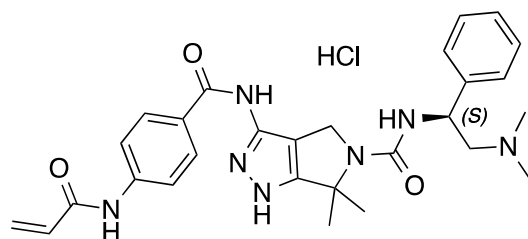


YKL-5-124

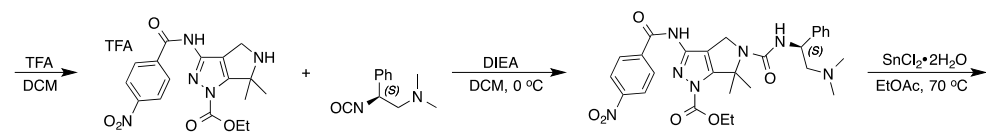
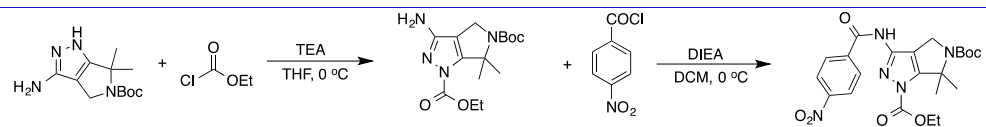


Chemical Formula: C₂₈H₃₃N₇O₃

Exact Mass: 515.26

HCl salt: 551.24

Category	Parameter	Description
Compound	Name	YKL-5-124
	Citation	"Development of a Selective CDK7 Covalent Inhibitor Reveals Predominant Cell-Cycle Phenotype" <i>Cell chemical biology</i> (2019)
	Chemical descriptors	<chem>O=C(N(C1)C(C)(C)C2=C1C(NC(C3=CC=C(NC(C=C)O)C=C3)O)=NN2)N[C@@H](C4=C(C=CC=C4)CN(C)C.[H]Cl</chem>
	Chemical name	(S)-3-(4-acrylamidobenzamido)-N-(2-(dimethylamino)-1-phenylethyl)-6,6-dimethyl-4,6-dihydropyrrolo[3,4-c]pyrazole-5(1H)-carboxamide hydrochloride
	Entries in chemical databases	CID 121443990
	Availability	
<i>In vitro</i> profiling	Target (potency)	CDK7 : IC ₅₀ = 9.7 nM (Invitrogen, biochemical assay), IC ₅₀ = 53.5 nM (Geyer, P32 biochemical assay), K _i = 2.2 nM (Westover, enzyme kinetics using mobility shift assay)
	Target (potency)	CDK12 : IC ₅₀ > 10 μM (Geyer, P32 biochemical assay), CDK13 : IC ₅₀ > 10 μM (Geyer, P32 biochemical assay), CDK2 : IC ₅₀ = 1.3 μM (Invitrogen, biochemical assay), CDK9 : IC ₅₀ = 3.0 μM (Invitrogen, biochemical assay)
	Selectivity	YKL-5-124 selectivity was assessed by KiNativ profiling in Jurkat cells @ 1 μM
	Potential reactivity	Cysteine reactive
	SAR	
	Mechanism of inhibition	Irreversible
Cellular profiling	Validation of cellular target	YKL-5-124 dose-dependently targets CDK7 in HAP1 and Jurkat cells as assessed by intracellular target engagement and IP kinase activity assays
	Validation of cellular specificity	HAP1 cells expressing a CDK7 mutant lacking the requisite cysteine (Cys312) is more than 150-fold less sensitive to YKL-5-124 (Note: TCA which codes for serine, was introduced into HAP1 genome via CRISPR Cas9-mediated allelic replacement, replacing TGT which codes for cysteine (C312S)); selectivity was also assessed by KiNativ profiling assay in Jurkat cells @ 1 μM
	Additional comments	the reversible inactive analog is YKL-5-167 (negative control)
Pharmacodynamics		N/A
Pharmacokinetics		N/A



Synthetic scheme

