Iris Biotech

LIGATION TECHNOLOGIES

Version: IB7_4

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.

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-analogs as well as specific linkers for controlled drug delivery and release.

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

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 analogs

Building Blocks

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

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, poly(acrylamide) resins, Cyclover

Linkerology® and Drug Delivery

Linkers for Solid Phase Peptide Synthesis

Cleavable Linkers

Val-Ala-based, Val-Cit-based, disulfide-based, Dde-helping hands, pH-sensitive linkers

Photo-Activatable Linkers

Functionalized Linkers

Clickable linkers, trifunctional linkers, linkers with maleimide function, cross-linkers, selective N-term acylation and biotinylation, 5HP2O

PROTACs

Ligands, linkers & modules

Fullerenes, Poly(2-oxazolines), Dextrans & Plant-Derived Cholesterol

Superparamagnetic Iron Oxide Nanoparticles

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, 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 & origin
- Impurity profiling
- Safety data sheets
- 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

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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.

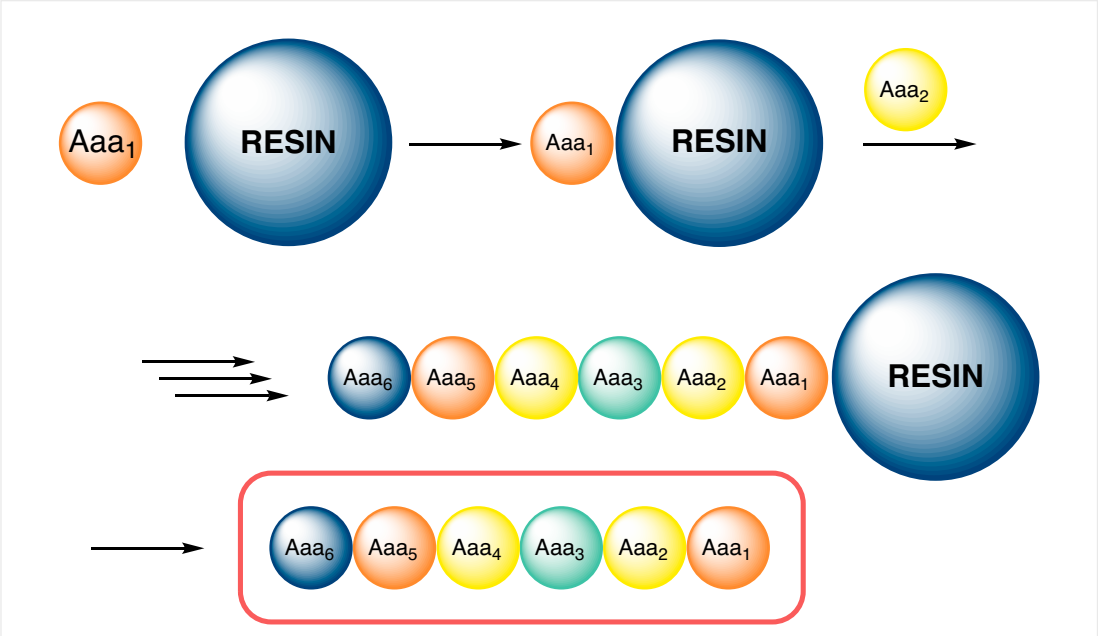

Fig. 1: Concept of solid phase peptide synthesis (SPPS): attachment of the first amino acid to a resin and repetitive cycles of deprotection, washing, coupling, washing, deprotection, ... and final cleavage from the resin and purification.

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.

Tab. 1: Final yield in SPPS depending on the yield per step.

	Yield per Step/Final Yield			
# of Steps	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%

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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.

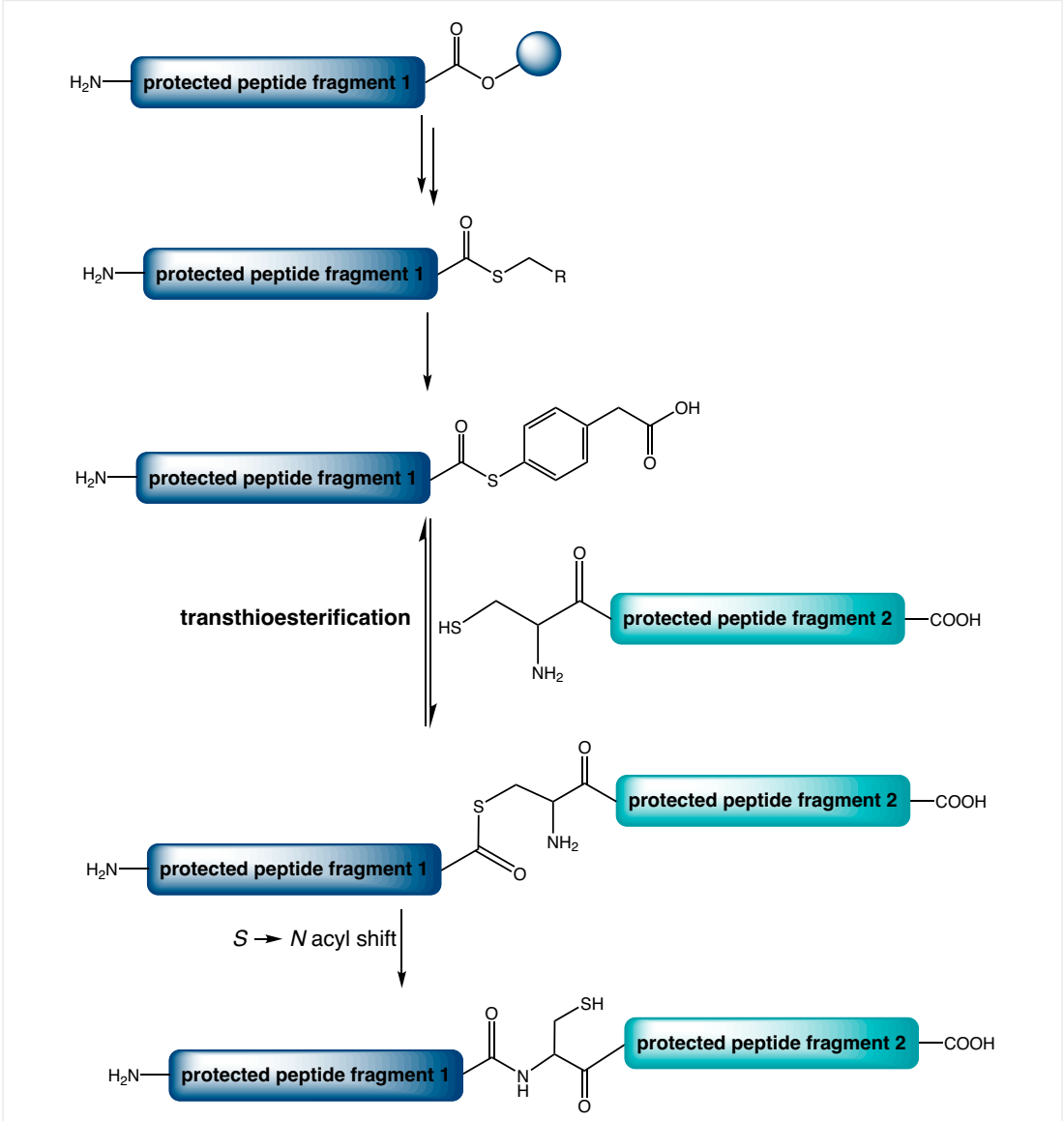

Fig. 2: Mechanism of native chemical ligation.

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.

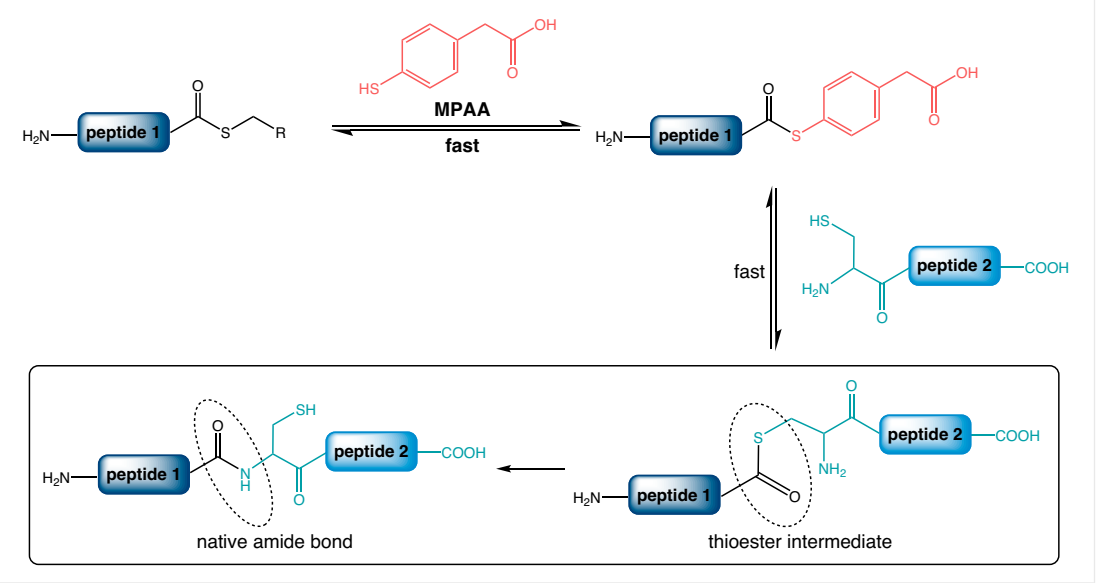

Fig. 3: The role of MPAA as an additive in native chemical ligation.

Tab. 2: General information - Elements in NCL, their electronegativity, atomic radius, and electron configuration.

