Electronic Supplementary Material (ESI) for Organic & Biomolecular Chemistry.

Supporting Information

Differentiation of Small Alkane and Alkyl Halide Constitutional Isomers via Encapsulation

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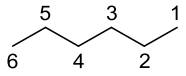
Materials and Instrumentation

Octa-acid host **1** was synthesized as previously reported.[1] All guests **2-6** (≥ 99% pure) were purchased from Aldrich Chemical Company and were used without further purification. Guests **7, 8, 10, 11, 12**, and **14** were purchased from Aldrich Chemical Company, guest **9** was purchased from BroadPharm and guest **13** was purchased from Enamine. All NMR spectra were recorded on a 500 MHz Bruker NMR spectrometer regulated at 25˚C. All competitions were performed in deuterium oxide (Cambridge Isotopes, 99.9%+) with each solution prepared on the day of analysis. Host **1** and guests **2-14** are displayed below with number assignments.



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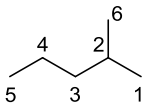

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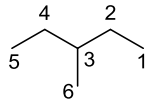

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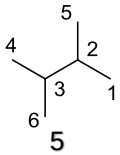

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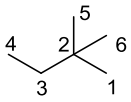

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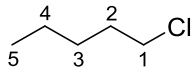

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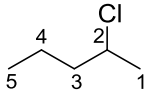

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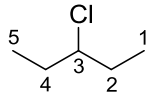

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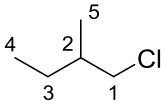

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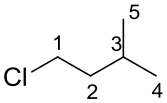

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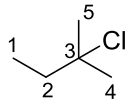

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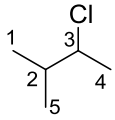

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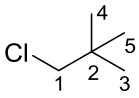

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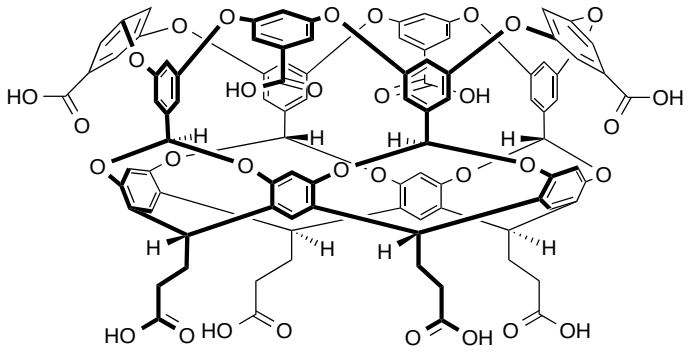

1

NMR Data for Capsular Complexes between Host 1 and Guests 2-6

A 1.0 mM stock solution of host **1** in 10 mM sodium borate/D_2O buffer was prepared. To analyze host-guest complexation, 0.6 mL of the host **1** stock solution was added to an NMR tube, followed by 1.0 µL (excess) of a pure guest. The resulting suspension was mixed thoroughly. A spectrum was recorded within 10 minutes of mixing, and again after 24 hours to confirm equilibrium. The ^{1}H NMR spectra utilized presaturation parameters for water suppression. The ^{1}H NMR of the complexes formed between **1** and guest **2**-**6** are displayed in Figures S1-S5.

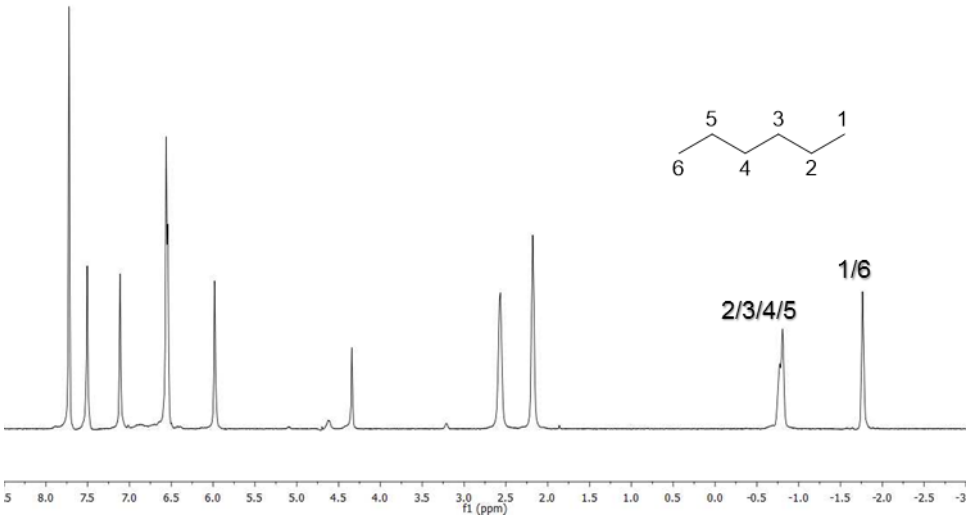

Figure S1: ^{1}H NMR of the complex formed between host **1** and guest **2**.

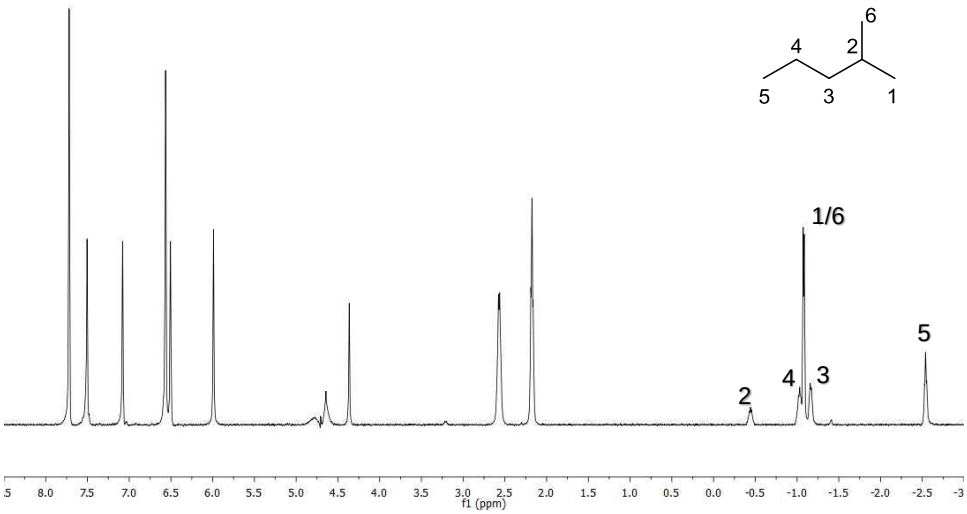

Figure S2: ^{1}H NMR of the complex formed between host **1** and guest **3**.

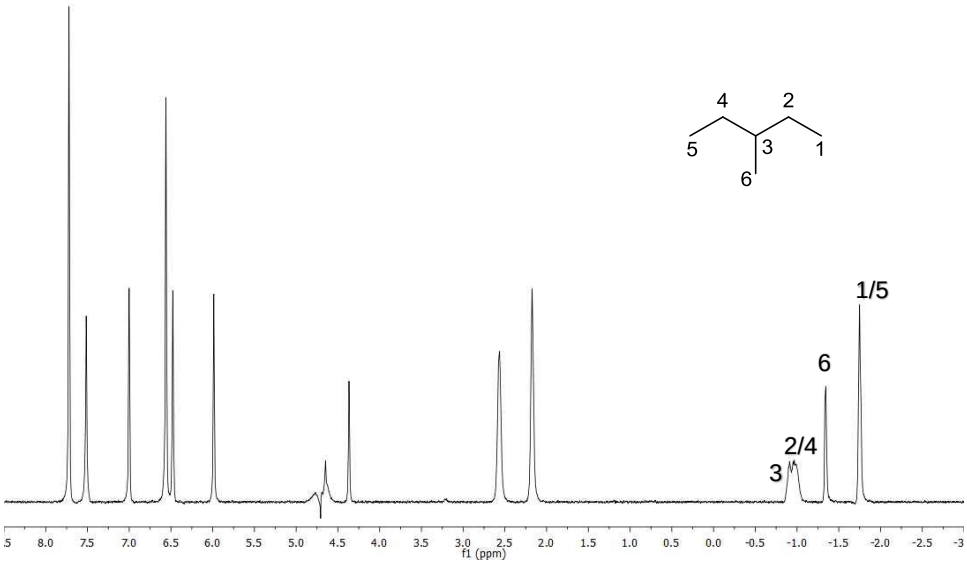

Figure S3: ^{1}H NMR of the complex formed between host **1** and guest **4**.

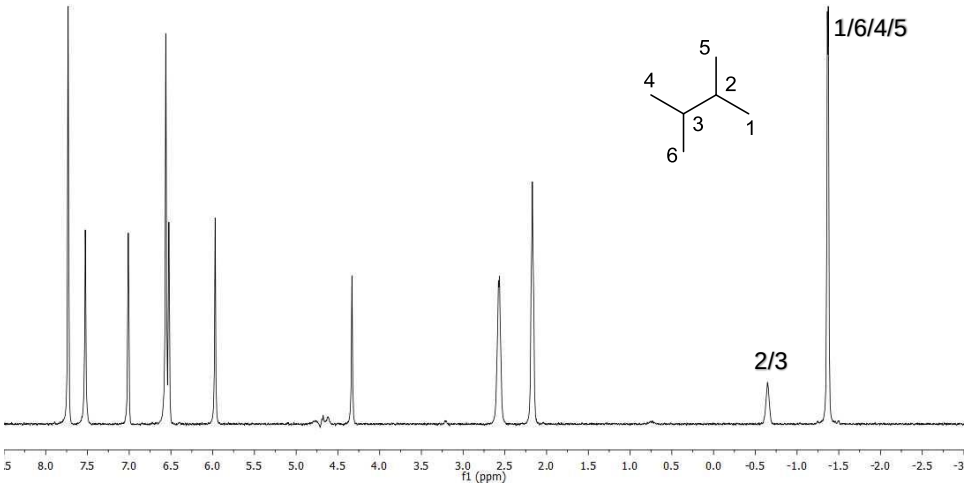

Figure S4: ^{1}H NMR of the complex formed between host **1** and guest **5**.

