NHC-triphosphate

Cat. No.: HY-135867

CAS No.: 34973-27-8

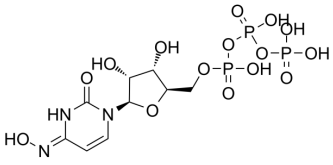
Molecular Formula: $C_9H_{16}N_3O_{15}P_3$

Molecular Weight: 499.16

Target: Topoisomerase; HCV; Endogenous Metabolite; Enterovirus; SARS-CoV

Pathway: Cell Cycle/DNA Damage; Anti-infection; Metabolic Enzyme/Protease

Storage: -20°C, protect from light, stored under nitrogen
* In solvent : -80°C, 6 months; -20°C, 1 month (protect from light, stored under nitrogen)



SOLVENT & SOLUBILITY

In Vitro

H_2O : 160 mg/mL (320.54 mM; Need ultrasonic)

Preparing Stock Solutions	Mass / Solvent / Concentration	1 mg	5 mg	10 mg
	1 mM	2.0034 mL	10.0168 mL	20.0337 mL
	5 mM	0.4007 mL	2.0034 mL	4.0067 mL
	10 mM	0.2003 mL	1.0017 mL	2.0034 mL

Please refer to the solubility information to select the appropriate solvent.

BIOLOGICAL ACTIVITY

Description

NHC-triphosphate is an active phosphorylated intracellular metabolite of β-d-N4-Hydroxycytidine (NHC) (HY-125033) as a triphosphate form[1]. NHC-triphosphate is a weak alternative substrate for the viral polymerase and can be incorporated into HCV replicon RNA[1][2].

In Vitro

In an intracellular metabolism assay, HCV replicon cells are treated with 10 μM ^{3}H-labeled NHC, and intracellular nucleotide levels are determined after 1, 2 and 8 hours incubations. NHC is rapidly convered into the mono-, di-, and triphosphate forms, and NHC-TP reaches up to 71.12 pM after 8 hours[1].

NHC-triphosphate (NHC-TP) (5-40 μM) absence leads to full-length polymerization products, it can be a weak alternative substrate. In addition, incorporation of NHC-TP instead of CTP increases the molecular weight of the polymerization product by 16 (one extra oxygen) for each event and an obvious electrophoretic shift is observed in cell-free HCV NS5B polymerization reactions[1].

Huh-7 cells are incubated with (10-50 μM; 4 h) NHC or a McGuigan phosphoramidate prodrug of NHC. Intracellular levels of the parental compounds and phosphorylated metabolites are measured using LC-MS/MS. Small amounts of NHC-monophosphate (MP) and NHC-diphosphate (DP) can be observed, while NHC-triphosphate (HY-135867) remains the most abundant metabolite[2].

NHC-triphosphate (NHC-TP) metabolite may directly target the viral polymerase and behave as a nonobligate chain

terminator. It plays a prominent role in inhibiting early negative-strand RNA synthesis, either through chain termination or mutagenesis, which may in turn interfere with correct replicase complex formation.

MCE has not independently confirmed the accuracy of these methods. They are for reference only.

CUSTOMER VALIDATION

- Nucleic Acids Res. 2021 Jan 8;49(D1):D1113-D1121.
- ACS Sens. 2022 May 27;7(5):1564-1571.
- Commun Biol. 2022 Feb 22;5(1):154.
- J Biol Chem. 2021 May 11;100770.
- ACS Bio Med Chem Au. October 24, 2022.

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REFERENCES

[1]. Stuyver LJ,et al. Ribonucleoside analogue that blocks replication of bovine viral diarrhea and hepatitis C viruses in culture.Antimicrob Agents Chemother. 2003 Jan;47(1):244-54.

[2]. Maryam Ehteshami, et al. Characterization of β-d- N4-Hydroxycytidine as a Novel Inhibitor of Chikungunya Virus.

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