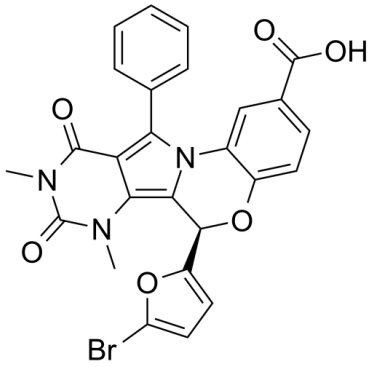
Data Sheet

Product Name:	(R)-BPO-27
Cat. No.:	CS-6272
CAS No.:	1415390-47-4
Molecular Formula:	C26H18BrN3O6
Molecular Weight:	548.34
Target:	Autophagy; CFTR
Pathway:	Autophagy; Membrane Transporter/Ion Channel
Solubility:	DMSO : ≥ 14.28 mg/mL (26.04 mM)



BIOLOGICAL ACTIVITY:

(R)-BPO-27 is a potent **CFTR** inhibitor with an **IC_{50}** of 4 nM. IC50 & Target: IC50: 4 nM[1] **In Vitro:** The benzopyrimido-pyrrolo-oxazinedione BPO-27 is an analogue of PPQ-102, which inhibits CFTR with an IC_{50} of 8 nM. The R enantiomer of BPO-27 inhibits CFTR chloride conductance with an IC_{50} of 4 nM, while S enantiomer is inactive. In vitro metabolic stability in hepatic microsomes shows both enantiomers as stable, with less than 5% metabolism in 4 h[1]. (R)-BPO-27 binds near the canonical ATP binding site. Whole-cell patch-clamp studies shows linear CFTR currents with a voltage-independent (R)-BPO-27 block mechanism. At a concentration of (R)-BPO-27 that inhibits CFTR chloride current by 50%, the EC_{50} for ATP activation of CFTR increases from 0.27 to 1.77 mM[2]. **In Vivo:** Following bolus interperitoneal administration in mice, serum (R)-1 decays with $t_{1/2}$ ≈ 1.6 h and gives sustained therapeutic concentrations in kidney[1].

PROTOCOL (Extracted from published papers and Only for reference)

Cell Assay: [2]Whole-cell recordings are done on CFTR-expressing CHO-K1 cells. After establishing the whole-cell configuration, BPO-27 is added for 5 minutes, and then CFTR is activated by the addition of forskolin (10 μM) in the continued presence of BPO-27 (0.5 or 1 μM). Whole-cell currents are elicited by applying hyperpolarizing and depolarizing voltage pulses from a holding potential of 0 mV to potentials between +80 and -80 mV in steps of 20 mV. Recordings are made at room temperature using an Axopatch-200B. Currents are digitized with a Digidata 1440A converter and filtered at 5 kHz[2]. **Animal Administration:** [1]Rats: (R)-BPO-27 is formulated at 1 mg/mL in 5% DMSO, 2.5% Tween-80 and 2.5% PEG400 in water. Male mice in a CD1 genetic background are administered 300 μL of the (R)-BPO-27 formulation by intraperitoneal injection. At specified times, blood samples are collected by eye bleed. At 4 h, kidneys are removed following renal arterial perfusion with PBS. Kidneys are weighed, mixed with acetic acid and homogenized for analysis[1].

References:

[1]. Snyder DS, et al. Absolute Configuration And Biological Properties of Enantiomers of CFTR Inhibitor BPO-27. ACS Med Chem Lett. 2013 May 9;4(5):456-459.

[2]. Kim Y, et al. Benzopyrimido-pyrrolo-oxazine-dione (R)-BPO-27 Inhibits CFTR Chloride Channel Gating by Competition with ATP. Mol Pharmacol. 2015 Oct;88(4):689-96.

CAIndexNames:

6H-Pyrimido[4',5':3,4]pyrrolo[2,1-c][1,4]benzoxazine-2-carboxylic acid, 6-(5-bromo-2-furanyl)-7,8,9,10-tetrahydro-7,9-dimethyl-8,10-dioxo-11-phenyl-, (6R)-

SMILES:

O=C(C1=CC=C(O[C@@H](C2=CC=C(Br)O2)C3=C(N(C)C4=O)C(C(N4C)=O)=C(C5=CC=CC=C5)N36)C6=C1)O

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

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