Iris Biotech

LIGATION TECHNOLOGIES

Version: IB7_3

Empowering Peptide Innovation

With this guiding theme in mind, Iris Biotech's mission is to support researchers by supplying

- innovative technologies,
- rare compounds,
- as well as a broad portfolio on standard consumables,

available in flexible quantities from small scale to bulk quantities. To fulfill our dedication "Empowering Peptide Innovation", we are attending various conferences, symposia, and exhibitions each year. This allows us to remain in direct contact with scientists all over the world, both from academia and industry, to exchange knowledge, and to gather new ideas to tackle your current challenges.

Guided by our dedication to provide

- competent service,
- as well as novel substances and
- latest technologies,

Iris Biotech is your trusted partner for the world of peptides, while having strong expertise in associated disciplines. Thus, our portfolio comprises reagents and tools for the synthesis and modification of peptides, e.g. amino acids, resins and solvents but also for related technologies such as Drug Delivery, Linkerology® and Life Sciences.

Amino Acids ***Building Blocks*** ***Life Sciences*** ***Drug Delivery*** ***Reagents*** ***Resins*** ***Linkerology®*** ***Click Chemistry***

Owed to the growing demand for tailor-made compounds, our portfolio is fine-tuned by our Custom Synthesis Service at Iris Biotech Laboratories. Our skilled scientists offer profound expertise in

- *de novo* route development,
- upscaling towards larger scale production,
- as well as synthesis optimization for increased efficiency.

Examples are the synthesis of rare chiral building blocks, unnatural amino acid derivatives, sophisticated orthogonal protecting groups, heterocycles, building blocks for nucleotides, PEGs and PEG-analogues as well as specific linkers for controlled drug delivery and release.

Portfolio Overview

Peptide Synthesis and Modification

(Protected) Amino Acids

Standards such as Fmoc-D/L-AAA and Boc-D/L-AAA, Smoc amino acids for peptide synthesis in water, variety of protecting groups (e.g. Pbf, Trt, ^{t}Bu, Bzl, Acm, Mob, SIT, Phacm, Allocam, Mmt), unusual amino acids, fluorinated derivatives, substituted prolines, arginine analogues

Building Blocks

Amino alcohols, amino aldehydes, diamines and hydrazines, (pseudoproline) dipeptides, polyamines and spermines, fatty acid derivatives

Reagents

Coupling reagents, solvents and scavengers, protecting groups

Resins

Preloaded resins (e.g. based on Trityl, TCP, TentaGel, Methoxybenzhydryl, Merrifield, PAM, Rink, Wang), scavenger resins, hydrazone resins

Linkerology® and Drug Delivery

Linkers for Solid Phase Peptide Synthesis

Cleavable Linkers

Val-Ala based, Val-Cit based, disulfide-based, Dde-helping hands

Photo-Activatable Linkers

Functionalized Linkers

Clickable linkers, trifunctional linkers, linkers with maleimide function, cross-linkers, selective N-term acylation and biotinylation

PROTACs

Ligands, linkers & modules

Fullerenes, Poly(2-oxazolines) & Dextrans

Poly-Amino Acids

Poly-Arg, Poly-Glu, Poly-Lys, Poly-Orn, Poly-Sar

PEGylation

Branched PEGylating reagents, (amino-)PEG-acids, PEG-amines & hydrazides & guanidines, reagents for Click-conjugation, Biotin-PEG-reagents, PEG-thiols, PEG-maleimides, other PEGylating reagents

Life Sciences

Biotinylation Reagents

Carbohydrates

Galactose, Glucose, Maltose, Mannose, Xylose and others

Drug Metabolites

Peptides

Substrates & Inhibitors

E.g. protein kinase inhibitors, substrates for fusion (Halo/Snap/Clip)-tagged proteins

Natural Products

Dyes and Fluorescent Labels

E.g. ICG, AMC, DAPI

Maillard & Amadori Reaction Products

Large portfolio of derivatives useful as standards for food, pharma and cosmetics industry

Vitamins

Custom Synthesis

Your project requires a compound not listed in our portfolio?
Get in contact and inquire about our custom synthesis capabilities.

Our experienced scientists are excited to accept your synthetic challenge!
In such cases, your request undergoes the following stages:

Step-by-Step Analysis

- Customer's demands

Process Evaluation

- Detailed literature review
- Synthetic possibilities

Strategy Development

- Protocol development
- Method development and validation
- Customized synthesis

Quality Consistency

- Identity confirmation
- Purity verification

Our Service Promise

All our services are based on high standards, transparency & documentation, trust, honesty & confidentiality, as well as the required know-how.

High Standards

- Values: sustainability & responsibility
- State-of-the-art equipment & latest technologies
- High quality standards
- Qualified suppliers & regular audits

Transparency & Documentation

- Talk to our specialists – customer care
- Certificates of analysis & impurity profiling
- Analytical and process reports

Trust, Honesty & Confidentiality

- Intergenerational business valuing partnerships
- Meeting the customer‘s expectations
- Integrity towards our customers

Our Know-How

- One-step reactions & complex multi-step synthesis
- Scalability from mg to kg quantities
- Route scouting

Ligation Technologies

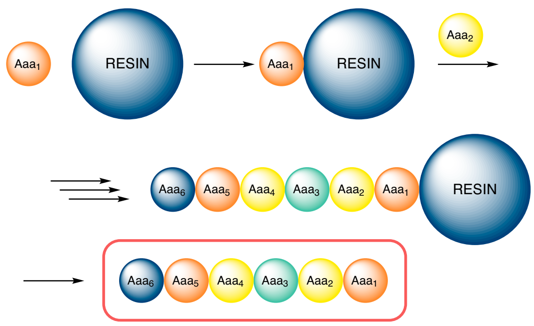
1. Description of the Technology

Background

Peptides are typically synthesized *via* solid phase (peptide) synthesis (SP(P)S). The main advantage in comparison to classical solution phase synthesis is the fast and easy separation of the desired product from excess reagents by filtration. Typically, in SP(P)S, the molecule being synthesized (e.g., a growing peptide chain) is attached to an insoluble solid support, while reagents are added to the suspension. This setup enables the removal of excess reagents and dissolved byproducts *via* simple disposal of the reaction solution. Filtration followed by washing of the resin with various solvents leaves the purified protected peptide on the carrier. Consequently, an excess of reagents can be employed in order to shorten reaction times and allow for a quantitative turnover of the substrate, which in turn leads to higher yields and less side products.

The Main Advantages of SPPS

1. Fast work-up through easy separation of solid support from dissolved reactants and by products by filtration, and multiple, rapid washing steps.
2. Improved reaction times, turnover and yield by use of excess amounts of reagents.
3. The syntheses can easily be automatized.
4. Toxic or hazardous materials can be handled safely while being attached to the resin.
5. Minimal physical product loss.
6. Pseudo-dilution phenomena on an individual bead can enable cyclization and avoid formation of dimers.



Protocol of solid phase synthesis of peptides:

Attachment of the first amino acid to a resin
Repetitive cycles of:

- Deprotection
- Washing
- Coupling
- Washing
- ...
- Deprotection

Final cleavage from the resin and purification.

# of Steps	Yield per Step/Final Yield			
	98,0%	99,0%	99,5%	99,9%
10	82%	90%	95%	99%
20	67%	82%	90%	98%
30	55%	74%	86%	97%
40	45%	67%	82%	96%
50	36%	61%	78%	95%
60	30%	55%	74%	94%
70	24%	49%	70%	93%
80	20%	45%	67%	92%
90	16%	40%	64%	91%
100	13%	37%	61%	90%
110	11%	33%	58%	90%
120	9%	30%	55%	89%
130	7%	27%	52%	88%
140	6%	24%	50%	87%
150	5%	22%	47%	86%
160	4%	20%	45%	85%
170	3%	18%	43%	84%
180	3%	16%	41%	84%
190	2%	15%	39%	83%
200	2%	13%	37%	82%

Fig. 1: Concept of solid phase peptide synthesis (SPPS).

Two reaction steps have to be carried out per amino acid of a peptide chain. I.e., the synthesis of a 50mer requires 100 chemical steps. Assuming, that the yield per chemical step is 98%, which in general means is rather high, there is only 13% yield of the target sequence left (*Fig. 1*). Nevertheless, within a long sequence, the probability that difficult fragments are appearing is rather high, which will lower the overall yield of the synthesis. In contrast, an extremely high average yield of 99.9% per coupling step will result in 90% global yield. As this is rather unrealistic, new chemical methodologies such as fragment condensation and native chemical ligation must be developed to facilitate access to longer peptides of 100 amino acids and more.

Native Chemical Ligation

Native chemical ligation (NCL) of unprotected peptide segments involves the reaction between a first peptide fragment α-thioester and a second peptide fragment, which carries a cysteine on the N-terminus, to yield a product with a native amide bond at the ligation site. Peptide-α-thioalkyl esters are commonly used because of their ease of preparation. These thioalkyl esters are rather unreactive, so the ligation reaction is catalyzed by *in situ* transthioesterification with thiol additives, which are either a mixture of thiophenol/benzyl mercaptan or other alkanethiols. Despite the use of this thiol additive, ligation reactions typically take 24–48 h.

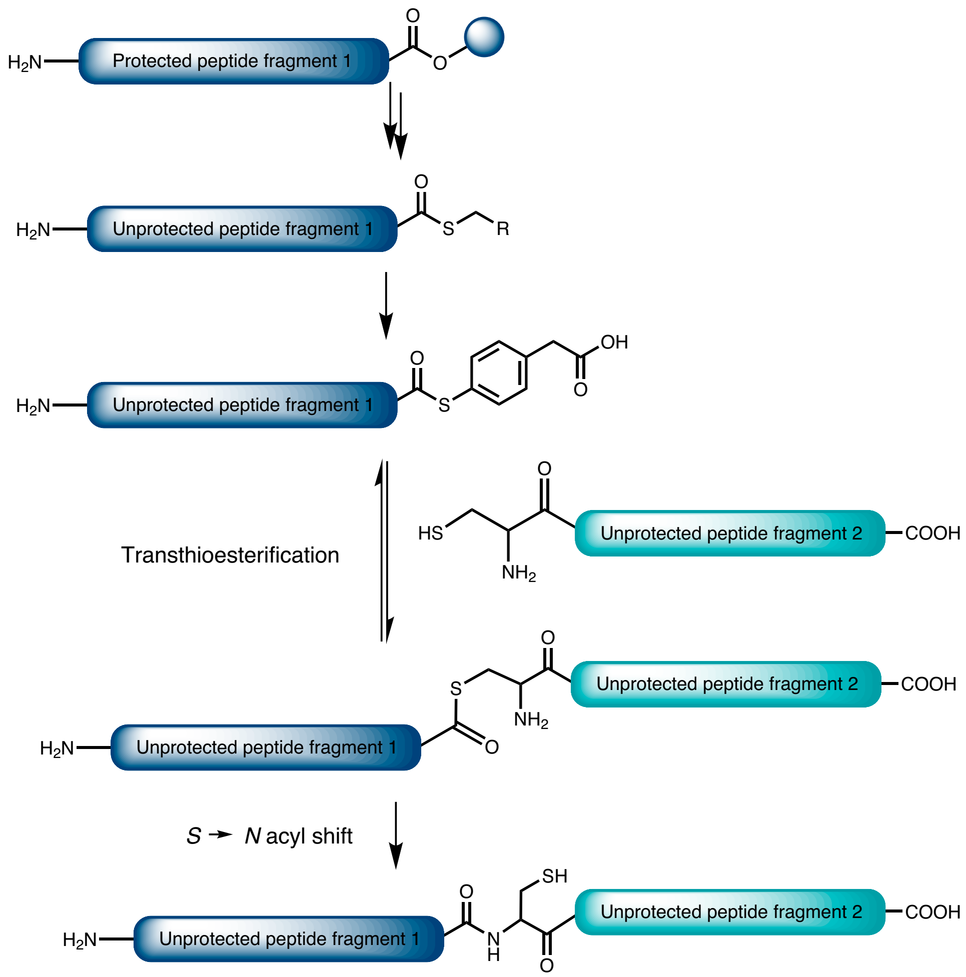


Fig. 2: Mechanism of native chemical ligation.

back to content ↑

Requirements

1. Unprotected peptide fragment as C-terminal thioester.
2. Cysteine on N-terminus of a second unprotected peptide fragment.

Limitations

1. Cysteine appears very rarely in natural sequences.
2. Multiple, consecutive ligations are hardly possible.
3. Cysteine is prone to racemization.
4. Slow kinetics, as ligations normally take 24-48 h; hence a good thiol additive, like 4-mercaptophenylacetic acid (MPAA), is necessary.

The main advantage of this ligation technology vs. fragment condensation is the usually good solubility of unprotected peptide fragments compared to fully protected peptides, which have very limited solubility. One main challenge, however, is that the presence of cysteine within a peptide sequence is a prerequisite for NCL, but at the same time cysteine is the least abundant of all proteinogenic amino acids since it occurs with an average frequency of only 1.4% within natural sequences. This becomes even more of an obstacle if multiple consecutive ligations are necessary to construct the target sequence. Hence, sophisticated variations must be implemented in the absence of cysteine.

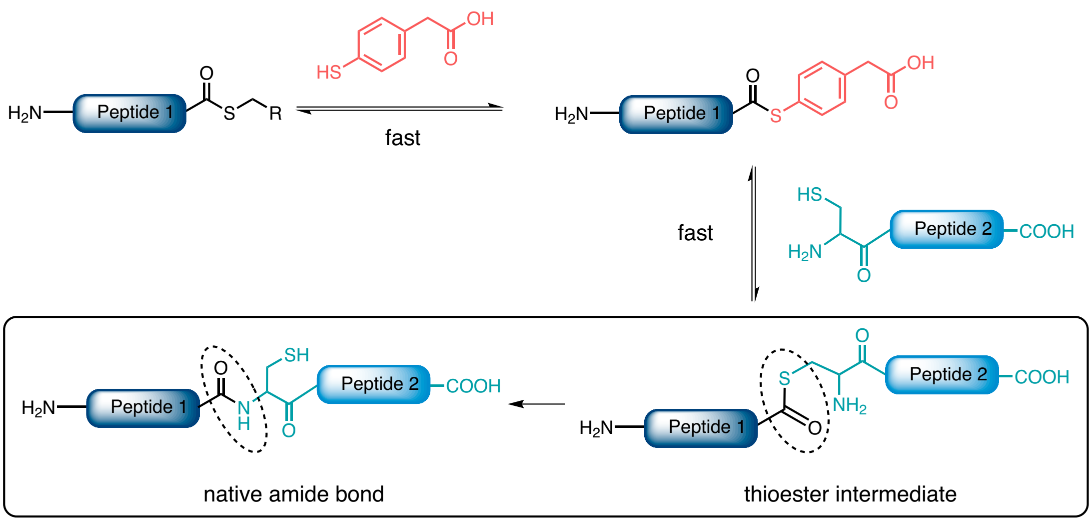
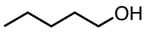
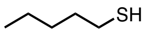
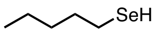
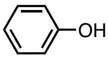
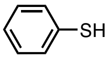
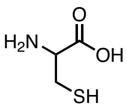
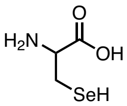
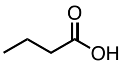


Fig. 3: The role of MPAA as an additive in native chemical ligation.

Element	Electronegativity	Atomic Radius	Electron Configuration
O	3.4	0.60^{0} Å, 1.38^{-2}_{4} Å	[He] $2s^2\ 2p^4$
S	2.6	1.04^{0} Å, 1.84^{-2}_{6} Å	[Ne] $3s^2\ 3p^4$
Se	2.6	1.16^{0} Å, 1.98^{-2}_{6} Å	[Ar] $3d^{10}\ 4s^2\ 4p^4$

Structure	Leaving Group	pK_a
	Alkyl Alcohol	16-18
	Alkyl Thiol	10-11
	Alkyl Selenol	7-8
	Phenol	9.89
	Thiophenol	6.6
	Cys S-H	8.3
	Sec Se-H	5.2
	Alkyl Carboxylic Acids	~4

The mechanistic details of NCL have been studied by several groups in order to find appropriate additives. Substituted thiophenols with pK_a > 6 were found to best combine the ability to exchange rapidly and completely with thioalkyl esters, and to then act as efficient leaving groups in the reaction of the peptide thioester with the thiol side chain of an N-terminal cysteine. 4-mercaptophenylacetic acid (MPAA), a non-malodorous, water-soluble thiol, proved to be a highly effective and practical additive. MPAA reacts orders of magnitude faster than other thiols in model studies of NCL and in the synthesis of small proteins, as demonstrated in the synthesis of turkey ovomucoid third domain (OMTKY3). MPAA should find broad use in native chemical ligation and in the total synthesis of proteins.

The need for a cysteine residue on the N-terminus of one of the reacting peptide fragments has motivated the development of β-, γ-, and δ-thiolated variants of other amino acids, as well as thiol-containing auxiliaries that can be used as Cys surrogates in ligation chemistry. After ligation reactions at these residues, the thiol auxiliary is desulfurized (usually by means of radical-based protocols) to yield native polypeptide products. However, this transformation is not chemoselective in the presence of other unprotected cysteine residues that might be found elsewhere in the sequence. This limitation of desulfurization chemistry has led chemists to expand the native chemical ligation toolbox to include the 21st amino acid, selenocysteine (Sec), as well as various non-natural selenoamino acids (to date specifically based on Pro and Phe). The key advantage of carrying out ligation chemistry with selenoamino acids rather than thioamino acids is that chemoselective deselenization can be performed under mild conditions (typically with a phosphine reductant and a hydrogen atom source) that do not affect unprotected Cys residues. Payne *et al.* and Dery *et al.* have demonstrated that ligation products can be subjected to oxidative deselenization to afford Ser in place of Sec at the ligation junction.

