

PF-9366

## Chemical Properties

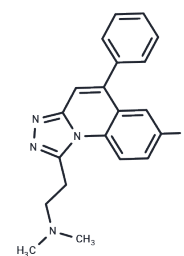
CAS No. : 72882-78-1

Formula: C<sub>20</sub>H<sub>19</sub>ClN<sub>4</sub>

Molecular Weight: 350.84

Storage: Powder: -20°C for 3 years | In solvent: -80°C for 1 year

Actual storage temperature shall be subject to the COA.



## Biological Description

Description	PF-9366 is a human methionine adenosyltransferase 2A (Mat2A) inhibitor with an IC <sub>50</sub> of 420 nM and a K <sub>d</sub> of 170 nM.
Targets(IC <sub>50</sub> )	Methionine Adenosyltransferase (MAT)
In vitro	H520 lung carcinoma cells were treated with PF-9366 for 6 h. PF-9366 inhibited cellular SAM production with an IC <sub>50</sub> of 1.2 μM. The IC <sub>50</sub> s of PF-9366 was modestly decreased in the H520 cells with Mat2B knockdown, to 0.86 μM. Huh-7 cells were more sensitive to compound exposure than the H520 cell line. After 6-h exposure to PF-9366, the IC <sub>50</sub> for SAM synthesis inhibition was 225 nM.
Kinase Assay	The Mat2A and Mat2B proteins are extensively dialyzed into a buffer containing 150 mM KCl, 25 mM HEPES, pH 7.4, 5 mM MgCl <sub>2</sub> , 5% (v/v) glycerol, 2 mM TCEP. Concentrations are determined spectrophotometrically using an ε <sub>280</sub> of 44,350 /M.cm for Mat2A and an ε <sub>280</sub> of 36,440 /M.cm for Mat2B. PF-9366 are diluted from 100% DMSO stocks into a buffer without DMSO. In a typical experiment, nineteen 15 μL injections of 200 μM compound or 30-35 μM Mat2B are made into 10 μM Mat2A on a VP ITC or nineteen 2 μL injections of 200 μM compound into 10 μM Mat2A on an Auto iTC200.
Cell Research	Huh-7 cells are seeded at a concentration of 15,000 cells per well for 6-h incubation with compound (PF-9366) and 4,000 cells per well for 72-h incubation with the compound in 96-well plates in 200 μL of growth medium. NCI-H520 MAT2B knockdown cells are seeded at a concentration of 20,000 cells per well for 6 h incubation or 10,000 cells per well for 72 h incubation with the compound in 96 well plates in 200 μL of growth medium. Cells are allowed to attach overnight at 37°C with 5% CO <sub>2</sub> . A 5× solution of cycloleucine is prepared fresh from powder stock in the growth medium. Other compounds (PF-9366) are diluted in 100% DMSO using a three-fold dilution scheme and further diluted in growth medium to give 0.5% DMSO final. Consistency of cellular confluence for each cell line is monitored with the IncuCyte Zoom live cell imager. Proliferation is measured using CellTiterGlo reagent. Growth media is removed from the cell plates following compound treatment and 80 μL/well CellTiter Glo diluted 1:1 in PBS added.

## Solubility Information

## A DRUG SCREENING EXPERT

Solubility	DMSO: 13.18 mg/mL (37.57 mM), Sonication is recommended. (< 1 mg/ml refers to the product slightly soluble or insoluble)
In vivo Formulation	10% DMSO+90% Saline: < 1.32 mg/mL (3.76 mM), Lower concentrations may be soluble, but exact solubility limit is unknown. 10% DMSO+40% PEG300+5% Tween 80+45% Saline: 1.32 mg/mL (3.76 mM), Solution. <i>Please add the solvents sequentially, clarifying the solution as much as possible before adding the next one. Dissolve by heating and/or sonication if necessary. Working solution is recommended to be prepared and used immediately. The formulation provided above is for reference purposes only. In vivo formulations may vary and should be modified based on specific experimental conditions.</i>

### Preparing Stock Solutions

	1mg	5mg	10mg
1 mM	2.8503 mL	14.2515 mL	28.503 mL
5 mM	0.5701 mL	2.8503 mL	5.7006 mL
10 mM	0.285 mL	1.4252 mL	2.8503 mL
50 mM	0.057 mL	0.285 mL	0.5701 mL

Please select the appropriate solvent to prepare the stock solution, according to the solubility of the product in different solvents. Please use it as soon as possible.

Note: The dilution table applies only to solid products. For liquid products, please calculate the stock solution based on the stated concentration and/or density.

### Reference

Quinlan CL, et al. Targeting S-adenosylmethionine biosynthesis with a novel allosteric inhibitor of Mat2A. Nat Chem Biol. 2017 Jul;13(7):785-792.

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