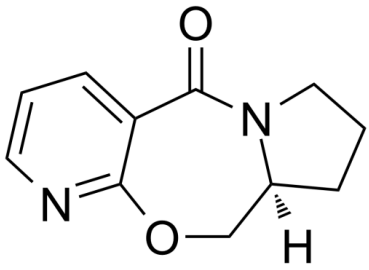
Data Sheet

Product Name:	Org-26576
Cat. No.:	CS-6250
CAS No.:	1026791-61-6
Molecular Formula:	C11H12N2O2
Molecular Weight:	204.23
Target:	iGluR
Pathway:	Membrane Transporter/Ion Channel; Neuronal Signaling
Solubility:	DMSO : 25 mg/mL (122.41 mM; Need ultrasonic)



BIOLOGICAL ACTIVITY:

Org-26576 is a **AMPA** receptor positive allosteric modulator. **In Vitro:** Org-26576 (Org 26576) represents structurally a distinct chemical series derived from the first generation ampakine CX516 and displays 10-30 fold greater potency when compared to CX516 in potentiating AMPA-mediated electrophysiological responses with an EC_{50} of 8-16 μM in rat hippocampal primary cultured neurons. Org-26576 demonstrates selectivity for AMPA receptors when tested at 10 μM against >60 molecular targets including G-Protein Coupled Receptors, ion channels and kinases[1]. **In Vivo:** Org-26576 (Org 26576; 1 mg/kg) produces significant increases in the anteroventral and laterodorsal thalamus, cingulate cortex, dentate gyrus and CA3 subfield of the hippocampus in mice[1]. Chronic administration of Org-26576 (Org 26576) increases progenitor cell proliferation in dentate gyrus (approximately 40%) and in prelimbic cortex (approximately 35%) at the 10-mg/kg dosage. Cells born in response to chronic Org-26576 in dentate gyrus exhibits increased rates of survival (approximately 30%) with the majority of surviving cells expressing a neuronal phenotype[2]. AMPA receptor potentiation by Org-26576 (Org 26576) exerts a positive modulatory influence on brain derived neurotrophic factor (BDNF) expression during ongoing neuronal activity. Total BDNF mRNA levels are significantly increased in the hippocampus of animals exposed to the combination of Org-26576 and stress[3].

PROTOCOL (Extracted from published papers and Only for reference)

Animal Administration: Org 26576 is prepared in saline.[1][3]Rats: Saline and Org-26576 (10 mg/kg) are administered, by intraperitoneal injection, 25 min before acute swim stress. Briefly, rats are subjected to a swim stress session for 5 min and sacrificed by decapitation 15 min after the end of the swim session. Brain regions are immediately dissected, frozen on dry ice and stored at -80°C[3].

Mice: Org-26576 (0.1, 1, 10 mg/kg) and Org 24448 (3, 10, 30 mg/kg) or vehicle (5% Mulgofenesaline) are administered intraperitoneally (i.p.) 10 min prior to the administration of the $_{14}$C-2-deoxyglucose. All drugs/vehicle are administered in the contralateral side of the abdomen to the $_{14}$C-2-deoxyglucose (2-DG) i.p. injection. A separate group of animals is also administered the AMPA receptor antagonist NBQX. NBQX (10 mg/kg) is injected either alone or 10 min prior to the administration of Org-26576 (10 mg/kg i.p.), Org 24448 (10 mg/kg i.p.) or vehicle (5% Mulgofenesaline i.p.). For each drug dose administered nZ5e7. The behavioural effects of all drugs administered are monitored throughout the entirety of procedure, and any alterations in behaviour noted[1].

References:

[1]. Jordan GR, et al. Regionally selective and dose-dependent effects of the ampakines Org 26576 and Org 24448 on local cerebral glucose utilisation in the mouse as assessed by 14C-2-deoxyglucose autoradiography. Neuropharmacology. 2005 Aug;49(2):254-64.

[2]. Su XW, et al. Chronic treatment with AMPA receptor potentiator Org 26576 increases neuronal cell proliferation and survival in adult rodent hippocampus. Psychopharmacology (Berl). 2009 Oct;206(2):215-22.

[3]. Fumagalli F, et al. The AMPA receptor potentiator Org 26576 modulates stress-induced transcription of BDNF isoforms in rat hippocampus. Pharmacol Res. 2012 Feb;65(2):176-81.

CAIndexNames:

5H,7H-Pyrido[3,2-f]pyrrolo[2,1-c][1,4]oxazepin-5-one, 8,9,9a,10-tetrahydro-, (9aS)-

SMILES:

O=C1N2[C@](CCC2)([H])COC3=NC=CC=C13

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