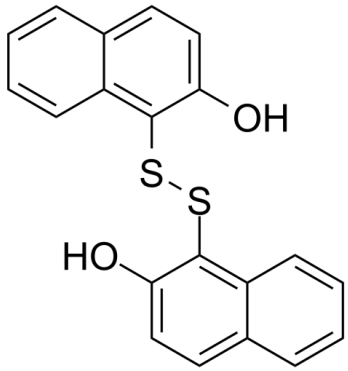
Data Sheet

Product Name:	IPA-3
Cat. No.:	CS-1432
CAS No.:	42521-82-4
Molecular Formula:	C20H14O2S2
Molecular Weight:	350.45
Target:	PAK
Pathway:	Cell Cycle/DNA Damage; Cytoskeleton
Solubility:	H2O : < 0.1 mg/mL (insoluble); DMSO : ≥ 100 mg/mL (285.35 mM)



BIOLOGICAL ACTIVITY:

IPA-3 is a selective non-ATP competitive **PAK1** inhibitor with **IC_{50}** of 2.5 μM, and shows no inhibition to group II PAKs (PAKs 4-6). **In Vitro:** IPA-3 inhibits Pak1 activation in part by binding covalently to the regulatory domain of Pak1. IPA-3 binds Pak1 covalently in a time- and temperature-dependent manner. IPA-3 prevents binding of the Pak1 activator Cdc42. IPA-3 binds directly to the Pak1 autoregulatory domain. IPA-3 reversibly inhibits PMA-induced membrane ruffling in cells[1]. IPA-3 (2 μM, 5 μM or 20 μM) reduces cell spreading in human primary Schwann and schwannoma cells. IPA-3 treatment significantly reduces the number of adherent Schwann and schwannoma cells in a dose-dependent manner[2]. IPA-3 is a non ATP-competitive, allosteric inhibitor of p21-activated kinase 1 (Pak1). PIR3.5 is the control compound of IPA-3. IPA-3 prevents Cdc42-stimulated Pak1 autophosphorylation on Thr423. IPA-3 also prevents sphingosine-dependent Pak1 autophosphorylation. IPA-3 does not target exposed cysteine residues on Pak1. The disulfide bond of IPA-3 is critical for inhibition of Pak1 and in vitro reduction by the reducing agent dithiothreitol (DTT) abolishes Pak1 inhibition by IPA-3. IPA-3 inhibits activation of Pak1 by diverse activators, but does not inhibit preactivated Pak1. IPA-3 inhibits PDGF-stimulated Pak activation in mouse embryonic fibroblasts[3].

PROTOCOL (Extracted from published papers and Only for reference)

Kinase Assay: [1]Pak1 (150 nM final) is pre-incubated with MBP (8.3 μM), indicated proteins, and IPA-3 or DMSO in Kinase buffer for 20 minutes at 4°C. Cdc42-GTPγS (3.2 μM) is then added and the reaction is pre-equilibrated 10 minutes at 30°C. Kinase reactions are started by the addition of ATP (to 30 μM) containing [^{32}P]ATP and are incubated 10 min and analyzed by SDS-PAGE and autoradiography. **Cell Assay:** [2]Human primary schwannoma cells are grown on 96 well plates for 2 days. Cells are left untreated or treated with 5 μM IPA-3, 20 μM IPA-3 or 20 μM PIR-3.5 for 24 hours. The MTS-solution is left on the cells for 3 hours, before the absorbance at 490 nm is measured. The experiments are conducted three times and mean and standard error of the mean is calculated with Excel.

References:

[1]. Viaud J, et al. An allosteric kinase inhibitor binds the p21-activated kinase autoregulatory domain covalently. Mol Cancer Ther. 2009 Sep;8(9):2559-65.

[2]. Flaiz C, et al. PAK kinase regulates Rac GTPase and is a potential target in human schwannomas. Exp Neurol. 2009 Jul;218(1):137-44.

[3]. Deacon SW, et al. An isoform-selective, small-molecule inhibitor targets the autoregulatory mechanism of p21-activated kinase. Chem Biol. 2008 Apr;15(4):322-31

CAIndexNames:

2-Naphthalenol, 1,1'-dithiobis-

SMILES:

OC1=CC=C2C=CC=CC2=C1SSC3=C4C=CC=CC4=CC=C3O

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