HYDROLYSIS STABLE ANALOGS

Phosphono Amino Acids

Chemical Mimicry

Transforming the phosphoester of Ser, Thr, and Tyr to a (fluorinated) phosphono derivative improves hydrolytic stability.

page 1

Phosphorylation is one of the most important activating post-translational modifications.
page 1

Cellular phosphatases are unable to remove phosphono groups.
page 1

Fluorination renders the phosphonic acid more acidic.
page 1

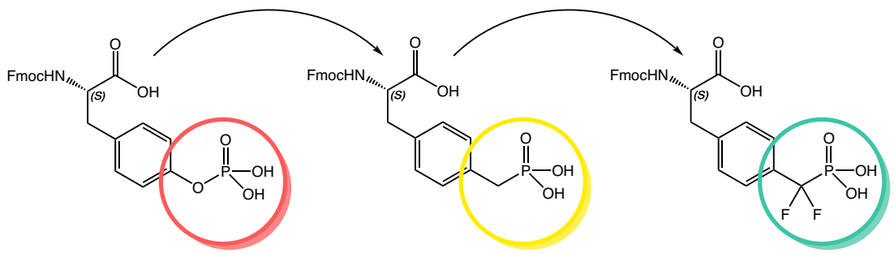
Version: IF9_3

Hydrolysis Stable Analogs

Phosphono Amino Acids

The preparation of synthetic phosphorylated peptides is of significant interest for research. Among posttranslational modifications that occur in organisms, phosphorylation of serine, threonine and tyrosine is counted among the most important activating ones. Nevertheless, from a chemical point of view, those phosphoesters are highly hydrolysis labile.

Iris Biotech presents hydrolysis-stable phosphono-amino acid derivatives of pSer, pThr, and pTyr, termed Pma (Ser), Pmab (Thr), and Pmp (Tyr) as well as their next generation fluorinated derivatives. Fluorination renders the phosphonic acid more acidic and thus an even better mimic of the parent phosphoamino acid while keeping the hydrolytic stability.



Improving stability: phosphoester vs. phosphono functionalization vs. fluorinated phosphono derivative.

The hydrolysis resistance of the phosphono-derivatives has an additional benefit: cellular phosphatases are unable to remove the phosphate group mimic. Consequently, peptides or semi-synthetic proteins that include Pma, Pmab or Pmp are valuable tools for cell-based experiments.

All derivatives are suitably protected for use in peptide synthesis by Fmoc strategy. The *tert*-butyl protecting groups prevent side reactions and can be removed during final deprotection of the peptide.

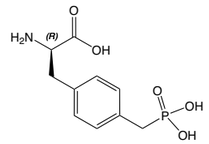
Interested in the difluoro phosphono derivatives of serine and threonine? Please contact our Custom Synthesis Service!

Product details

HAA6480 H-D-Pmp-OH

4-Phosphonomethyl-D-phenylalanine

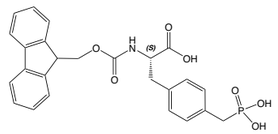
CAS-No.	120667-17-6
Formula	$C_{10}H_{14}NO_5P$
Mol. weight	259,19 g/mol



FAA1745 Fmoc-L-Pmp-OH

N-alpha-(9-Fluorenylmethyloxycarbonyl)-4-phosphonomethyl-L-phenylalanine

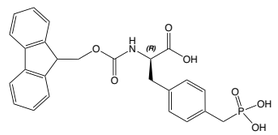
CAS-No.	229180-64-7
Formula	$C_{25}H_{24}NO_7P$
Mol. weight	481,42 g/mol



FAA1689 Fmoc-D-Pmp-OH

N-alpha-(9-Fluorenylmethyloxycarbonyl)-4-phosphonomethyl-D-phenylalanine

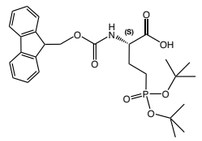
CAS-No.	229180-65-8
Formula	$C_{25}H_{24}NO_7P$
Mol. weight	481,42 g/mol



FAA5580 Fmoc-L-Pma(*t*Bu)2-OH

N-alpha-(9-Fluorenylmethyloxycarbonyl)-4-(di-*t*-butylphosphonomethyl)-L-alanine

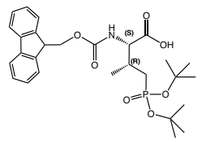
CAS-No.	2088020-71-5
Formula	$C_{27}H_{36}NO_7P$
Mol. weight	517,55 g/mol



FAA5600 Fmoc-L-Pmab(*t*Bu)2-OH

(2S,3R)-2-((9-fluorenylmethyloxycarbonyl) amino)-4-(di-*t*-butylphosphonomethyl)-3-methylbutyric acid

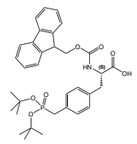
CAS-No.	1199612-89-9
Formula	$C_{28}H_{38}NO_7P$
Mol. weight	531,58 g/mol



FAA5590 Fmoc-L-Pmp(*t*Bu)2-OH

N-alpha-(9-Fluorenylmethyloxycarbonyl)-4-(di-*t*-butylphosphonomethyl)-L-phenylalanine

CAS-No.	166409-77-4
Formula	$C_{33}H_{40}NO_7P$
Mol. weight	593,65 g/mol

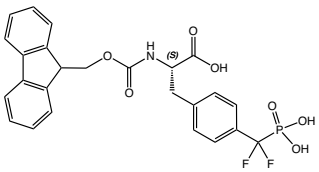


Product details

FAA5595 Fmoc-L-F2Pmp-OH

4-(Difluorophosphonomethyl)-N-(9-fluorenylmethyloxycarbonyl)-L-phenylalanine

CAS-No.	160751-44-0
Formula	$C_{25}H_{22}F_2NO_7P$
Mol. weight	517,42 g/mol



References:

→ *Phosphatase-Stable Phosphoamino Acid Mimetics That Enhance Binding Affinities with the Polo-Box Domain of Polo-like Kinase 1; D. Hymel, T. R. Burke;* ***Jr. Chem Med Chem*** *2017;* ***12****: 202-206. https://doi.org/10.1002/cmdc.201600574*

→ *An Intrinsic Hydrophobicity Scale for Amino Acids and Its Application to Fluorinated Compounds; W. Hoffmann, J. Langenhan, S. Huhmann, J. Moschner, R. Chang, M. Accorsi, J. Seo, J. Rademann, G. Meijer, B. Koksch, M. T. Bowers, G. von Helden, K. Pagel;* ***Angew Chem Int Ed Engl*** *2019;* ***58****: 8216-8220. https://doi.org/10.1002/anie.201813954*