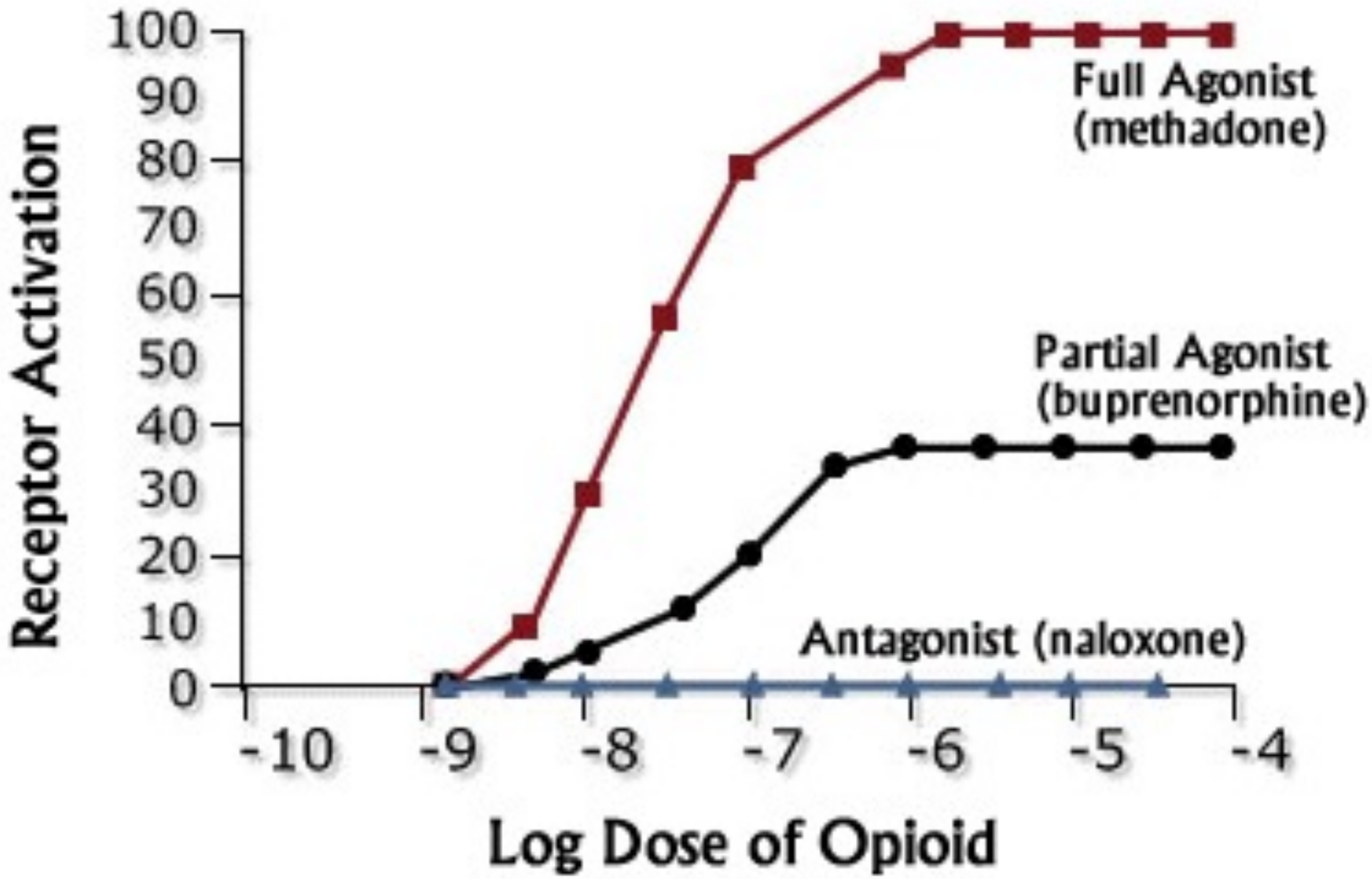
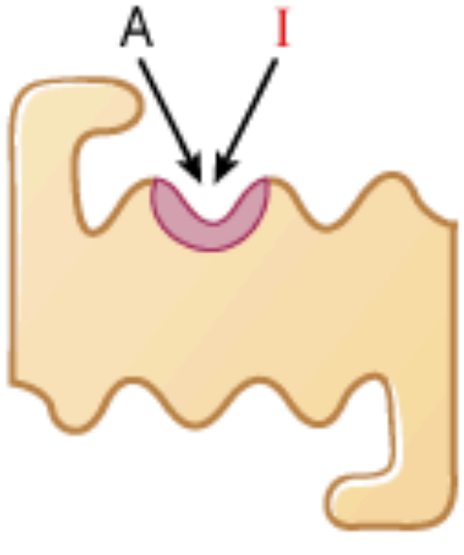
