Unusual Orientation And Reactivity Of Alkyl Halides In Water-Soluble Cavitands

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Electronic Supplementary Information

1. General Information

^{1}H and 2D NOESY NMR spectra were recorded on an Avance Bruker DRX-600 spectrometer with a 5mm QNP probe or a Varian Inova 400 MHz NMR spectrometer. Proton (^{1}H) chemical shifts are reported in parts per million (δ) with respect to tetramethylsilane (TMS, δ=0), and referenced internally with respect to the protio solvent impurity. Deuterated NMR solvents were obtained from Cambridge Isotope Laboratories, Inc., Andover, MA, and used without further purification. All added guests were obtained from Aldrich Chemical Company, St. Louis, MO and were used as received. Molecular modeling (molecular mechanics calculations) was carried out using the AMBER force field[1] with the solvation (dielectric) setting for water as implemented by Macromodel or Maestro (Schrödinger, Inc.) on a Silicon Graphics Octane workstation. Cavitand **1** and precursors were synthesized according to the literature procedure.[2]

2. NMR Spectral Data

Sample Chemical Shift Calculation for 1-Chloroundecane:
Assume external (unshifted) CH_3 is at +0.8 ppm and CH_2 groups are at +1.0 ppm

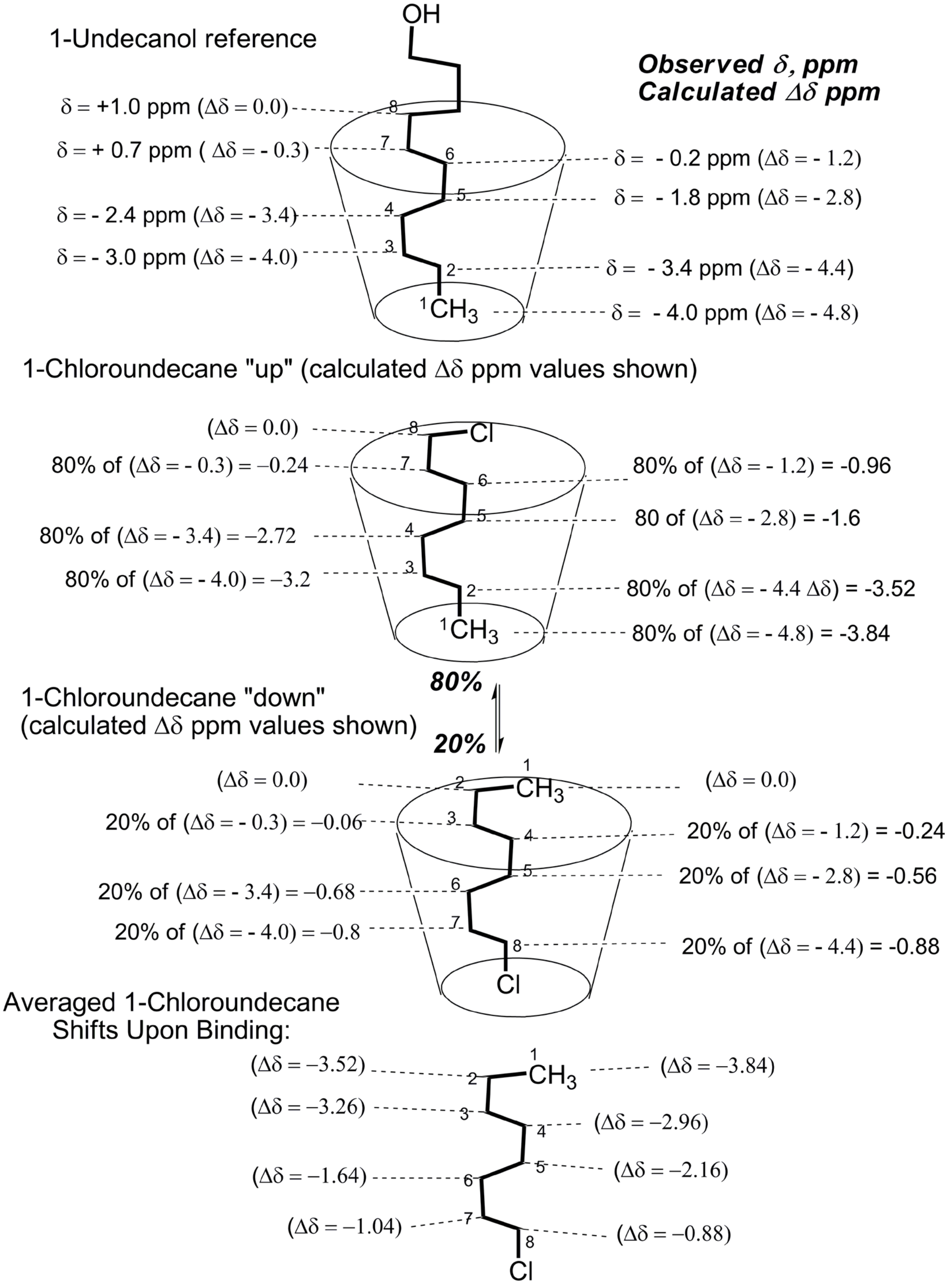
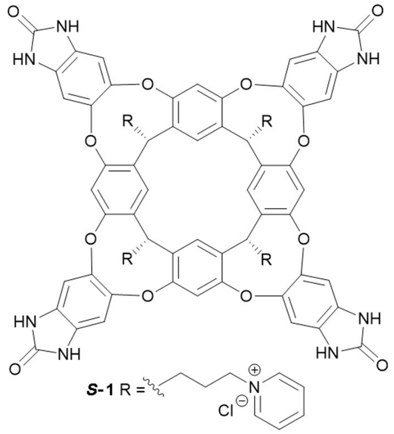
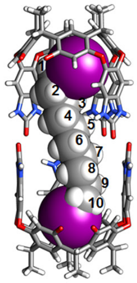


Figure S-1. A sample calculation of the averaged chemical shifts for alkyl halides in cavitand **1**, in this case for $C_{11}H_{23}X$. For the treatment of halide atoms in the cavity interior, Cl and Br are assumed to be in the position of, and of identical size to a terminal CH_3 group. Iodine is assumed to be in the position of, and of identical size to a terminal C_2H_5 group (see Figure S-2). In addition, it is assumed that C_{11} alcohol hydrolysis product defines the maximum upfield shifts for a compressed alkyl group at the values shown above.

