CYSTEINE DERIVATIVES

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CYSTEINE DERIVATIVES OFFERED BY BACHEM

Cystine disulfide bridges help to stabilize the biologically active conformation of peptides and proteins. They are generated by incorporation of cysteine residues followed by oxidation of the thiol functions yielding disulfides („folding“). For the chemical synthesis of peptides, a range of protecting groups has been developed for blocking these sensitive moieties which may be removed either directly before or during oxidative folding. When synthesizing peptides containing two or more disulfide bonds, S-protection may have to be varied to allow consecutive bridge formation for obtaining an unambiguous structure.

CYSTEINE DERIVATIVES

Bachem offers a broad selection of protected cysteine derivatives for most synthetic needs. Additionally, you will find a choice of derivatives of cystine, homocysteine, penicillamine, and thioproline in this brochure. Moreover, we offer a range of protected mercapto carboxylic acids, useful building blocks for synthesizing analogs of cystine-containing peptides.

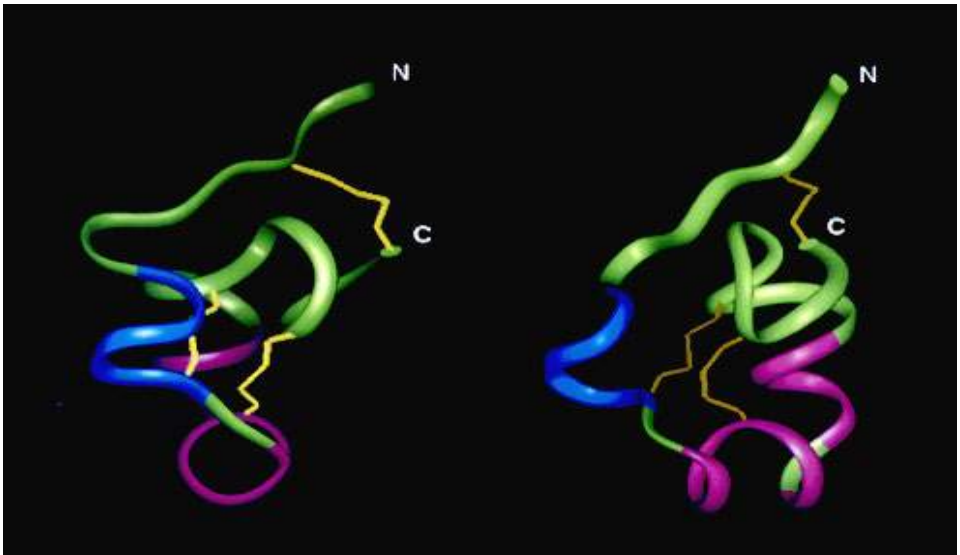
Synthesis of Cys-containing Peptides and Analogs

Peptides containing disulfide bridges

Albeit cysteine rarely occurs in bioactive peptides, its lateral thiol group is of utmost importance for stabilizing the tertiary structure due to its participation in disulfide bonds. Such links can be formed intra- and intermolecularly by oxidation. Protection of this very reactive moiety during the synthesis of peptides is mandatory. Hence the development of specifically cleavable thiol protecting groups has always been an issue in peptide chemistry. Selective deblocking of the thiol moiety allows disulfide bond formation at various stages of the peptide assembly as well as the consecutive formation of two or more disulfide bridges [1-5].
In solution synthesis, the strategy has to be adapted to the presence of Cys (or Met) in the growing peptide, as sulfur-containing amino acids “poison” hydrogenation catalysts.
In solid-phase peptide synthesis (SPPS), thiol protection has to be compatible with

the chosen strategy: trityl has become the most frequently used S-protection in Fmoc/tBu-SPPS, whereas Boc/Bzl-SPPS requires S-protecting groups withstanding repeated contact with TFA. Mbzl or Mob are split off during the final HF cleavage. Acm, which is removed in a separate step, is compatible with both strategies.
Furthermore, removal of S-protection and oxidation yielding the disulfide bridge may be performed either consecutively or concomitantly, by oxidative deprotection.
If two or more disulfide bonds have to be formed either pairwise orthogonal protection is used allowing selective, consecutive disulfide bridge formations or a single Cys protecting group is chosen. Then all the sulfhydryls are liberated simultaneously followed by bridging in buffered solutions containing redox systems such as oxidized and reduced glutathione; the term "oxidative folding" has been coined for this approach. Clearly, oxidative folding is the more convenient approach, but bioactive peptides are often derived from precursors, which are oxidized before being cleaved to generate the active circulating form. In such cases, the correct bridging may only be obtained by consecutive disulfide bond formation. This also applies for analogs and unnatural folding patterns [6].
Peptides containing a single intermolecular disulfide bond, i.e. dimers, can be obtained using any Cys protecting group compatible with the chosen combination of N^{α}/side-chain protecting groups. A different strategy is required when synthesizing heterodimers. SH-labile thiol protecting groups as NPys (often introduced post-synthetically [7]) allow the selective bridging of different peptide chains [8].
For modifying disulfide bridges, one Cys residue or both can be replaced by other β-mercapto amino acids as penicillamine (Pen) or Cys homologs as homocysteine (Hcy). A considerable number of analogs of bioactive peptides, e.g. vasopressin and oxytocin antagonists, has been obtained by substituting an N-terminal Cys by β-mercaptopropionic acid or β-mercapto-β,β-cyclopentamethylenepropionic acid. Cysteamine can replace C-terminal Cys.
Thioether bridges can be obtained by exploiting the high nucleophilicity of the sulfhydryl group, which smoothly reacts with lateral haloacetyl groups in the presence

