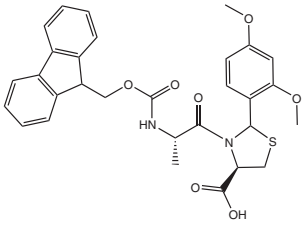
Novabiochem®
Letters 1 Vol. 15

Novabiochem®
30 Years of Innovation

New Building blocks for synthesis of difficult peptides

NEW • Cysteine pseudoproline dipeptides

Fmoc-Ala-Cys($\psi^{Dmp,H}$pro)-OH



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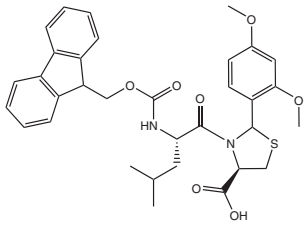
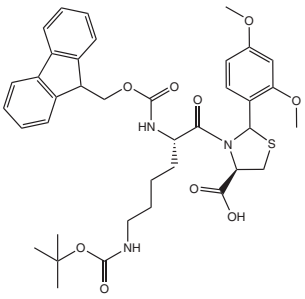
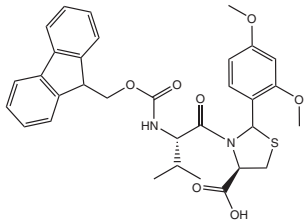


Fmoc-Lys(Boc)-Cys($\psi^{Dmp,H}$pro)-OH



Fmoc-Val-Cys($\psi^{Dmp,H}$pro)-OH



Features & Benefits

- Pseudoproline dipeptides for cysteine-containing peptides
- Prevents aggregation and helps helps improve yield and purity of desired peptide
- Couples without epimerization of cysteine residue

Mutter's pseudoproline dipeptides [1] are extremely powerful tools for enhancing synthetic efficiency in Fmoc SPPS. They work by mimicking the natural propensity of proline [2, 3] to disrupt the formation of the secondary structures during peptide assembly. Their use leads to better and more predictable

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acylation and deprotection kinetics, which results in higher purities and solubilities of crude products, easier HPLC purification and improved yields, with less need to repeat failed syntheses. They have proved particularly effective in the synthesis of intractable peptides [4 - 7], long peptides/small proteins [8 - 16], and cyclic peptides [17, 18], enabling in many cases the production of peptides that otherwise could not be made. Standard pseudoproline derivatives are only appropriate for use in Ser- or Thr-containing sequences as they consist of a dipeptide in which the Ser or Thr residue has been reversibly protected with acetone. Novabiochem is therefore pleased to offer cysteine-based pseudoproline dipeptides, to expand the scope of the structure breaking building blocks available for Fmoc SPPS.

These dipeptides are used in exactly the same manner as standard pseudoproline dipeptides. They can be coupled using any standard coupling method, such as PyBOP/DIPEA or DIPCDI/Oxyma Pure, substituting a Cys residue together with the preceding amino acid residue in the peptide sequence with the appropriate pseudoproline dipeptide (Figure 1). The thiazolidine ring is labile to TFA, so the native sequence cysteinyl-containg peptide is regenerated on cleavage and deprotection.

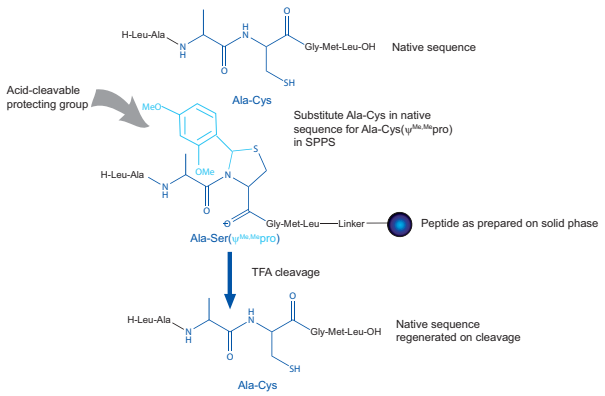


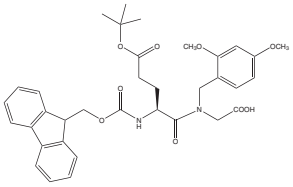
Fig. 1: Principles of using cysteinyl pseudoproline dipeptides.

