

## Supporting Information

for

### New ultra-high affinity host-guest complexes of cucurbit[7]uril with bicyclo[2.2.2]octane and adamantane guests: Thermodynamic analysis and evaluation of M2 affinity calculations

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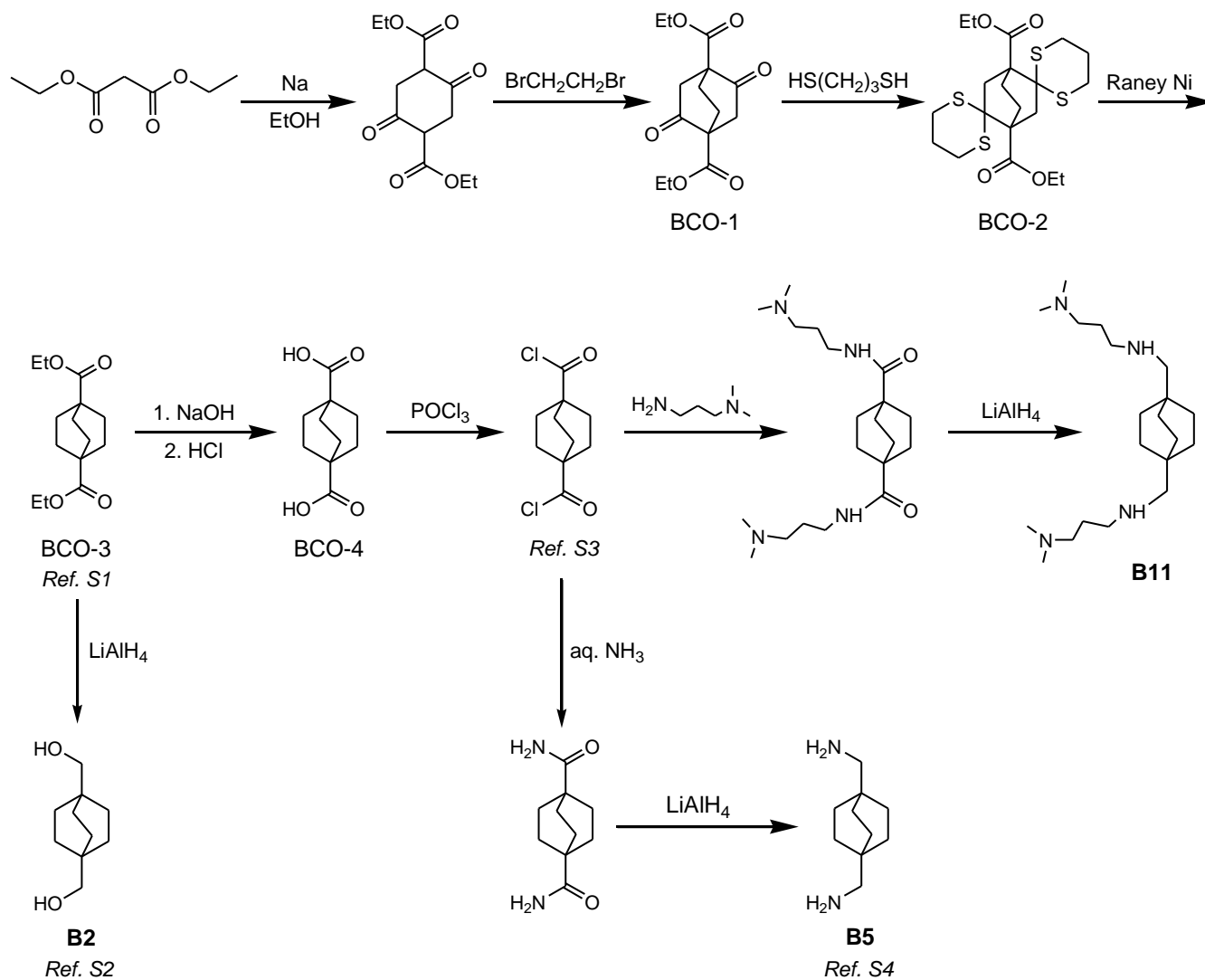
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**Ref 10:** MacKerell, A.; Bashford, D.; Bellott, M.; Dunbrack, R.; Evanseck, J.; Field, M.; Fischer, S.; Gao, J.; Guo, H.; Ha, S.; Joseph-McCarthy, D.; Kuchnir, L.; Kuczera, K.; Lau, F.; Mattos, C.; Michnick, S.; Ngo, T.; Nguyen, D.; Prodhom, B.; Reiher, W.; Roux, B.; Schlenkrich, M.; Smith, J.; Stote, R.; Straub, J.; Watanabe, M.; Wiorkiewicz-Kuczera, J.; Yin, D.; Karplus, M. *J. Phys. Chem. B.* **1998**, *102*, 3586-3616.

## Experimental section

Bicyclo[2.2.2]octane derivatives were synthesized as illustrated in Scheme S1, according to the procedures reported in the references S1-S3.

