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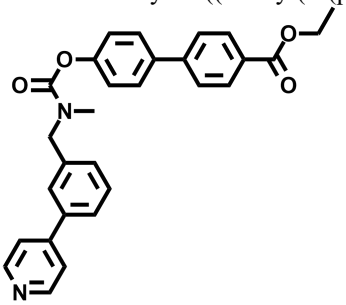
WWL113 --- Ces3 and Ces1f Inhibitor

Chemical Name: ethyl 4'-((methyl(3-(pyridin-4-yl)benzyl)carbamoyl)oxy)-[1,1'-biphenyl]-4-carboxylate



Molecular Weight:	466.53
Formula:	C29H26N2O4
Purity:	≥98%
CAS#:	947669-86-5
Solubility:	DMSO up to 50mM
Storage	Powder: 4ºC 1 year DMSO: 4ºC 3 month -20ºC 1 year

Biological Activity:

WWL113 is a novel potent and selective inhibitor of Ces3 and Ces1f with IC50 ~0.1 μM in cellular assays. WWL113 was discovered by a high throughput screen. Carboxylesterase 3 (Ces3, also known as Ces1d) plays a key role in lipid metabolism (e.g., hydrolyzing long-chain fatty acid esters and thioesters) and promotes lipid storage in adipocytes. Ces3 activity is markedly elevated during adipocyte differentiation. Treatment of two mouse models of obesity/diabetes with WWL113 ameliorates multiple features of metabolic syndrome, including enhancing insulin sensitivity and glucose tolerance and reducing hepatic diacylglycerol species. WWL113 serves as a very useful chemical tool to pharmacologically validate Ces3 as a new therapeutic target.

How to Use:

In vitro: WWL113 was used at 10 μM final concentration in various in vitro assays.

In vivo: WWL113 was administered by oral dosing once a day at a dose of 30-50 mg/kg in the model of diet-induced obesity ordb/db mice.

Reference:

1. Dominguez E, et al. Integrated phenotypic and activity-based profiling links Ces3 to obesity and diabetes. (2014) Nat Chem Biol. 10(2):113-21.