

The creation of a 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. The reagents listed in this section have been used in one or other of these steps in the synthesis of peptide molecules. An enormous body of literature exists on the subject of peptide synthesis, of which a selection of books and review articles is listed.¹⁻¹²

Protecting group reagents

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. References to methods of protection and deprotection can be found under specific items in the main Catalogue. Further information on the use of protecting groups in peptide synthesis can be found in the general references on peptide synthesis and in other specialist sources.¹³⁻¹⁵

CARBOXYL PROTECTION

Although a wide variety of esters and other groups have been used for the protection of carboxylic acids, only a limited number of these find significant use in peptide synthesis.

tert-Butyl ester

L08855 tert-Butyl acetate

L00431 N,N-Dimethylformamide di-tert-butyl acetal

B22039 tert-Butyl 2,2,2-trichloroacetimidate

L12338 tert-Butanol

1-Adamantyl ester

A10209 1-Adamantanol

Dicyclopropylmethyl ester

L01816 Dicyclopropylmethanol

Benzylic esters

A15188 9-Anthracenemethanol

L03292 Benzyl alcohol

A13535 Benzyl bromide

A12481 Benzyl chloride

A13579 9-(Chloromethyl)anthracene

A12859 4-(Chloromethyl)pyridine hydrochloride

A15212 9-Fluorenylmethanol

A15559 4-Methoxybenzyl alcohol

A15742 4-Nitrobenzyl alcohol

A13127 2-Nitrobenzyl bromide

A15236 4-Nitrobenzyl bromide

A15749 4-Nitrobenzyl chloride

L00555 2,3,4,5,6-Pentamethylbenzyl chloride

A14698 Pyridine-4-methanol

L00423 2,4,6-Trimethylbenzyl chloride

Alfa Aesar Worldwide Sales Offices

NORTH AMERICA

Tel: 1-800-343-0660 or
1-978-521-6300
Fax: 1-800-322-4757
Email: info@alfa.com

GERMANY

Tel: 00800 4566 4566 or
+49-721-84007-280
Fax: 00800 4577 4577 or
+49-721-84007-300
Email: Eurosales@alfa.com

UNITED KINGDOM

Tel: 0800-801812 or
+44 (0) 1524-850506
Fax: +44 (0) 1 524-850608
Email: UKsales@alfa.com

FRANCE

Tel: 0800 03 51 47 or
+33 03 88 62 26 90
Fax: 0800 10 20 67
Email: frventes@alfa.com

INDIA

Tel: +91 (0)44 2815 4153 or
+91 (0)44 2815 4154
Email: India@alfa.com

CHINA

Tel: +86 (010) 8567-8600
Fax: +86 (010) 8567-8601
Email: saleschina@alfa-asia.com

KOREA

Tel: 82-2-3410-6000
Fax: 82-2-3140-6001
Email: saleskorea@alfa-asia.com

Benzhydryl-type ester precursors

A12266 Benzophenone hydrazone

B21706 9-Fluorenone hydrazone

Phenacyl esters

A15576 2-Bromoacetophenone

A13415 2-Bromo-4'-methoxyacetophenone

Allyl ester

A15026 Allyl alcohol

A11766 Allyl bromide

2-Substituted ethyl esters

A10275 2-Bromoethanol

L19365 2-(p-Toluenesulfonyl)ethanol

B23579 2-(2-Hydroxyethyl)pyridine

L08163 2,2,2-Trichloroethanol

L05442 2-(Methylthio)ethanol

B20970 2-(Trimethylsilyl)ethanol

Miscellaneous carboxyl protecting reagents

A13005 Benzyl carbazate

A12018 N-(Chloromethyl)phthalimide

A12383 tert-Butyl carbazate

B21292 N-(Hydroxymethyl)phthalimide

A15238 2-Chloroacetamide

AMINO PROTECTION

The most popular protecting groups for the amino function are carbamates, particularly Benzyloxycarbonyl [Cbz, Z], Boc and Fmoc groups, but many other groups including trifluoroacetyl and trityl can be used.

