



Technical Support Information Bulletin 1100

HBTU

HBTU is an excellent coupling reagent that suppresses racemization. Its reactivity is similar BOP, but it liberates tetramethylurea upon reaction instead of carcinogenic HMPA. Couplings using HBTU proceed smoothly and can be enhanced by adding HOBt.¹

Preactivation and Coupling with HBTU

1. Dissolve 2.0 equivalents (based on resin substitution) of the protected amino acid in DMF (5 mL/g of resin).
2. Add 2.0 equivalents (based on resin substitution) of 1.0 M HBTU solution and 4.0 equivalents (based on resin substitution) of diisopropylethylamine (DIPEA). 2.0 equivalents (based on resin substitution) of 0.5 M HOBt solution in DMF can be added to suppress racemization.
3. Mix for 3 to 5 minutes at room temperature.
4. Remove the N-terminal protecting group using standard protocols.
5. Add the pre-activated amino acid solution to the resin.
6. Mix for 10-60 minutes until the Kaiser test is negative.
7. Filter and wash the resin with DMF.

¹ Knorr, R.; Trzeciak, A.; Bannwarth, W.; Gillessen, D. *Tetrahedron Lett.* **1989**, 30, 1927-1930.