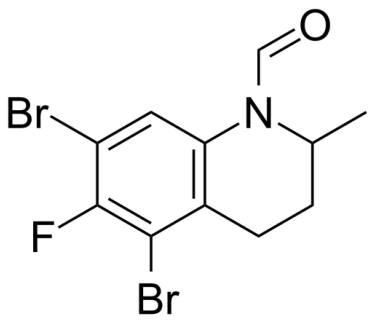
Data Sheet

Product Name:	CE3F4
Cat. No.:	CS-0029107
CAS No.:	143703-25-7
Molecular Formula:	$C_{11}H_{10}Br_2FNO$
Molecular Weight:	351.01
Target:	Ras
Pathway:	GPCR/G Protein
Solubility:	DMSO : 50 mg/mL (142.45 mM; Need ultrasonic)



BIOLOGICAL ACTIVITY:

CE3F4 is a selective antagonist of exchange protein directly activated by cAMP (**Epac1**), with **IC_{50}**s of 10.7 μM and 66 μM for Epac1 and Epac2(B), respectively. IC50 & Target: IC50: 10.7 μM (Epac1), 66 μM (Epac2(B))[1] **In Vitro:** CE3F4 is a selective antagonist of Epac1, with IC_{50}s of 10.7 μM and 66 μM for Epac1 and Epac2(B), respectively. CE3F4 is more active on Epac1 than (S)-stereoisomer ((S)-CE3F4, IC_{50}, 56 μM), but less active than (R)-CE3F4 (IC_{50}, 5.8 μM). CE3F4 (50 μM) shows more inhibitory activities against GEF activity of Epac1, than that of Epac2(AB) or Epac2(B)[1]. CE3F4 reduces the exchange activity of Epac1 induced by 007, with IC_{50} of 23 ± 3 μM. CE3F4 (40 μM) specifically inhibits Epac1 guanine nucleotide exchange activity without interference with Rap1 activity or Epac1-Rap1 interaction. CE3F4 has no influence on PKA activity. CE3F4 (20 μM) inhibits Epac-induced Rap1 activation in living cultured HEK293 cells[2]. CE3F4 (20 μM) significantly inhibits the late phase of ERK activation stimulated by glucose in INS-1 cells[3]. **In Vivo:** CE3F4 (1-3 mg/kg; through a catheter in the internal jugular vein) inhibits atrial fibrillation (AF) and CE3F4 (3 mg/kg; i.v.) inhibits ventricular arrhythmias[4].
CE3F4 (10 mg/kg; i.v.) improves cardiac function after myocardial infarction in mice[5].

PROTOCOL (Extracted from published papers and Only for reference)

Kinase Assay: [2]To determine Epac1 exchange activity, 200 nM of purified GST-Rap1A preloaded with bGDP are incubated at 22°C in exchange buffer (50 mM Tris-HCl (pH 7.5), 50 mM NaCl, 5 mM $MgCl_2$, 5 mM 1,4-dithioerythritol, 5% glycerol, 0.01% Nonidet P-40) in the presence of **100 nM purified GST-Epac1 or GST-Epac1-Cat**; 20 μM unlabeled GDP; and defined concentrations of cAMP, cyclic nucleotide analogs, and test compounds (**CE3F4**). Experiments are performed in black 384-well plates in a final volume of **30 μL**. bGDP fluorescence (excitation, 480 nm and emission, 535 nm) is measured using a multilabel plate reader[2]. **Cell Assay:** [3]Cells are cultured overnight in 96-well black-walled plates at 37°C and 5% CO_2, then washed twice in phosphate buffered saline. Cells are pre-incubated for two hours in glucose-free, modified KRBH supplemented with 0.05% fatty acid-free BSA at 37°C and 5% CO_2. The pre-incubation buffer is decanted, and cells are stimulated with 18 mM glucose in KRBH. Cells are incubated with or without inhibitors (**CE3F4**) in modified KRBH for 30 min at 37°C and 5 % CO_2 before **glucose stimulation**. The reactions are terminated at the indicated time points by decanting the treatments and fixing the cells with 4% formaldehyde. In experiments using pharmacological inhibitors, reactions are terminated 10 min after glucose stimulation is initiated. Total ERK and pERK is measured using the Phospho-ERK1 (T202/Y204) / ERK2 (T185/Y187) Cell-Based ELISA. Total ERK1/ERK2 is measured at 450 nm with excitation at 360 nm, and phosphorylated ERK1/ERK2 is measured at 600 nm with excitation at 540 nm, using a Synergy 4 Microplate Reader. The data are expressed as the ratio of pERK to total ERK then normalized and expressed as either fold over basal or % glucose response[3].

References:

[1]. Courilleau D, et al. The (R)-enantiomer of CE3F4 is a preferential inhibitor of human exchange protein directly activated by cyclic AMP isoform 1 (Epac1). Biochem Biophys Res Commun. 2013 Oct 25;440(3):443-8.

[2]. Courilleau D, et al. Identification of a tetrahydroquinoline analog as a pharmacological inhibitor of the cAMP-binding protein Epac. J Biol Chem. 2012 Dec 28;287(53):44192-202.

[3]. Pratt EP, et al. Ca2+ influx through L-type Ca2+ channels and Ca2+-induced Ca2+ release regulate cAMP accumulation and Epac1-dependent ERK 1/2 activation in INS-1 cells. Mol Cell Endocrinol. 2016 Jan 5;419:60-71.

[4]. Prajapati R, et al. Usefulness of Exchanged Protein Directly Activated by cAMP (Epac)1-Inhibiting Therapy for Prevention of Atrial and Ventricular Arrhythmias in Mice. Circ J. 2019;83(2):295-303.

[5]. Abstract 17548: Inhibition of Exchange Protein 1 Directly Activated by cAMP (Epac1) is Cardioprotective Against Ischemia-reperfusion Injury

CAIndexNames:

1(2H)-Quinolinecarboxaldehyde, 5,7-dibromo-6-fluoro-3,4-dihydro-2-methyl-

SMILES:

O=CN1C(C)CCC2=C1C=C(Br)C(F)=C2Br

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