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}

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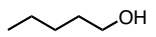
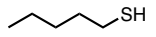
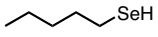
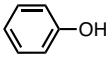
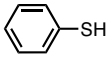
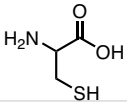
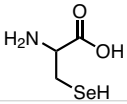
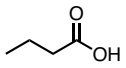
Tab. 3: Substituded alcohols, thiols and selenols and their respective pK_a values.

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 cysteine 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 proline and phenylalanine). 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 cysteine residues. Payne *et al.* and Dery *et al.* have demonstrated that ligation products can be subjected to oxidative deselenization to afford serine in place of selenocysteine at the ligation junction.

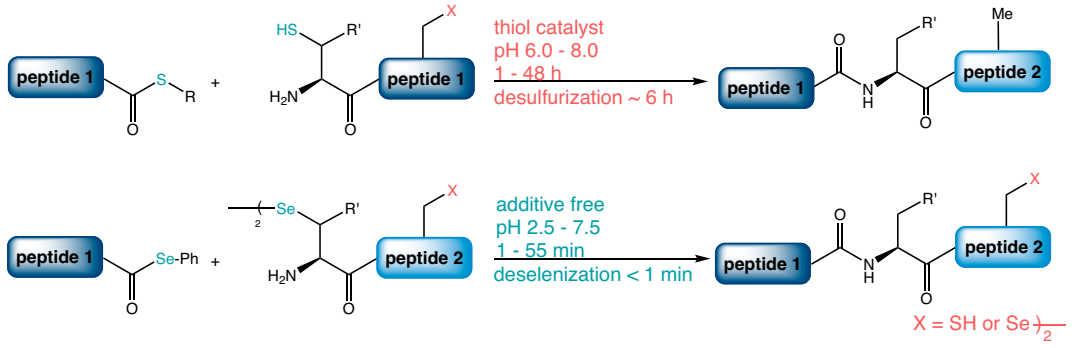


Fig. 4: Differences in properties and capabilities using either sulfur or selenium in native chemical ligation.

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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.

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.

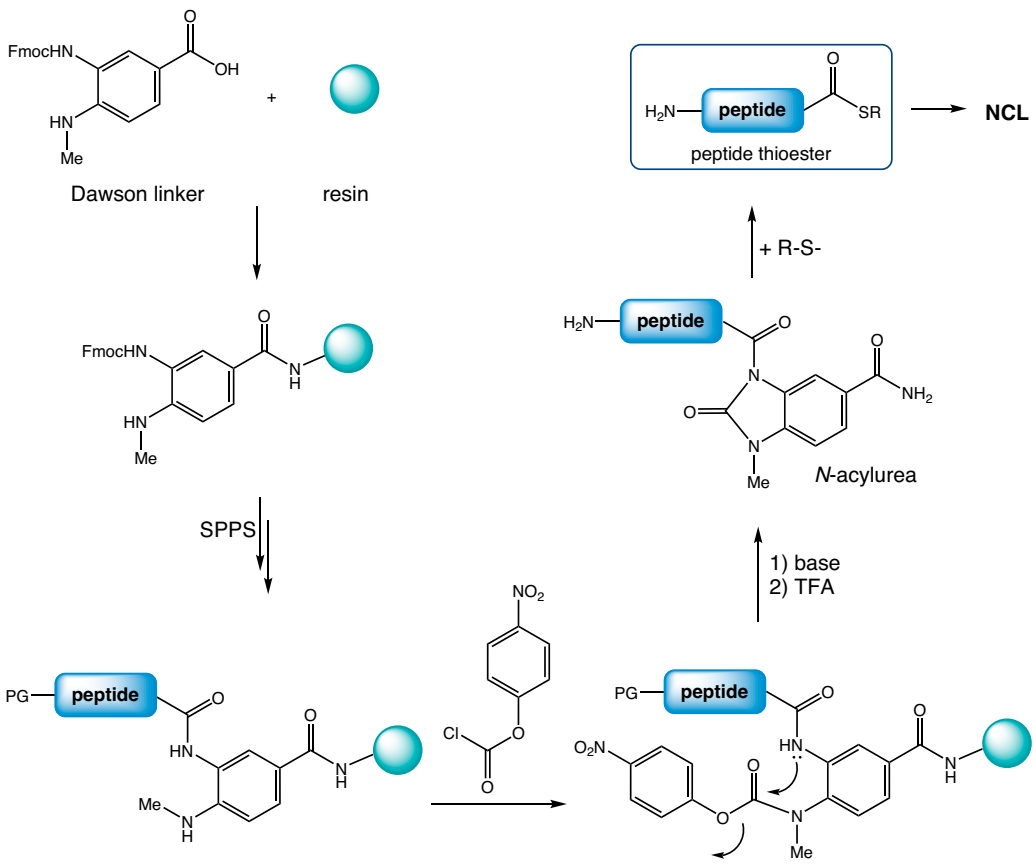

Fig. 5: Formation of thioesters via Dawson linker.

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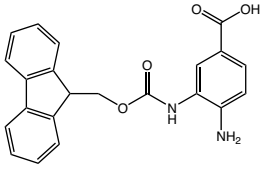
FAA3165 Fmoc-Dbz-OH

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



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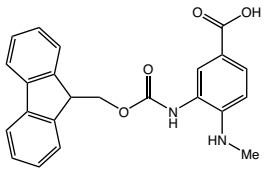
Product details

FAA3166 Fmoc-MeDbz-OH

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

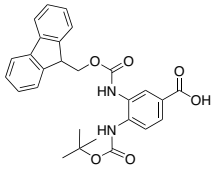
CAS-No.	1788861-35-7
Formula	$C_{23}H_{20}N_2O_4$
Mol. weight	388,44 g/mol



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

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

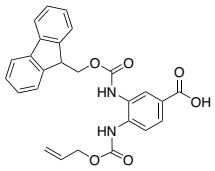
CAS-No.	1823479-63-5
Formula	$C_{27}H_{26}N_2O_6$
Mol. weight	474,51 g/mol



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

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

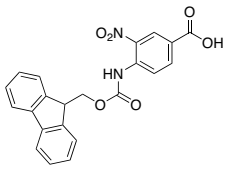
CAS-No.	2143465-53-4
Formula	$C_{26}H_{22}N_2O_6$
Mol. weight	458,46 g/mol



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

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

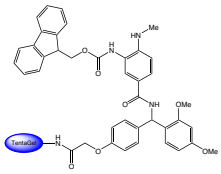
CAS-No.	1342864-48-5
Formula	$C_{22}H_{16}N_2O_6$
Mol. weight	404,37 g/mol



S-30091 Fmoc-MeDbz-RAM TG S

TentaGel S Dawson Fmoc-MeDbz RAM Resin

Mesh Size	90 µm
Loading	0.15 - 0.25 mmol/g



2.2. Hydrazone Resins

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.

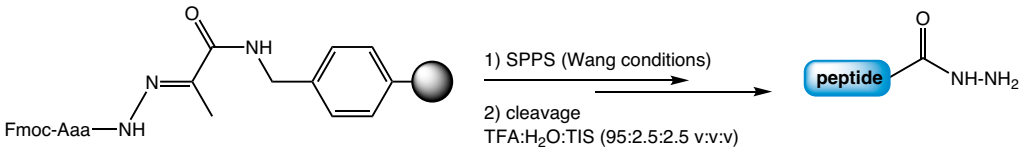


Fig. 6: Synthesizing peptide hydrazides utilizing hydrazone resin.

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.

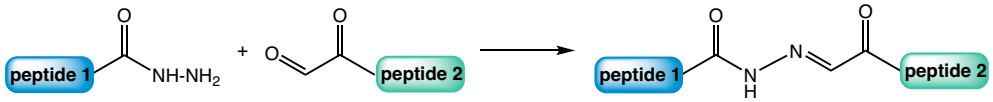


Fig. 7: Hydrazone ligation.

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.

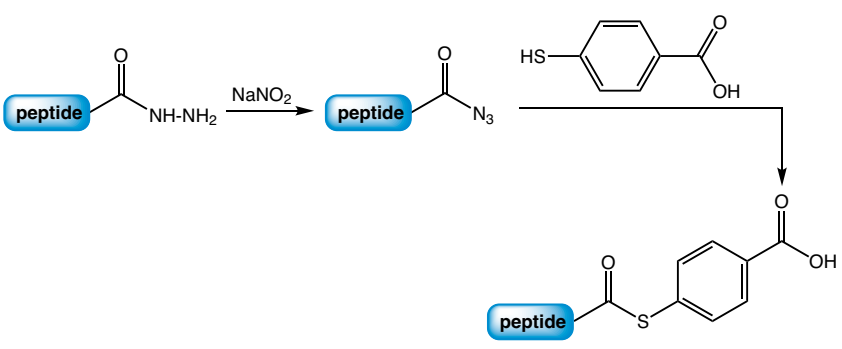


Fig. 8: Synthesizing peptide thioesters utilizing hydrazone resin via oxidation.

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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.

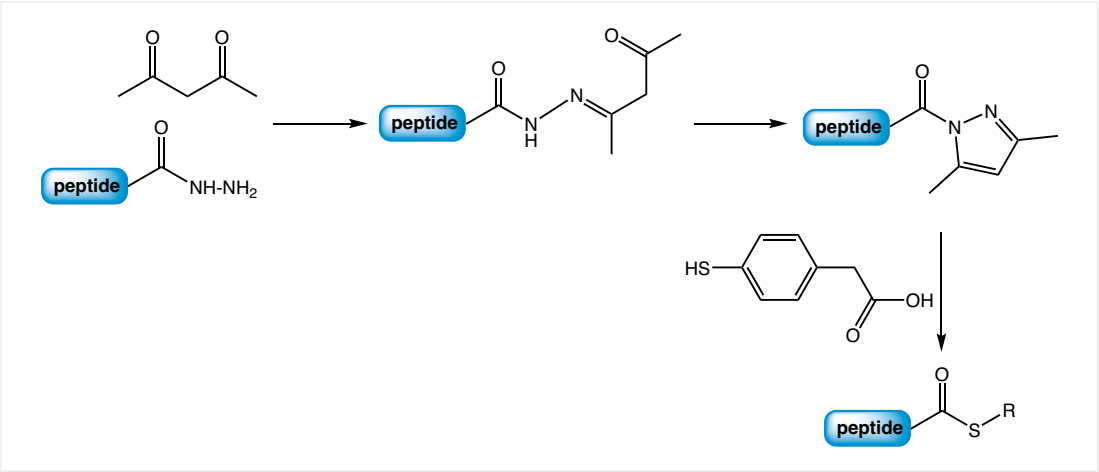

Fig. 9: General route for synthesizing peptide thioesters utilizing hydrazone resin.

