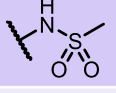
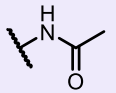
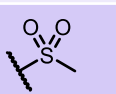
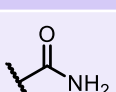
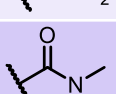
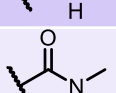
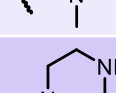

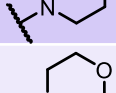

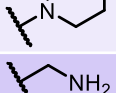
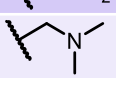





# LogD Cheat Sheet

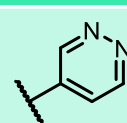
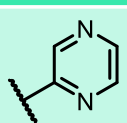
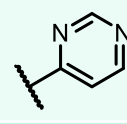
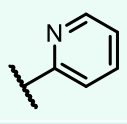
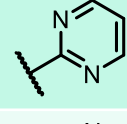
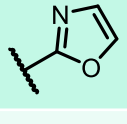
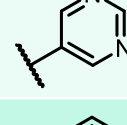
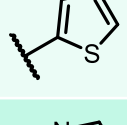
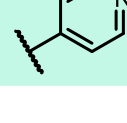
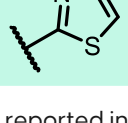
influence of substituents on  $\Delta\text{LogD}$  and expected "lipophilic potency"

-H changed to -R R =	median $\Delta\text{LogD}^*$ (# of matched pairs)	x-fold change in affinity/potency expected from lipophilicity alone	-H changed to -R R =	median $\Delta\text{LogD}^*$ (# of matched pairs)	x-fold change in affinity/potency expected from lipophilicity alone
Me	0.30 (8458)	2x gain	OMe	-0.05 (1579)	Insignificant
Et	0.72 (634)	5x gain	OEt	0.40 (100)	3x gain
n-Pr	1.05 (66)	11x gain	SMe	0.45 (30)	3x gain
i-Pr	1.10 (419)	13x gain	Oi-Pr	0.85 (76)	7x gain
t-Bu	1.30 (88)	20x gain	OCF <sub>3</sub>	1.00 (138)	10x gain
CHF <sub>2</sub>	0.40 (260)	3x gain	OCHF <sub>2</sub>	0.50 (88)	3x gain
CF <sub>3</sub>	0.90 (899)	8x gain		-1.00 (76)	10x loss
Ph	1.40 (570)	25x gain		-0.60 (139)	3x loss
CN	-0.28 (1092)	2x loss		-0.90 (192)	10x loss
F	0.2 (4249)	2x gain		-1.10 (269)	13x loss
Cl	0.6 (1782)	4x gain		-0.50 (140)	3x loss
Br	0.9 (356)	8x gain		-0.98 (148)	10x loss
I	1.1 (35)	13x gain		-1.90 (53)	100x loss
	0.9 (586)	8x gain		-0.20 (278)	2x loss
	1.30 (88)	20x gain		-2.33 (72)	200x loss
OH	-0.70 (1224)	4x loss		-1.10 (57)	13x loss
	-0.60 (560)	3x loss			
	-2.98 (106)	1000x loss			
	-1.90 (62)	100x loss			

\*data reported in M. Landry and J. Crawford, *ACS Med. Chem. Lett.* 2020, 11, 1, 72-76

expected changes to LogD from phenyl-group replacements

$$\Delta\Delta\text{LogD} = (\Delta\text{LogD}_{\text{H-to-R}} - \Delta\text{LogD}_{\text{H-to-Ph}})$$

Heterocycle	$\Delta\text{LogD}^*$ ( $\Delta\Delta\text{LogD}$ )	expt'd $\Delta$ potency H to R (Ph to R)	Heterocycle	$\Delta\text{LogD}^*$ ( $\Delta\Delta\text{LogD}$ )	expt'd $\Delta$ potency H to R (Ph to R)
	-0.80 (-2.20)	6x loss (160x loss)		0.20 (-1.20)	1.6x gain (16x loss)
	0.50 (-0.90)	3x gain (8x loss)		0.70 (-0.70)	5x gain (5x loss)
	0.90 (-0.50)	8x gain (3x loss)		0.05 (-1.35)	similar (22x loss)
	-0.20 (-1.60)	1.6x loss (40x loss)		1.20 (-0.20)	16x gain (1.6x loss)
	0.50 (-0.90)	3x gain (8x loss)		0.70 (-0.70)	5x gain (5x loss)

\*data reported in M. Landry and J. Crawford, *ACS Med. Chem. Lett.* 2020, 11, 1, 72-76