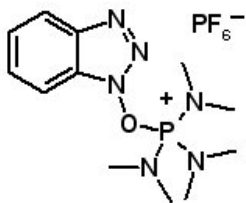




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BOP (Castro's Reagent)



BOP was developed by Bertrand Castro (B. Castro, et al. *Tetrahedron Lett.* 1975, 16, 1219-22), and is often referred to as Castro's Reagent. Although newer coupling reagents such as HBTU have been introduced, BOP still is used in peptide synthesis (S.J. Sachel, et al. *J. Med. Chem.* 2004, 47, 6447-50). It was used in the automated preparation of parallel library of peptide-platinum (II) complexes for anti cancer screening (M.S. Robillard, et al. *J. Comb. Chem.* 2003, 5, 821-5).

BOP is often used in difficult couplings, such as coupling to secondary amines (Y.S. Lee, et al. *J. Med. Chem.* 2007, 50, 5528-32) and weakly nucleophilic heteroaromatic amines (G. Quéféver, et al. *J. Comb. Chem.* 2004, 6, 695-8). BOP has also been utilized to form cyclic peptides by coupling the C-terminal to the N-terminal of linear precursor peptides (R.C. Reid, et al. *J. Org. Chem.* 2003, 68, 4464-71; Y. Singh, et al. *Org. Lett.* 2002, 4, 3367-70).

Lately BOP has been utilized in a different ways. It was recently used to convert aldoximes to the corresponding nitriles (M.K. Singh and M.K. Lakshman *J. Org. Chem.* 2009, 74, 3079-84). It was also utilized to couple 5-carboxy teramethylrhodamine (Tamara) to 4-hydroxypiperidine in a synthesis of Tamara phosphoramidite, which was used in turn for the solid phase synthesis of 5'-Tamara-DNA (M.H. Lyttle, et al. *J. Org. Chem.* 2000, 65, 9033-8). BOP's most significant other use has been to activate heterocyclic lactams and ureas to form substituted aromatic heterocycles Z.-K. Wan, et al. *J. Org. Chem.* 2007, 72, 10199-210; C.G. Lewis and Z.-K. Wan *Org. Lett.* 2008, 10, 1755-8). This process has been utilized in a synthesis of kinetin and the potential kinase inhibitor olomoucine (Z.-K. Wan, et al. *Org. Lett.* 2006, 8, 2425-8).

This chemistry has proven useful for preparing a wide variety of substituted nucleosides and nucleoside derivatives. (Z.-K. Wan, *Org. Lett.* 2005, 7, 5877-80; S. Bae and M.K. Lakshman *J. Am. Chem. Soc.* 2007, 129, 782-9; S. Bae and M.K. Lakshman *Org. Lett.* 2008, 10, 2203-6). These nucleoside derivatives have potential applications in synthesizing modified RNA and DNA.

BOP was introduced a little over 35 years ago, but it remains a very useful synthesis reagent. AAPPTec provides BOP at very competitive prices. AAPPTec can also provide BOP in bulk

Focus XC Series High Performance Solid Phase Peptide Synthesizers



Focus XC (6)

High performance solid phase peptide synthesis of long or difficult peptides may require the utilization of special coupling reagents for specific residues within the peptide sequence. The Focus XC Series of solid phase peptide synthesizers have the capacity and operational flexibility to allow you to use special reagents for selected couplings. If your peptide sequence contains an arylglycine residue, you can use the low-racemization coupling reagent DEPBT to couple the racemization-prone arylglycine, then return to standard coupling reagents for the remainder of the synthesis, all automatically.

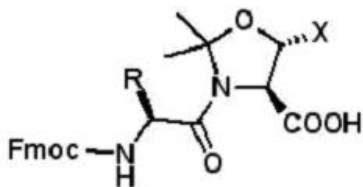
The Focus XC series has the physical capacity to utilize special reagents. In the standard configuration, Focus XC Peptide Instruments have two 5-liter solvent/reagent bottles, one 2-liter solvent/reagent bottle, two 1-liter solvent/reagent bottles and twenty-four 90 mL reaction vessels that may be used for amino acid monomers and special reagents. Optional configurations can have 36 or 48 reaction vessels or other combinations of solvent/reagent bottles.

Optional reaction monitoring and the heating and sonication options also contribute to the Focus XC peptide synthesizers' high performance. With the automatic reaction monitoring option, the Focus XC peptide instrument will not proceed to the next step until the current coupling is completed, thus assuring higher yields and purer crude peptides even when couplings are slow. Sonication and heating increase reaction yields of difficult couplings. Focus XC peptide synthesizers apply heat and sonication only during specified steps in the peptide synthesis to prevent damaging side

quantities for additional savings. E-mail AAPPTec at sales@aapptec.com for a quotation on bulk quantities.

