Supporting Information for

Recognition of the Persistent Organic Pollutant Chlordecone by a Hemicryptophane Cage

Augustin Long,[†] Sara Lefevre,[‡] Laure Guy, [‡] Vincent Robert,[§] Jean-Pierre Dutasta, [‡] Marion L. Chevallier[¶], Oriane Della-Negra[¶] Pierre-Loïc Saaidi,*[,¶] and Alexandre Martinez*[,†]

[†] Aix Marseille Univ, CNRS, Centrale Marseille, iSm2, Marseille, France
[‡] Laboratoire de Chimie, École Normale Supérieure de Lyon, CNRS, UCBL, 46 Allée d'Italie, F-69364 Lyon, France
[§] Laboratoire de Chimie Quantique Institut de Chimie, UMR CNRS 7177, Université de Strasbourg, 4, rue Blaise Pascal, F-67070 Strasbourg, France
[¶] Génomique Métabolique, Genoscope, Institut François Jacob, CEA, CNRS, Univ Evry, Université Paris-Saclay, Evry, France

*Corresponding authors. E-mails: alexandre.martinez@centrale-marseille.fr; plsaaidi@genoscope.cns.fr

Contents

Number of pages: **15**
Number of Figures: **13** (Figure S1 to Figure S13)
Number of Tables: **1** (Table S1)

1. Synthesis

1.1. Chemical and materials

Starting material and solvents were of commercial grade and were used without further purification. Chromatography was carried out with Merck 60 A (0.040 - 0.063 mm) silica gel. TLC was performed with Merck silica gel 60 F_{254} plates. ^{1}H NMR and ^{13}C NMR were recorded at 298 K either on a Bruker Avance III HD 400 MHz, a Bruker 300 MHz spectrometer or a a Bruker Avance 600 MHz NMR spectrometer equipped with a cryoprobe. ^{1}H NMR and ^{13}C NMR chemical shifts δ are reported in ppm referenced to the protonated residual solvent signal.

1.2. Hemicryptophane 1

Hemicryptophane **1** was prepared according to the common published procedure. ^{1}H NMR and ^{13}C NMR spectra were consistent with literature.[1]

^{1}H NMR ($CDCl_3$, 400 MHz, 298 K) δ 7.09 – 7.01 (m, 6H), 6.84 (s, 3H), 6.71 (d, J = 8.5 Hz, 6H), 6.39 (d, J = 8.5 Hz, 6H), 4.78 (d, J = 13.7 Hz, 3H), 4.53 – 4.46 (m, 3H), 4.39 – 4.32 (m, 3H), 4.29 – 4.16 (m, 9H), 3.75 (dd, J = 14.5, 4.4 Hz, 3H), 3.67 (s, 9H), 3.57 (d, J = 13.8 Hz, 3H), 3.15 (d, J = 16.5 Hz, 3H), 3.09 (d, J = 16.4 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$, 298 K) δ 169.6, 157.7, 148.5, 146.5, 133.1, 131.9, 130.5, 128.8, 116.9, 115.0, 113.8, 67.9, 67.7, 61.0, 55.9, 42.7, 36.5.

1.3. Hemicryptophane 2

Hemicryptophane **2** was prepared according to the common published procedure. ^{1}H NMR and ^{13}C NMR spectra were consistent with literature.[2]

^{1}H NMR ($CDCl_3$, 400 MHz, 298 K) δ 6.97 (s, 3H), 6.78 – 6.73 (m, 9H), 6.39 (d, J = 8.6 Hz, 6H), 4.70 (d, J = 13.6 Hz, 3H), 4.45 – 4.38 (m, 3H), 4.31 – 4.24 (m, 3H), 4.15 – 4.08 (m, 6H), 3.60 (s, 9H), 3.49 (d, J = 13.8 Hz, 3H), 3.44 – 3.39 (m, 3H), 3.31 (d, J = 13.2 Hz, 3H), 2.36 – 2.26 (m, 12H); ^{13}C NMR (100 MHz, $CDCl_3$, 298 K) δ 157.5, 148.6, 146.6, 133.1, 131.9, 129.2, 117.2, 114.9, 113.9, 67.9, 67.8, 56.0, 52.9, 47.0, 36.5.

1.4. 10-monohydrochlordecone

The title compound 10-monohydrochlordecone was successfully synthesized and properly purified in small quantities. Details will be reported separately.

^{1}H NMR $(CD_3)_2CO$, 600 MHz, 298 K) δ 6.82 (s, 2 H), 5.00 (s, 1 H); ^{13}C NMR ($(CD_3)_2CO$, 150 MHz, 298 K) δ 104.0, 81.5, 80.5, 76.9, 75.3, 67.9.