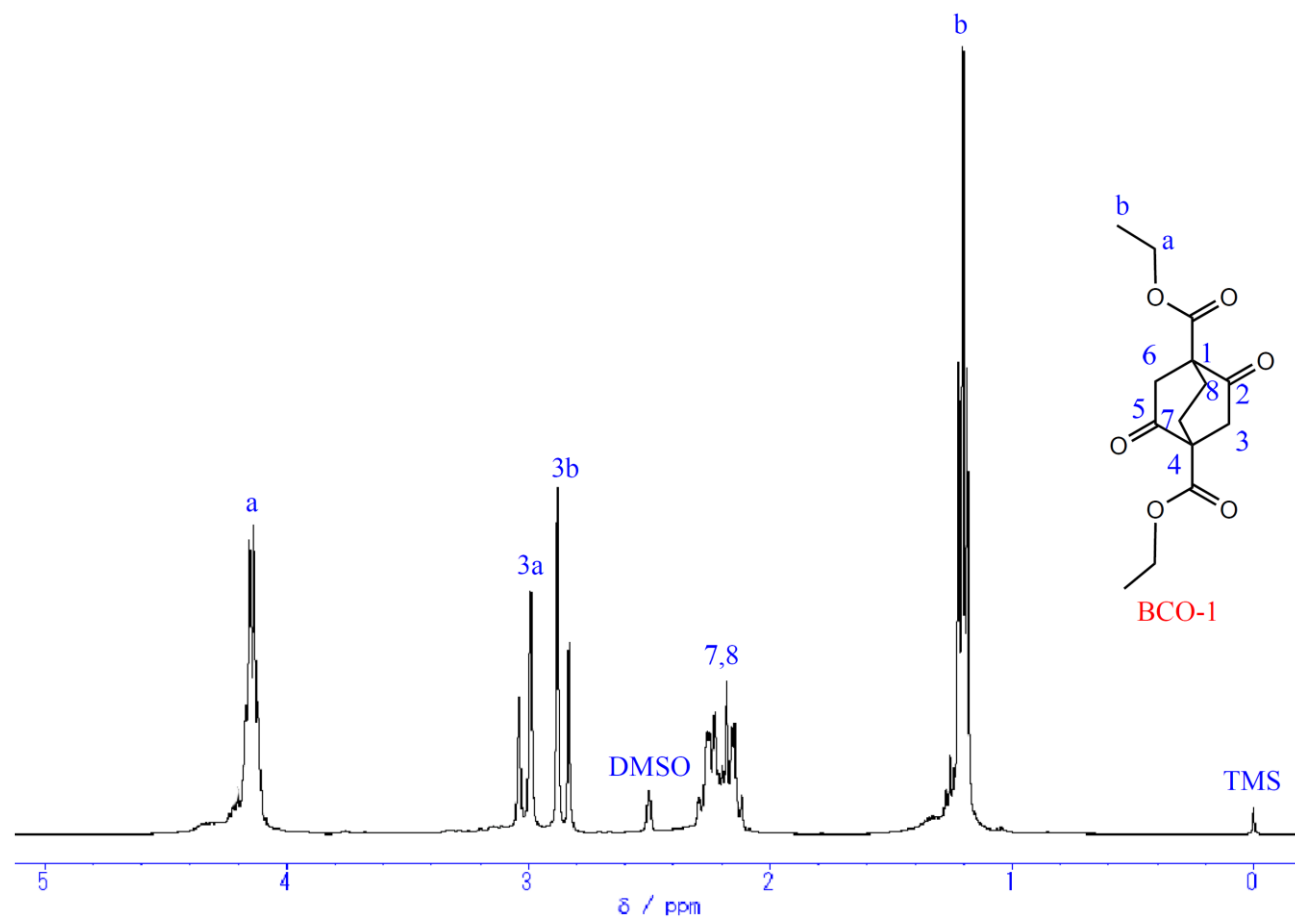


**Scheme S1.** Synthetic route for bicyclo[2.2.2]octane derivatives.

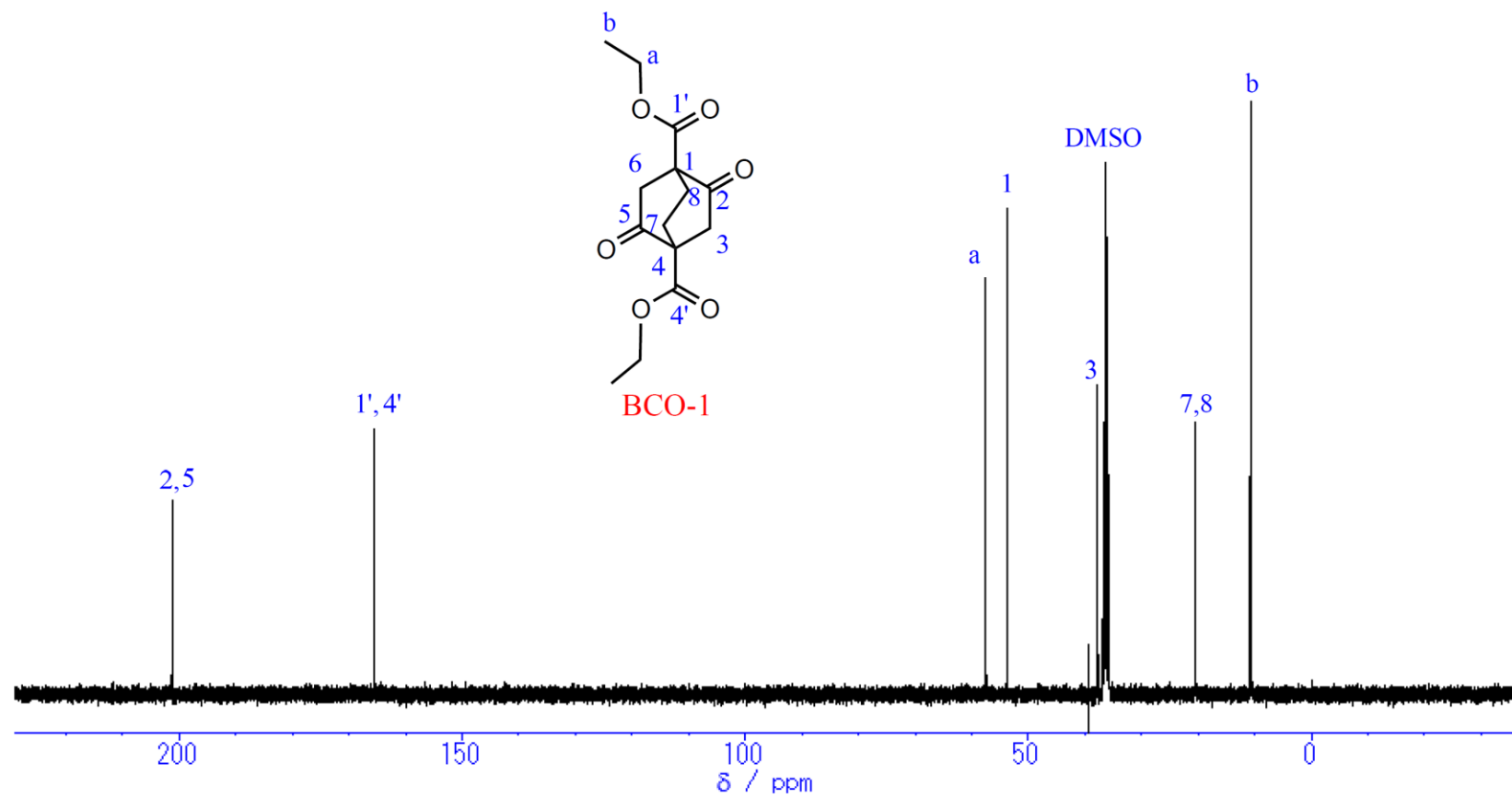
**Table S1.** Experimental Complex Stability Constant ( $K$ ), Standard Free Energy ( $\Delta G^\circ$ ), Enthalpy ( $\Delta H^\circ$ ), and Entropy Changes ( $T\Delta S^\circ$ ) for Complexation of Various Ferrocene, Bicyclo[2.2.2]octane, and Adamantane Guests with Cucurbit[7]uril in H<sub>2</sub>O at  $T = 298.15\text{ K}^a$

guest <sup>charge</sup>	$K/M^{-1}$	$\Delta G^\circ$ /kcal mol <sup>-1</sup>	$\Delta H^\circ$ /kcal mol <sup>-1</sup>	$T\Delta S^\circ$ /kcal mol <sup>-1</sup>
ferrocenylCH <sub>2</sub> OH ( <b>F1</b> )	$(3.3 \pm 0.5) \times 10^9$	$-13.0 \pm 0.1$	$-21.5 \pm 0.5$	$-8.6 \pm 0.5$
ferroceneCH <sub>2</sub> N <sup>+</sup> HMe <sub>2</sub> ( <b>F2</b> )	$(2.4 \pm 0.8) \times 10^{12}$	$-16.9 \pm 0.2$	$-21.0 \pm 0.5$	$-4.1 \pm 0.5$
ferroceneCH <sub>2</sub> N <sup>+</sup> Me <sub>3</sub> ( <b>F3</b> )	$(4.1 \pm 1.0) \times 10^{12}$	$-17.2 \pm 0.2$	$-21.5 \pm 0.2$	$-4.3 \pm 0.5$
1,1'-bis(CH <sub>2</sub> NMe <sub>3</sub> ) <sub>2</sub> ferrocene <sup>2+</sup> ( <b>F6</b> )	$(3.2 \pm 1.0) \times 10^{15}$	$-21.1 \pm 0.2$	$-21.5 \pm 0.2$	$-0.5 \pm 0.5$
1,4-bis(hydroxymethyl)bicyclo[2.2.2]octane <sup>0</sup> ( <b>B2</b> )	$(6.1 \pm 0.5) \times 10^9$	$-13.4 \pm 0.1$	$-15.8 \pm 0.2$	$-2.4 \pm 0.2$
1,4-bis(aminomethyl)bicyclo[2.2.2]octane <sup>2+</sup> ( <b>B5</b> )	$(2.0 \pm 0.5) \times 10^{14}$	$-19.5 \pm 0.2$	$-15.6 \pm 0.4$	$3.9 \pm 0.5$
1,4-bis(Me <sub>2</sub> NCH <sub>2</sub> CH <sub>2</sub> CH <sub>2</sub> NCH <sub>2</sub> ) <sub>2</sub> bicyclo[2.2.2]octane <sup>4+</sup> ( <b>B11</b> )	$(1.2 \pm 0.5) \times 10^{15}$	$-20.6 \pm 0.4$	$-16.3 \pm 0.4$	$4.3 \pm 0.5$
1-adamantanol <sup>0</sup> ( <b>A1</b> )	$(2.3 \pm 0.8) \times 10^{10}$	$-14.1 \pm 0.2$	$-19.0 \pm 0.4$	$-4.9 \pm 0.4$
1-adamantylamine <sup>1+</sup> ( <b>A2</b> )	$(1.7 \pm 0.8) \times 10^{14}$	$-19.4 \pm 0.1$	$-19.3 \pm 0.4$	$0.1 \pm 0.5$
1-aminomethyladamantane <sup>1+</sup> ( <b>A3</b> )	$9 \times 10^{14}{}^b$	$-20.3{}^b$	$-21.9 \pm 0.4$	$-1.7$
1-(2-aminoethylamino)adamantane <sup>2+</sup> ( <b>A4</b> )	$5 \times 10^{15}{}^b$	$-21.5{}^b$	$-20.1 \pm 0.4$	$1.4$
2-adamantylamine <sup>1+</sup> ( <b>A5</b> )	$(1.0 \pm 0.3) \times 10^{14}$	$-19.1 \pm 0.2$	$-19.5 \pm 0.4$	$-0.4 \pm 0.5$

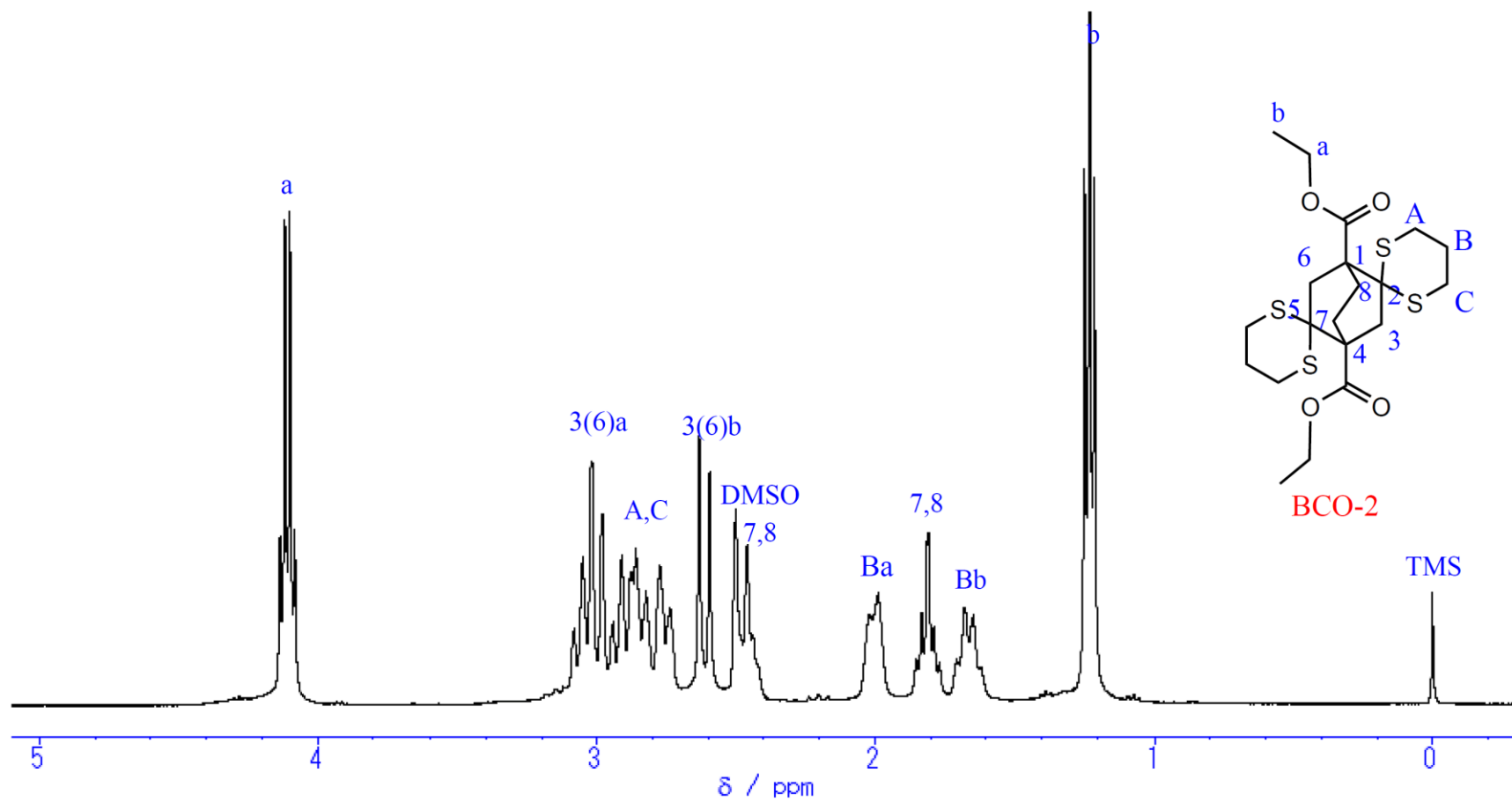
<sup>a</sup> Determined in pure water at 298.15 K by isothermal titration calorimetry (ITC-VT, Microcal), unless stated otherwise. <sup>b</sup> Binding constant was determined by NMR in the presence of competitor, while the enthalpic change was determined by microcalorimetry.



