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# Supporting Information



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# Chiral Recognition Inside a Chiral Cucurbituril – Supporting Information

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**Experimental Section.** The guests used in this study were prepared by the literature procedures or purchased from commercial suppliers and were used without further purification. Melting points were measured on a Meltemp apparatus in open capillary tubes and are uncorrected. IR spectra were recorded on commercial spectrophotometers as KBr pellets and are reported in $cm^{-1}$. NMR spectra were measured on spectrometers operating at 400 or 500 MHz for $^{1}H$ and 100 or 125 MHz for $^{13}C$. Mass spectrometry was performed using a VG 7070E magnetic sector instrument by fast atom bombardment (FAB) using the indicated matrix or on a JEOL AccuTOF electrospray instrument. Computational results were obtained using Spartan 02 running on a Macintosh personal computer. UV/Vis titrations were performed on a Cary 100 UV/Vis instrument with 1cm pathlength cells at 298K and analyzed using Associate v. 1.6.[1] $^{1}H$ NMR competition experiments were performed in the manner described in detail previously.[2,3]

**Trimer 1 and (±)-Bis-*ns*-CB[6].** A mixture of glycoluril (1.420 g, 9.99 mmol), paraformaldehyde (0.450 g, 14.99 mmol), and conc. HCl (8 mL) was heated at 80 °C for 30 minutes. The reaction mixture was cooled to room temperature and poured into methanol to give a precipitate. The precipitate was collected and washed with acetone to give an off-white solid. The solid was dried overnight under high vacuum. Chromatography on Dowex ion exchange resin (1:1 formic acid:HCl (aq.)) gave samples containing trimer **1** and (±)-bis-ns-CB[6]. These fractions were separately recrystallized from $CF_3CO_2H$ to give pure trimer **1** (50 mg, 0.105 mmol, 3%) and pure (±)-bis-ns-CB[6] (75 mg, 0.077 mmol, 5%). **Trimer 1**. M.p. > 300 °C. IR (KBr, $cm^{-1}$): 3334s, 2994w, 2920w, 1715s, 1465s, 1379s, 1229s, 1184s, 968s . $^{1}H$ NMR (400 MHz, 35% DCl): 5.69 (d, $J$ = 9.0, 2H), 5.58 (d, $J$ = 9.0, 2H), 5.53 (s, 2H), 5.38 (d, $J$ = 15.6, 4H), 4.36 (d, $J$ = 15.6, 4H). $^{13}C$ NMR (100 MHz, 35% DCl): 159.4, 158.3 (q, $J$ = 36, $CF_3\mathit{C}O_2H$), 155.8, 113.6 (q, $J$ = 290, $\mathit{C}F_3CO_2H$), 74.2, 69.9. 62.5, 50.9. ES-MS: $m/z$ 475 (100, $[M + H]^+$). HR-MS (ES-MS): $m/z$ 475.1540 ($[M + H]^+$, $C_{16}H_{19}N_{12}O_6$, calcd 475.1551). X-ray crystal structure. **(±)-Bis-*ns*-CB[6].** M.p. > 300 °C. IR (KBr, $cm^{-1}$): 3338m, 2994w, 2931w, 1717s, 1475s, 1418m, 1380m, 1334m, 1237s, 966m. $^{1}H$ NMR (400 MHz, $D_2O$): 5.61 (d, $J$ = 16.0, 4H), 5.55 (d, $J$ = 16.0, 4H), 5.50-5.40 (m, 12H), 4.58 (s, 4H), 4.17 (d, $J$ = 16.0, 4H), 4.15 (d, $J$ = 16.0, 4H). $^{13}C$ NMR (100 MHz, $D_2O$): 162.2 (q, $J$ = 36, $CF_3\mathit{C}O_2H$), 158.4, 157.9, 157.3, 156.9, 155.9, 155.4, 115.6 (q, $J$ = 290, $\mathit{C}F_3CO_2H$), 71.4, 71.2, 69.3, 66.5, 65.4, 65.2, 53.2, 51.9, 50.0, 49.7 (two sets of resonances are observed because TFA is not fully bound). MS (ES): $m/z$ 973 (100, $[M = H]^+$). HR-MS (ES): $m/z$ 1105.2031 ($[M + Cs]^+$), $C_{34}H_{36}N_{24}O_{12}Cs$, calcd. 1105.1999. X-ray crystal structure as the $CF_3CO_2H$ solvate.

**(±)-Bis-*ns*-CB[6] from Trimer 1.** To a solution of trimer **1** (20 mg, 0.041 mmol) in conc. HCl (0.2 mL) was added paraformaldehyde (1.2 mg, 0.041 mmol) at room temperature. After the

reaction mixture was stirred overnight it was poured into MeOH which gave a precipitate. The precipitate was centrifuged, the supernatant decanted, and dried at high vacuum to give a crude solid (20 mg). The crude solid contains 15% (±)-bis-*ns*-CB[6] along with starting material **1** as evidenced by $^{1}$H NMR.

**References:**

[1] B. R. Peterson, Ph.D. Thesis, University of California, Los Angeles, 1994.
[2] S. Liu, C. Ruspic, P. Mukhopadhyay, S. Chakrabarti, P. Y. Zavalij, L. Isaacs, *J. Am. Chem. Soc*. **2005**, *127*, 15959-15967.
[3] W. L. Mock, N.-Y. Shih, *J. Org. Chem*. **1986**, *51*, 4440-4446.

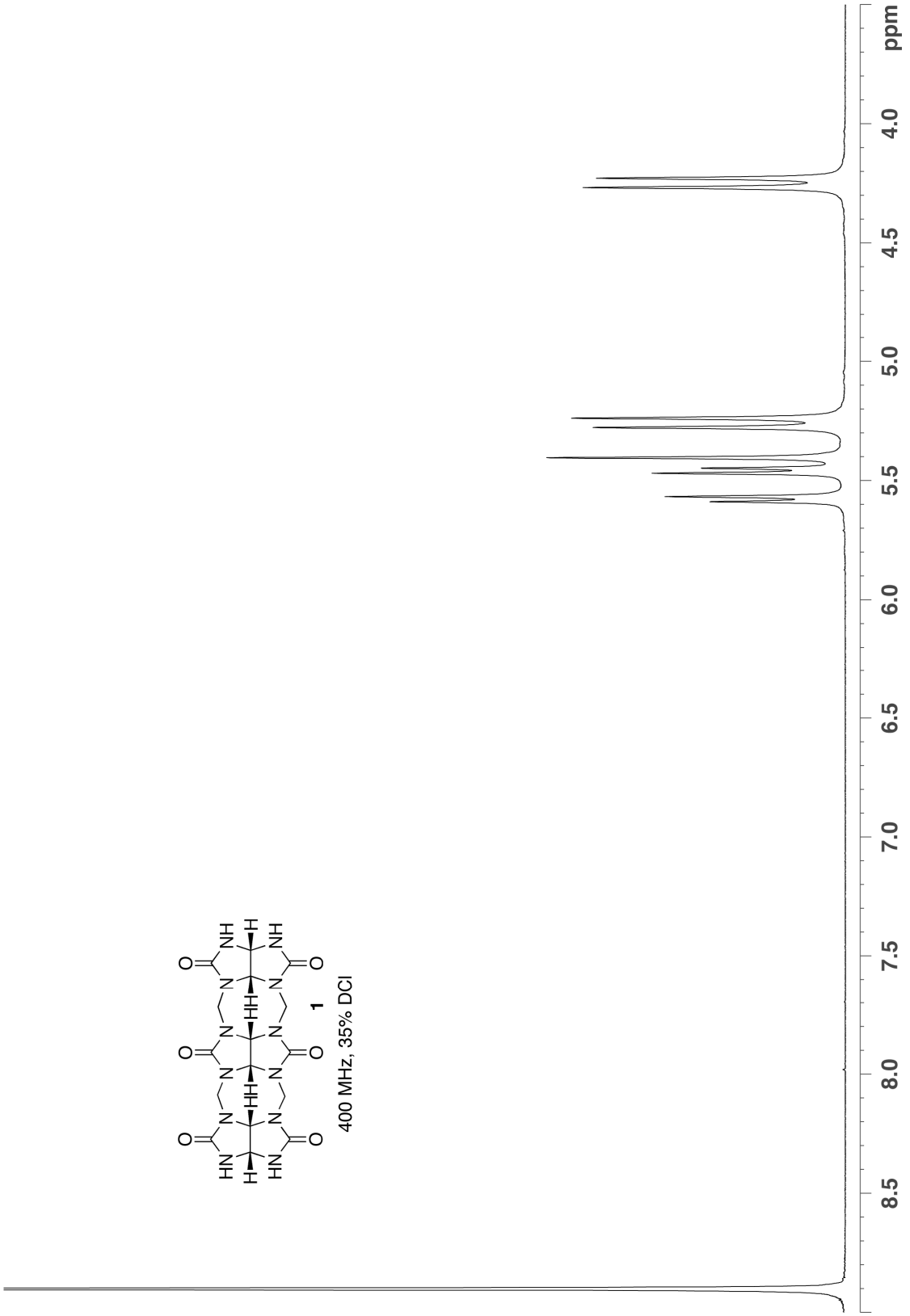


***Figure S1.*** $^{1}$H NMR spectrum recorded (400 MHz, 35% DCl) for **1**.

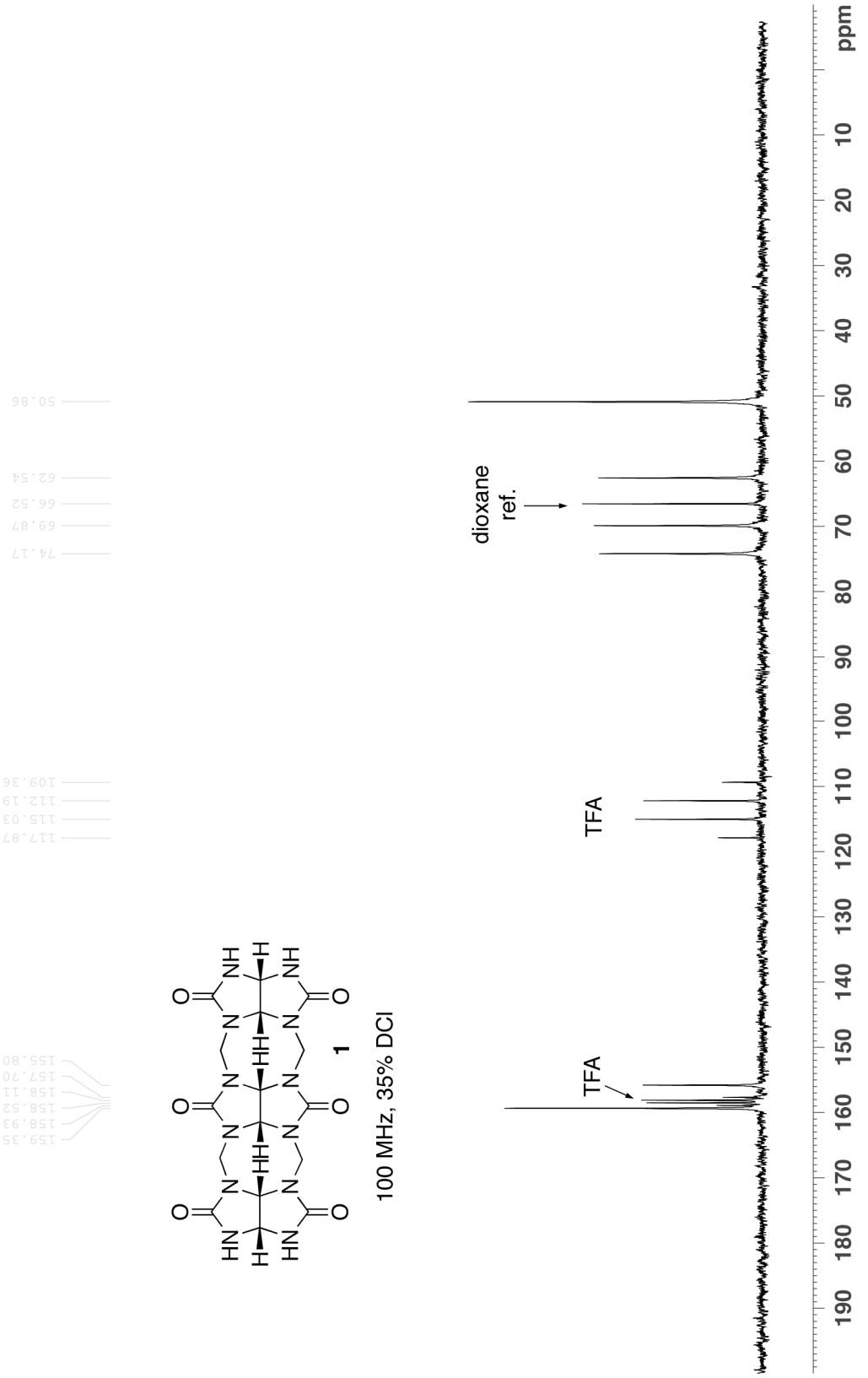


***Figure S2.*** $^{13}$C NMR spectrum recorded (100 MHz, 35% DCl) for **1**.

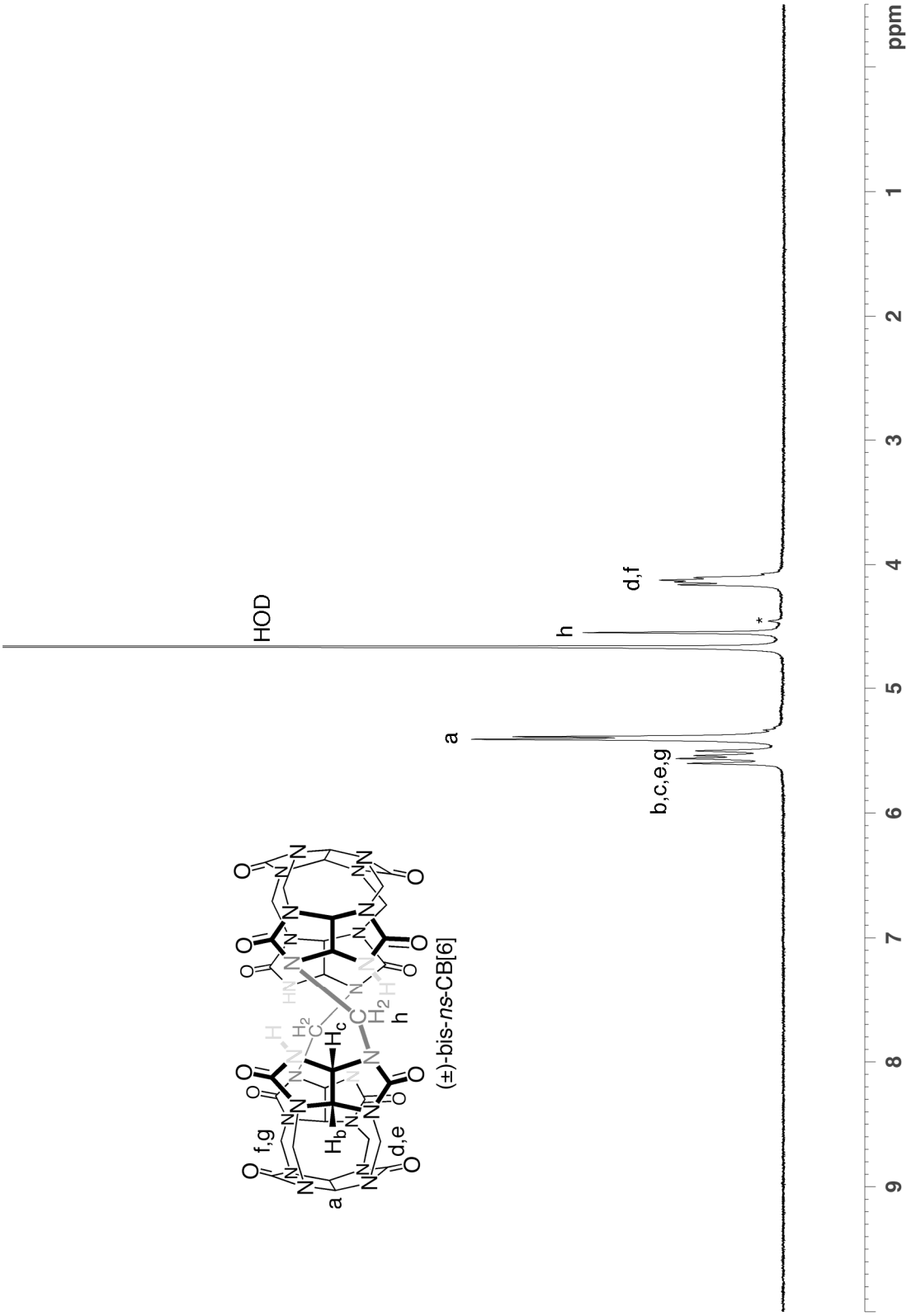


***Figure S3.*** $^{1}$H NMR spectrum recorded (400 MHz, $D_2O$) for (±)-bis-ns-CB[6]. * = bis-ns-CB[6]•TFA arising from TFA of crystallization.