Benzyl carbamate [Cbz, Z]

A15682 Benzyl chloroformate

A12153 N-(Benzyloxycarbonyloxy)succinimide

Substituted benzyl carbamates

B25632 4-Nitrobenzyl chloroformate

tert-Butyl carbamate [Boc]

A14708 Di-tert-butyl dicarbonate

A18906 Boc-ON [2-(tert-Butoxycarbonyloximino)

L00506 N-Boc-imidazole 2-phenylacetone nitrile]

B22435 S-Boc-2-mercapto-4,6-dimethylpyrimidine

A12383 tert-Butyl carbazate

Benzo[b]thiophenesulfoylmethyl carbamate [Bsmoc]

L19559 1,1-Dioxobenzo[b]thiophen-2-ylmethyl chloroformate

L19733 1,1-Dioxobenzo[b]thiophen-2-ylmethyl N-succinimidyl carbonate

2,2,2-Trichloroethyl carbamate [Troc]

L06875 2,2,2-Trichloroethyl chloroformate

Alfa Aesar Worldwide Sales Offices

NORTH AMERICA
Tel: 1-800-343-0660 or
1-978-521-6300
Fax: 1-800-322-4757
Email: info@alfa.com

GERMANY
Tel: 00800 4566 4566 or
+49-721-84007-280
Fax: 00800 4577 4577 or
+49-721-84007-300
Email: Eurosales@alfa.com

UNITED KINGDOM
Tel: 0800-801812 or
+44 (0) 1524-850506
Fax: +44 (0) 1 524-850608
Email: UKsales@alfa.com

FRANCE
Tel: 0800 03 51 47 or
+33 03 88 62 26 90
Fax: 0800 10 20 67
Email: frventes@alfa.com

INDIA
Tel: +91 (0)44 2815 4153 or
+91 (0)44 2815 4154
Fax: +91 (0)44 2815 4154
Email: India@alfa.com

CHINA
Tel: +86 (010) 8567-8600
Fax: +86 (010) 8567-8601
Email: saleschina@alfa-asia.com

KOREA
Tel: 82-2-3410-6000
Fax: 82-2-3140-6001
Email: saleskorea@alfa-asia.com

9-Fluorenylmethyl carbamate [Fmoc]

A11683 9-Fluorenylmethyl chloroformate

A13143 N-(9-Fluorenylmethoxycarbonyloxy)-succinimide

Allyl carbamate [Alloc]

B22332 Allyl chloroformate

Trifluoroacetyl group

A13614 Trifluoroacetic anhydride

L00135 Trifluoroacetylimidazole

Trityl groups (Trt, Mmt)

A12864 Bromotriphenylmethane

A11799 Chlorotriphenylmethane

A10545 4-Methoxytrityl chloride

Miscellaneous amino protecting groups

A14822 N-(Ethoxycarbonyl)phthalimide

L06432 Chlorocarbonylsulfonyl chloride

L00770 2-Chloro-3,5-dinitropyridine

B23627 2-Nitrobenzenesulfonyl chloride

A15857 3-Nitrophthalic anhydride

SIDE CHAIN PROTECTION

The presence of reactive side chains in certain amino acids can interfere with peptide synthesis. Some examples are given here of reagents used to mask this reactivity:

Hydroxyl protection

Of the vast range of groups available for the blocking of hydroxyl groups, only a few find regular use in peptide synthesis for serine, threonine and tyrosine derivatives. Benzyl ethers (from benzyl halides or alcohol) and tert-butyl ethers are widely used. For silyl protection, see Appendix 4. Among the most useful OH protecting reagents are:

L13471 N-(2-Bromobenzyloxycarbonyloxy)-succinimide

A12387 Benzyl 2,2,2-trichloroacetimidate

A10370 3-Bromocyclohexene

L13576 3-Bromopentane

B22039 tert-Butyl 2,2,2-trichloroacetimidate

A12859 4-(Chloromethyl)pyridine hydrochloride

L01050 2-Methoxyethoxymethyl chloride

Thiol protection

A variety of methods have been employed to mask the thiol group of cysteine, including benzyl, substituted benzyl, benzhydryl, trityl, Cbz and Boc groups.¹⁶ Examples of reagents for SH protection are given:

A12884 Benzhydryl

A13820 N-(Hydroxymethyl)acetamide

L14367 trans- β -Nitrostyrene

A10366 Triphenylmethanol

L13316 4-Vinylpyridine

Alfa Aesar Worldwide Sales Offices

NORTH AMERICA
Tel: 1-800-343-0660 or
1-978-521-6300
Fax: 1-800-322-4757
Email: info@alfa.com

GERMANY
Tel: 00800 4566 4566 or
+49-721-84007-280
Fax: 00800 4577 4577 or
+49-721-84007-300
Email: Eurosales@alfa.com

UNITED KINGDOM
Tel: 0800-801812 or
+44 (0) 1524-850506
Fax: +44 (0) 1 524-850608
Email: UKsales@alfa.com

FRANCE
Tel: 0800 03 51 47 or
+33 03 88 62 26 90
Fax: 0800 10 20 67
Email: frventes@alfa.com

INDIA
Tel: +91 (0)44 2815 4153 or
+91 (0)44 2815 4154
Email: India@alfa.com

CHINA
Tel: +86 (010) 8567-8600
Fax: +86 (010) 8567-8601
Email: saleschina@alfa-asia.com

KOREA
Tel: 82-2-3410-6000
Fax: 82-2-3140-6001
Email: saleskorea@alfa-asia.com

Carboxyl protection

The side chain carboxyl groups of aspartyl and glutamyl residues can be blocked by means of one of the reagents listed above for carboxyl protection, and also:

A10697 2-Adamantanol

A10381 Pyridine-3-methanol

Guanidino protection

The guanidino group of arginine has been protected by N-nitration, or by Cbz or Boc derivatives, amongst others. Arylsulfonyl protection has been found to be particularly useful:

A11775 Mesitylenesulfonyl chloride

L19561 2,2,4,6,7-Pentamethyldihydro-

L11829 4-Methoxy-2,3,6-trimethylbenzenesulfonyl chloride

benzo[b]furan-5-sulfonyl chloride

Imidazole protection

The imidazole ring in histidine can interfere with acylation reactions and can also promote racemization. It has been blocked by a variety of methods including formation of the Boc or Troc derivatives (reagents listed under Amino Protection) and the following:

A11871 2,4-Dinitro-1-fluorobenzene

A13127 2-Nitrobenzyl bromide

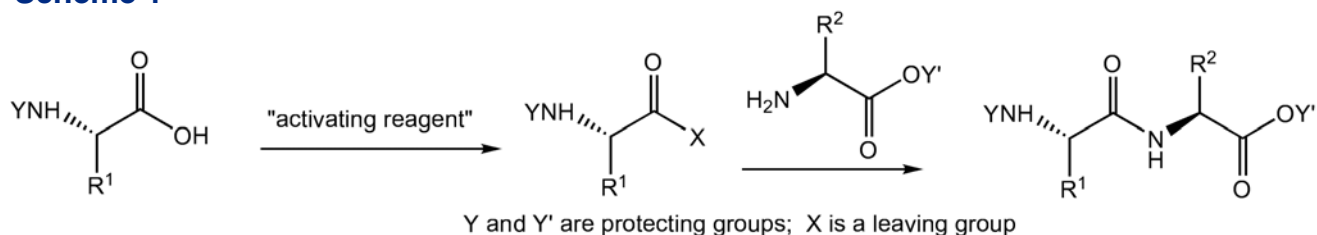
A13788 4-Methoxybenzenesulfonyl chloride

A14547 p-Toluenesulfonyl chloride

Activation and coupling methods

Formation of the peptide link under sufficiently mild conditions normally requires activation of the carboxylic acid function by conversion to a more electrophilic species, such as an acyl halide, azide, anhydride, mixed anhydride or active ester, which then undergoes coupling *in situ*, or as a separate step, with the amino function of the second component, as shown in Scheme 1.

Scheme 1



Acid chlorides have limited value in peptide coupling because of the danger of hydrolysis, racemization, cleavage of protecting groups and other side reactions.¹² These difficulties can generally be avoided by the use of acid fluorides as active intermediates.

