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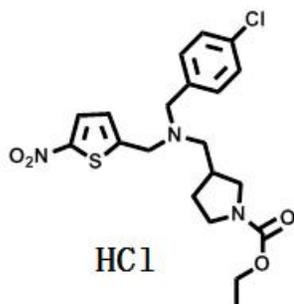
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## REV-ERB Agonist SR9009

**Chemical Name:** ethyl 3-(((4-chlorobenzyl)((5-nitrothiophen-2-yl)methyl)amino)methyl)pyrrolidine-1-carboxylate HCl salt



Molecular Weight:	474.40
Formula:	C <sub>20</sub> H <sub>25</sub> Cl <sub>2</sub> N <sub>3</sub> O <sub>4</sub> S
Purity:	≥98%
CAS#:	1379686-30-2
Solubility:	DMSO up to 100 mM
Storage	Powder: 4°C 1 year DMSO: 4°C 3 month -20°C 1 year

### Biological Activity:

SR9009 is a potent and specific synthetic REV-ERB agonist that binds to REV-ERB- $\alpha$  with an EC<sub>50</sub> ~670 nM and REV-ERB- $\beta$  with EC<sub>50</sub> ~800 nM. It also has good in vivo plasma/brain exposure. The nuclear receptors REV-ERB- $\alpha$  and REV-ERB- $\beta$  play an integral role in regulating the expression of core clock proteins, driving rhythms in activity and metabolism. Administration of SR9009 alters circadian behavior and the circadian pattern of core clock gene expression in the hypothalami of mice. The circadian expression pattern of an array of metabolic genes in the liver, skeletal muscle and adipose tissue was also altered, resulting in increased energy expenditure. Treatment of diet-induced obese mice with SR9009 decreased obesity by reducing fat mass and markedly improved dyslipidaemia and hyperglycaemia. It improves muscle mitochondrial function too. These results indicate that synthetic REV-ERB ligands that pharmacologically target the circadian rhythm may be beneficial in the treatment of sleep disorders as well as metabolic diseases.

### How to Use:

**In vitro:** SR9009 was used at 5-10  $\mu$ M concentration in vitro and in cellular assays.

**In vivo:** IP administration of SR9009 was used at 100 mg/kg once or twice per day for 12-30 days in different mouse models.

### Reference:

1. Solt LA, et al. Regulation of circadian behavior and metabolism by synthetic REV-ERB agonists. (2012) Nature 485(7396):62-8.
2. Cho H, et al. Regulation of circadian behavior and metabolism by REV-ERB- $\alpha$  and REV-ERB- $\beta$ . (2012) Nature 485(7396):123-7.
3. Woldt E, et al. Rev-erb- $\alpha$  modulates skeletal muscle oxidative capacity by regulating mitochondrial biogenesis and autophagy. (2013) Nat Med. 19(8):1039-46.
4. Banerjee S, et al. Pharmacological targeting of the mammalian clock regulates sleep architecture and emotional behaviour. (2014) Nat Commun. 5:5759.

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