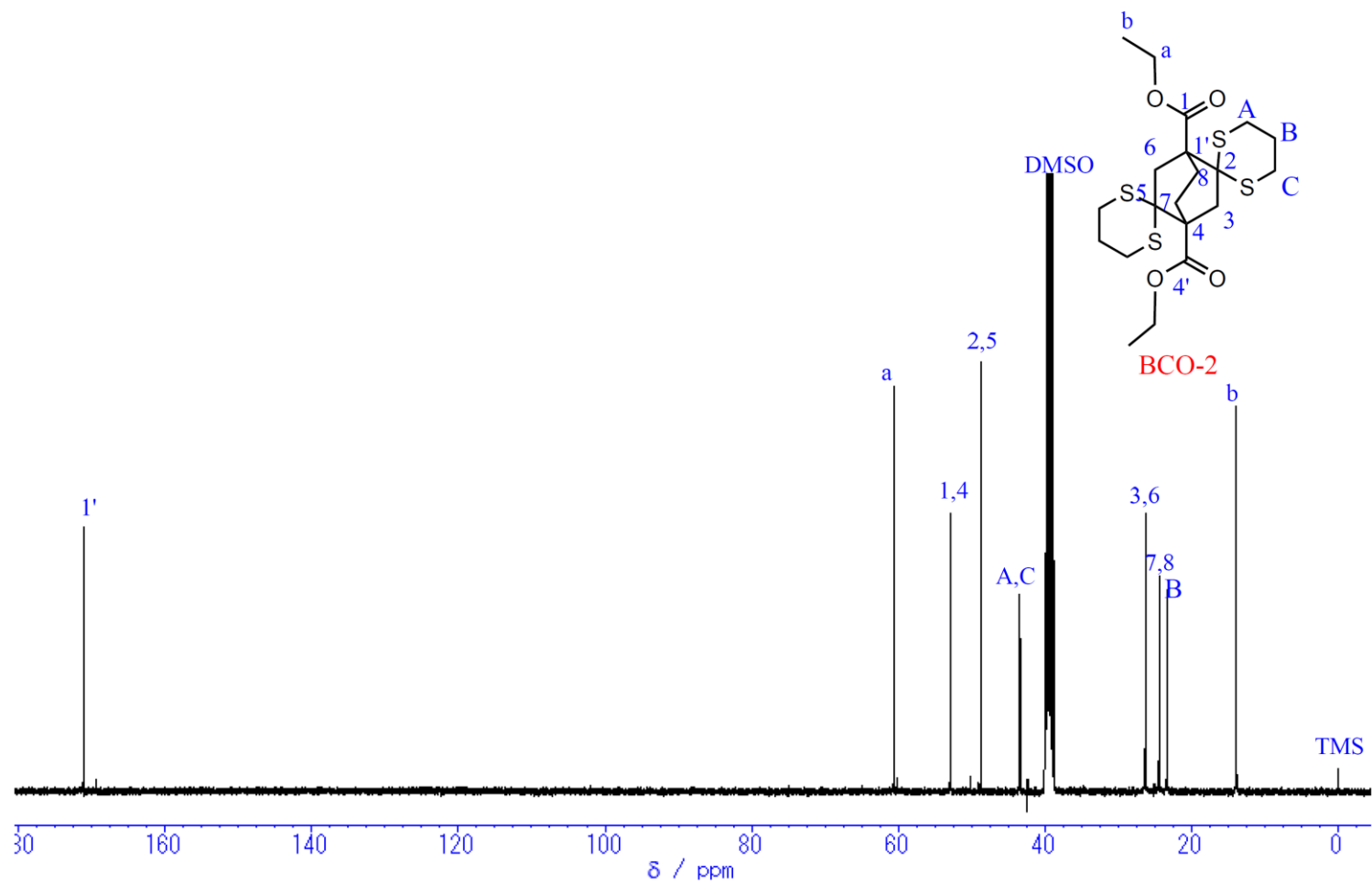
**Figure S1.**  $^1\text{H}$  NMR spectrum of BCO-1 in  $\text{DMSO-}d_6$  measured at 20 °C.



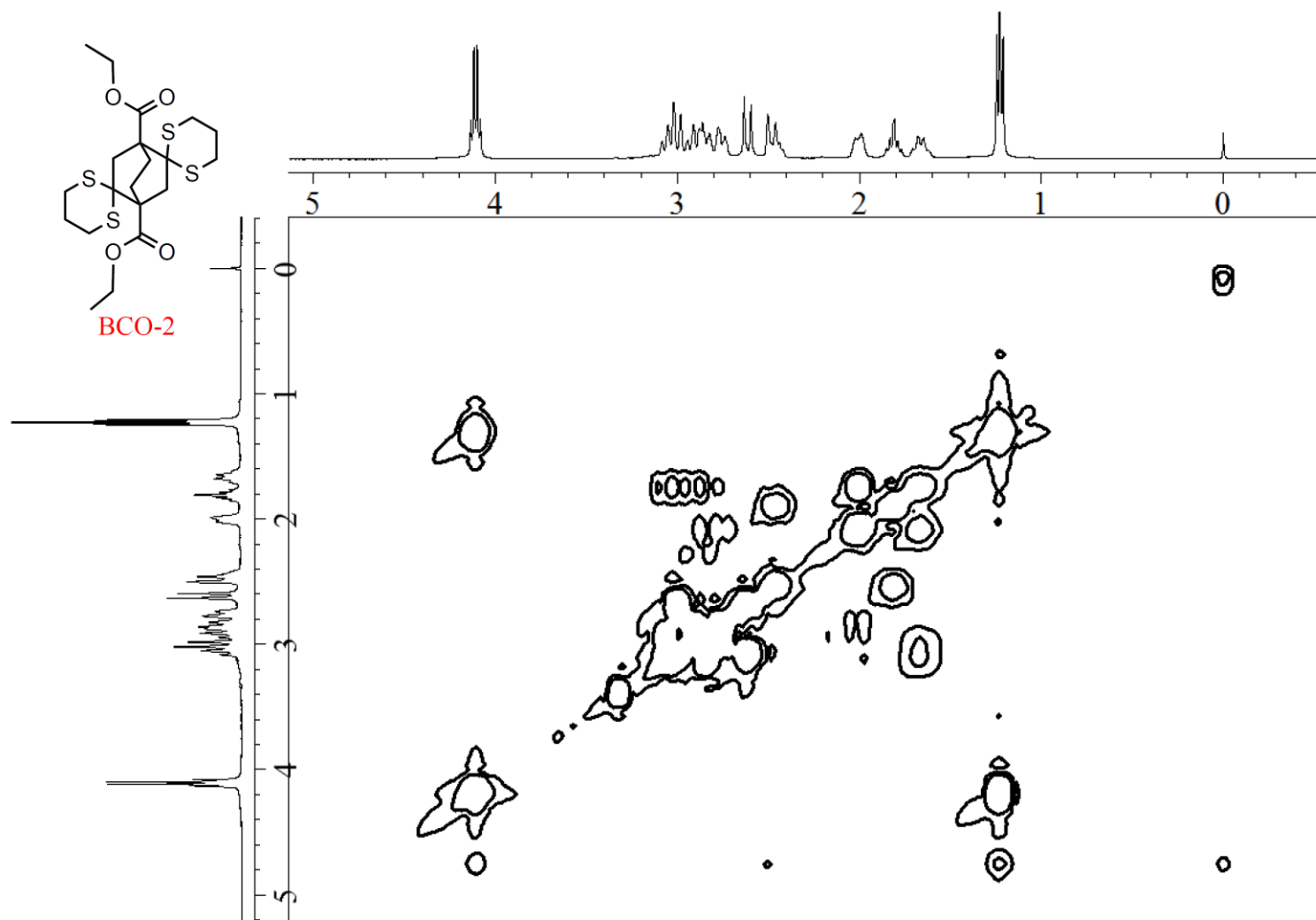
**Figure S2.** <sup>13</sup>C NMR spectrum of BCO-1 in DMSO-*d*<sub>6</sub> measured at 20 °C.



