Electronic Supplementary Material (ESI) for ChemComm.

Supporting Information

Index

1. Supplementary figures for the manuscript.

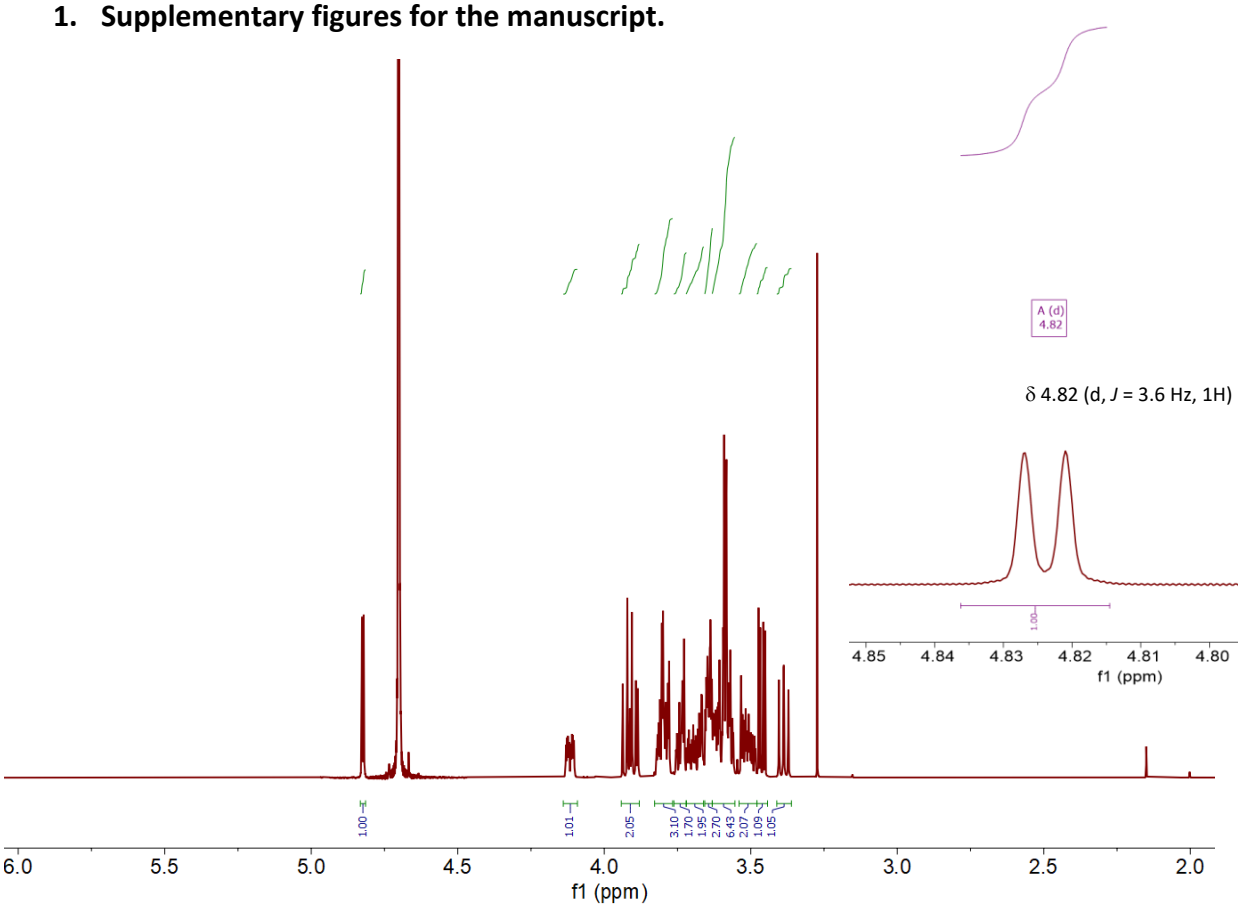


Figure S1 *1H NMR spectrum of receptor* ***8*** *(inset – H-1 proton of the receptor with the chemical shift and the coupling constant indicated).*

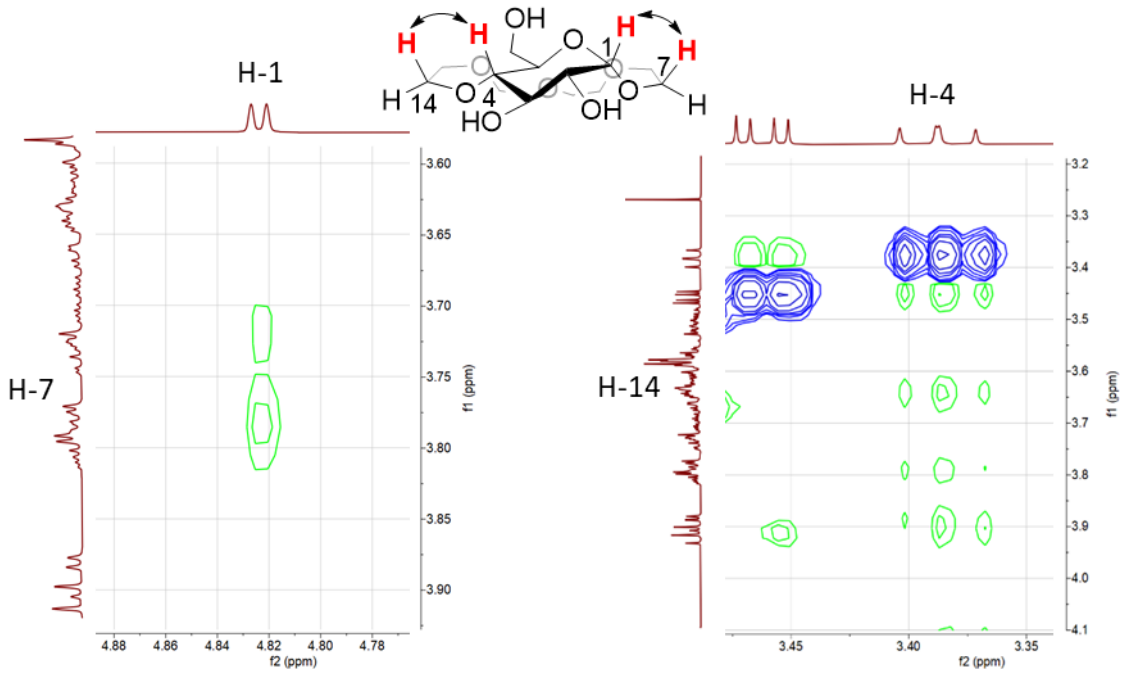


Figure S2 *Fragments of the NOESY spectrum of receptor* ***8*** *indicating the through space interactions between protons H-1, H-4 of the glucopyranose ring and the adjacent tetraethylene glycol protons.*

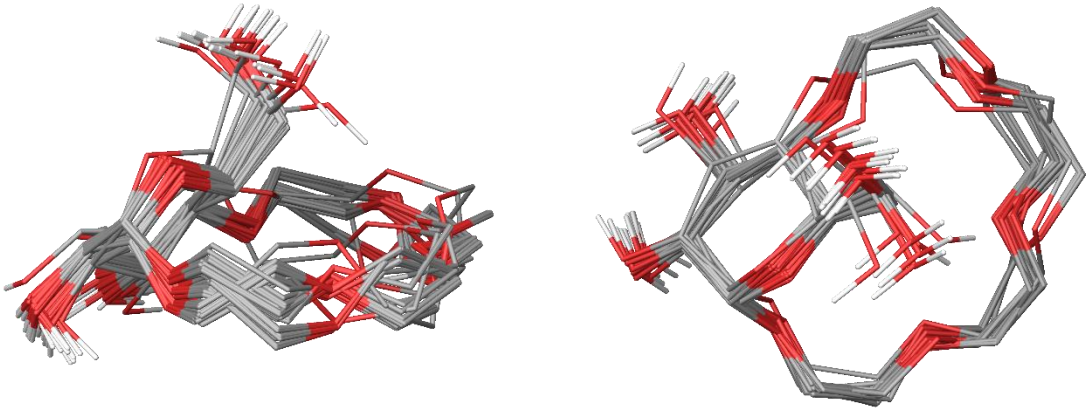


Figure S3 *Ensemble of lowest energy conformers (within 2 kcal/mol window) of receptor* ***8*** *obtained using the OPLSe3 Force Field calculations.*

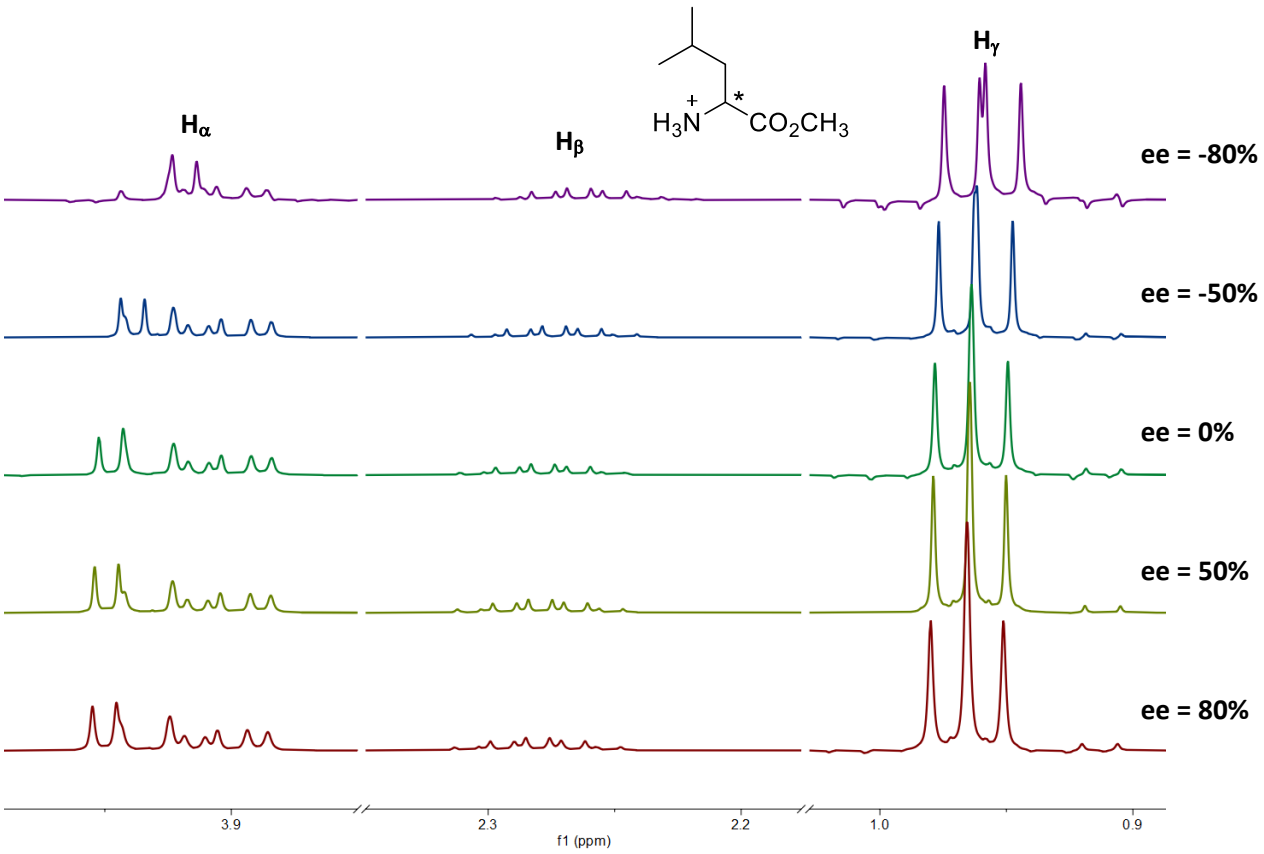


Figure S4 *^{1}H NMR (D_2O, selected regions) stacked plot: mixtures of D- and L-Val-OMe x HCl with different enantiomeric excesses and 1 equivalent of receptor* ***8****.*

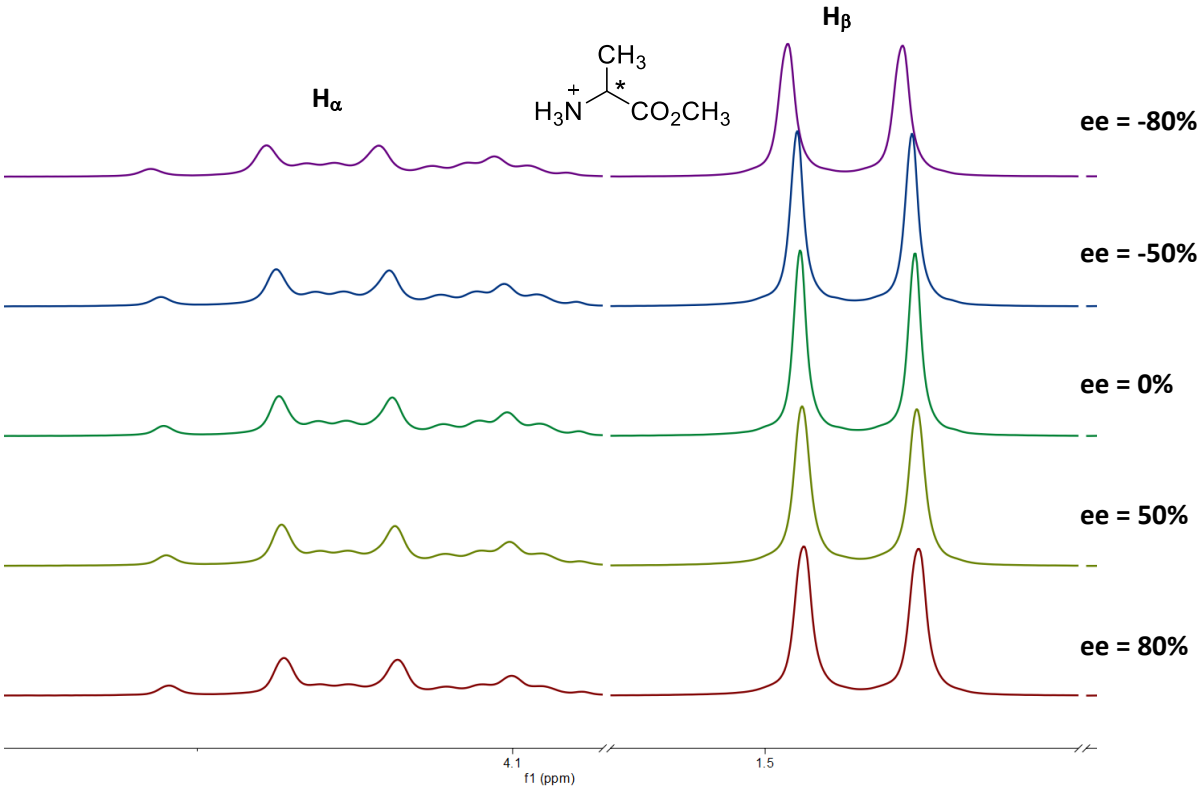


Figure S5 *^{1}H NMR (D_2O, selected regions) stacked plot: mixtures of D- and L-Ala-OMe x HCl with different enantiomeric excesses and 1 equivalent of receptor* ***8****.*

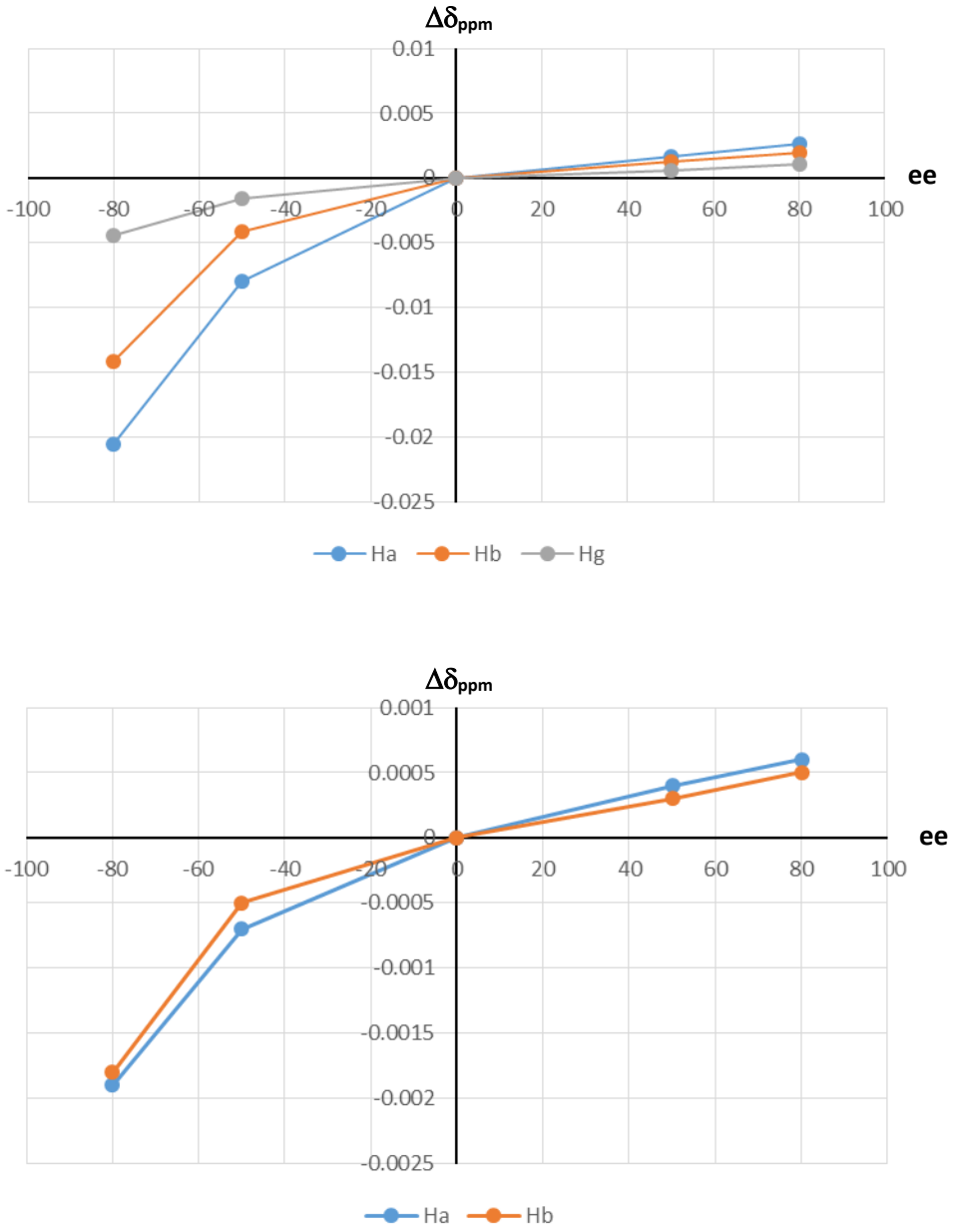


Figure S6 *Plots of chemical shift changes for different guest protons vs ee of the enantiomer mixture (top – H-Val-OMe, bottom – H-Ala-OMe).*

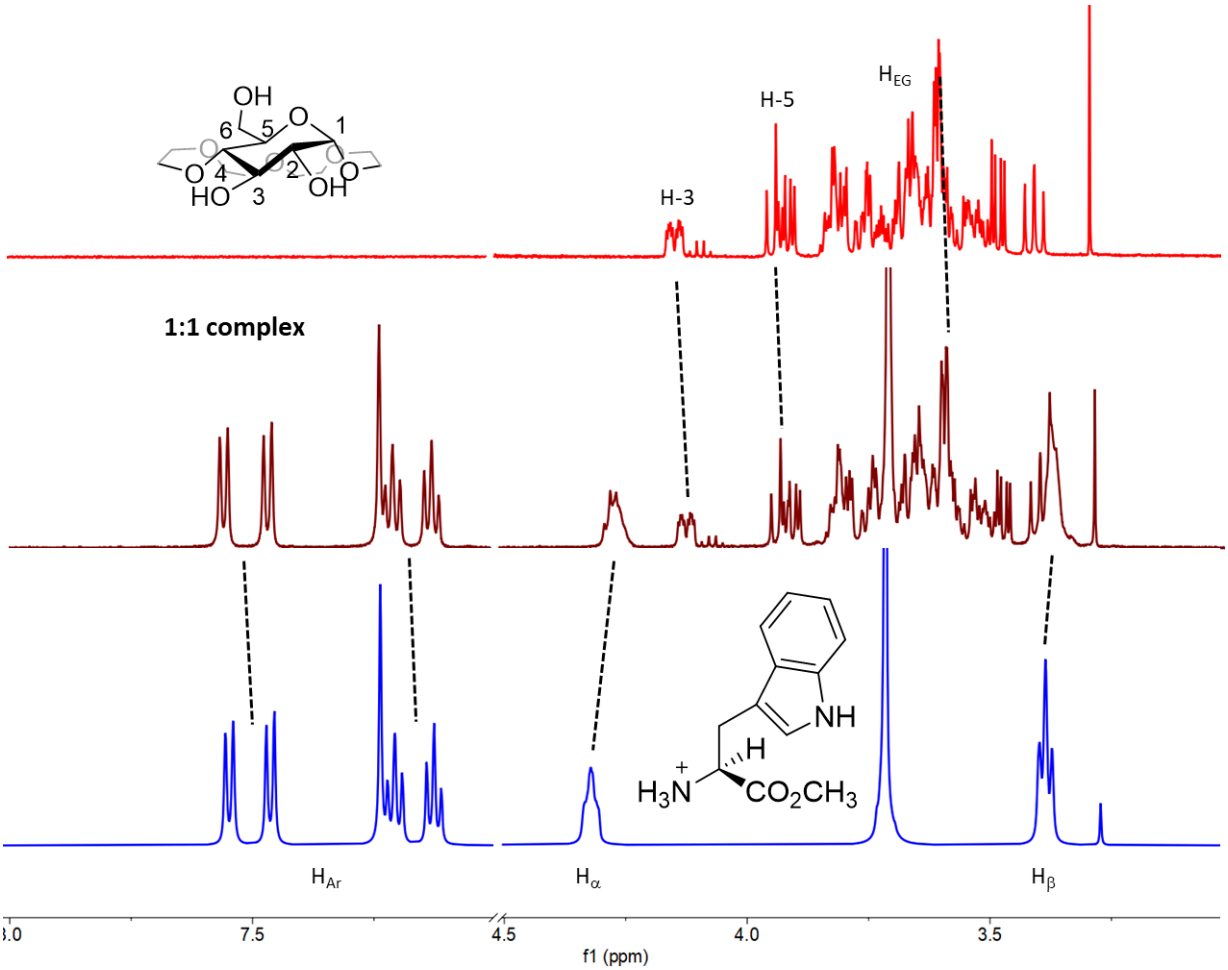


Figure S7 *^{1}H NMR (D_2O) stacked plot: top – receptor **8**; middle - H-L-Trp-OMe x HCl + receptor **8** (1:1); bottom - H-L-Trp-OMe x HCl ── the dotted lines indicate shifts of specific protons upon complex formation.*

2. Materials, methods and instruments

Materials

Solvents and reagents were of the highest commercially available grade and used without further purification. They were purchased from Sigma Aldrich, Fischer Scientific, Fluka, Bachem, BioMatrix, Biotage, IRIS Biotech, Protein Technologies and Acros Organics. Solvents used for MPLC were HPLC-grade quality.

Preparative medium pressure liquid chromatography (MPLC)

Purifications of the building blocks were carried out on a CombiFlash EZ Prep flash chromatography system (Teledyne ISCO). Two different solvent sets were used: 1. Solvent A was HPLC-grade DCM without stabilizer and solvent B was HPLC-grade methanol for the building blocks. 2. Solvent A was HPLC-grade hexane and solvent B HPLC-grade EtOAc.

Thin-layer chromatography (TLC)

TLC was conducted on aluminium sheets coated with silica gel 60 F_{254} (Merck) using UV fluorescence (254 and 366 nm). Analytical grade solvents were used.

Liquid chromatography - mass spectrometry (LC - MS)

Analytical reverse phase HPLC (RP-HPLC) was performed on a Dionex UHPLC, Ultimate 3000. Reprosil gold 120 C_{18} (150 x 4 mm, 5 µm) with a flow of 0.5 mL/min was used as the analytical column. Two different solvents were used. Solvent A was assigned to be pure acetonitrile and solvent B was a mixture of 1 % acetonitrile and 0.1 % TFA in Milli-Q pure water. The mass analysis was performed on an amaZone speed ion trap mass analyzer (Bruker, USA).

Nuclear magnetic resonance (NMR) spectroscopy

1D and 2D NMR spectra were recorded on 400 and 500 MHz Ultrashield spectrometers (Bruker, USA). ^{1}H-NMR chemical shifts (δ_H) are quoted in parts per million (ppm) and coupling constants (J) are quoted in Hertz (Hz). Abbreviations for NMR data are s (singlet), d (doublet), t (triplet), q (quartet), m (multiplet).

High-resolution mass spectrometry (HR-MS)

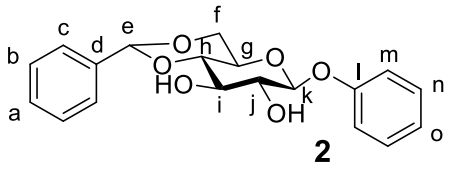
High-resolution electrospray ionization (HR-ESI) spectra were measured on a Bruker maXis spectrometer.

Isothermal titration calorimetry (ITC)

ITC experiments were carried out in a MicroCal PEAQ-ITC (Malvern), at 25°C, 750 rpm, high feedback and 10 µcal/s as reference power, using MilliQ water as a solvent.

3. Synthesis and characterisation of receptor 8.

4,6-*O*-benzylidene-phenyl-β-*D*-glucopyranoside (**2**):



2

A solution of phenyl-β-*D*-glucopyranoside (**1**) (10 g, 39 mmol), camphorsulphonic acid (50 mg) and benzaldehyde dimethylacetal (11.8 mL, 78.8 mmol) in MeCN (100 mL) was stirred for 16 h at room temperature. Triethylamine (2 mL) was added and the solution was allowed to stir for a further 1 h. Afterwards the solution was filtered through cellite and all volatiles were evaporated. The crude product was recrystallized from EtOH. Product **2** was obtained as white crystalline solid (10.8g, 31.7 mmol, 80% yield).

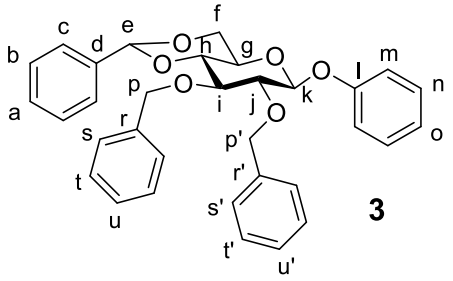
m.p. 173-176 °C

^{1}H NMR (400 MHz, DMSO-d_6) δ 7.54 – 7.46 (m, 2H, H_c), 7.43 – 7.37 (m, 3H, H_a+H_b), 7.37 – 7.28 (m, 2H, H_n), 7.14 – 7.08 (m, 2H, H_m), 7.07 – 7.00 (m, 1H, H_o), 5.63 (s, 1H, H_e), 5.16 (d, J = 7.7 Hz, 1H, H_k), 4.25 (dd, J = 9.6, 4.4 Hz, 1H, H_f), 3.81 – 3.59 (m, 3H, H_i + $H_{f'}$ + H_h), 3.53 (t, J = 9.1 Hz, 1H, H_g), 3.48 – 3.43 (m, 1H, H_j *overlap with the trace water signal in DMSO*).

^{13}C NMR (101 MHz, DMSO-d_6) δ 157.61 (C_l), 138.23 (C_d), 129.97 (C_n), 129.36 (C_b), 128.53 (C_a), 126.85 (C_c), 122.59 (C_o), 116.81 (C_m), 101.22 (C_e), 101.02 (C_k), 80.87 (C_h), 74.64 (C_j), 73.32 (C_i), 68.37 (C_f), 66.29 (C_g).

HR-ESI-MS: m/z: 367.1155 $[M + Na]^+$, calculated for $C_{19}H_{20}NaO_6^+$: 367.1152

4,6-*O*-benzylidene-2,3-di-*O*-benzyl-phenyl-β-*D*-glucopyranoside (**3**):



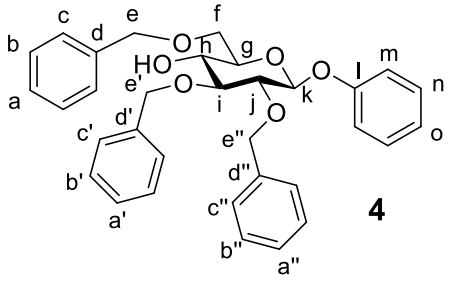
Compound **2** (6.88 g, 20 mmol) was dissolved in dry DMF (100 mL) under argon. The solution was cooled down to 0 °C. NaH (50 % suspension in mineral oil, 2.4g, 50 mmol) was then added in portions, under vigorous stirring. After additional 30 minutes benzyl bromide (5 mL, 42 mmol) was added dropwise. Afterwards the cooling was removed and the mixture was stirred at room temperature overnight. The reaction mixture was quenched with water and then partitioned between water and ethyl acetate (50 mL each). The aqueous layer was extracted with ethyl acetate (3 x 50 mL). The combined organic extracts were washed with water (30 mL), brine (30 mL) and 5% aqueous LiCl solution (30 mL), dried over $MgSO_4$, filtered and evaporated. The crude product mixture was separated by MPLC (hexane : ethyl acetate = 100 : 0 (4 min) → 60 : 40 (over 15 min) → 0 : 100 (over 1 min)) to afford **3** as a white powder (9.9 g, 19 mmol, 95 % yield).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.56 – 7.50 (m, 2H, H_c), 7.46 – 7.29 (m, 15H, H_a + H_b + H_n + $H_{s+s'}$ + $H_{t+t'}$ + $H_{u+u'}$), 7.14 – 7.06 (m, 3H, H_m + H_o), 5.63 (s, 1H, H_e), 5.17 (d, J = 7.5 Hz, 1H, H_k), 5.00 (dd, J = 14.3, 11.1 Hz, 2H, $H_{p+p'}$), 4.88 (dd, J = 12.6, 11.1 Hz, 2H, $H_{p+p'}$), 4.42 (dd, J = 10.5, 5.0 Hz, 1H, H_f), 3.92 – 3.74 (m, 4H, $H_{f'}$ + H_g + H_i + H_j), 3.58 (ddd, J = 10.0, 9.0, 5.0 Hz, 1H, H_h).

^{13}C NMR (101 MHz, $CDCl_3$) δ 157.09 (C_l), 138.42, 138.10 (2 x C, $C_{r+r'}$), 137.24 (C_d), 129.65, 129.02, 128.39, 128.35, 128.29, 128.25, 128.07, 127.84, 127.71 (9 x C, C_a + C_b + $C_{s+s'}$ + $C_{t+t'}$ + $C_{u+u'}$ + C_n), 126.04 (C_c), 123.05 (C_o), 116.92 (C_m), 102.04 (C_k), 101.25 (C_e), 81.81, 81.30, 80.90 (3 x C, C_g + C_i + C_j), 75.56, 75.21 (2 x C, $C_{p+p'}$), 68.77 (C_f), 66.23 (C_h).

HR-ESI-MS: m/z: 547.2090 $[M + Na]^+$, calculated for $C_{33}H_{32}NaO_6^+$: 547.2091

2,3,6-tri-*O*-benzyl-phenyl-β-*D*-glucopyranoside (**4**):



4

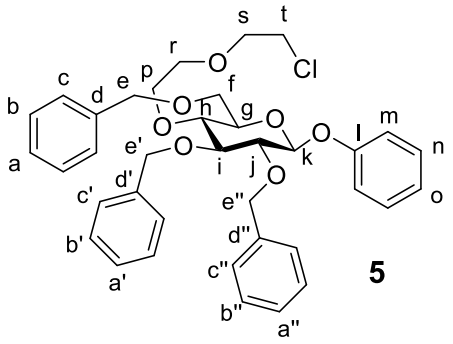
Compound **3** (5.2 g, 10 mmol) was dissolved in dry tetrahydrofuran (50 mL). Sodium cyanoborohydride (5 g, 80 mmol) was added. A 1N solution of HCl in dioxane was added in small portions until gas development ceased and the pH of the mixture remained acidic. The mixture was then concentrated to approximately 10 mL, CH_2Cl_2 (25 mL) was added and the mixture was neutralized by addition of 1N aqueous $NaHCO_3$. The layers were separated and the aqueous layer was extracted with CH_2Cl_2 (3 x 25 mL). The combined organic layers were washed with water (30 mL), dried ($MgSO_4$), filtered and evaporated. MPLC of the crude product (hexane : ethyl acetate = 100 : 0 (2 min) → 50 : 50 (over 17 min) → 0 : 100 (over 1 min)) afforded **4** as a colourless oil (2.9 g, 5.5 mmol, 55 % yield).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.43 – 7.30 (m, 17H, $H_{a+a'+a''}$ + $H_{b+b'+b''}$ + $H_{c+c'+c''}$ + H_n), 7.17 – 7.05 (m, 3H, H_m + H_o), 5.15 – 5.05 (m, 2H, H_k + H_e), 5.01 (d, J = 11.3 Hz, 1H), 4.93 – 4.75 (m, 2H), 4.73 – 4.70 (m, 2H) (5 x H, $H_{e+e'+e''}$), 3.87 (dd, J = 10.5, 3.6 Hz, 1H, H_f), 3.81 – 3.69 (m, 3H, $H_{f'}$ + H_g + H_j), 3.69 – 3.53 (m, 2H, H_h + H_i).

^{13}C NMR (101 MHz, CDCl3) δ 157.32 (C_l), 138.55, 138.19, 137.95 (3 x C, $C_{d+d'+d''}$), 129.59, 128.62, 128.46, 128.43, 128.30, 128.03, 127.92, 127.86, 127.75, 127.69, 127.02 (10 x C, $C_{a+a'+a''}$ + $C_{b+b'+b''}$ + $C_{c+c'+c''}$ + C_n), 122.77 (C_o), 116.91 (C_m), 101.73 (C_k), 84.07, 81.52 (2 x C, C_g + C_i), 75.40 , 74.99 (2 x C, $C_{e+e'}$), 74.47 (C_h), 71.29 (C_j), 70.11 (C_f), 65.37 ($C_{e''}$).

HR-ESI-MS: m/z: 544.2692 $[M + NH_4]^+$, calculated for $C_{33}H_{38}NO_6^+$: 544.2694

2,3,6-tri-*O*-benzyl-4-*O*-(2-(2-chloroethoxy)ethoxy)-phenyl-β-*D*-glucopyranoside (**5**):



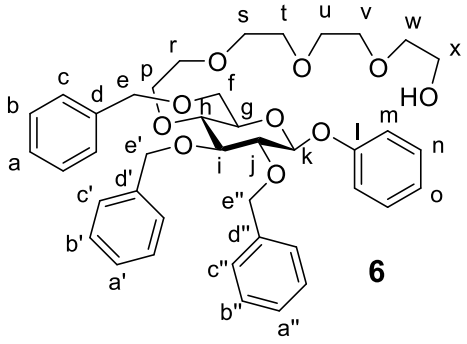
A solution of compound **4** (2.0 g, 3.8 mmol) in tetrahydrofuran (5 mL) was added dropwise into vigorously stirring solution of tetrabutylammonium hydrogen sulfate (100 mg, 0.3 mmole) in a mixture of bis-(2-chloroethyl)ether (8.5 mL, 78 mmol) and 50% aqueous KOH (15 mL). The resulting solution was stirred for 12h at 50 °C. After cooling water (20 mL) and $CHCl_3$ (25 mL) were added and the phases separated. The aqueous layer was washed with $CHCl_3$ (3x25 mL). The combined organic extracts were dried ($MgSO_4$), filtered and concentrated under reduced pressure. The residue was purified by MPLC ((hexane : ethyl acetate = 100 : 0 (4 min) → 70 : 30 (over 15 min) → 0 : 100 (over 1 min)) to afford product **5** as a pale yellow oil (2.15 g, 3.4 mmol, 90% yield).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.41 – 7.29 (m, 17H, $H_{a+a'+a''}$ + $H_{b+b'+b''}$ + $H_{c+c'+c''}$ + H_n), 7.17 – 7.03 (m, 3H, H_m + H_o), 5.11 – 4.98 (m, 2H, H_k + H_e), 4.98 – 4.90 (m, 1H), 4.85 (dd, J = 10.9, 7.6 Hz, 2H), 4.75 – 4.52 (m, 2H) (5 x H, $H_{e+e'+e''}$), 3.99 (ddd, J = 10.8, 5.2, 3.7 Hz, 1H, H_i), 3.86 (ddd, J = 13.0, 10.9, 1.9 Hz, 1H, H_f), 3.81 – 3.64 (m, 7H, $H_{f'}$ + H_g + H_j + H_p + H_r), 3.64 – 3.52 (m, 5H, H_h + H_s + H_t).

^{13}C NMR (101 MHz, $CDCl_3$) δ 157.42 (C_l), 138.61, 138.28, 138.26 (3 x C, $C_{d+d'+d''}$), 129.53, 128.40, 128.32, 128.25, 127.95, 127.91, 127.78, 127.70, 127.66, 127.55 (10 x C, $C_{a+a'+a''}$ + $C_{b+b'+b''}$ + $C_{c+c'+c''}$ + C_n), 122.66 (C_o), 116.93 (C_m), 101.69 (C_k), 84.44, 81.93 (2 x C, C_g + C_j), 78.34 (C_h), 75.70, 75.14 (2 x C, $C_{e+e'}$), 75.06 (C_p), 73.47 ($C_{e''}$), 72.15 (C_i), 71.25, 70.75 (2 x C, C_r + C_s), 68.76 (C_f), 42.69 (C_t).

HR-ESI-MS: m/z: 650.2867 $[M + NH_4]^+$, calculated for $C_{37}H_{45}ClNO_7^+$: 650.2879

2,3,6-tri-*O*-benzyl-4-*O*-(tetraethylene glycolyl)-phenyl-β-*D*-glucopyranoside (**6**):



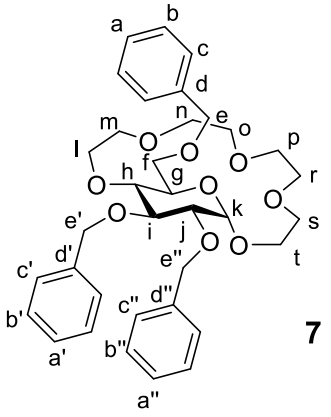
KOH (8.4 g, 150 mmol) was dissolved in diethylene glycol (40 mL) under stirring and moderate heating. The solution of substrate **5** (1.9 mg, 3 mmol) in THF (3 mL) was then added under vigorous stirring and subsequently heated for 8 h at 80 °C. After cooling, the mixture was diluted with water (30 mL) and extracted with DCM (30 mL). The aqueous layer was acidified to pH 3 with 1 N HCl and again extracted with DCM (3 x 30 mL). The combined organic extracts were washed with brine (25 mL), dried (MgSO4), filtered and concentrated under reduced pressure. The crude mixture was separated by MPLC ((hexane : ethyl acetate = 100 : 0 (2 min) → 70 : 30 (over 2 min) → 20 : 80 (over 15 min) → 0 : 100 (over 1 min)) to afford product **6** as a yellow oil (1.65 g, 2.4 mmol, 80% yield).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.41 – 7.23 (m, 17H, $H_{a+a'+a''}$ + $H_{b+b'+b''}$ + $H_{c+c'+c''}$ + H_n), 7.17 – 7.02 (m, 3H, H_m + H_o), 5.09 – 4.97 (m, 2H, H_k + H_e), 4.97 – 4.77 (m, 3H), 4.75 – 4.53 (m, 2H) (5 x H, $H_{e+e'+e''}$), 4.05 – 3.94 (m, 1H, H_i), 3.93 – 3.81 (m, 1H, H_f), 3.80 – 3.68 (m, 6H, $H_{f'}$ + H_g + H_p + H_r), 3.67 – 3.48 (m, 14H, H_h + H_j + H_s + H_t + $H_{u,v,w,x}$).

^{13}C NMR (101 MHz, $CDCl_3$) δ 157.41 (C_l), 138.65, 138.31, 138.29 (3 x C, $C_{d+d'+d''}$), 129.52, 128.39, 128.38, 128.30, 128.24, 127.98, 127.75, 127.66, 127.63, 127.52 (10 x C, $C_{a+a'+a''}$ + $C_{b+b'+b''}$ + $C_{c+c'+c''}$ + C_n), 122.63 (C_o), 116.92 (C_m), 101.65 (C_k), 84.43, 81.92 (2 x C, C_g + C_j), 78.41 (C_h), 75.67, 75.18, 75.05, 73.46, 72.48, 72.21, 70.76, 70.67, 70.60, 70.52, 70.36 (11 x C, C_i + $C_{e,e',e''}$ + $C_{p,r,s,t,u,v,w}$), 68.86 (C_f), 61.76 (C_x).

HR-ESI-MS: m/z: 725.3299 $[M + Na]^+$, calculated for $C_{41}H_{50}NaO_{10}^+$: 725.3296

2,3,6-tri-*O*-benzyl-glucose crown ether (**7**):



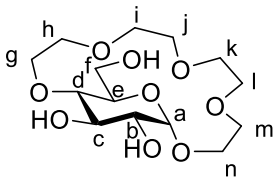
Compound **6** (700 mg, 1 mmol) was dissolved in dry MeCN (200 mL) under N_2 atmosphere. NH_4PF_6 (325 mg, 2 mmol) was added and the mixture was stirred for 1 h at room temperature. Then $FeCl_3$ (350 mg, 2.2 mmol) was added and the resulting solution was stirred for 48 h at 40 °C. The mixture was then concentrated to approx. 10% volume. DCM (30 mL) and 1N aqueous $NaHCO_3$ (30 mL) were added and the layers were separated. The aqueous layer was extracted with DCM (3 x 30 mL). The combined organic extracts were washed with water (25 mL), brine (25 mL), dried ($MgSO_4$), filtered and concentrated under reduced pressure. The crude mixture was separated by MPLC ((hexane : ethyl acetate = 100 : 0 (3 min) → 40 : 60 (over 16 min) → 0 : 100 (over 1 min)) to afford product **7** as a pale yellow oil (364 mg, 0.6 mmol, 60% yield).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.44 – 7.23 (m, 15H, $H_{a+a'+a''}$ + $H_{b+b'+b''}$ + $H_{c+c'+c''}$), 4.97 – 4.85 (m, 2H, $H_{e/e'/e''}$), 4.83 (d, J = 12.4 Hz, 1H, He/e'/e''), 4.74 (d, J = 3.4 Hz, 1H, Hk), 4.71 – 4.63 (m, 2H, $H_{e/e'/e''}$), 4.53 (d, J = 12.1 Hz, 1H, $H_{e/e'/e''}$), 4.38 (dt, J = 9.8, 2.6 Hz, 1H, H_g), 4.14 (dd, J = 11.0, 3.1 Hz, 1H, H_f), 4.05 (dd, J = 9.6, 8.7 Hz, 1H, H_i), 3.86 (ddd, J = 10.8, 8.9, 1.7 Hz, 1H, H_t), 3.81 – 3.73 (m, 2H, H_l), 3.73 – 3.49 (m, 15H, $H_{f'}$ + H_h + $H_{m,n,o,p,r,s,t'}$), 3.45 (ddd, J = 11.8, 9.4, 2.8 Hz, 1H, H_j).

^{13}C NMR (101 MHz, $CDCl_3$) δ 139.41, 138.57, 138.53 (3 x C, $C_{d+d'+d''}$), 128.37, 128.28, 128.16, 128.05, 127.91, 127.81, 127.74, 127.40, 127.34 (9 x C, $C_{a+a'+a''}$ + $C_{b+b'+b''}$ + $C_{c+c'+c''}$), 96.65 (C_k), 81.04 (C_i), 79.45 (C_j), 77.27 (C_h), 75.45, 73.29, 73.10 (3 x C, $C_{e,e',e''}$), 71.86, 70.79, 70.65, 70.63, 70.58, 70.50 (6 x C, $C_{m,n,o,p,r,s}$, 69.47 (C_l), 69.33 (C_g), 68.96 (C_f), 66.51 (C_t).

HR-ESI-MS: m/z: 626.3307 $[M + NH_4]^+$, calculated for $C_{35}H_{48}NO_9^+$: 626.3324

Glucose crown ether (**8**):



Compound **7** (304 mg, 0.5 mmol) was dissolved in MeOH (25 mL). Pd/C (30 mg, 10 wt.% loading, 0.025 mmol) was added and a H_2 balloon was appended to the flask. The mixture was stirred in H_2 atmosphere for 72h. Afterwards it was filtered through cellite and concentrated under reduced pressure. The product **8**, obtained as a colourless, thick oil, did not require further purification. (167 mg, 0.495 mmol, 99% yield).

^{1}H NMR (600 MHz, D_2O) δ 4.82 (d, J = 3.6 Hz, 1H, H_a), 4.14 – 4.10 (m, 1H, H_e), 3.94 – 3.87 (m, 2H, H_c + H_f), 3.84 – 3.77 (m, 3H, H_f + H_n), 3.76 – 3.72 (m, 2H), 3.72 – 3.66 (m, 2H), 3.66 – 3.63 (m, 2H, H_g), 3.62 – 3.57 (m, 6H, H_g), 3.54 – 3.48 (m, 2H) (12 x H, $H_{h,l,j,k,l,m}$), 3.46 (dd, J = 9.7, 3.6 Hz, 1H, H_b), 3.39 (dd, J = 10.2, 9.2 Hz, 1H, H_d).

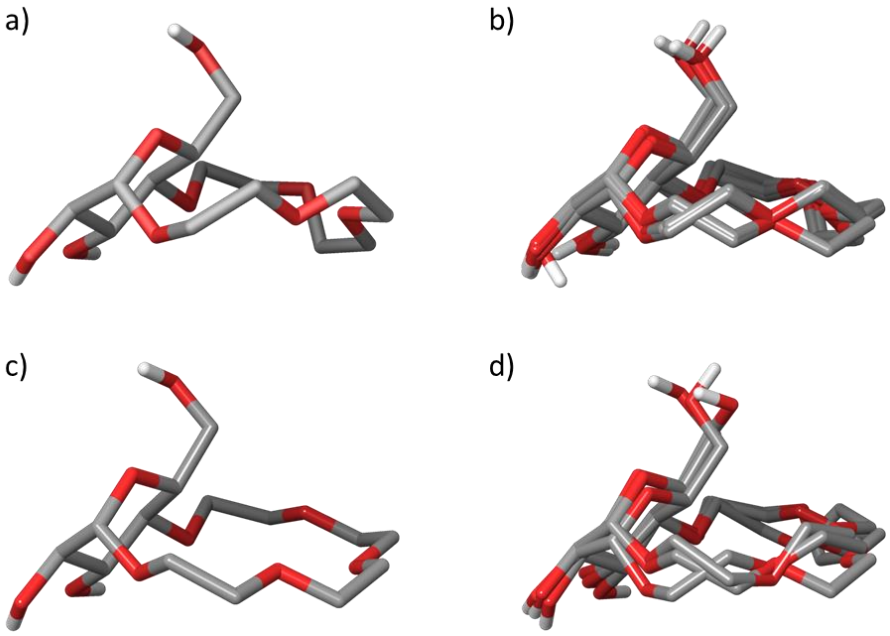
^{13}C NMR (151 MHz, D_2O) δ 98.18 (C_a), 75.92 (C_d), 71.57 (C_b), 70.85 (C_m), 70.44 (C_c), 70.04, 69.97, 69.93, 69.90, 69.64 (5 x C, $C_{h,l,j,k,l}$), 69.57 (C_e), 67.14 (C_g), 67.06 (C_n), 60.62 (C_f).

HR-ESI-MS: m/z: 361.1482 $[M + Na]^+$, calculated for $C_{14}H_{26}NaO_9^+$: 361.1485

4. Conformational analysis of receptor 8.

Computational simulations were performed with the Schrodinger Maestro Suite (Program version 2020-2 for MacOS). A conformational search was carried out starting from a random input geometry of receptor **8**, using the Mixed-torsional/Low mode conformational sampling of MacroModel combined with OPLS3e force field minimization (GB/SA water solvation model). The conformational search was performed with 10000 steps and a 21kJ/mol (~ 5 kcal/mol) relative potential energy cut-off was applied (0.5 Å maximum atom deviation).

All resulting conformers within 21 kJ/mol (~ 5 kcal/mol) of the global minimum were clustered according to the RMSD of the heavy atoms. The structure closest to the centroid in each cluster was chosen as a representative conformation. Representative conformers in between ~ 2 kcal/mol were superimposed for structural comparison.



*a) Lowest energy conformation of receptor **8**. b) Overlay of the six lowest energy conformers of receptor **8** in between 1 kcal/mol relative potential energy. c) Lowest energy structure nearest to centroid after conformational clustering (relative potential energy: 2.56 kJ/mol). d) Overlay of the three lowest energy structures nearest to centroids of clusters < 2kcal/mol relative potential energy. Note: For all structures non-polar hydrogen atoms have been omitted for clarity.*

5. Titration experiments.

5.1 NMR titrations.

5.1.1 NMR titrations with amino-acid methyl ester hydrochlorides.

The titration experiments were carried out in D_2O at room temperature.[1] The concentrations of the host and the guest solutions were 10 mM and 600 mM respectively. The starting volume of the host solution was 0.6 mL. The data was fitted to a single-site non-competitive binding equation using Prism ver.9.0.0 (GraphPad).