Alfa Aesar Worldwide Sales Offices

NORTH AMERICA
Tel: 1-800-343-0660 or
1-978-521-6300
Fax: 1-800-322-4757
Email: info@alfa.com

GERMANY
Tel: 00800 4566 4566 or
+49-721-84007-280
Fax: 00800 4577 4577 or
+49-721-84007-300
Email: Eurosales@alfa.com

UNITED KINGDOM
Tel: 0800-801812 or
+44 (0) 1524-850506
Fax: +44 (0) 1 524-850608
Email: UKsales@alfa.com

FRANCE
Tel: 0800 03 51 47 or
+33 03 88 62 26 90
Fax: 0800 10 20 67
Email: frventes@alfa.com

INDIA
Tel: +91 (0)44 2815 4153 or
+91 (0)44 2815 4154
Fax: +91 (0)44 2815 4154
Email: India@alfa.com

CHINA
Tel: +86 (010) 8567-8600
Fax: +86 (010) 8567-8601
Email: saleschina@alfa-asia.com

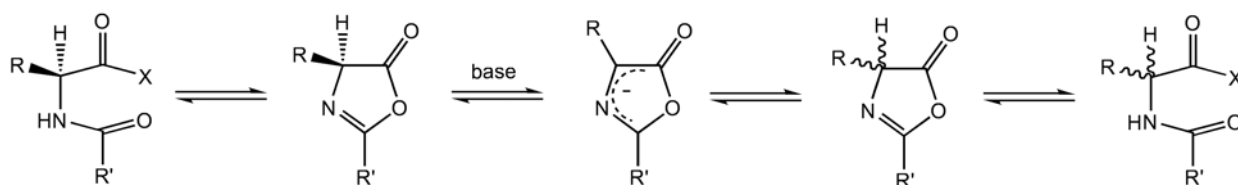
KOREA
Tel: 82-2-3410-6000
Fax: 82-2-3140-6001
Email: saleskorea@alfa-asia.com

Mixed anhydrides of various kinds, formed by reaction of a carboxylic acid with chloroformates, acid chlorides, etc., in the presence of a tertiary amine base, have a long history as peptide intermediates. A variety of phosphorus-based reagents have been employed to form mixed anhydrides and some have shown promising results, often with simplified procedures.

However, for more than four decades the most widely-used reagents have been carbodiimides, especially N,N-dicyclohexylcarbodiimide [DCC] and water-soluble carbodiimide¹⁷ [EDCI, "WSC"]. These will couple protected amino acids directly, but better results are often obtained with various additives or activating agents, most of which can form an "active ester", containing a good leaving group, with the carboxyl function. Frequently the coupling is performed as two separate steps: carbodiimide promoted formation (and possible isolation) of the active ester, followed by reaction with the free amino species.

The main problem is often partial loss of chirality caused by side reactions, the most important of which is considered to be azlactone (oxazolinone) formation by intramolecular cyclization of an N-acylated activated acid derivative with proton abstraction at the chiral center (Scheme 2).

Scheme 2



The suppression of racemization has been a major goal of much of the effort in development of coupling methods, and many techniques have been introduced, of which the use of active esters plays a prominent role. Newer coupling methods include the use of pyridinium salts, phosphonium salts and a variety of uronium salt reagents, some of which have been used to form active esters, giving superior results in specific coupling applications. Several other methods of peptide coupling are sometimes used, including the oldest of all, the azide method¹¹ due to Curtius,¹⁸ of which the use of diphenylphosphonic azide¹⁹ is a variation.

Alfa Aesar Worldwide Sales Offices

NORTH AMERICA
Tel: 1-800-343-0660 or
1-978-521-6300
Fax: 1-800-322-4757
Email: info@alfa.com

GERMANY
Tel: 00800 4566 4566 or
+49-721-84007-280
Fax: 00800 4577 4577 or
+49-721-84007-300
Email: Eurosales@alfa.com

UNITED KINGDOM
Tel: 0800-801812 or
+44 (0) 1524-850506
Fax: +44 (0) 1 524-850608
Email: UKsales@alfa.com

FRANCE
Tel: 0800 03 51 47 or
+33 03 88 62 26 90
Fax: 0800 10 20 67
Email: frventes@alfa.com

INDIA
Tel: +91 (0)44 2815 4153 or
Fax: +91 (0)44 2815 4154
Email: India@alfa.com

CHINA
Tel: +86 (010) 8567-8600
Fax: +86 (010) 8567-8601
Email: saleschina@alfa-asia.com

KOREA
Tel: 82-2-3410-6000
Fax: 82-2-3140-6001
Email: saleskorea@alfa-asia.com

ACTIVATING AND COUPLING REAGENTS

Further information and literature references on the use of most the following reagents can be found in the text entries in the main section of the Catalogue.

