Activators for Peptide Synthesis and Peptide Libraries

Success in the chemical synthesis of peptides, performed either in solution or via solid-phase techniques, relies heavily upon efficient coupling reagents. HOAt, HATU, and PyAOP, the newest coupling reagents from PerSeptive Biosystems, enhance coupling yields, minimize racemization, and reduce the need for multiple couplings.

**HOAt 1-HYDROXY-7-AZABENZOTRIAZOLE**
HOAt is a coupling additive that can be used in conjunction with active ester (OPfp, ODbht) and carbodiimide (DCC, DIPCDI, EDC) chemistry. Recent research has shown that HOAt is a superior coupling additive in both solution and solid-phase synthesis when compared to HOBt (1). HOAt enhances coupling yields in solution by 6-32 fold and reduces the loss of chiral integrity by up to 50% (2,3). The HOAt molecule incorporates both key elements of the 1:1 mixture of HOBt and a tertiary amine; in couplings involving active esters, this results in greater catalytic activity than HOBt alone. (1)

![HATU Structure](image)

**HATU: N-{(DIMETHYLAMINO)-1H-1,2,3,-TRIAZOL0[4,5-b]PYRIDIN-1-YLMETHYLENE]-N-METHYL METHANAMINUM HEXAFLUOROPHOSPHATE/N-OXIDE(4,5)**
HATU, the onium salt of HOAt, is a stand-alone coupling reagent that has been shown to be particularly effective in difficult couplings via both solution and solid-phase techniques. HATU has shown special utility for the synthesis of peptides containing hindered amino acids, N-methyl amino acids, and in segment condensations (2,3,6,7).

The benefits of HOAt and HATU
- Enhances coupling yields and reduces racemization
- Reduces cycle times
- Allows coupling of hindered amino acids and synthesis of difficult peptides
- Reliability and ease of use
- Compatible with tBoc- and Fmoc-based methods
- Suitable for the assembly of peptide libraries

**PyAOP 7-AZABENZOTRIAZOLE-1-YLOXYTRIS (PYRROLIDINO) PHOSPHONIUM HEXAFLUOROPHOSPHATE**
PyAOP, a phosphonium salt, is an activator for peptide synthesis. It is an HOAt derivative that is analogous to PyBOP.

The benefits of PyAOP
- Provides the phosphonium derivative with HOAt/HATU catalytic effect and benefits
- Particularly beneficial in the synthesis of cyclic peptides (see figure at left)
- Eliminates guanidinium formation
REFERENCES AND NOTES


5. Note: The systematic name given here for HATU differs from that previously given in the literature. Recent x-ray structural determinations for this compound as well as HBTU have clarified the crystal structures as guanidinium N-oxides rather than uronium salts (refer to reference #3).


HANDLING AND STORAGE

HOAt
CAS [39968-33-7] MW 136.1
Handling, Storage and Precautions: Very stable, not hygroscopic, and can be stored indefinitely. HOAt solutions in DMF (0.3 M) can be stored in an inert atmosphere for weeks. Syntheses of peptides carried out with freshly prepared and 4-week old solutions show similar quality for the crude product. Violent decomposition may occur when dried at elevated temperatures.

HATU
CAS [148893-10-1] MW 380.2
Handling, Storage, and Precautions: Very stable, not hygroscopic, and can be stored indefinitely at 0°C. HATU solutions in DMF (0.5 M) can be stored in an inert atmosphere for weeks (after 4 weeks, purity is 85%). Syntheses of peptides carried out with freshly prepared and 3-week old solutions show crude products of similar quality. Violent decomposition can occur when dried at elevated temperature.

PyAOP
CAS [156311-83-0] MW 521.4
Handling, Storage, and Precautions: Very stable, not hygroscopic, and can be stored indefinitely at 0°C. PyAOP solutions in DMF (0.5 M) can be stored in an inert atmosphere for 2 days. Violent decomposition can occur when dried at elevated temperature.

ORDERING INFORMATION

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