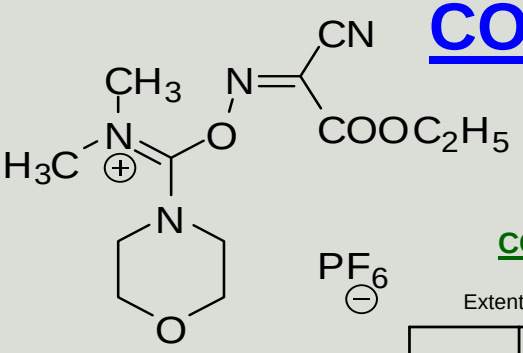
Luxembourg Bio Technologies Ltd.



COMU - A Safer and More Efficient Replacement for Benzotriazole-based Coupling Reagents

COMU – Reactivity

Extent of Coupling of Fmoc-Val-Val-NH_2

Time (min)	HATU (Yield %)		COMU (Yield %)	
	2 equiv	1 equiv	2 equiv	1 equiv
5	83.0	70.0	95.1	82.0
10	87.6	76.0	96.0	86.0
20	90.5	80.0	98.0	90.1
30	92.5	82.0	98.5	94.5
60	93.0	82.0	100.0	96.0
120	94.0	83.0	100.0	98.0

H-Tyr-Aib-Aib-Phe-Leu-NH2 was manually assembled on Fmoc-Rink Amide.AM-resin using amino acid/activator (3 eq.), DIEA (6 eq.), using 30 min coupling time except for the case of Aib-Aib, for which 1 h was used.

Coupling Reagent	Base (equiv.)	Penta (%)	Des-Aib (%) tetra
HATU	DIEA (2)	83.0	17
HBTU	DIEA (2)	47.0	53
HTOC	DIEA (2)	99.0	1.0
COMU	**DIEA (2)**	**99.7**	**0.26**

COMU – Stability and Solubility

To determine the compatibility of the new coupling reagents with peptide synthesis in both manual and automatic mode, their solubility and stability in solution and in solid state was tested

Coupling Reagent	5 h	24 h	48 h
HATU	99 %	95 %	76 %
HBTU	100 %	98 %	86 %
HOTU	100 %	95 %	84 %
COMU	100 %	100 %	93 %

Hydrolytic stability of immonium-type coupling reagents in DMF

Coupling Reagent	Wt/1mL	Molarity
HATU	0.165	0.43
HBTU	0.175	0.46
HOTU	0.420	1.09
COMU	0.620	1.44

Effect of Oxygen on the solubility of the uronium type coupling reagents

COMU - Features and Advantages:

-Comparable coupling efficiency to HATU and far better than HBTU, TBTU, HCTU, TNTU and even better than TOTU

- Safe to producer, safe to user (LD50 = 2000 mg/kg)
- Excellent solubility and stability in DMF and NMP (1.4 M)
- Low or non-existent explosivity
- Likely to have low potential for causing allergic reactions
- COMU enhances the coupling yield and reduce the racemization in comparison with HBTU, HCTU, and similar reagents

COMU gives a color which makes the reaction could be followed for completion

2 min reaction — 1 h reaction

For more information, trial samples, protocols and quotes please contact:

Dr. Shamis Marina

Marina@luxembourg.co.il

www.peptide-and-dna.com

Tel: +972-8-946 6040

Fax: +972-8-946 6402