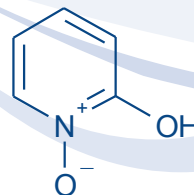


2-Hydroxypyridine-N-oxide: An HOBt replacement

Product Code: **FH05522**
 CAS Number: **13161-30-3**
 Chemical Formula: **C₅H₅NO₂**
 Molecular Weight: **111.10**



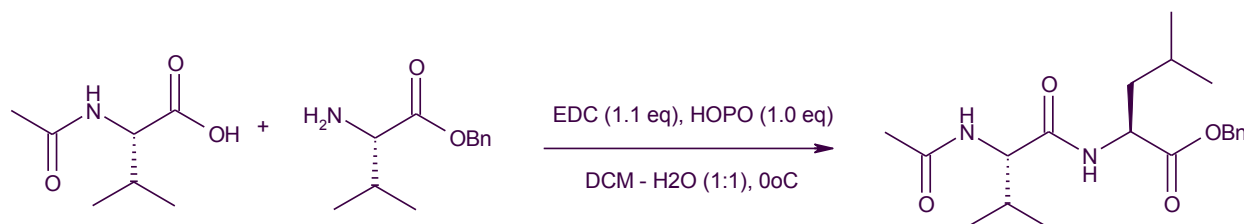
Synonyms: *HOPO*

N-Hydroxy compounds such as 1-hydroxybenzotriazole hydrate (HOBt, product code FH07279) or 1-hydroxy-7-azabenzotriazole (HOAt) have traditionally been used in amide coupling reactions to suppress side reactions and minimise racemisation, the latter challenge being a key one in peptide synthesis.^{1,2} However, racemisation can still be an issue with either additive.^{3,4}

A recent change in the UN classification of HOBt resulting in more restrictive shipping regulations has led to interest in the lesser known alternative, 2-hydroxypyridine-N-oxide (HOPO, product code FH05522).

2-Hydroxypyridine N-oxide is less frequently known by several other names: 2-hydroxypyridine 1-oxide, 2-pyridinol N-oxide, 2-Pyridinol 1-oxide, 1-hydroxypyridine-2-one, 1-hydroxy-2-pyridone and 1-hydroxy-2(1H)-pyridinone, 2-HPNO.

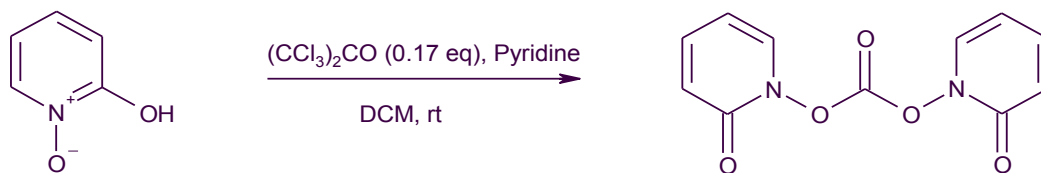
The major use for HOPO is in amide bond synthesis. A simple and efficient, biphasic (CH₂Cl₂ or EtOAc with water, 1:1) coupling protocol with EDC (product code FD05800) has been described, yielding di- or tri-peptides with low levels of racemisation, Scheme 1.⁵ HOPO had been previously used in a stepwise process via the initial formation of esters from activated amino acids (for example acid chlorides).^{6,7}



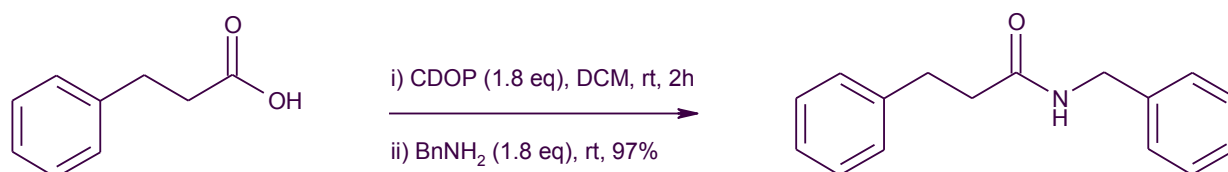
Scheme 1

Reider and colleagues have recently reported the use of a combination of HOPO and HOAt additives in the EDC-mediated coupling of doxorubicin, an anthracycline antibiotic used in cancer chemotherapy, with a heptapeptide. The resulting doxorubicin-peptide conjugate has potential utility in the treatment of prostate cancer.⁸

1,1'-Carbonyl-dioxydi[2(1*H*)-pyridone] (CDOP) can be prepared by the homo-coupling of 2-hydroxypyridine-N-oxide with triphosgene and pyridine, Scheme 2. CDOP is then used in coupling reactions to efficiently form amides, Scheme 3, and peptides, which proceed in the absence of basic promoters such as tertiary amines or substituted 4-dimethylaminopyridine (DMAP), further reducing racemisation in peptide synthesis.⁹



Scheme 2



Scheme 3

HOPO also has utility in areas outside of organic synthesis. For example, the ability of HOPO and derivatives to remove iron ions by chelation from human transferrin (a glycopeptide found in blood plasma) has been studied. This work raises the prospect for these molecules to be used as probes for studying the metabolism of iron in humans, and potentially in the treatment of disorders relating to iron imbalance.¹⁰ HOPO has also been recently studied as part of efforts to elucidate the mechanism of therapeutic action of iron chelators such as desferrioxamine, a clinically used treatment for iron poisoning.¹¹

The ability of self-assembled monolayers on mesoporous silica supports functionalised with HOPO to remove lanthanides (La, Ce, Pr, Nd, Eu, Gd and Lu) from aqueous solutions has been studied. Affinity for the lanthanides differs along the series, suggesting that this system may have utility in chromatographic lanthanide separation.¹²

HOPO has also found utility in the preservation of wood, proving to be efficacious against degradation by the white-rot fungus *Coriulus versicolor*.¹³ The fungistatic properties are believed to be related to the ability of the hydroxamic function to chelate metals which are required for the oxidative reactions involved in fungus mediated wood degradation.¹⁴

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