Supporting Information

Binding orientation and reactivity of alkyl α, ω -dibromide in water soluble cavitands

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General Information and experimental procedure

All commercially available chemicals were purchased from TCI, Alfa aesar, Energy chemicals, Macklin and used without further purification. Dry solvents directly purchased from Energy chemical and transferred *via* dry syringe. NMR solvents were obtained from Cambridge Isotope Laboratories, Inc. ¹H NMR, and COSY NMR spectra were recorded at 600 MHz on a Bruker DRX-600 spectrometer at the reported temperatures. Chemical shifts are reported in ppm using the residual solvent peaks as reference: $D_2O \delta = 4.79$ ppm (¹H NMR); CD₃OD $\delta = 3.34$ ppm (¹H NMR). GC analyses were performed by SHIMADZU Nexis GC 2030 gas chromatography.

Experimental procedures: In a vial, a solution of the guest (50 mM in MeOH, 14 μ L) was added and methanol was removed by reduced pressure. Cavitand **1** in D₂O (1.4 mM, 0.5 mL) was added to the vial in order to get a host-guest ratio 1:1. The final mixture was sonicated for 6 h and analyzed by ¹H NMR spectroscopy.

$\Delta \delta$ Calculation:

 $\Delta \delta$ (ppm) = the chemical shift of bound (ppm)-the chemical shift of free (ppm)

Synthesis of cavitand 1 (synthetic procedure followed as previously reported by our group).¹⁻³



Compound 1b: To a stirred solution of compound $1a^4$ (1.31 g, 1.0 mmol) in anhydrous DMF (90 mL) was added Cs₂CO₃ (7.68 g, 23.6 mmol) and MeI (11.3 g, 80 mmol) at room temperature under N₂ atmosphere. The mixture was stirred for 24 h at room temperature. After completion (checked

by TLC), DMF was removed by rotary evaporator. Then 60 mL of H₂O was added to the residual solid and sonication for 60 min and the resultant solid was filtered under vacuum. The solid was washed with water (3 × 20 mL) and collected. Again solid portion was mixed with 80 mL MeOH and sonicated for 60 min, filtered, washed with MeOH (3 × 20 mL) and dried under high vacuum at 50 °C to provided **1b**⁵ (1.27 g, 89% yield). ¹H NMR (600 MHz, DMSO-*d*₆, ppm): δ 7.86 (s, 4H), 7.76 (s, 4H), 7.72 (s, 8H), 5.69 (t, *J* = 6.0Hz, 4H), 3.76 (t, *J* = 6.0Hz, 8H), 3.14 (s, 24H), 1.75 (quintet, *J* = 7.0Hz, 8H). ¹³C NMR (150 MHz, DMSO-*d*₆, ppm): δ 155.19, 154.30, 146.30, 135.14, 127.03, 124.69, 116.38, 104.06, 45.03, 32.67, 31.05, 28.84, 27.18.

Compound 1: A homogeneous solution of **1b** (1.43g, 1.0mmol) in 80 mL of 1-methylimidazole was stirred at room temperature for 1 h and 14 h at 90 °C. After cooling to room temperature, the mixture was added to 100 mL acetone, and then kept it at 0 °C for 1 h. The solid was collected, suspended in 80 mL of acetone and refluxed at 65 °C for 24 h. The solid portion was filtered and washed with acetone (3 × 20 mL) gave **1** (1.32 g, 75% yield). ¹H NMR (600 MHz, DMSO- d_6 , ppm): δ 9.56 (s, 8H), 8.11 (s, 4H), 8.10 (s, 4H), 7.83 (s, 4H), 7.80 (s, 4H), 7.72 (s, 8H), 5.55 (t, *J* = 8.16 Hz, 4H), 4.34 (br, 8H), 3.89 (s, 12H), 3.14 (s, 24H), 2.70 (br, 8H). 1.76 (br, 8H). ¹³C NMR (150 MHz, DMSO- d_6 , ppm): δ 155.12, 154.39, 146.30, 136.76, 135.26, 127.00, 125.73, 123.45, 122.63, 116.23, 104.08, 49.29, 35.87, 33.42, 28.75, 28.07, 27.20. HRMS (ESI-TOF): Calcd for: C₉₂H₉₂Cl₂N₁₆O₁₂ [M-2Cl]²⁺ 841.3223, found: 841.3262 C₉₂H₉₂ClN₁₆O₁₂ [M-3Cl]³⁺ 549.5595, found: 549.5597 C₉₂H₉₂N₁₆O₁₂ [M-4Cl]⁴⁺ 403.4273, found: 403.4272.

