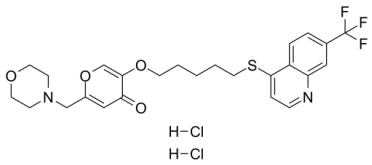
Data Sheet

Product Name:	EHT 1864
Cat. No.:	CS-3154
CAS No.:	754240-09-0
Molecular Formula:	C25H29Cl2F3N2O4S
Molecular Weight:	581.48
Target:	Ras
Pathway:	GPCR/G Protein
Solubility:	DMSO : ≥ 32 mg/mL (55.03 mM); H2O : ≥ 100 mg/mL (171.97 mM)



BIOLOGICAL ACTIVITY:

EHT 1864 is an inhibitor of **Rac family small GTPases**. EHT 1864 directly binds and impairs the ability of this small GTPase to engage critical downstream effectors required for growth transformation. The K_d values are 40, 50, 60, and 230 nM for Rac1, Rac1b, Rac2 and Rac3, respectively. EHT 1864 also potently inhibits other Rac-dependent transformation processes, Tiam1- and Ras-mediated growth transformation. EHT 1864 prevents Aβ 40 and Aβ 42 production in vivo[1][2][3]. **In Vivo:** EHT 1864 (oral administration) displays good tolerability, brain penetrance, and no genotoxicity. EHT 1864 (10 and 40 mg/kg/day; daily; 15 days; intraperitoneal injections) lowers brain Aβ 40 by 37% in guinea pigs[1].

PROTOCOL (Extracted from published papers and Only for reference)

Cell assay [2] To determine the effects of EHT 1864 treatment on the rate of cell proliferation, NIH 3T3 cells stably expressing oncogenic Ras were plated in 96-well plates at an initial density of 2 × 103 cells/well. The cells were cultured for up to 4 days in complete growth medium, either alone, or supplemented with 5 μM EHT 1864. Cell growth was then assessed using the conversion of 3-(4,5-dimethylthiazol-2-yl)-2,5-diphenyltetrazolium bromide (MTT, Sigma-Aldrich) to a formazan product (40). Briefly, the MTT reagent (from a 5 mg/ml solution diluted in PBS) was added to the wells at a final concentration of 0.5 mg/ml, and the cells were further incubated for 4 h at 37°C. The medium was then removed, and the reaction was terminated by adding 100 μl/well Me2SO. The absorbance was read at 570 nm using a microplate reader. Animal administration [1] EHT 1864 or vehicle (physiological saline) were injected in male Hartley albino guinea pigs, weighing 250–270 g at delivery and obtained from Charles River Laboratories (L'Arbresle, France), once a day for 15 consecutive days by the intraperitoneal route. 1 h after the final administration, the guinea pigs were killed; brains were immediately extracted and immersed in an oxygenated (95% O2, 5% CO2) physiological saline bath placed on ice (1–2 °C); and superficial vessels were removed. The whole brains were dissected to provide left and right cortices, which were weighed, snap-frozen in liquid nitrogen, and stored at –80 °C, separately. The maximum time between sacrifice and snap freezing was less than 15 min.

References:

[1]. Desire L, et al. RAC1 inhibition targets amyloid precursor protein processing by gamma-secretase and decreases Abeta production in vitro and in vivo. J Biol Chem. 2005 Nov 11;280(45):37516-25.

[2]. Shutes A, et al. Specificity and mechanism of action of EHT 1864, a novel small molecule inhibitor of Rac family small GTPases. J Biol Chem. 2007 Dec 7;282(49):35666-78.

[3]. Onesto C, et al. Characterization of EHT 1864, a novel small molecule inhibitor of Rac family small GTPases. Methods Enzymol. 2008;439:111-29.

CAIndexNames:

4H-Pyran-4-one, 2-(4-morpholinylmethyl)-5-[[5-[[7-(trifluoromethyl)-4-quinolinyl]thio]pentyl]oxy]-, hydrochloride (1:2)

SMILES:

O=C1C=C(CN2CCOCC2)OC=C1OCCCCCSC3=CC=NC4=CC(C(F)(F)F)=CC=C34.[H]Cl.[H]Cl

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