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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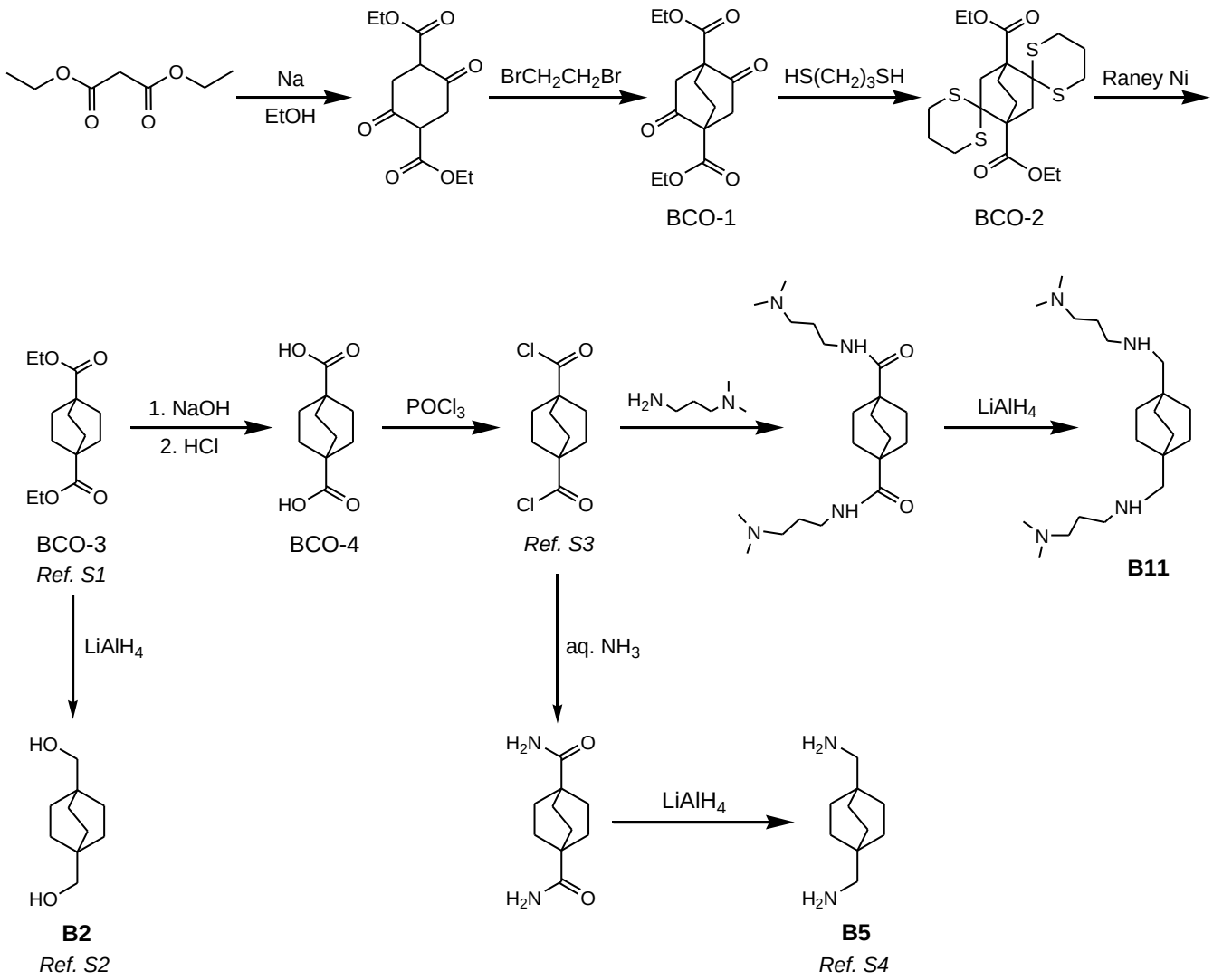
Ref 10: MacKerell, A.; Bashford, D.; Bellott, M.; Dunbrack, R.; Evanseck, J.; Field, M.; Fischer, S.; Gao, J.; Guo, H.; Ha, S.; Joseph-McCarthy, D.; Kuchnir, L.; Kuczera, K.; Lau, F.; Mattos, C.; Michnick, S.; Ngo, T.; Nguyen, D.; Prodhom, B.; Reiher, W.; Roux, B.; Schlenkrich, M.; Smith, J.; Stote, 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 ($\Delta G°$), Enthalpy ($\Delta H°$), and Entropy Changes ($T\Delta S°$) for Complexation of Various Ferrocene, Bicyclo[2.2.2]octane, and Adamantane Guests with Cucurbit[7]uril in H_2O at T = 298.15 K[a]

guest^{charge}	K/M^{-1}	$\Delta G°$ /kcal mol^{-1}	$\Delta H°$ /kcal mol^{-1}	$T\Delta S°$ /kcal mol^{-1}
ferrocenylCH_2OH (**F1**)	$(3.3 \pm 0.5) \times 10^9$	-13.0 ± 0.1	-21.5 ± 0.5	-8.6 ± 0.5
ferrocene$CH_2N^+HMe_2$ (**F2**)	$(2.4 \pm 0.8) \times 10^{12}$	-16.9 ± 0.2	-21.0 ± 0.5	-4.1 ± 0.5
ferrocene$CH_2N^+Me_3$ (**F3**)	$(4.1 \pm 1.0) \times 10^{12}$	-17.2 ± 0.2	-21.5 ± 0.2	-4.3 ± 0.5
1,1'-bis$(CH_2NMe_3)_2$ferrocene^{2+} (**F6**)	$(3.2 \pm 1.0) \times 10^{15}$	-21.1 ± 0.2	-21.5 ± 0.2	-0.5 ± 0.5
1,4-bis(hydroxylmethyl)bicyclo[2.2.2]octane^0 (**B2**)	$(6.1 \pm 0.5) \times 10^9$	-13.4 ± 0.1	-15.8 ± 0.2	-2.4 ± 0.2
1,4-bis(aminomethyl)bicyclo[2.2.2]octane^{2+} (**B5**)	$(2.0 \pm 0.5) \times 10^{14}$	-19.5 ± 0.2	-15.6 ± 0.4	3.9 ± 0.5
1,4-bis$(Me_2NCH_2CH_2CH_2NCH_2)_2$bicyclo[2.2.2]octane^{4+} (**B11**)	$(1.2 \pm 0.5) \times 10^{15}$	-20.6 ± 0.4	-16.3 ± 0.4	4.3 ± 0.5
1-adamantanol^0 (**A1**)	$(2.3 \pm 0.8) \times 10^{10}$	-14.1 ± 0.2	-19.0 ± 0.4	-4.9 ± 0.4
1-adamantylamine^{1+} (**A2**)	$(1.7 \pm 0.8) \times 10^{14}$	-19.4 ± 0.1	-19.3 ± 0.4	0.1 ± 0.5
1-aminomethyladamantane^{1+} (**A3**)	9×10^{14} [b]	-20.3 [b]	-21.9 ± 0.4	-1.7
1-(2-aminoethylamino)adamantane^{2+} (**A4**)	5×10^{15} [b]	-21.5 [b]	-20.1 ± 0.4	1.4
2-adamantylamine^{1+} (**A5**)	$(1.0 \pm 0.3) \times 10^{14}$	-19.1 ± 0.2	-19.5 ± 0.4	-0.4 ± 0.5