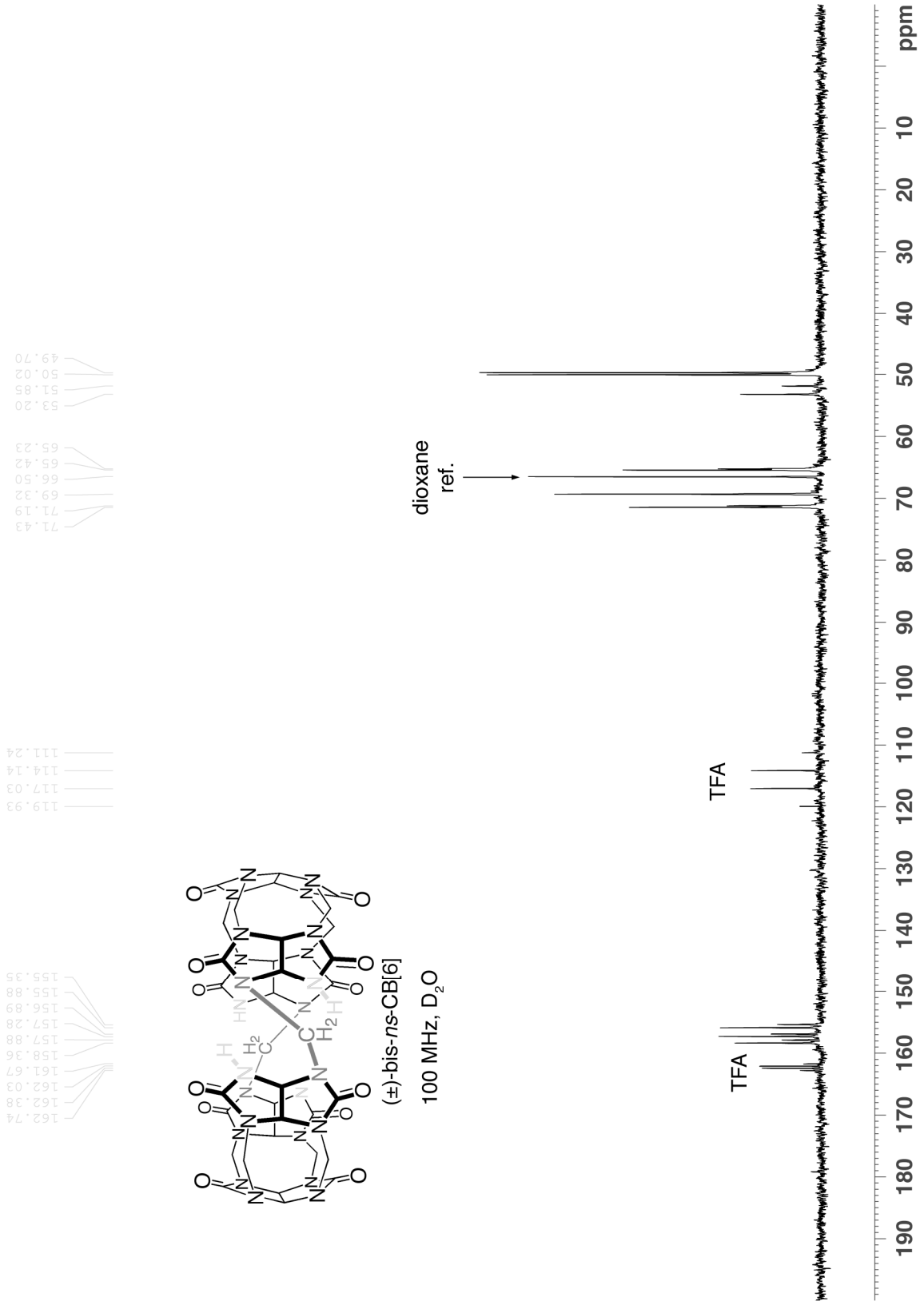


***Figure S4.*** $^{13}$C NMR spectrum recorded (100 MHz, $D_2O$) for (±)-bis-ns-CB[6].

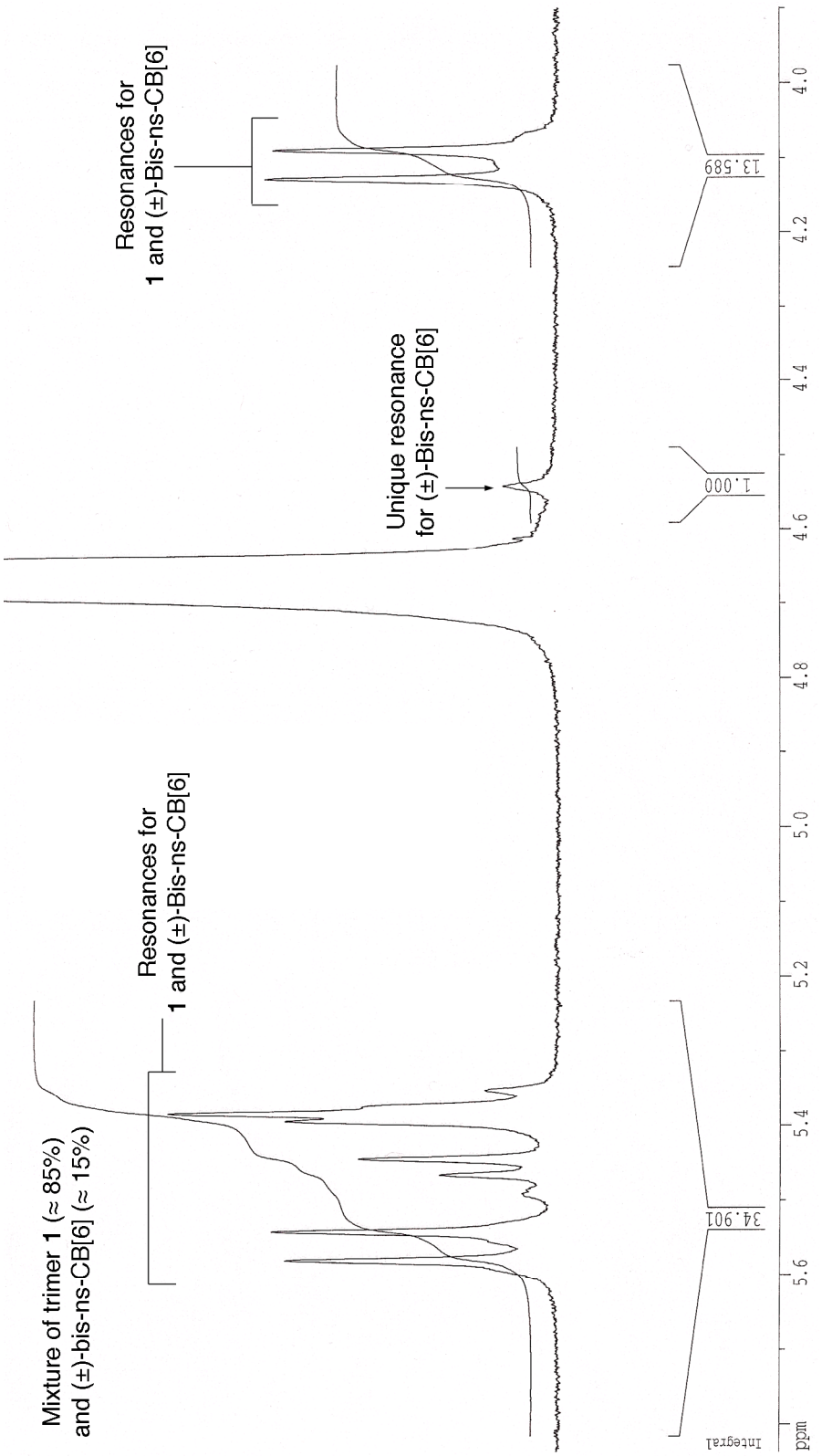


***Figure S5.*** $^{1}$H NMR spectrum (400 MHz, $D_2O$) for a mixture of trimer **1** and (±)-bis-ns-CB[6] (≈15%) obtained by the condensation of trimer with paraformaldehyde in HCl at RT.

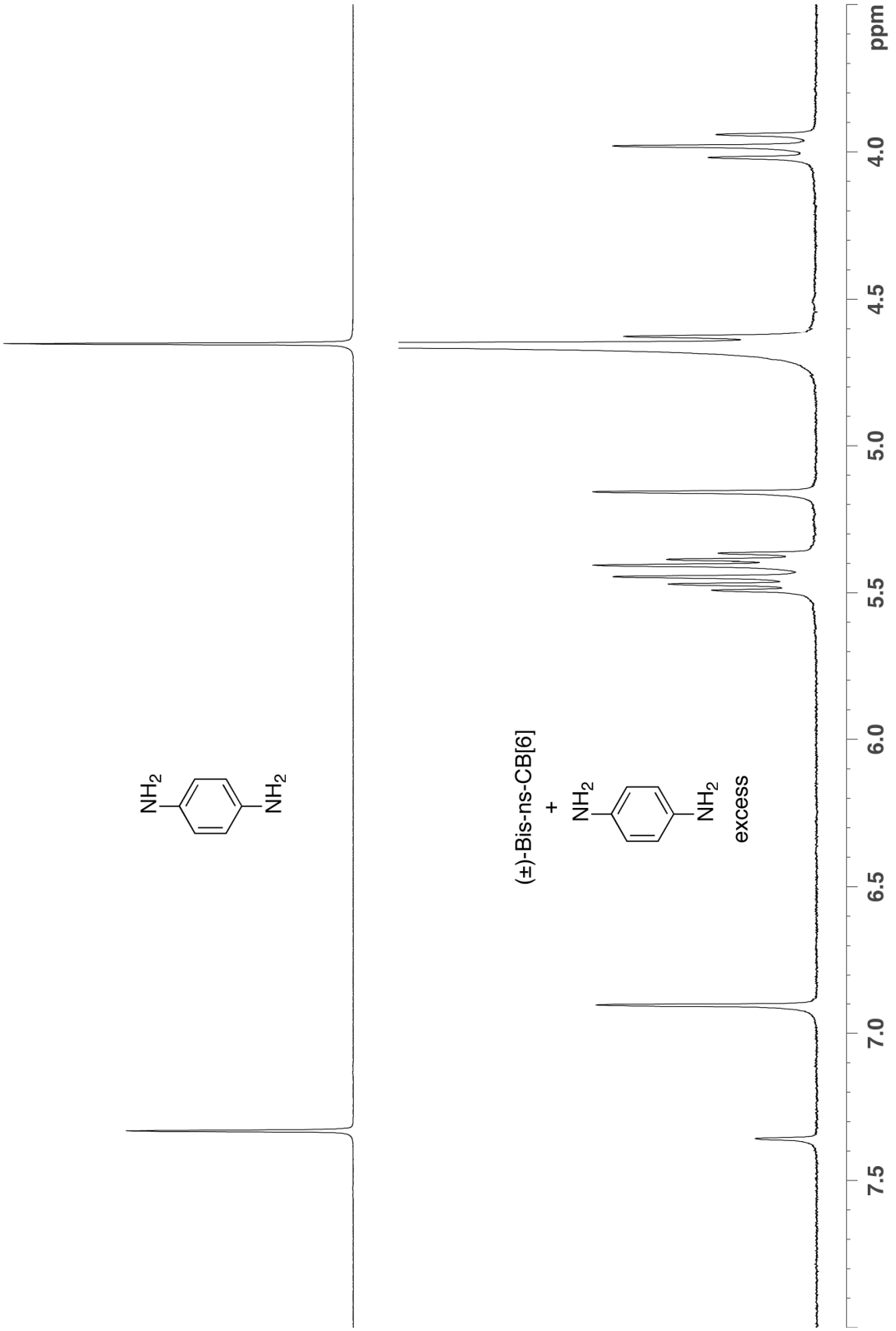


***Figure S6.*** $^{1}$H NMR spectrum recorded (400 MHz, $D_2O$) for: (left) phenylene diamine, and (right) (±)-bis-ns-CB[6] and excess phenylene diamine.

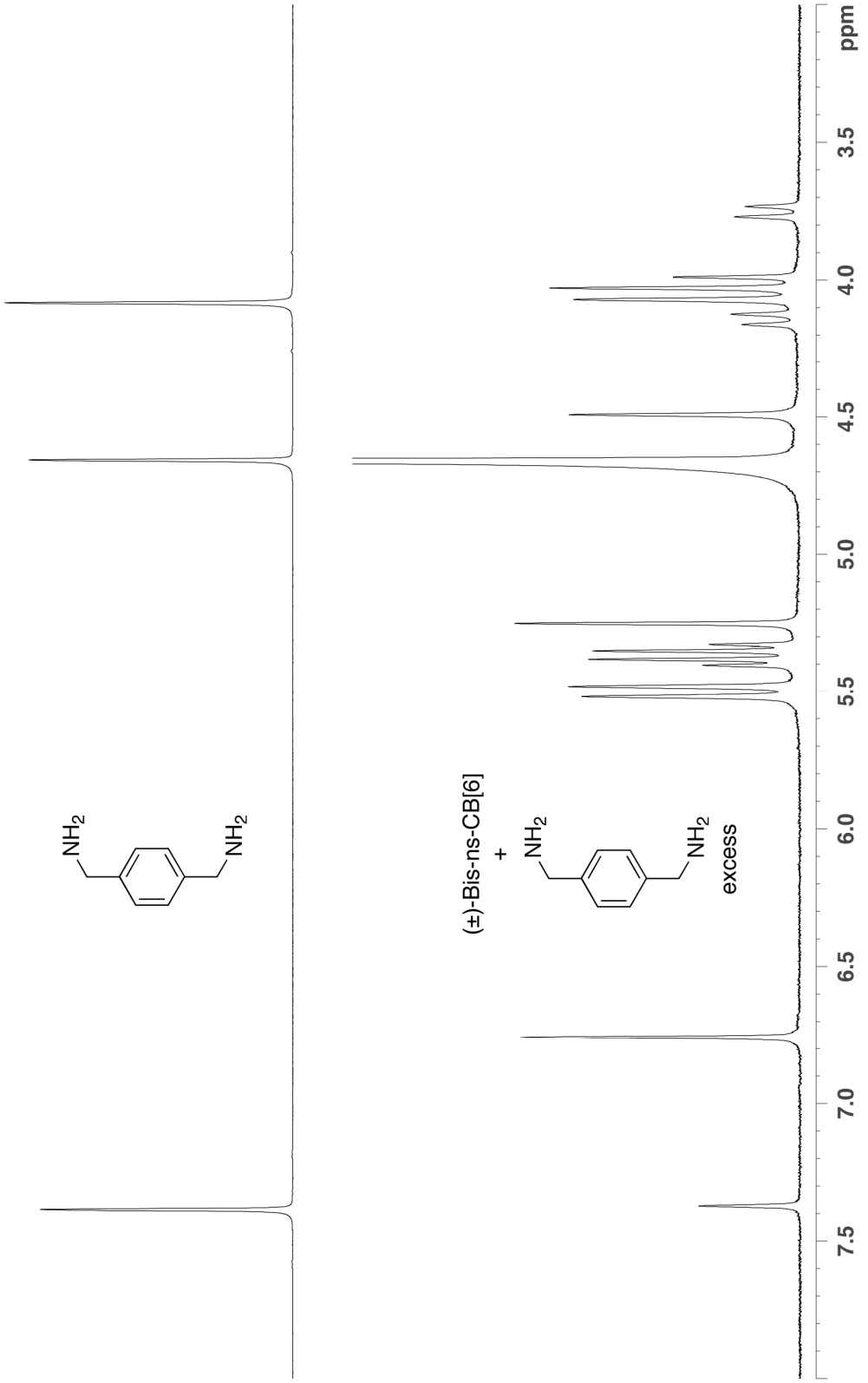


***Figure S7.*** $^{1}$H NMR spectrum recorded (400 MHz, $D_2O$) for: (left) p-xylylenediamine, and (right) (±)-bis-ns-CB[6] and excess p-xylylenediamine.