The cysteine pseudoprolines can be used in combination with standard pseudoprolines and Dmb-dipeptides. Positioning of these structure-breaking derivatives approximately 6 residues apart in the peptide sequence at regular intervals has proven to be an extremely effective approach for the synthesis of long and amyloidogenic peptides. This approach has been exemplified by the synthesis of a 95 residue peptide in remarkable purity through the expeditious use of 7 pseudoproline dipeptides [8], in the synthesis of 101mer related to d2 domain of VEGF receptor [12], and parallel production of ubiquitin analogs [13].

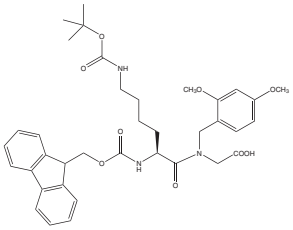
Cat.No.	Product	Contents	Price USD
852381	Fmoc-Ala-Cys($\psi^{Dmp,H}$pro)-OH	1 g	135.00
NEW		5 g	540.00
852382	Fmoc-Leu-Cys($\psi^{Dmp,H}$pro)-OH	1 g	135.00
NEW		5 g	540.00
852383	Fmoc-Val-Cys($\psi^{Dmp,H}$pro)-OH	1 g	135.00
NEW		5 g	540.00
852384	Fmoc-Lys(Boc)-Cys($\psi^{Dmp,H}$pro)-OH	1 g	135.00
NEW		5 g	540.00
852175	Fmoc-Ala-Ser($\psi^{Me,Me}$pro)-OH	1 g	65.00
		5 g	278.00
852180	Fmoc-Ala-Thr($\psi^{Me,Me}$pro)-OH	1 g	65.00
		5 g	278.00
852185	Fmoc-Asn(Trt)-Ser($\psi^{Me,Me}$pro)-OH	1 g	78.00
		5 g	312.00
852183	Fmoc-Asn(Trt)-Thr($\psi^{Me,Me}$pro)-OH	1 g	78.00
		5 g	312.00
852186	Fmoc-Asp(OtBu)-Ser($\psi^{Me,Me}$pro)-OH	1 g	78.00
		5 g	312.00
852199	Fmoc-Asp(OtBu)-Thr($\psi^{Me,Me}$pro)-OH	1 g	78.00
		5 g	312.00
852190	Fmoc-Gln(Trt)-Ser($\psi^{Me,Me}$pro)-OH	1 g	78.00
		5 g	312.00
852198	Fmoc-Gln(Trt)-Thr($\psi^{Me,Me}$pro)-OH	1 g	78.00
		5 g	312.00
852177	Fmoc-Glu(OtBu)-Ser($\psi^{Me,Me}$pro)-OH	1 g	78.00
		5 g	312.00
852196	Fmoc-Glu(OtBu)-Thr($\psi^{Me,Me}$pro)-OH	1 g	78.00
		5 g	312.00
852200	Fmoc-Gly-Ser($\psi^{Me,Me}$pro)-OH	1 g	65.00
		5 g	278.00
852197	Fmoc-Gly-Thr($\psi^{Me,Me}$pro)-OH	1 g	65.00
		5 g	278.00
852194	Fmoc-Ile-Ser($\psi^{Me,Me}$pro)-OH	1 g	65.00
		5 g	278.00
852193	Fmoc-Ile-Thr($\psi^{Me,Me}$pro)-OH	1 g	65.00
		5 g	278.00
852179	Fmoc-Leu-Ser($\psi^{Me,Me}$pro)-OH	1 g	65.00
		5 g	278.00
852184	Fmoc-Leu-Thr($\psi^{Me,Me}$pro)-OH	1 g	65.00
		5 g	278.00
852178	Fmoc-Lys(Boc)-Ser($\psi^{Me,Me}$pro)-OH	1 g	78.00
		5 g	312.00
852191	Fmoc-Lys(Boc)-Thr($\psi^{Me,Me}$pro)-OH	1 g	78.00
		5 g	312.00
852195	Fmoc-Phe-Ser($\psi^{Me,Me}$pro)-OH	1 g	65.00
		5 g	278.00
852201	Fmoc-Phe-Thr($\psi^{Me,Me}$pro)-OH	1 g	65.00
		5 g	278.00
852187	Fmoc-Ser(tBu)-Ser($\psi^{Me,Me}$pro)-OH	1 g	78.00
		5 g	312.00
852192	Fmoc-Ser(tBu)-Thr($\psi^{Me,Me}$pro)-OH	1 g	78.00
		5 g	312.00
852202	Fmoc-Trp(Boc)-Ser($\psi^{Me,Me}$pro)-OH	1 g	78.00
		5 g	312.00
852188	Fmoc-Trp(Boc)-Thr($\psi^{Me,Me}$pro)-OH	1 g	78.00
		5 g	312.00
852189	Fmoc-Tyr(tBu)-Ser($\psi^{Me,Me}$pro)-OH	1 g	78.00
		5 g	312.00
852182	Fmoc-Tyr(tBu)-Thr($\psi^{Me,Me}$pro)-OH	1 g	78.00
		5 g	312.00
852176	Fmoc-Val-Ser($\psi^{Me,Me}$pro)-OH	1 g	65.00
		5 g	278.00
852181	Fmoc-Val-Thr($\psi^{Me,Me}$pro)-OH	1 g	65.00
		5 g	278.00

