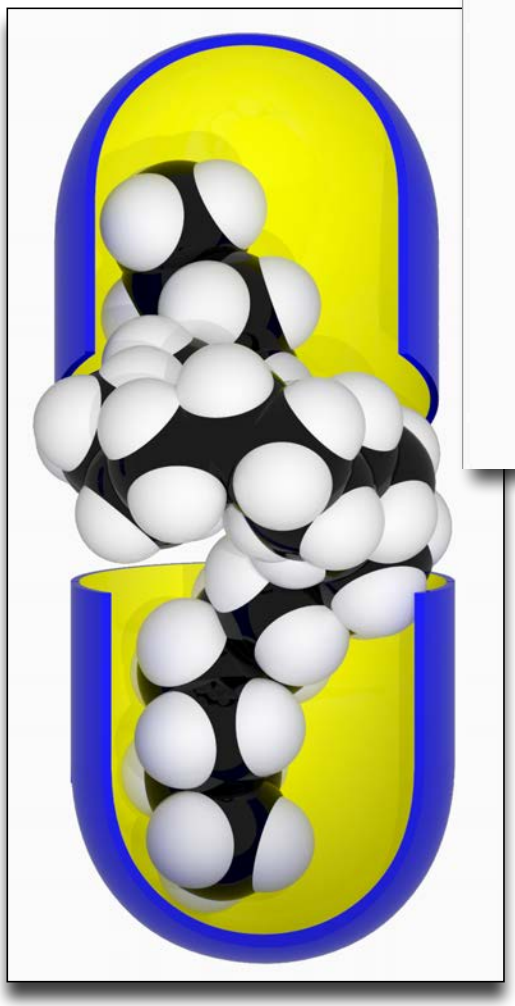
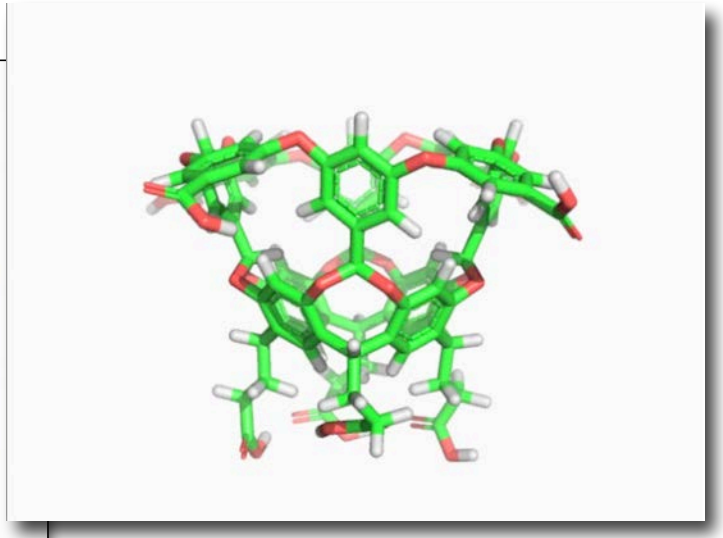
The Thermodynamics of Guest Binding to Deep-Cavity cavitands





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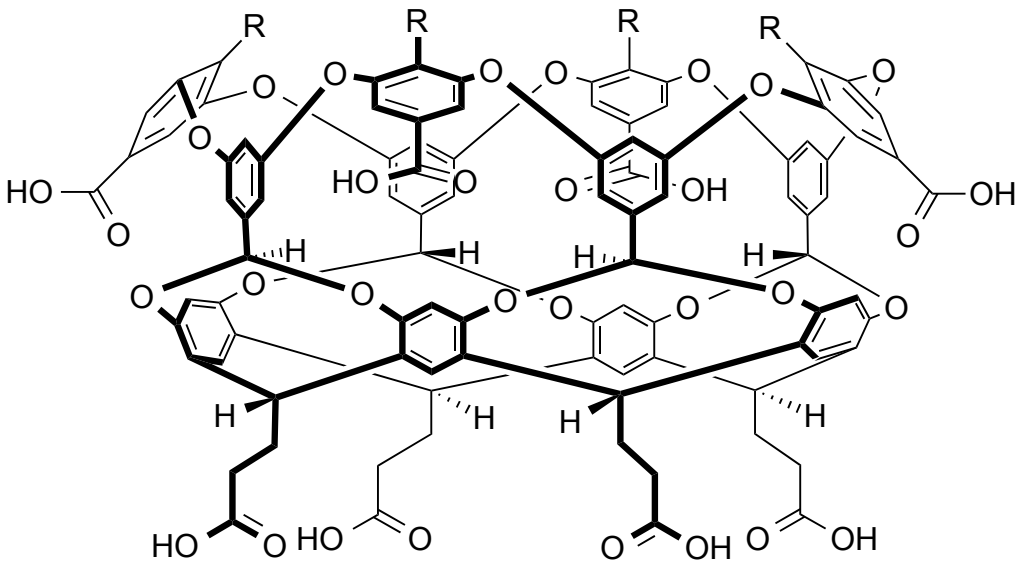
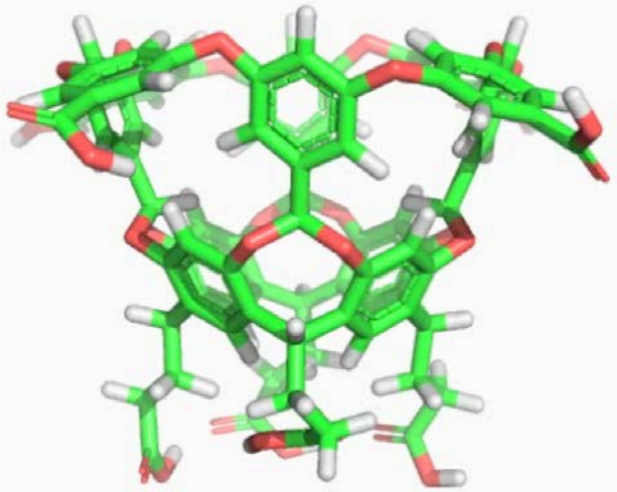
SAMPL Hosts



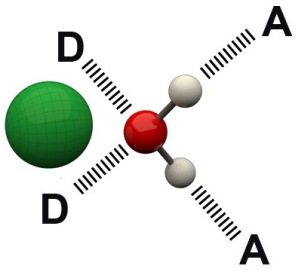
OA: R = H
TEMOA, R = Me



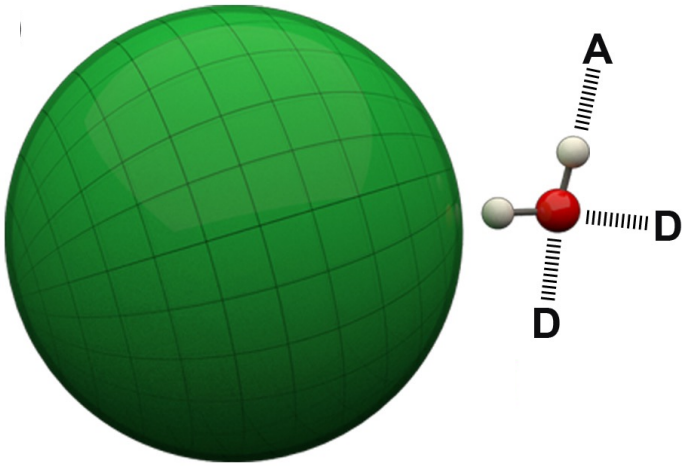
Movie courtesy of Prof. David Mobley

Sullivan, M. R., Sokalingam, P., Nguyen, T., Donahue, J. P., Gibb, B.C., *unpublished*.

