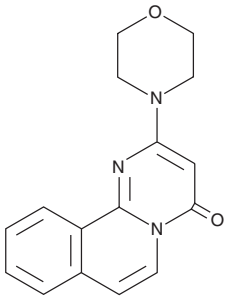
PRODUCT INFORMATION

Compound 401

Item No. 21769

CAS Registry No.:	168425-64-7
Formal Name:	2-(4-morpholinyl)-4H-pyrimido[2,1-a] isoquinolin-4-one
MF:	$C_{16}H_{15}N_3O_2$
FW:	281.3
Purity:	≥98%
UV/Vis.:	λ_{max}: 214, 252, 276 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

Compound 401 is supplied as a crystalline solid. A stock solution may be made by dissolving the compound 401 in the solvent of choice, which should be purged with an inert gas. Compound 401 is soluble in organic solvents such as ethanol, DMSO, and dimethyl formamide (DMF). The solubility of compound 401 in ethanol is approximately 0.5 mg/ml and approximately 1 mg/ml in DMSO and DMF.

Description

Compound 401 is an inhibitor of DNA-dependent protein kinase (DNA-PK) and mammalian target of rapamycin (mTOR; IC_{50}s = 0.28 and 5.3 µM, respectively).[1] It is selective for DNA-PK and mTOR over PI3K, ATM, and ATR (IC_{50}s = >100 µM for all). Compound 401 (10 µM) inhibits phosphorylation of the mTOR targets S6K1 and Akt in Rat-1 fibroblasts and in M059J glioma cells that lack DNA-PK.[2] It inhibits proliferation of mouse embryonic fibroblasts (MEFs) lacking tuberous sclerosis complex 1 (*TSC1*$^{-/-}$; IC_{50} = 2 µM), a complex associated with hamartomas that display hyperactive mTOR signaling, but not *TSC1*$^{+/+}$ MEFs. Compound 401 also induces apoptosis in *TSC1*$^{-/-}$ MEFs.

References

1. Griffin, R.J., Fontana, G., Golding, B.T., *et al.* Selective benzopyranone and pyrimido[2,1-a]isoquinolin-4-one inhibitors of DNA-dependent protein kinase: Synthesis, structure-activity studies, and radiosensitization of a human tumor cell line in vitro. *J. Med. Chem.* **48(2)**, 569-585 (2005).
2. Ballou, L.M., Selinger, E.S., Choi, J.Y., *et al.* Inhibition of mammalian target of rapamycin signaling by 2-(morpholin-1-yl)pyrimido[2,1-α]isoquinolin-4-one. *J. Biol. Chem.* **282(33)**, 24463-24470 (2007).

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