DISULFIDE BRIDGES STABILIZE THE TERTIARY STRUCTURES OF PROTEINS



ShK toxin, a 35-residue peptide toxin isolated from the sea anemone Stichodactyla helianthus, contains three intramolecular disulfide bonds to stabilize the compactly folded biologically active conformation.

of a base [9]. Peptides containing Cys and dehydroalanine yield lanthionine peptides upon cyclization.

Peptides containing unbridged cysteine
Besides its role in disulfide bridge formation, the sulfhydryl group of cysteine has further important biological functions, e.g. in the active site of SH-proteases. Moreover, it can be nitrosylated, palmitoylated, or prenylated posttranslationally.
The peptide chemist can benefit as well from this highly reactive moiety allowing a broad spectrum of selective modifications. Peptides containing an exposed single free sulfhydryl moiety, usually a C- or N-terminal cysteine, are used to prepare peptide-protein conjugates. The link is generated by reacting the thiol with maleimide bound to the carrier. ***Please ask about our custom synthesis services for conjugation to KLH, BSA or thyroglobulin carrier protein.***
Peptides containing several free thiol moieties can form complexes with metal ions such as Zn(II) ("zinc finger peptides"), Cu(I) and Ag(I). They are readily obtained by SPPS using a single SH protecting group, but they have to be protected from (random) oxidation [10].

Activation and coupling of Cys derivatives
Cys derivatives are notorious for base-catalyzed racemization during activation and coupling [11,12]. Considerable amounts of D-Cys epimer are obtained when coupling Cys(Trt) derivatives in the presence of bases. Cys(Acm) derivatives show a lower tendency to racemize, they tolerate weak bases as collidine. Attempted syntheses of peptides containing several disulfide bridges following standard Fmoc protocols may have failed for this reason. The extent of this side-reaction can be reduced by using weak bases as collidine in combination with uronium/aminium or phosphonium reagents or, more effectively, by coupling in the absence of bases, e.g. with carbodiimides and HOBt (or HOAt). Racemization is further impeded by using less polar solvents for the coupling.
Further side reactions of cysteine during peptide synthesis have been described in the literature, for a review see e.g. [13]. Usually, the extent of by-product formation from Cys depends on the nature of the thiol protecting group. This aspect should not be ignored when developing a synthetic strategy for peptides containing several Cys residues.

The role of Cys in Native Chemical Ligation
The cysteine sulfhydryl group plays a crucial role in the synthesis of large peptides by Native Chemical Ligation (NCL) [14,15]. The key step of NCL consists of the reaction of a peptide thioester with a peptide containing an N-terminal Cys. When assembling small proteins from three or more peptide fragments, the middle fragments have to be N-terminally protected to avoid oligomerization or an intramolecular reaction of the thioesters. Thz (thiazolidine-4-carboxylic acid) can be attached to such fragments as an equivalent for N-terminal Cys, as the thioaminal may be cleaved under mild conditions liberating the mercapto and amino moieties concomitantly [16,17].

Thiol Protection During Solid-Phase Synthesis

Thiol protecting groups
In Fmoc-based SPPS, Trt [18] is the preferred protecting group for the SH-moiety. In the presence of scavengers such as EDT Trt is smoothly removed with TFA. Additionally, Mob [19], the very acid-labile Mmt [20] or the orthogonal Acm [21] are frequently chosen for the synthesis of more complex Cys-containing peptides. If linked to the resin by an ester bond, C-terminal cysteine is prone to base-induced β-elimination followed by addition of piperidine during the subsequent Fmoc cleavage steps. C-Terminal Cys(Trt) should be preferred over Cys(Acm) in order to reduce the extent of this side reaction [22], especially in case of an adjacent Ser or Thr. Fmoc-Asp(OtBu)-OH should not be coupled to Cys(Acm), as the Asp(OtBu)-Cys(Acm) motif readily forms aspartimide in the presence of bases. The motif Asp(OtBu)-Cys(Trt) turned out to be far less sensitive towards the repetitive piperidine treatments during Fmoc-based SPPS [23].
Such limitations have to be kept in mind

when developing strategies for consecutive disulfide bridge formation. Mob and Mbzl [24] are the most commonly used protecting groups for the sulfhydryl function in Boc-based SPPS. Mbzl is more stable towards the repetitive acidolysis of the N^{α}-deprotection step. Hence it should be chosen when synthesizing long peptides. Both groups are removed during the final cleavage with HF. Orthogonal thiol protection is attained by selecting Acm, StBu [25], NPys, or base-labile Fm [26].

