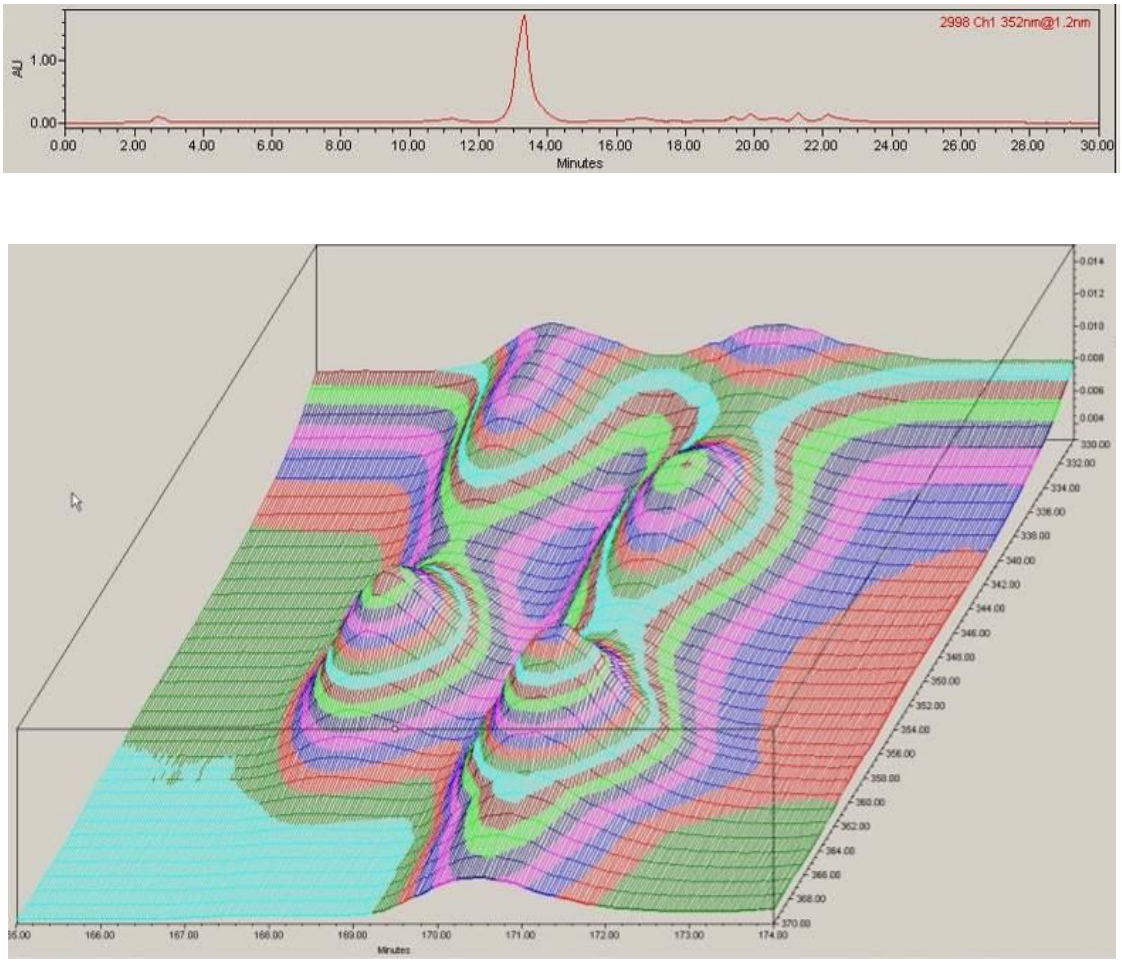


Figure S6. Preparative HPLC traces for: **top)** first purification monitored at 352 nm of crude product on a Waters CSH C_{18} column (80%>>18 min.>>92%>>2 min.>>100%>>2 min.80%); **bottom)** final purification of protected receptors **6** (166-169 min.) and **17** (170-173 min.) as monitored at 330-370nm, using an ACE 5 C_{18}-PFP column (70%(60min.)>>44 min.>>77%(33 min.)>>10 min.>>100%).

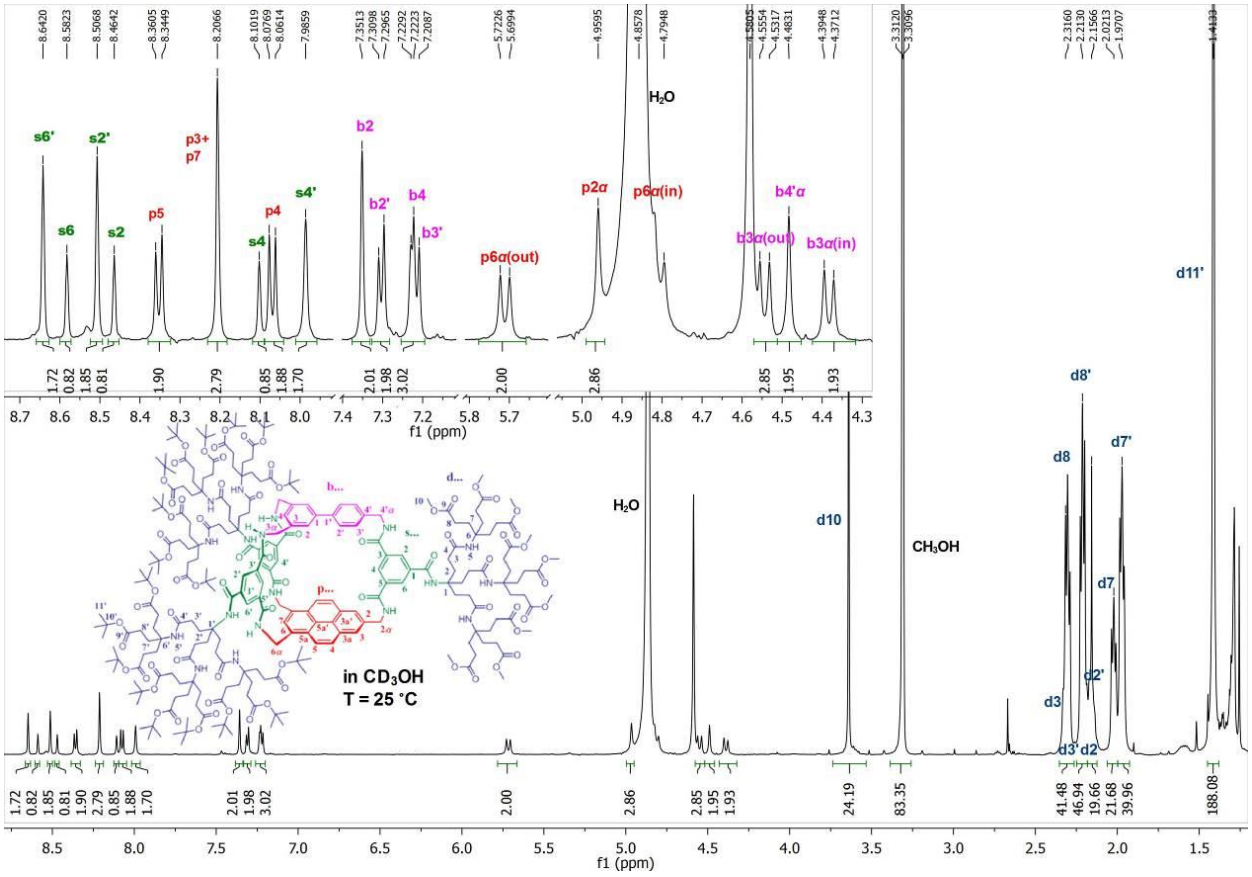


Figure S7. ^{1}H-NMR spectrum of protected receptor **6** recorded at 600 MHz in CD_3OD, with assignments.

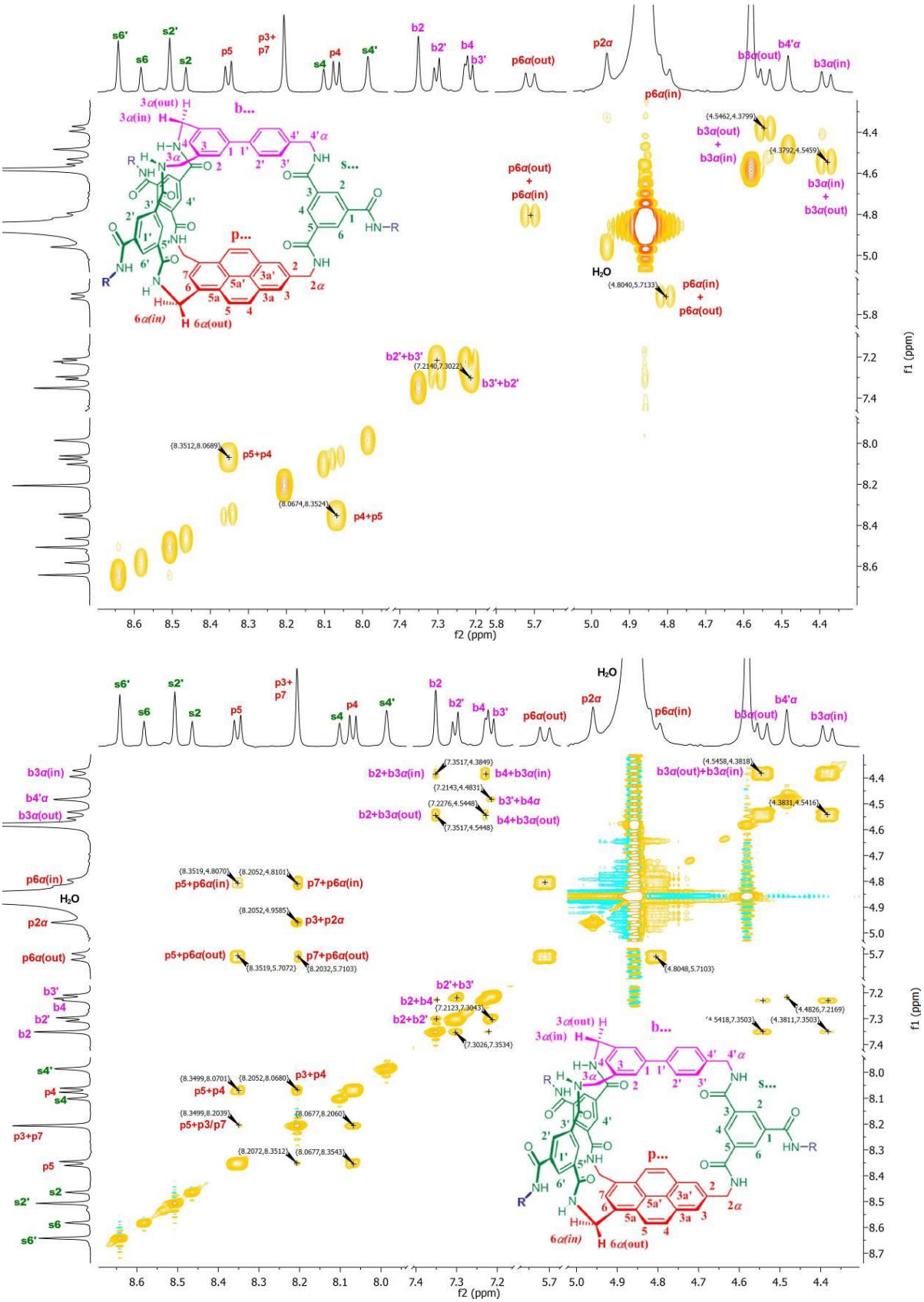


Figure S8. {^{1}H-^{1}H}-COSY (top) and {^{1}H-^{1}H}-NOESY (bottom) spectra of protected receptor **6**, with assignments. The spectra were recorded at 600 MHz in CD_3OD.

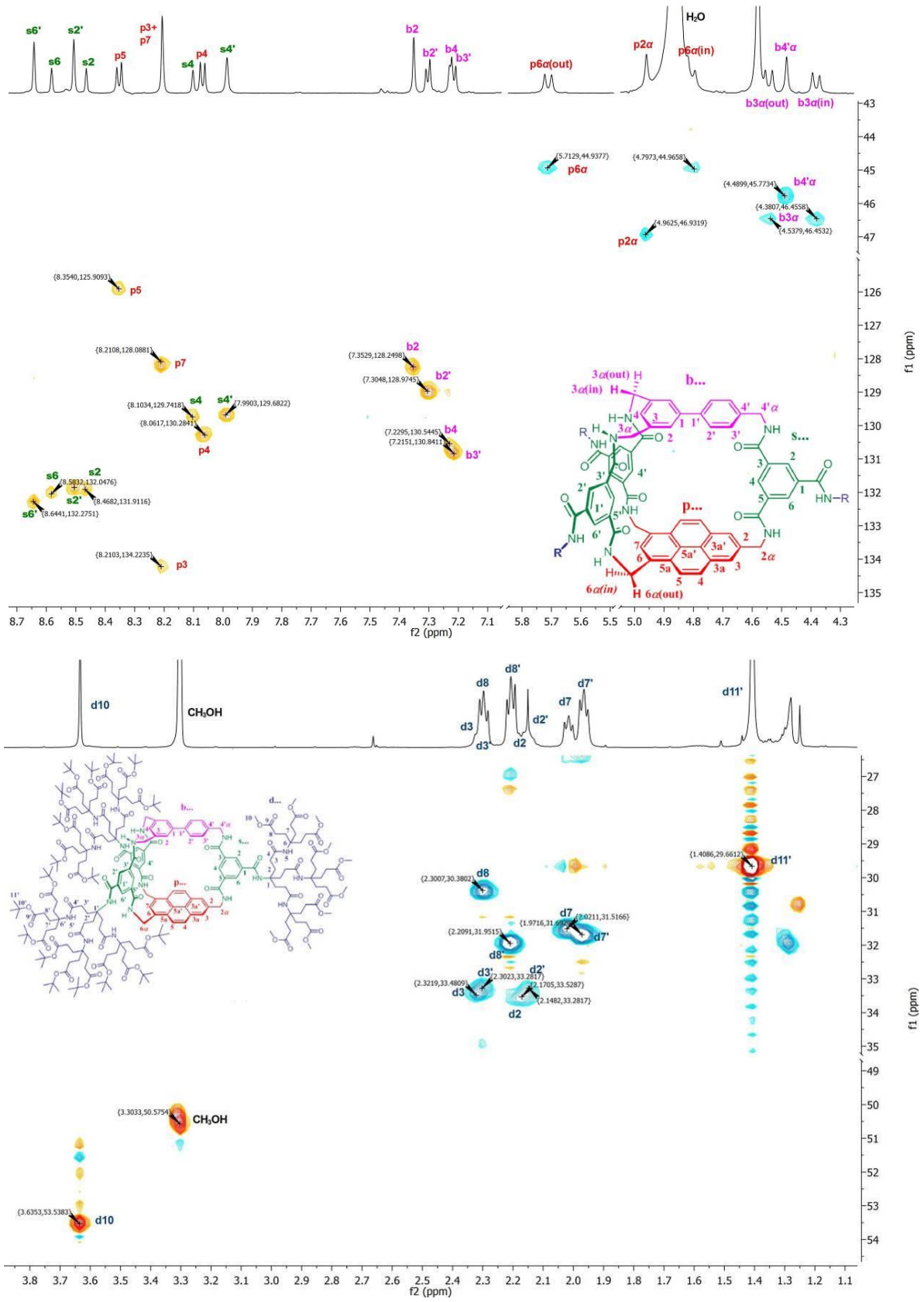


Figure S9. {^{1}H-^{13}C}-HSQC spectrum of protected receptor **6**, with assignments. The aromatic and aliphatic regions are shown top and bottom respectively. The spectrum was, as recorded at 600 MHz in CD_3OD.