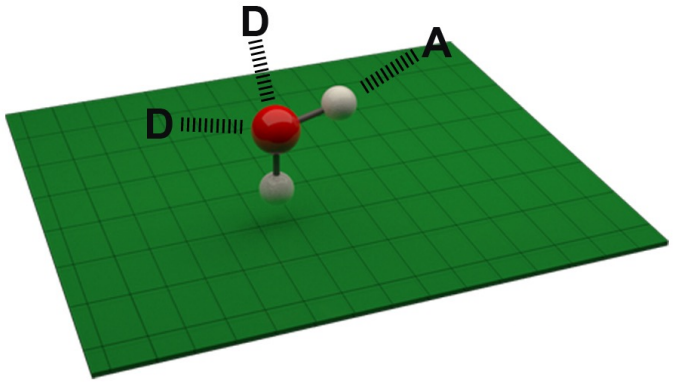
Shape and the Hydrophobic effect



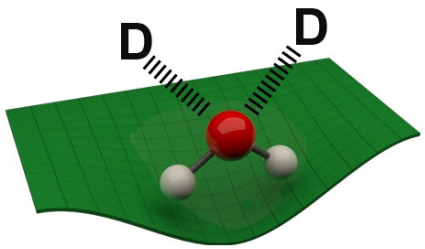
0
Dangling HBs



1
Dangling HBs



1
Dangling HBs



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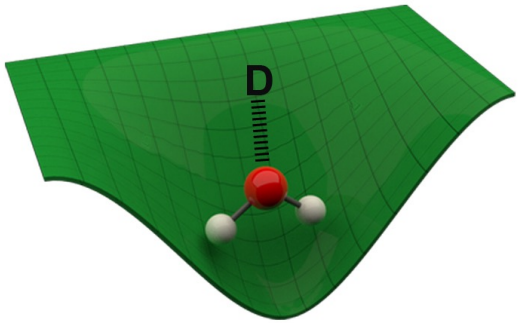
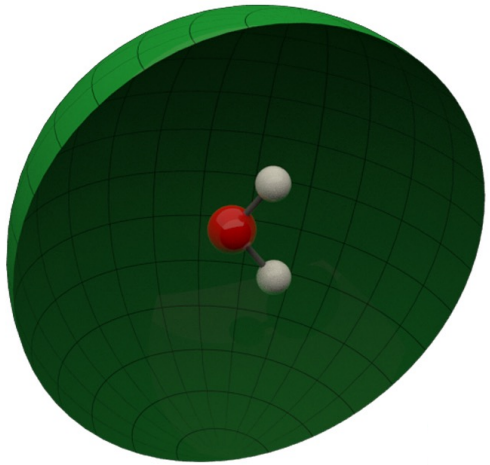
Dangling HBs



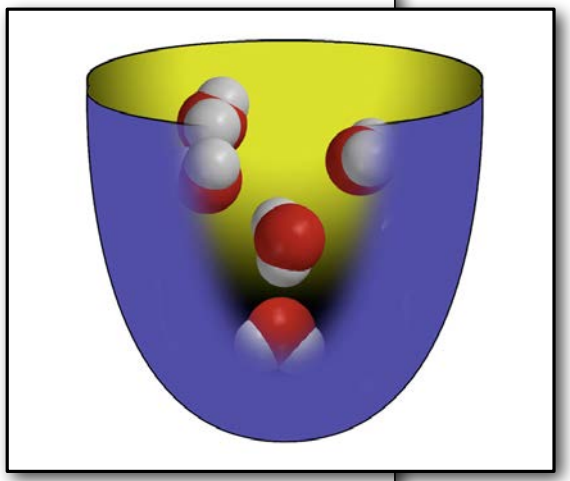
3
Dangling HBs



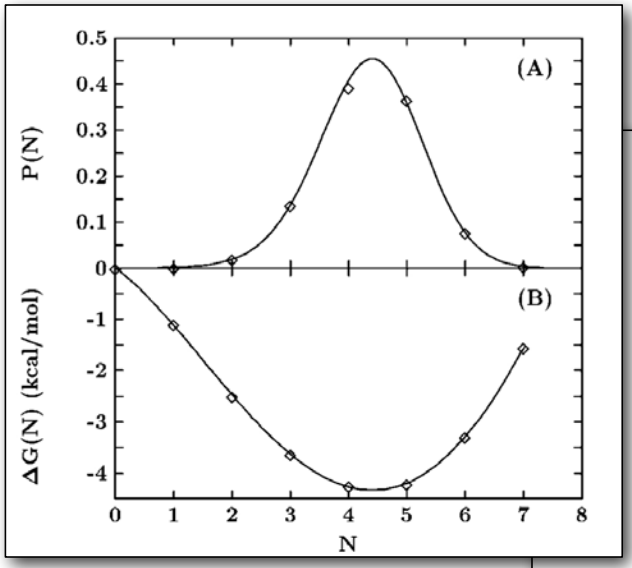
4
Dangling HBs

Hillyer, M. B., Gibb, B.C., *Annual Reviews of Physical Chemistry*, in press.

Water in the hydrophobic pocket



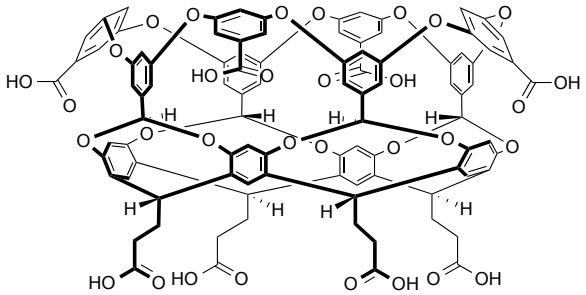
- Cavity contains 0-7 waters (Av. = 4.34).
- The lone water in the lowest layer averages 1.33 hydrogen bonds (as an acceptor).
- Those in the middle layer form on average 2.65 hydrogen bonds.
- Those in the upper layer at the interface with the bull have 3.33 hydrogen bonds on average. (Bulk water has 3.64.)

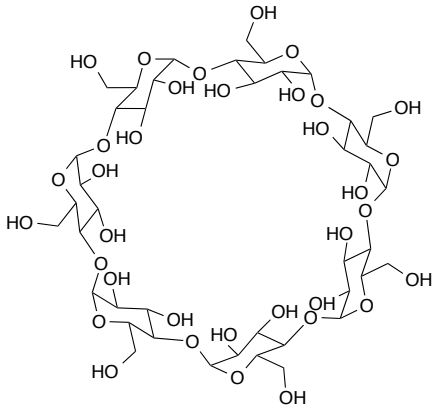


- Water within the cavity is stabilized by its interactions with the bulk; a small hydrophobe 4Å from the cavity triggers complete dewetting of the cavity.
- ΔG_{hyd} ΔH_{hyd} and $-T\Delta S_{hyd}$ of the cavity ≈ –5, –20 and 15 kcal mol^{-1} respectively.

Ewell, J.; Gibb, B. C.; Rick, S., *J. Phys. Chem.*, **2008**, *112*, 10272-10279.

