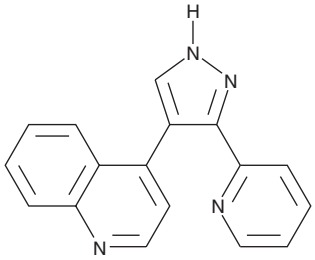
PRODUCT INFORMATION

LY364947

Item No. 13341

CAS Registry No.:	396129-53-6
Formal Name:	4-[3-(2-pyridinyl)-1H-pyrazol-4-yl]-quinoline
Synonyms:	HTS 466284, TGF-β RI Kinase Inhibitor
MF:	$C_{17}H_{12}N_4$
FW:	272.3
Purity:	≥98%
UV/Vis.:	λ_{max}: 229, 283 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

LY364947 is supplied as a crystalline solid. A stock solution may be made by dissolving the LY364947 in the solvent of choice, which should be purged with an inert gas. LY364947 is soluble in organic solvents such as DMSO and dimethyl formamide (DMF). The solubility of LY364947 in these solvents is approximately 1 and 2 mg/ml, respectively.

LY364947 is sparingly soluble in aqueous buffers. For maximum solubility in aqueous buffers, LY364947 should first be dissolved in DMF and then diluted with the aqueous buffer of choice. LY364947 has a solubility of approximately 0.5 mg/ml in a 1:1 solution of DMF:PBS (pH 7.2) using this method. We do not recommend storing the aqueous solution for more than one day.

Description

Transforming growth factor-β (TGF-β) signals through a cell surface heteromeric complex involving type I (TGF-β RI) and type II (TGF-β RII) receptors. Downstream signal transduction is mediated by the TGF-β RI kinase domain through the phosphorylation of Smad proteins. LY-364947 is a selective inhibitor of TGF-β RI (TGFR-I, TβR-I, ALK-5), with an IC_{50} value of 59 nM.[1] LY-364947 less effectively inhibits TGF-β RII (IC_{50} = 400 nM), p38 MAPK (IC_{50} = 740 nM), and mixed-lineage kinase 7 (MLK7; IC_{50} = 1,400 nM).[1,2] It inhibits TGF-β-induced cell growth (IC_{50} = 89 nM) in NIH 3T3 mouse fibroblasts and TGF-β-directed Smad phosphorylation, synthesis of fibronectin, PAI-1 and uPA protein, and matrigel invasion in MDA-MB-231 cells.[1,3]

References

1. Sawyer, J.S., Anderson, B.D., Beight, D.W., *et al*. Synthesis and activity of new aryl- and heteroaryl-substituted pyrazole inhibitors of the transforming growth factor-β type I receptor kinase domain. *J. Med. Chem* **46(19)**, 3953-3956 (2003).
2. Li, H., Wang, Y., Heap, C.R., *et al*. Dihydropyrrolopyrazole transforming growth factor-β type I receptor kinase domain inhibitors: A novel benzimidazole series with selectivity *versus* transforming growth factor-β type II receptor kinase and mixed lineage kinase-7. *J. Med. Chem* **49(6)**, 2138-2142 (2006).
3. Shiou, S.-R., Datta, P.K., Dhawan, P., *et al*. Smad4-dependent regulation of urokinase plasminogen activator secretion and RNA stability associated with invasiveness by autocrine and paracrine transforming growth factor. *J. Biol. Chem*. **281(45)**, 33971-33981 (2006).

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