**Figure S3.**  $^1\text{H}$  NMR spectrum of BCO-2 measured in  $\text{DMSO-}d_6$  at  $20\text{ }^\circ\text{C}$ .

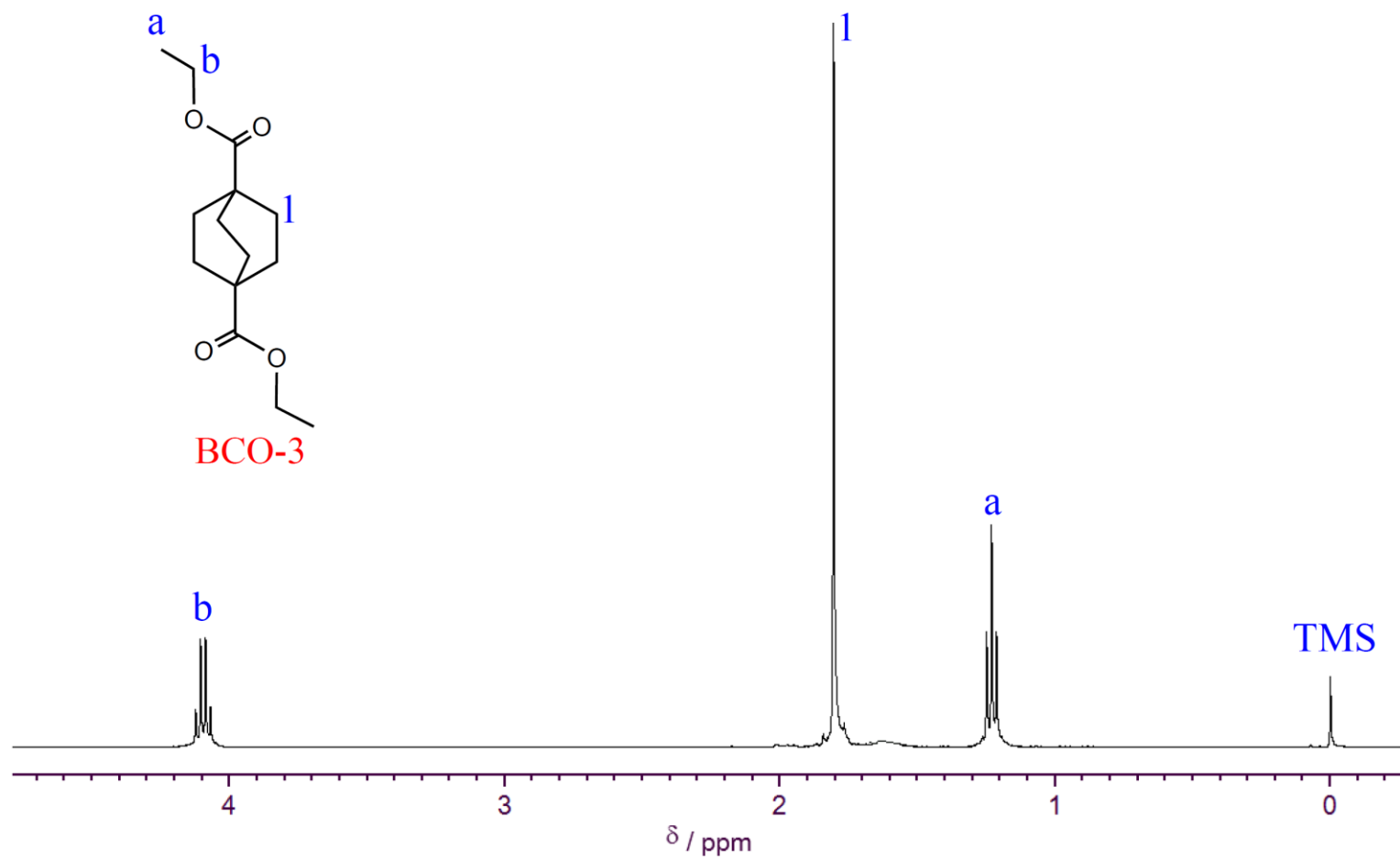


**Figure S4.**  $^{13}\text{C}$  NMR spectrum of BCO-2 measured in  $\text{DMSO-}d_6$  at 20 °C.

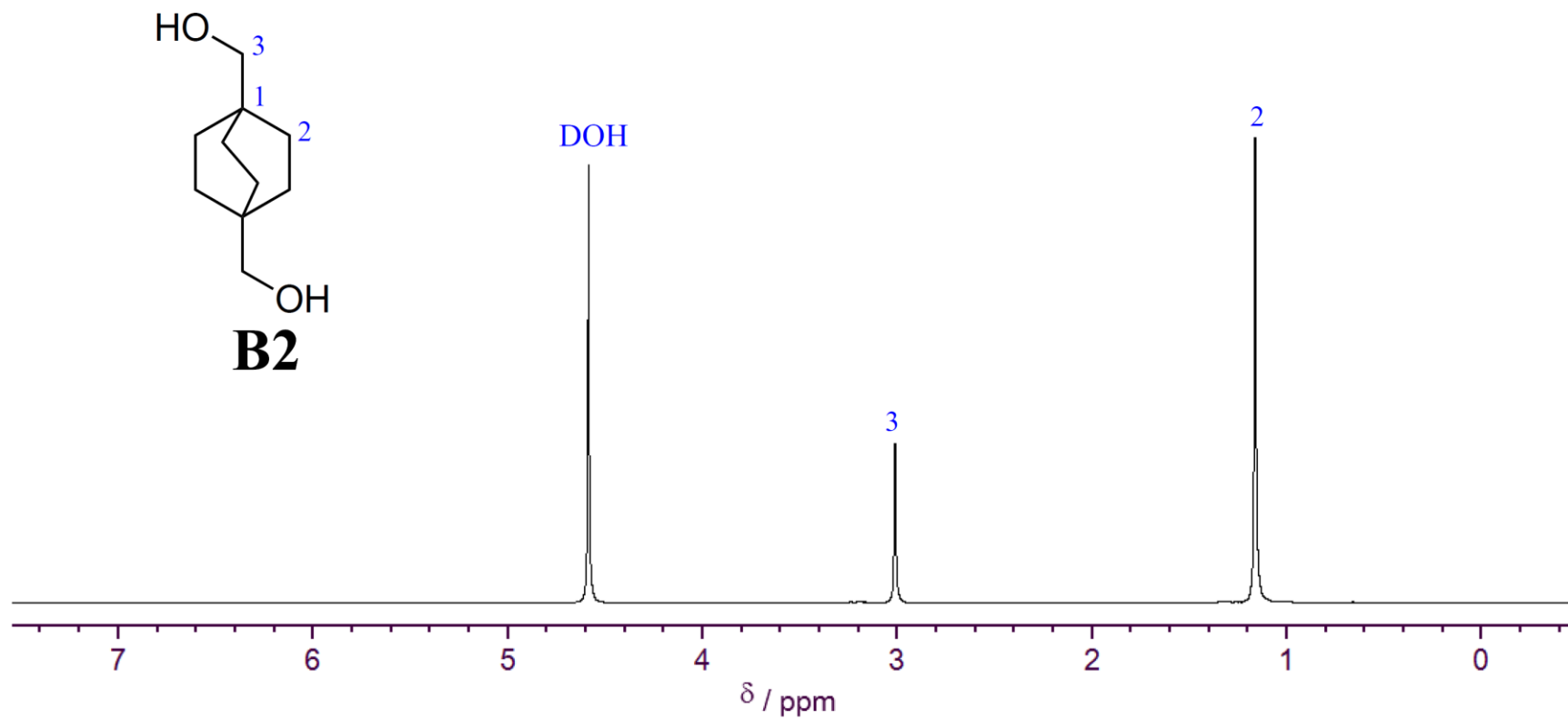


**Figure S5.**  $^1\text{H}$ - $^1\text{H}$  COSY spectrum of BCO-2 measured in  $\text{DMSO-}d_6$  at 20 °C.

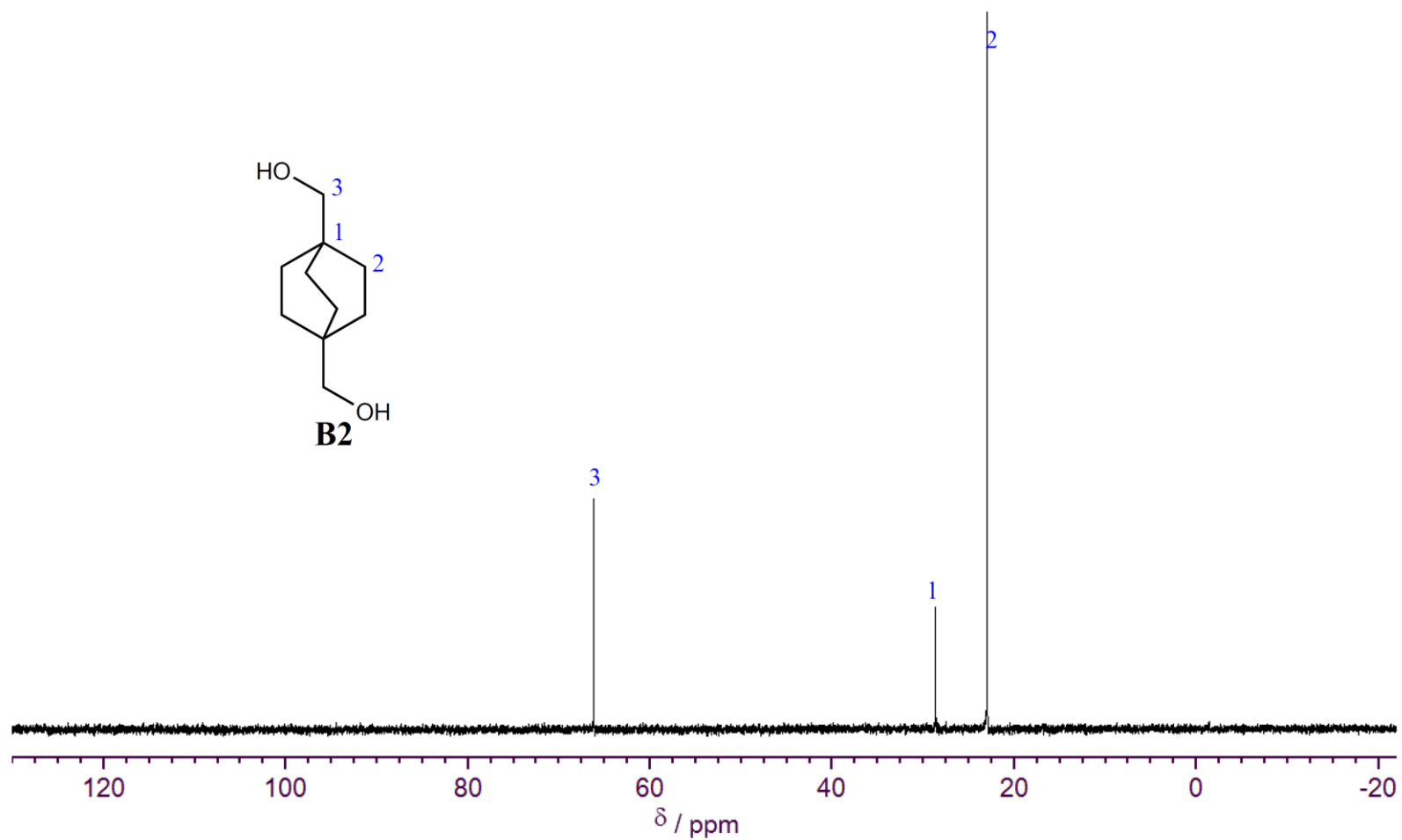