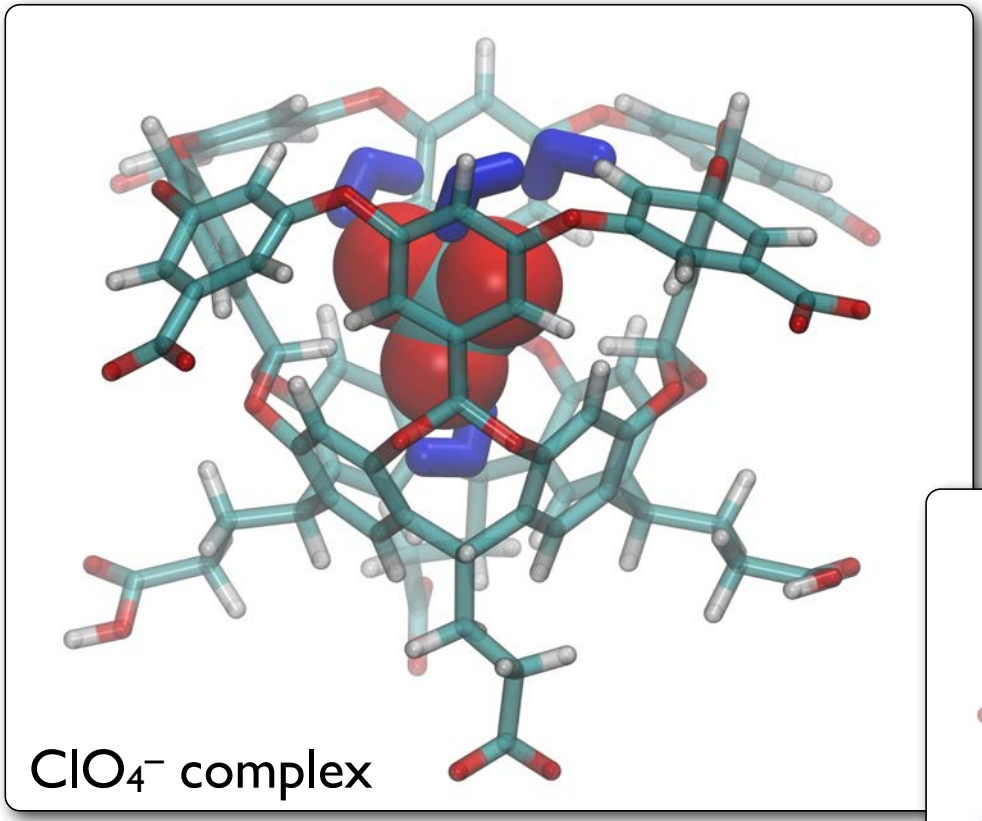
Octa-Acid verses β-Cyclodextrin



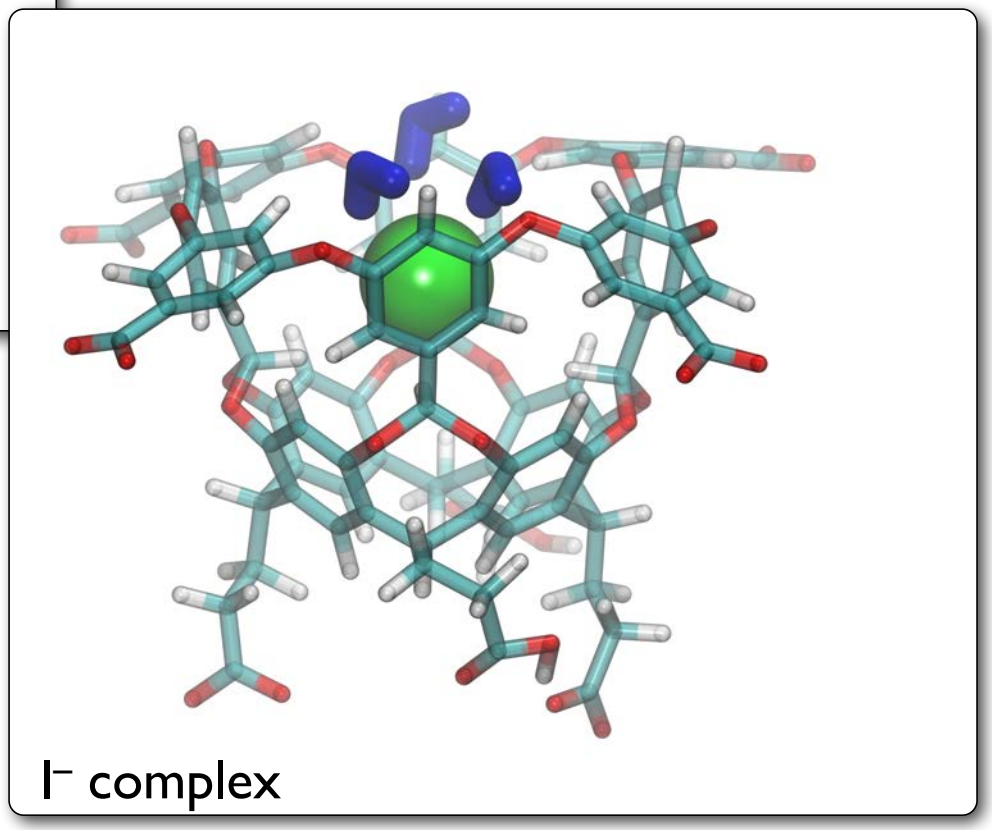


	Binding Constant (K_a, M^{-1})	
Benzoate	5.39×10^2	3.98×10^2
Hexanoate	3.64×10^3	6.76×10^1
Decanoate	1.49×10^5	6.60×10^3
Adamantane carboxylate	1.14×10^6	3.23×10^4

