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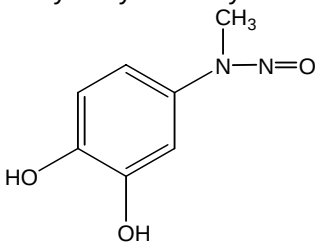
ProductInformation

Methyl-3,4-Dephostatin

Product Number **M 9440**
Storage Temperature 2–8 °C

Synonyms: 3,4-Dihydroxy-N-methyl-N-nitrosoaniline;



Product Description
Molecular Formula: $C_7H_8N_2O_3$
Molecular Weight: 168.15 (anhydrous)
Appearance: reddish brown powder
Purity: 98% by HPLC

Methyl-3,4-dephostatin is a stable synthetic analog of dephostatin and an inhibitor of the intracellular protein tyrosine phosphatases (PTPases) PTP-1B and SHPTP-1 (SHP-1).

Tyrosine phosphorylation and dephosphorylation are important regulatory components in signal transduction, neoplastic transformation, and the control of cell cycle progression. The activity of enzymes and regulatory proteins is tightly controlled by reversible phosphorylation of serine, threonine or tyrosine residues. PTPases catalyze the hydrolysis of the phosphoester bond of protein-bound phosphotyrosine. PTPases appear to be highly specific for phosphotyrosyl residues and do not structurally resemble either the protein serine/threonine phosphatases or the acid phosphatases and alkaline phosphatases. Mammalian PTPases can be subdivided into two broad categories. Transmembrane receptor PTPases contain linked cytoplasmic catalytic domains, while intracellular PTPases contain two tandem SRC homology 2 (SH2) domains. The transmembrane PTPases are involved in cell-cell or cell-matrix interactions and share properties with adhesion molecules.[1]

Dephostatin was isolated originally from the culture broth of a strain of *Streptomyces* MJ742-NF5.[2-4] In order to improve stability, the dephostatin analogues methyl-3,4-dephostatin and ethyl-3,4-dephostatin were synthesized.[3] However, only methyl-3,4-dephostatin inhibits the PTPase activity of CD45. This analogue is 10 times more stable than dephostatin in cell culture media.[3] It strongly inhibits the intracellular PTPases PTP1B and SHPTP-1, displaying an IC_{50} value of 0.58 µg/ml. Both PTP1B and SHPTP-1have been identified in insulin-sensitive tissues such as skeletal muscle, liver, and adipose tissue, and may play a role in the regulation of the insulin receptor or in insulin signaling.[3] Methyl-3,4-dephostatin prolongs the tyrosine phosphorylation and, thus, the activation of MAP kinase. Methyl-3,4-dephostatin competitively inhibits (K_i = 1.6 µM) the hydrolysis of p-nitrophenyl phosphate (pNPP) by *Streptomyces coelicolor* PTPAse.[4]

Research on the effect of the 3,4-dephostatin on the differentiation of rat pheochromocytoma PC12 cells has shown that the 3,4-dephostatin accelerated NGF-induced neurite formation in PC12h cells, a subline of PC12 cells, whereas the inhibitor alone did not induce neurite formation. It sustained the NGF-induced tyrosine phosphorylation of several proteins, most prominently that of mitogen-activated protein (MAP) kinase. EGF alone did not induce differentiation in PC12h cells, but it induced neurite formation in the presence of 3,4-dephostatin . The inhibitor also prolonged EGF-induced tyrosine phosphorylation.[5]

Preparation Instructions
Methyl-3,4-dephostatin is soluble in DMSO at 18 mg/ml with warming to 60 °C. It is insoluble in water.

Storage/Stability
Store under argon in a desiccator at 2–8 °C.

References

1. Kaplan, R., et al., Cloning of three human tyrosine phosphatases reveals a multigene family of receptor-linked protein-tyrosine-phosphatases expressed in brain. Proc. Nat. Acad. Sci, **87**, 7000-7004 (1990).
2. Imoto, M., et al., Dephostatin, a novel protein tyrosine phosphatase inhibitor produced by *Streptomyces*. I. Taxonomy, isolation, and characterization. J. Antibiot., **46,** 1342-1346 (1993).
3. Watanabe, T., et al., Structure-activity relationship and rational design of 3,4-dephostatin derivatives as protein tyrosine phosphatase inhibitors. Tetrahedron, **56**, 741-752 (2000).
4. Fujiwara, S., et al., Enhancement or induction of neurite formation by a protein tyrosine phosphatase inhibitor, 3,4-dephostatin, in growth factor-treated PC12h cells.Biochem. Biophys. Res. Commun**.**, **238**, 213-217 (1997).

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