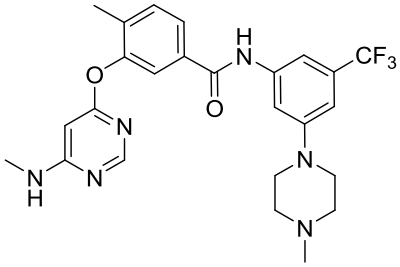
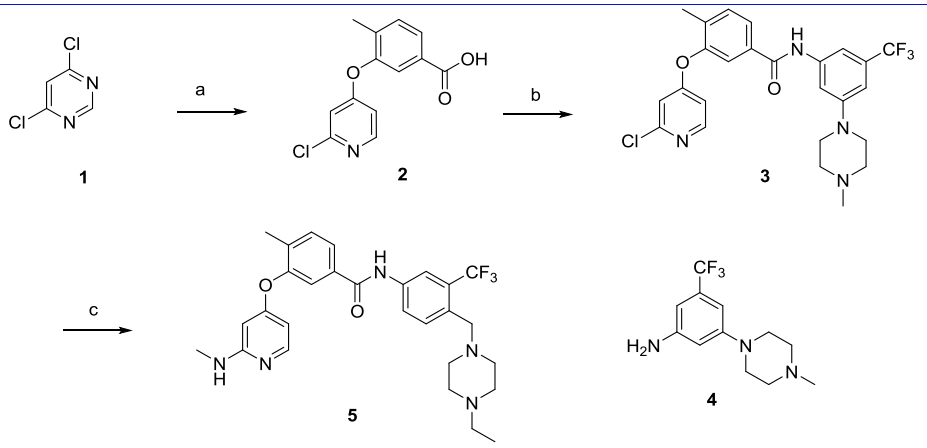
MAP4K2 inhibitor (TL4-12)



Chemical Formula: $C_{50}H_{54}F_6N_{12}O_4$
Molecular Weight: 1001.05

Category	Parameter	Description
Compound	Name	MAP4K2 inhibitor (TL4-12)
	Citation	*J Med Chem.* **2014** jm500480k.
	Chemical descriptors	CC1=CC=C(C(NC2=CC(N3CCN(C)CC3)=CC(C(F)(F)F)=C2)=O)C=C1OC4=NC=NC(NC)=C4
	Chemical name	4-methyl-3-((6-(methylamino)pyrimidin-4-yl)oxy)-*N*-(3-(4-methylpiperazin-1-yl)-5-(trifluoromethyl)phenyl)benzamide
	Availability	
In vitro profiling	Target (potency)	**MAP4K2** (37 nM IC50 in Z'-Lyte assay, 85% inhibition at 1.0 μM IC_{50} in ActivX KiNativ assay)
	Additional Target (potency)	
	Selectivity	
	Potential reactivity	None to our knowledge
	SAR	
	Mechanism of inhibition	ATP-competitive
	Structure of target-probe complex	
Cellular profiling	Validation of cellular target	TL4-12 dose-dependently inhibited MAP4K2 downstream signaling induced by TGFβ in TAK1-null MEF cells with IC50 between 0.1~0.5 μM. Compound phenotypes were compared to literature. The cellular effects were correlated with *in vitro* biochemical activities.
	Validation of cellular specificity	
Pharmacodynamics		
Pharmacokinetics		

Synthetic scheme



Reagents and conditions: (a) 3-hydroxy-4-methylbenzoic acid, NaOH, acetone/H_2O; (b) **4**, HATU, DMAP, DIEA, CH_2Cl_2; (c) methylamine, THF.