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.

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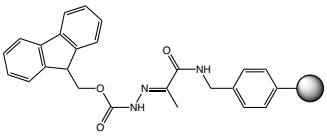
PYV1000 Fmoc-NHN=Pyv Resin

Fmoc-hydrazono-pyruvyl-aminomethylpolystyrene resin

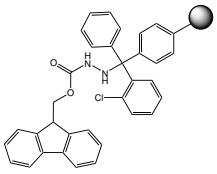
Mesh Size	100-200 mesh
Loading	> 0.3 mmol/g
DVB	1% DVB



BR-5279 Fmoc-NHNH-2CT Resin

Fmoc-hydrazine-2-chlorotrityl resin

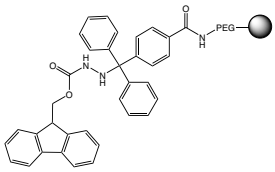
Mesh Size	100-200 mesh
Loading	0,4-1,4 mmol/g
DVB	1% DVB



BR-5280 Fmoc-NHNH-Trt-PEG Resin

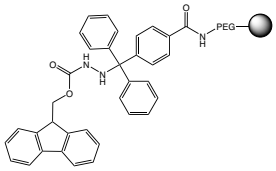
Fmoc-hydrazine-trityl polyethyleneglycol resin

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



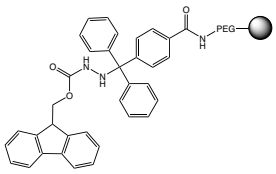
PEG8260 Fmoc-NHNH-Trt-PEG Resin HL

Fmoc-hydrazine-trityl polyethyleneglycol resin



PEG8265 Fmoc-NHNH-Trt-PEG Resin XV

Fmoc-hydrazine-trityl polyethyleneglycol resin



PYV1100 Fmoc-L-Ala-NHN=Pyv Resin

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

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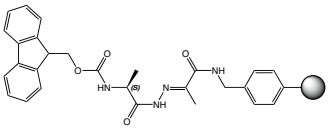
DVB	1% DVB



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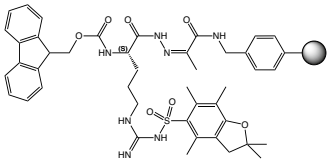
Product details

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

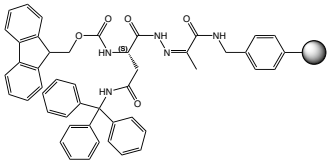
Fmoc-*N*'-2,2,4,6,7-pentamethyldihydrobenzo-furan-5-sulfonyl-L-arginyl-hydrazono-pyruvyl-amino-methylpolystyrene resin



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

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

Fmoc-N-beta-trityl-L-asparaginyl-hydrazono-pyru-vyl-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

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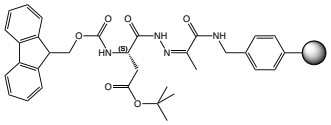

Mesh Size	100-200 mesh
Loading	> 0.3 mmol/g
DVB	1% DVB

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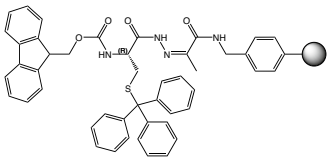

Mesh Size	100-200 mesh
Loading	> 0.3 mmol/g
DVB	1% DVB

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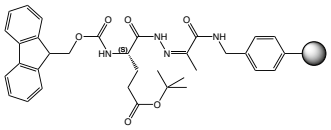
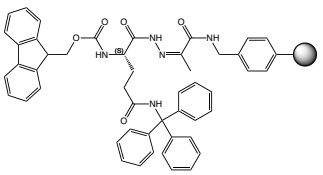


Mesh Size	100-200 mesh
Loading	> 0.3 mmol/g
DVB	1% DVB

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

Fmoc-N-gamma-trityl-L-glutaminyl-hydrazono-pyru-vyl-aminomethylpolystyrene resin



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

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Fmoc-glycyl-hydrazono-pyruvyl-aminomethylpolystyrene resin

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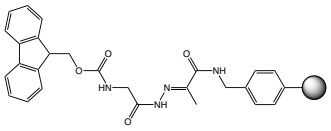
Loading	> 0.3 mmol/g
DVB	1% DVB



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

Fmoc-N-trityl-L-histidyl-hydrazono-pyruvyl-aminomethylpolystyrene resin

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Loading	> 0.3 mmol/g
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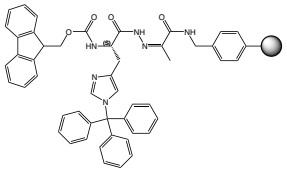

PYV1190 Fmoc-L-Ile-NHN=Pyv Resin

Fmoc-L-isoleucyl-hydrazono-pyruvyl-aminomethylpolystyrene resin

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Loading	> 0.3 mmol/g
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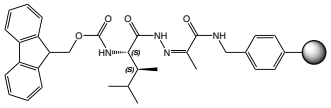

PYV1200 Fmoc-L-Leu-NHN=Pyv Resin

Fmoc-L-leucyl-hydrazono-pyruvyl-aminomethylpolystyrene resin

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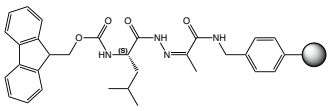
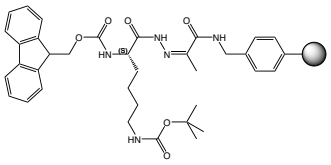
Loading	> 0.3 mmol/g
DVB	1% DVB



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

Fmoc-N-epsilon-t-butyloxycarbonyl-L-lysyl-hydrazono-pyruvyl-aminomethylpolystyrene resin

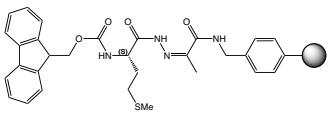
Mesh Size	100-200 mesh
Loading	> 0.3 mmol/g
DVB	1% DVB



PYV1220 Fmoc-L-Met-NHN=Pyv Resin

Fmoc-L-methionyl-hydrazono-pyruvyl-aminomethylpolystyrene resin

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



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Product details

PYV1230 Fmoc-L-Phe-NHN=Pyv Resin

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

Mesh Size	100-200 mesh
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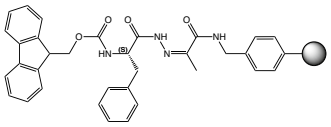
DVB	1% DVB



PYV1240 Fmoc-L-Pro-NHN=Pyv Resin

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

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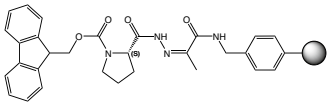
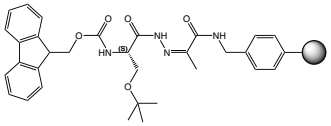
Loading	> 0.3 mmol/g
DVB	1% DVB



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

Fmoc-O-*t*-butyl-L-seryl-hydrazono-pyruvyl-amino-methylpolystyrene resin

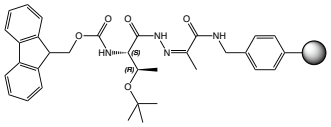
Mesh Size	100-200 mesh
Loading	> 0.3 mmol/g
DVB	1% DVB



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

Fmoc-O-*t*-butyl-L-threonyl-hydrazono-pyruvyl-amino-methylpolystyrene resin

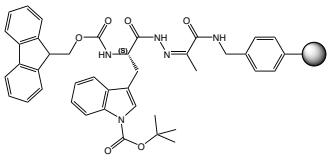
Mesh Size	100-200 mesh
Loading	> 0.3 mmol/g
DVB	1% DVB



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

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

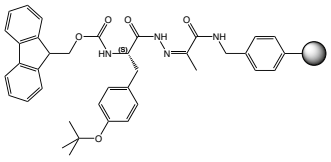
Mesh Size	100-200 mesh
Loading	> 0.3 mmol/g
DVB	1% DVB



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

Fmoc-O-*t*-butyl-L-tyrosyl-hydrazono-pyruvyl-amino-methylpolystyrene resin

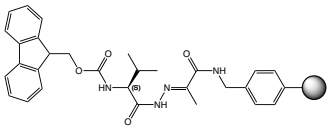
Mesh Size	100-200 mesh
Loading	> 0.3 mmol/g
DVB	1% DVB



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



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3. Building Blocks for Ligation

3.1. Cysteine Building Blocks for Ligation

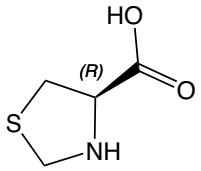
1,3-Thiazolidine-4-carboxylic acid (Thz) is a protected cysteine. It can be converted into free cysteine by reaction with aqueous 0.8 M methoxylamine ($MeONH_2$).