2. NMR spectra

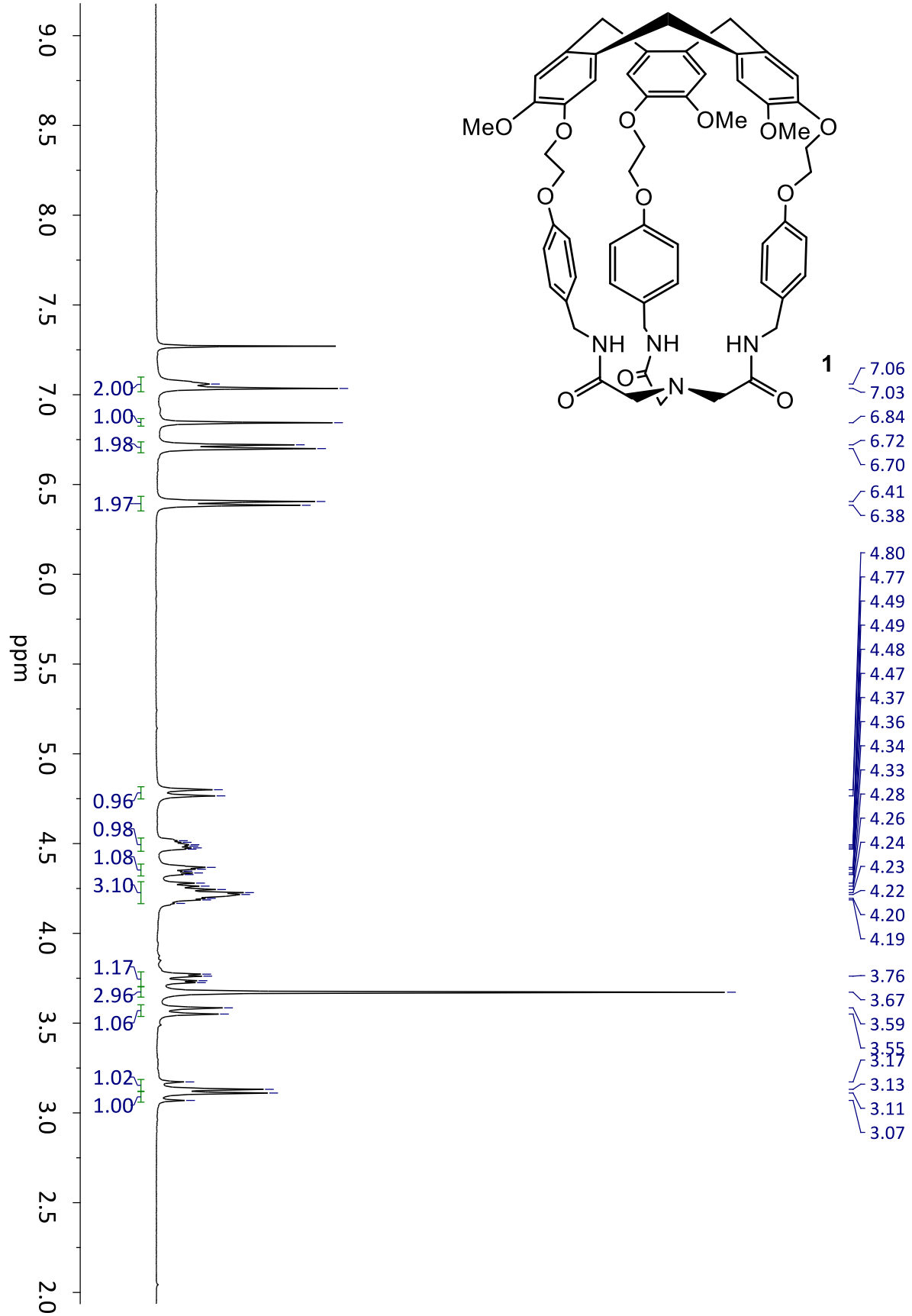


Figure S1. ^{1}H NMR spectrum of **1** ($CDCl_3$, 400 MHz, 298 K).

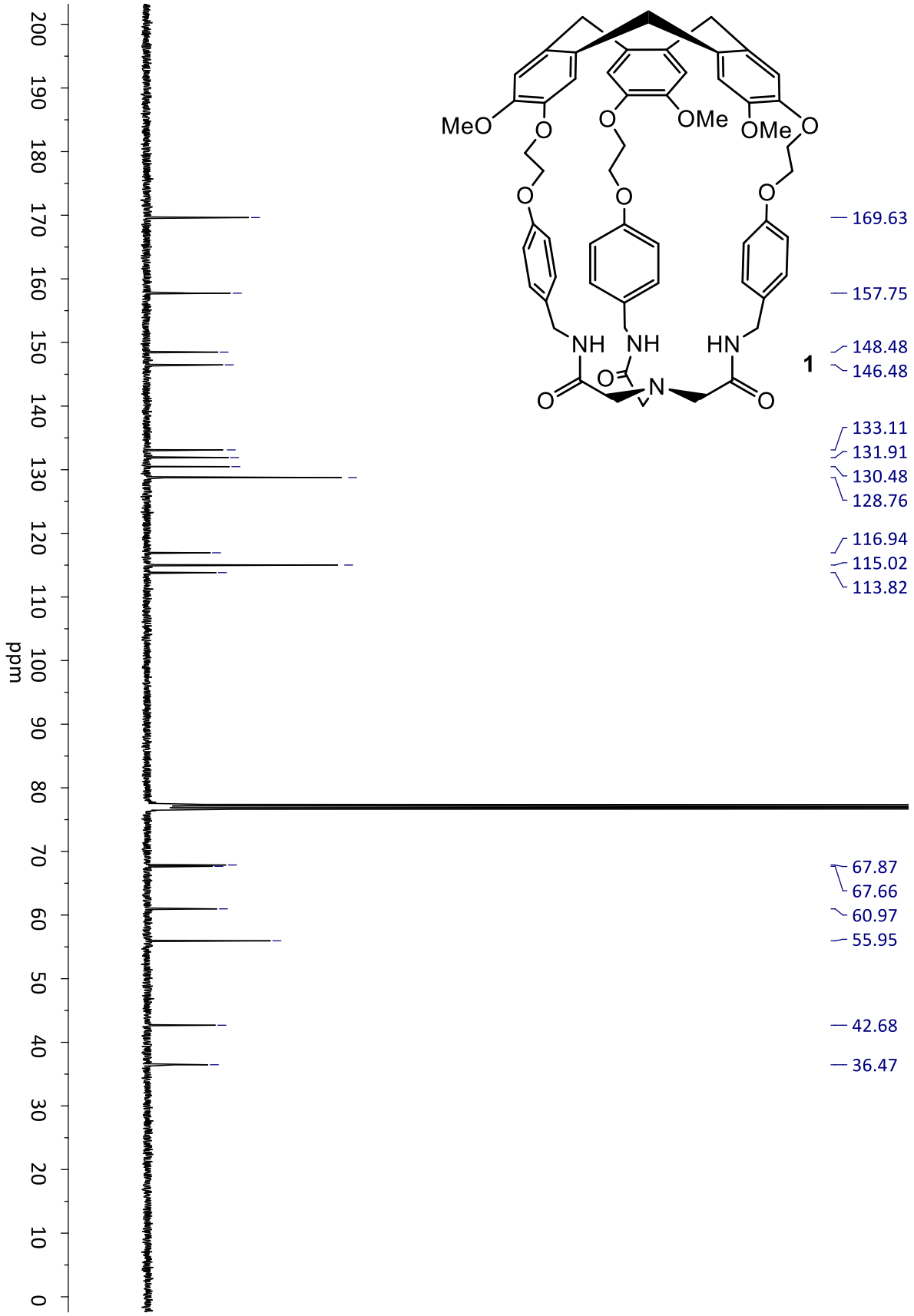


Figure S2. ^{13}C NMR spectrum of **1** ($CDCl_3$, 100 MHz, 298 K).

