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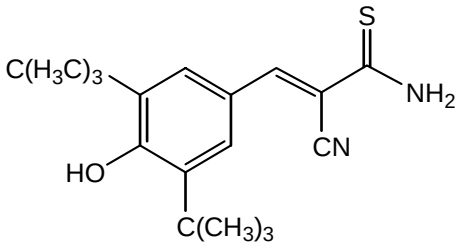
ProductInformation

TYRPHOSTIN AG 879

Product Number **T 2067**
Store at Room Temperature

Cas #: 148741-30-4
Synonyms: alpha-Cyano-(3,5-di-t-butyl-4-hydroxy)thiocinnamide; AG879



Product Description
Molecular Formula: $C_{18}H_{24}N_2OS$
Formula Weight: 316.47
Appearance: yellow solid
Purity: 99% by HPLC
Melting Point: 219-220°C

Tyrphostin AG 879 is a member of a family of synthetic tyrphostins, antineoplastic agents and protein tyrosine kinase antagonists and inhibitors. Tyrphostin AG 879 specifically inhibits nerve growth factor (NGF)-dependent TrkA tyrosine phosphorylation, as well as 140 *trk* protooncogene, and HER2/*neu*. HER2/Neu is a member of EGF receptors, the class I receptor tyrosine kinase family, which is the most frequently implicated in human cancer.[1,2]

Tyrphostin AG 879 inhibits NGF-dependent pp140c-trk tyrosine phosphorylation, without affecting tyrosine phosphorylation of epidermal growth factor or platelet-derived growth factor receptors. The tyrosine phosphorylation of the receptor-associated protein p38 is attenuated by tyrphostin AG 879 in time- and dose-dependent fashion. In addition, tyrphostin AG 879 also completely inhibits NGF-induced phosphorylation of PLC-γ1, phosphatidylinositol-3 (PI3) kinase activation, and MAP and raf-1 kinases induction. These results indicate that the tyrosine kinase activity of the TrkA NGF receptor is essential for the cellular actions of this growth factor. [3]

Tyrphostin AG-879 was used in *in vitro* studies of rat myogenic cell line L6, primary cultures of adult human myoblasts, and the human rhabdomyosarcoma cell line TE-671. All three cell types expressed NGF, p75 and TrKA receptors. Addition of tyrphostin AG879 in the low μM concentration inhibited TrkA signal transduction and resulted in a dramatic dose-dependent decrease in proliferation of all myogenic cell lines. This potent anti-proliferative effect of TrkA inhibitor on myogenic cells, and especially on the TE-671 rhabdomyosarcoma cell line, suggests that inhibition of NGF signal transduction could be effective in the control of the proliferation of these malignant cells.[4]

Note: Please refer to Sigma Catalog and Web Page for a full list of available Tyrphostins.

Preparation Instructions
Tyrphostin AG-879 is soluble in DMSO at 26 mg/ml and insoluble in water.

Storage/Stability
Store tightly sealed at room temperature.

References
1. Yeh, S., et al., From HER2/Neu signal cascade to androgen receptor and its coactivators: a novel pathway by induction of androgen target genes through MAP kinase in prostate cancer cells., Proc. Nat. Acad.Sci. U S A., **96**, 5458-5463 (1999).
2. Piccinotti, A., et al., Nerve growth factor induces sphingomyelin accumulation in pheochromocytoma cells. FEBS Lett., **472**, 143-147 (2000).
3. Ohmici, M., et al., The tyrosine kinase inhibitor tyrphostin blocks the cellular actions of nerve growth factor. Biochemistry, **17,** 4650-4658 (1993).
4. Rende, M., et al., Nerve growth factor (NGF) influences proliferation and differentiation of myogenic cells *in vitro* via TrKA. Int. J. Dev. Neurosci., **18,** 869-885 (2000).

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