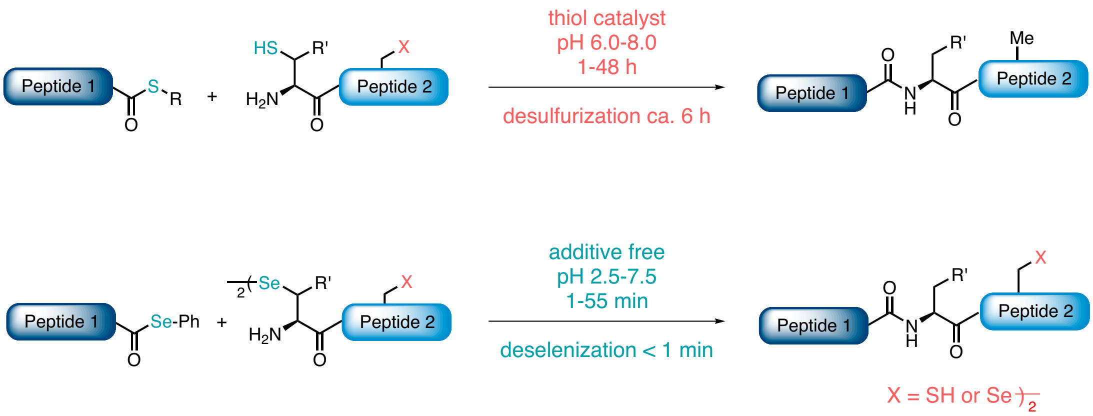


Fig. 4: Differences in properties and capabilities using either sulfur or selenium in native chemical ligation.

back to content ↑

References:

- [13] Protein synthesis by chemical ligation of unprotected peptides in aqueous solution; T. W. Muir, P. E. Dawson, S. B. H. Kent; **Solid-Phase Peptide Synthesis** 1997; **289**: Academic Press, 266-298.
- Accelerated Protein Synthesis via One-Pot Ligation-Deselenization Chemistry; N. J. Mitchell, J. Sayers, S. S. Kulkarni, D. Clayton, A. M. Goldys, J. Ripoll-Rozada, P. J. Barbosa Pereira, B. Chan, L. Radom, R. J. Payne; **Chem** 2017; **2**: 703-715. https://doi.org/10.1016/j.chempr.2017.04.003
- Chemical synthesis of proteins; B. L. Nilsson, M. B. Soellner, R. T. Raines; **Annu Rev Biophys Biomol Struct** 2005; **34**: 91-118. https://doi.org/10.1146/annurev.biophys.34.040204.144700
- Construction of Challenging Proline-Proline Junctions via Diselenide-Selenoester Ligation Chemistry; J. Sayers, P. M. T. Karpati, N. J. Mitchell, A. M. Goldys, S. M. Kwong, N. Firth, B. Chan, R. J. Payne; **J Am Chem Soc** 2018; **140**: 13327-13334. https://doi.org/10.1021/jacs.8b07877
- Expressed protein ligation: a general method for protein engineering; T. W. Muir, D. Sondhi, P. A. Cole; **Proc Natl Acad Sci U S A** 1998; **95**: 6705-6710. https://doi.org/10.1073/pnas.95.12.6705
- Free-radical-based, specific desulfurization of cysteine: a powerful advance in the synthesis of polypeptides and glycopolypeptides; Q. Wan, S. J. Danishefsky; **Angew Chem Int Ed Engl** 2007; **46**: 9248-9252. https://doi.org/10.1002/anie.200704195
- Insights into the mechanism and catalysis of the native chemical ligation reaction; E. C. Johnson, S. B. Kent; **J Am Chem Soc** 2006; **128**: 6640-6646. https://doi.org/10.1021/ja058344i
- Native Chemical Ligation of Peptides and Proteins; P. A. Cistrone, M. J. Bird, D. T. Flood, A. P. Silvestri, J. C. J. Hintzen, D. A. Thompson, P. E. Dawson; **Curr Protoc Chem Biol** 2019; **11**: e61. https://doi.org/10.1002/cpch.61
- Oxidative Deselenization of Selenocysteine: Applications for Programmed Ligation at Serine; L. R. Malins, N. J. Mitchell, S. McGowan, R. J. Payne; **Angew Chem Int Ed Engl** 2015; **54**: 12716-12721. https://doi.org/10.1002/anie.201504639
- Protein synthesis by native chemical ligation: expanded scope by using straightforward methodology; T. M. Hackeng, J. H. Griffin, P. E. Dawson; **Proc Natl Acad Sci U S A** 1999; **96**: 10068-10073. https://doi.org/10.1073/pnas.96.18.10068
- Rapid additive-free selenocystine-selenoester peptide ligation; N. J. Mitchell, L. R. Malins, X. Liu, R. E. Thompson, B. Chan, L. Radom, R. J. Payne; **J Am Chem Soc** 2015; **137**: 14011-14014. https://doi.org/10.1021/jacs.5b07237
- Selenopeptide chemistry; M. Muttenthaler, P. F. Alewood; **J Pept Sci** 2008; **14**: 1223-1239. https://doi.org/10.1002/psc.1075
- Syntheses and biological activities of selenium analogs of alpha-rat atrial natriuretic peptide; T. Koide, H. Itoh, A. Otaka, M. Furuya, Y. Kitajima, N. Fujii; **Chem Pharm Bull (Tokyo)** 1993; **41**: 1596-1600. https://doi.org/10.1248/cpb.41.1596
- Synthesis of proteins by native chemical ligation; P. E. Dawson, T. W. Muir, I. Clark-Lewis, S. B. Kent; **Science** 1994; **266**: 776-779. https://doi.org/10.1126/science.7973629
- Synthesis of selenocysteine peptides and their oxidation to diselenide-bridged compounds; D. Besse, L. Moroder; **Journal of Peptide Science** 1997; **3**: 442-453. https://doi.org/10.1002/(sici)1099-1387(199711)3:6<442::Aid-psc122>3.0.Co;2-2
- Synthetic study on selenocystine-containing peptides; T. Koide, H. Itoh, A. Otaka, H. Yasui, M. Kuroda, N. Esaki, K. Soda, N. Fujii; **Chem Pharm Bull (Tokyo)** 1993; **41**: 502-506. https://doi.org/10.1248/cpb.41.502
- Total chemical synthesis of enzymes; S. Kent; **J Pept Sci** 2003; **9**: 574-593. https://doi.org/10.1002/psc.475
- Über Peptidsynthesen. 8. Mitteilung Bildung von S-haltigen Peptiden durch intramolekulare Wanderung von Aminoacylresten; T. Wieland, E. Bokelmann, L. Bauer, H. U. Lang, H. Lau; **Justus Liebigs Annalen der Chemie** 1953; **583**: 129-149. https://doi.org/10.1002/jlac.19535830110

2. Tools for the Formation of Thioesters

2.1. Dawson Linkers

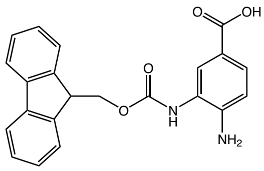
The straightforward C-terminal modification of peptides assembled on a solid support used to be a significant challenge in peptide and protein chemistry. This was also true for C-terminal thioester peptides, which are important intermediates in the generation of active esters, amides, and hydrazides. Moreover, they are also an essential component of many synthetic strategies for protein synthesis. The most efficient approach for the synthesis of peptidyl thioesters used to be the *in situ* neutralization protocol for Boc solid-phase peptide synthesis using thioester linkage.

Product details

FAA3165 Fmoc-Dbz-OH

3-[(9-Fluorenylmethyloxycarbonyl)amino]-4-amino-benzoic acid

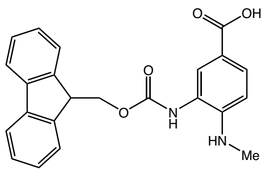
CAS-No.	1071446-05-3
Formula	$C_{22}H_{18}N_2O_4$
Mol. weight	374,39 g/mol



FAA3166 Fmoc-MeDbz-OH

3-[(9-Fluorenylmethyloxycarbonyl)amino]-4-(methylamino)benzoic acid

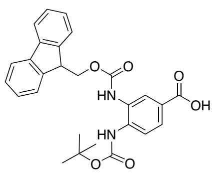
CAS-No.	1788861-35-7
Formula	$C_{23}H_{20}N_2O_4$
Mol. weight	388,44 g/mol



FAA3167 Fmoc-Dbz(*o*-Boc)-OH

3-(Fmoc-amino)-4-(Boc-amino)-benzoic acid

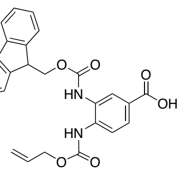
CAS-No.	1823479-63-5
Formula	$C_{27}H_{26}N_2O_6$
Mol. weight	474,51 g/mol



FAA3168 Fmoc-Dbz(*o*-Alloc)-OH

3-(Fmoc-amino)-4-(Alloc-amino)-benzoic acid

CAS-No.	2143465-53-4
Formula	$C_{26}H_{22}N_2O_6$
Mol. weight	458,46 g/mol



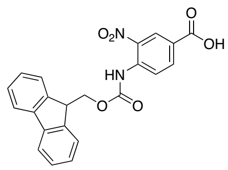
back to content ↑

Product details

FAA3169 Fmoc-Dbz(*o*-NO_2)-OH

4-(Fmoc-amino)-3-Nitro-benzoic acid

CAS-No.	1342864-48-5
Formula	$C_{22}H_{16}N_2O_6$
Mol. weight	404,37 g/mol



Importantly, the linker is a stable amide during chain assembly and the key activation step utilizes the most robust reaction in solid phase peptide synthesis: the acylation of an amine. As a result, the method is compatible with amino acid side chains and protecting groups commonly used in peptide synthesis.

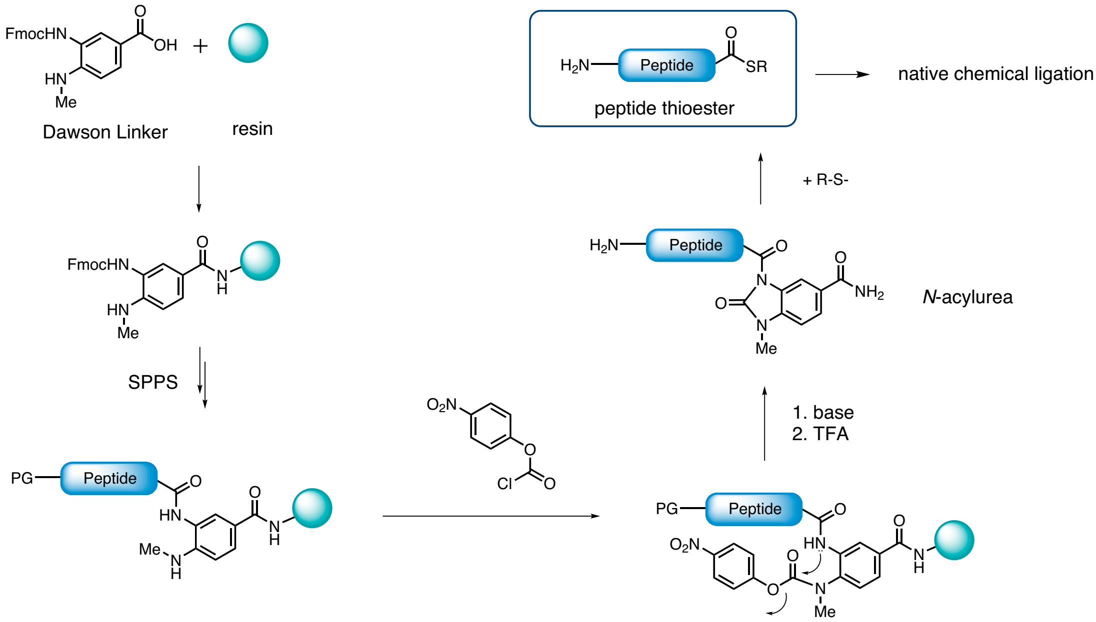


Fig. 5: Formation of thioesters via Dawson linker.

References:

→ *Alternative chemistries for the synthesis of thrombospondin-1 type 1 repeats; T. K. Tiefenbrunn, J. Blanco-Canosa, P. E. Dawson;* ***Biopolymers*** *2010;* ***94****: 405-413. https://doi.org/10.1002/bip.21486*

→ *An Efficient Fmoc-SPPS Approach for the Generation of Thioester Peptide Precursors for Use in Native Chemical Ligation; J. B. Blanco-Canosa, P. E. Dawson;* ***Angew Chem*** *2008;* ***120****: 6957-6961. https://doi.org/10.1002/ange.200705471*

→ *Protein synthesis assisted by native chemical ligation at leucine; Z. Harpaz, P. Siman, K. S. Kumar, A. Brik;* ***Chembiochem : a European journal of chemical biology*** *2010;* ***11****: 1232-1235. https://doi.org/10.1002/cbic.201000168*

→ *A reversible protection strategy to improve Fmoc-SPPS of peptide thioesters by the N-Acylurea approach; S. K. Mahto, C. J. Howard, J. C. Shimko, J. J. Ottesen;* ***Chembiochem : a European journal of chemical biology*** *2011;* ***12****: 2488-2494. https://doi.org/10.1002/cbic.201100472*

→ *A semisynthesis platform for investigating structure-function relationships in the N-terminal domain of the anthrax Lethal Factor; B. L. Pentelute, A. P. Barker, B. E. Janowiak, S. B. Kent, R. J. Collier;* ***ACS Chem Biol*** *2010;* ***5****: 359-364. https://doi.org/10.1021/cb100003r*

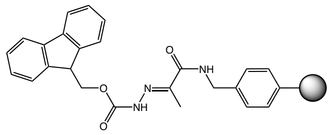
2.2. Hydrazone Resins

Product details

PYV1000 Fmoc-NHN=Pyv Resin

Fmoc-hydrazono-pyruvyl-aminomethylpolystyrene resin

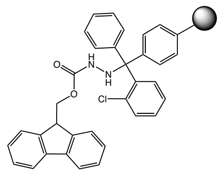
Mesh Size	100-200 mesh
Loading	> 0.3 mmol/g
DVB	1% DVB



BR-5279 Fmoc-NHNH-2CT Resin

Fmoc-hydrazine-2-chlorotrityl resin

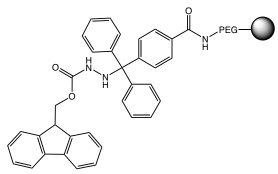
Mesh Size	100-200 mesh
Loading	0,4-1,4 mmol/g
DVB	1%



BR-5280 Fmoc-NHNH-Trt-PEG Resin

Fmoc-hydrazine-trityl polyethyleneglycol resin

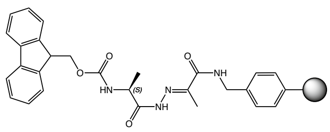
Loading	0,10-0,30 mmol/g
DVB	1% DVB



PYV1100 Fmoc-L-Ala-NHN=Pyv Resin

Fmoc-L-alanyl-hydrazono-pyruvyl-aminomethylpolystyrene resin

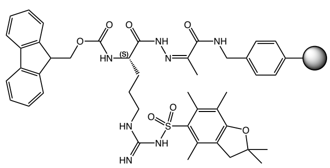
Mesh Size	100-200 mesh
Loading	> 0.3 mmol/g
DVB	1% DVB



PYV1110 Fmoc-L-Arg(Pbf)-NHN=Pyv Resin

Fmoc-*N*'-2,2,4,6,7-pentamethyldihydrobenzofuran-5-sulfonyl-L-arginyl-hydrazono-pyruvyl-aminomethylpolystyrene resin

Mesh Size	100-200 mesh
Loading	> 0.3 mmol/g
DVB	1% DVB

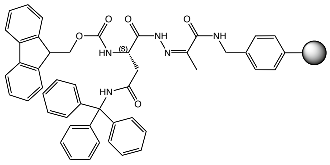


back to content ↑

Product details

PYV1120 Fmoc-L-Asn(Trt)-NHN=Pyv Resin

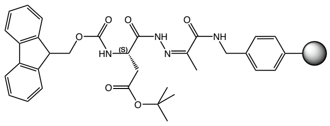
Fmoc-N-beta-trityl-L-asparaginyl-hydrazono-pyruvyl-aminomethylpolystyrene resin



Mesh Size	100-200 mesh
Loading	> 0.3 mmol/g
DVB	1% DVB

PYV1130 Fmoc-L-Asp(O*t*Bu)-NHN=Pyv Resin

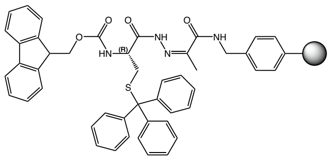
Fmoc-L-aspartyl-beta-*t*-butyl ester-alpha-hydrazono-pyruvyl-aminomethylpolystyrene resin



Mesh Size	100-200 mesh
Loading	> 0.3 mmol/g
DVB	1% DVB

PYV1140 Fmoc-L-Cys(Trt)-NHN=Pyv Resin

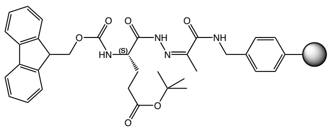
Fmoc-S-trityl-L-cysteinyl-hydrazono-pyruvyl-amino-methylpolystyrene resin



Mesh Size	100-200 mesh
Loading	> 0.3 mmol/g
DVB	1% DVB

PYV1150 Fmoc-L-Glu(*t*Bu)-NHN=Pyv Resin

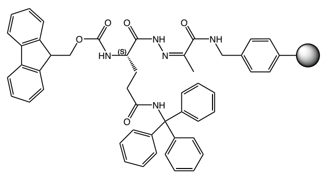
Fmoc-L-glutamyl-gamma-*t*-butyl ester-alpha-hydrazono-pyruvyl-aminomethylpolystyrene resin



Mesh Size	100-200 mesh
Loading	> 0.3 mmol/g
DVB	1% DVB

PYV1160 Fmoc-L-Gln(Trt)-NHN=Pyv Resin

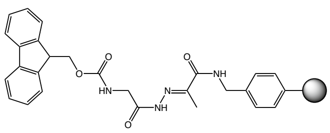
Fmoc-N-gamma-trityl-L-glutaminyl-hydrazono-pyruvyl-aminomethylpolystyrene resin