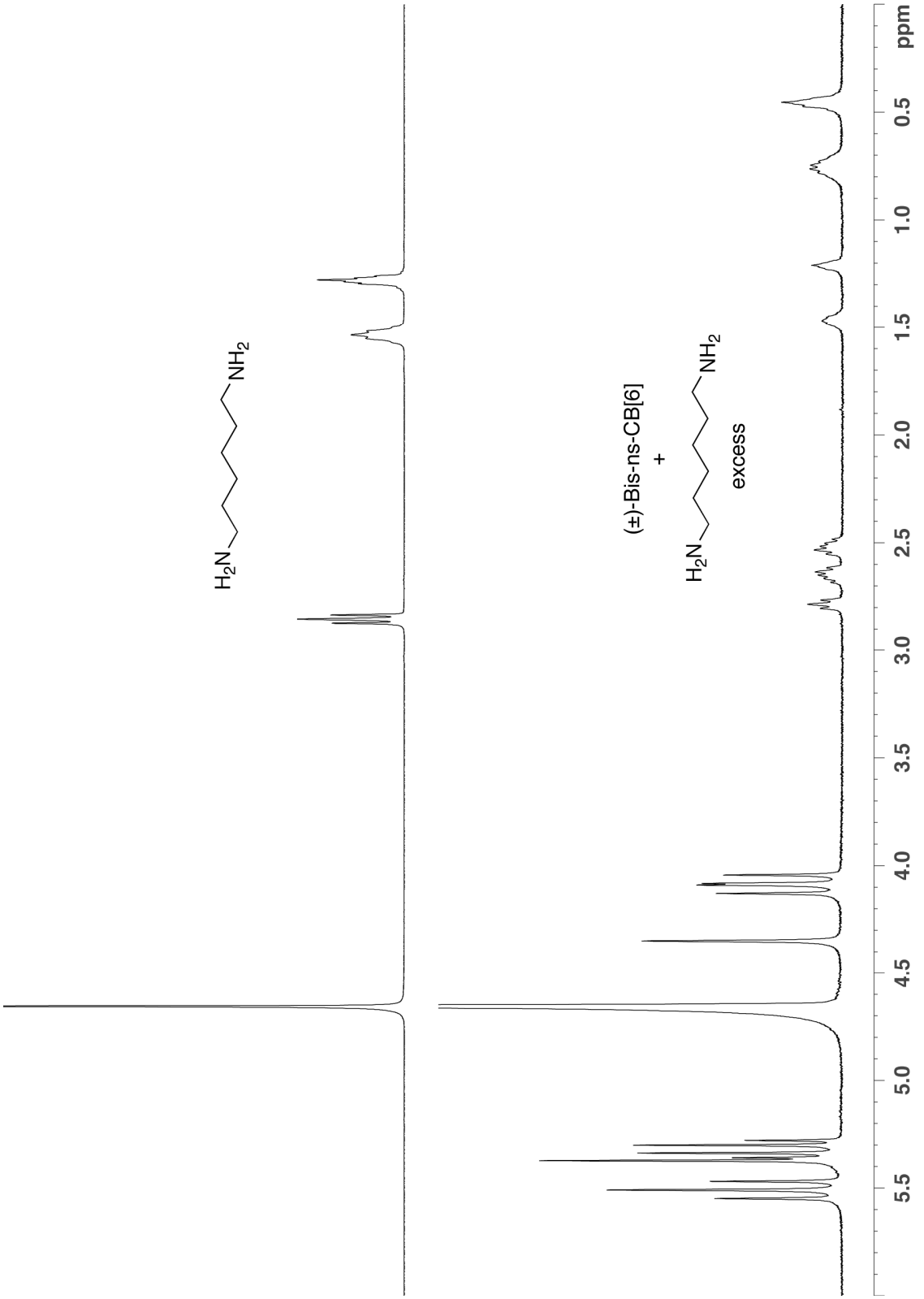


***Figure S8.*** $^{1}$H NMR spectrum recorded (400 MHz, $D_2O$) for: (left) hexanediamine, and (right) (±)-bis-ns-CB[6] and excess hexanediamine.

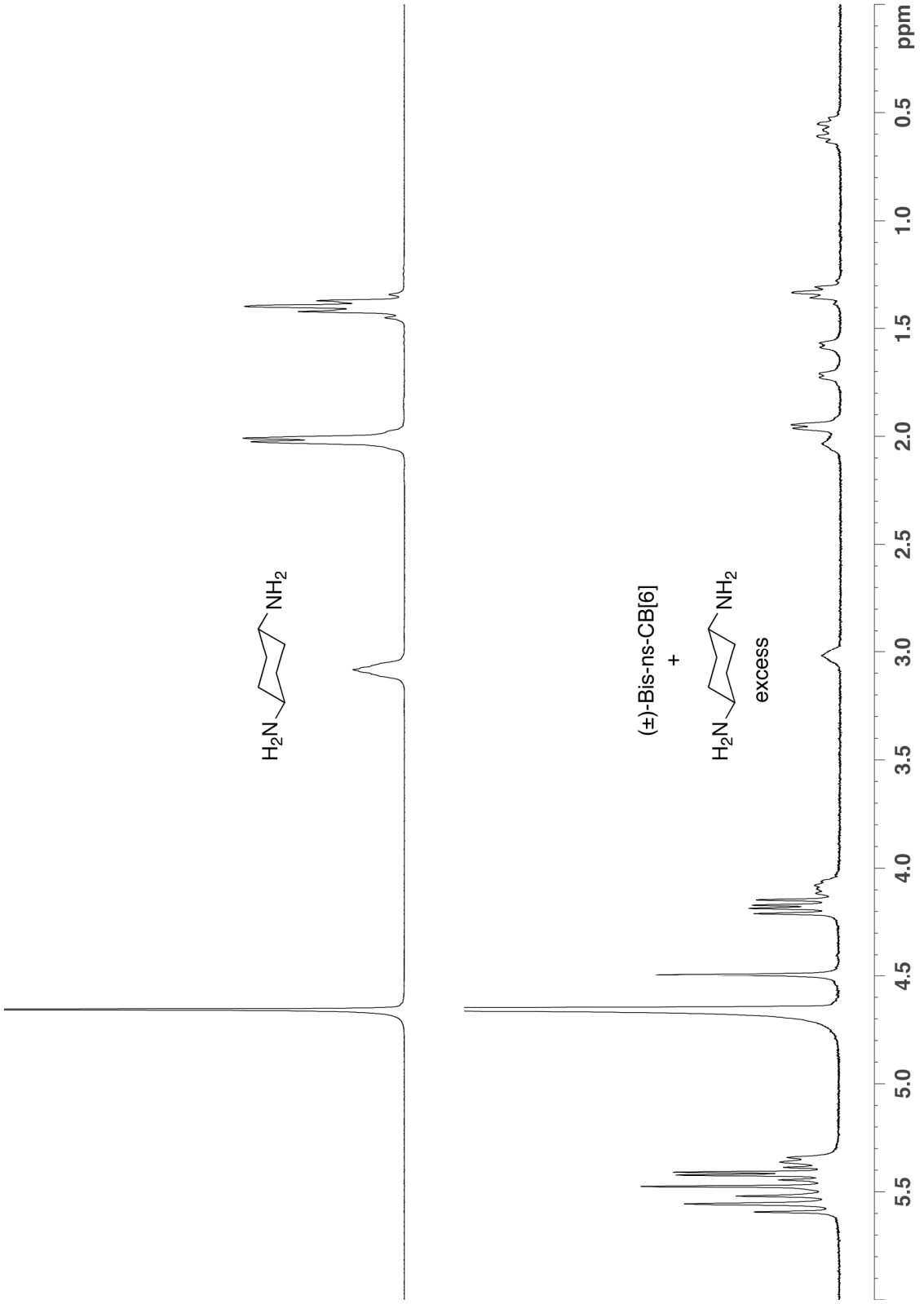


***Figure S9.*** $^{1}$H NMR spectrum recorded (400 MHz, $D_2O$) for: (left) cyclohexanediamine, and (right) (±)-bis-ns-CB[6] and excess cyclohexanediamine.

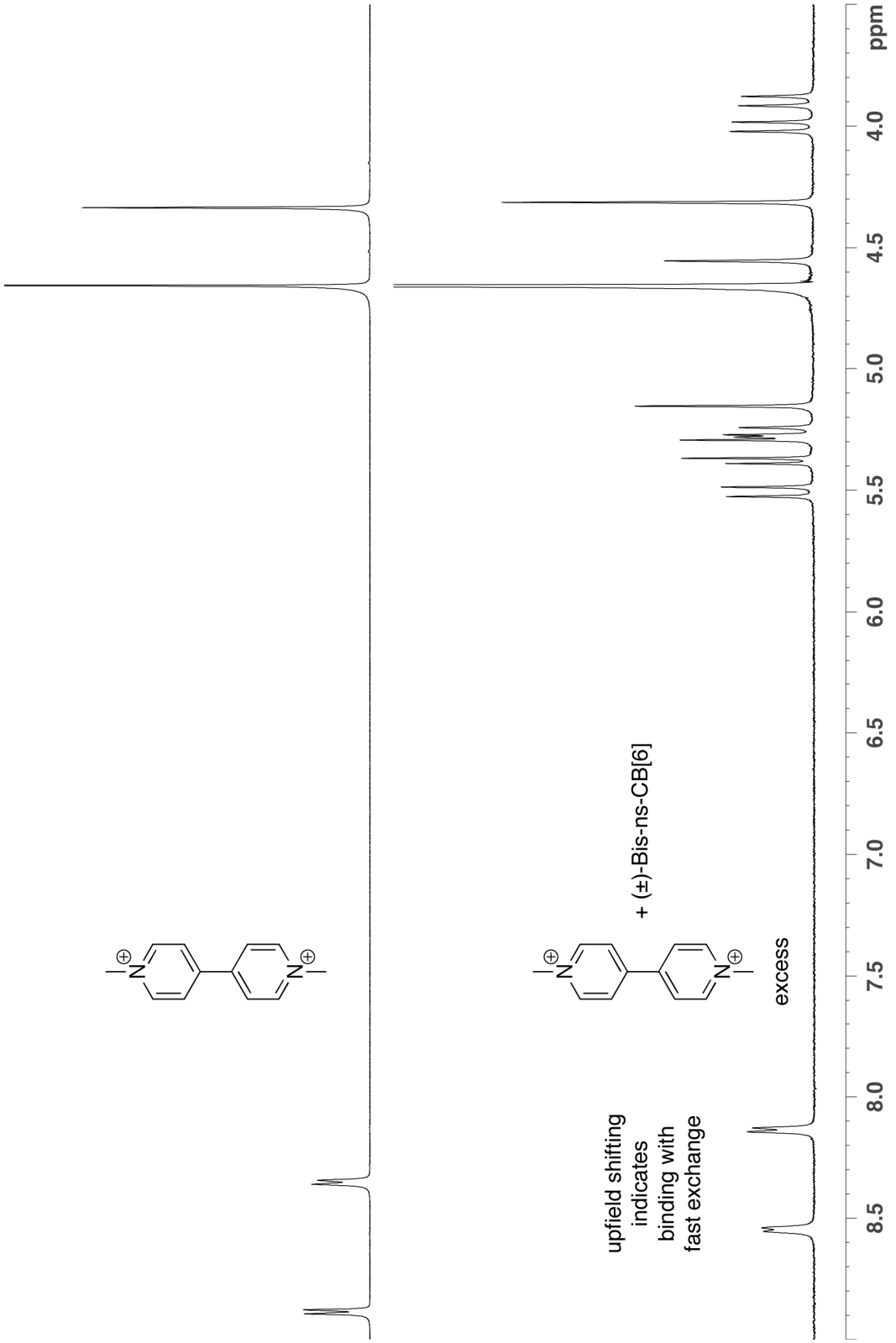


***Figure S10.*** $^{1}$H NMR spectrum recorded (400 MHz, $D_2O$) for: (left) methylviologen, and (right) (±)-bis-ns-CB[6] and excess methylviologen.

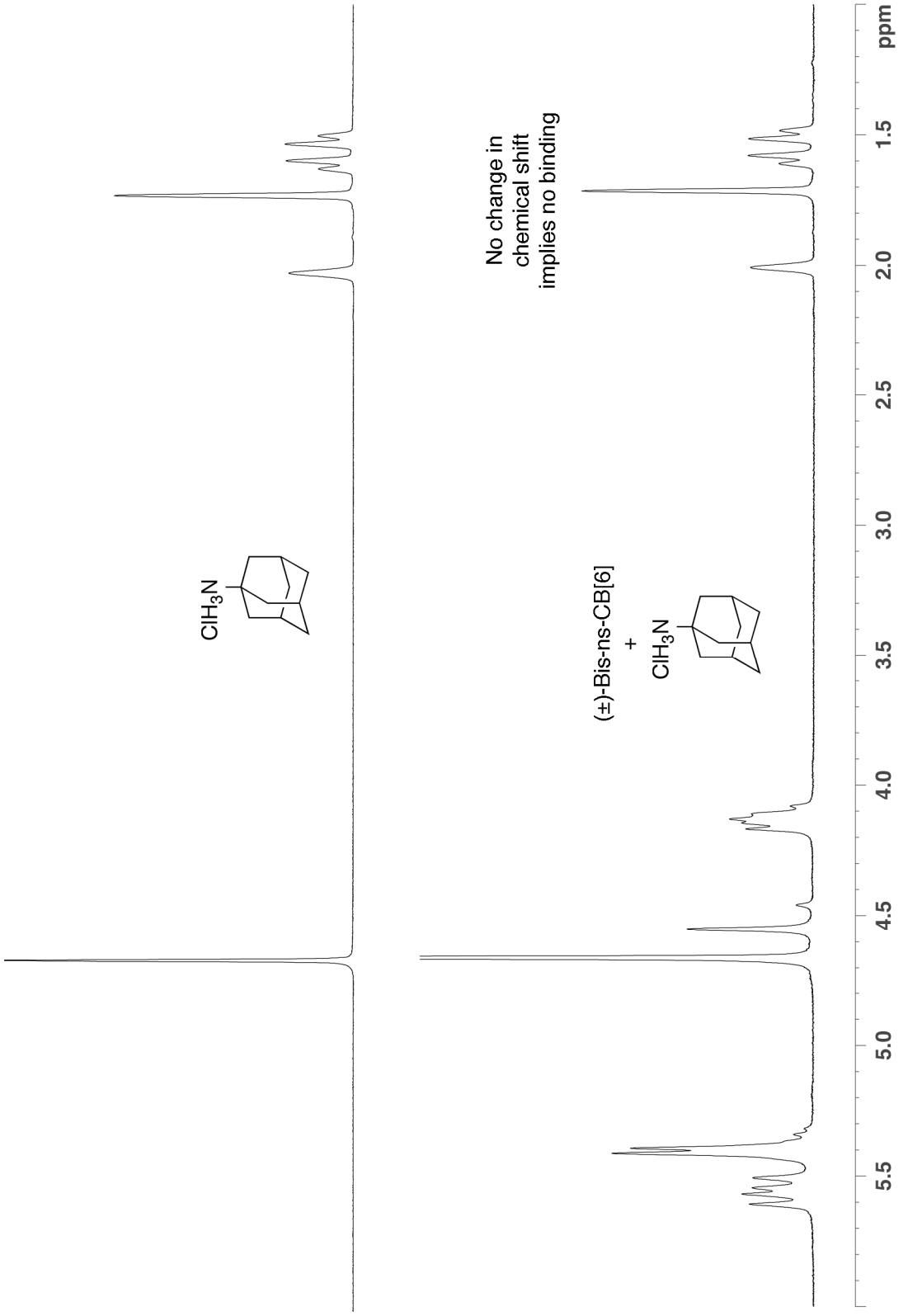


***Figure S11.*** $^{1}$H NMR spectrum recorded (400 MHz, $D_2O$) for: (left) adamantaneamine, and (right) the non-binding mixture of (±)-bis-ns-CB[6] and adamantaneamine.

