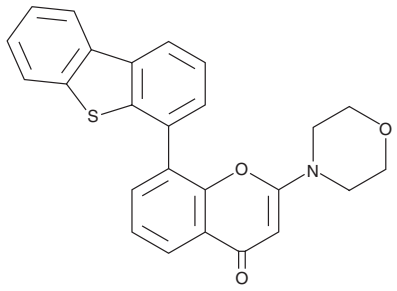
PRODUCT INFORMATION

NU 7441

Item No. 14881

CAS Registry No.:	503468-95-9
Formal Name:	8-(4-dibenzothienyl)-2-(4-morpholinyl)-4H-1-benzopyran-4-one
Synonym:	Ku-57788
MF:	$C_{25}H_{19}NO_3S$
FW:	413.5
Purity:	≥98%
UV/Vis.:	λ_{max}: 234, 288 nm
Supplied as:	A crystalline solid
Storage:	-20°C
Stability:	≥2 years



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

Laboratory Procedures

NU 7441 is supplied as a crystalline solid. A stock solution may be made by dissolving the NU 7441 in the solvent of choice. NU 7441 is soluble in organic solvents such as DMSO and dimethyl formamide (DMF), which should be purged with an inert gas. The solubility of NU 7441 in these solvents is approximately 0.12 and 1 mg/ml, respectively.

NU 7441 is sparingly soluble in aqueous buffers. For maximum solubility in aqueous buffers, NU 7441 should first be dissolved in DMF and then diluted with the aqueous buffer of choice. NU 7441 has a solubility of approximately 0.2 mg/ml in a 1:4 solution of DMF:PBS (pH 7.2) using this method. We do not recommend storing the aqueous solution for more than one day.

Description

DNA-dependent protein kinase (DNA-PK) catalyzes nonhomologous end-joining, which is required to repair lethal DNA double-strand breaks. Because cells that are defective in DNA double-strand break repair are highly sensitive to ionizing radiation and topoisomerase II poisons, modulating DNA-PK is one strategy to defer cancer cell resistance to radiation or chemotherapeutic treatments.[1] NU 7441 is a selective DNA-PK inhibitor with an IC_{50} value of 14 nM.[2] It inhibits other members of the PI3K-related kinase family, including mTOR, PI3K, ataxia telangiectasia mutated (ATM), and ataxia telangiectasia and Rad3 related (ATR) with IC_{50} values of 1.7, 5, >100, and >100 µM, respectively.[2] NU 7441 has been shown to increase the cytotoxicity of ionizing radiation and etoposide (Item No. 12092) in human colon cancer cell lines *in vitro* and to potentiate the effects of etoposide in mice bearing human colon cancer xenograft tumors *in vivo*.[3]

References

1. Veuger, S.J., Curtin, N.J., Richardson, C.J., *et al.* Radiosensitization and DNA repair inhibition by the combined use of novel inhibitors of DNA-dependent protein kinase and poly(ADP-ribose) polymerase-1. *Cancer Res.* **63(18)**, 6008-6015 (2003).
2. Leahy, J.J.J., Golding, B.T., Griffin, R.J., *et al.* Identification of a highly potent and selective DNA-dependent protein kinase (DNA-PK) inhibitor (NU7441) by screening of chromenone libraries. *Bioorg. Med. Chem. Lett.* **14(24)**, 6083-6087 (2004).
3. Zhao, Y., Thomas, H.D., Batey, M.A., *et al.* Preclinical evaluation of a potent novel DNA-dependent protein kinase inhibitor NU7441. *Cancer Res.* **66(10)**, 5354-5362 (2006).

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