Mesh Size	100-200 mesh
Loading	> 0.3 mmol/g
DVB	1% DVB

PYV1170 Fmoc-Gly-NHN=Pyv Resin

Fmoc-glycyl-hydrazono-pyruvyl-aminomethylpolystyrene resin

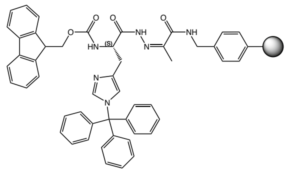


Mesh Size	100-200 mesh
Loading	> 0.3 mmol/g
DVB	1% DVB

Product details

PYV1180 Fmoc-L-His(Trt)-NHN=Pyv Resin

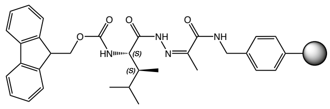
Fmoc-N-trityl-L-histidyl-hydrazono-pyruvyl-amino-methylpolystyrene resin



Mesh Size	100-200 mesh
Loading	> 0.3 mmol/g
DVB	1% DVB

PYV1190 Fmoc-L-Ile-NHN=Pyv Resin

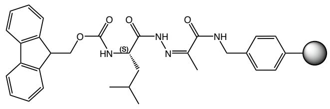
Fmoc-L-isoleucyl-hydrazono-pyruvyl-aminomethylpo-lystyrene resin



Mesh Size	100-200 mesh
Loading	> 0.3 mmol/g
DVB	1% DVB

PYV1200 Fmoc-L-Leu-NHN=Pyv Resin

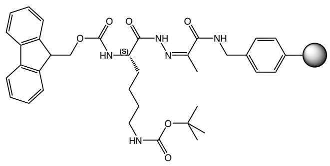
Fmoc-L-leucyl-hydrazono-pyruvyl-aminomethylpolys-tyrene resin



Mesh Size	100-200 mesh
Loading	> 0.3 mmol/g
DVB	1% DVB

PYV1210 Fmoc-L-Lys(Boc)-NHN=Pyv Resin

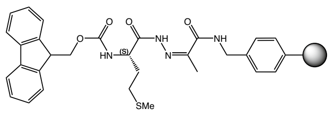
Fmoc-N-epsilon-*t*-butyloxycarbonyl-L-lysyl-hydrazo-no-pyruvyl-aminomethylpolystyrene resin



Mesh Size	100-200 mesh
Loading	> 0.3 mmol/g
DVB	1% DVB

PYV1220 Fmoc-L-Met-NHN=Pyv Resin

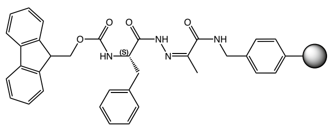
Fmoc-L-methionyl-hydrazono-pyruvyl-aminomethylpo-lystyrene resin



Mesh Size	100-200 mesh
Loading	> 0.3 mmol/g
DVB	1% DVB

PYV1230 Fmoc-L-Phe-NHN=Pyv Resin

Fmoc-L-phenylalanyl-hydrazono-pyruvyl-aminomethyl-polystyrene resin



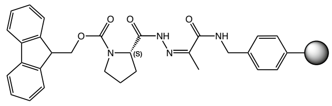
Mesh Size	100-200 mesh
Loading	> 0.3 mmol/g
DVB	1% DVB

back to content ↑

Product details

PYV1240 Fmoc-L-Pro-NHN=Pyv Resin

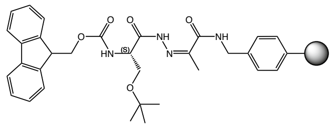
Fmoc-L-prolinyl-hydrazono-pyruvyl-aminomethylpolystyrene resin



Mesh Size	100-200 mesh
Loading	> 0.3 mmol/g
DVB	1% DVB

PYV1250 Fmoc-L-Ser(*t*Bu)-NHN=Pyv Resin

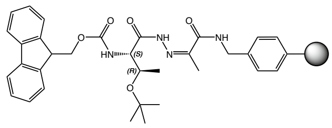
Fmoc-O-*t*-butyl-L-seryl-hydrazono-pyruvyl-aminomethylpolystyrene resin



Mesh Size	100-200 mesh
Loading	> 0.3 mmol/g
DVB	1% DVB

PYV1260 Fmoc-L-Thr(*t*Bu)-NHN=Pyv Resin

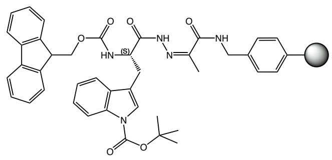
Fmoc-O-*t*-butyl-L-threonyl-hydrazono-pyruvyl-aminomethylpolystyrene resin



Mesh Size	100-200 mesh
Loading	> 0.3 mmol/g
DVB	1% DVB

PYV1270 Fmoc-L-Trp(Boc)-NHN=Pyv Resin

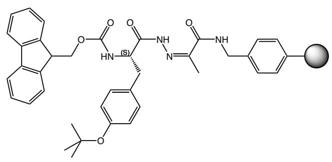
Fmoc-N-*t*-butyloxycarbonyl-L-tryptophyl-hydrazono-pyruvyl-aminomethylpolystyrene resin



Mesh Size	100-200 mesh
Loading	> 0.3 mmol/g
DVB	1% DVB

PYV1280 Fmoc-L-Tyr(*t*Bu)-NHN=Pyv Resin

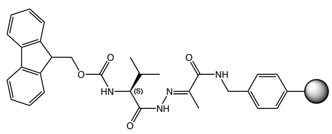
Fmoc-O-*t*-butyl-L-tyrosyl-hydrazono-pyruvyl-aminomethylpolystyrene resin



Mesh Size	100-200 mesh
Loading	> 0.3 mmol/g
DVB	1% DVB

PYV1290 Fmoc-L-Val-NHN=Pyv Resin

Fmoc-L-valyl-hydrazono-pyruvyl-aminomethylpolystyrene resin



Mesh Size	100-200 mesh
Loading	> 0.3 mmol/g
DVB	1% DVB

Peptide hydrazides can be easily synthesized using hydrazone resins, which are polystyrene resins functionalized with the hydrazone linker (Fig. 6). The hydrazone linker is completely stable in the course of standard Fmoc-SPPS. Moreover, it tolerates treatment with 5% TFA/DCM, thus permitting selective removal of Mtt or similar acid-labile protecting groups. Subsequent application of cleavage cocktails containing neat TFA permits to obtain the desired peptides in high yields and purity.

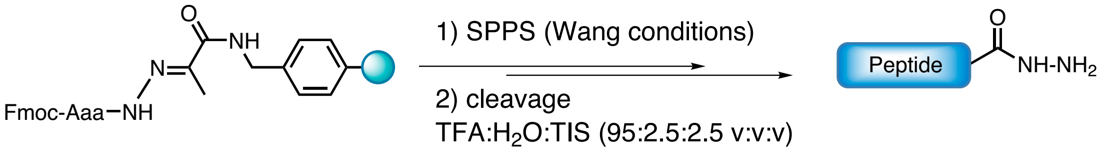


Fig. 6: Synthesizing peptide hydrazides utilizing hydrazone resin.

Synthesized peptide hydrazides can be applied as building blocks for the chemoselective conjugation to an aldehyde or ketone group on a second peptide (or other biomacromolecule) using the hydrazone ligation technique (Fig. 7). The resulting conjugate shows a non-natural hydrazone linkage replacing the natural amide bond. This, however, is in many cases tolerated, and the conjugate displays the same properties as a natural protein fragment.

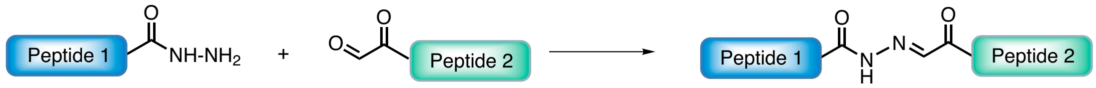


Fig. 7: Hydrazone ligation.

A peptide hydrazide can be converted into a peptide thioester. Two different protocols (Fig. 8 and Fig. 9) have been published recently. These methods include, but are not limited to, solution phase oxidation of C-terminal hydrazides to the corresponding acylazides. The required oxidants – typically used in large excess – cannot be employed in concert with N-terminal thiazolidines, a common peptide protecting strategy utilized in the synthesis of proteins requiring multiple ligations, aryl amines, or other redox-sensitive residues which can be incorporated *via* SPPS.

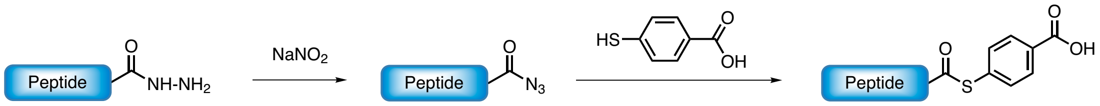


Fig. 8: Synthesizing peptide thioesters utilizing hydrazone resin via oxidation.

A more robust method for the generation of Fmoc-SPPS peptide thioesters compatible with multiple ligations utilizes mild and selective conditions at stoichiometric quantities of reactants. This process is suitable for multiple ligations to be performed sequentially in one pot, hence, has the potential for a general route to synthesize larger and complex proteins *via* multiple chemical ligation steps.

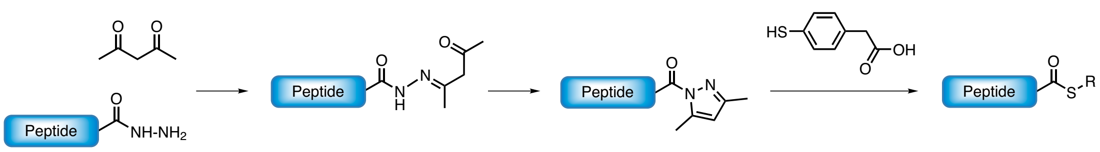


Fig. 9: General route for synthesizing peptide thioesters utilizing hydrazone resin.

back to content ↑

Peptide hydrazides exposed to acetylacetone (acac, 2.5 eq.) in a solution of 6 M guanidinium chloride and 2% thiophenol at acidic conditions will initially form a hydrazine. This cyclizes to pyrazole at low pH and can be replaced with thiols like MPAA resulting in the corresponding peptide thioester.

References:

→ *Chemical synthesis of proteins using peptide hydrazides as thioester surrogates; J. S. Zheng, S. Tang, Y. K. Qi, Z. P. Wang, L. Liu;* ***Nat Protoc*** *2013;* ***8****: 2483-2495. https://doi.org/10.1038/nprot.2013.152*

→ *Convenient method of peptide hydrazide synthesis using a new hydrazone resin; P. S. Chelushkin, K. V. Polyanichko, M. V. Leko, M. Y. Dorosh, T. Bruckdorfer, S. V. Burov;* ***Tetrahedron Letters*** *2015;* ***56****: 619-622. https://doi.org/10.1016/j.tetlet.2014.12.056*

→ *Leveraging the Knorr Pyrazole Synthesis for the Facile Generation of Thioester Surrogates for use in Native Chemical Ligation; D. T. Flood, J. C. J. Hintzen, M. J. Bird, P. A. Cistrone, J. S. Chen, P. E. Dawson;* ***Angew Chem Int Ed Engl*** *2018;* ***57****: 11634-11639. https://doi.org/10.1002/anie.201805191*

→ *Protein chemical synthesis by ligation of peptide hydrazides; G. M. Fang, Y. M. Li, F. Shen, Y. C. Huang, J. B. Li, Y. Lin, H. K. Cui, L. Liu;* ***Angew Chem Int Ed Engl*** *2011;* ***50****: 7645-7649. https://doi.org/10.1002/anie.201100996*

→ *Selective Coupling at the α-Amino Group of Cysteine Using Transfer Active-ester-condensation Technology to Synthesize a Linear Octadecapeptide; Y. Liao, Y. Kong, N. Hu, Z. Jin, P. Wang;* ***Chem Lett*** *2010;* ***39****: 196-197. https://doi.org/10.1246/cl.2010.196*

3. Building Blocks for Ligation

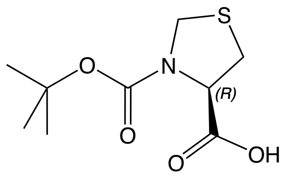
3.1. Cysteine Building Blocks for Ligation

Product details

BAA1135 Boc-L-Thz-OH

(R)-N-*t*-Butyloxycarbonyl-thiazolidine-4-carboxylic acid

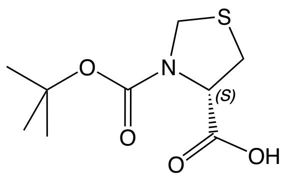
CAS-No.	51077-16-8
Formula	$C_9H_{15}NO_4S$
Mol. weight	233,29 g/mol



BAA1186 Boc-D-Thz-OH

(S)-N-(*t*-Butyloxycarbonyl)-thiazolidine-4-carboxylic acid

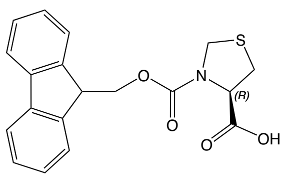
CAS-No.	63091-82-7
Formula	$C_9H_{15}NO_4S$
Mol. weight	233,29 g/mol



FAA1427 Fmoc-L-Thz-OH

(R)-N-(9-Fluorenylmethyloxycarbonyl)-thiazolidine-L-4-carboxylic acid

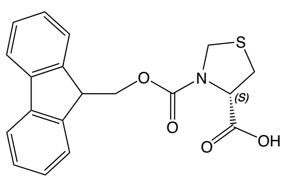
CAS-No.	133054-21-4
Formula	$C_{19}H_{17}NO_4S$
Mol. weight	355,42 g/mol



FAA1495 Fmoc-D-Thz-OH

(S)-N-alpha-(9-Fluorenylmethyloxycarbonyl)-thiazolidine-4-carboxylic acid

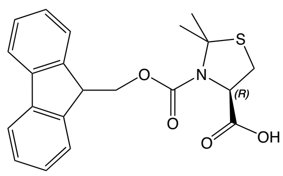
CAS-No.	198545-89-0
Formula	$C_{19}H_{17}NO_4S$
Mol. weight	355,42 g/mol



FAA1437 Fmoc-L-Thz(Me$_2$)-OH

(R)-N-(9-Fluorenylmethyloxycarbonyl)-2,2-dimethyl-thiazolidine-4-carboxylic acid

CAS-No.	873842-06-9
Formula	$C_{21}H_{21}NO_4S$
Mol. weight	383,46 g/mol



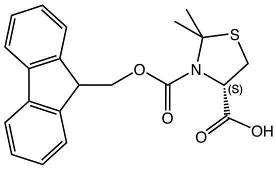
back to content ↑

Product details

FAA3160 Fmoc-D-Thz(Me2)-OH

(S)-N-(9-Fluorenylmethyloxycarbonyl)-2,2-dimethyl-thiazolidine-4-carboxylic acid

CAS-No.	1932198-36-1
Formula	$C_{21}H_{21}NO_4S$
Mol. weight	383,46 g/mol



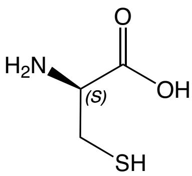
1,3-Thiazolidine-4-carboxylic acid (Thz) is a protected cysteine. It can be converted into free cysteine by reaction with aqueous 0.8 M methoxylamine ($MeONH_2$).

Product details

HAA1017 H-D-Cys-OH*HCl*H_2O

D-Cysteine Hydrochloride

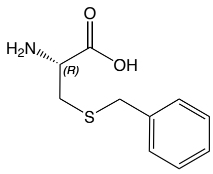
CAS-No.	32443-99-5
Formula	$C_3H_7NO_2S$*HCl*H_2O
Mol. weight	121,2*36,45*18,01 g/mol



HAA1574 H-L-Cys(Bzl)-OH

S-Benzyl-L-cysteine

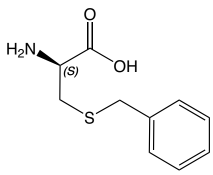
CAS-No.	3054-01-1
Formula	$C_{10}H_{13}NO_2S$
Mol. weight	211,29 g/mol



HAA6110 H-D-Cys(Bzl)-OH

S-Benzyl-D-cysteine

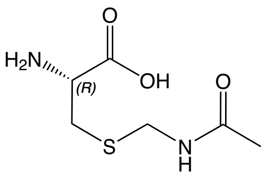
CAS-No.	23032-53-3
Formula	$C_{10}H_{13}NO_2S$
Mol. weight	211,29 g/mol



HAA6070 H-L-Cys(Acm)-OH*HCl

S-(Acetyl-aminomethyl)-L-cysteine hydrochloride

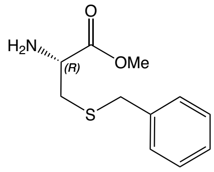
CAS-No.	28798-28-9
Formula	$C_6H_{12}N_2O_3S$*HCl
Mol. weight	192,24*36,45 g/mol



HAA6080 H-L-Cys(Bzl)-OMe*HCl

S-Benzyl-L-cysteine methyl ester hydrochloride

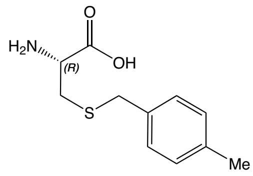
CAS-No. 16741-80-3
Formula $C_{11}H_{15}NO_2S$*HCl
Mol. weight 225,31*36,45 g/mol



HAA6090 H-L-Cys(MBzl)-OH

S-(4-Methylbenzyl)-L-cysteine

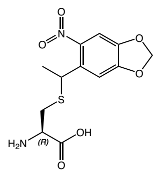
CAS-No. 42294-52-0
Formula $C_{11}H_{15}NO_2S$
Mol. weight 225,3 g/mol



HAA9270 H-L-Cys(MDNPE)-OH

1-[4‘,5‘-(methylenedioxy)-2‘-nitrophenyl]ethyl]-L-cysteine

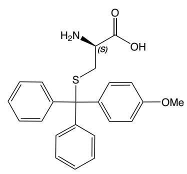
CAS-No. 1551078-43-3
Formula $C_{12}H_{14}N_2O_6S$
Mol. weight 314,31 g/mol