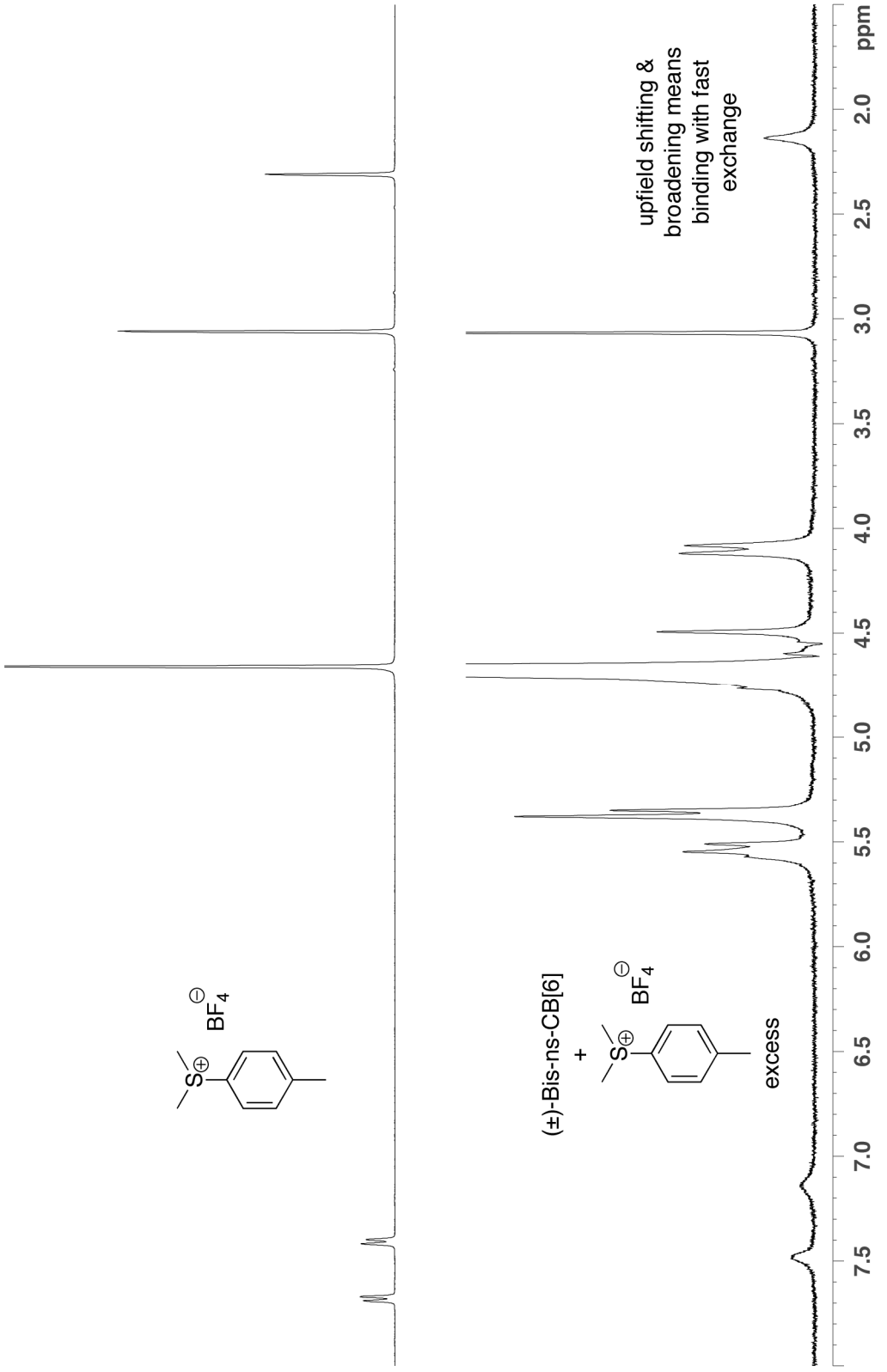


***Figure S12.*** $^{1}$H NMR spectrum recorded (400 MHz, $D_2O$) for: (left) p-tolyldimethylsulfonium tetrafluoroborate guest, and (right) mixture of (±)-bis-ns-CB[6] and excess guest.

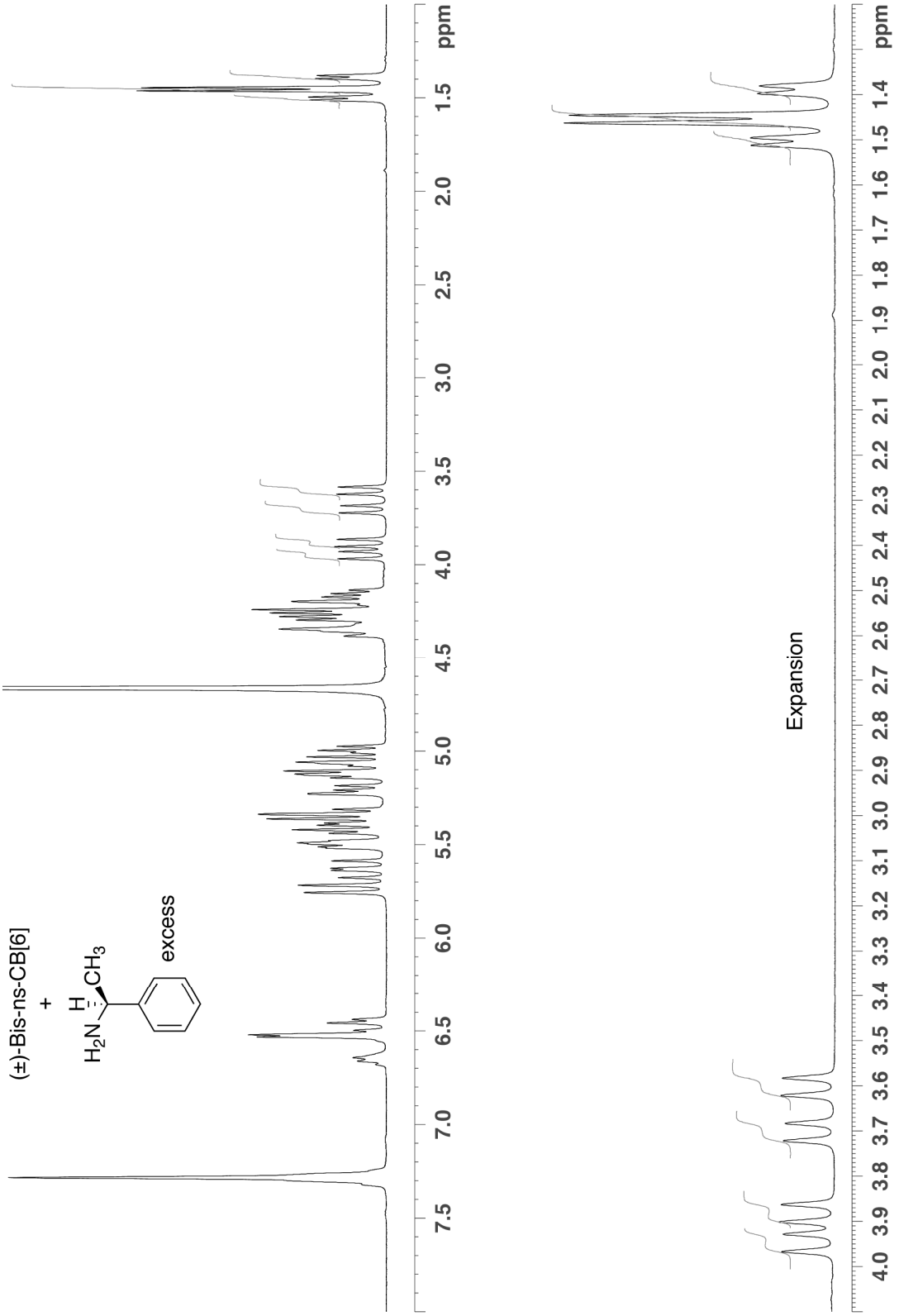


***Figure S13.*** $^{1}$H NMR spectrum recorded (400 MHz, $D_2O$) for: (left) (±)-bis-ns-CB[6] and excess D-phenethylamine, and (right) an expansion of the 1.2.4.0 ppm region.

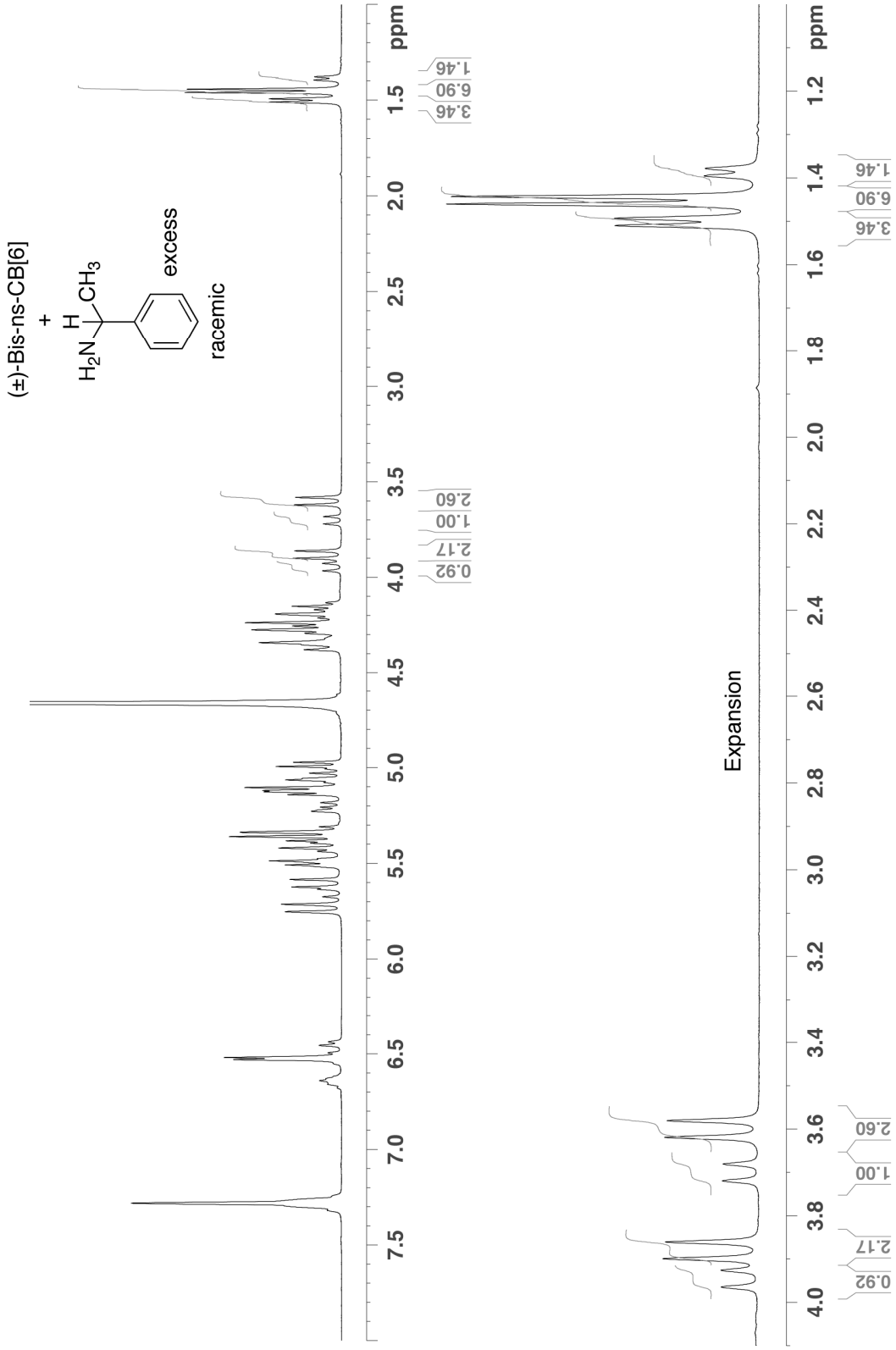


***Figure S14.*** $^{1}$H NMR spectrum recorded (400 MHz, $D_2O$) for: (left) (±)-bis-ns-CB[6] and excess (±)-phenethylamine, and (right) an expansion of the 1.2.4.0 ppm region.

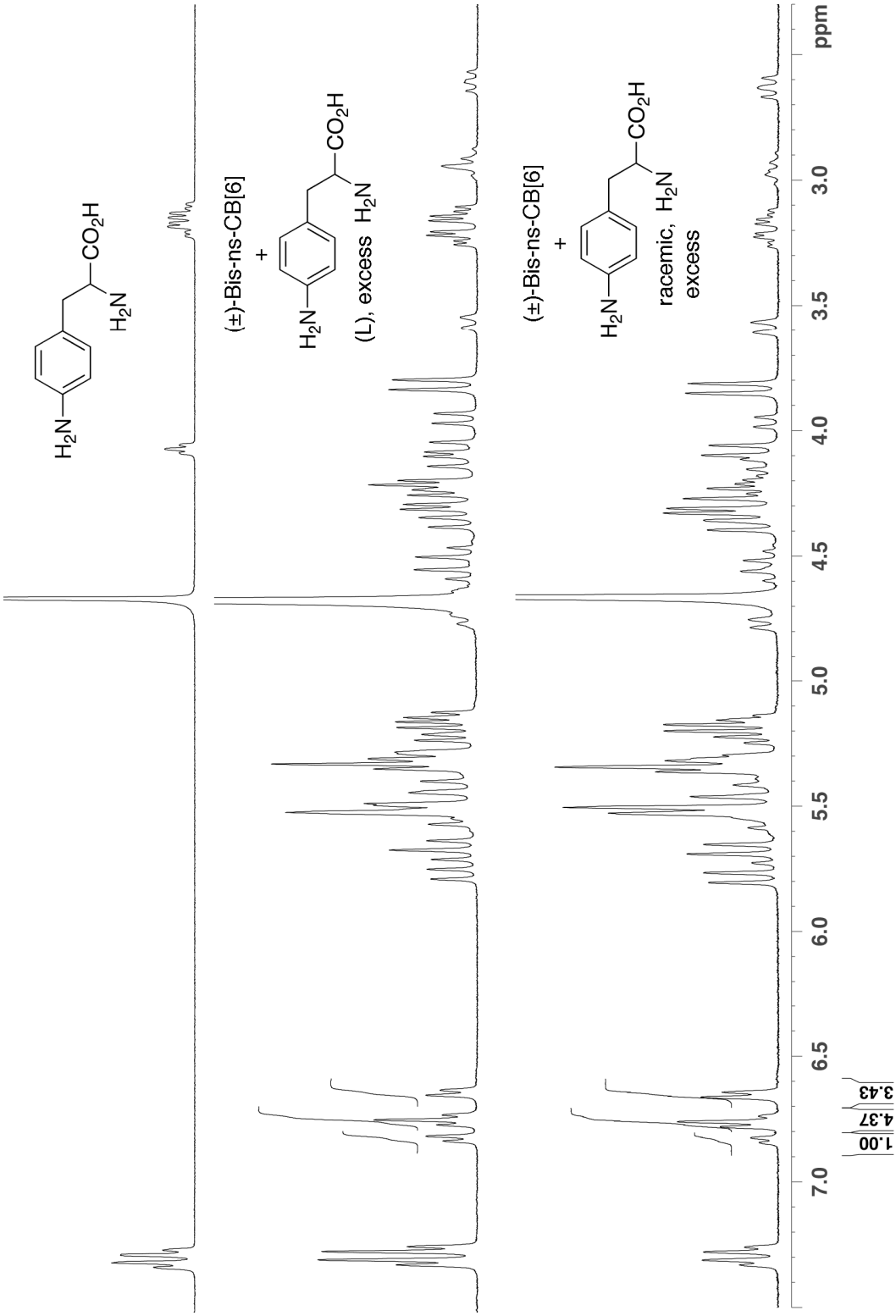


***Figure S15.*** $^{1}$H NMR spectrum recorded (400 MHz, $D_2O$) for: (left) aminophenylalanine, (middle) (±)-bis-ns-CB[6] and excess L-aminophenylalanine, and (right) (±)-bis-ns-CB[6] and excess racemic aminophenylalanine.