Peptides containing a single disulfide bridge

When applying Fmoc-Cys(Trt)-OH for incorporating both cysteines, cleavage with TFA/scavengers yields the crude deprotected linear peptide, which may be cyclized directly by atmospheric oxygen or other mild oxidants (e.g. potassium hexacyanoferrate (III)). The presence of scavengers during TFA cleavage is mandatory. Silanes as Et_3SiH are most efficient in removing the trityl cations as they reduce them to inert triphenylmethane. Usually, the oxidation is performed in very dilute solution to favor intramolecular reaction.

Protecting group	Cleavage conditions	Remarks
Trt	TFA/ scavengers	standard (Fmoc)
Mmt	1%TFA/DCM/ EDT or silanes	selective deprotection of Cys
Acm	Ag(I), Hg(II)	orthogonal to Fmoc and Boc
Dpm[1)]	TFA/scavengers	Fmoc
Mob	HF	standard (Boc)
Mbzl	HF	standard (Boc)
Fm	secondary amine	orthogonal , withstands HF
NPys	thiolysis/ reduction/ S-S interchange	orthogonal, withstands HF
StBu	reduction	orthogonal, withstands HF

[1)] Use of Dpm in place of Trt [42] also reduces oxidation of Cys to cysteic acid.

Fmoc-Cys(Acm)-OH is chosen when conducting cleavage and cyclization consecutively, with the option of purifying the crude S-protected peptide in between. On the other hand, the very acid-labile, selectively cleavable Mmt allows the oxidation of otherwise protected fragments. It can also be removed on-resin (e.g. on Wang resin).
In Boc/Bzl-based SPPS followed by HF-cleavage, use of Mob or Mbzl (the latter being more stable towards the repetitive TFA-treatments during the synthesis) yields the free peptide. Use of Acm yields an Acm-protected crude peptide, which may be oxidized with iodine. For a comparison of various oxidation methods (in solution and on-resin) see [27].

Peptides containing two disulfide bridges

Mispairings, which may occur when oxidizing the four free sulfhydryl groups concomitantly, can be excluded by consecutive formation of the disulfide bridges. The adequate combination of S-protecting groups allows specific cleavage and the use of optimal cyclization conditions. The order, in which the disulfide bonds are formed, may decide the outcome of the synthesis. In most cases, the "smaller cycle" is generated first.

Cysteine protecting groups	Cleavage of cysteine protecting groups	Cyclization conditions
Cys(Trt) + Cys(Trt)	95% aq. TFA+5% EDT	standard, separate steps, liberation of SH followed by oxidation (air, H_2O_2, iodine,...)
Cys(Acm) + Cys(Acm)	iodine in 80% AcOH[1)]	standard, oxidative cleavage, orthogonal to tBu/Wang
Cys(Trt) + Cys(Acm)	95% aq. TFA+5% EDT; 1 eq. iodine in 80% AcOH (iodine titration)	separate steps, Acm is cleaved concomitantly with bridge formation by titration with iodine

[1)] Precautions have to be taken in the presence of Tyr, His, Met and especially Trp. Trp can be protected by adding a large excess of Ac-Trp-OMe. Protected peptides are less susceptible to iodine-induced side-reactions.

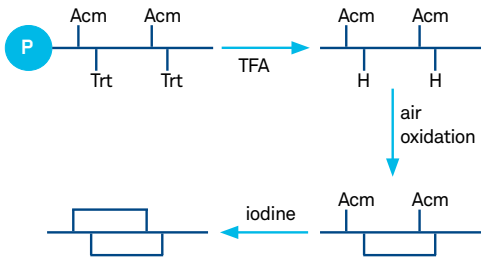
Formation of Disulfide Bridges by Air Oxidation
The peptide is dissolved at a concentration of 10^{-3} to 10^{-4} M in dilute acetic acid or 0.05 M ammonium acetate; the pH is adjusted and kept between 7.5 and 8 whilst stirring the solution at room temperature in the presence of atmospheric oxygen.

Additives such as 1-10% DMSO or 3% H_2O_2 can be used to accelerate the reaction (H_2O_2 must not be used if the peptide contains Met). The progress of the reaction is followed by HPLC.

The pH has to be checked regularly and readjusted if required. After complete conversion, the solution is acidified with acetic acid. It can be applied directly to preparative HPLC.