HAA3500 H-D-Cys(Mmt)-OH

S-*p*-methoxytrityl-D-cysteine

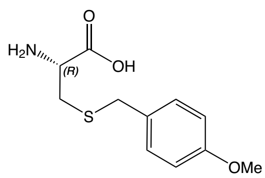
CAS-No. 926935-33-3
Formula $C_{23}H_{23}NO_3S$
Mol. weight 393,5 g/mol



HAA6100 H-L-Cys(Mob)-OH

S-(4-Methoxybenzyl)-L-cysteine

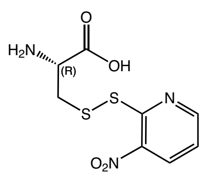
CAS-No. 2544-31-2
Formula $C_{11}H_{15}NO_3S$
Mol. weight 241,3 g/mol



HAA3510 H-L-Cys(Npys)-OH*HCl

S-(3-nitro-2-pyridylthio)-L-cysteine hydrochloride

CAS-No. 108807-66-5
Formula $C_8H_9N_3O_4S_2$*HCl
Mol. weight 275,30*36,45 g/mol



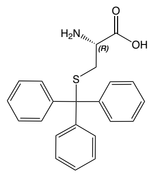
back to content ↑

Product details

HAA6160 H-L-Cys(Trt)-OH

S-Trityl-L-cysteine

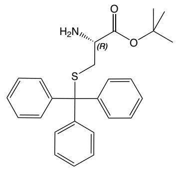
CAS-No. 2799-07-7
Formula $C_{22}H_{21}NO_2S$
Mol. weight 363,48 g/mol



HAA1995 H-L-Cys(Trt)-O*t*Bu*HCl

S-Trityl-L-cysteine *t*-butyl ester hydrochloride

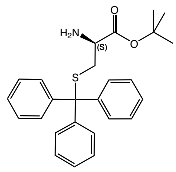
CAS-No. 158009-03-1
Formula $C_{26}H_{29}NO_2S$*HCl
Mol. weight 419,58*36,45 g/mol



HAA2100 H-D-Cys(Trt)-O*t*Bu*HCl

S-Trityl-D-cysteine *t*-butyl ester hydrochloride

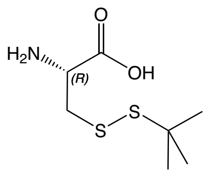
CAS-No. 439089-10-8
Formula $C_{26}H_{29}NO_2S$*HCl
Mol. weight 419,58*36,45 g/mol



HAA6140 H-L-Cys(S*t*Bu)-OH

S-Thio-*t*-butyl-L-cysteine

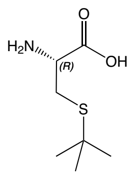
CAS-No. 30044-51-0
Formula $C_7H_{15}NO_2S_2$
Mol. weight 209,32 g/mol



HAA6150 H-L-Cys(*t*Bu)-OH*HCl

S-*t*-Butyl-L-cysteine hydrochloride

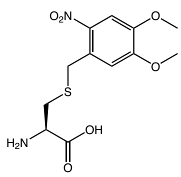
CAS-No. 2481-09-6
Formula $C_7H_{15}NO_2S$*HCl
Mol. weight 177,26*36,45 g/mol



HAA9320 H-L-Cys(DMNB)-OH

S-(4,5-dimethoxy-2-nitrobenzyl)-L-cysteine

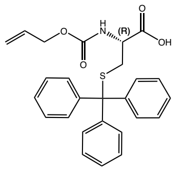
CAS-No. 214633-68-8
Formula $C_{12}H_{16}N_2O_6S$
Mol. weight 316,33 g/mol



AAA2015 Aloc-L-Cys(Trt)-OH

N-alpha-Allyloxycarbonyl-S-trityl-L-cysteine

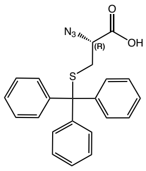
CAS-No.	96865-72-4
Formula	$C_{26}H_{25}NO_4S$
Mol. weight	447,55 g/mol



HAA2810 N_3-L-Cys(Trt)-OH*CHA

(R)-2-azido-3-(tritylthio)propanoic acid cyclohexylamine

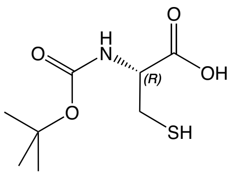
CAS-No.	1286670-90-3
Formula	$C_{22}H_{19}N_3O_2S*C_6H_{13}N$
Mol. weight	389,47*99,17 g/mol



BAA1083 Boc-L-Cys-OH

N-alpha-*t*-Butyloxycarbonyl-L-cysteine

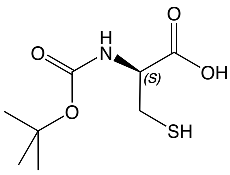
CAS-No.	20887-95-0
Formula	$C_8H_{15}NO_4S$
Mol. weight	221,27 g/mol



BAA1170 Boc-D-Cys-OH

N-alpha-*t*-Butyloxycarbonyl-D-cysteine

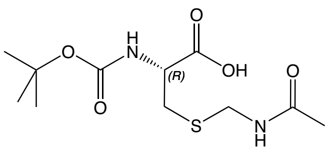
CAS-No.	149270-12-2
Formula	$C_8H_{15}NO_4S$
Mol. weight	221,27 g/mol



BAA1078 Boc-L-Cys(Acm)-OH

N-alpha-*t*-Butyloxycarbonyl-S-(acetyl-aminomethyl)-L-cysteine

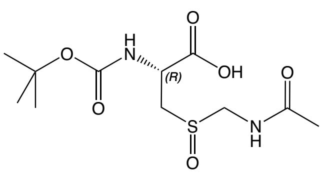
CAS-No.	19746-37-3
Formula	$C_{11}H_{20}N_2O_5S$
Mol. weight	292,36 g/mol



BAA1510 Boc-L-Cys(Acm,O)-OH

N-alpha-*t*-Butyloxycarbonyl-S-(acetyl-aminomethyl)-S-oxo-L-cysteine

CAS-No.	75893-04-8
Formula	$C_{11}H_{20}N_2O_6S$
Mol. weight	308,35 g/mol



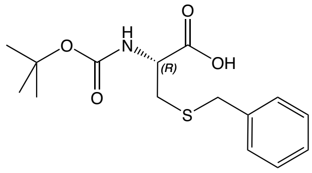
back to content ↑

Product details

BAA1079 Boc-L-Cys(Bzl)-OH

N-alpha-*t*-Butyloxycarbonyl-S-benzyl-L-cysteine

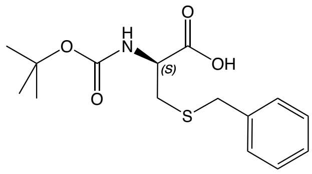
CAS-No.	5068-28-0
Formula	$C_{15}H_{21}NO_4S$
Mol. weight	311,38 g/mol



BAA5410 Boc-D-Cys(Bzl)-OH

N-alpha-*t*-Butyloxycarbonyl-S-benzyl-D-cysteine

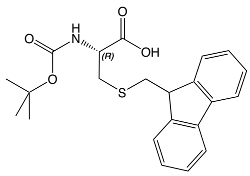
CAS-No.	102830-49-9
Formula	$C_{15}H_{21}NO_4S$
Mol. weight	311,38 g/mol



BAA5510 Boc-L-Cys(Fm)-OH

N-alpha-*t*-Butyloxycarbonyl-S-(9-fluorenyl-methyl)-L-cysteine

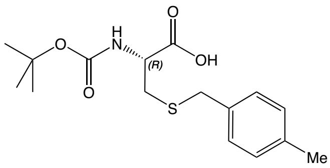
CAS-No.	84888-35-7
Formula	$C_{22}H_{25}NO_4S$
Mol. weight	399,51 g/mol



BAA1080 Boc-L-Cys(MBzl)-OH

N-alpha-*t*-Butyloxycarbonyl-S-(4-methyl-benzyl)-L-cy-steine

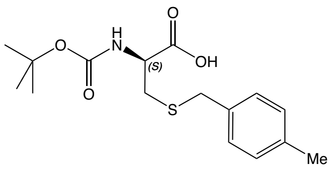
CAS-No.	61925-77-7
Formula	$C_{16}H_{23}NO_4S$
Mol. weight	325,43 g/mol



BAA5420 Boc-D-Cys(MBzl)-OH

N-alpha-*t*-Butyloxycarbonyl-S-(4-methyl-benzyl)-D-cy-steine

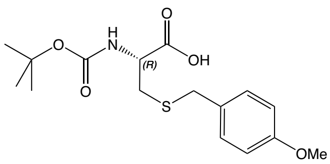
CAS-No.	61925-78-8
Formula	$C_{16}H_{23}NO_4S$
Mol. weight	325,43 g/mol



BAA1081 Boc-L-Cys(Mob)-OH

N-alpha-*t*-Butyloxycarbonyl-S-(4-methoxy-benzy-l)-L-cysteine

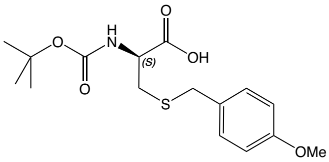
CAS-No.	18942-46-6
Formula	$C_{16}H_{23}NO_5S$
Mol. weight	341,43 g/mol



Product details

BAA5430 Boc-D-Cys(Mob)-OH

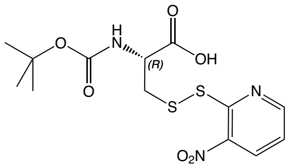
N-alpha-*t*-Butyloxycarbonyl-S-(4-methoxy-benzy-l)-D-cysteine



CAS-No.	58290-35-0
Formula	$C_{16}H_{23}NO_5S$
Mol. weight	341,43 g/mol

BAA1860 Boc-L-Cys(Npys)-OH

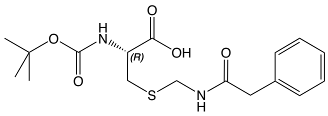
N-alpha-*t*-Butyloxycarbonyl-S-(3-nitro-2-pyridylthi-o)-L-cysteine



CAS-No.	76880-29-0
Formula	$C_{13}H_{17}N_3O_6S_2$
Mol. weight	375,42 g/mol

BAA6390 Boc-L-Cys(Phacm)-OH

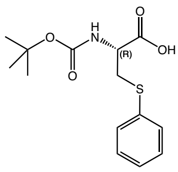
N-alpha-*t*-Butyloxycarbonyl-S-(Phenylacetylamino-methyl)-L-cysteine



CAS-No.	57084-73-8
Formula	$C_{17}H_{24}N_2O_5S$
Mol. weight	368,45 g/mol

BAA3140 Boc-L-Cys(Ph)-OH

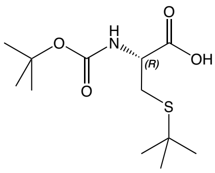
N-alpha-*t*-Butyloxycarbonyl-S-phenyl-L-cysteine



CAS-No.	163705-28-0
Formula	$C_{14}H_{19}NO_4S$
Mol. weight	297,37 g/mol

BAA1082 Boc-L-Cys(tBu)-OH

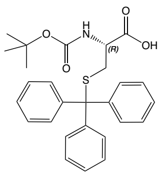
N-alpha-*t*-Butyloxycarbonyl-S-*t*-butyl-L-cysteine



CAS-No.	56976-06-8
Formula	$C_{12}H_{23}NO_4S$
Mol. weight	277,37 g/mol

BAA1084 Boc-L-Cys(Trt)-OH

N-alpha-*t*-Butyloxycarbonyl-S-trityl-L-cysteine



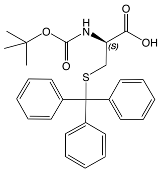
CAS-No.	21947-98-8
Formula	$C_{27}H_{29}NO_4S$
Mol. weight	463,59 g/mol

back to content ↑

Product details

BAA5000 Boc-D-Cys(Trt)-OH

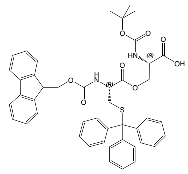
N-alpha-*t*-Butyloxycarbonyl-S-trityl-D-cysteine



CAS-No.	87494-13-1
Formula	$C_{27}H_{29}NO_4S$
Mol. weight	463,59 g/mol

IAD1040 Boc-L-Ser[Fmoc-L-Cys(Trt)]-OH

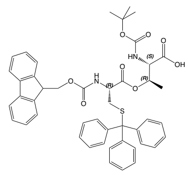
O-(N-(((9H-fluoren-9-yl)methoxy)carbonyl)-S-trityl-L-cysteinyl)-N-(*tert*-butoxycarbonyl)-L-serine



Formula	$C_{45}H_{44}N_2O_8S$
Mol. weight	772,9

IAD2040 Boc-L-Thr[Fmoc-L-Cys(Trt)]-OH

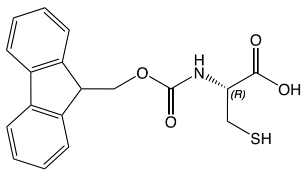
O-(N-(((9H-fluoren-9-yl)methoxy)carbonyl)-S-trityl-L-cysteinyl)-N-(*tert*-butoxycarbonyl)-L-threonine



CAS-No.	944283-30-1
Formula	$C_{46}H_{46}N_2O_8S$
Mol. weight	786,93 g/mol

FAA1362 Fmoc-L-Cys-OH*H_2O

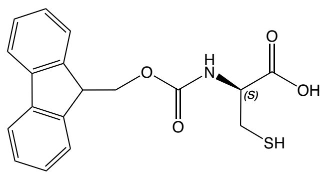
N-alpha-(9-Fluorenylmethyloxycarbonyl)-L-cysteine monohydrat



CAS-No.	135248-89-4net
Formula	$C_{18}H_{17}NO_4S$*H_2O
Mol. weight	343,40*18,01 g/mol

FAA1470 Fmoc-D-Cys-OH*H_2O

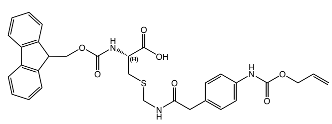
N-alpha-(9-Fluorenylmethyloxycarbonyl)-D-cysteine monohydrat



CAS-No.	157355-80-1 net
Formula	$C_{18}H_{17}NO_4S$*H_2O
Mol. weight	343,4*18,01 g/mol

FAA5150 Fmoc-L-Cys(Aapam)-OH

N-alpha-(9-Fluorenylmethyloxycarbonyl)-S-((4-(allyloxycarbonylamino)phenylacetylaminomethyl)-L-cysteine

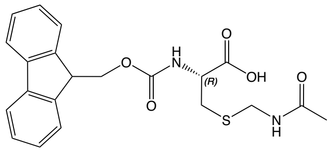


CAS-No.	1946783-89-6
Formula	$C_{31}H_{31}N_3O_7S$
Mol. weight	589,66 g/mol

FAA1506 Fmoc-L-Cys(Acm)-OH

N-alpha-(9-Fluorenylmethyloxycarbonyl)-S-(acetyl-aminomethyl)-L-cysteine

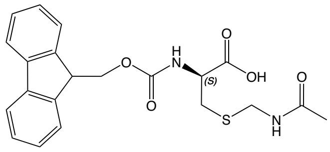
CAS-No.	86060-81-3
Formula	$C_{21}H_{22}N_2O_5S$
Mol. weight	414,48 g/mol



FAA6230 Fmoc-D-Cys(Acm)-OH

N-alpha-(9-Fluorenylmethyloxycarbonyl)-S-(acetyl-aminomethyl)-D-cysteine

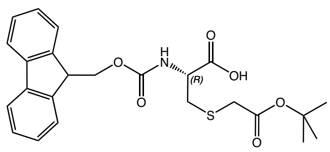
CAS-No.	168300-88-7
Formula	$C_{21}H_{22}N_2O_5S$
Mol. weight	414,48 g/mol



FAA4751 Fmoc-L-Cys(Ac-OtBu)-OH*DCHA

N-alpha-(9-Fluorenylmethyloxycarbonyl)-S-(*t*-butoxycarbonylmethyl)-L-cysteine dicyclohexylamine

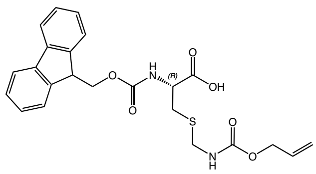
CAS-No.	269730-62-3 net
Formula	$C_{24}H_{27}NO_6S*C_{12}H_{23}N$
Mol. weight	457,54*181,32 g/mol



FAA7610 Fmoc-L-Cys(Allocam)-OH

N-alpha-(9-Fluorenylmethyloxycarbonyl)-S-((allyloxycarbonylamino)methy)-L-cysteine

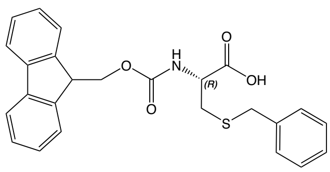
CAS-No.	232953-09-2
Formula	$C_{23}H_{24}N_2O_6S$
Mol. weight	456,51 g/mol



FAA6270 Fmoc-L-Cys(Bzl)-OH

N-alpha-(9-Fluorenylmethyloxycarbonyl)-S-benzyl-L-cysteine

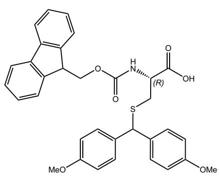
CAS-No.	53298-33-2
Formula	$C_{25}H_{23}NO_4S$
Mol. weight	433,52 g/mol



FAA6940 Fmoc-L-Cys(Ddm)-OH

N-alpha-(9-Fluorenylmethyloxycarbonyl)-S-di(4-methoxyphenyl)methyl-L-cysteine

CAS-No.	1403825-56-8
Formula	$C_{33}H_{31}NO_6S$
Mol. weight	569,67 g/mol



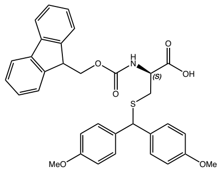
back to content ↑

Product details

FAA6950 Fmoc-D-Cys(Ddm)-OH

N-alpha-(9-Fluorenylmethyloxycarbonyl)-S-di(4-methoxyphenyl)methyl-D-cysteine

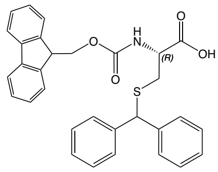
Formula	$C_{33}H_{31}NO_6S$
Mol. weight	569,67 g/mol



