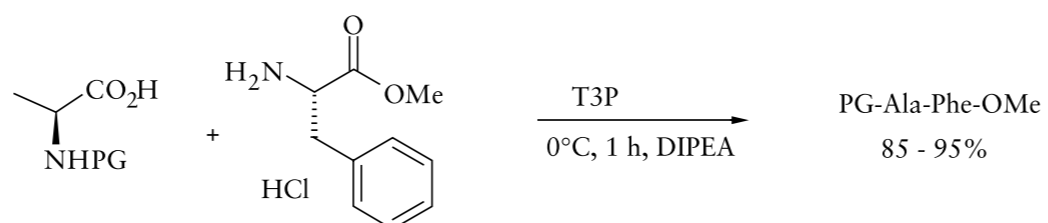


# High-Performance Amide/Peptide Bond Formations with <sup>®</sup>T3P

Claudius Böhm, Andreas Meudt, Shigeki Tanaka, Yoshiharu Ono

We have developed Propane Phosphonic Acid Anhydride (<sup>®</sup>T3P) as a mild and non-toxic amide bond forming reagent. In addition to easy application and product isolation by simple extraction, selectivities with <sup>®</sup>T3P are usually superior to other coupling reagents. Furthermore, because of the properties of <sup>®</sup>T3P, common but hazardous additives (e.g. HOBt) are not required anymore in peptide couplings. Recent studies also suggest high potential for this reagent in other reactions of multi-functional molecules, e.g. dehydrations of amides to nitriles where all the advantages of <sup>®</sup>T3P are maintained.

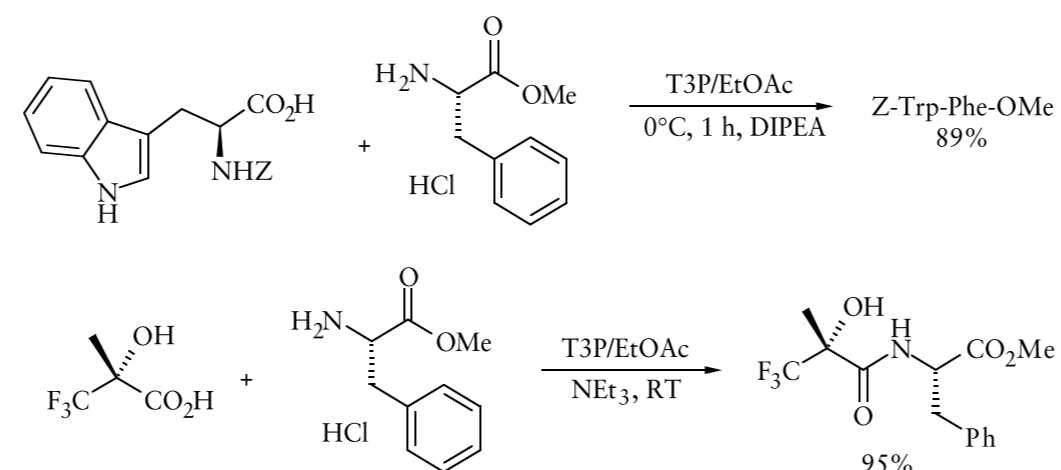
## 1. Standard peptide couplings



PG = Z, Boc, Fmoc; solvents, e.g. EtOAc, BuOAc, DMF, Toluene, THF, DCM, ACN

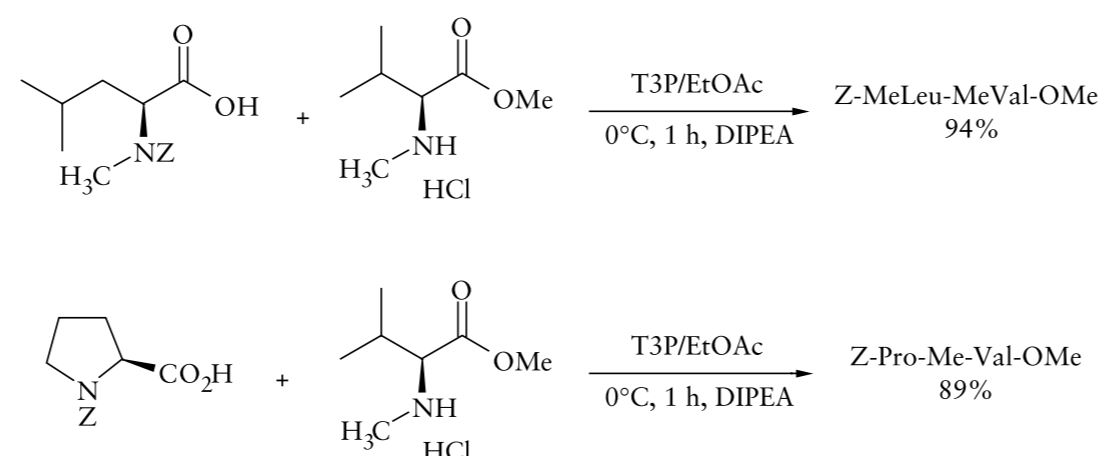
- Standard peptide couplings can be done in many different solvents and with common protecting groups
- Several pharma applications on up to 100 tonnes scale

