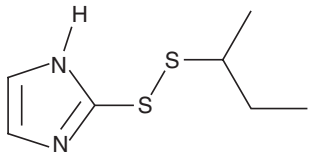
PRODUCT INFORMATION

PX 12

Item No. 14192

CAS Registry No.:	141400-58-0
Formal Name:	2-[(1-methylpropyl)dithio]-1H-imidazole
MF:	$C_7H_{12}N_2S_3$
FW:	188.3
Purity:	≥98%
UV/Vis.:	λ_{max}: 235 nm
Supplied as:	A crystalline solid
Storage:	-20°C
Stability:	≥4 years



Information represents the product specifications. Batch specific analytical results are provided on each certificate of analysis.

Laboratory Procedures

PX 12 is supplied as a crystalline solid. A stock solution may be made by dissolving the PX 12 in the solvent of choice. PX 12 is soluble in organic solvents such as ethanol, DMSO, and dimethyl formamide, which should be purged with an inert gas. The solubility of PX 12 in these solvents is approximately 20, 14, and 16 mg/ml, respectively.

PX 12 is sparingly soluble in aqueous solutions. To enhance aqueous solubility, dilute the organic solvent solution into aqueous buffers or isotonic saline. If performing biological experiments, ensure the residual amount of organic solvent is insignificant, since organic solvents may have physiological effects at low concentrations. We do not recommend storing the aqueous solution for more than one day.

Description

PX 12 is a competitive, irreversible inhibitor of thioredoxin 1 (Trx1), acting by binding to Cys^{73} of this enzyme.[1] As Trx1 is overexpressed in certain cancers, PX 12 is effective in suppressing the growth of cancer cells, with growth inhibition in a panel of 60 human tumors significantly correlated with expression of Trx1 mRNA.[2,3] Through its effects on Trx1, PX 12 reduces hypoxia-induced HIF-1α protein levels (IC_{50} = 7.2 µM), as well as expression of VEGF (IC_{50} = 10.4 µM) and iNOS (IC_{50} = 18.1 µM), culminating in attenuation of the proliferation of MCF-7 cells (IC_{50} = 1.9 µM) and HT-29 cells (IC_{50} = 2.9 µM) as well as reduced microvessel density in MCF-7 tumor xenografts.[4] PX 12 also blocks Trx-mediated activation of extracellular transglutaminase 2 (IC_{50} = ~3 µM) and Trx-1-increased expression and translation of CYP1B1.[5,6]

References

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2. Powis, G. and Montfort, W.R. Properties and biological activities of thioredoxins. *Annu. Rev. Biophys. Biomol. Struct.* **30**, 421-455 (2001).
3. Mukherjee, A. and Martin, S.G. The thioredoxin system: A key target in tumour and endothelial cells. *Br. J. Radiol.* **81**, S57-S68 (2008).
4. Welsh, S.J., Williams, R.R., Birmingham, A., *et al.* The thioredoxin redox inhibitors 1-methylpropyl 2-imidazolyl disulfide and pleurotin inhibit hypoxia-induced factor 1α and vascular endothelial growth factor formation. *Mol. Cancer Ther.* **2(3)**, 235-243 (2003).
5. Jin, X., Stamnaes, J., Klöck, C., *et al.* Activation of extracellular transglutaminase 2 by thioredoxin. *J. Biol. Chem.* **286(43)**, 37866-37873 (2011).
6. Husbeck, B. and Powis, G. The redox protein thioredoxin-1 regulates the constitutive and inducible expression of the estrogen metabolizing cytochromes P450 1B1 and 1A1 in MCF-7 human breast cancer cells. *Carcinogenesis* **23(10)**, 1625-1630 (2002).

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