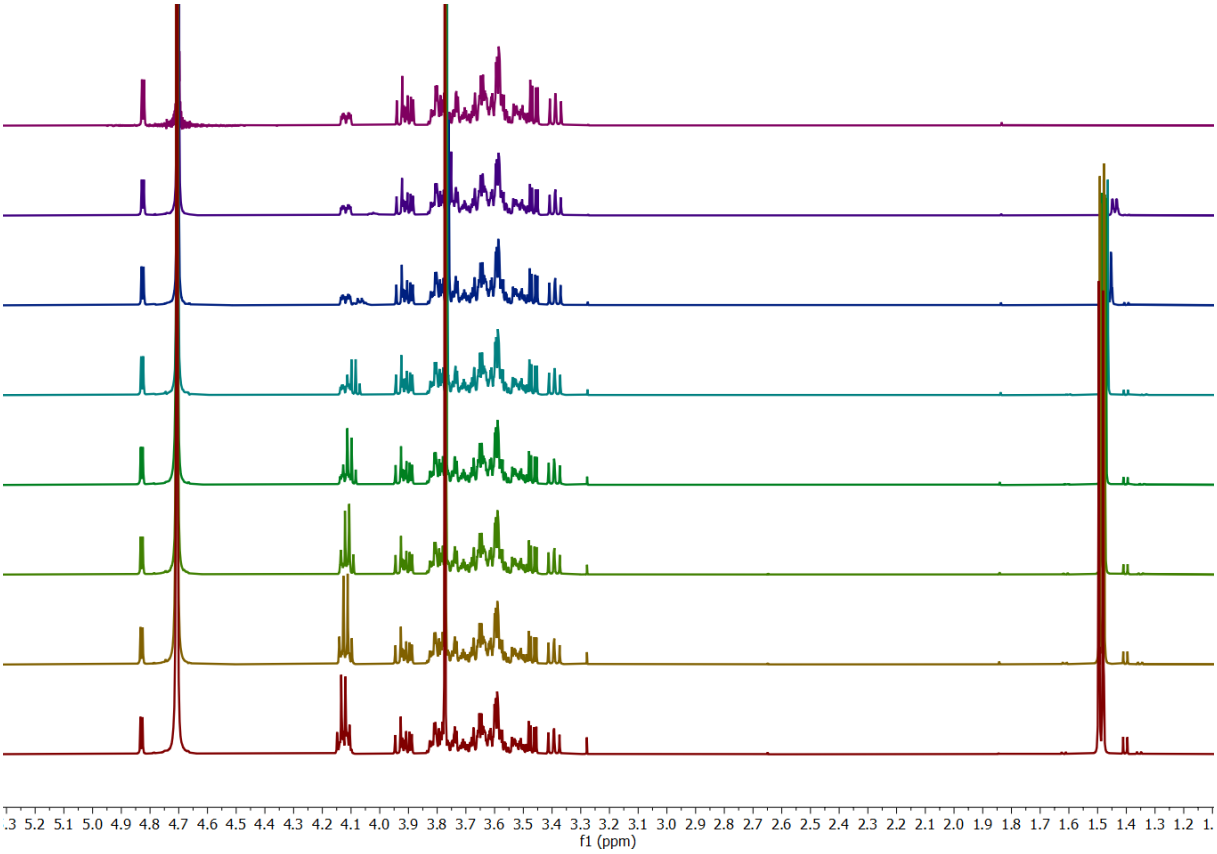
Injection table valid for all titration experiments:

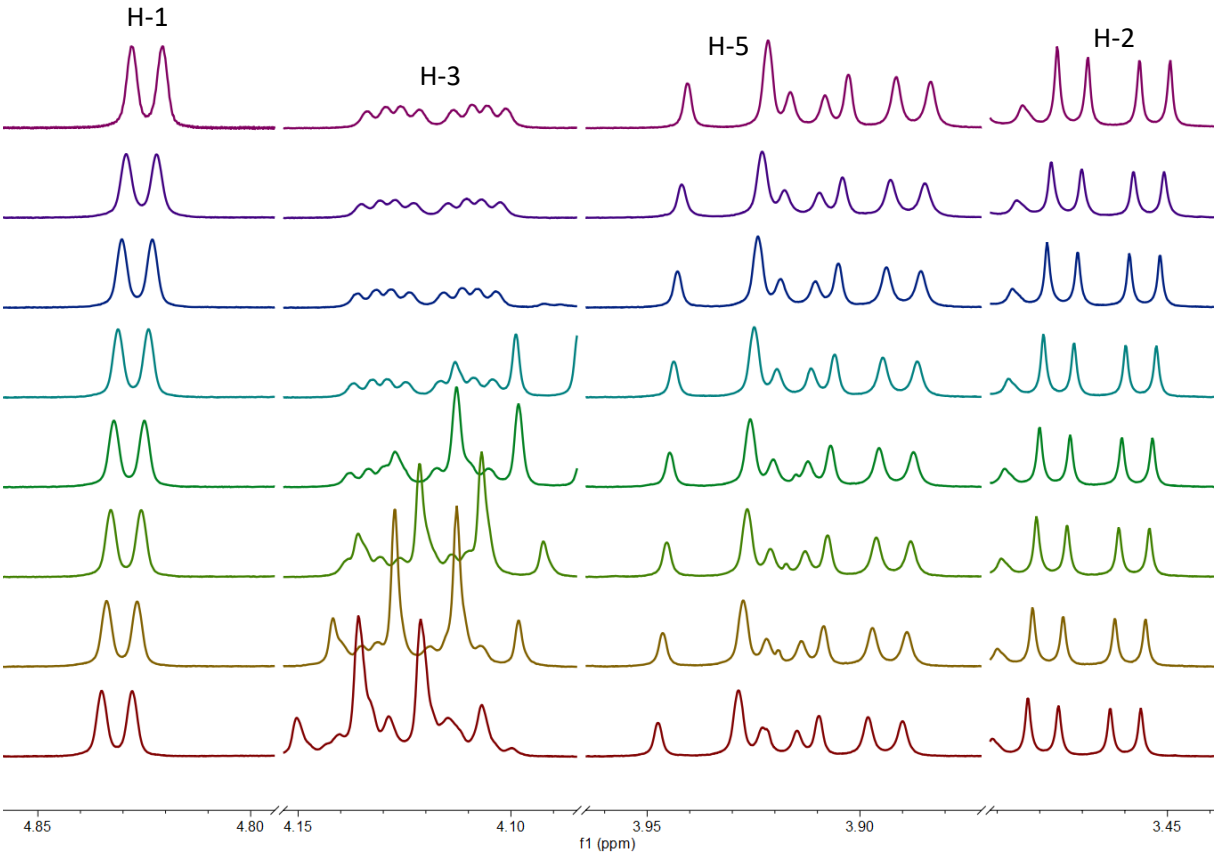
Titration	Portion of guest solution added (µL)	Total volume of guest solution added (µL)	Equivalents of guest added	Concentration of guest (mM)
1	0	0	0	0
2	1	1	0.1	1.0
3	1.5	2.5	0.25	2.49
4	2.5	5	0.5	4.96
5	3	8	0.8	7.89
6	4	12	1.2	11.76
7	6	18	1.8	17.48
8	20	38	3.8	35.74

[1] *For titrations of H-Phe-OH the guest was dissolved in a 20:1 D_2O : DMSO-d_6 solution to reach a concentration of 400 mM (the solubility in pure D_2O was too low to achieve sufficient concentration of the guest).*

H-L-Ala-OMe x HCl to receptor 8:

^{1}H NMR spectra (top – full, bottom – enhanced view on specific receptor protons):

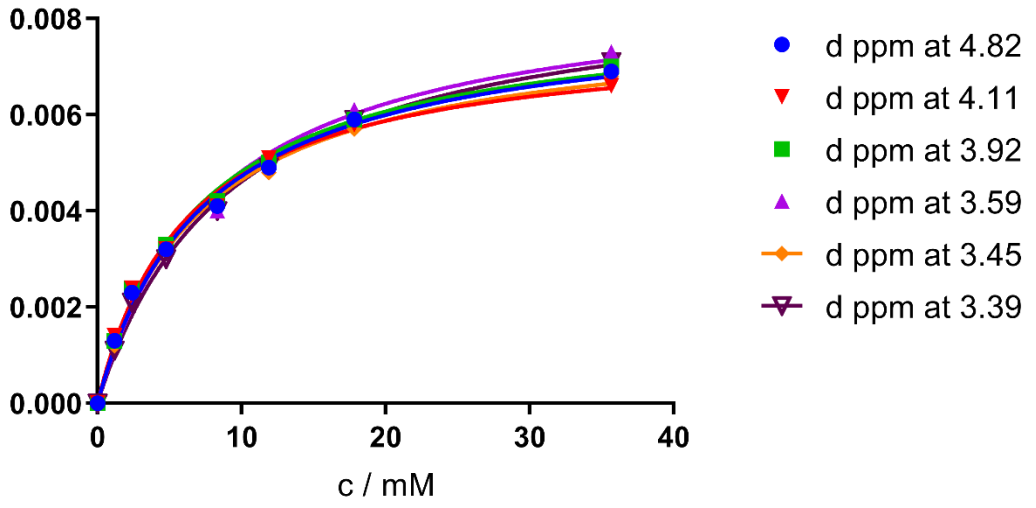




Summary of chemical shift changes:

Titration	4.82	Δppm	4.11	Δppm	3.92	Δppm	3.59	Δppm	3.45	Δppm	3.39	Δppm
1	4.8207	0.0000	4.1337	0.0000	3.9216	0.0000	3.5857	0.0000	3.4566	0.0000	3.3879	0.0000
2	4.8220	0.0013	4.1351	0.0014	3.9229	0.0013	3.587	0.0013	3.4578	0.0012	3.389	0.0011
3	4.8230	0.0023	4.1361	0.0024	3.924	0.0024	3.5881	0.0024	3.4589	0.0023	3.39	0.0021
4	4.8239	0.0032	4.1369	0.0032	3.9249	0.0033	3.589	0.0033	3.4598	0.0032	3.3909	0.0030
5	4.8248	0.0041	4.1378	0.0041	3.9258	0.0042	3.5897	0.0040	3.4607	0.0041	3.3919	0.0040
6	4.8256	0.0049	4.1388	0.0051	3.9266	0.0050	3.5907	0.0050	3.4614	0.0048	3.3928	0.0049
7	4.8266	0.0059	4.1395	0.0058	3.9275	0.0059	3.5918	0.0061	3.4623	0.0057	3.3938	0.0059
8	4.8276	0.0069	4.1403	0.0066	3.9286	0.0070	3.593	0.0073	3.4634	0.0068	3.395	0.0071

Plot of chemical shift change vs guest concentration:



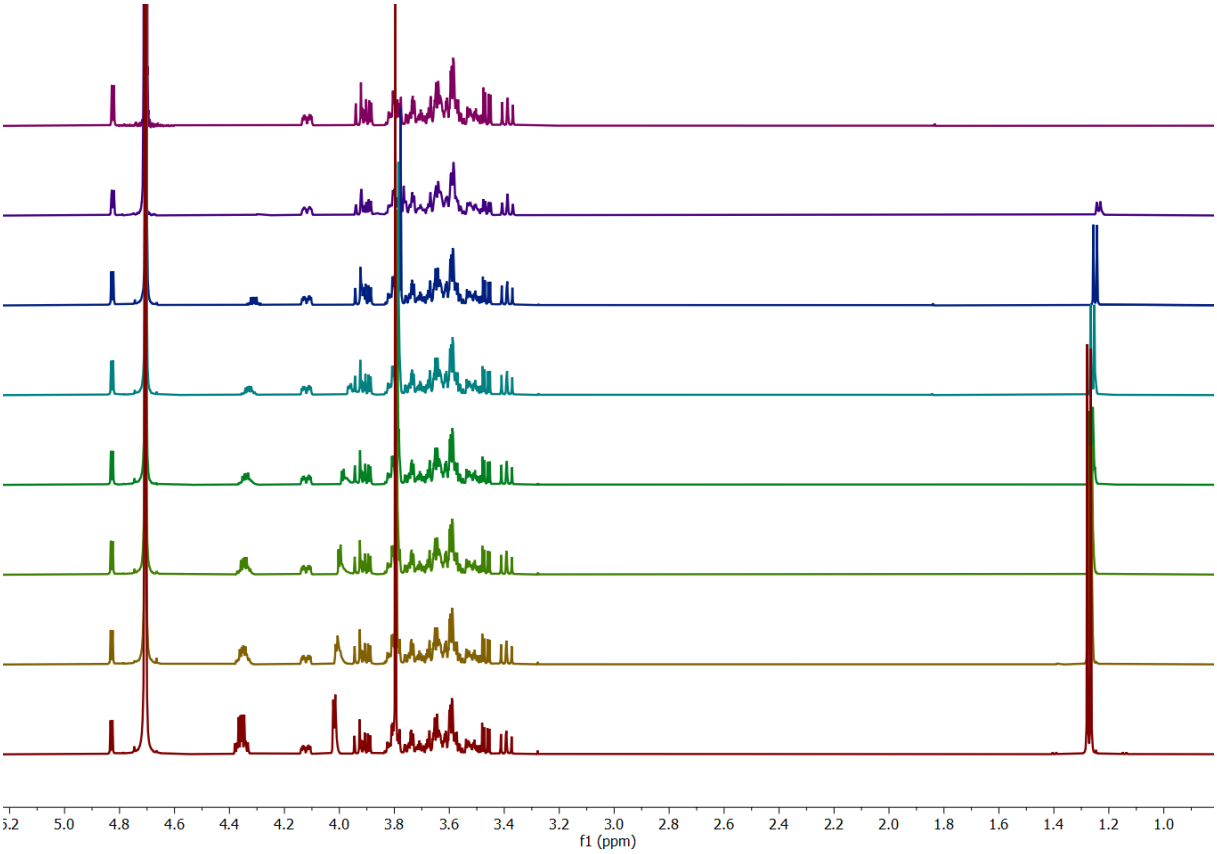
K_d values obtained by fitting the data for each proton into the single-site specific binding model:

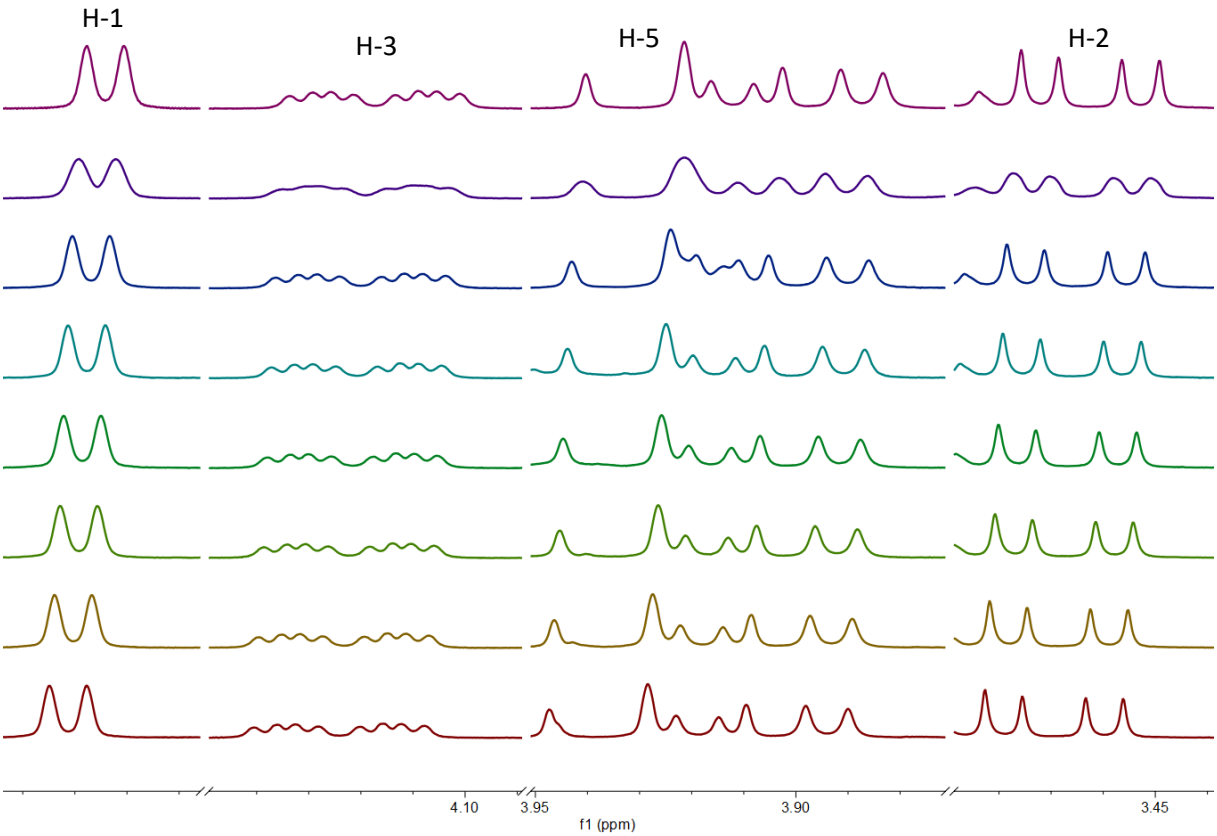
K_d	7.353	6.216	7.037	8.208	7.179	9.200
Std. error	0.753	0.647	0.714	1.181	0.694	0.756
R squared	0.994	0.994	0.994	0.989	0.995	0.997

K_d = 7.53 ± 0.79 mM

H-L-Thr-OMe x HCl to receptor 8:

^{1}H NMR spectra (top – full, bottom – enhanced view on specific receptor protons):

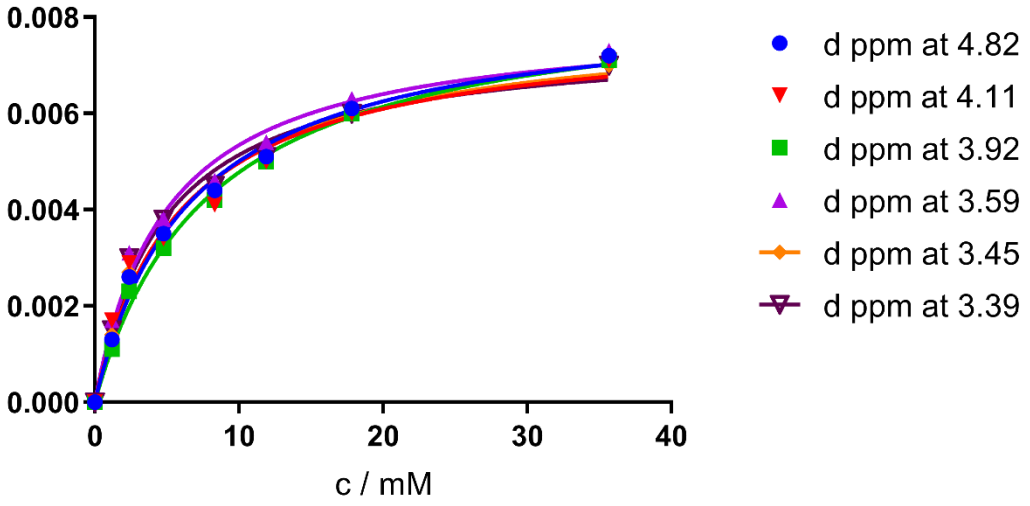




Summary of chemical shift changes:

Titration	4.82	Δppm	4.11	Δppm	3.92	Δppm	3.59	Δppm	3.45	Δppm	3.39	Δppm
1	4.8206	0.0000	4.1133	0.0000	3.9214	0.0000	3.5851	0.0000	3.4564	0.0000	3.3876	0.0000
2	4.8219	0.0013	4.115	0.0017	3.9225	0.0011	3.5868	0.0017	3.4578	0.0014	3.3891	0.0015
3	4.8232	0.0026	4.1162	0.0029	3.9237	0.0023	3.5882	0.0031	3.4591	0.0027	3.3906	0.0030
4	4.8241	0.0035	4.1167	0.0034	3.9246	0.0032	3.5889	0.0038	3.4599	0.0035	3.3914	0.0038
5	4.8250	0.0044	4.1174	0.0041	3.9256	0.0042	3.5897	0.0046	3.4607	0.0043	3.3921	0.0045
6	4.8257	0.0051	4.1183	0.0050	3.9264	0.0050	3.5905	0.0054	3.4614	0.0050	3.3927	0.0051
7	4.8267	0.0061	4.1193	0.0060	3.9274	0.0060	3.5914	0.0063	3.4625	0.0061	3.3936	0.0060
8	4.8278	0.0072	4.1204	0.0071	3.9285	0.0071	3.5924	0.0073	3.4634	0.0070	3.3946	0.0070

Plot of chemical shift change vs guest concentration:



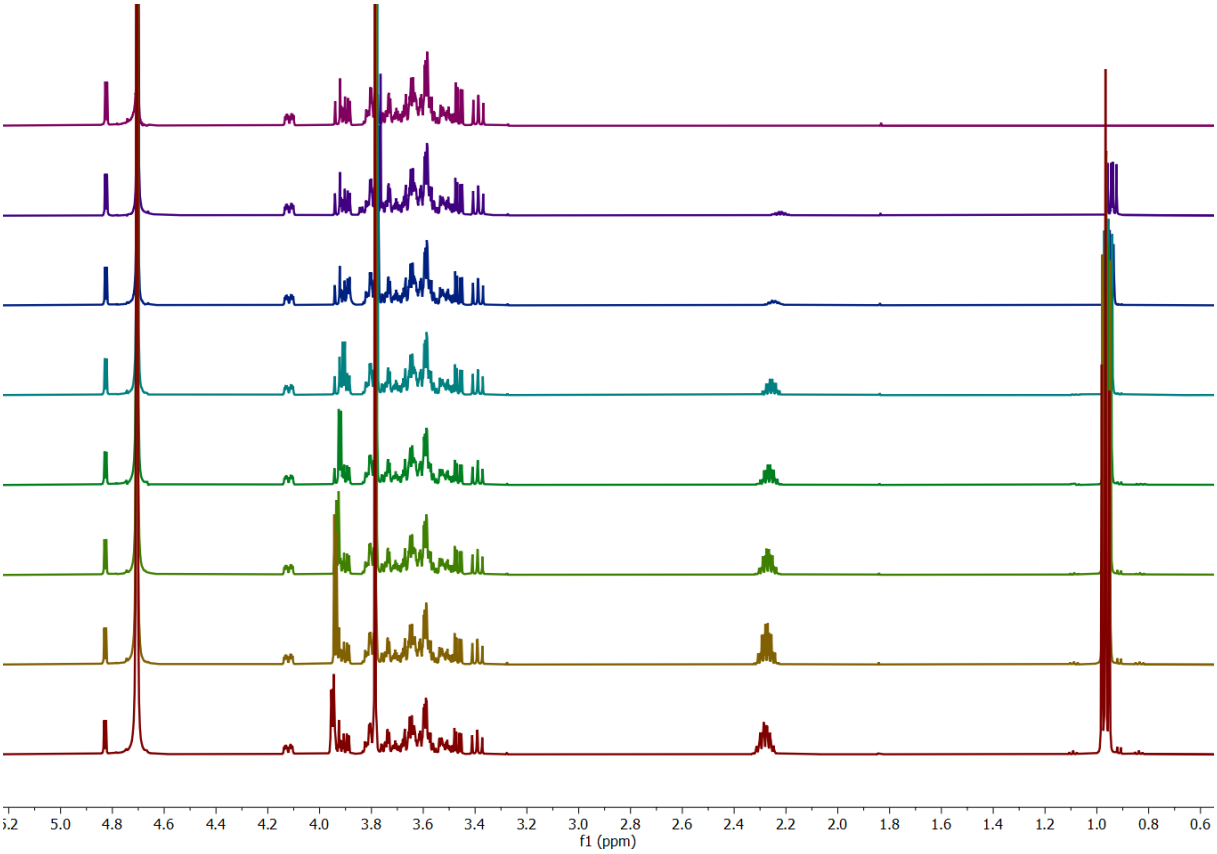
K_d values obtained by fitting the data for each proton into the single-site specific binding model:

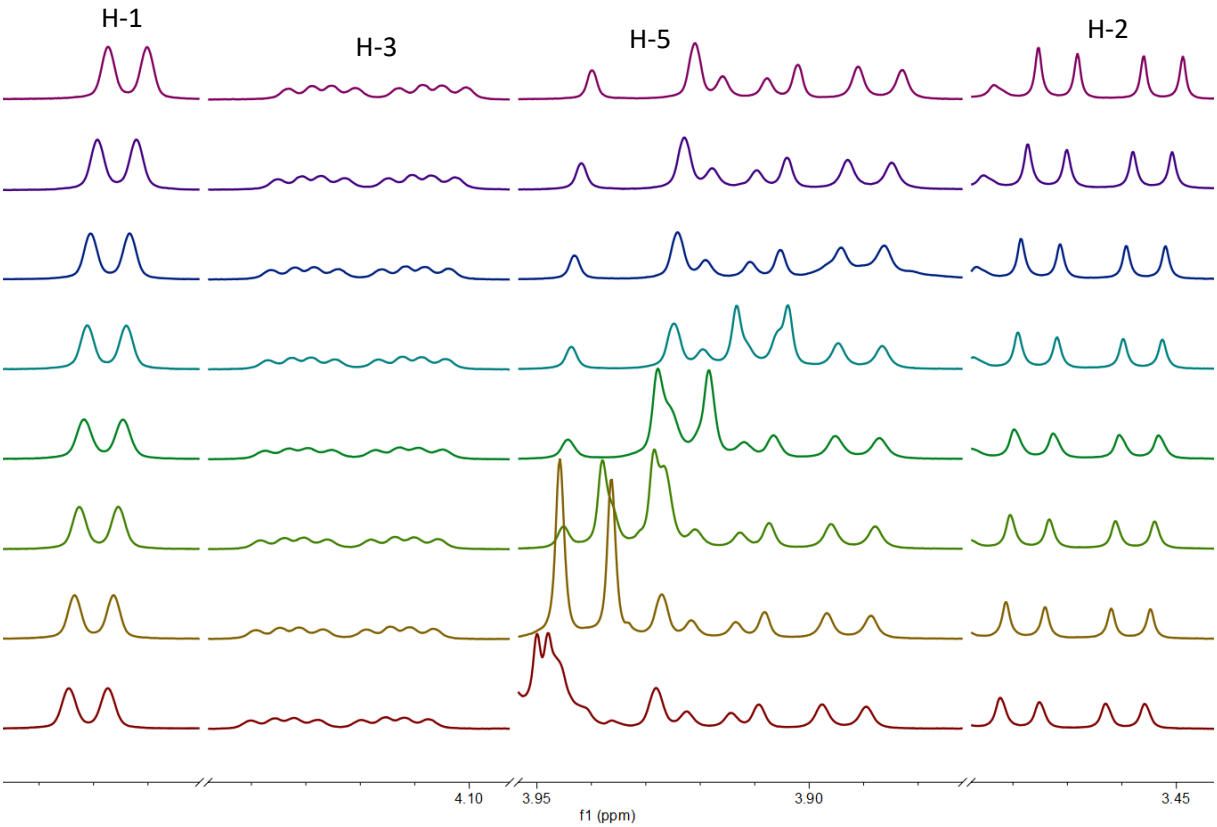
K_d	6.611	5.800	7.993	4.957	6.037	4.798
Std. error	0.762	1.232	0.703	0.772	0.848	0.727
R squared	0.993	0.973	0.996	0.985	0.989	0.986

K_d = 6.03 ± 0.84 mM

H-L-Val-OMe x HCl to receptor 8:

^{1}H NMR spectra (top – full, bottom – enhanced view on specific receptor protons):

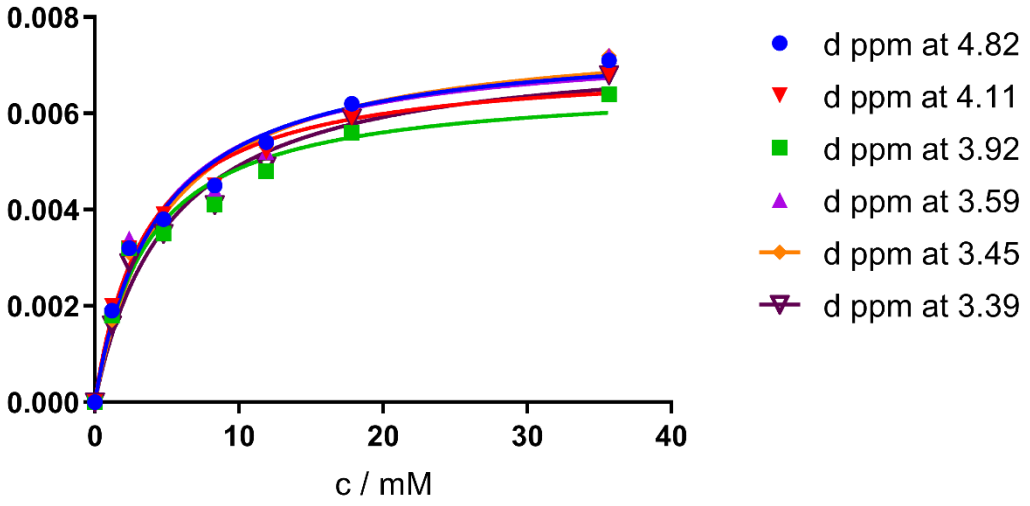




Summary of chemical shift changes:

Titration	4.82	Δppm	4.11	Δppm	3.92	Δppm	3.59	Δppm	3.45	Δppm	3.39	Δppm
1	4.8201	0.0000	4.1128	0.0000	3.8829	0.0000	3.585	0.0000	3.4559	0.0000	3.3876	0.0000
2	4.8220	0.0019	4.1148	0.0020	3.8847	0.0018	3.5869	0.0019	3.4576	0.0017	3.3892	0.0016
3	4.8233	0.0032	4.116	0.0032	3.8861	0.0032	3.5884	0.0034	3.4590	0.0031	3.3905	0.0029
4	4.8239	0.0038	4.1167	0.0039	3.8864	0.0035	3.5889	0.0039	3.4597	0.0038	3.3911	0.0035
5	4.8246	0.0045	4.1173	0.0045	3.887	0.0041	3.5894	0.0044	3.4604	0.0045	3.3917	0.0041
6	4.8255	0.0054	4.118	0.0052	3.8877	0.0048	3.5902	0.0052	3.4612	0.0053	3.3925	0.0049
7	4.8263	0.0062	4.1187	0.0059	3.8885	0.0056	3.5912	0.0062	3.4620	0.0061	3.3935	0.0059
8	4.8272	0.0071	4.1196	0.0068	3.8893	0.0064	3.5922	0.0072	3.4631	0.0072	3.3944	0.0068

Plot of chemical shift change vs guest concentration:



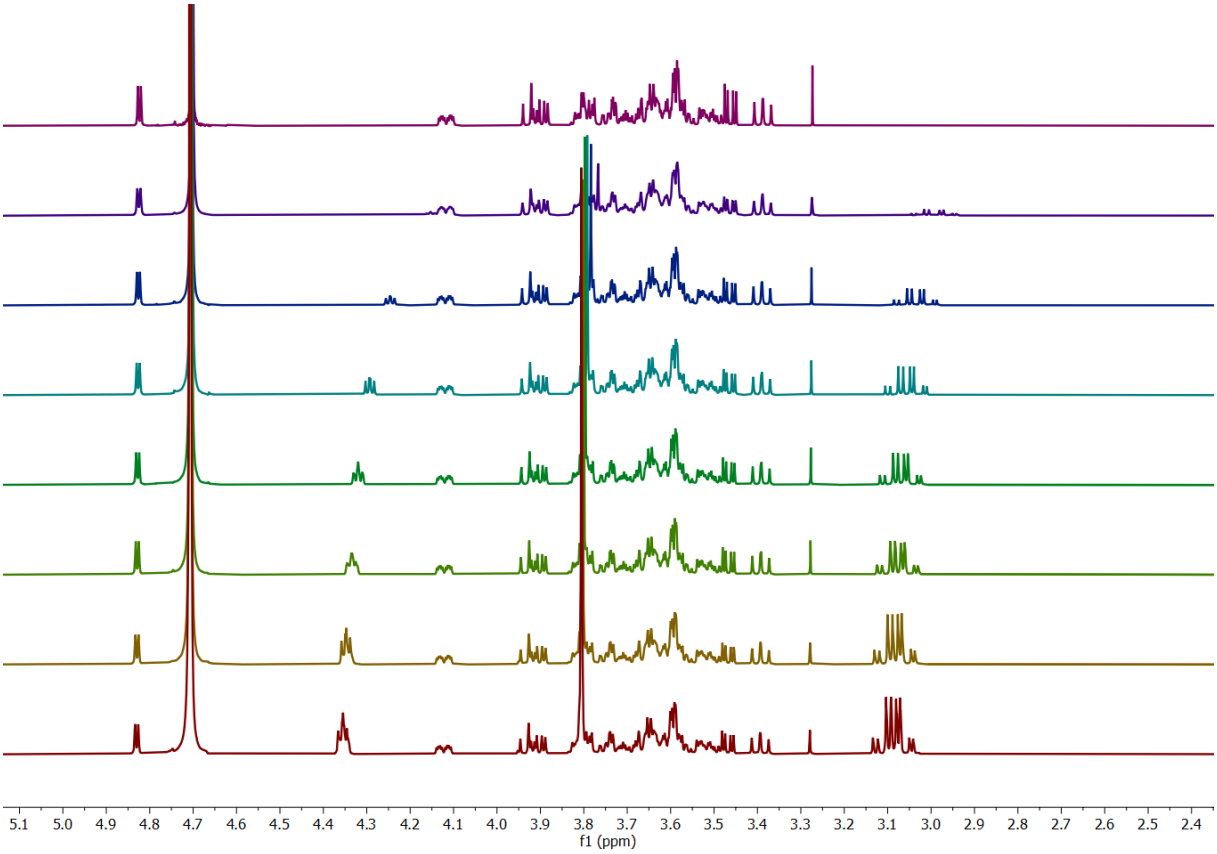
K_d values obtained by fitting the data for each proton into the single-site specific binding model:

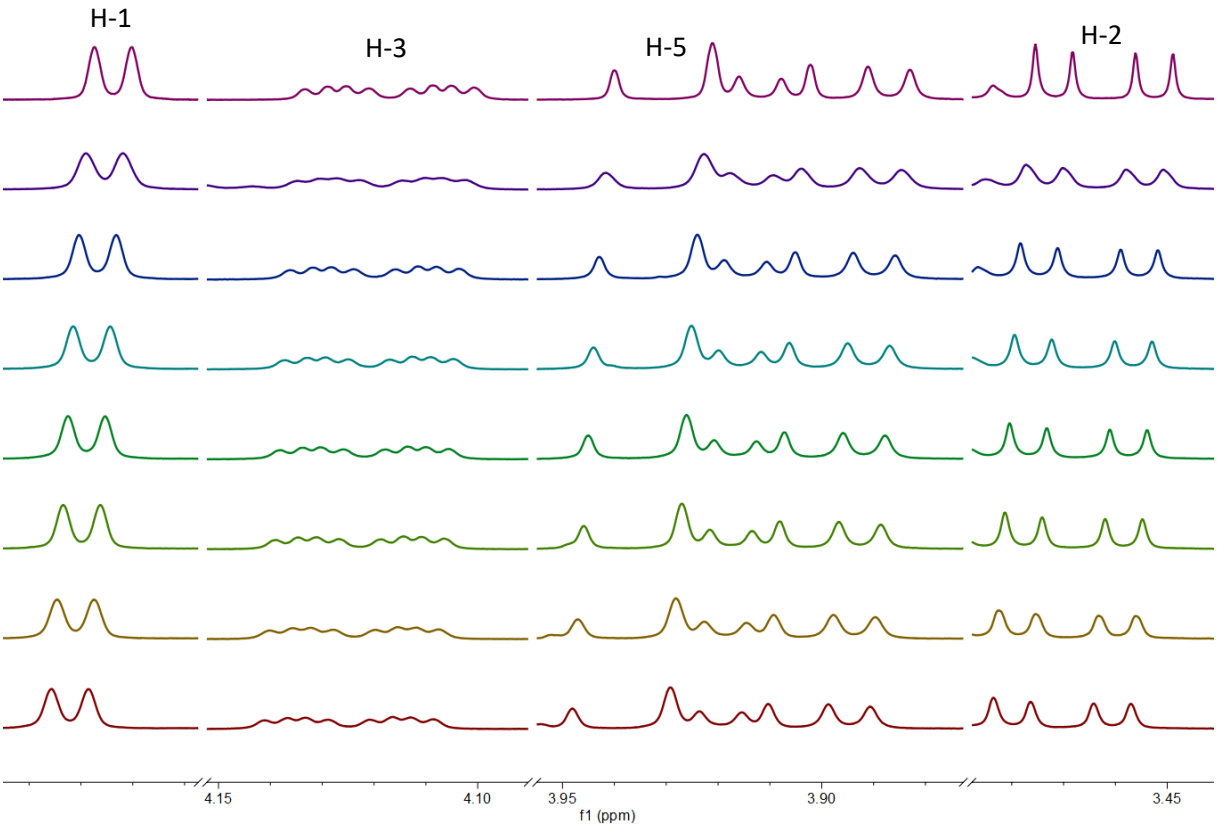
K_d	4.309	3.571	3.660	4.119	4.768	5.146
Std. error	0.763	0.598	0.807	0.947	0.798	0.989
R squared	0.980	0.982	0.969	0.967	0.983	0.978

K_d = 4.26 ± 0.81 mM

H-L-Cys-OMe x HCl to receptor 8:

^{1}H NMR spectra (top – full, bottom – enhanced view on specific receptor protons):

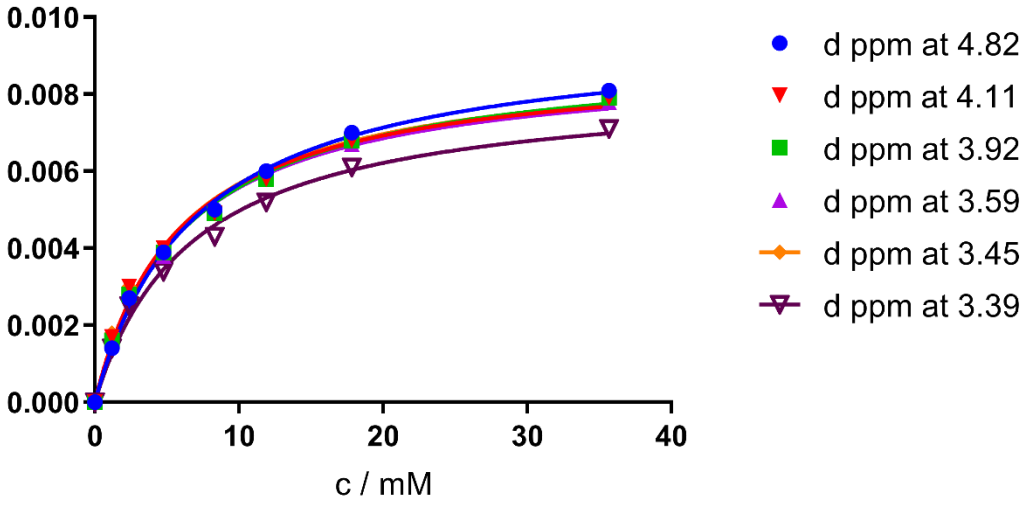




Summary of chemical shift changes:

Titration	4.82	Δppm	4.11	Δppm	3.92	Δppm	3.59	Δppm	3.45	Δppm	3.39	Δppm
1	4.8203	0.0000	4.1067	0.0000	3.9211	0.0000	3.5851	0.0000	3.4560	0.0000	3.3876	0.0000
2	4.8217	0.0014	4.1084	0.0017	3.9227	0.0016	3.5868	0.0017	3.4578	0.0018	3.389	0.0014
3	4.8230	0.0027	4.1097	0.0030	3.9239	0.0028	3.588	0.0029	3.4590	0.0030	3.3901	0.0025
4	4.8242	0.0039	4.1107	0.0040	3.925	0.0039	3.5889	0.0038	3.4600	0.0040	3.391	0.0034
5	4.8253	0.0050	4.1116	0.0049	3.926	0.0049	3.59	0.0049	3.4609	0.0049	3.3919	0.0043
6	4.8263	0.0060	4.1125	0.0058	3.9269	0.0058	3.5909	0.0058	3.4618	0.0058	3.3928	0.0052
7	4.8273	0.0070	4.1135	0.0068	3.9279	0.0068	3.5918	0.0067	3.4628	0.0068	3.3937	0.0061
8	4.8284	0.0081	4.1146	0.0079	3.929	0.0079	3.5929	0.0078	3.4640	0.0080	3.3947	0.0071

Plot of chemical shift change vs guest concentration:



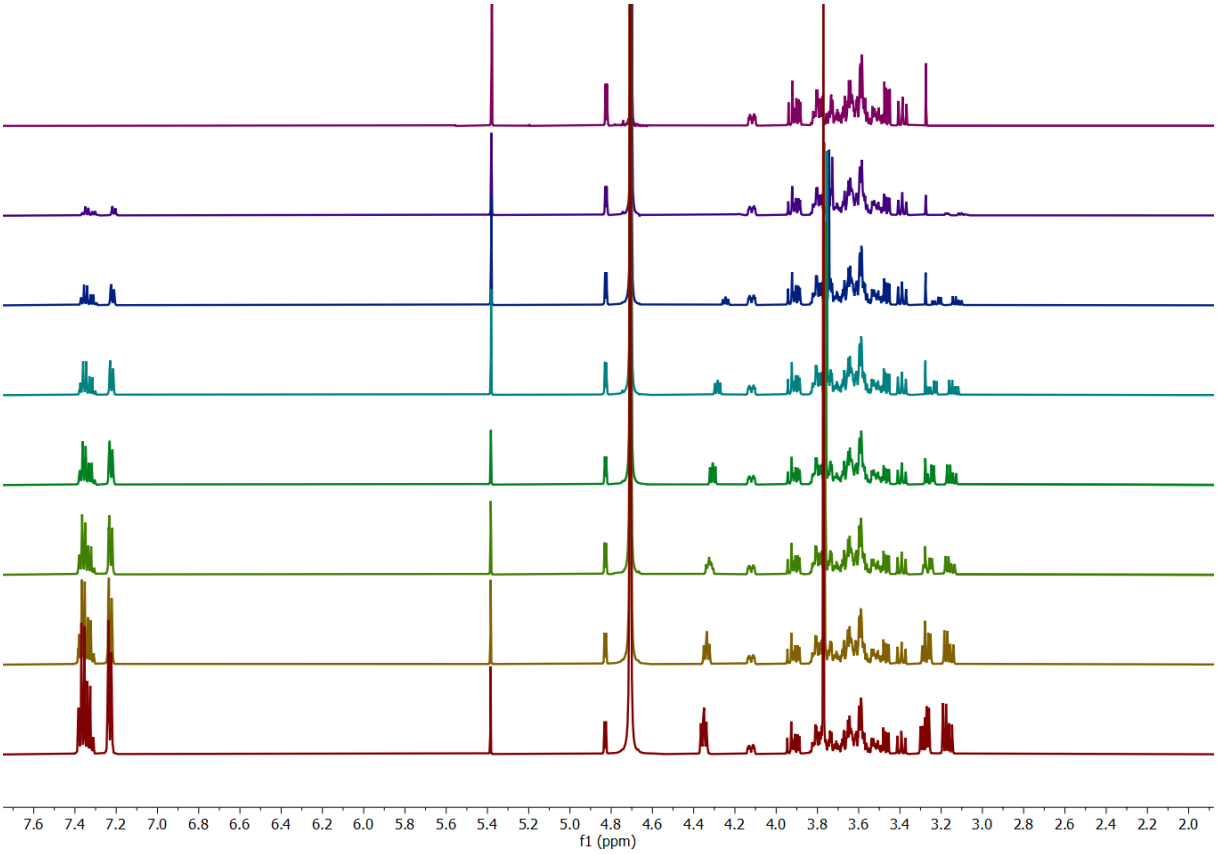
K_d values obtained by fitting the data for each proton into the single-site specific binding model:

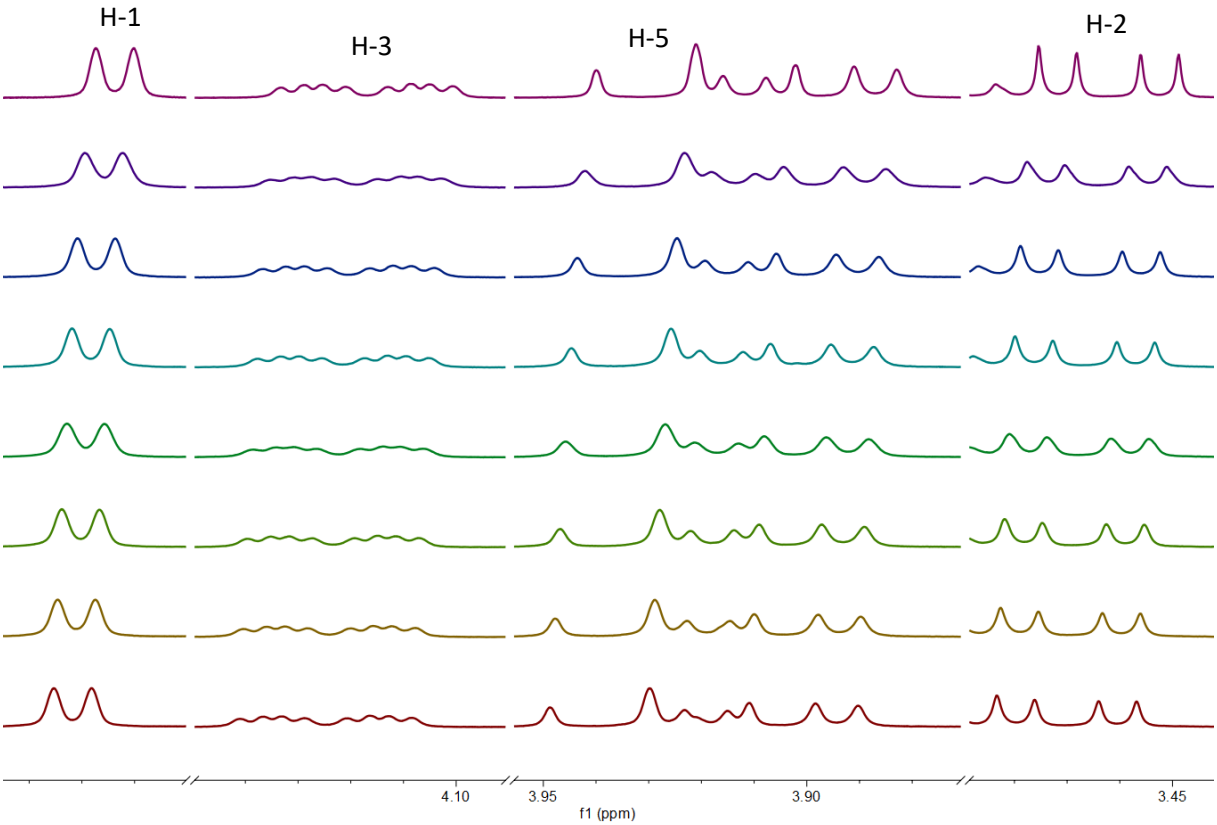
K_d	6.997	5.786	6.327	5.985	5.846	6.684
Std. error	0.462	0.696	0.588	0.647	0.774	0.692
R squared	0.998	0.992	0.995	0.993	0.990	0.994

K_d = 6.27 ± 0.64 mM

H-L-Phe-OMe x HCl to receptor 8:

^{1}H NMR spectra (top – full, bottom – enhanced view on specific receptor protons):

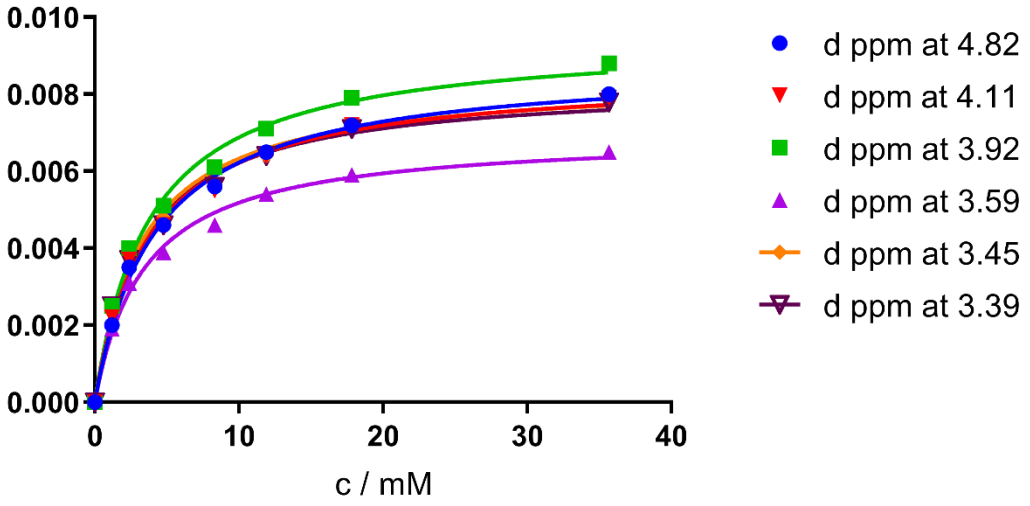




Summary of chemical shift changes:

Titration	4.82	Δppm	4.11	Δppm	3.92	Δppm	3.59	Δppm	3.45	Δppm	3.39	Δppm
1	4.8201	0.0000	4.1048	0.0000	3.9208	0.0000	3.5851	0.0000	3.4559	0.0000	3.3874	0.0000
2	4.8221	0.0020	4.107	0.0022	3.9233	0.0025	3.587	0.0019	3.4583	0.0024	3.3899	0.0025
3	4.8236	0.0035	4.1085	0.0037	3.9248	0.0040	3.5882	0.0031	3.4598	0.0039	3.3911	0.0037
4	4.8247	0.0046	4.1094	0.0046	3.9259	0.0051	3.589	0.0039	3.4606	0.0047	3.392	0.0046
5	4.8257	0.0056	4.1103	0.0055	3.9269	0.0061	3.5897	0.0046	3.4615	0.0056	3.393	0.0056
6	4.8266	0.0065	4.1112	0.0064	3.9279	0.0071	3.5905	0.0054	3.4623	0.0064	3.3938	0.0064
7	4.8273	0.0072	4.112	0.0072	3.9287	0.0079	3.591	0.0059	3.4631	0.0072	3.3945	0.0071
8	4.8281	0.0080	4.1127	0.0079	3.9296	0.0088	3.5916	0.0065	3.4639	0.0080	3.3952	0.0078

Plot of chemical shift change vs guest concentration:



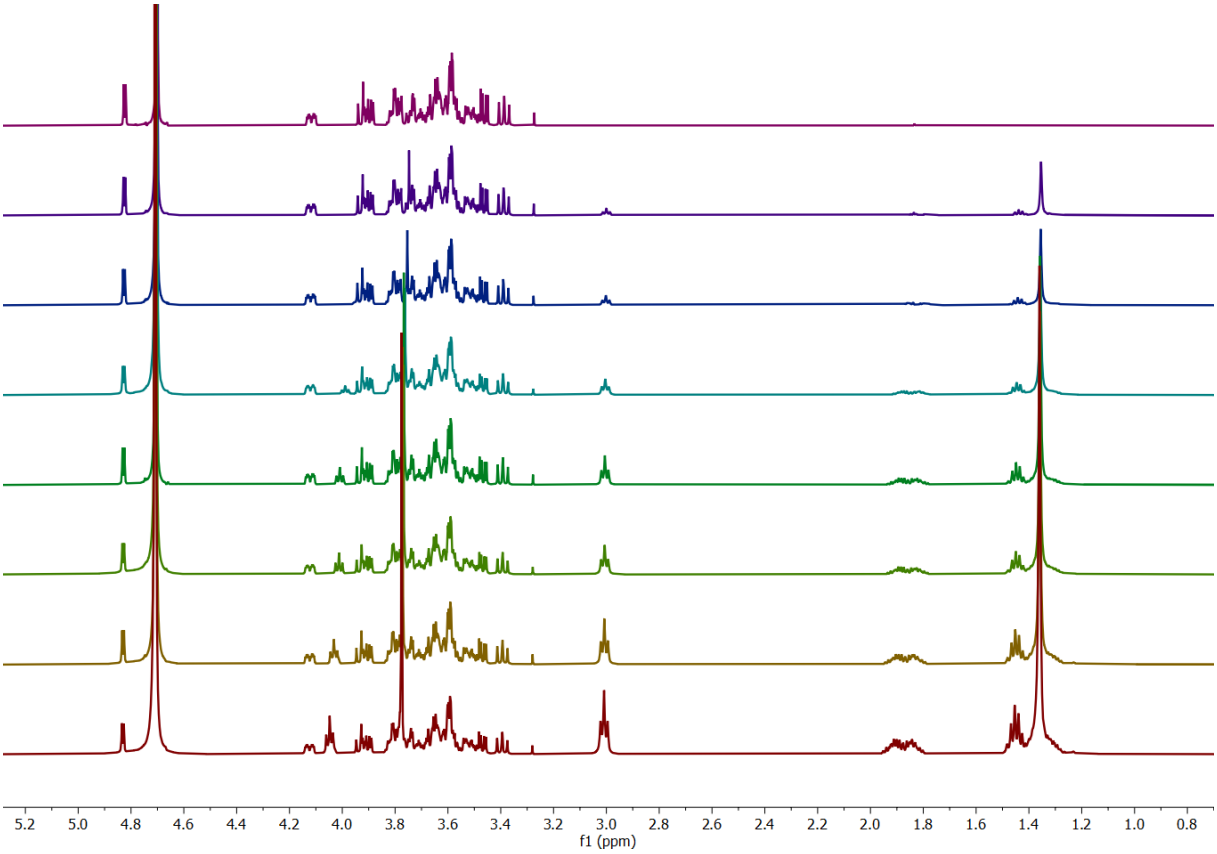
K_d values obtained by fitting the data for each proton into the single-site specific binding model:

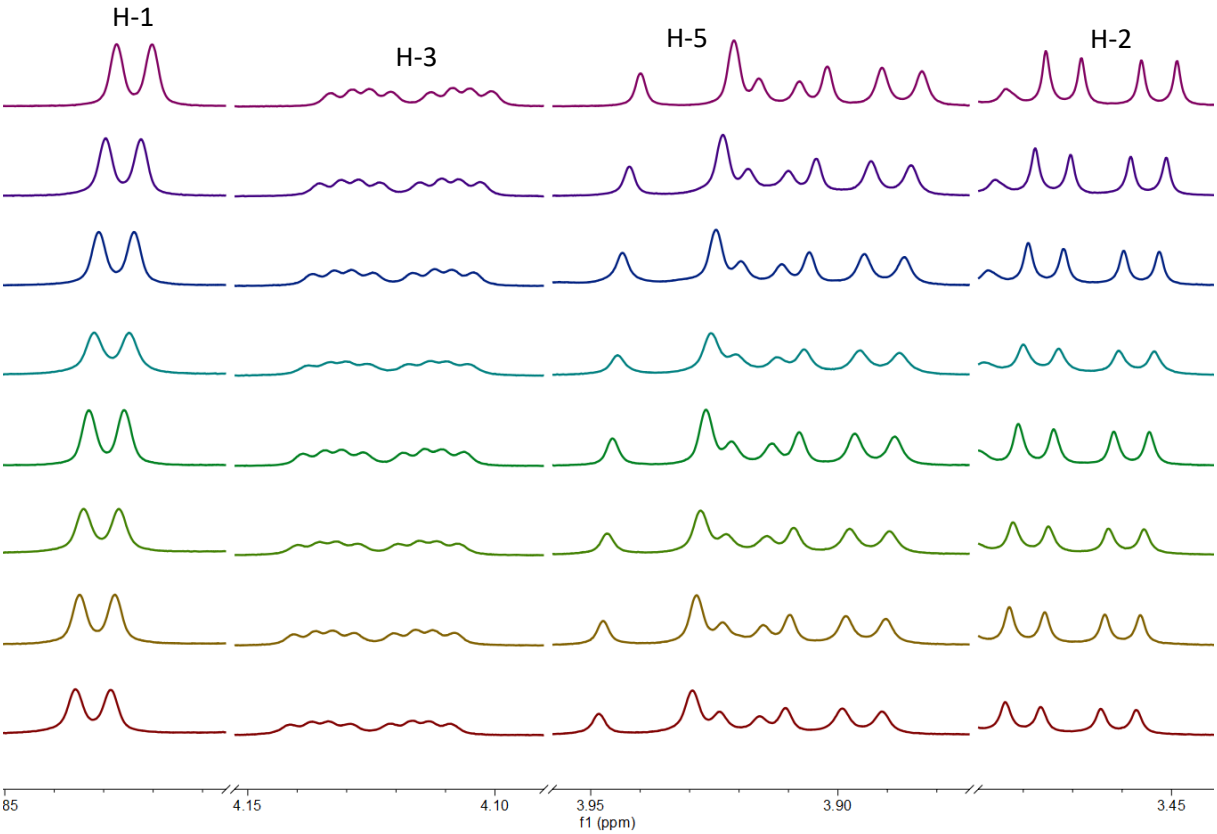
K_d	4.147	3.723	3.769	3.449	3.303	3.326
Std. error	0.317	0.425	0.404	0.357	0.421	0.384
R squared	0.996	0.992	0.993	0.993	0.990	0.991

K_d = 3.62 ± 0.38 mM

H-L-(Boc)Lys-OMe x HCl to receptor 8:

^{1}H NMR spectra (top – full, bottom – enhanced view on specific receptor protons):

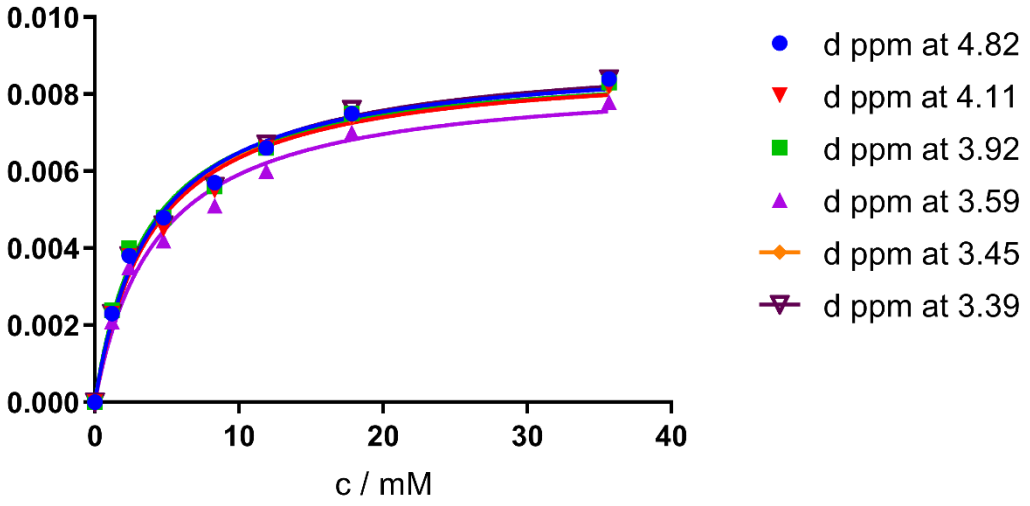




Summary of chemical shift changes:

Titration	4.82	Δppm	4.11	Δppm	3.92	Δppm	3.59	Δppm	3.45	Δppm	3.39	Δppm
1	4.8201	0.0000	4.1067	0.0000	3.9208	0.0000	3.5851	0.0000	3.4560	0.0000	3.3873	0.0000
2	4.8224	0.0023	4.109	0.0023	3.9232	0.0024	3.5872	0.0021	3.4583	0.0023	3.3896	0.0023
3	4.8239	0.0038	4.1105	0.0038	3.9248	0.0040	3.5886	0.0035	3.4598	0.0038	3.3911	0.0038
4	4.8249	0.0048	4.1112	0.0045	3.9256	0.0048	3.5893	0.0042	3.4607	0.0047	3.3919	0.0046
5	4.8258	0.0057	4.1122	0.0055	3.9264	0.0056	3.5902	0.0051	3.4616	0.0056	3.3929	0.0056
6	4.8267	0.0066	4.1133	0.0066	3.9274	0.0066	3.5911	0.0060	3.4626	0.0066	3.394	0.0067
7	4.8276	0.0075	4.1141	0.0074	3.9283	0.0075	3.5921	0.0070	3.4634	0.0074	3.3949	0.0076
8	4.8285	0.0084	4.1149	0.0082	3.9291	0.0083	3.5929	0.0078	3.4642	0.0082	3.3957	0.0084

Plot of chemical shift change vs guest concentration:



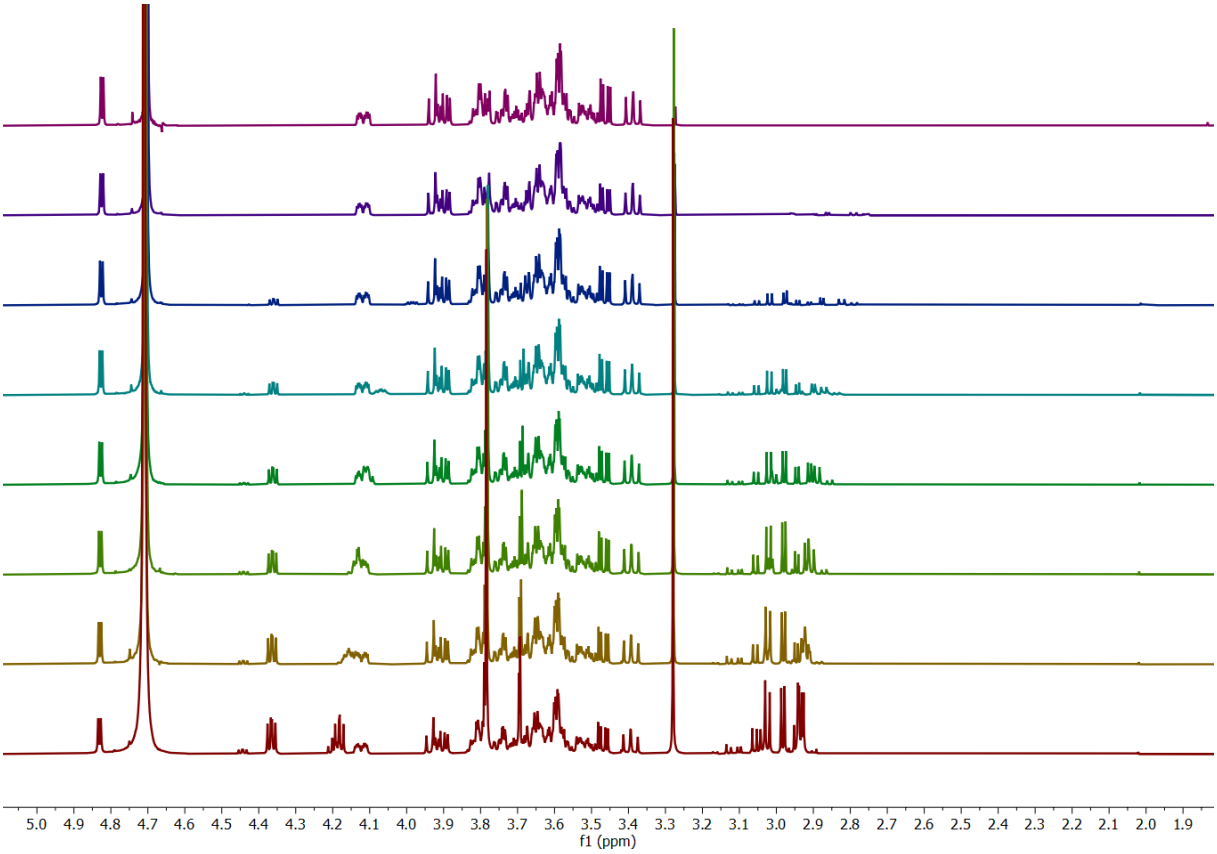
K_d values obtained by fitting the data for each proton into the single-site specific binding model:

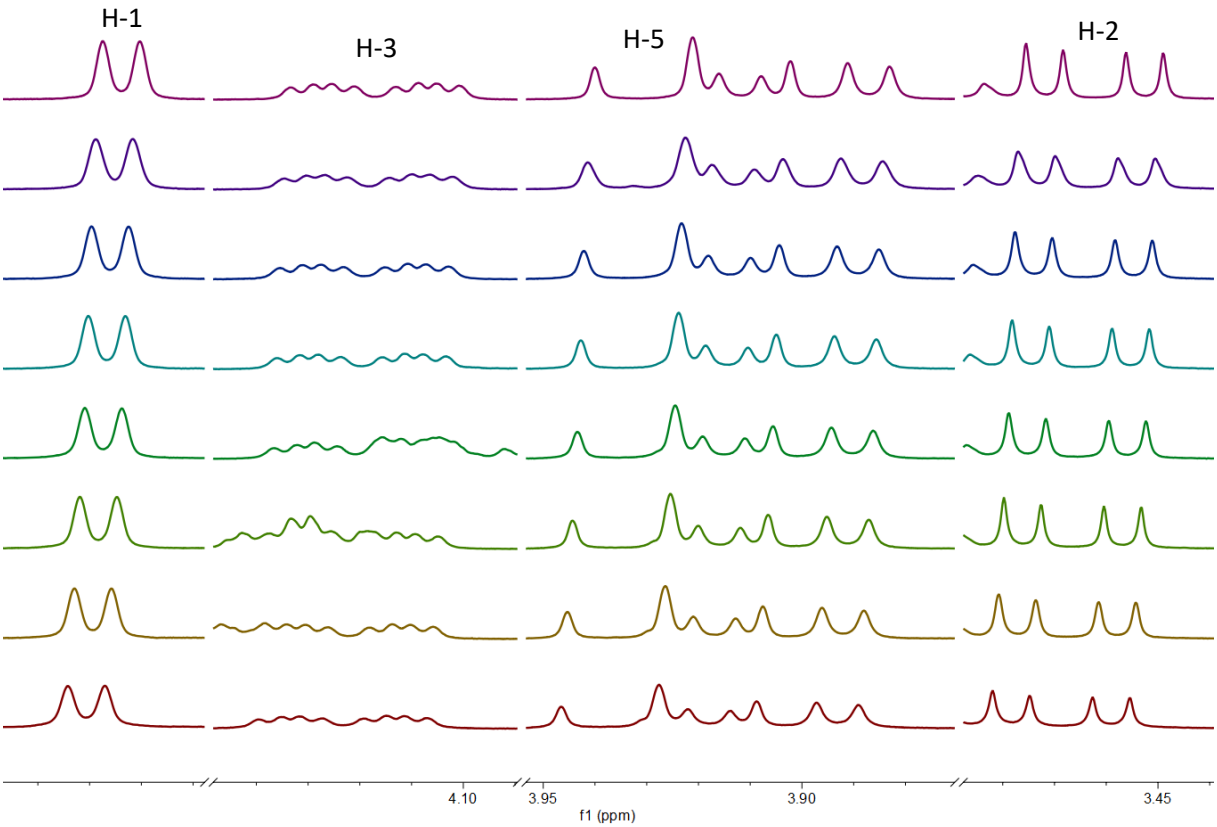
K_d	3.923	3.989	3.591	4.308	3.803	4.157
Std. error	0.482	0.591	0.546	0.682	0.478	0.590
R squared	0.991	0.986	0.985	0.984	0.990	0.987

K_d = 3.96 ± 0.56

H-L-Asn-OMe x HCl to receptor 8:

^{1}H NMR spectra (top – full, bottom – enhanced view on specific receptor protons):

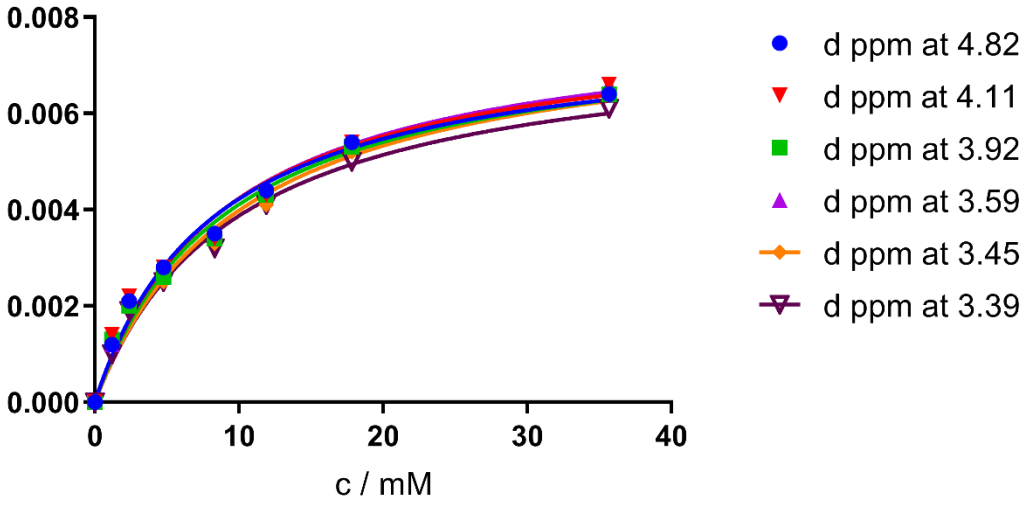




Summary of chemical shift changes:

Titration	4.82	Δppm	4.11	Δppm	3.92	Δppm	3.59	Δppm	3.45	Δppm	3.39	Δppm
1	4.8203	0.0000	4.1068	0.0000	3.9211	0.0000	3.5852	0.0000	3.4562	0.0000	3.3876	0.0000
2	4.8215	0.0012	4.1082	0.0014	3.9224	0.0013	3.5864	0.0012	3.4574	0.0012	3.3886	0.0010
3	4.8224	0.0021	4.109	0.0022	3.9231	0.0020	3.5873	0.0021	3.4582	0.0020	3.3895	0.0019
4	4.8231	0.0028	4.1096	0.0028	3.9237	0.0026	3.588	0.0028	3.4587	0.0025	3.3901	0.0025
5	4.8238	0.0035	4.1102	0.0034	3.9245	0.0034	3.5887	0.0035	3.4595	0.0033	3.3908	0.0032
6	4.8247	0.0044	4.1111	0.0043	3.9254	0.0043	3.5896	0.0044	3.4603	0.0041	3.3917	0.0041
7	4.8257	0.0054	4.1122	0.0054	3.9264	0.0053	3.5906	0.0054	3.4614	0.0052	3.3926	0.0050
8	4.8267	0.0064	4.1134	0.0066	3.9275	0.0064	3.5918	0.0066	3.4626	0.0064	3.3937	0.0061

Plot of chemical shift change vs guest concentration:



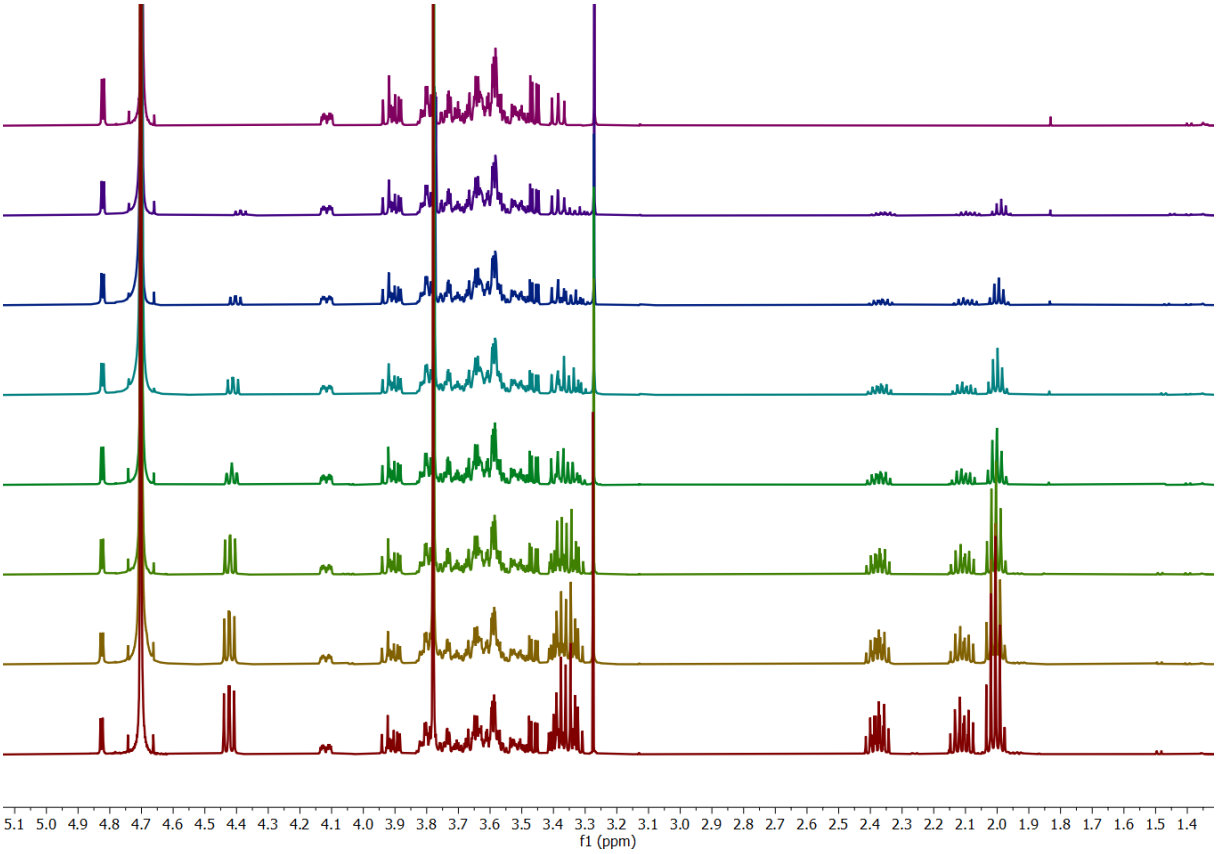
K_d values obtained by fitting the data for each proton into the single-site specific binding model:

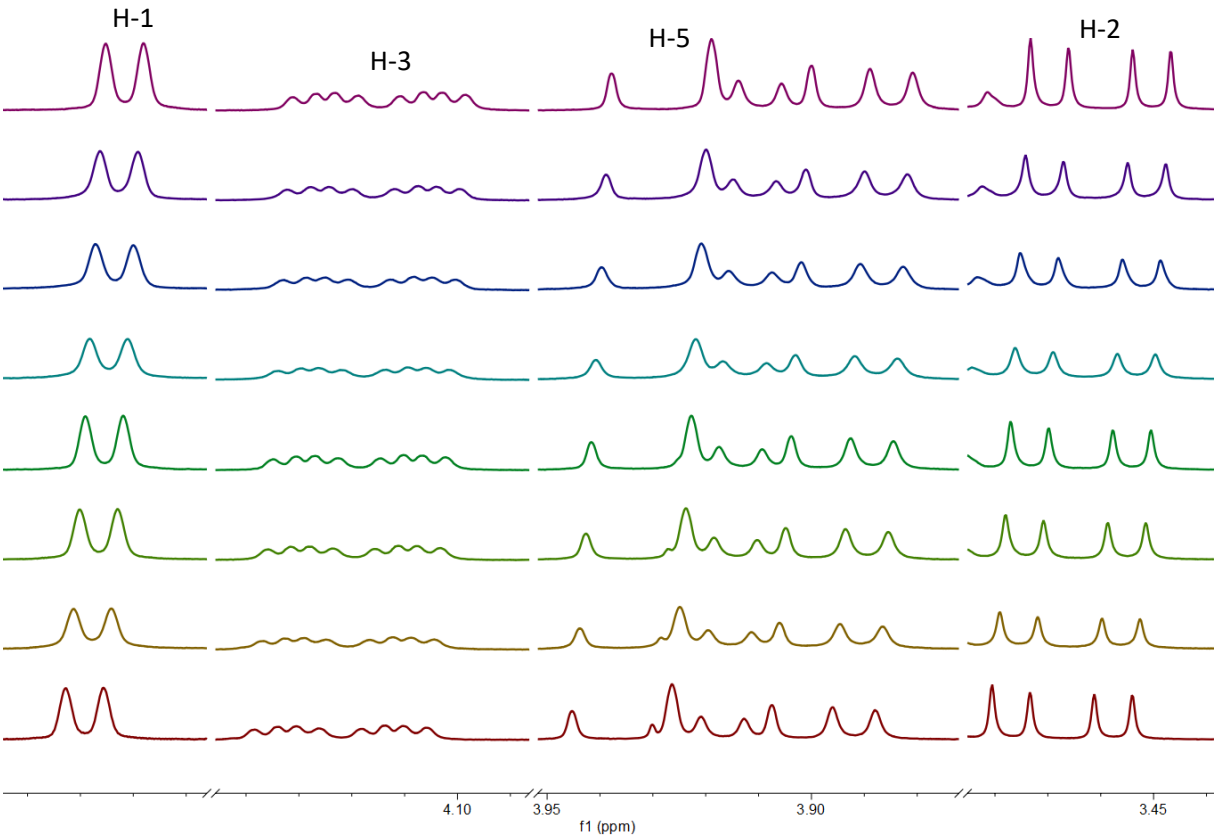
K_d	8.387	8.803	9.263	9.087	10.200	9.715
Std. error	1.247	1.875	1.554	1.425	1.863	1.396
R squared	0.988	0.975	0.985	0.987	0.983	0.989

K_d = 9.24 ± 1.56

H-L-Pro-OMe x HCl to receptor 8:

^{1}H NMR spectra (top – full, bottom – enhanced view on specific receptor protons):

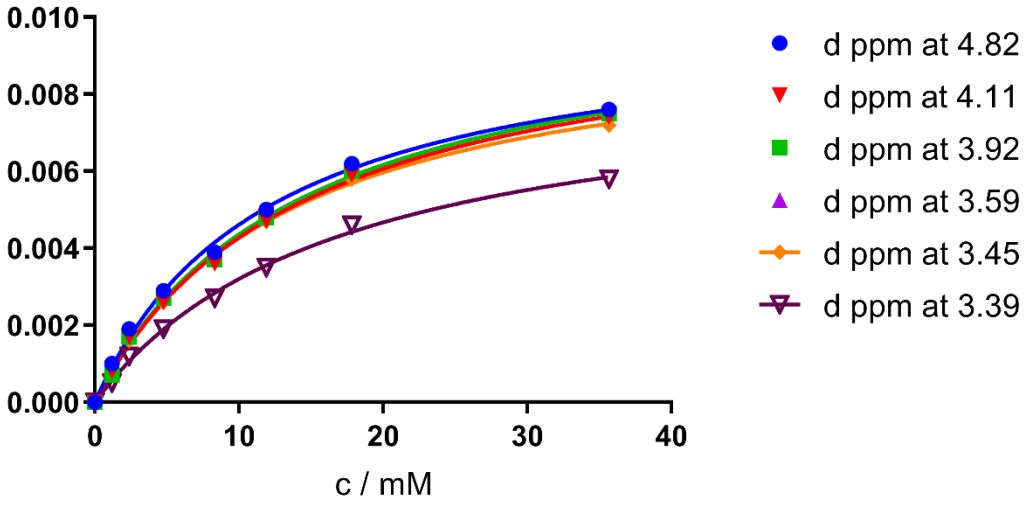




Summary of chemical shift changes:

Titration	4.82	Δppm	4.11	Δppm	3.92	Δppm	3.59	Δppm	3.45	Δppm	3.39	Δppm
1	4.8180	0.0000	4.1065	0.0000	3.9189	0.0000	3.5832	0.0000	3.4540	0.0000	3.4048	0.0000
2	4.8190	0.0010	4.1073	0.0008	3.9196	0.0007	3.5839	0.0007	3.4548	0.0008	3.4053	0.0005
3	4.8199	0.0019	4.1082	0.0017	3.9206	0.0017	3.5848	0.0016	3.4556	0.0016	3.406	0.0012
4	4.8209	0.0029	4.1091	0.0026	3.9216	0.0027	3.5857	0.0025	3.4566	0.0026	3.4067	0.0019
5	4.8219	0.0039	4.1101	0.0036	3.9226	0.0037	3.5868	0.0036	3.4577	0.0037	3.4075	0.0027
6	4.8230	0.0050	4.1112	0.0047	3.9237	0.0048	3.588	0.0048	3.4587	0.0047	3.4083	0.0035
7	4.8242	0.0062	4.1124	0.0059	3.9249	0.0060	3.5892	0.0060	3.4598	0.0058	3.4094	0.0046
8	4.8256	0.0076	4.1139	0.0074	3.9264	0.0075	3.5908	0.0076	3.4612	0.0072	3.4106	0.0058

Plot of chemical shift change vs guest concentration:



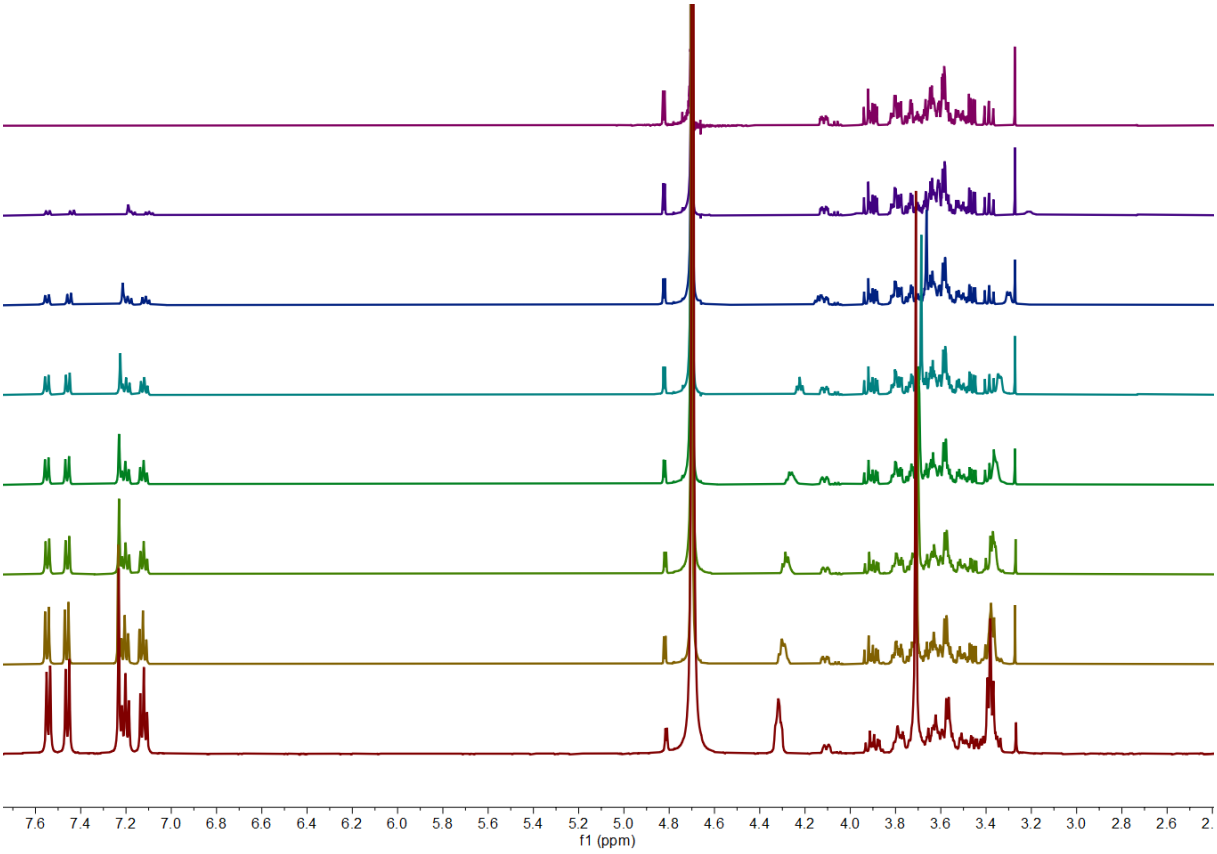
K_d values obtained by fitting the data for each proton into the single-site specific binding model:

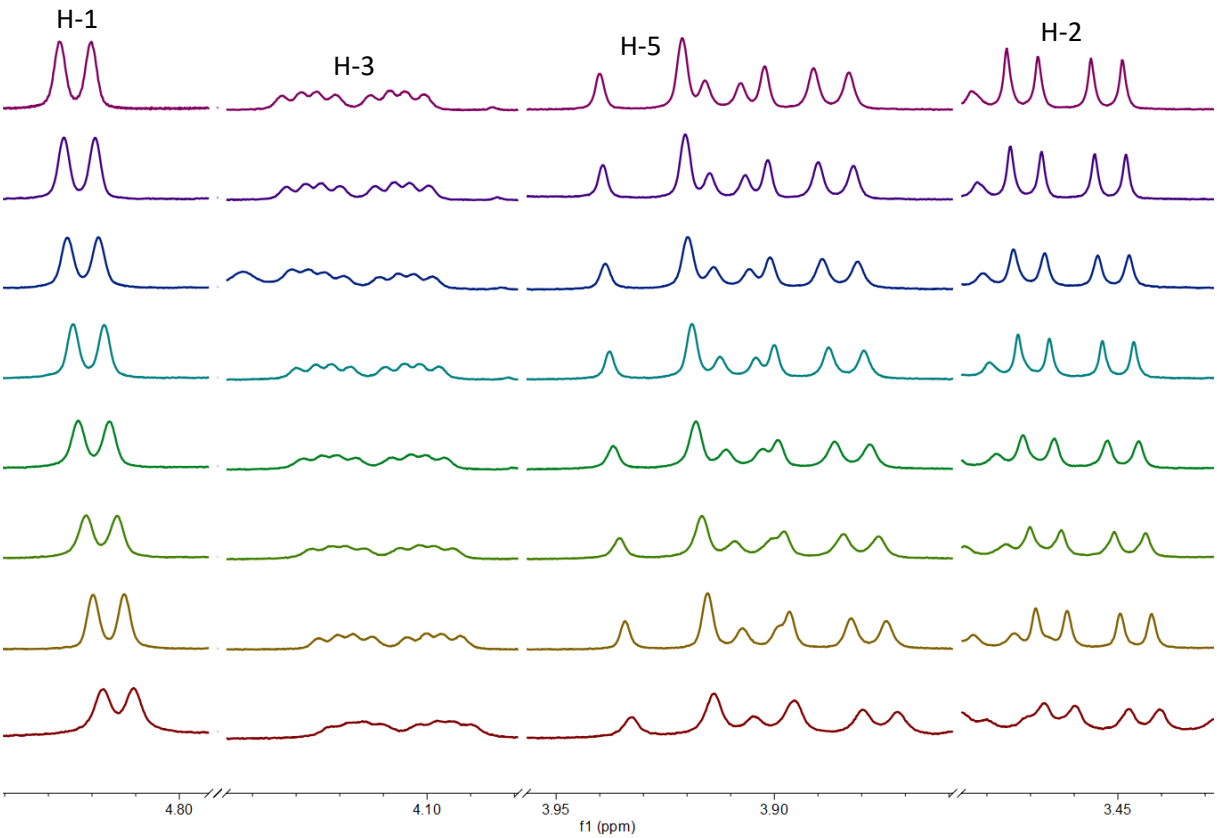
K_d	12.060	14.340	14.120	14.120	13.320	16.960
Std. error	0.959	1.095	1.025	1.025	0.586	1.435
R squared	0.997	0.998	0.998	0.998	0.999	0.997

K_d = 14.46 ± 1.02

H-L-Trp-OMe x HCl to receptor 8:

^{1}H NMR spectra (top – full, bottom – enhanced view on specific receptor protons):

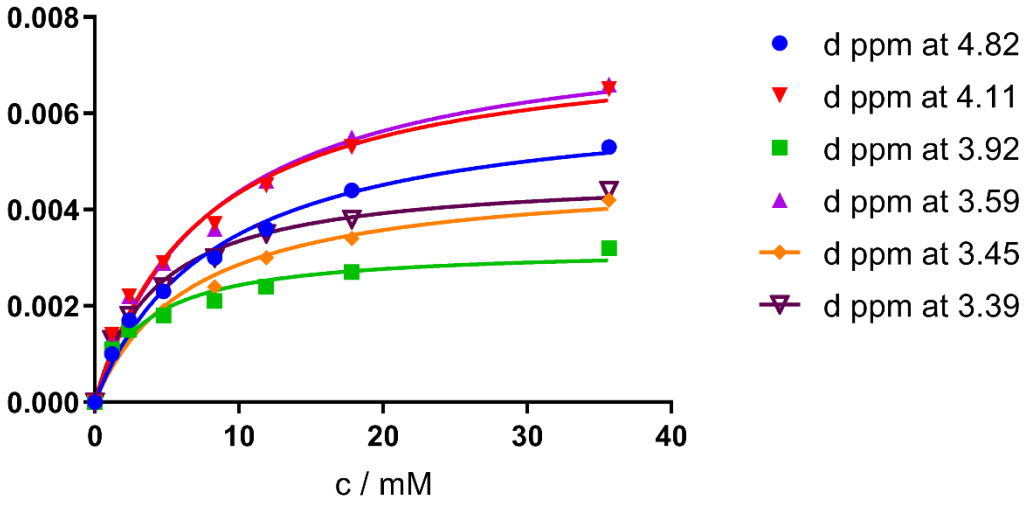




Summary of chemical shift changes:

Titration	4.82	Δppm	4.11	Δppm	3.92	Δppm	3.59	Δppm	3.45	Δppm	3.39	Δppm
1	4.8203	0.0000	4.1131	0.0000	3.9213	0.0000	3.8911	0.0000	3.4562	0.0000	3.4071	0.0000
2	4.8193	0.0010	4.1117	0.0014	3.9202	0.0011	3.8898	0.0013	3.4552	0.0010	3.4058	0.0013
3	4.8186	0.0017	4.1109	0.0022	3.9198	0.0015	3.8889	0.0022	3.4547	0.0015	3.4053	0.0018
4	4.8180	0.0023	4.1102	0.0029	3.9195	0.0018	3.8882	0.0029	3.4543	0.0019	3.4047	0.0024
5	4.8173	0.0030	4.1094	0.0037	3.9192	0.0021	3.8875	0.0036	3.4538	0.0024	3.4041	0.0030
6	4.8167	0.0036	4.1086	0.0045	3.9189	0.0024	3.8865	0.0046	3.4532	0.0030	3.4036	0.0035
7	4.8159	0.0044	4.1078	0.0053	3.9186	0.0027	3.8856	0.0055	3.4528	0.0034	3.4033	0.0038
8	4.8150	0.0053	4.1066	0.0065	3.9181	0.0032	3.8845	0.0066	3.4520	0.0042	3.4027	0.0044

Plot of chemical shift change vs guest concentration:



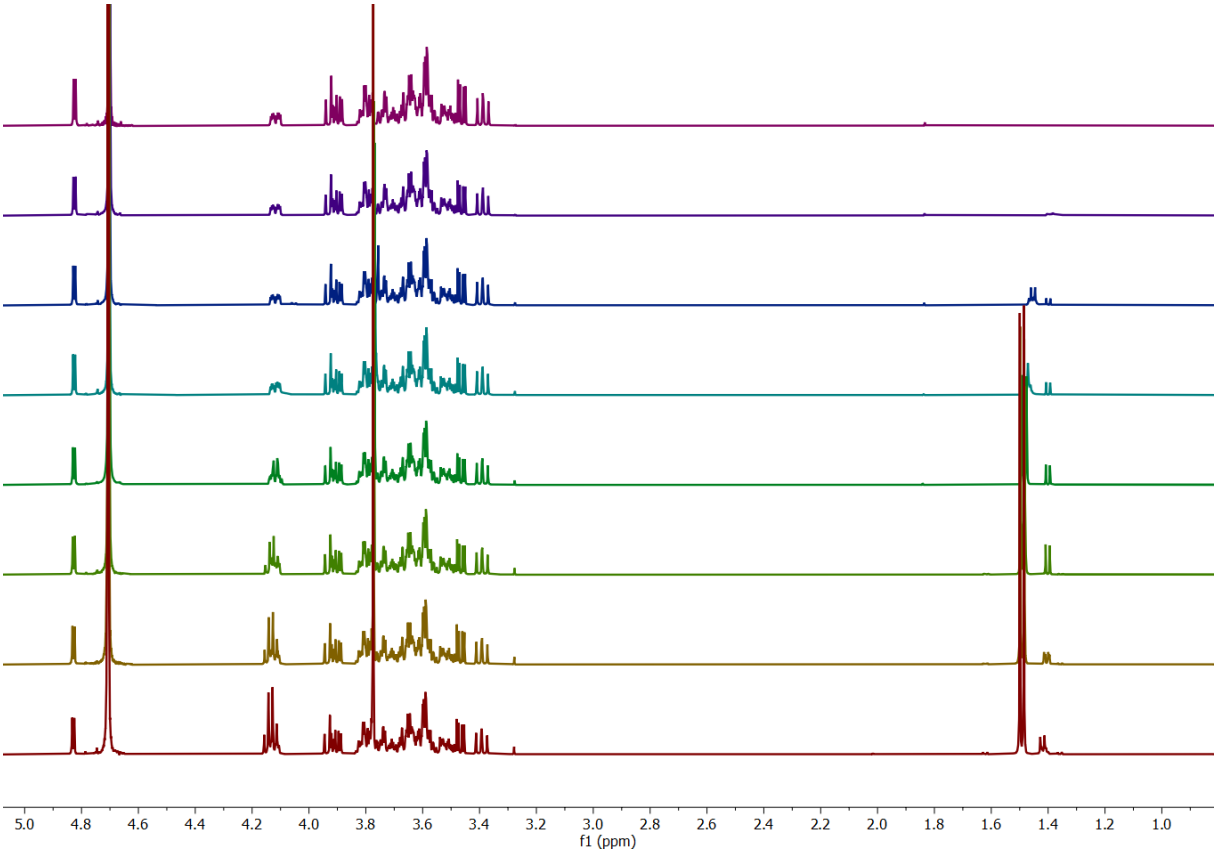
K_d values obtained by fitting the data for each proton into the single-site specific binding model:

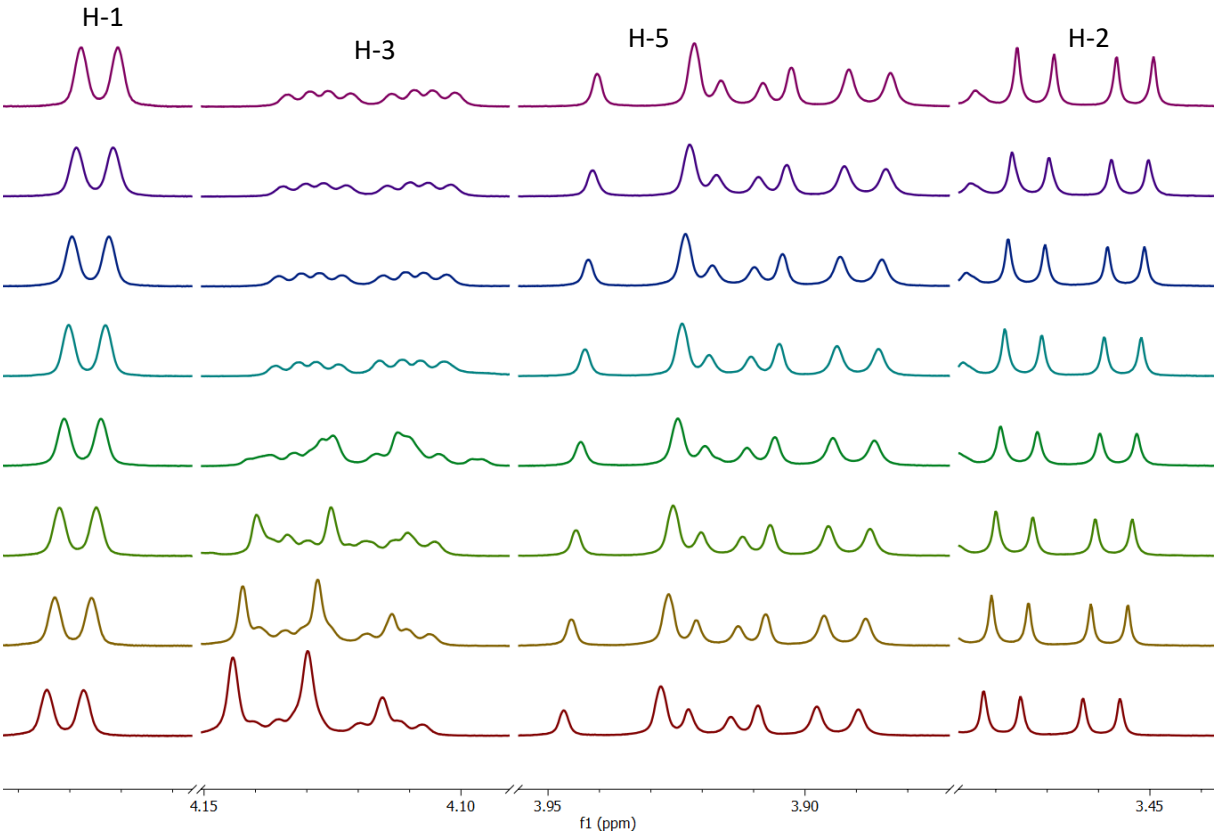
K_d	8.313	7.423	3.213	8.104	6.706	4.197
Std. error	1.070	1.149	0.692	1.260	1.208	0.503
R squared	0.991	0.986	0.970	0.987	0.981	0.991

K_d = 6.03 ± 0.98 mM

H-D-Ala-OMe x HCl to receptor 8:

^{1}H NMR spectra (top – full, bottom – enhanced view on specific receptor protons):

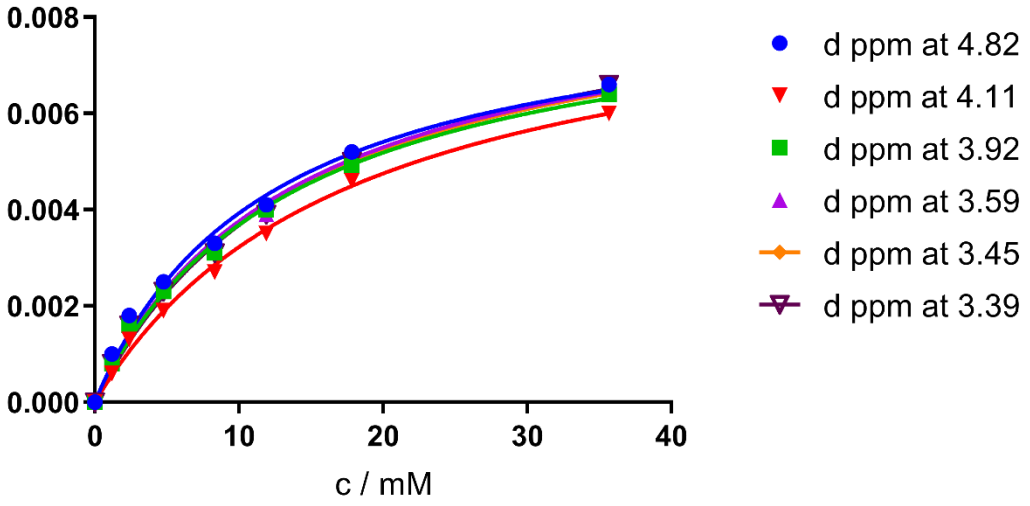




Summary of chemical shift changes:

Titration	4.82	Δppm	4.11	Δppm	3.92	Δppm	3.59	Δppm	3.45	Δppm	3.39	Δppm
1	4.8206	0.0000	4.1013	0.0000	3.9216	0.0000	3.5857	0.0000	3.4565	0.0000	3.388	0.0000
2	4.8216	0.0010	4.1019	0.0006	3.9224	0.0008	3.5866	0.0009	3.4574	0.0009	3.3888	0.0008
3	4.8224	0.0018	4.1026	0.0013	3.9232	0.0016	3.5874	0.0017	3.4581	0.0016	3.3896	0.0016
4	4.8231	0.0025	4.1032	0.0019	3.9239	0.0023	3.5881	0.0024	3.4588	0.0023	3.3903	0.0023
5	4.8239	0.0033	4.104	0.0027	3.9247	0.0031	3.5889	0.0032	3.4596	0.0031	3.3911	0.0031
6	4.8247	0.0041	4.1048	0.0035	3.9256	0.0040	3.5896	0.0039	3.4605	0.0040	3.3919	0.0039
7	4.8258	0.0052	4.1059	0.0046	3.9265	0.0049	3.5907	0.0050	3.4615	0.0050	3.393	0.0050
8	4.8272	0.0066	4.1073	0.0060	3.928	0.0064	3.5923	0.0066	3.4630	0.0065	3.3946	0.0066

Plot of chemical shift change vs guest concentration:



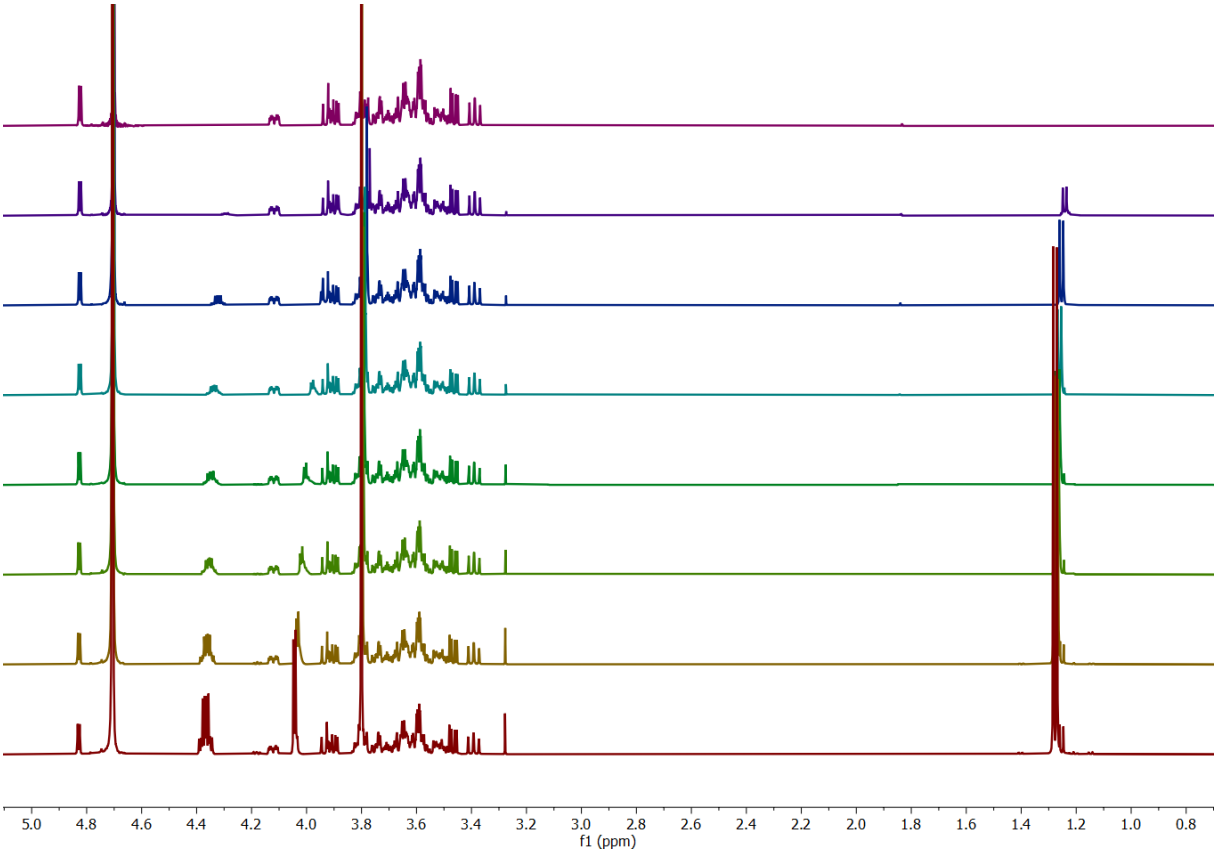
K_d values obtained by fitting the data for each proton into the single-site specific binding model:

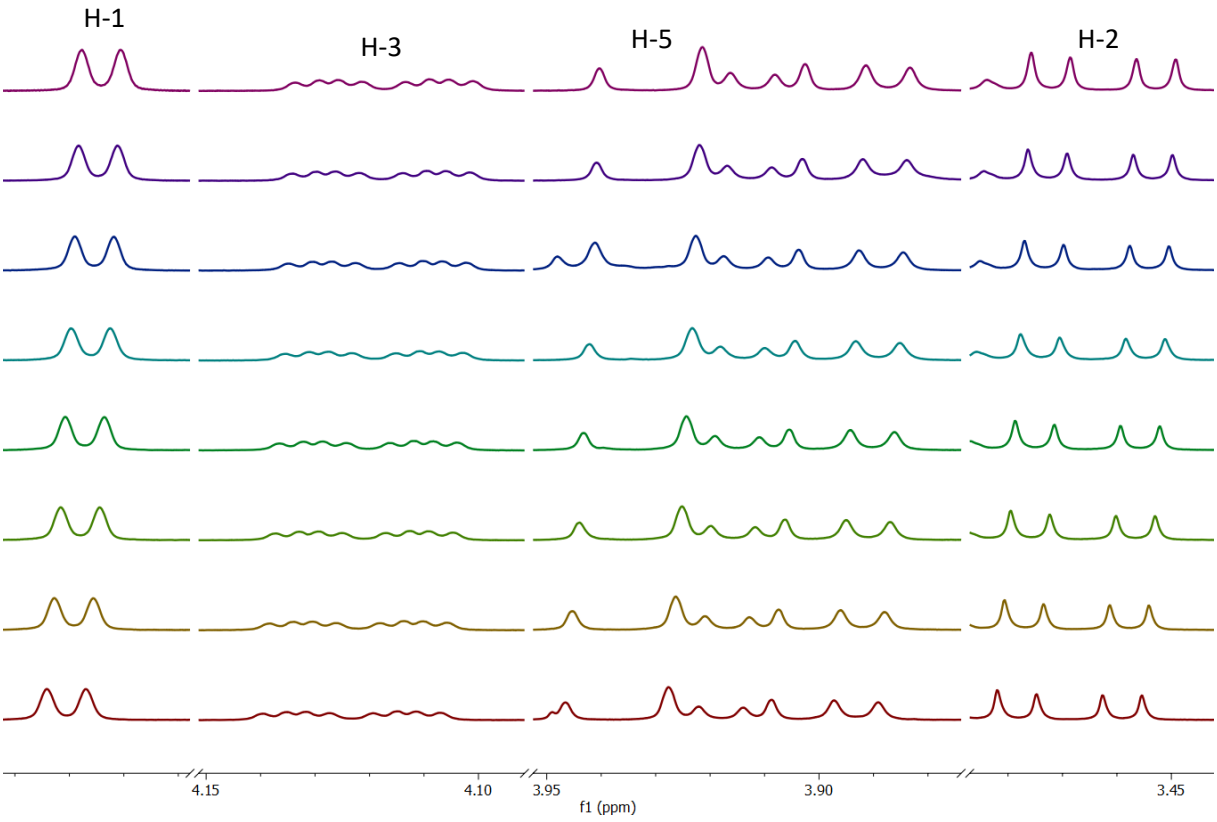
K_d	12.130	17.970	13.710	13.830	14.110	15.250
Std. error	1.657	1.733	1.440	1.960	1.651	1.843
R squared	0.991	0.996	0.995	0.991	0.994	0.994

K_d = 14.50 ± 1.71 mM

H-D-Thr-OMe x HCl to receptor 8:

^{1}H NMR spectra (top – full, bottom – enhanced view on specific receptor protons):

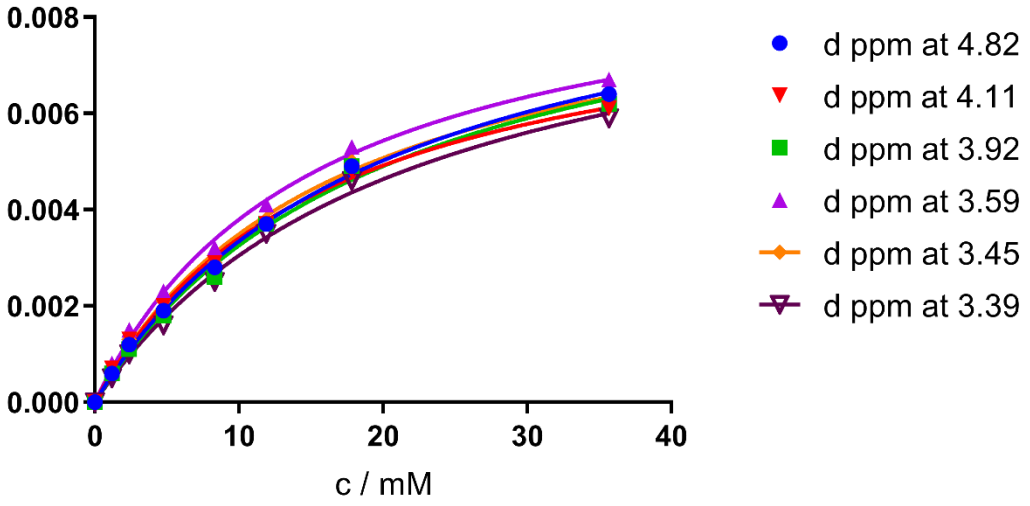




Summary of chemical shift changes:

Titration	4.82	Δppm	4.11	Δppm	3.92	Δppm	3.59	Δppm	3.45	Δppm	3.39	Δppm
1	4.8206	0.0000	4.1132	0.0000	3.9214	0.0000	3.5854	0.0000	3.4563	0.0000	3.388	0.0000
2	4.8212	0.0006	4.1139	0.0007	3.922	0.0006	3.5862	0.0008	3.4570	0.0007	3.3885	0.0005
3	4.8218	0.0012	4.1145	0.0013	3.9225	0.0011	3.5869	0.0015	3.4576	0.0013	3.389	0.0010
4	4.8225	0.0019	4.1152	0.0020	3.9232	0.0018	3.5877	0.0023	3.4584	0.0021	3.3896	0.0016
5	4.8234	0.0028	4.1161	0.0029	3.924	0.0026	3.5886	0.0032	3.4592	0.0029	3.3905	0.0025
6	4.8243	0.0037	4.1169	0.0037	3.9251	0.0037	3.5895	0.0041	3.4601	0.0038	3.3915	0.0035
7	4.8255	0.0049	4.118	0.0048	3.9263	0.0049	3.5907	0.0053	3.4613	0.0050	3.3926	0.0046
8	4.8270	0.0064	4.1193	0.0061	3.9276	0.0062	3.5921	0.0067	3.4626	0.0063	3.3939	0.0059

Plot of chemical shift change vs guest concentration:



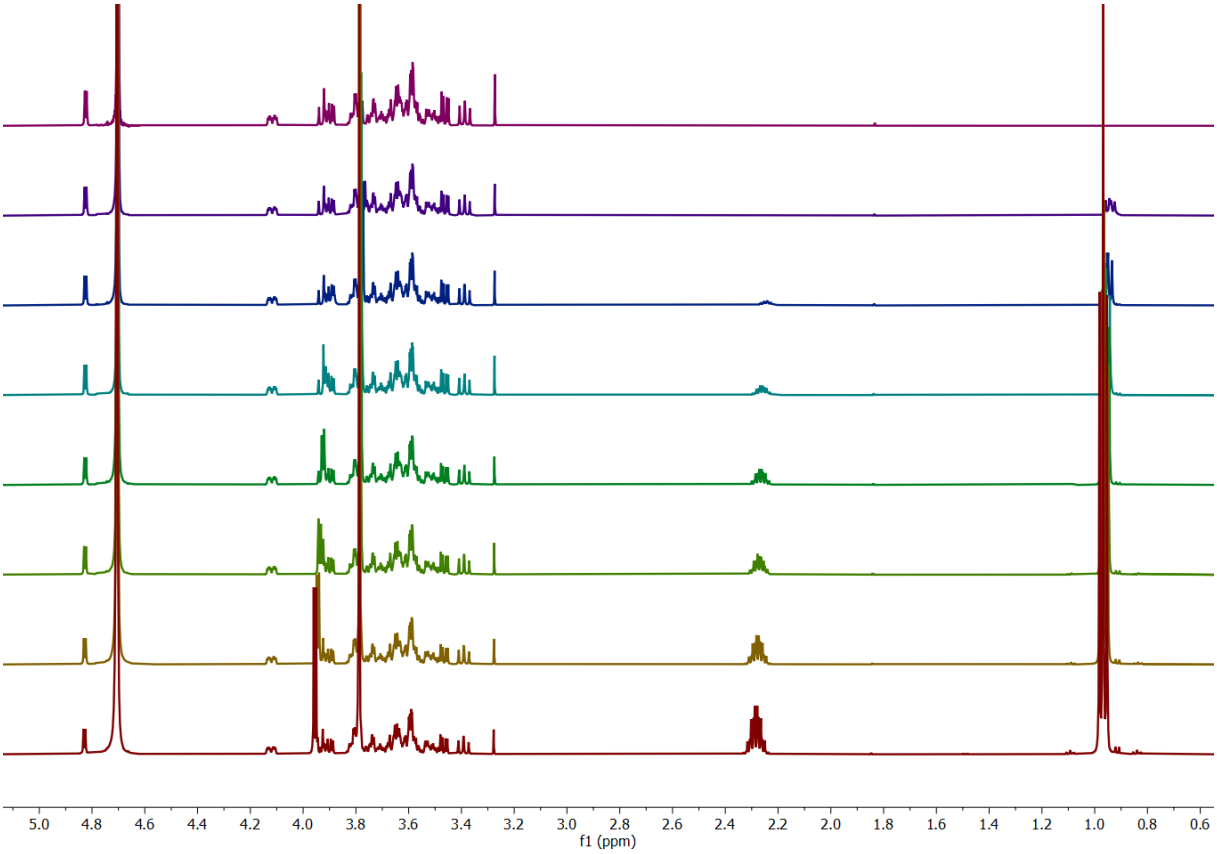
K_d values obtained by fitting the data for each proton into the single-site specific binding model:

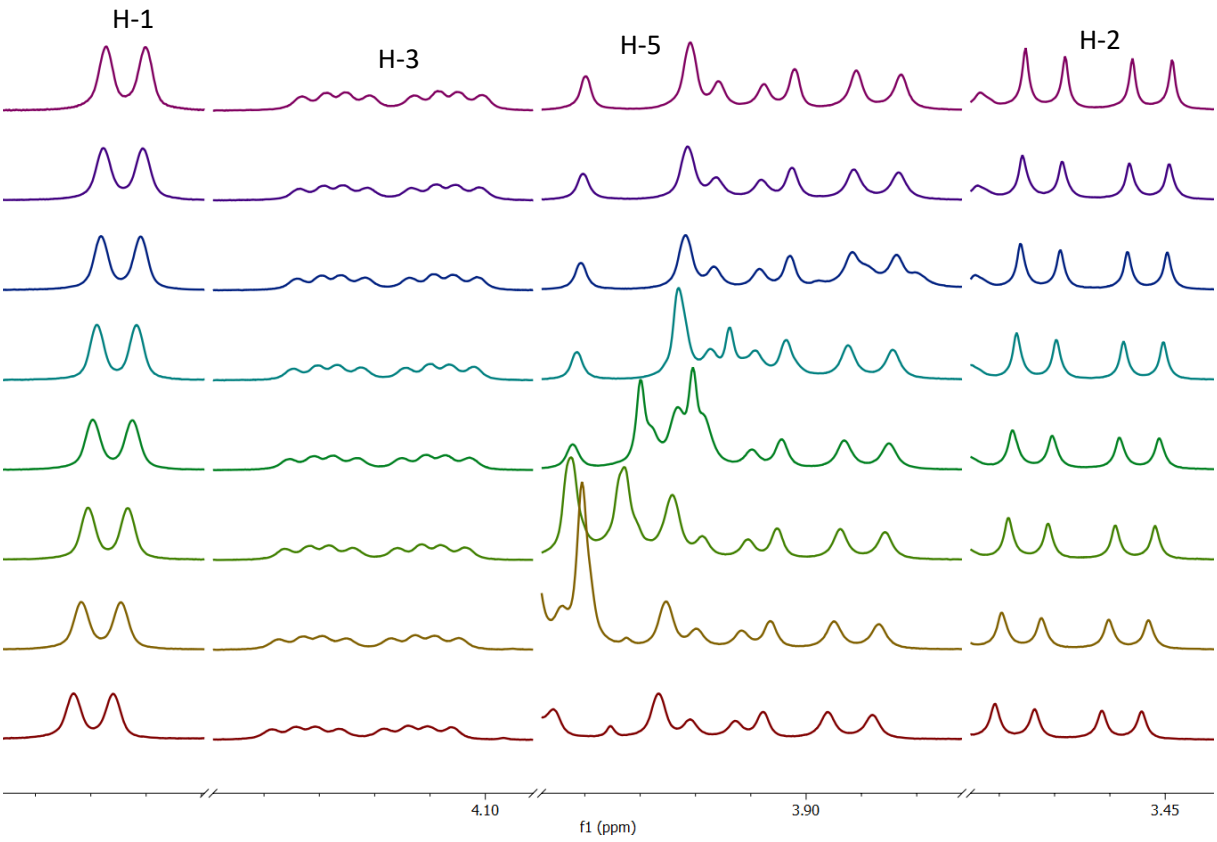
K_d	20.120	16.090	20.500	15.170	16.610	21.650
Std. error	1.556	1.217	2.537	1.305	1.506	2.451
R squared	0.998	0.998	0.995	0.997	0.997	0.996

K_d = 18.36 ± 1.76 mM

H-D-Val-OMe x HCl to receptor 8:

^{1}H NMR spectra (top – full, bottom – enhanced view on specific receptor protons):

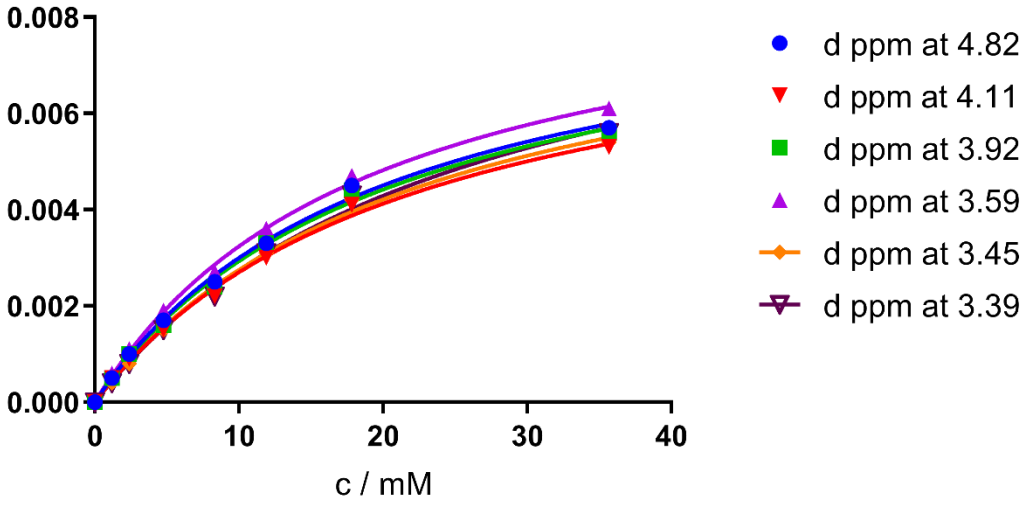




Summary of chemical shift changes:

Titration	4.82	Δppm	4.11	Δppm	3.92	Δppm	3.59	Δppm	3.45	Δppm	3.39	Δppm
1	4.8200	0.0000	4.1128	0.0000	3.902	0.0000	3.585	0.0000	3.4559	0.0000	3.3874	0.0000
2	4.8205	0.0005	4.1133	0.0005	3.9025	0.0005	3.5856	0.0006	3.4563	0.0004	3.3878	0.0004
3	4.8210	0.0010	4.1137	0.0009	3.903	0.0010	3.5861	0.0011	3.4567	0.0008	3.3882	0.0008
4	4.8217	0.0017	4.1143	0.0015	3.9036	0.0016	3.5869	0.0019	3.4574	0.0015	3.3889	0.0015
5	4.8225	0.0025	4.115	0.0022	3.9044	0.0024	3.5877	0.0027	3.4582	0.0023	3.3896	0.0022
6	4.8233	0.0033	4.1158	0.0030	3.9053	0.0033	3.5886	0.0036	3.4590	0.0031	3.3905	0.0031
7	4.8245	0.0045	4.1169	0.0041	3.9064	0.0044	3.5897	0.0047	3.4601	0.0042	3.3917	0.0043
8	4.8257	0.0057	4.1181	0.0053	3.9076	0.0056	3.5911	0.0061	3.4613	0.0054	3.393	0.0056

Plot of chemical shift change vs guest concentration:



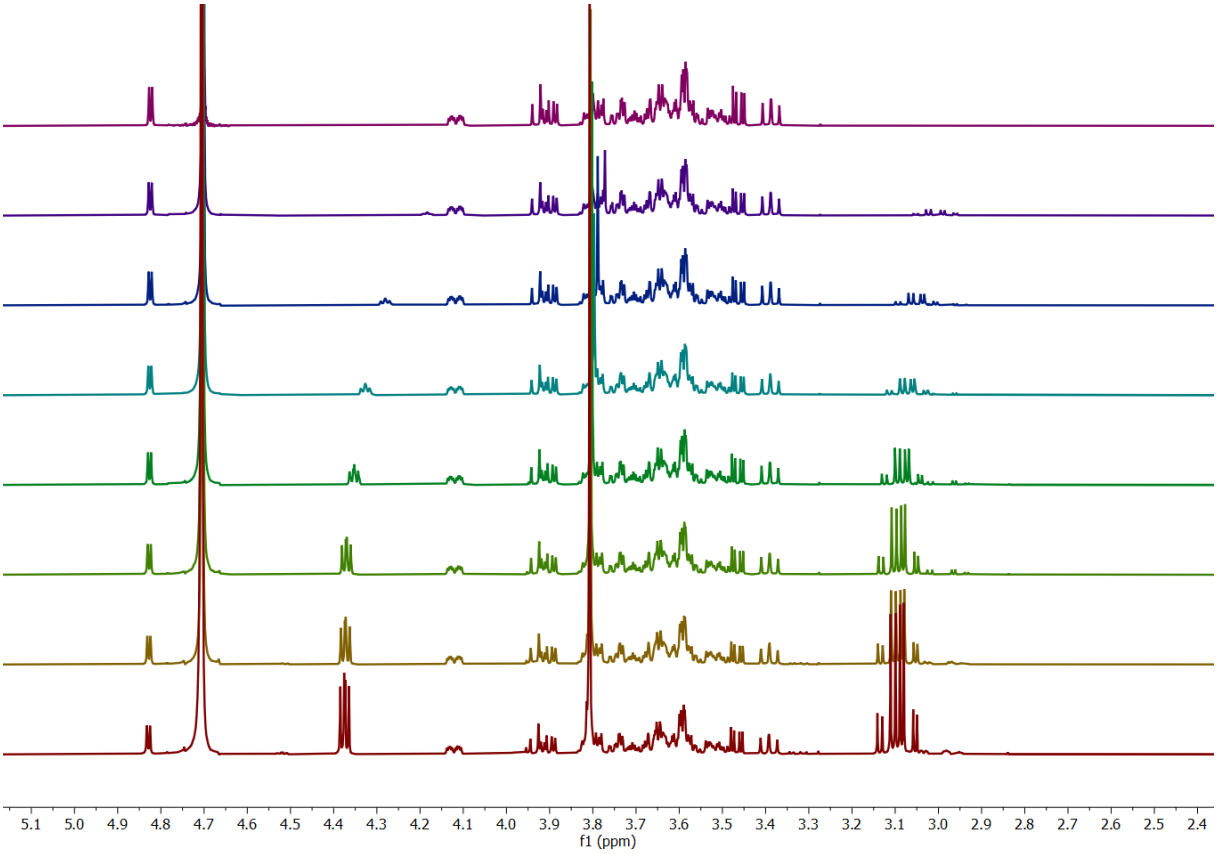
K_d values obtained by fitting the data for each proton into the single-site specific binding model:

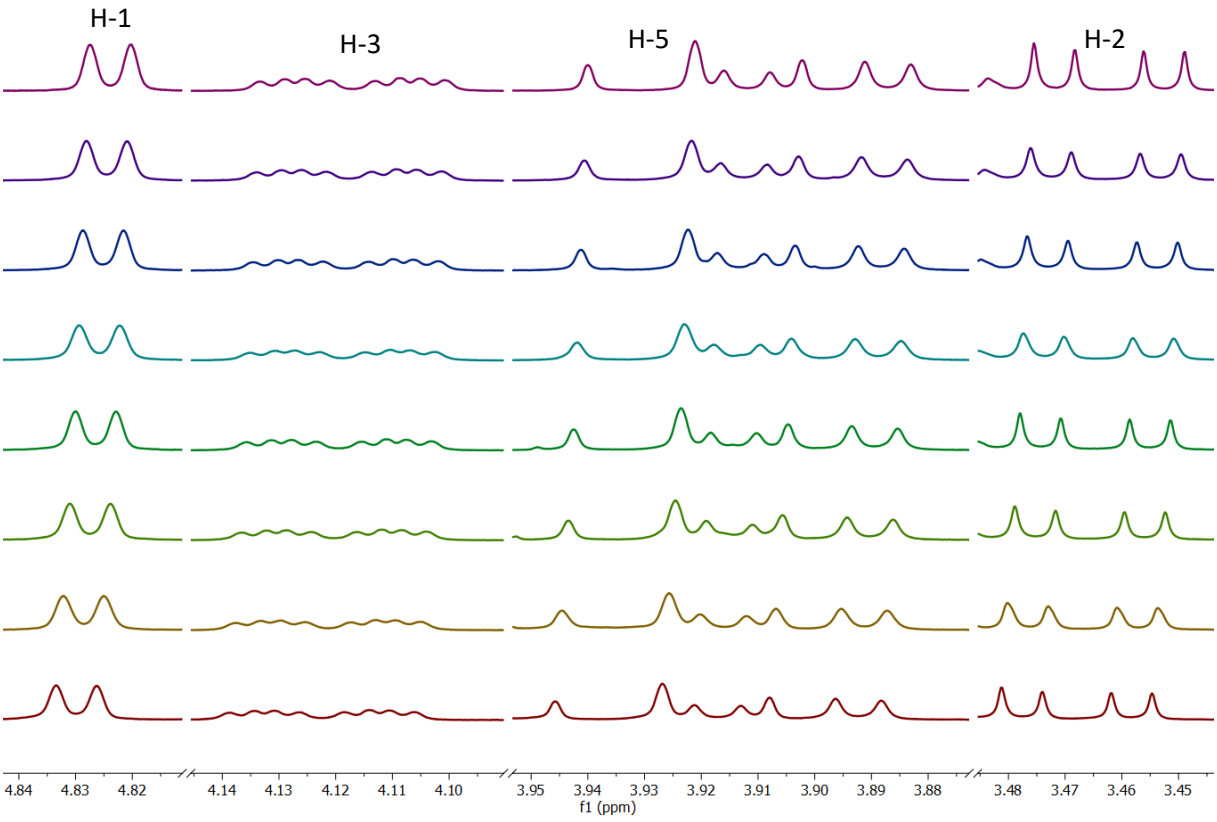
K_d	20.210	22.360	20.670	19.130	22.710	25.840
Std. error	2.012	2.426	2.234	1.328	2.380	3.334
R squared	0.997	0.996	0.996	0.998	0.997	0.995

K_d = 21.82 ± 2.29 mM

H-D-Cys-OMe x HCl to receptor 8:

^{1}H NMR spectra (top – full, bottom – enhanced view on specific receptor protons):

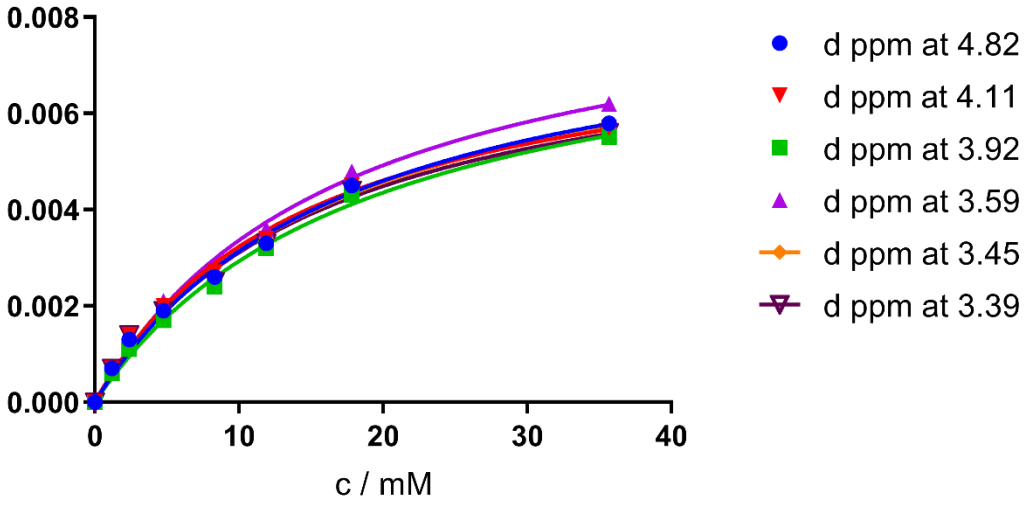




Summary of chemical shift changes:

Titration	4.82	Δppm	4.11	Δppm	3.92	Δppm	3.59	Δppm	3.45	Δppm	3.39	Δppm
1	4.8202	0.0000	4.113	0.0000	3.9212	0.0000	3.5852	0.0000	3.4561	0.0000	3.3875	0.0000
2	4.8209	0.0007	4.1137	0.0007	3.9218	0.0006	3.5859	0.0007	3.4568	0.0007	3.3882	0.0007
3	4.8215	0.0013	4.1144	0.0014	3.9223	0.0011	3.5866	0.0014	3.4574	0.0013	3.3889	0.0014
4	4.8221	0.0019	4.115	0.0020	3.9229	0.0017	3.5873	0.0021	3.4580	0.0019	3.3894	0.0019
5	4.8228	0.0026	4.1157	0.0027	3.9236	0.0024	3.5879	0.0027	3.4586	0.0025	3.39	0.0025
6	4.8235	0.0033	4.1164	0.0034	3.9244	0.0032	3.5888	0.0036	3.4595	0.0034	3.3908	0.0033
7	4.8247	0.0045	4.1175	0.0045	3.9255	0.0043	3.59	0.0048	3.4606	0.0045	3.3919	0.0044
8	4.8260	0.0058	4.1187	0.0057	3.9267	0.0055	3.5914	0.0062	3.4618	0.0057	3.3931	0.0056

Plot of chemical shift change vs guest concentration:



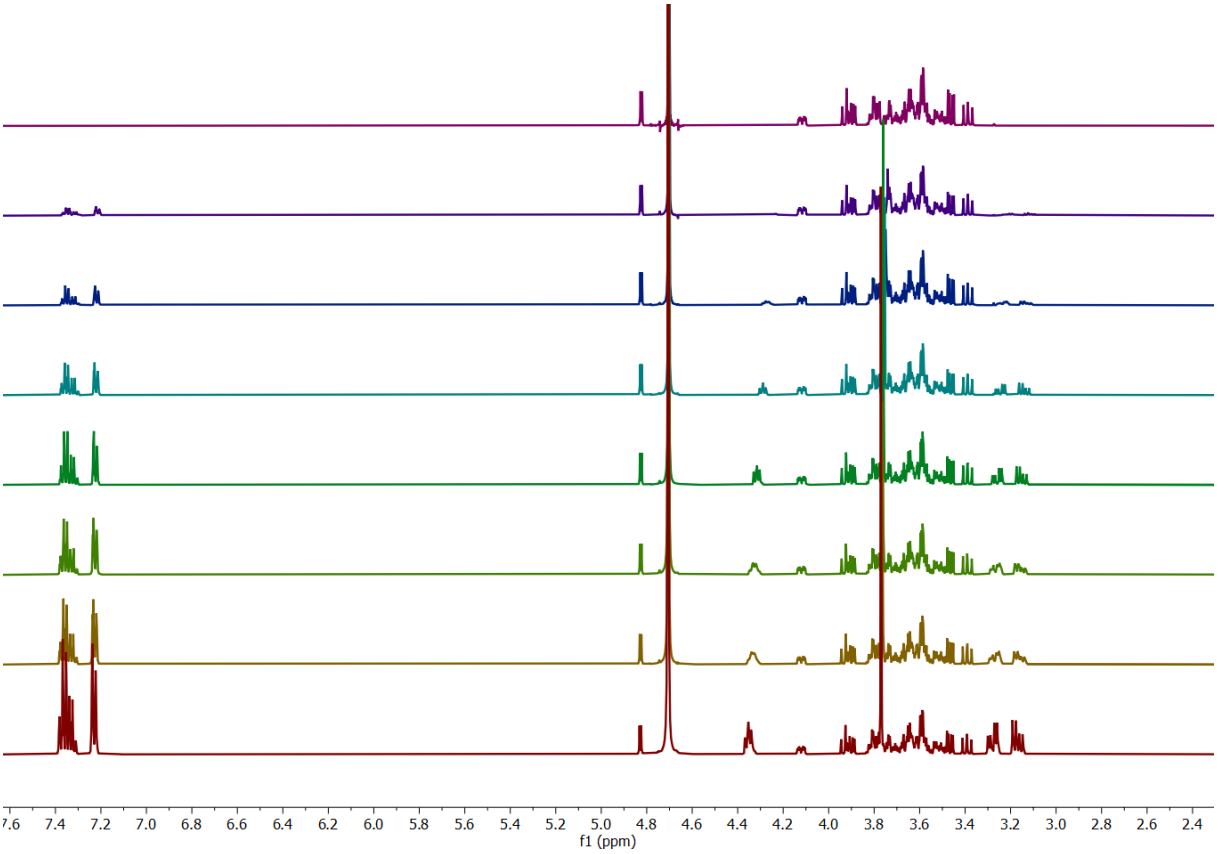
K_d values obtained by fitting the data for each proton into the single-site specific binding model:

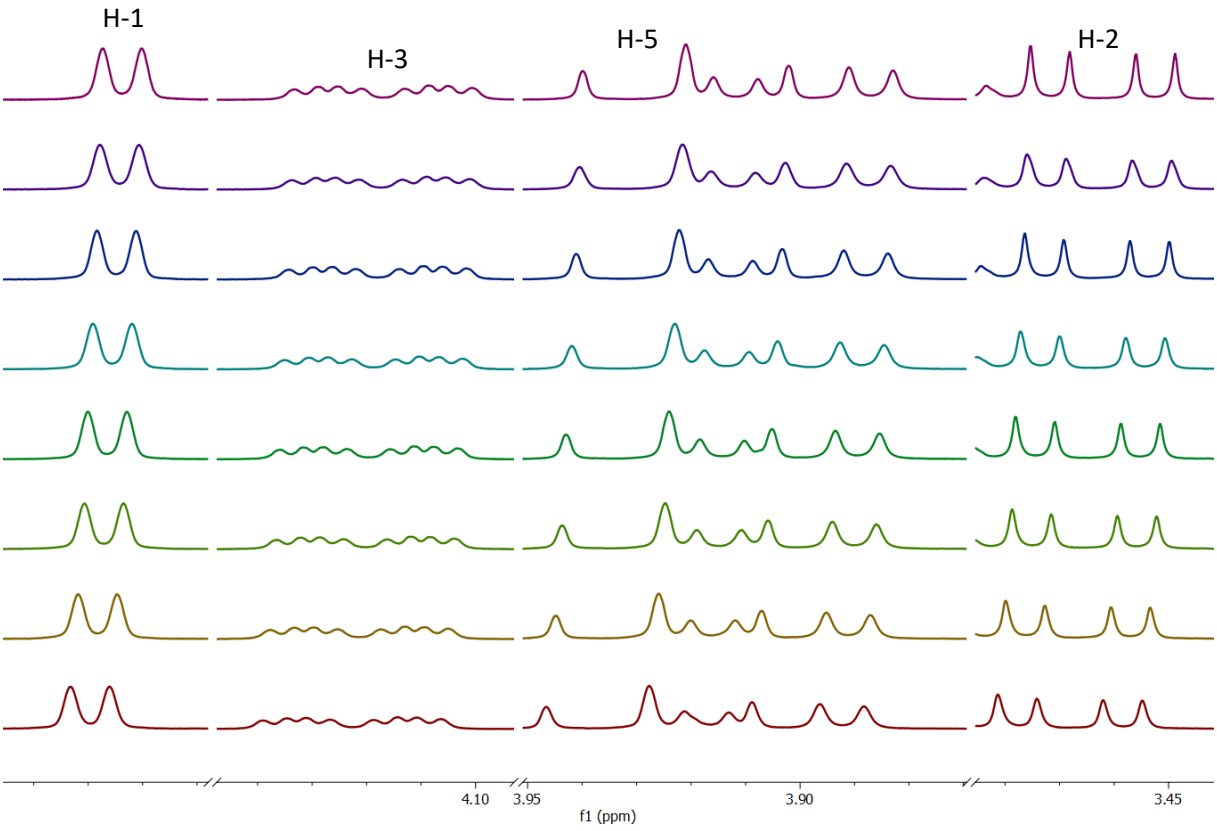
K_d	17.470	14.820	18.930	17.310	16.760	15.950
Std. error	2.307	1.850	2.055	2.359	2.325	2.503
R squared	0.993	0.993	0.996	0.993	0.992	0.990

K_d = 16.87 ± 2.23 mM

H-D-Phe-OMe x HCl to receptor 8:

^{1}H NMR spectra (top – full, bottom – enhanced view on specific receptor protons):

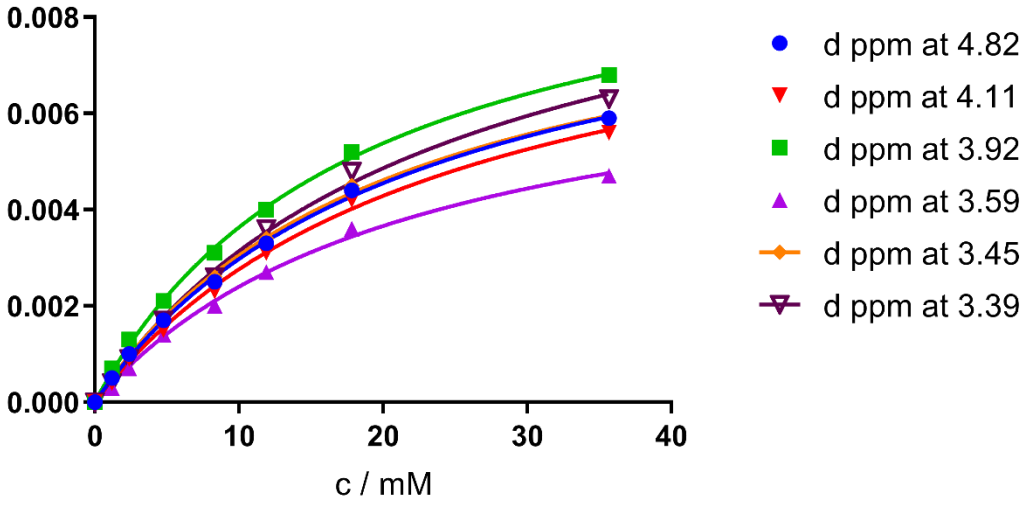




Summary of chemical shift changes:

Titration	4.82	Δppm	4.11	Δppm	3.92	Δppm	3.59	Δppm	3.45	Δppm	3.39	Δppm
1	4.8202	0.0000	4.113	0.0000	3.9209	0.0000	3.5852	0.0000	3.4560	0.0000	3.3874	0.0000
2	4.8207	0.0005	4.1134	0.0004	3.9216	0.0007	3.5855	0.0003	3.4565	0.0005	3.3878	0.0004
3	4.8212	0.0010	4.1139	0.0009	3.9222	0.0013	3.5859	0.0007	3.4570	0.0010	3.3883	0.0009
4	4.8219	0.0017	4.1145	0.0015	3.923	0.0021	3.5866	0.0014	3.4577	0.0017	3.3891	0.0017
5	4.8227	0.0025	4.1153	0.0023	3.924	0.0031	3.5872	0.0020	3.4586	0.0026	3.39	0.0026
6	4.8235	0.0033	4.1161	0.0031	3.9249	0.0040	3.5879	0.0027	3.4594	0.0034	3.391	0.0036
7	4.8246	0.0044	4.1172	0.0042	3.9261	0.0052	3.5888	0.0036	3.4605	0.0045	3.3922	0.0048
8	4.8261	0.0059	4.1186	0.0056	3.9277	0.0068	3.5899	0.0047	3.4619	0.0059	3.3937	0.0063

Plot of chemical shift change vs guest concentration:



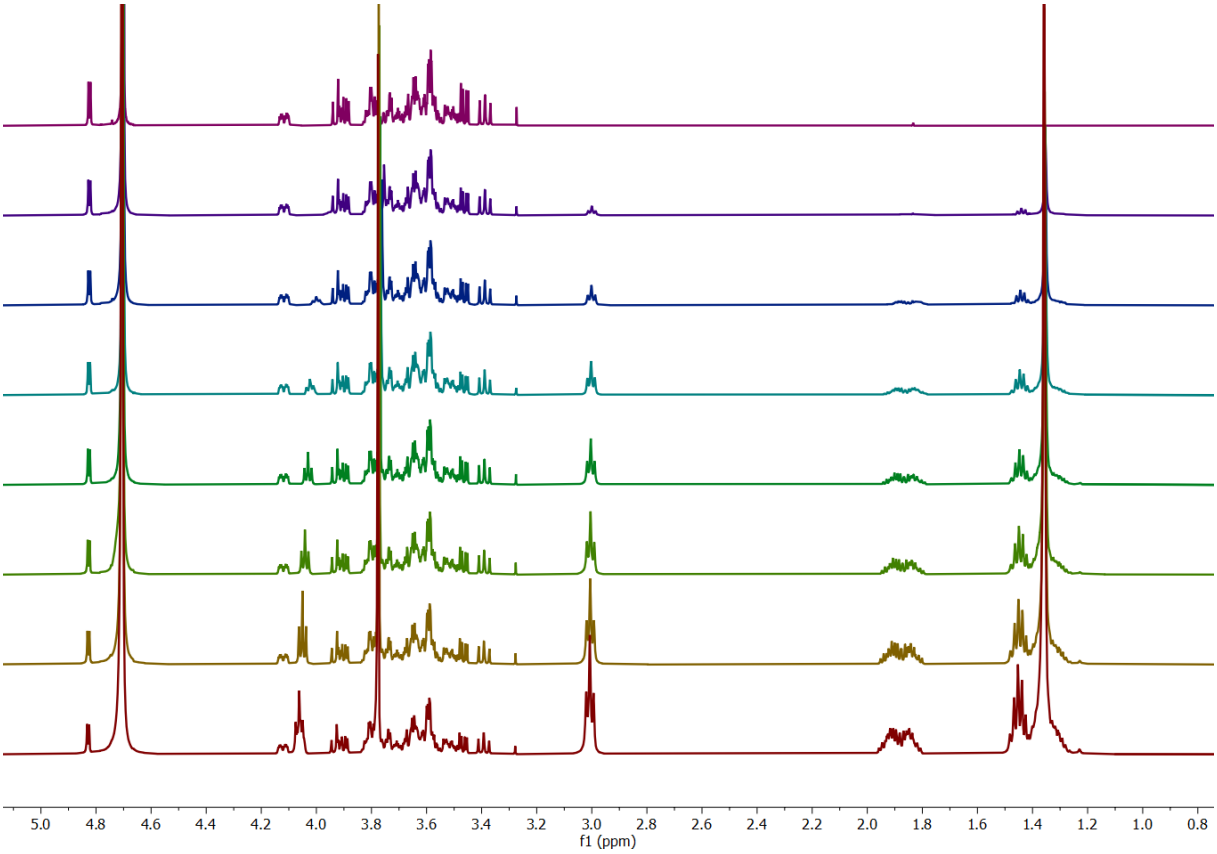
K_d values obtained by fitting the data for each proton into the single-site specific binding model:

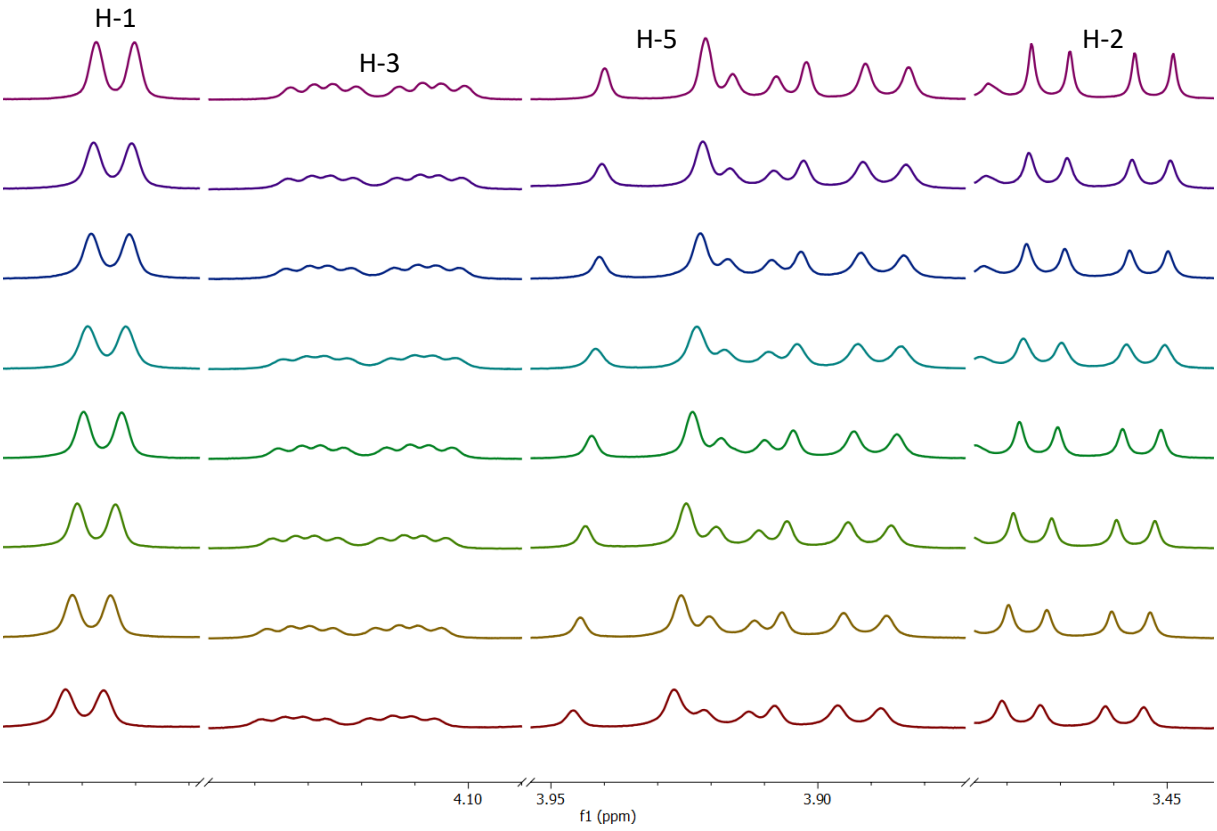
K_d	22.510	24.680	18.510	22.190	21.030	24.280
Std. error	1.388	2.077	1.085	2.038	1.296	2.517
R squared	0.999	0.998	0.999	0.997	0.999	0.997

K_d = 22.20 ± 1.73 mM

H-D-(Boc)Lys-OMe x HCl to receptor 8:

^{1}H NMR spectra (top – full, bottom – enhanced view on specific receptor protons):

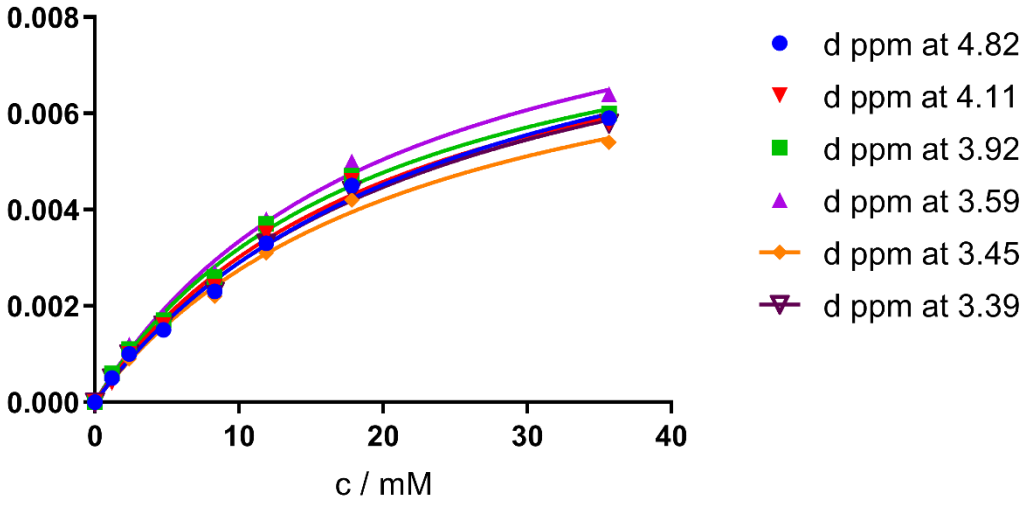




Summary of chemical shift changes:

Titration	4.82	Δppm	4.11	Δppm	3.92	Δppm	3.59	Δppm	3.45	Δppm	3.39	Δppm
1	4.8202	0.0000	4.1128	0.0000	3.9209	0.0000	3.585	0.0000	3.4561	0.0000	3.3875	0.0000
2	4.8207	0.0005	4.1132	0.0004	3.9215	0.0006	3.5856	0.0006	3.4566	0.0005	3.388	0.0005
3	4.8212	0.0010	4.1138	0.0010	3.922	0.0011	3.5862	0.0012	3.4570	0.0009	3.3885	0.0010
4	4.8217	0.0015	4.1144	0.0016	3.9226	0.0017	3.5868	0.0018	3.4576	0.0015	3.3891	0.0016
5	4.8225	0.0023	4.1152	0.0024	3.9235	0.0026	3.5877	0.0027	3.4583	0.0022	3.3898	0.0023
6	4.8235	0.0033	4.1163	0.0035	3.9246	0.0037	3.5888	0.0038	3.4592	0.0031	3.3908	0.0033
7	4.8247	0.0045	4.1174	0.0046	3.9256	0.0047	3.59	0.0050	3.4603	0.0042	3.3919	0.0044
8	4.8261	0.0059	4.1186	0.0058	3.9269	0.0060	3.5914	0.0064	3.4615	0.0054	3.3933	0.0058

Plot of chemical shift change vs guest concentration:



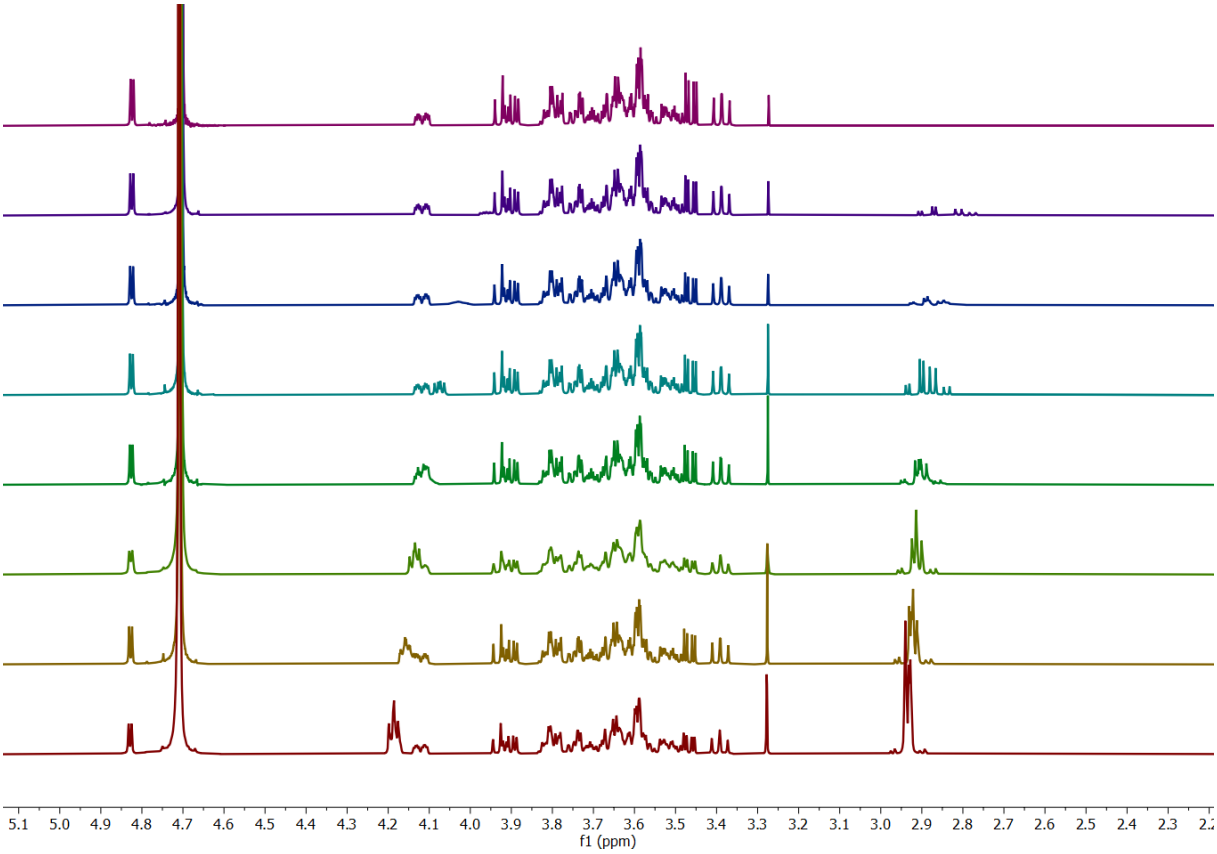
K_d values obtained by fitting the data for each proton into the single-site specific binding model:

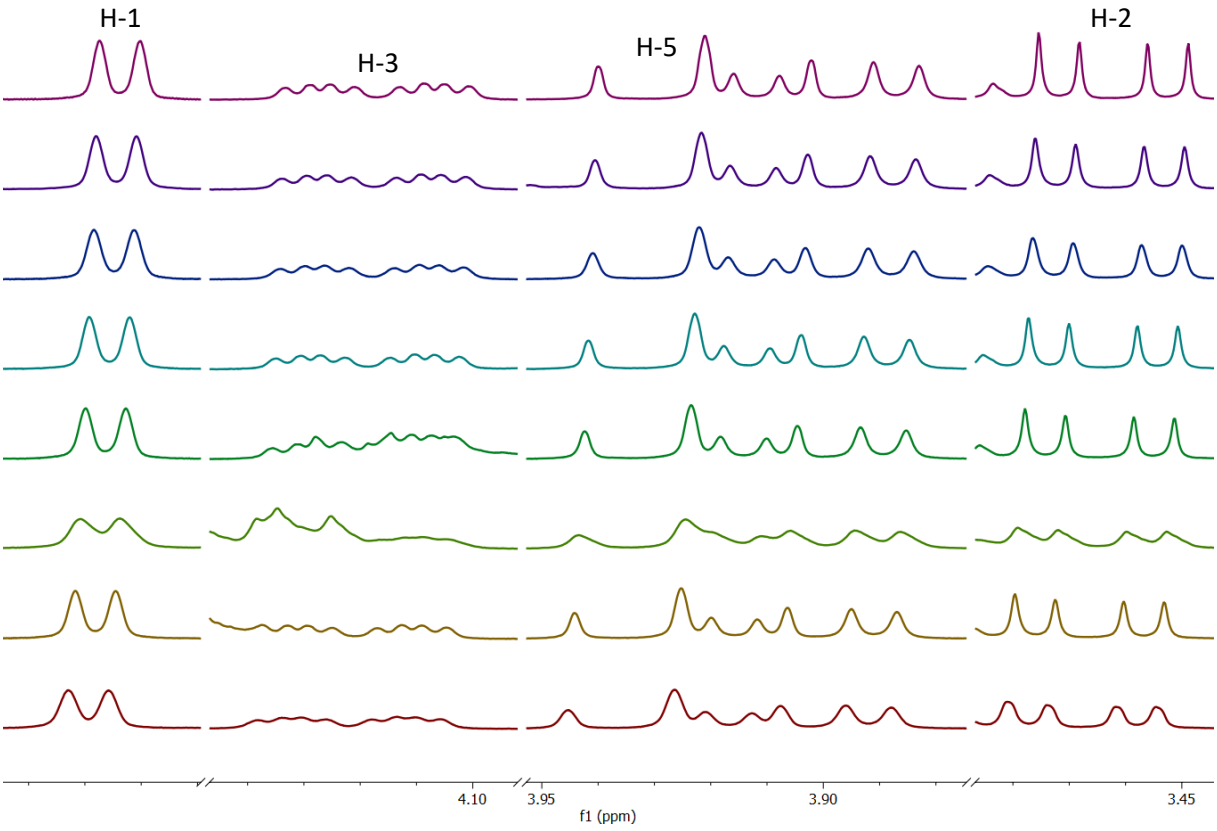
K_d	25.390	21.580	19.540	20.700	22.690	23.640
Std. error	3.460	3.120	2.224	2.444	2.775	2.717
R squared	0.994	0.993	0.995	0.995	0.995	0.996

K_d = 22.26 ± 2.79 mM

H-D-Asn-OMe x HCl to receptor 8:

^{1}H NMR spectra (top – full, bottom – enhanced view on specific receptor protons):

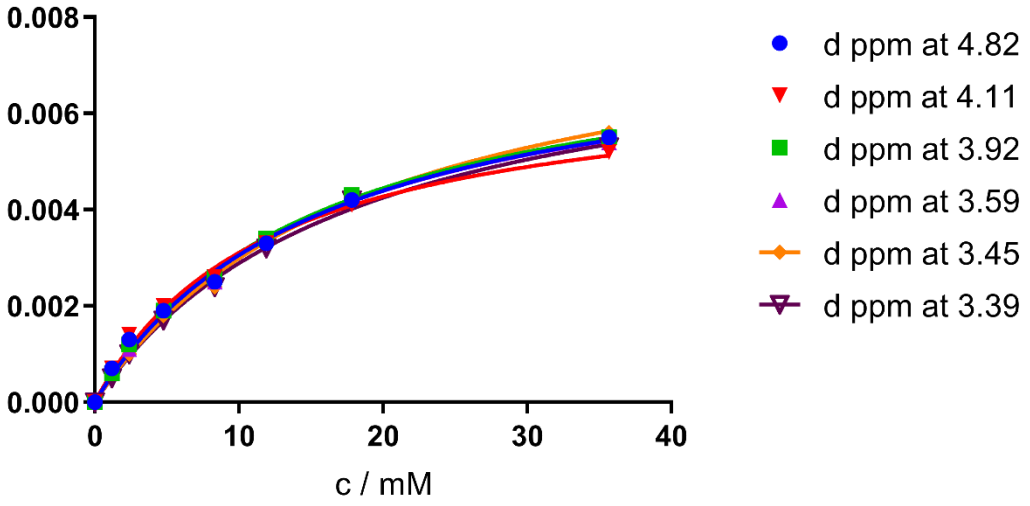




Summary of chemical shift changes:

Titration	4.82	Δppm	4.11	Δppm	3.92	Δppm	3.59	Δppm	3.45	Δppm	3.39	Δppm
1	4.8203	0.0000	4.1005	0.0000	3.921	0.0000	3.5852	0.0000	3.4561	0.0000	3.3875	0.0000
2	4.8210	0.0007	4.1012	0.0007	3.9216	0.0006	3.5858	0.0006	3.4567	0.0006	3.388	0.0005
3	4.8216	0.0013	4.1019	0.0014	3.9222	0.0012	3.5863	0.0011	3.4571	0.0010	3.3885	0.0010
4	4.8222	0.0019	4.1025	0.0020	3.9229	0.0019	3.5871	0.0019	3.4579	0.0018	3.3892	0.0017
5	4.8228	0.0025	4.1031	0.0026	3.9236	0.0026	3.5877	0.0025	3.4585	0.0024	3.3899	0.0024
6	4.8236	0.0033	4.1038	0.0033	3.9244	0.0034	3.5886	0.0034	3.4595	0.0034	3.3907	0.0032
7	4.8245	0.0042	4.1046	0.0041	3.9253	0.0043	3.5895	0.0043	3.4604	0.0043	3.3917	0.0042
8	4.8258	0.0055	4.1057	0.0052	3.9265	0.0055	3.5906	0.0054	3.4617	0.0056	3.3928	0.0053

Plot of chemical shift change vs guest concentration:



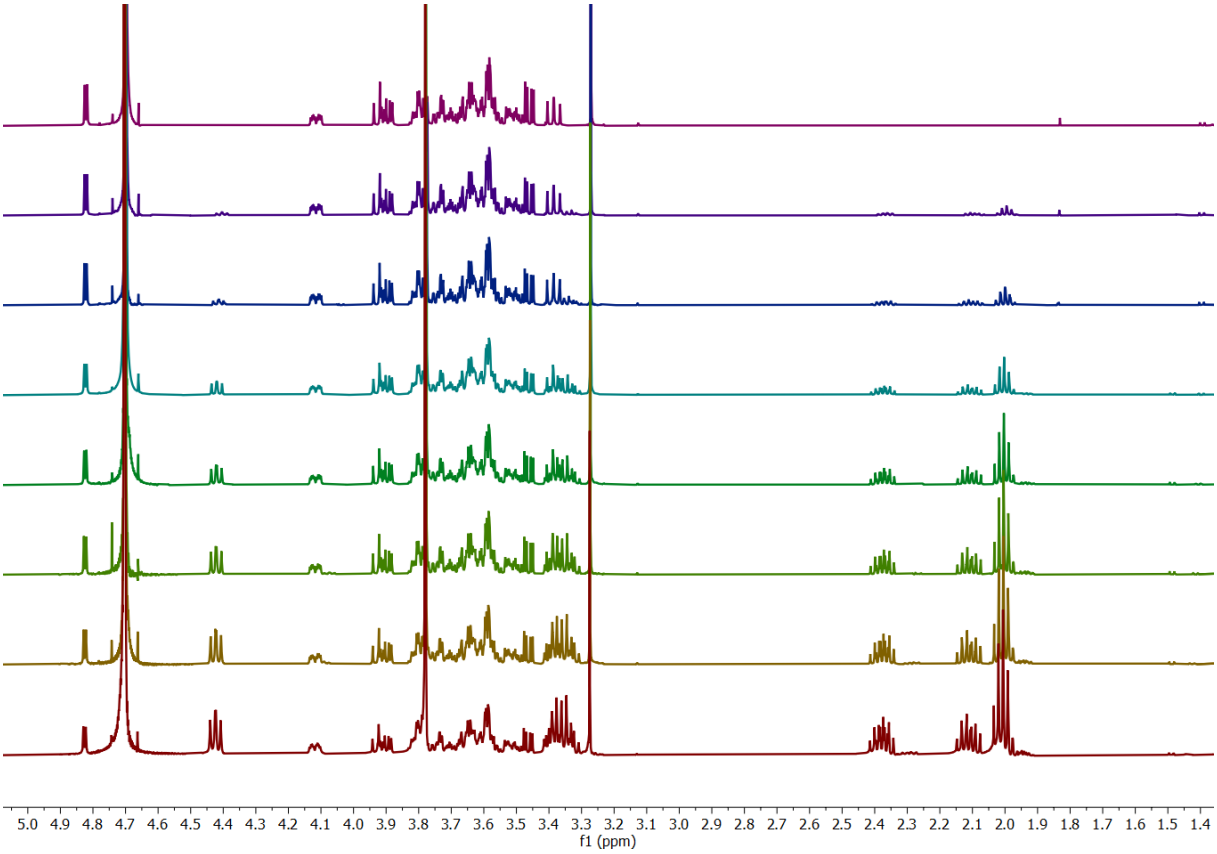
K_d values obtained by fitting the data for each proton into the single-site specific binding model:

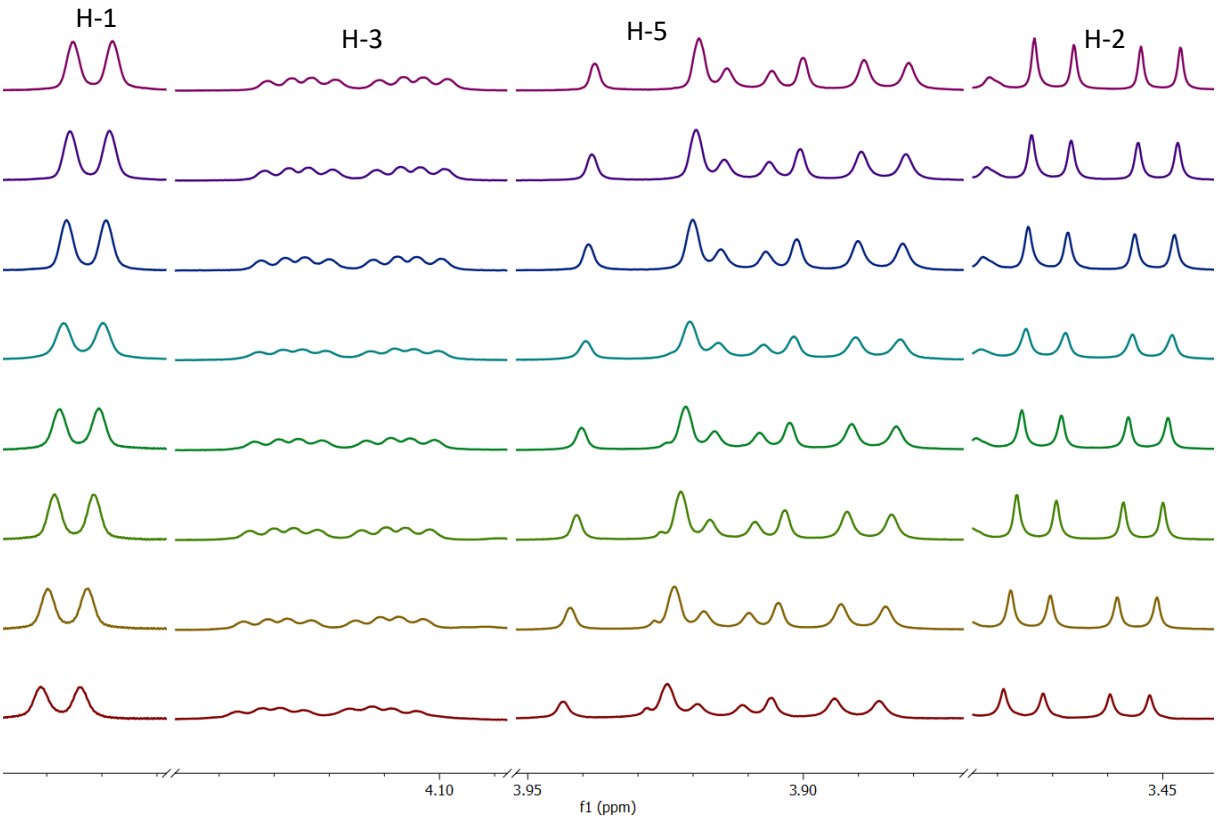
K_d	15.640	12.090	15.400	15.520	18.750	17.870
Std. error	1.943	1.420	1.139	1.365	1.782	1.498
R squared	0.993	0.994	0.998	0.997	0.997	0.997

K_d = 15.88 ± 1.52

H-D-Pro-OMe x HCl to receptor 8:

^{1}H NMR spectra (top – full, bottom – enhanced view on specific receptor protons):

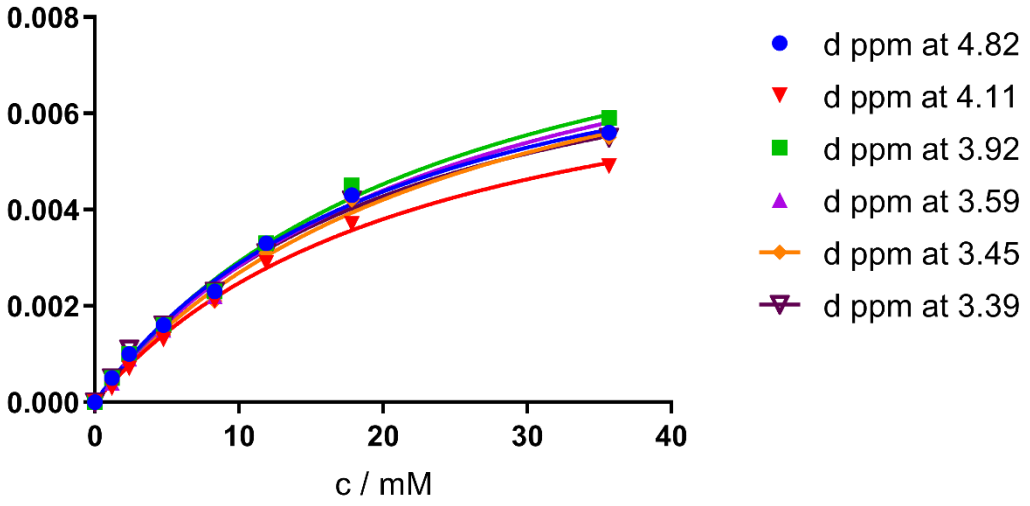




Summary of chemical shift changes:

Titration	4.82	Δppm	4.11	Δppm	3.92	Δppm	3.59	Δppm	3.45	Δppm	3.39	Δppm
1	4.8181	0.0000	4.111	0.0000	3.9189	0.0000	3.5832	0.0000	3.4540	0.0000	3.4048	0.0000
2	4.8186	0.0005	4.1113	0.0003	3.9194	0.0005	3.5836	0.0004	3.4544	0.0004	3.4053	0.0005
3	4.8191	0.0010	4.1117	0.0007	3.9199	0.0010	3.5841	0.0009	3.4549	0.0009	3.4059	0.0011
4	4.8197	0.0016	4.1123	0.0013	3.9205	0.0016	3.5847	0.0015	3.4554	0.0014	3.4064	0.0016
5	4.8204	0.0023	4.1131	0.0021	3.9212	0.0023	3.5854	0.0022	3.4561	0.0021	3.4071	0.0023
6	4.8214	0.0033	4.1139	0.0029	3.9222	0.0033	3.5865	0.0033	3.4571	0.0031	3.4079	0.0031
7	4.8224	0.0043	4.1147	0.0037	3.9234	0.0045	3.5876	0.0044	3.4582	0.0042	3.409	0.0042
8	4.8237	0.0056	4.1159	0.0049	3.9248	0.0059	3.5889	0.0057	3.4595	0.0055	3.4103	0.0055

Plot of chemical shift change vs guest concentration:



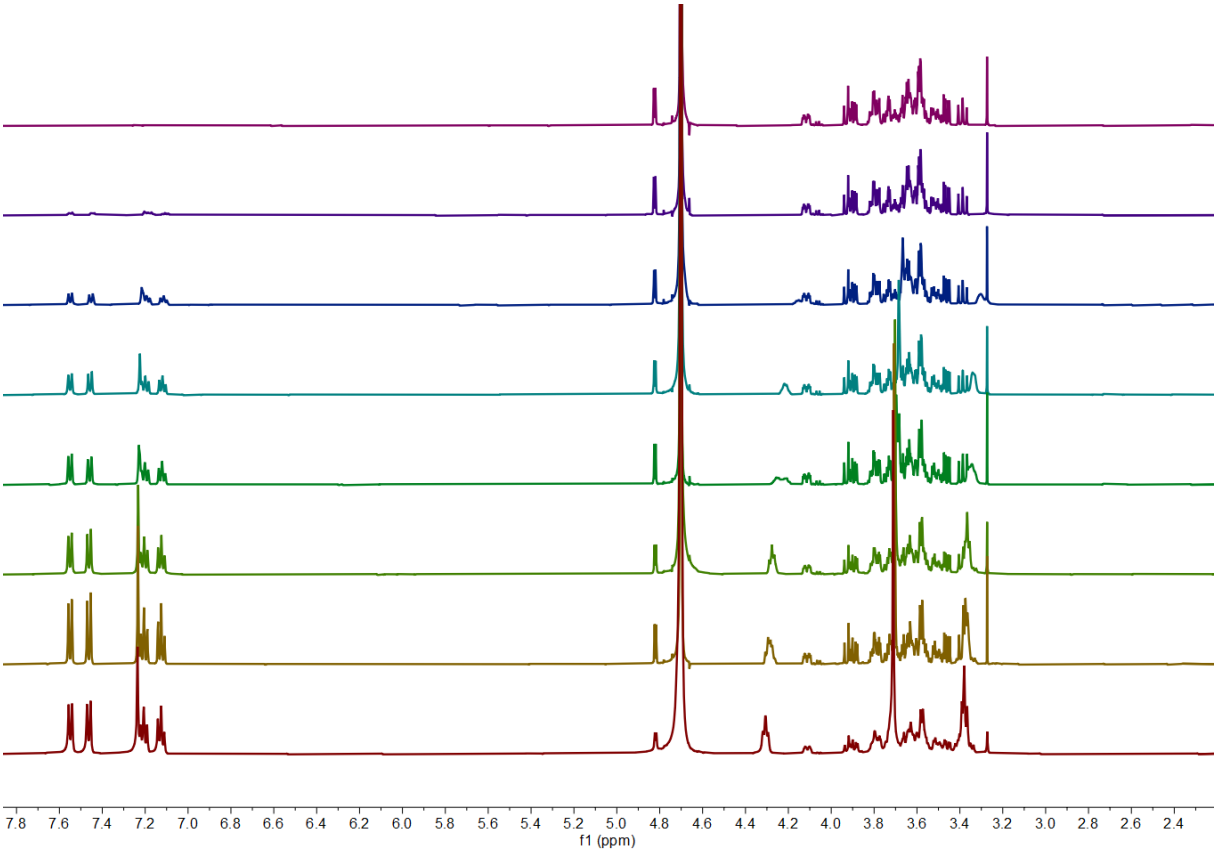
K_d values obtained by fitting the data for each proton into the single-site specific binding model:

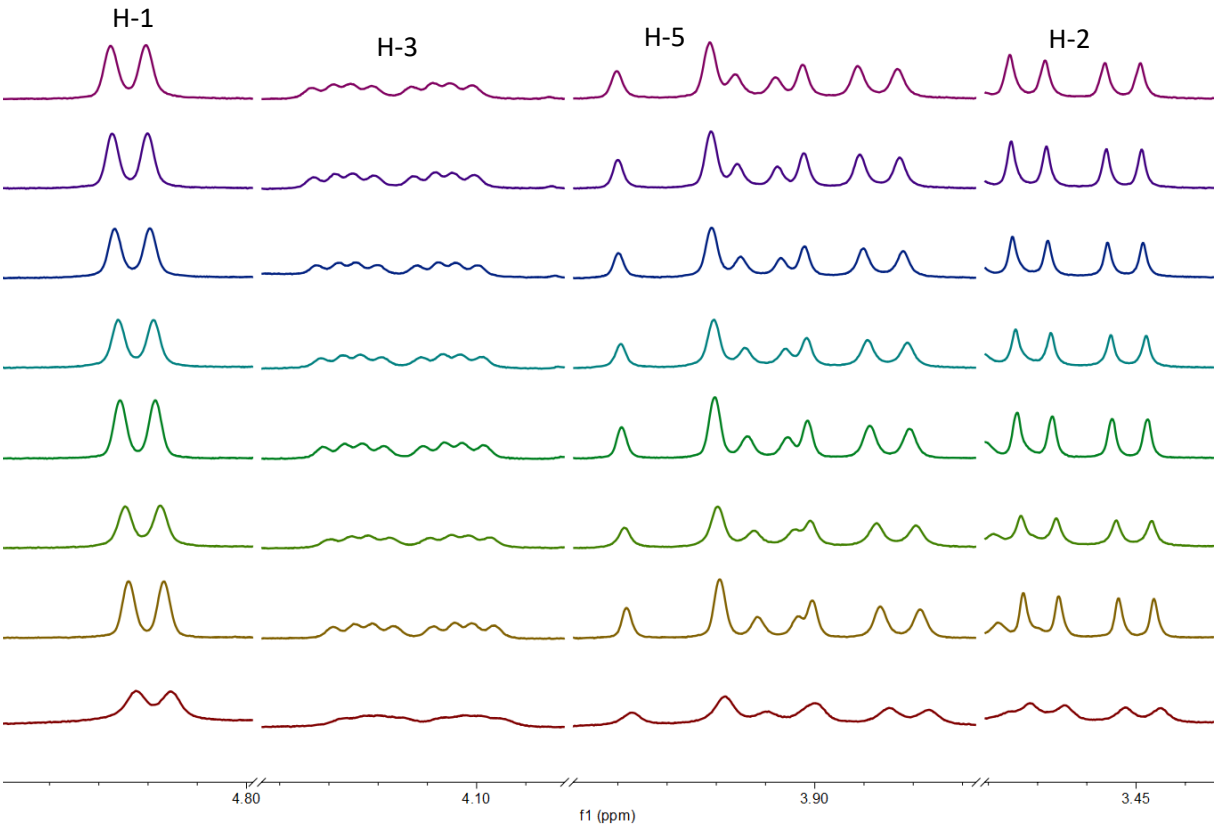
K_d	21.550	23.120	24.610	24.830	25.990	21.300
Std. error	2.365	2.297	3.156	3.694	3.777	2.453
R squared	0.996	0.997	0.995	0.993	0.994	0.995

K_d = 23.57 ± 2.96 mM

H-D-Trp-OMe x HCl to receptor 8:

^{1}H NMR spectra (top – full, bottom – enhanced view on specific receptor protons):

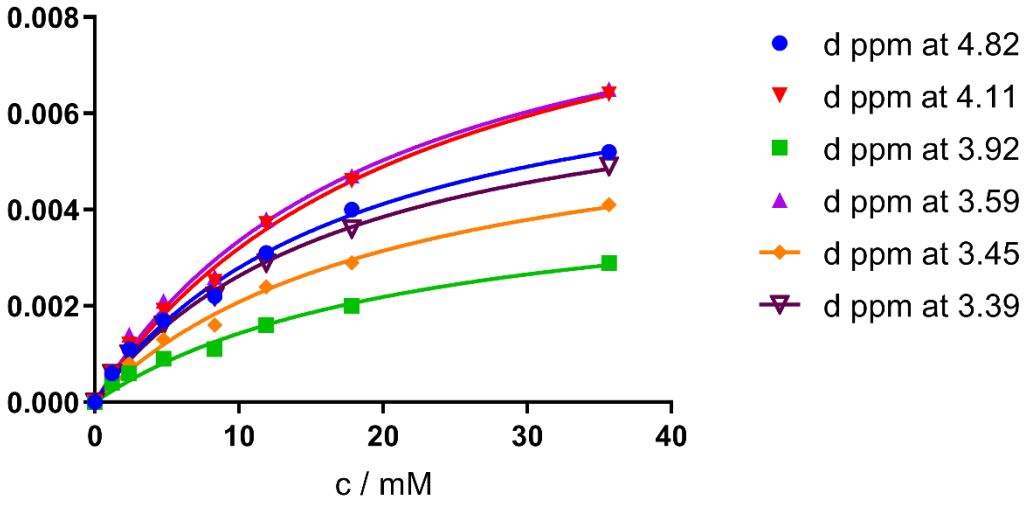




Summary of chemical shift changes:

Titration	4.82	Δppm	4.11	Δppm	3.92	Δppm	3.59	Δppm	3.45	Δppm	3.39	Δppm
1	4.8206	0.0000	4.1133	0.0000	3.9213	0.0000	3.8913	0.0000	3.4564	0.0000	3.4072	0.0000
2	4.8200	0.0006	4.1127	0.0006	3.9209	0.0004	3.8907	0.0006	3.4559	0.0005	3.4066	0.0006
3	4.8195	0.0011	4.1121	0.0012	3.9207	0.0006	3.8899	0.0014	3.4556	0.0008	3.4062	0.0010
4	4.8189	0.0017	4.1114	0.0019	3.9204	0.0009	3.8892	0.0021	3.4551	0.0013	3.4056	0.0016
5	4.8184	0.0022	4.1108	0.0025	3.9202	0.0011	3.8887	0.0026	3.4548	0.0016	3.405	0.0022
6	4.8175	0.0031	4.1096	0.0037	3.9197	0.0016	3.8875	0.0038	3.4540	0.0024	3.4043	0.0029
7	4.8166	0.0040	4.1087	0.0046	3.9193	0.0020	3.8866	0.0047	3.4535	0.0029	3.4036	0.0036
8	4.8154	0.0052	4.1069	0.0064	3.9184	0.0029	3.8848	0.0065	3.4523	0.0041	3.4023	0.0049

Plot of chemical shift change vs guest concentration:



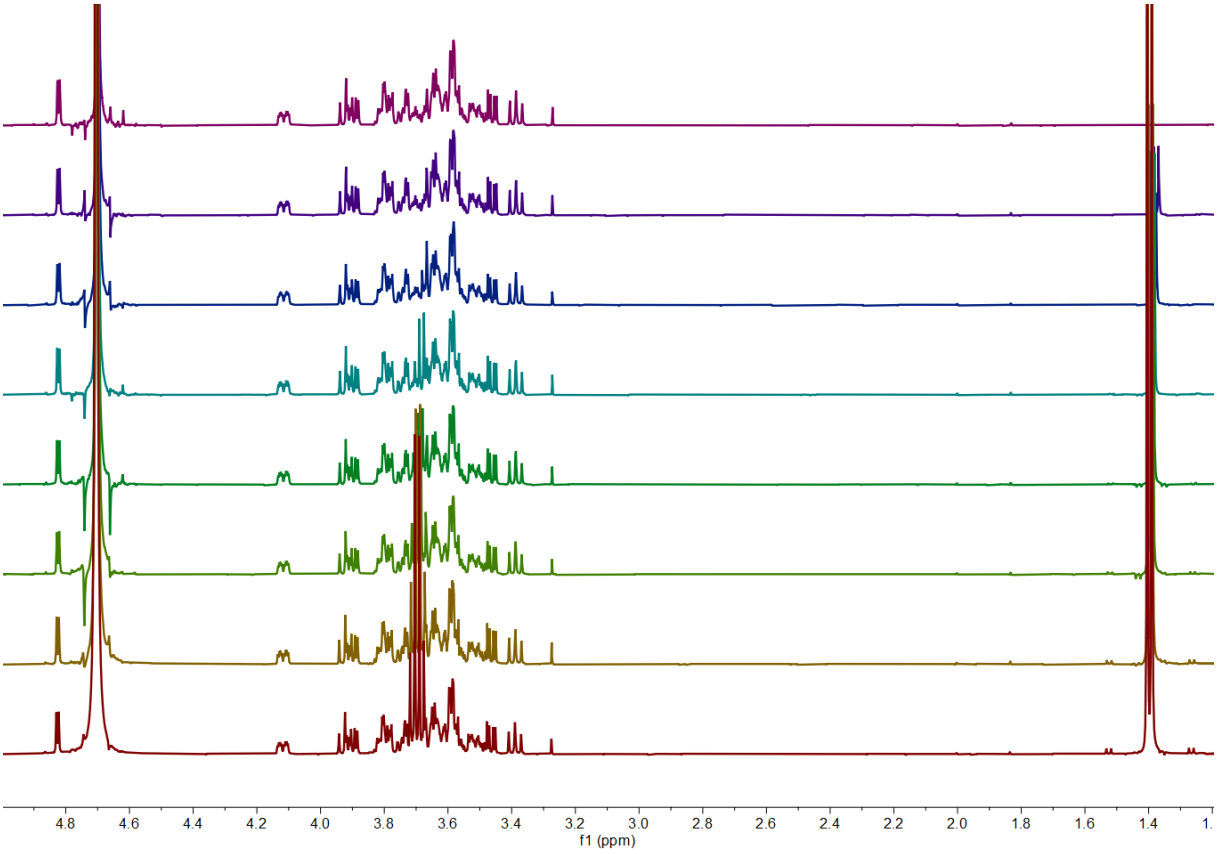
K_d values obtained by fitting the data for each proton into the single-site specific binding model:

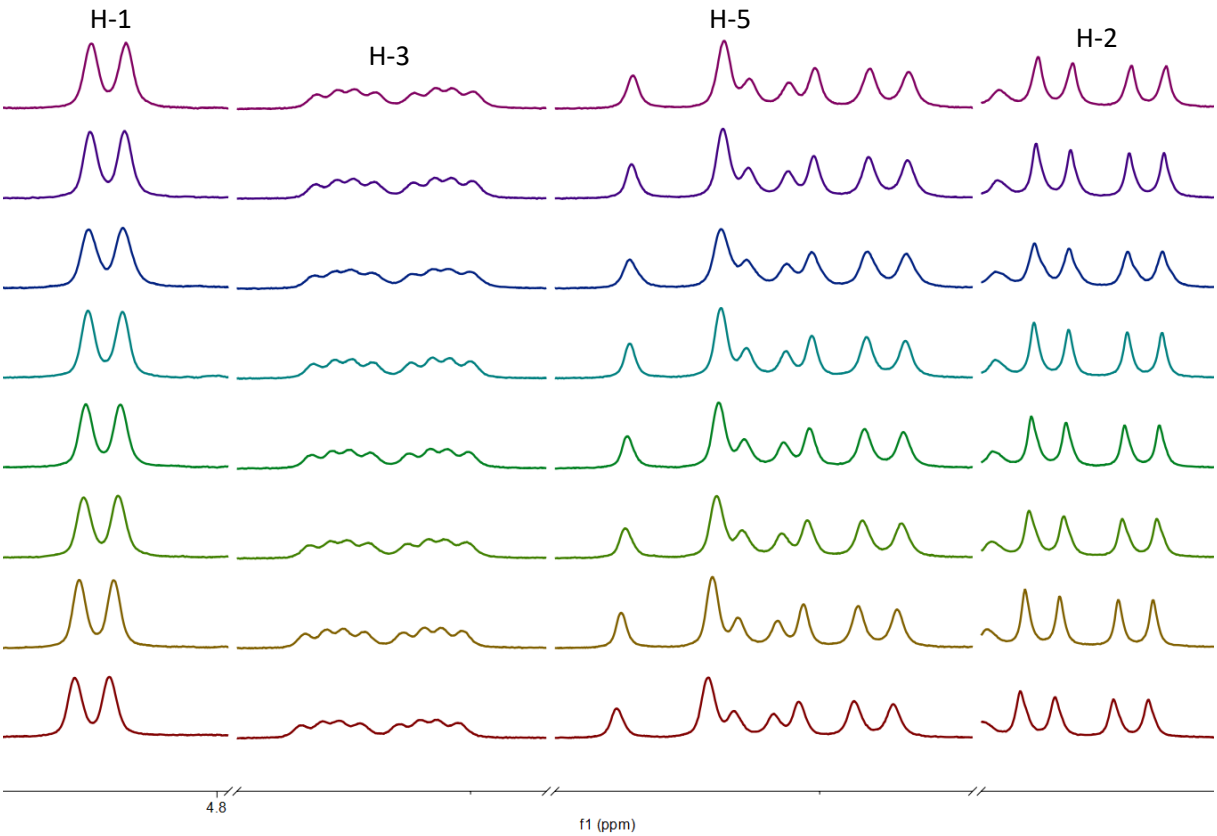
K_d	18.090	22.590	22.520	20.010	20.870	17.580
Std. error	2.304	2.732	4.534	2.983	3.324	1.609
R squared	0.994	0.995	0.986	0.992	0.991	0.997

K_d = 20.28 ± 2.92 mM

H-L-Ala-OH to receptor 8:

^{1}H NMR spectra (top – full, bottom – enhanced view on specific receptor protons):

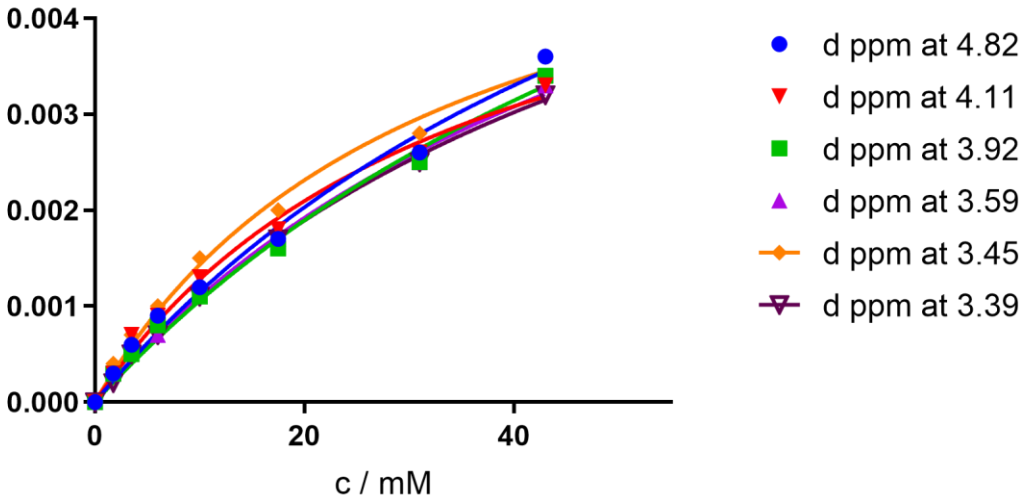




Summary of chemical shift changes:

Titration	4.82	Δppm	4.11	Δppm	3.92	Δppm	3.59	Δppm	3.45	Δppm	3.39	Δppm
1	4.8188	0.0000	4.1116	0.0000	3.9198	0.0000	3.5893	0.0000	3.4546	0.0000	3.3863	0.0000
2	4.8191	0.0003	4.1119	0.0003	3.9201	0.0003	3.5896	0.0003	3.4550	0.0004	3.3865	0.0002
3	4.8194	0.0006	4.1123	0.0007	3.9203	0.0005	3.5899	0.0006	3.4553	0.0007	3.3868	0.0005
4	4.8197	0.0009	4.1125	0.0009	3.9206	0.0008	3.59	0.0007	3.4556	0.0010	3.387	0.0007
5	4.8200	0.0012	4.1129	0.0013	3.9209	0.0011	3.5904	0.0011	3.4561	0.0015	3.3874	0.0011
6	4.8205	0.0017	4.1134	0.0018	3.9214	0.0016	3.591	0.0017	3.4566	0.0020	3.388	0.0017
7	4.8214	0.0026	4.1142	0.0026	3.9223	0.0025	3.5918	0.0025	3.4574	0.0028	3.3888	0.0025
8	4.8224	0.0036	4.1149	0.0033	3.9232	0.0034	3.5926	0.0033	3.4582	0.0036	3.3895	0.0032

Plot of chemical shift change vs guest concentration:



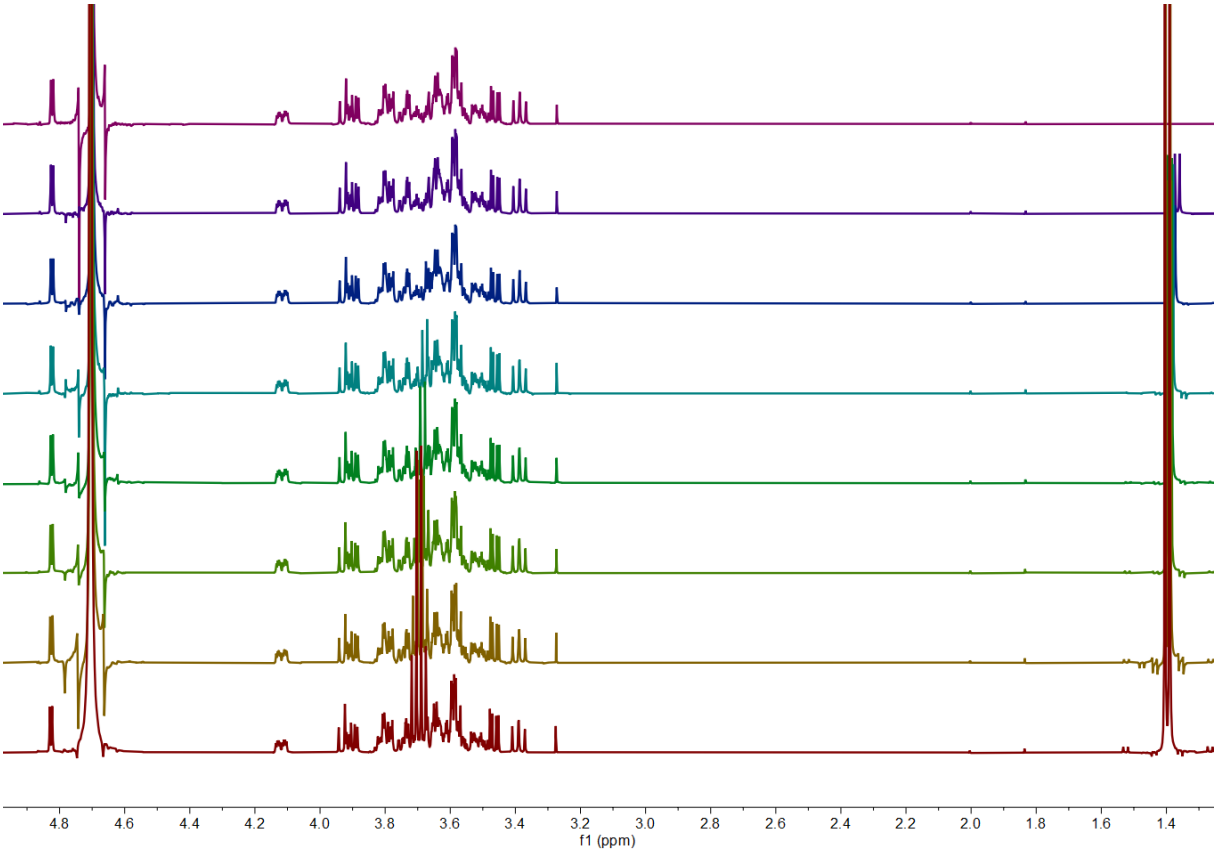
K_d values obtained by fitting the data for each proton into the single-site specific binding model:

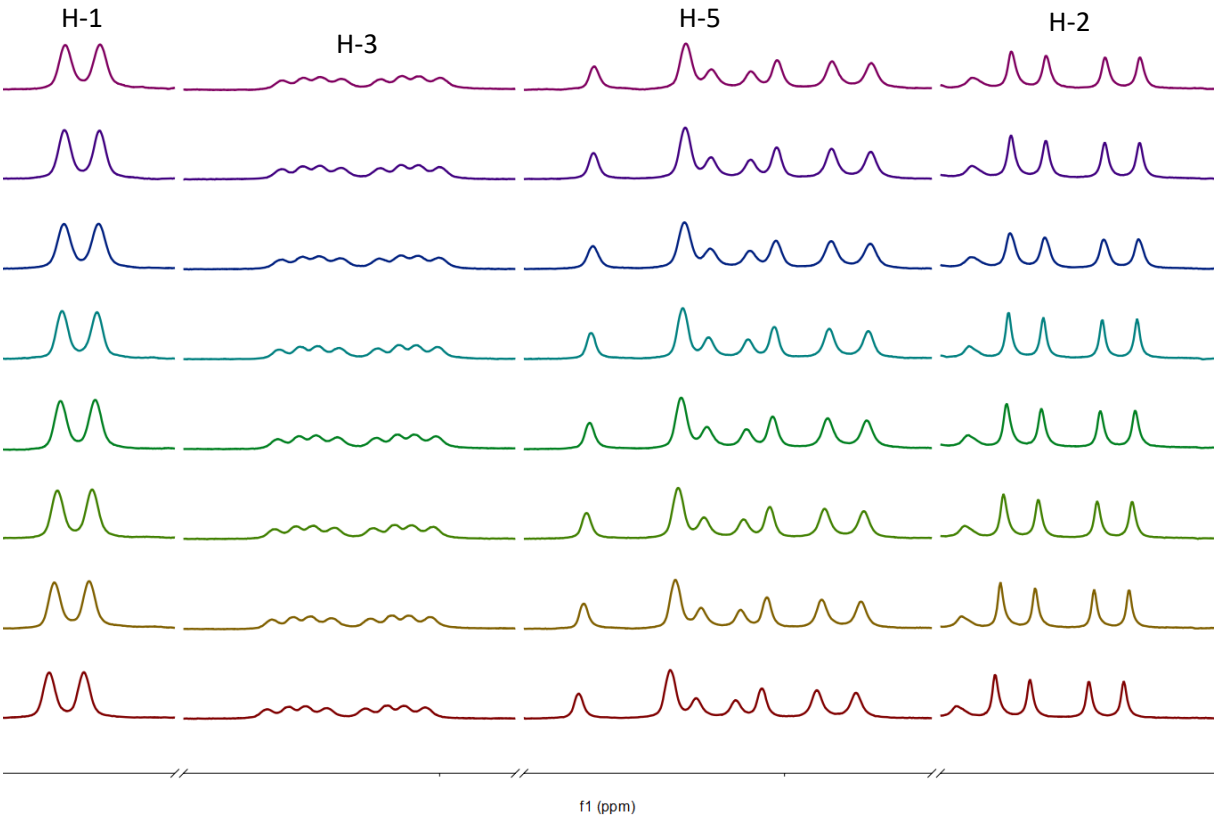
K_d	66.61	35.54	77.26	60.67	32.19	58.9
Std. error	22.82	6.76	23.12	13.89	5.871	6.74
R squared	0.9865	0.9916	0.9916	0.9933	0.9915	0.9983

K_d = 55.20 ± 13.2 mM

H-D-Ala-OH to receptor 8:

^{1}H NMR spectra (top – full, bottom – enhanced view on specific receptor protons):

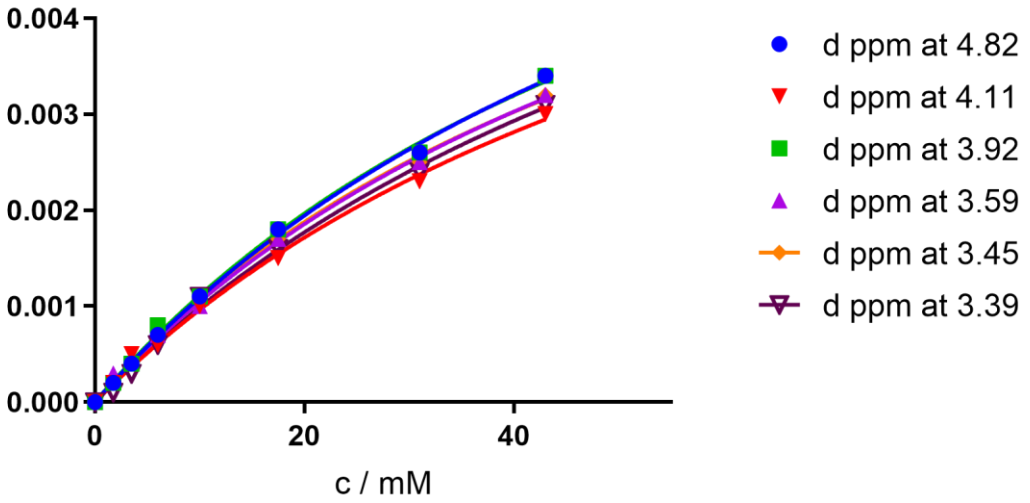




Summary of chemical shift changes:

Titration	4.82	Δppm	4.11	Δppm	3.92	Δppm	3.59	Δppm	3.45	Δppm	3.39	Δppm
1	4.8193	0.0000	4.1121	0.0000	3.9202	0.0000	3.5898	0.0000	3.4481	0.0000	3.3868	0.0000
2	4.8195	0.0002	4.1123	0.0002	3.9204	0.0002	3.5901	0.0003	3.4483	0.0002	3.3869	0.0001
3	4.8197	0.0004	4.1126	0.0005	3.9206	0.0004	3.5902	0.0004	3.4484	0.0003	3.3871	0.0003
4	4.8200	0.0007	4.1127	0.0006	3.921	0.0008	3.5905	0.0007	3.4488	0.0007	3.3874	0.0006
5	4.8204	0.0011	4.1131	0.0010	3.9213	0.0011	3.5908	0.0010	3.4492	0.0011	3.3879	0.0011
6	4.8211	0.0018	4.1136	0.0015	3.922	0.0018	3.5915	0.0017	3.4498	0.0017	3.3884	0.0016
7	4.8219	0.0026	4.1144	0.0023	3.9228	0.0026	3.5923	0.0025	3.4507	0.0026	3.3892	0.0024
8	4.8227	0.0034	4.1151	0.0030	3.9236	0.0034	3.593	0.0032	3.4515	0.0034	3.3899	0.0031

Plot of chemical shift change vs guest concentration:



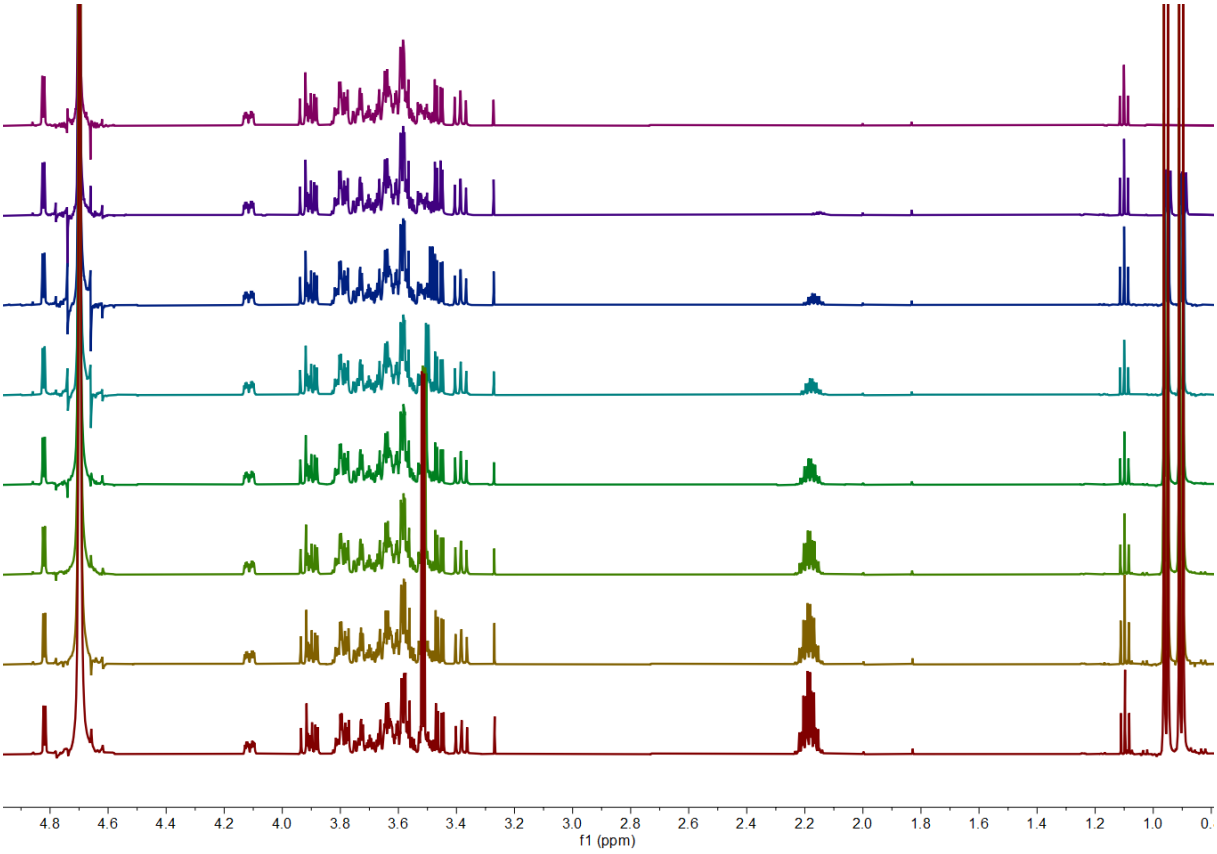
K_d values obtained by fitting the data for each proton into the single-site specific binding model:

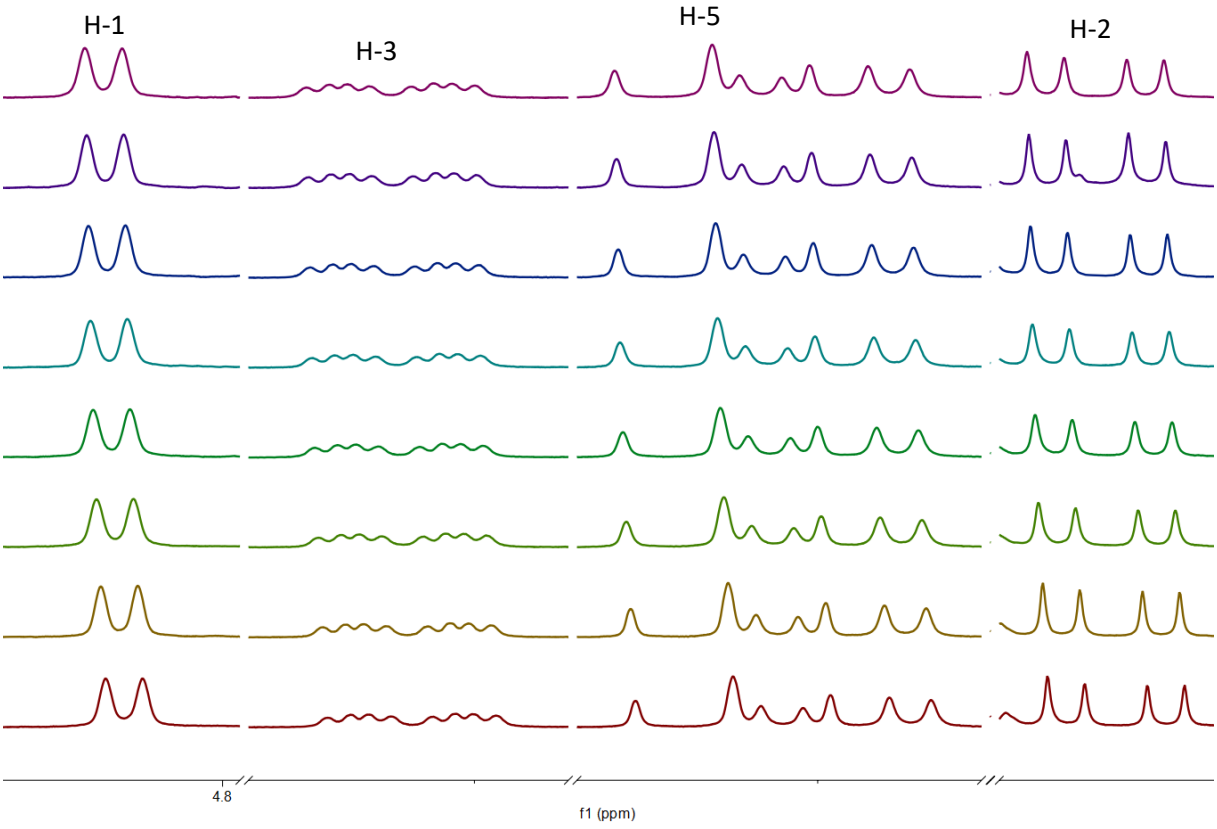
K_d	73.13	71.42	66.53	68.42	62.87	76.07
Std. error	8.85	13.74	10.03	9.32	5.47	15.15
R squared	0.9986	0.9962	0.9975	0.998	0.9991	0.9965

K_d = 69.74 ± 10.42 mM

H-L-Val-OH to receptor 8:

^{1}H NMR spectra (top – full, bottom – enhanced view on specific receptor protons):

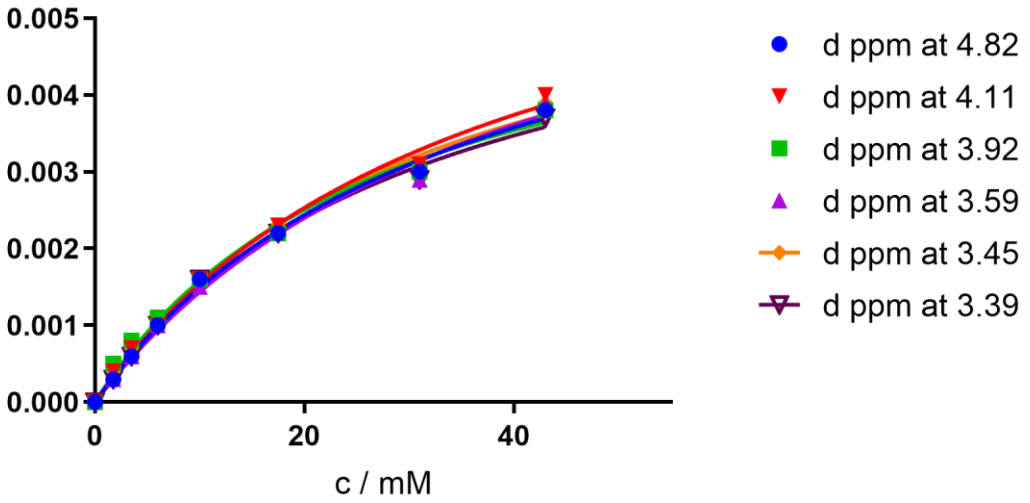




Summary of chemical shift changes:

Titration	4.82	Δppm	4.11	Δppm	3.92	Δppm	3.59	Δppm	3.45	Δppm	3.39	Δppm
1	4.8195	0.0000	4.1123	0.0000	3.9205	0.0000	3.5936	0.0000	3.4554	0.0000	3.3868	0.0000
2	4.8192	0.0003	4.1119	0.0004	3.92	0.0005	3.5933	0.0003	3.4550	0.0004	3.3865	0.0003
3	4.8189	0.0006	4.1116	0.0007	3.9197	0.0008	3.593	0.0006	3.4547	0.0007	3.3862	0.0006
4	4.8185	0.0010	4.1113	0.0010	3.9194	0.0011	3.5926	0.0010	3.4543	0.0011	3.3858	0.0010
5	4.8179	0.0016	4.1107	0.0016	3.9189	0.0016	3.5921	0.0015	3.4538	0.0016	3.3852	0.0016
6	4.8173	0.0022	4.11	0.0023	3.9183	0.0022	3.5914	0.0022	3.4531	0.0023	3.3846	0.0022
7	4.8165	0.0030	4.1092	0.0031	3.9175	0.0030	3.5906	0.0030	3.4524	0.0030	3.3839	0.0029
8	4.8157	0.0038	4.1083	0.0040	3.9167	0.0038	3.5896	0.0040	3.4515	0.0039	3.383	0.0038

Plot of chemical shift change vs guest concentration:



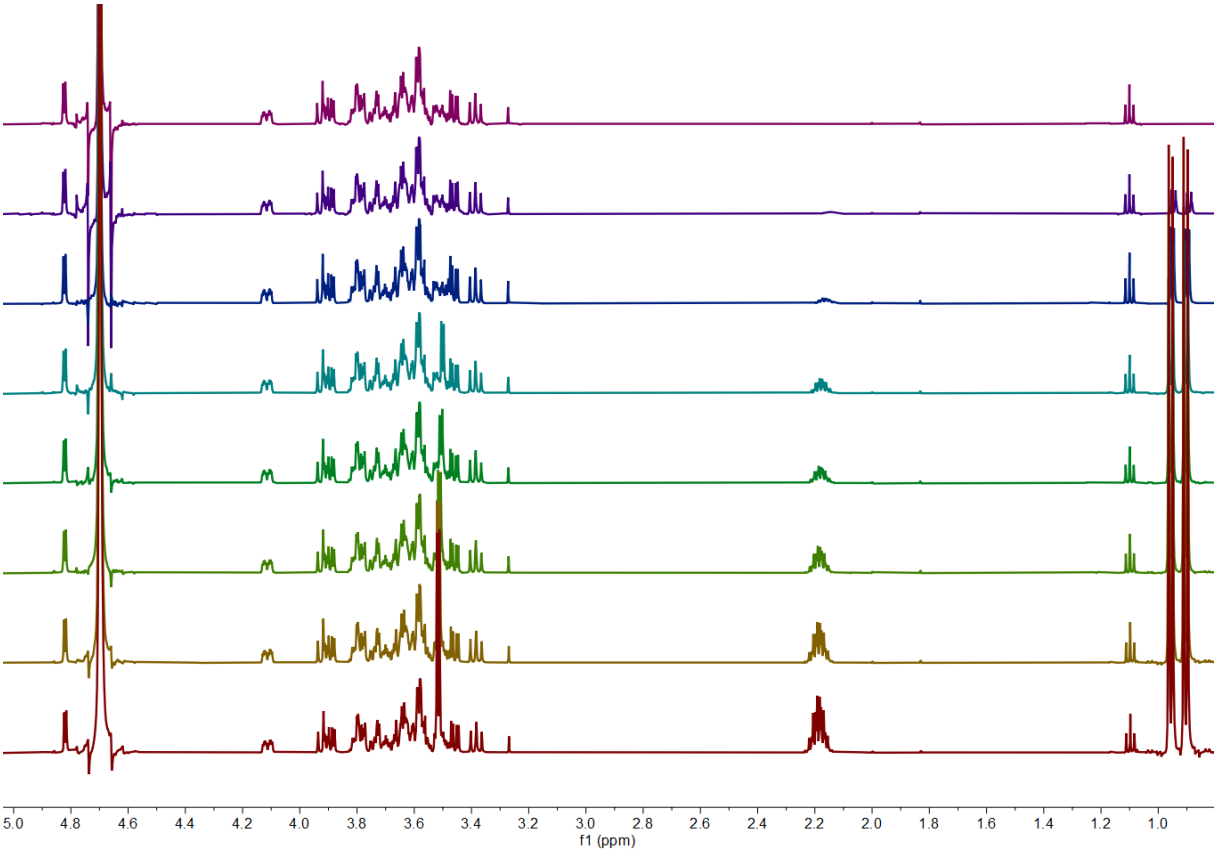
K_d values obtained by fitting the data for each proton into the single-site specific binding model:

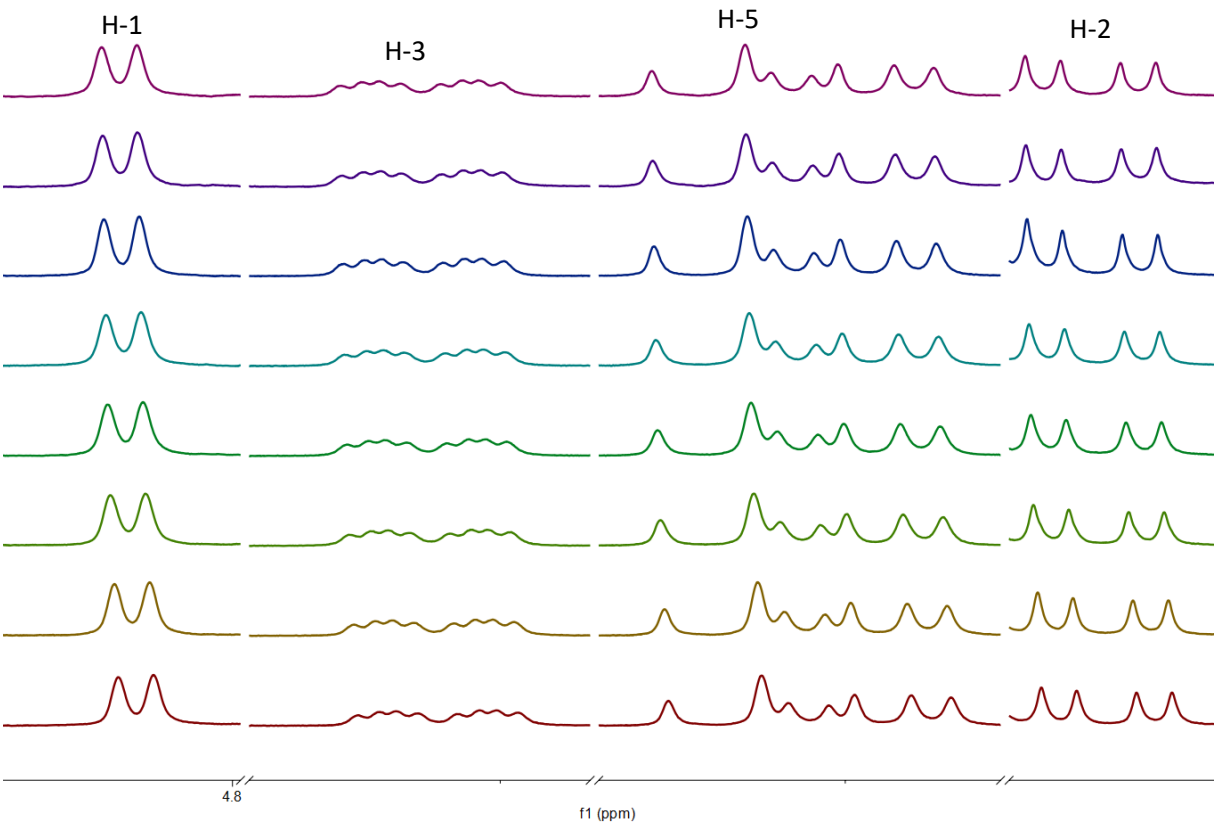
K_d	35.02	36.51	28.07	40.79	31.18	31.87
Std. error	4.48	5.41	4.87	7.95	4.95	4.46
R squared	0.9963	0.9951	0.9912	0.9926	0.9935	0.9952

K_d = 33.91 ± 5.35 mM

H-D-Val-OH to receptor 8:

^{1}H NMR spectra (top – full, bottom – enhanced view on specific receptor protons):

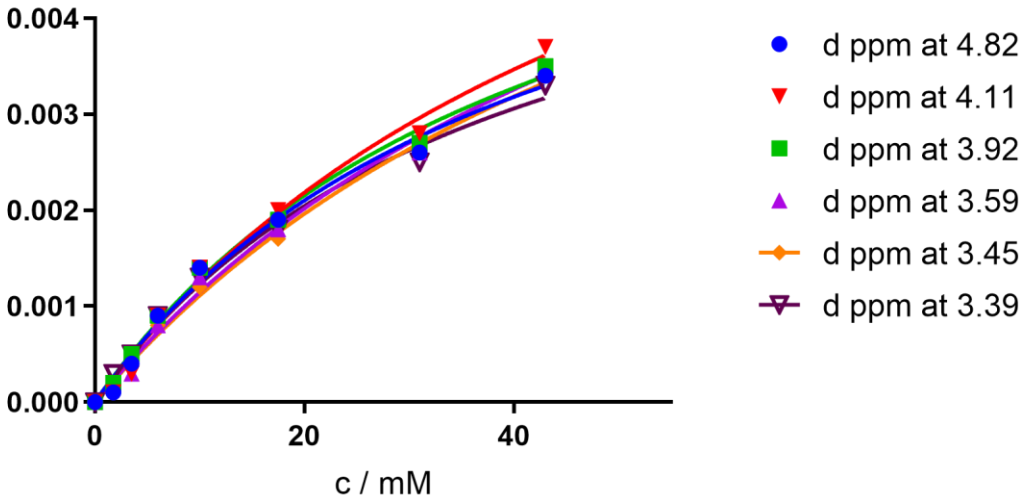




Summary of chemical shift changes:

Titration	4.82	Δppm	4.11	Δppm	3.92	Δppm	3.59	Δppm	3.45	Δppm	3.39	Δppm
1	4.8194	0.0000	4.1122	0.0000	3.9204	0.0000	3.5934	0.0000	3.4481	0.0000	3.3867	0.0000
2	4.8193	0.0001	4.1121	0.0001	3.9202	0.0002	3.5932	0.0002	3.4479	0.0002	3.3864	0.0003
3	4.8189	0.0005	4.1119	0.0003	3.9199	0.0005	3.5931	0.0003	3.4477	0.0004	3.3862	0.0005
4	4.8185	0.0009	4.1113	0.0009	3.9195	0.0009	3.5926	0.0008	3.4473	0.0008	3.3858	0.0009
5	4.8180	0.0014	4.1108	0.0014	3.919	0.0014	3.5921	0.0013	3.4469	0.0012	3.3854	0.0013
6	4.8175	0.0019	4.1102	0.0020	3.9185	0.0019	3.5916	0.0018	3.4464	0.0017	3.3849	0.0018
7	4.8168	0.0026	4.1094	0.0028	3.9177	0.0027	3.5908	0.0026	3.4455	0.0026	3.3842	0.0025
8	4.8160	0.0034	4.1085	0.0037	3.9169	0.0035	3.5899	0.0035	3.4447	0.0034	3.3834	0.0033

Plot of chemical shift change vs guest concentration:



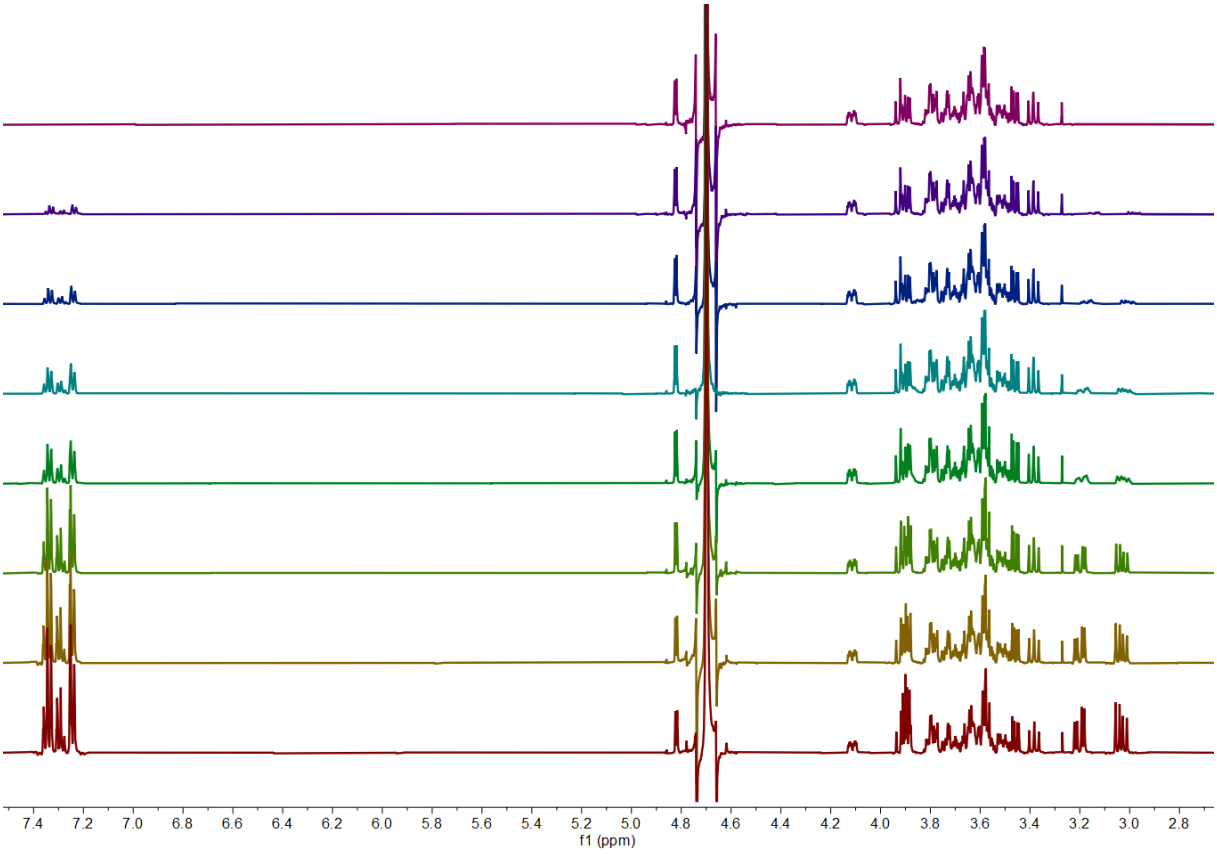
K_d values obtained by fitting the data for each proton into the single-site specific binding model:

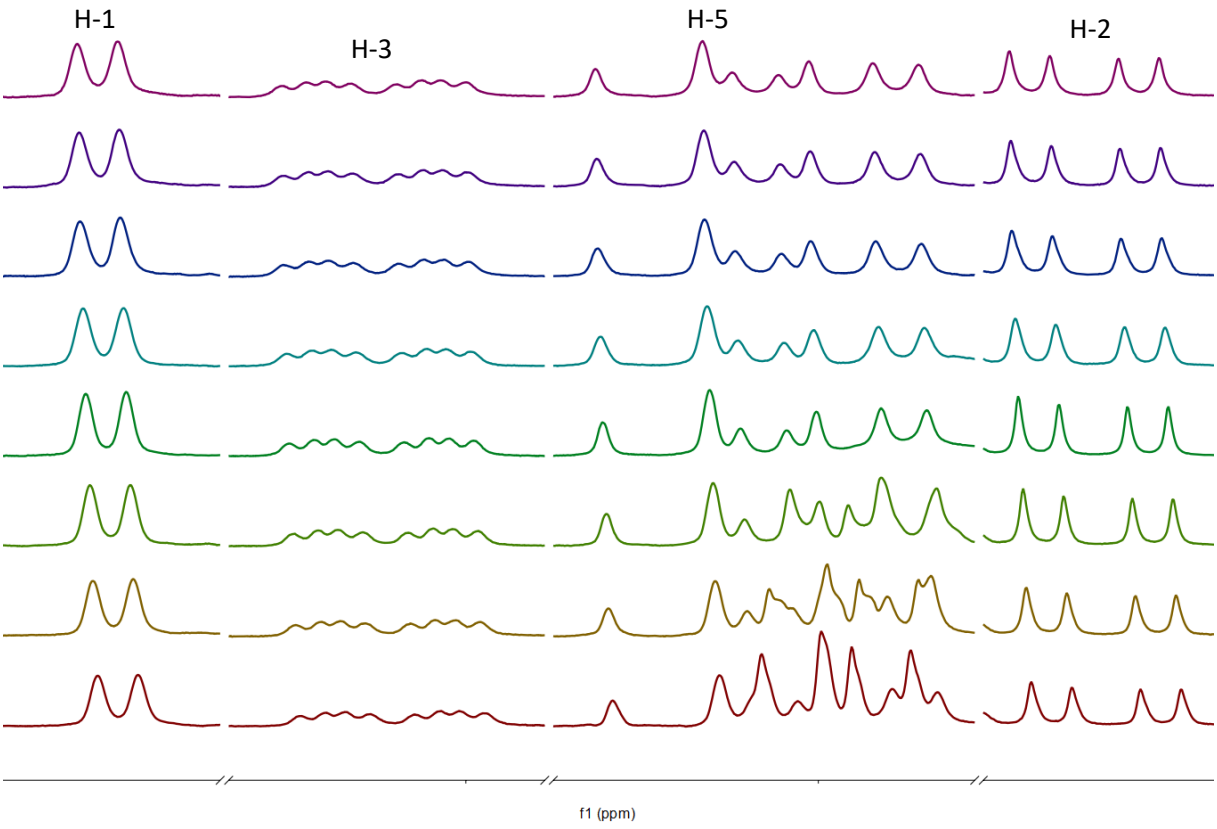
K_d	42.29	56.88	43.26	64.03	66.09	39.51
Std. error	9.93	15.69	7.54	16.95	12.05	7.55
R squared	0.9902	0.9904	0.9945	0.9921	0.9963	0.9926

K_d = 52.01 ± 11.62 mM

H-L-Phe-OH to receptor 8:

^{1}H NMR spectra (top – full, bottom – enhanced view on specific receptor protons):

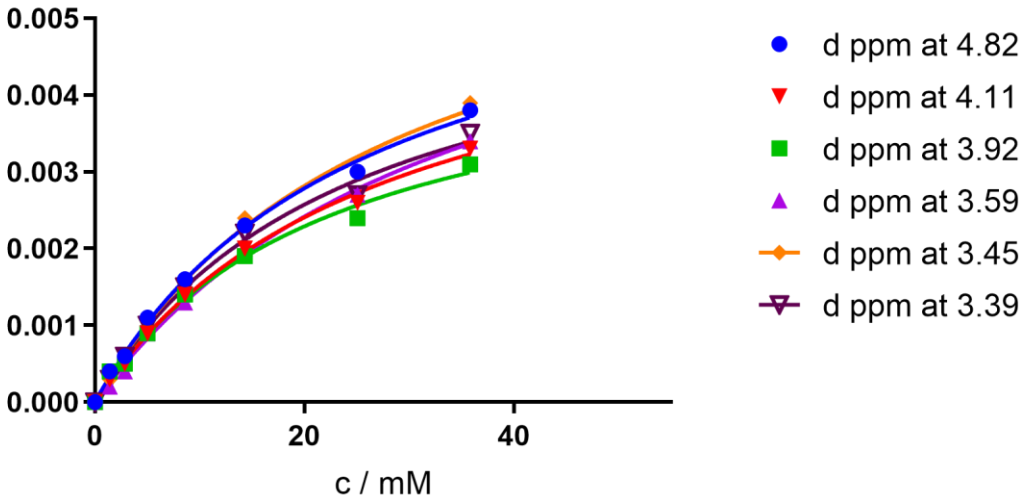




Summary of chemical shift changes:

Titration	4.82	Δppm	4.11	Δppm	3.92	Δppm	3.59	Δppm	3.45	Δppm	3.39	Δppm
1	4.8197	0.0000	4.1124	0.0000	3.9206	0.0000	3.5937	0.0000	3.4555	0.0000	3.387	0.0000
2	4.8193	0.0004	4.1121	0.0003	3.9202	0.0004	3.5935	0.0002	3.4552	0.0003	3.3867	0.0003
3	4.8191	0.0006	4.1119	0.0005	3.9201	0.0005	3.5933	0.0004	3.4550	0.0005	3.3864	0.0006
4	4.8186	0.0011	4.1115	0.0009	3.9197	0.0009	3.5928	0.0009	3.4544	0.0011	3.386	0.0010
5	4.8181	0.0016	4.111	0.0014	3.9192	0.0014	3.5924	0.0013	3.4539	0.0016	3.3855	0.0015
6	4.8174	0.0023	4.1104	0.0020	3.9187	0.0019	3.5917	0.0020	3.4531	0.0024	3.3848	0.0022
7	4.8167	0.0030	4.1098	0.0026	3.9182	0.0024	3.591	0.0027	3.4525	0.0030	3.3843	0.0027
8	4.8159	0.0038	4.1091	0.0033	3.9175	0.0031	3.5903	0.0034	3.4516	0.0039	3.3835	0.0035

Plot of chemical shift change vs guest concentration:



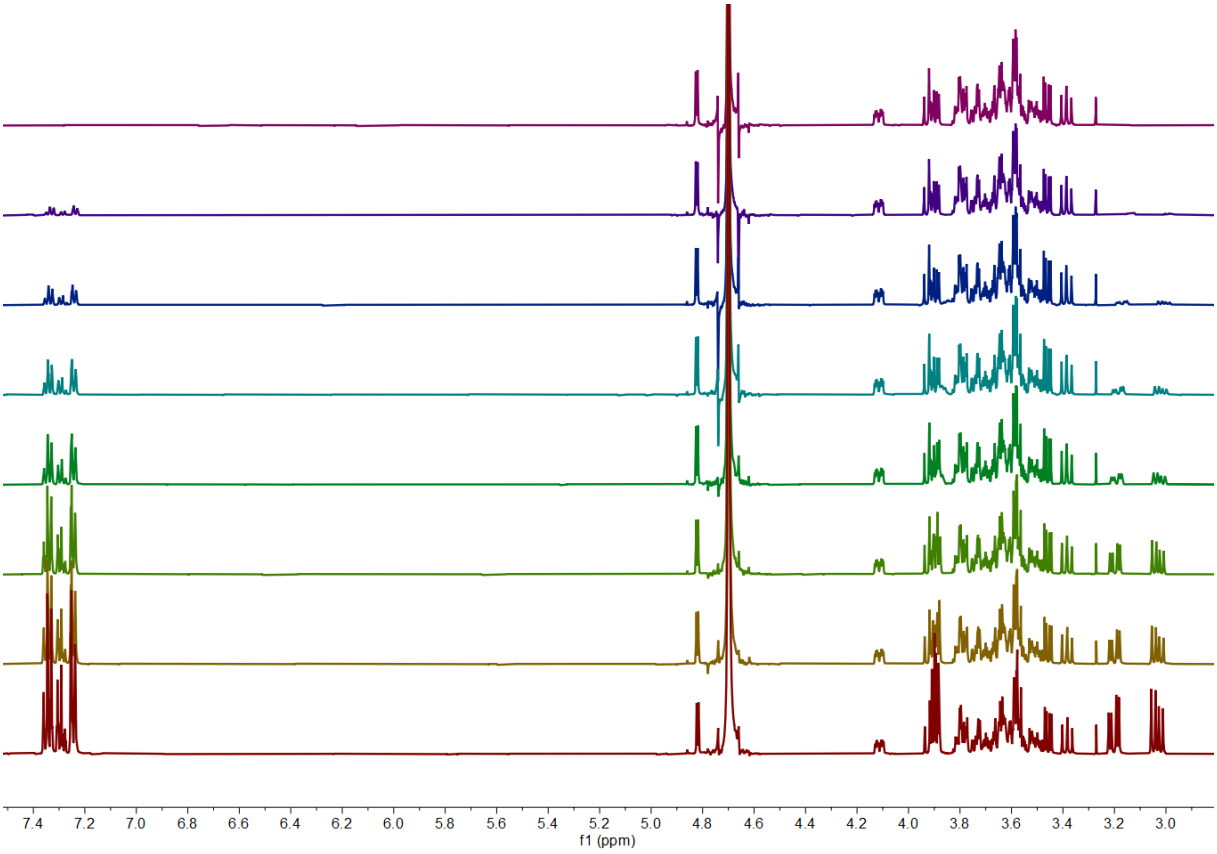
K_d values obtained by fitting the data for each proton into the single-site specific binding model:

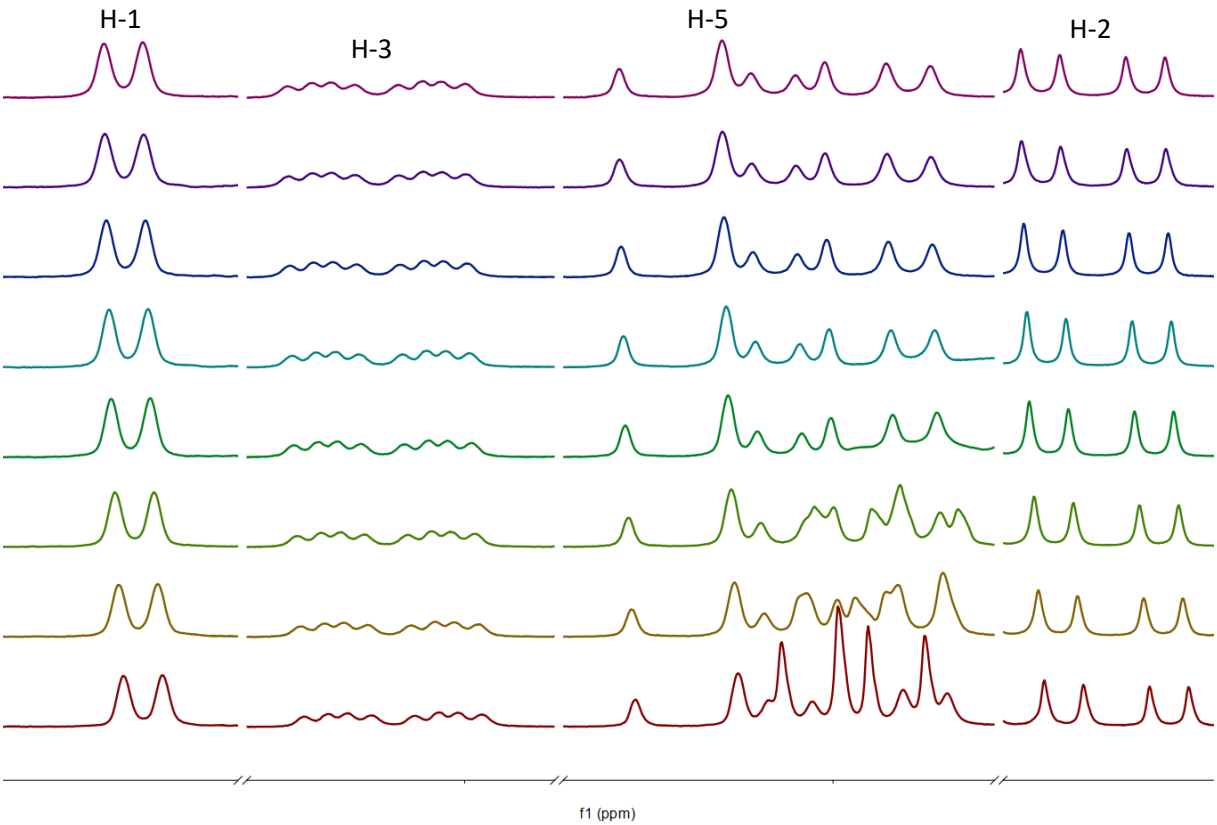
K_d	25.83	27.27	22.62	35.59	28.47	24.17
Std. error	2.84	2.86	3.51	4.46	4.67	3.4
R squared	0.9969	0.9973	0.9929	0.9971	0.9938	0.9947

K_d = 27.33 ± 3.62 mM

H-D-Phe-OH to receptor 8:

^{1}H NMR spectra (top – full, bottom – enhanced view on specific receptor protons):

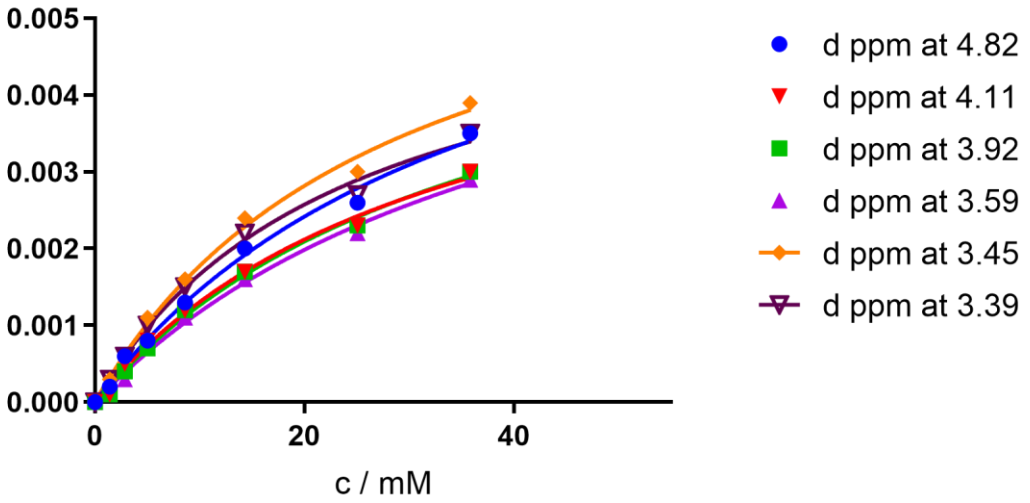




Summary of chemical shift changes:

Titration	4.82	Δppm	4.11	Δppm	3.92	Δppm	3.59	Δppm	3.45	Δppm	3.39	Δppm
1	4.8266	0.0000	4.1123	0.0000	3.9204	0.0000	3.5937	0.0000	3.4554	0.0000	3.3868	0.0000
2	4.8264	0.0002	4.1122	0.0001	3.9203	0.0001	3.5936	0.0001	3.4552	0.0002	3.3866	0.0002
3	4.8261	0.0005	4.1119	0.0004	3.9201	0.0003	3.5934	0.0003	3.4550	0.0004	3.3864	0.0004
4	4.8258	0.0008	4.1115	0.0008	3.9197	0.0007	3.593	0.0007	3.4543	0.0011	3.3858	0.0010
5	4.8253	0.0013	4.1111	0.0012	3.9192	0.0012	3.5926	0.0011	3.4537	0.0017	3.3854	0.0014
6	4.8246	0.0020	4.1106	0.0017	3.9187	0.0017	3.5921	0.0016	3.4530	0.0024	3.3848	0.0020
7	4.8239	0.0027	4.1099	0.0024	3.918	0.0024	3.5914	0.0023	3.4520	0.0034	3.384	0.0028
8	4.8229	0.0037	4.1092	0.0031	3.9172	0.0032	3.5907	0.0030	3.4512	0.0042	3.3832	0.0036

Plot of chemical shift change vs guest concentration:



K_d values obtained by fitting the data for each proton into the single-site specific binding model:

K_d	44.52	38.85	55.17	52.17	43.39	38.29
Std. error	9.397	7.674	9.039	11.67	6.11	4.471
R squared	0.9922	0.9922	0.9933	0.9929	0.9922	0.9932

K_d = 47.40 ± 8.05 mM

5.2 Isothermal Titration Calorimetry (ITC) measurements.

ITC experiments were carried out in a MicroCal PEAQ-ITC (Malvern), at 25°C, 750 rpm, high feedback and 10 µcal/s as reference power, using MilliQ water as a solvent.

The concentrations of the host and the guest solutions were 3 mM and 100 mM respectively. The guest solution was added in 1µL portions at 2 min intervals unless stated otherwise.

The data was analysed by fitting to a one set of sites model using the MicroCal PEAQ-ITC Control Software.

Summary of ITC results (for raw calorimetry data and fitted curves see following pages):

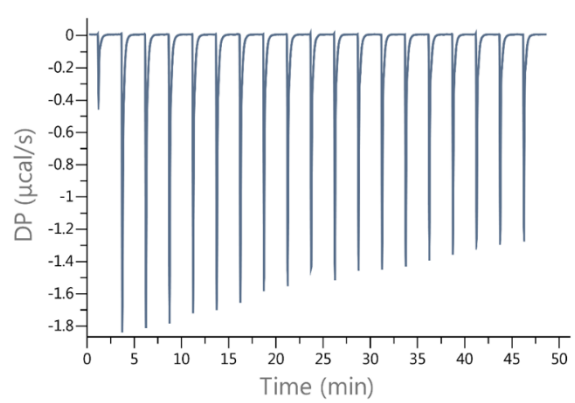
Entry	Guest	K_d*L*	K_d*D*
1	Ala	8.1±1.3	13.5±1.8
2	Thr	6.1±1.5	14.2±2.7
3	Val	3.4±1.1	18.2±3.1
4	Cys	5.3±1.8	17.7±2.7
5	Phe	2.6±0.7	24.6±3.9
6	N_ε-Boc-Lys	2.9±1.3	21.2±2.9
7	Asn	9.1±1.4	n.a.[a]
8	Pro	15.7±2.7	n.a.[a]
9	Trp	n.a.[b]	n.a.[b]

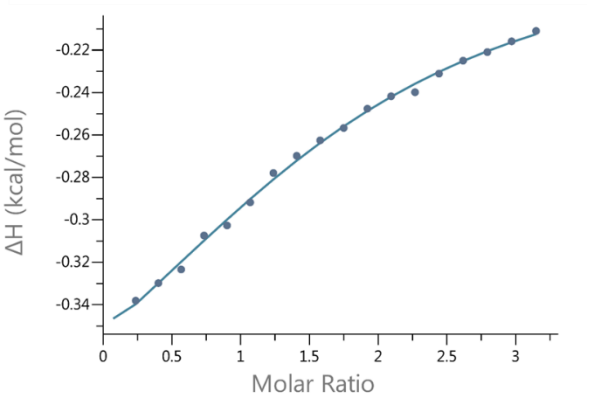
n.a. – not available

[a]*the raw calorimetry data could not be fitted to the equation due to very low levels of released heat;*

[b]*the high dissolution heats of the guest upon titration were overriding the heats associated with the interactions with the receptor*

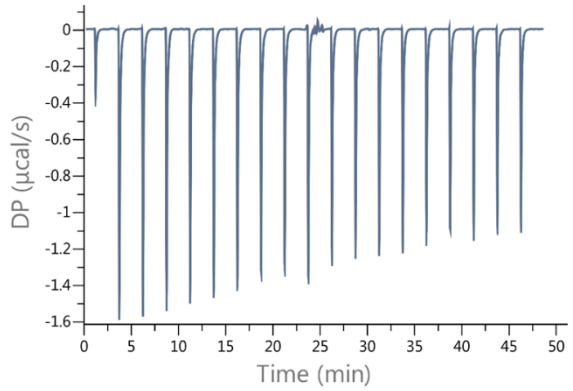
H-L-Ala-OMe x HCl to receptor 8:

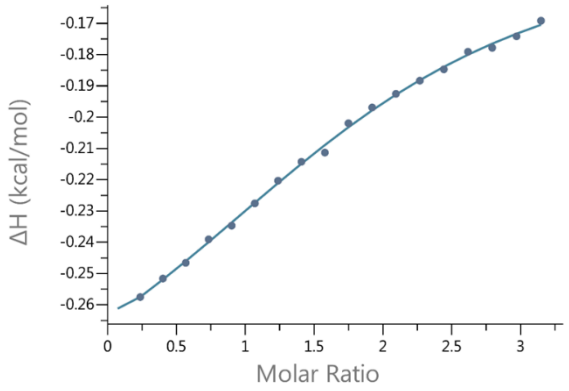




Kd (mM)	N (sites)	ΔG (kcal/mol)	ΔH (kcal/mol)	-TΔS (kcal/mol)
8.13 ± 1.32	1.2	-2.85	-0.28	-2.57

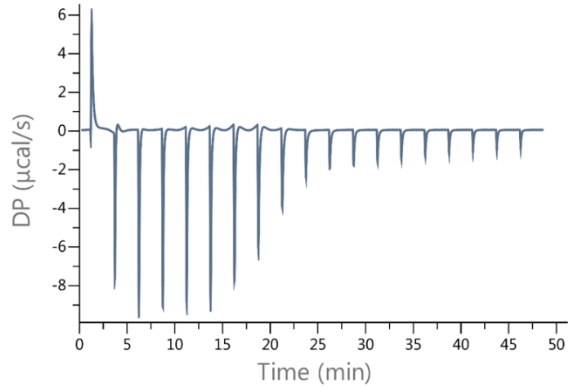
H-L-Thr-OMe x HCl to receptor 8:

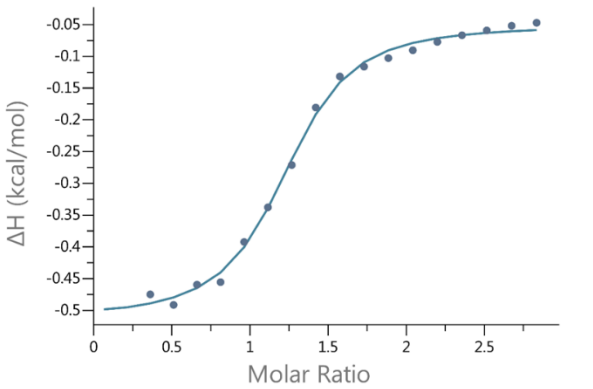




Kd (mM)	N (sites)	ΔG (kcal/mol)	ΔH (kcal/mol)	-TΔS (kcal/mol)
6.13 ± 1.68	1.4	-3.02	-0.32	-2.72

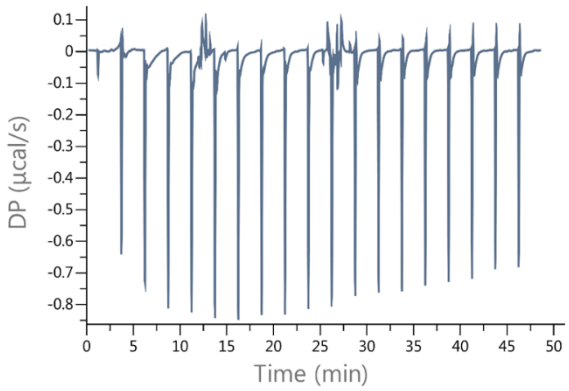
H-L-Val-OMe x HCl to receptor 8:

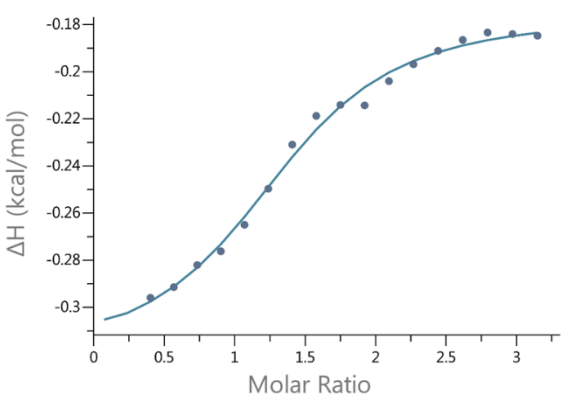




Kd (mM)	N (sites)	ΔG (kcal/mol)	ΔH (kcal/mol)	-TΔS (kcal/mol)
3.42 ± 1.11	1.37	-3.41	-0.73	-2.68

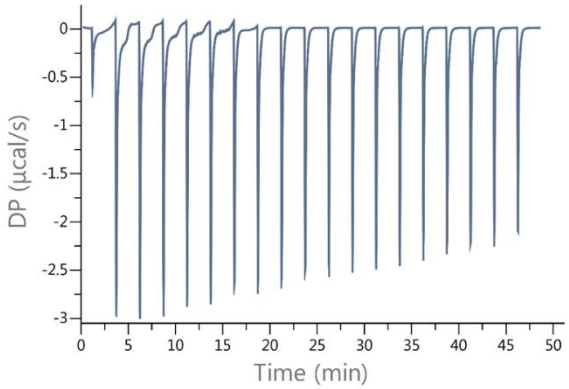
H-L-Cys-OMe x HCl to receptor 8:

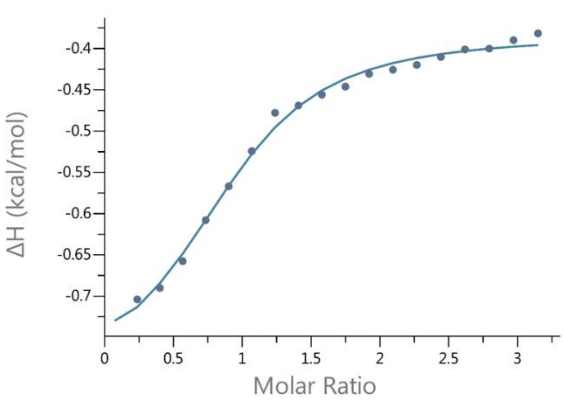




Kd (mM)	N (sites)	ΔG (kcal/mol)	ΔH (kcal/mol)	-TΔS (kcal/mol)
6.68 ± 1.77	1.18	-2.96	-0.35	-2.62

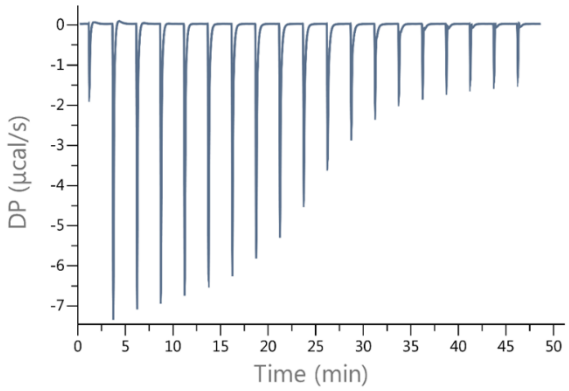
H-L-Phe-OMe x HCl to receptor 8:

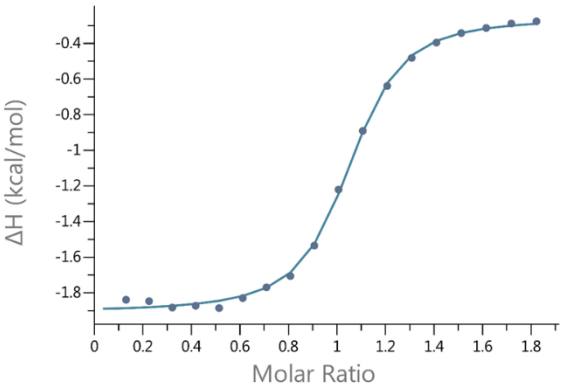




Kd (mM)	N (sites)	ΔG (kcal/mol)	ΔH (kcal/mol)	-TΔS (kcal/mol)
2.62 ± 0.81	0.93	-3.52	-0.96	-2.56

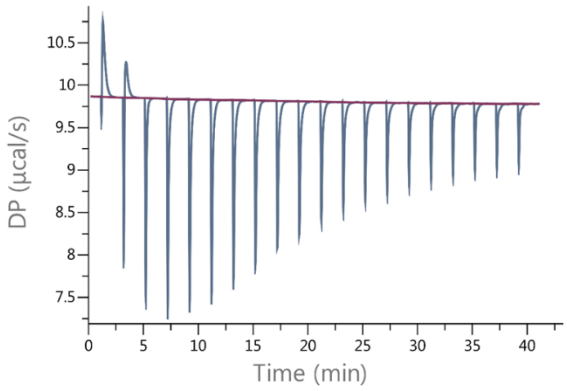
H-L-(Boc)Lys-OMe x HCl to receptor 8:

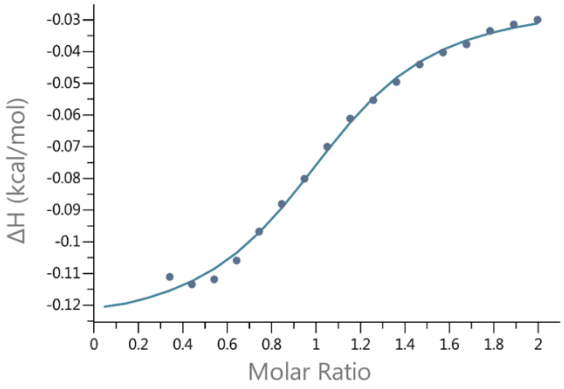




Kd (mM)	N (sites)	ΔG (kcal/mol)	ΔH (kcal/mol)	-TΔS (kcal/mol)
2.88 ± 1.31	1.01	-3.46	-1.23	-2.23

