

Proximal charge effects on guest binding to a non-polar pocket^{† ‡}

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[†] A contribution of reference data for the seventh statistical assessment of modeling of proteins and ligands (SAMPL7)

[‡] Dedicated to Eric V Anslyn on the imminent arrival of his 60th birthday.

The Hosts

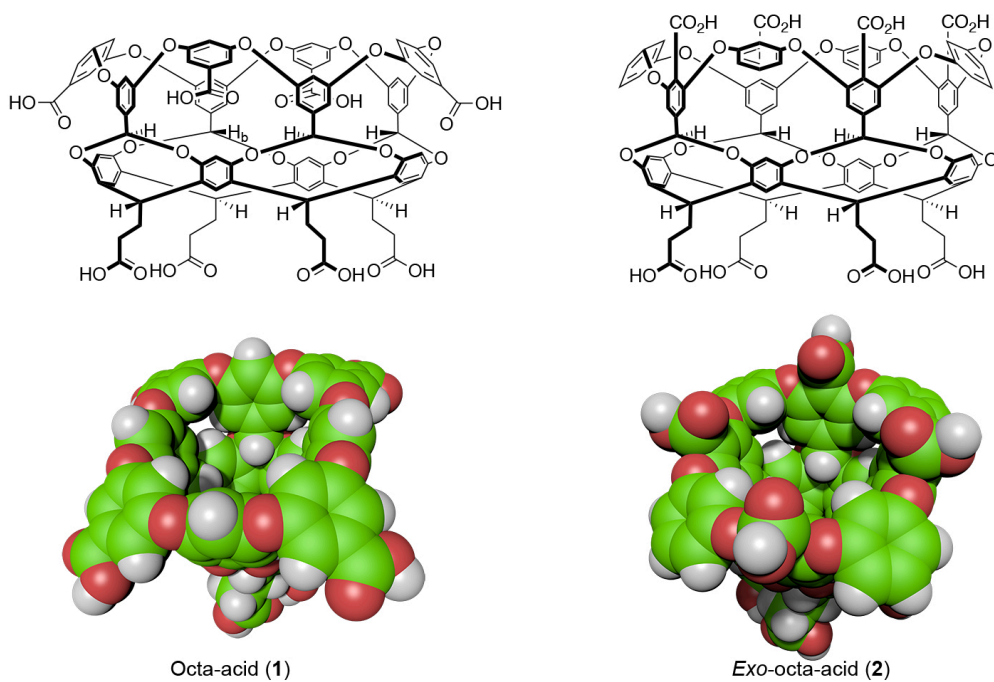


Figure 1: Structures and space-filling models of the two hosts in this study: octa-acid (1) and exo-octa-acid (2).

The guests

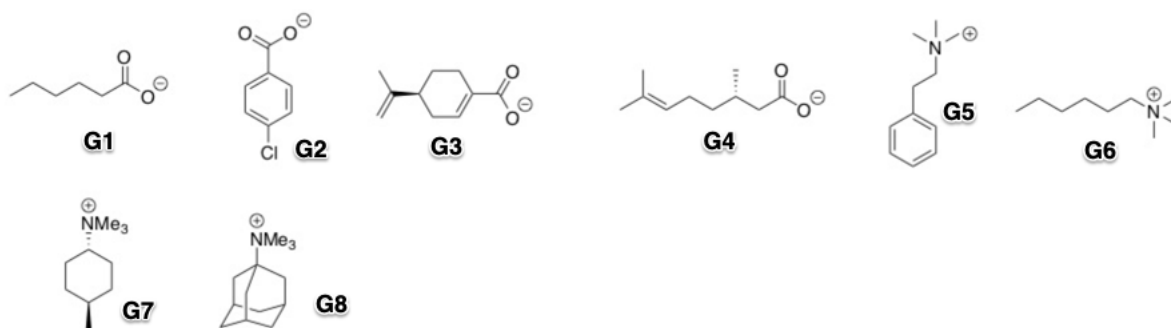


Figure 2: Guests used in this study. Guests **G5-G8** were used as their chloride salts.

The data

Table 1: Thermodynamic data from ITC for the binding of guests G1-G8 with hosts OA and Exo-OA.

Guest	Octa acid 1			exo-Octa acid 2		
	ΔG (kJ mol ⁻¹)	ΔH (kJ mol ⁻¹)	$-T\Delta S$ (kJ mol ⁻¹)	ΔG (kJ mol ⁻¹)	ΔH (kJ mol ⁻¹)	$-T\Delta S$ (kJ mol ⁻¹)
G1	-20.8(1) ^a	-23.2(4) ^a	2.4(6) ^a	— ^b	— ^b	— ^b
G2	-28.9(1) ^a	-40(1) ^a	11(1) ^a	-9(3) ^c	—	—
G3	-33.9(2)	-50.2(1)	16.3(1)	-14.1(1)	-25.2(5)	11.7(1)
G4	-28.4(2)	-28.0(6)	-0.3(1)	-15.1(1)	-31(2)	15(3)
G5	-19.8(1) ^d	-31.3(2) ^d	11.5(2) ^d	-23.3(1)	-25.8(1)	2.5(1)
G6	-20.8(1) ^d	-30(1) ^d	10(1) ^d	-24.4(1)	-13.6(1)	-10.8(2)
G7	-25.4(2)	-24.0(6)	-1.4(6)	-29.2(5)	-20.8(3)	-8.4(9)
G8	-34(2)	-32.7(7)	-1.7(9)	-32.1(4)	-21.1(2)	-11(1)

^a Data for this host-guest combination was determined as part of SAMPL4 in 50 mM borate.¹

^b No binding observed.

^c Determined by ¹H NMR spectroscopy.

^d Data for this host-guest combination was determined as part of SAMPL5 in 50 mM phosphate.²

The numbers in parentheses are the indicated errors in the last digit, e.g. 19(1) indicates 19±1, and 20.2(3) indicates 20.2 ± 0.3. All uncertainties were determined by taking the standard deviation of three different ITC runs (each experiment is triplicated, or in some instances, quadruplicated). The three runs were performed on two different instruments set to the same experimental parameters, and the runs were performed using three different solutions of host, and three different solutions of guest. The three different solutions (of host and guest) were made using the same stock of sample. The numerical errors also account for slight (<5%) variations in buffer and solute concentrations.

No evidence of binding could be observed by ITC for G4@exo-OA; similarly, no clear evidence of binding could be observed by ¹H NMR spectroscopy, indicating a binding constant $K_a(\text{G1@exo-OA}) < 5$. Very weak binding was observed via ITC for G2@exo-OA, so much so that ¹H NMR was the only way to determine a binding constant. All ¹H NMR titrations were done in triplicate, with similar solution preparation as those of the ITC experiments.

References

1. Gibb C. L. D., Gibb B. C. *Binding of cyclic carboxylates to octa-acid deep-cavity cavitand*. J. Comput. Aided Mol. Des., **2014**, 28(4), 319-25. doi: 10.1007/s10822-013-9690-2. PubMed PMID: 24218290; PubMed Central PMCID: PMC4018434.
2. Sullivan M. R., Sokkalingam P., Nguyen T., Donahue J. P., Gibb B. C. *Binding of carboxylate and trimethylammonium salts to octa-acid and TEMOA deep-cavity cavitands*.

J. Comput. Aided Mol. Des., **2017**, 31(1), 21-8. Epub 2016/07/20. doi: 10.1007/s10822-016-9925-0. PubMed PMID: 27432339; PubMed Central PMCID: PMC5571645.