

Product Data Sheet

Product Name: NS 1738

Cat. No.: GC13064

Chemical Properties

Cas. No. 501684-93-1

Chemical Name 1-(5-chloro-2-hydroxyphenyl)-3-(2-chloro-5-(trifluoromethyl)phenyl)urea

SMILES ClC1=CC(=C(C(F)(F)F)C=C1)NC(=O)NC2=CC(Cl)=CC=C2O

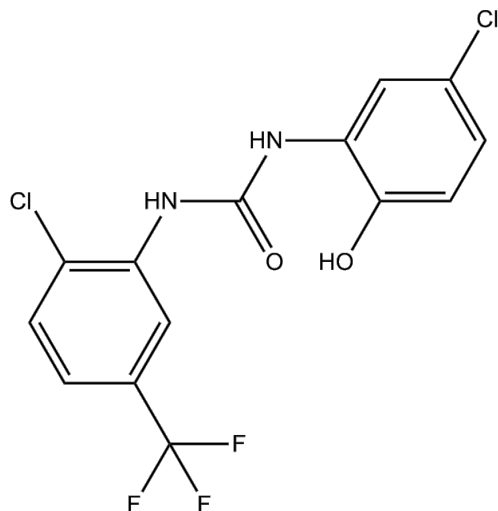
Formula $C_{14}H_9Cl_2F_3N_2O_2$ M.Wt 365.13

Solubility DMF: 25 mg/ml, DMSO: 25 mg/ml, DMSO: PBS (pH 7.2) (1:3): 0.25 mg/ml, Ethanol: 10 mg/ml
Storage Store at -20°C

General tips For obtaining a higher solubility, please warm the tube at 37 °C and shake it in the ultrasonic bath for a while. Stock solution can be stored below -20°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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Animal experiment: Rats[1]Sprague-Dawley rats are used. Adult (2-4 months; 400-450 g) and juvenile (50-60 g) animals are allowed to acclimate to the test room for 90 to 120 min before starting. After acclimation, adult rats are placed alone in their respective test cages. After a brief habituation period (30 min), they are allowed to interact for 5 min with a juvenile rat (trial; T1). During the interactive trial, the adult exhibits investigative behaviors that include close following, grooming, and/or sniffing of the juvenile for as much as 40 to 50% of the trial duration. The time of the investigative interaction is recorded in seconds. The juvenile rat is then removed, and the adult rats are immediately administered varying doses of NS 1738 (10 and 30 mg/kg NS-1738 i.p.) [prepared in 5% ethanol/95% hydroxypropyl-B-cyclodextrin (34% solution); 2.0 mL/kg i.p.] or Nicotine (0.1 mg/kg i.p.), and then they are returned to their home cage. A second 5-min interactive trial (T2) is conducted 120 min later in the same test cage, and investigative behavior of the adult rat is again monitored and the time is recorded. Recognition ratios of time spent investigating the familiar juvenile in T2 divided by time spent investigating the juvenile in T1 are calculated.

References:

[1]. Timmermann DB, et al. An allosteric modulator of the $\alpha 7$ nicotinic acetylcholine receptor possessing cognition-enhancing properties in vivo. J Pharmacol Exp Ther. 2007 Oct;323(1):294-307.

Background

NS 1738 (NSC 213859) is a novel positive allosteric modulator of the $\alpha 7$ nAChR, with respect to positive modulation of $\alpha 7$ nAChR ($EC_{50}=3.4 \mu M$ in oocyte experiments).

NS 1738 acts by increasing the peak amplitude of acetylcholine (ACh)-evoked currents at all concentrations; thus, it increased the maximal efficacy of ACh. Plotting peak current amplitude against the logarithm of the NS 1738 concentration used for preincubation reveals a sigmoidal concentration-response relationship that is well fit by the Hill equation ($EC_{50}=3.4 \mu M$). Under similar experimental conditions, NS 1738 shows comparable efficacy and potency at the rat $\alpha 7$ nAChR ($EC_{50}=3.9 \mu M$)[1].

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To estimate the ability of NS 1738 to permeate the blood-brain barrier, rats are administered 10 mg/kg NS 1738 intraperitoneally. Peak brain concentrations are measured approximately 30 min after injection, and they amount to ~80 ng/mL (~200 nM) at this dose. The ratio between the amount of compound entering the brain and that in plasma is $AUC_{\text{brain}} / AUC_{\text{plasma}} = 0.50$. The half-life in plasma is estimated to 42 min. Incubation of NS1738 with isolated liver microsomes in vitro indicates that approximately 60 and 75% of NS 1738 is metabolized via the cytochrome P450 system in mouse and rat, respectively, within 1 h. Adult rats administered NS 1738 at 10 and 30 mg/kg i.p. immediately following the initial exposure to a juvenile rat (T1) display significant decreases in the investigative duration of a subsequent exposure to the same juvenile (T2) 2 h later (T2/T1 ratio of 0.69 ± 0.13 and 0.61 ± 0.07 , respectively)[1].

Reference:

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