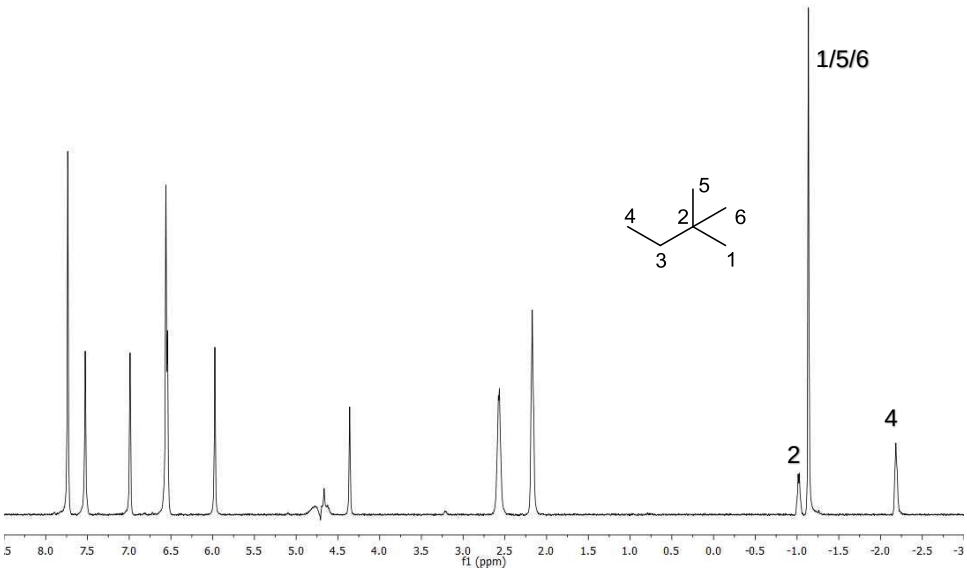

Figure S5: ^{1}H NMR of the complex formed between host **1** and guest **6**.

^{1}H NMR Shift Data (Δδ, ppm) for Guests 2-6 Encapsulated in Host 1

All ^{1}H NMR data listed in Table S1 were calculated in reference to free guest peaks found in D_2O and corresponding bound guest peaks encapsulated within **1**.

Table S1: ^{1}H NMR Shift Data (Δδ, ppm) for guests **2-6** encapsulated in **1**.

Proton / Guest	H1	H2	H3	H4	H5	H6
2	-2.68	-2.13	-2.13	-2.13	-2.13	-2.68
3	-2.00	-2.04	-2.37	-2.38	-3.45	-2.00
4	-2.65	-2.75	-1.97	-2.75	-2.65	-2.67
5	-1.46	-1.91	-1.91	-1.46	-1.46	-1.46
6	-3.07	NA	-2.59	-1.91	-3.07	-3.07

Competition Experiments

All competition experiments were performed with excess guest and 1.0 mM stock solution of **1** in 10 mM sodium borate/D_2O buffer. For the competitions, 0.6 mL of the **1** stock solution was added to an NMR tube and 1.0 µL each of two guests were added and mixed thoroughly. A spectrum was recorded within 10 minutes of mixing, and again after 24 hours to confirm equilibrium. The NMR spectra utilized presaturation parameters for water suppression. The ^{1}H NMR spectra of selected competitions are displayed in Figures S6-S10.

^{1}H NMR Spectra of Selected Competition Experiments for Guests 2-6

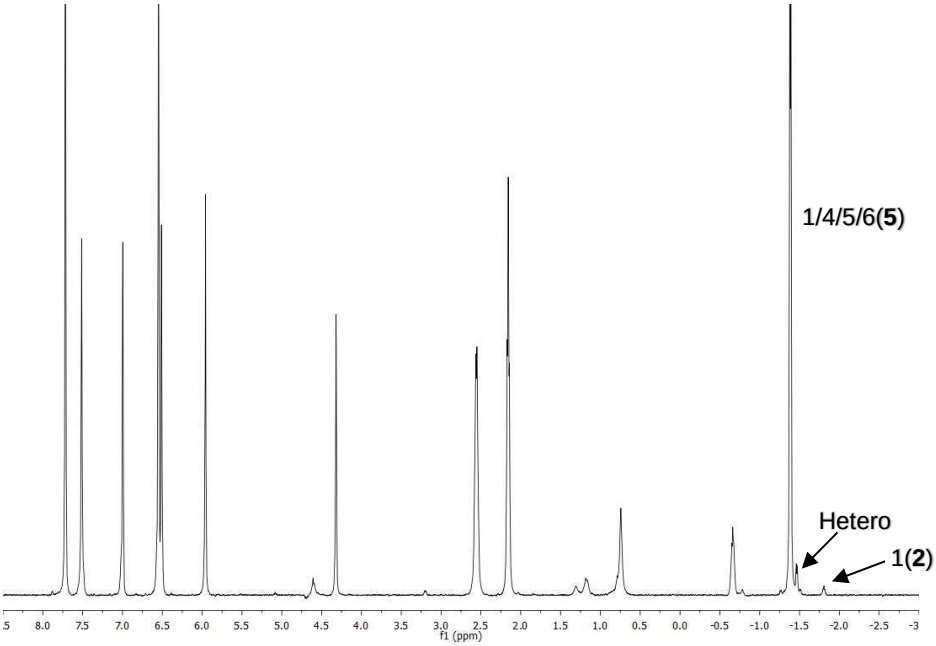

Figure S6: ^{1}H NMR of the complexes formed between host **1** and guest **2** and **5**.

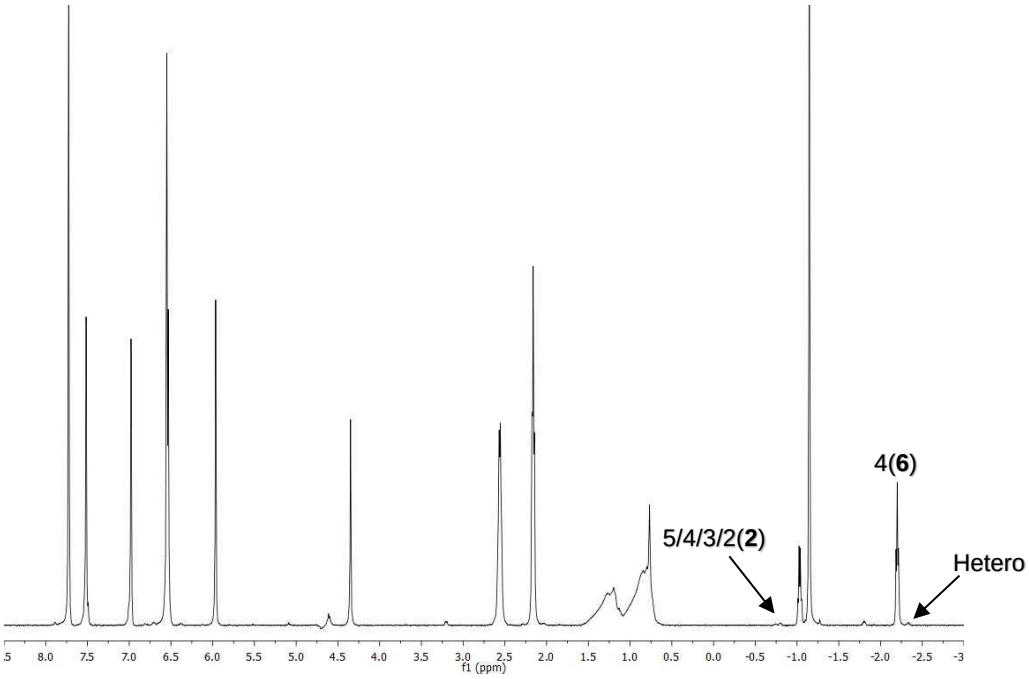

Figure S7: ^{1}H NMR of the complexes formed between host **1** and guest **2** and **6**.

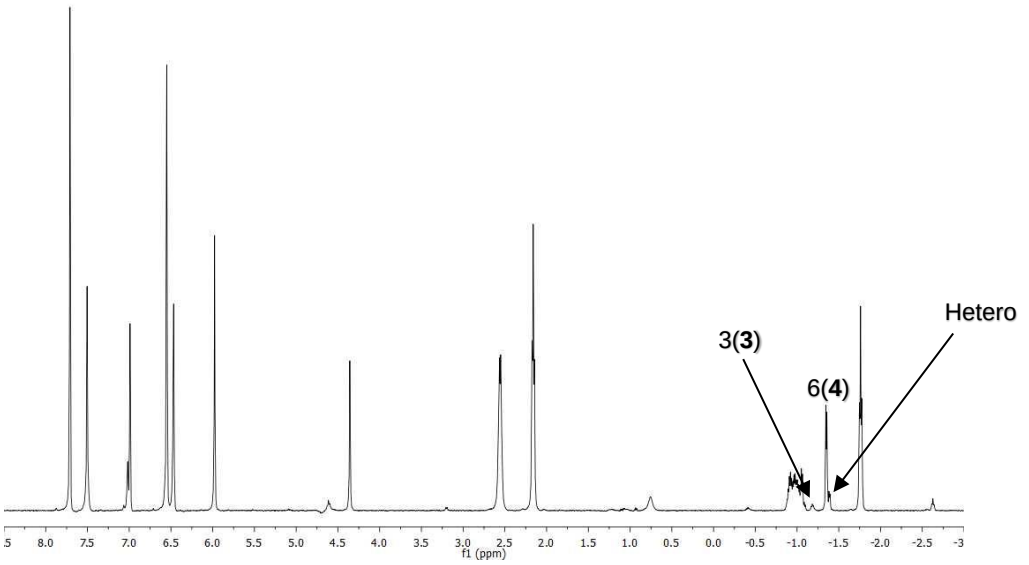

Figure S8: ^{1}H NMR of the complexes formed between host **1** and guest **3** and **4**.

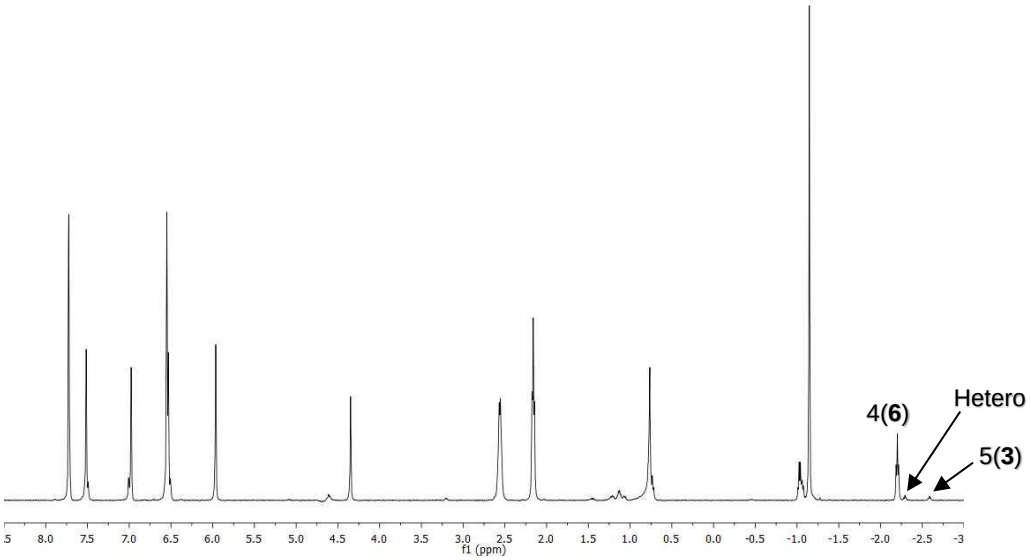

Figure S9: ^{1}H NMR of the complexes formed between host **1** and guest **3** and **6**.

