

BAY-390: A Chemical Probe for TRPA1

Version 2.0 (6th February 2023)

Web link for more details: <https://www.sgc-ffm.uni-frankfurt.de/#!/specificprobeoverview/BAY-390>

Overview

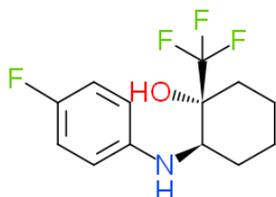
TRPA1 acts as a damage sensor activated by a wide range of endogenous mediators. Activated TRPA1 induces pain, central sensitization, neurogenic inflammation and mast cell-driven inflammation.

Summary

Chemical Probe Name	BAY-390
Negative control compound	BAY-9897
Target(s) (synonyms)	TRPA1 (transient receptor potential cation channel subfamily A member 1; ANKTM1)
Recommended <i>in vitro</i> assay concentration	Use at concentration of 100 nM for BAY-390 and BAY-9897; use with negative control and orthogonal probe for best interpretation of data
Suitability for <i>in vivo</i> use and recommended dose	BAY-390 shows a suitable pharmacokinetic profile for <i>in vivo</i> studies in rodents. It was tested in rats with 30 to 90 mg/kg PO twice a day for 10 days.
Publications	PMID: 36622903
Orthogonal chemical probes	A-079
<i>In vitro</i> assay(s) used to characterise	FLIPR
Cellular assay(s) for target-engagement	Ephys (Patchliner, CHO cells)

Chemical Probe & Negative Control Structures and Use

BAY-390 Chemical Probe



SMILES: C1CC[C@@]([C@@H](C1)Nc1ccc(cc1)F)(C(F)(F)F)O

InChiKey: IESAJAZKMLPVIB-VXGBXAGGSA-N

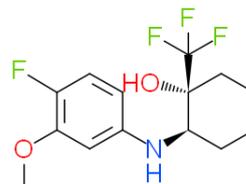
Molecular weight: 277.11

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

BAY-9897 Negative Control



SMILES: COc1cc(ccc1F)N[C@@H]1CCCC[C@@]1(C(F)(F)F)O

InChiKey: CWRARANSONEPBZ-CHWSQXEVSAN

Molecular weight: 307.12

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:

BAY-390 shows potent activity in a FLIPR Ca²⁺ assay (CHO or HEK cells): human TRPA1 (IC₅₀ = 16 nM), dog (IC₅₀ = 19 nM), rat (IC₅₀ = 63 nM, equipotent on rat, mouse, guinea pig and monkey TRPA1). Selectivity against family members was tested and for all > 30 fold (IC₅₀ [μM]: hTRPV1 (>25), hTRPV4 (>25), hTRPC3 (>25), hTRPC5 (5.6), hTRPC6 (>25), hKCNK9 (TASK-3) (>30), hCACNA1H (Cav3.2) (>25). Selectivity in Eurofins Lead Profiling Screen, GPCR Profiling Screen and Bayer Kinase Panel was performed. Closest off-targets are hSLC6A3 (K_i = 0.9 μM), hPGR (K_i = 4 μM) and ESR1 (EC₅₀ = 2.1 μM). BAY-9897 shows no activity in the FLIPR assay (IC₅₀ > 25 μM).

Potency in Cells and Cellular Target Engagement:

BAY-390 displays potent binding in an Ephys human TRPA1 (Patchliner, CHO cells) assay (IC₅₀ = 82 nM).