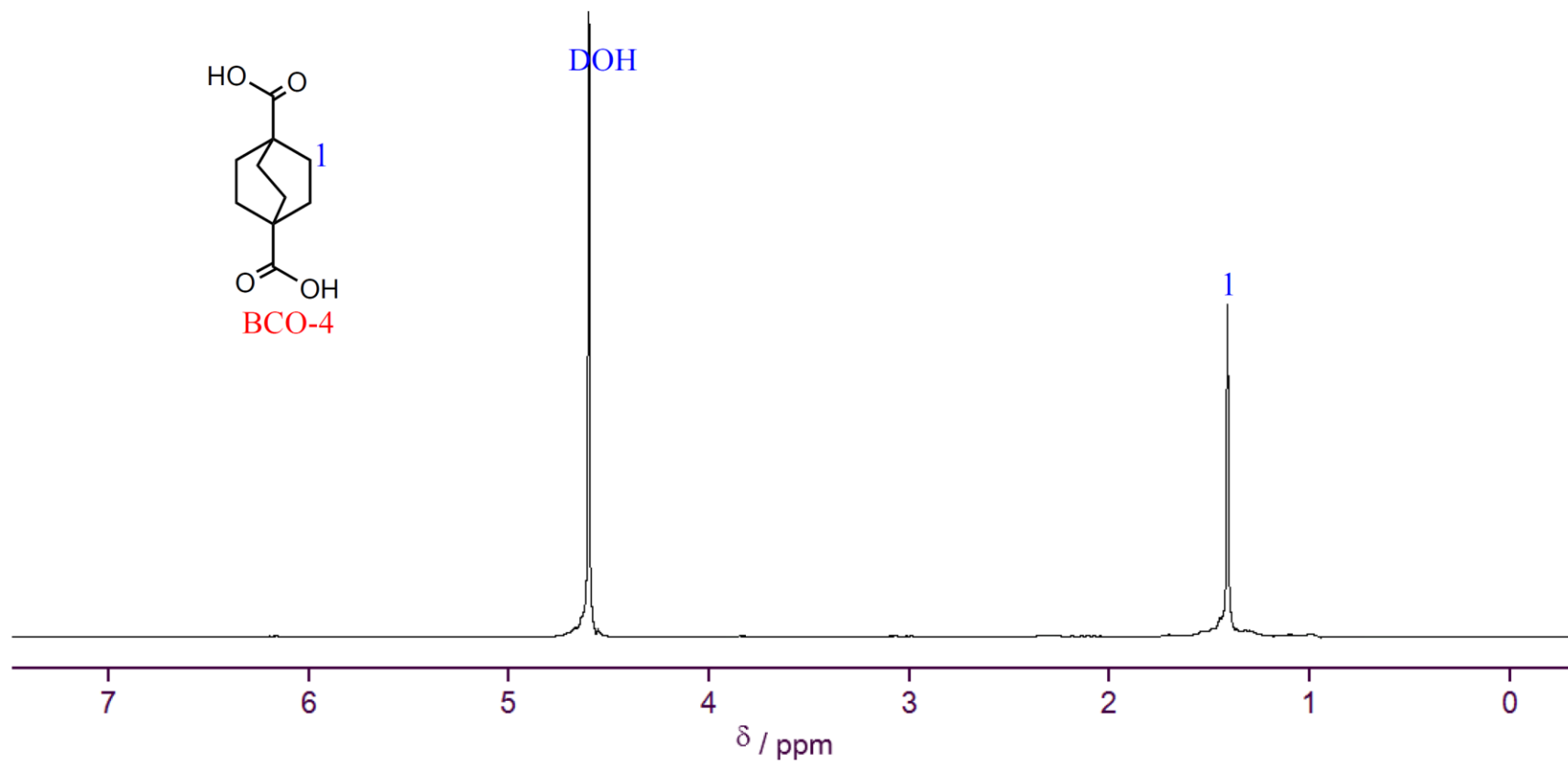
**Figure S6.** <sup>1</sup>H NMR spectrum of BCO-3 measured in CDCl<sub>3</sub> at 20 °C.



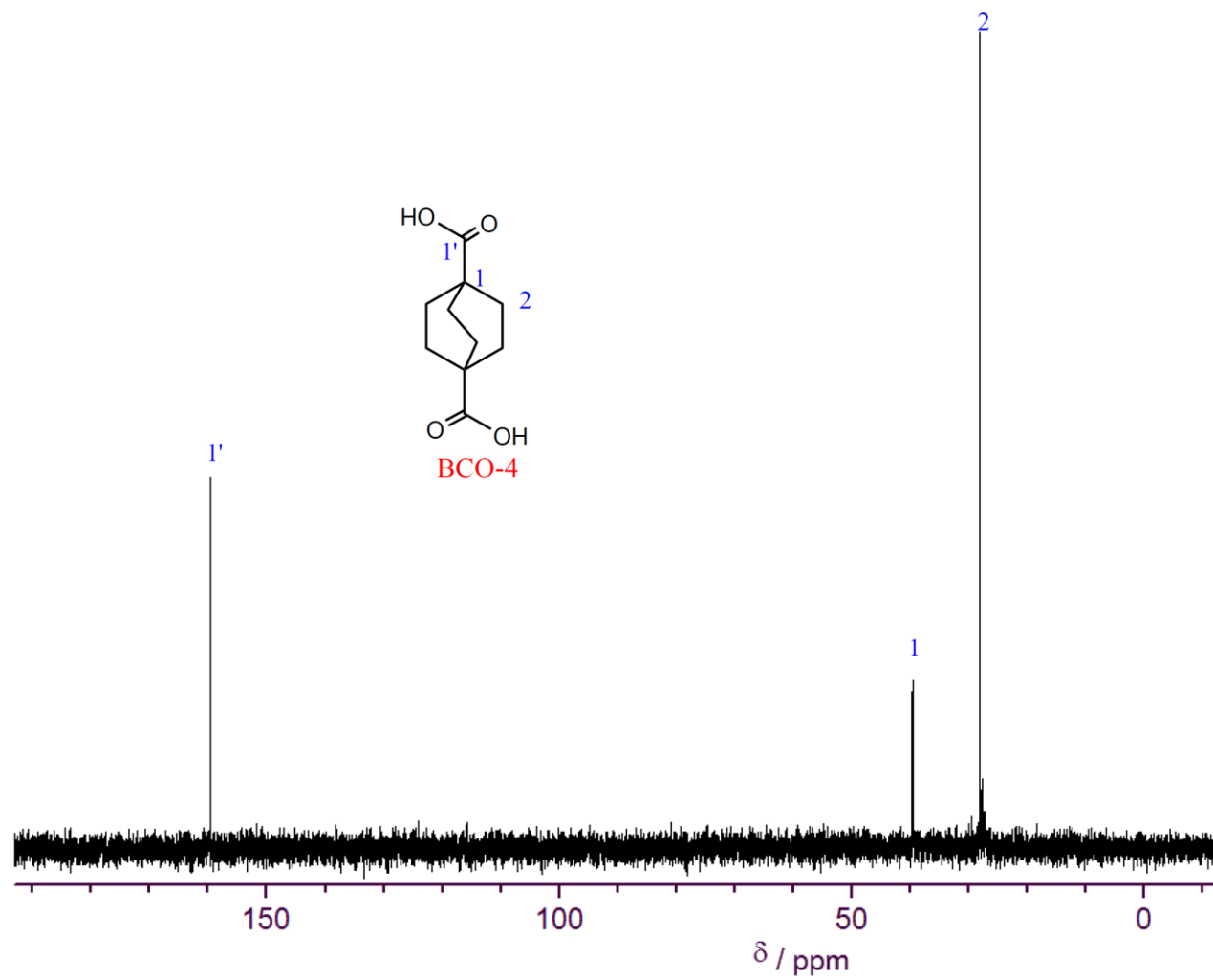
**Figure S7.** <sup>1</sup>H NMR spectrum of **B2** measured in CDCl<sub>3</sub> at 20 °C.



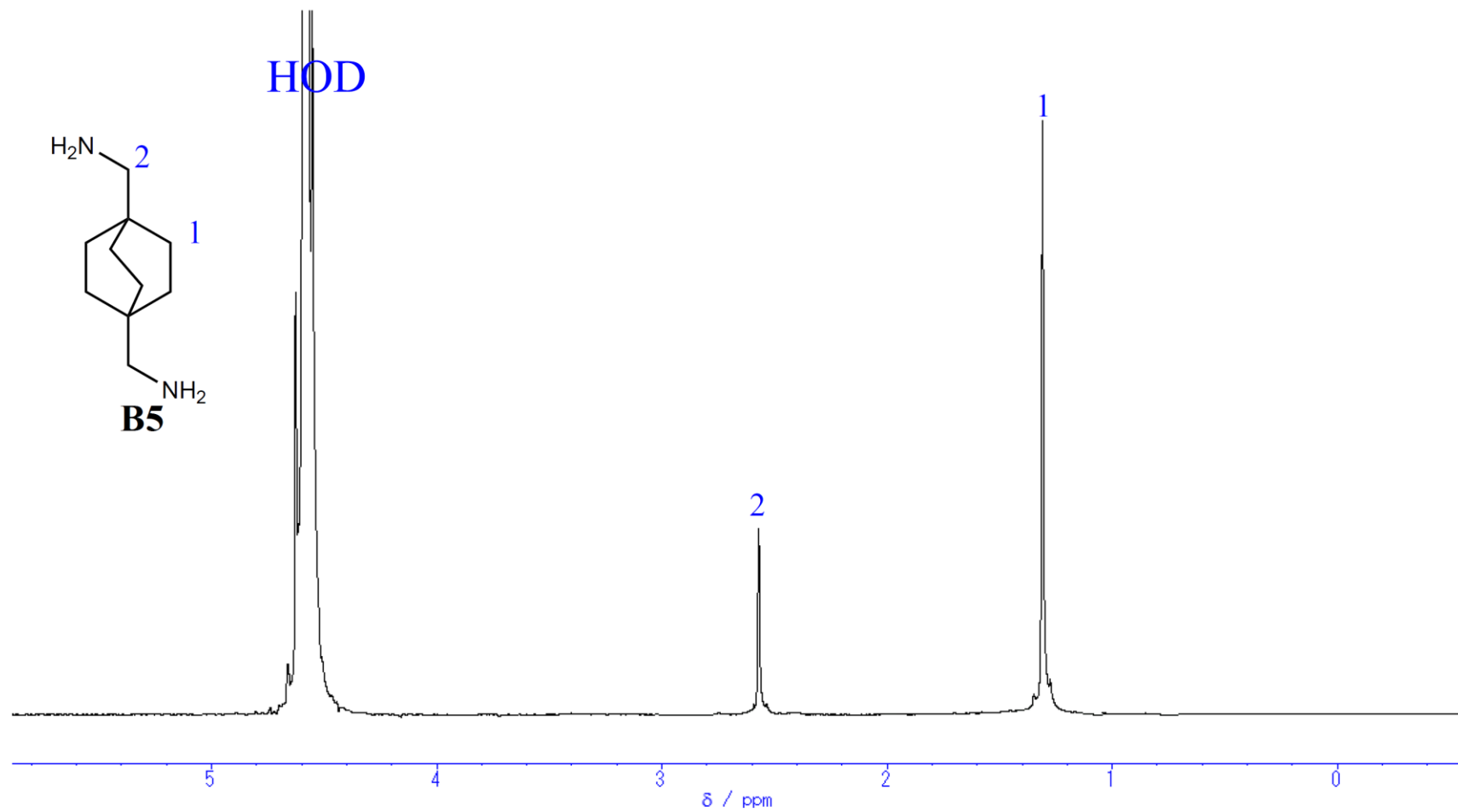
**Figure S8.**  $^{13}\text{C}$  NMR spectrum of **B2** measured in  $\text{DMSO-}d_6$  at  $20\text{ }^\circ\text{C}$ .