Small anionic guests



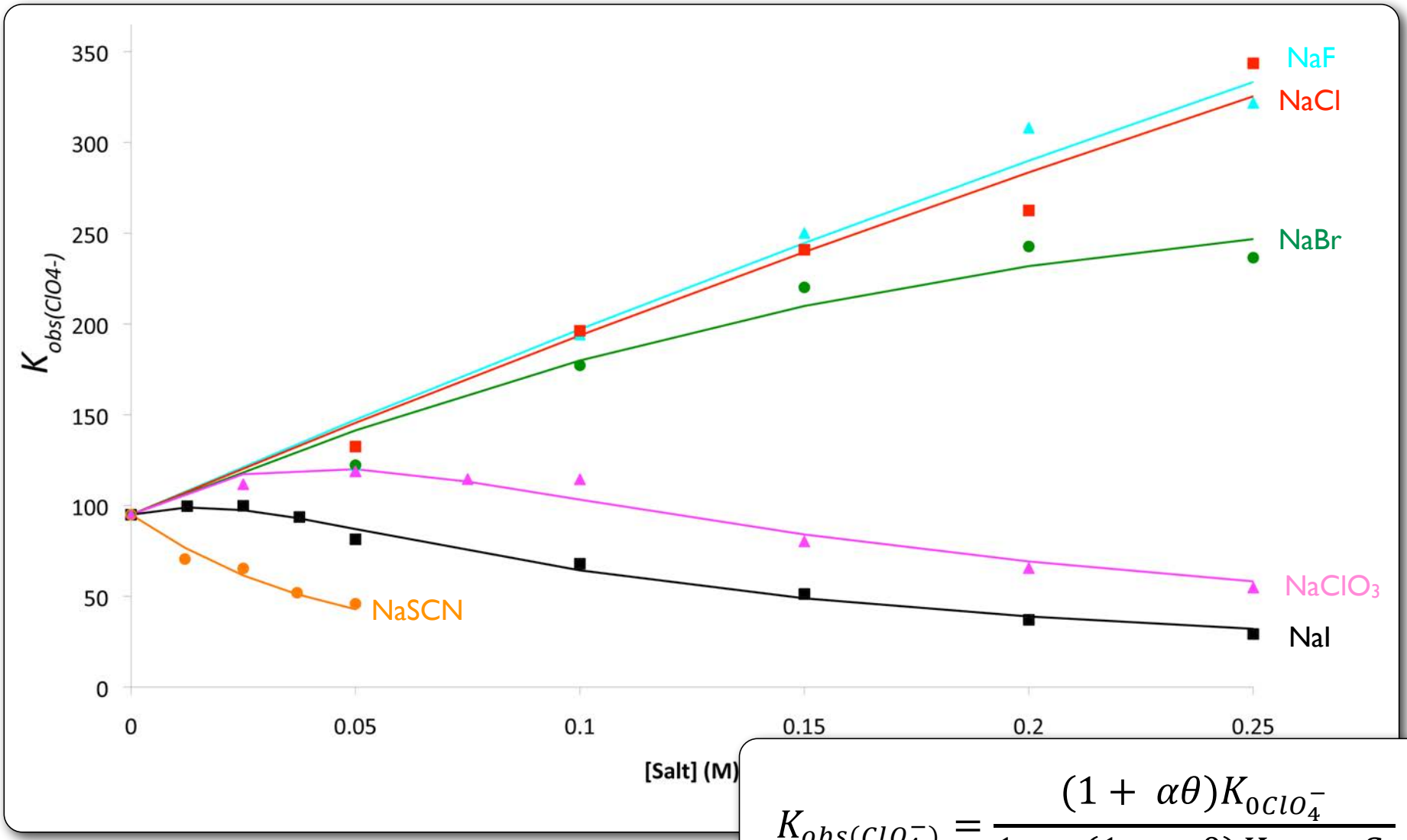
ClO_4^- complex



I^- complex

Sokkalingam, P., Shraberg, J., Rick, S.W., Gibb B. C., *J. Am. Chem. Soc.* **2016**, *138*, 48-51

Data fits a two-interaction model



$$K_{obs(ClO_4^-)} = \frac{(1 + \alpha\theta)K_{0ClO_4^-}}{1 + (1 + \alpha\theta)K_{0(salt)}S_t}$$

Carnagie, R.; Gibb, C. L. D.; Gibb, B. C., *Angew. Chem. Int. Ed.* **2014**, 53, 11498-11500.

