**APPLICATIONS OF PEPTIDE COUPLING REAGENTS – AN UPDATE**

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Accepted on: 01-02-2011; Finalized on: 01-05-2011.

**ABSTRACT**

Peptide synthesis includes a wide range of techniques and procedures that enable the preparation of molecules ranging from small peptides to large proteins. This review focuses on the coupling reagents and major advances that have had a great impact in the field of peptide synthesis. Coupling reagents have gained substantial popularity in peptide coupling reactions involving formation of azide, mixed anhydride and acid halide intermediates. Another significant development in the field of peptide coupling reactions is the discovery of the racemisation suppressants. Racemisation can occur at C-terminal amino acid residue in the course of a coupling reaction due to the ionization of the α-hydrogen and the formation of an oxazolone intermediate. A peptide coupling reagent with an appropriate racemisation suppressing agent assures suppression of the undesired racemisation and other side reactions. 

**Keywords:** Peptides, peptide coupling reagents, carbodiimides, phosphonium-based reagents, uranium reagents.

**INTRODUCTION**

A key step in the peptide production process is the formation of the peptide bond. This requires the activation of a carboxylic acid, which is usually carried out using the peptide coupling reagents. The peptide linkage between two amino acid segments is one of the most important reactions in organic and bioorganic chemistry. Many different strategies have been devised for selective amide bond formation from a carboxylic acid and an amino group, usually involving protection, activation, coupling and deprotection steps. 

To ensure specific coupling between the required carboxyl and amino groups, a range of protecting groups have been developed which can be selectively introduced and removed. In recent years, peptide coupling reactions have been significantly advanced in accordance with the development of new peptide coupling reagents in organic synthesis. The development of new peptide coupling reagents has been steadily accelerated in the past few years. DCC as a peptide-coupling reagent has particularly attracted organic chemists in their synthesis of complex molecules. Moreover, the development of onium-type coupling reagents has made the incorporation of sterically hindered amino acids including N-methylated and α,α-dialkylated amino acids smoothly into the corresponding peptides possible. In some cases, racemisation suppressants are also used as additives to the peptide coupling reagent. The additive plays a role as not only a racemisation suppressor but also as a rate enhancer.

This review evaluates advantages, disadvantages, and effectiveness of newly developed peptide coupling reagents. Different types of coupling reagents include phosphonium, uronium, immonium, carbodiimide, imidazolium, organophosphorous, acid halogenating and other coupling reagents, according to the structural similarity.

**FIGURE 1**

![Diagram of peptide coupling reaction](image)

**PEPTIDE COUPLING REAGENTS**

**Carbodiimides**

Dicyclohexylcarbodiimide (DCC) and diisopropylcarbodiimide (DIC) are commonly used to prepare amides, esters and acid anhydrides from carboxylic acids. DCC was first reported by Sheehan.

**Applications and Advances**

- Carbodiimides have dramatically expanded their scope with the aid of various additives such as HOPO, HOAt, HODhbt and more recently HOCT.
- The coupling reaction between the aminobaccatin and oxazoline was achieved by using DCC/DMAP to provide the desired product in good yield.
- Maryanoff successfully constructed the macrocycle in a cyclic pentapeptide, cyclotheonamide A, employing DCC/HOBt, in 47% yield.
- Boger applied EDC/HOBt to the synthesis of the vancomycin aglycon AB ring system.
- In Fmoc solid-phase peptide synthesis, the DIC/additive method was investigated in various conditions by changing the additive, base, and solvent. Carpio demonstrated that DIC/HOAt was superior to DIC/other additives.
- Further variations of the carbodiimide such as BMC, BEC, and N,N-dicyclopentylcarbodiimide were reported. Rapoport developed the hydrophilic side-chain-containing carbodiimide, BDDC, in 1994.
BDDC in THF, DMF, or toluene gave a reasonable yield for the coupling reaction with a Boc-protected amino acid and the by-product was easily removed by an acid wash. A combination method using carbodiimides with appropriate activators has been widely applied in peptide coupling reactions since the pioneering work by Bodanszky with p-nitrophenol.  

Active esters can be produced from activators such as N-hydroxyphthalimide, and N-hydroxysuccinimide.  