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

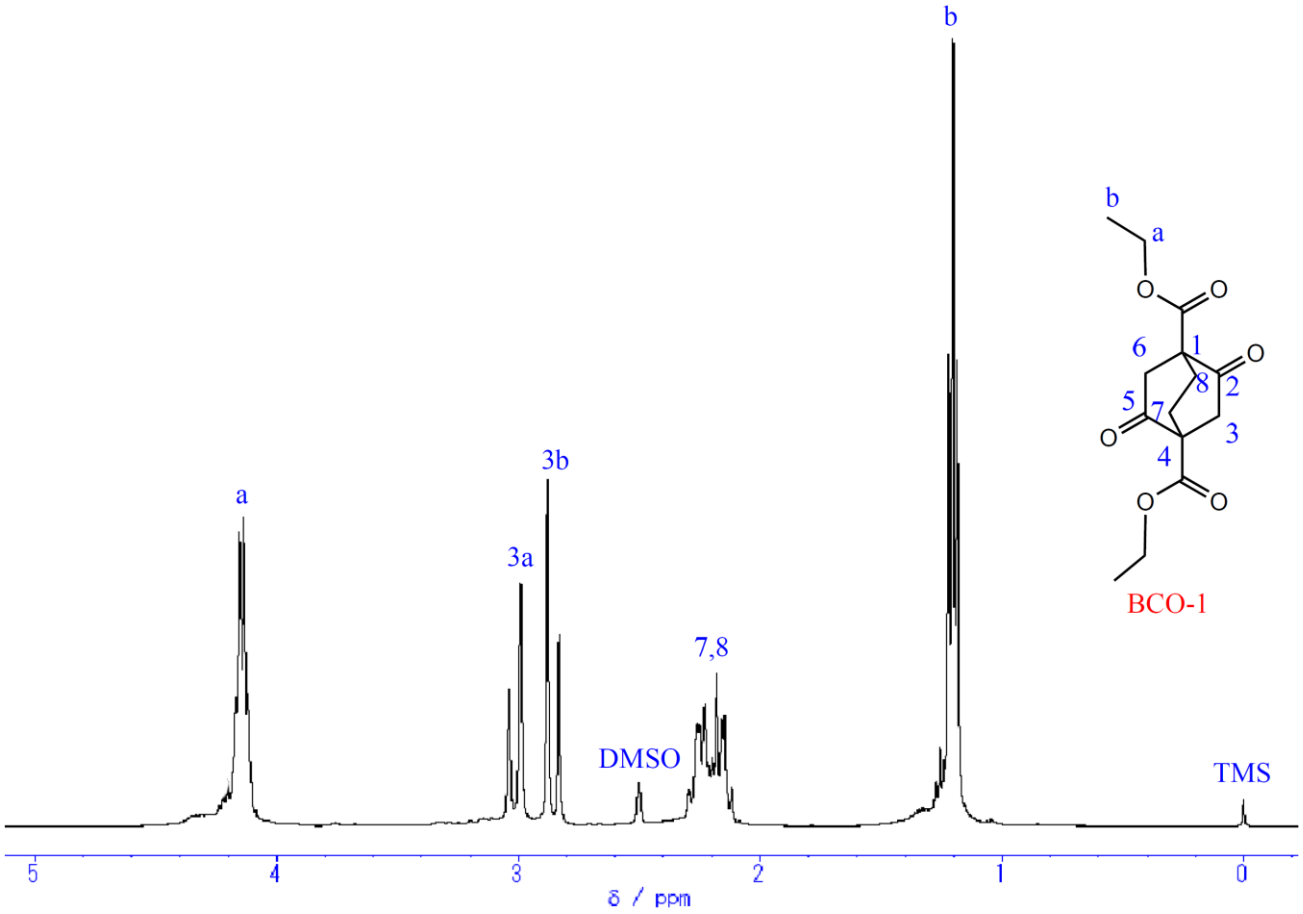


Figure S1. ^{1}H NMR spectrum of BCO-1 in DMSO-d_6 measured at 20 °C.

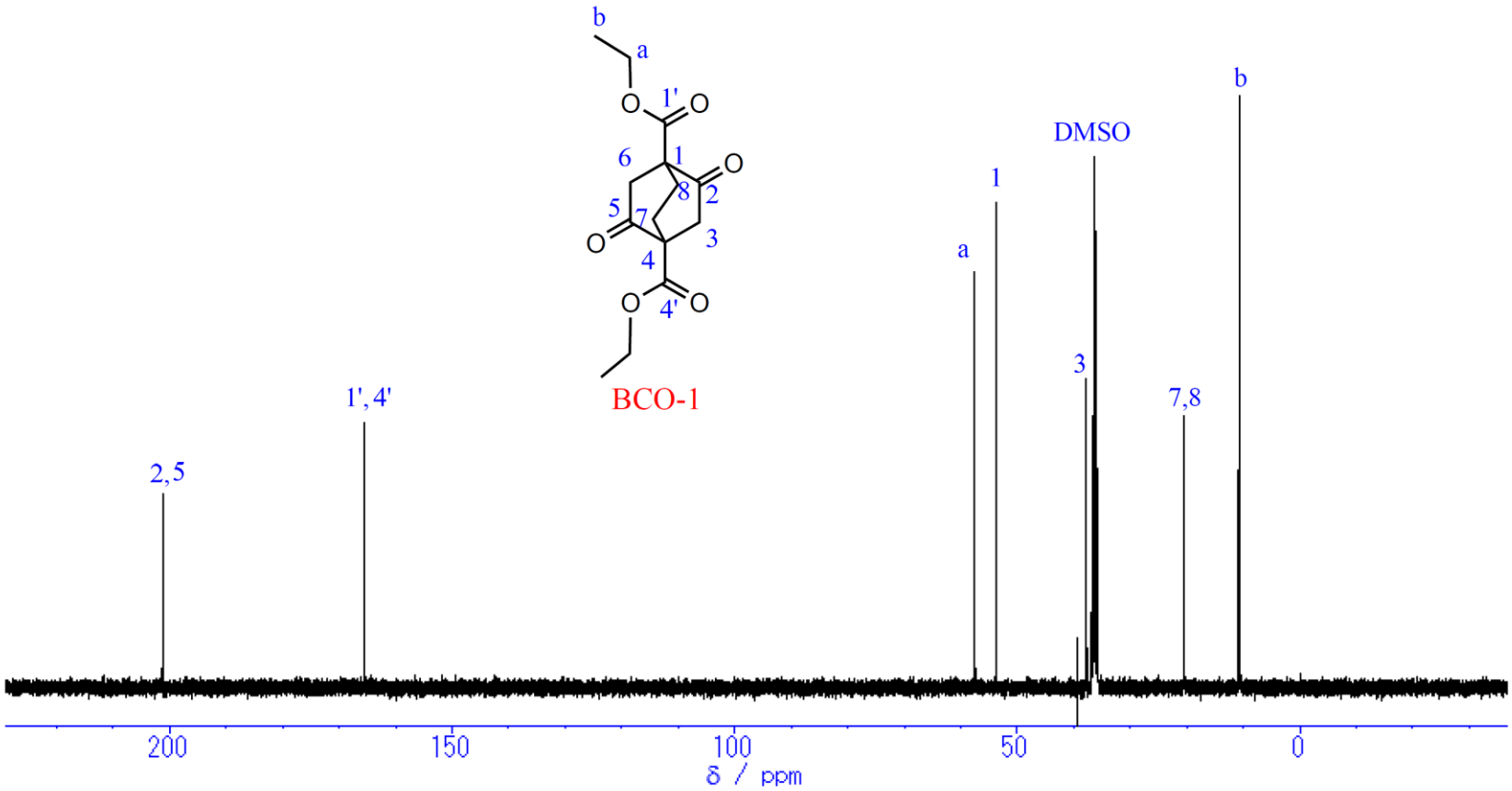


Figure S2. ^{13}C NMR spectrum of BCO-1 in DMSO-d_6 measured at 20 °C.

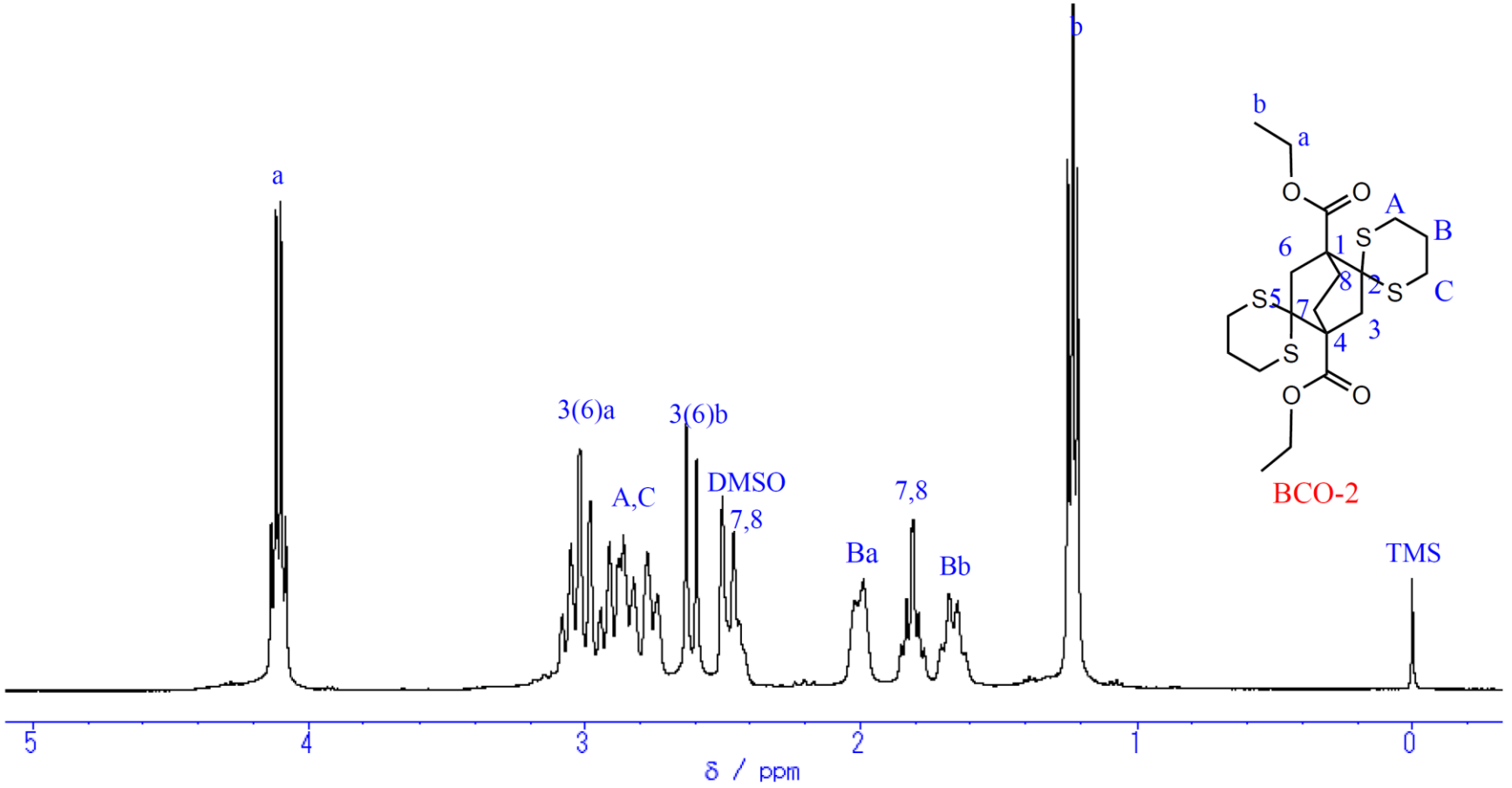


Figure S3. ^{1}H NMR spectrum of BCO-2 measured in DMSO-d_6 at 20 °C.