Salt Modulation of *trans*-4-Methyl-Cyclohexane Carboxylate Binding

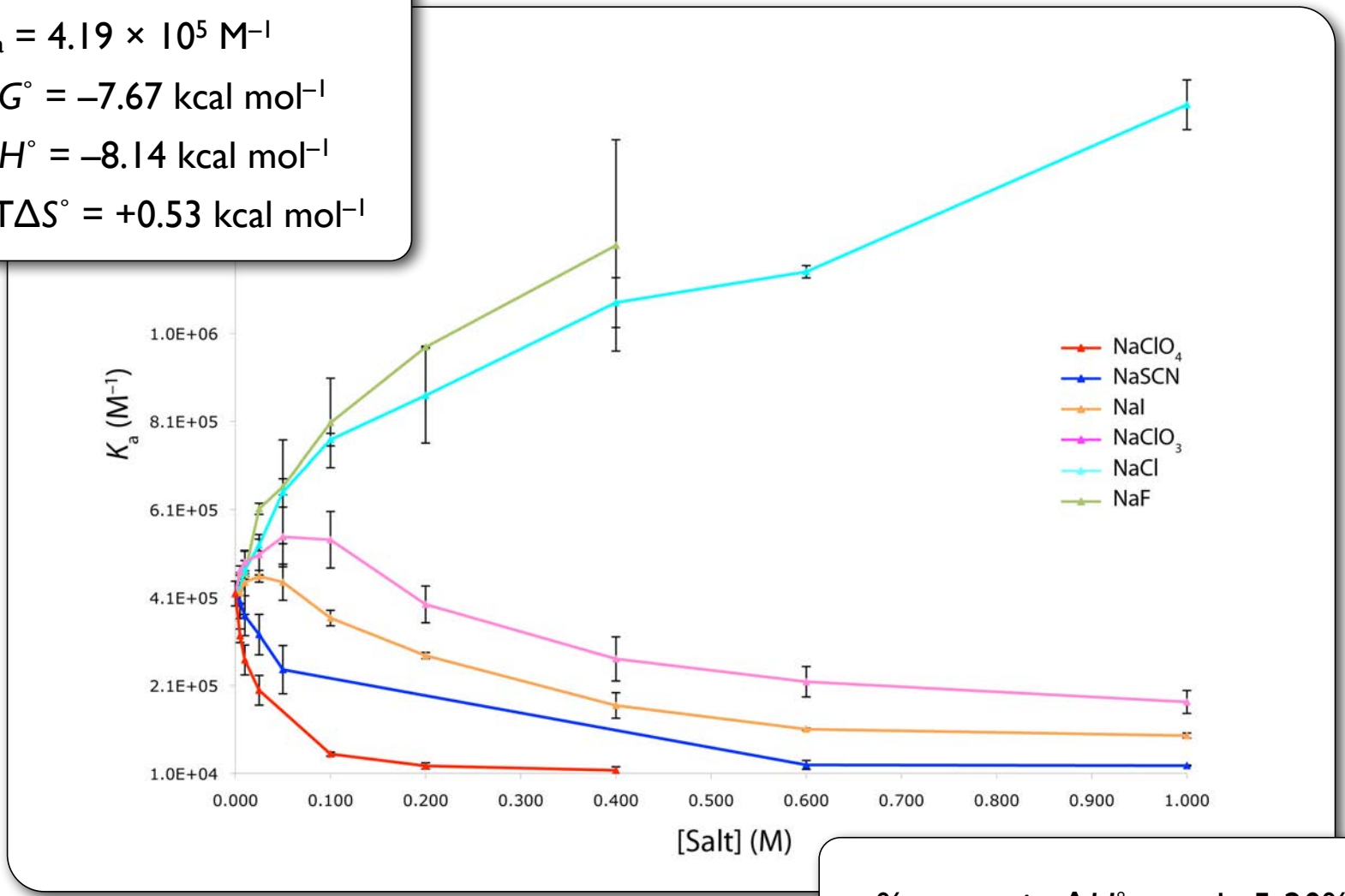
'Salt-free' data

$K_a = 4.19 \times 10^5\ M^{-1}$

$\Delta G^\circ = -7.67$ kcal mol^{-1}

$\Delta H^\circ = -8.14$ kcal mol^{-1}

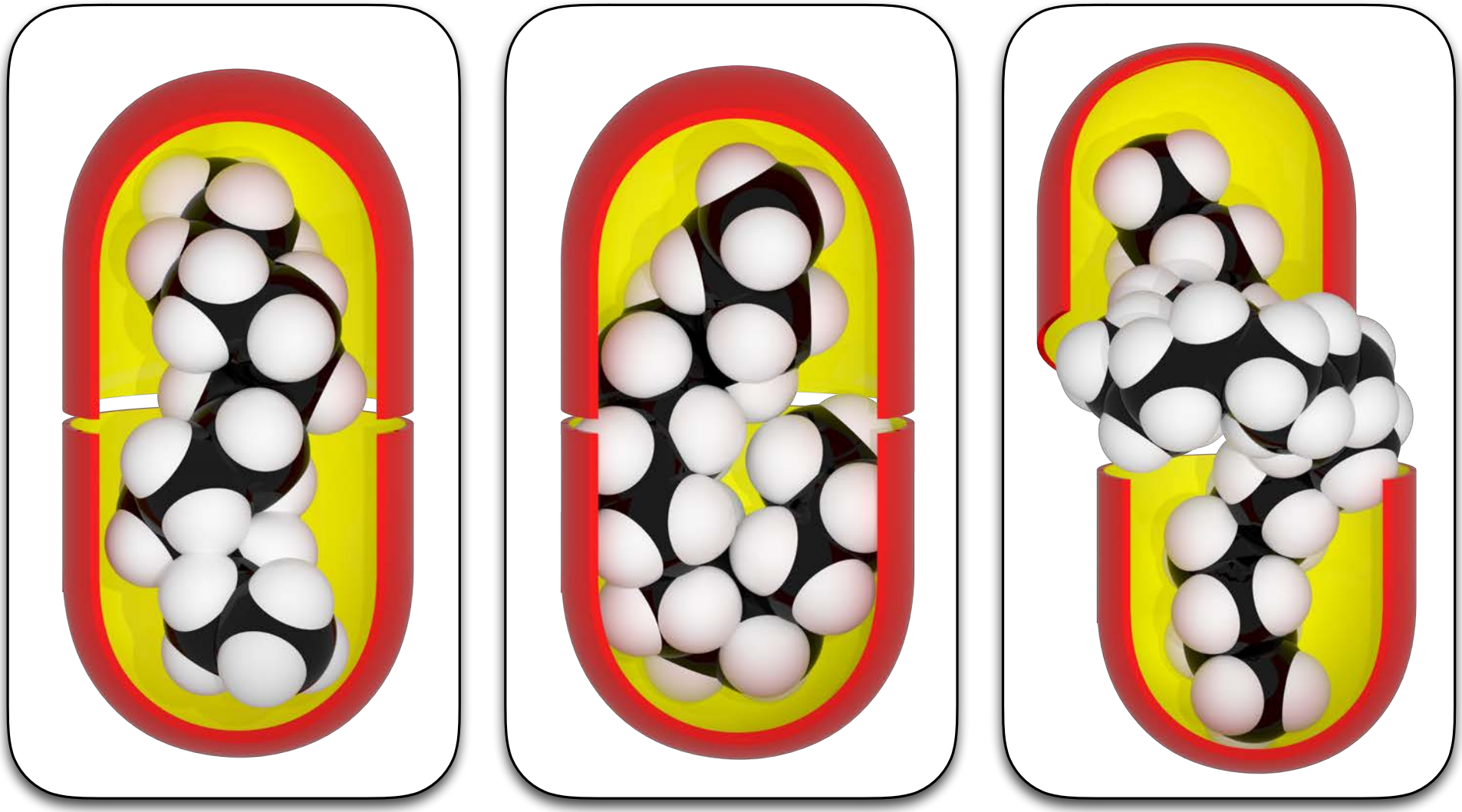
$-T\Delta S^\circ = +0.53$ kcal mol^{-1}



- % errors in ΔH° mostly 5-20%. % errors in ΔH° for NaI, $NaClO_3$, NaCl and NaF < 10%.
- Errors in first derivative data are mostly < 30%. Poorer data when ΔH° is small.

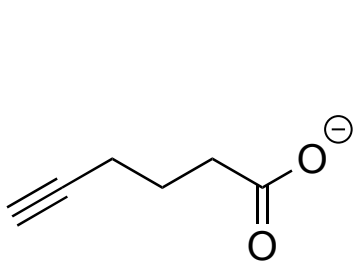
Gibb, C. L. D., Oertling, E,. E., Velaga, S. and Gibb, B. C., *J. Phys. Chem. B,* **2015**, *119,* 5624-5638.

n-Alkane Packing



Gibb, C. L. D., Gibb, B. C., *Chem. Commun*., **2007**, 1635-1637.
Jordan J. H., Gibb B. C. Chem. Soc. Rev., **2015**, *44*(2), 547-85.

SAMPL5 Guests



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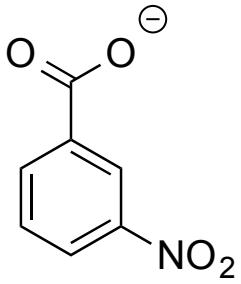

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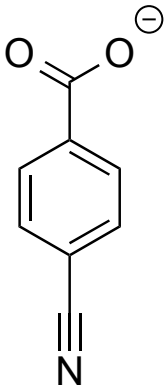

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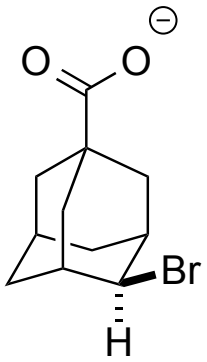

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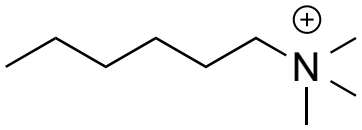