Evidence for the assumption that bound Iodine is assumed to be in the position of, and of identical size to a terminal C_2H_5 group:



Peak	Free δ (ppm)	Bound δ (ppm)	Δδ (ppm)
1,10	3.358	-0.765	-4.123
2,9	2.010	-1.409	-3.419
3,8	1.580	-1.071	-2.651
4,7	1.491	-0.743	-2.234
5,6	1.491	-0.279	-1.77



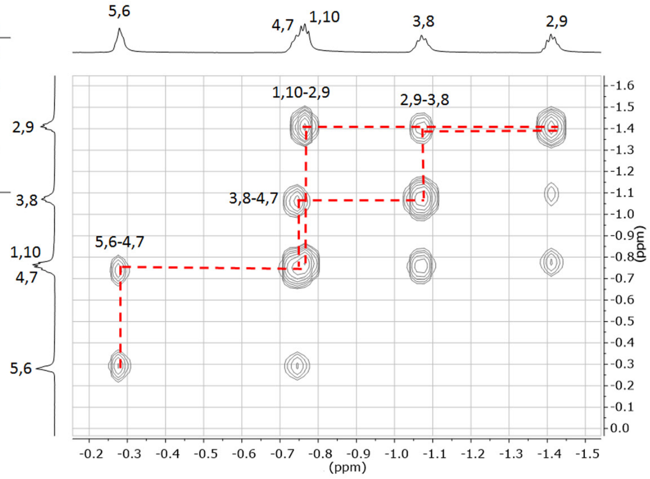


Figure S-2. Upfield region of the 2D COSY spectrum (600 MHz, 15% hexafluoroisopropanol/D_2O) of an analogous capsular diiodoalkane complex to **1**•iodooctane, $(\textbf{\textit{S}-1})_2$•$I(CH_2)_{10}I$.[3,4] [***S*-1**] = 0.00279 M: 2 μL of neat diiodododecane were added to 400 μL of cavitand solution in an NMR tube, then sonicated for 2 h.

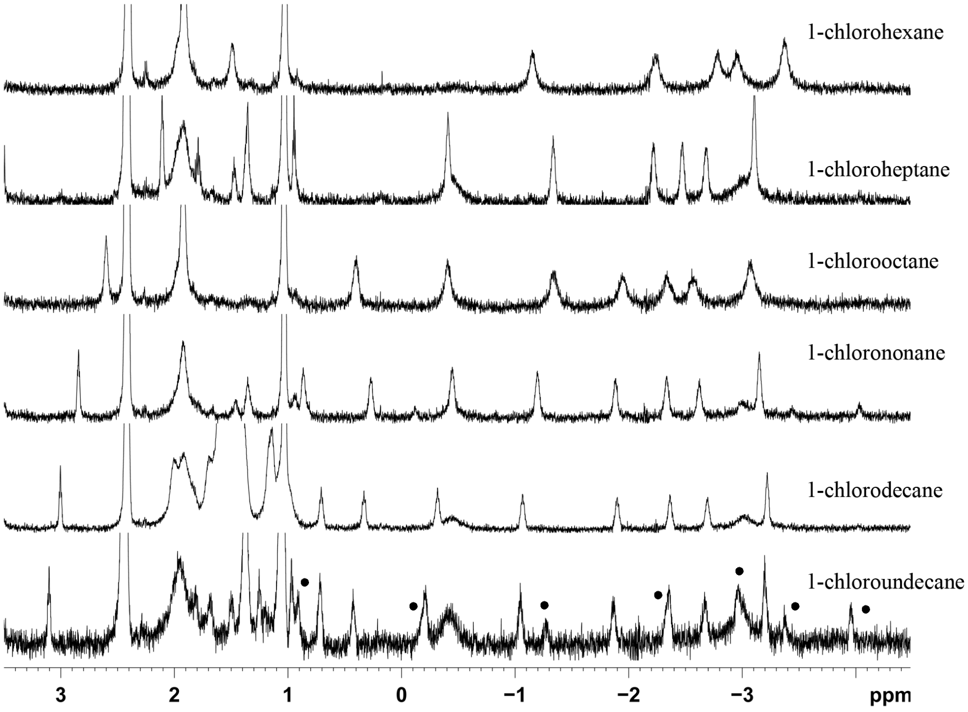


Figure S-3. Upfield ^1H NMR spectra (600MHz, D_2O, 298K) of excess 1-chloroalkanes (C_6-C_{11}) in a 1 mM solution of **1** in D_2O. ● = peaks for bound alcohol product (C_6-C_{11}) after hydrolysis.