Approximate upfield shifts ($-\Delta\delta$) experienced by nuclei in cavitands 1 and 2



Figure S1. Approximate upfield shifts $(-\Delta\delta)$ experienced by nuclei in cavitand 1 and 2.





Figure S2. Stacked full ¹H NMR spectra of α, ω -dibromo alkanes (**3a-f**) binding in cavitand **1**. Black circle refers to free guest.



Figure S3. Partial COSY NMR spectrum of 3f in cavitand 1.

Br 2 1	1,12-dibromododecane			
3 4		Free	Bound	Δδ
		(ppm)	(ppm)	(ppm)
	1	3.44	1.51	-1.93
$11 \frac{12}{Br}$	2	1.91	-0.36	-2.27
	3	1.5	-0.67	-2.17
4	4	1.37	-0.67	-2.04
l IV	5	1.37	-0.43	-1.80
Br	6	1.37	-0.30	-1.67
	7	1.37	-0.43	-1.80
	8	1.37	-0.30	-1.67
5 6	9	1.37	-0.67	-2.04
	10	1.50	-0.67	-2.17
Br	11	1.91	-0.36	-2.27
	12	3.44	1.51	-1.93

Figure S4. Cartoon conformation and relative chemical shifts of **3f** in cavitand **1**. The average $\Delta \delta$ value for each methylene is recorded on the structure.



Figure S5. Partial COSY NMR spectrum of 3d in cavitand 1.

Br	1,10-dibromodecane			
4 3		Free	Bound	Δδ
5-6		(ppm)	(ppm)	(ppm)
	1	3.46	1.25	-2.21
Br	2	1.92	-0.58	-2.50
	3	1.50	-0.58	-2.08
	4	1.39	-0.79	-2.18
Br	5	1.39	-0.79	-2.18
9-10	6	1.39	-0.79	-2.18
	7	1.39	-0.58	-1.97
	8	1.39	-0.79	-2.18
	9	1.92	-0.58	-2.50
Br	10	3.46	1.25	-2.21

Figure S6. Cartoon conformation and relative chemical shifts of **3d** in cavitand **1**. The average $\Delta\delta$ value for each methylene is recorded on the structure.



Figure S7. Partial ¹H NMR spectra of solvent screening: (a) Acetone (b) DMSO; (c) DMF; (d) acetic acid; (e) 1,4-dioxane; (f) acetonitrile. Cavitand **1** (1.4 mM) in D₂O, **3f** (1.4 mM) in respective solvents (14 μ L, 50 mM) stirred at 50 °C for 12 h. * mono hydroxyl product.



Figure S8. Stacked full ¹H NMR spectra **3c** in cavitand **1**. Reaction progress were recorded after sequential addition of DMSO- d_6 (4 µL) and stirred at 50 °C: (a) after 6 h under sonication at 25 °C without DMSO- d_6 ; (b) sample a, DMSO- d_6 (4 µL), 24 h; (c) sample b, DMSO- d_6 (4 µL), 56 h; (d) sample c, DMSO- d_6 (4 µL), 112 h; (e) sample d, 136 h; (f) 172 h; (g) spectra of authentic C₉ monobromo alcohol. Blue circle = Oligomer



Figure S9. Stacked full ¹H NMR spectra of **3d** in cavitand **1**. Reaction progress were recorded after sequential addition of DMSO- d_6 (4 µL) and stirred at 50 °C; (a) after 6 h of sonication at 25 °C without DMSO- d_6 ; (b) sample a, DMSO- d_6 (4 µL), 24 h; (c) sample b, DMSO- d_6 (4 µL), 56 h; (d) sample c, DMSO- d_6 (4 µL), 112 h; (e) sample d, 136 h; (f) 172 h; (g) spectra of authentic (C₁₀) monobromo alcohol.