Formation of Disulfide Bridges from Bis-Acm Peptides
The peptide is dissolved at a concentration of 10^{-3} to 10^{-4} M in 40% aqueous acetic acid.
Iodine (25 to 50 fold excess) dissolved in 40% acetic acid (or in methanol) is added.
The solution is stirred at room temperature, the progress of the reaction is monitored by analytical HPLC.
To stop the reaction the excess of iodine is destroyed with 1 M aqueous ascorbic acid (the solution is added slowly up to disappearance of the iodine color).
The solution is diluted with water to lower the concentration of acetic acid to approximately 10% before applying it to a preparative HPLC column.

Several combinations of protecting groups may be chosen [1-5,27]. We have described in our "Recommended Standard Procedure" protocol the most used combination Trt/Acm depicted below:



Peptides containing three disulfide bridges

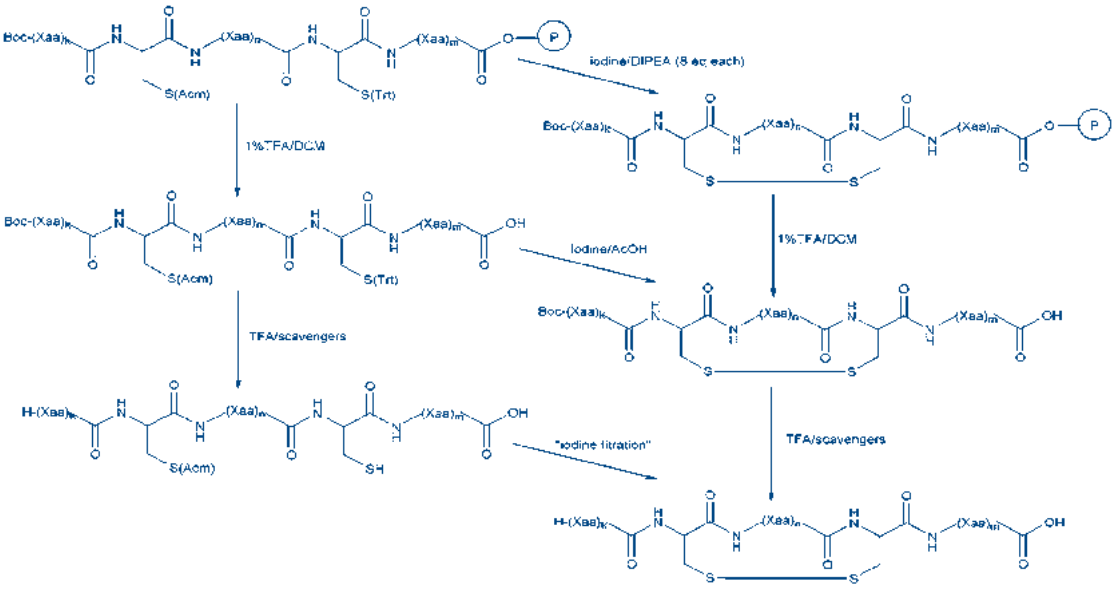
The combination Acm/Mob/Trt has been successfully used for the preparation of several peptides (amongst them relaxin [28], defensins [29], sapecin [30]) containing three disulfide bridges employing Fmoc/tBu-SPPS and selective bridging. It should be kept in mind that the consecutive formation of the disulfide bridges is a long and tedious process. If the peptide to be prepared corresponds to a naturally occurring sequence, not excised from a prepeptide and showing the natural bridging pattern, the simultaneous formation of disulfide bridges (random oxidation) can render very good results [31,32]. Both methods can be combined [33].

Simultaneous formation of disulfide bridges

Using this approach a single kind of protecting group must be chosen for the protection of the sulfhydryl function. In Fmoc-based SPPS, Trt is the most commonly used thiol protection cleaved during the final TFA deprotection; Acm or Mbzl have been used in Boc SPPS. The crude peptide can be prepurified or subjected directly to oxidation. The Acm group is stable to acidolysis. Hence the SH moieties of the peptide obtained after the final TFA (or HF) deprotection still are blocked, which facilitates the purification.

Pairing of Cys protecting groups	Cleavage of Cys protecting group	Cyclization conditions
Cycle 1: Cys(Trt)	TFA/H_2O_2/ scavengers	Air oxidation
Cycle 2: Cys(Acm)	Concomitant cleavage and cyclization with iodine	
Cycle 3: Cys(Mob)	TFMSA/TFA/ anisole+5% EDT)	Air or DMSO-oxidation, or iodine titration

The Acm group can then be cleaved by mercuric acetate followed by oxidative folding. The reaction is mediated by redox systems such as reduced and oxidized glutathione, cysteine/cystine or DTT/oxidized DTT. This approach has been used in the preparation of muscarinic toxin 1 (MTX1) [34] a 66-resi-



Strategies for the Fmoc-SPPS of a peptide containing a single disulfide bridge employing a highly acid-labile resin, e.g. SASRIN or 2-chlorotrityl resin.