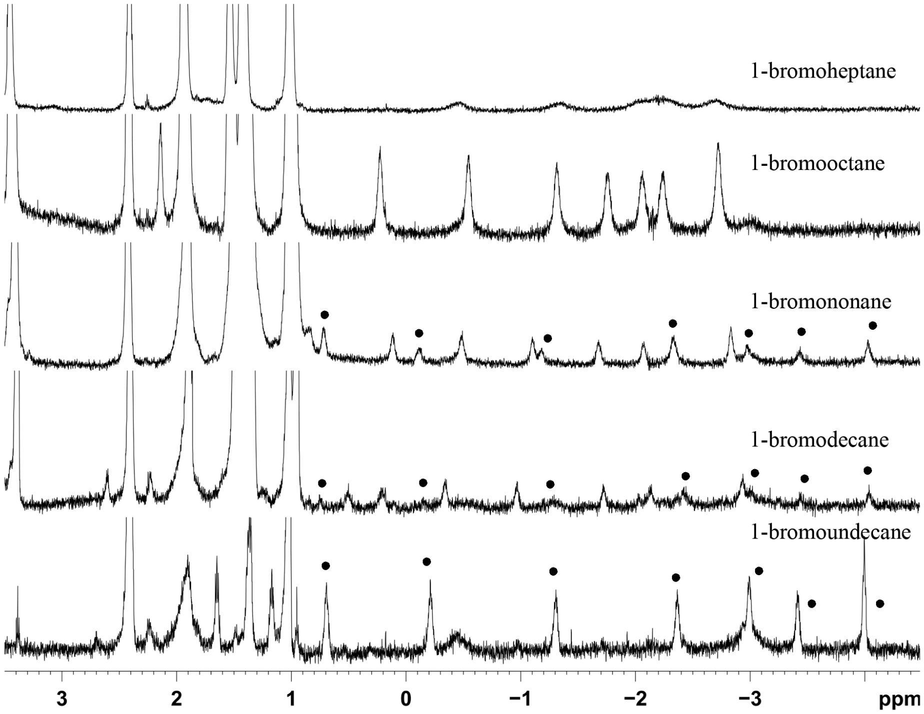


***Figure S*-4.** Upfield ^{1}H NMR spectra (600MHz, D_2O, 298K) of excess 1-bromoalkanes (C_6-C_{11}) in a 1 mM solution of **1** in D_2O. ● = peaks for bound alcohol product (C_6-C_{11}) after hydrolysis.

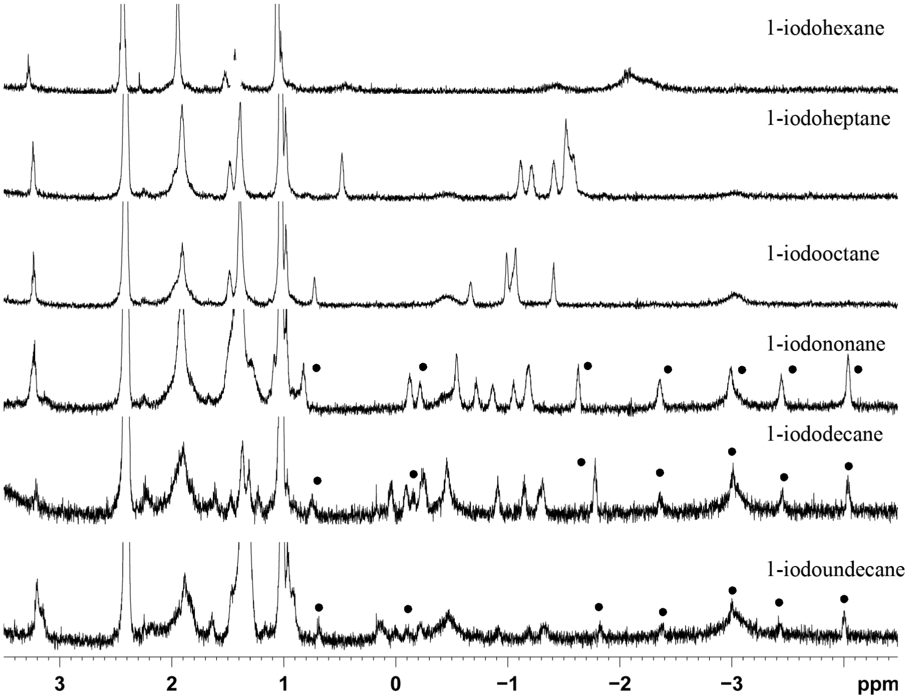


***Figure S*-5.** Upfield ^{1}H NMR spectra (600MHz, D_2O, 298K) of excess 1-iodoalkanes (C_6-C_{11}) in a 1 mM solution of **1** in D_2O. ● = peaks for bound alcohol product (C_6-C_{11}) after hydrolysis.

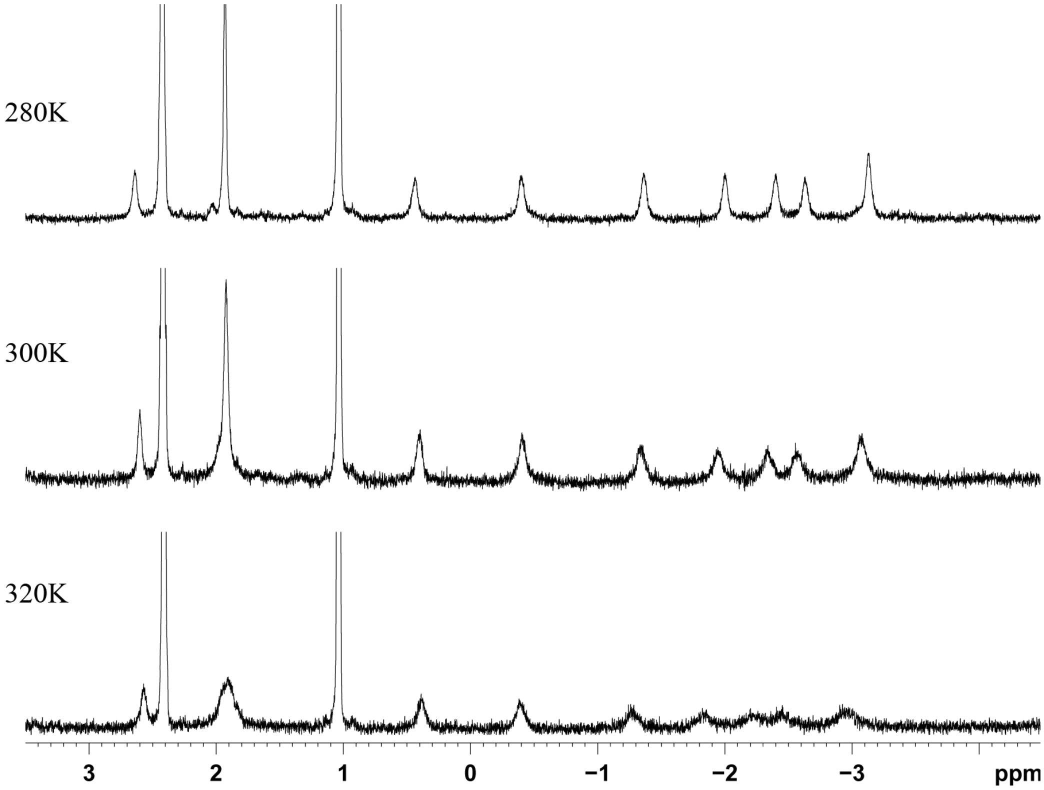


***Figure S*-6.** Upfield ^{1}H NMR spectra (600MHz, D_2O) of excess 1-chlorooctane in a 1 mM solution of **1** in D_2O at various temperatures.

