

Product Data Sheet

Product Name: CA 074
Cat. No.: GC16317

Chemical Properties

Cas. No. 134448-10-5

Chemical Name (2S)-1-[(2S,3S)-3-methyl-2-[[[(3S)-3-(propylcarbamoyl)oxirane-2-carbonyl]amino]pentanoyl]pyrrolidine-2-carboxylic acid

SMILES CCCNC(=O)C1C(O1)C(=O)NC(C(C)CC)C(=O)N2CCCC2C(=O)O

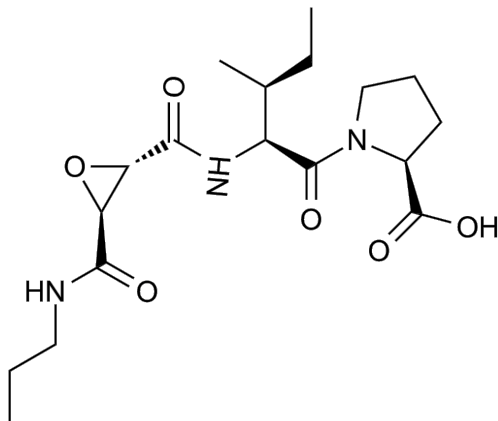
Formula $C_{18}H_{29}N_3O_6$ M.Wt 383.44

Solubility $\geq 19.17\text{mg/mL}$ in DMSO Storage Store at -20°C

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

Cell experiment [1]:

Cell lines HT29, DLD1, SW480 cells

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Preparation Method HT29, DLD1, and SW480 cells were cultured in soft agarose in the presence or absence of 10 μ M CA 074 for 2–3 week.

Reaction Conditions 10 μ M; 2–3 week

Applications CA 074 significantly inhibited cell invasion through Matrigel by approximately 45–60%.

Animal experiment [2]:

Animal models CD-1 male nude (nu/nu) mice

Preparation Method MM4 cells were injected into the hind leg muscle of mice. Beginning on day 6 after tumor implantation (tumor mass approximately 250mg), mice were treated with CA 074 at 10 mg/kg intravenously for eight consecutive days.

Dosage form 10mg/kg; i.v.

Applications CA 074 significantly inhibited tumor growth and suppressed the number of metastases in artificial lungs.

References:

[1]Bian B, Mongrain S, Cagnol S, et al. Cathepsin B promotes colorectal tumorigenesis, cell invasion, and metastasis[J]. Molecular carcinogenesis, 2016, 55(5): 671-687.

[2]Matarrese P, Ascione B, Ciarlo L, et al. Cathepsin B inhibition interferes with metastatic potential of human melanoma: an in vitro and in vivo study[J]. Molecular cancer, 2010, 9: 1-14.

Background

CA 074 is a selective inhibitor of cathepsin B with a K_i value of 2-5 nM. CA 074 is 10000-30000 times more potent against purified rat cathepsin B than against cathepsin H and L^[1]. CA 074 is a synthetic

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analog of E-64, a natural peptidyl epoxide that irreversibly inhibits most lysosomal cysteine proteases^[2]. CA 074 cannot cross cell membranes, but its methyl ester form, CA-074 Me (GC15917), can cross cell membranes^[3].

In vitro, CA 074 (10 μ M) treatment of HT29, DLD1, and SW480 cells for 2-3 weeks significantly inhibited cell invasion through Matrigel by approximately 45-60% ^[4].

In vivo, CA 074 (10 mg/kg) treated intravenously in mice inoculated with human melanoma cells significantly inhibited tumor growth and the number of lung metastases ^[5]. CA 074 (50 mg/kg) was injected intraperitoneally into 4T1.2 tumor-bearing mice, which significantly inhibited tumor growth, reduced tumor cathepsin B activity, and inhibited lung and bone metastasis^[6]. CA 074 (4 mg/kg) was injected intravenously into rats with focal cerebral ischemia, which significantly reduced the levels of cathepsin B and L and increased the number of eosinophilic (necrotic) and apoptotic neurons in brain tissue^[7].

References:

- [1] Towatari T, Nikawa T, Murata M, et al. Novel epoxysuccinyl peptides A selective inhibitor of cathepsin B, in vivo[J]. FEBS letters, 1991, 280(2): 311-315.
- [2] Matsumoto K, Mizoue K, Kitamura K, et al. Structural basis of inhibition of cysteine proteases by E-64 and its derivatives[J]. Peptide Science, 1999, 51(1): 99-107.
- [3] Patel N, Nizami S, Song L, et al. CA-074Me compound inhibits osteoclastogenesis via suppression of the NFATc1 and c-FOS signaling pathways[J]. Journal of Orthopaedic Research, 2015, 33(10): 1474-1486.
- [4] Bian B, Mongrain S, Cagnol S, et al. Cathepsin B promotes colorectal tumorigenesis, cell invasion, and metastasis[J]. Molecular carcinogenesis, 2016, 55(5): 671-687.
- [5] Matarrese P, Ascione B, Ciarlo L, et al. Cathepsin B inhibition interferes with metastatic potential of human melanoma: an in vitro and in vivo study[J]. Molecular cancer, 2010, 9: 1-14.
- [6] Withana N P, Blum G, Sameni M, et al. Cathepsin B inhibition limits bone metastasis in breast cancer[J]. Cancer research, 2012, 72(5): 1199-1209.
- [7] Özkara E, Durmaz R, Özbek Z, et al. The Effect of Ca-074 (Cathepsin B Inhibitor) on Necrotic and Apoptotic Neuronal Cell Death in Model of Cerebral Ischemia[J]. Osmangazi Tıp Dergisi, 2023, 45(5): 781-790.

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