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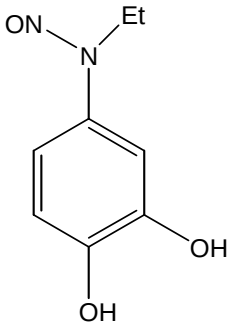
ProductInformation

Ethyl-3,4-Dephostatin

Product Number **E 1904**
Storage Temperature 2–8 °C

Synonyms: 3,4-Dihydroxy-N-ethyl-N-nitrosoaniline,



Product Description
Molecular Formula: $C_8H_{10}N_2O_3$
Molecular Weight: 182.18
Appearance: brown solid
Purity: >99% by HPLC
Melting Point: 130 °C

Ethyl-3,4-dephostatin is a stable synthetic analog of dephostatin that strongly inhibits the intracelular protein tyrosine phosphatases (PTPases) PTP-1B and SHPTP1 (SHP-1).[1,2]

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.[3]

Dephostatin was isolated originally from the culture broth of a strain of *Streptomyces* MJ742-NF5.[1,4] In order to improve stability, the dephostatin analogues methyl-3,4-dephostatin and ethyl-3,4-dephostatin were synthesized.[1]

Ethyl-3,4-dephostatin inhibits the intracellular PTPases PTP1B and SHPTP-1, which were 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.[1,2]
Ethyl-3,4-dephostatin inhibits PTP1B PTPase with an IC_{50} value of 0.58 µg/ml.[1] It also increases the phosphorylation of Akt, induces GLUT4 translocation, and mimics or potentiates the various activities of insulin; it activates the PI 3-kinase-independent signaling pathway. These effects are the result of ethyl-3,4-dephostatin-induced increase in tyrosine phosphorylation of the insulin receptor and insulin receptor substrate-1 with or without insulin.[2]

When administered orally to mice with high blood glucose, ethyl-3,4-dephostatin effectively lowers their blood glucose levels, producing a significant anti-diabetic effect. It also enhances the phosphorylation of other proteins, such as c-Cbl, phospholipase Cγ (PLCγ), phosphatidylinositol 3-kinase (PI3K) and insulin receptor 3 substrate (IRS-3). However, unlike dephostatin, this analog did not effectively inhibit CD45-associated PTPase.[2]

Preparation Instructions
Ethyl-3,4-dephostatin is soluble in DMSO at 22 mg/ml and in water at 8 mg/ml.

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

References
1. 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).

2. Suzuki, T., et al., Potentiation of insulin-related signal transduction by a novel protein-tyrosine phosphatase inhibitor, Et-3,4-dephostatin, on cultured 3T3-L1 adipocytes. J. Biol. Chem., **276**, 27511-27518 (2001).
3. 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).
4. 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).

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