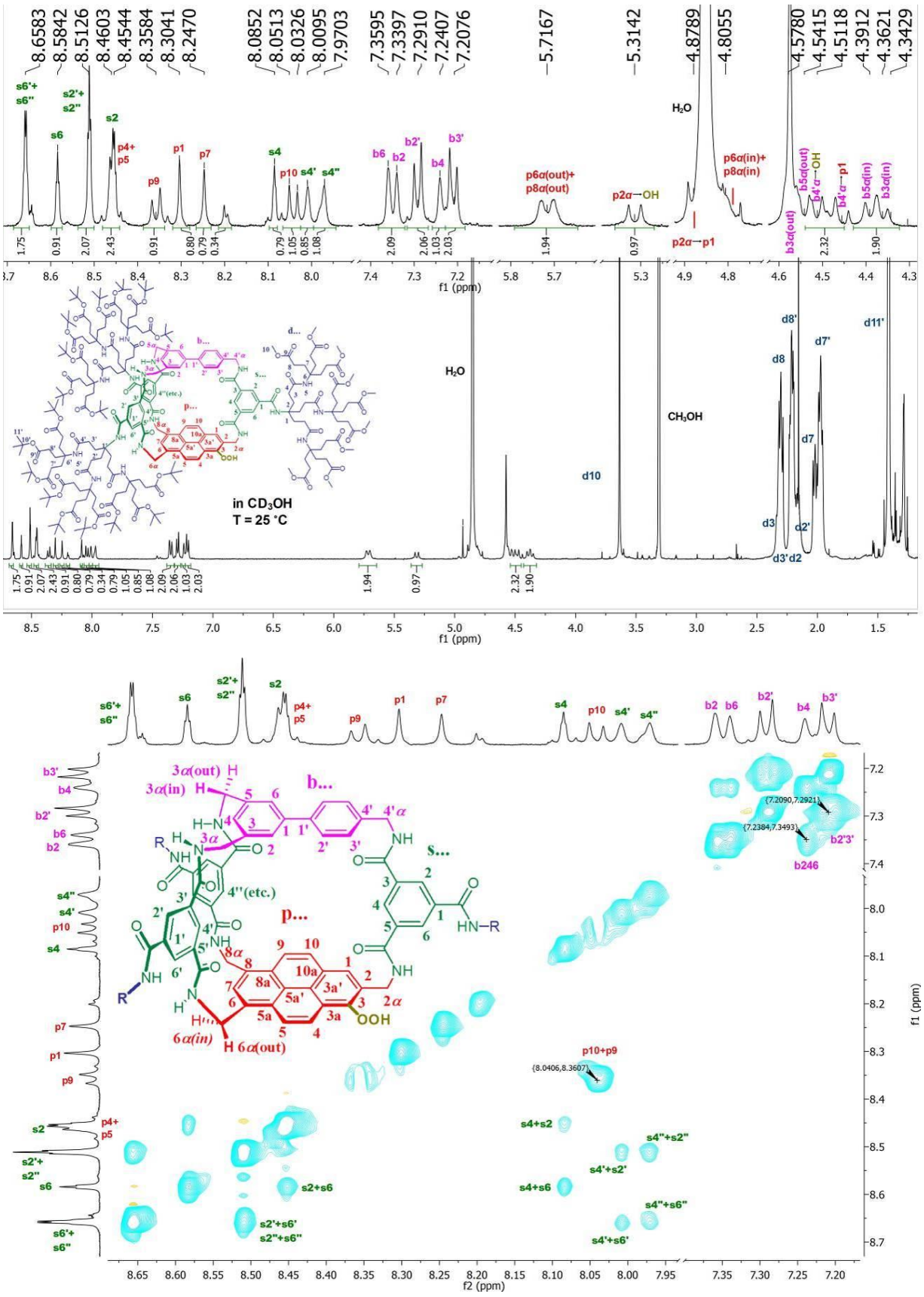


Figure S10. ^{1}H-NMR (top) and {^{1}H-^{1}H}-TOCSY (bottom) spectra of protected receptor **17** recorded at 600 MHz in CD_3OD, with assignments.

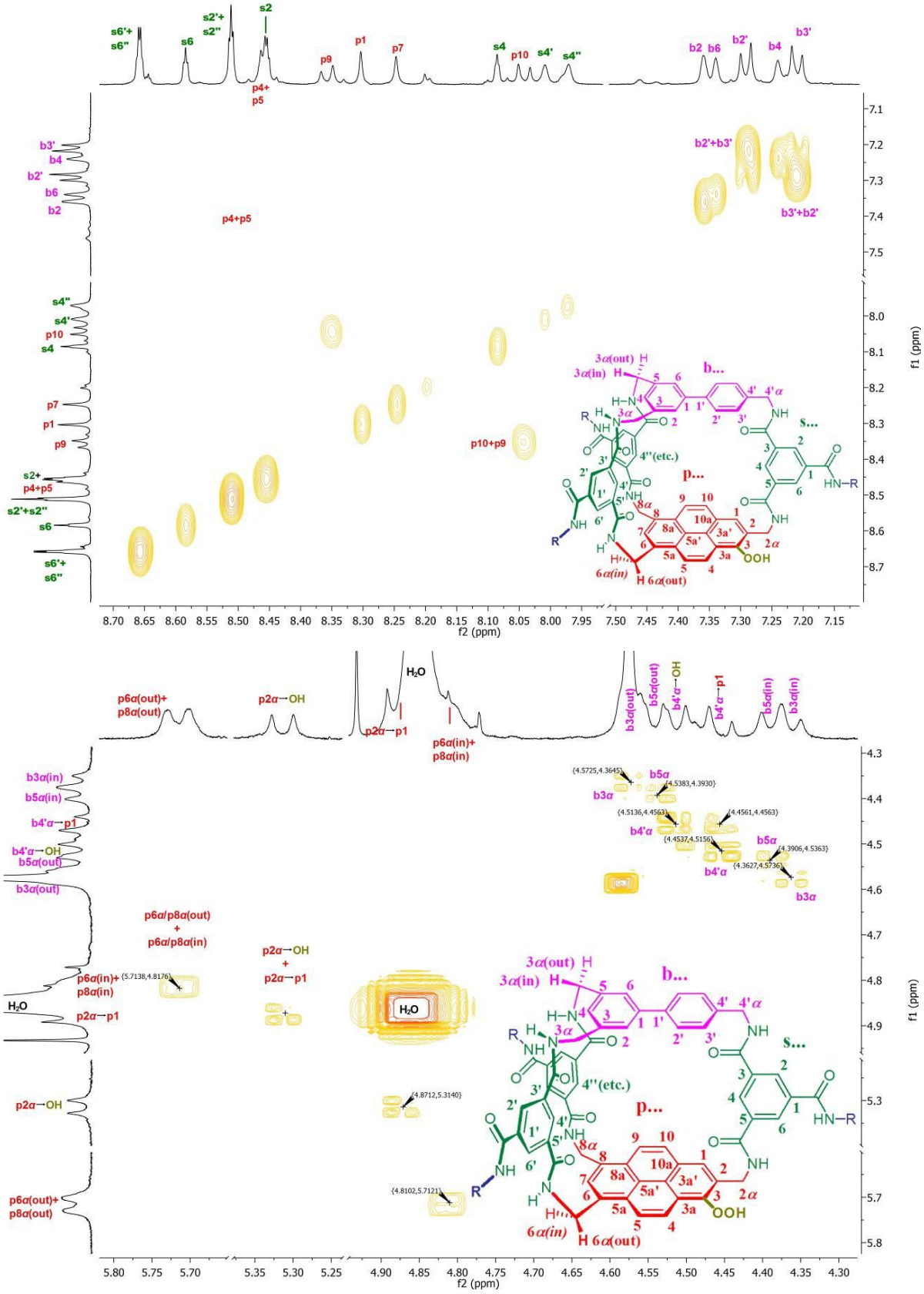


Figure S11. Partial {^{1}H-^{1}H}-COSY spectra of protected receptor **17** recorded at 600 MHz in CD_3OD, with assignments.

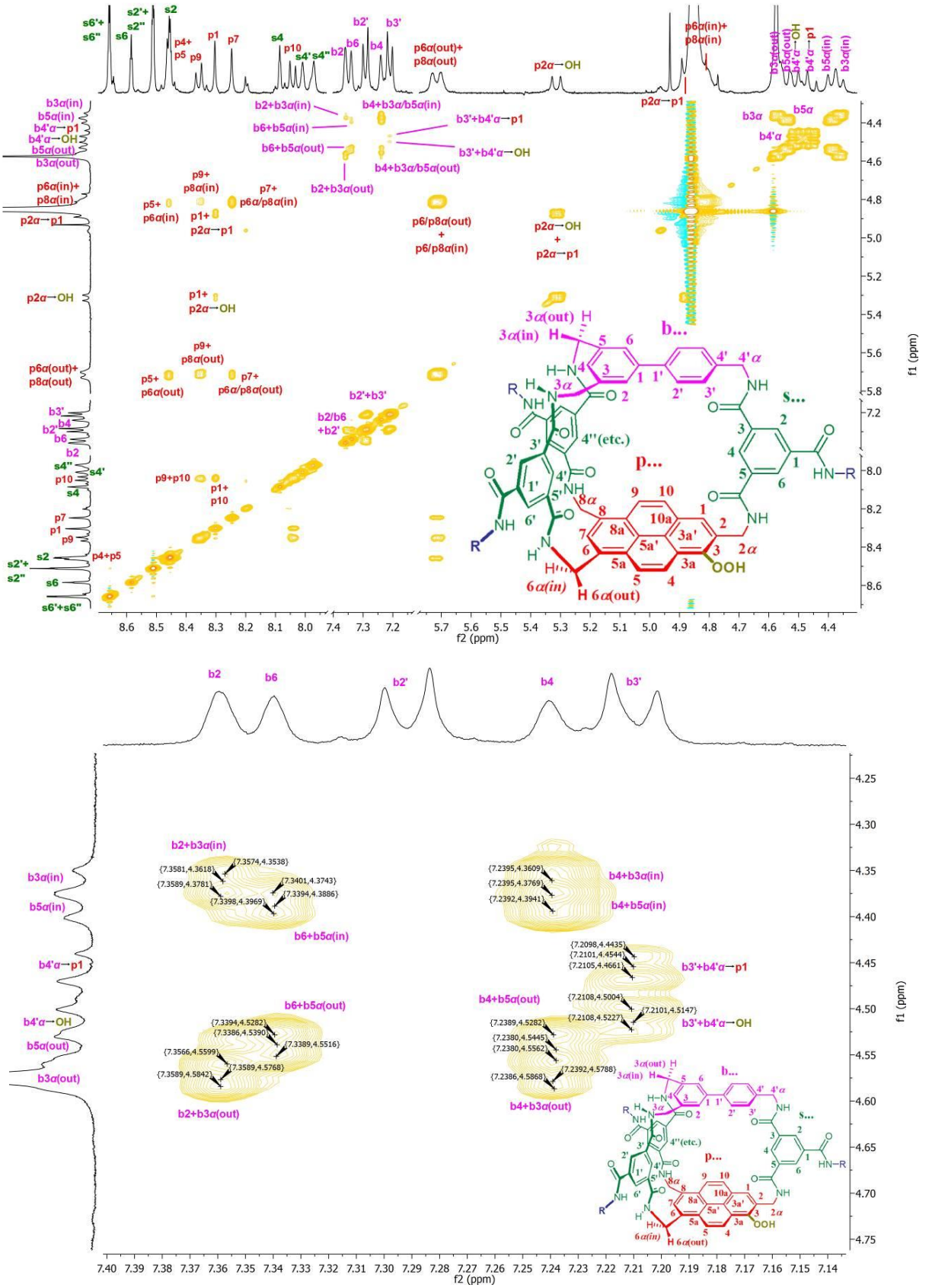


Figure S12. Partial {^{1}H-^{1}H}-NOESY spectra of protected receptor **17** recorded at 600 MHz in CD_3OD, with assignments.