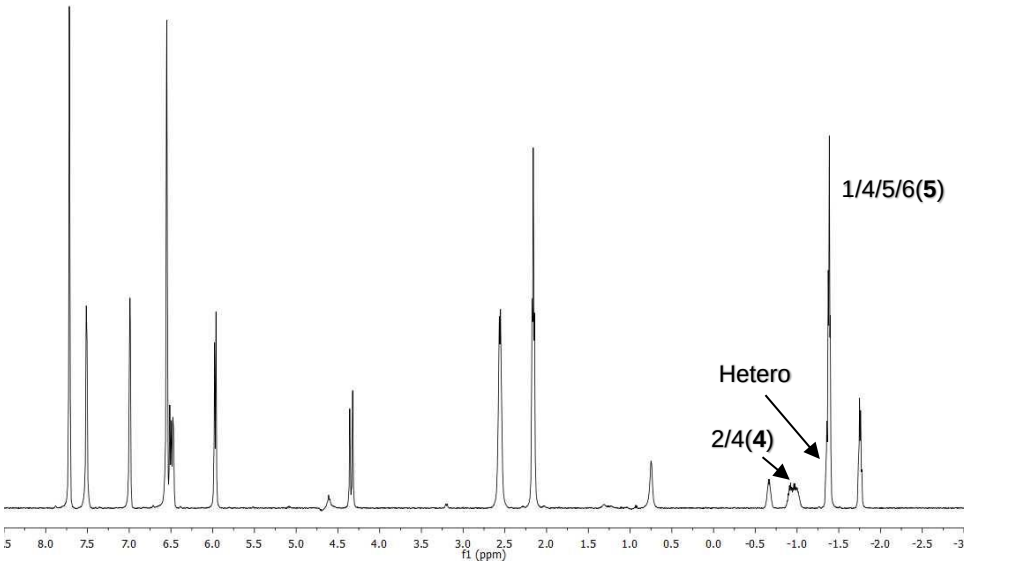

Figure S10: ^{1}H NMR of the complexes formed between host **1** and guest **4** and **5**.

^{1}H NMR Analysis of Chloropentane Isomer Guests 7-14

The procedure for analysis of guests **7-14** was the same as that described previously for guests **2-6**. The ^{1}H NMR spectra for guests **7-14** encapsulated in **1** are shown in Figures S11-S18. Additionally, COSY or NOESY experiments were carried out when necessary to determine unidentified peaks from ^{1}H NMR. Select 2-D NMR spectra are displayed in Figures S19-S22.

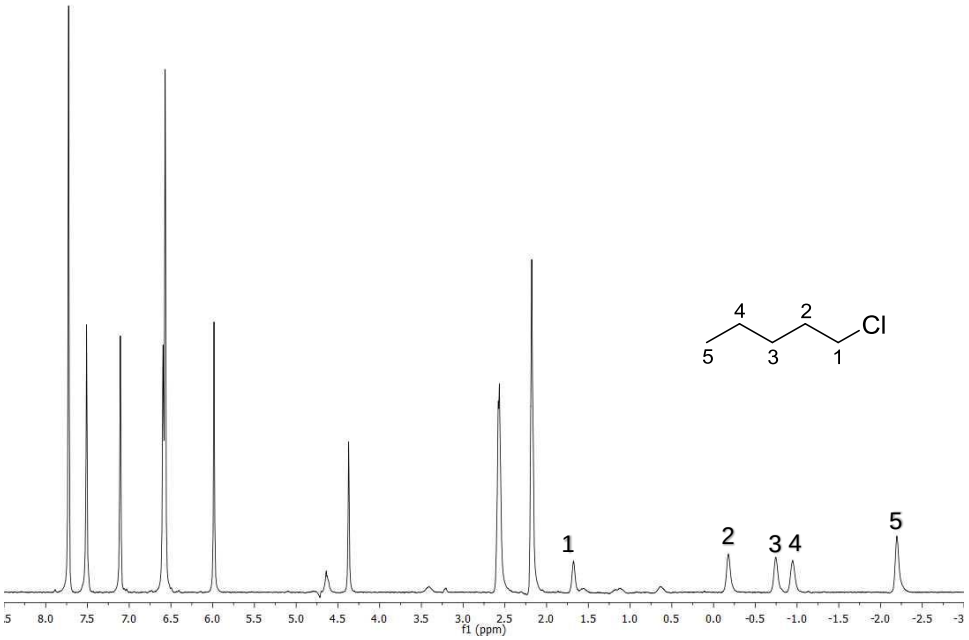

Figure S11: ^{1}H NMR of the complex formed between host **1** and guest **7**.

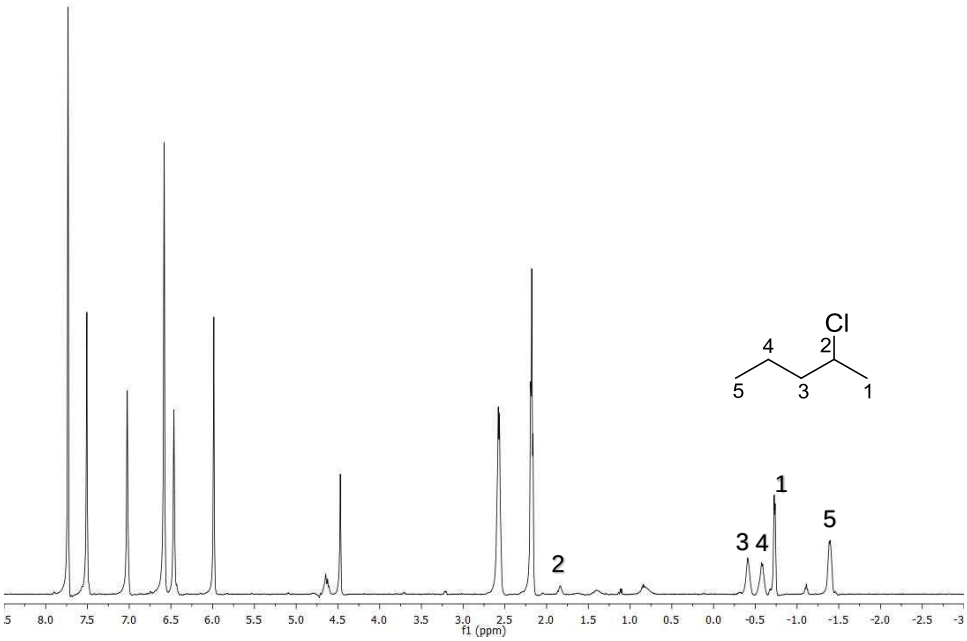

Figure S12: ^{1}H NMR of the complex formed between host **1** and guest **8**.

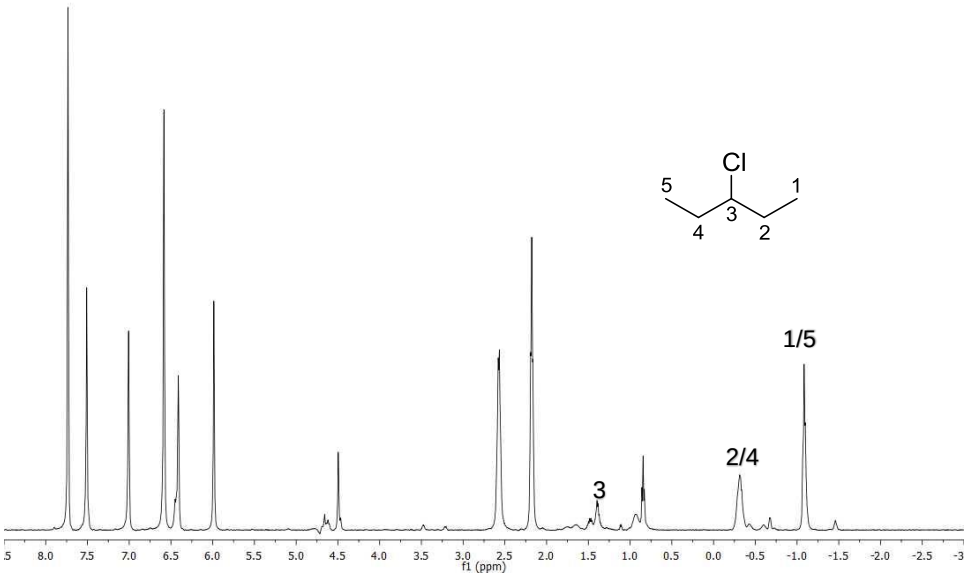

Figure S13: ^{1}H NMR of the complex formed between host **1** and guest **9**.

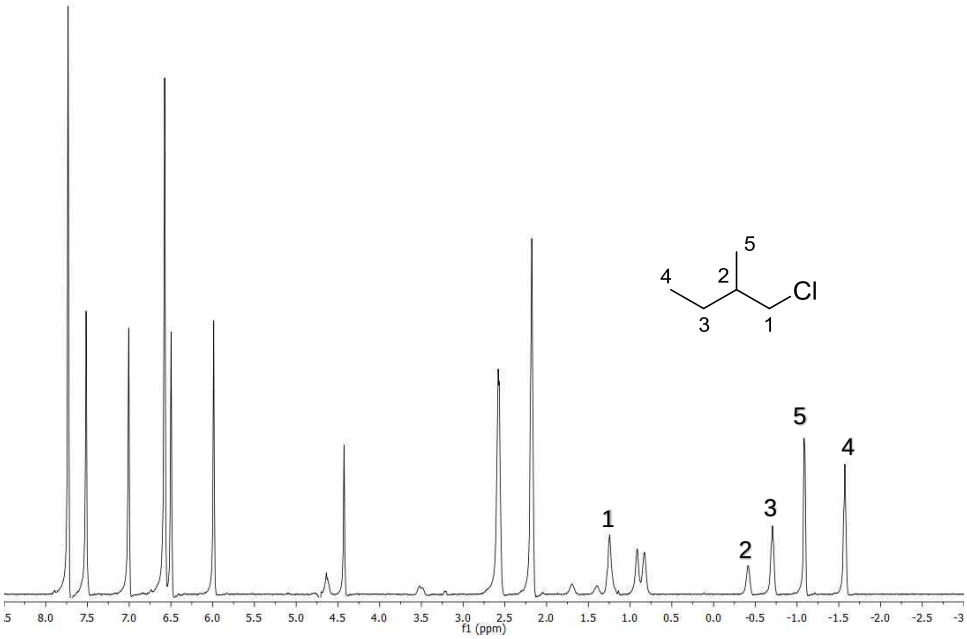

Figure S14: ^{1}H NMR of the complex formed between host **1** and guest **10**.