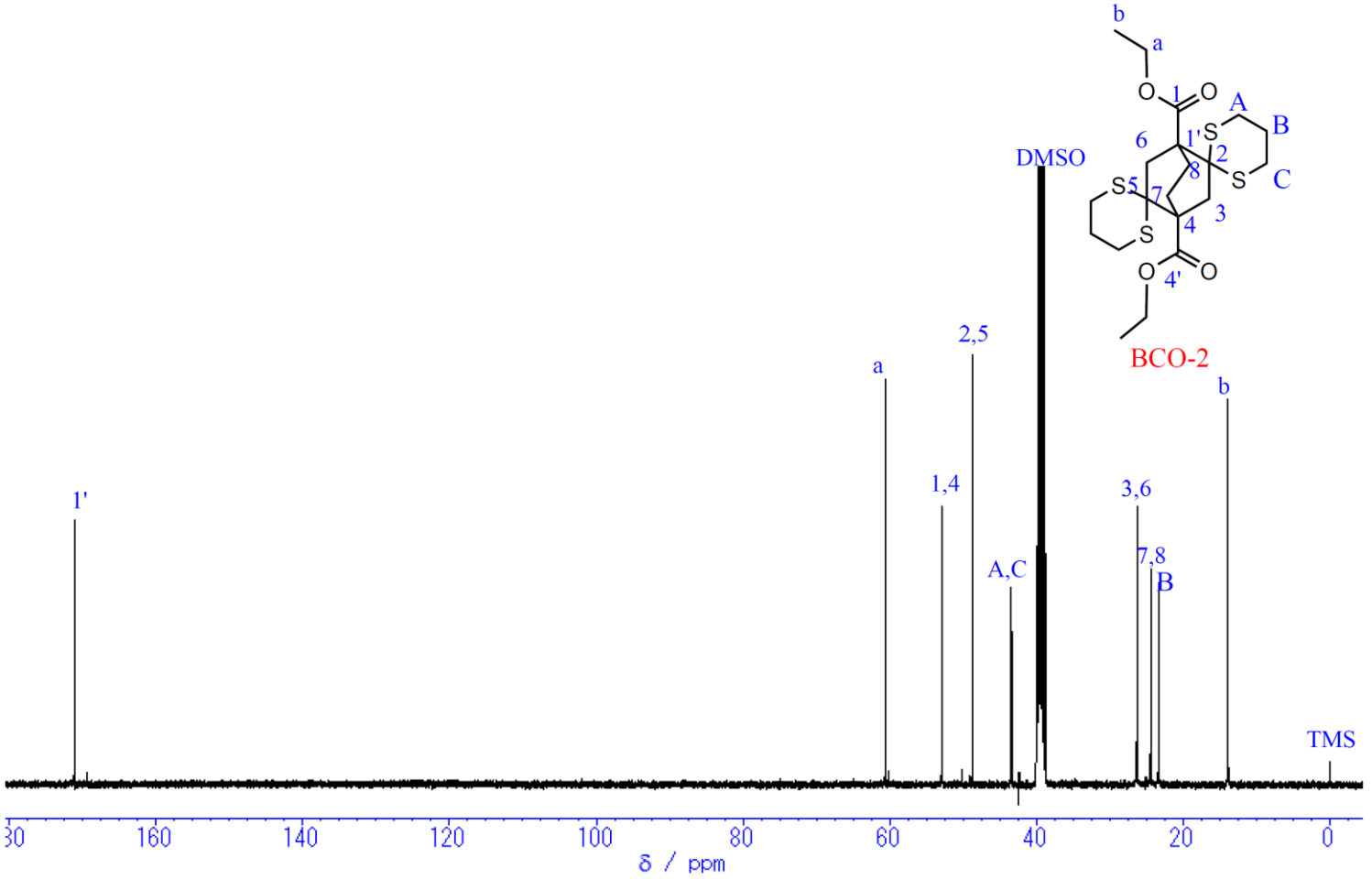


Figure S4. ^{13}C NMR spectrum of BCO-2 measured in DMSO-d_6 at 20 °C.

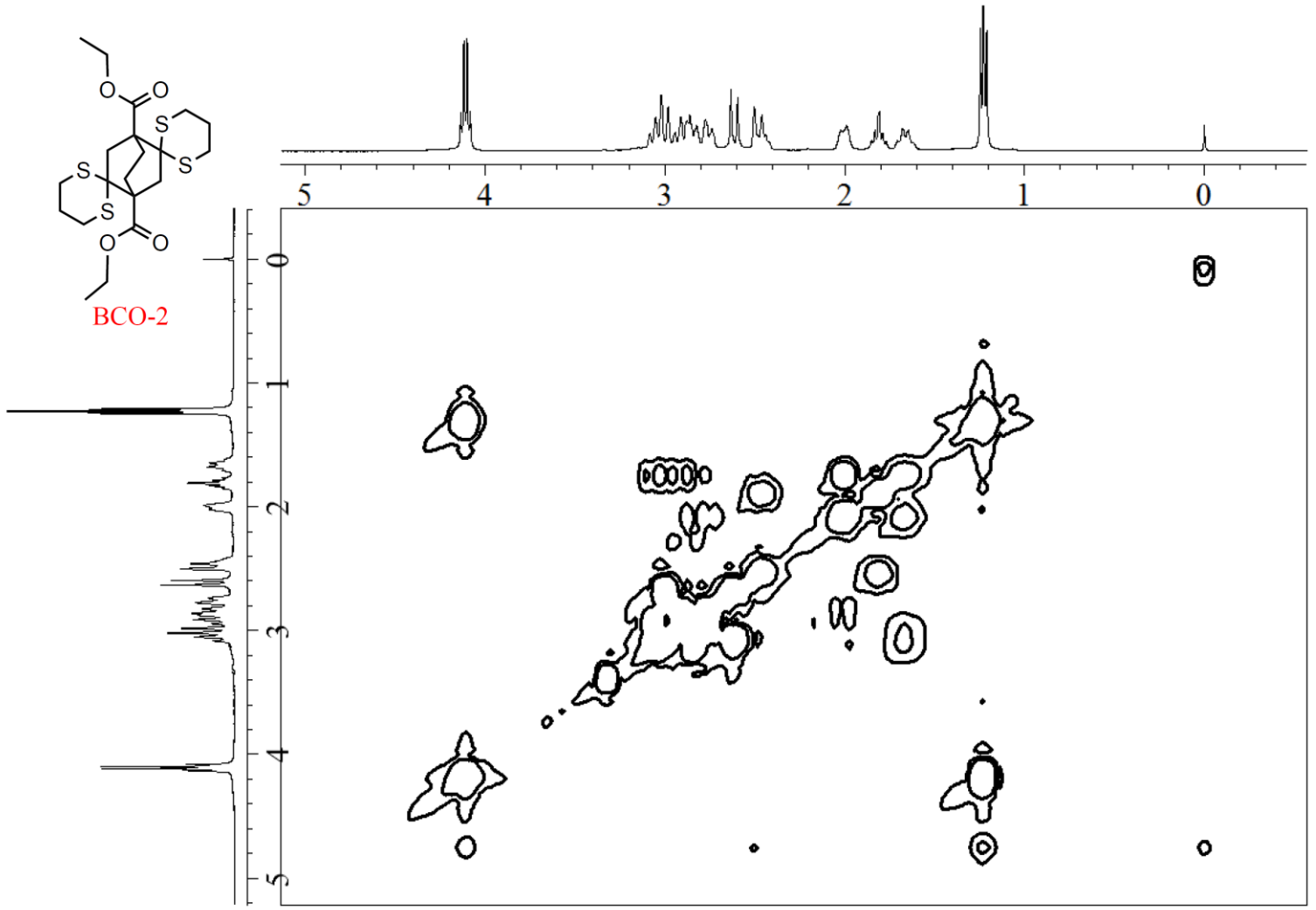


Figure S5. ^{1}H-^{1}H COSY spectrum of BCO-2 measured in DMSO-d_6 at 20 °C.