FAA3190 Fmoc-L-Cys(Dpm)-OH

N-alpha-(9-Fluorenylmethyloxycarbonyl)-S-diphenylmethyl-L-cysteine

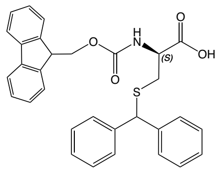
CAS-No.	247595-29-5
Formula	$C_{31}H_{27}NO_4S$
Mol. weight	509,62 g/mol



FAA5650 Fmoc-D-Cys(Dpm)-OH

N-alpha-(9-Fluorenylmethyloxycarbonyl)-S-diphenylmethyl-D-cysteine

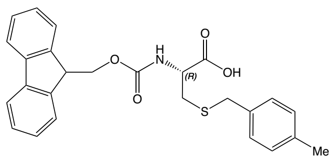
Formula	$C_{31}H_{27}NO_4S$
Mol. weight	509,62 g/mol



FAA1714 Fmoc-L-Cys(MBzl)-OH

N-alpha-(9-Fluorenylmethyloxycarbonyl)-S-(4-methylbenzyl)-L-cysteine

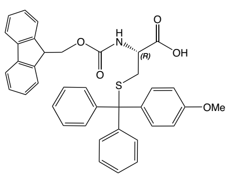
CAS-No.	136050-67-4
Formula	$C_{26}H_{25}NO_4S$
Mol. weight	447,53 g/mol



FAA1030 Fmoc-L-Cys(Mmt)-OH

N-alpha-(9-Fluorenylmethyloxycarbonyl)-S-*p*-methoxytrityl-L-cysteine

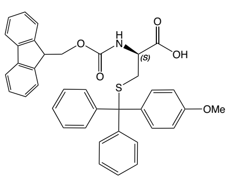
CAS-No.	177582-21-7
Formula	$C_{38}H_{33}NO_5S$
Mol. weight	615,74 g/mol



FAA1614 Fmoc-D-Cys(Mmt)-OH

N-alpha-(9-Fluorenylmethyloxycarbonyl)-S-*p*-methoxytrityl-D-cysteine

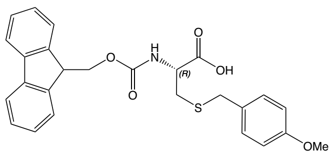
CAS-No.	1198791-73-9
Formula	$C_{38}H_{33}NO_5S$
Mol. weight	615,74 g/mol



FAA1715 Fmoc-L-Cys(Mob)-OH

N-alpha-(9-Fluorenylmethyloxycarbonyl)-S-(4-methoxybenzyl)-L-cysteine

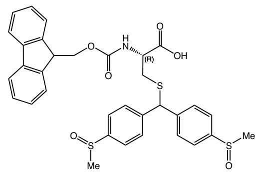
CAS-No.	141892-41-3
Formula	$C_{26}H_{25}NO_5S$
Mol. weight	463,55 g/mol



FAA4155 Fmoc-L-Cys(Msbh)-OH

N-alpha-(9-Fluorenylmethyloxycarbonyl)-S-(4,4'-dimethylsulfinylbenzhydryl)-L-cysteine

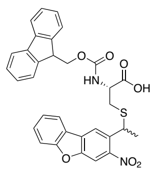
CAS-No.	1584646-97-8
Formula	$C_{33}H_{31}NO_6S_3$
Mol. weight	633,80 g/mol



FAA8420 Fmoc-L-Cys(NDBF)-OH

N-alpha-(9-Fluorenylmethyloxycarbonyl)-S-(1-(3-nitro-dibenzofuran-2-yl)-ethyl)-L-cysteine

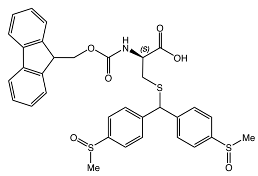
CAS-No.	1895883-28-9
Formula	$C_{32}H_{26}N_2O_7S$
Mol. weight	582,62 g/mol



FAA8150 Fmoc-D-Cys(Msbh)-OH

N-alpha-(9-Fluorenylmethyloxycarbonyl)-S-(4,4'-dimethylsulfinylbenzhydryl)-D-cysteine

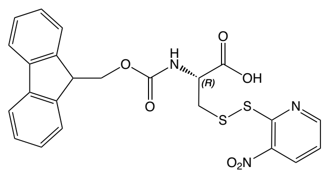
Formula	$C_{33}H_{31}NO_6S_3$
Mol. weight	633,80 g/mol



FAA1975 Fmoc-L-Cys(Npys)-OH

N-alpha-(9-Fluorenylmethyloxycarbonyl)-S-(3-nitro-2-pyridylthio)-L-cysteine

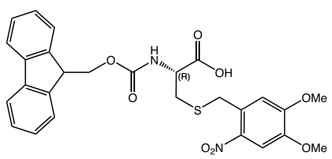
CAS-No.	159700-51-3
Formula	$C_{23}H_{19}N_3O_6S_2$
Mol. weight	497,54 g/mol



FAA3970 Fmoc-L-Cys(oNv)-OH

N-alpha-(9-Fluorenylmethyloxycarbonyl)-S-(2-nitroveratryl)-L-cysteine

CAS-No.	214633-71-3
Formula	$C_{27}H_{26}N_2O_8S$
Mol. weight	538,57 g/mol

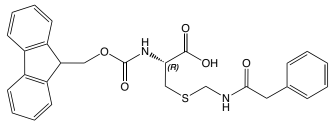


back to content ↑

Product details

FAA6910 Fmoc-L-Cys(Phacm)-OH

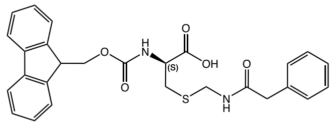
N-alpha-(9-Fluorenylmethyloxycarbonyl)-S-Phenylacetylaminomethyl)-L-cysteine



CAS-No.	159680-21-4
Formula	$C_{27}H_{26}N_2O_5S$
Mol. weight	490,57 g/mol

FAA3710 Fmoc-D-Cys(Phacm)-OH

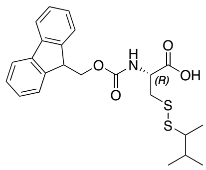
N-alpha-(9-Fluorenylmethyloxycarbonyl)-S-(phenylacetylaminomethyl)-D-cysteine



CAS-No.	1565818-55-4
Formula	$C_{27}H_{26}N_2O_5S$
Mol. weight	490,57 g/mol

FAA8495 Fmoc-L-Cys(SIT)-OH

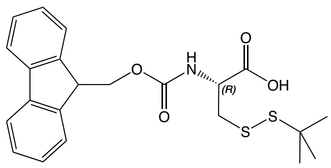
N-alpha-(9-Fluorenylmethyloxycarbonyl)-S-(sec-isoamyl mercaptan)-L-cysteine



CAS-No.	2545642-31-5
Formula	$C_{23}H_{27}NO_4S_2$
Mol. weight	445,59 g/mol

FAA1575 Fmoc-L-Cys(StBu)-OH

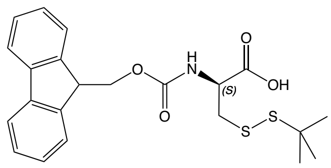
N-alpha-(9-Fluorenylmethyloxycarbonyl)-S-(*t*-butylthio)-L-cysteine



CAS-No.	73724-43-3
Formula	$C_{22}H_{25}NO_4S_2$
Mol. weight	431,57 g/mol

FAA1965 Fmoc-D-Cys(StBu)-OH

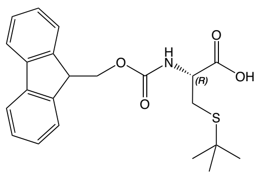
N-alpha-(9-Fluorenylmethyloxycarbonyl)-S-(*t*-butylthio)-D-cysteine



CAS-No.	501326-55-2
Formula	$C_{22}H_{25}NO_4S_2$
Mol. weight	431,57 g/mol

FAA1716 Fmoc-L-Cys(*t*Bu)-OH

N-alpha-(9-Fluorenylmethyloxycarbonyl)-S-*t*-butyl-L-cysteine

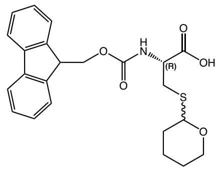


CAS-No.	67436-13-9
Formula	$C_{22}H_{25}NO_4S$
Mol. weight	399,51 g/mol

Product details

FAA4160 Fmoc-L-Cys(Thp)-OH

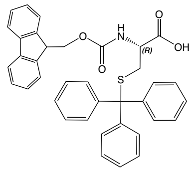
N-alpha-(9-Fluorenylmethyloxycarbonyl)-S-tetrahydro-pyranyl-L-cysteine



CAS-No.	1673576-83-4
Formula	$C_{23}H_{25}NO_5S$
Mol. weight	427,15 g/mol

FAA1040 Fmoc-L-Cys(Trt)-OH

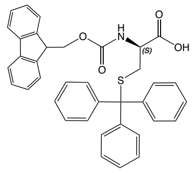
N-alpha-(9-Fluorenylmethyloxycarbonyl)-S-trityl-L-cy-steine



CAS-No.	103213-32-7
Formula	$C_{37}H_{31}NO_4S$
Mol. weight	585,71 g/mol

FAA1035 Fmoc-D-Cys(Trt)-OH

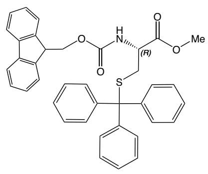
N-alpha-(9-Fluorenylmethyloxycarbonyl)-S-trityl-D-cy-steine



CAS-No.	167015-11-4
Formula	$C_{37}H_{31}NO_4S$
Mol. weight	585,71 g/mol

FAA5670 Fmoc-L-Cys(Trt)-OMe

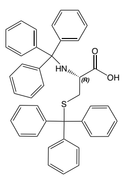
N-alpha-(9-Fluorenylmethyloxycarbonyl)-S-trityl-L-cy-steine methyl ester



CAS-No.	245088-56-6
Formula	$C_{38}H_{33}NO_4S$
Mol. weight	599,74 g/mol

TAA1508 Trt-L-Cys(Trt)-OH*DEA

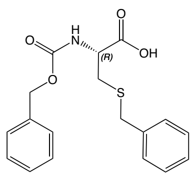
N-alpha-S-Bistrityl-L-cysteine diethylamine



CAS-No.	27486-88-0
Formula	$C_{41}H_{35}NO_2S*C_4H_{11}N$
Mol. weight	678,9 g/mol

ZAA1161 Z-L-Cys(Bzl)-OH

N-alpha-Benzyloxycarbonyl-S-benzyl-L-cysteine



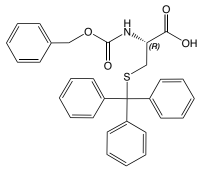
CAS-No.	3257-18-9
Formula	$C_{18}H_{19}NO_4S$
Mol. weight	345,42 g/mol

back to content ↑

Product details

ZAA1310 Z-L-Cys(Trt)-OH

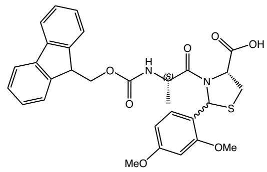
N-alpha-Benzyloxycarbonyl-S-trityl-L-cysteine



CAS-No.	26311-04-6
Formula	$C_{30}H_{27}NO_4S$
Mol. weight	497,60 g/mol

PSI1450 Fmoc-L-Ala-L-Cys[PSI(Dmp,H)pro]-OH

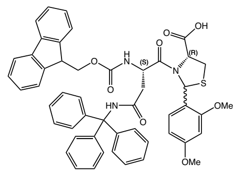
(S)-3-(N-(9-Fluorenylmethyloxycarbonyl)-L-alanyl)-2-(2,4-dimethoxphenyl)thiazolidine-4-carboxylic acid



CAS-No.	2022956-37-0
Formula	$C_{30}H_{30}N_2O_7S$
Mol. weight	562,63 g/mol

PSI1460 Fmoc-L-Asn(Trt)-L-Cys[PSI(Dmp,H)pro]-OH

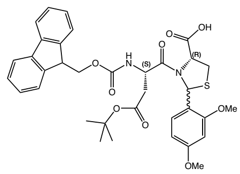
(S)-3-(N-(9-Fluorenylmethyloxycarbonyl)-beta-trityl-L-asparaginyl)-2-(2,4-dimethoxphenyl)thiazolidine-4-carboxylic acid



Formula	$C_{50}H_{45}N_3O_8S$
Mol. weight	847,97 g/mol

PSI1470 Fmoc-L-Asp(*t*Bu)-L-Cys[PSI(Dmp,H)pro]-OH

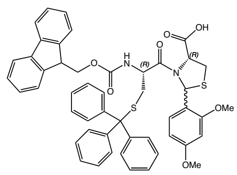
(S)-3-(N-(9-Fluorenylmethyloxycarbonyl)-beta-*t*-butyl-L-aspartyl)-2-(2,4-dimethoxphenyl)thiazolidine-4-carboxylic acid



CAS-No.	1359754-16-7
Formula	$C_{35}H_{39}N_2O_9S$
Mol. weight	662,75 g/mol

PSI1580 Fmoc-L-Cys(Trt)-L-Cys(Psi(Dmp,H)pro)-OH

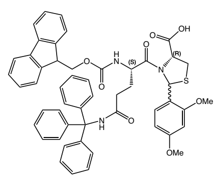
(R)-3-(N-(9-Fluorenylmethyloxycarbonyl)-S-trityl-L-cysteinyl)-2-(2,4-dimethoxphenyl)thiazolidine-4-carboxylic acid



CAS-No.	2022956-75-6
Formula	$C_{49}H_{44}N_2O_7S_2$
Mol. weight	837,01 g/mol

PSI1480 Fmoc-L-Gln(Trt)-L-Cys[PSI(Dmp,H)pro]-OH

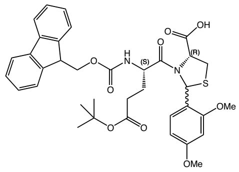
(S)-3-(N-(9-Fluorenylmethyloxycarbonyl)-gamma-trityl-L-glutaminyl)-2-(2,4-dimethoxphenyl)thiazolidine-4-carboxylic acid



Formula	$C_{51}H_{47}N_3O_8S$
Mol. weight	862,00 g/mol

PSI1490 Fmoc-L-Glu(*t*Bu)-L-Cys[PSI(Dmp,H)pro]-OH

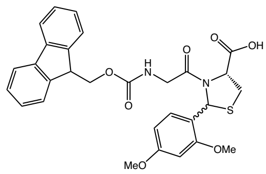
(S)-3-(N-(9-Fluorenylmethyloxycarbonyl)-gamma-*t*-butyl-L-glutamyl)-2-(2,4-dimethoxphenyl)thiazolidine-4-carboxylic acid



Formula	$C_{36}H_{40}N_2O_9S$
Mol. weight	676,78 g/mol

PSI1440 Fmoc-Gly-L-Cys[PSI(Dmp,H)pro]-OH

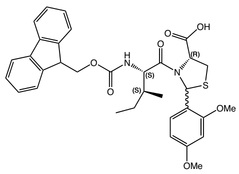
(S)-3-(N-(9-Fluorenylmethyloxycarbonyl)-glycyl)-2-(2,4-dimethoxphenyl)thiazolidine-4-carboxylic acid



CAS-No.	1926163-05-4
Formula	$C_{29}H_{28}N_2O_7S$
Mol. weight	548,61 g/mol

PSI1500 Fmoc-L-Ile-L-Cys[PSI(Dmp,H)pro]-OH

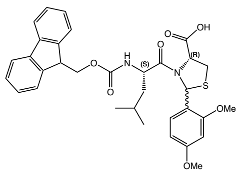
(S)-3-(N-(9-Fluorenylmethyloxycarbonyl)-L-isoleucyl)-2-(2,4-dimethoxphenyl)thiazolidine-4-carboxylic acid



Formula	$C_{33}H_{36}N_2O_7S$
Mol. weight	604,71 g/mol

PSI1510 Fmoc-L-Leu-L-Cys[PSI(Dmp,H)pro]-OH

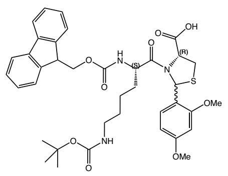
(S)-3-(N-(9-Fluorenylmethyloxycarbonyl)-L-leucyl)-2-(2,4-dimethoxphenyl)thiazolidine-4-carboxylic acid



CAS-No.	1926163-06-5
Formula	$C_{33}H_{36}N_2O_7S$
Mol. weight	604,71 g/mol

PSI1520 Fmoc-L-Lys(Boc)-L-Cys[PSI(Dmp,H)pro]-OH

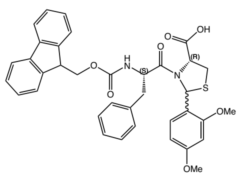
(S)-3-(N-(9-Fluorenylmethyloxycarbonyl)-N-epsilon-*t*-butyloxycarbonyl-L-lysyl)-2-(2,4-dimethoxphenyl) thiazolidine-4-carboxylic acid



CAS-No.	1926163-07-6
Formula	$C_{38}H_{45}N_3O_9S$
Mol. weight	719,84 g/mol

PSI1530 Fmoc-L-Phe-L-Cys[PSI(Dmp,H)pro]-OH

(S)-3-(N-(9-Fluorenylmethyloxycarbonyl)-L-phenylalanyl)-2-(2,4-dimethoxphenyl)thiazolidine-4-carboxylic acid



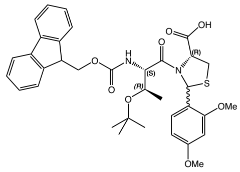
Formula	$C_{36}H_{34}N_2O_7S$
Mol. weight	638,73 g/mol

back to content ↑

Product details

PSI1550 Fmoc-L-Thr(*t*Bu)-L-Cys[PSI(Dmp,H)pro]-OH

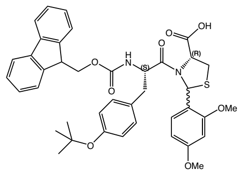
(S)-3-(N-(9-Fluorenylmethyloxycarbonyl)-O-*t*-butyl-L-threonyl)-2-(2,4-dimethoxphenyl)thiazolidine-4-carboxylic acid



Formula	$C_{35}H_{40}N_2O_8S$
Mol. weight	648,77 g/mol

PSI1560 Fmoc-L-Tyr(*t*Bu)-L-Cys[PSI(Dmp,H)pro]-OH

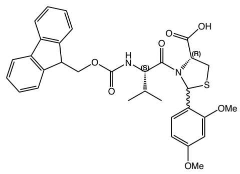
(S)-3-(N-(9-Fluorenylmethyloxycarbonyl)-O-*t*-butyl-L-thyrosyl)-2-(2,4-dimethoxphenyl)thiazolidine-4-carboxylic acid



Formula	$C_{40}H_{42}N_2O_8S$
Mol. weight	710,84 g/mol

PSI1570 Fmoc-L-Val-L-Cys[PSI(Dmp,H)pro]-OH

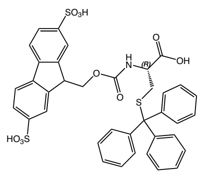
(S)-3-(N-(9-Fluorenylmethyloxycarbonyl)-L-valyl)-2-(2,4-dimethoxphenyl)thiazolidine-4-carboxylic acid



CAS-No.	1926163-08-7
Formula	$C_{32}H_{34}N_2O_7S$
Mol. weight	590,69 g/mol

SAA1110 Smoc-L-Cys(Trt)-OH

N-(((2,7-disulfo-9H-fluoren-9-yl)methoxy)carbonyl)-S-trityl-L-cysteine potassium salt



CAS-No.	2442552-68-1 (net)
Formula	$C_{37}H_{29}K_2NO_{10}S_3$
Mol. weight	822,01 g/mol

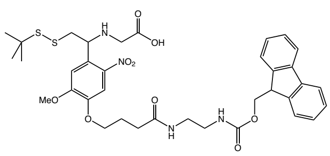
3.2. Ligation at the Position of Glycine

On average, cysteine occurs at a very low frequency in natural peptide sequences, a fact that frequently causes challenges when planning NCL strategies. On the other hand, glycine is a much more common amino acid, and being the simplest amino acid in nature, lends itself ideally for the construction of an NCL auxiliary.