As an example, the HOSu/DCC method was used in the synthesis of the peptidyl nucleoside antibiotic, polyoxin J.  

The hexadecameric tandem repeat H-(AlaAlaLysPro)4-OH was synthesized in good yield from the corresponding Tfc esters using di-Tfc-carbonate, thus obviating the need to use DCC.  

Advantages

- These reagents can also convert primary amides to nitriles, which can be useful in organic synthesis.
- Dicyclohexylurea, the byproduct formed from DCC, is nearly insoluble in most organic solvents and precipitates from the reaction mixture as the reaction progresses.
- DCC is very useful in solution phase reactions. It is not appropriate for reactions on resin.
- DIC is used instead in solid phase synthesis since the urea byproduct is more soluble and will remain in solution.
- In certain applications, such as modifying proteins, ethyl-(N', N'-dimethylamino) propylcarbodiimide hydrochloride (EDC) is used. This carbodiimide reagent and its urea by-product are water soluble, so the byproduct and any excess reagent are removed by aqueous extraction. In peptide synthesis, adding an equivalent of 1-hydroxybenzotriazole (HOBt) minimizes this problem.

Since the ureas from DIC and CIC were relatively soluble in CH2Cl2, these reagents were more suitable for solid-phase peptide synthesis than DCC.

Carbodiimide reagents have been widely used in peptide synthesis because they show a moderate activity and they are reasonably cheap.

Drawbacks

It gives troublesome side reaction of asparagine and glutamine residues in peptide synthesis. Carbodiimide activation of amino acid derivatives often causes a partial racemization of the amino acid.  

PHOSPHONIUM-BASED REAGENTS

To avoid the racemization and side reactions that can occur with carbodiimide reagents, many alternative reagents were developed to generate OBt esters in situ. Castro introduced CloP and BroP as peptide coupling reagents with noticeable racemisation in Young’s test.  

Applications and Advances

- After HOBt was discovered as a racemisation suppressant, a new CloP-HOBt combined coupling reagent, known as BOP, was introduced. BOP is a non-hygroscopic crystalline compound which can easily be prepared in large quantities.
- Schreiber reported the use of BOP in the ring closure of 12-membered tetrapeptides such as trapoxin B. Schmidt’s pentafluorophenyl ester protocol gave unsatisfactory results.
- Later, PyCloP, PyBroP, and PyBOP were introduced, where the dimethylamine moiety was replaced by pyrrolidine. These reagents could avoid the generation of poisonous hexamethylphosphoramid (HMPA) by-product.

Advantages

- BOP does not generate asparagine and glutamine dehydration byproducts and racemization is minimal BOP is also useful for preparing esters under mild conditions.
- (Benzotriazol-1-ylxylo) tripyrrolidino phosphonium hexafluorophosphate couples amino acids efficiently as BOP, but the by-products are less hazardous. Coupling reactions are rapid, being nearly complete within a few minutes.
- Bromotripyrrolidinophosphonium hexafluoro phosphate is a more reactive coupling reagent. It is especially useful in difficult coupling, such as...
coupling N-methyl amino acids or α,α-dialkylglycines, where other coupling reagents are inefficient.

**Drawback**

BOP must be handled with caution as highly carcinogenic hexamethylphosphoramide is formed as a byproduct in coupling reactions.

**IMIDAZOLIUM REAGENTS**

The search for better coupling reagents based on DCC led to the development of CDI. 55

**Applications and Advances**

- Kiso developed modified imidazolium reagents, BOI, and its precursor, CIP, as new peptide coupling reagents and, later, as new esterification reagents to avoid the toxic HMPA by-product of the BOP reagent. 56
- The efficiency of CIP was also evaluated in peptide coupling reactions between sterically hindered α,α-dialkylated amino acids. The CIP/HOAt combined coupling reagents showed the best result in the formation of a dipeptide, Cbz-Aib-Aib-OMe, compared with PyBroP, TODT, TOTT, and CIP alone.
- Recently, Kato has reported the synthesis of analogues of a gastrokinetic agent, mosapride, using CDI. 57
- Xu also introduced a thiazolium-type reagent, BEMT. 58,59 The mechanism of BEMT may involve the sequential conversion of a carboxylic acid of an amino acid into the corresponding acyloxythiazolium salt and then to the acid bromide, leaving N-ethyl-4-ethythiazolidone as the by-product. The efficacy of BEMT and BEP was elegantly demonstrated in fragment coupling reactions containing N-alkylated amino acids during the synthesis of the immunosuppressive cyclosporin O. 60
- More recently, Wischnat has introduced the crystalline and non-hygroscopic BMTB as a new peptide coupling reagent. BMTB was produced by alkylation of its precursor with methyl bromide (MeBr), while BEMT was prepared with triethylxonium tetrafluoroborate (Et3OBF4) from the common intermediate. 61

