

Novabiochem®

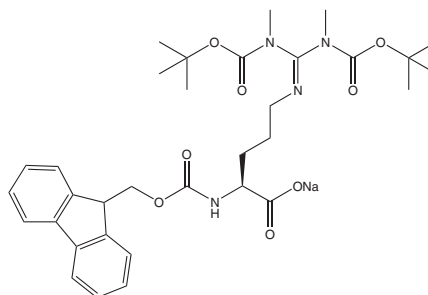
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NEW Fmoc amino acid derivatives

Fmoc-SDMA(Boc)₂-ONa



Features & Benefits

- Direct synthesis of dimethylated Arg-containing peptides by automated methods
- Improved stability compared to Fmoc-SDMA(Boc)₂-OH
- Introduced using standard activation methods
- Compatible with Fmoc SPPS

Post-translational methylation of arginine side chains is now recognized as an important control mechanism for the regulation of protein expression in eukaryotes [1, 2]. However, research into the role of arginine methylation has until quite recently been hampered by lack of efficient methods for the production of the appropriate peptide tools. This situation was remedied with the introduction in 2008 of Novabiochem®'s range of fully protected methylated arginine derivatives for Fmoc SPPS: Fmoc-Arg(Me,Pbf)-OH, Fmoc-ADMA(Pbf)-OH and

Fmoc-SDMA(Boc)₂-OH. Since this time, these derivatives have become the standard tools for the synthesis of monomethyl-, asymmetric- and symmetric dimethylarginine containing peptides, owing to their ease of use and lack of side-reactions.

Unfortunately, it has become apparent that Fmoc-SDMA(Boc)₂-OH is not particularly stable when stored above -20 °C. It appears that the carboxylic acid can promote partial loss of one of the guanidine Boc groups. For this reason, we have decided to replace this product with the corresponding sodium salt, Fmoc-SDMA(Boc)₂-ONa.

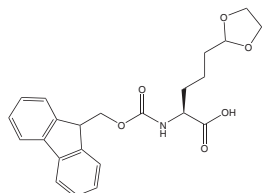
This derivative is best coupled using phosphonium or uronium-based coupling reagents, such as PyBOP and HBTU; only one equivalent of DIPEA is required, since the derivative is a salt. The Boc side-chain protecting groups are cleaved with standard TFA cleavage cocktails.

852310 Fmoc-SDMA(Boc)₂-ONa
NEW

852105 Fmoc-Arg(Me,Pbf)-OH

852107 Fmoc-ADMA(Pbf)-OH

Fmoc-allysine ethylene acetal (Fmoc-Aea-OH)



Features & Benefits

- Versatile derivative for the introduction of a highly reactive aldehyde functionality to a peptide side chain
- Compatible with Fmoc SPPS
- Aldehyde is unmasked during TFA cleavage reaction

Fmoc-Aea-OH is a fully protected derivative of allysine suitably protected for use with Fmoc SPPS methods. It is compatible with all standard coupling conditions such as PyBOP or HBTU. Treatment with TFA/water cleaves the cyclic acetal, liberating the side chain aldehyde group. (The use of thiol-based TFA cleavage cocktails should be avoided as their use can lead to thioacetal formation.) Owing to the high reactivity of this functionality, the resulting product depends on the peptide sequence, in particular the nature of the adjacent residues. Vinyl sulfide bridged analogs of angiotensin II have been prepared by utilizing the reaction between cysteine and an allysine separated by an amino acid residue [3]. Adjacent cysteine or homocysteine residues can form bicycles [4], analogous to the drug Vanlev. N-Terminal

allysine will spontaneously form 1-piperidine-6-carboxyl peptides [5]. If the N-terminal residue attached to the allysine is unhindered, the product is likely to be the corresponding peptide containing either 2-hydroxypiperidine carboxylic or 2-piperidine-6-carboxylic acid [5].

Peptides containing lysine and allysine residues may also have applications as models for collagen cross-linking. Allysine is produced naturally by the action of lysyl oxidase on protein residues. Cross-links formed between the reaction of allysine and lysine and hydroxylysine residues are responsible for giving collagen fibrils their tensile strength.

852305
NEW

Fmoc-Aea-OH

100 mg
500 mg

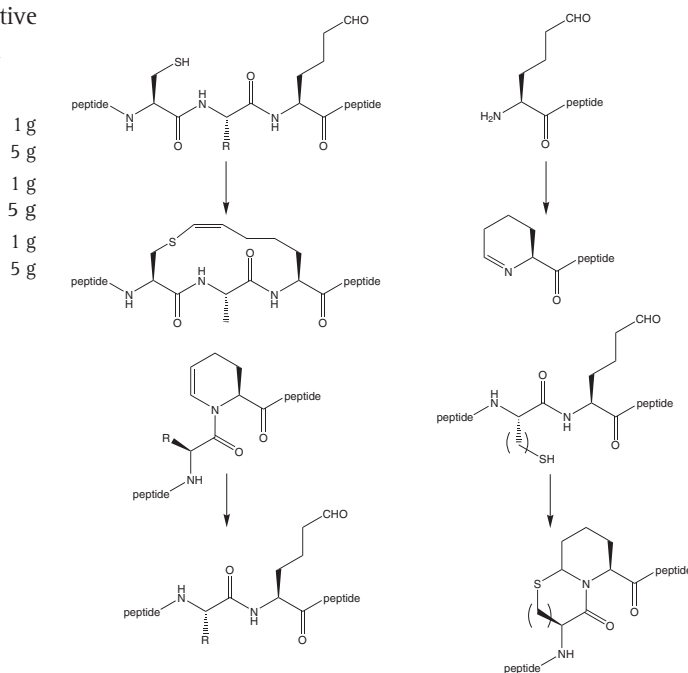
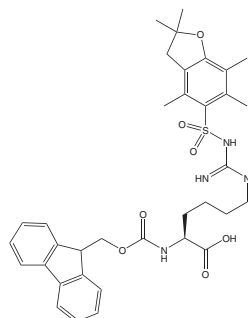


Figure 1: Possible products derived from Aea.