Figure S10. Stacked full ¹H NMR spectra **3e** in cavitand **1**. Reaction progress were recorded sequential addition of DMSO- d_6 (4 µL) and stirred at 50 °C; (a) after 6 h of sonication at 25 °C without DMSO- d_6 ; (b) sample a, DMSO- d_6 (4 µL), 12 h; (c) sample b, DMSO- d_6 (4 µL), 12 h; (d) sample c, DMSO- d_6 (4 µL), 12 h; (e) sample d, 12 h; (f)12 h; (g) spectra of authentic (C₁₁) monobromo alcohol.



Figure S11. Stacked full ¹H NMR spectra of **3f** in cavitand **1**. Reaction progress were recorded sequential addition of DMSO- d_6 (4 µL) and stirred at 50 °C; (a) after 6 h of sonication at 25 °C without DMSO- d_6 ; (b) sample a, DMSO- d_6 (4 µL), 12 h; (c) sample b, DMSO- d_6 (4 µL), 12 h; (d) sample c, DMSO- d_6 (4 µL), 12 h; (e) sample d, 12 h; (f)12 h; (g) spectra of authentic (C₁₂) monobromo alcohol.

Mono hydroxyl bromide conformational study and stability



Figure S12. Partial COSY NMR spectrum of 10-bromodecan-1-ol in cavitand 1.

10-bromodecan-1-ol				[
ОН		Free	Bound	Δδ
		(ppm)	(ppm)	(ppm)
\rangle_2	1	3.58	3.44	-0.14
3	2	1.56	1.19	-0.37
	3	1.49	0.73	-0.76
	4	1.36	0.20	-1.16
	5	1.36	-0.29	-1.65
	6	1.36	-0.98	-2.34
	7	1.36	-1.82	-3.18
	8	1.36	-2.26	-3.62
	9	1.89	-2.34	-4.23
	10	3.48	-0.51	-3.99

Figure S13. Cartoon conformation and relative chemical shifts of 10-bromodecan-1-ol in cavitand **1**. The average $\Delta\delta$ value for each methylene is recorded on the structure.



Figure S14. Partial COSY NMR spectrum of 12-bromododecan-1-ol in cavitand 1.

	12-bromododecan-1-ol			
		Free	Bound	Δδ
OH 1		(ppm)	(ppm)	(ppm)
2	1	3.61	3.59	-0.02
3	2	1.89	1.56	-0.33
54	3	1.49	1.14	-0.35
$\left(\begin{array}{c} & & \\ & & & \\ & & \\ & & & \\ & & & \\ & & \\ & & & \\ & & \\ & & & \\ & & \\ & & & \\ & & \\ & & & \\ & & & \\ & & & \\ & $	4	1.36	0.83	-0.53
7	5	1.36	0.53	-0.83
	6	1.36	-0.03	-1.39
	7	1.36	-0.52	-1.88
12 11	8	1.36	-1.19	-2.55
	9	1.36	-1.90	-3.26
	10	1.35	-2.16	-3.51
	11	1.49	-1.99	-3.48
	12	3.44	-0.03	-3.47

Figure S15. Cartoon conformation and relative chemical shifts of 12-bromododecan-1-ol in cavitand **1**. The average $\Delta\delta$ value for each methylene is recorded on the structure.



Figure S16. ¹H NMR spectra of **3c-f.** Spectra recorded after one month.