**Advantages**

- Rapoport introduced a new imidazolium reagent, CBMIT, by bismethylating CDI with methyl triflate. 62 CBMIT is particularly useful in peptide coupling reactions with sterically hindered amino acids such as Val or Aib, and showed no sign of racemisation in the presence of CuCl2 or Cu(OTf)2.

**Drawbacks**

CBMIT is moisture sensitive and should be handled in the air for a very short period of time. Due to the polarity of CBMIT, the choice of solvent is restricted to polar solvents such as nitro methane. 63

**ORGANOPHOSPHOROUS REAGENTS**

Since the mixed carboxylic-phosphoric anhydride method was first proposed in peptide chemistry by Yamada using DPPA from diphenylphosphorochloridate and sodium azide, various organophosphorous compounds have been developed as new peptide coupling reagents. 64

**Applications and Advances**

- This method usually gave a higher regioselectivity towards nucleophilic attack by the amine component than a mixed carboxylic anhydride method. 65 DPP-CI was first introduced. 66
- Shortly after, Palomo-Coll developed BOP-CI and it quickly became popular in practical applications. BOP-CI was well known as a powerful reagent for peptide coupling reactions involving N-alkylamino acids. 67,68
- Brady applied an improved DPPA technique, in which the triethylamine base was replaced by sodium bicarbonate, in the macrocyclisation step during the synthesis of a cyclic hexapeptide analogue of somatostatin. 69
- The DPPA/NaHCO3 method was also employed for the 32-membered macrocyclisation of (2)-sandramycin. 70 The key advantage of the use of this method relied on the insolubility of NaHCO3 in the reaction medium, where a mild reaction condition was required. DECP was easily prepared by the reaction of triethyl phosphate with cyanogen bromide. 71,72
- Itoh reported the synthesis of N 5-substituted glutamine analogues, which displayed potent antitumour activities against MTX-resistant tumours by inhibition of dihydrofolate reductase, using several coupling reagents including DECP and compared their results.
- On the other hand, DECP was useful for more nucleophilic amines containing electron-donating substituents in an aromatic ring, whereas phosphorus trichloride was effective for less nucleophilic amines.
One of the notable variations in organophosphorous reagents was the development of the phosphinic acid derivatives.

In the macrocyclisation step during the synthesis of the cyclooctadepsipeptide, PF1022A, BOP-Cl gave a high yield (87%) with negligible racemisation, whereas the Pfp active ester or EDC/HOBt method gave only moderate yields (28 and 59%, respectively).74

FDPP has been widely used as a new coupling reagent in macrocyclisation since its development.75

Shioiri employed FDPP for the synthesis of a cyclic depsipeptide, alterobactin A, containing two types of noncoded amino acids such as L-threo-b-hydroxyaspartic acid and (3R, 4S)-4, 8-diamino-3-hydroxyoctanoic acid.

Cyclisation between Gly and b-OH-Asp was accomplished with FDPP in 53% yield for 2 steps. The choice of glycin as the C-terminal residue in the macrocyclisation gave the synthetic advantages of non-epimerisation and non-steric hindrance.76 When the hydroxyl group of the eastern hemisphere was not protected prior to the macrocyclisation, an aspartimide derivative was formed as the byproduct.