On-Resin Disulfide Bridge Formation
The resin is left to swell in DCM/MeOH/H_2O (60:25:4,v/v/v; 18 ml/g resin) for 0.5 to 1 hr before adding 8 eq I_2 in DCM (12 ml/g resin) and 8 eq DIPEA Reaction time: 1 hr or less. Washes: DMF, aq. ascorbic acid/ DMF, aq. DMF, DMF, DCM or IPA.

due peptide containing 5 disulfide bridges following a convergent Boc synthesis based on a combined solid phase-solution approach. However, folding does not yield automatically the correct disulfide bridging. In certain cases, a product containing an unnatural folding pattern could be isolated predominantly at first [35]. The fine-tuning of the cyclization conditions (reaction at 5°C in the presence of 2 M sodium sulfate) has resulted in the isolation of the correctly folded, bioactive molecule as the main product.

On-resin cyclization

Peptides containing a single disulfide bridge can be obtained via SPPS by various synthetic strategies, which are summarized in the scheme on p. 6 (for SASRIN or other highly acid-sensitive resins). Either the (partially) protected peptide or the deprotected peptide may be oxidized in solution, but as to enhance intramolecular disulfide formation, the oxidation is performed in very dilute solution thus making work-up rather tedious. Oxidation of a resin-bound peptide circumvents this problem. Quite a number of papers dealing with variations of this approach as employing different types of resin, sulfhydryl protecting groups and oxidants has been published [36], though, to our knowledge, a systematic overview is still lacking. Cyclization yields depend on several factors, amongst them the peptide load (a low load should reduce intermolecular reaction and thus enhance cyclization, i.e. the pseudodilution effect), the size of the ring to be formed (probably best below 10 amino acids), and the solvent which should properly swell the peptide resin. Oxidations proceeding smoothly in solution may also work well if performed with the resin-bound peptide (for a noteworthy exception see [37]). The N-terminus should be protected. When oxidizing peptides linked to highly acid-sensitive carriers (e.g. SASRIN, ClTrt-resin) with iodine, the concomitantly formed HI should be neutralized. At Bachem, oxidative cyclization has been performed successfully on SASRIN. The conditions described here have been evaluated for [Cys^1(Acm), Cys^7(Trt)]-salmon calcitonin (1-10) and [Cys^2(Acm or Trt), Cys^7(Trt)]-α-CGRP (human) (1-14) [38].

The resin (load of fully protected peptide approximately 0.1 mmol/g or below) is left to swell in DCM/MeOH/H_2O (60:25:4, approx. 18 ml/g resin) for at least 30 minutes. A solution of iodine (8 eq) in DCM (12 ml/g resin) is added rapidly, followed by DIPEA (max 8 eq) to neutralize the hydrogen iodide evolved during the reaction. Oxidation time should not exceed one hour, the rate has to be determined by taking samples and quenching them with ascorbic acid before cleavage and analysis. Eventually excess iodine is removed by filtering and washing the resin with DMF and DMF/ascorbic acid in aqueous buffer of pH7. Nevertheless the resin may remain slightly yellow. As usual, all polar impurities have to be removed before cleaving with 1% TFA/DCM. The yield obtained may be lower than the cleavage yield of the linear fully protected peptide. Yields depend on the conditions of oxidation, especially on the solvent, thus preliminary experiments optimizing this parameter should be conducted if possible.
Other synthetic strategies may be chosen, e.g. generation of sulfhydryl groups and oxidation as separate steps.
If S-t-butylthio protection is employed the peptide resin is first treated with tributylphosphine [39,40] (or β-mercaptoethanol), thoroughly washed and then treated with an oxidant. The incorporation of Cys(Mmt) allows consecutive on-resin deprotection and cyclization during Fmoc-SPPS [20].
Further modes of on-resin cyclization involving Cys, e.g. via thioether bond [41], have been described in the literature.

Cleavage of Mob and Disulfide Bridge Formation
The cleavage cocktail (TFMSA/TFA/anisole 1:8:1) is prepared and cooled in an ice bath. The cooled mixture is added to the peptide (3 mg/ml). The resulting solution is stirred at 0°C for 45 min.
The reaction solution is diluted 50-fold with ice-cold water and extracted 3 times with ether.
DMSO (10% of total volume) is added to the aqueous phase. The cyclization is monitored by analytical HPLC. If complete conversion is achieved, the reaction solution is diluted with water and used directly for preparative HPLC purification. The cyclization can also be performed by iodine titration: addition of a methanolic solution of iodine up to persistent yellow colour and destruction of the excess of iodine with ascorbic acid.