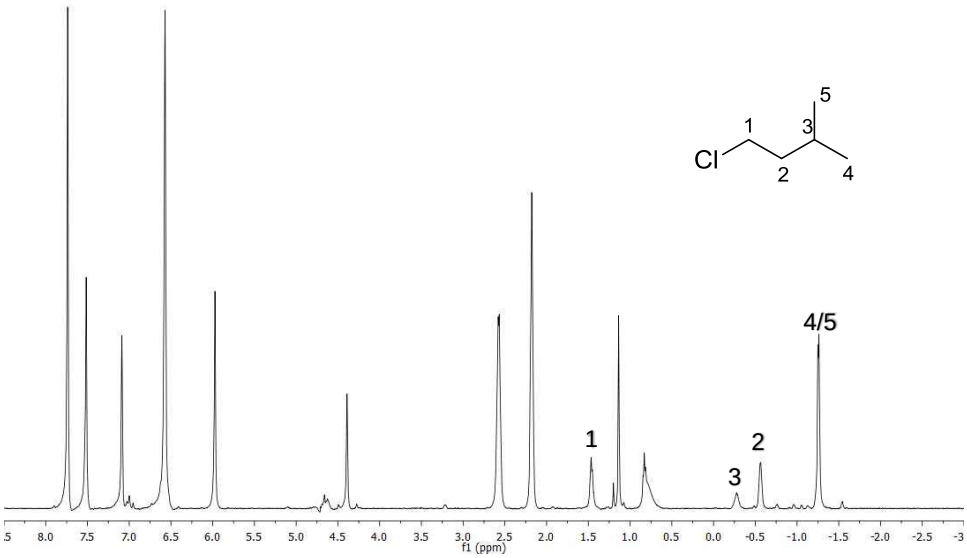

Figure S15: ^{1}H NMR of the complex formed between host **1** and guest **11**.

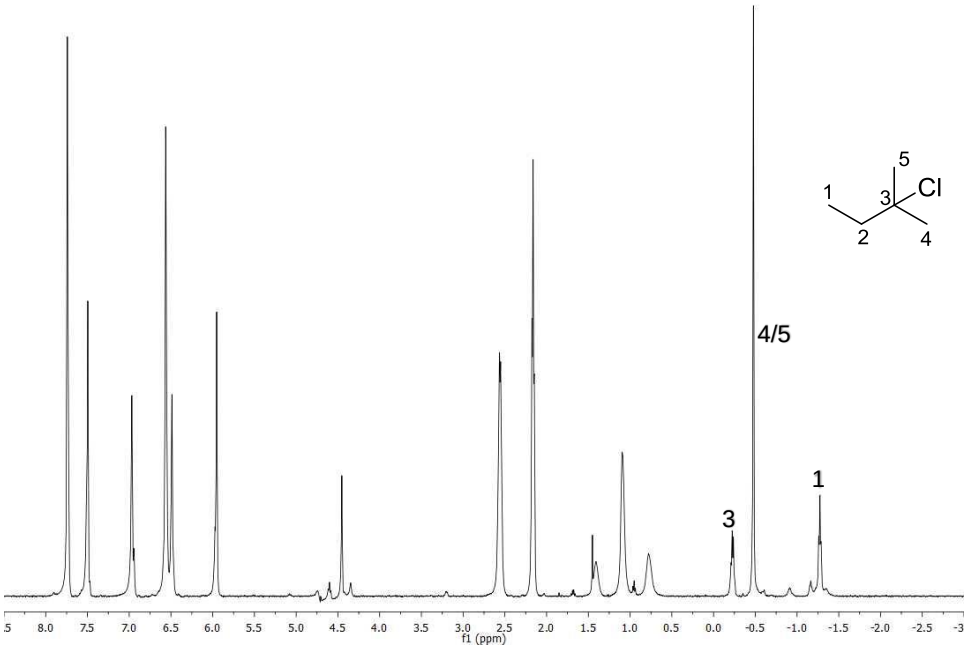

Figure S16: ^{1}H NMR of the complex formed between host **1** and guest **12**.

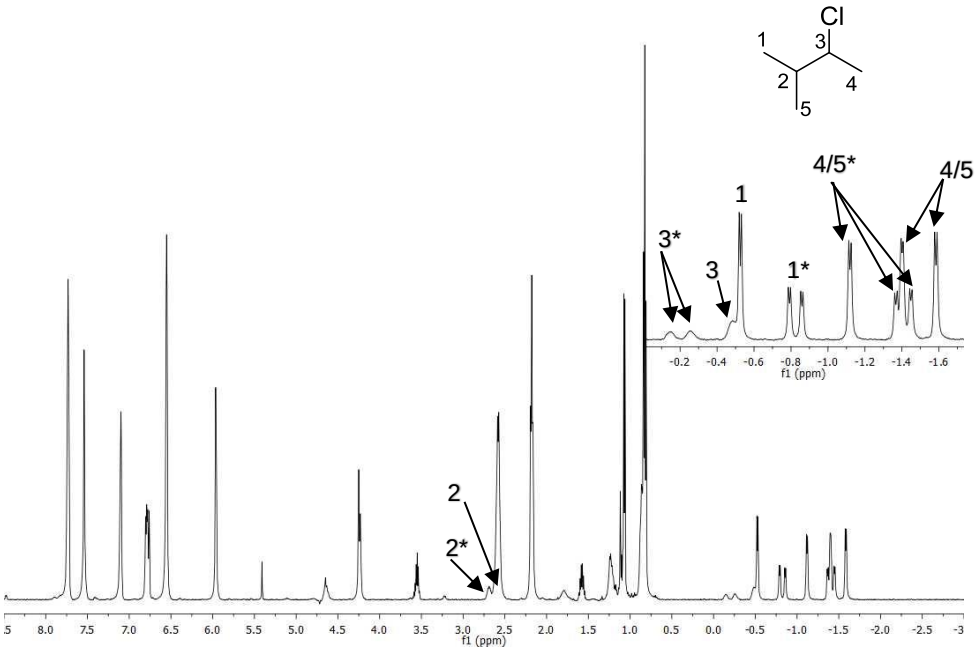

Figure S17: ^{1}H NMR of the complex formed between host **1** and guest **13** *(R/S) complex).

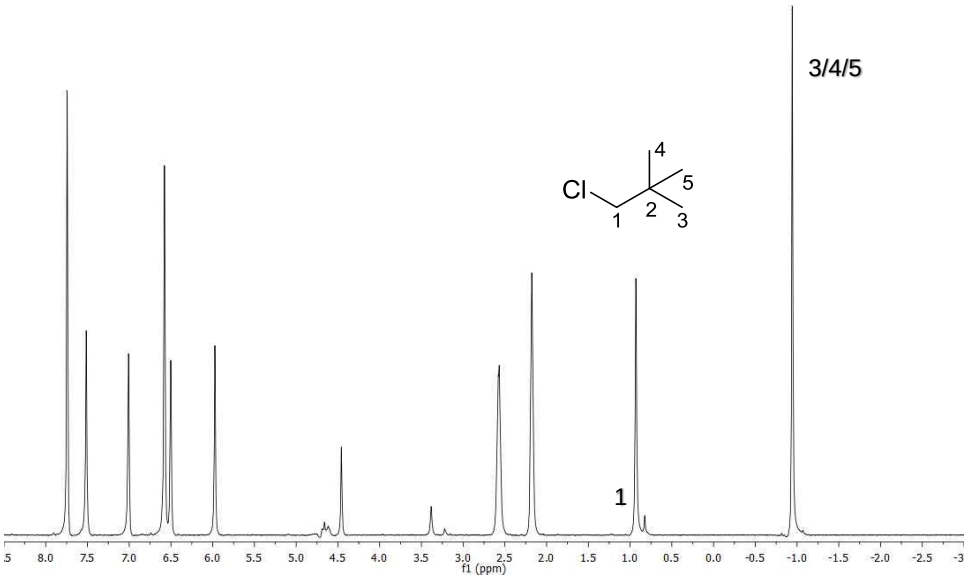

Figure S18: ^{1}H NMR of the complex formed between host **1** and guest **14**.

Select 2-D NMR Analysis of Chloropentane Isomer Guests 7-14

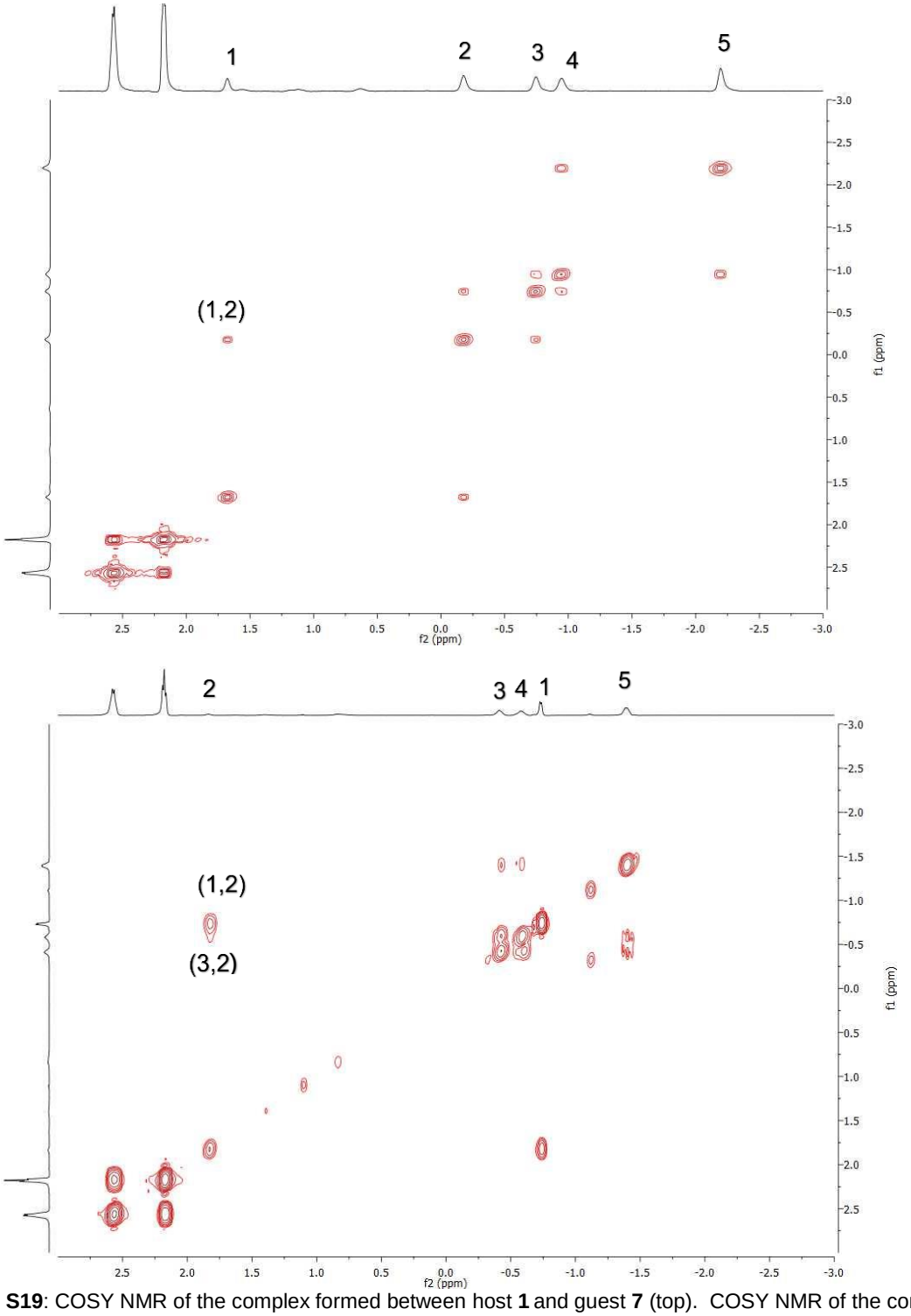

Figure S19: COSY NMR of the complex formed between host **1** and guest **7** (top). COSY NMR of the complex formed between host **1** and guest **8** (bottom).