Fmoc-hArg(Pbf)-OH



Fmoc-homoArg(Pbf)-OH, the latest addition to the Novabiochem® brand's range of arginine analogs, is the ideal tool for the introduction of homoarginine by Fmoc SPPS. It can be used in exactly the same manner as Fmoc-Arg(Pbf)-OH.

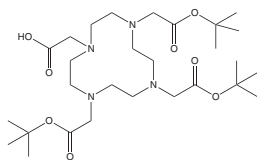
852267
NEW

Fmoc-homoArg(Pbf)-OH

1 g
5 g

NEW Derivatives for labeling peptides with metals

DOTA tris-t-Bu ester



Features & Benefits

- Building block for the synthesis of lanthanide labeled peptides
- Compatible with Fmoc SPPS

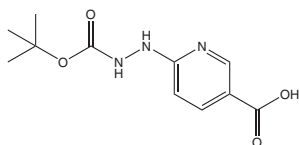
Peptides labeled with metals are valuable tools for targeted imaging and for use as therapeutic radiopharmaceuticals and MRI contrast agents. The most versatile and frequently used metal-binding ligand for this application is DOTA [6], owing to the thermodynamic stability and kinetic inertness of its lanthanide complexes.

The most convenient reagent for the labeling of a peptide with DOTA is the tris-t-butyl ester. This reagent has good solubility in DMF and DCM, and its free carboxyl group can be easily activated using uronium or phosphonium coupling reagents, enabling it to be attached to peptide amino groups. The simplest approach is to couple it to the N-terminus of a resin-bound peptide as the last step of peptide assembly. Alternatively, an amino acid bearing an orthogonally protected side-chain amino functionality, such as Lys(ivDde), can be introduced into the sequence to provide a site of attachment for the DOTA.

Removal of the t-butyl ester groups from the DOTA occurs during the course of the TFA-mediated cleavage reaction. The progress of the reaction should be monitored as the cleavage of these esters is slow, owing to the proximity of the basic ring nitrogens.

851200 DOTA tris-t-Bu ester 100 mg
NEW 250 mg

Hynic



Features & Benefits

- Building block for synthesis of ^{99m}Tc labeled peptides
- Compatible with Fmoc SPPS

2-Hydrazinonicotinic acid (Hynic or HNA) is the favored chelator for labeling peptides with ^{99m}Tc for use in molecular imaging [7]. It is most conveniently introduced to the N-terminal or side-chain amino functionality of a peptide using Boc-HNA, using uronium-based activating reagents such as HBTU and HATU.

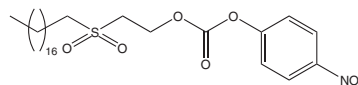
Cleavage from the resin and side chain deprotection of the Boc-HNA peptide is effected by treatment with TFA/water/TIS. The liberated hydrazine is very reactive and will readily form hydrazones with traces of aldehyde and ketones present in the environment or undergo oxidation in basic media. Inclusion of acetone into buffers containing HNA-peptides can be used to help stabilize the hydrazine. Alternatively, extending the cleavage reaction leads to trifluoroacetylation of HNA, which can serve to protect the HNA from hydrazone formation and oxidation. Both hydrazone formation and triacetylation are reversed during the chelation of the peptide with ^{99m}Tc .

851079 Hydralink 6-Boc-HNA Reagent 100 mg
500 mg

851078 Hydralink 6-Fmoc-HNA Reagent 100 mg
500 mg

Chemoselective purification tag

p-Nitrophenyl-2-(octadecylsulfonyl)ethyl carbonate (C₁₈ Tag)



Features & Benefits

- Reversible tag for chemoselective purification of peptides by RP-HPLC
- Tag increases retention time of product by 5 – 10 min compared to capped by-products, facilitating purification
- Tag removed with 5% ammonia

Whilst RP-HPLC is an extremely powerful tool for the purification of small to medium sized peptides, for long peptides the technique lacks the resolution necessary to separate the target molecule from the melange of closely related impurities that arise during synthesis. Such HPLC purified long peptides, despite giving the appearance of being

homogeneous by HPLC, are in fact microheterogeneous, contaminated with numerous coeluting species which, because they are individually present in small amounts, escape detection by mass spectroscopy.

A complementary approach to the purification of long peptides from failure sequences is to utilize a chemoselective tag. By capping unreacted amino groups after each coupling step, deletion sequences are converted to shorter truncation sequences. In the final step of the synthesis, prior to cleavage of the peptide from the resin, the *N*-terminal amino functionality of the full length peptide is labeled with an affinity tag which permits selective separation of the tagged target peptide from these truncation sequences. Following affinity purification, the tag is cleaved and the desired peptide isolated.

For chemoselective purification, the Novabiochem® brand offers *p*-nitrophenyl-2-(octadecylsulfonyl)ethyl carbonate (C₁₈ Tag) [8]. This lipophilic tag allows separation of the tagged peptide by RP-HPLC. Typically, tagged peptides elute 5 - 10 minutes later than the capped by-products. Removal of the tag is effected by treatment with 5% aq. ammonia [8]. For detailed description and protocols on the use of lipophilic tags, see [9].

851092 C₁₈ Tag
NEW

250 mg
1 g

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