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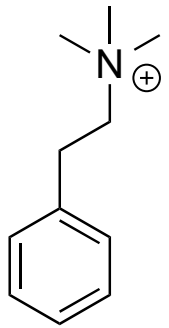
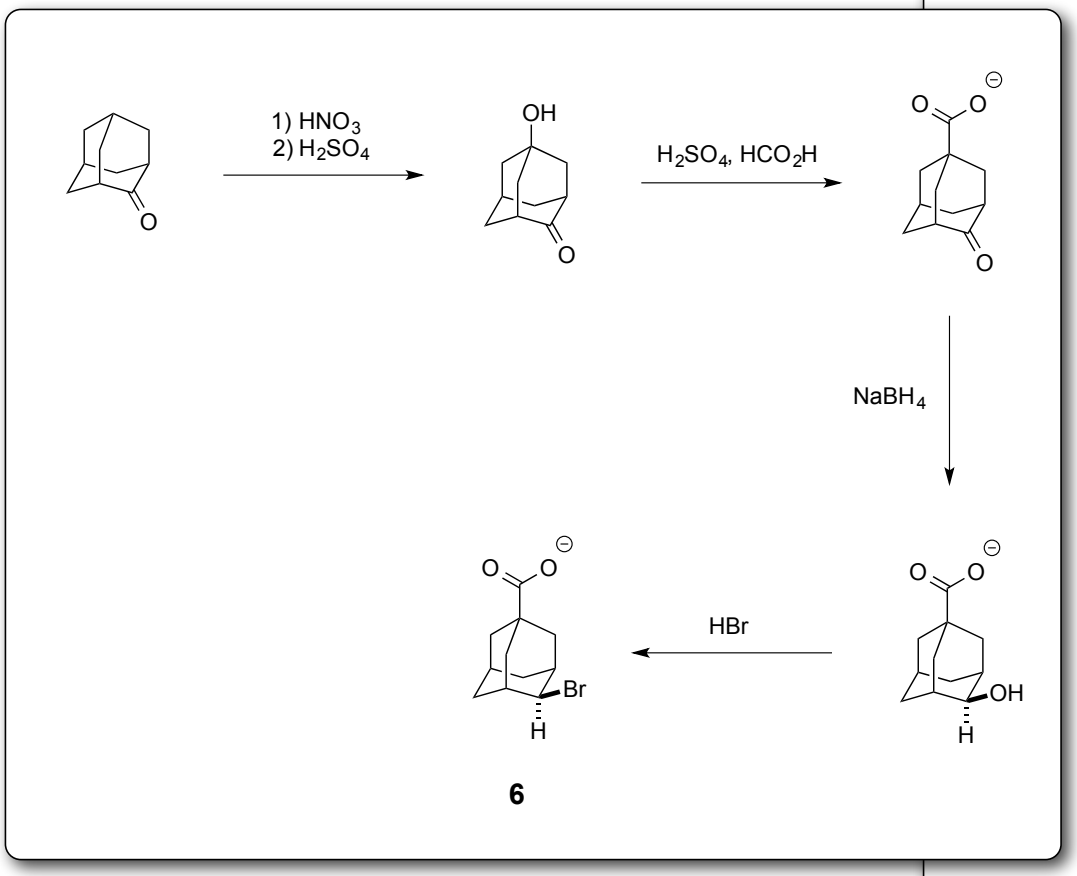
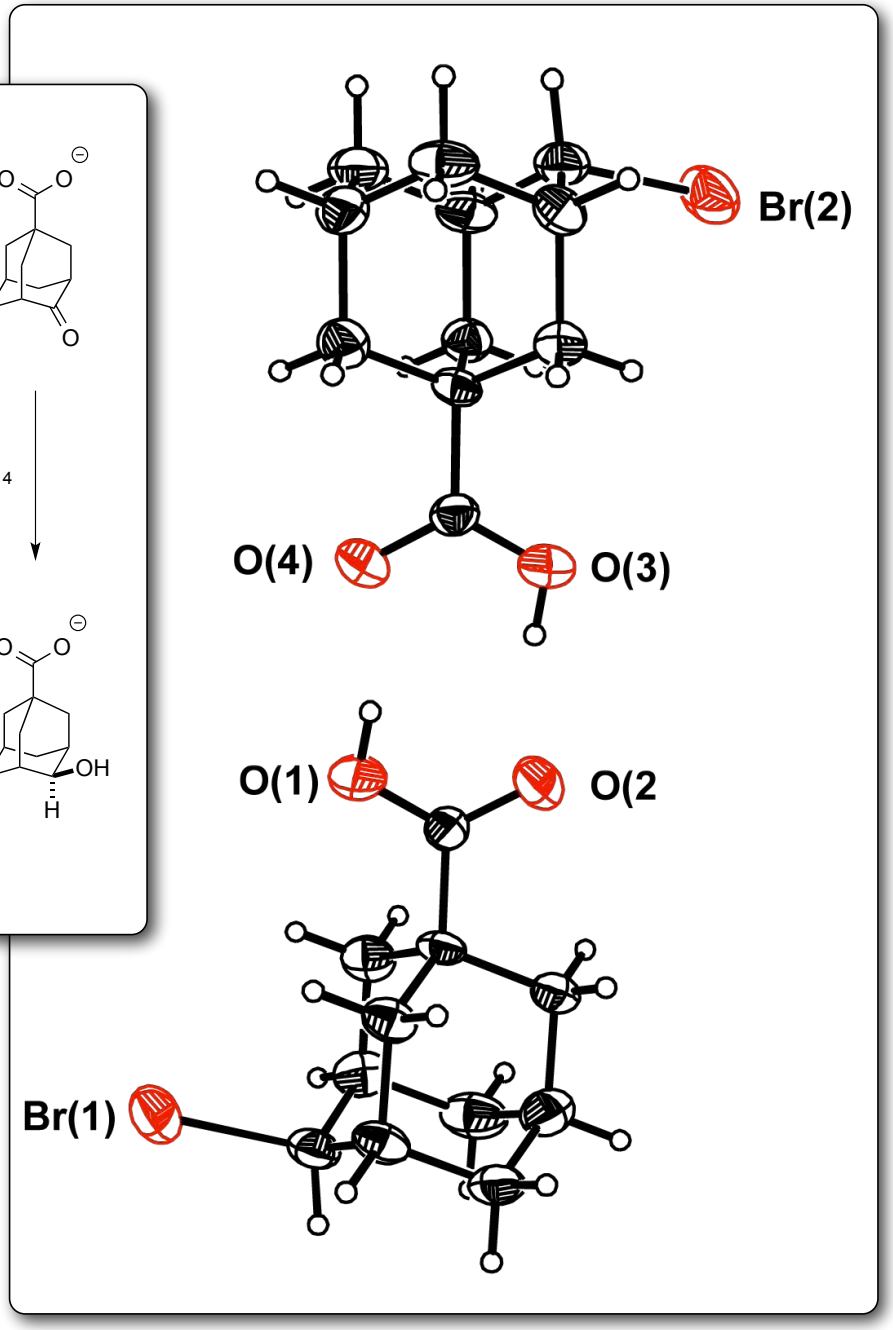


8

Sullivan, M. R., Sokalingam, P., Nguyen, T., Donahue, J. P., Gibb, B.C., *unpublished*.

