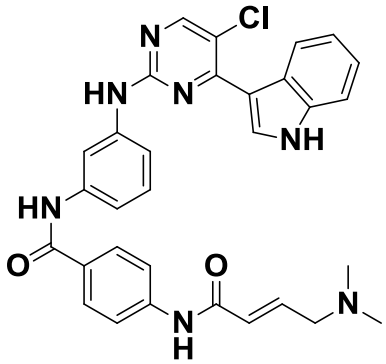
CDK7/CDK12 inhibitor-THZ1



Category	Parameter	Description
Compound	Name	CDK7/CDK12 inhibitor (THZ1)
	Citation	Nature. 2014 Jul 31;511(7511):616-20. doi: 10.1038/nature13393. Epub 2014 Jun 22.
	Chemical descriptors	ClC1=CN=C(NC2=CC(NC(C3=CC=C(NC(/C=C/CN(C)C)=O)C=C3)=O)=CC=C2)N=C1C4=CNC5=C4C=CC=C5
	Chemical name	(E)-N-(3-((5-chloro-4-(1H-indol-3-yl)pyrimidin-2-yl)amino)phenyl)-4-(4-(dimethylamino)but-2-enamido)benzamide
	Availability	EMD , Chemexpress
In vitro profiling	Target (potency)	**CDK7** (3.3 nM)
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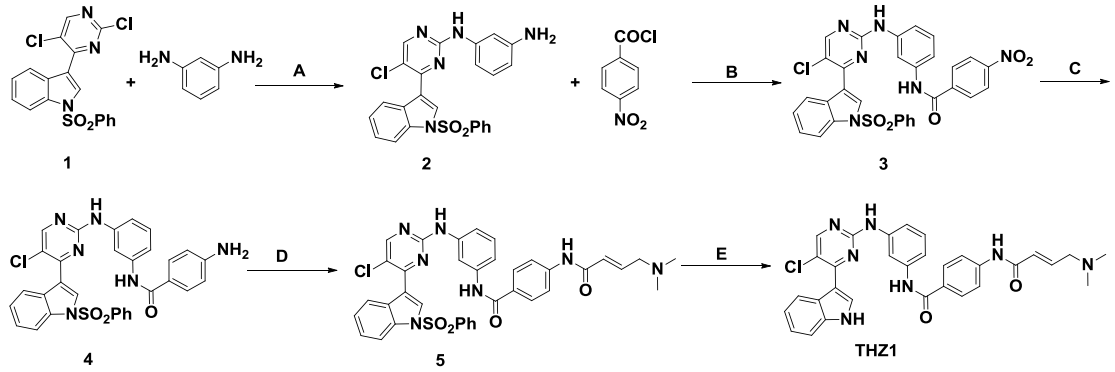
	Selectivity	
	Potential reactivity	None to our knowledge
	SAR	
	Mechanism of inhibition	ATP-competitive
	Structure of target-probe complex	
Cellular profiling	Validation of cellular target	THZ1 dose-dependently inhibited Pol II CTD ser phosphorylation at 50-100 nM
	Validation of cellular specificity	
Pharmacodynamics		
Pharmacokinetics		$T_{1/2}$ = 13.8 hours, CL = 37 (mL/min/Kg), Vss = 20 (L/Kg), F = 2%

Synthetic scheme



Reagents and conditions: (A) NMP, 130°C (B) pyridine, 80 °C (C) $SnCl_2$, 80°C, ethyl acetate and methanol (D) *(E)*-4-bromobut-2-enoyl chloride, acetonitrile and then $NHMe_2$, 0°C-RT (E) 1M NaOH, 1,4-dioxane, RT