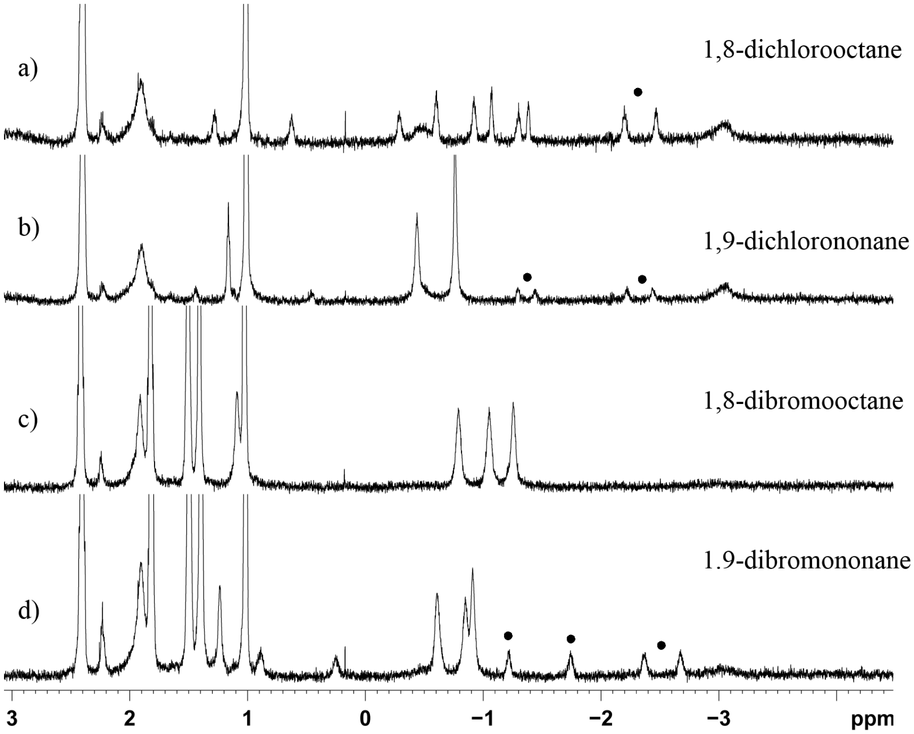


***Figure S*-7.** Upfield ^{1}H NMR spectra (600MHz, D_2O, 298K) of excess α,ω-dihaloalkanes in a 1 mM solution of **1** in D_2O. ● = peaks for bound alcohol product (C_6-C_{11}) after hydrolysis.

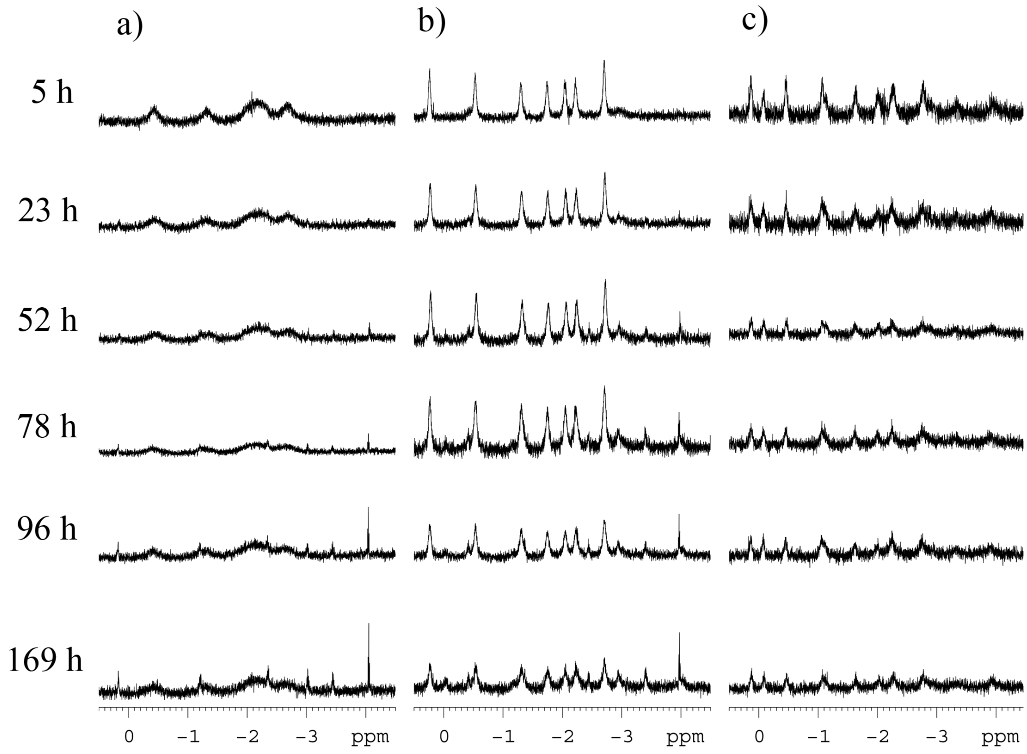


***Figure S*-8.** Upfield ^{1}H NMR spectra (600MHz, D_2O, 298K) of 40 eq. a) 1-bromoheptane, b) 1-bromooctane and c) 1-bromononane in a 1 mM solution of **1** in D_2O over time.