Modification of DPPA led to the development of thiophosphinic-type coupling reagents such as MPTA and MPTO.77

As DPPA is an oil, these reagents are crystalline and stable for long-term storage. Since MPTA generated a carbamoyl azide or urea derivative as the by-product, Ueki introduced MPTO, in which the azide group of MTPA was replaced by a 2-oxazolone group. When the coupling conditions were compared for the Cyclisation of H-D-Trp-DGlU (Obn)-Ala-D-Val-Leu-Oh, MPTA/HOBt/ DIEA gave 84% yield (.0.1% of epimer) in 8 h and MPTO/HOBt/ DIEA gave 78% yield (.0.1% of epimer) in 3 h, whereas DPPA/HOBt/DIEA gave only 66% yield in 3 days (6.0% of epimer).

In addition to the earlier development of organophosphorous reagents, a great deal of effort has been focused on creating various coupling reagents of a similar kind. For example, NDPP, Cpt-Cl, BMP-Cl, DEBP, BDP, bis(o-iodoxyphenyl)phenyl phosphonate, (5-nitro-pyridyl)-diphenyl phosphinate, diphenyl 2-oxo-3-oxazolinyl phosphonate, and 1,2-benzisoxazol-3-yl diphenyl phosphate were prepared by various research groups.78-84

More recently, Ye developed DEPBO, DOPBO, DOPBT, and DEPB.85 DEPB derived from DEPC and HODHbt was evaluated against other peptide coupling reagents and gave good results in segment coupling reactions.86

Advantages

- DEPBT was efficient for the synthesis of N-protected peptide alcohols and N-Glycopeptides.87 When DEPBT was used as the coupling reagent, the carboxylic group selectively reacted with the amino group in the presence of unprotected hydroxyl functional groups.

ACID HALOGENATING REAGENTS

Acid chlorides

The acid chloride method was first introduced to peptide chemistry by Fisher. Since then, chlorination of amino acids was carried out with various chlorinating reagents such as pivaloyl chloride, phthaloyl dichloride, thionyl chloride and oxalic chloride.88-90 The acid halide technique is frequently recommended in peptide coupling reactions of extremely hindered amino acids.

Applications and Advances

- Gani reported the synthesis of cis-peptidyl prolyl peptide mimetics. The coupling reaction between proline and methyl hydrazide was achieved with IBCF in 74% yield. However, when the steric bulkiness of the N-substituent in the hydrazide was increased, a more powerful activation of the carboxylic acid was required. Thionyl chloride in pyridine was applied to the coupling reactions for this purpose.

- Other useful acid halogenating reagents are cyanuric chloride and CDMT.95,96

- Due to the weak basicity of the triazine moiety, the by-product and excess coupling reagent were easily removed by washing with dilute acid.

- Gilon has recently reported the use of BTC as a chlorinating reagent in solid-phase peptide synthesis.97-99

- Coupling reactions mediated by BTC gave good results for Fmoc-amino acids containing acid-labile side-chains. Since NMP reacted with BTC to form the chlororiminium ion and led to racemisation, inert solvents such as THF or dioxane were required.
Acid fluorides

Since amino acid fluorides showed a better stability towards moisture and acid-labile functional groups than amino acid chlorides, several acid fluorinating reagents were developed. Cyanuric fluoride easily converted amino acids into the corresponding acid fluorides.\textsuperscript{100}

Applications and Advances

- Danishefsky elegantly applied the acid fluoride method to the peptide coupling reaction in the crucial chain-elongation step during the synthesis of a potential MDR reversal agent, 5-N-acetyldeimamin.\textsuperscript{101}
- The most notable advance in acid halogenations has been the development of fluoroformamidinium salts. Carpino reported TFFH, BTFFH, and DFIH as new acid fluorinating reagents which act by in situ generating amino acid fluorides in peptide coupling reactions.\textsuperscript{102}
- BTFFH may be more useful than TFFH due to its lack of toxic by-product forming ability.\textsuperscript{103}
- Han applied the acid fluoride method to the synthesis of a 14-membered cyclic enamide, the key intermediate of C3-epimauritine.\textsuperscript{104}
- The in situ-generated acid fluoride with TFFH in the presence of HOAt successfully afforded the desired macro lactam in 75% yield for 2 steps, while the corresponding Pfp activated ester gave none of the product.\textsuperscript{105-108}

Advantages

- For sterically hindered amino acids, such as Deg, MeAib and Iva, the acid fluoride method gave excellent yields in peptide coupling reactions.\textsuperscript{109}
   These fluorinating reagents are especially useful for His and Arg because the corresponding amino acid fluoride intermediates are not stable on shelf storage.