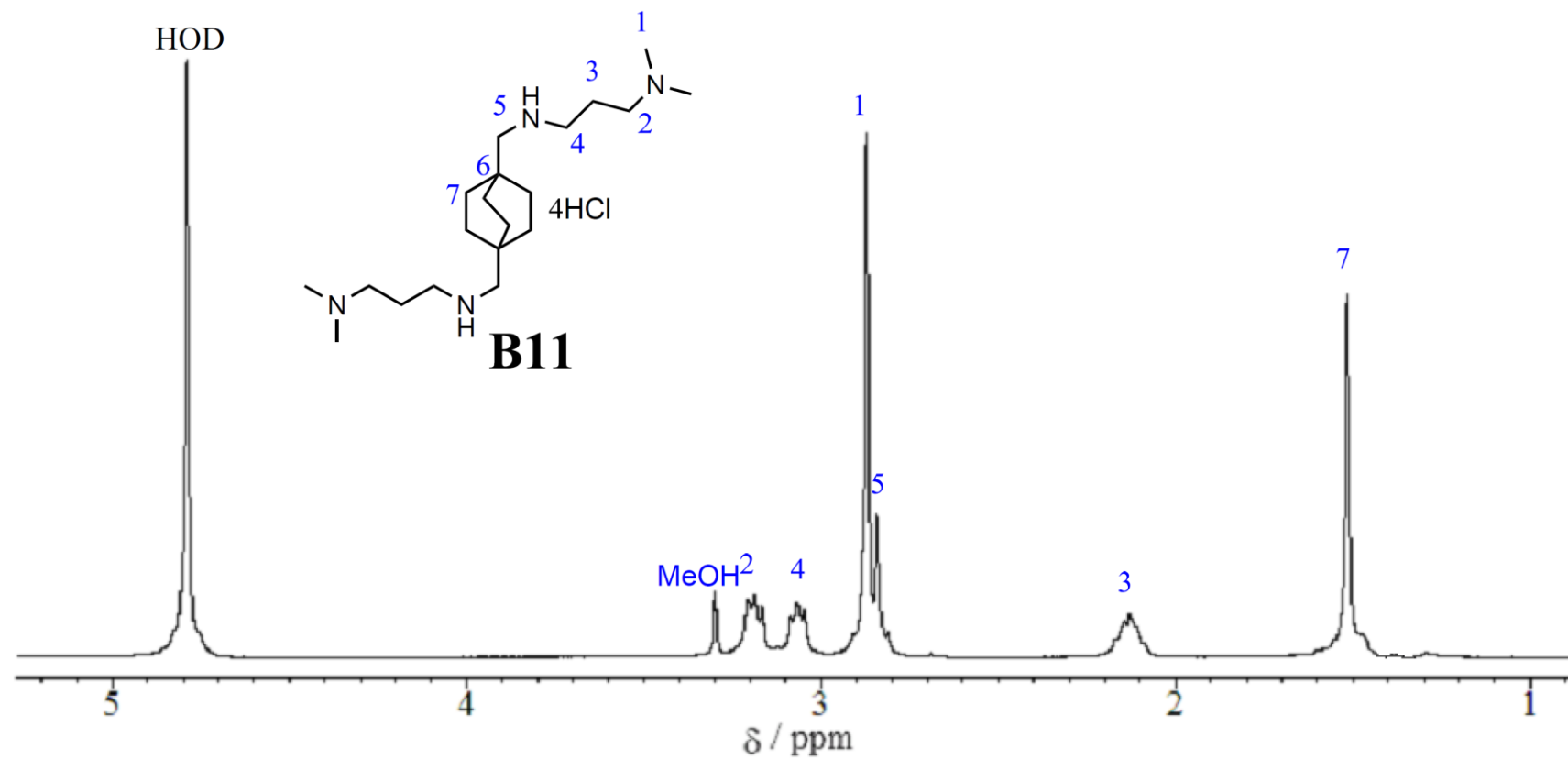
**Figure S9.**  $^1\text{H}$  NMR spectrum of BCO-4 measured in  $\text{D}_2\text{O}$  at  $20\text{ }^\circ\text{C}$ .



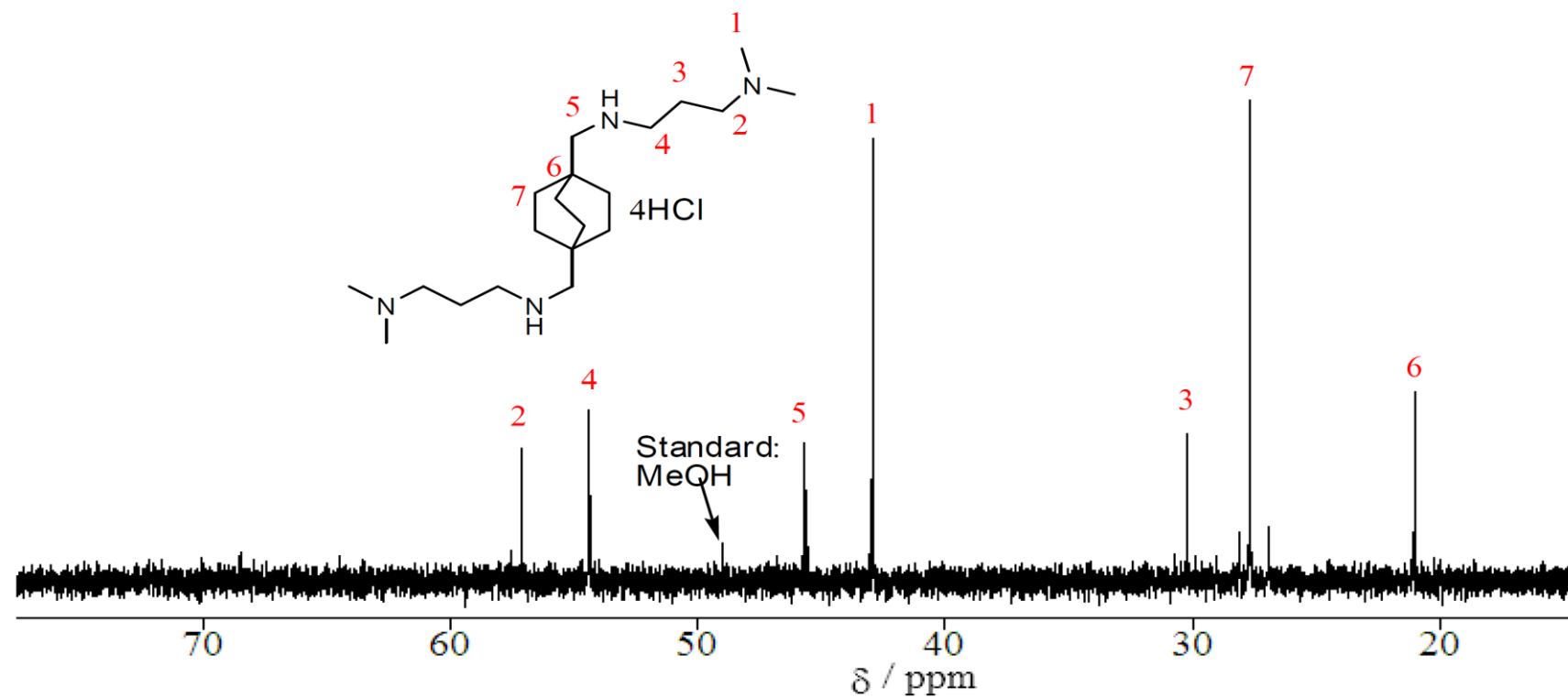
**Figure S10.** <sup>13</sup>C NMR spectrum of BCO-4 measured in D<sub>2</sub>O at 20 °C.



**Figure S11.**  $^1\text{H}$  NMR spectrum of **B5** measured in  $\text{D}_2\text{O}$  at  $20\text{ }^\circ\text{C}$ .



**Figure S12.**  $^1\text{H}$  NMR spectrum of **B11** measured in  $\text{D}_2\text{O}$  at  $20^\circ\text{C}$  with MeOH added as an internal standard.



**Figure S13.**  $^{13}\text{C}$  NMR spectrum of **B11** measured in  $\text{D}_2\text{O}$  at 20 °C with MeOH as an internal standard.