Relative yield calculations of mono hydroxylation α,ω-dibromo alkane

Dimethyl sulfone was used as water soluble internal standard (NMR chemical shift for six protons = 3.15 ppm). Concentration of the internal standard (IS) was always used 1.4 mM. The reaction substrates (**3c-f**) (1.4 mM), and cavitand **1** (1.4 mM) was added and sonicated for 6 h to ensure complete complexation. After complexation, internal standard (IS) was added and recorded the ¹H NMR spectroscopy. Integration of IS and bound guest peaks (**3c-f**) was checked before the reaction. Again, the integration of IS and product nuclei was checked after reaction with sequencial addition DMSO- d_6 at given temperature and time.

% of yield was calculated by following equation using selective known peak integration.

% of yield = $\frac{Integration number of after reaction for 2 protons}{Integration number of before reaction for 2 protons} \times 100$





Figure S17. Full ¹H NMR spectra of **3c** with internal standard for quantifying the yield. Spectrum A is before reaction; Spectrum B is after reaction.





Figure S18. Full ¹H NMR spectra of **3d** with internal standard for quantifying the yield. Spectrum A is before reaction; Spectrum B is after reaction.





Figure S19. Full ¹H NMR spectra of **3e** with internal standard for quantifying the yield. Spectrum A is before reaction; Spectrum B is after reaction.





Figure S20. Full ¹H NMR spectra of **3f** with internal standard for quantifying the yield. Spectrum A is before reaction; Spectrum B is after reaction.

Control experiments without cavitand 1

General procedure: A solution of 3d in DMSO (1.4 mM, 18 µL) was mixed with 0.5 mL of

 $D_2O/Acetone$ mixture (25% of acetone, v/v) and stirred at 50 °C. Reaction progress was monitored using NMR spectroscopy. The product distribution was checked by gas chromatography.



Figure S21. Stacked full ¹H NMR spectra of **3d** without cavitand **1**. (a) initial (b) after 24 h; (c) after 48 h; (d) 60 h; (e) 86 h; (f) 120 h; (g) 136 h; (h) 160 h; (i) 8 days (j) 9 days; (K) 10 days at 50 °C; (l) authetic 10-bromodecan-1-ol; (m) authetic decane-1,10-diol.



Figure S22. Full expanded ¹H NMR spectrum of **3d** without cavitand **1** after 60 h. Green arrow indicates 10-bromodecan-1-ol; blue circles are decane-1,10-diol, and red arrow peak is related to α, ω -dibromo alkane **3d**.



Figure S23. GC spectrum of reaction mixture after 24 h.



Figure S24. Gas chromatography spectrum of reaction mixture after 116 h.



Figure S25. GC spectrum of authentic α, ω -dibromo alkane (C₁₀) 3d.



Figure S26. GC spectrum of authentic 10-bromodecan-1-ol.



Fugure S27. GC spectrum of authentic decane-1,10-diol.

Capsule formation in cavitand 2, conformation and reactivity.



Figure S28. Stacked full ¹H NMR spectra (600 MHz, 298K, D_2O) of **3b-f** in **2**. Host-guest (2:1) with 15% of Hexafluroisopropyl alcohol (HFIPA).



Figure S29. Partial COSY NMR spectrum (600MHz, D₂O, 298K) of 3d in 2.

	1,10-dibromodecane			
		Free	Bound	Δδ
2/Br		(ppm)	(ppm)	(ppm)
3 4 5 6 7 8 9 Br 10	1,10	3.46	-1.05	-4.51
	2,9	1.92	-1.81	-3.73
	3,8	1.58	-1.43	-3.01
	4,7	1.39	-0.93	-2.32
	5,6	1.39	-0.48	-1.87

Figure S30. Cartoon conformation and relative chemical shifts of **3d** in cavitand **2**. The average $\Delta \delta$ value for each methylene is recorded on the structure.



Figure S31. Stacked full ¹H NMR spectra of guests **3b-f** in **2** after reaction. Each spectrum was recorded after sequential addition of DMSO- d_6 and stirred at 50 °C for 56 h.

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