Drawbacks

Nonetheless, an amino acid chloride-bearing acid labile protecting group can be easily racemised to the oxazolone so that the practical application of the acid chloride is restricted, despite its high reactivity and low cost.
Third generation of Uronium-type coupling reagent

- COMU is a third generation of uronium-type coupling reagent based on ethyl 2-cyano-2-(hydroxyimino) acetate (Oxyma) as well as a morpholino carbon skeleton. The presence of the morpholino group has a marked influence on the solubility, stability and reactivity of the reagent.

- COMU performed extremely well in the presence of only 1 equiv. of base, thereby confirming the effect of the hydrogen bond acceptor in the reaction.

- The by-products of COMU are water soluble and easily removed, making it an excellent choice of coupling reagent for solution-phase peptide synthesis.

- Finally, COMU shows a less hazardous safety profile than benzotriazole-based reagents, such as HATU and HBTU, which in addition exhibit unpredictable autocatalytic decompositions and therefore a higher risk of explosion.

- Furthermore, in contrast to benzotriazole-based reagents, COMU is significantly less likely to cause allergic reaction.

Applications and Advantages

- BOMI and BDMP showed a higher reactivity than other immonium reagents such as AOMP, FOMP, DOMP, BPMP, and SOMP for the synthesis of a tripeptide.

- Interestingly, immonium reagents gave better results than uronium compounds such as HAPyU and HBPyU, presumably due to the fact that resonance stabilisation of uronium reagents from the amine substituent on the central carbon atom contributed to the retardation of reactivity and such a nitrogen atom was not available in the immonium reagents.

- A suitable base for the immonium reagents was found to be 2,6-lutidine in THF or MeCN. BOMI was applied to the synthesis of an oligopeptide, Leu-enkephalin, both in solution and in the solid phase.

PYRIDINIUM AND OTHER COUPLING REAGENTS

Mukaiyama introduced pyridinium reagents such as BMPI and CMPI to peptide chemistry. CMPI was applied to the synthesis of a b-lactam carbacepham skeleton.

Advances

- Recently, Xu reported novel pyridinium reagents such as BEP, FEP, BEPH, and FEPH.

- Tetrafluoroborate or hexachloroantimonate was chosen as the nonnucleophilic counterion to improve the solubility of the pyridinium reagents, compared to Mukaiyama’s reagents. BEP was applied in the synthesis of a tetrapeptide fragment of cyclosporin A and a pentapeptide moiety of dolastatin 15.

- Datta applied (Boc)₂O/DMAP to peptide coupling reactions in the presence of pyridine. The (Boc)₂O-mediated coupling reaction gave the dipeptide in good yield with very little racemisation comparable to DCC/HOBt method. This method was efficient in terms of its low cost, non-toxicity, and stability on storage compared with other coupling reagents.

- Taddei reported DMTMM, which was derived from CDMT and NMM, as a new coupling reagent, and has applied it to solid-phase synthesis.

IMMONIUM REAGENTS

Xu designed new immonium reagents by modifying known uronium reagents. The structural distinction of immonium reagents is the replacement of the amino group of the central carbon atom in uronium reagents with hydrogen, an alkyl, or an aryl group.
Racemisation suppressants

Ko¨nig and Geiger first reported the use of HOBt as a racemisation suppressant in peptide coupling reactions with carbodiimide coupling reagents. With this technique, additives such as HOBt, HOAt, HODhbt, N-hydroxytetrazole, HOCl, and PTF have roles in not only suppressing racemisation, but also enhancing the reactivity. HODhbt has been limited in its widespread adoption due to the side reaction of ring opening.

HOAt has been reported to be more efficient than HOBt because of an Anchimeric assistance effect caused by the pyridine ring. Later, N-hydroxytriazoles and N-hydroxytetrazole were examined for their coupling efficiency. Ramage reported the coupling reaction of dipeptide with DIC and the newly designed HOCl for a racemisation study. Racemisation with DIC/HOCl activation was negligible for all amino acids except histidine.

