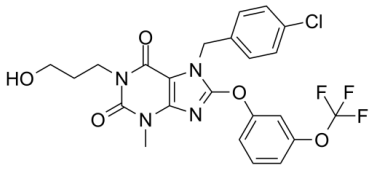
Data Sheet

Product Name:	Pico145
Cat. No.:	CS-0021610
CAS No.:	1628287-16-0
Molecular Formula:	C23H20ClF3N4O5
Molecular Weight:	524.88
Target:	TRP Channel
Pathway:	Membrane Transporter/Ion Channel; Neuronal Signaling
Solubility:	DMSO : ≥ 100 mg/mL (190.52 mM)



BIOLOGICAL ACTIVITY:

Pico145 is a remarkable inhibitor of **TRPC1/4/5** channels, inhibits (−)-englerin A-activated TRPC4/TRPC5 channels, with **IC_{50}**s of 0.349 and 1.3 nM in cells, and shows no effect on TRPC3, TRPC6, TRPV1, TRPV4, TRPA1, TRPM2, TRPM8. IC50 & Target: IC50: 0.349 nM (TRPC4, cell assay), 1.3 nM (TRPC5, cell assay), 0.03 nM (TRPC4-TRPC1, cell assay), 0.2 nM (TRPC5-TRPC1, cell assay)[1] **In Vitro:** Pico145 (Compound 31, C31) is a remarkable small-molecule inhibitor of TRPC1/4/5 channels, inhibits (−)-englerin A-activated TRPC4/TRPC5 channels, with IC_{50}s of 0.349 and 1.3 nM in cells; Pico145 shows no effect on TRPC3, TRPC6, TRPV1, TRPV4, TRPA1, TRPM2, TRPM8. Pico145 also inhibits human TRPC4-TRPC1 and TRPC5-TRPC1 concatemers expressed in HEK 293 Tet^+ cells (IC_{50}, 0.03 nM and 0.2 nM, respectively). The potency of Pico145 can be reduced by increased (−)-englerin A concentration. Furthermore, Pico145 potently inhibits RPC4-TRPC1 channels activated by sphingosine 1-phosphate (S1P), and suppresses S1P-evoked Ca^{2+} entry through TRPC4-TRPC1 channels with an IC_{50} of 0.011 nM. Pico145 also sensitizes EA-sensitive cancer cell line (Hs578T cells) (IC_{50}, 0.11 nM). Pico145 (100 nM) lacks effect on store-operated Ca^{2+} entry and histamine-evoked Ca^{2+} entry into endothelial cells[1].

PROTOCOL (Extracted from published papers and Only for reference)

Cell Assay: Pico145 is dissolved in DMSO, and diluted before use[1].[1]Cells are seeded at 90% confluence into 96-well clear-bottomed poly-d-lysine-coated black plates for **HEK 293 cells** and clear-bottomed Nunc plates for A498 cells, Hs578T cells, and HUVECs 24 h before experimentation. Fura-2 Ca^{2+} indicator dye is used to monitor changes in intracellular ionized Ca^{2+} concentration. To perform the experiment, the cells are incubated for 1 h with fura-2-AM (2 μM) in standard bath solution (SBS) at 37°C in the presence of 0.01% pluronic acid. SBS contains 135 mM NaCl, 5 mM KCl, 1.2 mM $MgCl_2$, 1.5 mM $CaCl_2$, 8 mM glucose, and 10 mM Hepes (pH titrated to 7.4 using NaOH). Subsequently, the cells are washed twice with SBS before adding **Pico145** or ML204 for 30 min before making **Ca^{2+} measurements**. The fura-2 fluorescence is recorded using a 96-well fluorescence plate reader and the excitation wavelengths of 340 and 380 nm. For TRPV4 recordings, fluo-4/AM is used in place of fura-2/AM, and 2.5 mM probenecid is included to inhibit leak of fluo-4. Fluo-4 is excited at 485 nm, and emitted light is collected at 525 nm. Ca^{2+} is indicated by the ratio of the fluorescence (F) emission intensities for the two excitation wavelengths. Measurements are made at room temperature (21 ± 3°C)[1].

References:

[1]. Rubaiy HN, et al. Picomolar, selective, and subtype-specific small-molecule inhibition of TRPC1/4/5 channels. J Biol Chem. 2017 May 19;292(20):8158-8173.

CAIndexNames:

1H-Purine-2,6-dione, 7-[(4-chlorophenyl)methyl]-3,7-dihydro-1-(3-hydroxypropyl)-3-methyl-8-[3-(trifluoromethoxy)phenoxy]-

SMILES:

O=C1C2=C(N=C(OC3=CC=CC(OC(F)(F)F)=C3)N2CC4=CC=C(Cl)C=C4)N(C)C(N1CCCO)=O

Caution: Product has not been fully validated for medical applications. For research use only.

Tel: 732-484-9848 Fax: 888-484-5008 E-mail: sales@ChemScene.com

Address: 1 Deer Park Dr, Suite Q, Monmouth Junction, NJ 08852, USA