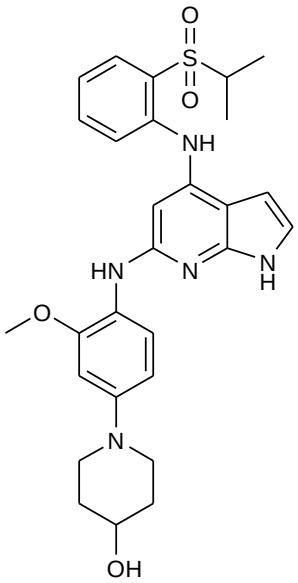
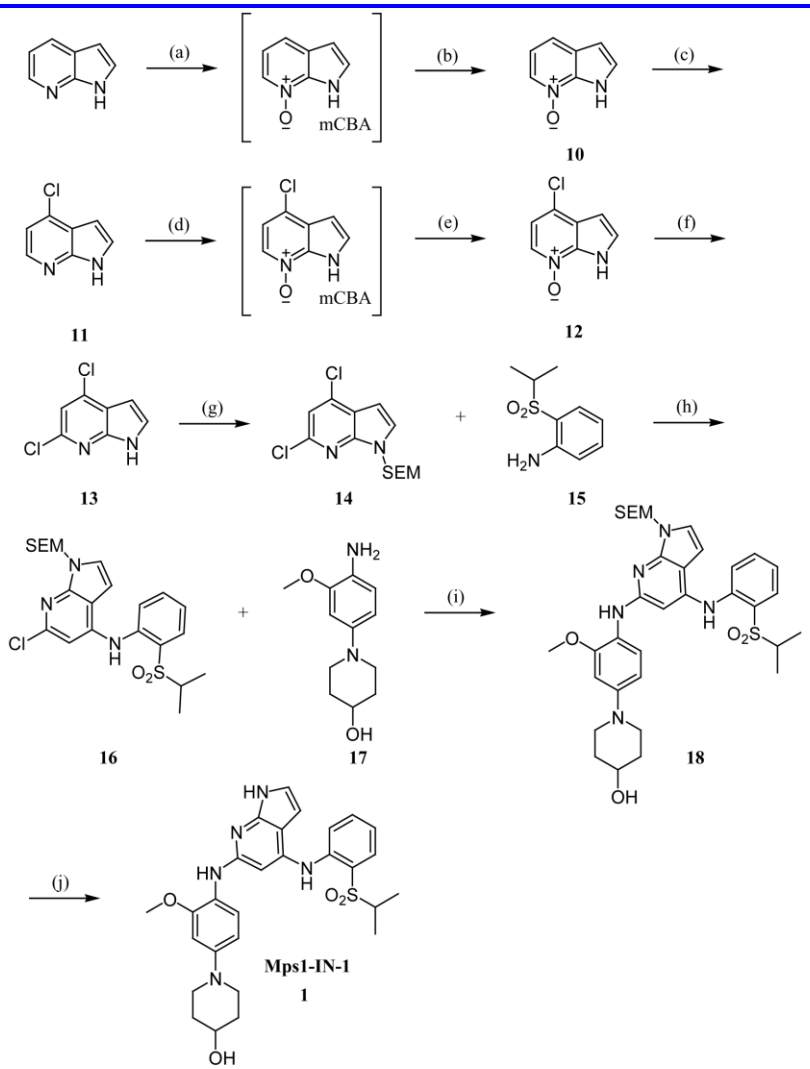
Chemical probe data: 1. Mps1-IN-1



Chemical Formula: $C_{28}H_{33}N_5O_4S$
Molecular Weight: 535.6577

Category	Parameter	Description
Compound	Name	Mps1-IN-1
	Citation	*Nat. Chem. Biol.* **2010**, 6(5), 359-68.
	Chemical descriptors	COC(C=C(N1CCC(O)CC1)C=C2)=C2NC3=CC(NC4=C(S(C(C)C)(=O)=O)C=CC=C4)=C5C(NC=C5)=N3
	Chemical Name	1-(4-(4-(2-(isopropylsulfonyl)phenylamino)-1H-pyrrolo[2,3-b]pyridin-6-ylamino)-3-methoxyphenyl)piperidin-4-ol
	Availability	Compound can be made available from the laboratory of Dr. Gray, DFCI and HMS
	Papers that used the compounds	*J. Cell Biol.* **2010**, 191(2), 281-90. http://www.ncbi.nlm.nih.gov.ezp-prod1.hul.harvard.edu/pubmed/20937696 *Proc Natl Acad Sci USA* **2011**, 108(5), 1949-54. http://www.ncbi.nlm.nih.gov.ezp-prod1.hul.harvard.edu/pubmed/21245318
In vitro profiling	Target (potency)	Mps1 - 367 nM IC_{50} in Invitrogen biochemical assay, 27 nM K_D in Ambit binding assay
	Additional Target (potency)	Alk – 21 nM K_D in Ambit binding assay Ltk – 29 nM K_D in Ambit binding assay
	Selectivity	*Nat. Chem. Biol.* **2010**, 6(5), 359-68, Supplementary Tables S1 and S2
	Potential reactivity	None to our knowledge
	SAR	*Nat. Chem. Biol.* **2010**, 6(5), 359-68, Supplementary Fig. S3
	Mechanism of inhibition	ATP-competitive
	Structure of the target-probe complex	3GFW

Cellular profiling	Validation of cellular target	Dose-dependently inhibited spindle checkpoint at 1 μM -10 μM in Hela and U2OS cells *Nat. Chem. Biol.* **2010**, 6(5), 359-68, Fig. 2. For Mps1-IN-1 dose-dependently inhibited Mps1 autophosphorylation at 1 μM -10 μM in U2OS cells *Nat. Chem. Biol.* **2010**, 6(5), 359-68, Supp. Fig. S7c. Compound phenotypes were compared to literature and empirically determined phenotypes of RNAi against Mps1 *Nat. Chem. Biol.* **2010**, 6(5), 359-68, Fig. 2, 3, 4.
	Validation of cellular specificity	An inhibitor resistant mutant was developed to assess intracellular specificity of both compounds *Nat. Chem. Biol.* **2010**, 6(5), 359-68, Fig. 2, Supp. Fig. S7.
Pharmacodynamics		Not studied.
Pharmacokinetics		Not studied.
Synthetic Scheme		 [a]Reagents and conditions: (a) mCPBA, EA, 0°C, 18h; (b) K_2CO_3, H_2O, 0°C, 18h; (c) MsCl, DMF, 50°C to 70°C, 2h; (d) mCPBA, EA, 0°C, 18h; (e) K_2CO_3, H_2O, 0°C, 18h; (f) MsCl, DMF, 50°C to 80°C, 2h; (g)NaH, SEMCl, DMF, 0°C, 3h; (h) K_2CO_3, $Pd_2(dba)_3$, X-Phos, t-BuOH, 100°C, 5h; (i) K_2CO_3, $Pd_2(dba)_3$, X-Phos, t-BuOH, 100°C, 5h; (j) a. TFA, DCM, 0°C, 5h; b. LiOH/H_2O, H_2O:THF:MeOH, room temperature, 6h.