## 2. Coupling of sidechain-protected amino- and carboxylic acids



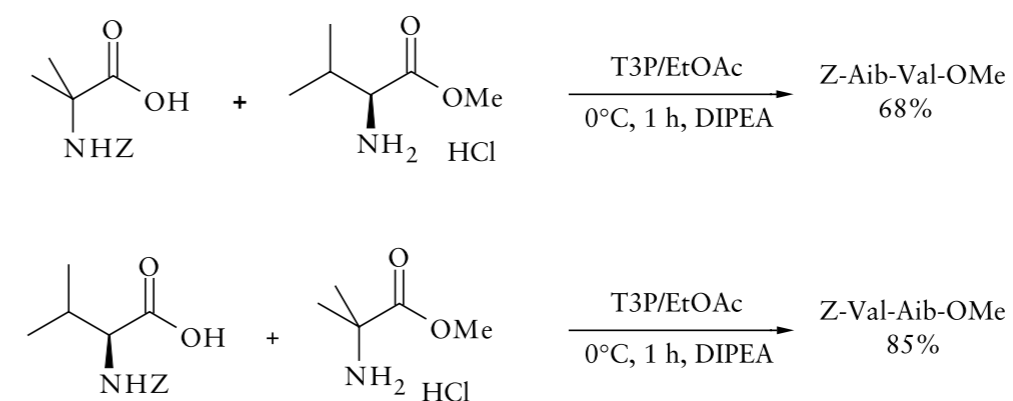
- Economically superior to PyBOP (w.r.t. reagent costs, work-up problems, toxicity)
- High yields despite an  $\alpha$ -hydroxy group or steric hindrance

## 3. Coupling of N-methylated amino acids



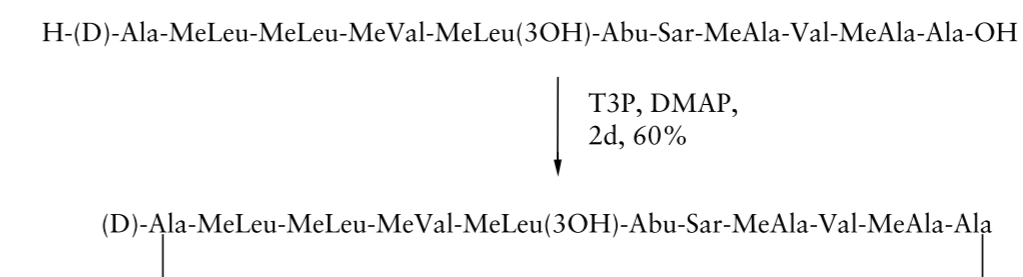
- Very mild conditions, high yields, easy application

## 4. Coupling of sterically hindered amino acids

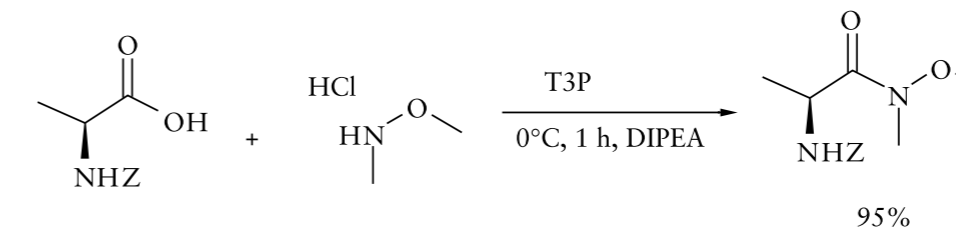


- Very mild conditions, high yields, easy application

## 5. Intramolecular cyclization reaction of oligopeptides



## 6. High ee chiral Weinreb amides



## Advantages of <sup>®</sup>T3P

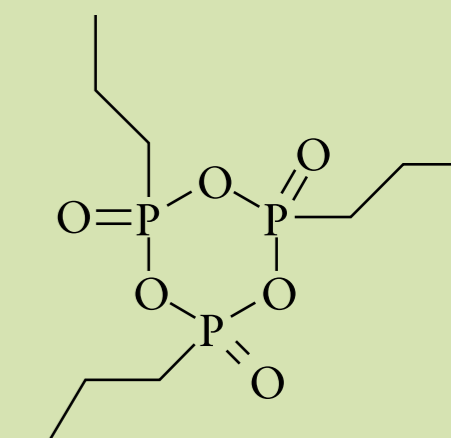
- Broad functional group tolerance
- Reduced overall process costs (economic application)
- Easy purification/workup (only water-soluble by-products)
- Low epimerization without any additives
- High yields
- Low toxicity
- Detailed technical package available on request

## Standard Procedure for Amide/Peptide Couplings

- Reaction:** 1 mol Acid, 1 mol Amine, 2 mol Base (e.g. N-Methylmorpholine, DIPEA) and 1.2 mol <sup>®</sup>T3P are stirred in EtOAc (or other appropriate solvent) at 0°C for 20 minutes and overnight at room temperature.
- Product Isolation:** Quench with water, adjust pH to 7, phase separation, water wash, phase separation and evaporation.

## Production

<sup>®</sup>T3P is produced in an ISO 9001 certified facility on a multiton scale and is available from stock. We supply as a 50% (w/w) solution in DMF, EtOAc, and BuOAc and can also deliver in any other solvent appropriate to the customer's needs. With years of experience in using this technology, we are ready to support you to achieve optimal benefits and performance from <sup>®</sup>T3P.



Archimica

archimica.com