

(R)-ZINC-3573: A Chemical Probe for MRGPRX2

Version 1.0 (23rd March 2021)



Web link for more details: [https://www.sgc-ffm.uni-frankfurt.de/#!/specificprobeoverview/\(R\)-ZINC-3573](https://www.sgc-ffm.uni-frankfurt.de/#!/specificprobeoverview/(R)-ZINC-3573)

Overview

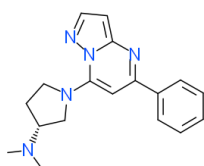
[MRGPRX2](#) is a class A orphan GPCR expressed in small diameter neurons in the dorsal root and trigeminal ganglia and mast cells. It is activated by basic secretagogues and neurokinins and mediates pseudo-allergic reactions. It is involved in neurogenic inflammation, pain and itch.

Summary

Chemical Probe Name	(R)-ZINC-3573
Negative control compound	(S)-ZINC-3573
Target(s) (synonyms)	MRGPRX2 (MAS related GPR family member X2)
Recommended cell assay concentration	< 1 μ M for (R)-ZINC-3573 and (S)-ZINC-3573; use with negative control for best interpretation of data
Suitability for <i>in vivo</i> use and recommended dose	This chemical probe was not tested for <i>in vivo</i> use
Publications	PMID: 28288109
Orthogonal chemical probes	
<i>In vitro</i> assay(s) used to characterise	
Cellular assay(s) for target-engagement	PRESTO-Tango concentration response assay, FLIPR
ChemicalProbes.org	Link to chemicalprobes.org

Chemical Probe & Negative Control Structures and Use

(R)-ZINC-3573 Chemical Probe



SMILES: CN(C)[C@@H]1CCN(C1)c1cc(c2ccccc2)nc2ccnn12

InChIKey: XKBSPA ZCFAIBJL-OAHLLOKOSA-N

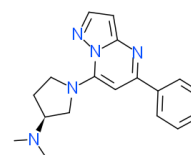
Molecular weight: 307.2

Storage: As a dry powder or as DMSO stock solutions (10 mM) at -20 °C.

DMSO stocks beyond 3-6 months or 2 freeze/thaw cycles should be tested for activity before use

Dissolution: Soluble in DMSO up to 10 mM; use only 1 freeze/thaw cycle per aliquot

(S)-ZINC-3573 *Negative* Control



SMILES: CN(C)[C@H]1CCN(C1)c1cc(c2ccccc2)nc2ccnn12

InChIKey: XKBSPA ZCFAIBJL-HNNXBMFYSA-N

Molecular weight: 307.2

Storage: As a dry powder or as DMSO stock solutions (10 mM) at -20 °C.

DMSO stocks beyond 3-6 months or 2 freeze/thaw cycles should be tested for activity before use

Dissolution: Soluble in DMSO up to 10 mM; use only 1 freeze/thaw cycle per aliquot

Chemical Probe Profile

In vitro Potency & Selectivity:

No off-target activity was found in concentration-response studies (tested 315 GPCRS in PRESTO-Tango GPCRome screening). Little activity was measured for 97 representative kinases in DiscoverX KINOMEScan at 10 μ M. The closest hits are [BTK](#) (Kd = 27 μ M), [MAPK8](#) (Kd = 19 μ M) and [MAPK10](#) (Kd > 30 μ M).

Potency in Cells and Cellular Target Engagement:

For (R)-ZINC-3573 an EC₅₀ = 740 nM was measured in the PRESTO-Tango concentration response assay and an EC₅₀ = 1 μ M in the FLIPR assay. Furthermore, (R)-ZINC-3573 induced intracellular calcium release and degranulation in LAD2 mast cells. In comparison, for (S)-ZINC-3573 an EC₅₀ > 100 μ M was found in the PRESTO-Tango and the FLIPR assay.