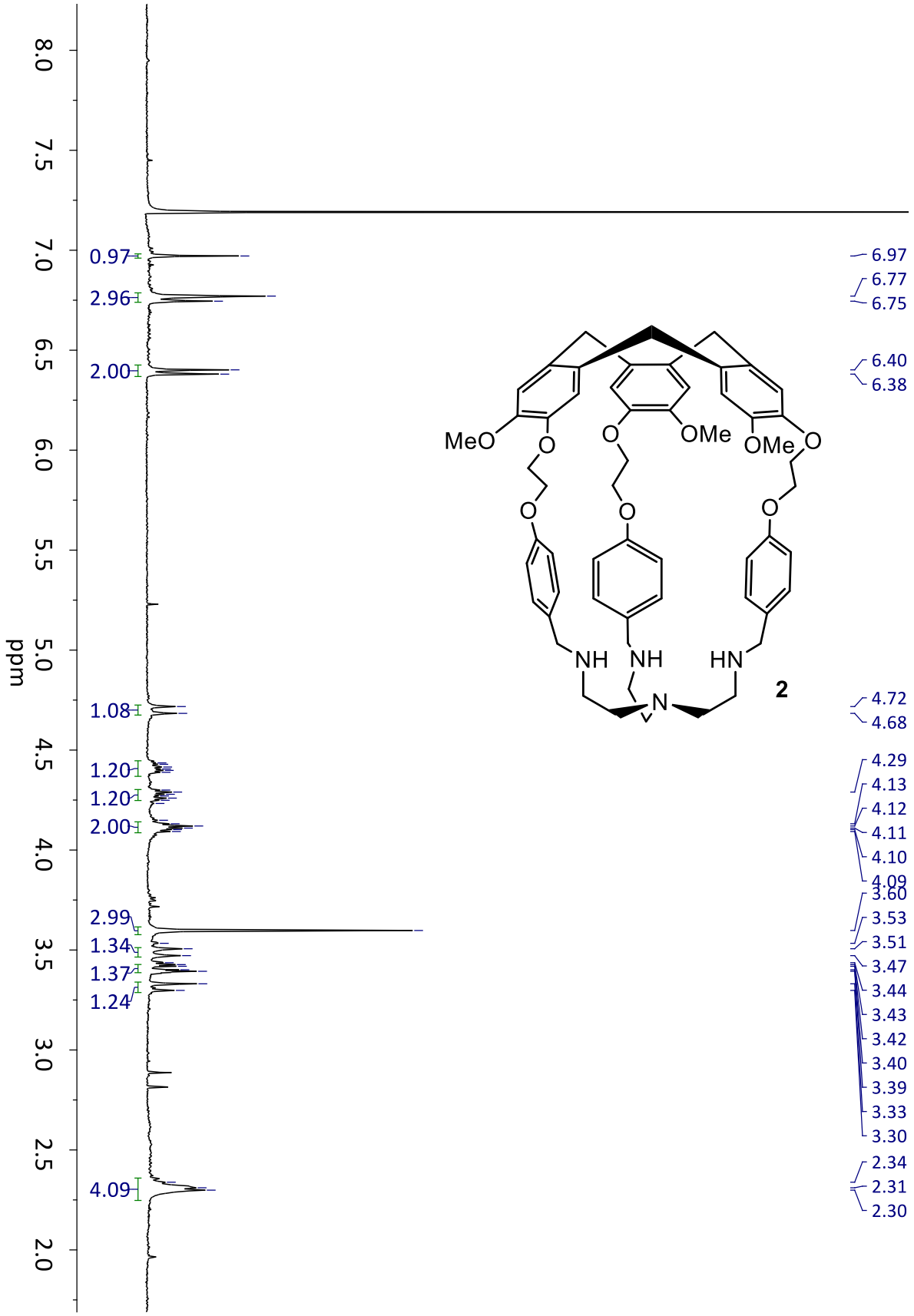


Figure S3. ^{1}H NMR spectrum of **2** ($CDCl_3$, 400 MHz, 298 K).

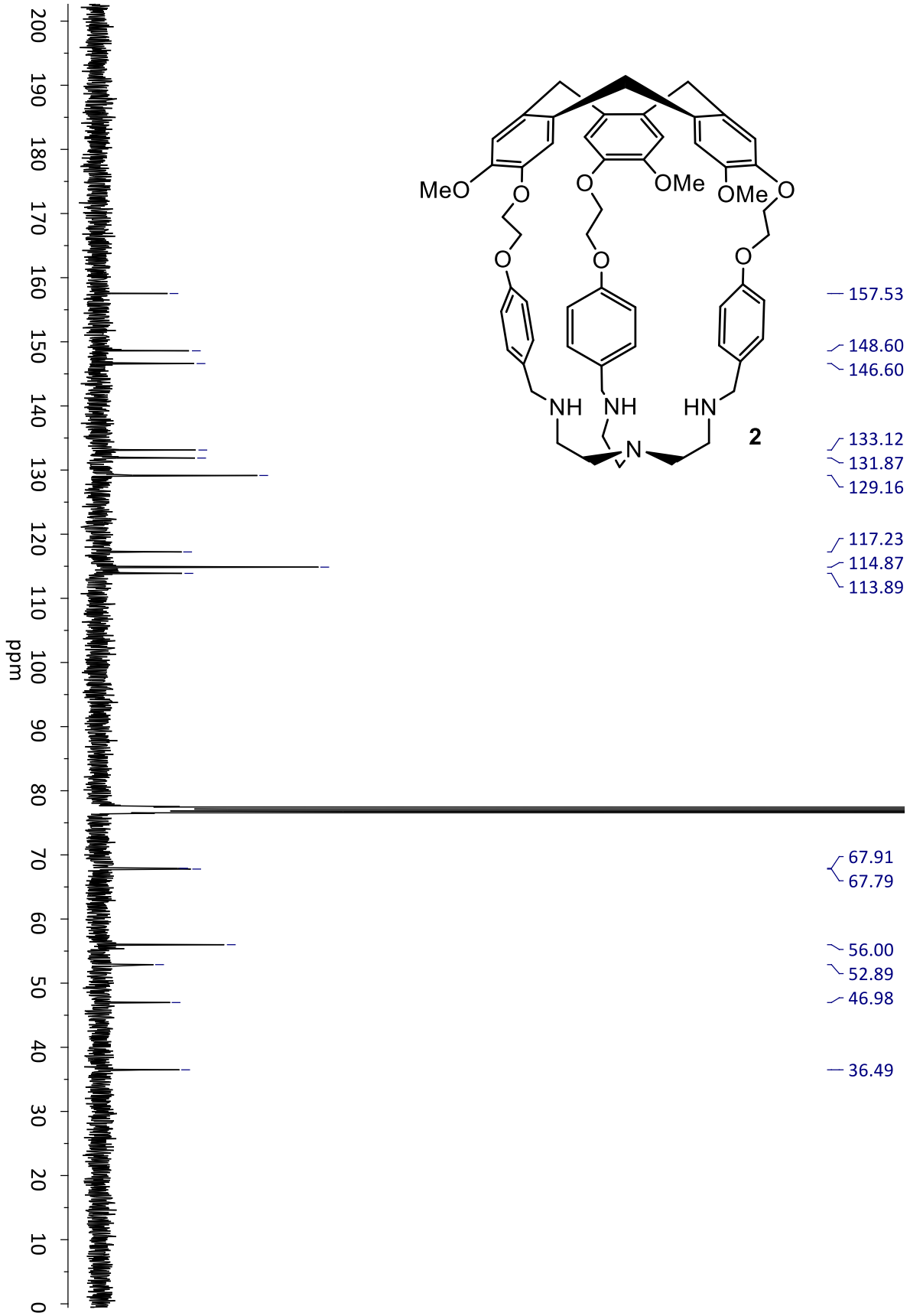


Figure S4. ^{13}C NMR spectrum of **2** ($CDCl_3$, 100 MHz, 298 K).