Acyl halides

L18013 Bis(tetramethylene)fluoroformamidinium hexafluorophosphate [BTFFH]

A15666 Cyanuric fluoride

A11992 Diethylaminosulfur trifluoride

A18012 Oxalyl chloride

Carbonyl and carboxylic mixed anhydrides

A14688 N,N'-Carbonyldiimidazole

A13724 2-Ethoxy-1-ethoxycarbonyl-1,2-dihydroquinoline [EEDQ]

A14692 Isobutyl chloroformate

L14159 2,4,6-Trichlorobenzoyl chloride

A15051 Trimethylacetyl chloride

Phosphorus mixed anhydrides

L08775 Bis(2-oxo-3-oxazolidinyl)phosphinic chloride [BOP-Cl]

L09919 Diethyl chlorophosphite

A11721 Diphenylphosphinic chloride

A13546 Diphenyl phosphorochloridate

A12724 Ethylene chlorophosphite

A14530 Lawesson's Reagent

L19271 1-Propylphosphonic acid cyclic anhydride, [®T3P], 50+% soln. in DMF

L11911 50+% soln. in ethyl acetate

Sulfonic mixed anhydride

L12147 3,5-Dichloro-2-hydroxybenzenesulfonyl chloride

Carbodiimides

L19463 N-Cyclohexylcarbodiimide on Merrifield resin

L00822 1-Cyclohexyl-3-(2-morpholinoethyl)-carbodiimide methyl-p-toluenesulfonate

A10973 N,N'-Dicyclohexylcarbodiimide [DCC]

A19292 N,N'-Diisopropylcarbodiimide

B25057 1-(3-Dimethylaminopropyl)-3-ethylcarbodiimide

A10807 1-(3-Dimethylaminopropyl)-3-ethylcarbodiimide hydrochloride [EDCI]

A10962 1-(3-Dimethylaminopropyl)-3-ethylcarbodiimide methiodide

L19462 N-Isopropylcarbodiimide on Merrifield resin

Active ester reagents

A10802 Acetone oxime

L00290 Bis(4-nitrophenyl) carbonate

B24153 2,5-Diphenyl-4-hydroxy-3-oxo-2,3-dihydrothiophene 1,1-dioxide [HOTDO]

L13513 4,6-Diphenylthieno[3,4-d]-1,3-dioxol-2-one 5,5-dioxide [TDO activated carbonate]

A12892 1-Hydroxybenzotriazole hydrate [HOBT]

A13205 endo-N-Hydroxy-5-norbornene-2,3-dicarboximide [HONB]

A13862 N-Hydroxyphthalimide

A14522 2-Hydroxypyridine

A10312 N-Hydroxysuccinimide

A15312 3-Nitrophenol

A14376 4-Nitrophenol

L00359 4-Nitrophenyl trifluoroacetate

A15574 Pentafluorophenol [PFP]

B25671 2,4,5-Trichlorophenol

A10788 2,2,2-Trifluoroethanol

Alfa Aesar Worldwide Sales Offices

NORTH AMERICA
Tel: 1-800-343-0660 or
1-978-521-6300
Fax: 1-800-322-4757
Email: info@alfa.com

GERMANY
Tel: 00800 4566 4566 or
+49-721-84007-280
Fax: 00800 4577 4577 or
+49-721-84007-300
Email: Eurosales@alfa.com

UNITED KINGDOM
Tel: 0800-801812 or
+44 (0) 1524-850506
Fax: +44 (0) 1 524-850608
Email: UKsales@alfa.com

FRANCE
Tel: 0800 03 51 47 or
+33 03 88 62 26 90
Fax: 0800 10 20 67
Email: frventes@alfa.com

