

Product Data Sheet

Product Name: β -Nicotyrine

Cat. No.: GC15056

Chemical Properties

Cas. No. 487-19-4

Chemical Name 3-(1-methyl-1H-pyrrol-2-yl)-pyridine

SMILES CN1C=CC=C1C2=CC=CN=C2

Formula $C_{10}H_{10}N_2$

M.Wt 158.2

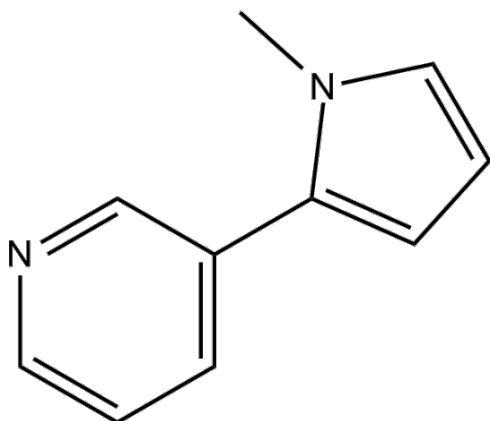
Solubility $\leq 50\text{mg/ml}$ in ethanol; 30mg/ml in DMSO; 50mg/ml in dimethyl formamide

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

Cell experiment [1]:

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Cell lines	Human HepaRG cells (metabolically competent hepatocyte cell line)
Preparation Method	HepaRG cells were treated with β -Nicotyrine (5–50 μ M) and the tobacco-specific nitrosamine NNK (100 μ M) for 12 hours.
Reaction Conditions	5-50 μ M; 12h
Applications	β -Nicotyrine significantly inhibited NNK bioactivation-induced DNA single-strand and double-strand breaks in HepaRG cells. The protective effect was comparable to the known CYP inhibitor PPITC. β -Nicotyrine achieved this by inhibiting the activity of cytochrome P450 (CYP) enzymes, particularly CYP2A6 and CYP2A13, thereby interfering with the metabolic activation of NNK.

Animal experiment [2]:

Animal models	Sprague-Dawley rats
Preparation Method	Rats were administered β -Nicotyrine (0.05-1.0mg/kg) and nicotine (0.0125-0.2mg/kg) subcutaneously either alone or in combination, with behavioral testing conducted at 10- and 60-minute pretreatment intervals using drug discrimination paradigms.
Dosage form	0.05-1.0mg/kg; s.c.; Single injection.

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Applications

β -Nicotyrine significantly slowed nicotine clearance by approximately 50% and prolonged nicotine's half-life from 68 to 125 minutes when administered at clinically relevant doses (25% of nicotine dose). β -Nicotyrine enhanced and prolonged the discriminative stimulus effects of nicotine, particularly at the 60-minute pretreatment interval, indicating increased nicotine discriminability. Unlike nicotine and nornicotine, β -Nicotyrine showed no binding affinity to nicotinic acetylcholine receptors ($\alpha 2\beta 2$, $\alpha 3\beta 4$, $\alpha 4\beta 2$) or other noncholinergic targets, and produced only weak nicotine-like subjective effects in female rats with no effects in males.

References:

- [1] Ordonez P, Sierra AB, Camacho OM, et al. Nicotine, cotinine, and β -nicotyrine inhibit NNK-induced DNA-strand break in the hepatic cell line HepaRG. *Toxicol In Vitro*. 2014 Jul 15:S0887-2333(14)00135-0.
- [2] Smethells JR, Wilde S, Muelken P, et al. β -Nicotyrine and e-cigarette abuse liability I: Pharmacodynamics and interaction with pharmacokinetics and discriminative stimulus effects of nicotine in rats. *Drug Alcohol Depend*. 2025 Dec 1;277:112949.

Background

β -Nicotyrine is a pyrolysis product of nicotine that can bind to cytochrome P450 (CYP) isoforms CYP2A6 and CYP2A13, and more effectively inhibit the activity of CYP2A6^[1-2]. By inhibiting CYP2A subtypes, β -Nicotyrine is able to suppress DNA strand breaks induced by genotoxic tobacco metabolites^[3-4].

In vitro, β -Nicotyrine (5–50 μ M) and Tobacco Nitrosamine (NNK; 100 μ M) were co-administered to metabolically active human hepatocyte cell line HepaRG for 12 hours, significantly inhibiting DNA single-strand and double-strand breaks induced by NNK bioactivation^[5].

In vivo, β -Nicotyrine (0.05–1.0mg/kg) and nicotine (0.0125–0.2mg/kg) were co-administered subcutaneously to Sprague-Dawley rats that had undergone nicotine discrimination training, with testing conducted at 10- and 60-minute pretreatment intervals. This treatment significantly enhanced

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and prolonged the discriminative stimulus effects of nicotine^[6].

References:

- [1] Kramlinger VM, von Weymarn LB, Murphy SE. Inhibition and inactivation of cytochrome P450 2A6 and cytochrome P450 2A13 by menthofuran, β -nicotyrine and menthol. *Chem Biol Interact.* 2012 May 30;197(2-3):87-92.
- [2] Denton TT, Zhang X, Cashman JR. Nicotine-related alkaloids and metabolites as inhibitors of human cytochrome P-450 2A6. *Biochem Pharmacol.* 2004 Feb 15;67(4):751-6.
- [3] Shigenaga MK, Kim BH, Caldera-Munoz P, et al. Liver and lung microsomal metabolism of the tobacco alkaloid beta-nicotyrine. *Chem Res Toxicol.* 1989 Sep-Oct;2(5):282-7.
- [4] Kurgat C, Kibet J, Cheplogoi P. Molecular modeling of major tobacco alkaloids in mainstream cigarette smoke. *Chem Cent J.* 2016 Jul 15;10:43.
- [5] Ordonez P, Sierra AB, Camacho OM, et al. Nicotine, cotinine, and β -nicotyrine inhibit NNK-induced DNA-strand break in the hepatic cell line HepaRG. *Toxicol In Vitro.* 2014 Jul 15:S0887-2333(14)00135-0.
- [6] Smethells JR, Wilde S, Muelken P, et al. β -Nicotyrine and e-cigarette abuse liability I: Pharmacodynamics and interaction with pharmacokinetics and discriminative stimulus effects of nicotine in rats. *Drug Alcohol Depend.* 2025 Dec 1;277:112949.

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