Product details

HAA1132 H-L-Thz-OH

(R)-Thiazolidine-4-carboxylic acid

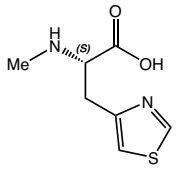
CAS-No.	34592-47-7
Formula	$C_4H_7NO_2S$
Mol. weight	133,16 g/mol



HAA3840 H-L-MeAla(4-Thz)-OH

N-alpha-Methyl-beta-(4-thiazolyl)-L-alanine

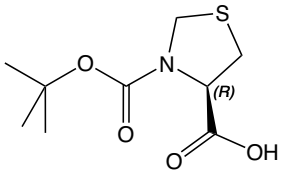
CAS-No.	2131118-50-6
Formula	$C_7H_{10}N_2O_2S$
Mol. weight	186,23 g/mol



BAA1135 Boc-L-Thz-OH

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

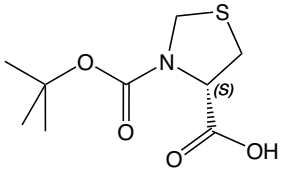
CAS-No.	51077-16-8
Formula	$C_9H_{15}NO_4S$
Mol. weight	233,29 g/mol



BAA1186 Boc-D-Thz-OH

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

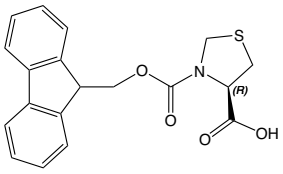
CAS-No.	63091-82-7
Formula	$C_9H_{15}NO_4S$
Mol. weight	233,29 g/mol



FAA1427 Fmoc-L-Thz-OH

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

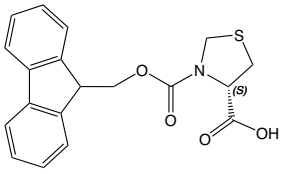
CAS-No.	133054-21-4
Formula	$C_{19}H_{17}NO_4S$
Mol. weight	355,42 g/mol



FAA1495 Fmoc-D-Thz-OH

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

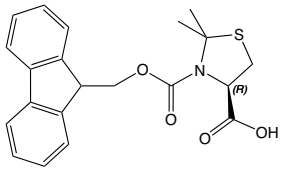
CAS-No.	198545-89-0
Formula	$C_{19}H_{17}NO_4S$
Mol. weight	355,42 g/mol



FAA1437 Fmoc-L-Thz(Me_2)-OH

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

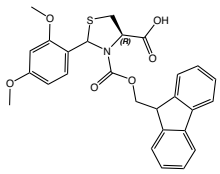
CAS-No.	873842-06-9
Formula	$C_{21}H_{21}NO_4S$
Mol. weight	383,46 g/mol



FAA9200 Fmoc-L-Thz(Dmp)-OH

(4R)-3-(((9H-fluoren-9-yl)methoxy)carbonyl)-2-(2,4-dimethoxyphenyl)thiazolidine-4-carboxylic acid

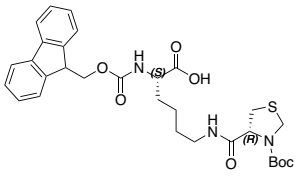
CAS-No.	2648642-22-0
Formula	$C_{27}H_{25}NO_6S$
Mol. weight	491,56 g/mol



FAA9320 Fmoc-L-Lys(Boc-Thz)-OH

N2-(((9H-fluoren-9-yl)methoxy)carbonyl)-N6-((R)-3-(*tert*-butoxycarbonyl)thiazolidine-4-carbonyl)-L-lysine

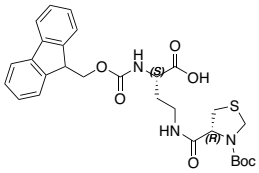
Formula	$C_{30}H_{37}N_3O_7S$
Mol. weight	583,70 g/mol



FAA9330 Fmoc-L-Dab(Boc-Thz)-OH

(S)-2-((((9H-fluoren-9-yl)methoxy)carbonyl)amino)-4-((R)-3-(*tert*-butoxycarbonyl)thiazolidine-4-carboxamido)butanoic acid

CAS-No.	2968514-54-5
Formula	$C_{28}H_{33}N_3O_7S$
Mol. weight	555,65 g/mol



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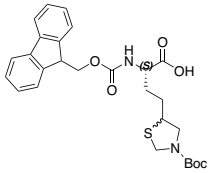
Product details

FAA9340 Fmoc-L-Lys(4-Thz, Boc)-OH

(2S)-2-((((9H-fluoren-9-yl)methoxy)carbonyl) amino)-4-(3-(*tert*-butoxycarbonyl)thiazolidin-5-yl) butanoic acid

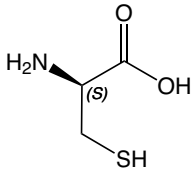
CAS-No.	1240666-28-7
Formula	$C_{27}H_{32}N_2O_6S$
Mol. weight	512,62 g/mol



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

D-Cysteine hydrochloride monohydrate

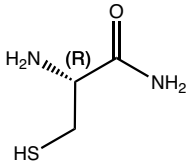
CAS-No.	32443-99-5
Formula	$C_3H_7NO_2S*HCl*H_2O$
Mol. weight	121,2*36,45*18,01 g/mol



HAA3530 H-L-Cys-NH_2*HCl

L-Cysteine amide hydrochloride

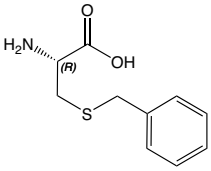
CAS-No.	16359-98-1
Formula	$C_3H_8N_2OS*HCl$
Mol. weight	120,17*36,45 g/mol



HAA1574 H-L-Cys(Bzl)-OH

S-Benzyl-L-cysteine

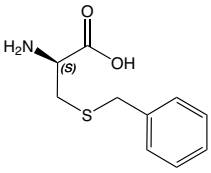
CAS-No.	3054-01-1
Formula	$C_{10}H_{13}NO_2S$
Mol. weight	211,29 g/mol



HAA6110 H-D-Cys(Bzl)-OH

S-Benzyl-D-cysteine

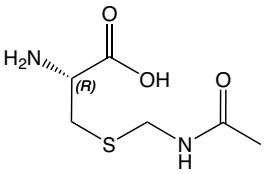
CAS-No.	23032-53-3
Formula	$C_{10}H_{13}NO_2S$
Mol. weight	211,29 g/mol



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

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

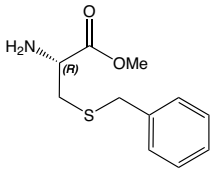
CAS-No.	28798-28-9
Formula	$C_6H_{12}N_2O_3S*HCl$
Mol. weight	192,24*36,45 g/mol



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

S-Benzyl-L-cysteine methyl ester hydrochloride

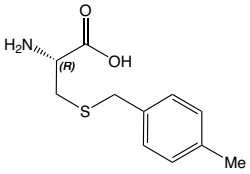
CAS-No.	16741-80-3
Formula	$C_{11}H_{15}NO_2S*HCl$
Mol. weight	225,31*36,45 g/mol



HAA6090 H-L-Cys(MBzl)-OH

S-(4-Methylbenzyl)-L-cysteine

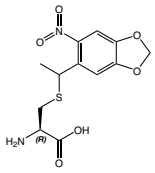
CAS-No.	42294-52-0
Formula	$C_{11}H_{15}NO_2S$
Mol. weight	225,3 g/mol



HAA9270 H-L-Cys(MDNPE)-OH

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

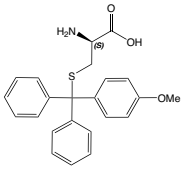
CAS-No.	1551078-43-3
Formula	$C_{12}H_{14}N_2O_6S$
Mol. weight	314,31 g/mol



HAA3500 H-D-Cys(Mmt)-OH

S-*p*-methoxytrityl-D-cysteine

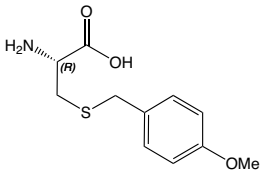
CAS-No.	926935-33-3
Formula	$C_{23}H_{23}NO_3S$
Mol. weight	393,5 g/mol



HAA6100 H-L-Cys(Mob)-OH

S-(4-Methoxybenzyl)-L-cysteine

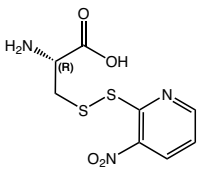
CAS-No.	2544-31-2
Formula	$C_{11}H_{15}NO_3S$
Mol. weight	241,3 g/mol



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



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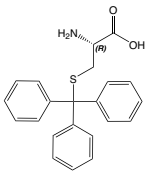
Product details

HAA6160 H-L-Cys(Trt)-OH

S-Trityl-L-cysteine

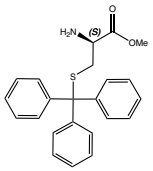
CAS-No.	2799-07-7
Formula	$C_{22}H_{21}NO_2S$
Mol. weight	363,48 g/mol



HAA3520 H-D-Cys(Trt)-OMe*HCl

S-trityl-D-cysteine methyl ester hydrochloride

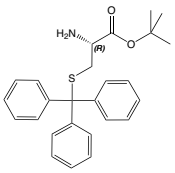
CAS-No.	1020369-32-7
Formula	$C_{23}H_{23}NO_2S*HCl$
Mol. weight	377,50*36,45 g/mol



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

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

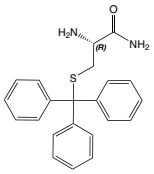
CAS-No.	158009-03-1
Formula	$C_{26}H_{29}NO_2S*HCl$
Mol. weight	419,58*36,45 g/mol



HAA1560 H-L-Cys(Trt)-NH_2

S-Trityl-L-cysteine amide

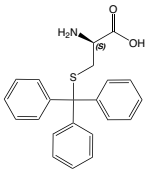
CAS-No.	166737-85-5
Formula	$C_{22}H_{22}N_2OS$
Mol. weight	362,49 g/mol