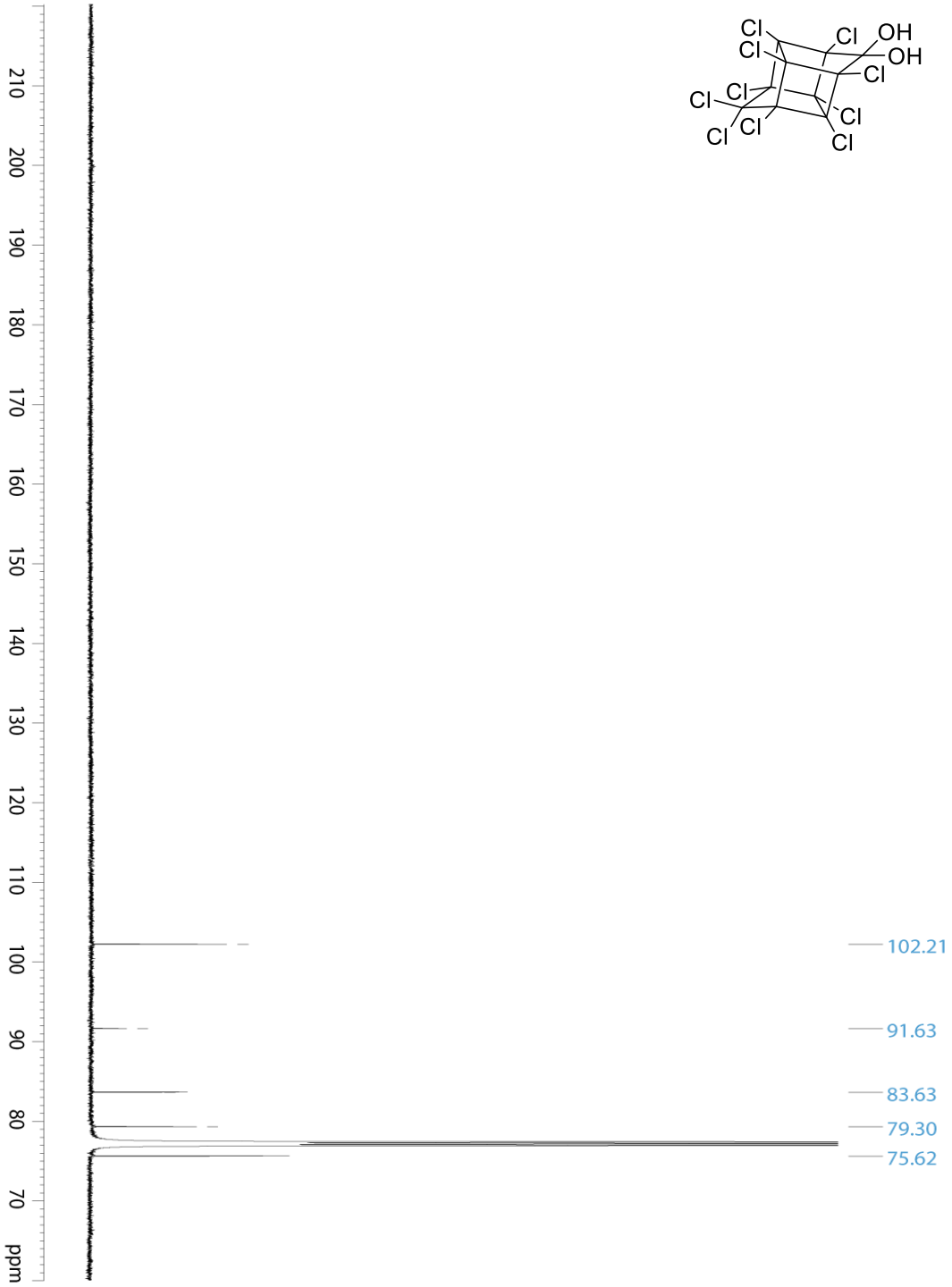
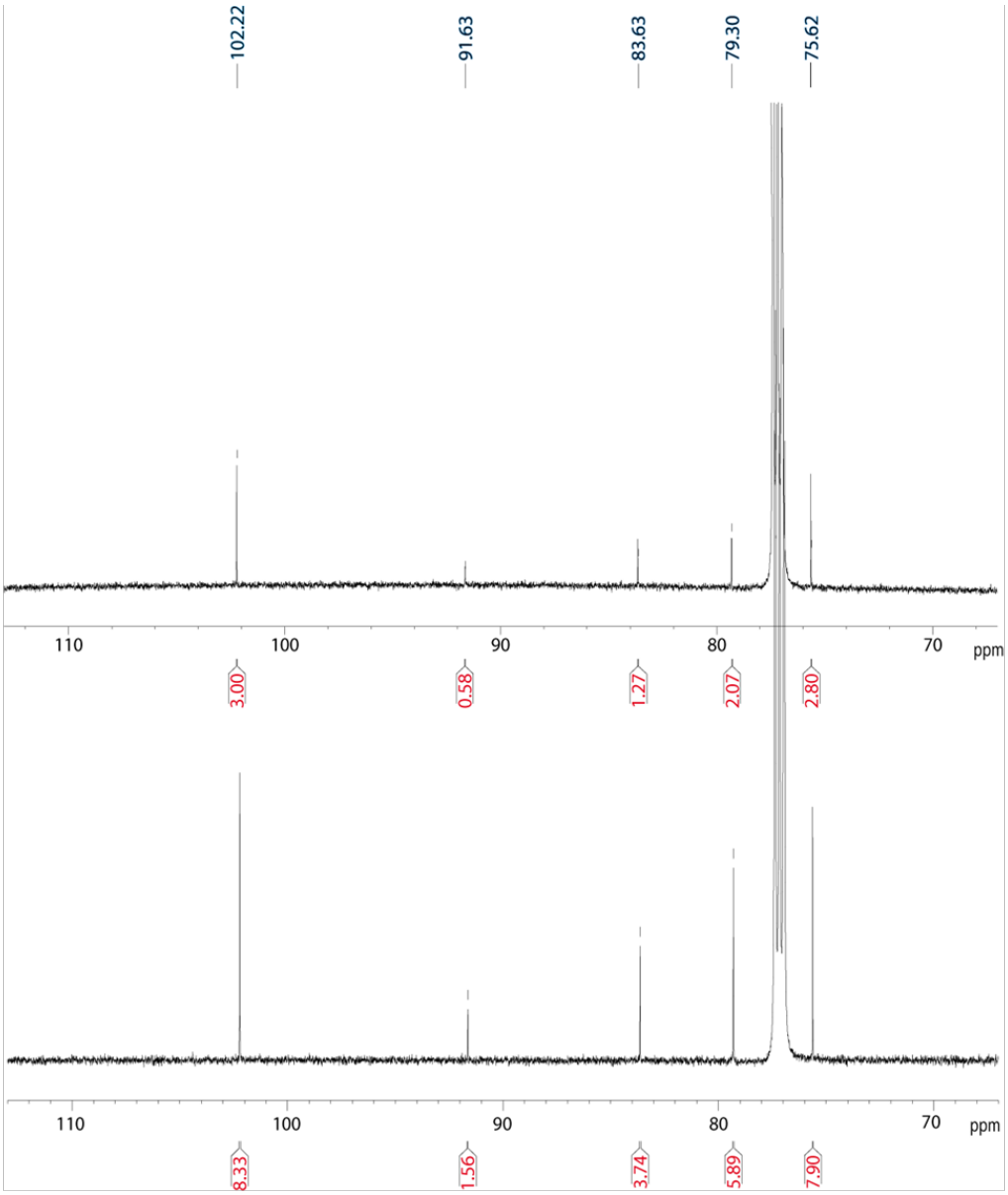


Figure S5. Long-term ^{13}C NMR spectrum of a chlordecone saturated solution in $CDCl_3$ (10 mg of chlordecone in 750 µL $CDCl_3$, 20 000 scans, 150 MHz, 298 K).