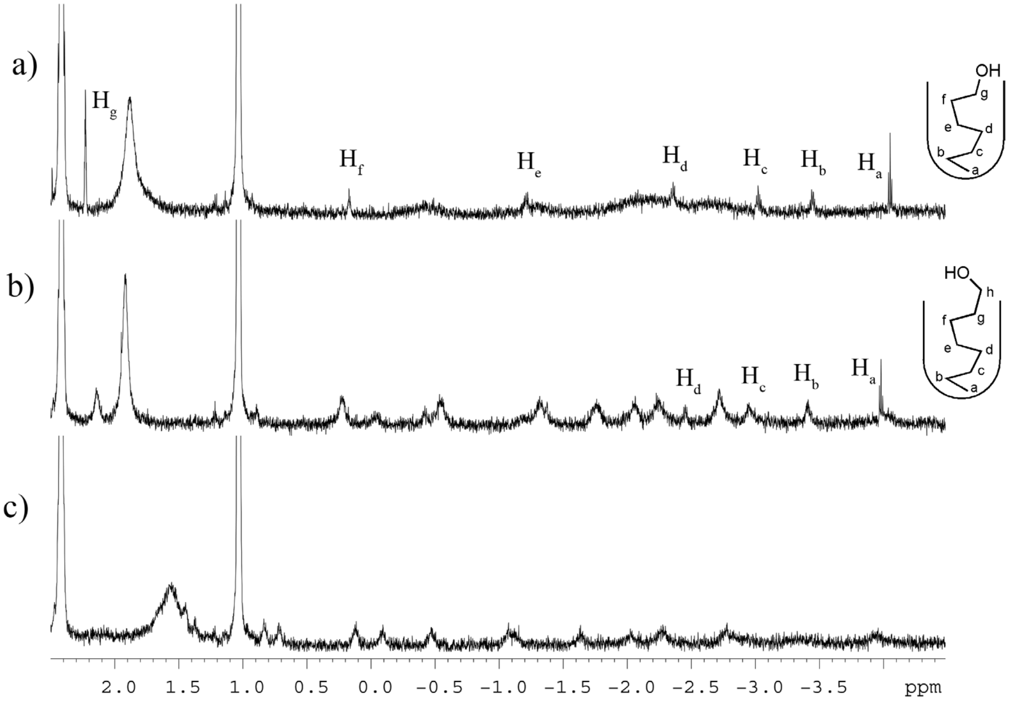


***Figure S*-9.** Upfield ^{1}H NMR spectra (600MHz, D_2O, 298K) of 40 eq. a) 1-bromoheptane, b) 1-bromooctane and c) 1-bromononane in a 1 mM solution of **1** in D_2O after 169h.

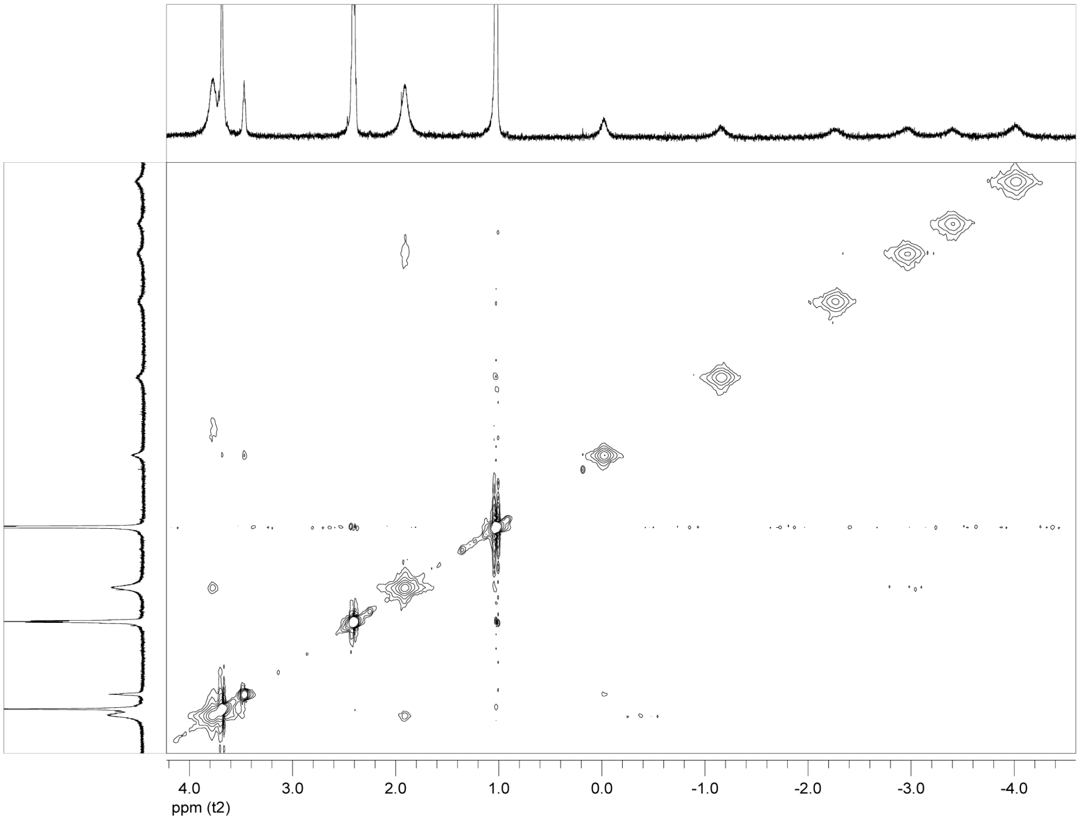


***Figure S*-10.** The upfield regions of the 2D NOESY spectra of 1-octanol in **1** (600 MHz, D_2O, 2 mM **1**, 298K, 300 ms mixing time).

