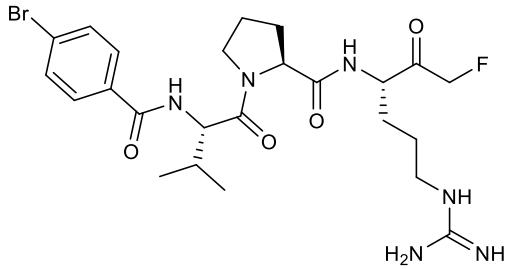
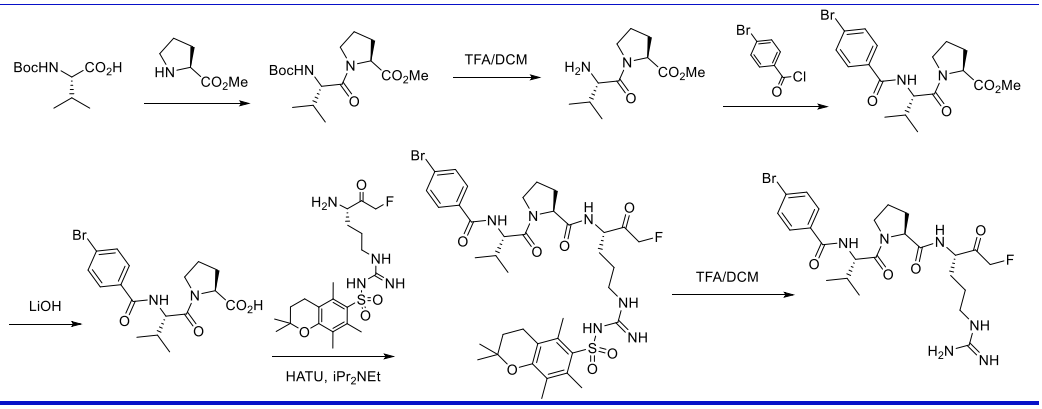
SCM-02-138



Chemical Formula: $C_{24}H_{34}BrFN_6O_4$
Molecular Weight: 569.48

Category	Parameter	Description
Compound	Name	SCM-02-138 (Cpd 3 in J Clin Inv; Cpd 22 in BMCL)
	Citation	*J Clin Invest.* **2018**, *128*, 4397. https://www.ncbi.nlm.nih.gov/pubmed/30024860 *Bioorg Med Chem Lett.* **2019**, 29, 1336 https://www.ncbi.nlm.nih.gov/pubmed/30954428
	Chemical descriptors	O=C(CF)[C@H](CCCNC(N)=N)NC([C@@H]1CCCN1C([C@@H](NC(C2=CC=C(Br)C=C2)=O)C(C)C)=O)=O
	Chemical name	(S)-1-((4-bromobenzoyl)-L-valyl)-N-((S)-1-fluoro-6-guanidino-2-oxohexan-3-yl)pyrrolidine-2-carboxamide
	Entries in chemical databases	
	Availability	None
	Papers that use the compounds	
	Additional comments	Compound was prepared as racemic at arginine residue for in vivo work
In vitro profiling	Target (potency)	MALT1 Ki 10nM;
	Target (potency)	
	Selectivity	Limited activity on other cysteine and serine proteases
	Potential reactivity	Forms covalent bond to cysteine at MALT1 active site, and
	SAR	Published in BMCL – good potency retained with modifications at proline, valine and LHS
	Mechanism of inhibition	Irreversible
	Structure of target-probe complex	Published in *J Clin Inv* reference
Cellular profiling	Validation of cellular target	Compound waspotent in cellular MALT1 protease assay, and OCI-Ly3 cell proliferation IC50 0.13uM (MALT1-dependent cell line).
	Validation of cellular specificity	The two cells assays showed a good correlation for the compounds tested.
Pharmacodynamics		Effects on hIL10 in TMD8 PD model. Moderate efficacy in TMD8 and OCI-LY3 xenograft models upon IP dosing.
Pharmacokinetics		Mouse IV PK: $T_{1/2}$ 0.25hr; Cl 13ml/min/kg


BocHN
CO2H
HN
CO2Me
BocHN
N
CO2Me
O
TFA/DCM
H2N
N
CO2Me
O
Br
Cl
O
Br
NH
N
CO2Me
O
O
LiOH
Br
NH
N
CO2H
O
O
H2N
O
F
NH
HN
NH
S
O
O
O
HATU, iPr2NEt
Br
NH
N
H
N
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TFA/DCM
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NH