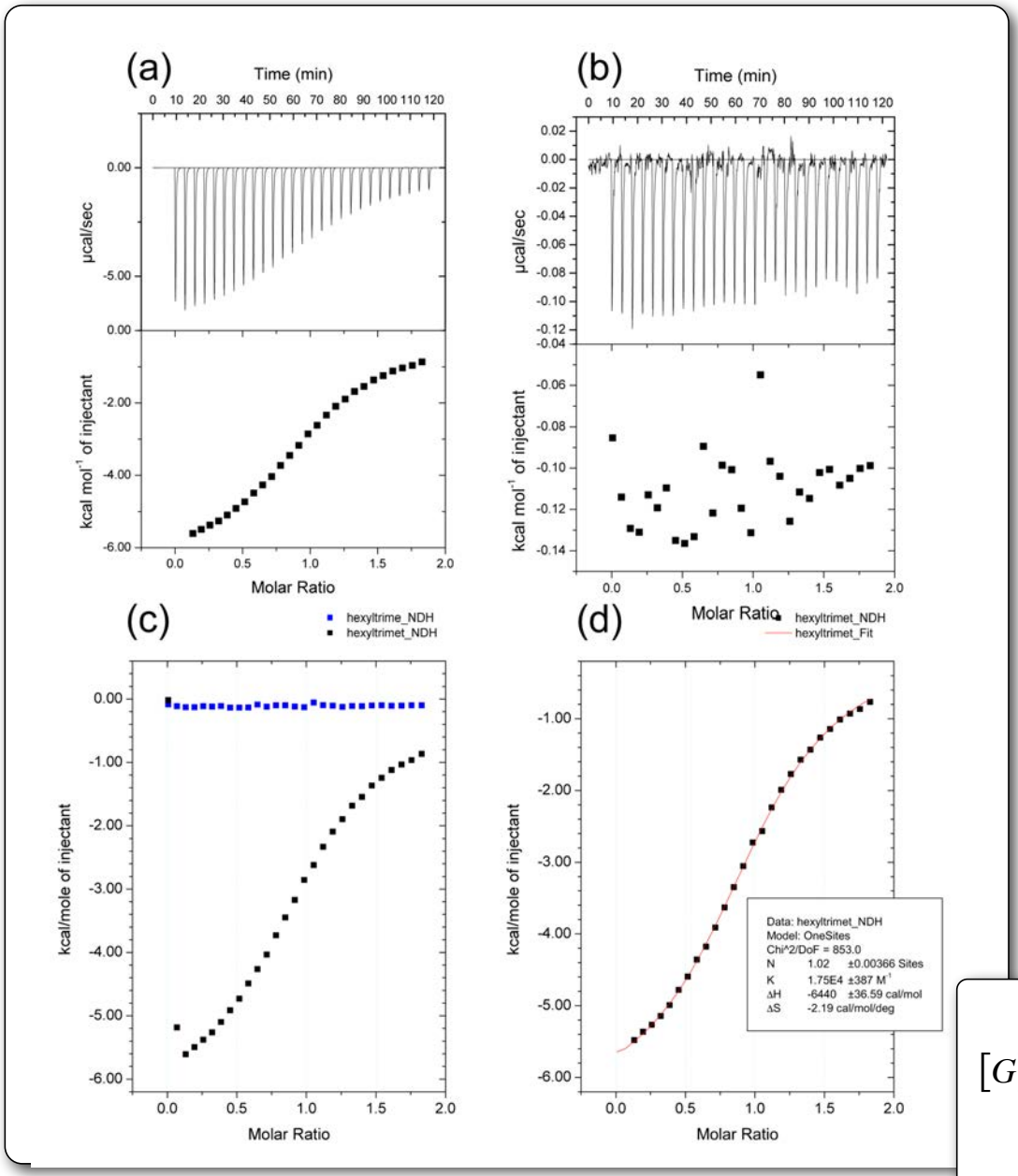
Z-4-Bromo-adamantane-1-carboxylic acid

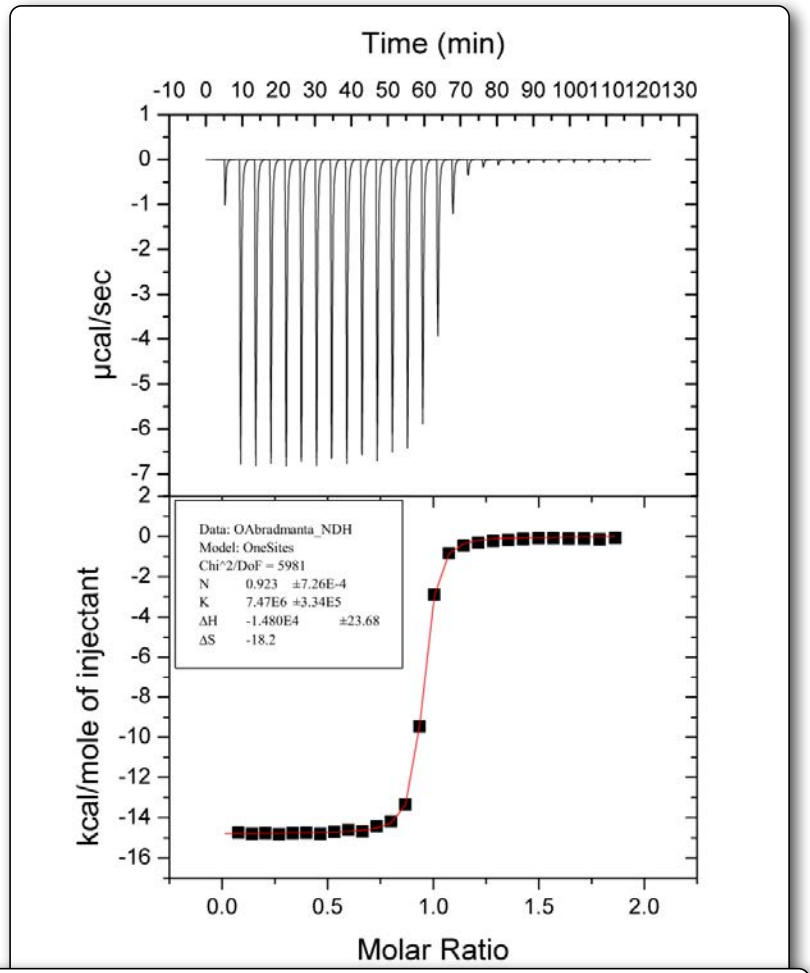




Sullivan, M. R., Sokalingam, P., Nguyen, T., Donahue, J. P., Gibb, B.C., *unpublished*.

ITC data for SAMPL5



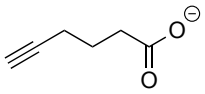
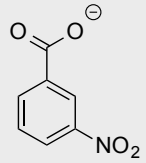
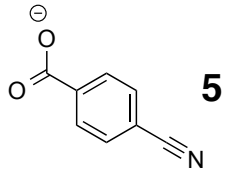
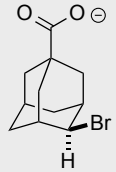
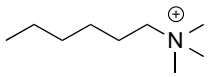
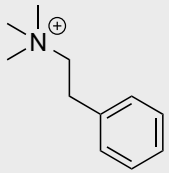


$$[G] = \frac{-(1 - K_a G_t + K_a H_t) \pm \sqrt{(1 - K_a G_t + K_a H_t)^2 + 4 K_a G_t}}{2 K_a}$$

$$Q = [HG] V_o \Delta H^\circ = (G_t - [G]) V_o \Delta H^\circ$$

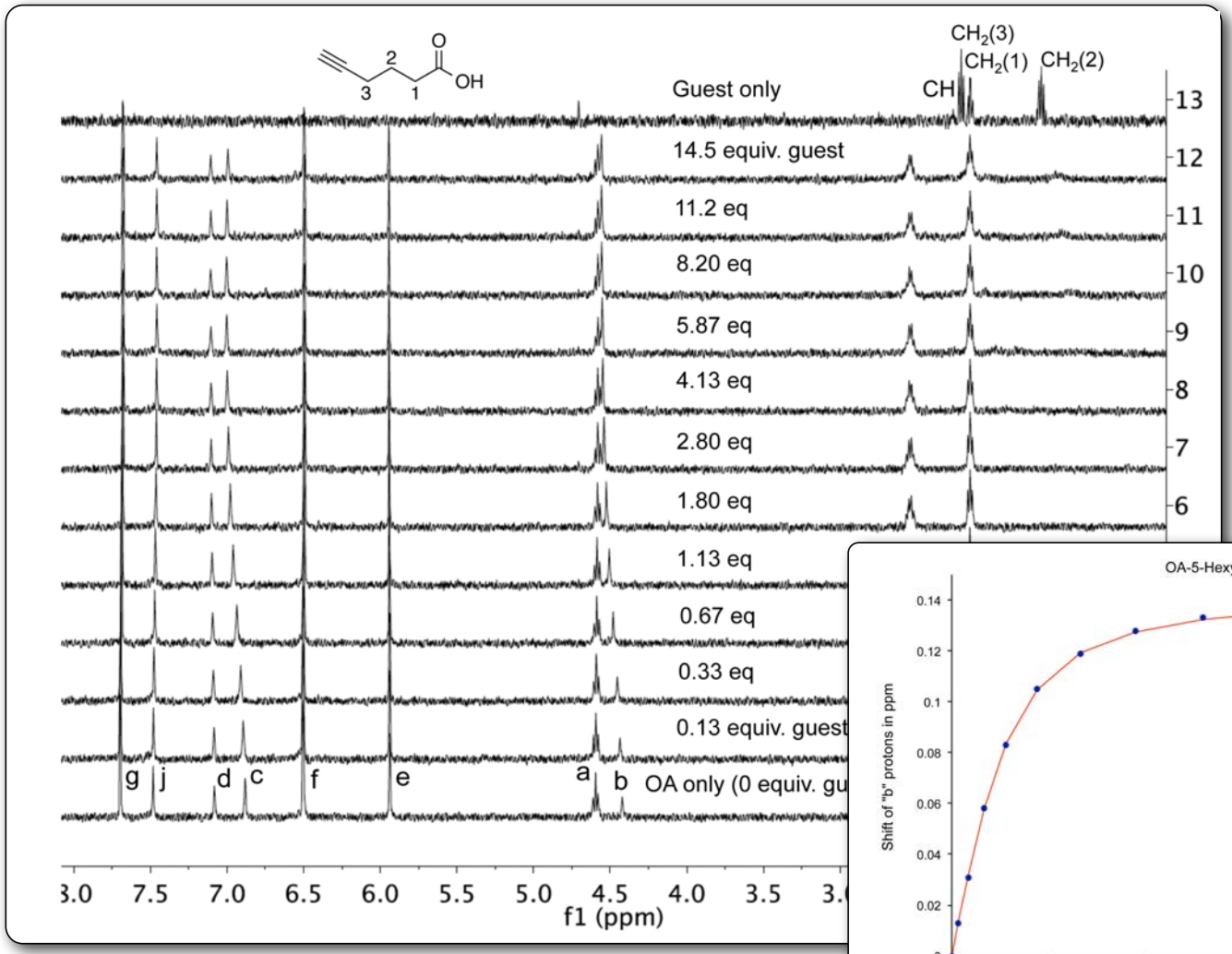
Sullivan, M. R., Sokalingam, P., Nguyen, T., Donahue, J. P., Gibb, B.C., *unpublished*.

