

## Product Data Sheet

Product Name: BPTU  
Cat. No.: GC19081

### Chemical Properties

Cas. No. 870544-59-5

SMILES O=C(NC1=CC=C(OC(F)(F)F)C=C1)NC2=CC=CN=C2OC3=CC=CC=C3C(C)(C)C

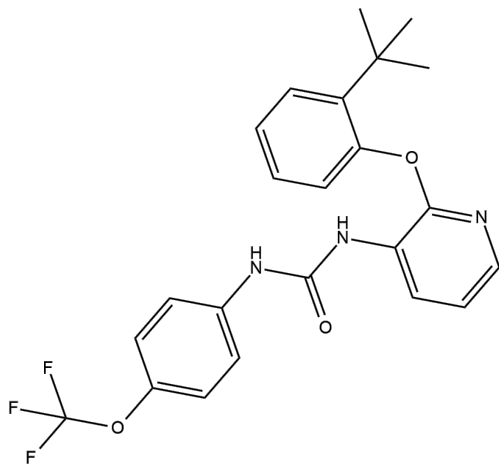
Formula  $C_{23}H_{22}F_3N_3O_3$  M.Wt 445.43

Solubility DMSO :  $\geq 33.3$  mg/mL (74.76 mM); Water :  $< 0.1$  mg/mL (insoluble) Storage Store at  $-20^{\circ}\text{C}$

General tips For obtaining a higher solubility, please warm the tube at  $37^{\circ}\text{C}$  and shake it in the ultrasonic bath for a while. Stock solution can be stored below  $-20^{\circ}\text{C}$  for several months.

Shipping Condition Evaluation sample solution : ship with blue ice All other available size: ship with RT, or blue ice upon request.

Structure



### Protocol

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

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**Cell experiment:** Electrophysiological experiments are performed with colonic rat and mouse strips. Inhibitory junction potentials (IJP) are elicited by electrical field stimulation (EFS) using two silver chloride plates placed 1.5 cm apart perpendicular to the longitudinal axis of the preparation. The protocol consists of single pulse trains of EFS (0.4 ms pulse duration) at increasing voltages (8, 12, 16, 20, 24, 28, 32, 36, 40 V). The voltage responsible for the supramaximal response is used to elicit single pulses during incubation with BPTU at increasing concentrations ( $1 \times 10^{-8}$  M,  $1 \times 10^{-7}$  M,  $3 \times 10^{-7}$  M,  $1 \times 10^{-6}$  M and  $3 \times 10^{-6}$  M). Another train of single pulses at increasing voltages is elicited after the highest dose of BPTU. The amplitude of the IJP (mV) is measured considering it as the difference between the maximal hyperpolarization and the resting membrane potential (RMP)[1].

**Animal experiment:** Mice are given BPTU intraperitoneally at doses of 3.15 mg of boron per kg body weight. Injection volumes range from 0.25 to 0.5 mL for both intravenous and intraperitoneal administrations. Six mice are not given any drug to allow measurement of boron background levels. Animals are killed with carbon dioxide 0.2, 0.4, 1, 2, 4, 24 and 48 h after drug administration and samples are taken from tumor, blood, skin, muscle, brain, kidneys and liver. Tumor tissue from mice bearing B16.013 tumor is checked by eye for the absence of pigmentation. BPTU is also given in a multiple dose scheme. Every 2 h 0.4 to 0.5 mL of the above-mentioned BPTU solution is given intraperitoneally ( $4 \times 3.15$  mg/kg boron). Twenty-four hours after the last administration, the animals are sacrificed and samples are taken[2].

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- [1]. Ma é N, et al. BPTU, an allosteric antagonist of P2Y<sub>1</sub> receptor, blocks nerve mediated inhibitory neuromuscular responses in the gastrointestinal tract of rodents. *Neuropharmacology*. 2016 Nov;110(Pt A):376-385.
- [2]. Verrijk R, et al. Pharmacokinetics in melanoma-bearing mice of 5-dihydroxyboryl-6-propyl-2-thiouracil (BPTU), a candidate compound for boron neutron capture therapy. *Br J Cancer*. 1994 Apr;69(4):641-7.

### Background

BPTU is a novel P2Y<sub>1</sub> allosteric antagonist.

BPTU blocks the supramaximal fast inhibitory junction potentials (fIJP) in a concentration-dependent manner both in the rat and mouse colon ( $P < 0.0001$  for both). The EC<sub>50</sub> of BPTU is approximately 0.3  $\mu$ M and 0.06  $\mu$ M for the rat and mouse colon, respectively. In the rat colon, addition of the P2Y agonist ADP $\beta$ S at 10  $\mu$ M significantly reduces spontaneous contractions to a  $43.2 \pm 13.4\%$  ( $N=5$ ) ( $P=0.0002$ ), and this reduction is blocked by 15 min incubation with BPTU at a concentration of 3  $\mu$ M ( $93.3 \pm 5.1\%$ ). Similar results are obtained in the murine colon where ADP $\beta$ S at 10  $\mu$ M reduces the area under the curve (AUC) of contractions to a  $15.8 \pm 5.1\%$  ( $N=4$ ) ( $P < 0.0001$ ) and its effect is reversed with BPTU at 3  $\mu$ M ( $82.7 \pm 3.6\%$ ). Addition of MRS2365, a selective P2Y<sub>1</sub> agonist, at a concentration of 5  $\mu$ M significantly reduces spontaneous contractions to a  $21.2 \pm 4.8\%$  ( $N=5$ ) ( $P=0.0002$ ) in the murine colon, and this reduction is blocked by 15 min incubation with BPTU at a concentration of 3  $\mu$ M ( $93.1 \pm 3.8\%$ ). The blockage of the MRS2365-induced response by BPTU at 3  $\mu$ M also occurs in control conditions ( $N=5$ ) ( $10.2 \pm 5.5\%$  vs.  $86.7 \pm 5.0\%$ )[1].

Uptake of BPTU from the peritoneal cavity is relatively rapid. Blood boron levels are maximal within 1 h after administration. After only 1 h, a boron tumor-to-blood ratio above 1 is found for BPTU in pigmented tumors, which is indicative of drug retention. This is not seen in the non-pigmented tumor variant, in which tumor boron levels closely follow blood levels. Up to 24 h, Borocaptate sodium (BSH) exhibits no selective retention in either tumor, but achieves higher maximum tumor boron concentrations than BPTU as a result of the administration of higher amounts of boron. During the tissue distribution phase, liver-to-kidney boron concentration ratios range from 2 to 4 for BSH and from 0.5 to 1 for BPTU[2].

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