NEW • Dmb-dipeptides

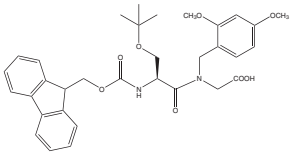
Fmoc-Glu(OtBu)-(Dmb)Gly-OH



Fmoc-Lys(Boc)-(Dmb)Gly-OH



Fmoc-Ser(tBu)-(Dmb)Gly-OH



Features & Benefits

- Helps prevent aggregation in glycine-containing peptides
- Use leads to improved yields and purity of desired peptide

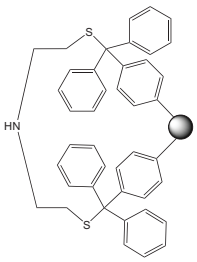
Novabiochem is pleased to introduce three new Dmb-dipeptides derivatives [19, 20]: They work in exactly the same way and offer the same benefits as pseudoproline dipeptides i.e. faster and more predictable acylation reactions, higher yields and purities of crude products, and less failed syntheses. Using them is very straightforward, one simply substitutes a Gly residue together with the preceding amino acid residue in the peptide sequence with the appropriate dipeptide (Figure 3-15). The native sequence is regenerated on TFA-mediated cleavage and deprotection. For peptides containing the Asp-Gly motif, Fmoc-Asp(OtBu)-(Dmb)Gly-OH is highly recommended as its use for introduction of the Asp-Gly dipeptide completely prevents aspartimide formation [20].

Cat.No.	Product	Contents	Price EUR
852405	Fmoc-Glu(OtBu)-(Dmb)Gly-OH	1 g	200.00
NEW		5 g	800.00
852407	Fmoc-Lys(Boc)-(Dmb)Gly-OH	1 g	200.00
NEW		5 g	800.00
852406	Fmoc-Ser(tBu)-(Dmb)Gly-OH	1 g	200.00
NEW		5 g	800.00
852108	Fmoc-Ala-(Dmb)Gly-OH	1 g	291.00
		5 g	1066.00
852115	Fmoc-Asp(OtBu)-(Dmb)Gly-OH	1 g	282.00
		5 g	1122.00
852109	Fmoc-Gly-(Dmb)Gly-OH	1 g	291.00
		5 g	1066.00
852114	Fmoc-Ile-(Dmb)Gly-OH	1 g	291.00
		5 g	1066.00
852114	Fmoc-Leu-(Dmb)Gly-OH	1 g	291.00
		5 g	1066.00
852116	Fmoc-Val-(Dmb)Gly-OH	1 g	306.00
		5 g	1071.00