More recently, Carpino and Henklein reported polyhydrogen fluoride additives, Py(HF)n. For example, the efficiency of the Coupling reaction for HBTU combined with PTF was as good as HATU.

Unfortunately, PTF was unsuitable for phosphonium or organophosphorourous reagents due to the high strength of the P–F linkage. For inorganic additives, the lowest level of racemisation was occasionally found in the presence of CuCl2 combined with various coupling reagents.

However, the improvement in yield was not sufficient by addition of CuCl2. In addition, the Cu (II)-based complexes, Cu (OBt)2 and Cu(OAt)2 also showed the ability to function as racemisation suppressants.

The choice of base is also important in peptide coupling reactions. Tertiary amines such as DIEA and NMM have been considered as practically useful bases in peptide reactions. Tertiary amines such as DIEA and NMM have been considered as practically useful bases in peptide reactions. Tertiary amines such as DIEA and NMM have been considered as practically useful bases in peptide reactions. Tertiary amines such as DIEA and NMM have been considered as practically useful bases in peptide reactions. Tertiary amines such as DIEA and NMM have been considered as practically useful bases in peptide reactions.
hour at room temperature. Filter the resin and wash with DCM.

**Coupling with HBTU or TBTU**

Dissolve 2.0 equivalents (based on resin substitution) of the protected amino acid in DMF (5 mL/g of resin) and add to the resin. 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 1.0 M HBTU solution and 4.0 equivalents (based on resin substitution) of 0.5 M HOBt solution in DMF can be added to suppress racemization. Mix for 10-60 minutes until the Kaiser test is negative. Filter and wash the resin with DMF.

**Coupling with TSTU in Aqueous Solvent Mixtures**

Dissolve the acid in a 2:2:1 mixture of DMF/dioxane/water. Add 3 equivalents of diisopropylethylamine and 1.3 equivalents of TSTU. After the formation of the T-OSu ester is complete, add 1.5 equivalents of the amine. After the reaction is complete, the solvents are removed and the crude product is isolated.

**CONCLUSION**

In addition to peptides, amide bonds are present in a huge array of other organic compounds of biological interest such as peptoids, oligocarbazates, oligoamides, β-lactams, polyenamides, benzodiazepines, diketopiperazines and hydantoins. The development of new peptide coupling reagents and reactions has become a most fascinating field of research for many organic chemists with various backgrounds. This review has presented an overview of the recent development of peptide coupling reagents including racemisation suppressants. Perhaps one of the most significant advances in peptide coupling reagents was the emergence of the onium or fluoroformamidinium salts. Moreover, the discovery of racemisation suppressants has reinforced the coupling reagents by enhancing the reactivity as well as reducing racemisation and side reactions. It is believed that this report serves as an excellent guideline for the organic synthesis of bioactive molecules bearing peptide linkages.

**Acknowledgement:** We are thankful to ITP, SPMVV, Tirupati for providing the necessary facilities and UGC, New Delhi for granting the RFSMS.

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**Abbreviations**

Alb, a-aminoisobutyric acid

AOMP, (7-azabenzotriazol-1-yl)-oxo

AOPT, (7-azabenzotriazol-1-yl)oxytris(dimethylamino) phosphonium hexafluorophosphosphate

BDD, bis([4-(2,2-dimethyl-1,3-dioxolyl)-1-methyl] carbodiimide

BDMP, 5-[(1H-benzotriazol-1-yl)-oxy]-3,4-dihydro-1-methyl 2H-pyrrolo[1,2-c]pyrimidinone

BDD, benzotriazol-1-yl) diethyl phosphosphate

BEC, N-tet-butyl-N0-ethylcarbodiimide

BEMT, 3-bromophenyl methyl thiazolium tetrfluoroborate

BEP, 2-bromo-1-ethyl pyridinium tetrfluoroborate

BEPH, 2-bromo-1-ethyl pyridinium hexa chloro antimonate

BMI, N-tet-butyl-N0-methylcarbodiimide

BMP-Cl, N,N,N0-bis(morpholino) phosphinic chloride

BNMX, N0-bis(methyloxoy)-1,3-dimethylimidazolium hexafluorophosphosphate

BOMI, benzotriazol-1-yl-oxy-N,N0-dimethylmethaniminium hexafluorocloroantimone

BOP, benzotriazol-1-oxotris(dimethyl-amino)-phosphonium hexafluorophosphosphate

BOP-Cl, N,N0-bis(2-oxo-3-oxazolidinyl)-phosphinic chloride

BPM, 1-(1H-benzotriazol-1-yl)phenyl-methylene pyrrolidinium hexafluorocloroantimone