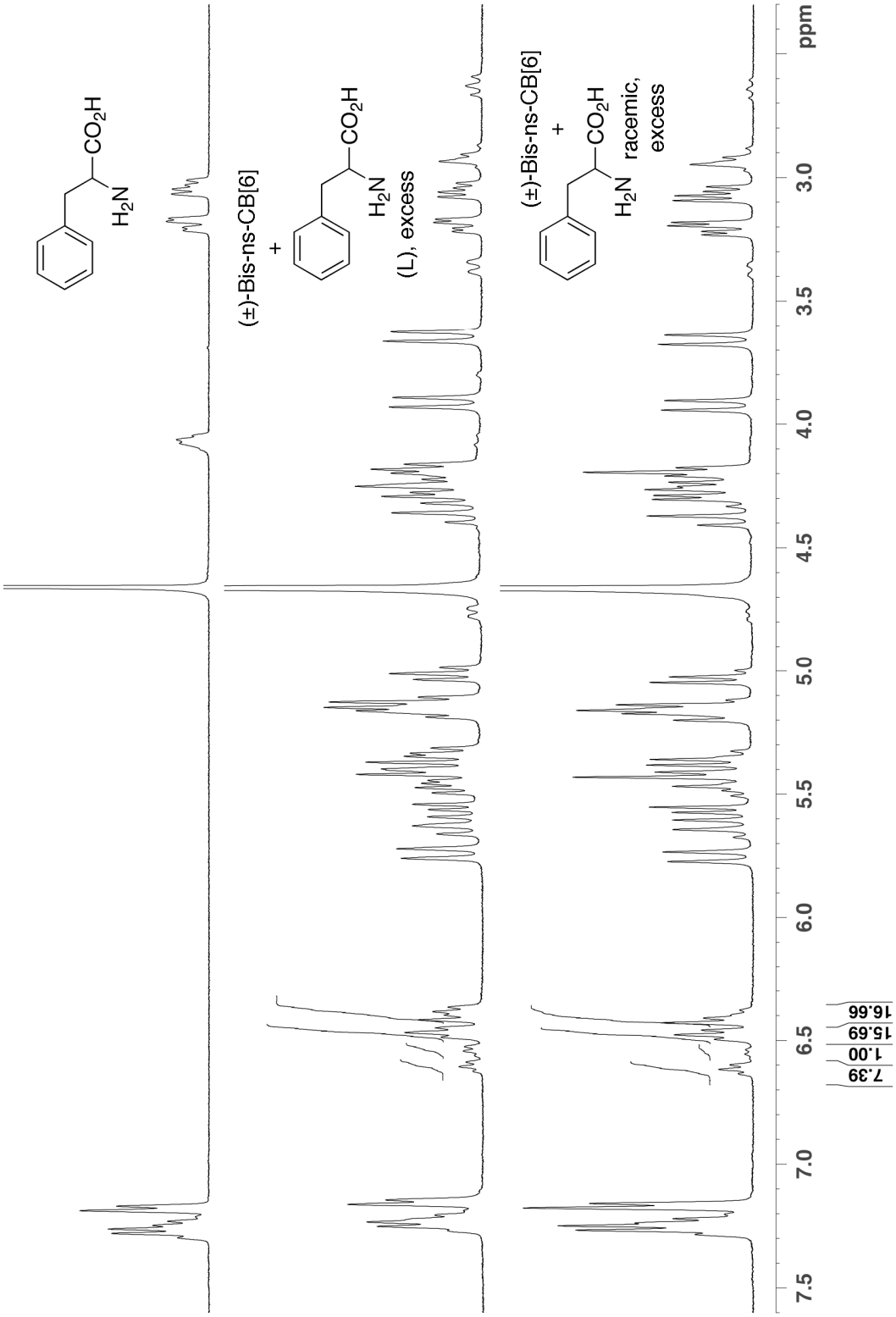


***Figure S16.*** $^{1}$H NMR spectrum recorded (400 MHz, $D_2O$) for: (left) phenylalanine, (middle) (±)-bis-ns-CB[6] and excess L-phenylalanine, and (right) (±)-bis-ns-CB[6] and excess racemic phenylalanine.

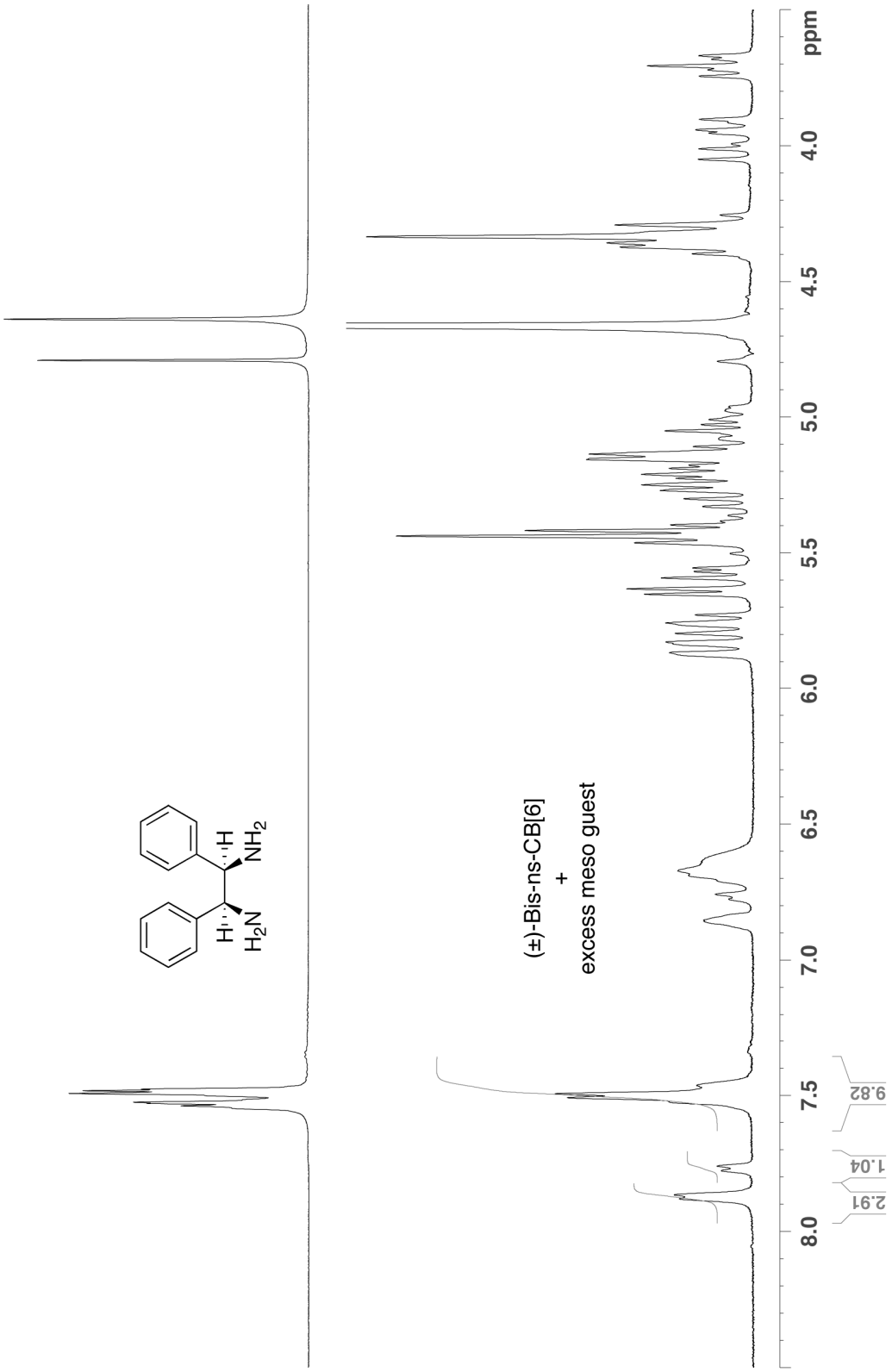


***Figure S17.*** $^{1}$H NMR spectrum recorded (400 MHz, $D_2O$) for: (left) meso-diphenylethylenediamine, and (right) (±)-bis-ns-CB[6] and excess diphenylethylenediamine.

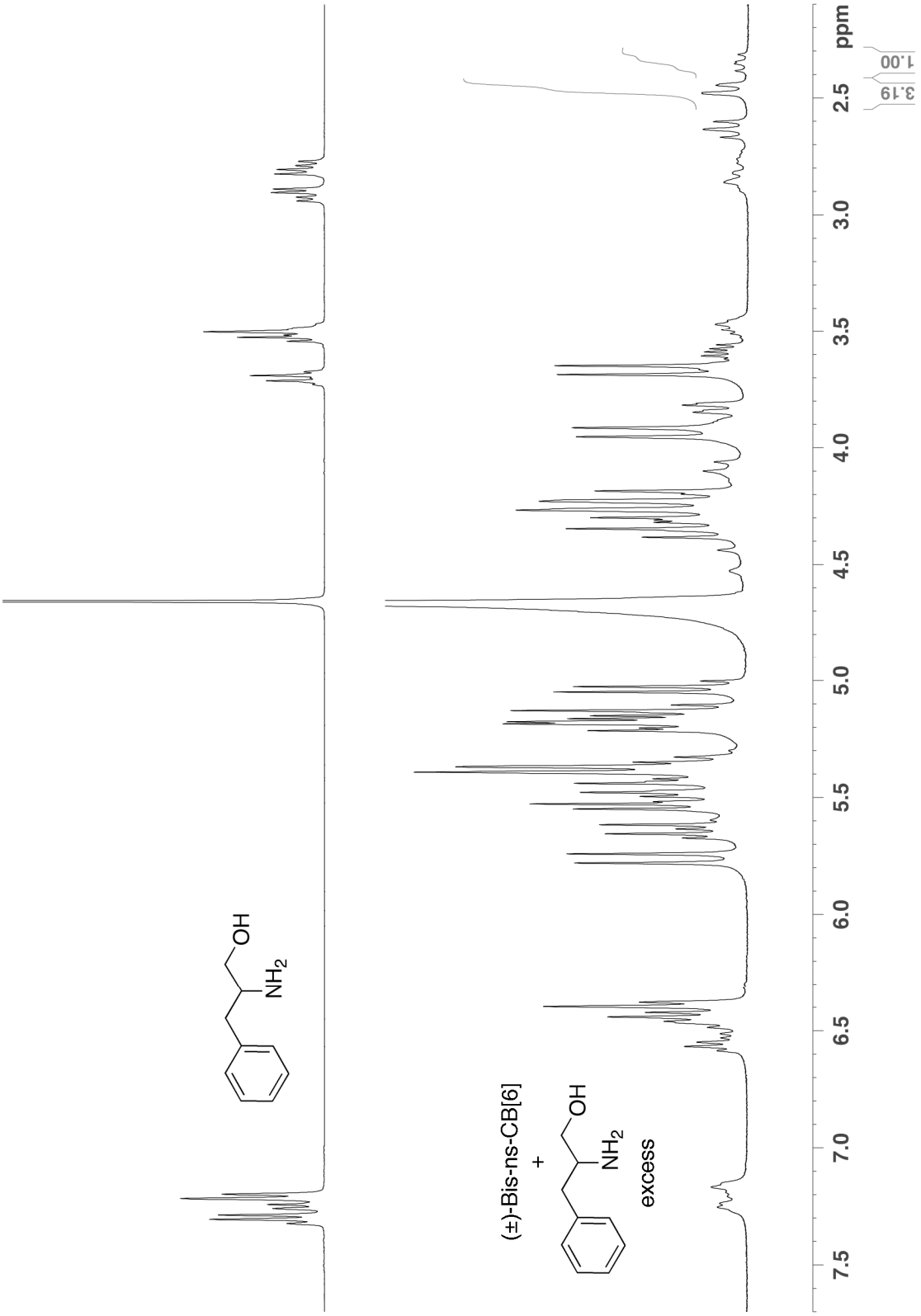


***Figure S18.*** $^{1}$H NMR spectrum recorded (400 MHz, $D_2O$) for: (left) amino alcohol **11**, and (right) (±)-bis-ns-CB[6] and excess **11**.

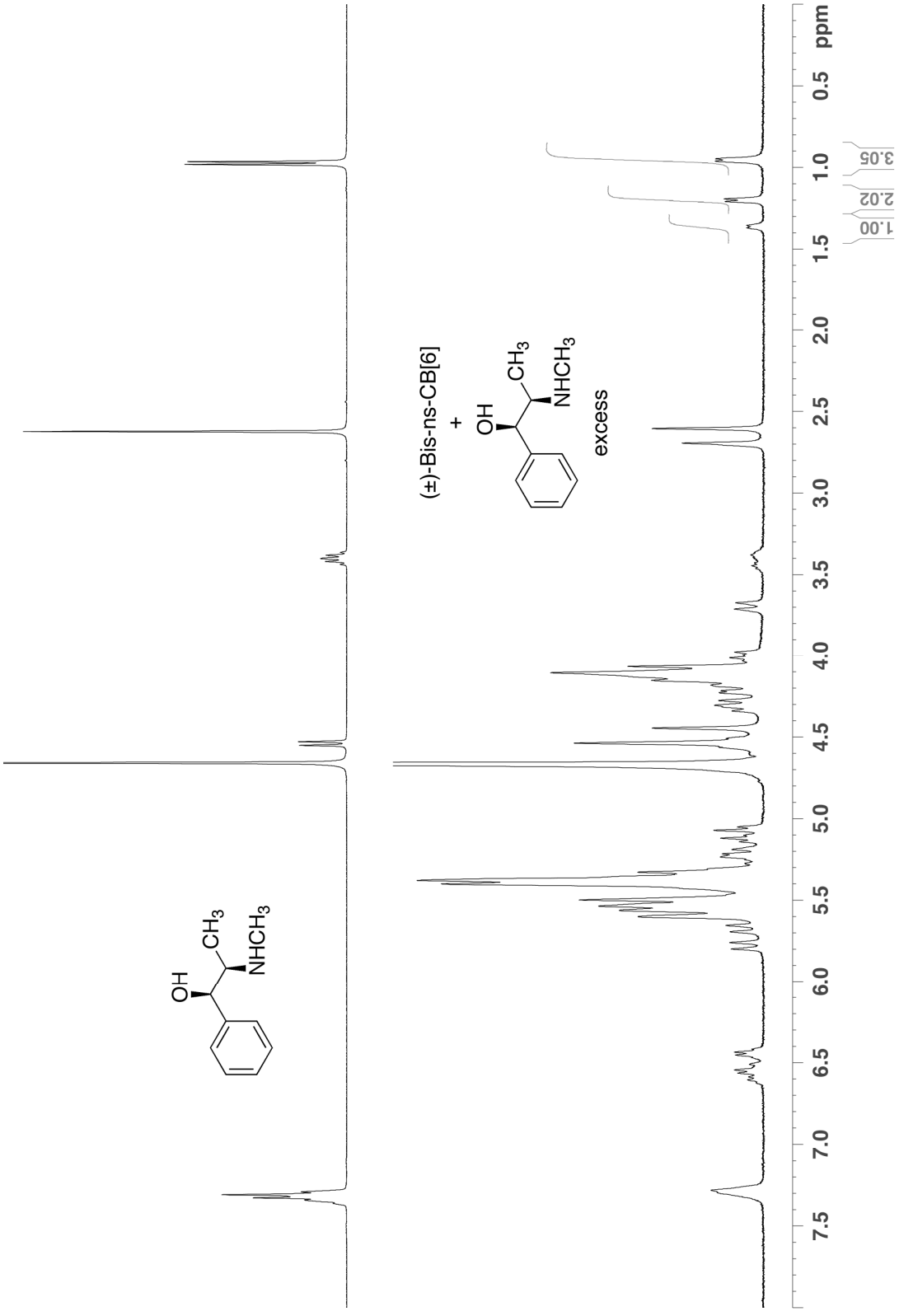


***Figure S19.*** $^{1}$H NMR spectrum recorded (400 MHz, $D_2O$) for: (left) ephedrine, and (right) (±)-bis-ns-CB[6] and excess ephedrine.

