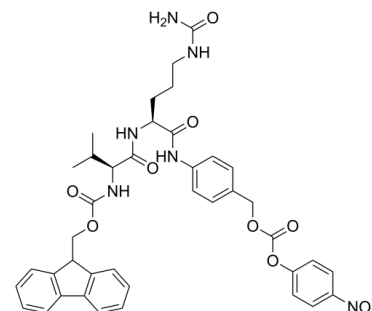


Data Sheet

Product Name:	Fmoc-Val-Cit-PAB-PNP
Cat. No.:	CS-5172
CAS No.:	863971-53-3
Molecular Formula:	C ₄₀ H ₄₂ N ₆ O ₁₀
Molecular Weight:	766.80
Target:	ADC Linker
Pathway:	Antibody-drug Conjugate/ADC Related
Solubility:	DMSO : ≥ 40 mg/mL



BIOLOGICAL ACTIVITY:

Fmoc-Val-Cit-PAB-PNP is a cleavable ADC linker used in the synthesis of antibody-drug conjugates (ADCs). Fmoc-Val-Cit-PAB-PNP has superior plasma stability comparable to that of non-cleavable linkers^{[1][2][3]}. *In Vitro*: Fmoc-Val-Cit-PAB-PNP contains peptide sequence degradable by a lysosome enzyme^[1].

Cathepsin B in the lysosome cleaves the peptide bond between Cit-PAB of dipeptide linkers containing Valine (Val)-citrulline (Cit) and p-aminobenzylalcohol (PAB). When PAB and a drug are binded covalently with carbamate bonds, the drug can be released by hydrolysis after cleavage of the peptide bond between Cit-PAB. Antibody-drug conjugates (ADCs) has been developed using this mechanism^[2].

In Vivo: Fmoc-Val-Cit-PAB-PNP linker stabilization in the mouse is an essential prerequisite for designing successful efficacy and safety studies in rodents during preclinical stages of ADC programs^[3].

Conjugation site plays an important role in determining VC-PABC linker stability in mouse plasma, and that the stability of the linker positively correlates with ADC cytotoxic potency both in vitro and in vivo^[3].

References:

- [1]. Dubowchik GM, et al. Cathepsin B-labile dipeptide linkers for lysosomal release of doxorubicin from internalizing immunoconjugates: model studies of enzymatic drug release and antigen-specific in vitro anticancer activity. *Bioconjug Chem.* 2002 Jul-Aug;13(4):855-69.
- [2]. Yoneda Y, et al. A cell-penetrating peptidic GRP78 ligand for tumor cell-specific prodrug therapy. *Bioorg Med Chem Lett.* 2008 Mar 1;18(5):1632-6.
- [3]. Dorywalska M, et al. Effect of attachment site on stability of cleavable antibody drug conjugates. *Bioconjug Chem.* 2015 Apr 15;26(4):650-9.

CAIndexNames:

L-Ornithinamide, N-[(9H-fluoren-9-ylmethoxy)carbonyl]-L-valyl-N5-(aminocarbonyl)-N-[4-[[[(4-nitrophenoxy)carbonyl]oxy]methyl]phenyl]-

SMILES:

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

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