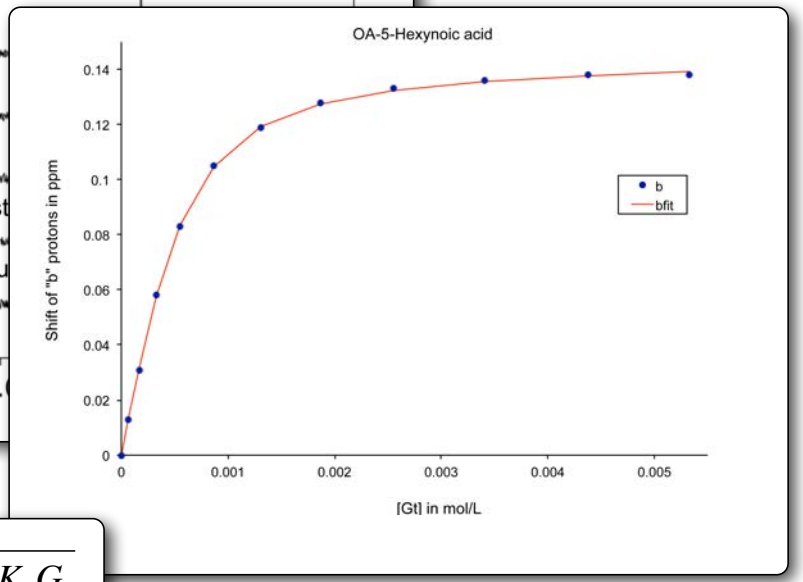
ITC data for SAMPL5 guests

Guest	OA				TEMOA			
	K_a (M^{-1})	ΔG° (cal/mol)	ΔH° (cal/mol)	$-T\Delta S^\circ$ (cal/mol)	K_a (M^{-1})	ΔG° (cal/mol)	ΔH° (cal/mol)	$-T\Delta S^\circ$ (cal/mol)
 **3**	9040 (40)	-5398 (3)	-7713 (48)	2315 (45)	10150 (50)	-5476 (10)	-9961 (6)	4485 (15)
 **4**	8140 (60)	-5335 (5)	-5669 (7)	334 (12)	2050 (70)	-4521 (19)	-9051 (130)	4530 (150)
 **5**	2890 (20)	-4731 (14)	-4445 (81)	-286 (79)	7085 (155)	-5255 (14)	-7559 (103)	2304 (117)
 **6**	7.43 x 10^6 (4 x 10^4)	-9369 (7)	-14783 (23)	5414 (20)	NB	NB	NB	NB
 **7**	1960 (20)	-4492 (10)	-5913 (95)	1421 (102)	16000 (1500)	-5732 (55)	-6619 (180)	887 (234)
 **8**	535 (7)	-3724 (9)	-9962 (108)	6238 (99)	NB	NB	NB	NB

Sullivan, M. R., Sokalingam, P., Nguyen, T., Donahue, J. P., Gibb, B.C., *unpublished*.

NMR data for SAMPL5



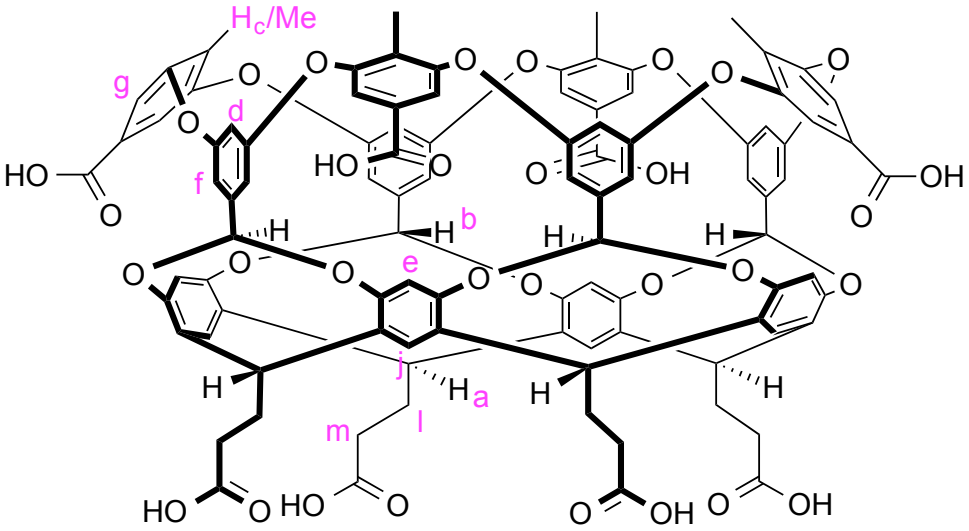


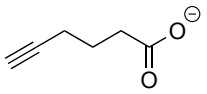
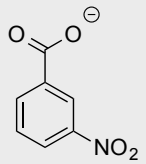
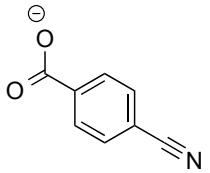
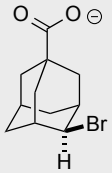
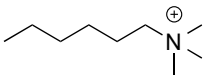
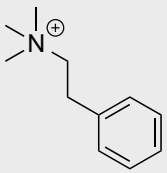
$$[G] = \frac{-(1 - K_a G_t + K_a H_t) \pm \sqrt{(1 - K_a G_t + K_a H_t)^2 + 4 K_a G_t}}{2K_a}$$

$$\Delta\delta_{obs} = \frac{\Delta\delta_{\max} K_a [G]}{1 + K_a [G]}$$

Sullivan, M. R., Sokalingam, P., Nguyen, T., Donahue, J. P., Gibb, B.C., *unpublished*.

NMR data for SAMPL5 guests



		OA	TEMOA
Guest		K_a (M^{-1})	K_a (M^{-1})
	**3**	5002	6941
	**4**	3935 (H_f)	1817 (CH_3)
	**5**	1307	4956
	**6**	-	56 (H_e) at 5˚C
	**7**	5164	2.31×10^4
	**8**	1997 (H_c)	729

Sullivan, M. R., Sokalingam, P., Nguyen, T., Donahue, J. P., Gibb, B.C., *unpublished*.

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CHE-MSN, CHE-CTMC, and CHE-CSDM-B

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