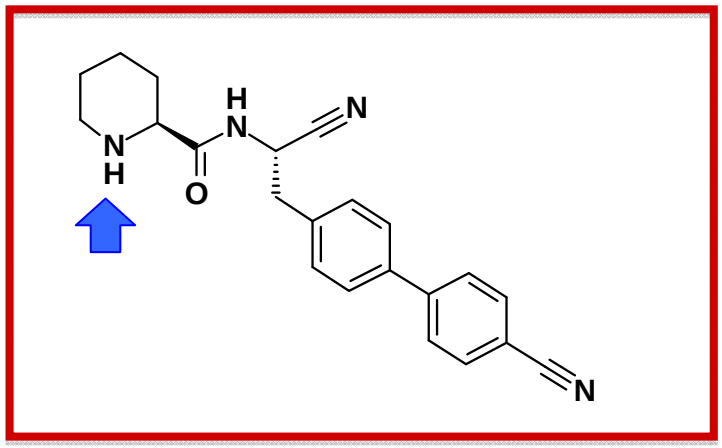
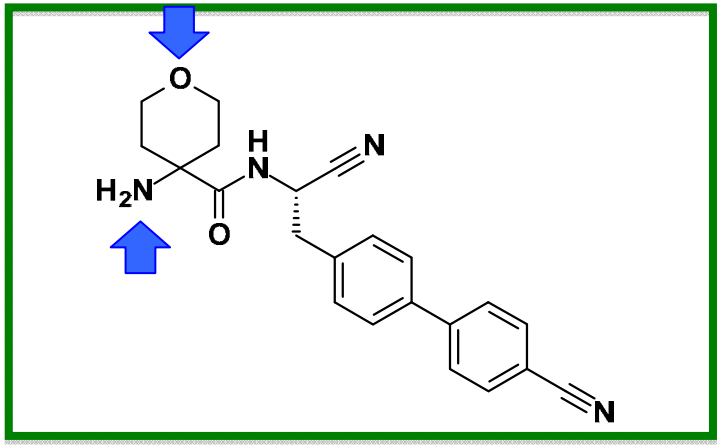
54 A Potent, Stable Cathepsin C Inhibitor With a Step Change in Properties Achieved Through Lead Hopping





Potency		
DPP1 enzyme pIC_{50}	7.7	**9.2**
DPP1 THP-cell pIC_{50}	8.0	**8.4**
WBP (calc)	6.3	**7.4**
Selectivity		
CatK pIC_{50}	6.6	**<5**
hERG IC_{50} (µM)	**1.4**	27
PLD EC_{50} (µM)	**9.2**	**>97** (top eff 34%)
DMPK		
In vitro Cl (µl/min/10^6 cells)		
rat,dog,human (heps)	6,11, 2	**3,<1,0.7**
Rat Cl (ml/min/kg) & F (%)	16, **75**	**9 ($T_{1/2}$ 4h), 92**
Dog Cl (ml/min/kg) & F (%)	22, **17**	**2, 72**
Predicted human uid dose (mg)	**106**	**6**

Come and see how we did it

Also revealing 'lowering levels of four active enzymes by inhibiting one'