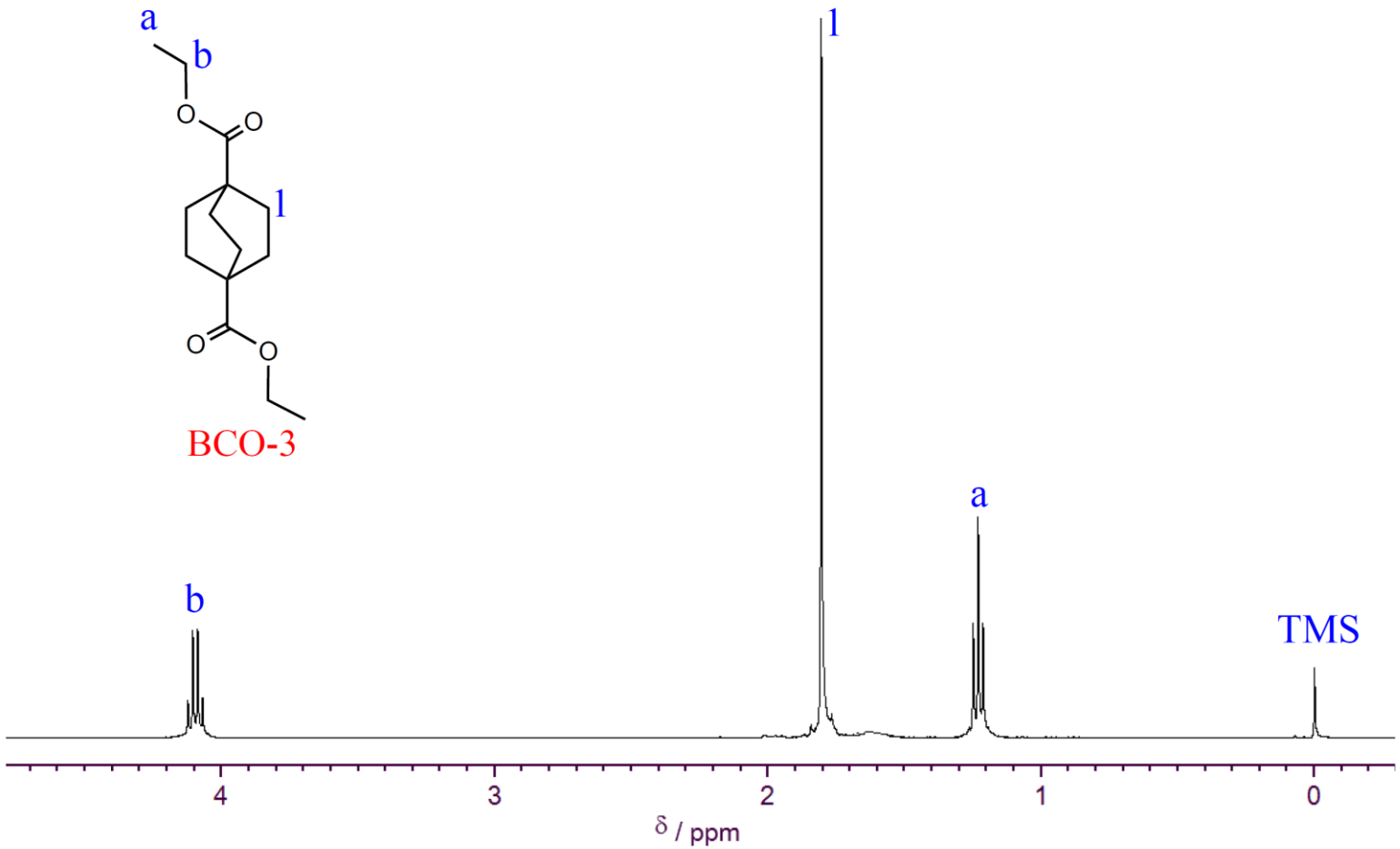


Figure S6. ^{1}H NMR spectrum of BCO-3 measured in $CDCl_3$ at 20 °C.

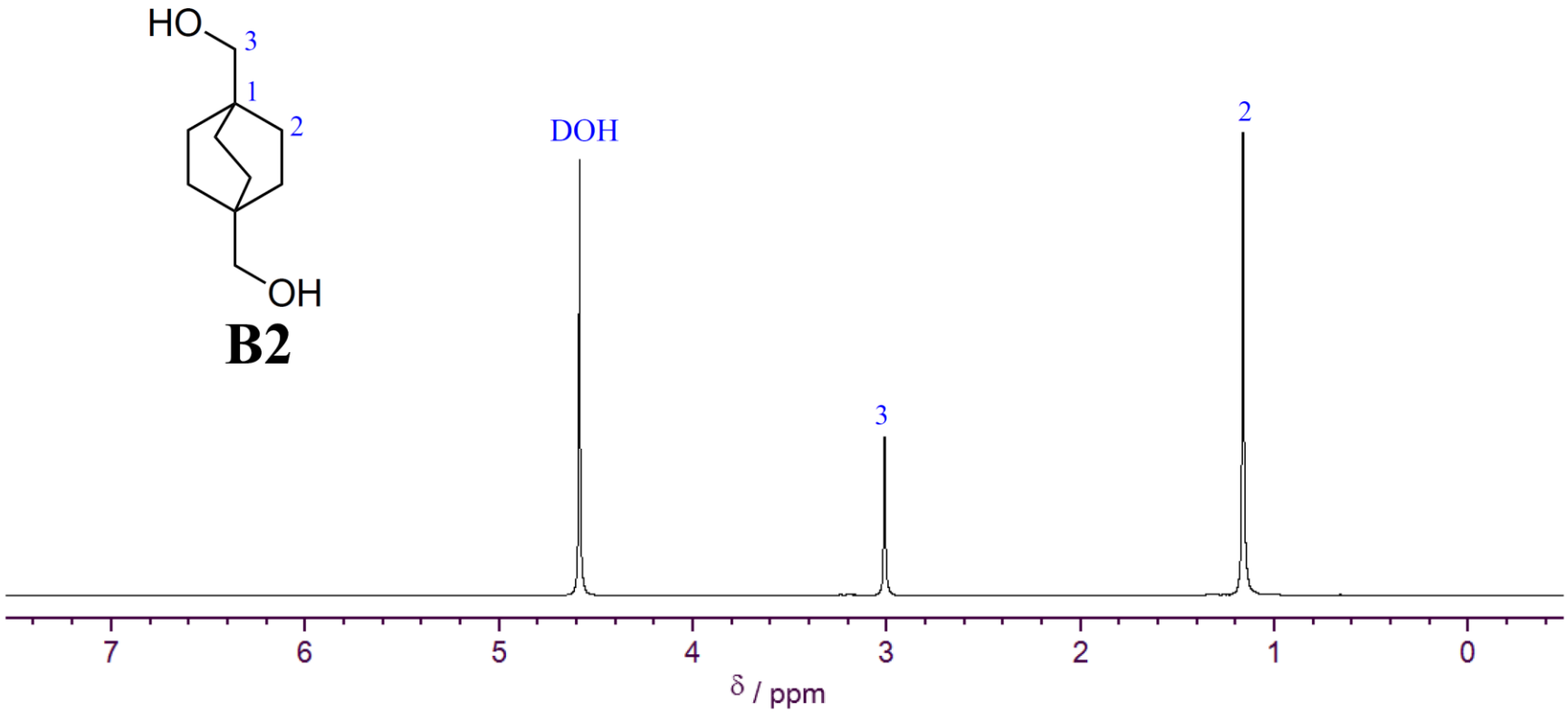


Figure S7. ^{1}H NMR spectrum of **B2** measured in $CDCl_3$ at 20 °C.

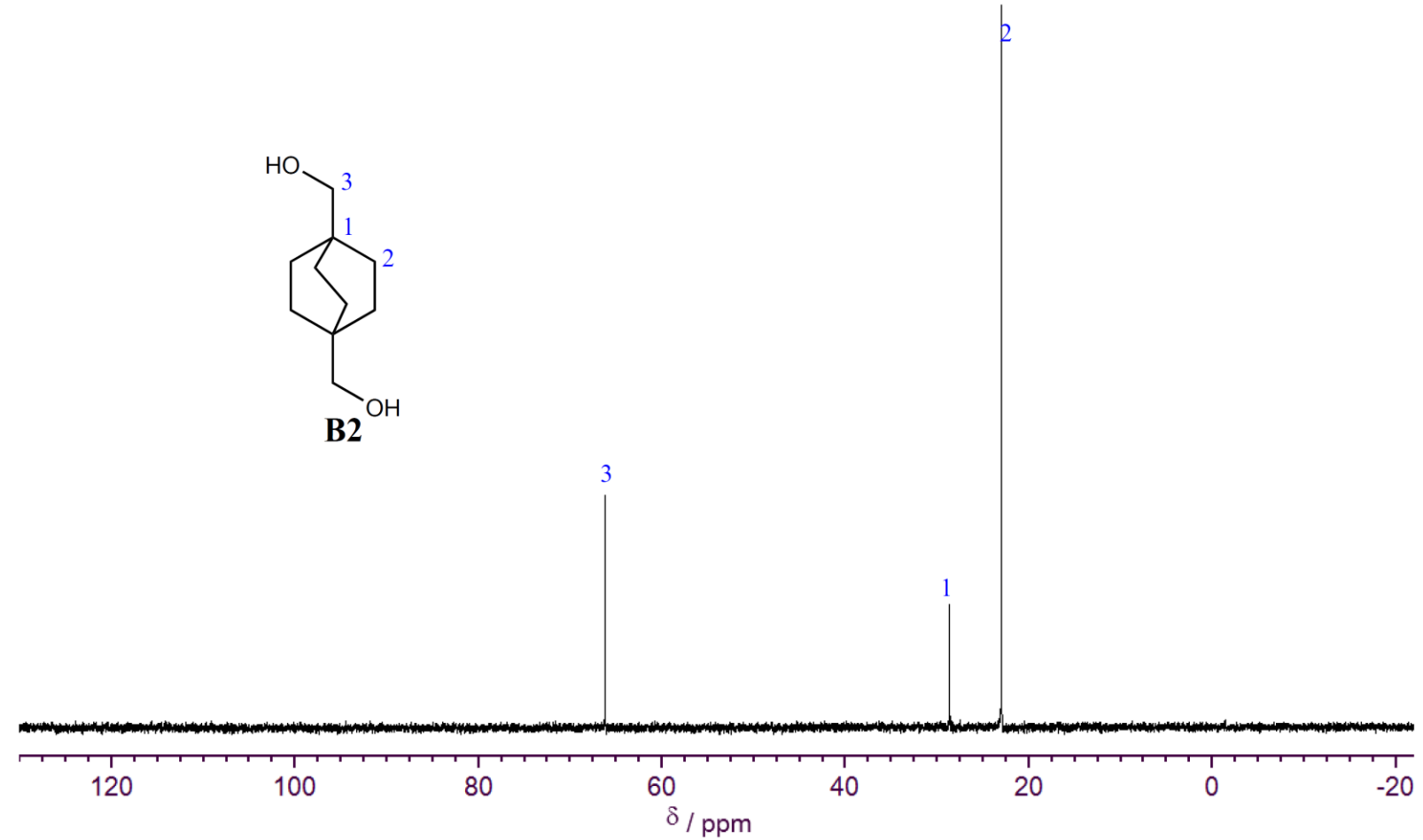


Figure S8. ^{13}C NMR spectrum of **B2** measured in DMSO-d_6 at 20 °C.