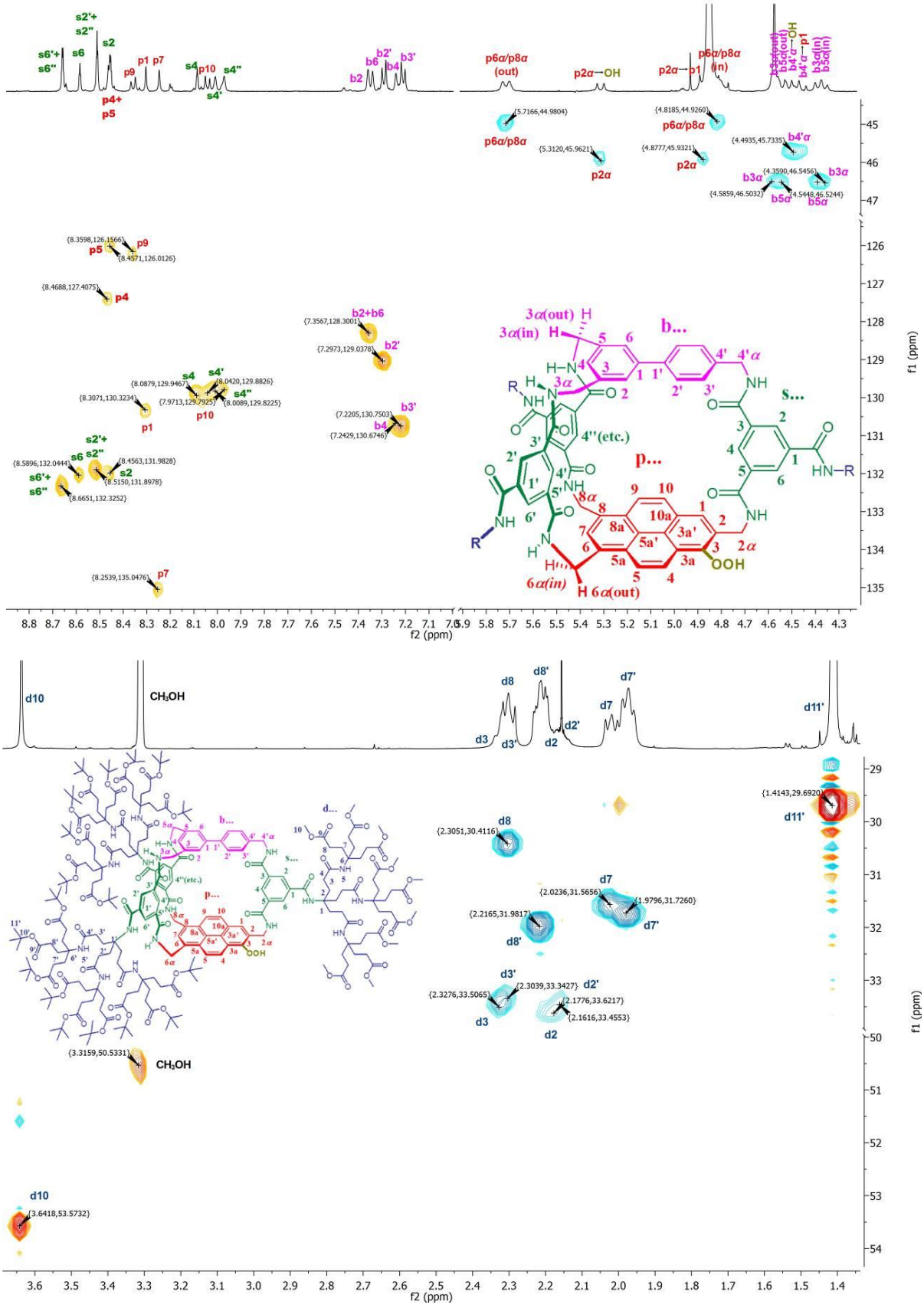
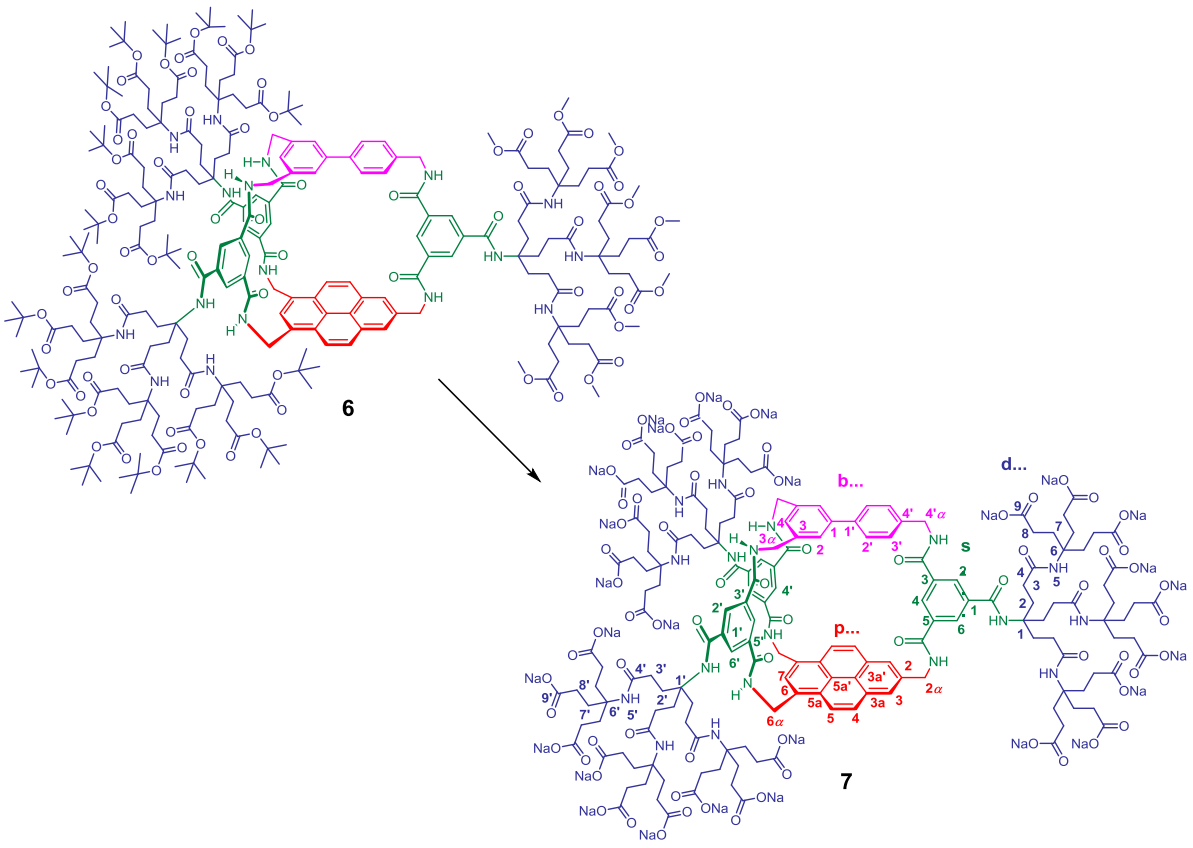


Figure S13. Partial {^{1}H-^{1}H}-HSQC spectra of protected receptor **17** recorded at 600 MHz in CD_3OD, with assignments.



Receptor 7

A 25 mL round-bottomed flask was charged with N_2, a magnetic stirrer, protected receptor (7.45 mg, 1.50 μmol), and dry DCM (5 mL). The solution was cooled to 0 °C, and TFA (5 mL) was added dropwise. The resulting solution was allowed to warm slowly to laboratory temperature (ca. 25 °C), then stirred for about 12 h. The volatiles were removed by passing a N_2 stream over the solution and the remaining solid was suspended in water (10 mL) and freeze-dried (twice). The resulting white solid was then suspended in water (3 mL), NaOH was added (0.2 mL, 5 M), and the resulting solution was stirred for 15 minutes. Ion exchange resin (Amberlyst 15, hydrogen form; thoroughly washed with water) was then added until pH < 3. The resulting suspension was then neutralized using NaOH (5 M, 1 M, and 0.1 M solutions) to pH ≈ 7.1. After passing the resulting solution through 45 then 20 μm filters, it was freeze-dried to yield the receptor in its sodium form as an off-white solid in ~100% yield (6.60 mg, 1.50 μmol). A full assignment of the ^{1}H-NMR spectrum could be made based on {^{1}H-^{1}H}-COSY, TOCSY, and NOESY spectroscopy, as detailed in Figure S14-Figure S16. A dilution study (Figure S17) implied that the receptor was monomeric at least below 0.35 mM. ^{1}H NMR (600 MHz, D_2O): δ = 8.31 (s, 2H, H-s6'), 8.25-8.15 (m, 11H, H-s2, s2', s6, p3, p5, p7), 8.07 (d, 2H, H-p4), 7.27 (s, 1H, H-s4), 7.16 (s, 2H, H-s4'), 5.60 (d, 2H, ^2J = 11.1 Hz, H-p6α(out)), 4.87 (s, 2H, H-p2α), 4.73 (d, 2H, H-p6α(in)), 4.40 (m, 4H, H-b3α(out)+b4'α), 4.28 (d, 2H, ^2J = 11.3 Hz, H-b3α), 2.21 (m, 18H, H-d3, d3'), 2.03 (m, 78H, D-d2, d7, d8, d8'), 1.81 (m, 48H, H-d2', d7') ppm.

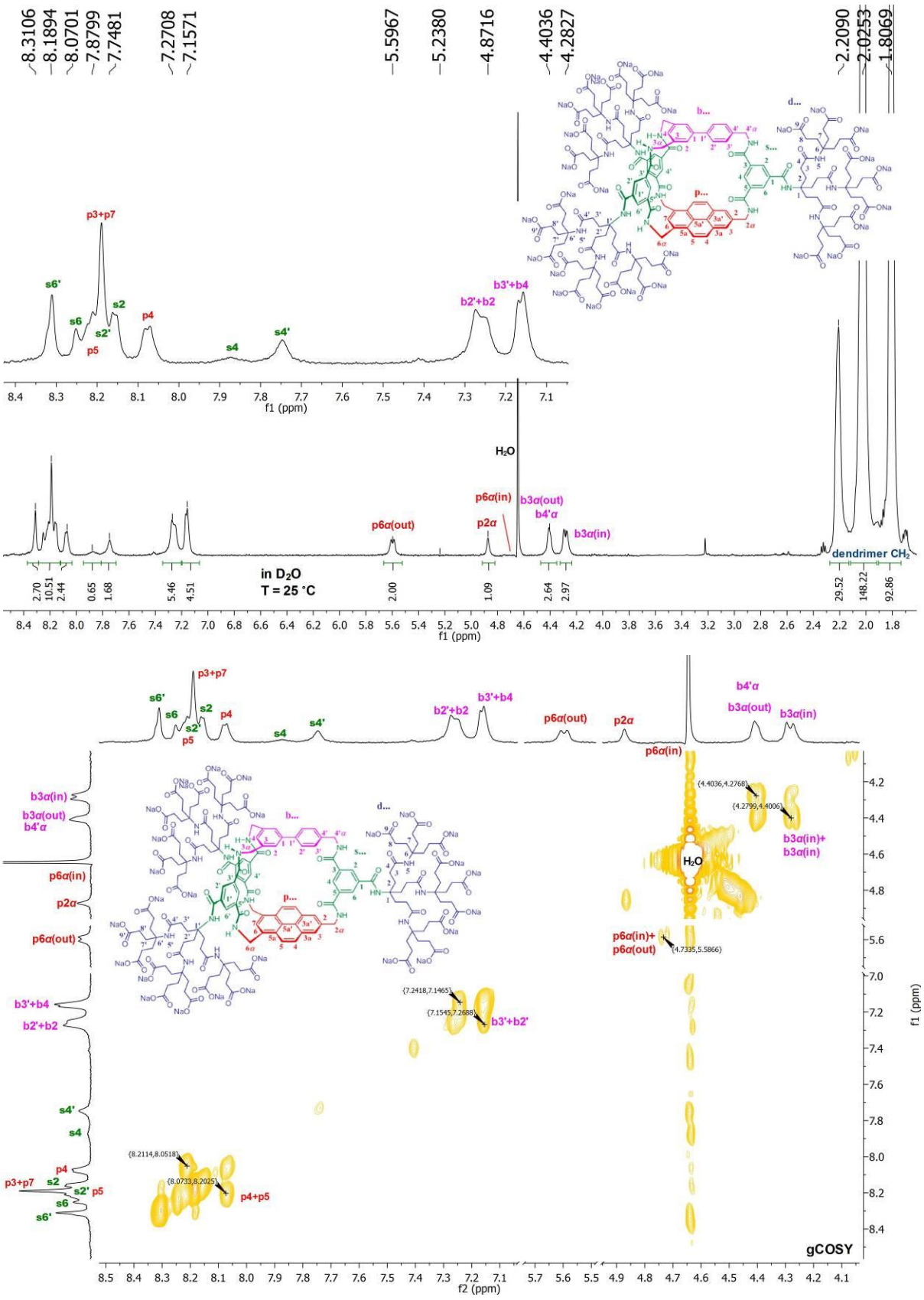


Figure S14. ^{1}H-NMR (top) and partial {^{1}H-^{1}H}-COSY (bottom) spectra of receptor **7**, with assignments. The spectra were recorded at 600 MHz in D_2O.

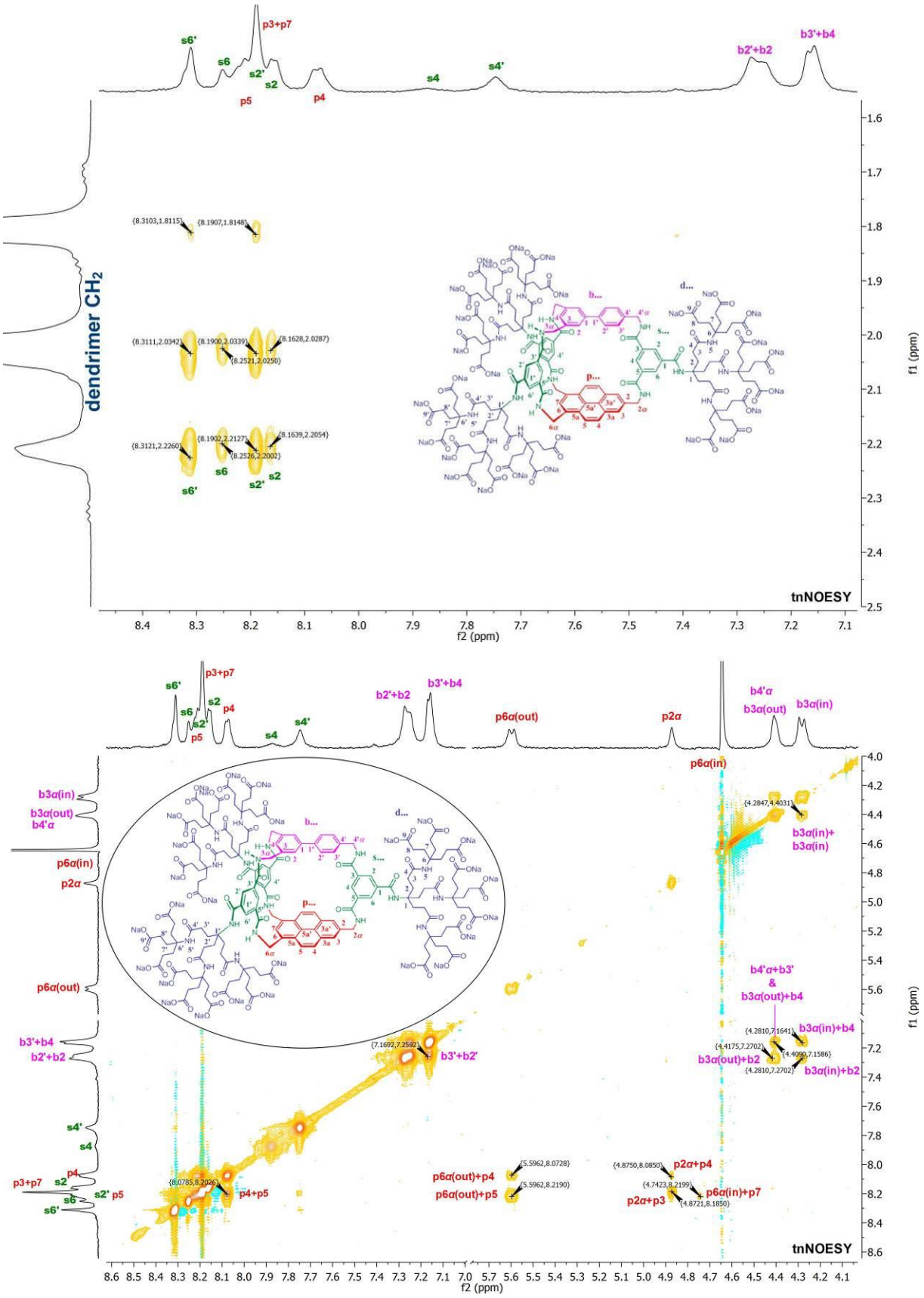


Figure S15. Partial {^{1}H-^{1}H}-NOESY spectra of receptor **7** recorded at 600 MHz in D_2O, with assignments.

