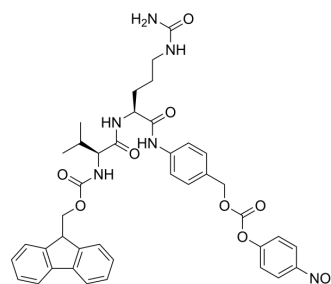


## Fmoc-Val-Cit-PAB-PNP

<b>Cat. No.:</b>	HY-41189
<b>CAS No.:</b>	863971-53-3
<b>Molecular Formula:</b>	C <sub>40</sub> H <sub>42</sub> N <sub>6</sub> O <sub>10</sub>
<b>Molecular Weight:</b>	766.8
<b>Sequence Shortening:</b>	Fmoc-V-Cit-PAB-PNP
<b>Target:</b>	ADC Linker
<b>Pathway:</b>	Antibody-drug Conjugate/ADC Related
<b>Storage:</b>	-20°C, stored under nitrogen
	* In solvent : -80°C, 6 months; -20°C, 1 month (stored under nitrogen)



### SOLVENT & SOLUBILITY

<b>In Vitro</b>	DMSO : ≥ 40 mg/mL (52.16 mM)				
	* "≥" means soluble, but saturation unknown.				
		<b>Mass</b>	<b>1 mg</b>	<b>5 mg</b>	<b>10 mg</b>
	<b>Preparing Stock Solutions</b>	<b>Concentration</b>			
	<b>1 mM</b>	1.3041 mL	6.5206 mL	13.0412 mL	
	<b>5 mM</b>	0.2608 mL	1.3041 mL	2.6082 mL	
	<b>10 mM</b>	0.1304 mL	0.6521 mL	1.3041 mL	
Please refer to the solubility information to select the appropriate solvent.					
<b>In Vivo</b>	1. Add each solvent one by one: 10% DMSO >> 90% corn oil Solubility: ≥ 5.25 mg/mL (6.85 mM); Clear solution				

### BIOLOGICAL ACTIVITY

<b>Description</b>	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 <sup>[1][2][3]</sup> .	
<b>IC<sub>50</sub> &amp; Target</b>	Protease Cleavable Linker	Cleavable Linker
<b>In Vitro</b>	Fmoc-Val-Cit-PAB-PNP contains peptide sequence degradable by a lysosome enzyme <sup>[1]</sup> . 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 <sup>[2]</sup> . MCE has not independently confirmed the accuracy of these methods. They are for reference only.	

## 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<sup>[3]</sup>.

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<sup>[3]</sup>.

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

## 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.

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

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