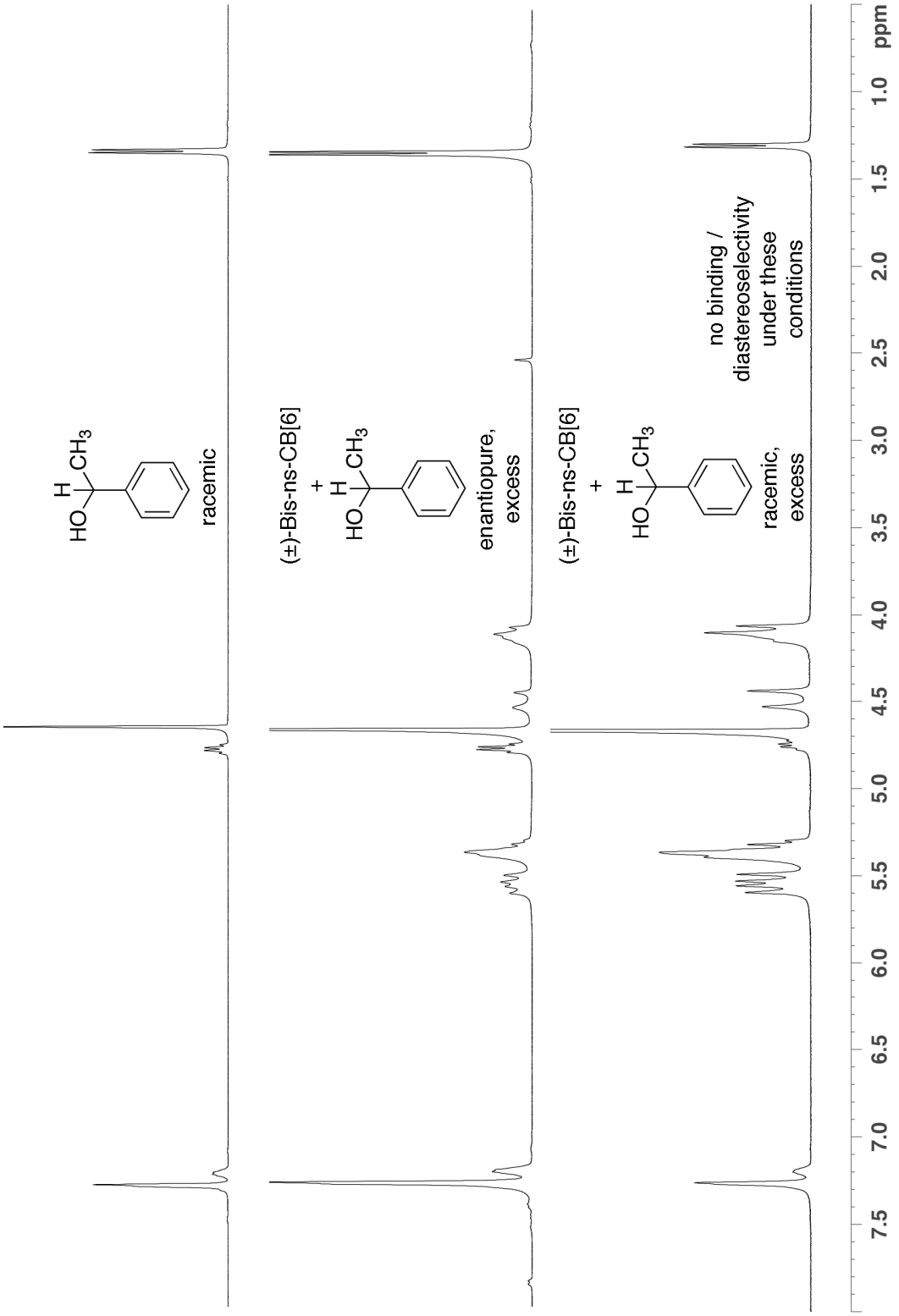


***Figure S20.*** $^{1}$H NMR spectrum recorded (400 MHz, $D_2O$) for: (left) phenylethanol, (middle) the non-binding mixture of (±)-bis-ns-CB[6] and excess (R)-phenylethanol, and (right) the non-binding mixture of (±)-bis-ns-CB[6] and excess racemic phenylethanol.

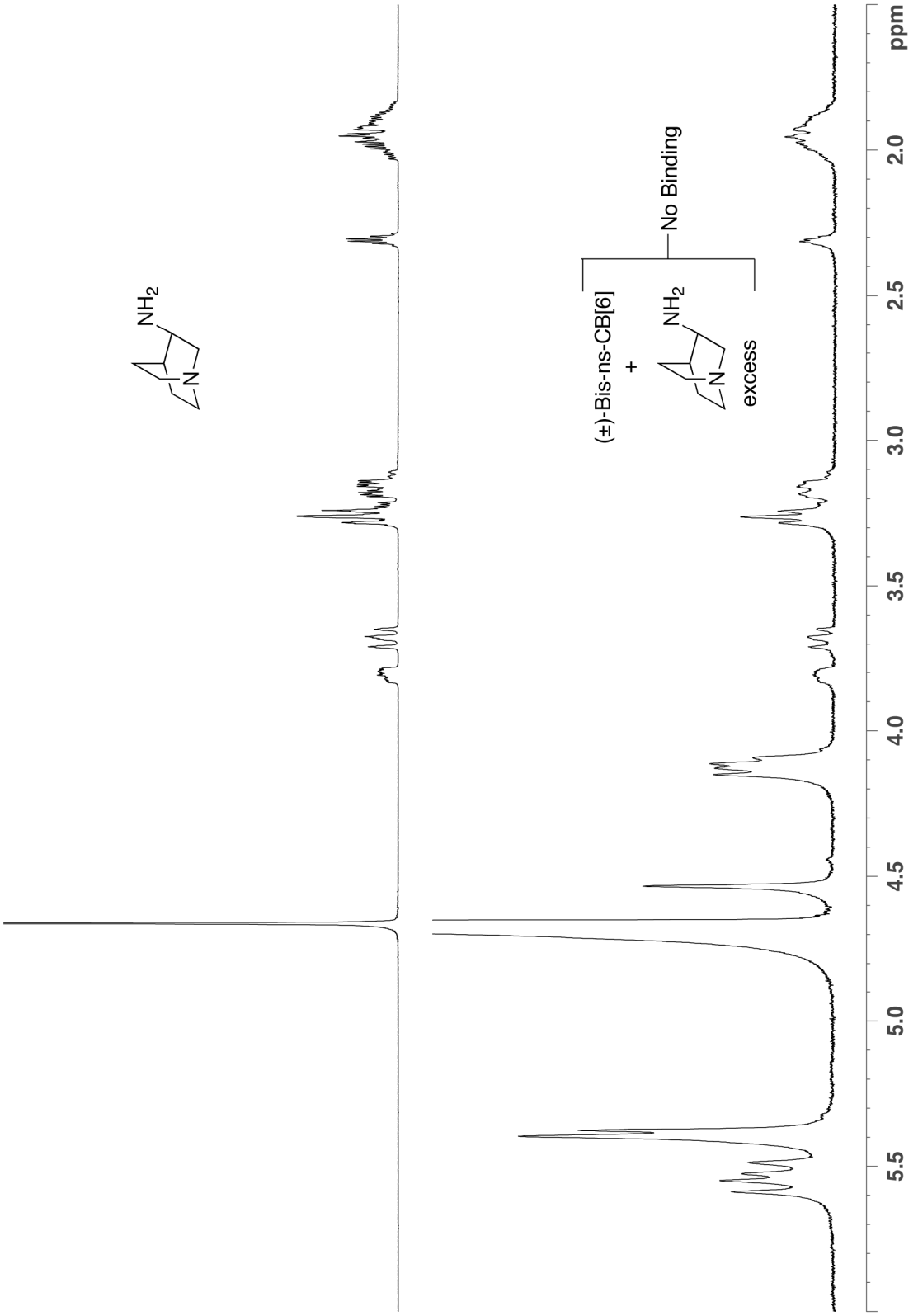


***Figure S21.*** $^{1}$H NMR spectrum recorded (400 MHz, $D_2O$) for: (left) (S)-aminoquinuclidine, and (right) the non-binding mixture of (±)-bis-ns-CB[6] and (S)-aminoquinuclidine.

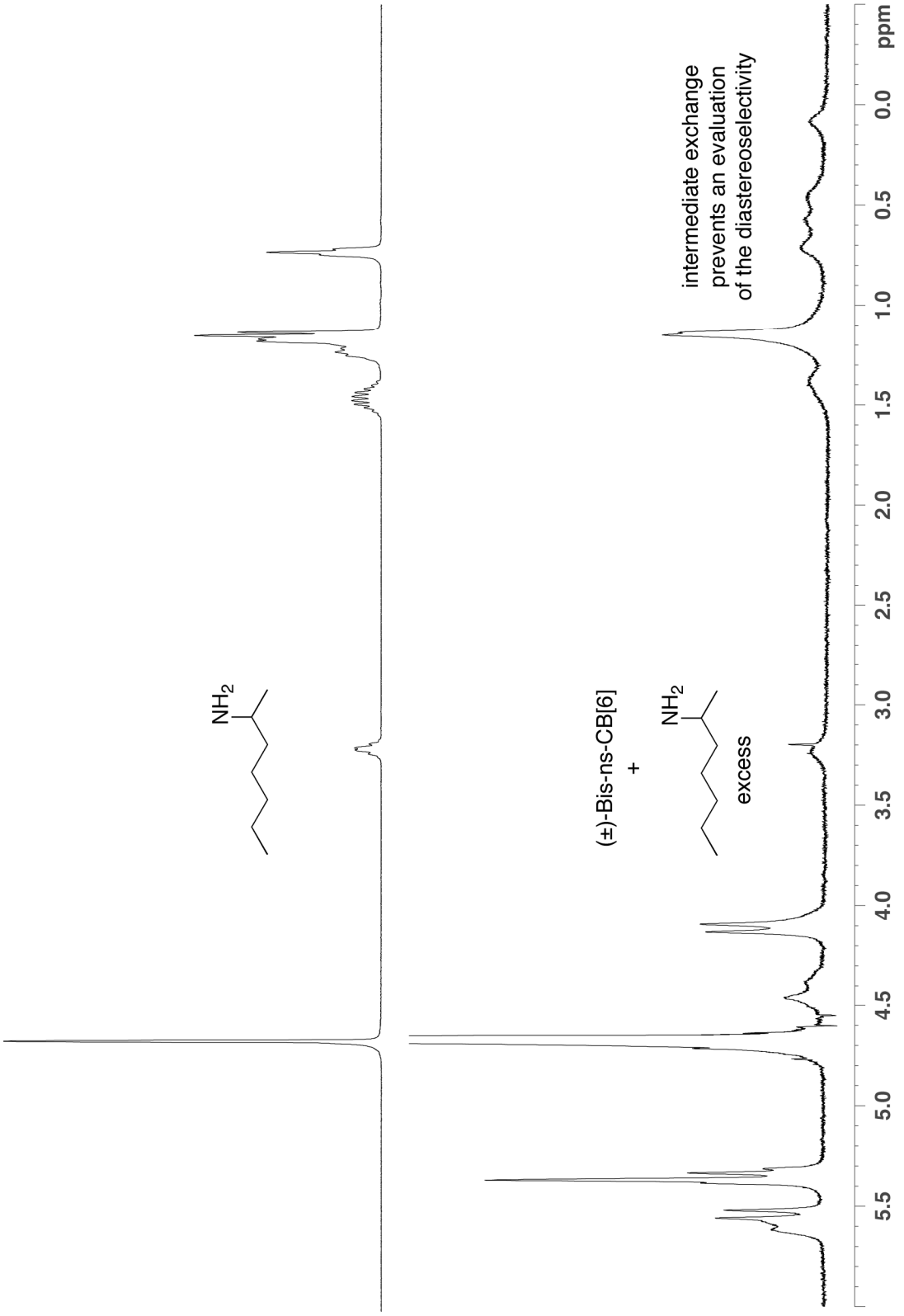


***Figure S22.*** $^{1}$H NMR spectrum recorded (400 MHz, $D_2O$) for: (left) 2-aminoheptane, and (right) mixture of (±)-bis-ns-CB[6] and excess 2-aminoheptane.

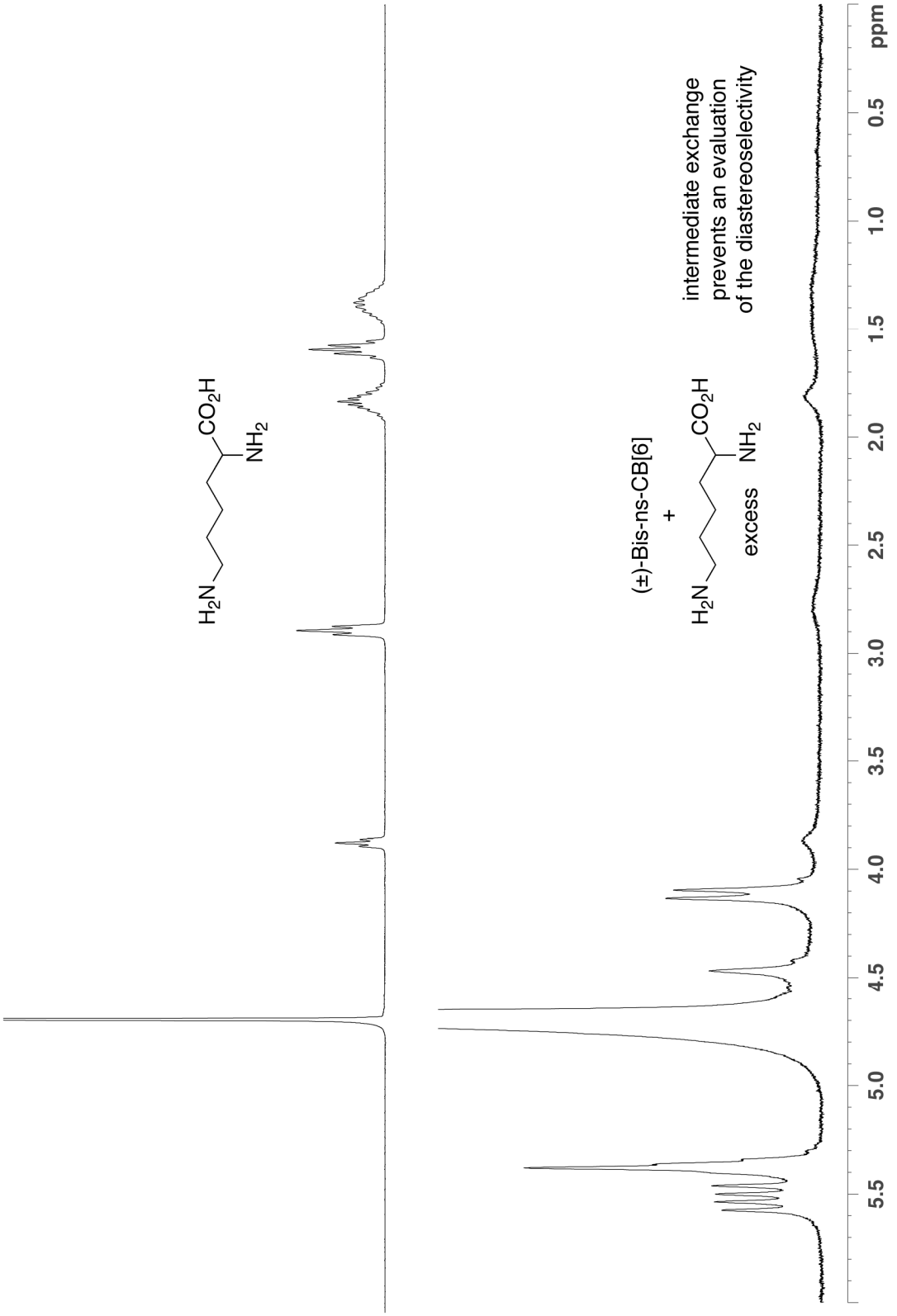


***Figure S23.*** $^1$H NMR spectrum recorded (400 MHz, $D_2O$, pH 2.0) for: (left) lysine, and (right) mixture of (±)-bis-ns-CB[6] and excess lysine.

