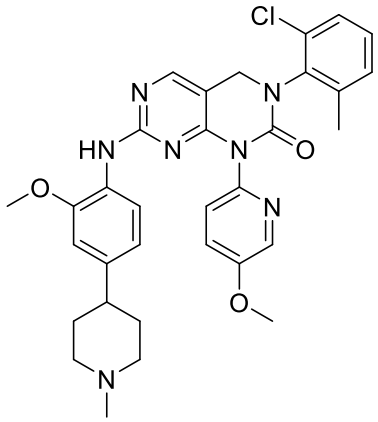
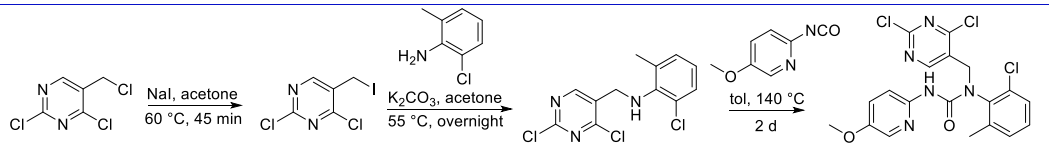
YKL-05-099



Chemical Formula: $C_{32}H_{34}ClN_7O_3$
Molecular Weight: 600.12

Category	Parameter	Description
Compound	Name	YKL-05-099
	Citation	*ACS Chem. Biol.*, **2016**, *11* (8), pp 2105–2111. http://pubs.acs.org/doi/abs/10.1021/acschembio.6b00217 *Nat. Commun*. **2016**, *7*, 13176. https://www.nature.com/articles/ncomms13176
	Chemical descriptors	O=C1N(C2=CC=C(OC)C=N2)C3=NC(NC4=C(OC)C=C(C5CCN(C)CC5)C=C4)=NC=C3CN1C6=C(C)C=CC=C6Cl
	Chemical name	3-(2-chloro-6-methylphenyl)-7-((2-methoxy-4-(1-methylpiperidin-4-yl)phenyl)amino)-1-(5-methoxypyridin-2-yl)-3,4-dihydropyrimido[4,5-*d*]pyrimidin-2(1*H*)-one
	Entries in chemical databases	CAS# 1936529-65-5
	Availability	MedChem Express https://www.medchemexpress.com/YKL-05-099.html
	Papers that use the compounds	https://www.ncbi.nlm.nih.gov/pubmed/?term=YKL-05-099
In vitro profiling	Target (potency)	SIK2 (IC_{50} 40 ± 25 nM)
	Target (potency)	SIK1 (IC_{50} 10.9 nM), SIK3 (IC_{50} 30.2 nM)
	Selectivity	S-score (35) = 0.16 (Ambit)
	Potential reactivity	
	SAR	
	Mechanism of inhibition	reversible
	Structure of target-probe complex	
Cellular profiling	Validation of cellular target	YKL-05-099 upregulates IL10 production with EC_{50} of 460 ± 110 nM in BMDCs. YKL-05-099 leads to dose-dependent reduction in HDAC4 S246 phosphorylation and causes SOST down-regulation and RANKL up-regulation in Ocy454 cells.
	Validation of cellular specificity	YKL-05-099 reduces production of several inflammatory cytokines including TNFα, IL-6, IL-12 in BMDCs. Cytotoxicity in BMDC CC_{50} > 10 µM.
Pharmacodynamics		YKL-05-099 reduces p-HDAC5 (Ser259) levels and modulates inflammatory cytokine responses *in vivo* following IP administration prior to stimulation with LPS.
Pharmacokinetics		MLM $T_{1/2}$ = 120 min.



Synthetic scheme