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Simultaneous Formation of Multiple Disulfide Bridges
The linear peptide is solubilized at a concentration of 10^{-3} to 10^{-4} M in 0.05 M ammonium acetate/0.1 M guanidinium hydrochloride (optional) and the pH is adjusted to 7.5. Redox additives are often used to accelerate the reaction.
Glutathione reduced (GSH)/glutathione oxidized (GSSG) is added to the oxidation solution at a ratio of 1:100:10 (peptide/GSH/GSSG).
The reaction is monitored by analytical HPLC and at the end, after acidification with acetic acid, the solution is directly subjected to preparative HPLC.

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ABBREVIATIONS

Ac	Acetyl
Acm	Acetamidomethyl
AMC	7-Amino-4-methylcoumarin
Boc	t-Butyloxycarbonyl
Bzl	Benzyl
tBu	t-Butyl
DCM	Dichlorormethane
DIPEA	Diisopropylethylamine
DMF	N,N-Dimethylformamide
DMSO	Dimethylsulfoxide
Dpm	Diphenylmethyl (Dityl)
DTT	Dithiothreitol
EDT	Ethanedithiol
Et	Ethyl
Fm	9-Fluorenylmethyl
Fmoc	9-Fluorenylmethoxycarbonyl
HOAt	1-Hydroxy-7-azabezotriazole
HOBt	1-Hydroxybenzotriazole
IPA	Isopropanol
4MβNA	4-Methoxy-β-naphthyl
Mbzl	4-Methylbenzyl
Me	Methyl
Mob	4-Methoxybenzyl
Mmt	4-Methoxytrityl
Mtt	4-Methyltrityl
βNA	β-Naphthyl
pNA	4-Nitroanilide
NPys	3-Nitro-2-pyridinesulfenyl
ONp	4-Nitrophenyl ester
OSu	N-Hydroxysuccinimidyl ester
OPfp	Pentafluorophenyl ester
SASRIN	Super Acid Labile Resin
SEt	Ethylthio
StBu	t-Butylthio
TFA	Trifluoroacetic acid
TFMSA	Trifluoromethanesulfonic acid
Trt	Trityl
Z	Benzyloxycarbonyl

CYSTEINE AND CYSTEINE DERIVA-TIVES

Bachem offers a broad selection of protected Cys derivatives for most synthetic needs, especially for Fmoc/tBu-based SPPS. A host of cysteine derivatives for peptide synthesis by Boc/Bzl-based approaches, on resin or in solution, are available in our online shop shop.bachem.com

