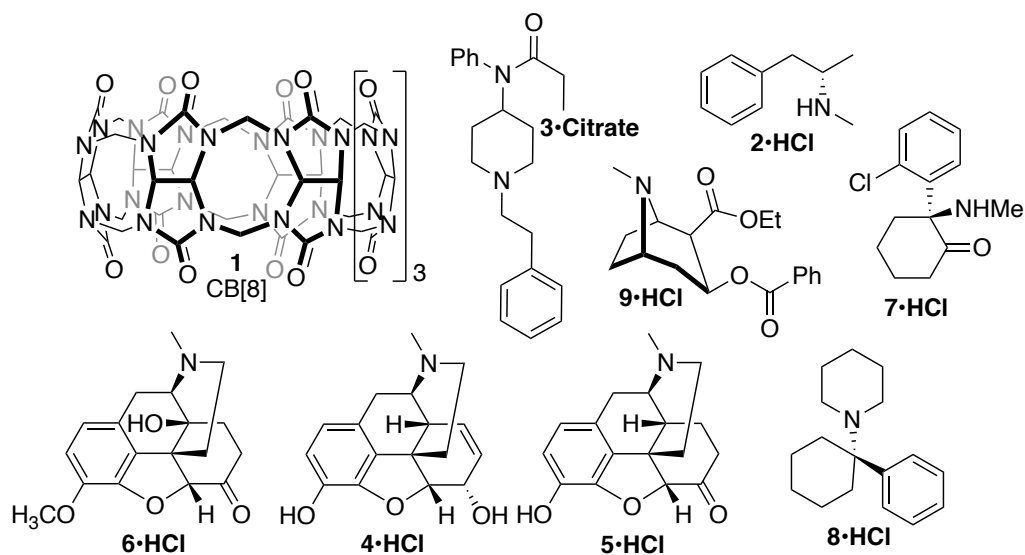


Guests	CB[8]					G2: Methamphetamine Hydrochloride G3: Fentanyl Citrate G4: Morphine Hydrochloride G5: Hydromorphone Hydrochloride G6: Oxycodone Hydrochloride G7: Ketamine Hydrochloride G8: Phencyclidine Hydrochloride G9: Cocaine Hydrochloride C1: Cycloheptanamine Hydrochloride (competitor) C2: Cyclooctanamine Hydrochloride (competitor)
	K_a (M ⁻¹)	ΔG° (kcal/mol)	ΔH° (kcal/mol)	$-T\Delta S$ (kcal/mol /K)	n	
G2 ^[a]	$(1.4 \pm 0.09) \times 10^5$	-7.05	(-7.84 ± 0.1)	0.788	1	
G3 ^[a]	$(1.9 \pm 0.09) \times 10^7$	-9.94	(-10.8 ± 0.06)	0.872	1	
	$(3.7 \pm 0.04) \times 10^5$	-7.60	(-7.67 ± 0.04)	0.073	2	
G4 ^[b]	$(1.7 \pm 0.11) \times 10^8$	-11.6	(-13.6 ± 0.04)	1.93	1	
G5 ^[b]	$(3.41 \pm 0.15) \times 10^8$	-11.2	(-15.8 ± 0.1)	4.54	1	
G6 ^[b]	$(3.42 \pm 0.05) \times 10^7$	-10.3	(-19.6 ± 0.04)	9.30	1	
G7 ^[c]	$(1.09 \pm 0.07) \times 10^9$	-12.3	(-17.3 ± 0.16)	5.01	1	
G8 ^[c]	$(2.1 \pm 0.2) \times 10^{10}$	-14.1	(-14.9 ± 0.04)	0.797	1	
G9 ^[a]	$(8.1 \pm 0.56) \times 10^5$	-7.79	(-6.57 ± 0.1)	-1.22	1	
C1	$(5.35 \pm 0.22) \times 10^6$	-9.18	(-7.62 ± 0.03)	-1.55	1	
C2	$(3.18 \pm 0.24) \times 10^7$	-10.2	(-8.26 ± 0.04)	-1.98	1	

Table 1. Isothermal titration calorimetry data for CB[8] towards guests **G2** – **G9**. [a] Direct ITC titration, [b] competitive ITC titration with **C1**, and [c] competitive ITC titration with **C2**.



Measurement Details: All measurements have been measured in duplicate in 20 mM sodium phosphate buffer at pH = 7.4 at 25°C.

- 2 C[C@H](NC)CC1=CC=CC=C1
- 3 O=C(CC)N(C1=CC=CC=C1)C(CC2)CCN2CCC3=CC=CC=C3
- 4 CN(CC1)[C@H]2[C@]3([H])C=C[C@H](O)[C@@]4([H])[C@]31C5=C(O4)C(O)=CC=C5C2
- 5 CN(CC1)[C@H]2[C@]([C@]1([C@@]3([H])O4)C5=C4C(O)=CC=C5C2)([H])CCC3=O
- 6 CN(CC1)[C@H]2[C@]([C@]1([C@@]3([H])O4)C5=C4C(OC)=CC=C5C2)(O)CCC3=O
- 7 O=C1CCCC[C@@]1(C2=CC=CC=C2Cl)NC
- 8 N1(C2(C3=CC=CC=C3)CCCCC2)CCCCC1
- 9 CN1[C@H]2CC[C@@H]1[C@@H](C(OCC)=O)[C@@H](OC(C3=CC=CC=C3)=O)C2