δ (ppm)	102.22	91.63	83.63	79.30	75.62	Average	Standard deviation
Integration (a)	3.00	0.58	1.27	2.07	2.80		
Integration (b)	8.33	1.56	3.74	5.89	7.90		
Integration (b)/Integration (a)	2.78	2.69	2.94	2.84	2.82	2.8	0.1
Chlordecone solubility in $CDCl_3$ (g/L)	11.1	10.8	11.8	11.4	11.3	11.3	0.2

Figure S6. (a) ^{13}C NMR spectrum of 3 mg of chlordecone in 750 µL $CDCl_3$ (150 MHz, 6000 scans, exponential broadening of 0.5 Hz, 298 K) (b) ^{13}C NMR spectrum (150 MHz, 6000 scans, exponential broadening of 0.5 Hz, 298 K) of a saturated solution of chlordecone in $CDCl_3$ (10 mg of chlordecone in 750 µL $CDCl_3$) (c) The signal integration ratio enables the solubility of chlordecone in $CDCl_3$ to be estimated at 11.3±0.2 g/L.

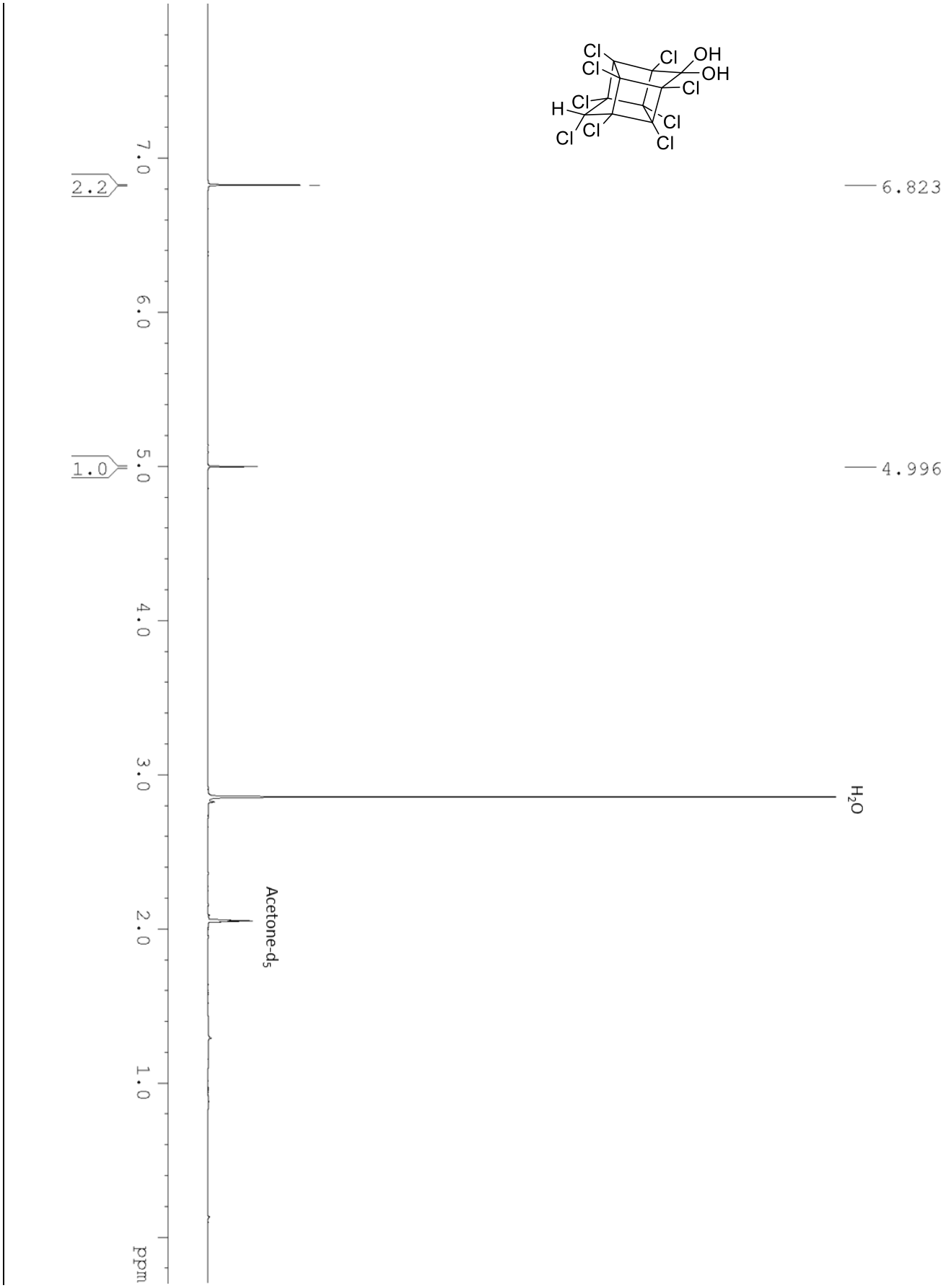


Figure S7. ^{1}H NMR spectrum of 10-monohydrochlordecone ($(CD_3)_2CO$, 600 MHz, 298 K).