FMOC-CYSTEINE DERIVATIVES, RESINS AND CYSTEINE PSEUDO-PROLINE DIPEPTIDES

Fmoc-Cys(Acm)-OH
4006622

Fmoc-D-Cys(Acm)-OH
4014984

Fmoc-Cys(Acm)-OPfp
4011855

Fmoc-Cys(Acm)-Wang resin (200-400 mesh)
4006437

Fmoc-Cys(tBu)-OH
4003574

Fmoc-D-Cys(tBu)-OH
4011898

Fmoc-Cys(tBu)-OPfp
4011863

Fmoc-Cys(tBu)-Wang resin (200-400 mesh)
4009137

Fmoc-Cys(Bzl)-OH
4016149

Fmoc-D-Cys(Bzl)-OH
4029075

Fmoc-Cys(Dpm)-OH
4081840

Fmoc-Cys(4-methoxytrityl)-OH
4025726

Fmoc-D-Cys(4-methoxytrityl)-OH
4027076

Fmoc-Cys(Mob)-OH
4007329

Fmoc-D-Cys(Mob)-OH
4017836

Fmoc-Cys(Mtt)-OH
4028614

Fmoc-D-Cys(Mtt)-OH
4066063

Fmoc-Cys(NPys)-OH
4016999

Fmoc-Cys(StBu)-OH
4007445

Fmoc-D-Cys(StBu)-OH
4026662

Fmoc-Cys(SO_3H)-OH · disodium salt
4016589

Fmoc-Cys(Trt)-OH
4007272

Fmoc-D-Cys(Trt)-OH
4017507

Fmoc-Cys(Trt)-OPfp
4030624

Fmoc-D-Cys(Trt)-OPfp
4017508

Fmoc-Cys(Trt)-Wang resin (100-200 mesh)
4028211

Fmoc-Cys(Trt)-Wang resin (200-400 mesh)
4014510

Fmoc-Cys(Trt)-SASRIN™ resin (200-400 mesh)
4013511

Fmoc-Cys(SASRIN™ resin)-OH (200-400 mesh)
4026902

Fmoc-Ser(tBu)-Cys(Psi(Me,Me) pro)-OH
4096165

Fmoc-Gly-Cys(Psi(Dmp,H)pro)-OH
4096169

Fmoc-Ala-Cys(Psi(Dmp,H)pro)-OH
4096166

Fmoc-Leu-Cys(Psi(Dmp,H)pro)-OH
4096175

Fmoc-Val-Cys(Psi(Dmp,H)pro)-OH
4096177

CYSTEINE DERIVATIVES LINKED TO 2-CHLOROTRITYL RESIN

H-Cys(Acm)-2-chlorotrityl resin (200-400 mesh)
4026171

H-Cys(4-methoxytrityl)-2-chlorotrityl resin (200-400 mesh)
4028399

H-Cys(Trt)-2-chlorotrityl resin (100-200 mesh)
4072954

H-Cys(Trt)-2-chlorotrityl resin (200-400 mesh)
4026170

H-Cys(Trt)-2-chlorotrityl resin (200-400 mesh) (Low Substitution)
4073355

BOC-CYSTEINE DERIVATIVES AND RESINS

Boc-Cys(Acm)-OH
4001136

Boc-D-Cys(Acm)-OH
4026800

Boc-Cys(Acm)-OSu
4018238

Boc-Cys(Bzl)-OH
4001957

Boc-D-Cys(Bzl)-OH
4030402

Boc-Cys(Bzl)-OSu
4011151

Boc-Cys(Fm)-OH
4018970

Boc-Cys(Mbzl)-OH
4010026
Boc-D-Cys(Mbzl)-OH
4019735

Boc-Cys(Mbzl)-PAM resin (200-400 mesh)
4014351

Boc-Cys(Mob)-OH
4000525

Boc-D-Cys(Mob)-OH
4013583

Boc-Cys(Mob)-OSu
4000309

Boc-Cys(Mob)-Merrifield resin (100-200 mesh)
4027257

Boc-Cys(NPys)-OH
4014705

Boc-D-Cys(NPys)-OH
4019702

Boc-Cys(SEt)-OH · DCHA
4000384

Boc-Cys(Trt)-OH
4003922

Boc-D-Cys(Trt)-OH
4017511

CYSTEINE AND PROTECTED DERIVATIVES

H-Cys-OH · HCl · H_2O
4030461

H-D-Cys-OH · HCl · H_2O
4030537

H-Cys(Acm)-OH · HCl
4000839

H-D-Cys(tBu)-OH · HCl
4011897

H-Cys(Bzl)-OH
4012083

H-D-Cys(Bzl)-OH
4011709

H-Cys(Bzl)-OEt · HCl
4012395

H-Cys(Fm)-OH
4018969

H-Cys(4-methoxytrityl)-OH
(H-Cys(Mmt)-OH)
4025808

H-Cys(Mob)-OH
4000523

H-Cys(StBu)-OH
4030538

H-Cys(SO_3H)-OH · sodium salt
4016588

H-Cys(Trt)-OH
4001485

H-D-Cys(Trt)-OH
4017506

H-Cys(Trt)-NH_2
4015634

Ac-Cys-OH
4031426

Ac-Cys(Trt)-OH
4018217

Trt-Cys(Trt)-OH
4006901

Trt-Cys(Trt)-OH · DEA
4017514

Z-CYSTEINE DERIVATIVES

Z-Cys(Bzl)-OH
4004225

Z-Cys(Z)-OH
4001212

S-ALKYLATED CYSTEINE DERIVATIVES

H-Cys(aminoethyl)-OH · HCl
(L-Thialysine · HCl)
4001430

Boc-Cys(Et)-OH
4027437

Boc-Cys(Me)-OH
4018560

Boc-Cys(Z-aminoethyl)-OH
(Boc-L-thialysine(Z))
4020253

Fmoc-Cys(3-(Boc-amino)-propyl)-OH
4028163

Fmoc-Cys(Et)-OH
4016168

Fmoc-Cys(2-hydroxyethyl)-OH
4026001

Fmoc-Cys((R)-2,3-di(palmitoyloxy)-propyl)-OH
4042951

Fmoc-Cys((RS)-2,3di(palmitoyloxy)-propyl)-OH
(Fmoc-Pam_2Cys-OH)
4038236

Fmoc-Cys((S)-2,3-di(palmitoyloxy)-propyl)-OH
4074791

Palmitoyl-Cys((RS)-2,3di(palmitoyloxy)-propyl)-OH
(Pam_3Cys-OH)
4015000

CYSTEINE SUBSTRATES AND INHIBITORS

Ac-Cys(farnesyl)-OH
(AFC)
4018082

Ac-Cys(farnesyl)-OMe
(AFCME)
4018083

H-Cys(aminoethyl)-OH · HCl
(L-Thialysine · HCl)
4001430

H-Cys(Bzl)-AMC
4007281

H-Cys(Bzl)-pNA
4002666

H-Cys(carbamoyl)-OH
4027858

MERCAPTO AMINO ACIDS

Here you will find a choice of cystine derivatives as well as S-protected derivatives of homocysteine, homocysteic acid, penicillamine, and thioproline.

We also offer a range of protected β-mercapto carboxylic acids, which are useful building blocks for synthesizing analogs of cystine-containing peptides.

