SL-84. Modulators of TRPC 3/6/7 Channels

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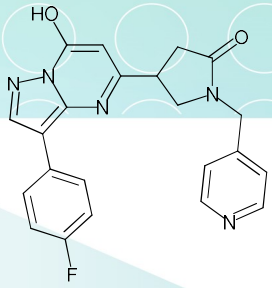
Canonical transient receptor potential channels (TRPC) constitute a family of polymodal ion channels permeable to cations, with a selectivity of calcium over sodium variable among the different members [1]. Structurally and functionally mammalian TRPCs can be divided into 4 major groups where the group consisting of TRPC3, TRPC6, and TRPC7 share a high degree of sequence similarity [2]. Effective and selective modulators of the TRPC3/6/7 ion channels are needed for understanding of their functional activity and drug development in cancer, kidney and cardiovascular diseases [2]. Using HTS and further SAR-enabling optimization a series of pyrazolopyrimidine derivatives has been recently discovered as potent agonists of TRPC3/6/7 channels [2]

Structural analogs of the reported ion channel modulators were included into this library



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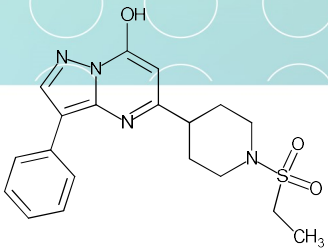

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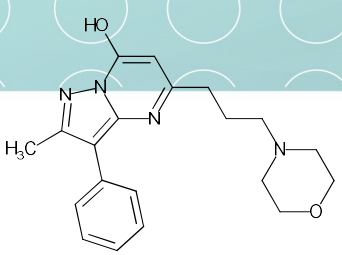

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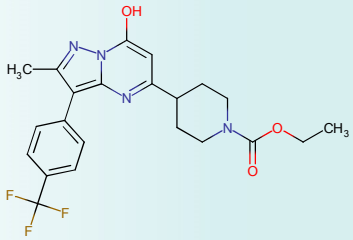
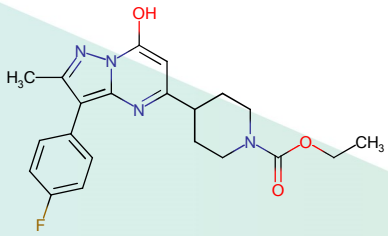
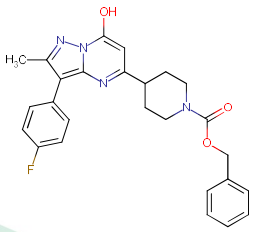


4n (potent lead) [2]



4o (primary hit) [2]



4p (potent lead) [2]

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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#84_TRPC_3_6_7.sdf

References:

1. *Physiol Rev. 2007 Jan;87(1):165-217*. doi: 10.1152/physrev.00021.2006
2. *J Med Chem. 2017 Jun 8;60(11):4680-4692*. doi: 10.1021/acs.jmedchem.7b00304

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