[ Mass Spectrum ]  
Data : HR083009 Date : 21-Aug-2009 09:25  
Sample: BCO-5  
Note :  
Inlet : Direct Ion Mode : FFB+  
Spectrum Type : Normal Ion (EF-Linear)  
RT : 1.75 min Scan# : 15  
BP : m/z 93.0552 Int. : 80.62  
Output m/z range : 85.0000 to 190.0000 Cut Level : 0.00 %

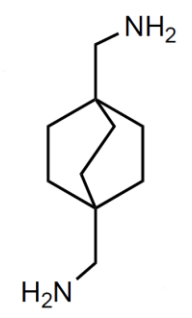
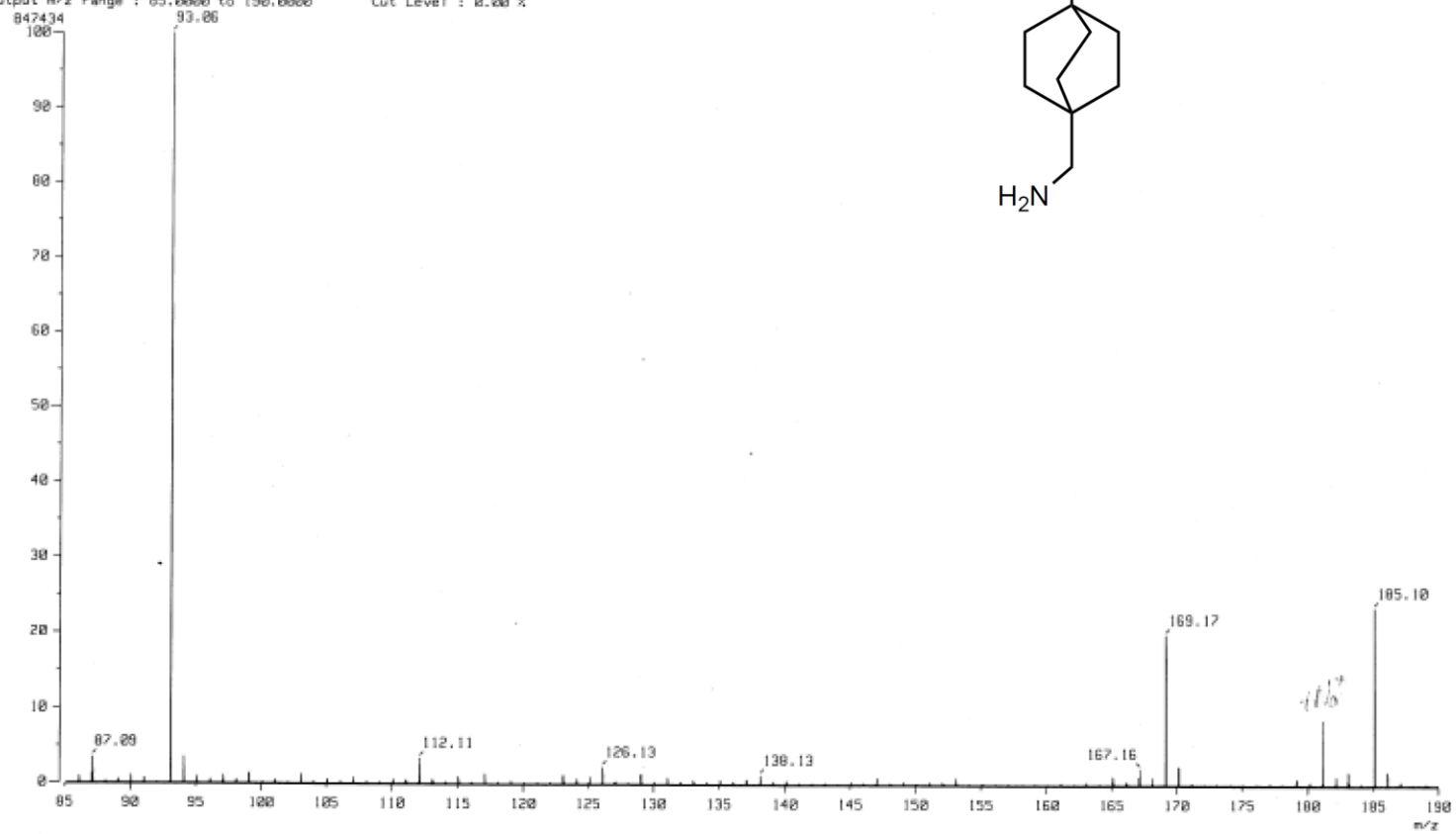


Figure S14. High-Resolution Mass Spectrum of B5.

[ Mass Spectrum ]  
Data : HR009004 Date : 20-Aug-2009 17:13  
Sample: BCO-6  
Note :  
Inlet : Direct Ion Mode : FRR+  
Spectrum Type : Normal Ion [EF-Linear]  
RT : 0.70 min Scan# : 8  
BP : m/z 277.1498 Int. : 21.87  
Output m/z range : 270.0000 to 375.0000 Cut Level : 0.00 %