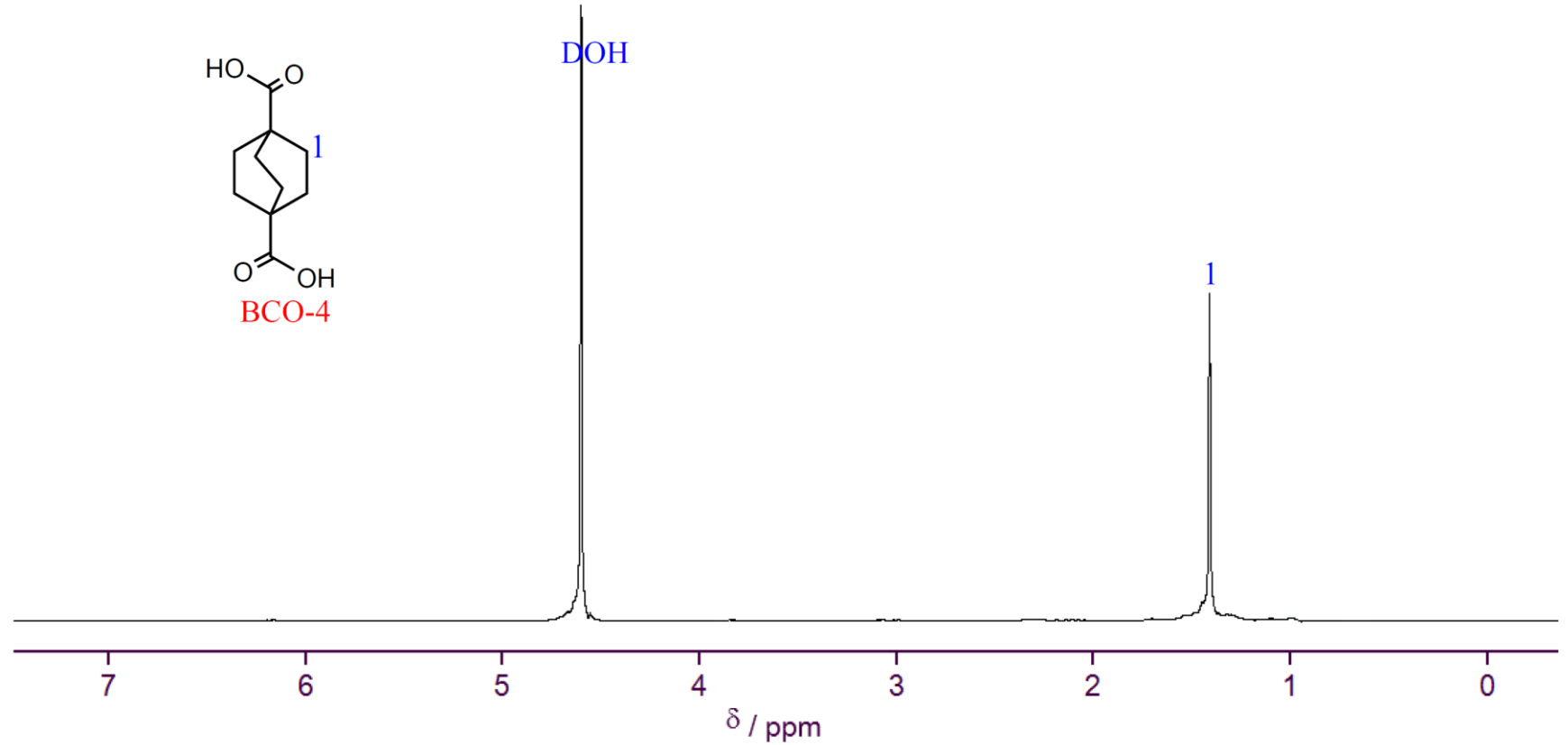


Figure S9. ^{1}H NMR spectrum of BCO-4 measured in D_2O at 20 °C.

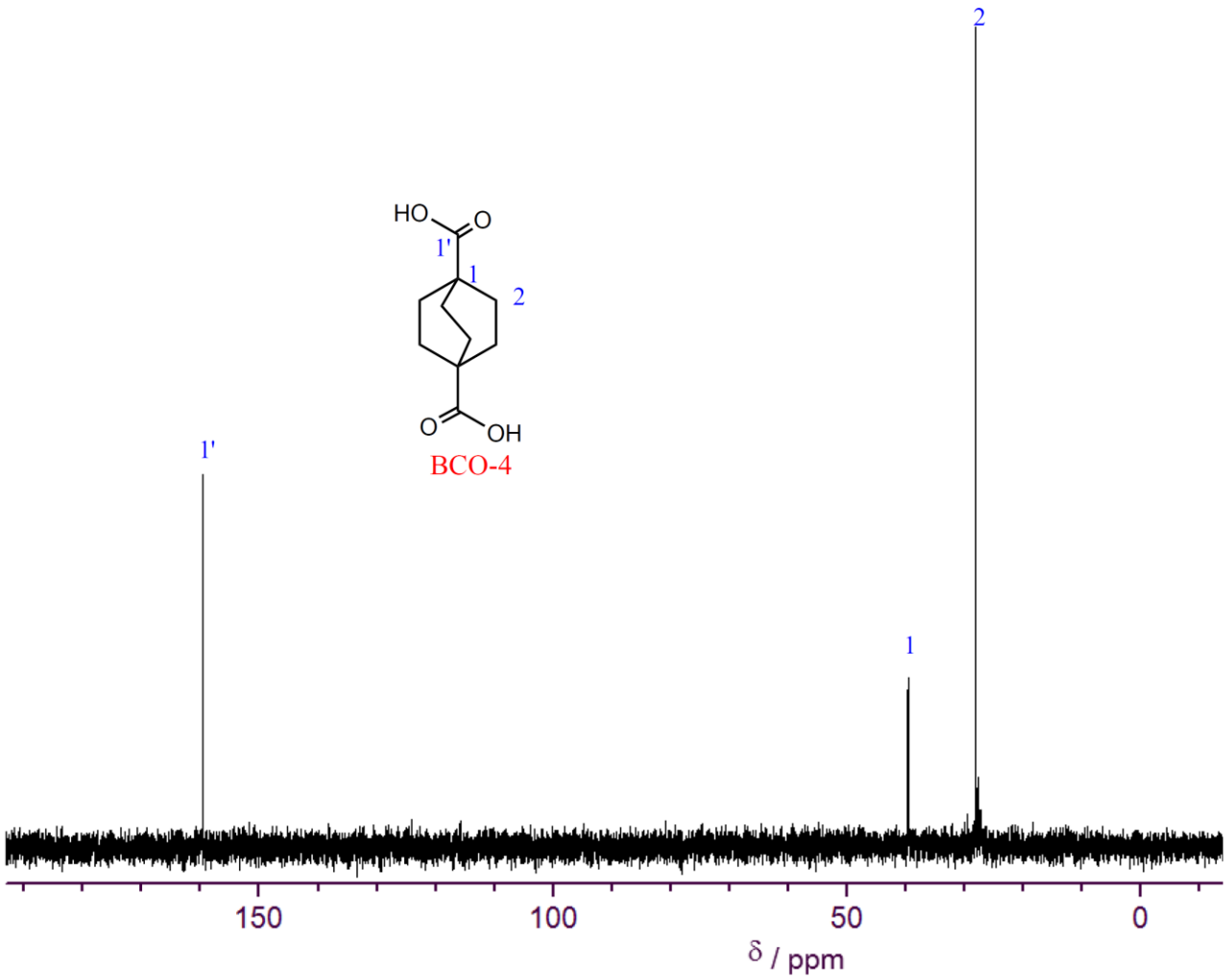


Figure S10. ^{13}C NMR spectrum of BCO-4 measured in D_2O at 20 °C.