BroP bromotrimethylammonium hexafluorophosphate

BTC bis(trichloromethyl)carbonate

BTFFH, bis[tetramethylethyl]fluorophosphate

CBBM1, 10-carboxylicis [3-methylimidazolium]-triltricate

CDI, 10-carboxylicidimazole

CDMT 2-chloro-4,6-dimethoxy-1,3,5-triazine

CIC N-cyclohexylo-N0-isopropylcarbodiimide

CIP 2-chloro-1, 3-dimethylimidazolium hexafluorophosphate

CBMIT 1, 10 methoxytris(dimethyl-amino)-phenyl-methylene pyrrolidinium hexafluorochloroantimone

CMII 2-chloro-1, 3-dimethyl 1H-benzimidazolium hexafluorophosphate
HOBt, HOAt, tetramethyluronium hexafluorophosphate, HDTU, HBTU, hexafluorophosphate, HBPyU, dimethyleneuronium hexafluorophosphate, Deg a,a-diethylglycine, DEPB, diethyl phosphorobromidate, DEPBO, N-diethoxyphosphoryl benzoxazole, DEPBT, 3-(diethoxycarbonyloxy)-1,2,3-benzotriazin-4(3H)-one, DEPC, diphenylphosphorochloridate, DFH, 1, 3-dimethyl-2-fluoro-4,5-dihydro-1H-imidazolium hexafluorophosphate, DIC, N,N-diisopropylcarbodiimide, DIEA (DIPEA), diisopropylethylamine, DPPA, diphenylphosphoryl azide, DOPBT, 3-phenoxybenzyltriphenylphosphonium dihydrogen trifluoride, DOPBO, norbornene, NDPP, norborn-5-ene-2,3-dicarboximido-diphenylphosphate, PTF, benzyltriphenylphosphonium dihydrogen trifluoride, PyAOP, [7-azabenzotriazol-1-yl]oxytris-(pyrrolidino) phosphonium hexafluorophosphate, PyBOP, benzotriazol-1-yl-oxytriyi(pyrrolidino)-phosphonium hexafluorophosphate, PyClO P, chlorotri(pyrrolidino)phosphonium hexafluorophosphate, PyClU, chloro-1,1,3,3-bis(tetramethylene)-formamidinium hexafluorophosphate, SOMP, 5-(succinimidyl)oxy-3,4-dihydro-1-methyl 2H-pyrrolium hexachloroantimonate, TATU, O-(7-azabenzotriazol-1-yl)oxytris-(pyrrolidino)phosphonium hexafluorophosphate, TBTU, benzotriazol-1-yl-1,1,3,3-tetramethylyuronium tetrafluoroborate, TDBTU2, (3,4-dihydro-4-oxo-1,2,3-benzotriazin-3-yl)-1,1,3,3-tetramethylyuronium tetrafluoroborate, TEMP, 2,3,5,6-tetramethylpyridine, TFFH, tetramethylfluorormamidinium hexafluorophosphate, Ths-Cl, 5-methyl-1,3,4-thiadiazole-2-sulfonyl chloride, TNTU, 2-(5-norbornene-2,3-dicarboximido)-1,1,3,3-tetramethyllyuronium tetrafluoroborate, TOTT, S-(1-oxido-2-pyridinyll)-1,3-dimethyl-1,3-trimethylxenithiouronium tetrafluoroborate, TOTU, S-(1-oxido-2-pyridinyll)-1,1,3,3-tetramethylxenithiouronium tetrafluoroborate, TOTU(4-[cyano(ethoxycarbonyl)methyleneamino]-N,N,N,N-tetramethyluronium tetrafluoroborate, TSTU, 2-succinimido-1,1,3,3-tetramethylyuronium tetrafluoroborate.