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## Product Data Sheet

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Product Name: NHC-triphosphate tetrasodium

Cat. No.: GC61961

### Chemical Properties

Cas. No.

SMILES O[C@H]1[C@H](N(C=C/C2=N/O)C(N2)=O)O[C@H](COP(OP(OP(O[Na]))(O[Na])=O)(O[Na])=O)(O[Na])=O)[C@H]1OFormula  $C_9H_{12}N_3Na_4O_{15}P_3$  M.Wt 587.08Solubility Water : 100 mg/mL  
(170.33 mM) Storage Store at -20°C, sealed storage, away from moisture and light

General tips For obtaining a higher solubility , please warm the tube at 37 °C and shake it in the ultrasonic bath for a while. Stock solution can be stored below -20°C for several months.

Shipping Condition Evaluation sample solution : ship with blue ice All other available size: ship with RT , or blue ice upon request.

Structure NHC-triphosphate tetrasodium

### Background

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

In an intracellular metabolism assay, HCV replicon cells are treated with 10  $\mu$ M 3H-labeled NHC, and intracellular nucleotide levels are determined after 1, 2 and 8 hours incubations. NHC is rapidly converted 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  $\mu$ M) 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  $\mu$ M; 4 h) NHC or a McGuigan phosphoramidate prodrug of NHC. Intracellular levels of the parental compounds and

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phosphorylated metabolites are measured using LC-MS/MS. Small amounts of NHC-monophosphate (MP) and NHC-diphosphate (DP) can be observed, while NHC-triphosphate 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.

### 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  $\beta$ -d- N4-Hydroxycytidine as a Novel Inhibitor of Chikungunya Virus.

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