Catalog Number	Product	Quantity	Price
CXZ090	BOP	25g	\$30
		100g	\$90
		500g	\$275

AAPPTec Pseudoproline Dipeptides



Fmoc-Xxx-Ser($\Psi^{Me, Me}$ pro)-OH X=H

Fmoc-Xxx-Thr($\Psi^{Me, Me}$ pro)-OH X=Me

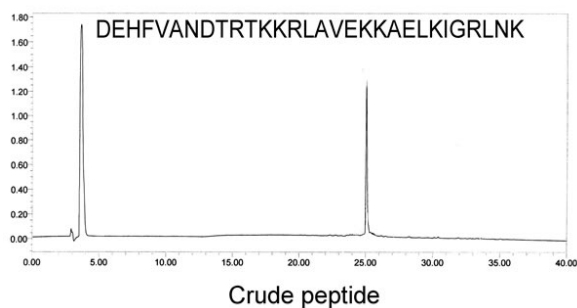
Pseudoproline dipeptides are useful building blocks developed by Mutter for preparing long or difficult peptides (Mutter M., et al. *Pept. Res.* 1995, 8, 145, Wöhr T., et al. *J. Am. Chem. Soc.* 1996, 118, 9218, White P, et al., *J. Pept. Sci.* 2004, 10, 18.) In the peptide chain, the amide bond between the pseudoproline dipeptide and the preceding amino acid preferentially adopts a cis configuration. This creates a kink in the peptide backbone that prevents self-association, β -sheet formation and peptide aggregation. Recently, hAmylin 1-37 has been prepared in excellent purity using pseudoproline dipeptides. (Abedini A, Raleigh, *Org. Lett.* 2005, 7, 693.) Using conventional synthesis methods, the peptide was obtained as a heterogeneous mixture.

By disrupting aggregation and β -sheet formation, incorporation of pseudoproline dipeptides into peptides used for fragment condensation reactions can markedly improve solubility. The tendency for pseudoprolines to form a kink in the peptide backbone promotes cyclization of linear peptides. Park and coworkers (Page K, et al. *J. Pept. Sci.* 2007, 13, 833.) found that incorporating a pseudoproline dipeptide accelerated the on resin cyclization of linear amylin (1-13). In addition, C-terminal pseudoprolines eliminate the risk of epimerization at the C-terminal during fragment coupling.

Most commercial pseudoproline dipeptides contain oxazolidines formed from Ser or Thr. The steric hindrance and reduced nucleophilicity of the oxazolidine nitrogen atom make coupling to pseudoprolines at peptide N-terminals difficult, usually resulting in unacceptably low yields. In peptide synthesis therefore pseudoprolines are introduced as preformed dipeptide units of the type Xaa-Oxa. The oxazolidine is converted back to Ser or Thr when the peptide is cleaved from the resin with TFA. The pseudoproline unit is stable to AcOH/TFE/DCM however, so peptides for fragment condensation can be prepared on and cleaved from 2-chlorotrityl resins with the pseudoproline unit intact. These peptides have improved solubility properties, making them very useful in fragment condensation reactions.

Pseudoproline dipeptides are powerful tools for enhancing the synthesis of cyclic peptides, long peptides and "difficult" peptides, often enabling the production of peptides that otherwise were impossible or impractical to synthesize.

reactions to the peptide in synthesis.



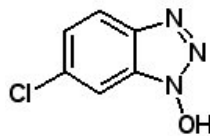
Crude 30mer Peptide Prepared on the Focus XC

Focus XC solid phase peptide synthesizers are versatile, low maintenance instruments that deliver high performance yet are small enough to fit on a laboratory benchtop. Their compact design assures accurate, efficient operation with minimum wastage.

Despite their sophisticated high performance, Focus XC series peptide synthesizers are easy to operate. Even novice users can begin preparing high quality peptides with very little training. Focus XC solid phase peptide synthesizers are the high performance instruments required for current and future advanced peptide synthesis

Visit our website at www.aapptec.com to learn about AAPPTec solid phase peptide synthesizers and other excellent products for efficient high yield peptide production.

6 Cl-HOBt



6 Cl-HOBt is an alternative to HOBt. The chlorine atom attached to the ring increases the acidity and the effectiveness as a leaving group of 6 Cl-HOBt compared to HOBt. Like HOBt, 6 Cl-HOBt efficiently suppresses racemization during coupling. Cl-HOBt can be used in place of HOBt with equal or superior results.