HAA6120 H-D-Cys(Trt)-OH

S-Trityl-D-cysteine

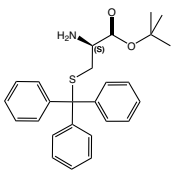
CAS-No.	25840-82-8
Formula	$C_{22}H_{21}NO_2S$
Mol. weight	363,48 g/mol



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

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

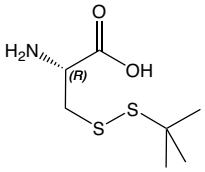
CAS-No.	439089-10-8
Formula	$C_{26}H_{29}NO_2S*HCl$
Mol. weight	419,58*36,45 g/mol



HAA6140 H-L-Cys(*St*Bu)-OH

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

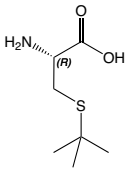
CAS-No.	30044-51-0
Formula	$C_7H_{15}NO_2S_2$
Mol. weight	209,32 g/mol



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

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

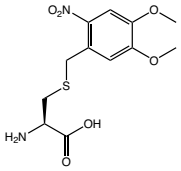
CAS-No.	2481-09-6
Formula	$C_7H_{15}NO_2S$*HCl
Mol. weight	177,26*36,45 g/mol



HAA9320 H-L-Cys(*o*Nv)-OH

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

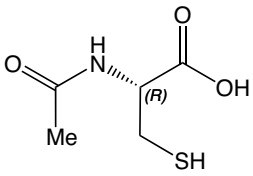
CAS-No.	214633-68-8
Formula	$C_{12}H_{16}N_2O_6S$
Mol. weight	316,33 g/mol



AAA1300 Ac-L-Cys-OH

N-alpha-Acetyl-L-cysteine

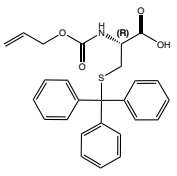
CAS-No.	616-91-1
Formula	$C_5H_9NO_3S$
Mol. weight	163,19 g/mol



AAA2015 Aloc-L-Cys(Trt)-OH

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

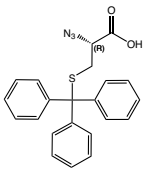
CAS-No.	96865-72-4
Formula	$C_{26}H_{25}NO_4S$
Mol. weight	447,55 g/mol



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



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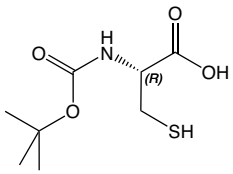
Product details

BAA1083 Boc-L-Cys-OH

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

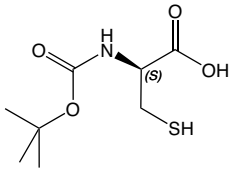
CAS-No.	20887-95-0
Formula	$C_8H_{15}NO_4S$
Mol. weight	221,27 g/mol



BAA1170 Boc-D-Cys-OH

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

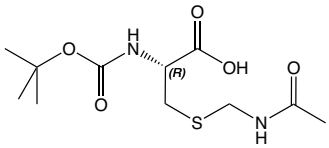
CAS-No.	149270-12-2
Formula	$C_8H_{15}NO_4S$
Mol. weight	221,27 g/mol



BAA1078 Boc-L-Cys(Acm)-OH

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

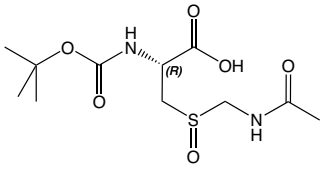
CAS-No.	19746-37-3
Formula	$C_{11}H_{20}N_2O_5S$
Mol. weight	292,36 g/mol



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

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

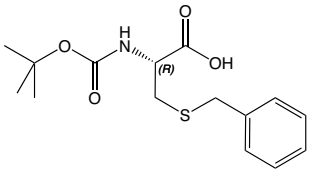
CAS-No.	75893-04-8
Formula	$C_{11}H_{20}N_2O_6S$
Mol. weight	308,35 g/mol



BAA1079 Boc-L-Cys(Bzl)-OH

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

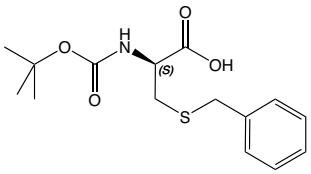
CAS-No.	5068-28-0
Formula	$C_{15}H_{21}NO_4S$
Mol. weight	311,38 g/mol



BAA5410 Boc-D-Cys(Bzl)-OH

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

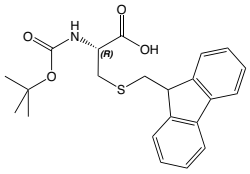
CAS-No.	102830-49-9
Formula	$C_{15}H_{21}NO_4S$
Mol. weight	311,38 g/mol



BAA5510 Boc-L-Cys(Fm)-OH

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

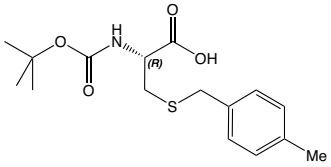
CAS-No.	84888-35-7
Formula	$C_{22}H_{25}NO_4S$
Mol. weight	399,51 g/mol



BAA1080 Boc-L-Cys(MBzl)-OH

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

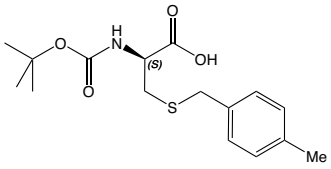
CAS-No.	61925-77-7
Formula	$C_{16}H_{23}NO_4S$
Mol. weight	325,43 g/mol



BAA5420 Boc-D-Cys(MBzl)-OH

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

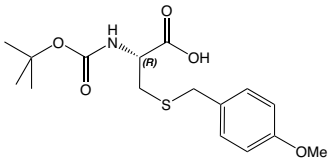
CAS-No.	61925-78-8
Formula	$C_{16}H_{23}NO_4S$
Mol. weight	325,43 g/mol



BAA1081 Boc-L-Cys(Mob)-OH

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

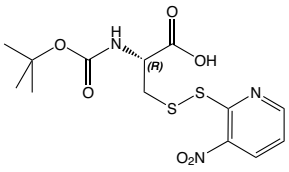
CAS-No.	18942-46-6
Formula	$C_{16}H_{23}NO_5S$
Mol. weight	341,43 g/mol



BAA1860 Boc-L-Cys(Npys)-OH

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

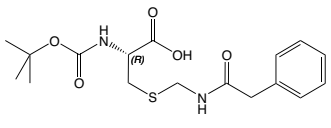
CAS-No.	76880-29-0
Formula	$C_{13}H_{17}N_3O_6S_2$
Mol. weight	375,42 g/mol



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



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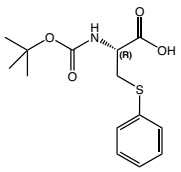
Product details

BAA3140 Boc-L-Cys(Ph)-OH

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

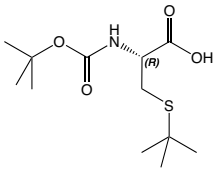
CAS-No.	163705-28-0
Formula	$C_{14}H_{19}NO_4S$
Mol. weight	297,37 g/mol



BAA1082 Boc-L-Cys(tBu)-OH

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

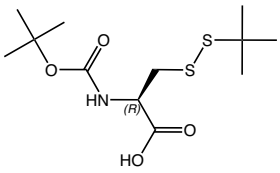
CAS-No.	56976-06-8
Formula	$C_{12}H_{23}NO_4S$
Mol. weight	277,37 g/mol



BAA6415 Boc-L-Cys(S*t*Bu)-OH

N-(*tert*-butoxycarbonyl)-S-(*tert*-butylthio)-L-cysteine

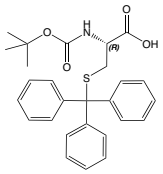
CAS-No.	30044-61-2
Formula	$C_{12}H_{23}NO_4S_2$
Mol. weight	309,44 g/mol



BAA1084 Boc-L-Cys(Trt)-OH

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

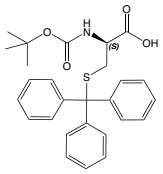
CAS-No.	21947-98-8
Formula	$C_{27}H_{29}NO_4S$
Mol. weight	463,59 g/mol



BAA5000 Boc-D-Cys(Trt)-OH

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

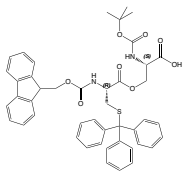
CAS-No.	87494-13-1
Formula	$C_{27}H_{29}NO_4S$
Mol. weight	463,59 g/mol



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

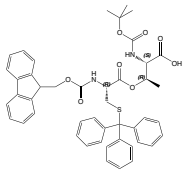
CAS-No.	944283-13-0
Formula	$C_{45}H_{44}N_2O_8S$
Mol. weight	772,9



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

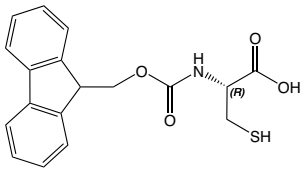
CAS-No.	944283-30-1
Formula	$C_{46}H_{46}N_2O_8S$
Mol. weight	786,93 g/mol



FAA1362 Fmoc-L-Cys-OH*H_2O

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

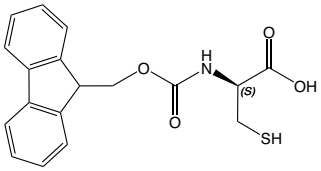
CAS-No.	135248-89-4
Formula	$C_{18}H_{17}NO_4S*H_2O$
Mol. weight	343,40*18,01 g/mol



FAA1470 Fmoc-D-Cys-OH*H_2O

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

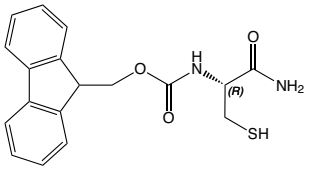
CAS-No.	157355-80-1
Formula	$C_{18}H_{17}NO_4S*H_2O$
Mol. weight	343,4*18,01 g/mol



