TECHNICAL NOTE

Formation of *In-Situ* Acid Fluorides using TFFH on the Pioneer™ Peptide Synthesis System

Fmoc amino acid fluorides have been shown to exhibit advantages over standard coupling agents, especially in the coupling of sterically hindered amino acids[1-4]. More recently, the onium reagent, tetramethylfluoroformamidinium hexafluorophosphate (TFFH), has been shown to effect efficient conversion of *N*-protected amino acids to the corresponding *N*-protected amino acid fluorides[5,6]. Because the reaction conditions for the formation of acid fluorides *via* TFFH are compatible with the normal protocols for peptide synthesis, TFFH is suitable for use as a coupling reagent which takes advantage of the exceptional properties of Fmoc amino acid fluorides without the need for their isolation. In addition, TFFH can be used with especially sensitive amino acids such as Arginine, Histidine and Asparagine, a task impossible with pre-formed acid fluorides.

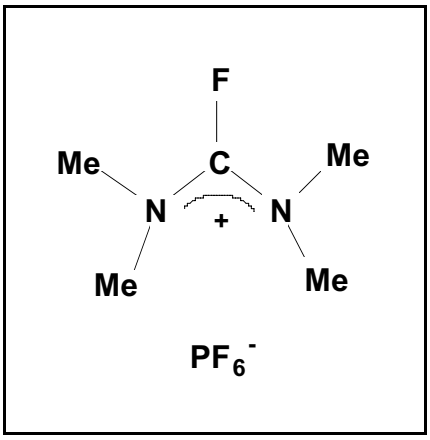

Figure 1. The Structure of TFFH

Properties and Handling Requirements

- TFFH is a non-hydroscopic crystalline solid (MW = 264.1). It is stable in air at ambient temperature and can be manipulated without special precautions.
- We recommend TFFH to be stored in a tightly closed plastic container at 4 ¡C and that the container be brought to room temperature before opening.
- TFFH has a greater sensitivity to water when dissolved in solvent.
- Only high quality solvents should be used when working with TFFH, especially the commonly used polar solvents such as DMF. DMF containing < 300 ppm of water gives excellent results.

Use of TFFH on the Pioneer™ Peptide Synthesis System

Single bottle activation is used, and is consistant with the other base-mediated chemistries such as HATU or TBTU (i.e. 4 fold xs of amino acid, two fold molarity of base to amino acid):

- Activator bottle (1, 2 or 3) : 1.0 M DIEA in DMF
- Amino acid vial: 1:1 molar ratio of dry TFFH to amino acid.

Ordering Information

GEN076541	5 grams
GEN076543	25 grams
GEN076545	100 grams

References

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