Recent publications utilizing 6 Cl-HOBt

S. Boitano, et al *J. Med. Chem.* 2011, 54, 1308.
H. Qu, et al. *J. Med. Chem.* 2009, 52, 3627.
K. Takahashi, et al *Biochem.* 2009, 48, 1654.
J.S. Josan, et al. *Org. Lett.* 2009, 11, 2479.
T. Yamamoto, et al. *J. Med. Chem.* 2008, 51, 1369.

AAPPTec supplies 6 Cl-HOBt in laboratory and bulk quantities at competitive prices. For a quotation on bulk quantities of 6 Cl-HOBt, send an e-mail to AAPPTec at sales@aapptec.com.

Catalog Number	Product	Quantity	Price
CXZ096	6 Cl-HOBt	100g	\$80.00
		500g	\$320.00
		1kg	\$485.00

To learn more about AAPPTec's highest quality chemicals for peptide synthesis, go to AAPPTec's online catalog at www.aapptec.com.

Catalog Number	Pseudoproline Dipeptide	1g	5g
PPD001	Fmoc-Ala-Ser($\psi^{Me,Me}$ pro)-OH	\$50	\$200
PPD002	Fmoc-Ala-Thr($\psi^{Me,Me}$ pro)-OH	\$50	\$200
PPD003	Fmoc-Asn(Trt)-Ser($\psi^{Me,Me}$ pro)-OH	\$50	\$200
PPD004	Fmoc-Asn(Trt)-Thr($\psi^{Me,Me}$ pro)-OH	\$50	\$200
PPD005	Fmoc-Asp(OtBu)-Ser($\psi^{Me,Me}$ pro)-OH	\$50	\$200
PPD006	Fmoc-Asp(OtBu)-Thr($\psi^{Me,Me}$ pro)-OH	\$50	\$200
PPD007	Fmoc-Gln(Trt)-Ser($\psi^{Me,Me}$ pro)-OH	\$50	\$200
PPD008	Fmoc-Gln(Trt)-Thr($\psi^{Me,Me}$ pro)-OH	\$50	\$200
PPD009	Fmoc-Glu(OtBu)-Ser($\psi^{Me,Me}$ pro)-OH	\$50	\$200
PPD010	Fmoc-Glu(OtBu)-Thr($\psi^{Me,Me}$ pro)-OH	\$50	\$200
PPD011	Fmoc-Gly-Ser($\psi^{Me,Me}$ pro)-OH	\$50	\$200
PPD012	Fmoc-Gly-Thr($\psi^{Me,Me}$ pro)-OH	\$50	\$200
PPD013	Fmoc-Ile-Ser($\psi^{Me,Me}$ pro)-OH	\$50	\$200
PPD014	Fmoc-Ile-Thr($\psi^{Me,Me}$ pro)-OH	\$50	\$200
PPD015	Fmoc-Leu-Ser($\psi^{Me,Me}$ pro)-OH	\$50	\$200
PPD016	Fmoc-Leu-Thr($\psi^{Me,Me}$ pro)-OH	\$50	\$200
PPD017	Fmoc-Lys(Boc)-Ser($\psi^{Me,Me}$ pro)-OH	\$50	\$200
PPD018	Fmoc-Lys(Boc)-Thr($\psi^{Me,Me}$ pro)-OH	\$50	\$200
PPD019	Fmoc-Phe-Ser($\psi^{Me,Me}$ pro)-OH	\$50	\$200
PPD020	Fmoc-Phe-Thr($\psi^{Me,Me}$ pro)-OH	\$50	\$200
PPD021	Fmoc-Ser(tBu)-Ser($\psi^{Me,Me}$ pro)-OH	\$50	\$200
PPD022	Fmoc-Ser(tBu)-Thr($\psi^{Me,Me}$ pro)-OH	\$50	\$200
PPD023	Fmoc-Trp(Boc)-Ser($\psi^{Me,Me}$ pro)-OH	\$50	\$200
PPD024	Fmoc-Trp(Boc)-Thr($\psi^{Me,Me}$ pro)-OH	\$50	\$200
PPD025	Fmoc-Tyr(tBu)-Ser($\psi^{Me,Me}$ pro)-OH	\$50	\$200
PPD026	Fmoc-Tyr(tBu)-Thr($\psi^{Me,Me}$ pro)-OH	\$50	\$200
PPD027	Fmoc-Val-Ser($\psi^{Me,Me}$ pro)-OH	\$50	\$200
PPD028	Fmoc-Val-Thr($\psi^{Me,Me}$ pro)-OH	\$50	\$200

UPCOMING EVENTS

[22nd American Peptide Symposium](#)

June 25-30, 2011
San Diego, CA
Booths #12, 13, 62

[ACS Fall Meeting 2011](#)

August 28 - September 1, 2011
Booth #608