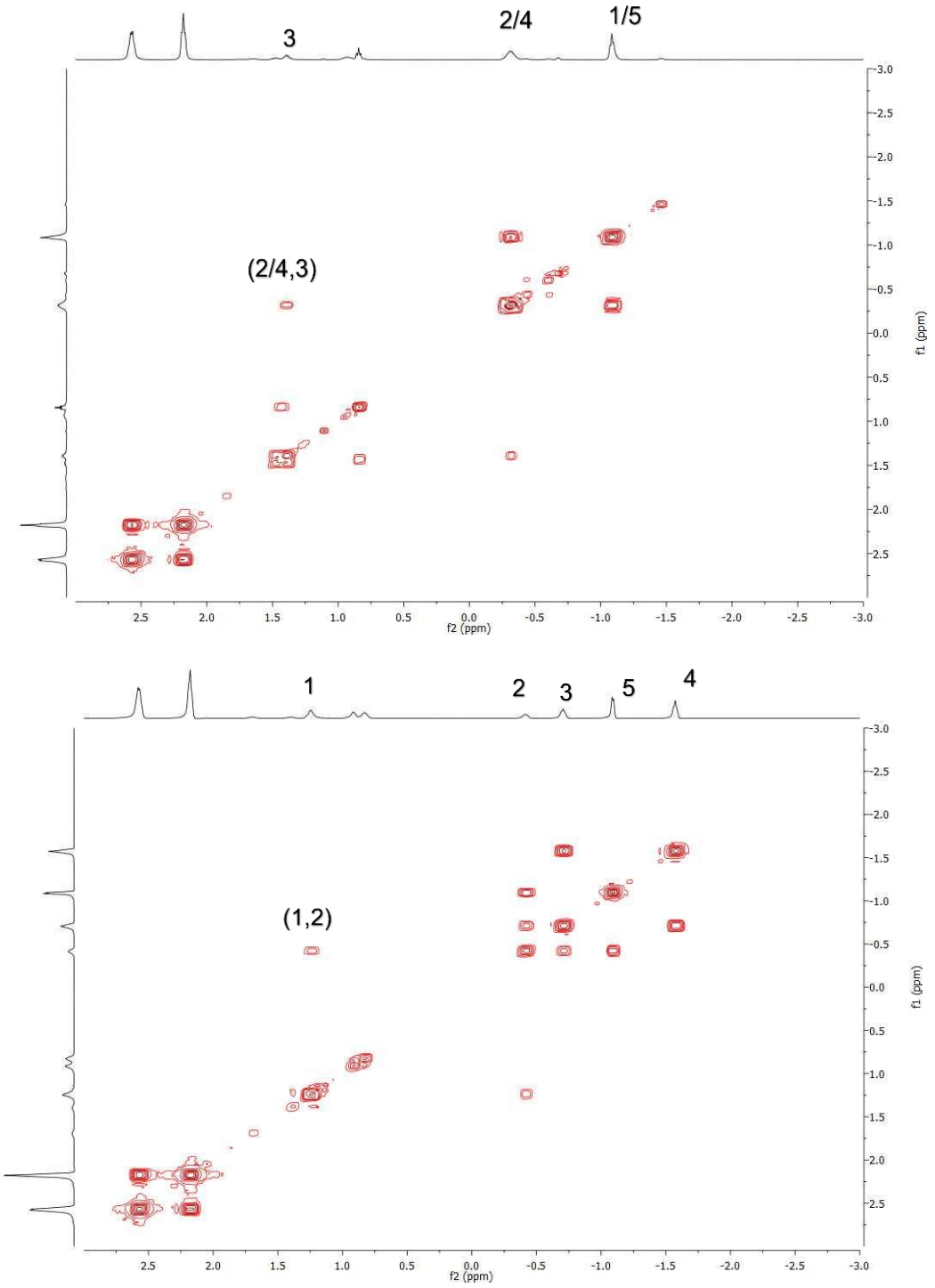

Figure S20: COSY NMR of the complex formed between host **1** and guest **9** (top). COSY NMR of the complex formed between host **1** and guest **10** (bottom).

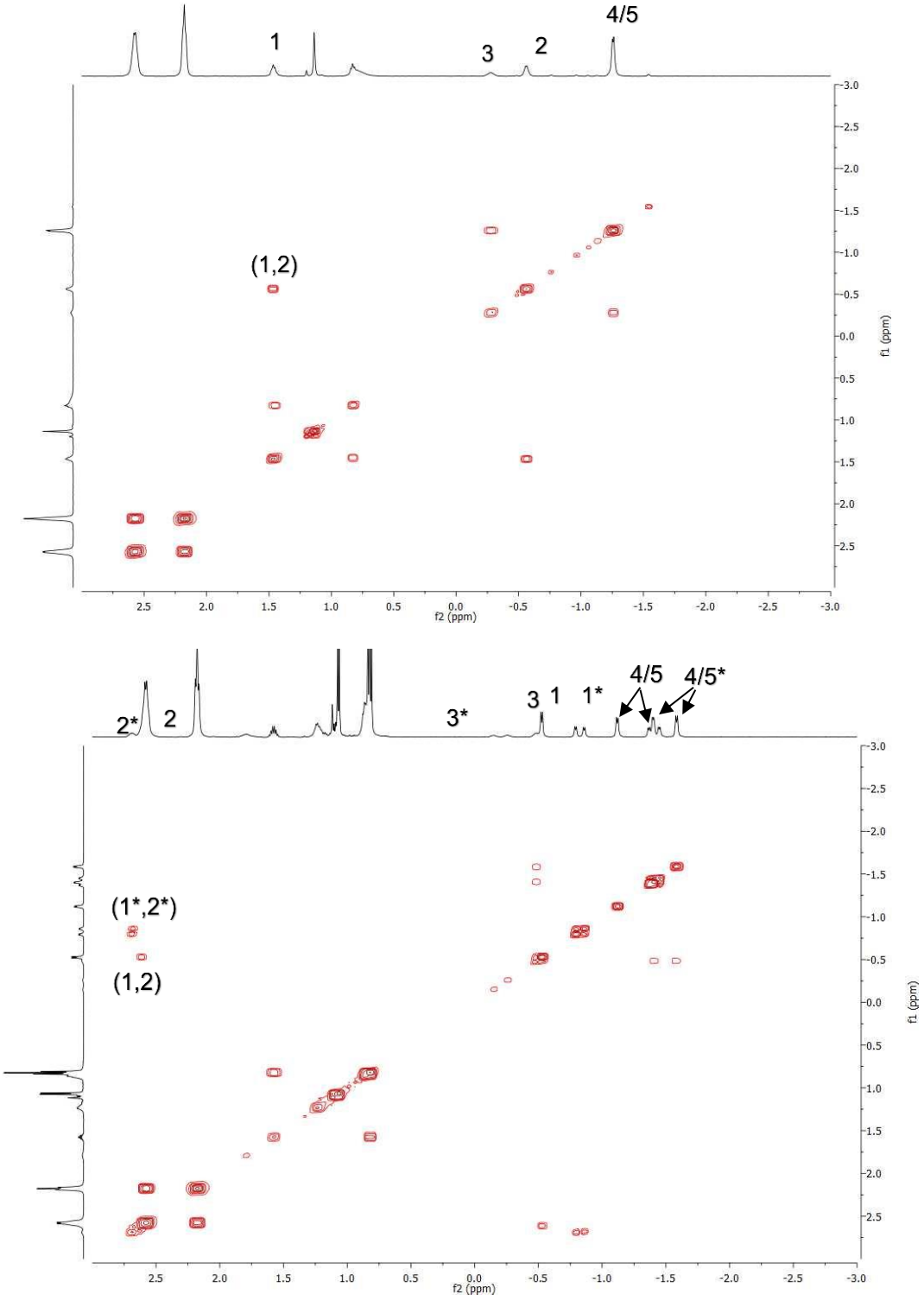

Figure S21: COSY NMR of the complex formed between host **1** and guest **11** (top). COSY NMR of the complex formed between host **1** and guest **13** (bottom).

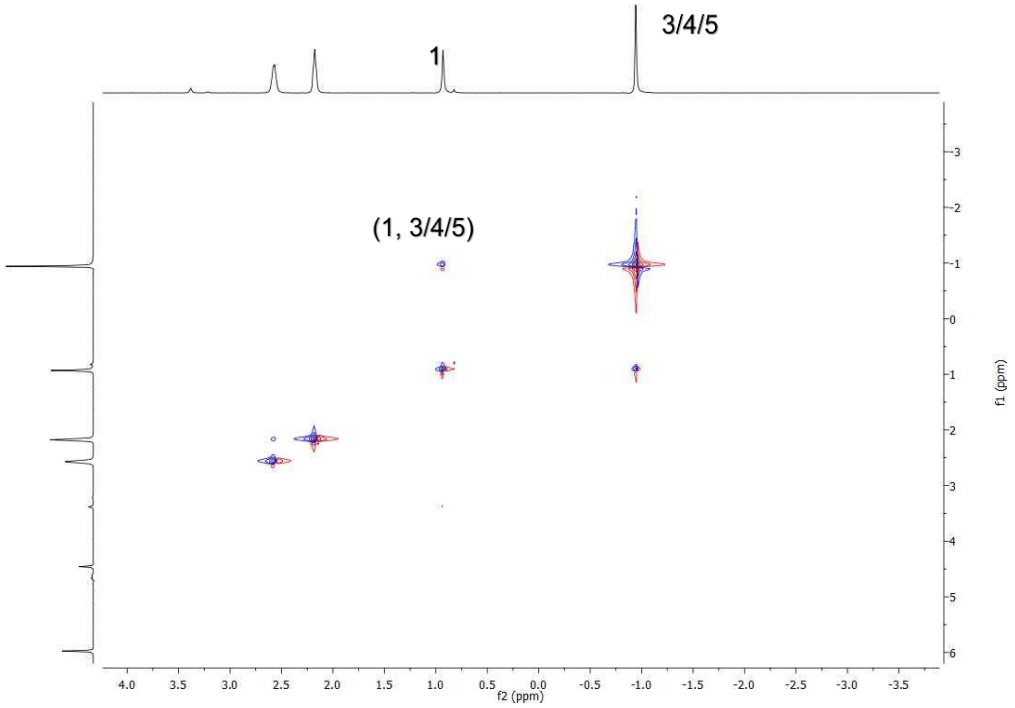

Figure S22: NOESY NMR of the complex formed between host **1** and guest **14**.