Product details

PAA2000 *t*Bu-SS-Photo(Fmoc)-Gly-OH

Photocleavable-NCL-auxiliary-Gly-OH



CAS-No.	1994388-93-0
Formula	$C_{36}H_{44}N_4O_9S_2$
Mol. weight	740,89 g/mol

The building block *t*Bu-SS-Photo(Fmoc)-Gly-OH is based on a glycine scaffold that is *N*-alkylated with a photolabile thiol-bearing auxiliary. This auxiliary mimics the action of an N-terminal cysteine's sulfhydryl group in NCL, and can be tracelessly removed following ligation, leaving only a glycine behind. Being able to perform NCL at the position of glycine residues enables the synthetic chemist with a much higher flexibility for the design of peptides and proteins. Following SPPS, this building block is attached to the N-terminus of a peptide sequence in lieu of a glycine residue. The auxiliary's Fmoc-protected amino functionality can subsequently be deprotected and functionalized, e.g., with a PEG, which is useful for increasing the solubility of peptide fragments, and for facilitating their purification by precipitation with EtOH/Et_2O. This is particularly valuable if the peptide's amino acid side chains are supposed to be further derivatized post-SPPS.

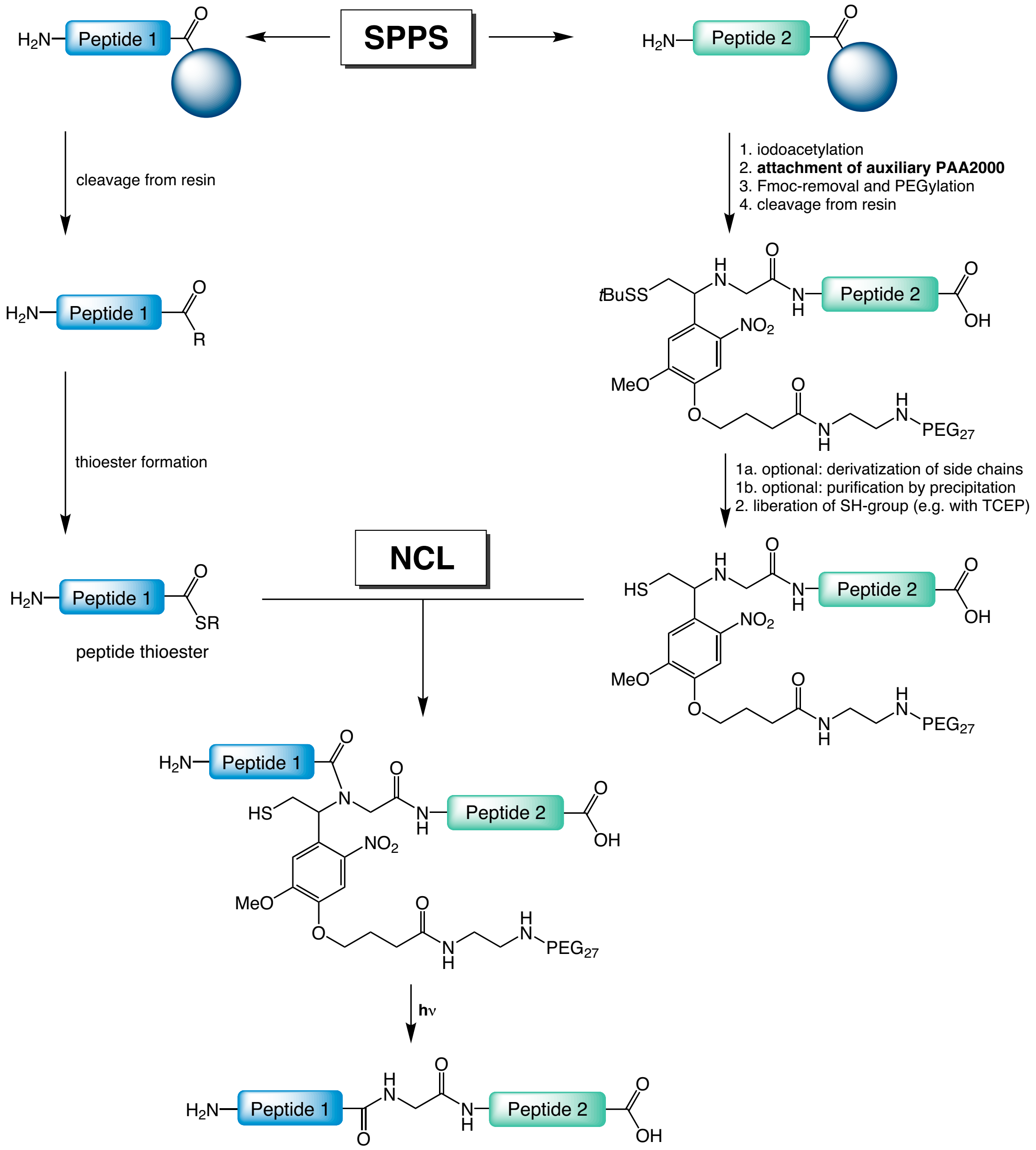


Fig. 10: Photo-cleavable glycine auxiliary building block enabling native chemical ligation at the position of glycine. It has additional capabilities to be conjugated with a solubilizing tag, e.g. PEG, in order to improve the solubility of hydrophobic peptide sequences.

back to content ↑

Reference:

→ *A PEGylated photocleavable auxiliary mediates the sequential enzymatic glycosylation and native chemical ligation of peptides; C. Bello, S. Wang, L. Meng, K. W. Moremen, C. F. Becker;* ***Angew Chem Int Ed Engl*** *2015;* ***54****: 7711-7715. https://doi.org/10.1002/anie.201501517*

3.3. Building Blocks and Reagents for Ligation with Seleno Amino Acids

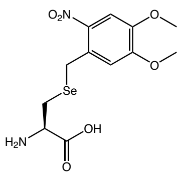
Our portfolio contains a variety of selenocysteine (Sec) derivatives as well as selenazolidine carboxylic acids (Sez derivatives). Sez can be deprotected and converted to Sec by treatment with O-methylhydroxylamine ($MeONH_2$) at pH 4 or by using Cu(II) salts.

Product details

HAA9255 H-L-Sec(DMNB)-OH*TFA

Dimethoxynitrobenzyl selenocysteine TFA salt

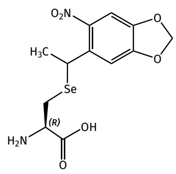
CAS-No.	1644398-13-9
Formula	$C_{12}H_{16}N_2O_6Se*CF_3COOH$
Mol. weight	363,24*114,02 g/mol



HAA9360 H-L-Sec(MDNPE)-OH

Se-(Methyl-*o*-nitropiperonyl)-selenocysteine

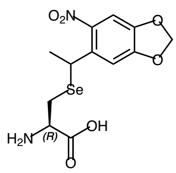
CAS-No.	2235373-47-2
Formula	$C_{12}H_{14}N_2O_6Se$
Mol. weight	361,21 g/mol



HAA9230 H-L-Sec(MDNPE)*TFA

(2R)-2-amino-3-((1-(6-nitrobenzo[d][1,3]dioxol-5-yl) ethyl)selanyl)propanoic acid trifluoroacetate

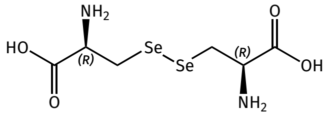
CAS-No.	2235373-48-3
Formula	$C_{12}H_{14}N_2O_6Se*CF_3CO_2H$
Mol. weight	361,22*114,02 g/mol



Product details

HAA9350 (H-L-Sec-OH)2

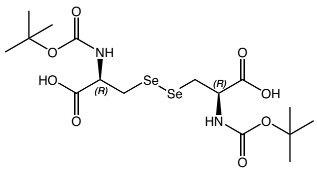
L-Selenocystine, (H-Sec)2, (H-L-Sec)2



CAS-No.	29621-88-3
Formula	$C_6H_{12}N_2O_4Se_2$
Mol. weight	334,11 g/mol

BAA3680 (Boc-L-Sec)$_2$

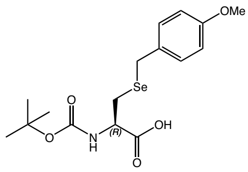
N-alpha-*t*-Butyloxycarbonyl-L-selenocystine



CAS-No.	877754-71-7
Formula	$C_{16}H_{28}N_2O_8Se_2$
Mol. weight	534,35 g/mol

BAA3760 Boc-L-Sec(Mob)-OH

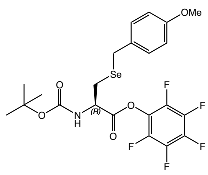
N-alpha-*t*-Butyloxycarbonyl-Se-(4-methoxybenzy-l)-L-selenocysteine



CAS-No.	959415-39-5
Formula	$C_{16}H_{23}NO_5Se$
Mol. weight	388,32 g/mol

BAA4830 Boc-L-Sec(Mob)-OPfp

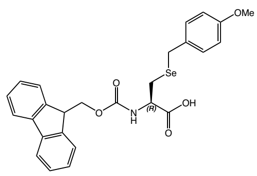
N-alpha-*tert*-Butoxycarbonyl-4-methoxybenzyl-L-selenocysteine pentafluorophenyl ester



CAS-No.	1257525-48-6
Formula	$C_{22}H_{22}F_5NO_5Se$
Mol. weight	554,38 g/mol

FAA8705 Fmoc-L-Sec(Mob)-OH

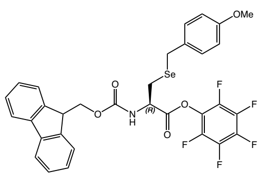
N-alpha-(9-Fluorenylmethyloxycarbonyl)-Se-(4-methoxybenzyl)-L-selenocysteine



CAS-No.	150308-80-8
Formula	$C_{26}H_{25}NO_5Se$
Mol. weight	510,46 g/mol

FAA8760 Fmoc-L-Sec(Mob)-OPfp

N-alpha-(9-Fluorenylmethyloxycarbonyl)-L-4-methoxybenzyl selenocysteine pentafluorophenyl ester



CAS-No.	939431-43-3
Formula	$C_{32}H_{24}F_5NO_5Se$
Mol. weight	676,51 g/mol

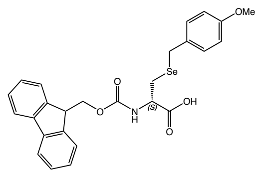
back to content ↑

Product details

FAA8710 Fmoc-D-Sec(Mob)-OH

N-alpha-(9-Fluorenylmethyloxycarbonyl)-Se-(4-methoxybenzyl)-D-selenocysteine

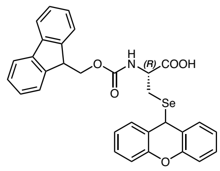
Formula	$C_{26}H_{25}NO_5Se$
Mol. weight	510,46 g/mol



FAA8465 Fmoc-L-Sec(Xan)-OH

Fmoc-Se-xanthyl-L-selenocysteine

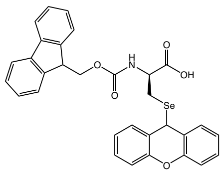
CAS-No.	1639843-35-8
Formula	$C_{31}H_{25}NO_5Se$
Mol. weight	570,49 g/mol



FAA8600 Fmoc-D-Sec(Xan)-OH

Fmoc-Se-xanthyl-D-selenocysteine

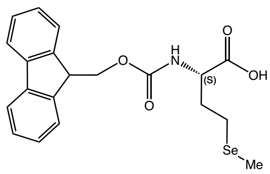
Formula	$C_{31}H_{25}NO_5Se$
Mol. weight	570,49 g/mol



FAA4205 Fmoc-L-Selenomethionine

N-alpha-(9-Fluorenylmethyloxycarbonyl)-L-selenomethionine

CAS-No.	1217852-49-7
Formula	$C_{20}H_{21}NO_4Se$
Mol. weight	418,35 g/mol



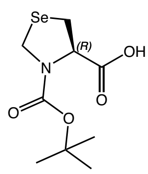
Besides Sec, our portfolio contains a variety of selenazolidine carboxylic acids (Sez derivatives). Sez can be deprotected and converted to Sec by treatment with O-methylhydroxylamine ($MeONH_2$) at pH 4 or by using Cu(II) salts.

Product details

BAA4880 Boc-L-Sez-OH

Boc selenazolidine carboxylic acid

CAS-No.	1841180-44-6
Formula	$C_9H_{15}NO_4Se$
Mol. weight	280,19 g/mol

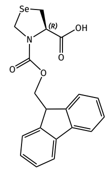


Product details

FAA8860 Fmoc-L-Sez-OH

Fmoc selenazolidine carboxylic acid

CAS-No.	1985651-74-8
Formula	$C_{19}H_{17}NO_4Se$
Mol. weight	402,31 g/mol



General Procedure for the Synthesis of Selenoesters

The peptide residue after Fmoc-SPPS is dissolved in anhydrous DMF and cooled to 0 °C. Diphenyl diselenide (DPDS) (30 eq. in DMF) and Bu_3P (30 eq.) are subsequently added. After 3 h at 0 °C, the solvent is removed *in vacuo*.

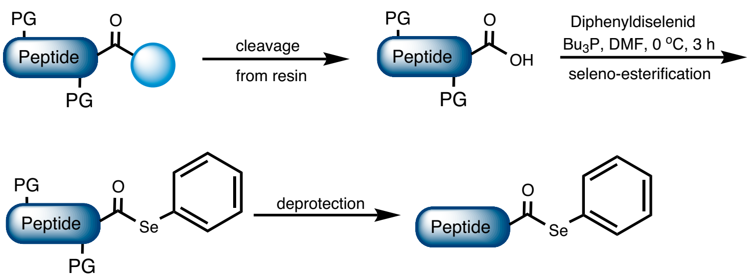


Fig. 11: Formation of selenoesters.

One-Pot Additive-Free Diselenide-Selenoester Ligation-Deselenization Reactions

Conditions of Additive-free Ligation:

2.5 mM final concentration of diselenide dimer in 6 M Gdn*HCl, and 0.1 M Na_2HPO_4 (pH 7.2; reduced to 6.2–6.5 upon addition to peptide fragments).

Conditions of One-Pot Deselenization:

Hexane extraction (×5) followed by the addition of 0.25 M TCEP, 25 mM DTT in 6 M Gdn*HCl, and 0.1 M Na_2HPO_4 (pH 5–6).

Reference:

→ *Accelerated Protein Synthesis via One-Pot Ligation-Deselenization Chemistry; N. J. Mitchell, J. Sayers, S. S. Kulkarni, D. Clayton, A. M. Goldys, J.Ripoll-Rozada, P. J. Barbosa Pereira, B. Chan, L. Radom, R. J. Payne;* ***Chem*** *2017;* ***2****: 703-715. https://doi.org/10.1016/j.chempr.2017.04.003*

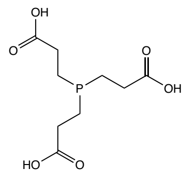
back to content ↑

Product details

LS-3405 TCEP*HCl

3-[bis(2-carboxyethyl)phosphanyl]propanoic acid, hydrochloride

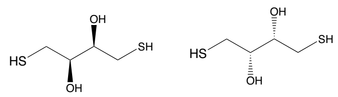
CAS-No.	51805-45-9
Formula	$C_9H_{15}O_6P$*HCl
Mol. weight	250,19*36,45 g/mol



RL-1020 DTT (racemic)

DL-Dithiothreitol

CAS-No.	3483-12-3
Formula	$C_4H_{10}O_2S_2$
Mol. weight	154,25 g/mol



3.4. Oxime Ligation using Aminooxy-Amino Acids

Replacing the primary amino group of an amino acid by an aminooxy moiety leads to an increase in nucleophilicity. Thus, after completion of the peptide synthesis and deprotection of the aminooxy-function, chemoselective reactions with carbonyl compounds under formation of a kinetically stable oxime bond can be performed. Compared to imines, oximes display much higher stability toward hydrolysis. This increased stability is explained by the α-effect provided by the heteroatom adjacent to the sp^2 nitrogen.