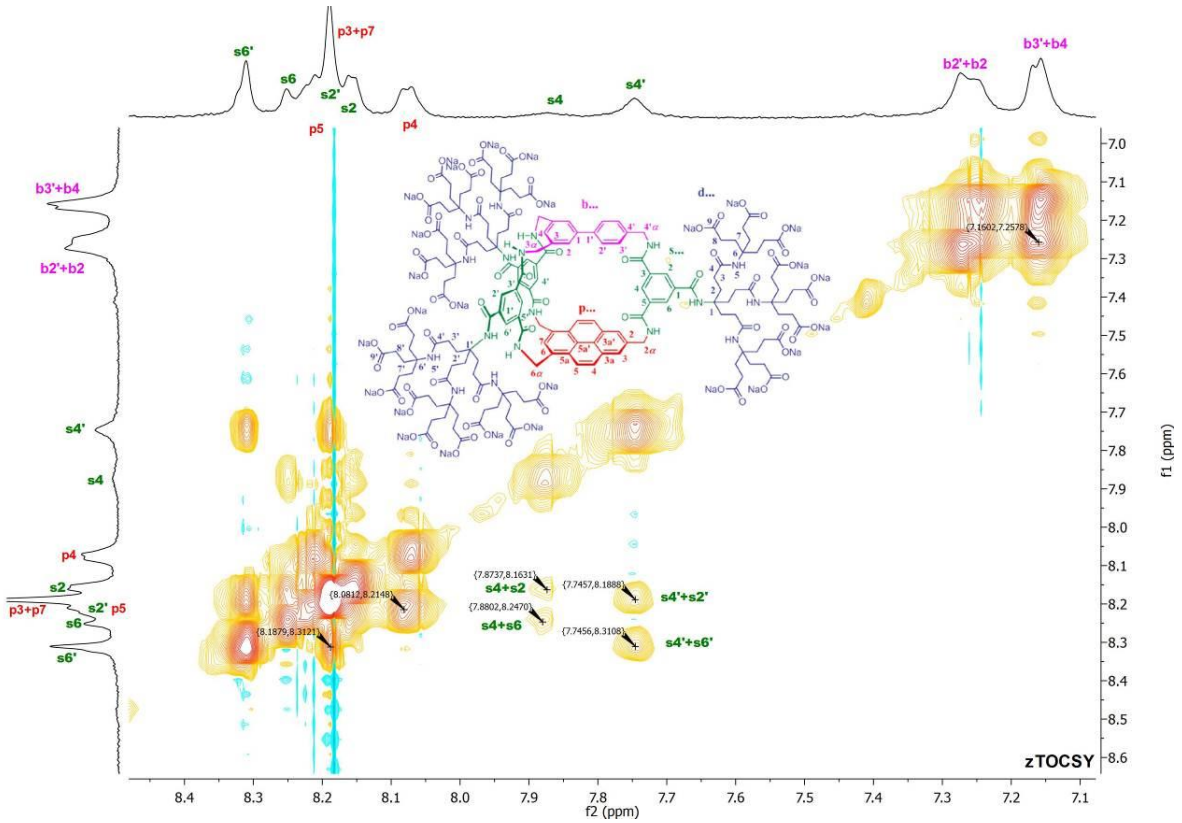


Figure S16. Partial {^{1}H-^{1}H}-TOCSY spectra of receptor **7** recorded at 600 MHz in D_2O, with assignments.

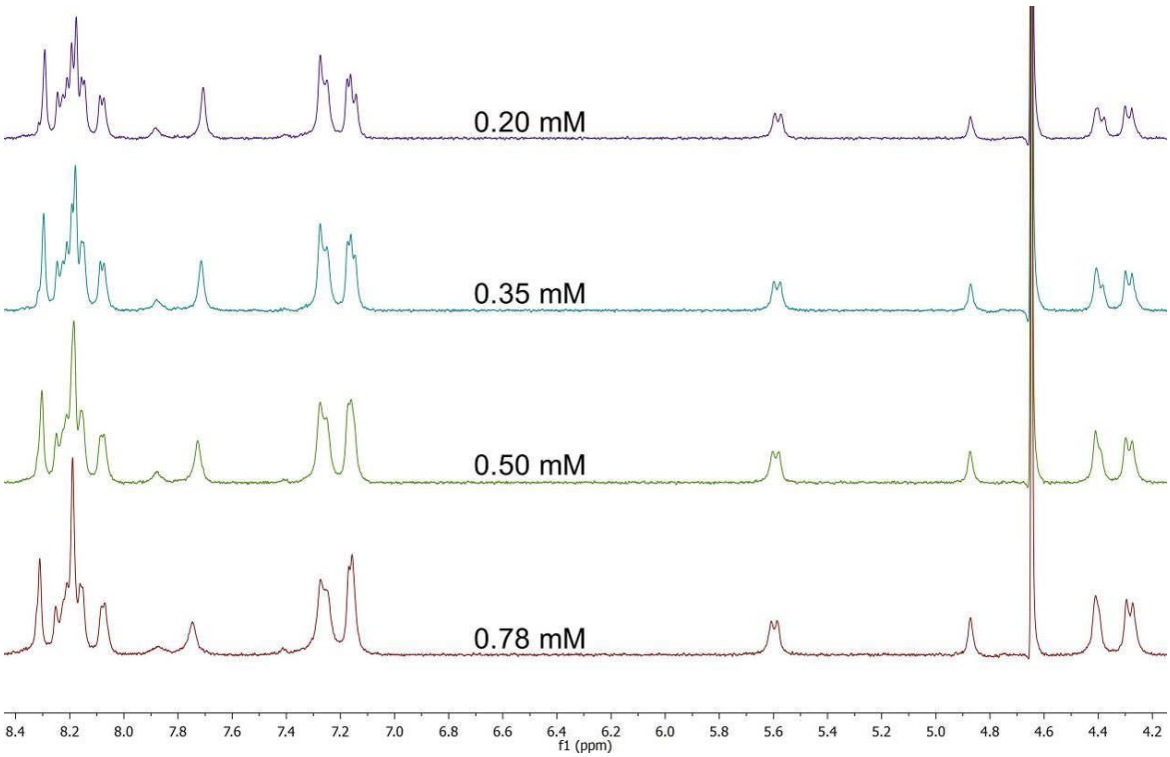
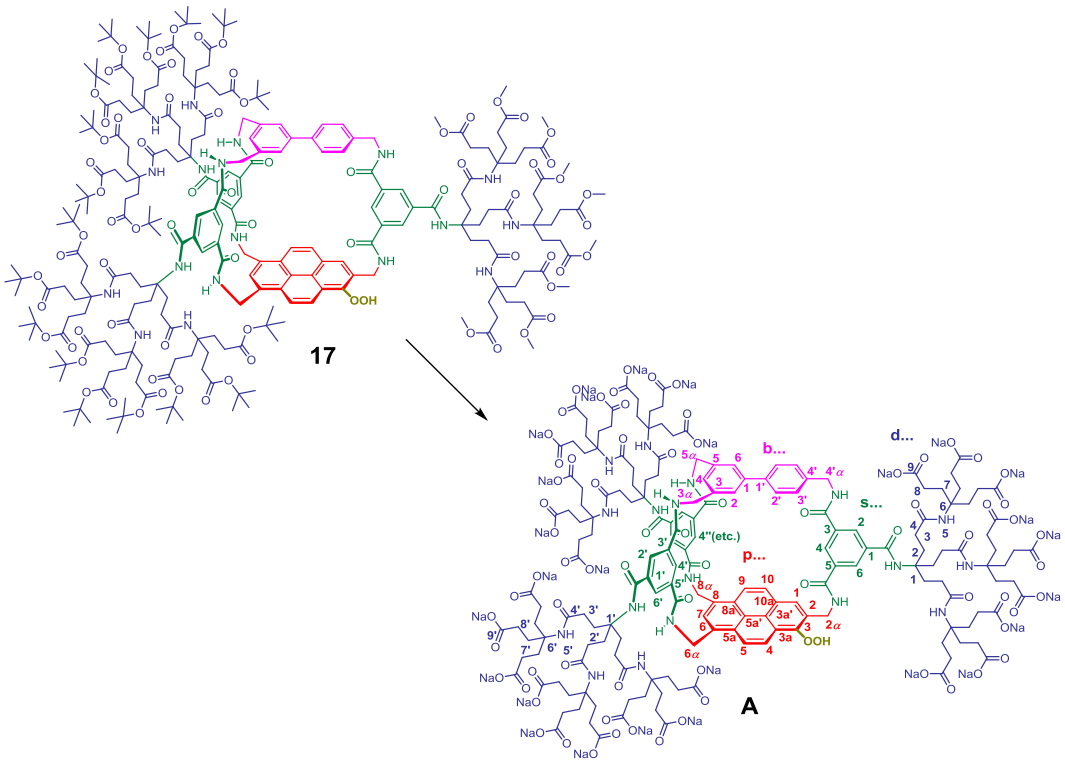


Figure S17. Dilution study of receptor **7** at pH = 7.0 and T = 25 °C as followed by ^{1}H-NMR spectroscopy (600 MHz, D_2O).



Deprotection of 17

A 25 mL roundbottom flask was charged with N_2, a magnetic stirrer, protected receptor (8.2 mg, 1.65 μmol), and dry DCM (5 mL). The solution was cooled to 0 °C, and TFA (5 mL) was added dropwise. The resulting solution was allowed to slowly warm to laboratory temperature (ca. 25 °C), where it was stirred for about 12 h. The volatiles were removed by passing a N_2 stream over the solution and the remaining solid was suspended in water (10 mL) and freeze-dried (twice). The resulting white solid was then suspended in water (3 mL), NaOH was added (0.2 mL, 5 M), and the resulting solution was stirred for 15 minutes. Ion exchange resin (Amberlyst 15, hydrogen form; thoroughly washed with water) was then added until pH < 3. The resulting suspension was then neutralized using NaOH (5 M, 1 M, and 0.1 M solutions) to pH ≈ 7.1. After passing the resulting solution through a 45 and a 20 μm filter, it was freeze-dried to yield the receptor, presumed to be **A**,[11] in its sodium form as an off-white solid in 100% yield (7.31 mg, 1.65 μmol). A dilution study (Figure S21) implied that the receptor was monomeric at concentrations below 0.9 mM. ^{1}H NMR (600 MHz, D_2O): δ = 8.49 (d, 1H, H-p4), 8.37 (d, 1H, H-p5), 8.30 (s, 1H, H-s6', s6''), 8.27 (s, 1H, H-p7), 8.26 (s, 1H, H-s6), 8.22 (d, 1H, H-p9), 8.19 (s, 1H, H-p1), 8.18 (s, 1H, H-s2', s2''), 8.16 (s, 1H, H-s2), 8.07 (d, 1H, H-p10), 7.91 (s, 1H, H-s4), 7.75 (s, 1H, H-s4', s4''), 7.26 (s, 1H, H-b2, b6), 7.22 (d, 2H, H-b2'), 7.15 (s, 1H, H-b4), 7.14 (d, 2H, H-b3'), 5.59 (d, 1H, H-p8α(out)), 5.25 (d, 1H, H-p2α→OH),

[11] See discussion on page S2.

4.88 (d, 1H, H-p2*α*→p1), 4.75 (d, 1H, H-p6*α*(in), p8*α*(in)), 4.61 (d, 1H, H-p6*α*(out)), 4.42 (d, 1H, H-b5*α*(out)), 4.41 (d, 1H, H-b4'*α*→OH), 4.38 (d, 1H, H-b3*α*(out)), 4.29 (d, 1H, H-b5*α*(in)), 4.27 (d, 1H, H-b4'*α*→p1), 4.25 (d, 1H, H-b3*α*(in)), 2.21 (m, 18H, H-d3, d3', d3''), 2.03 (m, 78H, D-d2, d7, d8, d8', d8''), 1.81 (m, 48H, H-d2', d2'', d7', d7'') ppm.

