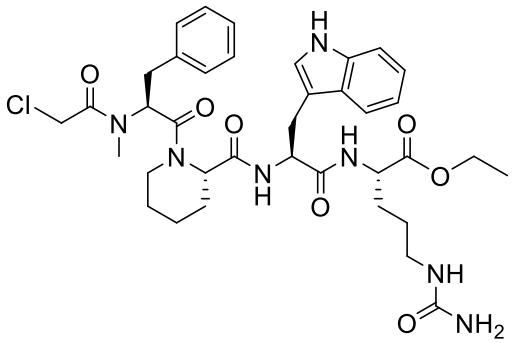
BJP-06-005-3



Chemical Formula: $C_{37}H_{48}ClN_7O_7$
Molecular Weight: 738.28

Category	Parameter	Description
Compound	Name	BJP-06-005-3
	Citation	Pinch, B.J. et al. Identification of a potent and selective covalent Pin1 inhibitor. Nature Chem Biol. (2020) https://doi.org/10.1038/s41589-020-0550-9
	Chemical descriptors	O=C(N1CCCC[C@H]1C(N[C@H](C(N[C@@H](CCCNC(N)=O)C(OCC)=O)=O)CC2=CNC3=C2C=CC=C3)=O)[C@H](CC4=CC=CC=C4)N(C(CCl)=O)C
	Chemical name	Ethyl (S)-2-((S)-2-((S)-1-(N-(2-chloroacetyl)-N-methyl-L-phenylalanyl)piperidine-2-carboxamido)-3-(1H-indol-3-yl)propanamido)-5-ureidopentanoate
	Entries in chemical databases	N/A
	Availability	N/A
	Additional comments	Negative control, BJP-06-115-3, also available. As well as Desthiobiotin-tagged probe, BJP-DTB (BJP-05-171-3)
In vitro profiling	Target (potency)	Pin1: K_i = 15 nM (FP assay); IC_{50} = 48 nM (PPIase assay)
	Selectivity	Highly selective for Pin1 Cys113 (by CITe-Id)
	Potential reactivity	Chloroacetamide electrophile
	SAR	Described in Pinch et al. Nature Chem Biol (2020).
	Mechanism of inhibition	Covalent inhibitor targeting Pin1 Cys113
	Structure of target-probe complex	PDB 6O34 (Pin1 bound to BJP-07-017-3, derivative of BJP-06-005-3 with C-terminal amide)
Cellular profiling	Validation of cellular target	Pin1 target engagement in competition pull-down assays with BJP-DTB. Target engagement achieved at 5-10 µM doses in live cells.
	Validation of cellular specificity	CITe-Id in PATU-8988T cell lysates
Pharmacodynamics		N/A – poor mouse microsome stability
Pharmacokinetics		

Synthetic scheme