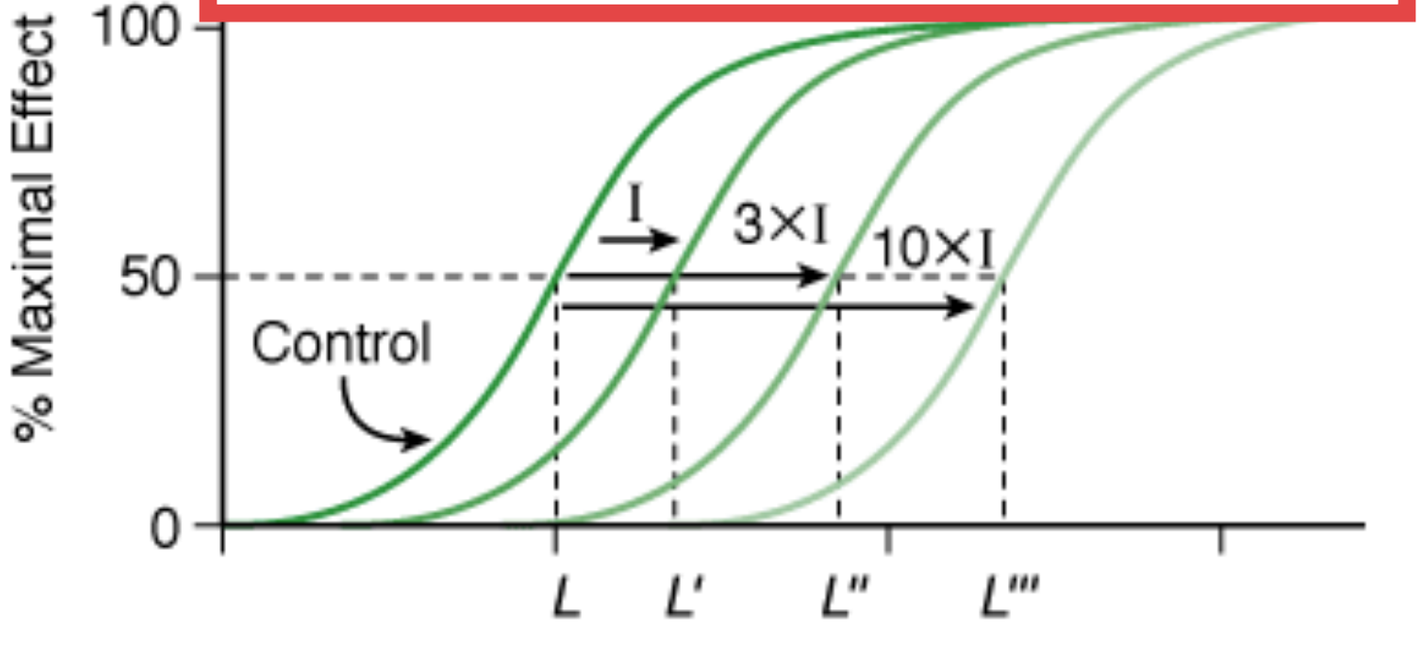
Antagonism