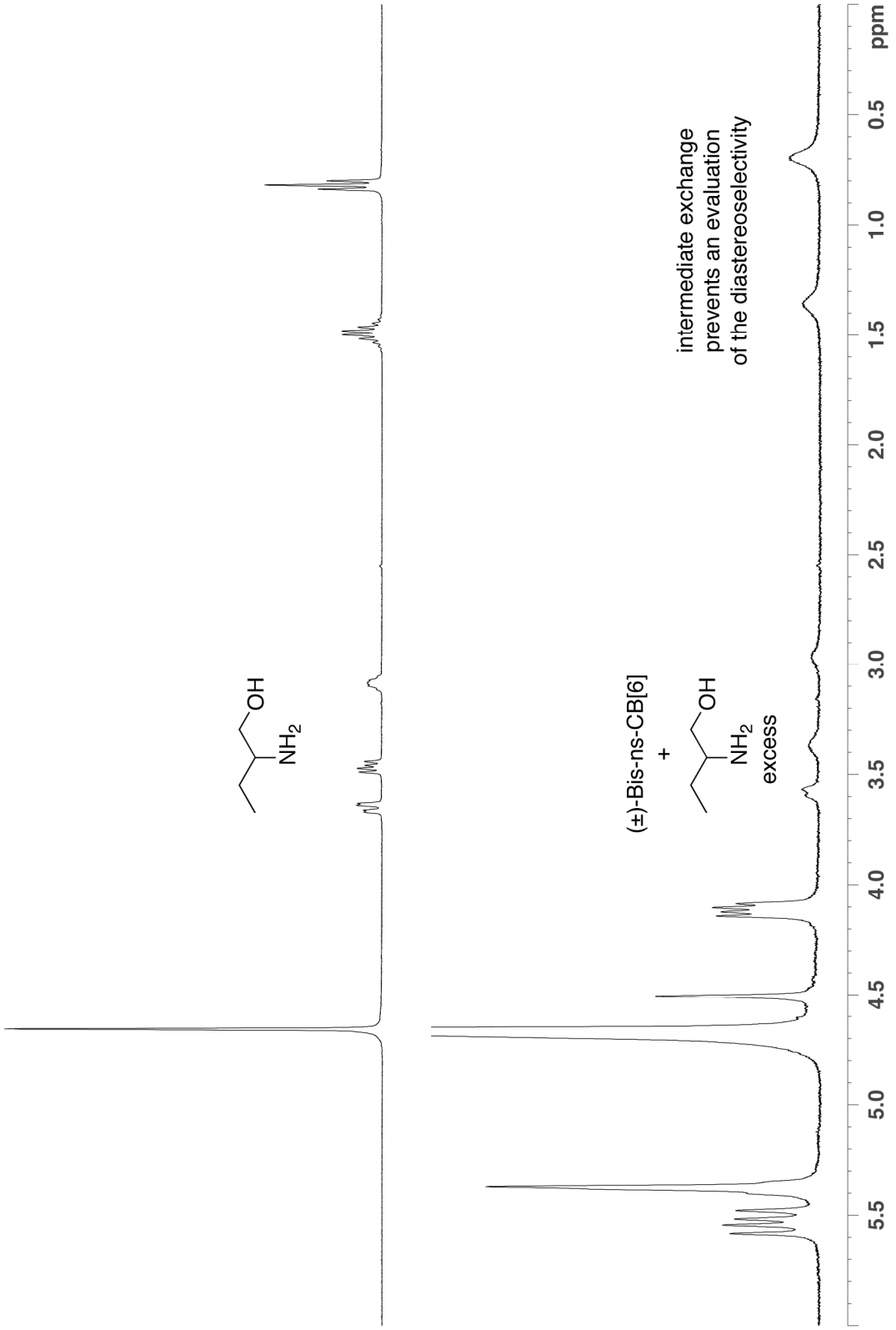


***Figure S24.*** $^{1}$H NMR spectrum recorded (400 MHz, $D_2O$) for: (left) 2-amino-1-butanol, and (right) mixture of (±)-bis-ns-CB[6] and excess guest.

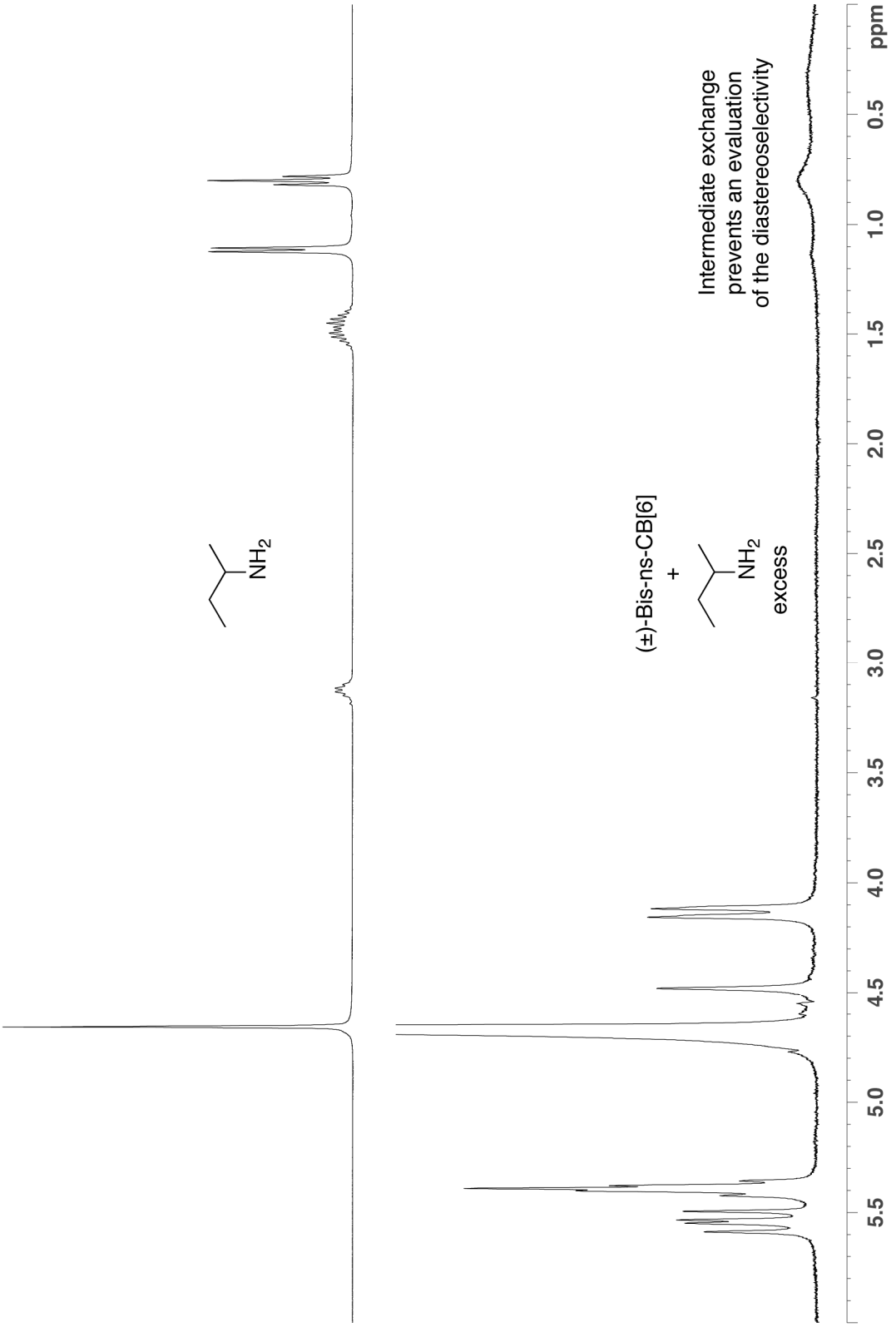


***Figure S25.*** $^{1}$H NMR spectrum recorded (400 MHz, $D_2O$) for: (left) 2-amino-1-butanol, and (right) mixture of (±)-bis-ns-CB[6] and excess guest.

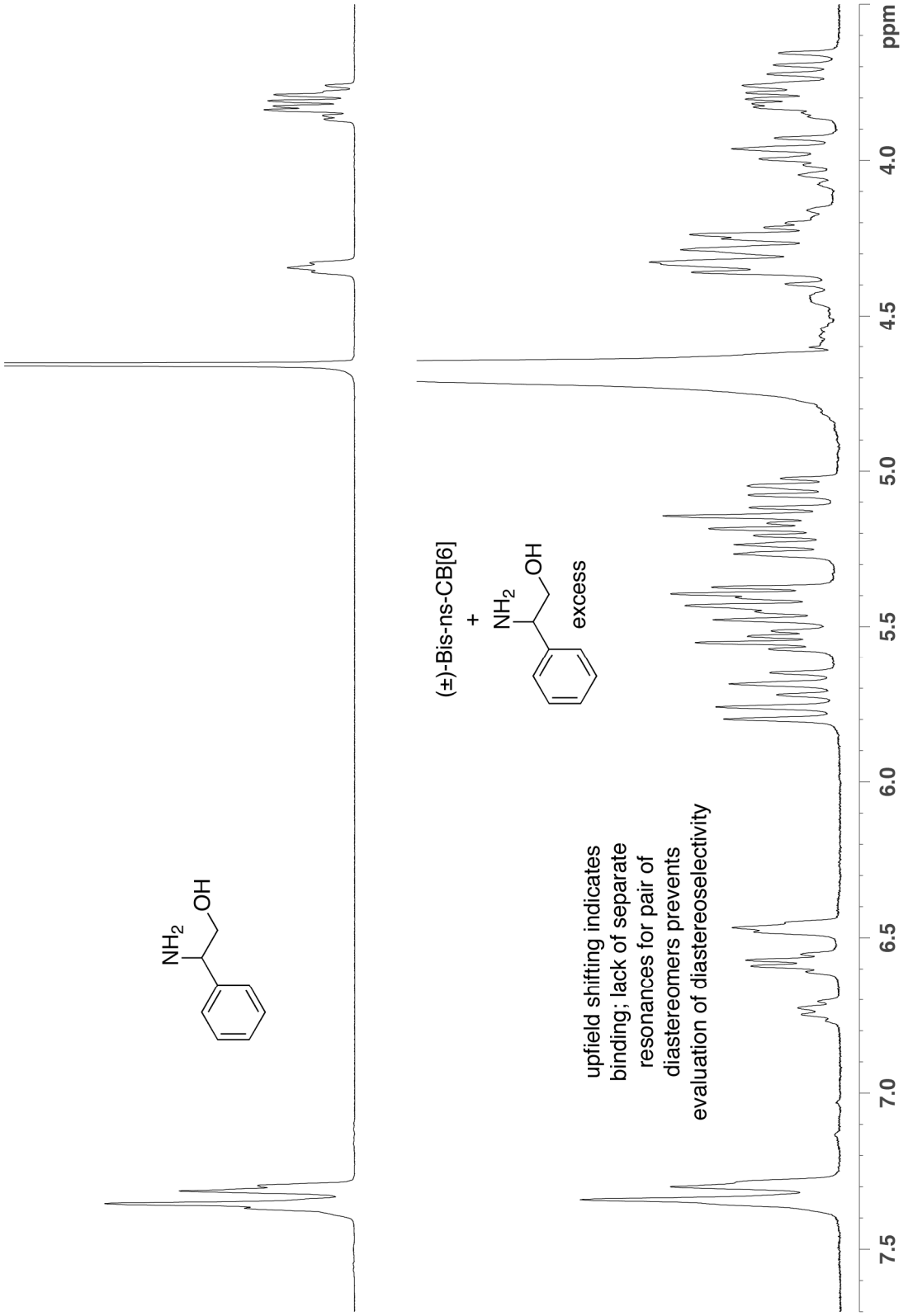


***Figure S26.*** $^{1}$H NMR spectrum recorded (400 MHz, $D_2O$) for: (left) phenylglycinol, and (right) mixture of (±)-bis-ns-CB[6] and excess phenylglycinol.

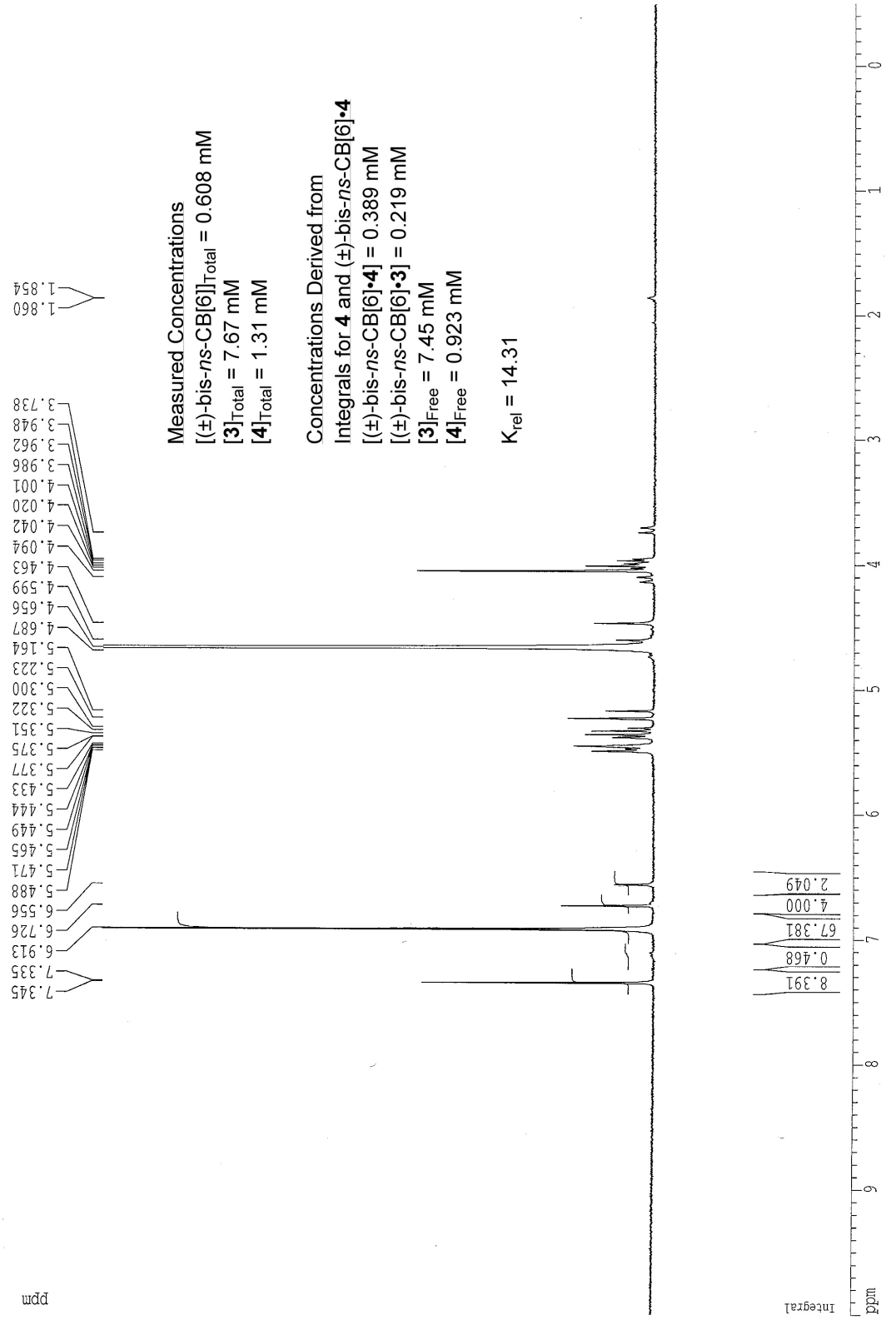


***Figure S27.*** $^{1}$H NMR spectrum recorded (400 MHz, $D_2O$) for the competition between **3** and **4** for a limiting quantity of (±)-bis-*ns*-CB[6].