Purity Analysis of Chloropentane Isomer Guests 7-14

^{1}H NMR spectra were collected for each guest in deuterated chloroform (Cambridge Isotopes, 99.8%+). The purity of the guests was determined by comparing integration of known peaks. Guests **7, 10, 11, 12,** and **14** arrived with little or no compromise to purity. Guests **8**, **9**, and **13** had more obtrusive amounts of impurity upon arrival. The spectra of impurities for guests **8, 9** and **13** are shown in Figures S23-S25.

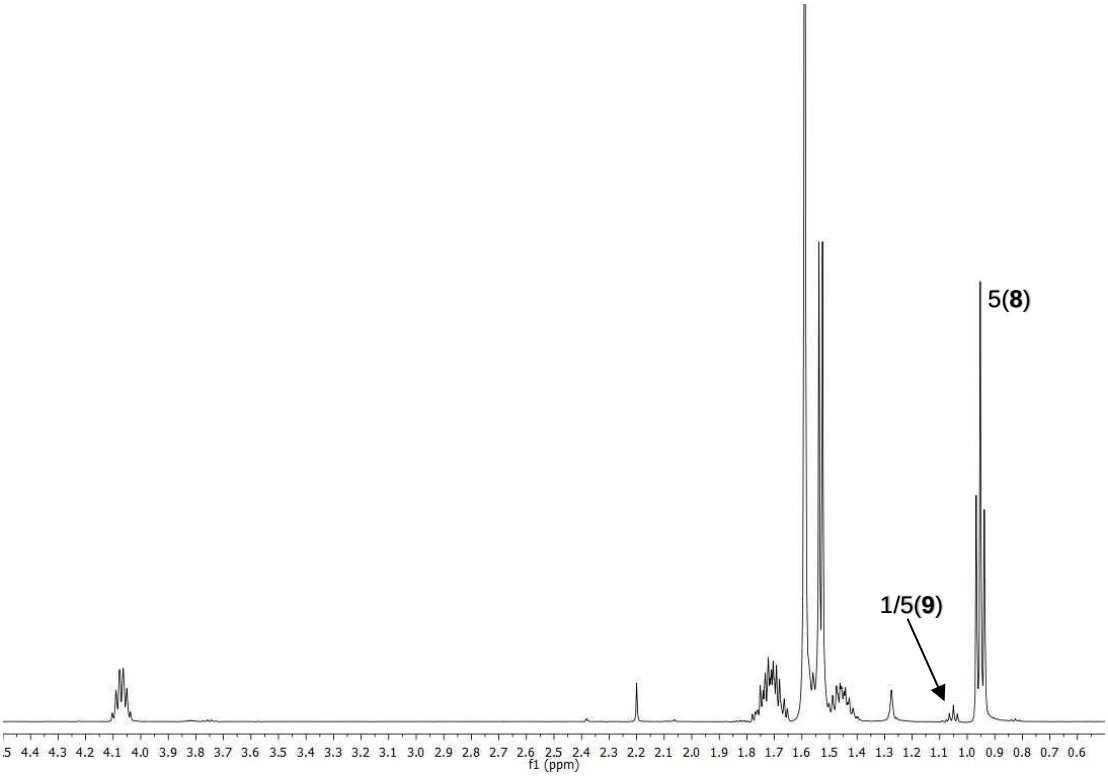

Figure S23: ^{1}H NMR of the guest **8** in $CDCl_3$.

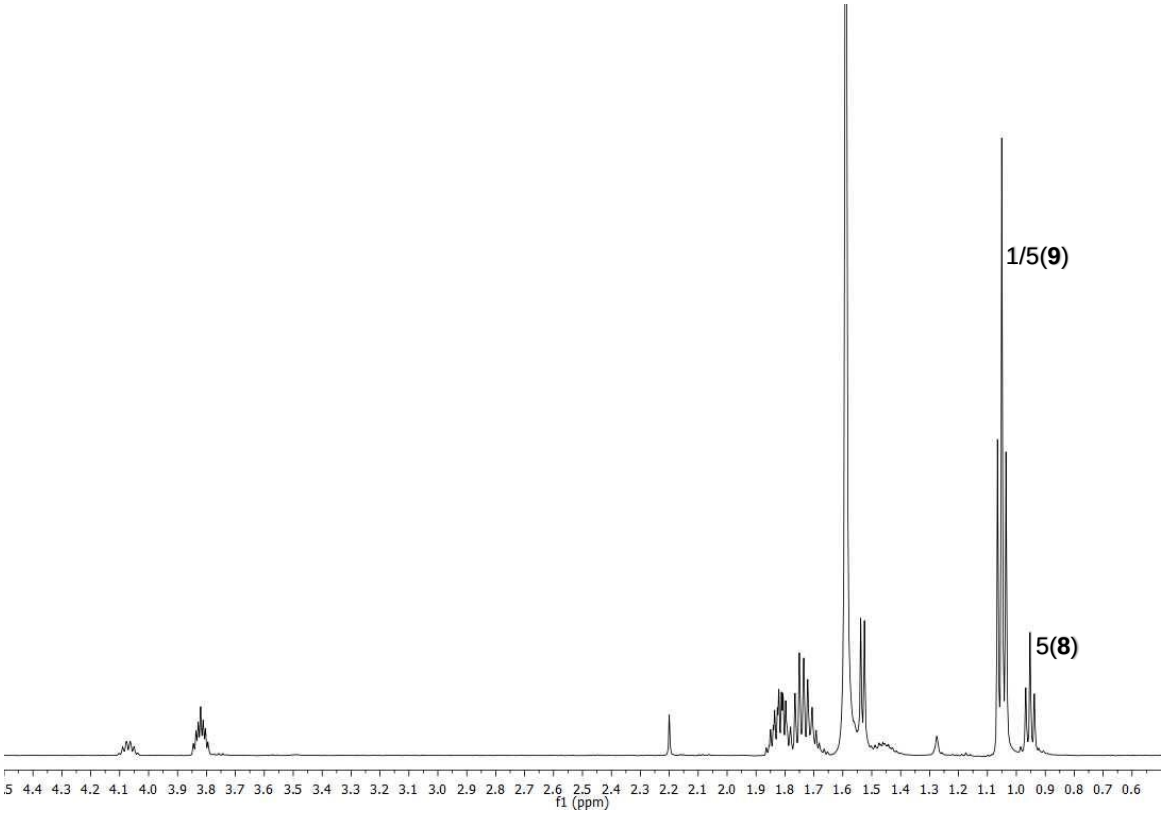

Figure S24: ^{1}H NMR of the guest **9** in $CDCl_3$.

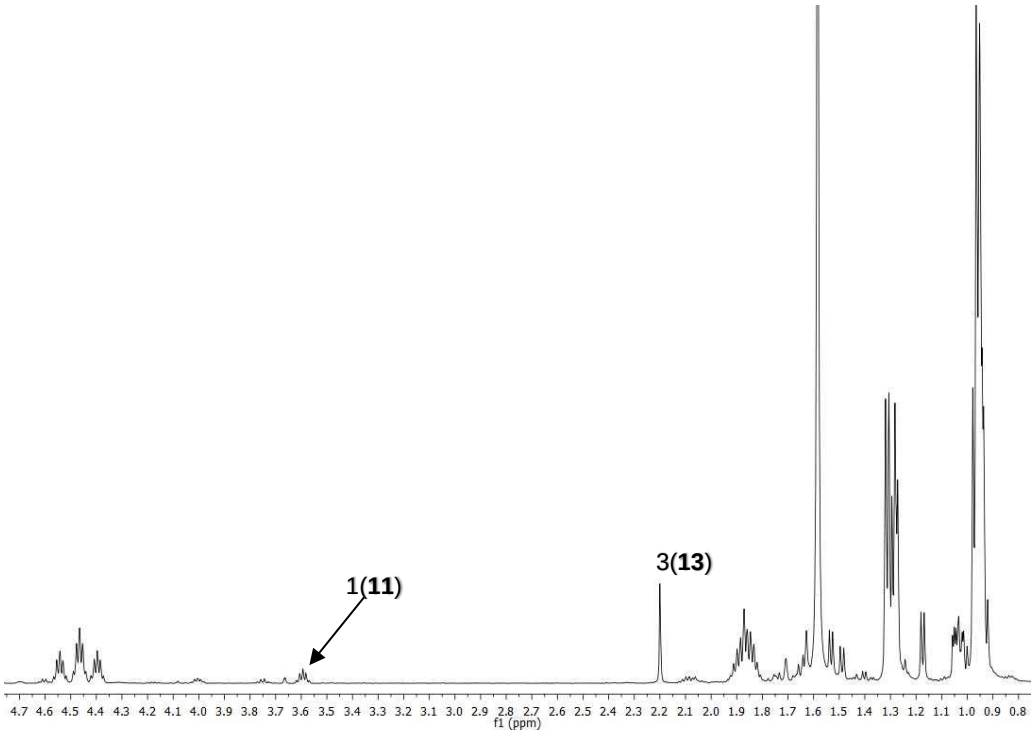

Figure S25: ^{1}H NMR of the guest **13** in $CDCl_3$.

^{1}H NMR Shift Data (Δδ, ppm) for Guests 7-14 Encapsulated in 1

All ^{1}H NMR data listed in Table S2 were calculated in reference to free guest peaks found in D_2O and corresponding encapsulated guest peaks in host **1**. Number assignments of protons are labeled in previous figures.

Table S2: ^{1}H NMR Shift Data (Δδ, ppm) for guests **7-14** encapsulated in **1**.

Proton / Guest	H1	H2	H3	H4	H5
7	-1.85	-1.50	-2.03	-2.18	-2.98
8	-2.09	-2.08	-2.04	-1.99	-2.21
9	-1.93	-1.74	-2.08	-1.74	-1.93
10	-2.25	-2.10	-2.11	-2.41	-2.01
11	-1.97	-2.16	-2.02	-2.12	-2.12
12	-1.57	NA	-1.64	-2.05	-1.57
13 (R/R)(S/S)	-1.60	-0.86	-2.06	-2.23	-2.41
13 (R/S)	-1.89	-0.93	-1.78	-1.94	-2.23
14	-2.45	NA	-1.87	-1.87	-1.87

^{1}H NMR Spectra of Selected Competition Experiments for Guests 7-14

Competition experiments were performed for each combination of guests **7-14** using the same procedure described previously for guests **2-6**. From these experiments, select ^{1}H NMR of competitions are displayed in Figures S26-S32.