INDIA
Tel: +91 (0)44 2815 4153 or
+91 (0)44 2815 4154
Email: India@alfa.com

CHINA
Tel: +86 (010) 8567-8600
Fax: +86 (010) 8567-8601
Email: saleschina@alfa-asia.com

KOREA
Tel: 82-2-3410-6000
Fax: 82-2-3140-6001
Email: saleskorea@alfa-asia.com

Pyridinium salts

A12820 2-Chloro-1-methylpyridinium iodide

L11088 2-Fluoro-1-methylpyridinium p-toluenesulfonate

Phosponium salts

A16140 Benzotriazol-1-yloxytris-(dimethylamino) phosphonium hexafluorophosphate [BOP]

L19384 Bromotri(pyrrolidino)phosponium hexafluorophosphate [PyBroP]

B25251 Benzotriazol-1-yloxytris(pyrrolidino) phosphonium hexafluorophosphate [PyBOP]

Uronium salts

B23597 O-(1H-Benzotriazol-1-yl)-N,N,N',N'-tetramethyluronium hexafluorophosphate [HBTU]

L18496 O-[(Ethoxycarbonyl)cyanomethylene-amino]-N,N,N,N'-tetramethyluronium tetrafluoroborate [TOTU]

L13470 O-(1H-Benzotriazol-1-yl)-N,N,N',N'-tetramethyluronium tetrafluoroborate [TBTU]

L13538 2-Succinimido-1,1,3,3,-tetramethyluronium tetrafluoroborate [TSTU]

L19494 O-(1,2-Dihydro-2-oxo-1-pyridyl)-N,N,N,N'-tetramethyluronium tetrafluoroborate [TPTU]

Miscellaneous coupling reagents

L14107 Diethyl cyanophosphonate

A15087 Ethyl diphenylphosphinite

A12124 Diphenylphosphonic azide

L14159 2,4,6-Trichlorobenzoyl chloride

A11118 2,2'-Dipyridyl disulfide

BASES

Most coupling reactions require the presence of a tertiary amine base such as triethylamine. Milder bases, especially 4-methylmorpholine, are less likely to promote racemization and other side reactions. Non-nucleophilic bases such as N-ethyl-diisopropylamine (Hünig's Base) are also widely used. The 4-dialkylaminopyridines are frequently used in substoichiometric amounts, in combination with another amine, as hyper-nucleophilic catalysts in mixed anhydride or carbodiimide coupling reactions. Tertiary amine bases are often also required in the introduction of protecting groups.

Tertiary amine bases

A11058 2,4,6-Collidine

A12158 4-Methylmorpholine

L14143 2,6-Di-tert-butyl-4-methylpyridine

L03398 1-Methylpiperidine

L05265 1-Diethylamino-2-propanol

L19372 Morpholine, polymer supported

A11081 N-Ethyl-diisopropylamine

[Methylmorpholine on polystyrene]

A11905 4-Ethylmorpholine

A12314 1,1,3,3-Tetramethylguanidine

A16294 1-Ethylpiperidine

B23797 Tribenzylamine

A10478 2,6-Lutidine

A12646 Triethylamine

Acylation catalysts

A13016 4-Dimethylaminopyridine [DMAP]

A12575 1-Methylimidazole

B23989 4-(1-Pyrrolidino)pyridine

A11597 1,2,4-Triazole

Alfa Aesar Worldwide Sales Offices

NORTH AMERICA
Tel: 1-800-343-0660 or
1-978-521-6300
Fax: 1-800-322-4757
Email: info@alfa.com

GERMANY
Tel: 00800 4566 4566 or
+49-721-84007-280
Fax: 00800 4577 4577 or
+49-721-84007-300
Email: Eurosales@alfa.com

UNITED KINGDOM
Tel: 0800-801812 or
+44 (0) 1524-850506
Fax: +44 (0) 1 524-850608
Email: UKsales@alfa.com

FRANCE
Tel: 0800 03 51 47 or
+33 03 88 62 26 90
Fax: 0800 10 20 67
Email: frventes@alfa.com

INDIA
Tel: +91 (0)44 2815 4153 or
+91 (0)44 2815 4154
Email: India@alfa.com

CHINA
Tel: +86 (010) 8567-8600
Fax: +86 (010) 8567-8601
Email: saleschina@alfa-asia.com

KOREA
Tel: 82-2-3410-6000
Fax: 82-2-3140-6001
Email: saleskorea@alfa-asia.com

MISCELLANEOUS REAGENTS AND SOLVENTS

The Alfa Aesar product range includes many other items useful in peptide chemistry. This section lists a limited number of examples of materials not covered by earlier sections of this Appendix. The Catalogue also contains a comprehensive listing of natural and unnatural amino acids and their protected derivatives.