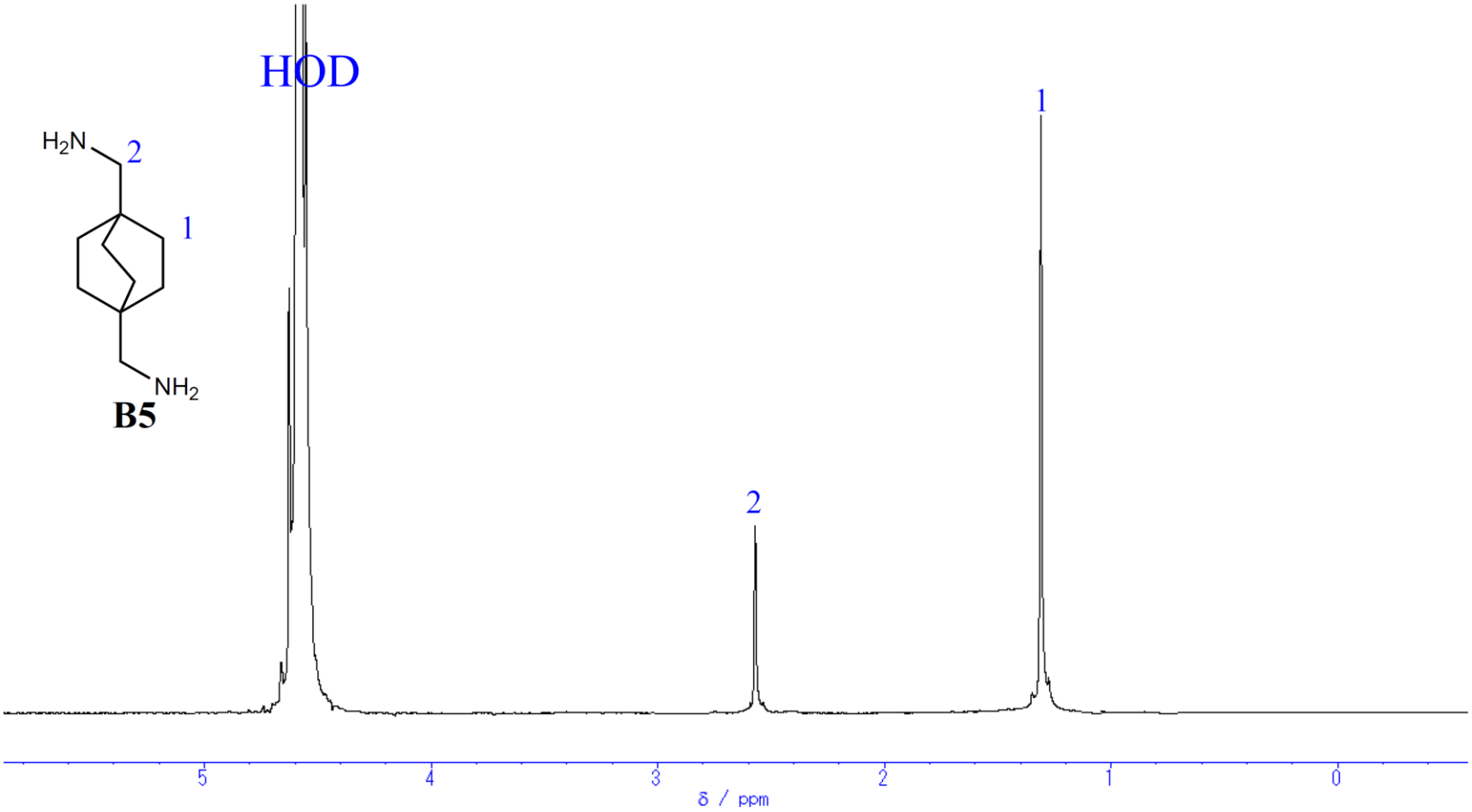


Figure S11. ^{1}H NMR spectrum of **B5** measured in D_2O at 20 °C.

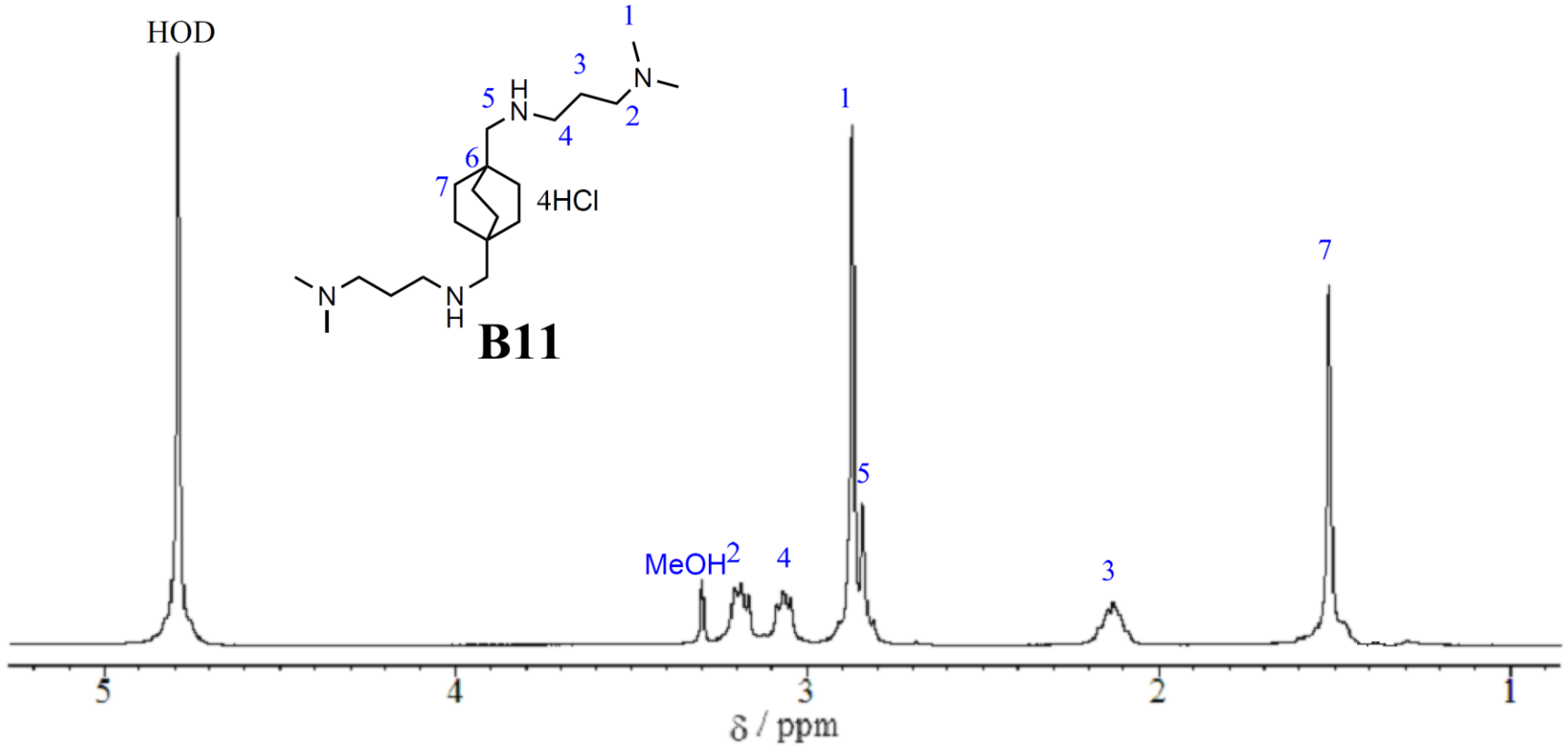


Figure S12. ^{1}H NMR spectrum of **B11** measured in D_2O at 20 °C with MeOH added as an internal standard.

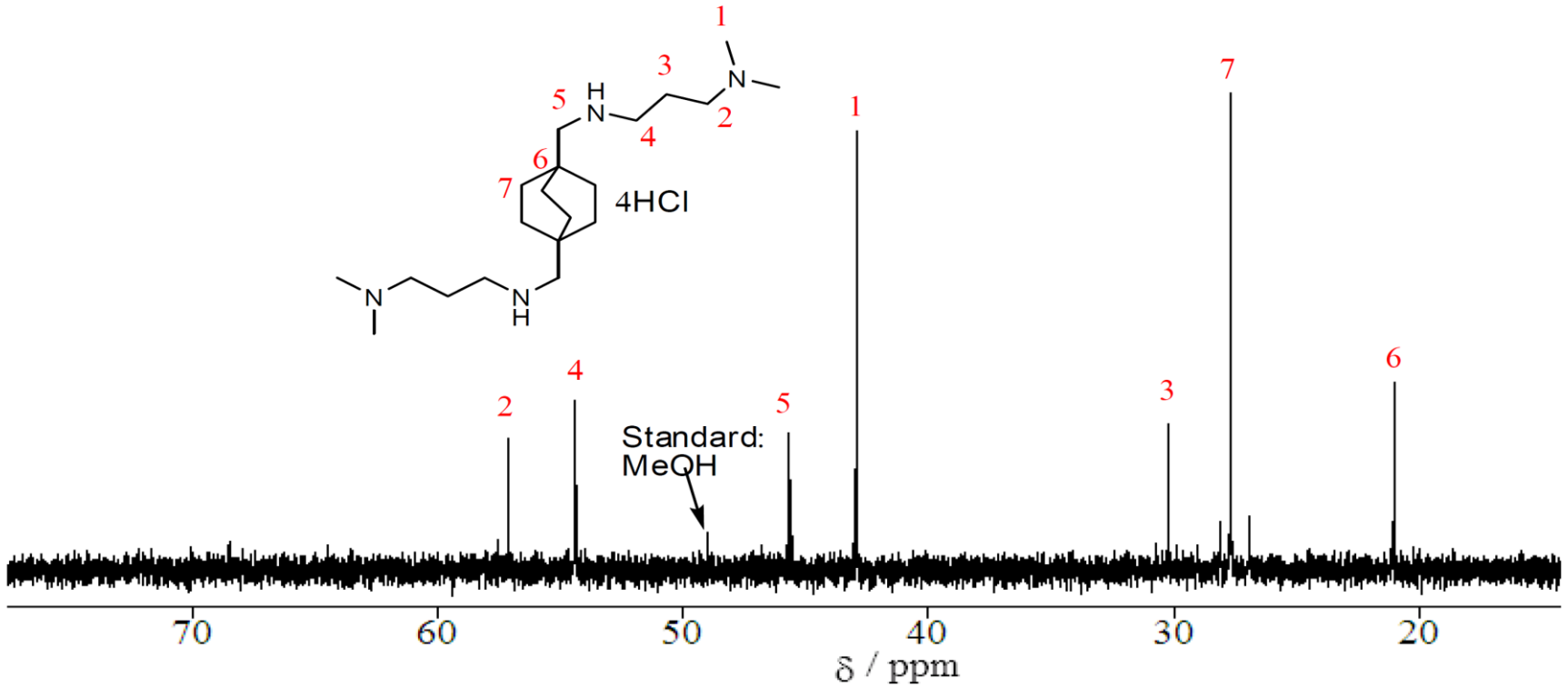


Figure S13. ^{13}C NMR spectrum of **B11** measured in D_2O at 20 °C with MeOH as an internal standard.