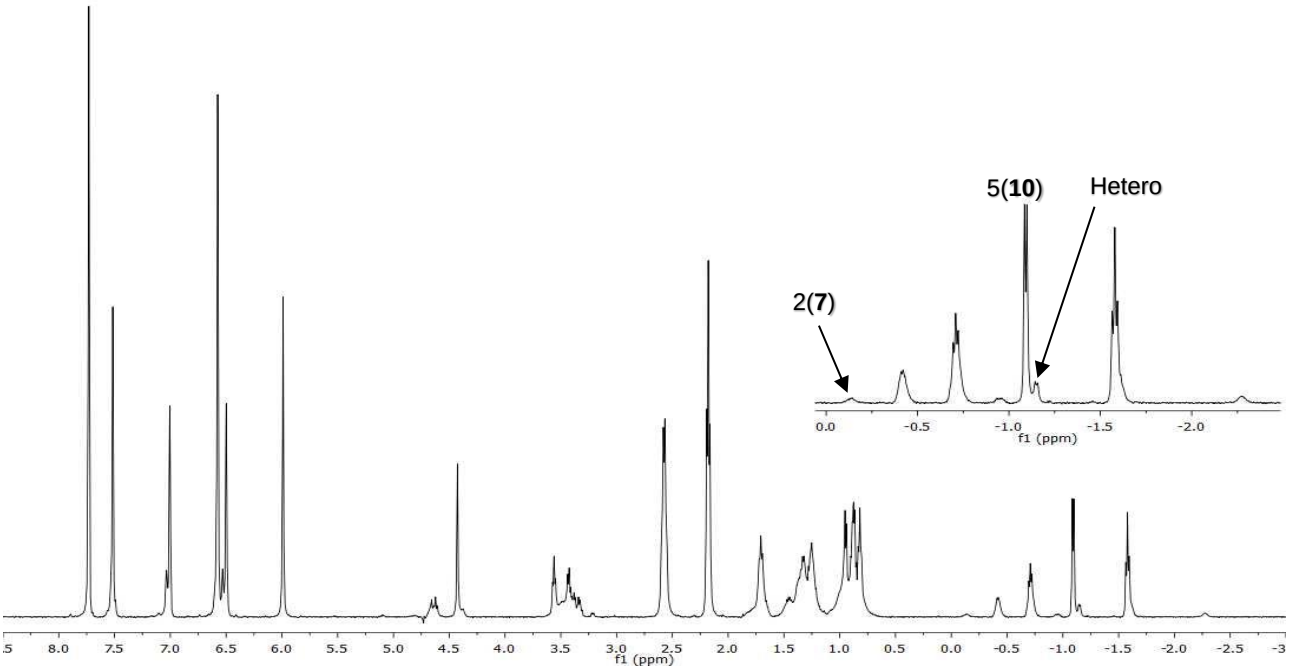

Figure S26: ^{1}H NMR of the complexes formed between host **1** and guests **7** and **10**.

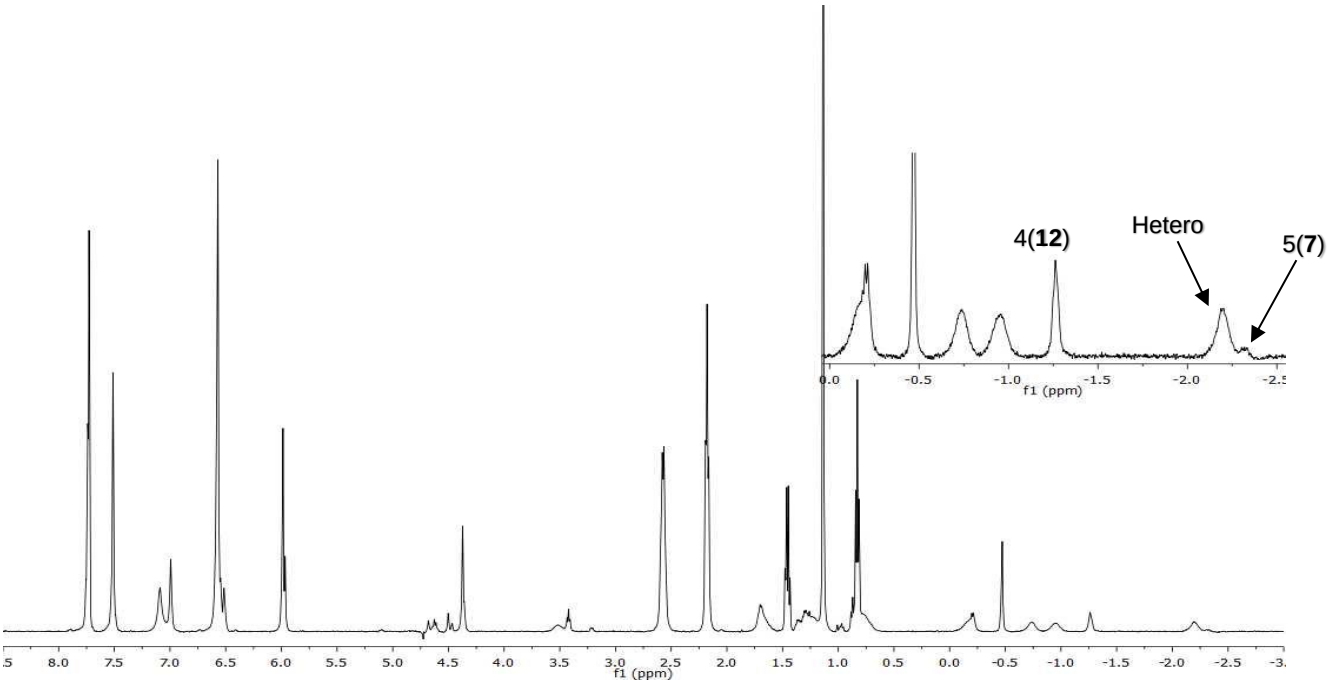

Figure S27: ^{1}H NMR of the complexes formed between host **1** and guests **7** and **12**.

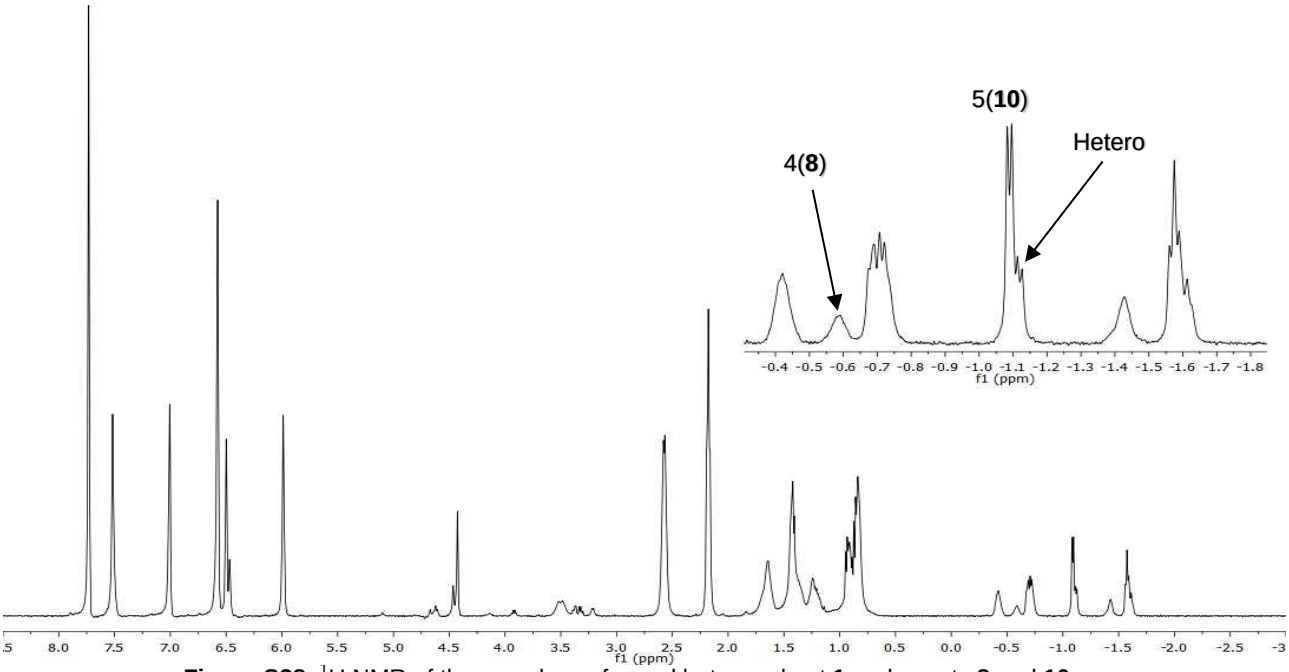

Figure S28: ^{1}H NMR of the complexes formed between host **1** and guests **8** and **10**.

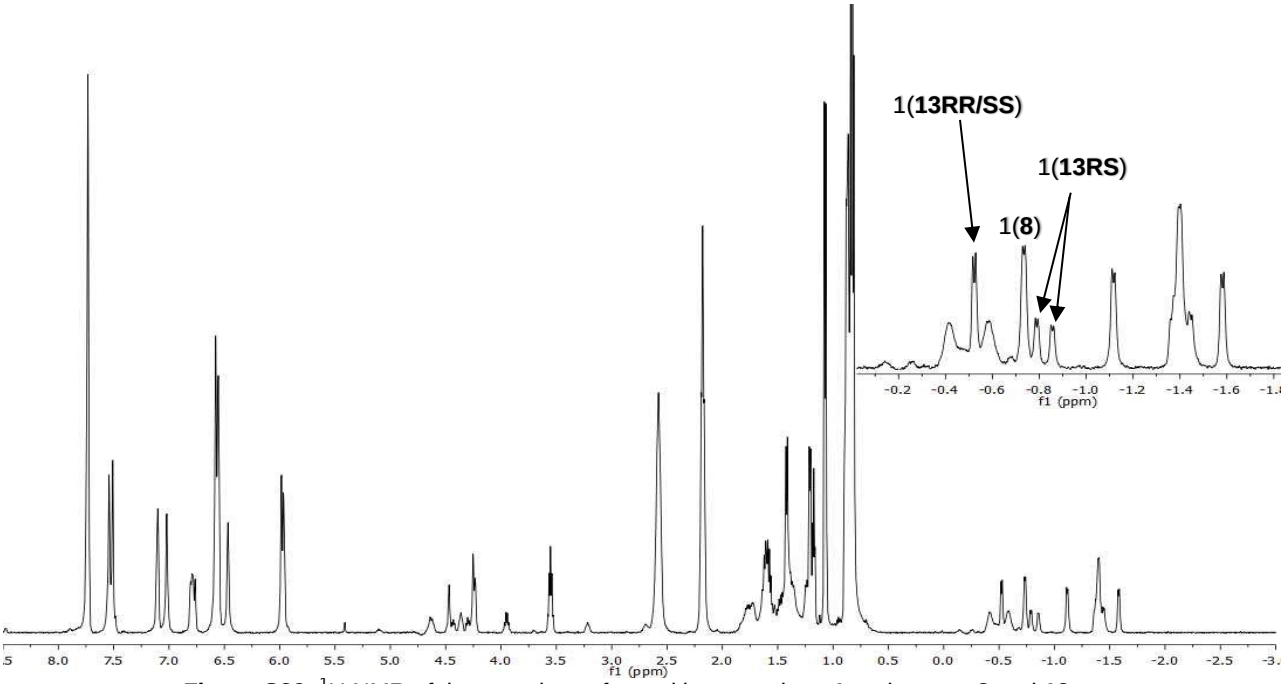

Figure S29: ^{1}H NMR of the complexes formed between host **1** and guests **8** and **13**.