FAA1980 Fmoc-L-Cys-NH_2

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

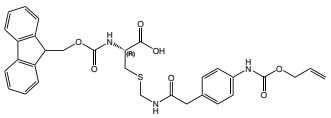
CAS-No.	623177-62-8
Formula	$C_{18}H_{18}N_2O_3S$
Mol. weight	342,41 g/mol



FAA5150 Fmoc-L-Cys(Aapam)-OH

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

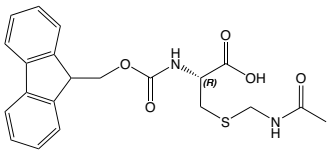
CAS-No.	1946783-89-6
Formula	$C_{31}H_{31}N_3O_7S$
Mol. weight	589,66 g/mol



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



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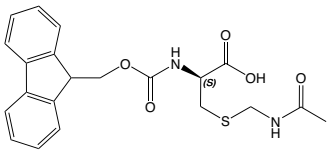
FAA6230 Fmoc-D-Cys(Acm)-OH

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

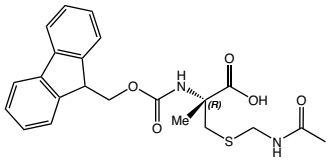
CAS-No.	168300-88-7
Formula	$C_{21}H_{22}N_2O_5S$
Mol. weight	414,48 g/mol



FAA6720 Fmoc-L-MeCys(Acm)-OH

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

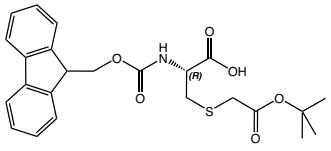
CAS-No.	481642-19-7
Formula	$C_{22}H_{24}N_2O_5S$
Mol. weight	428,5 /mol



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

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

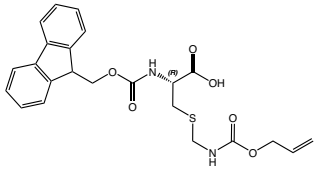
CAS-No.	269730-62-3 net
Formula	$C_{24}H_{27}NO_6S*C_{12}H_{23}N$
Mol. weight	457,54*181,32 g/mol



FAA7610 Fmoc-L-Cys(Allocam)-OH

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

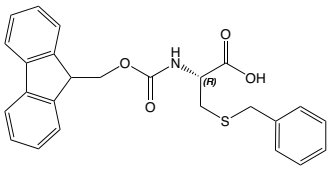
CAS-No.	232953-09-2
Formula	$C_{23}H_{24}N_2O_6S$
Mol. weight	456,51 g/mol



FAA6270 Fmoc-L-Cys(Bzl)-OH

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

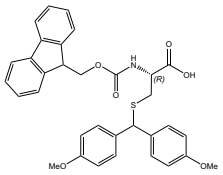
CAS-No.	53298-33-2
Formula	$C_{25}H_{23}NO_4S$
Mol. weight	433,52 g/mol



FAA6940 Fmoc-L-Cys(Ddm)-OH

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

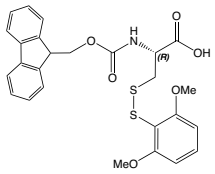
CAS-No.	1403825-56-8
Formula	$C_{33}H_{31}NO_6S$
Mol. weight	569,67 g/mol



FAA3180 Fmoc-L-Cys(S-DMP)-OH

N-alpha-(9-Fluorenylmethyloxycarbonyl)-S-(2,6-dimethoxythiophenol)-L-cysteine

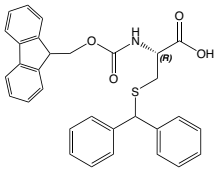
CAS-No.	1403834-73-0
Formula	$C_{26}H_{25}NO_6S_2$
Mol. weight	511,61 g/mol



FAA3190 Fmoc-L-Cys(Dpm)-OH

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

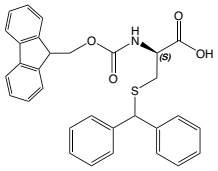
CAS-No.	247595-29-5
Formula	$C_{31}H_{27}NO_4S$
Mol. weight	509,62 g/mol



FAA5650 Fmoc-D-Cys(Dpm)-OH

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

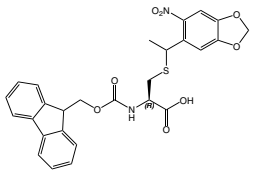
CAS-No.	2389078-16-2
Formula	$C_{31}H_{27}NO_4S$
Mol. weight	509,62 g/mol



FAA7945 Fmoc-L-Cys(MDNPE)-OH

N-(((9H-fluoren-9-yl)methoxy)carbonyl)-S-(1-(6-nitrobenzo[d][1,3]dioxol-5-yl)ethyl)-L-cysteine

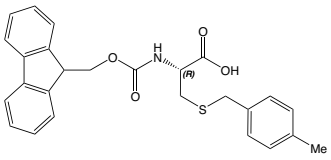
Formula	$C_{27}H_{24}N_2O_8S$
Mol. weight	536,56 g/mol



FAA1714 Fmoc-L-Cys(MBzl)-OH

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

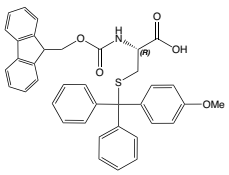
CAS-No.	136050-67-4
Formula	$C_{26}H_{25}NO_4S$
Mol. weight	447,53 g/mol



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



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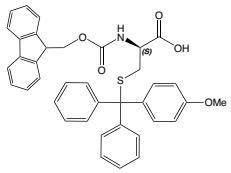
FAA1614 Fmoc-D-Cys(Mmt)-OH

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

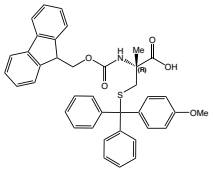
CAS-No.	1198791-73-9
Formula	$C_{38}H_{33}NO_5S$
Mol. weight	615,74 g/mol



FAA4845 Fmoc-alpha-Me-L-Cys(Mmt)-OH

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

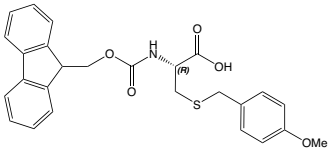
CAS-No.	1198791-74-0
Formula	$C_{39}H_{35}NO_5S$
Mol. weight	629,76 g/mol



FAA1715 Fmoc-L-Cys(Mob)-OH

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

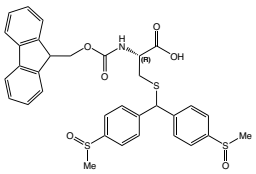
CAS-No.	141892-41-3
Formula	$C_{26}H_{25}NO_5S$
Mol. weight	463,55 g/mol



FAA4155 Fmoc-L-Cys(Msbh)-OH

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

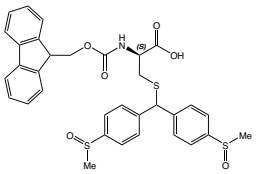
CAS-No.	1584646-97-8
Formula	$C_{33}H_{31}NO_6S_3$
Mol. weight	633,80 g/mol



FAA8150 Fmoc-D-Cys(Msbh)-OH

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

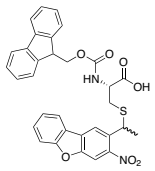
Formula	$C_{33}H_{31}NO_6S_3$
Mol. weight	633,80 g/mol



FAA8420 Fmoc-L-Cys(NDBF)-OH

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

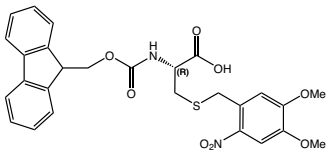
CAS-No.	1895883-28-9
Formula	$C_{32}H_{26}N_2O_7S$
Mol. weight	582,62 g/mol



FAA3970 Fmoc-L-Cys(oNv)-OH

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

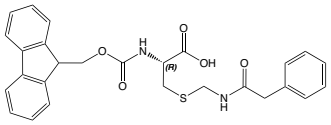
CAS-No.	214633-71-3
Formula	$C_{27}H_{26}N_2O_8S$
Mol. weight	538,57 g/mol



FAA6910 Fmoc-L-Cys(Phacm)-OH

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

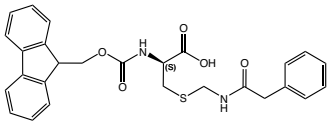
CAS-No.	159680-21-4
Formula	$C_{27}H_{26}N_2O_5S$
Mol. weight	490,57 g/mol



FAA3710 Fmoc-D-Cys(Phacm)-OH

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

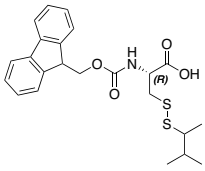
CAS-No.	1565818-55-4
Formula	$C_{27}H_{26}N_2O_5S$
Mol. weight	490,57 g/mol



FAA8495 Fmoc-L-Cys(SIT)-OH

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

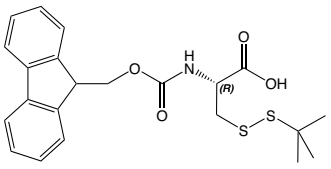
CAS-No.	2545642-31-5
Formula	$C_{23}H_{27}NO_4S_2$
Mol. weight	445,59 g/mol



FAA1575 Fmoc-L-Cys(StBu)-OH

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

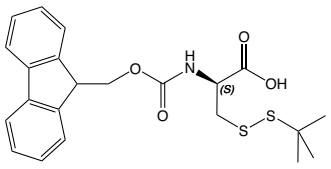
CAS-No.	73724-43-3
Formula	$C_{22}H_{25}NO_4S_2$
Mol. weight	431,57 g/mol



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



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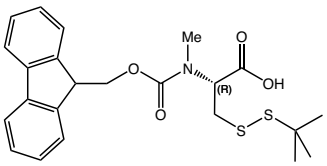
FAA3340 Fmoc-L-MeCys(S-*t*Bu)-OH