CYSTINE DERIVATIVES

$(Boc\text{-}Cys\text{-}OH)_2$
(Disulfide bond)
4001680

$(Fmoc\text{-}Cys\text{-}OH)_2$
(Disulfide bond)
4011808

$(Fmoc\text{-}Cys\text{-}OSu)_2$
(Disulfide bond)
4011809

$(Fmoc\text{-}Cys\text{-}OtBu)_2$
(Disulfide bond)
4027211

$(Z\text{-}Cys\text{-}OH)_2$
(Disulfide bond)
4000631

$(H\text{-}Cys\text{-}OH)_2$
(Disulfide bond)
4030444

$(H\text{-}Cys\text{-}NH_2)_2 \cdot 2\ HCl$
(Disulfide bond)
4011703

$(H\text{-}Cys\text{-}allyl\ ester)_2 \cdot 2$ p-tosylate
(Disulfide bond)
4028317

$(H\text{-}Cys\text{-}OtBu)_2 \cdot 2\ HCl$
(Disulfide bond)
4014989

$(H\text{-}Cys\text{-}OEt)_2 \cdot 2\ HCl$
(Disulfide bond)
4016470

$(H\text{-}Cys\text{-}OMe)_2 \cdot 2\ HCl$
(Disulfide bond)
4002631

$(H\text{-}D\text{-}Cys\text{-}OMe)_2 \cdot 2\ HCl$
(Disulfide bond)
4026225

$(H\text{-}Cys\text{-}\beta NA)_2$
(Disulfide bond)
4030540

$(H\text{-}Cys\text{-}\beta NA)_2 \cdot 2\ HCl$
(Disulfide bond)
4025042

$(H\text{-}Cys\text{-}pNA)_2$
(Disulfide bond)
4001884

$(Ac\text{-}Cys\text{-}OH)_2$
(Disulfide bond)
4017817

$(Ac\text{-}Cys\text{-}OMe)_2$
(Disulfide bond)
4002343

HOMOCYSTEINE, HOMOCYSTINE, HOMOCYSTEIC ACID

Boc-Homocys(Mbzl)-OH
4018998

Boc-Homocys(Trt)-OH
4025120

Boc-D-Homocys(Trt)-OH
4041792

Fmoc-Homocys(Trt)-OH
4025118

Fmoc-D-Homocys(Trt)-OH
4039317

Fmoc-N-Me-Homocys(Trt)-OH
4042205

$(H\text{-}Homocys\text{-}OH)_2$
(Disulfide bond)
4018994

Fmoc-4-(neopentyloxysulfonyl)-Abu-OH
(Fmoc-Homocya(OnP)-OH)
4034632

PENICILLAMINE DERIVATIVES

Boc-Pen(NPys)-OH
4025289

Boc-D-Pen(NPys)-OH
4025288

Boc-Pen(Trt)-OH
4019781

Boc-D-Pen(Trt)-OH
4019780

Fmoc-Pen(Acm)-OH
4016442

Fmoc-D-Pen(Acm)-OH
4017083

Fmoc-Pen(Trt)-OH
4019778

Fmoc-D-Pen(Trt)-OH
4019031

H-Pen-OH
4031087

H-D-Pen-OH
4032629

CYSTEIC ACID

Fmoc-L-cysteic acid · disodium salt
(Fmoc-Cya-OH · disodium salt)
4039171

THIAZOLIDINE-4-CARBOXYLIC ACID

Boc-L-thiazolidine-4-carboxylic acid
(Boc-Thz-OH)
4029316

Fmoc-L-thiazolidine-4-carboxylic acid
(Fmoc-Thz-OH)
4037410

L-Thiazolidine-4-carboxylic acid
4028717

D-Thiazolidine-4-carboxylic acid
4027488

L-2-Oxathiazolidine-4-carboxylic acid
4012415

S-PROTECTED β-MERCAPTO CARBOXYLIC ACIDS

[1-(4-Methoxy-benzylsulfanyl)-cyclohexyl]-acetic acid
4013918

[1-(4-Methyl-benzylsulfanyl)-cyclohexyl]-acetic acid
4028383

3-(Acetamido-methylsulfanyl)-propionic acid
4017035

3-(Tritylsulfanyl)-propionic acid
(S-Trityl-deamino-cysteine)
4012270

3-(4-Methoxy-benzylsulfanyl)-3-methyl-butyric acid
(S-(4-Methoxybenzyl)-deamino-penicllamine)
4009768

FURTHER THIOL COMPOUNDS

Fmoc-Cysteamine-SASRIN™ resin (200-400 mesh)
4026901

DL-Thiorphan
4010438

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Marketing & Sales Contact

Americas

Bachem Americas, Inc.
Tel. +1 888 422 2436 (toll free in USA & Canada)
+1 310 539 4171
sales.us@bachem.com

Asia Pacific

Bachem Japan K.K.
Tel. +81 3 6661 0774
sales.jp@bachem.com

Europe, Africa, Middle East and India

Bachem AG
Tel. +41 58 595 2020
sales.ch@bachem.com

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