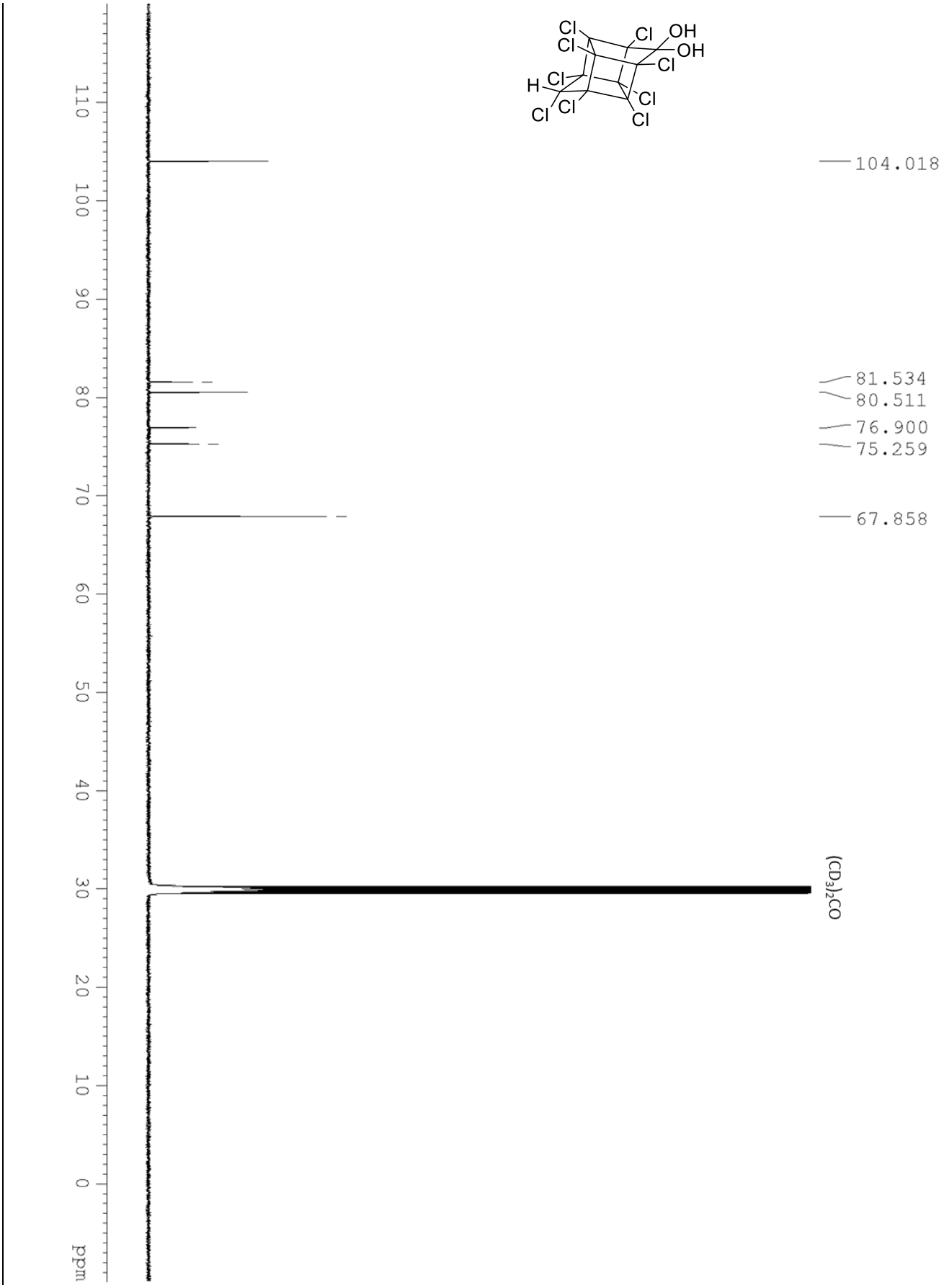


Figure S8. ^{13}C NMR spectrum of 10-monohydrochlordecone ($(CD_3)_2CO$, 150 MHz, 298 K).

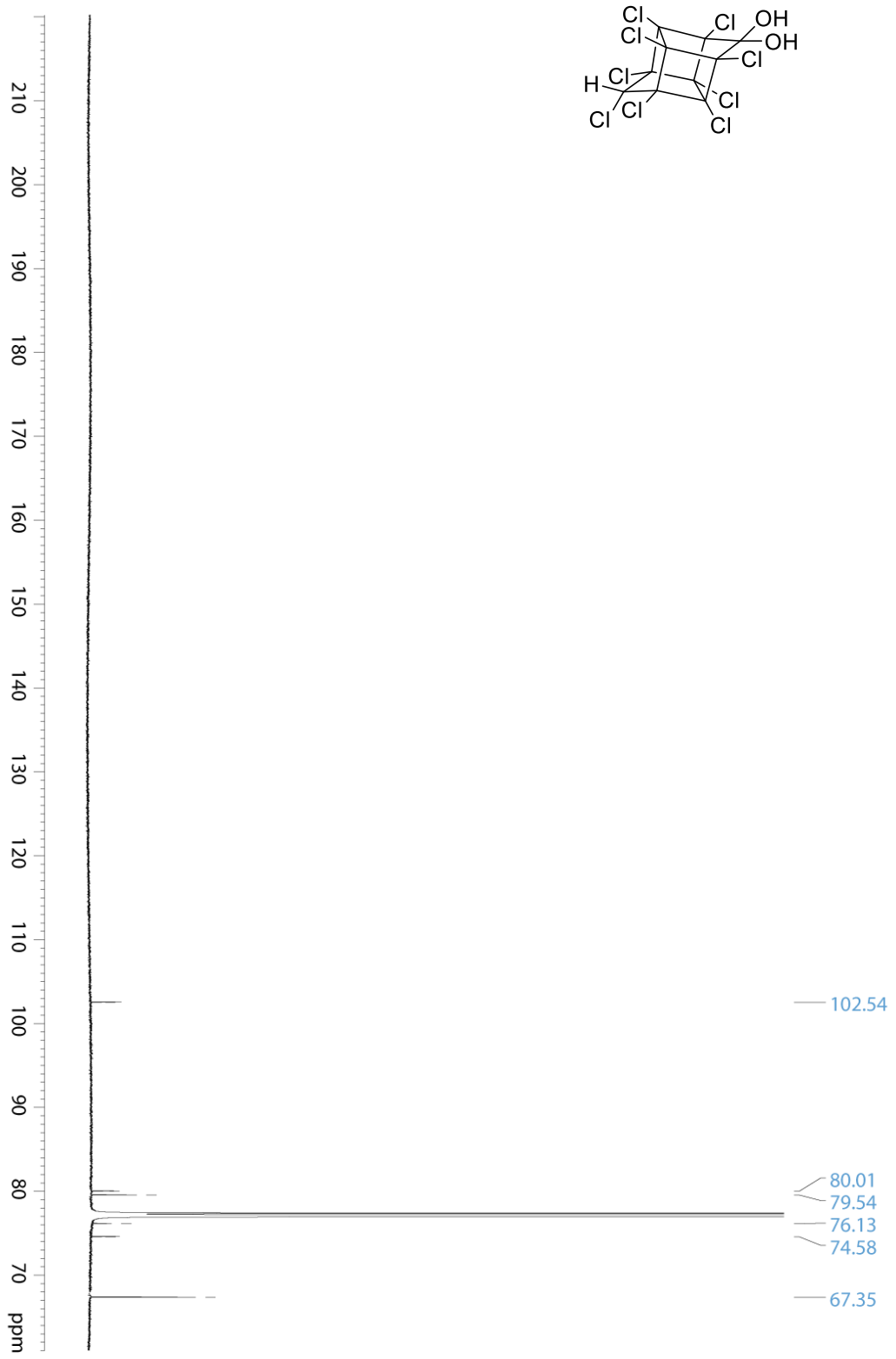


Figure S9. ^{13}C NMR spectrum of 10-monohydrochlordecone (saturated solution in $CDCl_3$, 150 MHz, 298 K).

3. ^{1}H NMR titrations

3.1. General procedure

A solution of hemicryptophane host (3.0 mM in $CDCl_3$, 600 µL) was titrated in NMR tubes with aliquots of a concentrated solution (7.0 mM in the same solvent) of chlordecone. ^{1}H NMR titration was performed on a Bruker Avance III HD 500 MHz. The shifts Δδ of the host's protons signals around 6.4 ppm were measured after each addition and plotted as a function of the guest/host ratio ([G]/[H]). Association constant K_a was obtained by nonlinear least-squares fitting of these plots using bindfit program from Thordarson's group.[3] K_a, covariance and RMS are reported for each titration

3.2. Fit parameters

Host	Guest	K_a (L.mol^{-1})	cov	RMS (ppm)
1	Chlordecone	126 ± 3.7%	3.03×10^{-3}	8.98×10^{-5}
2	Chlordecone	2.1×10^{4} ± 3.4%	3.91×10^{-4}	7.43×10^{-4}
2	Monohydrochlordecone	2.6×10^{4} ± 5.1%	1.42×10^{-3}	9.52×10^{-4}
2	Chlordecone alcohol	136 ± 2.9%	1.48×10^{-3}	9.47×10^{-5}

Table S1. K_a, covariance and RMS obtained from fits of the titration curves.

