

Product Data Sheet

Product Name: CRT0044876

Cat. No.: GC17231

Chemical Properties

Cas. No. 6960-45-8

Chemical Name 7-nitro-1H-indole-2-carboxylic acid

SMILES C1=CC2=C(C(=C1)[N+](=O)[O-])NC(=C2)C(=O)O

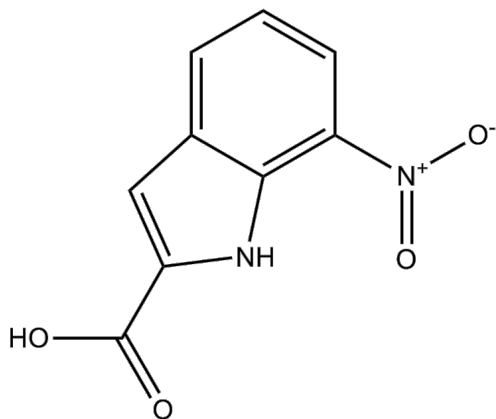
Formula $C_9H_6N_2O_4$ M.Wt 206.15

Solubility $\geq 55.6\text{mg/mL}$ in DMSO Storage Store at -20°C , protect from light

General tips For obtaining a higher solubility, please warm the tube at 37°C and shake it in the ultrasonic bath for a while. Stock solution can be stored below -20°C for several months.

Shipping Condition Evaluation sample solution: ship with blue ice All other available size: ship with RT, or blue ice upon request.

Structure



Protocol

Kinase experiment [1]:

Caution: Product has not been fully validated for medical applications. For research use only.

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AP site cleavage assay

BER reaction buffer comprised 40 mM HEPES-KOH (pH 7.8), 5 mM MgCl₂, 0.5 mM DTT and 0.1 mM EDTA. A 10 µL AP site cleavage reaction comprised of BER buffer mix, purified protein (3.3 nM final concentration of APE1) and 0.75 ng reduced AP site double-stranded oligonucleotide. The mixture was incubated at 37 °C for 1 hr. A total of 1 µL of stop buffer (50% glycerol, 10 mM Tris-HCl, 1 mM EDTA, 0.1% bromophenol blue and 0.1% Xylene cyanol) was added, and the sample mixture was denatured at 90 ~ 100 °C for 2 mins. The sample was then loaded on a 15% TBE Criterion Pre-Cast Gel, with electrophoresis at a constant current of 30 mA for 30 mins, and the radiolabeled substrate and reaction products were visualized using a phosphorImager. The inhibitory activity of potential APE1-targeting compounds was analyzed at drug concentrations ranging from 0.1 to 100 µM. The resolved radiolabeled bands were quantified using ImageQuant software analysis, and IC₅₀ values were calculated.

Cell experiment [1]:

Cell lines Human HT1080 fibrosarcoma cells

Preparation method The solubility of this compound in DMSO is > 55.6 mg/mL. General tips for obtaining a higher concentration: Please warm the tube at 37 °C for 10 minutes and/or shake it in the ultrasonic bath for a while. Stock solution can be stored below - 20 °C for several months.

Reacting condition 1 ~ 2 hrs

Applications In Human HT1080 fibrosarcoma cells, CRT0044876 significantly increased apurinic/apryrimidinic (AP) site accumulation. HT1080 cells treated with methylmethane sulfonate (MMS) also elevated the level of AP sites. The combination of CRT0044876 and MMS caused a synergistic increase in the level of AP sites.

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References:

[1]. Madhusudan S, Smart F, Shrimpton P, et al. Isolation of a small molecule inhibitor of DNA base excision repair. *Nucleic Acids Res*, 2005, 33(15): 4711-4724.

Background

CRT0044876 is a potent and selective inhibitor of APE1 with IC₅₀ value of 3.06 μ M [1].

Apurinic/apyrimidinic endonuclease-1 (APE1) is a member of the highly conserved exonuclease

III family of AP endonucleases and plays an important role in DNA repair. APE1 exhibits 3'-phosphodiesterase activity and weak 3'-phosphatase activity, 3'-5'-exonuclease activity and RNaseH activity [1].

CRT0044876 is a potent and selective APE1 inhibitor. In HeLa whole cell extract, CRT0044876 inhibited apurinic/apyrimidinic (AP) site cleavage catalyzed by APE1. CRT0044876 inhibited both the AP endonuclease and exonuclease activities of exonuclease III, the bacterial homologue of APE1. CRT0044876 inhibited the 3'-phosphoglycolate diesterase activity of APE1 with IC₅₀ value of 5 μ M and also inhibited 3'-phosphatase activity through binding to DNA repair active site of APE1. In HT1080 fibrosarcoma cells, CRT0044876 significantly increased AP site accumulation and was non-toxic at concentrations up to 400 μ M. Also, CRT0044876 potentiated the cytotoxicity induced by alkylating agent MMS, temozolomide, hydrogen peroxide and hmdUrd through specific inhibition of the base excision repair (BER) pathway [1].

Reference:

[1]. Madhusudan S, Smart F, Shrimpton P, et al. Isolation of a small molecule inhibitor of DNA base excision repair. *Nucleic Acids Res*, 2005, 33(15): 4711-4724.

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