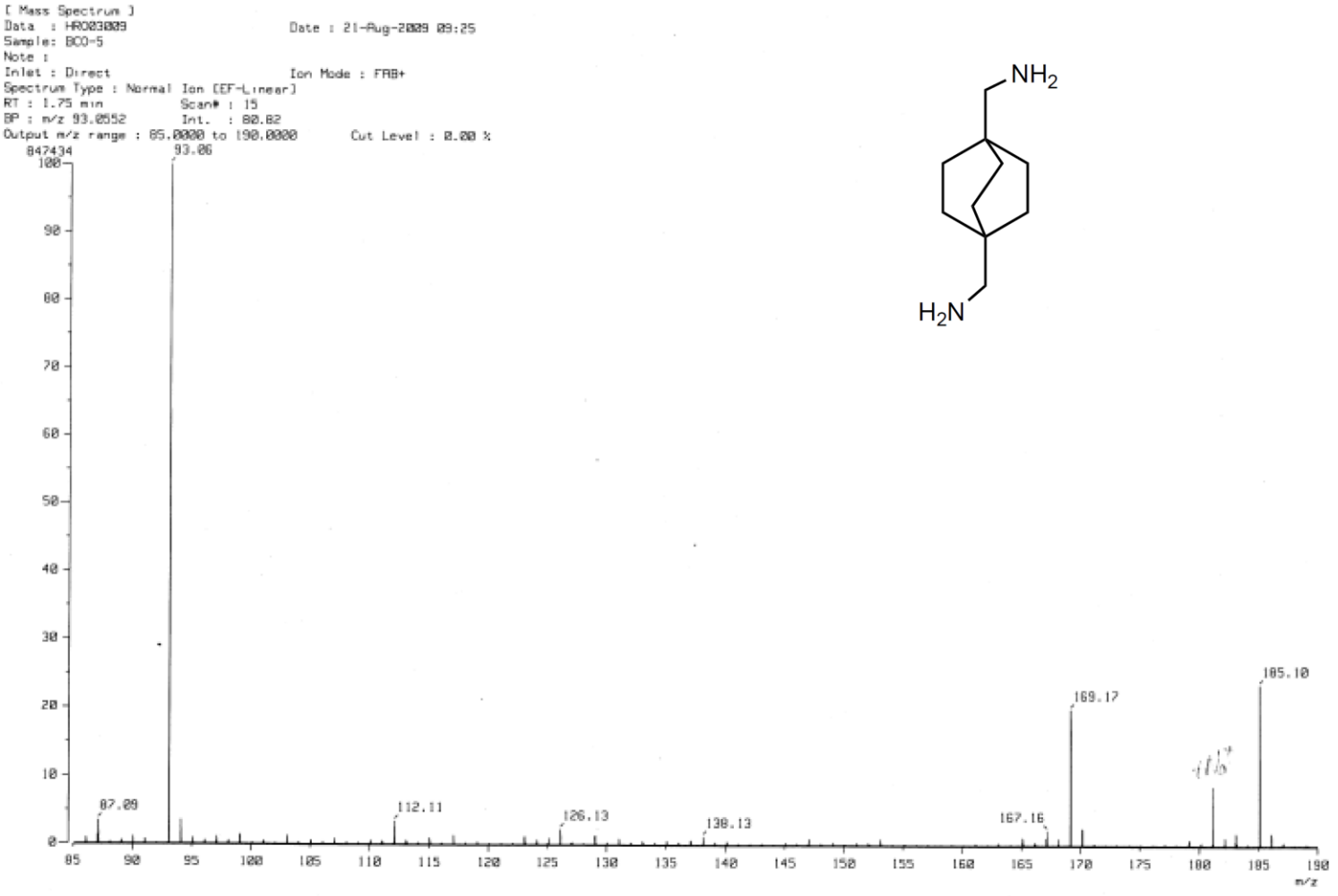


Figure S14. High-Resolution Mass Spectrum of **B5**.

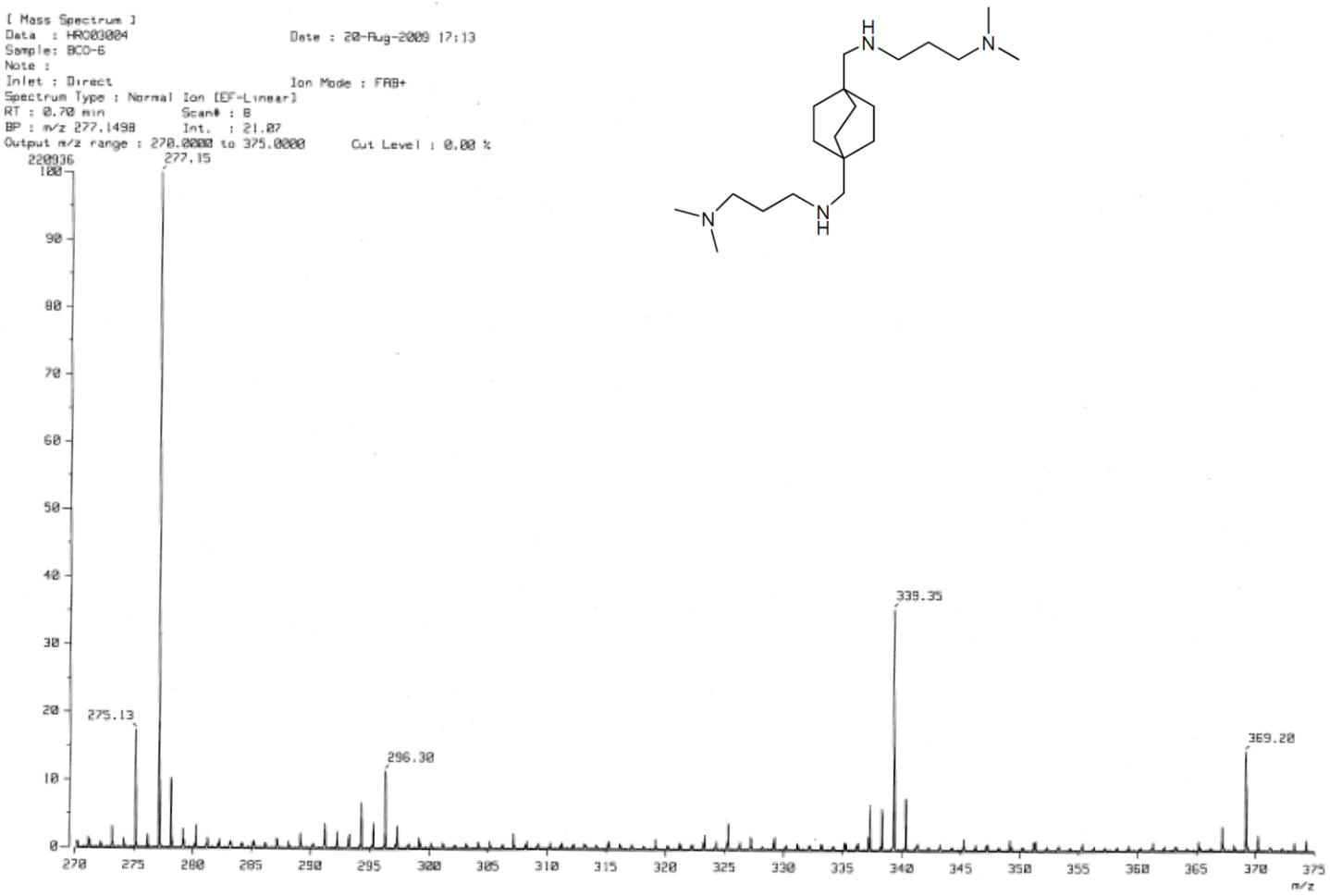


Figure S15. High-Resolution Mass Spectrum of **B11.**

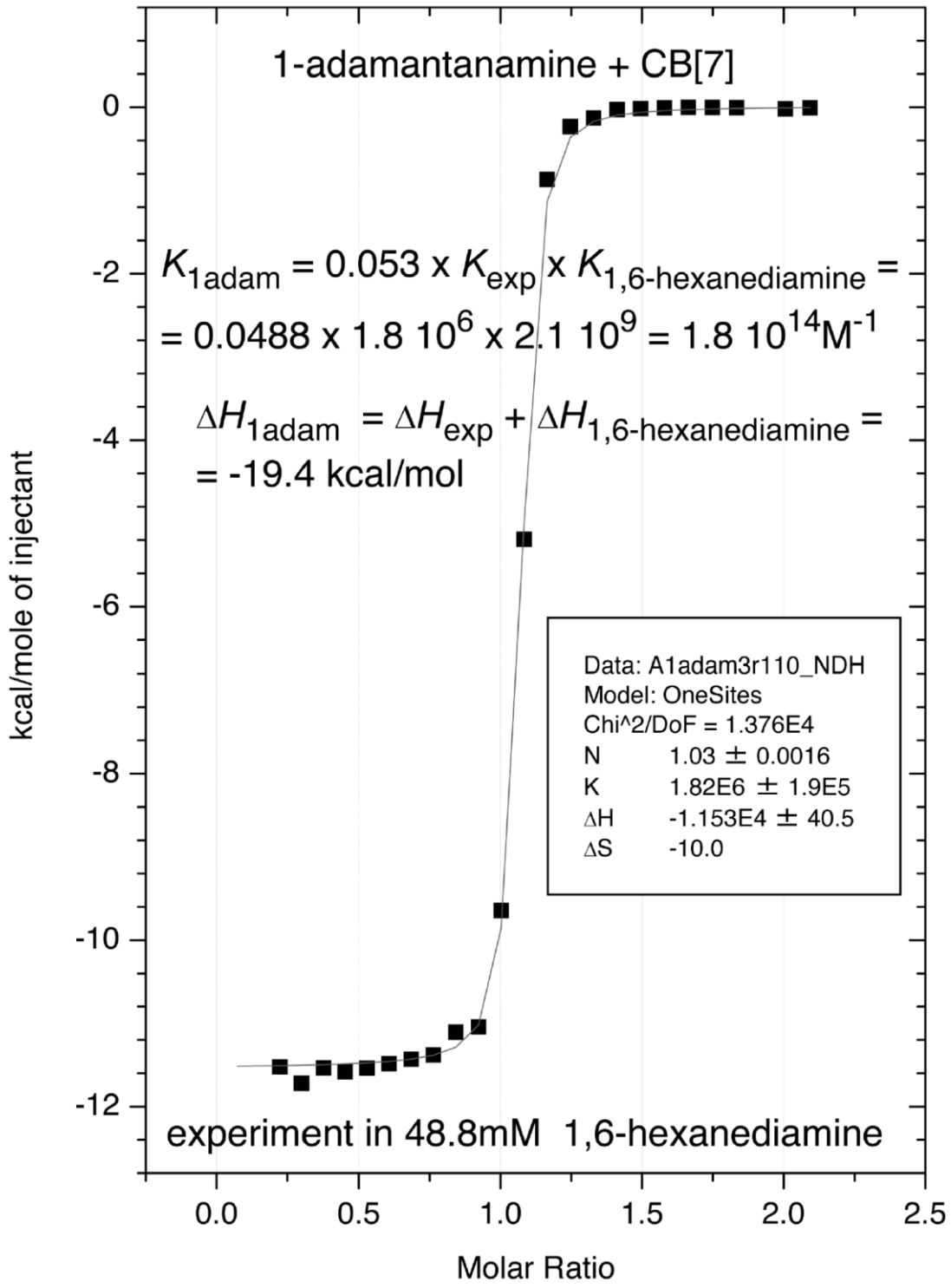


Figure 16. Competition ITC experiment on complexation of **A2** with CB[7] in water at 298.15 K in the presence of 1,6-hexanediamine (48.8 mM) as competitor.