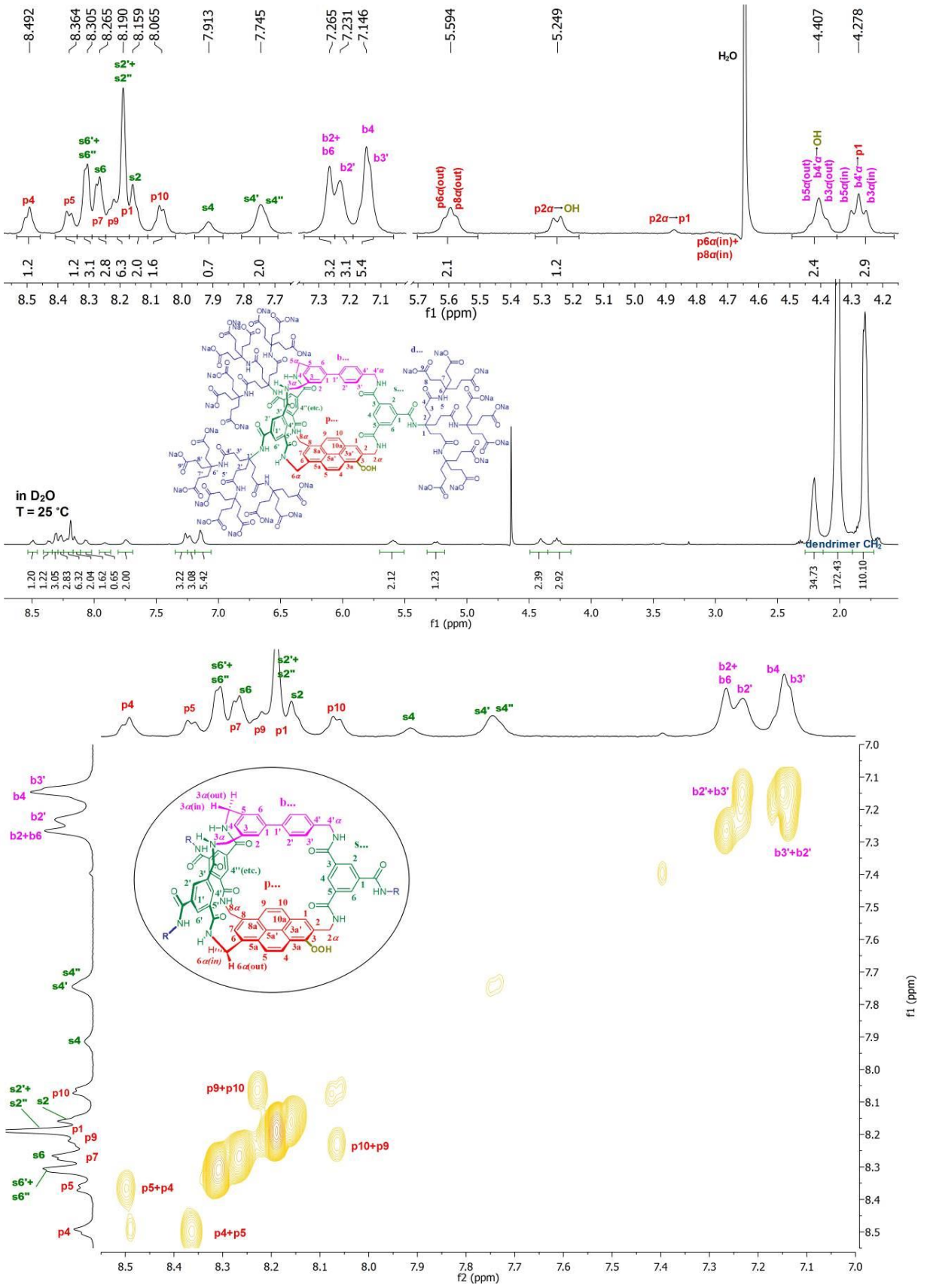


Figure S18. ^{1}H-NMR (top) and partial {^{1}H-^{1}H}-COSY (bottom) spectra of deprotected **17**, presumed to be **A**, with assignments. The spectra were recorded at 600 MHz in D_2O.

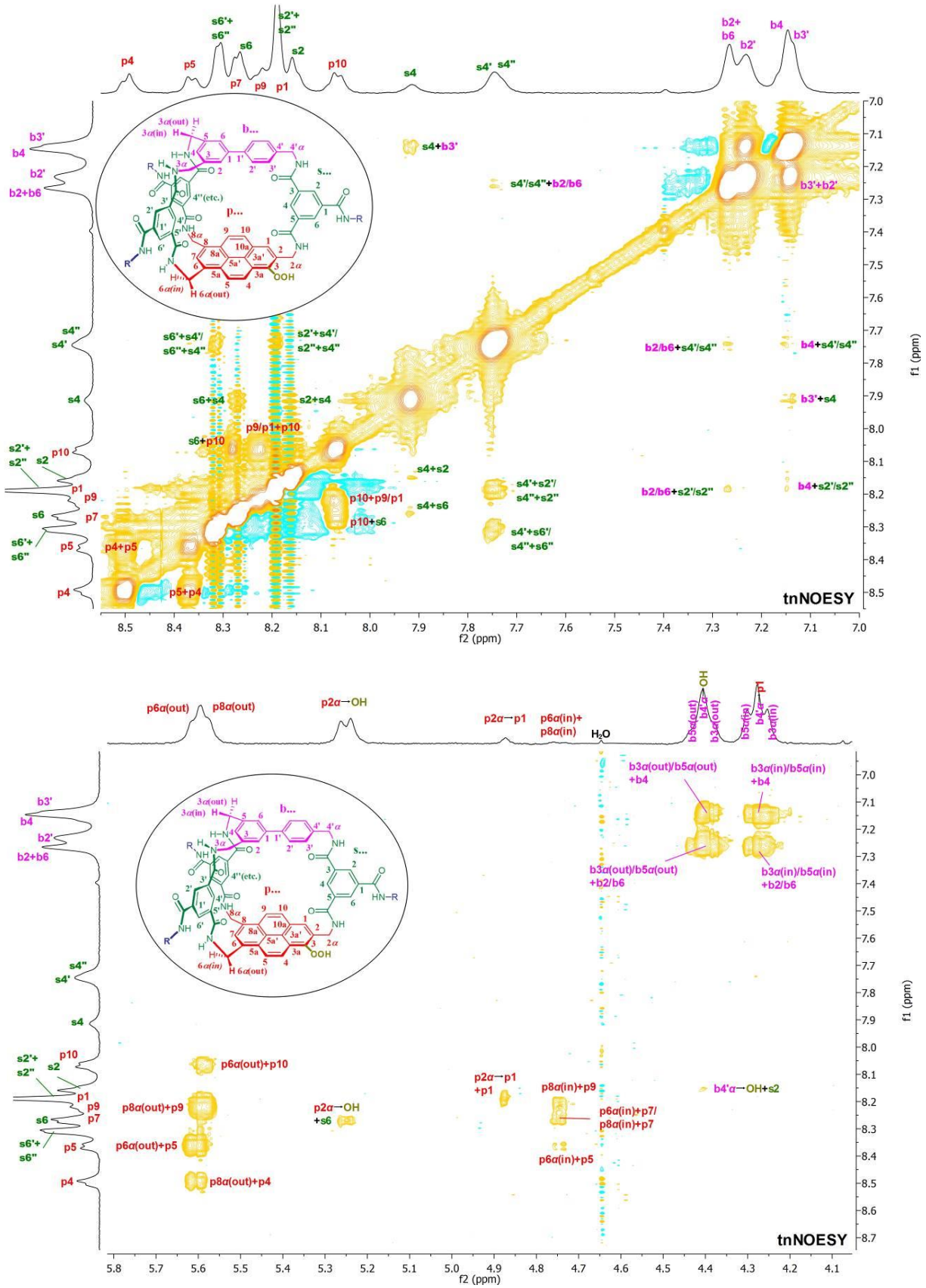


Figure S19. Partial {^{1}H-^{1}H}-NOESY spectra of deprotected **17**, presumed to be **A**, with assignments. The spectra were recorded at 600 MHz in D_2O.

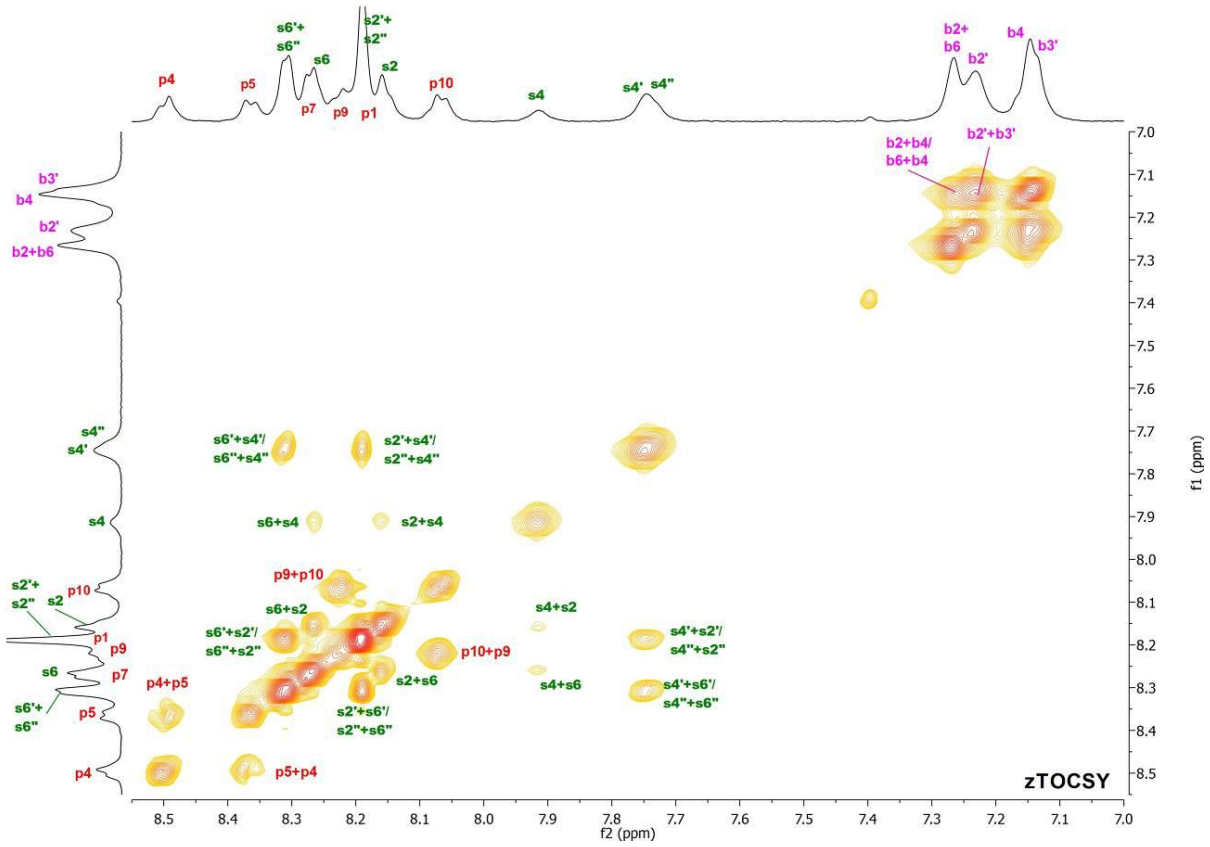


Figure S20. Partial {^{1}H-^{1}H}-TOCSY spectrum of deprotected **17**, presumed to be **A**, with assignments. The spectrum was recorded at 600 MHz in D_2O.

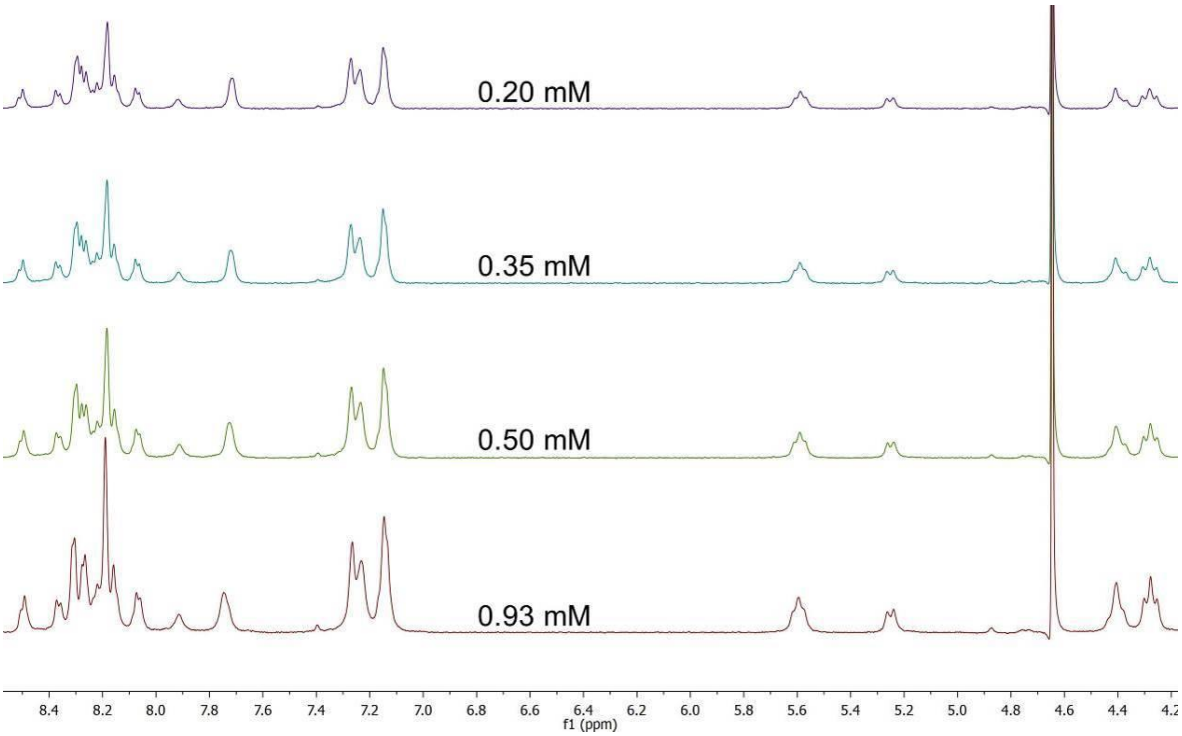


Figure S21. Dilution studies of deprotected **17**, presumed to be **A**, at pH = 7.0 and T = 25 °C as followed by ^{1}H-NMR spectroscopy (600 MHz, D_2O).

2. ^{1}H NMR binding studies

A solution of receptor in D_2O (99.9% -D, 0.20 mM) was prepared and typically 500 μL was transferred into a new or thoroughly cleaned and dried NMR tube. This same receptor solution was then used to prepare a stock solution of carbohydrate. For reducing sugars, the stock solution was allowed to equilibrate between the α and β forms overnight; in other cases (e.g. methyl β-D-glucoside) the stock solution could be used immediately. Aliquots of increasing volume were added from the stock solution into the NMR tube and –after thorough mixing– the ^{1}H NMR spectrum was recorded. Typically the first addition was 0.5 μL, while subsequent additions were double the volume of the previous addition (i.e. 1.0, 2.0, 4.0, 8.0 μL, etc.). The δ-values of receptor resonances that shifted upon addition of carbohydrate were collected and $\Delta\delta$ (*vs*. unbound receptor) was plotted as a function of total carbohydrate concentration. These data were fitted to a 1:1 binding model using a non-linear least squares curve-fitting programme implemented within Excel. Thus, K_a and δ_{HG} (i.e. chemical shift of the Host-Guest complex) could be derived. An estimated error for K_a could be obtained from individual data points by assuming the determined Ka and δ_{HG}. The assumption of 1:1 stoichiometry is supported by the generally good fits between observed and calculated data. The binding constants for the two receptors are summarised in Table S1 below.