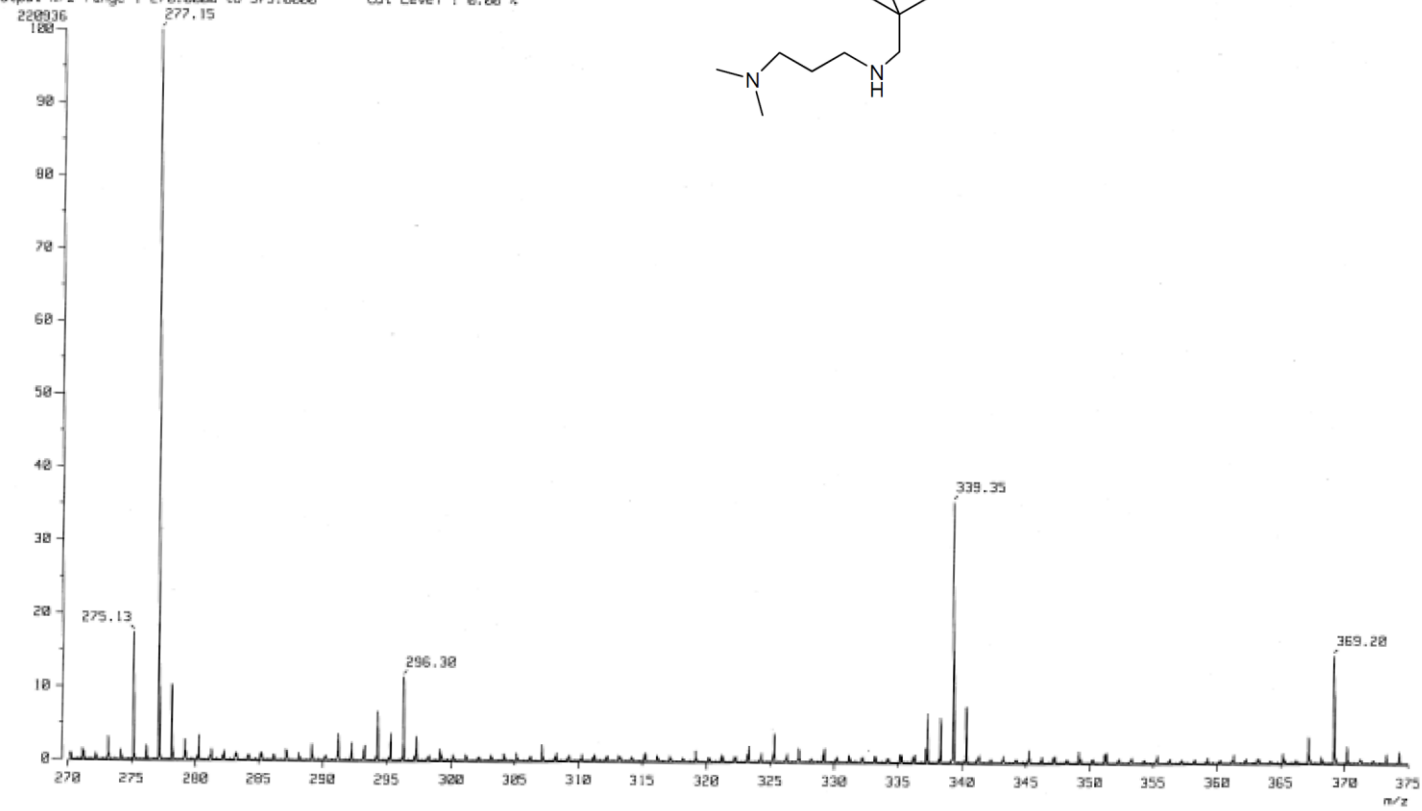
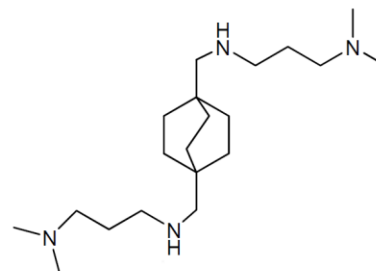
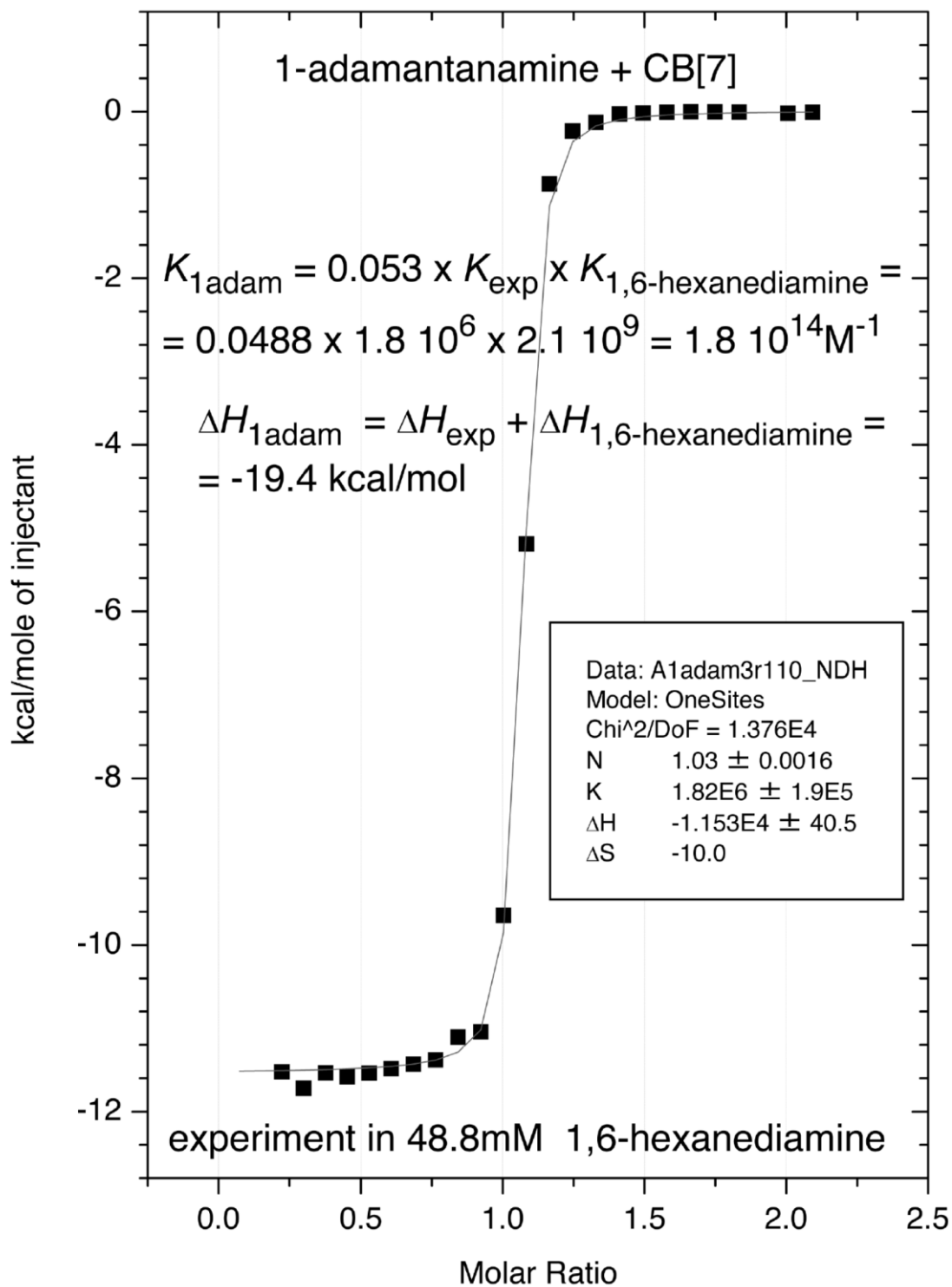
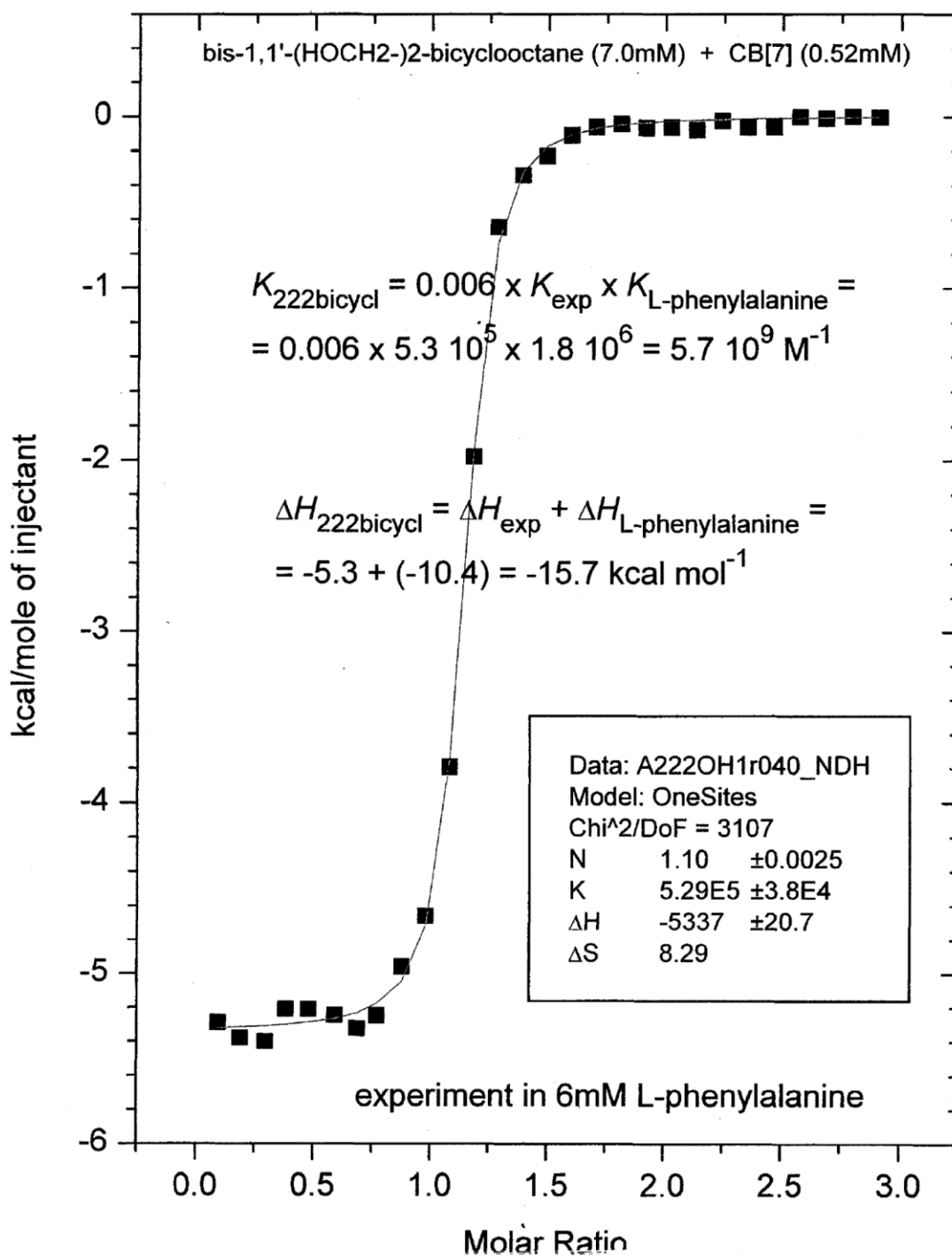


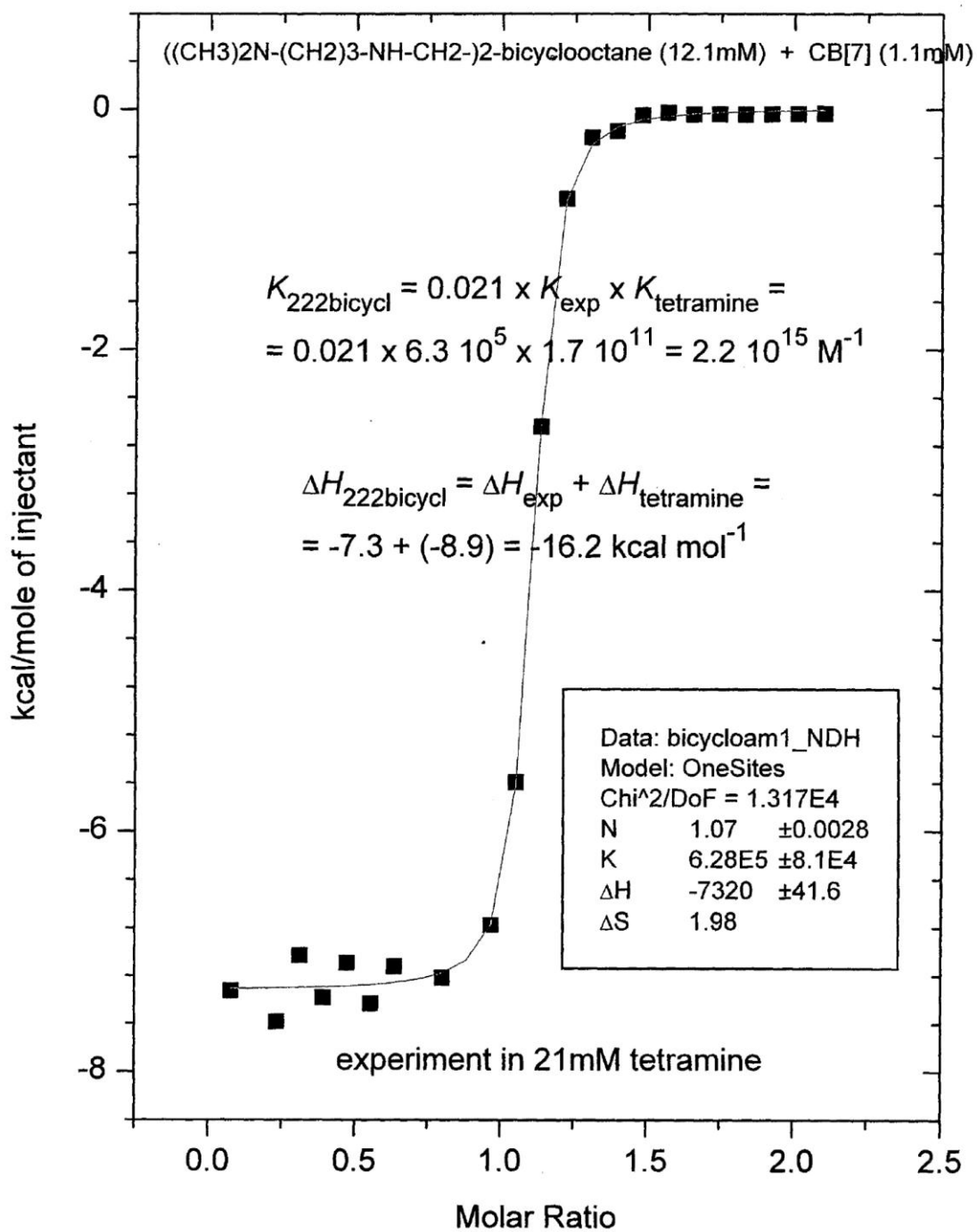
Figure S15. High-Resolution Mass Spectrum of B11.



**Figure 16.** Competition ITC experiment on complexation of **A2** with CB[7] in water at 298.15 K in the presence of 1,6-hexanediamine (48.8 mM) as competitor.



**Figure 17.** Competition ITC experiment on complexation of **B2** with CB[7] in water at 298.15 K in the presence of L-phenylalanine as competitor.



**Figure 18.** Competition ITC experiment on complexation of **B11** with CB[7] in water at 298.15 K in the presence of triethylenetetramine as competitor

## References

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