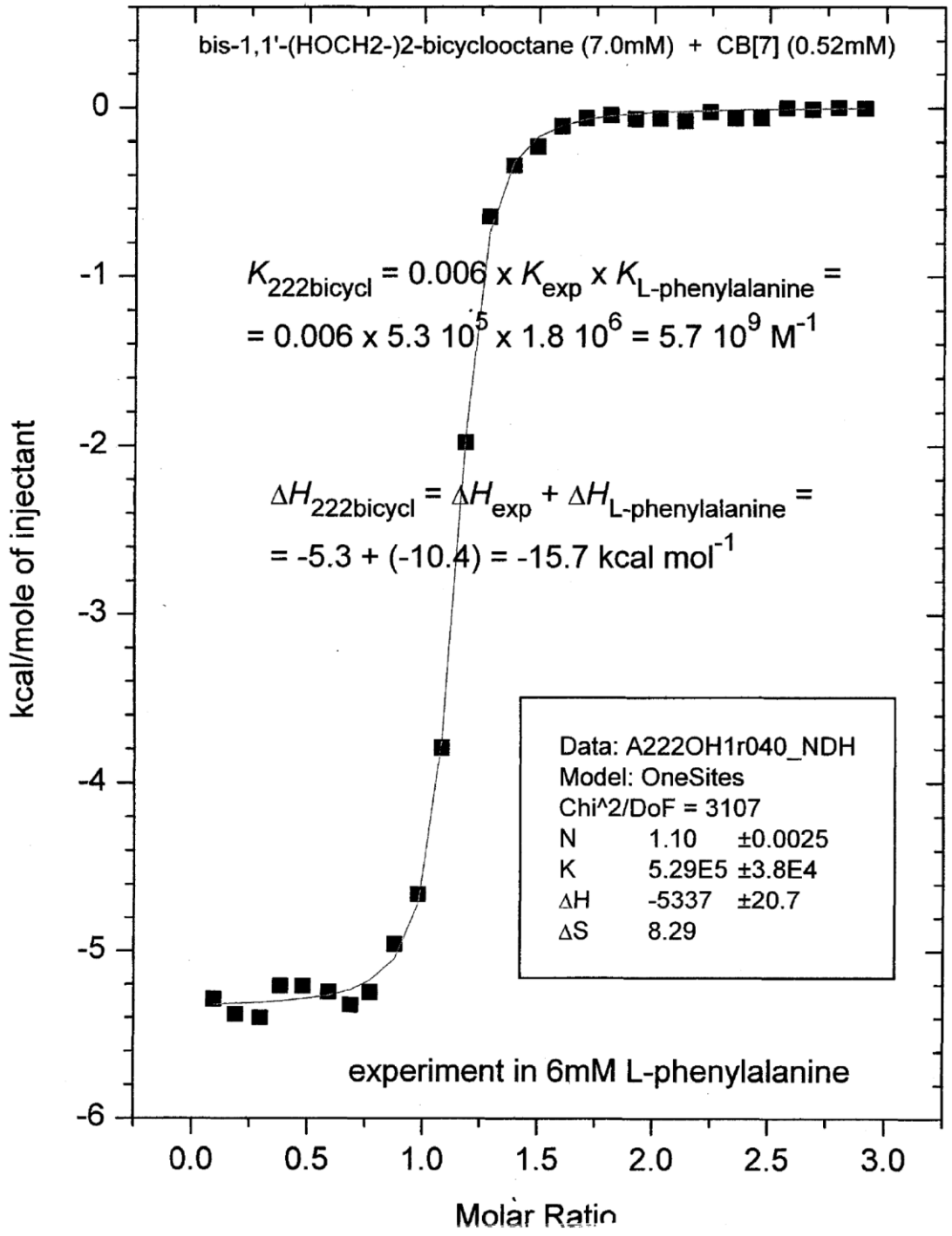


Figure 17. Competition ITC experiment on complexation of **B2** with CB[7] in water at 298.15 K in the presence of L-phenylalanine as competitor.

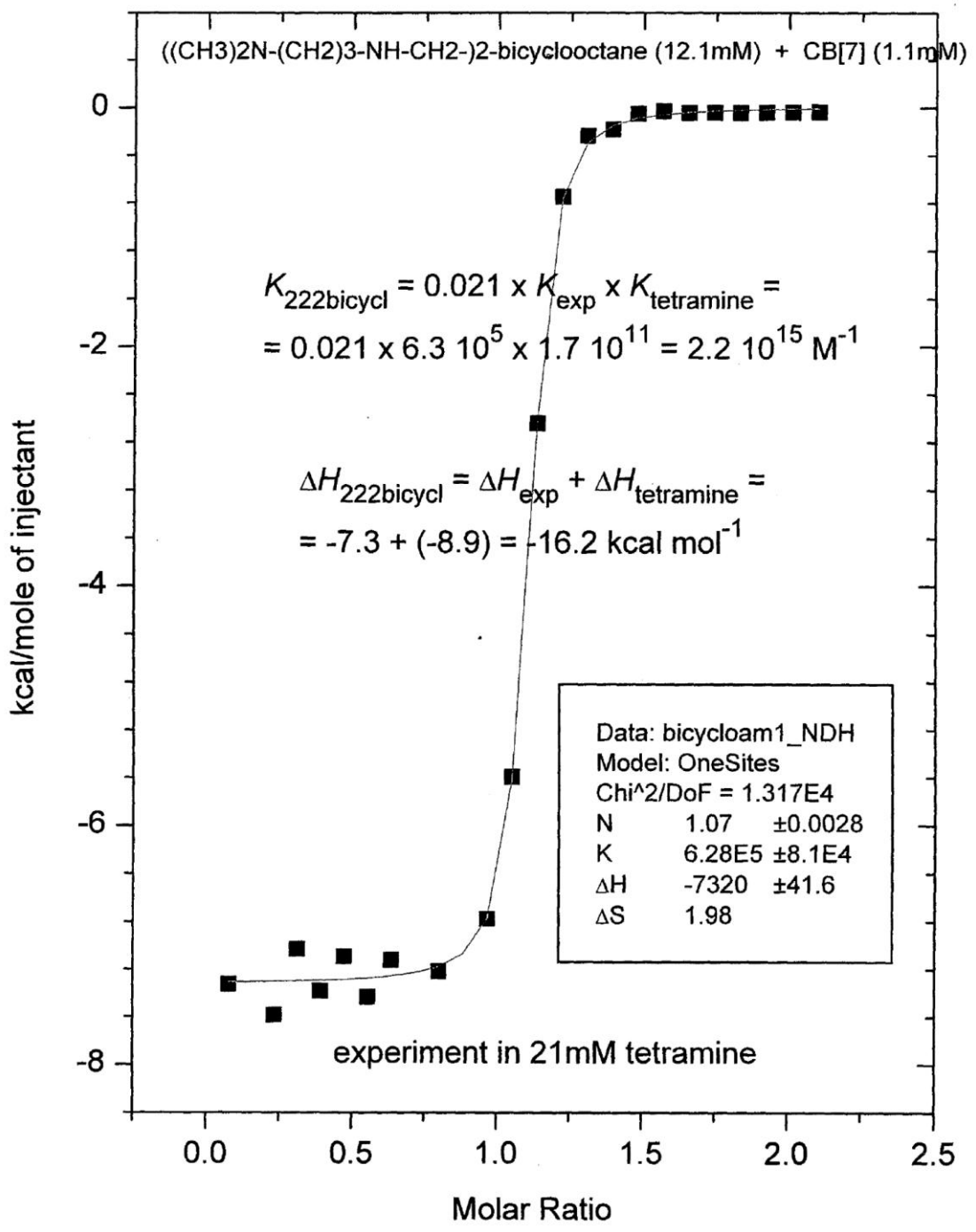


Figure 18. Competition ITC experiment on complexation of **B11** with CB[7] in water at 298.15 K in the presence of triethylenetetramine as competitor

References

(S1) Roberts, J. D.; Moreland, W. T.; Frazer, W. *J. Org. Chem.* **1953**, 18, 637.

(S2) Kumar, K.; Wang, S. S.; Sukenik, C. N. *J. Org. Chem.* **1984**, 49, 665.

(S3) Kauer, J. C.; Benson, R. E.; Parshall, G. W. *J. Org. Chem.*, **1965**, 30, 1431.

(S4) Cannon, J. G.; Yang, K. W.; Rodriguez, M.; Buckley, J. P. *J. Pharm. Sci.* **1971**, 1534.