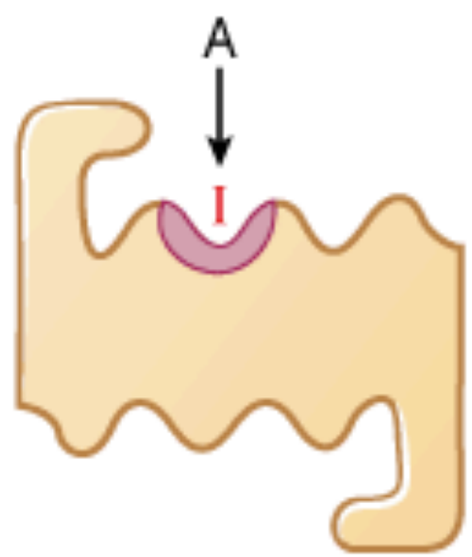
Antagonists have **affinity** but not **efficacy** (alpha = 0)

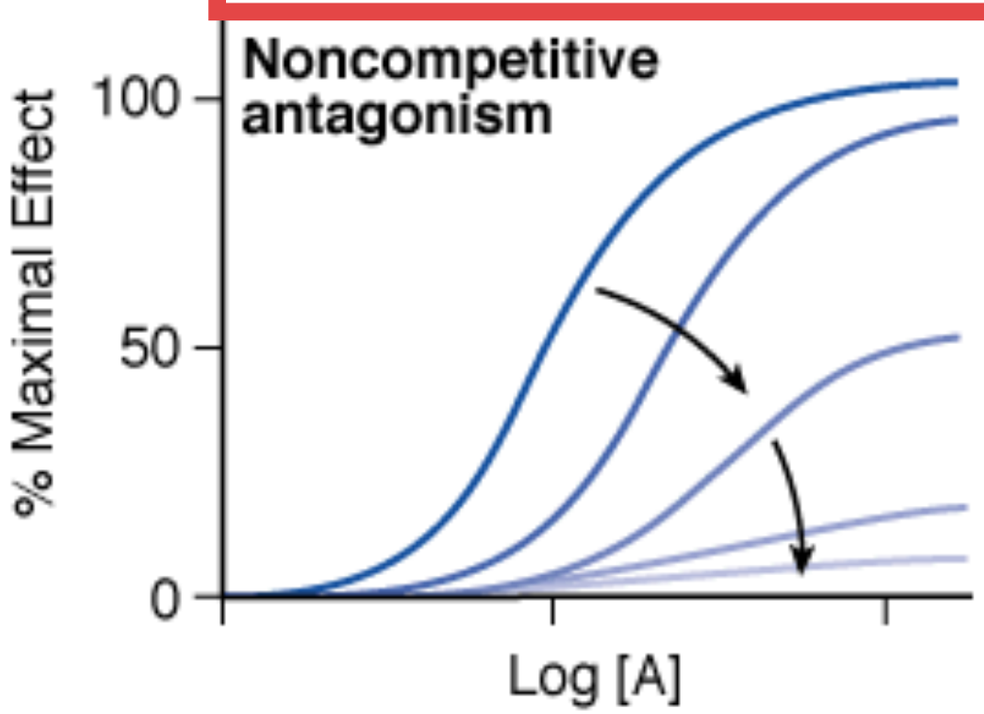


Competitive antagonism

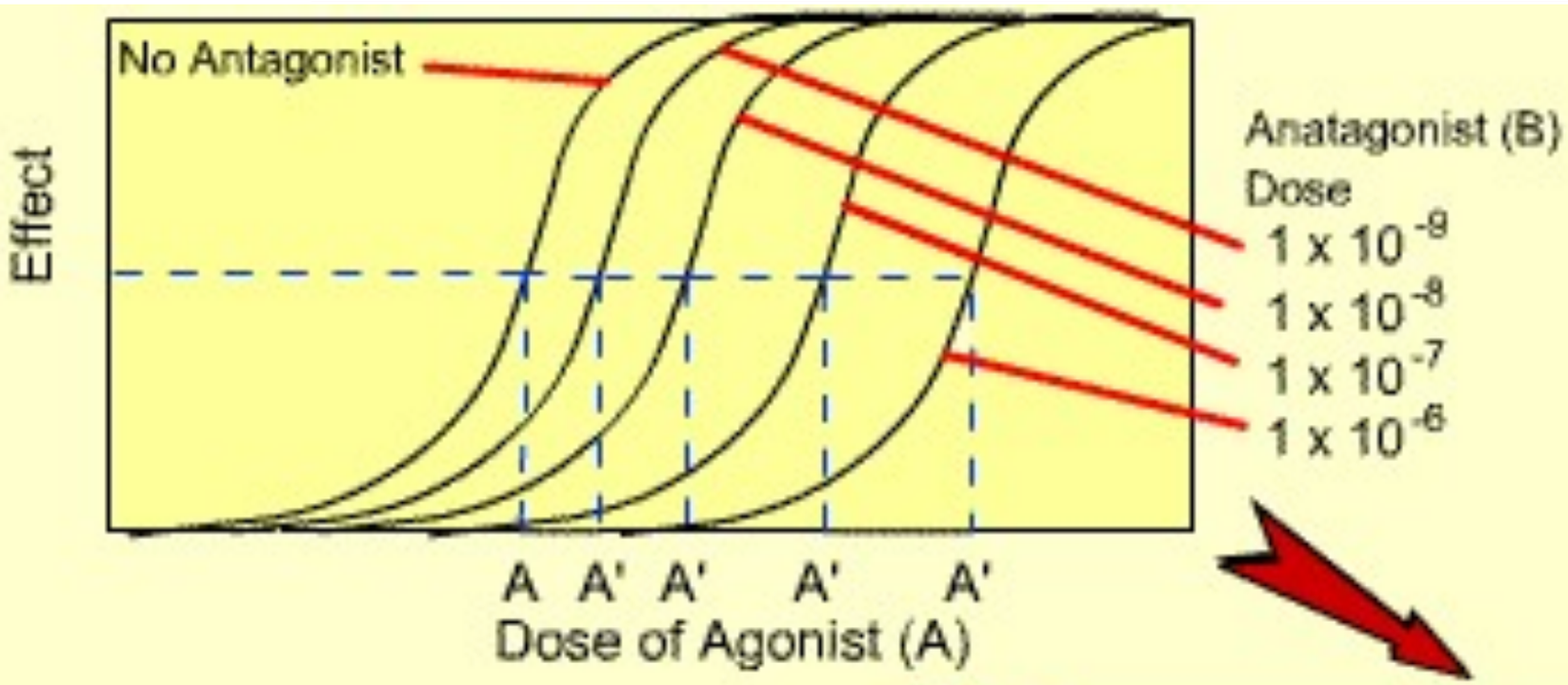


Irreversible antagonism

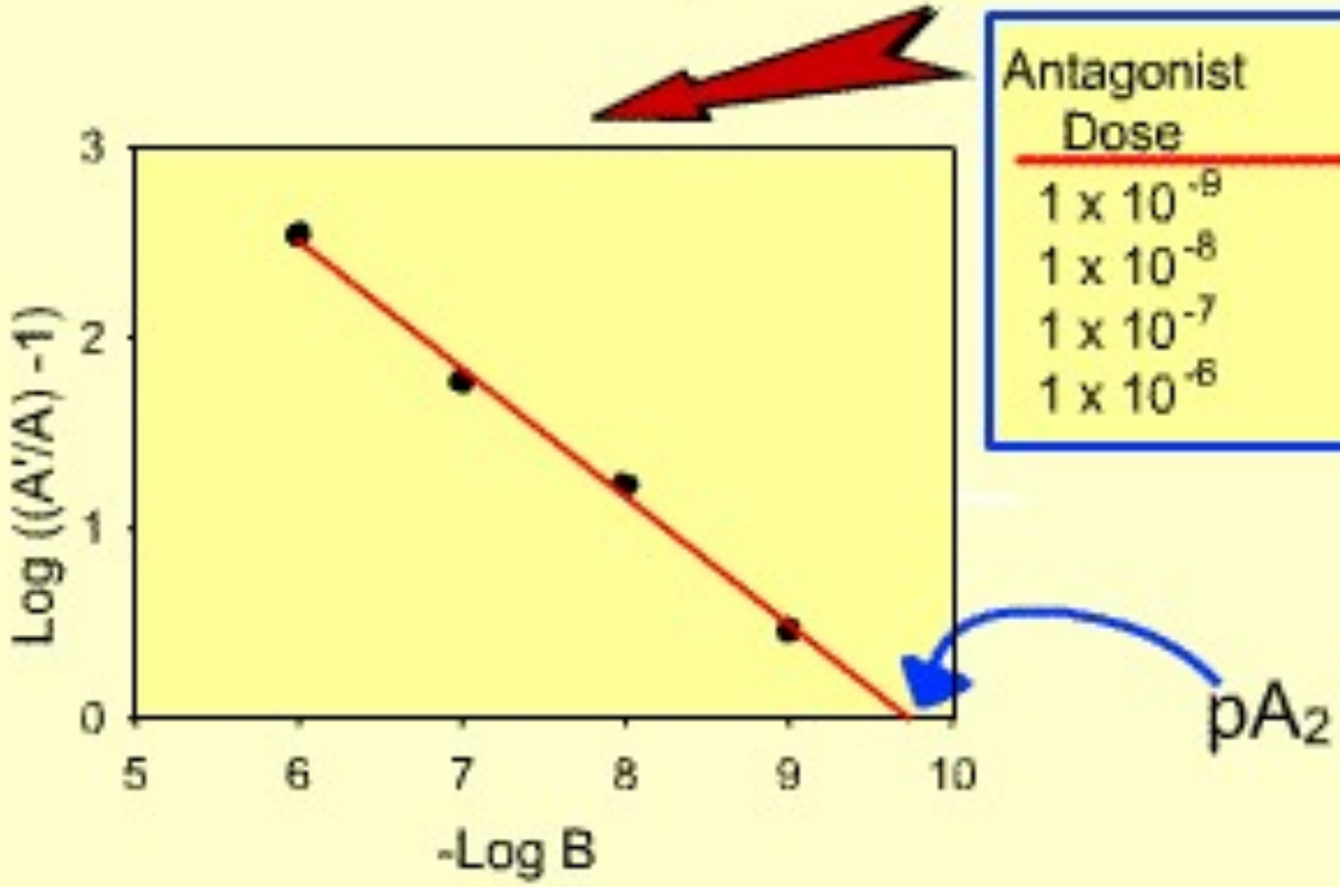




Schild Plot for pA2 determination



pA2 is the measure of the affinity of a reversible competitive antagonist for a specific receptor