New Resins for Fmoc SPPS

NEW • Resins for native chemical ligation

SEA-PS



Features & Benefits

- Generates a thioester surrogate for native chemical ligation

SEA-PS resin is a new tool for the synthesis of peptides for native chemical ligation (NCL) by Fmoc SPPS [21 - 23]. This resin on treatment with TFA cleavage generates peptides bearing a bis(2-sulfanylethyl)amide (SEA) on their *C*-terminus. These peptide at neutral pH exist as a mixture of amide and thioester forms. In presence of added thiol, the SEA group is cleaved to give the peptide thioester, which can be isolated or used *in situ* for NCL (Figure 2).

Loading of the resin with the *C*-terminal residue is best done using Fmoc-amino acid coupled activated with HATU. After peptide assembly, the peptide-SEA is cleaved from the resin using standard TFA cocktails. To stabilize the peptide and to simplify HPLC analysis and purification in acidic buffers, the SEA peptide should be converted to the disulfide form by air or iodine oxidation (Figure 5-12). In the presence of a reducing agent such as TCEP, peptide-SEA disulfides undergo rapid NCL or can be converted to thioesters. In the absence of a reducing reagent, peptide-SEA disulfides do not undergo ligation, which has been exploited to perform one-pot three segment ligations [24].

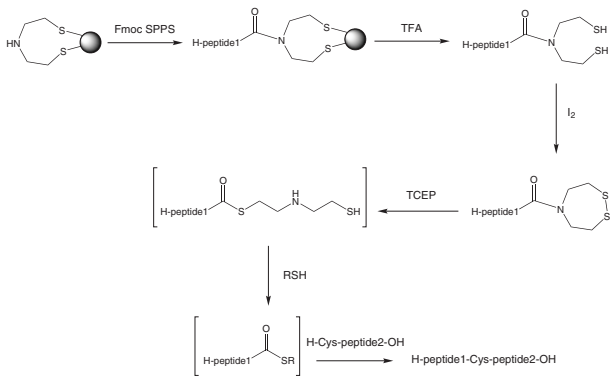
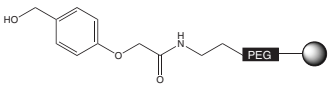


Fig. 2: SEA strategy [21-24].

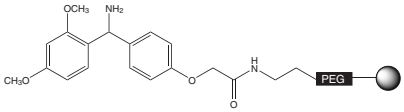
Cat.No.	Product	Contents	Price EUR
855152	SEA-PS	1 g	220.00
NEW		5 g	709.00

NEW • High swell PEG-PS resins

NovaSyn® TG^{XV} A resin



NovaSyn® TG^{XV} R resin



NovaSyn® TG^{XV} A and NovaSyn® TG^{XV} R resins are special formulations of NovaSyn® TGA and NovaSyn® TGR, with swelling properties comparable to Chemmatrix resins. They are therefore excellent tools for the synthesis of long and difficult peptides.

Cat.No.	Product	Contents	Price USD
855156	NovaSyn® TG^{XV} A resin	1 g	78.00
NEW		5 g	234.00
		25 g	734.00
855155	NovaSyn® TG^{XV} R resin	1 g	78.00
NEW		5 g	234.00
		25 g	734.00
855127	NovaSyn® TG^{R} A resin	1 g	64.00
		5 g	224.00
855128	NovaSyn® TG^{R} R resin	1 g	24.00
		5 g	245.00
855005	NovaSyn® TG A resin	1 g	50.00
		5 g	201.00
855009	NovaSyn® TG R resin	1 g	81.00
		5 g	321.00

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