

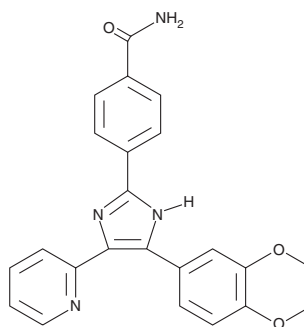
PRODUCT INFORMATION



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: C₂₃H₁₈N₄O₃
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 kinase 1 (CK1; IC₅₀ = 200 nM from *S. pombe*, 300 nM for CK1δ).^{1,2} It is a less effective inhibitor of PKD1 (IC₅₀ = 9.1 μM) and p38α MAPK (IC₅₀ = 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

1. Rena, G., Bain, J., Elliot, M., *et al.* D4476, a cell-permeant inhibitor of CK1, suppresses the site-specific phosphorylation and nuclear exclusion of FOXO1a. *EMBO reports* **5(1)**, 60-65 (2004).
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).

WARNING

THIS PRODUCT IS FOR RESEARCH ONLY - NOT FOR HUMAN OR VETERINARY DIAGNOSTIC OR THERAPEUTIC USE.

SAFETY DATA

This material should be considered hazardous until further information becomes available. Do not ingest, inhale, get in eyes, on skin, or on clothing. Wash thoroughly after handling. Before use, the user must review the complete Safety Data Sheet, which has been sent via email to your institution.

WARRANTY AND LIMITATION OF REMEDY

Buyer agrees to purchase the material subject to Cayman's Terms and Conditions. Complete Terms and Conditions including Warranty and Limitation of Liability information can be found on our website.

Copyright Cayman Chemical Company, 03/14/2024

CAYMAN CHEMICAL

1180 EAST ELLSWORTH RD
ANN ARBOR, MI 48108 · USA

PHONE: [800] 364-9897

[734] 971-3335

FAX: [734] 971-3640

CUSTSERV@CAYMANCHEM.COM
WWW.CAYMANCHEM.COM