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

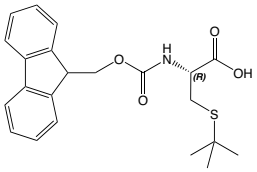
CAS-No.	1013096-03-1
Formula	$C_{23}H_{27}NO_4S_2$
Mol. weight	445,59 g/mol



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

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

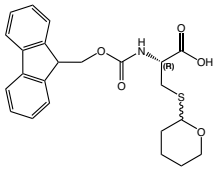
CAS-No.	67436-13-9
Formula	$C_{22}H_{25}NO_4S$
Mol. weight	399,51 g/mol



FAA4160 Fmoc-L-Cys(Thp)-OH

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

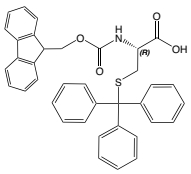
CAS-No.	1673576-83-4
Formula	$C_{23}H_{25}NO_5S$
Mol. weight	427,15 g/mol



FAA1040 Fmoc-L-Cys(Trt)-OH

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

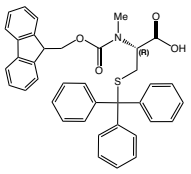
CAS-No.	103213-32-7
Formula	$C_{37}H_{31}NO_4S$
Mol. weight	585,71 g/mol



FAA3570 Fmoc-L-MeCys(Trt)-OH

N-alpha-(9-Fluorenylmethyloxycarbonyl)-N-alpha-methyl-S-trityl-L-cysteine

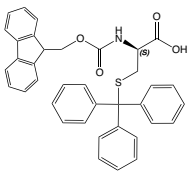
CAS-No.	944797-51-7
Formula	$C_{38}H_{33}NO_4S$
Mol. weight	599,74 g/mol



FAA1035 Fmoc-D-Cys(Trt)-OH

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

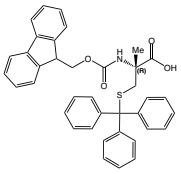
CAS-No.	167015-11-4
Formula	$C_{37}H_{31}NO_4S$
Mol. weight	585,71 g/mol



FAA4840 Fmoc-alpha-Me-L-Cys(Trt)-OH

N-alpha-(9-Fluorenylmethyloxycarbonyl)-alpha-methyl-S-trityl-L-cysteine

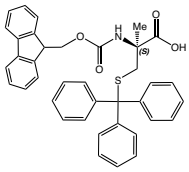
CAS-No.	725728-43-8
Formula	$C_{38}H_{33}NO_4S$
Mol. weight	599,74 g/mol



FAA4850 Fmoc-alpha-Me-D-Cys(Trt)-OH

N-alpha-(9-Fluorenylmethyloxycarbonyl)-alpha-methyl-S-trityl-D-cysteine

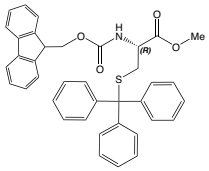
CAS-No.	725728-37-0
Formula	$C_{38}H_{33}NO_4S$
Mol. weight	599,74 g/mol



FAA5670 Fmoc-L-Cys(Trt)-OMe

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

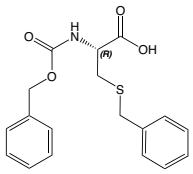
CAS-No.	245088-56-6
Formula	$C_{38}H_{33}NO_4S$
Mol. weight	599,74 g/mol



ZAA1161 Z-L-Cys(Bzl)-OH

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

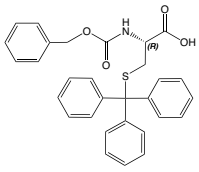
CAS-No.	3257-18-9
Formula	$C_{18}H_{19}NO_4S$
Mol. weight	345,42 g/mol



ZAA1310 Z-L-Cys(Trt)-OH

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

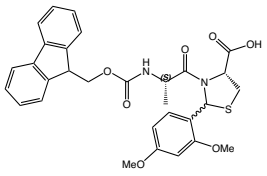
CAS-No.	26311-04-6
Formula	$C_{30}H_{27}NO_4S$
Mol. weight	497,60 g/mol



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



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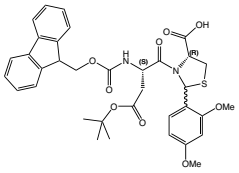
PSI1470 Fmoc-L-Asp(*t*Bu)-L-Cys[PSI(Dmp,H)pro]-OH

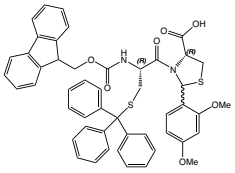
(S)-3-(N-(9-Fluorenylmethyloxycarbonyl)-beta-*t*-butyl-L-aspartyl)-2-(2,4-dimethoxphenyl)thiazolidine-4-carboxylic acid



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

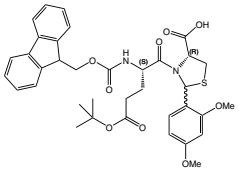
(R)-3-(N-(9-Fluorenylmethyloxycarbonyl)-S-trityl-L-cysteinyl)-2-(2,4-dimethoxphenyl)thiazolidine-4-carboxylic acid



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

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

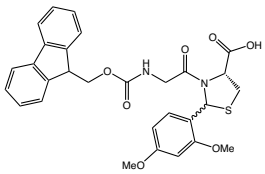
(S)-3-(N-(9-Fluorenylmethyloxycarbonyl)-gamma-*t*-butyl-L-glutamyl)-2-(2,4-dimethoxphenyl)thiazolidine-4-carboxylic acid



CAS-No.	2565804-44-4
Formula	$C_{36}H_{40}N_2O_9S$
Mol. weight	676,78 g/mol

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

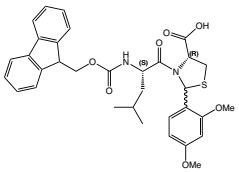
(S)-3-(N-(9-Fluorenylmethyloxycarbonyl)-glycyl)-2-(2,4-dimethoxphenyl)thiazolidine-4-carboxylic acid



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

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

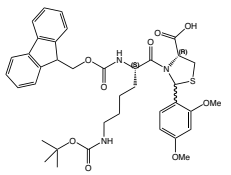
(S)-3-(N-(9-Fluorenylmethyloxycarbonyl)-L-leucyl)-2-(2,4-dimethoxphenyl)thiazolidine-4-carboxylic acid



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

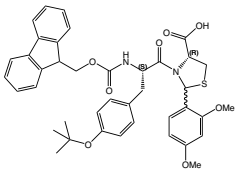
(S)-3-(N-(9-Fluorenylmethyloxycarbonyl)-N-epsilon-*t*-butyloxycarbonyl-L-lysyl)-2-(2,4-dimethoxphenyl) thiazolidine-4-carboxylic acid



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

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

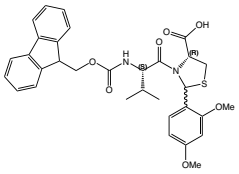
(S)-3-(N-(9-Fluorenylmethyloxycarbonyl)-O-*t*-butyl-L-thyrosyl)-2-(2,4-dimethoxphenyl)thiazolidine-4-carboxylic acid



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

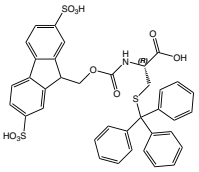
(S)-3-(N-(9-Fluorenylmethyloxycarbonyl)-L-valyl)-2-(2,4-dimethoxphenyl)thiazolidine-4-carboxylic acid



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
Formula	$C_{37}H_{29}K_2NO_{10}S_3$
Mol. weight	822,01 g/mol

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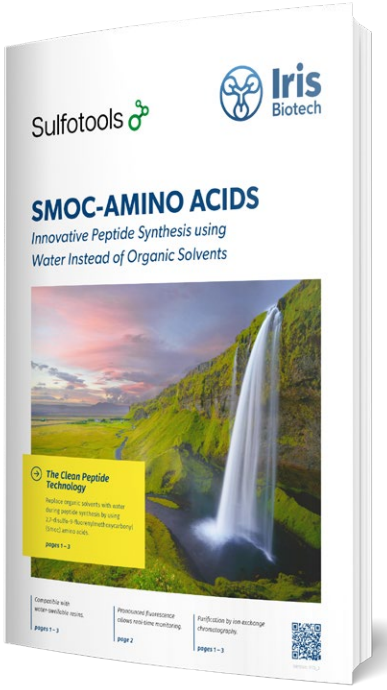

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3.2. Ligation at the Position of Glycine

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.

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.