This simple reaction can be utilized for the synthesis of large proteins by fragment assembly = oxime ligation. Successive deprotection of aldehyde and/or aminooxy moieties allows for the controlled and sequential ligation of peptide fragments.

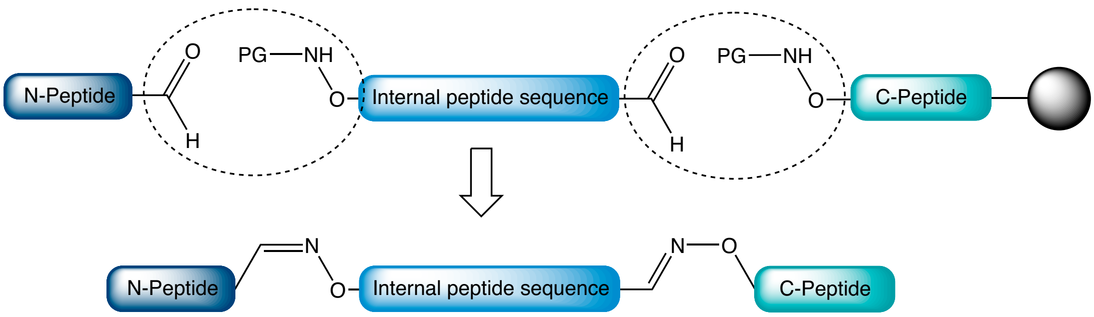


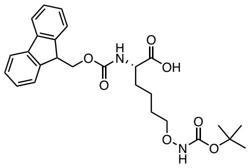
Fig. 12: Illustration of oxime ligation.

The oxime linkage is reported as good peptidomimetic instead of the amide bond. The low usage of this ligation type is most probably due to the possible hydrolysis of the oxime linkage as well as the formation of a mixture of products due to *E*/*Z*-isomerization.

FAA8450 Fmoc-AAHA(Boc)-OH (S)

(S)-2-(Fmoc-amino)-6-(Boc-aminoxy)hexanoic acid

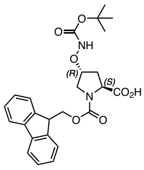
CAS-No.	357278-11-6
Formula	$C_{26}H_{32}N_2O_7$
Mol. weight	484,54 g/mol



FAA8455 Fmoc-L-*trans*-Hyp(NHBoc)-OH

Fmoc-4-(Boc-amino)oxy)-proline (2S,4R)

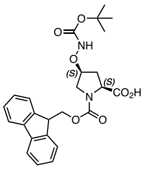
CAS-No.	1015426-45-5
Formula	$C_{25}H_{28}N_2O_7$
Mol. weight	468,50 g/mol



FAA8460 Fmoc-L-*cis*-Hyp(NHBoc)-OH

Fmoc-4-(Boc-amino)oxy)-proline (2S,4S)

CAS-No.	1015426-31-9
Formula	$C_{25}H_{28}N_2O_7$
Mol. weight	468,50 g/mol



References:

→ *Site-specific cross-linking of proteins to DNA via a new biorthogonal approach employing oxime ligation; S. S. Pujari, Y. Zhang, S. Ji, M. D. Distefano, N. Y. Tretyakova;* ***Chem. Commun.*** *2018;* ***54****: 6296-6299. https://doi.org/10.1039/C8CC01300D*

→ *44. Amino-oxy-derivatives. Part I. Some a-amino-oxy-acids and a-amino-oxy-hydrazides. D. Mchale, J. Green, P. Mamalis;* ***J. Chem. Soc.*** *1960; 225-229. https://doi.org/10.1039/JR9600000225*

→ *SAR by Oxime-Containing Peptide Libraries: Application to Tsg101 Ligand Optimization; F. Liu, A. G. Stephen, A. A. Waheed, M. J. Aman, E. O. Freed, R. J. Fisher, T. R. Burke;* ***ChemBioChem*** *2008;* ***9(12)****: 2000-2004. https://doi.org/10.1002/cbic.200800281*

→ *A Versatile Set of Aminooxy Amino Acids for the Synthesis of Neoglycopeptides; M. R. Carrasco, R. T. Brown;* ***J. Org. Chem.*** *2003;* ***68****: 8853-8858. https://doi.org/10.1021/jo034984x*

3.5. Activated Cysteine-Based Protein Ligation (ACPL)

This method is based on the direct activation of Cysteine by the small molecule cyanylating reagent 2-nitro-5-thiocyanatobenzoic acid (NTCB). The transferred cyanide then forms a thiocyanate which undergoes a reversible intramolecular addition with the Cys N-amide to generate a five-membered 1-acyl-2-iminothiazolidine intermediate which can be reacted with nucleophiles. When the nucleophile is hydrazine, the afforded peptide hydrazide can then undergo ligation, either *via* reaction with an aldehyde/ketone (hydrazone ligation) or *via* transformation to a peptide thioester and subsequent chemical ligation, both as described above. Without addition of a nucleophilic amine, the formed five-membered ring undergoes hydrolysis.

back to content ↑

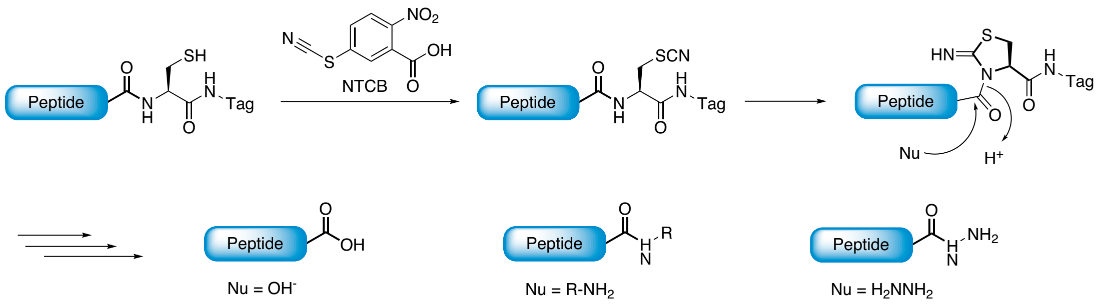


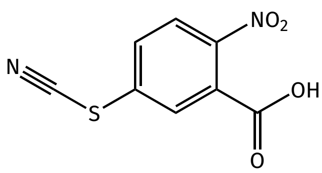
Fig. 13: Schematic illustration of the activated Cysteine-based protein ligation.

Product details

RL-4080 NTCB

2-nitro-5-thiocyanatobenzoic acid

CAS-No.	30211-77-9
Formula	$C_8H_4N_2O_4S$
Mol. weight	224,19 g/mol



Reference:

→ *Expressed Protein Ligation without Intein; Y. Qiao, G. Yu, K. C. Kratch, X. Aria Wang, W. Wei Wang, S. Z. Leeuwon, S. Xu, J. S. Morse, W. Ray Liu;* ***J. Am. Chem. Soc.*** *2002;* ***142****: 7057-7054.*
https://doi.org/10.1021/jacs.0c00252

4. Enzyme-mediated Ligation

The transpeptidase activity of sortase can be used to produce fusion proteins *in vitro*. The enzyme recognition motif (LPXTG) is added to the C-terminus of a protein of interest, while an oligo (glycine) motif is added to the N-terminus of the second protein. Upon addition of sortase A, the two peptides are covalently linked through a native peptide bond while losing one glycine residue.

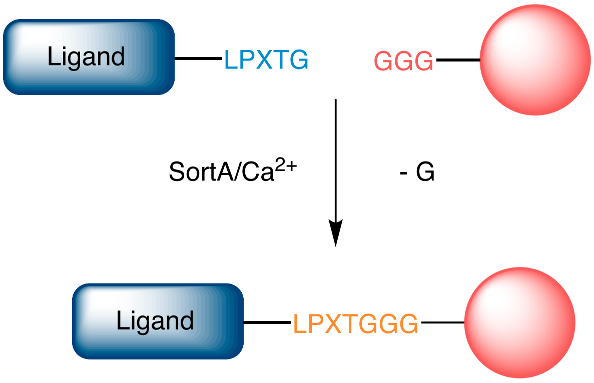


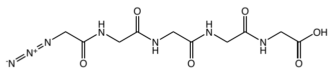
Fig. 14: Enzymatically supported conjugation utilizing sortase A.

Here we present several building blocks, which can be used for convenient N-terminal oligo-glycine design of ligation fragments.

Product details

HAA2860 N_3-Gly-Gly-Gly-Gly-Gly-OH

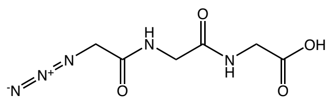
CAS-No. 2250433-77-1
Formula $C_{10}H_{15}N_7O_6$
Mol. weight 329,27 g/mol



HAA2840 N_3-Gly-Gly-Gly-OH

Azido-glycylglycylglycine

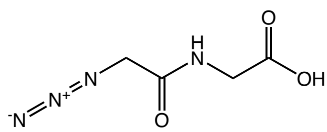
CAS-No. 1993176-75-2
Formula $C_6H_9N_5O_4$
Mol. weight 215,17 g/mol



HAA2850 N_3-Gly-Gly-OH*DCHA

Azido-glycylglycine dicyclohexylamine

CAS-No. 855750-87-7 net
Formula $C_4H_6N_4O_3$*$C_{12}H_{23}N$
Mol. weight 158,12*181,32 g/mol



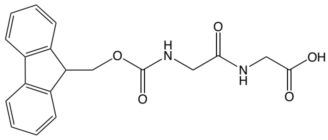
back to content ↑

Product details

FDP1030 Fmoc-Gly-Gly-OH

N-alpha-(9-Fluorenylmethyloxycarbonyl)-glycinyl-glycin

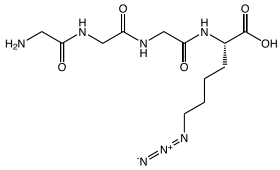
CAS-No.	35665-38-4
Formula	$C_{19}H_{18}N_2O_5$
Mol. weight	354,36 g/mol



HAA2870 H-(Gly)$_3$-Lys(N$_3$)-OH*HCl

Triglycyl-epsilon-azido-L-lysine hydrochloride

CAS-No.	2250437-45-5 net
Formula	$C_{12}H_{21}N_7O_5$*HCl
Mol. weight	343,34*36,45 g/mol



References:

- *Assembly of Oligoglycine Layers on Mica Surface; S. V. Tsygankova, A. A. Chinarev, A. B. Tuzikov, I. S. Zaitsev, N. Severin, A. A. Kalachev, J. P. Rabe, N. V. Bovin;* ***Journal of Biomaterials and Nanobiotechnology*** *2011;* ***02****: 91-97. https://doi.org/10.4236/jbnb.2011.21012*
- *Biantennary oligoglycines and glyco-oligoglycines self-associating in aqueous medium; S. V. Tsygankova, A. A. Chinarev, A. B. Tuzikov, N. Severin, A. A. Kalachev, J. P. Rabe, A. S. Gambaryan, N. V. Bovin;* ***Beilstein J Org Chem*** *2014;* ***10****: 1372-1382. https://doi.org/10.3762/bjoc.10.140*
- *DNA-bending finger: artificial design of 6-zinc finger peptides with polyglycine linker and induction of DNA bending; M. Imanishi, Y. Hori, M. Nagaoka, Y. Sugiura;* ***Biochemistry*** *2000;* ***39****: 4383-4390. https://doi.org/10.1021/bi992989b*
- *Effects of the length of a glycine linker connecting the N-and C-termini of a circularly permuted dihydrofolate reductase; M. Iwakura, T. Nakamura;* ***Protein Eng*** *1998;* ***11****: 707-713. https://doi.org/10.1093/protein/11.8.707*
- *Linkers in the structural biology of protein-protein interactions; V. P. Reddy Chichili, V. Kumar, J. Sivaraman;* ***Protein Sci*** *2013;* ***22****: 153-167. https://doi.org/10.1002/pro.2206*
- *Optimizing the stability of single-chain proteins by linker length and composition mutagenesis; C. R. Robinson, R. T. Sauer;* ***Proc Natl Acad Sci U S A*** *1998;* ***95****: 5929-5934. https://doi.org/10.1073/pnas.95.11.5929*
- *Sortase-mediated protein ligation: a new method for protein engineering; H. Mao, S. A. Hart, A. Schink, B. A. Pollok;* ***J Am Chem Soc*** *2004;* ***126****: 2670-2671. https://doi.org/10.1021/ja039915e*
- *Sortase-tag expressed protein ligation: combining protein purification and site-specific bioconjugation into a single step; R. Warden-Rothman, I. Caturegli, V. Popik, A. Tsourkas;* ***Anal Chem*** *2013;* ***85****: 11090-11097. https://doi.org/10.1021/ac402871k*

Iris Biotech

5. Examples

5.1. Kinetically Controlled Four-Fragment Ligation for the Convergent Chemical Synthesis of Proteins

The convergent synthesis of proteins by the chemical ligation of multiple peptide segments is achieved by a kinetically controlled four-fragment ligation. This was made possible by the controlled extension of the key Cys-peptide intermediate by ligation at either the N- or C-termini. For more information, please refer to the following publication:

Reference:

→ *Kinetically controlled ligation for the convergent chemical synthesis of proteins; D. Bang, B. L. Pentelute, S. B. Kent;* ***Angew Chem Int Ed Engl*** *2006;* ***45****: 3985-3988.*

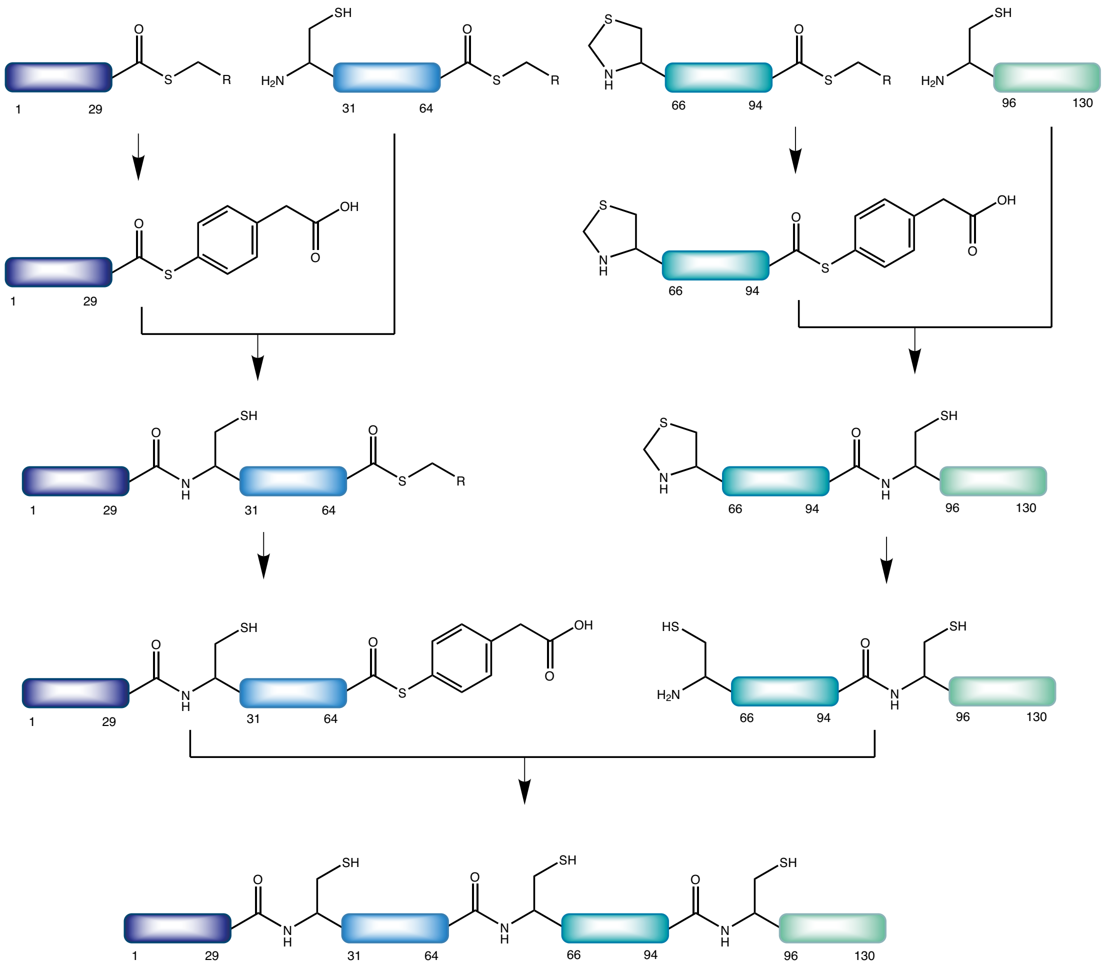


Fig. 15: Kinetically controlled four-fragment ligation.

back to content ↑

5.2. Three-Fragment Synthesis of a 116mer with Desulfurization

The discovery of native chemical ligation, the regio- and chemoselective coupling of two unprotected peptide segments, facilitated the synthesis of polypeptides with more than 200 amino acids. However, this approach initially relied on the presence of at least one cysteine residue in the sequence at a convenient position. Hence, postligation-desulfurization protocols were developed that allowed for ligation at amino acid residues other than cysteine. Please refer to the following review for a comprehensive overview of "the development and recent progress on the chemical synthesis of peptides and proteins encompassing postligation-desulfurization at alanine, valine, lysine, threonine, leucine, proline, arginine, aspartic acid, glutamate, phenylalanine, glutamine, and tryptophan".