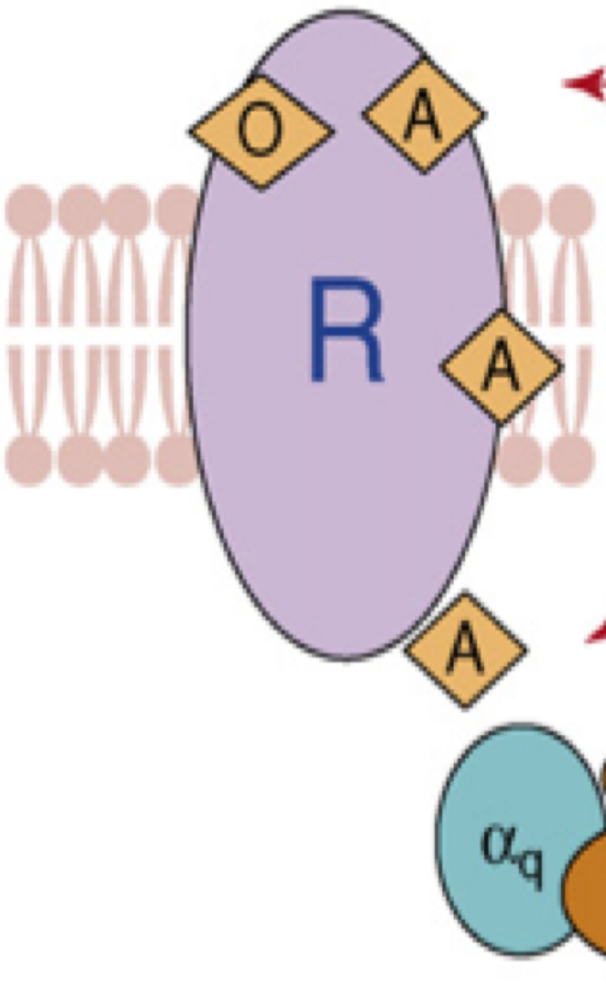


Antagonist Dose	A'/A	-logB	log((A'/A-1)
1 x 10 -9	4	9	0.47
1 x 10 -8	18	8	1.23
1 x 10 -7	60	7	1.77
1 x 10 -6	350	6	2.54

pA2 is the negative log of molar concentration of the antagonist which will reduce the effect of double the concentration of the agonist to that of a single dose

Allosteric ligands

Orthosteric site = O Allosteric site = A



1 — Modulate orthosteric ligand binding

2 — Modulate orthosteric ligand efficacy independent of orthosteric ligand binding or G protein coupling sites

3 — Modulate G protein binding

Allosteric modulators work only in the presence of orthosteric ligand, but don't necessarily alter orthosteric ligand binding

TRENDS in Pharmacological Sciences

Allosteric ligands