Table S1. Association constants to carbohydrates for receptor **7** and the oxidised analogue resulting from deprotection of hydroperoxide **17**, measured in D_2O at 25 ^oC.

Carbohydrate	K_a [M^{-1}]	
	7	Deprotected **17** (presumed to be **A**)
D-Mannose	4	2
D-Galactose	4	4
Methyl β-D-glucoside (**1**, R = Me)	20	38
Methyl β-D-*N*-acetylglucosaminide (**2**, R = Me)	38	32
D-Cellobiose **15**	260	335

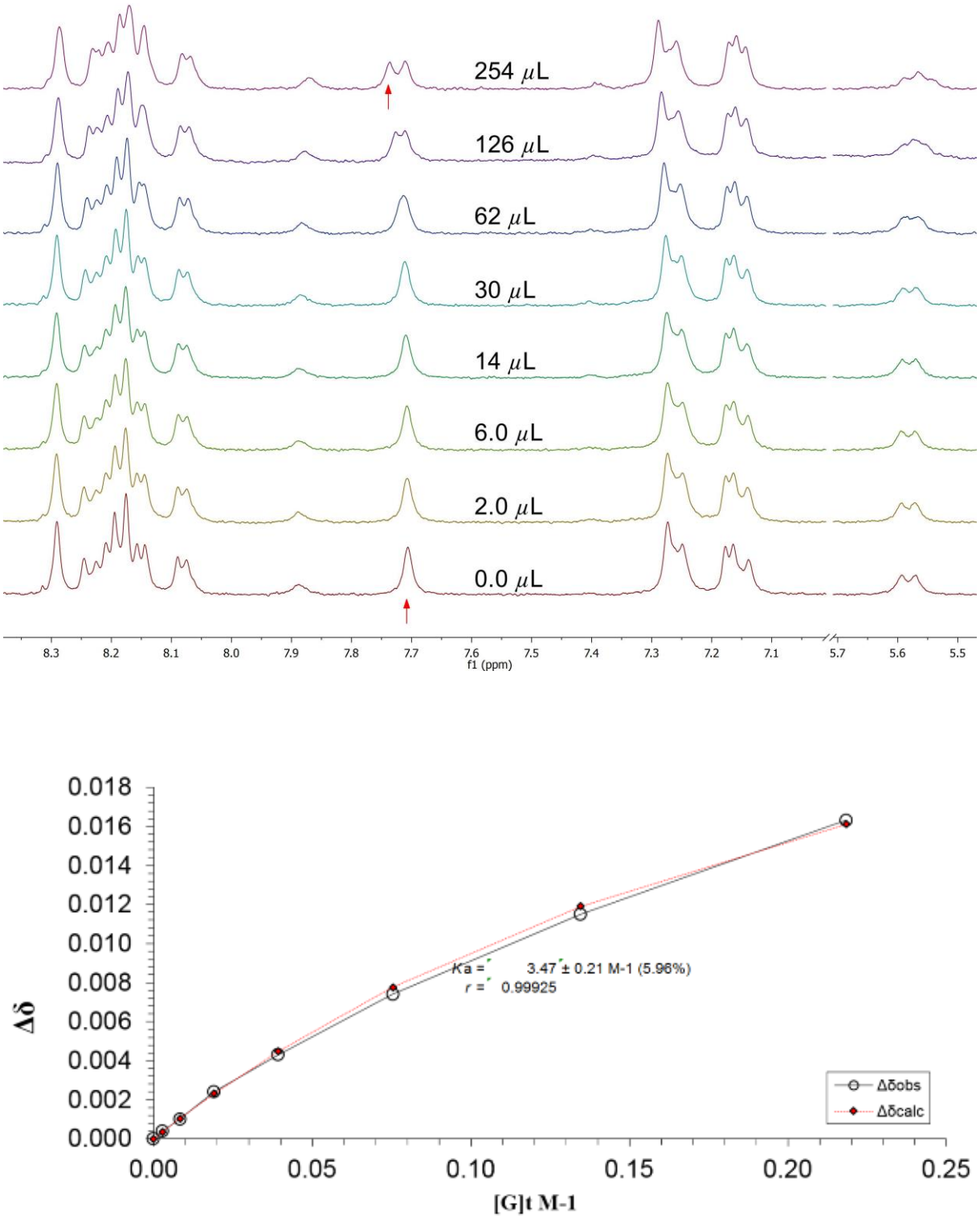


Figure S22. Binding study of receptor **7** (0.20 mM) titrated with D-mannose (562.5 mM, also containing 0.20 mM receptor) in D_2O as followed by ^{1}H-NMR at 600 MHz (top). The shift of the resonance around 7.7 ppm was plotted as a function of the total concentration of D-mannose and fitted to a 1:1 binding model (bottom) indicating K_a = 3.47 ± 0.21 M^{-1} (5.96%) and r = 0.99925.

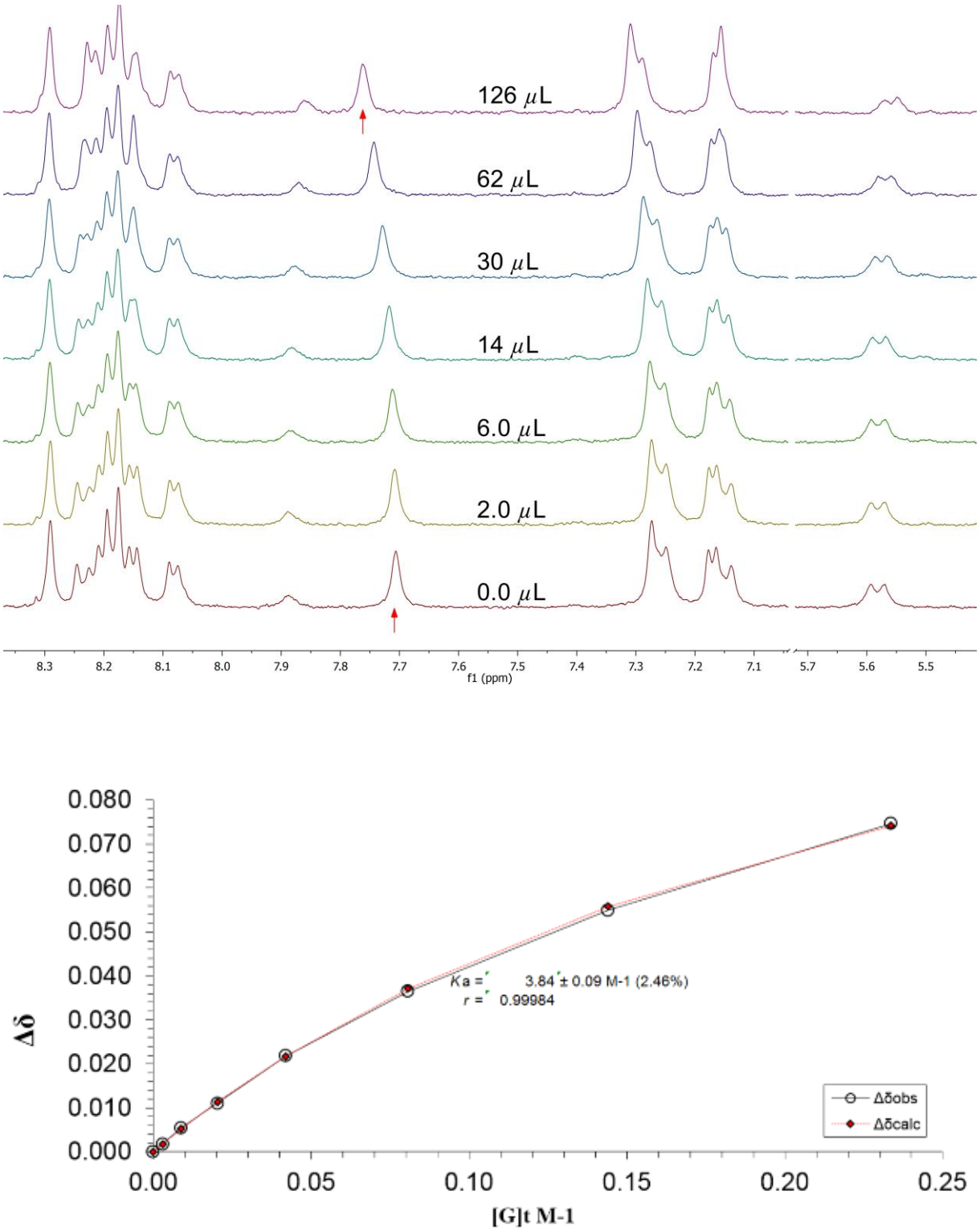


Figure S23. Binding study of receptor **7** (0.20 mM) titrated with D-galactose (601.3 mM, also containing 0.20 mM receptor) in D_2O as followed by ^{1}H-NMR at 600 MHz (top). The shift of the resonance around 8 ppm was plotted as a function of the total concentration of D-galactose and fitted to a 1:1 binding model (bottom) indicating K_a = 3.84 ± 0.09 M^{-1} (2.46%) and r = 0.99984.

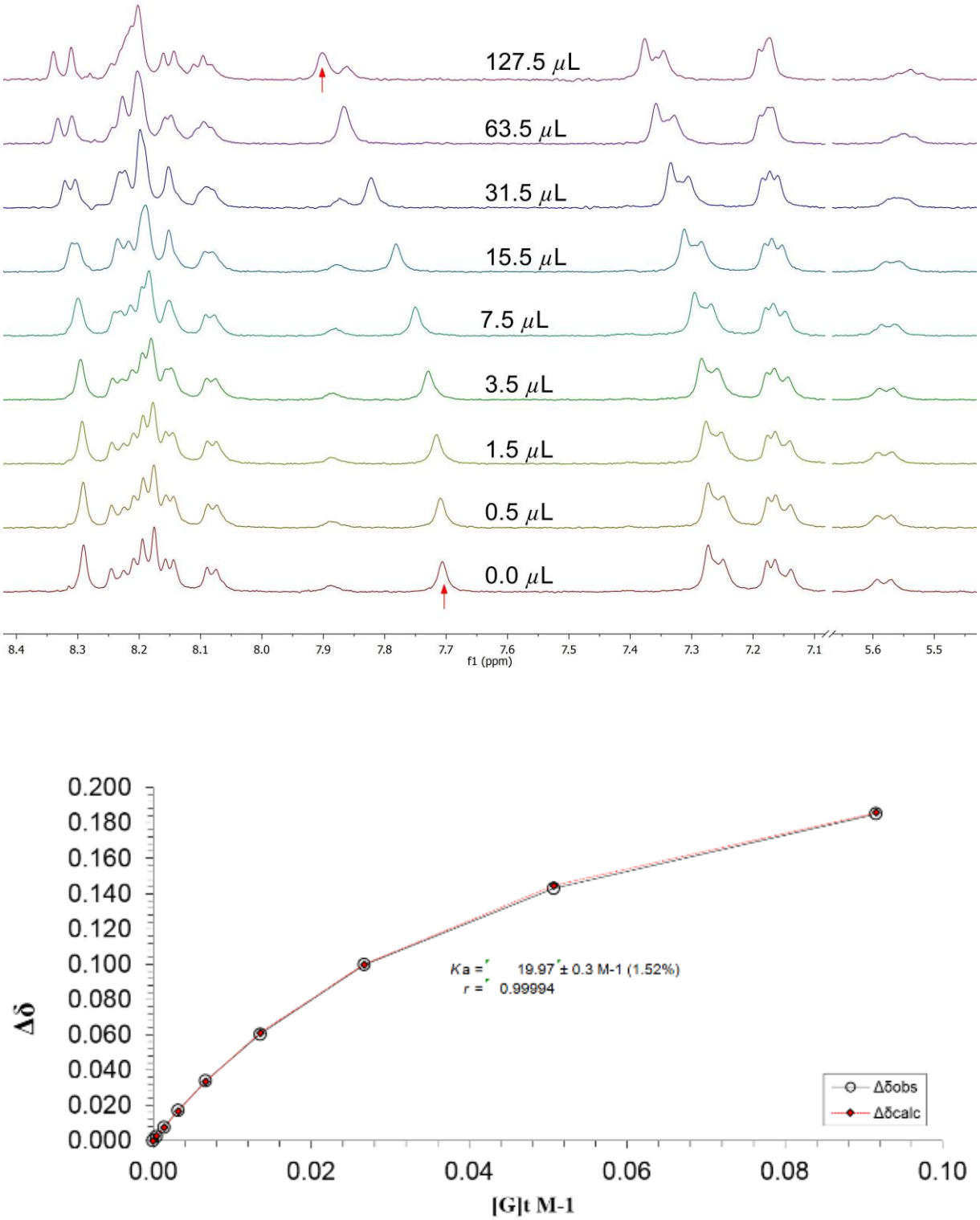


Figure S24. Binding study of receptor **7** (0.20 mM) titrated with methyl *β*-D-glucoside (460.9 mM, also containing 0.20 mM receptor) in D_2O as followed by ^{1}H-NMR at 600 MHz (top). The shift of the resonance around 8.65 ppm was plotted as a function of the total concentration of methyl-*β*-D-glucoside and fitted to a 1:1 binding model (bottom) indicating K_a = 19.97 ± 0.30 M^{-1} (1.52%) and r = 0.99994.