Deprotecting reagents

The Catalogue text entries for the protecting reagents listed in this Appendix give some details of methods of cleavage. Some of the most frequently-used reagents are listed below. For further information, see the general references.¹⁻¹⁵

L11577 4-(Aminomethyl)piperidine	42578 Palladium hydroxide on carbon [Pearlman's Catalyst]
A15275 Boron trifluoride diethyl ether complex	A12442 Piperidine
A14740 Dichloroacetic acid	L13303 Tetra-n-butylammonium fluoride trihydrate
A14005 Hydrazine monohydrate	L06374 Trifluoroacetic acid, 99%
A14475 Hydrobromic acid, 45% in acetic acid	A12198 Trifluoroacetic acid, 99%
L17117 Hydrogen fluoride pyridine complex	A14365 Trifluoroacetic acid, biochem. grade, 9.5+%
A10355 Morpholine	A10173 Trifluoromethanesulfonic acid
A13565 Methanesulfonic acid	B21789 Tris(2-aminoethyl)amine
A12623 Palladium, 5% on carbon	L19373 Tris(2-aminoethyl)amine, polymer- supported
A12012 Palladium, 10% on carbon	

Cation scavengers

Cleavage of protecting groups under acidic conditions often liberates cations (for example tert-butyl, benzyl, or trityl ions) which can undergo unwanted side reactions with the peptide molecule. The following compounds are among the most useful cation scavengers for these reactive species:

A12997 Anisole	A14846 Thioanisole
L12865 Ethanedithiol	A10320 Triethylsilane
L04163 Pentamethylbenzene	L09585 Triisopropylsilane

Solvents

A wide variety of solvents can be used in peptide synthesis. Those listed are among the most useful. Lack of solubility often dictates the use of relatively polar, including dipolar aprotic, solvents. Solvent mixtures can also be used:

A19862 Acetonitrile	A12747 1,1,1,3,3,3-Hexafluoro-2-propanol
L13089 Dichloromethane	A12260 1-Methyl-2-pyrrolidinone
A10924 N,N-Dimethylacetamide	L13304 Tetrahydrofuran
A13547 N,N-Dimethylformamide	A10788 Trifluoroethanol
A13280 Dimethyl sulfoxide	

Alfa Aesar Worldwide Sales Offices

NORTH AMERICA
Tel: 1-800-343-0660 or
1-978-521-6300
Fax: 1-800-322-4757
Email: info@alfa.com

GERMANY
Tel: 00800 4566 4566 or
+49-721-84007-280
Fax: 00800 4577 4577 or
+49-721-84007-300
Email: Eurosales@alfa.com

UNITED KINGDOM
Tel: 0800-801812 or
+44 (0) 1524-850506
Fax: +44 (0) 1 524-850608
Email: UKsales@alfa.com

FRANCE
Tel: 0800 03 51 47 or
+33 03 88 62 26 90
Fax: 0800 10 20 67
Email: frventes@alfa.com

INDIA
Tel: +91 (0)44 2815 4153 or
Fax: +91 (0)44 2815 4154
Email: India@alfa.com

CHINA
Tel: +86 (010) 8567-8600
Fax: +86 (010) 8567-8601
Email: saleschina@alfa-asia.com

KOREA
Tel: 82-2-3410-6000
Fax: 82-2-3140-6001
Email: saleskorea@alfa-asia.com

Miscellaneous reagents and materials

L19593 N-Acryloylsarcosine methyl ester resin
[Sheppard acrylamide resin]