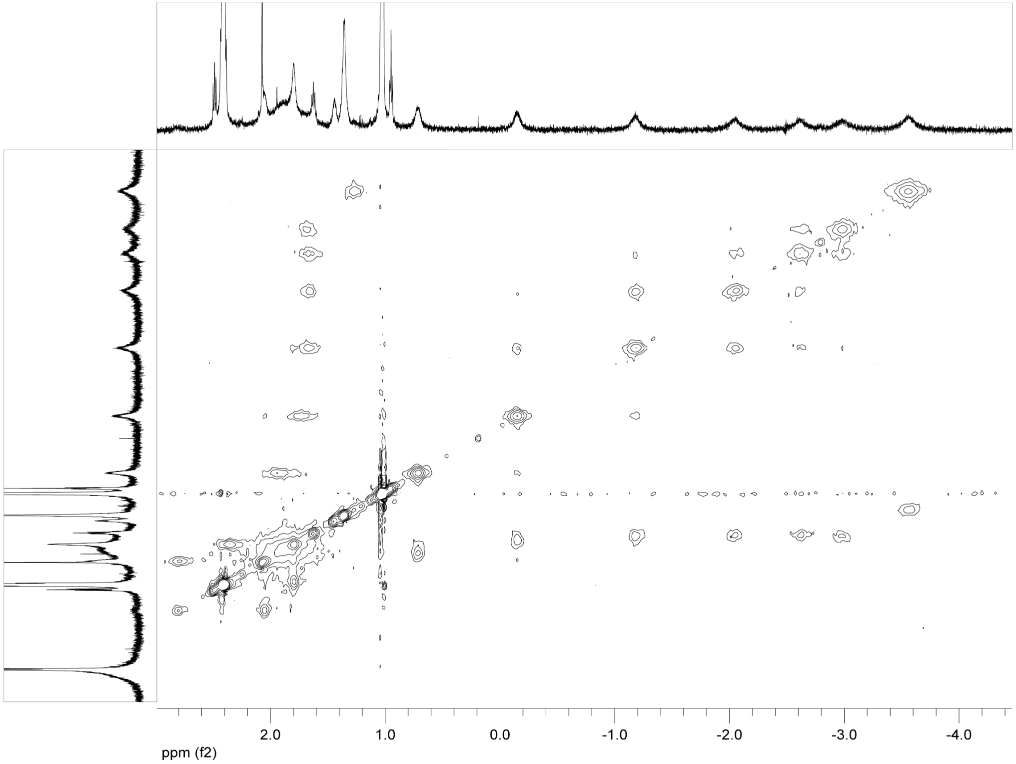


***Figure S*-11.** The upfield region of the 2D NOESY spectrum of 1-octanethiol in **1** (600 MHz, D_2O, 2 mM **1**, 298K, 300 ms mixing time).

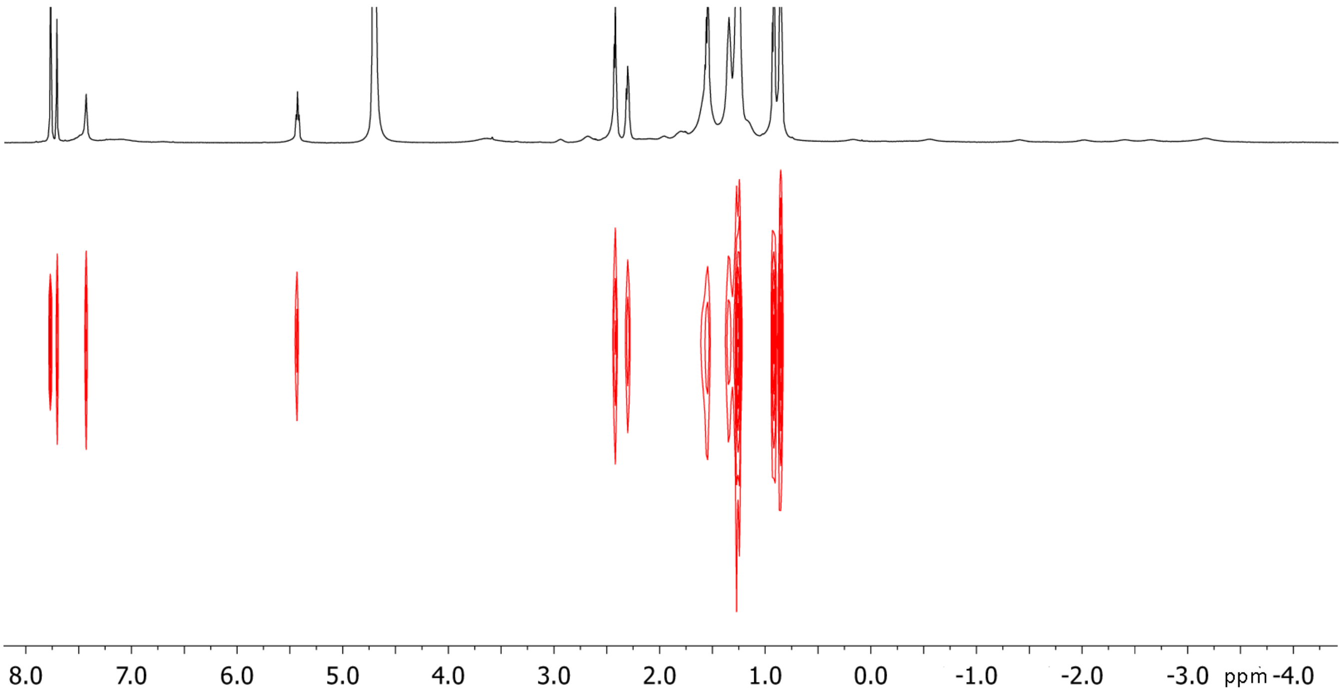


***Figure S*-12.** 2D DOSY spectrum of 1-octanethiol in **1** (600 MHz, D_2O, 4.5 mM **1**, 298K, $\Delta = 6$ ms, $\delta = 30$ µs, diffusion coefficient = 2.00×10^{-10} m^2/s). Note that the guest peaks are too broad and the signal:noise too low for accurate analysis; the free thiol and cavitand co-diffuse.