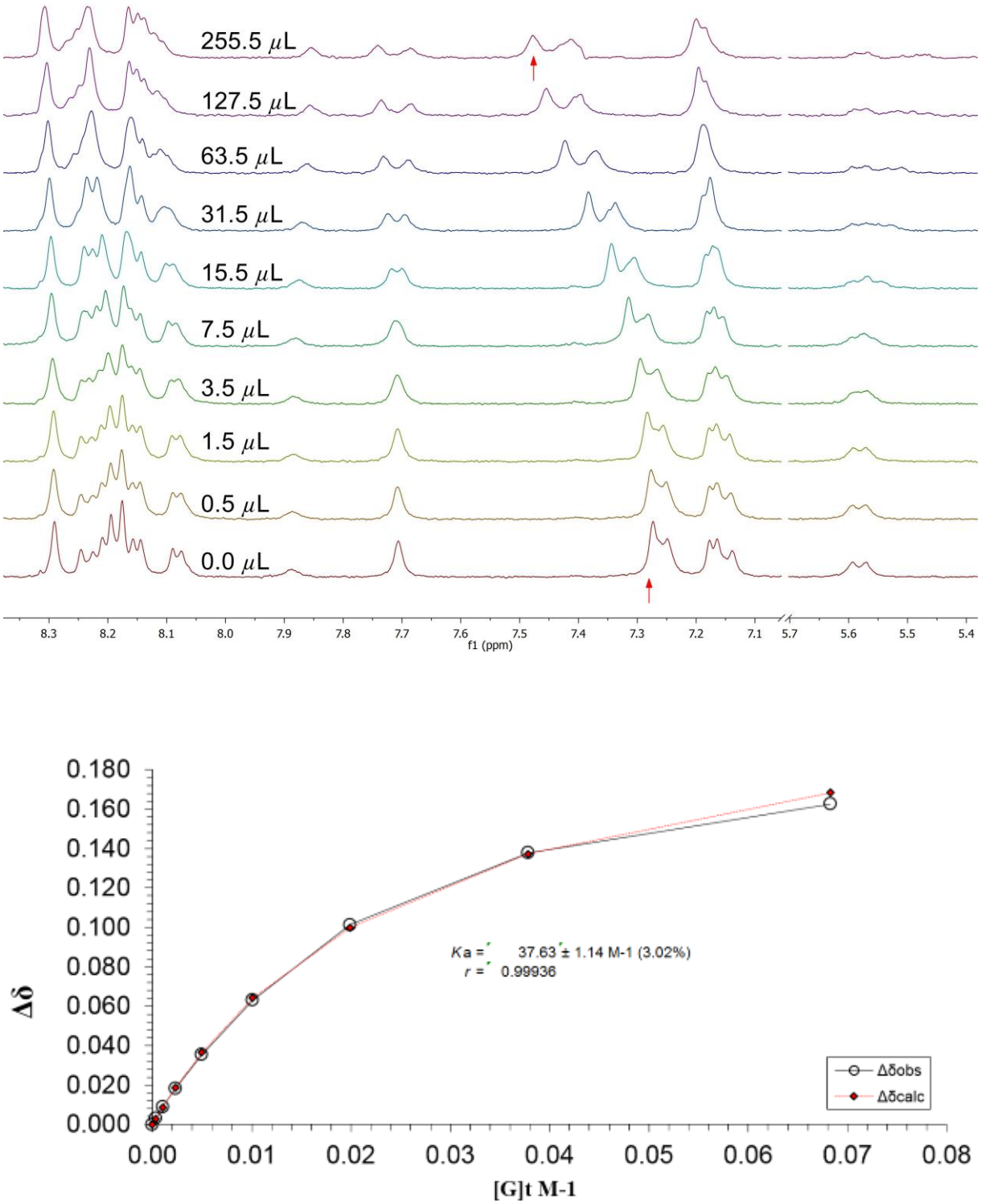


Figure S25. Binding study of receptor **7** (0.20 mM) titrated with *N*-acetyl-methyl-*β*-D-glucosamine (340.1 mM, also containing 0.20 mM receptor) in D_2O as followed by ^{1}H-NMR at 600 MHz (top). The shift of the resonance around 8.65 ppm was plotted as a function of the total concentration of *N*-acetyl-methyl-*β*-D-glucosamine and fitted to a 1:1 binding model (bottom) indicating K_a = 37.63 ± 1.14 M^{-1} (3.02%) and r = 0.99936.

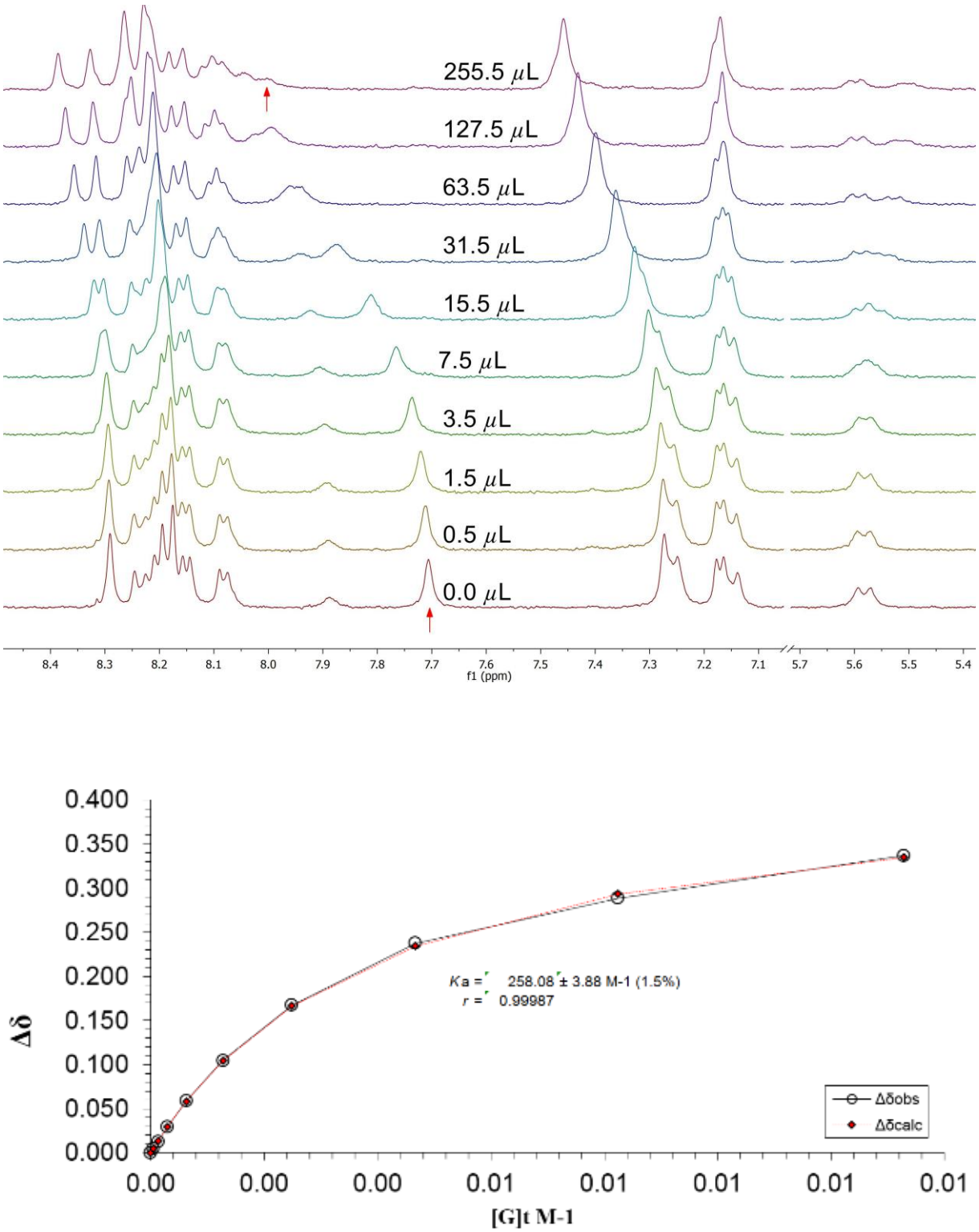


Figure S26. Binding study of receptor **7** (0.20 mM) titrated with D-cellobiose **15** (34.1 mM, also containing 0.20 mM receptor) in D_2O as followed by ^{1}H-NMR at 600 MHz (top). The shift of the resonance around 8.65 ppm was plotted as a function of the total concentration of D-cellobiose and fitted to a 1:1 binding model (bottom) indicating K_a = 258.08 ± 3.88 M^{-1} (1.50%) and r = 0.99987.

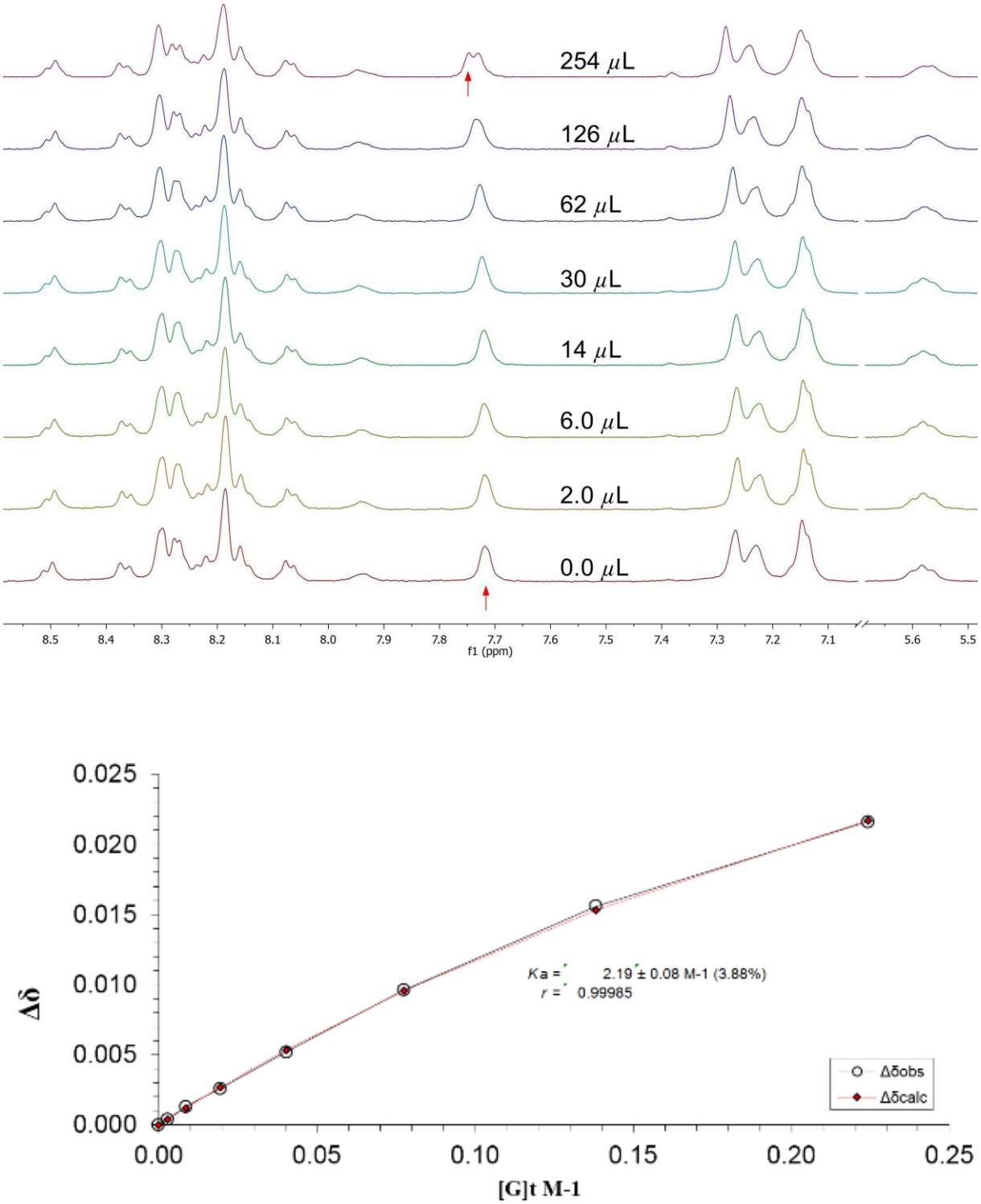


Figure S27. Binding study of deprotected **17**, presumed to be **A** (0.20 mM), titrated with D-mannose (577.3 mM, also containing 0.20 mM receptor) in D_2O as followed by ^{1}H-NMR at 600 MHz (top). The shift of the resonance around 8 ppm was plotted as a function of the total concentration of D-mannose and fitted to a 1:1 binding model (bottom) indicating K_a = 2.19 ± 0.08 M^{-1} (3.88%) and r = 0.99985.

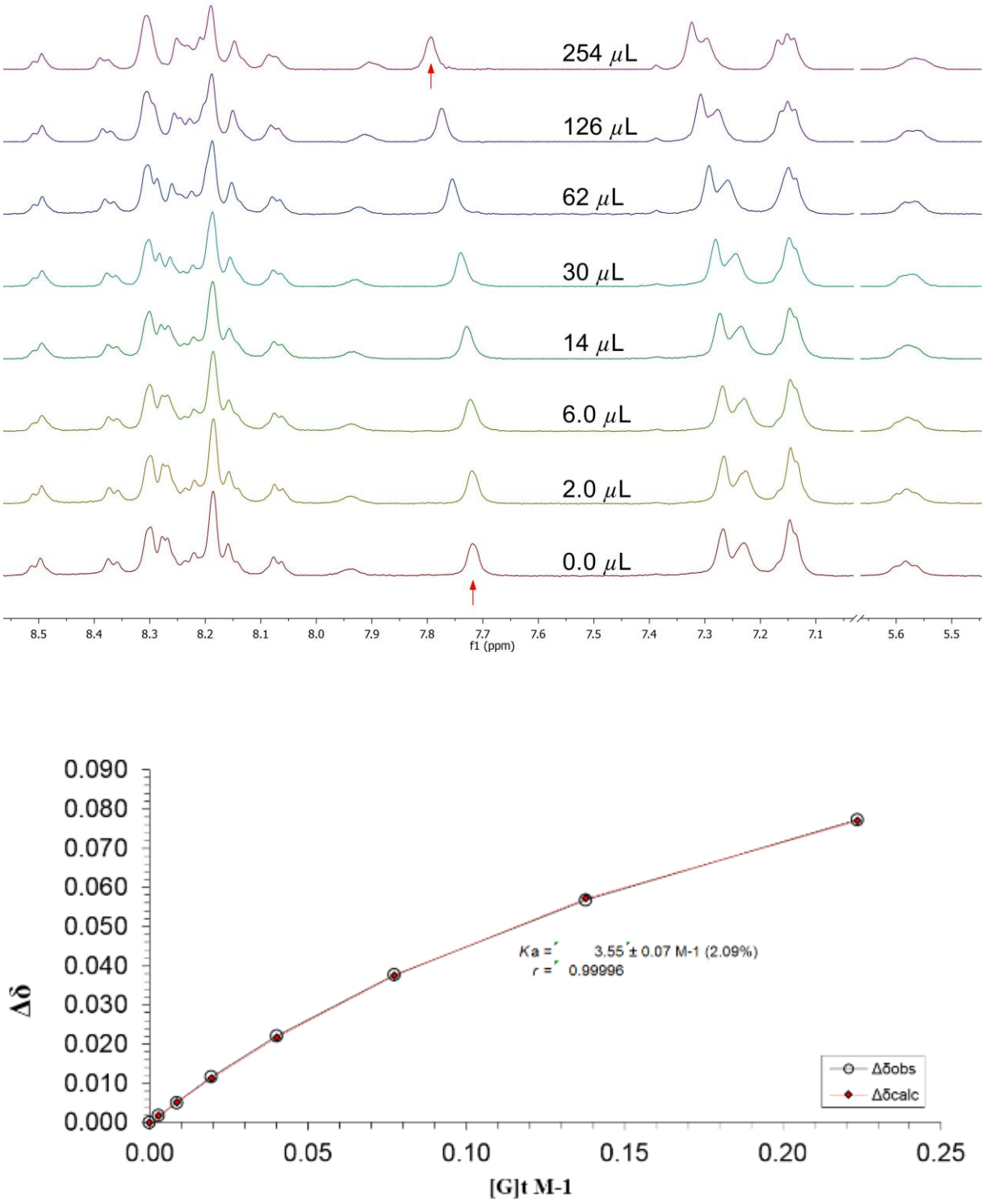


Figure S28. Binding study of deprotected **17**, presumed to be **A** (0.20 mM), titrated with D-galactose (575.4 mM, also containing 0.20 mM receptor) in D_2O as followed by ^{1}H-NMR at 600 MHz (top). The shift of the resonance around 8 ppm was plotted as a function of the total concentration of D-galactose and fitted to a 1:1 binding model (bottom) indicating K_a = 3.55 ± 0.07 M^{-1} (2.09%) and r = 0.99994.