Reference:

→ *Postligation-Desulfurization: A General Approach for Chemical Protein Synthesis; J. Ma, J. Zeng, Q. Wan;* ***Protein Ligation and Total Synthesis II*** *2015; (Ed.: L. Liu): Springer International Publishing, Cham, 57-101.*

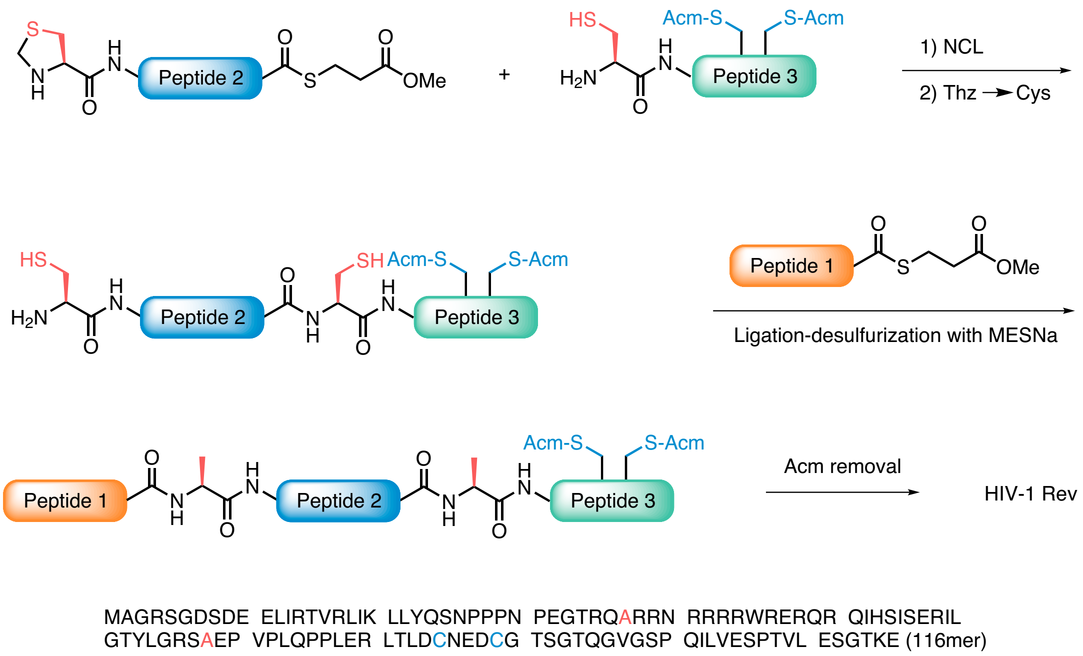


Fig. 16: Example of a synthesis of a peptide via ligation of three segments and thiazolidine as temporarily protected cysteine.

Notes

back to content ↑

Code of Conduct

As business activity of Iris Biotech GmbH impacts people's lives and health, it must be operated in ethical and correct manner and act with integrity and responsibility. To ensure high ethical standards and fair business practices, Iris Biotech GmbH applies an integrated policy known as its Code of Conduct.

In 2001 Iris Biotech GmbH was founded just at the beginning of the Biotech movement and the first remarkable breakthrough of biotech pharma products. Although the biotech field is rather young compared to other industries we believe on long-term business, a good partnership between our business partners and Iris Biotech GmbH and a good reputation. It is our duty as well as our responsibility to maintain and to extend this over the next generations – based on the principles of an honourable and prudent tradesman which based upon the concept of honourable entrepreneurship.

This Code of Conduct has been developed following the "Voluntary Guidelines for Manufacturers of Fine Chemical Intermediates and Active Ingredients" issued by AIME (Agrochemical & Intermediates Manufacturers in Europe) and the requirements of some of our business associates.

Iris Biotech GmbH commits to hold this Code of Conduct and to include and apply its principles in the management system and the company policies.

Ethics

Iris Biotech GmbH undertakes business in an ethical manner and acts with integrity. All corruption, extortion and embezzlement are prohibited. We do not pay or accept bribes or participate in other illegal inducements in business or government relationships. We conduct our business in compliance with all applicable anti-trust laws. Employees are encouraged to report concerns or illegal activities in the workplace, without threat of reprisal, intimidation or harassment.

Labour

Iris Biotech GmbH is committed to uphold the human rights of workers and to treat them with dignity and respect. Child labour, workplace harassment, discrimination, and harsh and inhumane treatment are prohibited. Iris Biotech GmbH respects the rights of the employees to associate freely, join or not join labour unions, seek representation and join workers' councils. Employees are paid and their working timetable is established according to applicable wage and labour laws. Employees are able to communicate openly with management regarding working conditions without threat of reprisal, intimidation or harassment.

General Policies

Contracts and Secrecy Agreements are binding and the confidential information received is only used for intended purposes. Clear management and organizational structures exist to provide efficient normal working and to address problems quickly. Know-how is protected and intellectual property isrespected.

Health and Safety

Iris Biotech GmbH provides a safe and healthy working environment to the employees and protects them from overexposure to chemical and physical hazards. Products are produced, stored and shipped under the guidelines of the relevant chemical and safety legislation. Risks and emergency scenarios are identified and evaluated, and their possible impact is minimized by implementing emergency plans and written procedures. Safety information regarding hazardous materials is available to educate, train and protect workers from hazards. Preventive equipment and facilities maintenance is performed at suitable periods to reduce potential hazards. Employees are regularly trained in health and safety matters and are informed about product properties and risk classification when it is required.

Environment

Iris Biotech GmbH operates in an environmentally responsible and efficient manner, minimizing adverse impacts on the environment. Waste streams are managed to ensure a safe handling, movement, storage, recycling and reuse, before and after being generated. Systems to prevent and mitigate accidental spills and releases to the environment are in place. All required environmental permits and licenses are obtained and their operational and reporting requirements are complied with.

Production and Quality Management

A quality management system following the Good Distribution Practices (GDP rules) of Active Pharmaceutical Ingredients is established covering all the aspects of the worldwide distribution of products. Regular audits are performed to evaluate the efficiency and fulfilling of the quality system. Process controls to provide reproducible product quality are established. There are preventive maintenance procedures to ensure plant reliability and the lowest risk of failure. Staff is trained periodically about GMP and GDP rules. Procedures are established and installations are designed to avoid cross contamination. Batch and analytical records are kept for inspection and audit purposes for suitable periods according guidelines.

Research and Development

Research and development staff education is appropriate to their functional activity and they are trained to develop, optimize and scale-up the processes. Intellectual property is respected and know-how protected. Development of manufacturing processes reflects the principles of the Green Chemistry according to the American Chemical Society Green Chemistry Institute. Animal testing is not used unless alternatives are not scientifically valid or accepted by regulators. If animal testing is carried out, animals are treated so that pain and stress are minimized.

back to content ↑

Terms and Conditions of Sales

All orders placed by a buyer are accepted and all contracts are made subject to the terms which shall prevail and be effective notwithstanding any variations or additions contained in any order or other document submitted by the buyer. No modification of these terms shall be binding upon Iris Biotech GmbH unless made in writing by an authorised representative of Iris Biotech GmbH.

Placing of Orders

Every order made by the buyer shall be deemed an offer by the buyer to purchase products from Iris Biotech GmbH and will not be binding on Iris Biotech GmbH until a duly authorised representative of Iris Biotech GmbH has accepted the offer made by the buyer. Iris Biotech GmbH may accept orders from commercial, educational or government organisations, but not from private individuals and Iris Biotech GmbH reserves the right to insist on a written order and/or references from the buyer before proceeding.

There is no minimum order value. At the time of acceptance of an order Iris Biotech GmbH will either arrange prompt despatch from stock or the manufacture/acquisition of material to satisfy the order. In the event of the latter Iris Biotech GmbH will indicate an estimated delivery date. In addition to all its other rights Iris Biotech GmbH reserves the right to refuse the subsequent cancellation of the order if Iris Biotech GmbH expects to deliver theproduct on or prior to the estimated delivery date. Time shall not be of the essence in respect of delivery of the products. If Iris Biotech GmbH is unable to deliver any products by reason of any circumstances beyond its reasonable control („Force Majeure“) then the period for delivery shall be extended by the time lost due to such Force Majeure. Details of Force Majeure will be forwarded by Iris Biotech GmbH to the buyer as soon as reasonably practicable.

Prices, Quotations and Payments

Prices are subject to change. For the avoidance of doubt, the price advised by Iris Biotech GmbH at the time of the buyer placing the order shall supersede any previous price indications. The buyer must contact the local office of Iris Biotech GmbH before ordering if further information is required. Unless otherwise agreed by the buyer and Iris Biotech GmbH, the price shall be for delivery ex-works. In the event that the buyer requires delivery of the products otherwise than ex-works the buyer should contact the local office of Iris Biotech GmbH in order to detail its requirements. Iris Biotech GmbH shall, at its discretion, arrange the buyer‘s delivery requirements including, without limitation, transit insurance, the mode of transit (Iris Biotech GmbH reserves the right to vary the mode of transit if any regulations or other relevant considerations so require) and any special packaging requirements (including cylinders). For the avoidance of doubt all costs of delivery and packaging in accordance with the buyer‘s requests over and above that of delivery in standard packaging ex-works shall be for the buyer‘s account unless otherwise agreed by both parties. Incoterms 2020 shall apply. Any tax, duty or charge imposed by governmental authority or otherwise and any other applicable taxes, duties or charges shall be for the buyer‘s account. Iris Biotech GmbH may, on request and where possible, provide quotations for multiple packs or bulk quantities, and non-listed items. Irrespective of the type of request or means of response all quotations must be accepted by the buyer without condition and in writing before an order will be accepted by Iris Biotech GmbH. Unless agreed in writing on different terms, quotations are valid for 30 days from the date thereof. Payment terms are net 30 days from invoice date unless otherwise agreed in writing. Iris Biotech GmbH reserves the right to request advance payment at its discretion. For overseas transactions the buyer shall pay all the banking charges of Iris Biotech GmbH. The buyer shall not be entitled to withhold or set-off payment for the products for any reason whatsoever. Government/

Corporate Visa and MasterCard (and other such credit cards) may be accepted on approved accounts for payment of the products. Personal credit cards are not acceptable. Failure to comply with the terms of payment of Iris Biotech GmbH shall constitute default without reminder. In these circumstances Iris Biotech GmbH may (without prejudice to any other of its rights under these terms) charge interest to accrue on a daily basis at the rate of 2% per month from the date upon which payment falls due to the actual date of payment (such interest shall be paid monthly). If the buyer shall fail to fulfil the payment terms in respect of any invoice of Iris Biotech GmbH Iris Biotech GmbH may demand payment of all outstanding balances from the buyer whether due or not and/or cancel all outstanding orders and/or decline to make further deliveries or provision of services except upon receipt of cash or satisfactory securities. Until payment by the buyer in full of the price and any other monies due to Iris Biotech GmbH in respect of all other products or services supplied or agreed to be supplied by Iris Biotech GmbH to the buyer (including but without limitation any costs of delivery) the property in the products shall remain vested in Iris Biotech GmbH.

Shipping, Packaging and Returns

The buyer shall inspect goods immediately on receipt and inform Iris Biotech GmbH of any shortage or damage within five days. Quality problems must be notified within ten days of receipt. Goods must not be returned without prior written authorisation of Iris Biotech GmbH. Iris Biotech GmbH shall at its sole discretion replace the defective products (or parts thereof) free of charge or refund the price (or proportionate price) to buyer. Opened or damaged containers cannot be returned by the buyer without the written prior agreement of Iris Biotech GmbH. In the case of agreed damaged containers which cannot be so returned, the buyer assumes responsibility for the safe disposal of such containers in accordance with all applicable laws.

Product Quality, Specifications and Technical Information

Products are analysed in the Quality Control laboratories of Iris Biotech GmbH’s production partners by methods and procedures which Iris Biotech GmbH considers appropriate. In the event of any dispute concerning reported discrepancies arising from the buyer’s analytical results, determined by the buyer’s own analytical procedures, Iris Biotech GmbH reserves the right to rely on the results of own analytical methods of Iris Biotech GmbH. Certificates of Analysis or Certificates of Conformity are available at the discretion of Iris Biotech GmbH for bulk orders but not normally for prepack orders. Iris Biotech GmbH reserves the right to make a charge for such certification. Specifications may change and reasonable variation from any value listed should not form the basis of a dispute. Any supply by Iris Biotech GmbH of bespoke or custom product for a buyer shall be to a specification agreed by both parties in writing. Technical information, provided orally, in writing, or by electronic means by or on behalf of Iris Biotech GmbH, including any descriptions, references, illustrations or diagrams in any catalogue or brochure, is provided for guidance purposes only and is subject to change.

Safety

All chemicals should be handled only by competent, suitably trained persons, familiar with laboratory procedures and potential chemical hazards. The burden of safe use of the products of Iris Biotech GmbH vests in the buyer. The buyer assumes all responsibility for warning his employees, and any persons who might reasonably be expected to come into contact with the products, of all risks to person and property in any way connected with the products and for instructing them in their safe handling and use. The buyer also assumes the responsibility for the safe disposal of all products in accordance with all applicable laws.

back to content ↑

Uses, Warranties and Liabilities

All products of Iris Biotech GmbH are intended for laboratory research purposes and unless otherwise stated on product labels, in the catalogue and product information sheet of Iris Biotech GmbH or in other literature furnished to the buyer, are not to be used for any other purposes, including but not limited to use as or as components in drugs for human or animal use, medical devices, cosmetics, food additives, household chemicals, agricultural or horticultural products or pesticides. Iris Biotech GmbH offers no warranty regarding the fitness of any product for a particular purpose and shall not be responsible for any loss or damage whatsoever arising there from. No warranty or representation is given by Iris Biotech GmbH that the products do not infringe any letters patent, trademarks, registered designs or other industrial rights. The buyer further warrants to Iris Biotech GmbH that any use of the products in the United States of America shall not result in the products becoming adulterated or misbranded within the meaning of the Federal Food, Drug and Cosmetic Act (or such equivalent legislation in force in the buyer's jurisdiction) and shall not be materials which may not, under sections 404, 505 or 512 of the Act, be introduced into interstate commerce. The buyer acknowledges that, since the products of Iris Biotech GmbH are intended for research purposes, they may not be on the Toxic Substances Control Act 1976 („TSCA") inventory. The buyer warrants that it shall ensure that the products are approved for use under the TSCA (or such other equivalent legislation in force in the buyer's jurisdiction), if applicable. The buyer shall be responsible for complying with any legislation or regulations governing the use of the products and their importation into the country of destination (for the avoidance of doubt to include, without limitation, the TSCA and all its amendments, all EINECS, ELINCS and NONS regulations). If any licence or consent of any government or other authority shall be required for the acquisition, carriage or use of the products by the buyer the buyer shall obtain the same at its own expense and if necessary produce evidence of the same to Iris Biotech GmbH on demand. Failure to do so shall not entitle the buyer to withhold or delay payment. Any additional expenses or charges incurred by Iris Biotech GmbH resulting from such failure shall be for the buyer's account. Save for death or personal injury caused by negligence of Iris Biotech GmbH, sole obligation of Iris Biotech GmbH and buyer's exclusive remedy with respect to the products proved to the satisfaction of Iris Biotech GmbH to be defective or products incorrectly supplied shall be to accept the return of said products to Iris Biotech GmbH for refund of the actual purchase price paid by the buyer (or proportionate part thereof), or replacement of the defective product (or part thereof) with alternative product. Iris Biotech GmbH shall have no liability to the buyer under or arising directly or indirectly out of or otherwise in connection with the supply of products by Iris Biotech GmbH to the buyer and/or their re-sale or use by the buyer or for any product, process or services of the buyer which in any way comprises the product in contract tort (including negligence or breach of statutory duty) or otherwise for pure economic loss, loss of profit, business, reputation, depletion of brand, contracts, revenues or anticipated savings or for any special indirect or consequential damage or loss of any nature except as may otherwise be expressly provided for in these terms. All implied warranties, terms and representations in respect of the products (whether implied by statute or otherwise) are excluded to the fullest extent permitted by law. The buyer shall indemnify Iris Biotech GmbH for and against any and all losses, damages and expenses, including legal fees and other costs of defending any action, that Iris Biotech GmbH may sustain or incur as a result of any act or omission by the buyer, its officers, agents or employees, its successors or assignees, its customers or all other third parties, whether direct or indirect, in connection with the use of any product. For the avoidance of doubt and in the event that Iris Biotech GmbH supplies bespoke or custom product to the buyer's design or specification, this indemnity shall extend to include any claim by a third party that the manufacture of the product for the buyer or the use of the product by the buyer infringes the intellectual property rights of any third party.

General

Iris Biotech GmbH shall be entitled to assign or sub-contract all or any of its rights and obligations hereunder. The buyer shall not be entitled to assign, transfer, sub-contract or otherwise delegate any of its rights or obligations hereunder. Any delay or forbearance by Iris Biotech GmbH in exercising any right or remedy under these terms shall not constitute a waiver of such right or remedy. If any provision of these terms is held by any competent authority to be invalid or unenforceable in whole or in part the validity of the other provisions of these terms and the remainder of the provision in question shall not be affected. These terms shall be governed by German Law and the German Courts shall have exclusive jurisdiction for the hearing of any dispute between the parties save in relation to enforcement where the jurisdiction of the German Courts shall be non-exclusive.

Notes

back to content ↑

Index

back to content ↑

Get in Contact

Iris Biotech GmbH
Adalbert-Zoellner-Str. 1
95615 Marktredwitz
Germany

+49 (0) 9231 97121-0
+49 (0) 9231 97121-99
info@iris-biotech.de
www.iris-biotech.de

Distribution Partners

The list contains the current distributors of Iris Biotech in different regions of the world. The latest list of distribution partners and contact details is available at: **www.iris-biotech.de/distribution-partner**

China:

Chengdu Yoo Technology Co., Ltd.

Japan:

BizCom Japan, Inc.

Shigematsu & Co., Ltd

Cosmo Bio Co., Ltd.

USA & Canada:

Peptide Solutions LLC

India, Bangladesh, Oman, Sri Lanka, United Arab Emirates:

Sumit Biosciences Pvt Ltd.

Singapore, Thailand, Malaysia, Indonesia, Vietnam, Philippines, Brunei, Burma (Myanmar), Laos, Cambodia, Timor-Leste:

SciClix Pte. Ltd.

Empowering Peptide Innovation