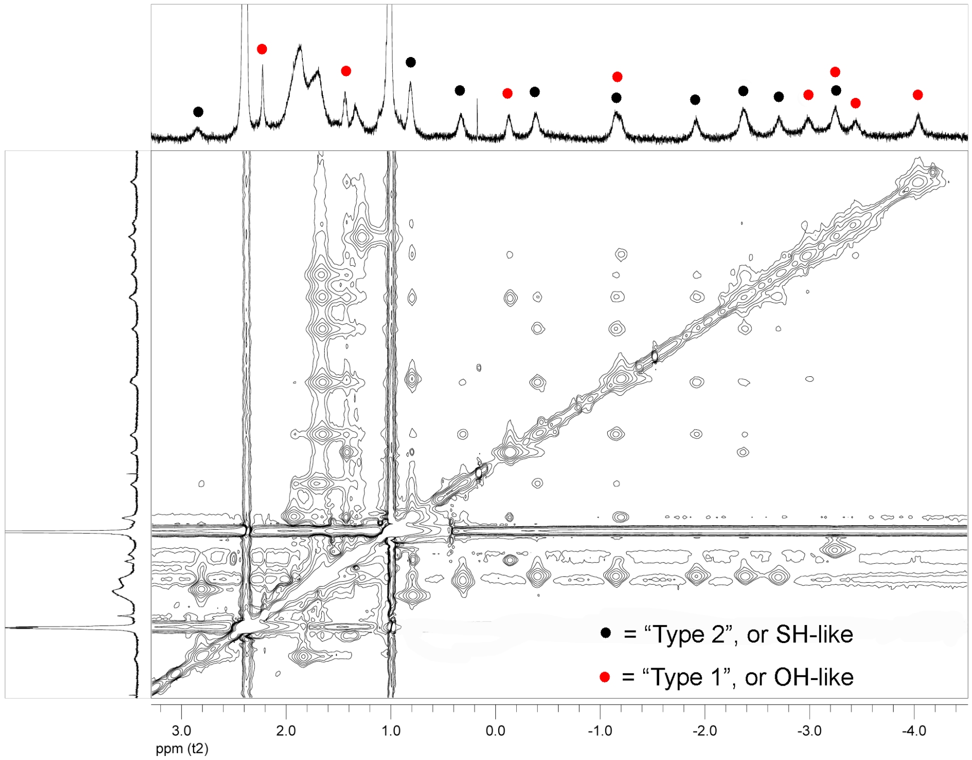


***Figure S*-13.** The upfield region of the 2D NOESY spectrum of 1-nonanethiol in **1** (600 MHz, D_2O, 2 mM **1**, 298K, 300 ms mixing time). The identifying circles from the image in the text are not present for spectral clarity.

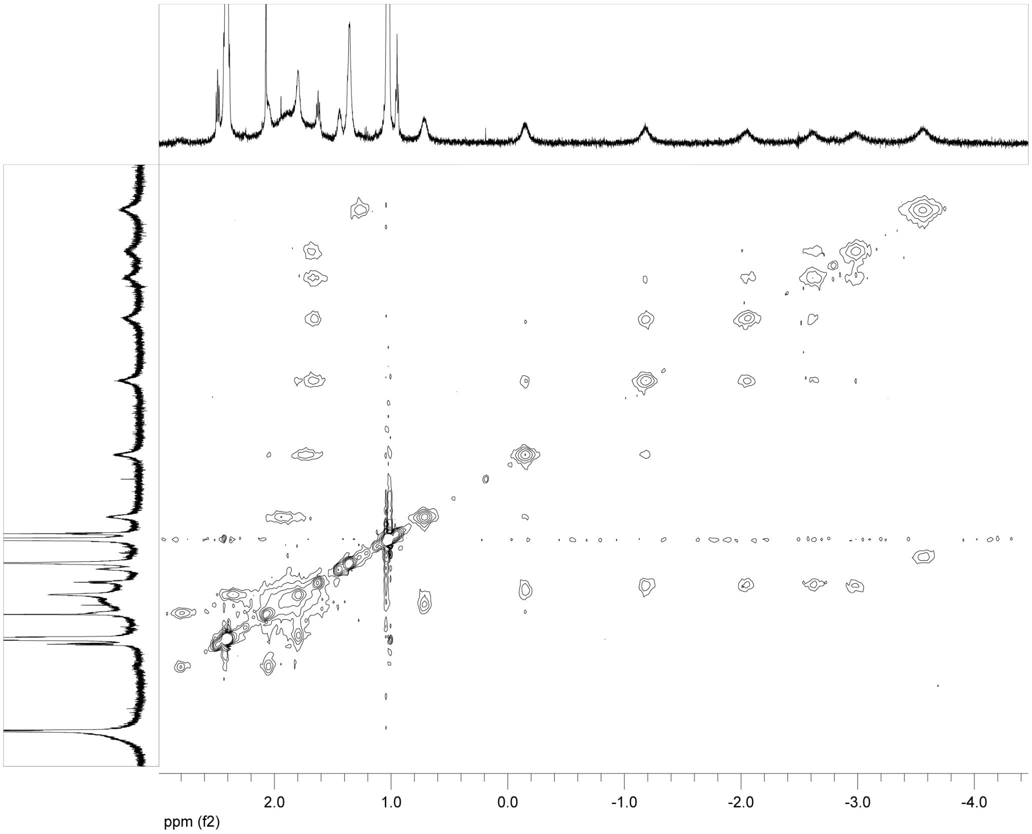


***Figure S*-14.** The upfield region of the 2D NOESY spectrum of 1-octylmethylsulfide in **1** (600 MHz, D_2O, 2 mM **1**, 298K, 300 ms mixing time).