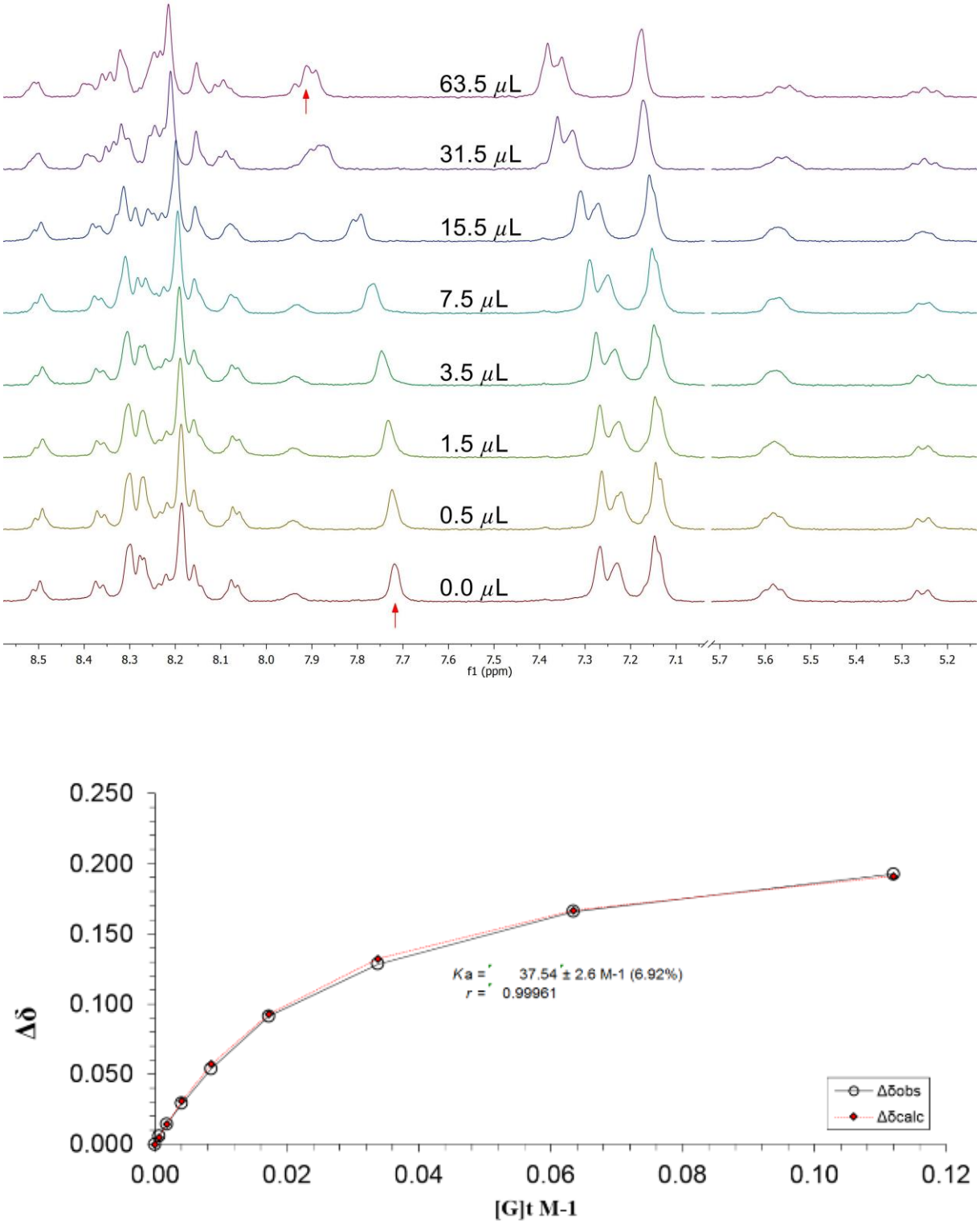


Figure S29. Binding study of deprotected **17**, presumed to be **A** (0.20 mM), titrated with methyl *β*-D-glucoside (463.5 mM, also containing 0.20 mM receptor) in D_2O as followed by ^{1}H-NMR at 600 MHz (top). The shift of the resonance around 8.65 ppm was plotted as a function of the total concentration of methyl-*β*-D-glucoside and fitted to a 1:1 binding model (bottom) indicating K_a = 37.54 ± 2.60 M^{-1} (6.92%) and r = 0.99961.

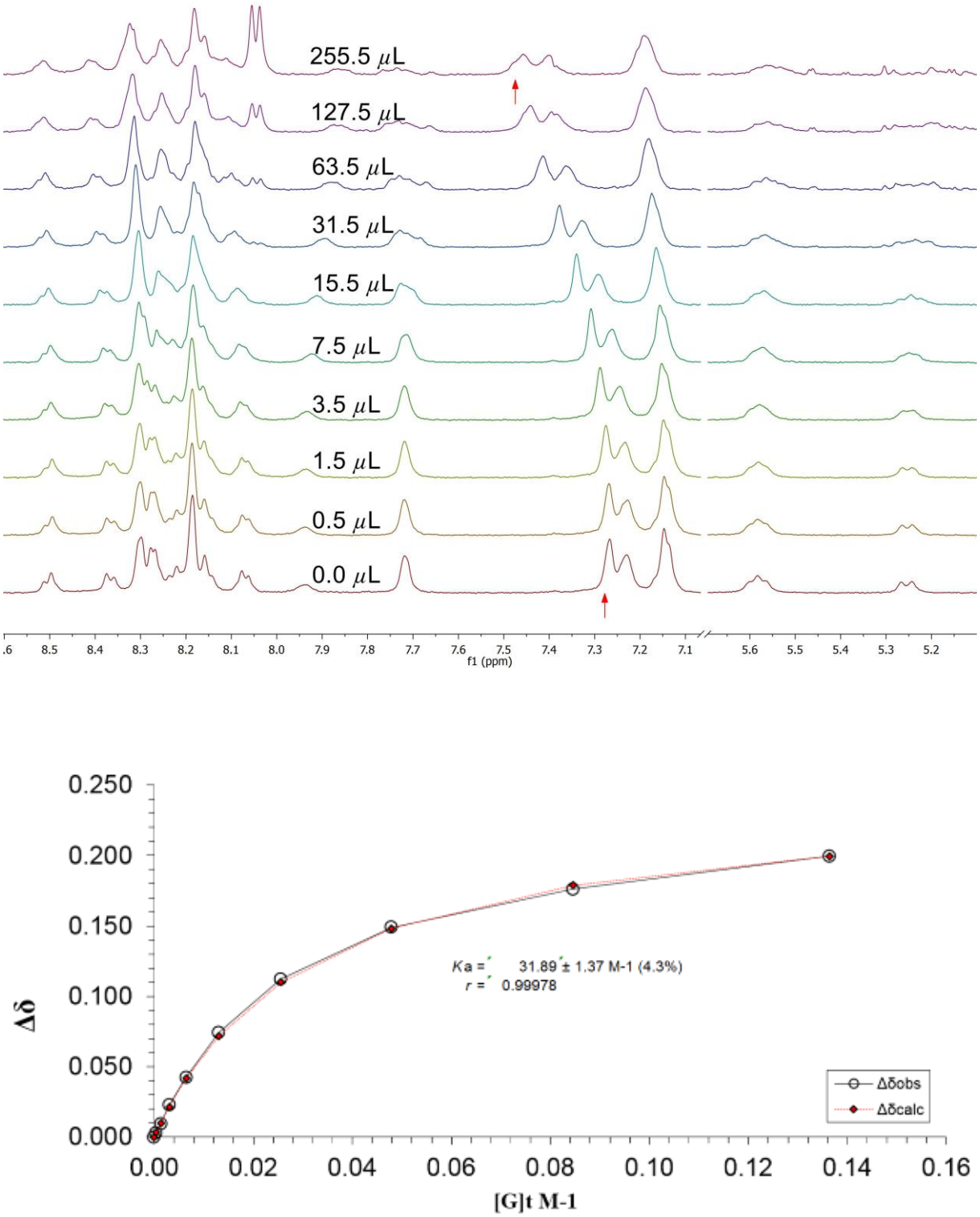


Figure S30. Binding study of deprotected **17**, presumed to be **A** (0.20 mM), titrated with *N*-acetyl-methyl-*β*-D-glucosamine (463.5 mM, also containing 0.20 mM receptor) in D_2O as followed by ^{1}H-NMR at 600 MHz (top). The shift of the resonance around 8.65 ppm was plotted as a function of the total concentration of *N*-acetyl-methyl-*β*-D-glucosamine and fitted to a 1:1 binding model (bottom) indicating K_a = 31.89 ± 1.37 M^{-1} (4.30%) and r = 0.99978.

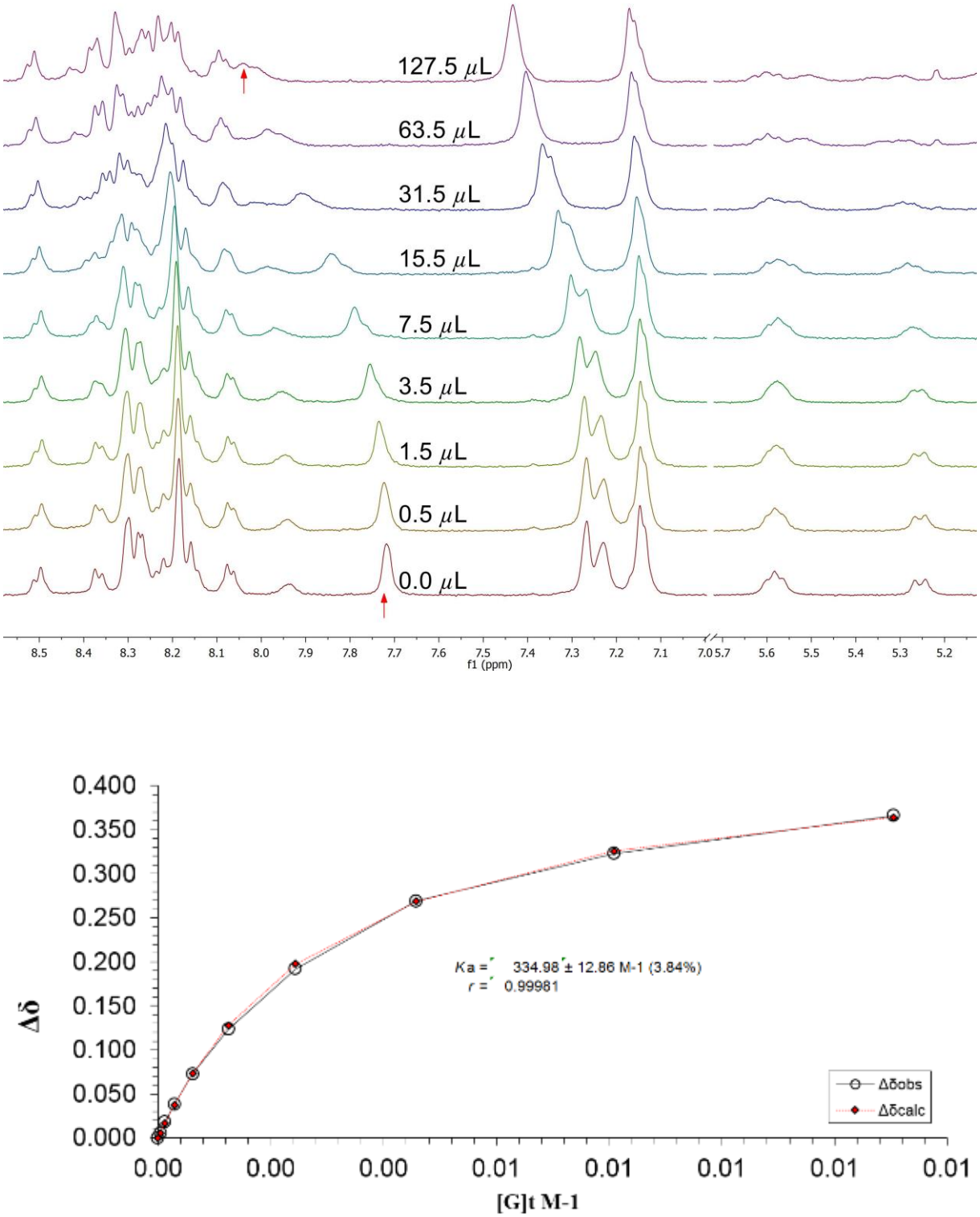


Figure S31. Binding study of deprotected **17**, presumed to be **A** (0.20 mM), titrated with D-cellobiose **15** (33.4 mM, also containing 0.20 mM receptor) in D_2O as followed by ^{1}H-NMR at 600 MHz (top). The shift of the resonance around 8.65 ppm was plotted as a function of the total concentration of D-cellobiose and fitted to a 1:1 binding model (bottom) indicating K_a = 335 ± 12.86 M^{-1} (3.84%) and r = 0.99981.