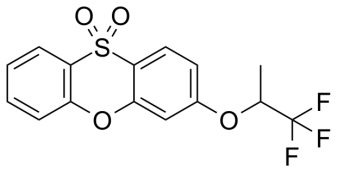
2614W94

Cat. No.:	HY-101578
CAS No.:	205187-35-5
Molecular Formula:	$C_{15}H_{11}F_3O_4S$
Molecular Weight:	344.31
Target:	Monoamine Oxidase
Pathway:	Neuronal Signaling
Storage:	Please store the product under the recommended conditions in the Certificate of Analysis.



BIOLOGICAL ACTIVITY

Description	2614W94 is a selective, reversible inhibitor of monoamine oxidase-A with a competitive mechanism of inhibition and IC_{50} of 5 nM and K_i of 1.6 nM with serotonin as substrate.
IC_{50} & Target	IC50: 5 nM (Monoamine Oxidase)[1] Ki: 1.6 nM (Monoamine Oxidase)[1]
In Vitro	2614W94 shows potent inhibitory activity against MAO-A, but shows no inhibition of MAO-B at 30 nM[1]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.
In Vivo	2614W94 (5 mg/kg, p.o.) produces selective inhibition of MAO-A in brains and livers of rats. 2614W94 (5 mg/kg, p.o.) also causes an elevation of neurotransmitter amines in brain, inparticular serotonin and norepinephrine, with a concomitant decrease in their oxidized metabolites. 2614W94 (0.5, 1, 2 mg/kg, p.o.) potentiates 5-hydroxytryptophan-induced head twitches in rats in a dose-dependent manner, with an extrapolated ED_{50} of 1.1 mg/kg[1]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

PROTOCOL

Kinase Assay [1]	MAO-A and -B forms are assayed. Rat brain mito-chondrial extract is pre-incubated with the inhibitor for 15 min at 37°C in 50 mM potassium phosphate buffer (pH 7.4). Substrates [^{3}H]serotonin (0.2 mM, 5 Ci/mol) and [^{14}C]β-phene-thylamine (10 μM, 3 Ci/mol) are then added, and incubation at 37°C is continued for 20 min. Blank assays contain 2 mM pargyline to inhibit all MAO activity. The reaction is terminated with 0.2 mL of 2 N HCl, and products are extracted with 6 mL of ethyl acetate/toluene (1:1). A 4 mL aliquot of the organic layer is countedin 10 mL of Ecolite in a scintillation spectrometer programmed for double-label counting. Assays are performed in triplicate unless otherwise indicated. At the above concentrations, serotonin is a selective substrate for MAO-A, and β-phenethylamine is aselective substrate for MAO-B. MCE has not independently confirmed the accuracy of these methods. They are for reference only.
Animal Administration [1]	Rats: Nonfasted Sprague-Dawley male rats (250-350 g) are dosed by gavage with 0.5% methyl cellulose or with 2614W94 or other compounds suspended in the methyl cellulose vehicle. For all groups, n = 3 unless otherwise specified. For oral administration, dosing volume is 10 mL/kg of body weight. For intravenous dosing, the vehicle is a mixture of PEG 400 (polyethylene glycol; molecular weight, 400), ethanol, and physiologic saline in a volume ratio of 1.5/1.5/1.0, respectively, and the dosing volume is 1 mL/kg. After dosing, rats are returned to their cages and allowed free access to water. Any

	animals kept overnight are also given food. Death is by CO_2 asphyxiation, after which brains and livers are promptly removed, frozen on dry ice, and stored at -70°C. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

REFERENCES

[1]. Helen L. White, et al. Biochemical and Pharmacologic Properties of 2614W94, a Reversible, Competitive Inhibitor of MonoamineOxidase-A. DRUG DEVELOPMENT RESEARCH 45:1-9 (1998).

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