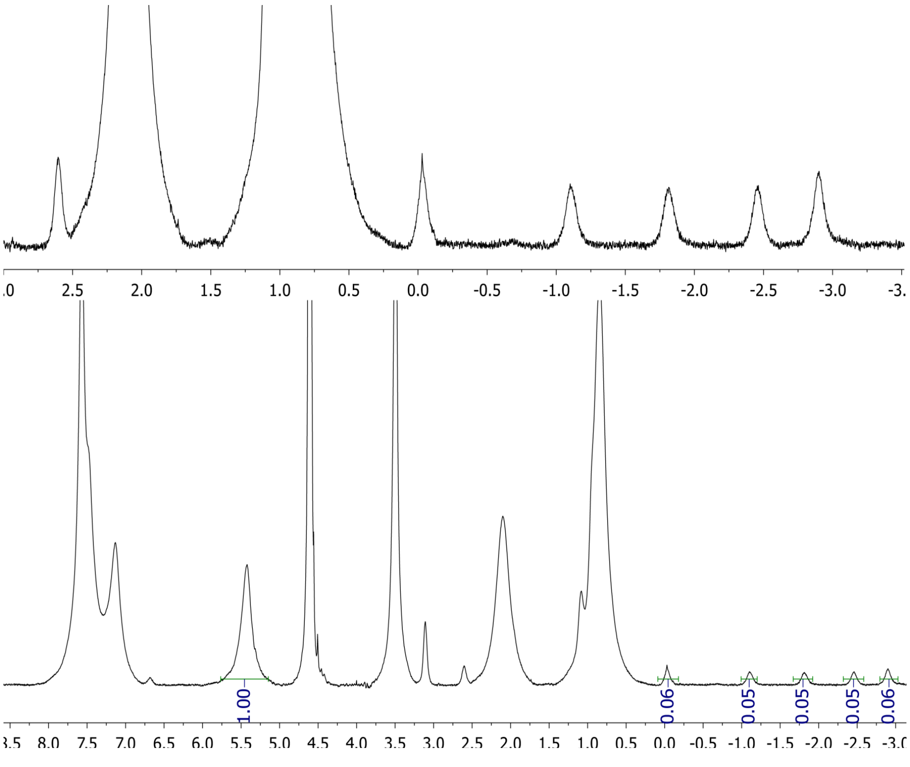


***Figure S*-15.** ^{1}H NMR spectra (400MHz, D_2O, 298K) of 1,12-dodecanol in a 1 mM solution of **1**.

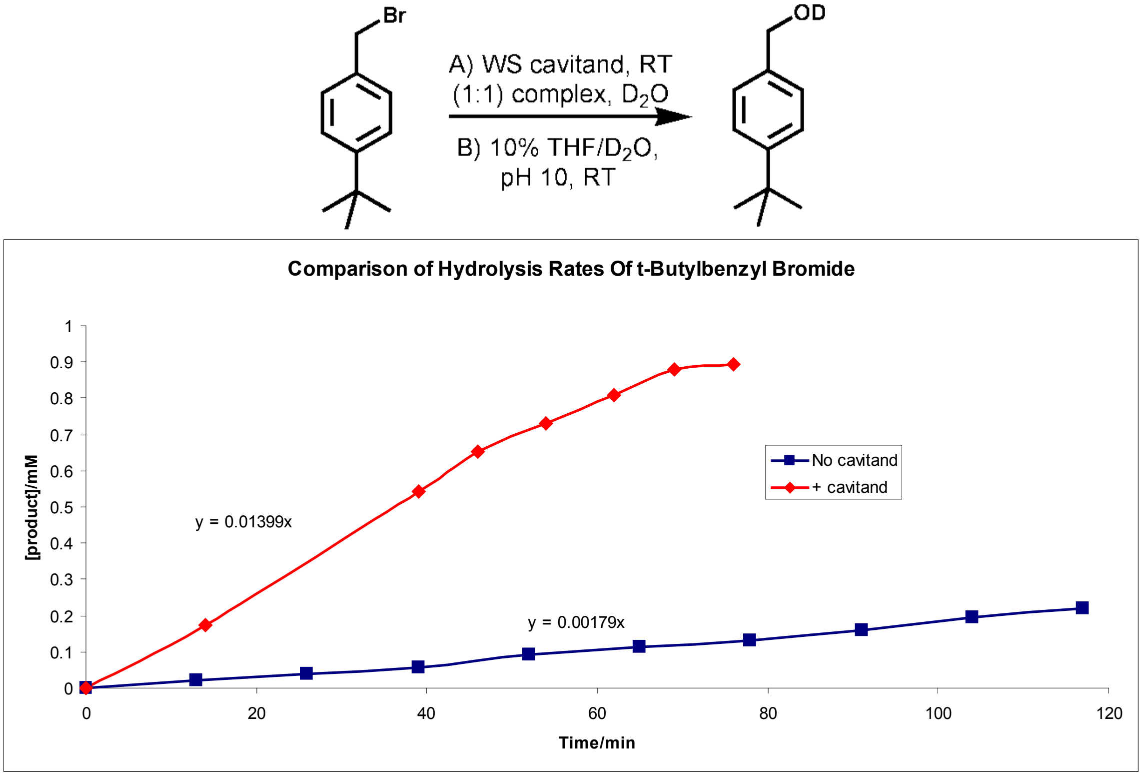


***Figure S*-16.** Graphical analysis of the rate increase of the solvolysis of encapsulated 4-*t*-butylbenzyl bromide.

References

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1) F. Mohamadi, N. G. J. Richards, W. C. Guida, R. Liskamp, M. Lipton, C. Caufield, G. Chang, T. Hendrickson, W. C. Still, *J. Comput. Chem.* **1990,** *11*, 440-467.

2) S. M. Biros, E. C. Ullrich, F. Hof, L. Trembleau and J. Rebek, Jr. *J. Am. Chem. Soc.* 2004, **126**, 2870-2876.

3) K.-D. Zhang, D. Ajami and J. Rebek, Jr. *J. Am. Chem. Soc.* **2013**, *135*, 18064.

4) K.-D. Zhang, D. Ajami, J. V.Gavette and J. Rebek, Jr. *Chem. Commun.* **2014**, *50*, 4895.