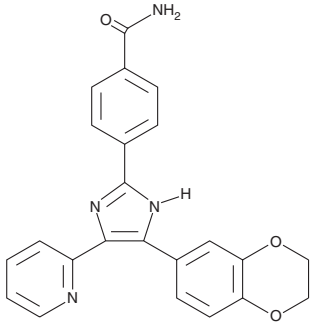
PRODUCT INFORMATION

D 4476

Item No. 13305

CAS Registry No.:	301836-43-1
Formal Name:	4-[4-(2,3-dihydro-1,4-benzodioxin-6-yl)-5-(2-pyridinyl)1H-imidazol-2-yl]-benzamide
Synonym:	Casein Kinase 1 Inhibitor
MF:	$C_{23}H_{18}N_4O_3$
FW:	398.4
Purity:	≥98%
UV/Vis.:	λ_{max}: 329 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

D 4476 is supplied as a crystalline solid. A stock solution may be made by dissolving the D 4476 in the solvent of choice, which should be purged with an inert gas. D 4476 is soluble in organic solvents such as ethanol, DMSO, and dimethyl formamide (DMF). The solubility of D 4476 in ethanol is approximately 10 mg/ml and approximately 30 mg/ml in DMSO and DMF.

D 4476 is sparingly soluble in aqueous buffers. For maximum solubility in aqueous buffers, D 4476 should first be dissolved in DMSO and then diluted with the aqueous buffer of choice. D 4476 has a solubility of approximately 0.1 mg/ml in a 1:10 solution of DMSO:PBS (pH 7.2) using this method. We do not recommend storing the aqueous solution for more than one day.

Description

D 4476 is a cell-permeant inhibitor of casein kianse 1 (CK1; IC_{50} = 200 nM from *S. pombe*, 300 nM for CK1δ).[1,2] It is a less effective inhibitor of PKD1 (IC_{50} - 9.1 µM) and p38α MAPK (IC_{50} = 5.8 µM), and only weakly affects the activities of a panel of kinases tested.[2] D 4476 blocks CK1-mediated phosphorylation of FOXO1a, RhoB, and p53.[1,3,4] As an inhibitor of ALK5, D 4476 prevents Smad3 activation and suppresses TGF-β1-induced gene expression without cytotoxicity in A498 cells.[5]

References

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2. Bain, J., Plater, L., Elliot, M., *et al*. The selectivity of protein kinase inhibitors: A further update. *Biochem. J*. **408(3)**, 297-315 (2007).
3. Tillement, V., Lajoie-Mazenc, I., Casanova, A. , *et al*. Phosphorylation of RhoB by CK1 impedes actin stress fiber organization and epidermal growth factor receptor stabilization. *Exp. Cell Res*. **314(15)**, 2811-2821 (2008).
4 MacLaine, N.J., Øster, B., Bundgaard, B., *et al*. A central role for CK1 in catalyzing phosphorylation of the p53 transactivation domain at serine 20 after HHV-6B viral infection. *J. Biol. Chem*. **283(42)**, 28563-28573 (2008).
5 Callahan, J.F., Burgess, J.L., Fornwald, J.A., *et al*. Identification of novel inhibitors of the transforming growth factor β1 (TGF-β1) type 1 receptor (ALK5). *J. Med. Chem*. **45(5)**, 999-1001 (2002).

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