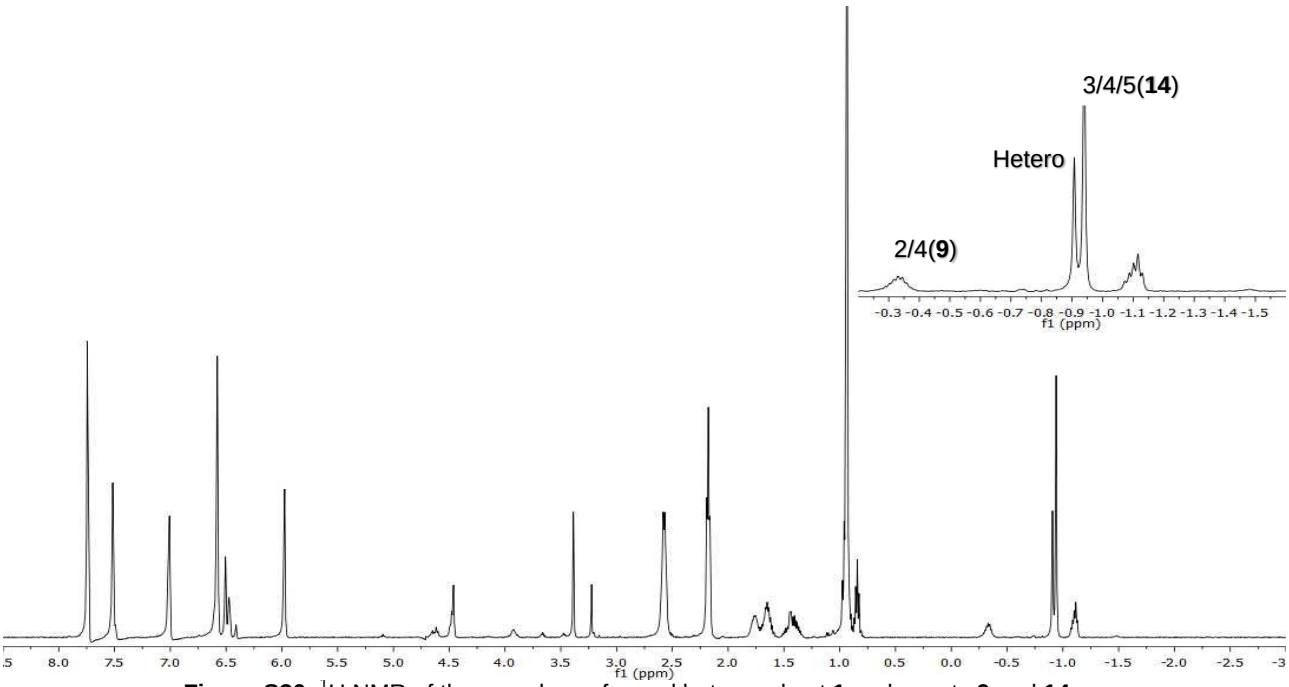

Figure S30: ^{1}H NMR of the complexes formed between host **1** and guests **9** and **14**.

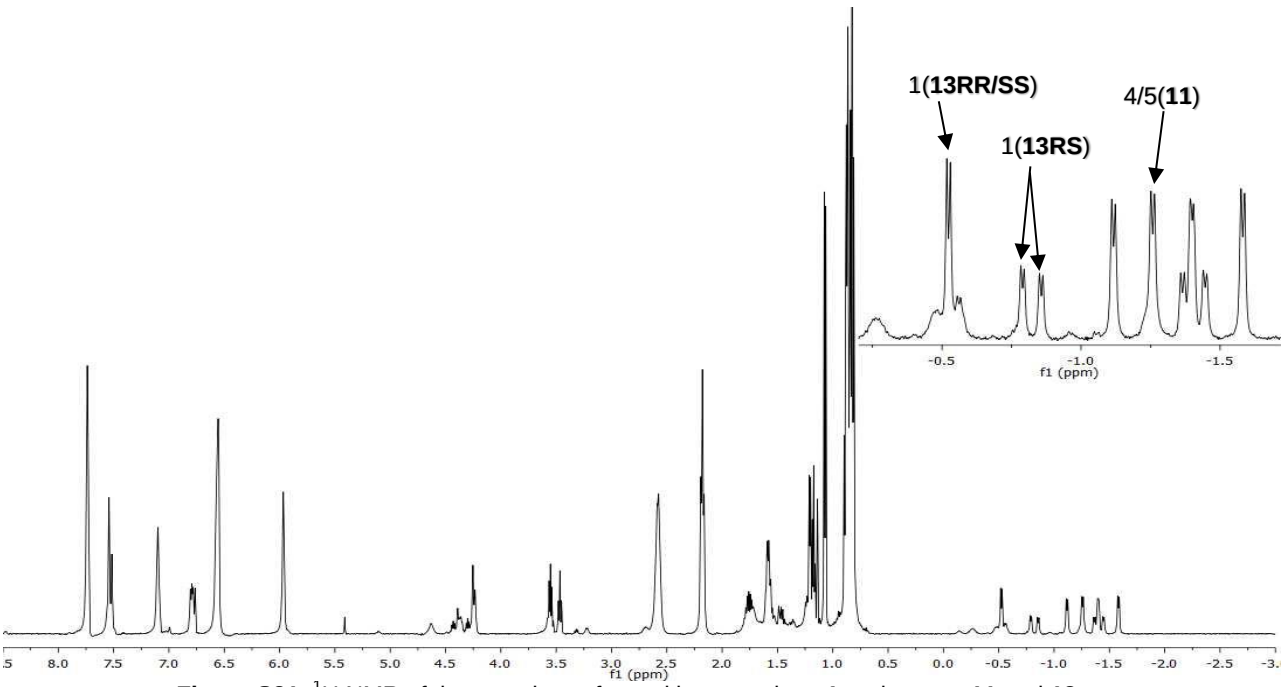

Figure S31: ^{1}H NMR of the complexes formed between host **1** and guests **11** and **13**.

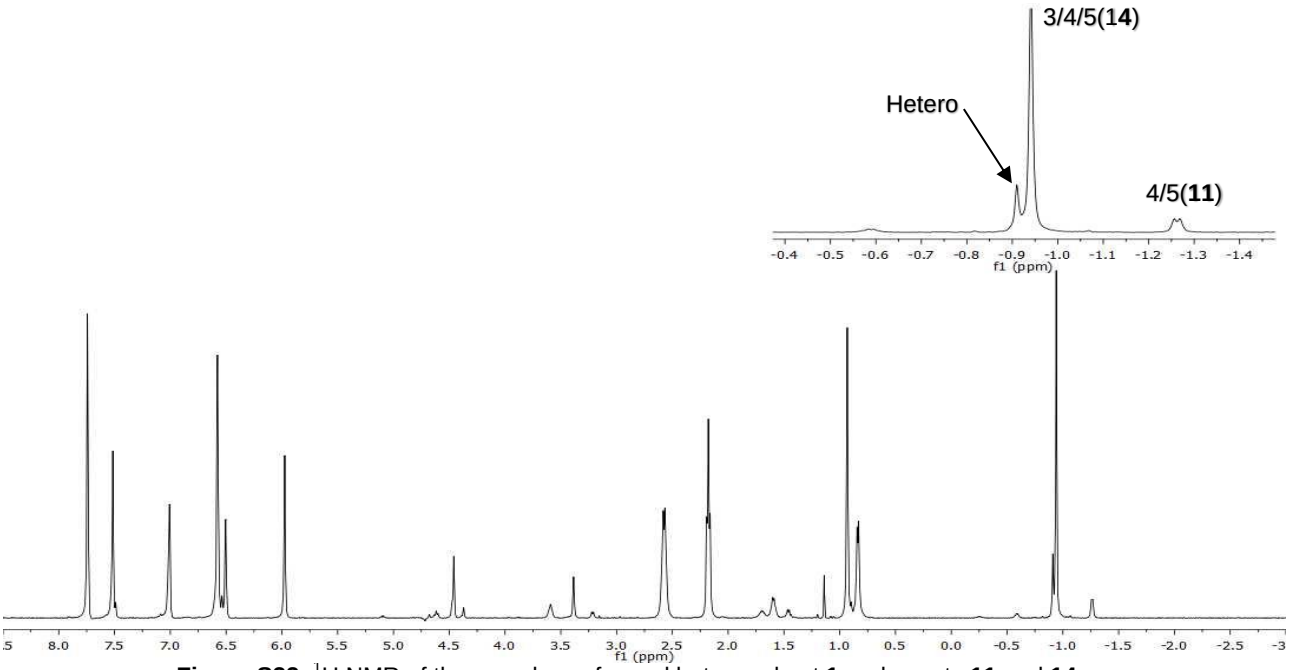

Figure S32: ^{1}H NMR of the complexes formed between host **1** and guests **11** and **14**.

Diffusion coefficient data for guests upon encapsulation within 1

DOSY (Diffusion-Ordered spectroscopy) NMR experiments were performed to confirm the formation of 2:2 capsular complexes rather than 1:1 complexes. The experiments were run at 25 °C with a host concentration of 1mM (in 10 mM sodium tetraborate) and a slight excess of guest. Diffusion coefficient data was determined using at least five of the aromatic host signals in each system examined. Selected data are presented below for free octa-acid host **1** as well as guests **4** and **7** encapsulated within host **1** (Table S3).

Table S3: Selected NMR Diffusion data for host 1 and its complexes.

System	**Diffusion Constant ($\times 10^{-6}$ cm^{2}s^{-1})**	**Hydrodynamic Volume (nm^3)[a]**
Host **1**	1.82	7.2
1.**4**	1.34	18.1
1.**7**	1.34	18.1

[a] As determined using the Stokes-Einstein Equation: $R_H = \frac{k_B T}{6\pi\eta D}$, where η is the viscosity, R_H *is* the hydrodynamic radius, k_B is the Boltzmann constant, *T* is the temperature, and *D* is the diffusion constant. In this study we assumed the particles examined have spherical shape and thus the corresponding hydrodynamic volume can be determined from: $V = \frac{4}{3}\pi R_H^3$.

References

1) Liu, S., Whisenhunt-Ioup, S. E., Gibb, C. L. D. & Gibb, B. C. An improved synthesis of ‘octa-acid’ deep-cavity cavitand. *Supramolecular Chemistry* **24**, 480-485 (2011).