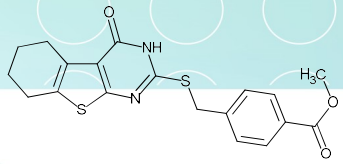
SL-83. Matrix Metalloproteinase 13 (MMP13) Inhibitors

A member of matrix metalloproteinase (MMP) family, MMP13 degrades fibrillar collagens at neutral pH. Abnormal expression of MMP13 is associated in several pathologic conditions including osteoarthritis and cancer [1]. Inhibitors for MMPs are under investigation for the treatment of cancer, arthritis, and cardiovascular disease [2]. The development of potent subclass-selective inhibitors of these enzymes has been challenging. Recent advances in structure-based drug discovery provides many opportunities for a rational design of novel MMP13 inhibitors with improved selectivity, safety and bioavailability [3]. Several highly potent and isoform-selective MMP13 inhibitors have been developed by rational merging of pyrimidine-containing pharmacophore core with Zn^{2+} chelating and non-chelating units.

Several analogs of the reported inhibitors containing pyrimidine core were included into this library



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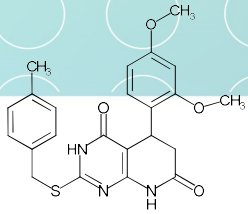

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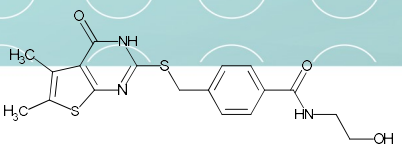

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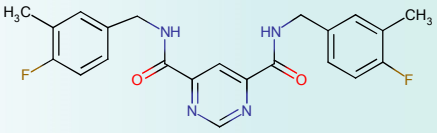
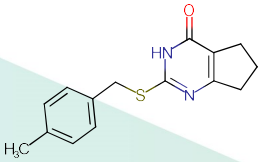
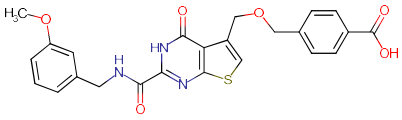


Compound 4 [1]



Compound 5 [2]



Compounds 4 [2]

Signature Library 83

Formats	Supplementary Information
80 compounds per plate 0.1 mg; 1 mg; 2 mg dry film/powder 0.1 µmol; 1 µmol DMSO solutions	SL#83_MPP13_inhibitors.sdf

References:

1. *Chem Biol. 2005 Feb;12(2):181-9*. doi: 10.1016/j.chembiol.2004.11.014
2. *Nat Rev Drug Discov. 2007 Jun;6(6):480-98.*. doi: 0.1038/nrd2308

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