Mc-MMAE

Cat. No.: HY-15741

CAS No.: 863971-24-8

Molecular Formula: $C_{49}H_{78}N_6O_{10}$

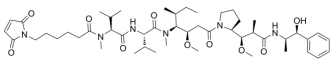
Molecular Weight: 911.18

Target: Microtubule/Tubulin; Drug-Linker Conjugates for ADC

Pathway: Cell Cycle/DNA Damage; Cytoskeleton; Antibody-drug Conjugate/ADC Related

Storage: 4°C, stored under nitrogen

* The compound is unstable in solutions, freshly prepared is recommended.



SOLVENT & SOLUBILITY

In Vitro

DMSO : 180 mg/mL (197.55 mM; Need ultrasonic)

H_2O : < 0.1 mg/mL (ultrasonic;warming;heat to 60°C) (insoluble)

Preparing Stock Solutions

Solvent / Mass / Concentration	1 mg	5 mg	10 mg
1 mM	1.0975 mL	5.4874 mL	10.9748 mL
5 mM	0.2195 mL	1.0975 mL	2.1950 mL
10 mM	0.1097 mL	0.5487 mL	1.0975 mL

Please refer to the solubility information to select the appropriate solvent.

In Vivo

1. Add each solvent one by one: 10% DMSO >> 90% (20% SBE-β-CD in saline)
   Solubility: 4.5 mg/mL (4.94 mM); Suspended solution; Need ultrasonic
2. Add each solvent one by one: 10% DMSO >> 90% corn oil
   Solubility: ≥ 4.5 mg/mL (4.94 mM); Clear solution

BIOLOGICAL ACTIVITY

Description

Mc-MMAE is a protective group (maleimidocaproyl)-conjugated monomethyl auristatin E (MMAE), which is a potent tubulin inhibitor. Mc-MMAE is a agent-linker conjugate for ADC.

IC_{50} & Target

Auristatin

In Vitro

Synthesis of maleimidocaproyl-MMAE (mc-MMAE) requires the addition of maleimidocaproic acid to a solution of MMAE in dichloromethane followed by the addition of diethyl cyanophosphonate and diisopropylethylamine[1].

MCE has not independently confirmed the accuracy of these methods. They are for reference only.

PROTOCOL

Kinase Assay [1]

Horseradish peroxidase (HRP) is thiolated with 2-iminothiolane and conjugated to mc-MMAE to generate the HRP-MMAE reporter enzyme-drug conjugate. Briefly, a thiolation reaction mixture containing 0.2 mM HRP (8 mg/mL) and 50 mM 2-iminothiolane in 25 mM sodium borate decahydrate ($Na_2B_4O_7•10H_2O$) buffer (pH 9.0) is incubated for 1 hour at 37°C. Unreacted 2-iminothiolane is removed by passage through a PD-10 desalting column equilibrated in PBS (pH 7.4). Peak fractions are pooled and mc-MMAE is coupled to thiolated HRP (HRP-SH) at a molar ratio of 3:1. The final conjugation reaction mixture contained 80 μM HRP-SH (3.2 mg/mL) in sodium borate buffer [50 mM H_3BO_3, 50 mM NaCl (pH 8.0); 80% v/v] and 240 μM mc-MMAE in ice-cold CH_3CN (20% v/v). After 30 minutes on ice, the reaction is terminated with a 20-fold molar excess of free cysteine (4.8 mM) before PD-10 chromatography. Peak fractions containing HRP-MMAE (exchanged into PBS) are pooled and evaluated for extent of modification using the thiol-reactive dye, Alexa Fluor 594 C_5 maleimide[1].

MCE has not independently confirmed the accuracy of these methods. They are for reference only.

REFERENCES

[1]. Sanderson RJ, et al. In vivo drug-linker stability of an anti-CD30 dipeptide-linked auristatin immunoconjugate. Clin Cancer Res. 2005 Jan 15;11(2 Pt 1):843-52.

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