3.3. Titration curve for chlordecone

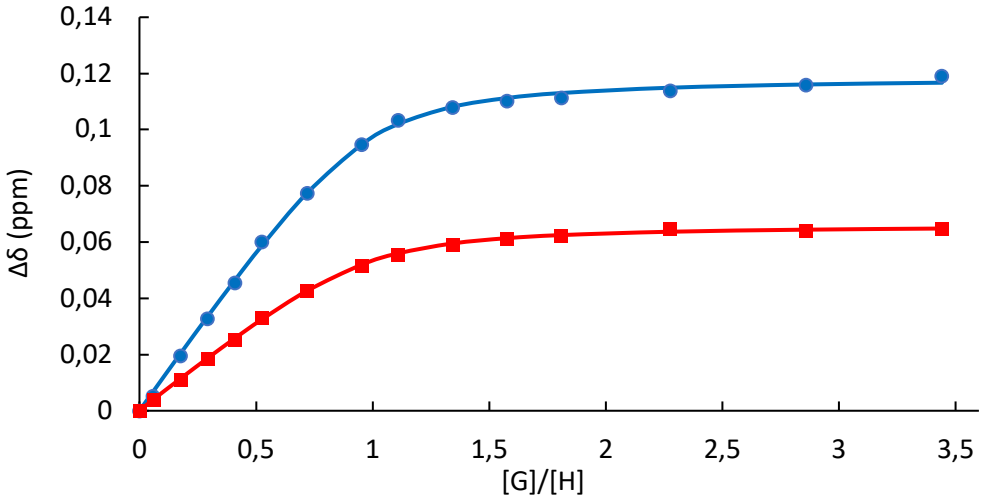


Figure S10. Titration curve of host **2** with chlordecone. The chemical induced shifts Δδ of host's protons at 6.46 ppm (●) and 3.67 ppm (■) were measured and plotted as a function of the ratio [G]/[H] (dots). Curves were fitted with Bindfit program (lines).

3.4. ^{13}C NMR complex spectra

A ^{13}C NMR spectrum of a saturated solution of chlordecone in $CDCl_3$ was recorded. 1 Equivalent of hemicryptophane **2** was then added to the NMR tube and another ^{13}C NMR was recorded with the same parameters. A third experiment with addition of 1 equivalent of chlordecone was performed (containing a 1:2 mixture of cage:chlordecone). The spectra were compared with that of the free cage.

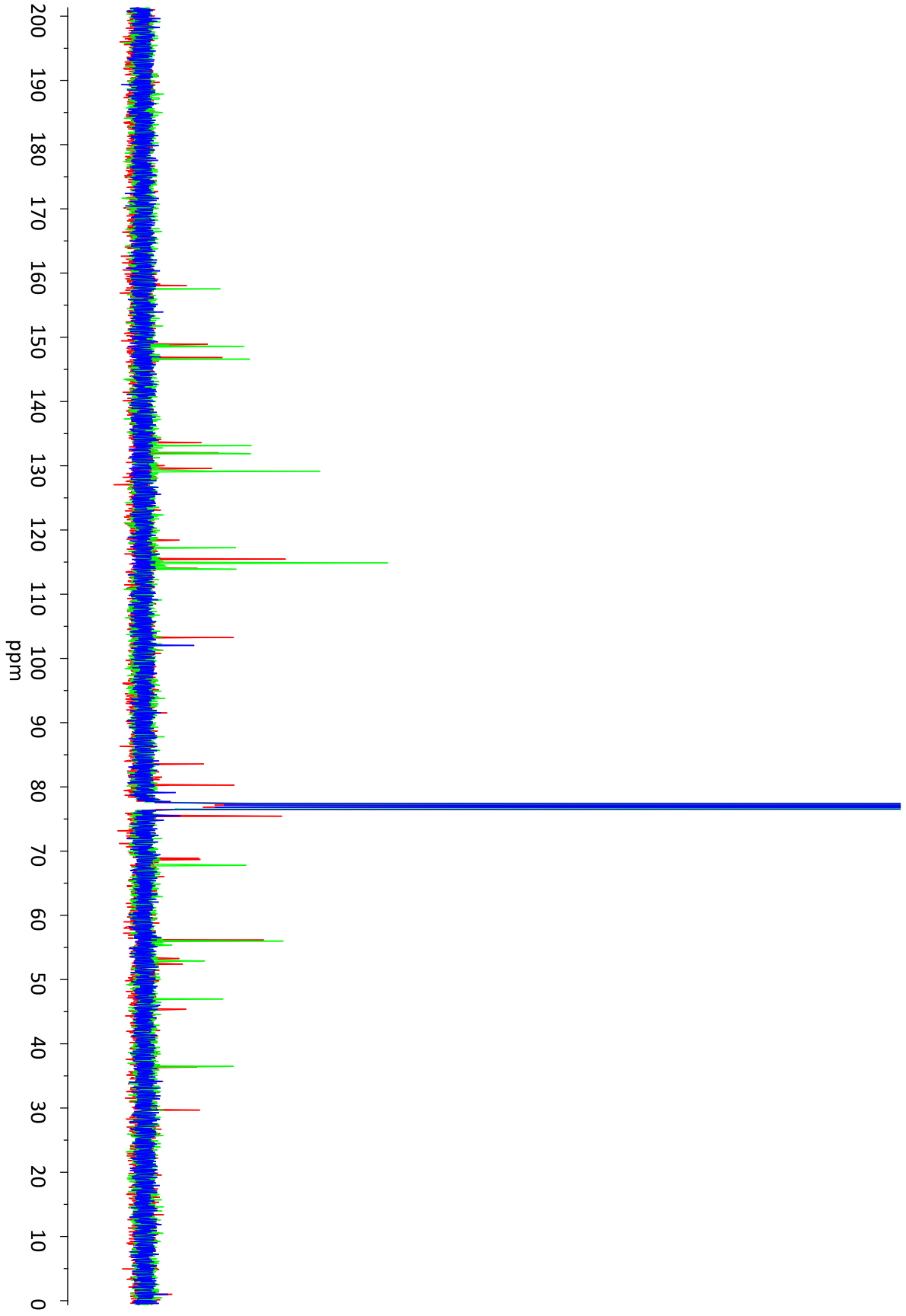


Figure S11. Superposition of ^{13}C NMR spectra of the saturated solution of chlordecone in $CDCl_3$ (100 MHz, 298 K) in blue, the free hemicryptophane **2** in $CDCl_3$ (100 MHz, 298 K) in green and the complex of chlordecone and hemicryptophane in $CDCl_3$ (100 MHz, 298 K) in red.

3.5. Evolution of ^{1}H NMR with time

A solution of hemicryptophane host **2** (3.0 mM in $CDCl_3$, 600 µL) containing 1 equivalent of chlordecone was added in a NMR tube and ^{1}H NMR spectra were recorded every day during 10 days.