L19600 BT-Core resin

L19602 2-Chlorotriyl alcohol on polystyrene

12457 Copper(II) chloride

A10138 1,4-Dithioerythritol

A15797 1,4-Dithio-DL-threitol

B22183 4-(Hydroxymethyl)benzoic acid

L15721 4-(Hydroxymethyl)phenoxyacetic acid

L17027 Merrifield Resin, 1% crosslinked

A16087 Merrifield Resin, 2% crosslinked

L17028 Wang Resin, 1% crosslinked

L19369 Wang Resin, 2% crosslinked

References

- (1) P. D. Bailey, *An Introduction to Peptide Chemistry*, Wiley, Chichester (1990).
- (2) J. Jones, *The Chemical Synthesis of Peptides*, OUP, Oxford (1991).
- (3) M. Bodansky, *Peptide Chemistry: a Practical Textbook*, Springer-Verlag, Berlin (1993).
- (4) M. Bodansky, *Principles of Peptide Synthesis*, 2nd ed., Springer-Verlag, Berlin (1993).
- (5) M. Bodansky, A. Bodansky, *Practice of Peptide Synthesis*, 2nd ed., Springer-Verlag, Berlin (1994).
- (6) *Peptides: Synthesis, Structures and Applications*, B. Gutte, Ed., Academic Press, San Diego (1995).
- (7) E. Atherton, R. C. Sheppard, *Solid Phase Peptide Synthesis*, IRL Press, Oxford (1989).
- (8) 'Side reactions in peptide synthesis', M. Bodansky, J. Martinez, *Synthesis*, 333 (1981).
- (9) 'Convergent solid-phase peptide synthesis', P. Lloyd-Williams *et al*, *Tetrahedron*, **49**, 11065 (1993).
- (10) 'Synthesis of peptides with mixed anhydrides', N. F. Albertson, *Org. React.*, **12**, 157 (1962).
- (11) 'The azide method in peptide synthesis', Y. S. Klausner, M. Bodansky, *Synthesis*, 549 (1974).
- (12) 'Peptide synthesis via amino acid halides', L. A. Carpino *et al*, *Acc. Chem. Res.*, **29**, 268 (1996).
- (13) T. W. Greene, P. G. M. Wuts, *Protective Groups in Organic Synthesis*, 3rd ed., Wiley, N.Y. (1999).
- (14) P. J. Kocienski, *Protecting Groups*, Thieme, Stuttgart (1994).
- (15) 'Protecting group strategies in organic synthesis', M. Schelhaas, H. Waldmann, *Angew. Chem. Int. Ed.*, **35**, 2057 (1996).
- (16) 'Bibliographical and critical study of the protection of the thiol function in peptide synthesis', F. Cavelier, J. Daunis, R. Jacquier, *Bull. Soc. Chim. Fr.*, 210 (1990).
- (17) J. C. Sheehan, G. P. Hess, *J. Am. Chem. Soc.*, **77**, 1067 (1955); J. C. Sheehan, P. A. Cruickshank, G. L. Boshart, *J. Org. Chem.*, **26**, 2525 (1961).
- (18) T. Curtius, *Ber.*, **35**, 3226 (1902).
- (19) T. Shiori, K. Ninomiya, S. Yamada, *J. Am. Chem. Soc.*, **94**, 6203 (1972).

Alfa Aesar Worldwide Sales Offices

NORTH AMERICA
Tel: 1-800-343-0660 or
1-978-521-6300
Fax: 1-800-322-4757
Email: info@alfa.com

GERMANY
Tel: 00800 4566 4566 or
+49-721-84007-280
Fax: 00800 4577 4577 or
+49-721-84007-300
Email: Eurosales@alfa.com

UNITED KINGDOM
Tel: 0800-801812 or
+44 (0) 1524-850506
Fax: +44 (0) 1 524-850608
Email: UKsales@alfa.com

FRANCE
Tel: 0800 03 51 47 or
+33 03 88 62 26 90
Fax: 0800 10 20 67
Email: frventes@alfa.com

INDIA
Tel: +91 (0)44 2815 4153 or
Fax: +91 (0)44 2815 4154
Email: India@alfa.com

CHINA
Tel: +86 (010) 8567-8600
Fax: +86 (010) 8567-8601
Email: saleschina@alfa-asia.com

KOREA
Tel: 82-2-3410-6000
Fax: 82-2-3140-6001
Email: saleskorea@alfa-asia.com