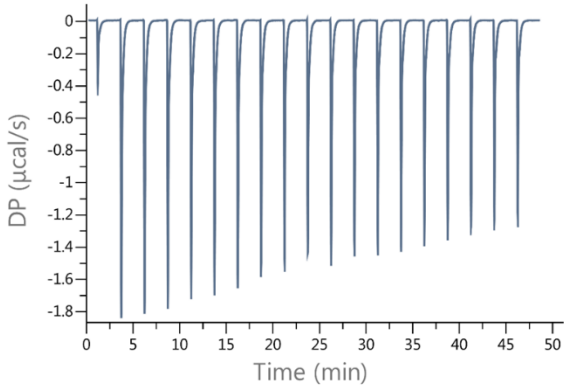
H-L-Asn-OMe x HCl to receptor 8:

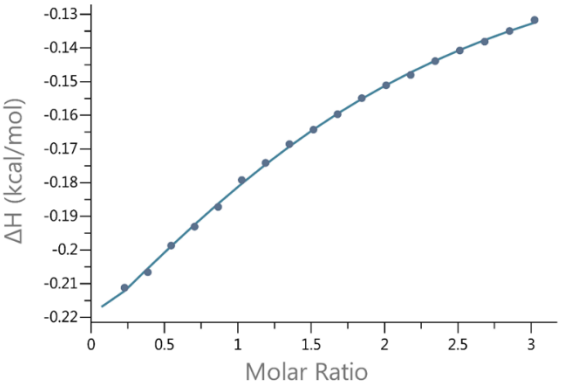




Kd (mM)	N (sites)	ΔG (kcal/mol)	ΔH (kcal/mol)	-TΔS (kcal/mol)
9.09 ± 2.54	1.01	-2.78	-0.17	-2.61

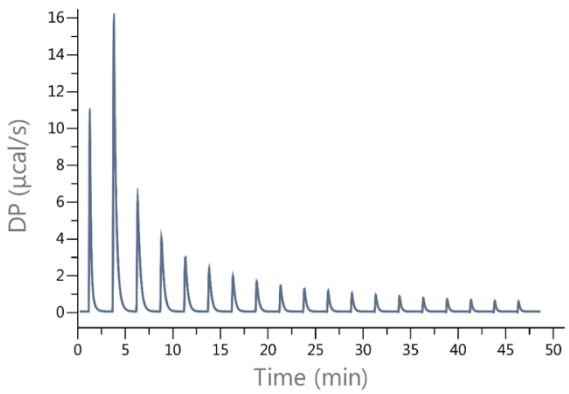
H-L-Pro-OMe x HCl to receptor 8:

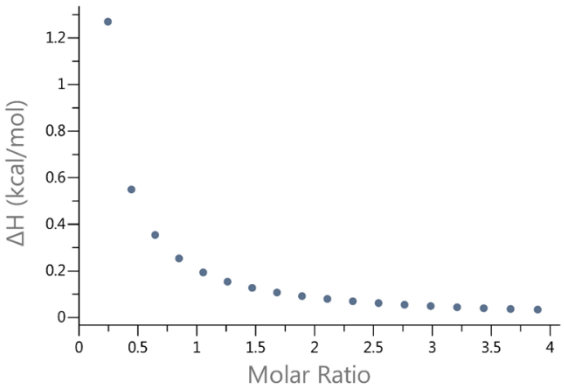




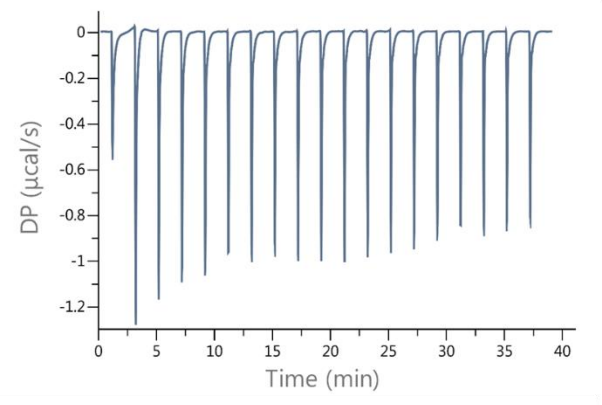
Kd (mM)	N (sites)	ΔG (kcal/mol)	ΔH (kcal/mol)	-TΔS (kcal/mol)
15.71 ± 2.99	1.03	-2.46	-0.11	-2.35

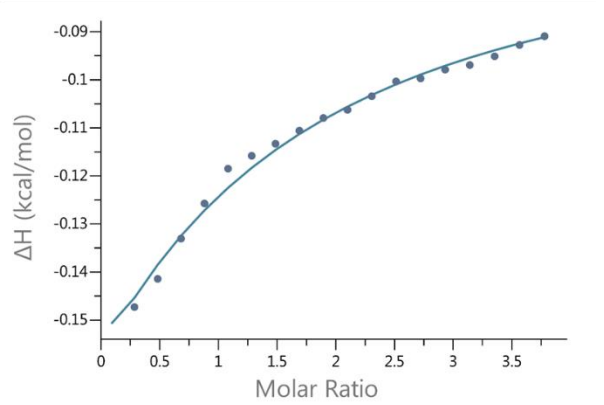
H-L-Trp-OMe x HCl to receptor 8:





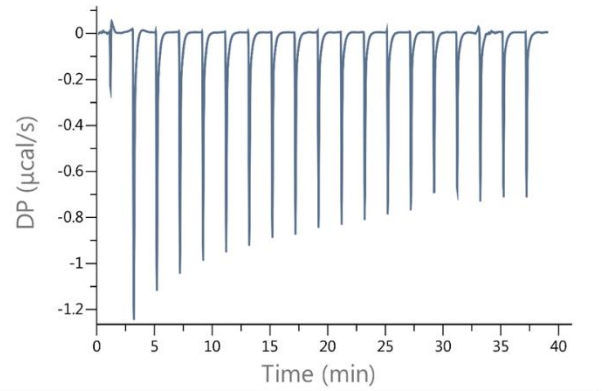
H-D-Ala-OMe x HCl to receptor 8:

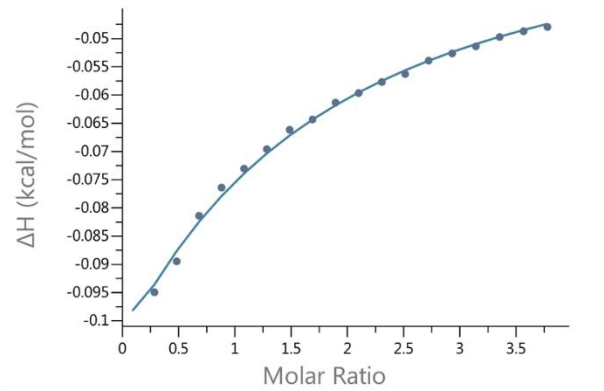




Kd (mM)	N (sites)	ΔG (kcal/mol)	ΔH (kcal/mol)	-TΔS (kcal/mol)
13.5 ± 2.78	1.4	-2.55	-0.12	-2.43

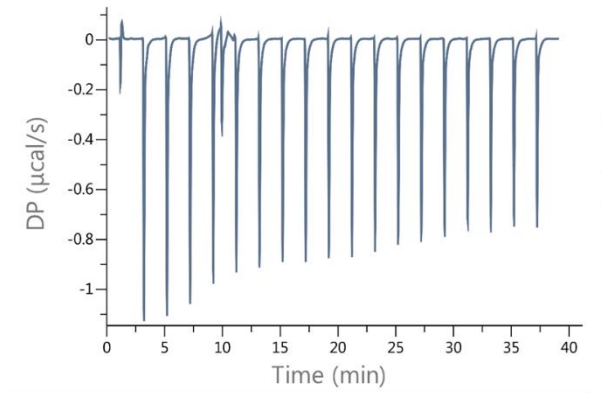
H-D-Thr-OMe x HCl to receptor 8:

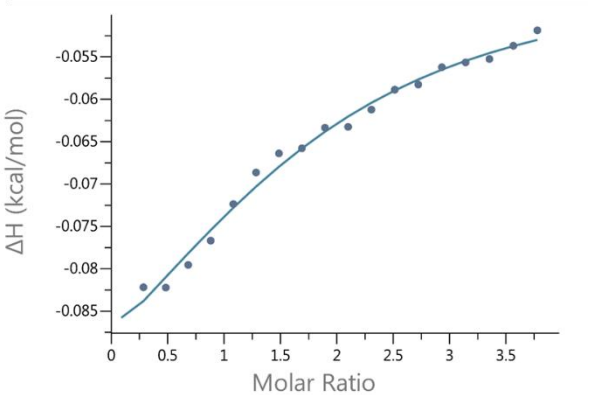




Kd (mM)	N (sites)	ΔG (kcal/mol)	ΔH (kcal/mol)	-TΔS (kcal/mol)
14.2 ± 3.82	1.2	-2.52	-0.11	-2.41

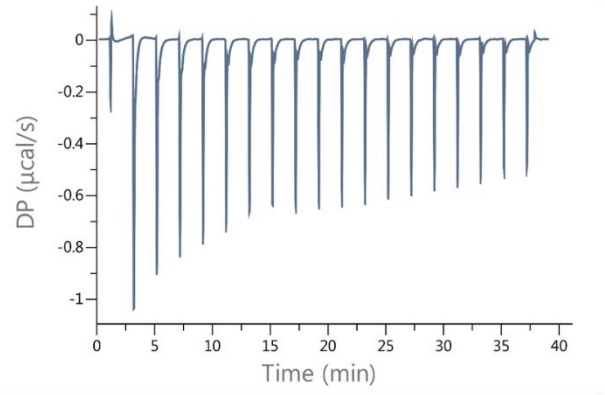
H-D-Val-OMe x HCl to receptor 8:

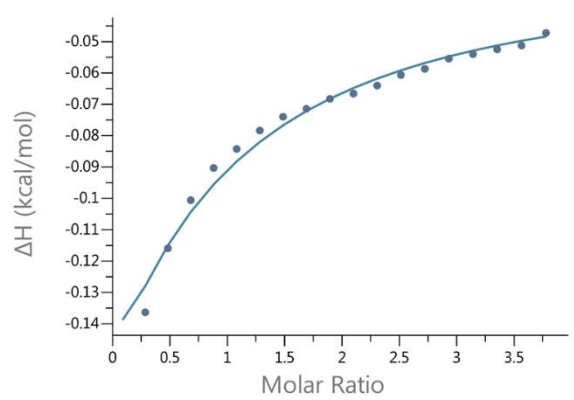




Kd (mM)	N (sites)	ΔG (kcal/mol)	ΔH (kcal/mol)	-TΔS (kcal/mol)
18.23 ± 5.31	1.2	-2.37	-0.1	-2.27

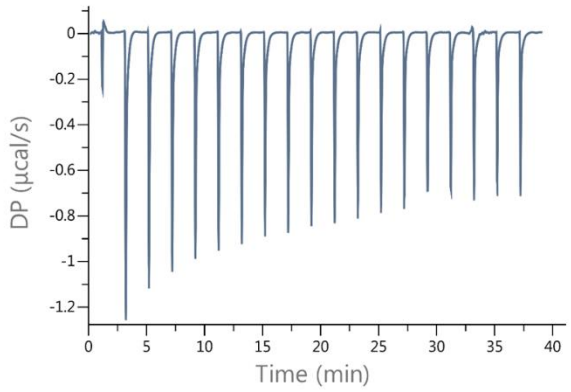
H-D-Cys-OMe x HCl to receptor 8:

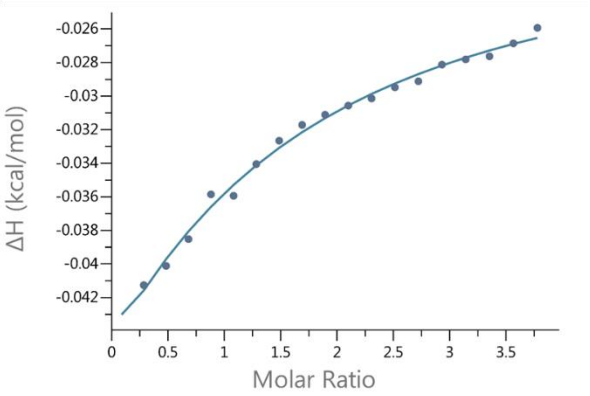




Kd (mM)	N (sites)	ΔG (kcal/mol)	ΔH (kcal/mol)	-TΔS (kcal/mol)
16.21 ± 4.52	1.36	-2.44	-0.08	-2.31

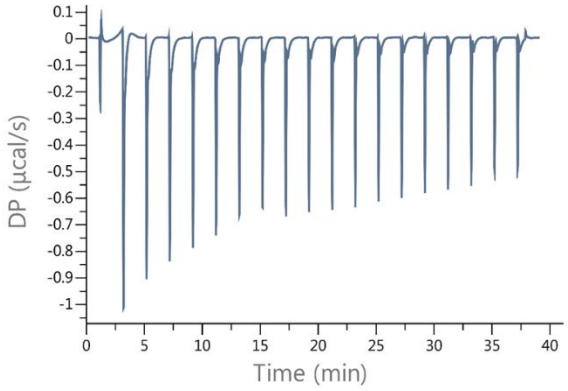
H-D-Phe-OMe x HCl to receptor 8:

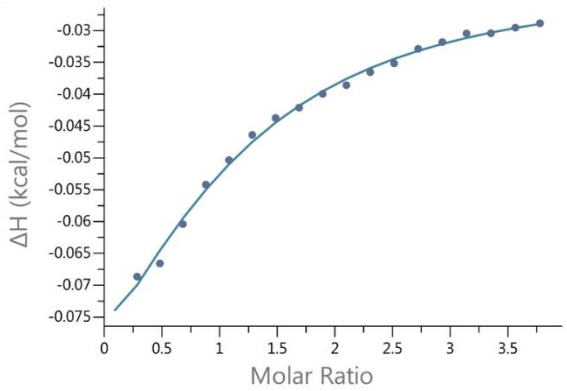




Kd (mM)	N (sites)	ΔG (kcal/mol)	ΔH (kcal/mol)	-TΔS (kcal/mol)
24.60 ± 4.65	0.86	-2.19	-0.09	-2.1

H-D-(Boc)Lys-OMe x HCl to receptor 8:

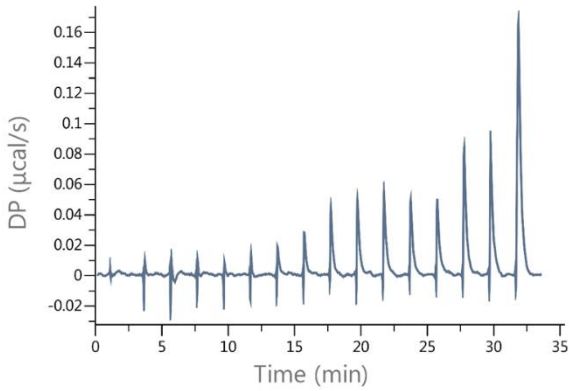




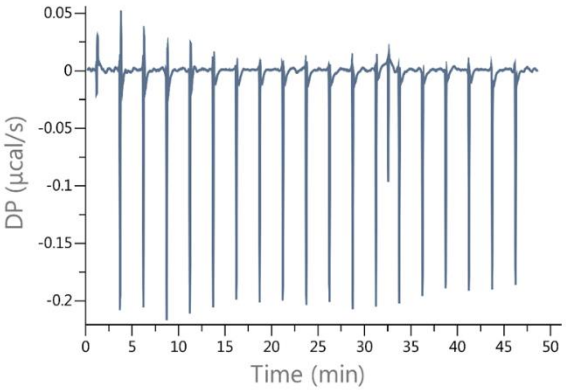
Kd (mM)	N (sites)	ΔG (kcal/mol)	ΔH (kcal/mol)	-TΔS (kcal/mol)
21.22 ± 4.33	0.86	-2.28	-0.21	-2.07

Control experiments:

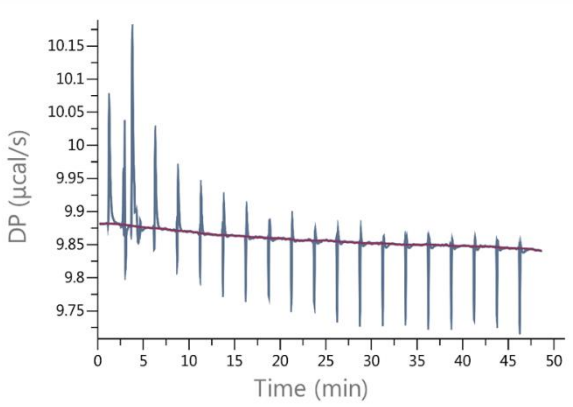
H_2O to receptor 8:



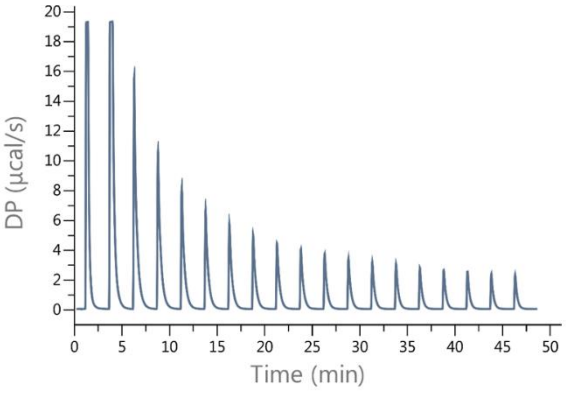
H-L-Ala-OMe x HCl to H_2O:



H-L-Phe-OMe x HCl to H_2O:



H-L-Trp-OMe x HCl to H_2O:



6. Job Plot.

The Job Plot was obtained by recording ^{1}H NMR spectra of the following D_2O solutions:

1: 5 mM receptor + 0 mM guest

2: 4 mM receptor + 1 mM guest

3: 3 mM receptor + 2 mM guest

4: 2.5 mM receptor + 2.5 mM guest

5: 2 mM receptor + 3 mM guest

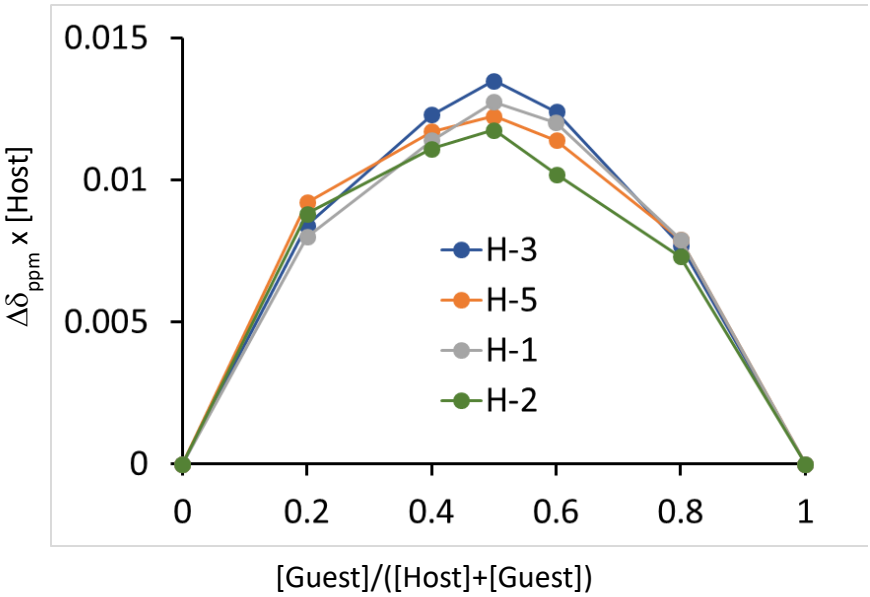
6: 1 mM receptor + 4 mM guest

7: 0 mM receptor + 5 mM guest

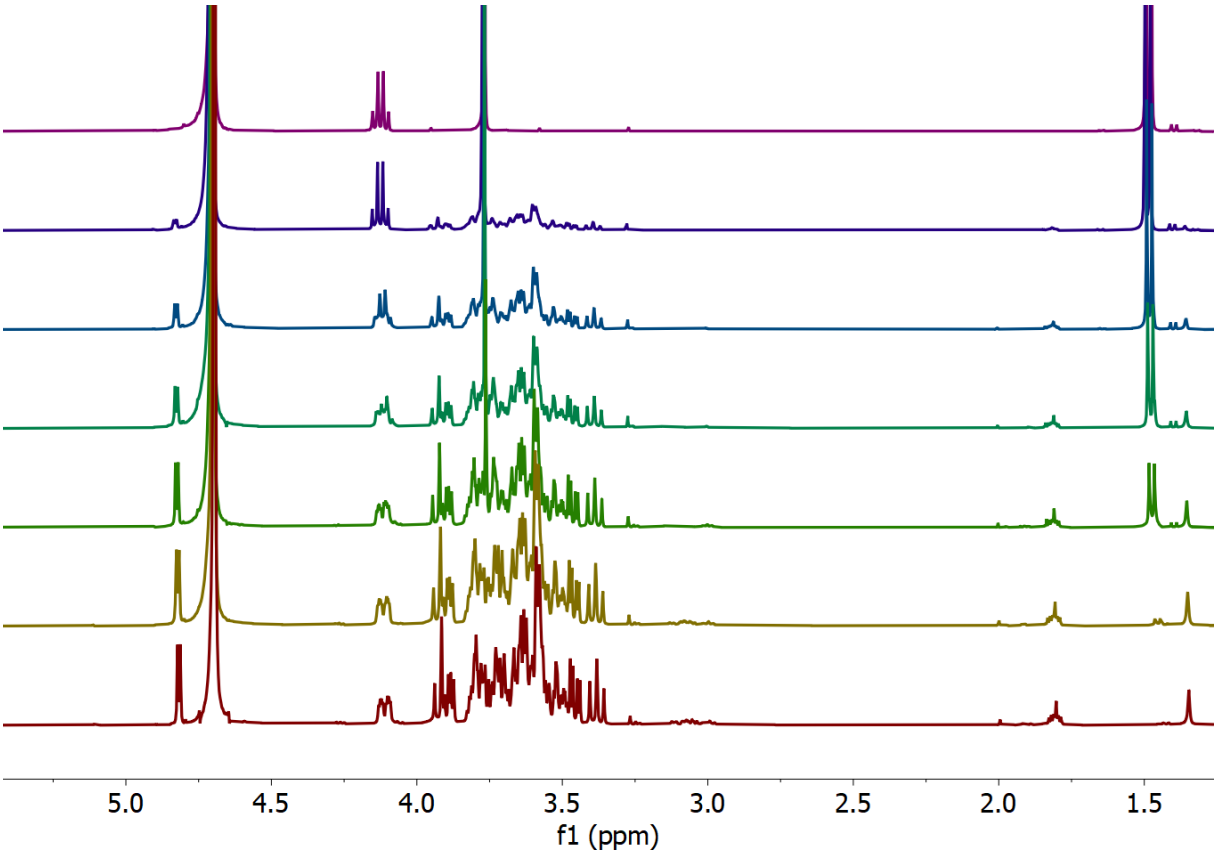
Summary of chemical shift changes of receptor protons (H-1, H-2, H-3 and H-5):

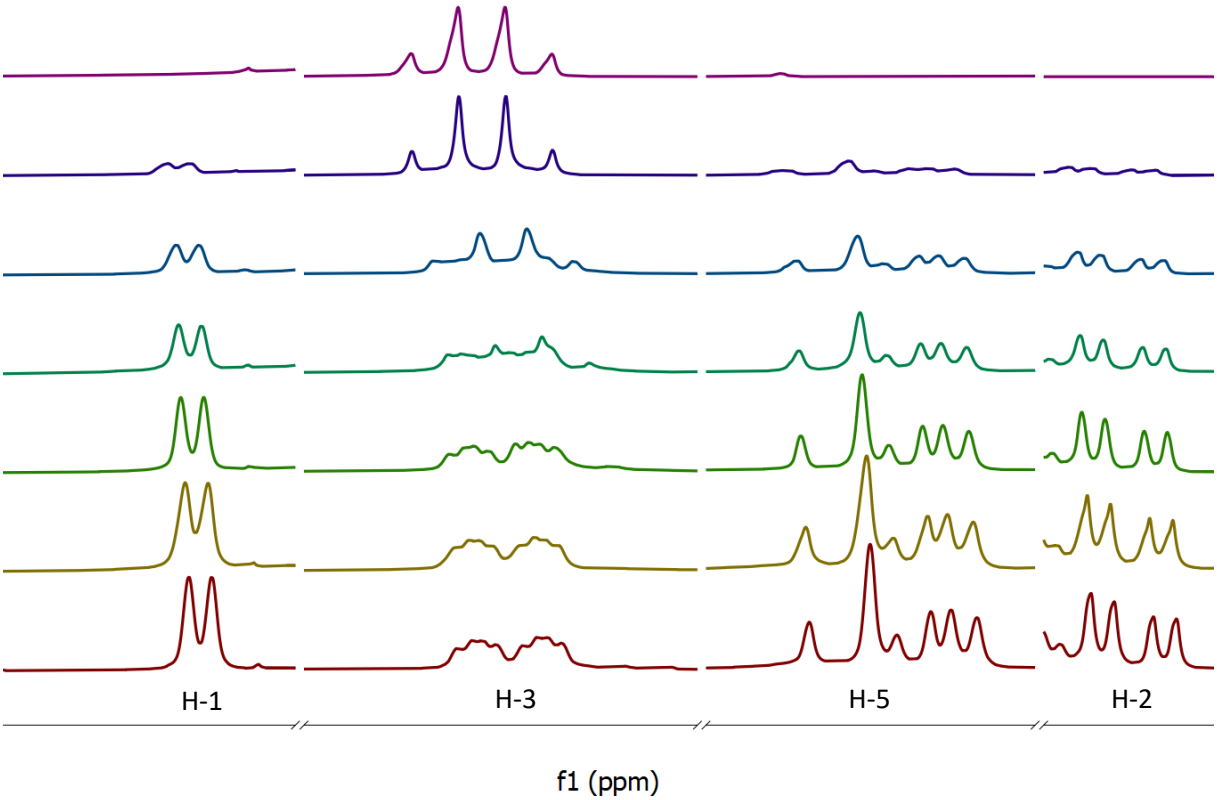
[Host] [mM]	[Guest] [mM]	δ ppm H-1	Δδ ppm H-1	Δδppm x [H]	δ ppm H-3	Δδ ppm H-3	Δδppm x [H]
5	0	4.8178	0	0	3.9145	0	0
4	1	4.8218	0.0023	0.0092	3.9181	0.0021	0.0084
3	2	4.8244	0.0039	0.0117	3.9152	0.0041	0.0123
2.5	2.5	4.8262	0.0049	0.01225	3.9236	0.0054	0.0135
2	3	4.8274	0.0057	0.0114	3.925	0.0062	0.0124
1	4	4.831	0.0079	0.0079	3.9275	0.0077	0.0077
0	5	0	0	0	0	0	0
[Host] [mM]	[Guest] [mM]	δ ppm H-5	Δδ ppm H-5	Δδppm x [H]	δ ppm H-2	Δδ ppm H-2	Δδppm x [H]
5	0	3.7287	0	0	3.4439	0	0
4	1	3.7322	0.002	0.008	3.4473	0.0022	0.0088
3	2	3.7352	0.0038	0.0114	3.45	0.0037	0.0111
2.5	2.5	3.7373	0.0051	0.01275	3.4518	0.0047	0.01175
2	3	3.7388	0.006	0.012	3.45	0.0051	0.0102
1	4	3.7421	0.0079	0.0079	3.4564	0.0073	0.0073
0	5	0	0	0	0	0	0

Job Plot:



^{1}H NMR spectra (top – full, bottom – enhanced view on specific receptor protons):





7. NMR experiments with enantiomer mixtures.

The experiments were performed in D_2O at room temperature. The following solutions were prepared and analysed with ^1H NMR:

1: 1 mM H-L-AA-OMe, 9 mM H-D-AA-OMe, 10 mM receptor **8**.

2: 2.5 mM H-L-AA-OMe, 7.5 mM H-D-AA-OMe, 10 mM receptor **8**.

3: 5 mM H-L-AA-OMe, 5 mM H-D-AA-OMe, 10 mM receptor **8**.

4: 7.5 mM H-L-AA-OMe, 2.5 mM H-D-AA-OMe, 10 mM receptor **8**.

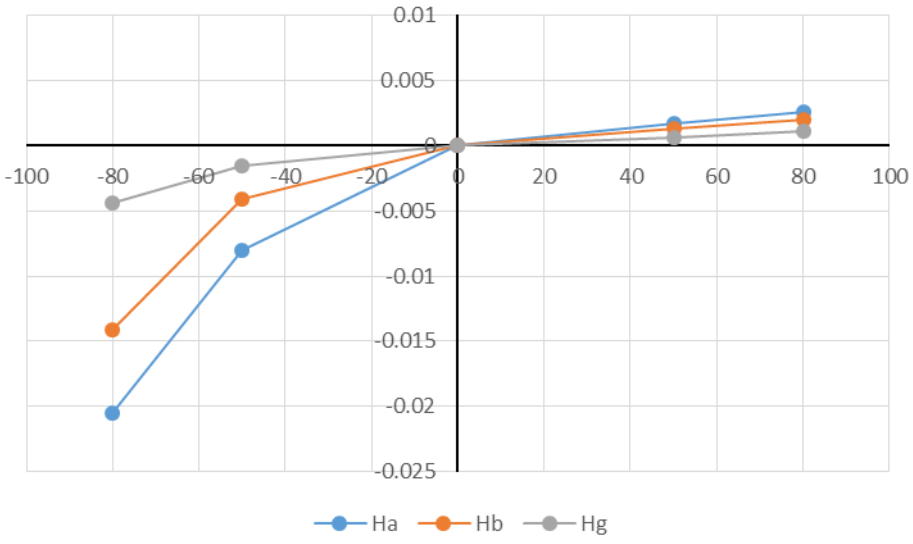
5: 9 mM H-L-AA-OMe, 1 mM H-D-AA-OMe, 10 mM receptor **8**.

7.1 H-Val-OMe:

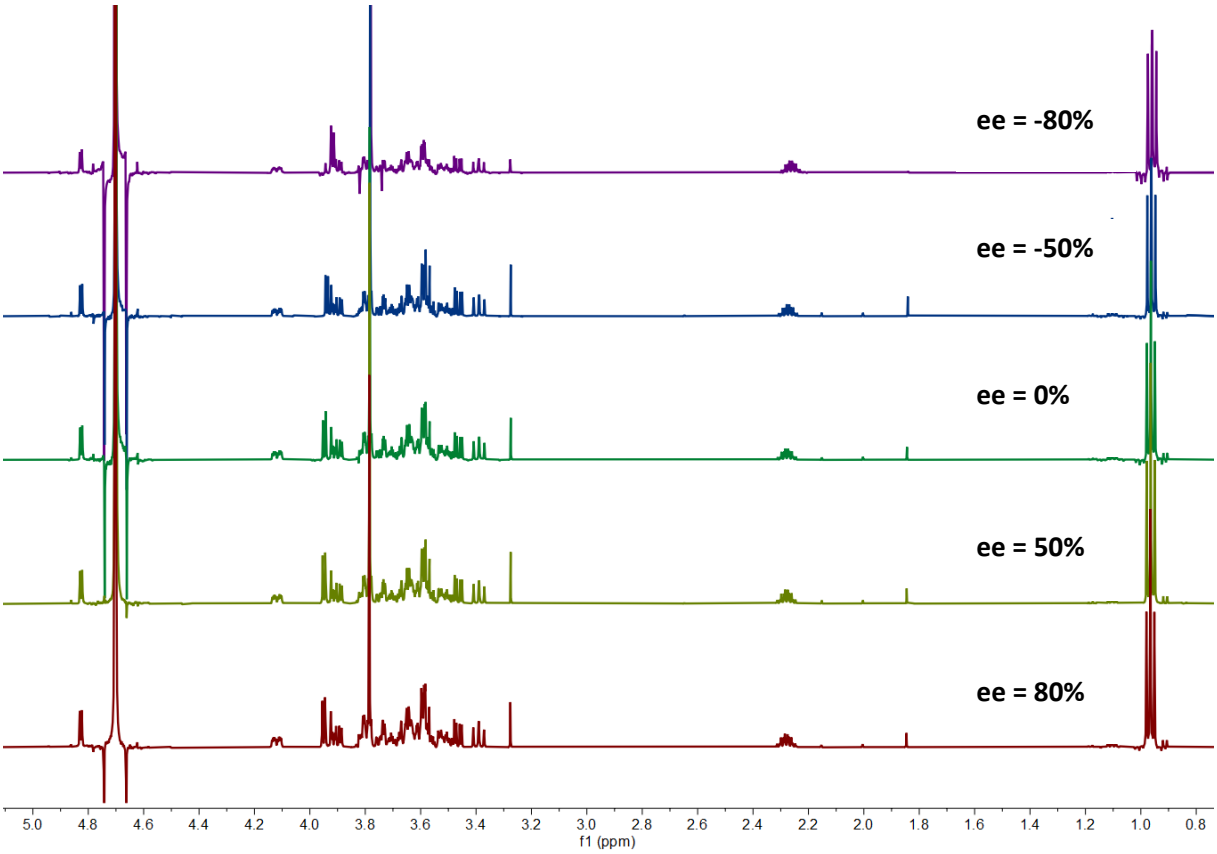
Summary of chemical shift changes of guest protons (H_α, H_β, H_γ):

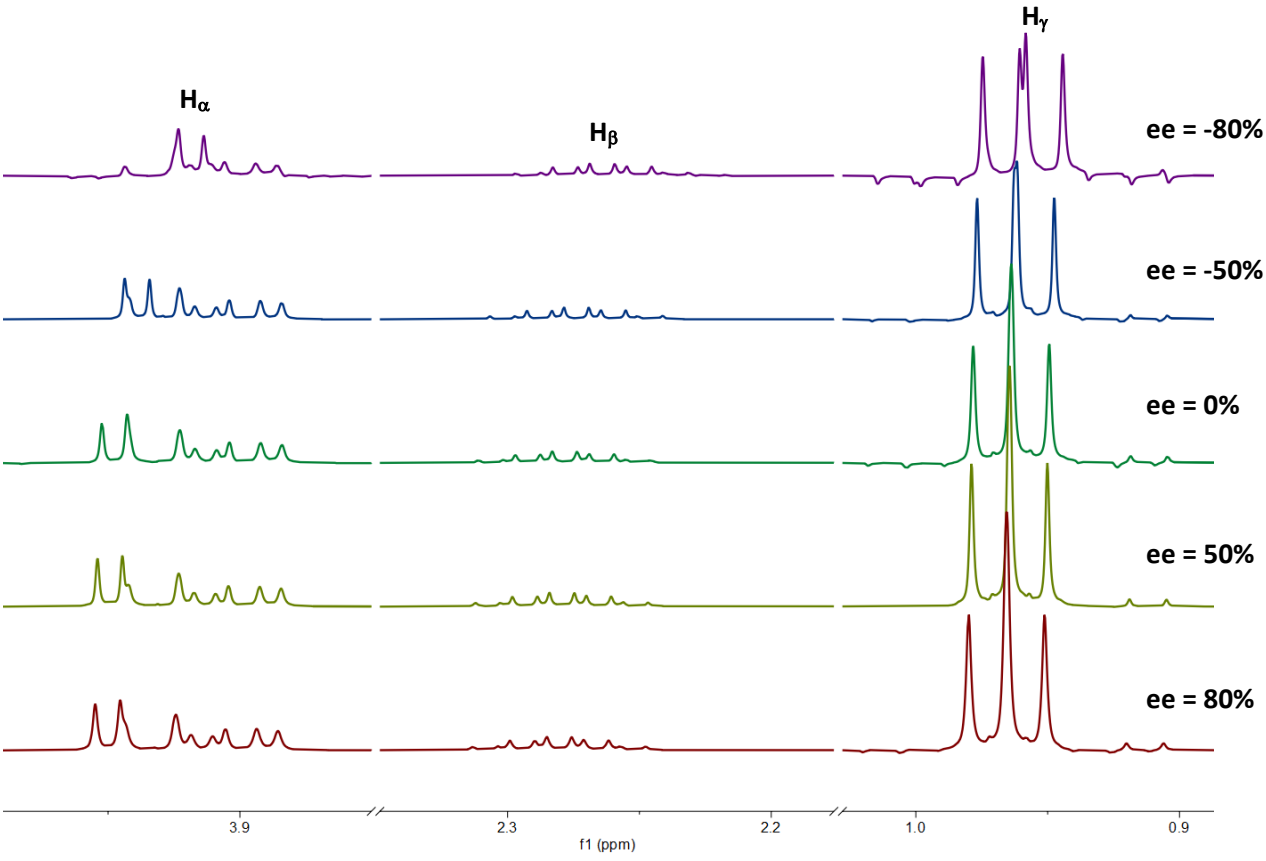
ee	H_α	H_β	H_γ
	Δδ ppm	Δδ ppm	Δδ ppm
-80	-0.0205	-0.0141	-0.0044
-50	-0.008	-0.0041	-0.0016
0	0	0	0
50	0.0017	0.0013	0.0006
80	0.0026	0.002	0.0011

Plot of chemical shift changes of each proton vs ee of the enantiomer mixture:



^{1}H NMR spectra (top – full, bottom – enhanced view on specific receptor protons):



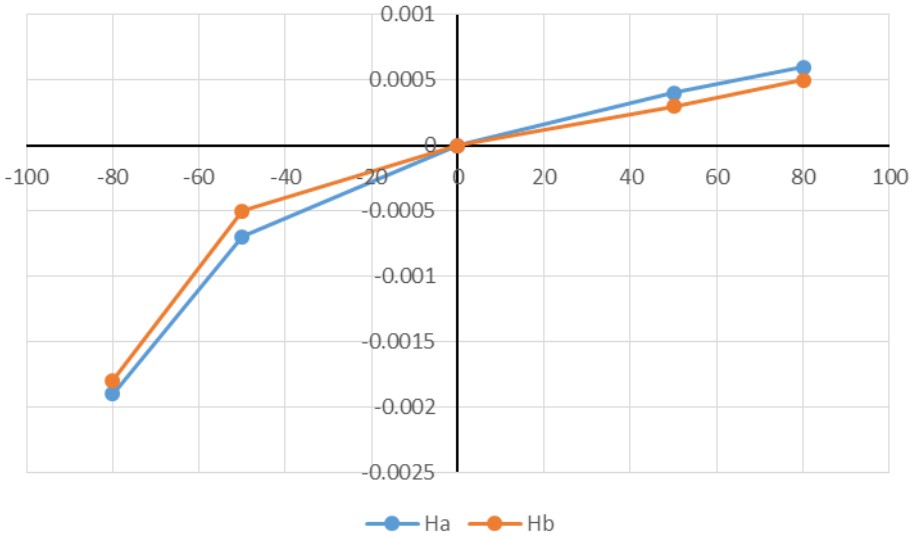


7.2 H-Ala-OMe:

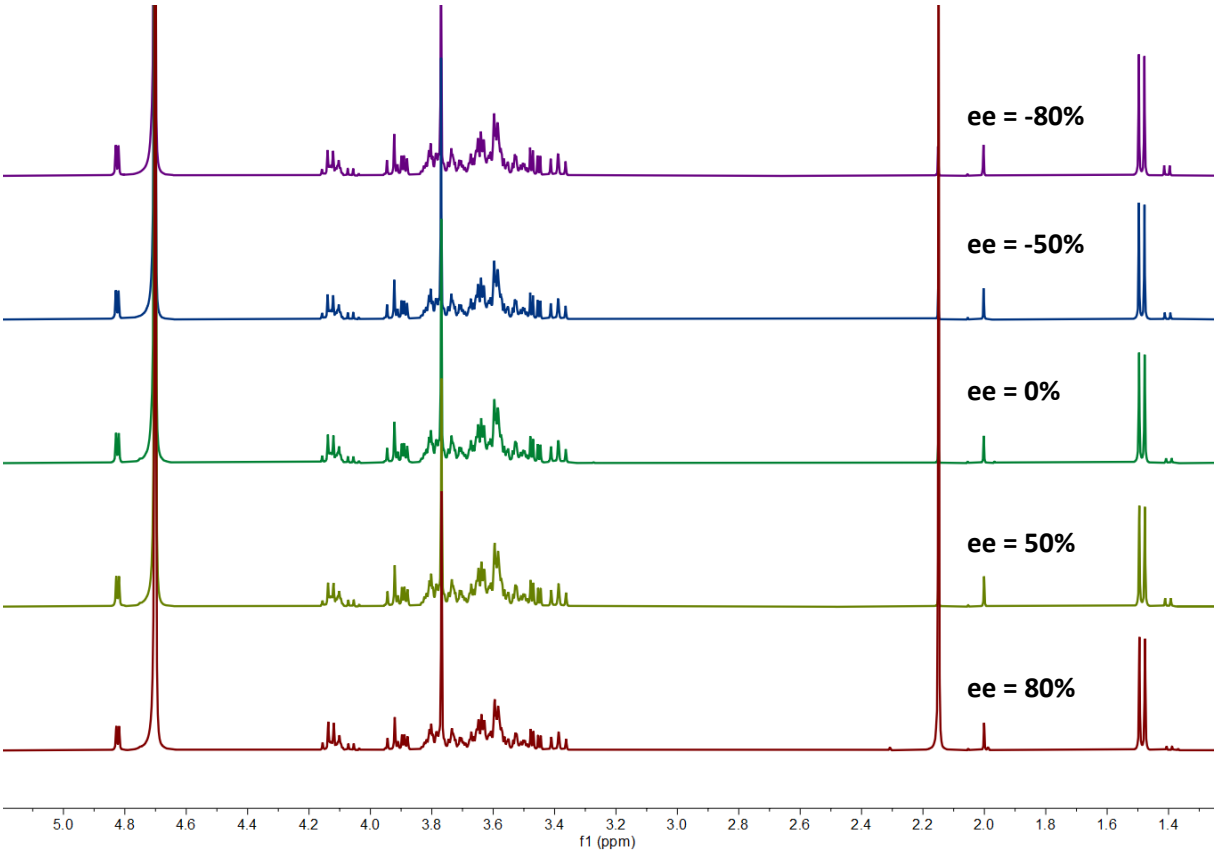
Summary of chemical shift changes of guest protons (H_α, H_β):

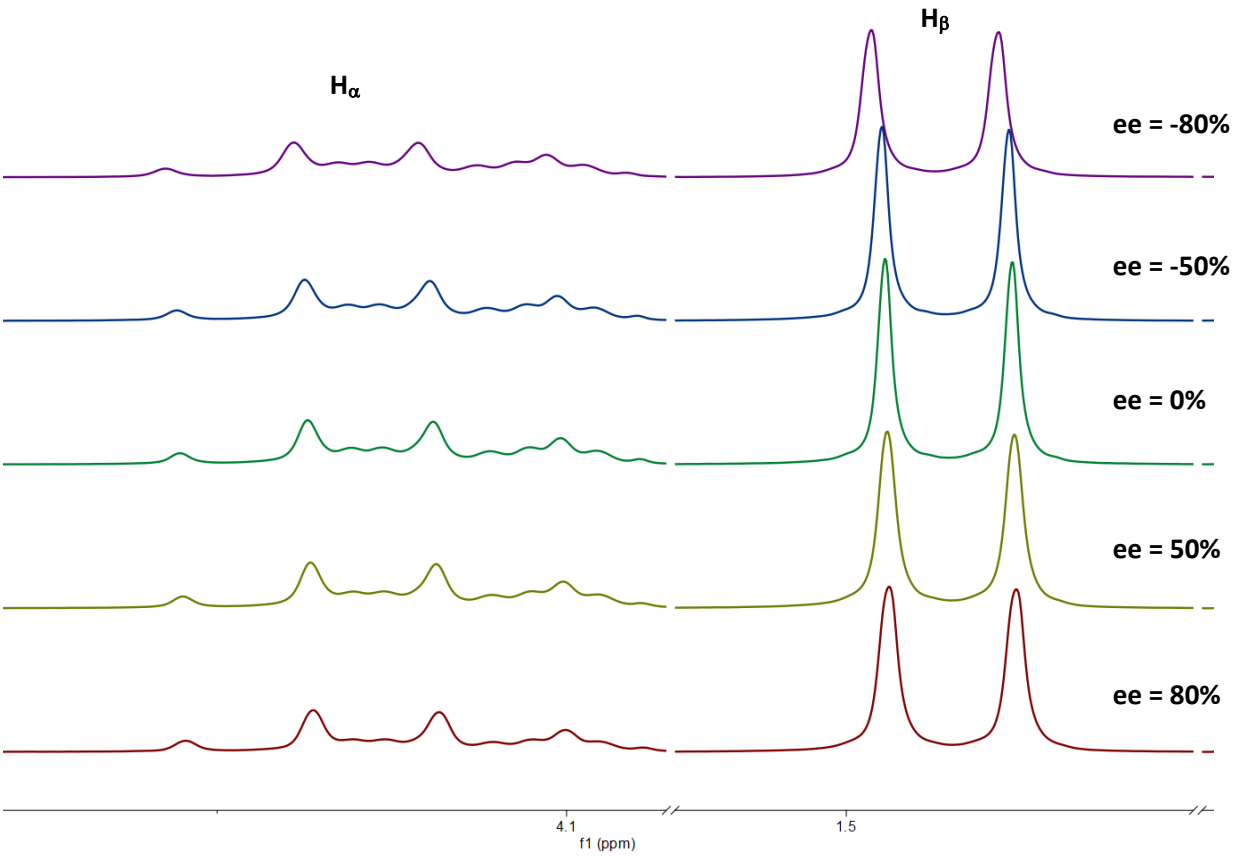
ee	H_α	H_β
	$\Delta\delta$ ppm	$\Delta\delta$ ppm
-80	-0.0019	-0.0018
-50	-0.0007	-0.0005
0	0	0
50	0.0004	0.0003
80	0.0006	0.0005

Plot of chemical shift changes of each proton vs ee of the enantiomer mixture:



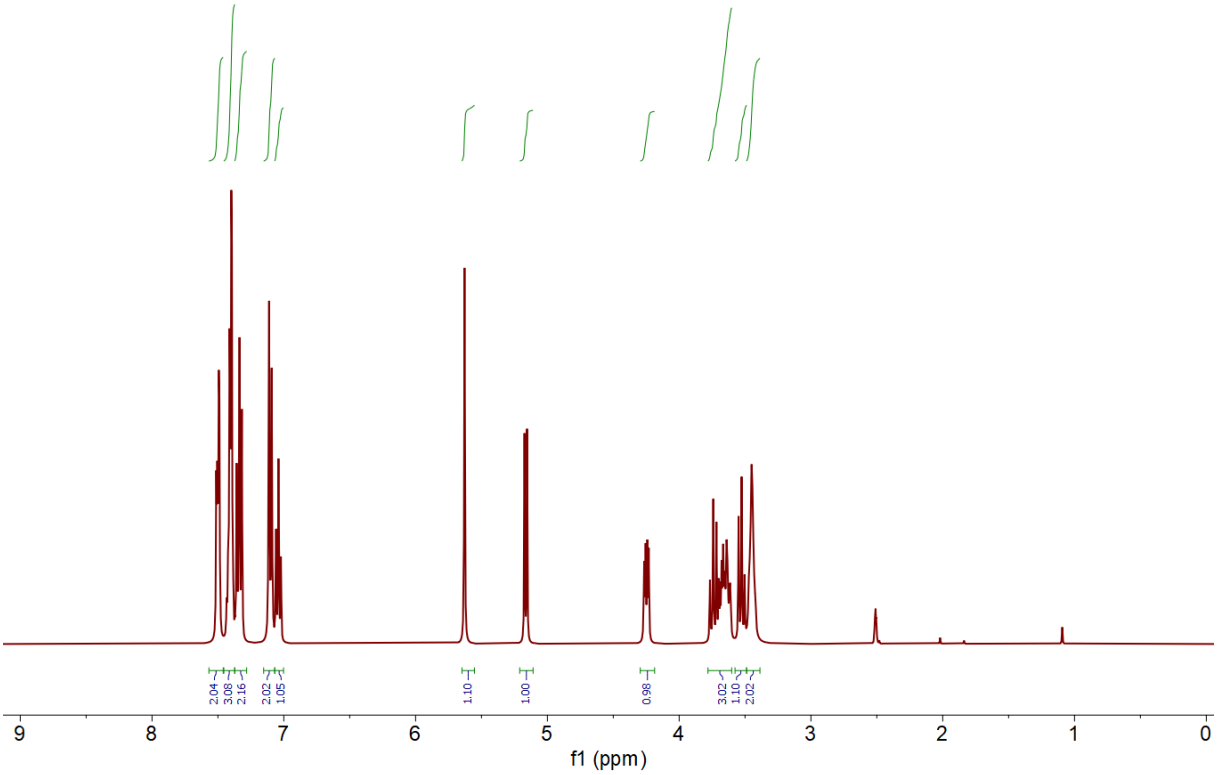
^{1}H NMR spectra (top – full, bottom – enhanced view on specific receptor protons):