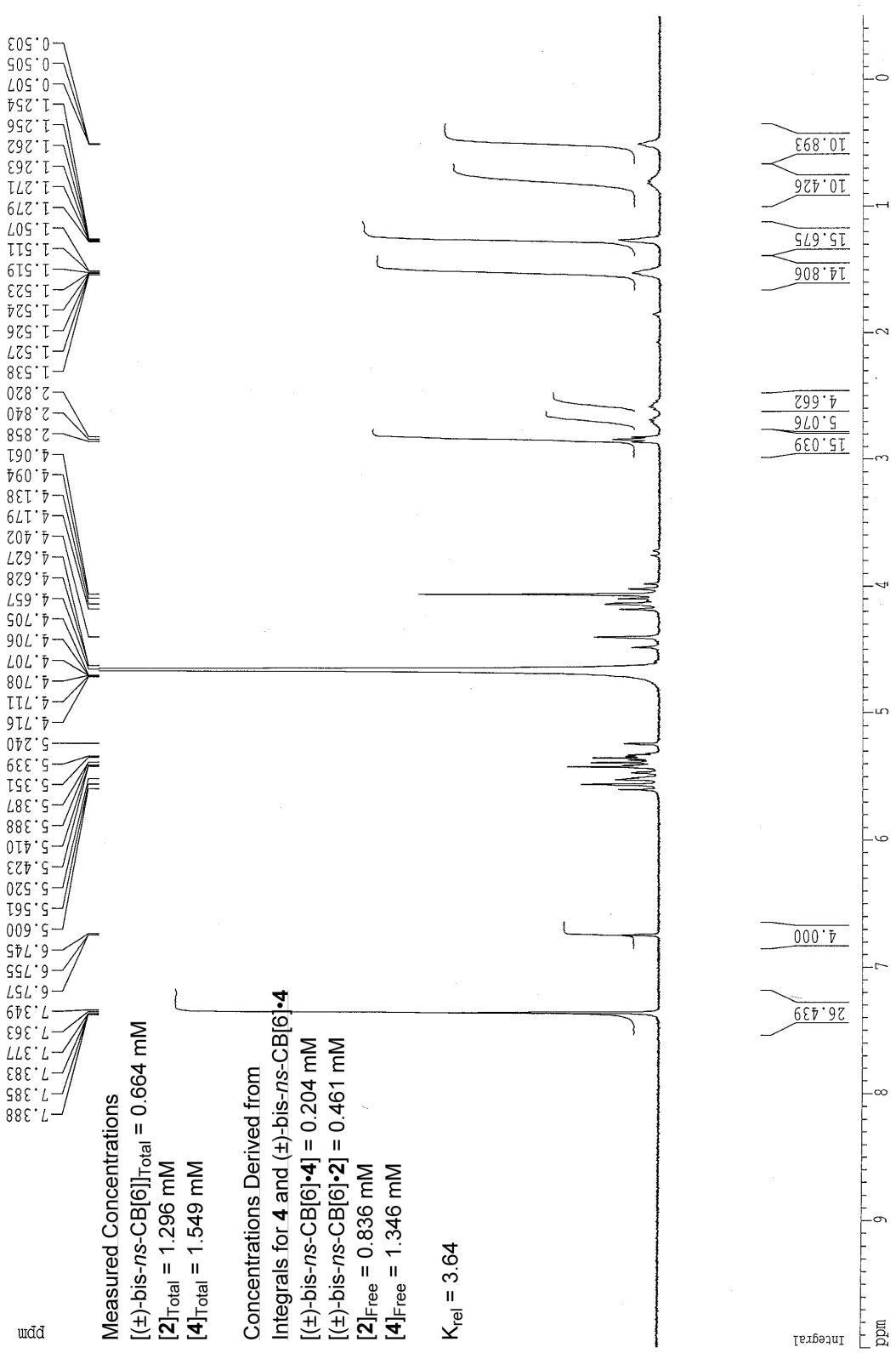


***Figure S28.*** $^{1}$H NMR spectrum recorded (400 MHz, $D_2O$) for the competition between **4** and **2** for a limiting quantity of (±)-bis-*ns*-CB[6].

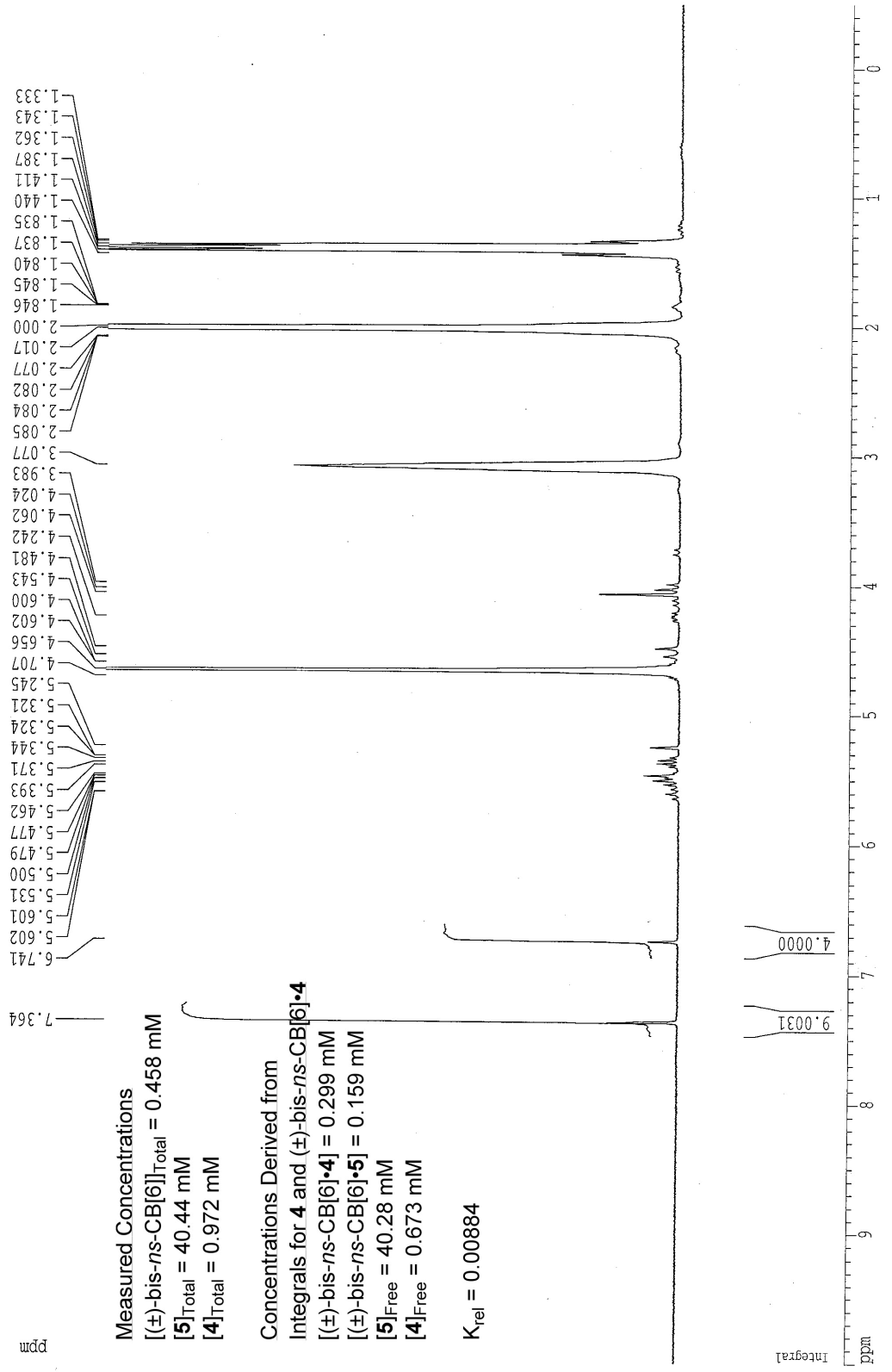


***Figure S29.*** $^{1}$H NMR spectrum recorded (400 MHz, $D_2O$) for the competition between **4** and **5** for a limiting quantity of (±)-bis-*ns*-CB[6].

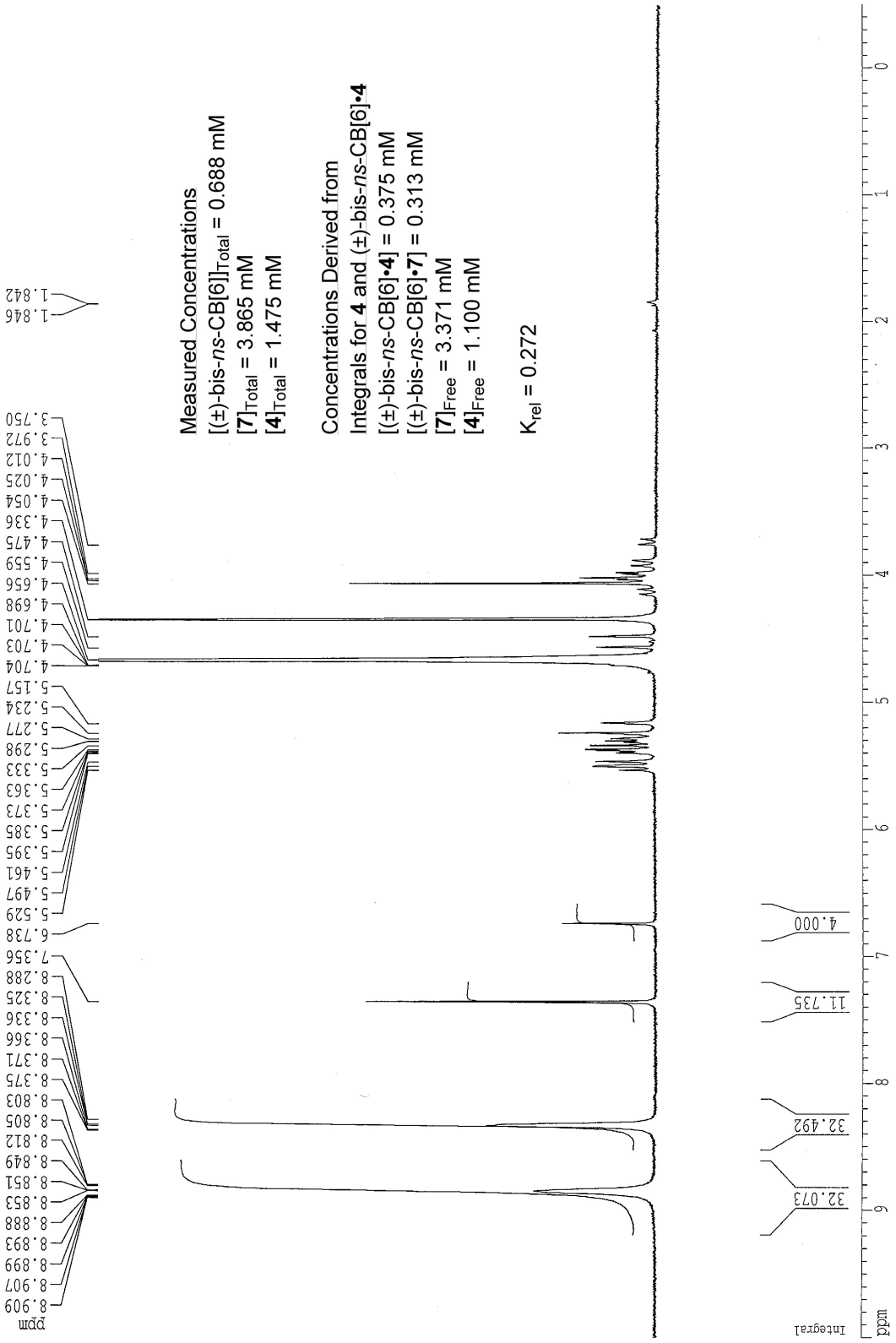


***Figure S30.*** $^{1}$H NMR spectrum recorded (400 MHz, $D_2O$) for the competition between **4** and **7** for a limiting quantity of (±)-bis-*ns*-CB[6].

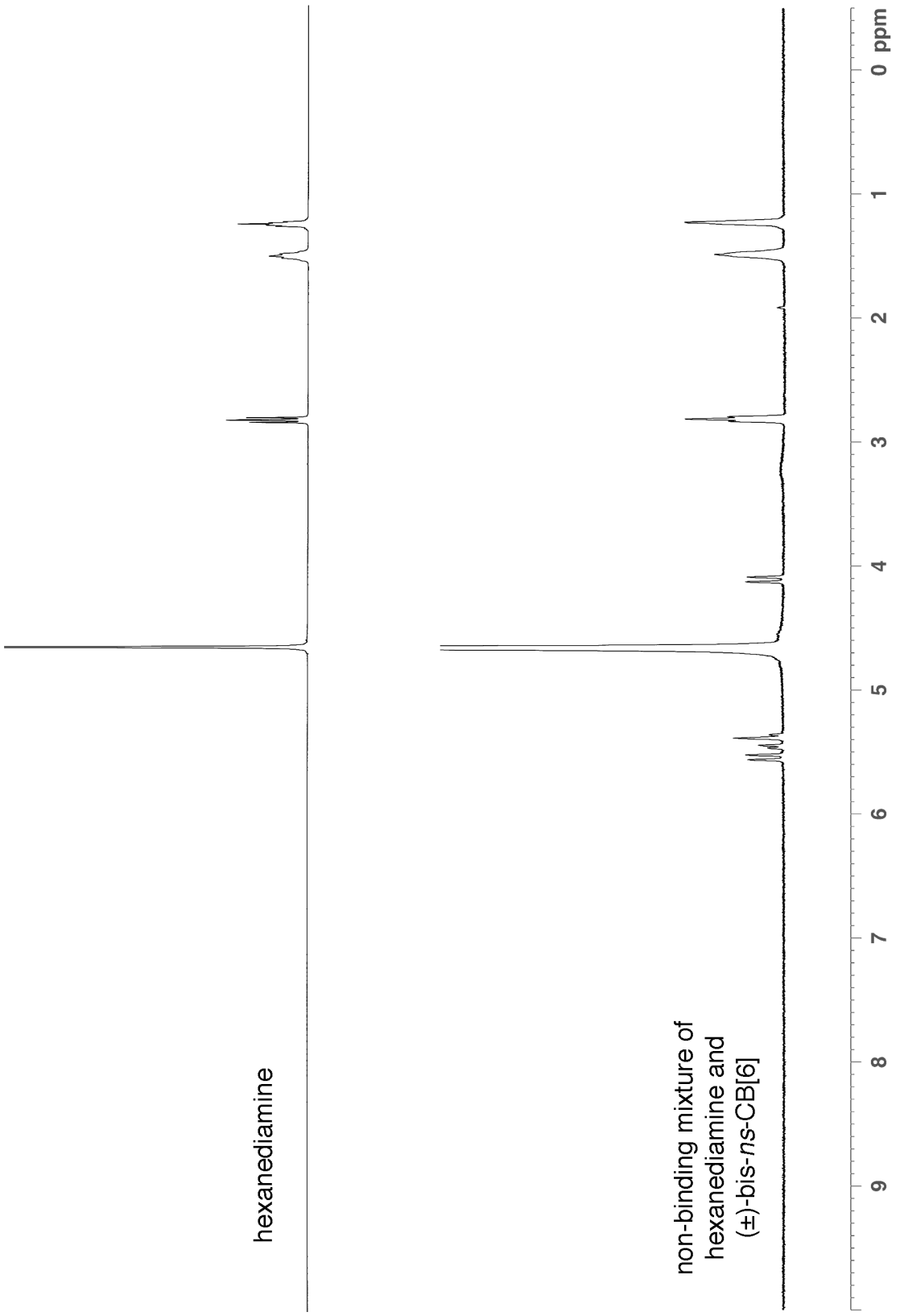


***Figure S31.*** $^{1}$H NMR spectrum recorded (400 MHz, $D_2O$) for **2** (left) and a non-binding mixture of **2** and trimer **1**.