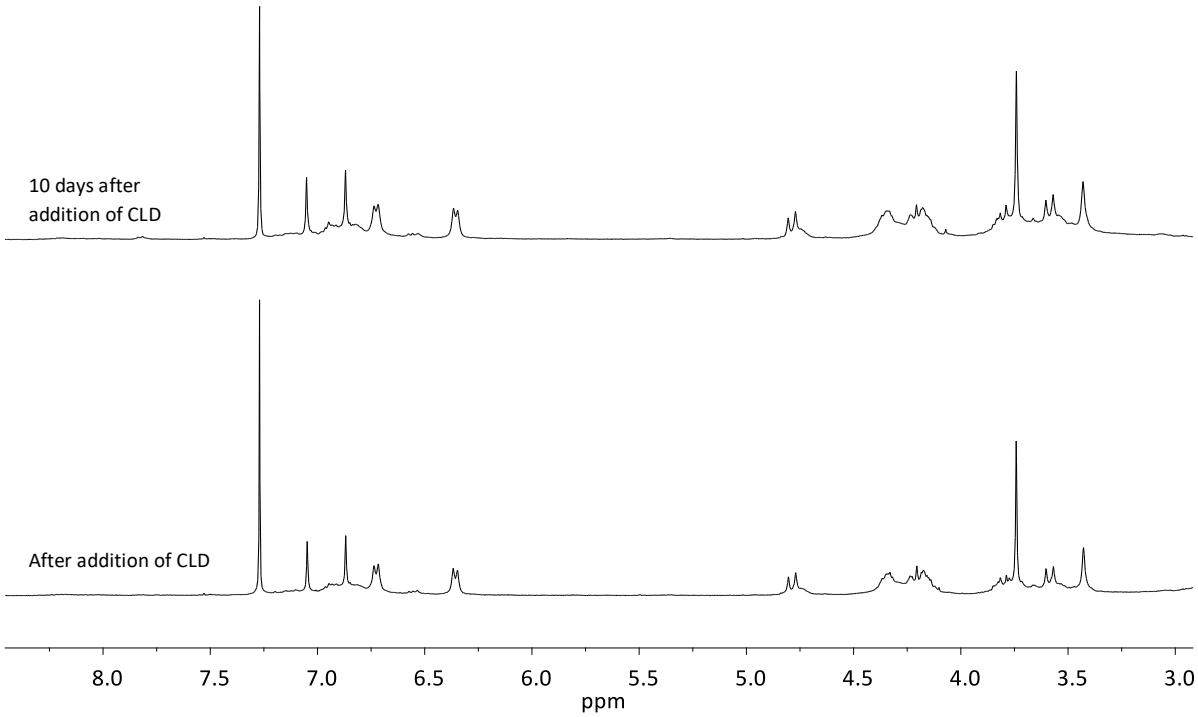


Figure S12. ^{1}H NMR spectra of the CLD@hemicryptophane-**2** complex ($CDCl_3$, 400 MHz, 298 K) after addition of chlordecone and 10 days after addition.

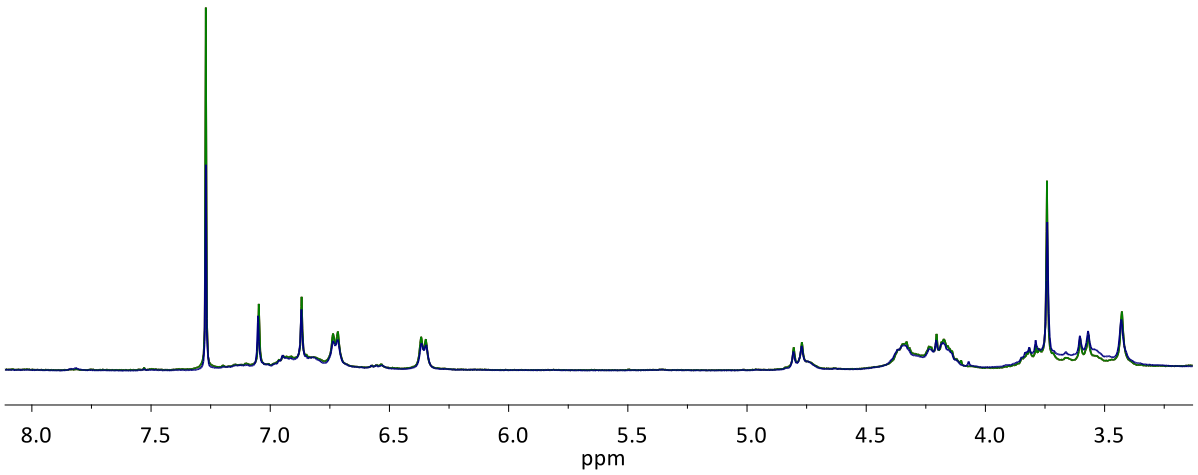


Figure S13. Superposition of ^{1}H NMR spectra of the CLD@hemicryptophane-**2** complex ($CDCl_3$, 400 MHz, 298 K) just after addition (in green) and 10 days after addition (in blue) of CLD.

4. Computational methods

All electronic structure calculations were carried out within density functional theory (DFT) framework. Since the inspected systems are particularly flexible, intramolecular interactions are likely to dictate their shape. Therefore, weak interactions corrections were included by means of a nowadays current procedure. The energy contributions arising from atoms polarizabilities are added on top of the DFT electronic energy. [4, 5] Full geometry optimizations were performed using the B3LYP functional and 6-31G* a basis set in the Gaussian G09 suite of programs.[6]

References

1 P. D. Raytchev, O. Perraud, C. Aronica, A. Martinez and J.-P. Dutasta, *J. Org. Chem.*, 2010, **75**, 2099–2102.

2 B. Chatelet, E. Payet, O. Perraud, P. Dimitrov-Raytchev, L.-L. Chapellet, V. Dufaud, A. Martinez and J.-P. Dutasta, *Org. Lett.*, 2011, **13**, 3706–3709.

3 D. B. Hibbert and P. Thordarson, *Chem. Commun.*, 2016, **52**, 12792–12805.

4 S. Grimme, *Comput. Mol. Sci.* 2011, **1**, 211-228.

5 S. Grimme, J. Antony, S. Ehrlich, S. Krieg, *J. Chem. Phys.* 2010, **132**, 154104.

6 M. J. Frisch, G. W. Trucks, H. B. Schlegel, G. E. Scuseria, M. A. Robb, J. R. Cheeseman, G. Scalmani, V. Barone, B. Mennucci, G. A. Petersson, H. Nakatsuji, M. Caricato, X. Li, H. P. Hratchian, A. F. Izmaylov, J. Bloino, G. Zheng, J. L. Sonnenberg, M. Hada, M. Ehara, K. Toyota, R. Fukuda, J. Hasegawa, M. Ishida, T. Nakajima, Y. Honda, O. Kitao, H. Nakai, T. Vreven, J. A. J. Montgomery, J. E. Peralta, F. Ogliaro, M. Bearpark, J. J. Heyd, E. Brothers, K. N. Kudin, V. N. Staroverov, R. Kobayashi, J. Normand, K. Raghavachari, A. Rendell, J. C. Burant, S. S. Iyengar, J. Tomasi, M. Cossi, N. Rega, J. M. Millam, M. Klene, J. E. Knox, J. B. Cross, V. Bakken, C. Adamo, J. Jaramillo, R. Gomperts, R. E. Stratmann, O. Yazyev, A. J. Austin, R. Cammi, C. Pomelli, J. W. Ochterski, R. L. Martin, K. Morokuma, V. G. Zakrzewski, G. A. Voth, P. Salvador, J. Dannenberg, S. Dapprich, A. D. Daniels, O. Farkas, J. B. Foresman, J. V. Ortiz, J. Cioslowski and D. J. Fox, *Gaussian Inc Wallingford CT*.