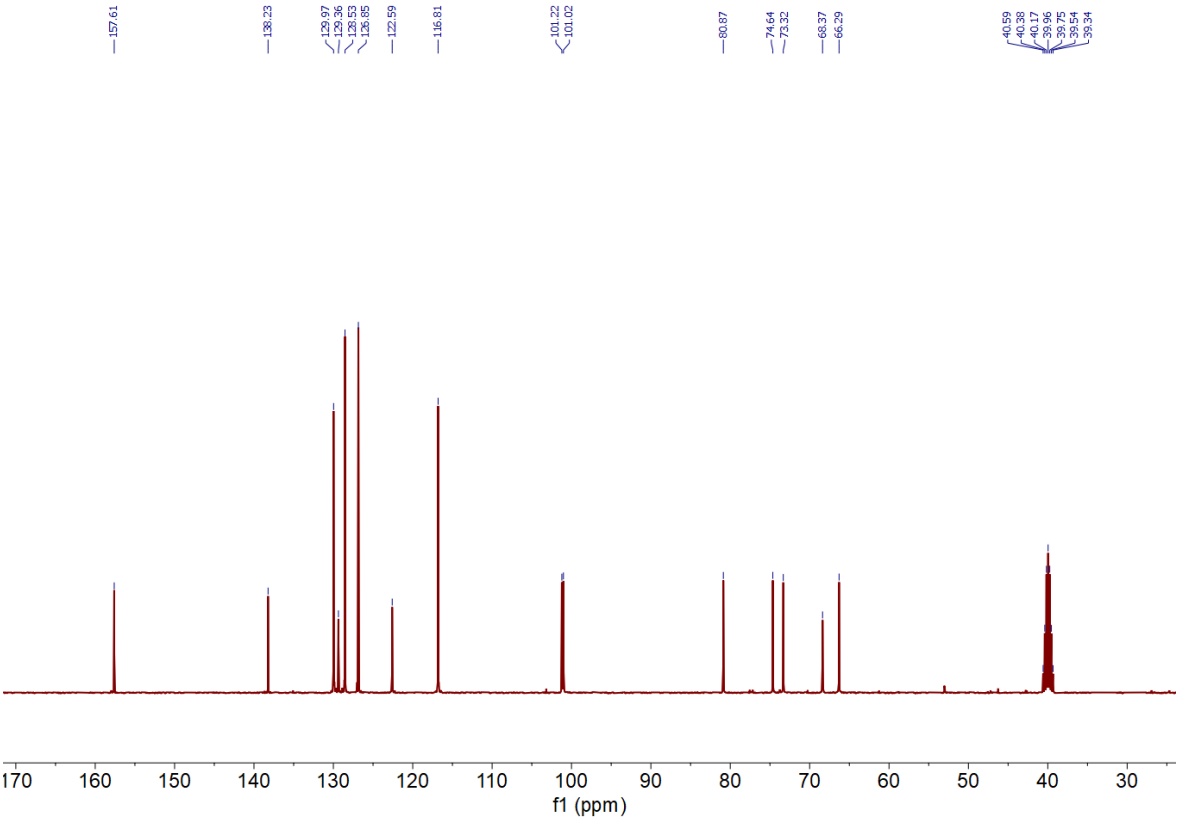


8. NMR spectra - sugar building blocks.

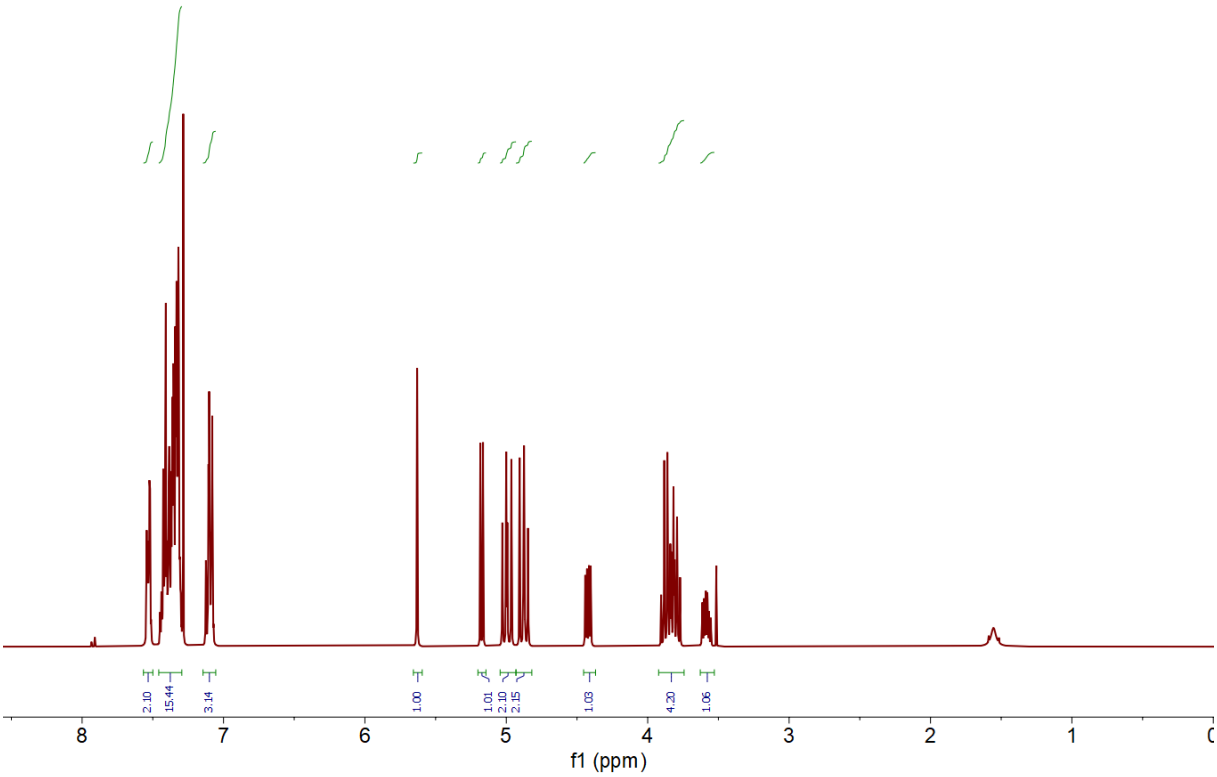
^{1}H NMR spectrum - compound **2**



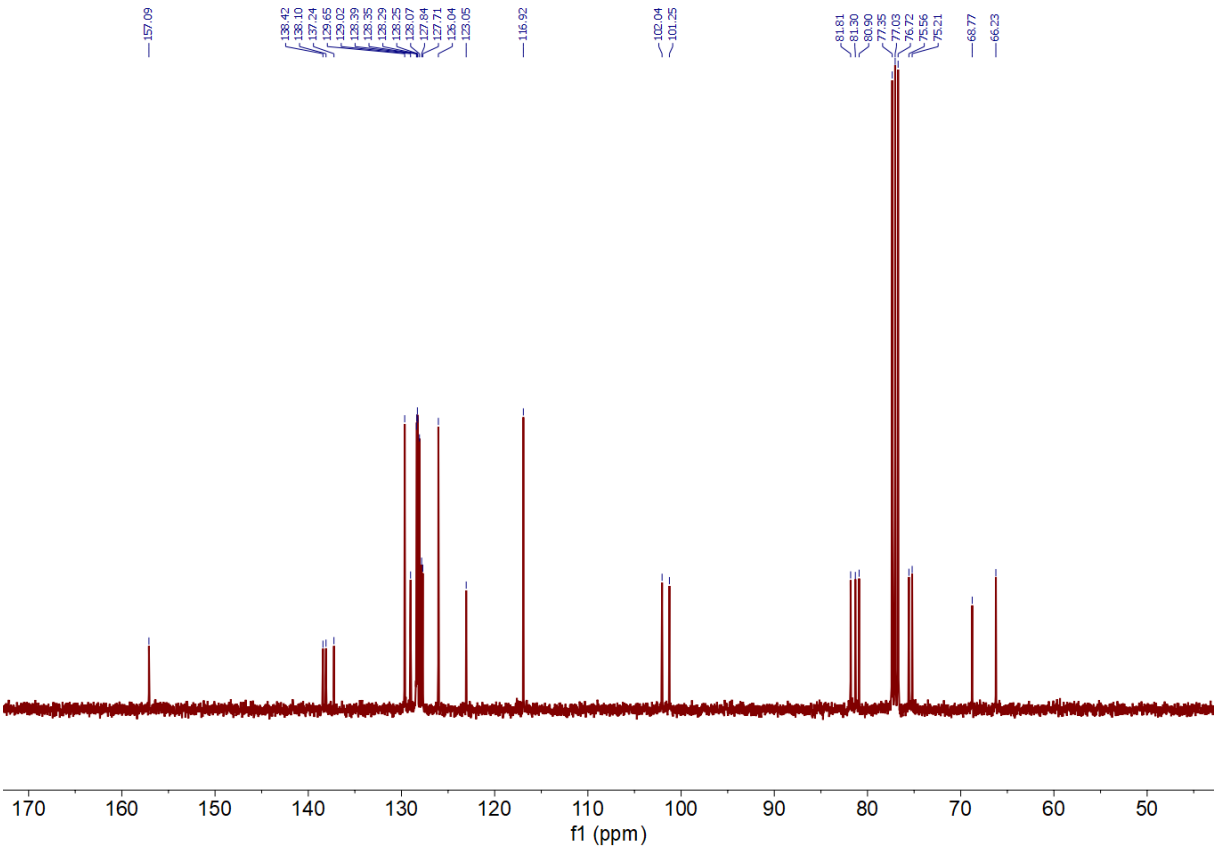
^{13}C NMR spectrum - compound **2**



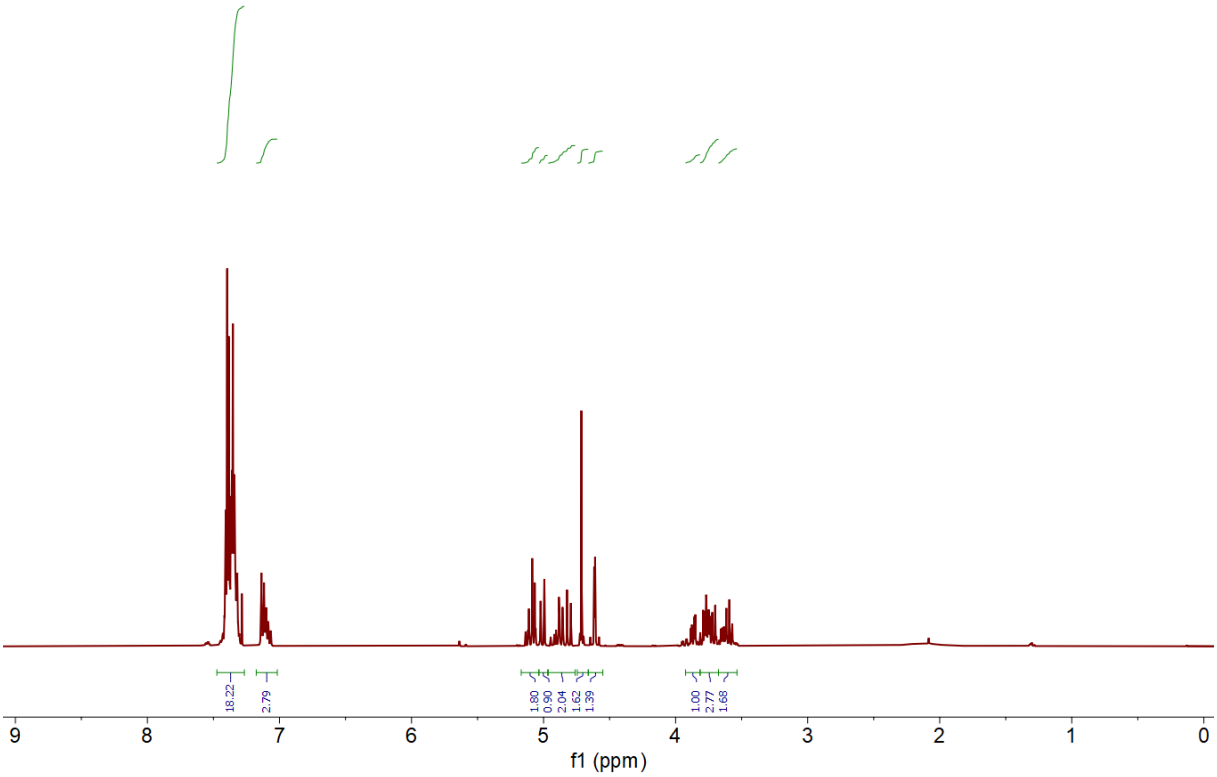
^{1}H NMR spectrum - compound **3**



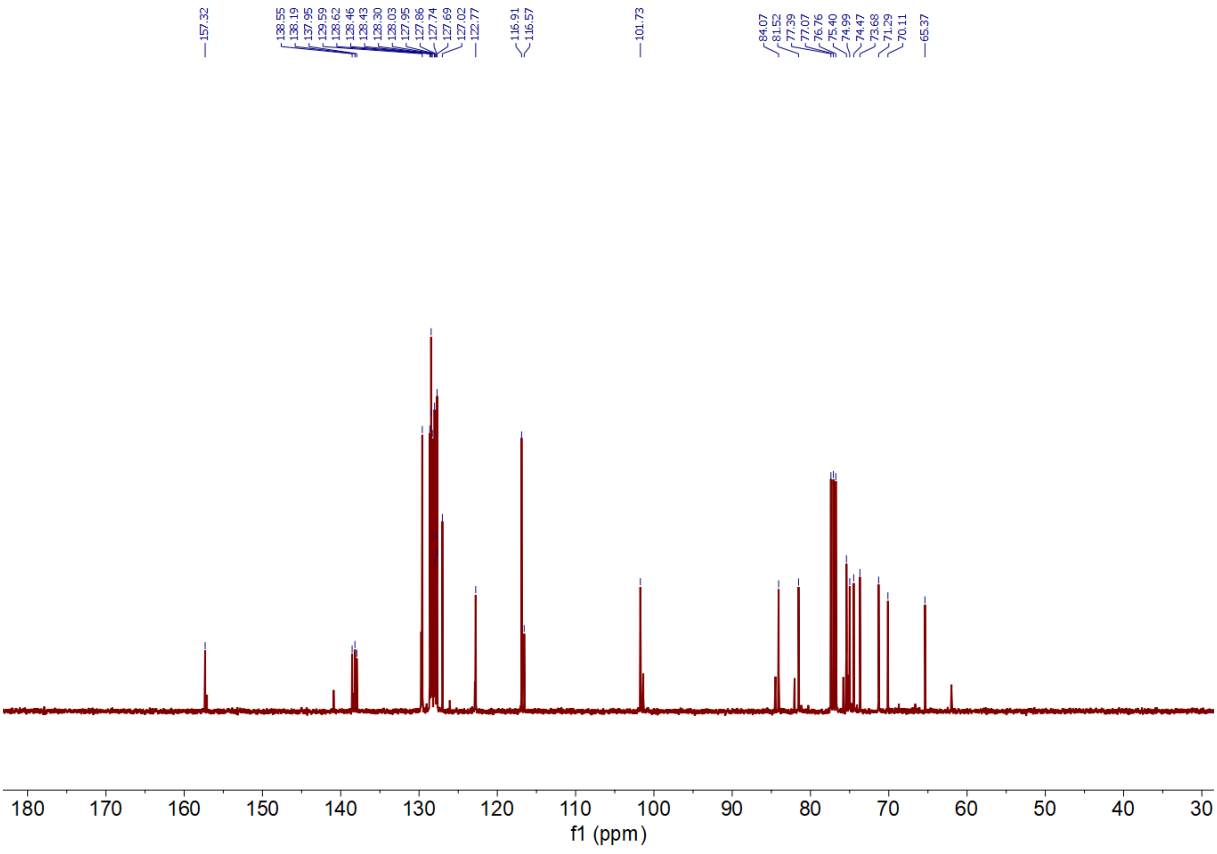
^{13}C NMR spectrum - compound **3**



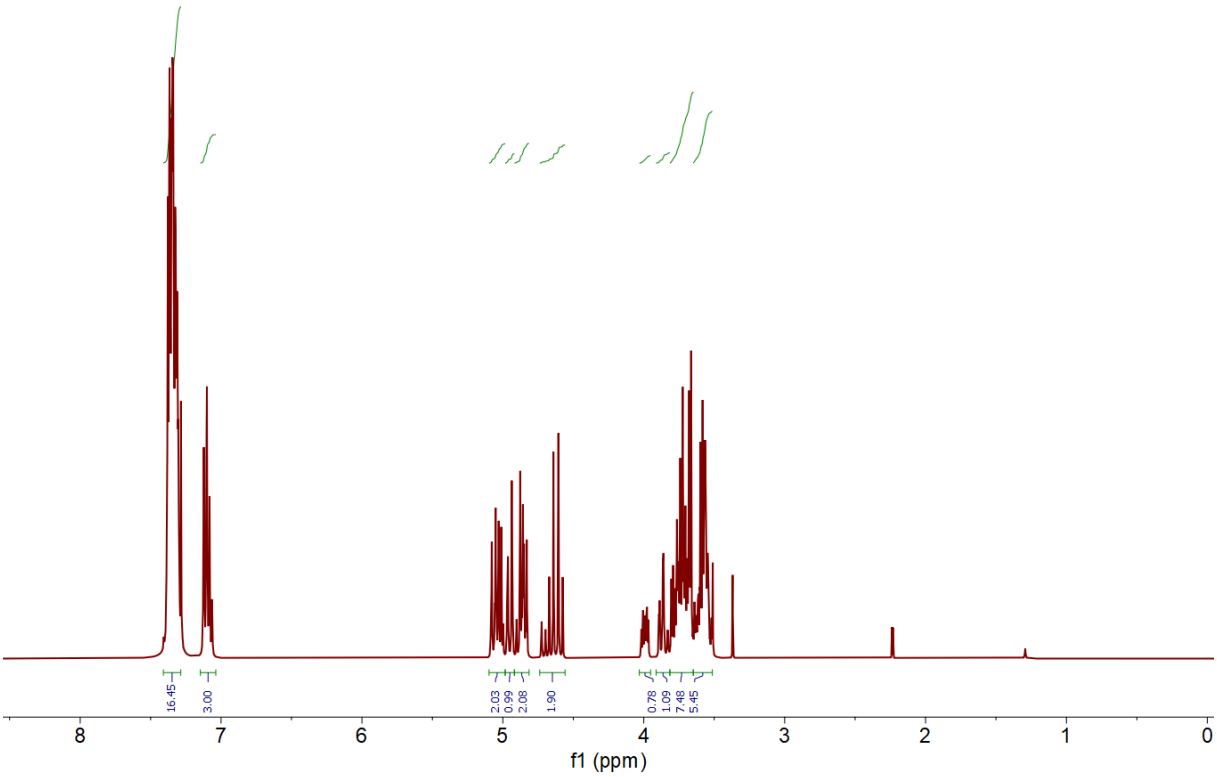
^{1}H NMR spectrum - compound **4**



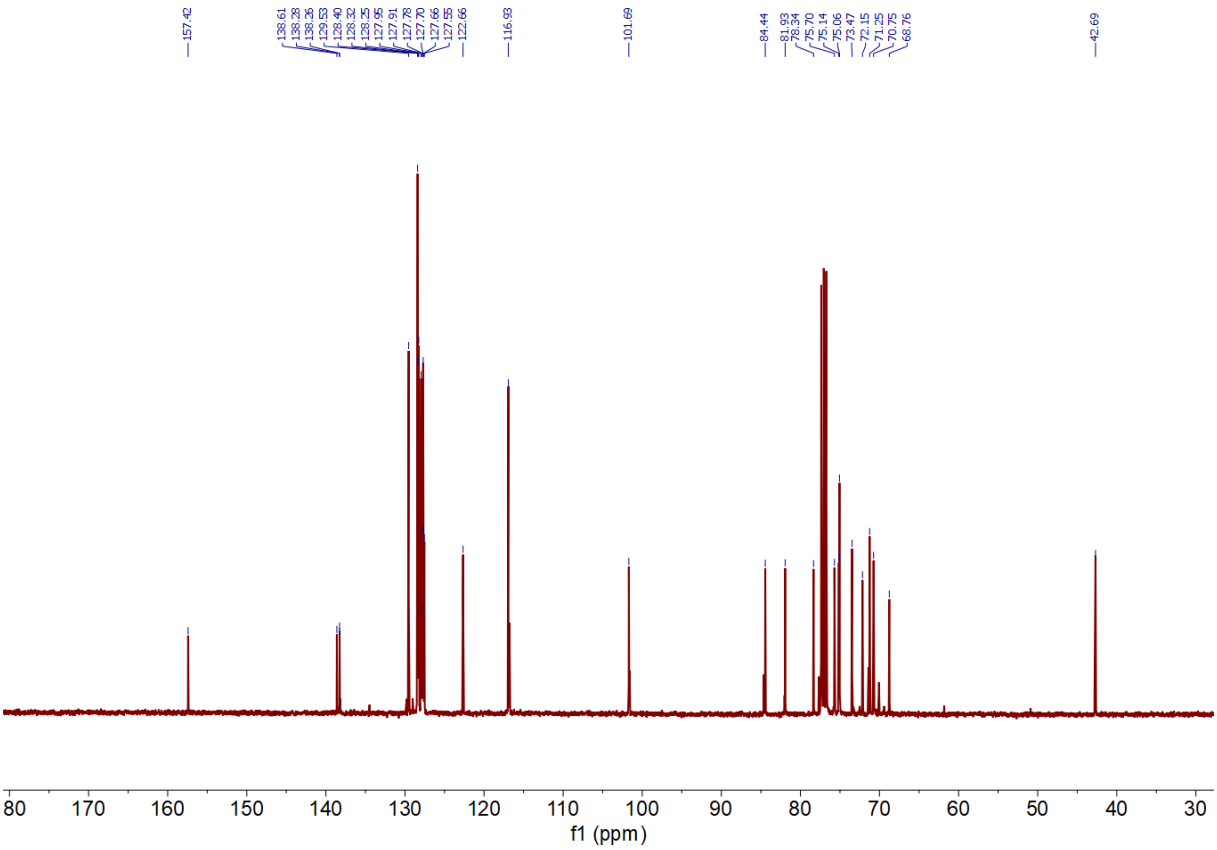
^{13}C NMR spectrum – compound **4**



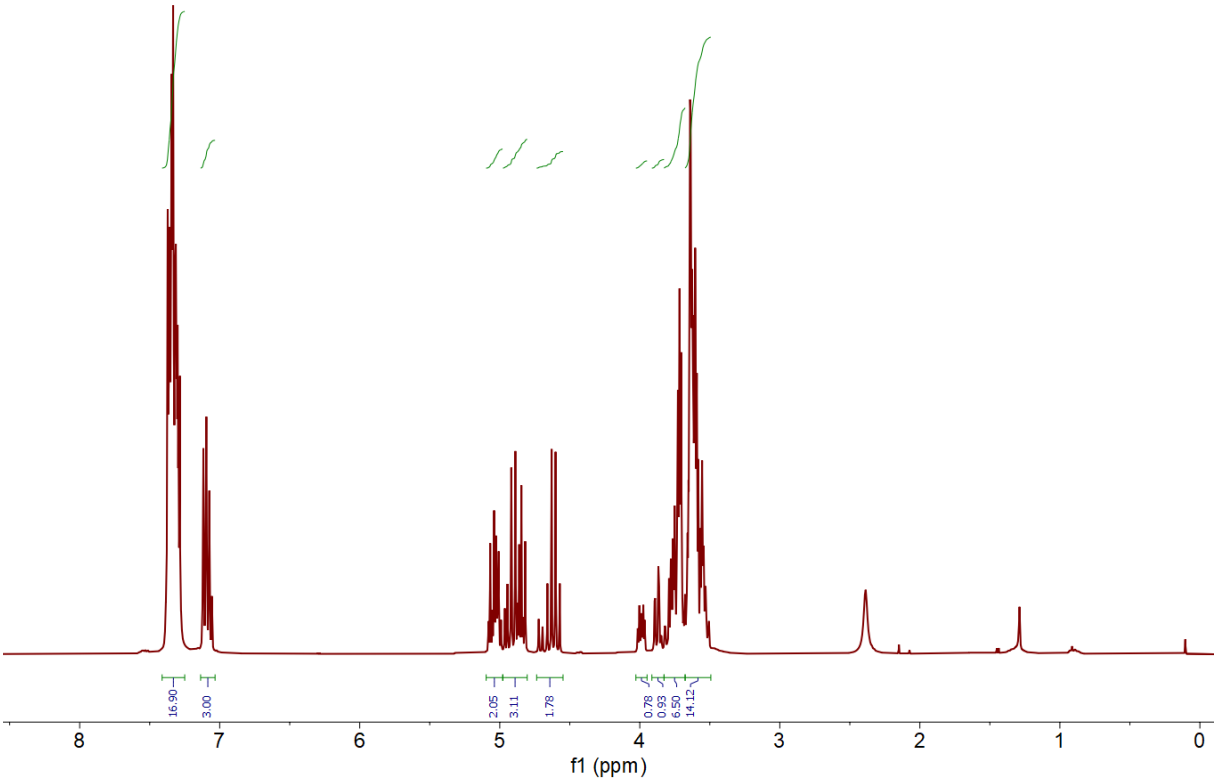
^{1}H NMR spectrum – compound **5**



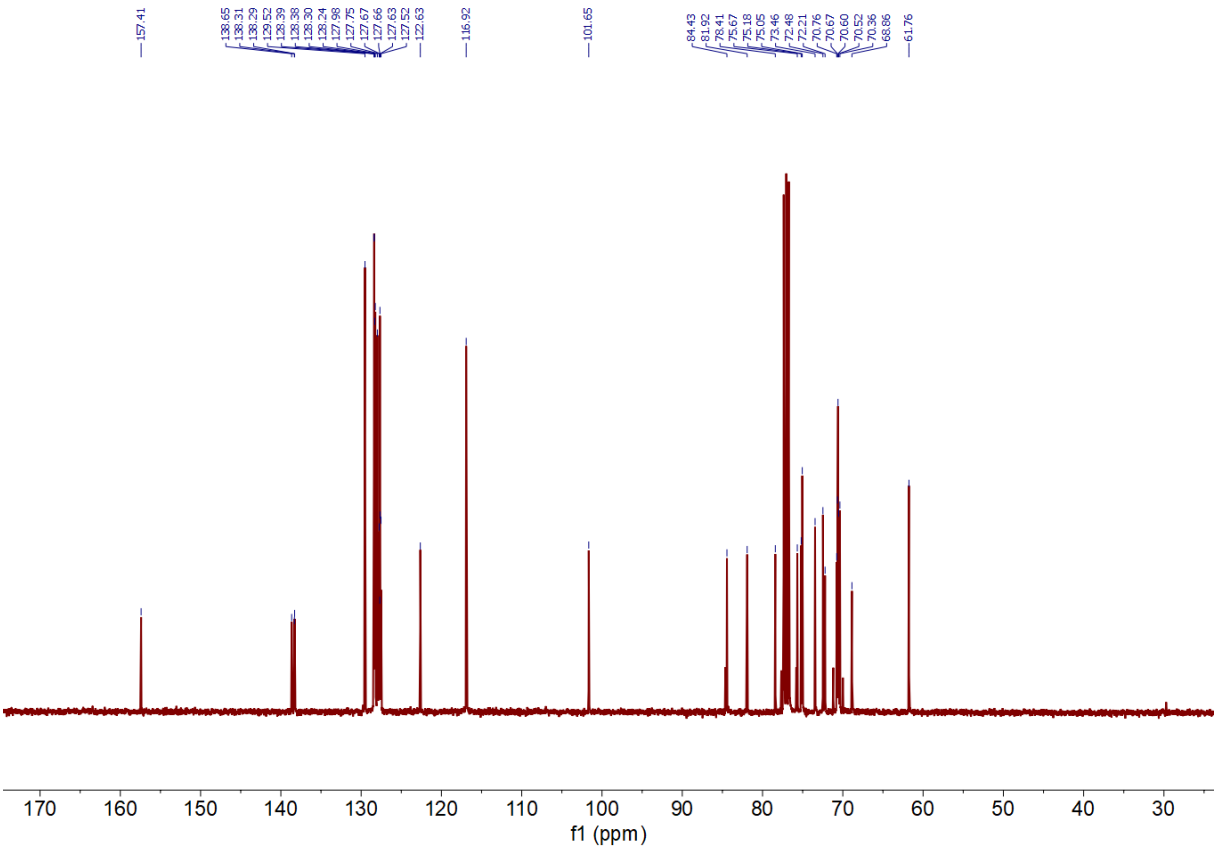
^{13}C NMR spectrum – compound **5**



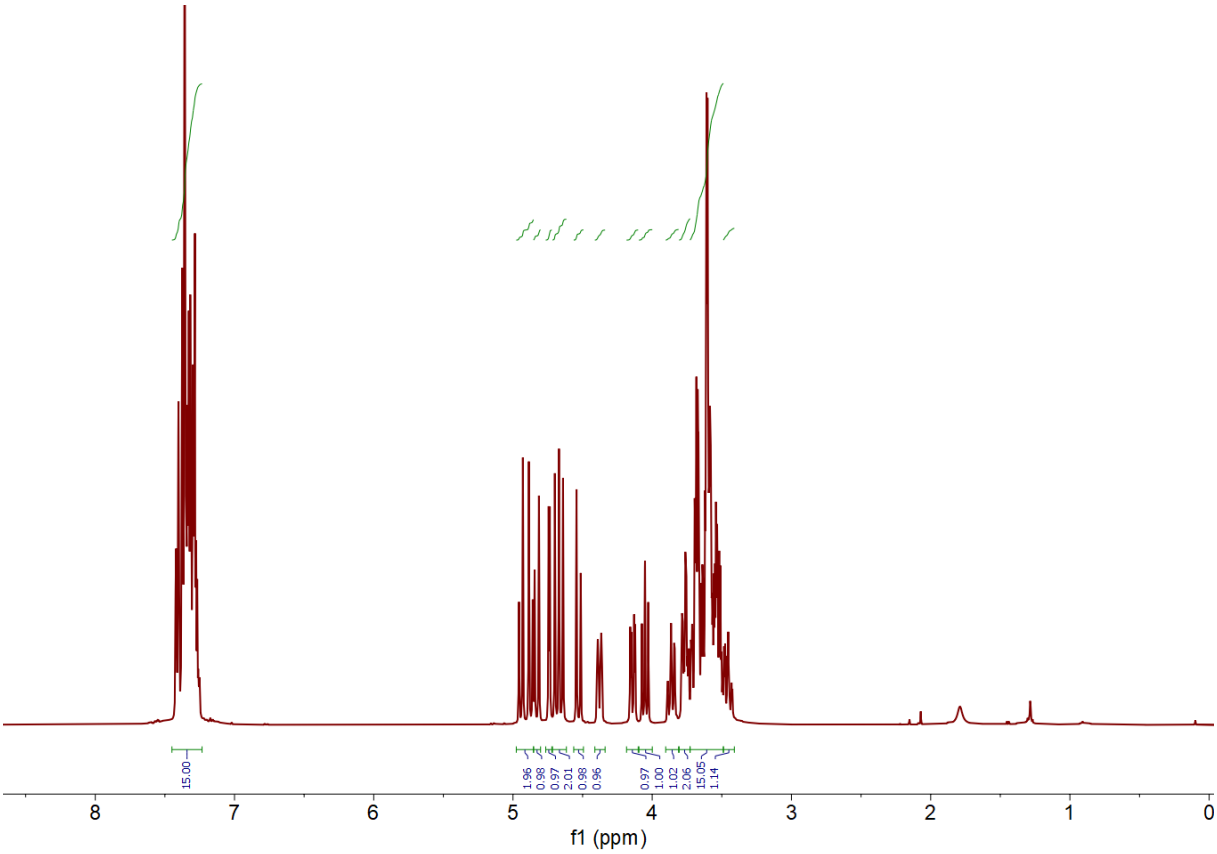
^{1}H NMR spectrum – compound **6**



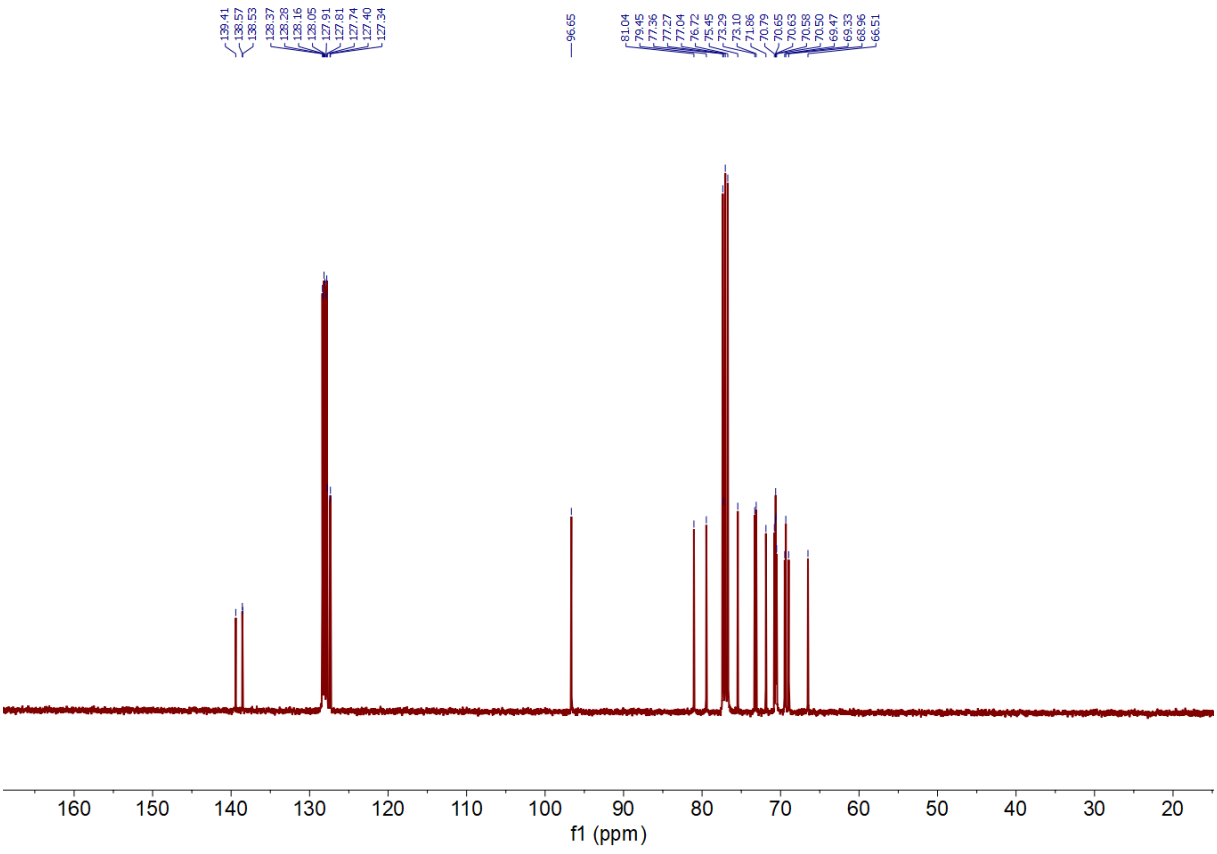
^{13}C NMR spectrum – compound **6**



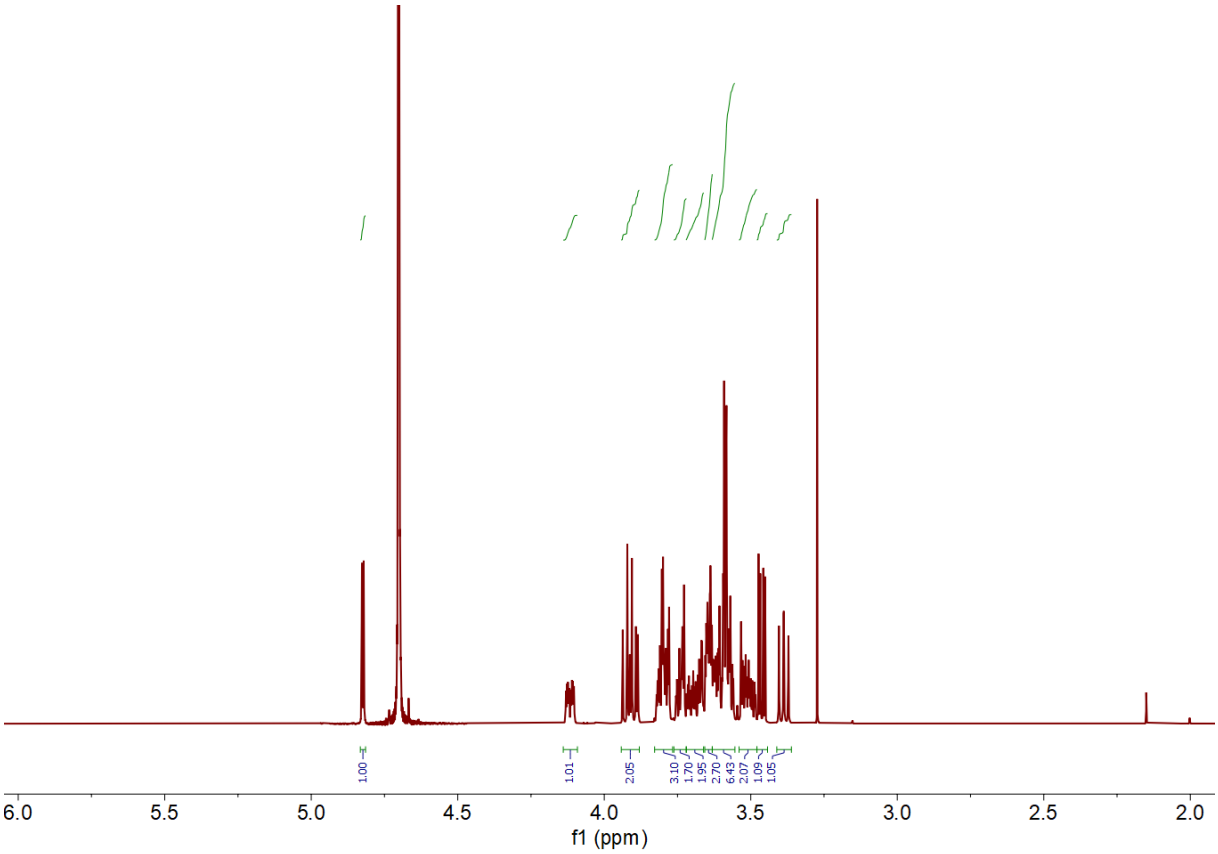
^{1}H NMR spectrum – compound **7**



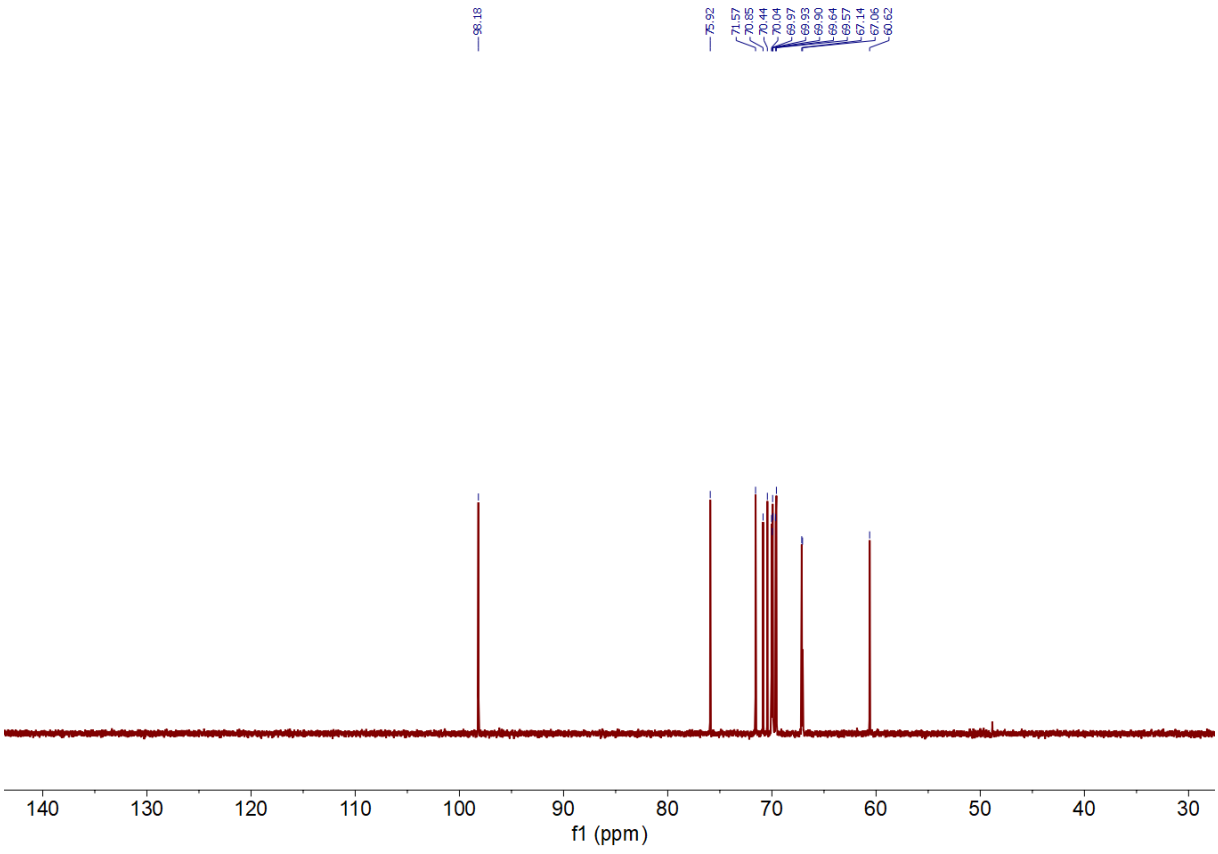
^{13}C NMR spectrum – compound **7**



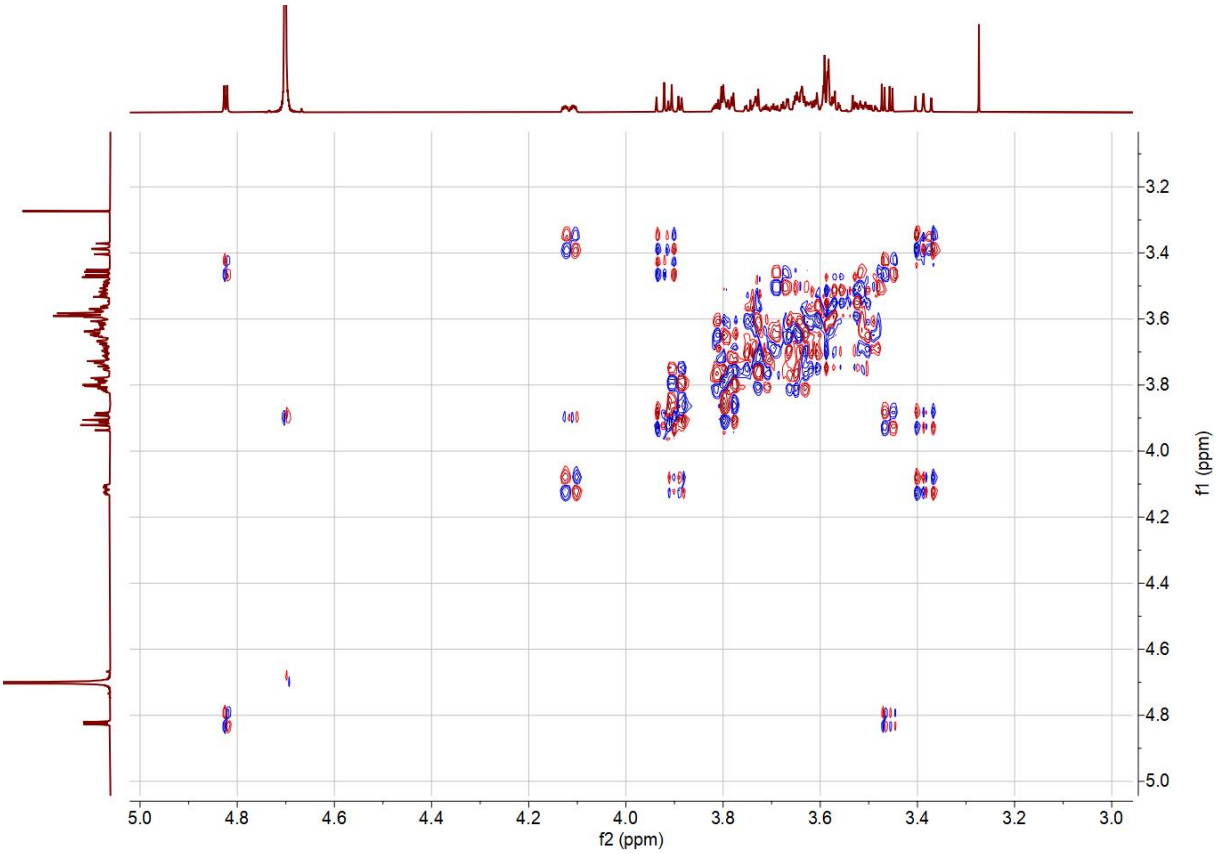
^{1}H NMR spectrum – compound **8**



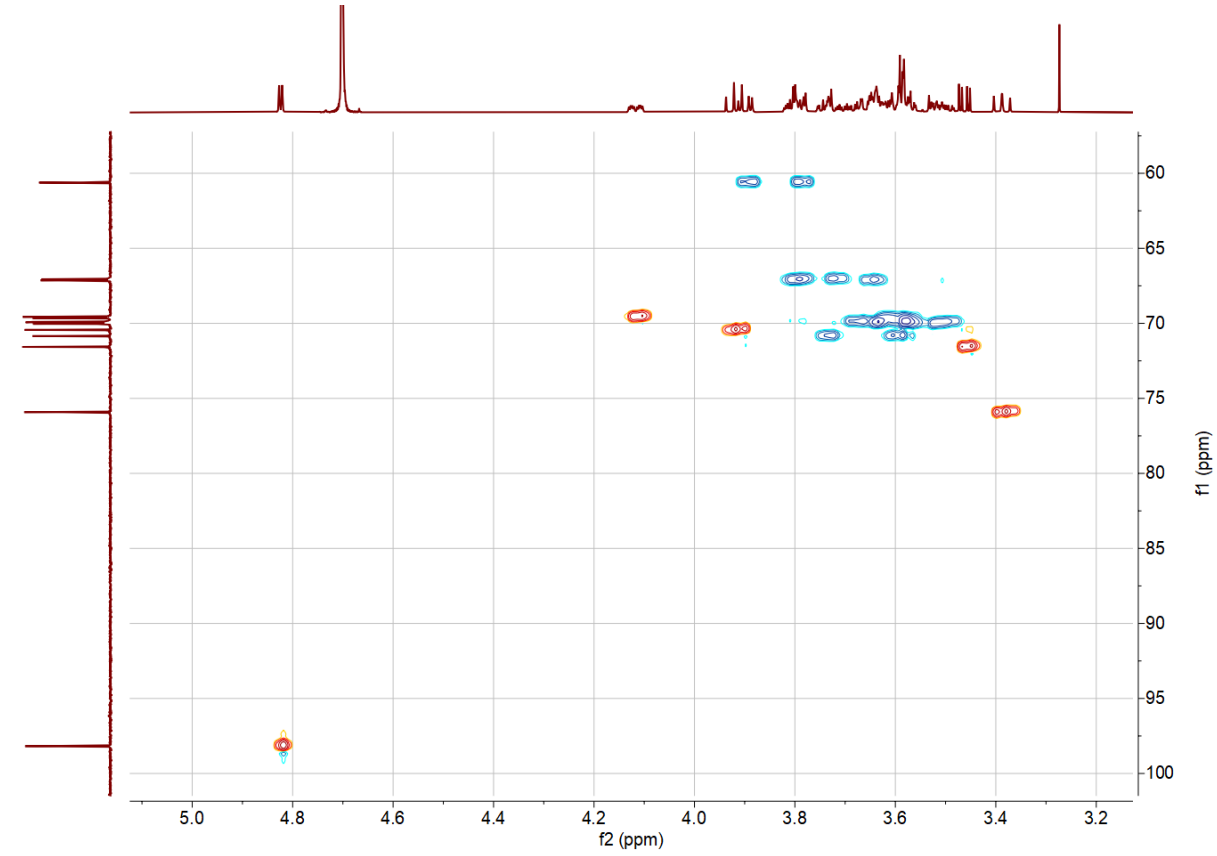
^{13}C NMR spectrum – compound **8**



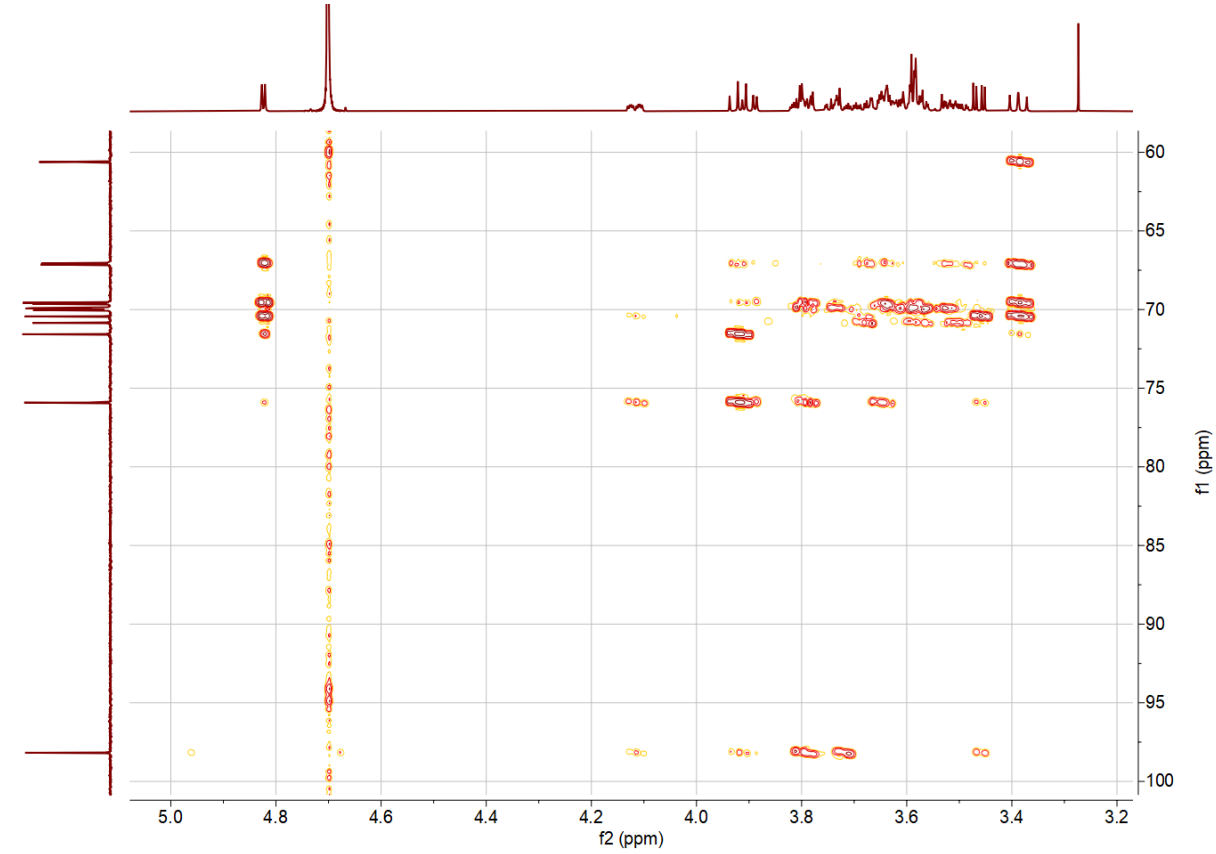
2D COSY spectrum – compound **8**



2D HSQC spectrum – compound **8**



2D HMBC spectrum – compound **8**



2D NOESY spectrum – compound **8**