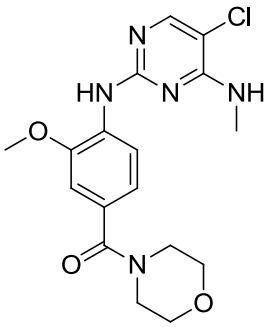
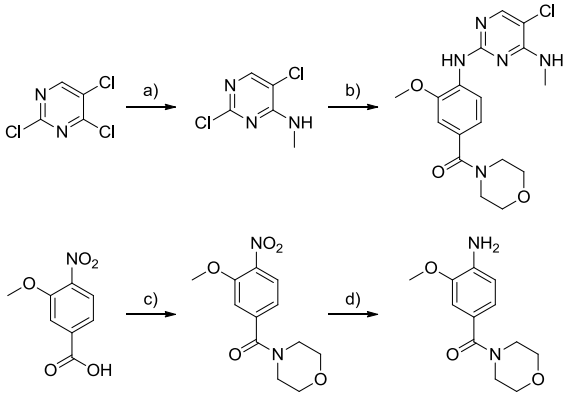
HG-10-102-01



Chemical Formula: $C_{17}H_{20}ClN_5O_3$
Exact Mass: 377.13

Category	Parameter	Description
Compound	Name	HG-10-102-01
	Citation	ACS Med Chem Lett. 2012 Aug 9;3(8):658-662
	Chemical descriptors	COC(C=C(C(N1CCOCC1)=O)C=C2)=C2NC3=NC=C(Cl)C(NC)=N3
	Chemical name	(4-((5-chloro-4-(methylamino)pyrimidin-2-yl)amino)-3-methoxyphenyl)(morpholino)methanone
In vitro profiling	Target (potency)	LRRK2 Wild-type IC_{50} = 20.3 nM, LRRK2 G2019S IC_{50} = 3.2 nM,
	Additional Target (potency)	MNK2, MLK1
	Selectivity	Highly selective, S(35) = 0.02
	Potential reactivity	None to our knowledge
	SAR	
	Mechanism of inhibition	ATP-competitive type I inhibitor
	Structure of target-probe complex	
Cellular profiling	Validation of cellular target	phosphorylation of wild-type LRRK2 and LRRK2[G2019S] mutant at Ser910 and Ser935 at 0.3-1.0 µM in cell culture
	Validation of cellular specificity	
Pharmacodynamics		
Pharmacokinetics		T1/2 hours = 0.13, CL (mL/min/Kg) = 222.04, Vss (L/Kg) = 1.68, F (%) = 67, BBB property = good

Synthetic scheme



Reagents and conditions: a) 2.0 M $MeNH_2$ in THF, THF, 0 ^oC to RT, 6 h, 85%, b) aniline, TFA, 2-BuOH, 110 ^oC, 12 h, 76%, c) i. thionyl chloride, toluene, 120 ^oC, 2 h, ii. morpholine, DIEA, THF, 0 ^oC to RT, 1 h, 92%, d) 10% Pd/C, MeOH, RT, 12 h, 98%.