Reference:

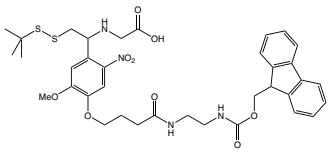
→ *A PEGylated photocleavable auxiliary mediates the sequential enzymatic glycosylation and native chemical ligation of peptides; C. Bello, S. Wang, L. Meng, K. W. Moremen, C. F. Becker;* ***Angew Chem Int Ed Engl*** *2015;* ***54****: 7711-7715.* https://doi.org/10.1002/anie.201501517

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



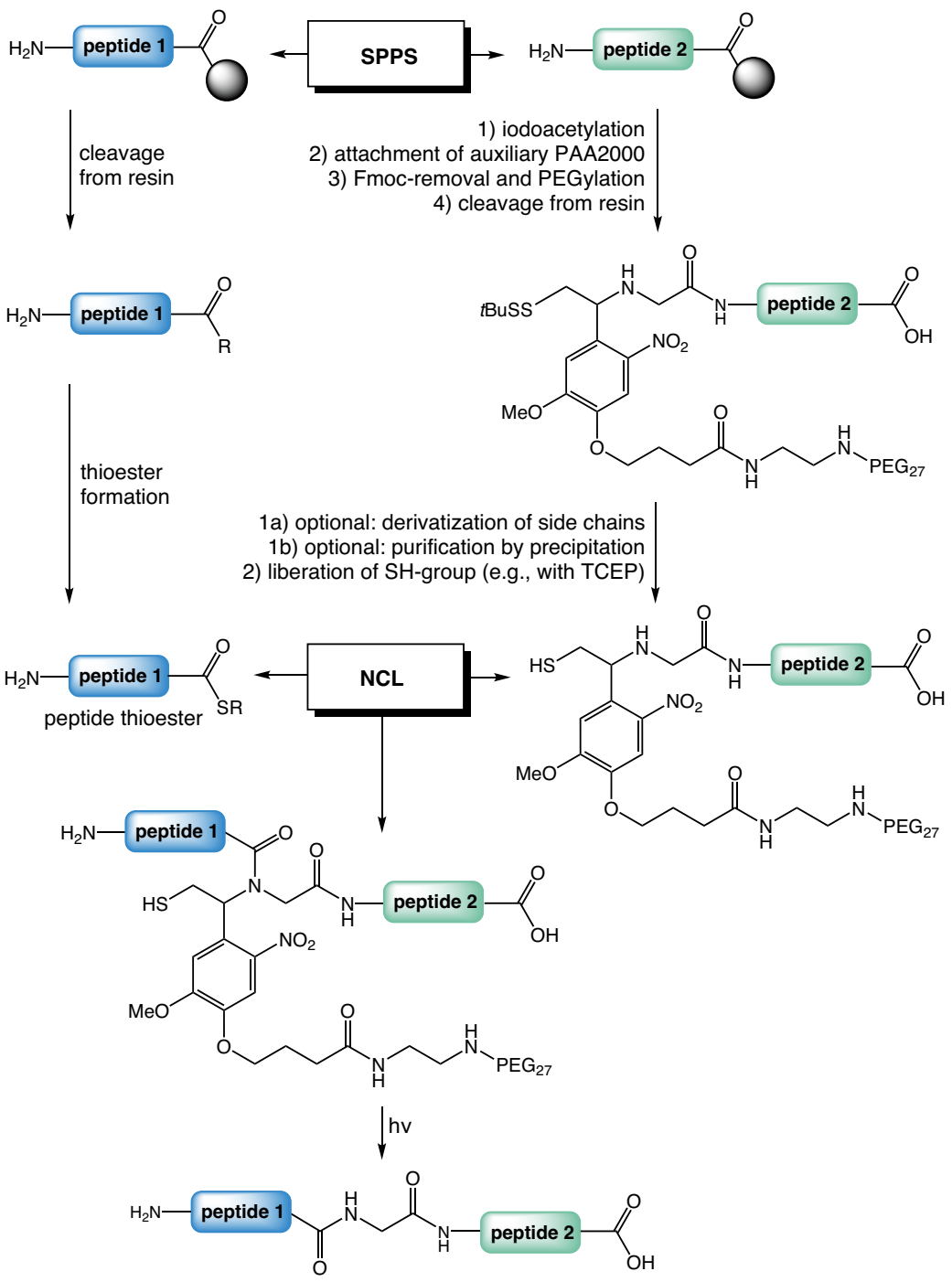


Fig. 10: Photo-cleavable glycine auxiliary building block enabling native chemical ligation at the position of glycine. It has additional capabilities to be conjugated with a solubilizing tag, e.g., PEG, in order to improve the solubility of hydrophobic peptide sequences.

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

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*.

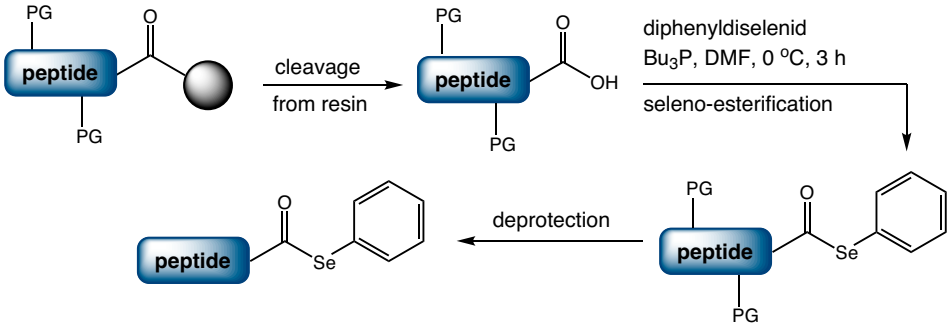


Fig. 11: Formation of selenoesters.

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:

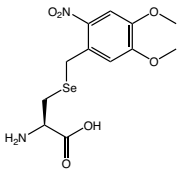
→ *Accelerated Protein Synthesis via One-Pot Ligation-Deselenization Chemistry; N. J. Mitchell, J. Sayers, S. S. Kulkarni, D. Clayton, A. M. Goldys, J.Ripoll-Rozada, P. J. Barbosa Pereira, B. Chan, L. Radom, R. J. Payne;* ***Chem*** *2017;* ***2****: 703-715.* https://doi.org/10.1016/j.chempr.2017.04.003

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.

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

Dimethoxynitrobenzyl selenocysteine TFA salt

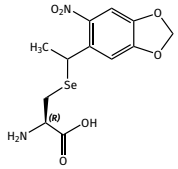
CAS-No.	1644398-13-9
Formula	$C_{12}H_{16}N_2O_6Se*CF_3COOH$
Mol. weight	363,24*114,02 g/mol



HAA9360 H-L-Sec(MDNPE)-OH

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

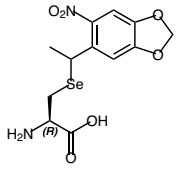
CAS-No.	2235373-47-2
Formula	$C_{12}H_{14}N_2O_6Se$
Mol. weight	361,21 g/mol



HAA9230 H-L-Sec(MDNPE)*TFA

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

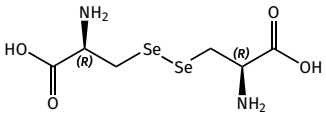
CAS-No.	2235373-48-3
Formula	$C_{12}H_{14}N_2O_6Se*CF_3CO_2H$
Mol. weight	361,22*114,02 g/mol



HAA9350 (H-L-Sec-OH)2

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

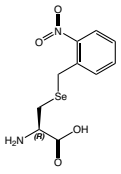
CAS-No.	29621-88-3
Formula	$C_6H_{12}N_2O_4Se_2$
Mol. weight	334,11 g/mol



HAA9465 H-L-Sec(oNB)-OH*HCl

(R)-2-amino-3-((2-nitrobenzyl)selanyl)propanoic acid

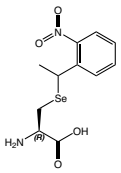
CAS-No.	324582-23-2 net
Formula	$C_{10}H_{12}N_2O_4Se*HCl$
Mol. weight	303,18*36,46 g/mol



HAA9475 H-L-Sec(NPE)-OH*HCl

(2R)-2-amino-3-((1-(2-nitrophenyl)ethyl)selanyl)propanoic acid

Formula	$C_{11}H_{14}N_2O_4Se*HCl$
Mol. weight	317,02*36,46 g/mol



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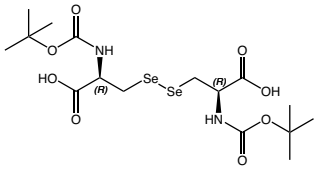
Product details

BAA3680 (Boc-L-Sec)$_2$

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

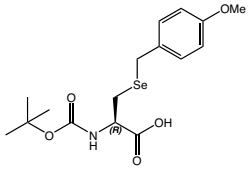
CAS-No.	877754-71-7
Formula	$C_{16}H_{28}N_2O_8Se_2$
Mol. weight	534,35 g/mol



BAA3760 Boc-L-Sec(Mob)-OH

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

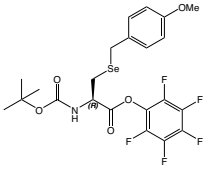
CAS-No.	959415-39-5
Formula	$C_{16}H_{23}NO_5Se$
Mol. weight	388,32 g/mol



BAA4830 Boc-L-Sec(Mob)-OPfp

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

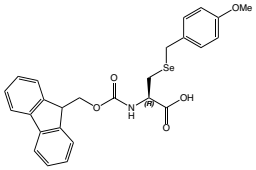
CAS-No.	1257525-48-6
Formula	$C_{22}H_{22}F_5NO_5Se$
Mol. weight	554,38 g/mol



FAA8705 Fmoc-L-Sec(Mob)-OH

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

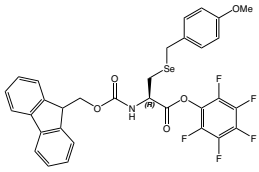
CAS-No.	150308-80-8
Formula	$C_{26}H_{25}NO_5Se$
Mol. weight	510,46 g/mol



FAA8760 Fmoc-L-Sec(Mob)-OPfp

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

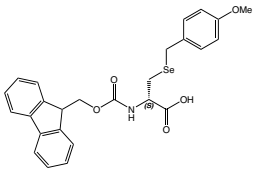
CAS-No.	939431-43-3
Formula	$C_{32}H_{24}F_5NO_5Se$
Mol. weight	676,51 g/mol



FAA8710 Fmoc-D-Sec(Mob)-OH

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

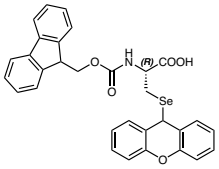
CAS-No.	2987041-11-0
Formula	$C_{26}H_{25}NO_5Se$
Mol. weight	510,46 g/mol



FAA8465 Fmoc-L-Sec(Xan)-OH

Fmoc-Se-xanthyl-L-selenocysteine

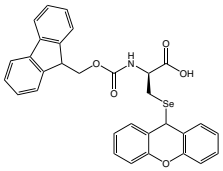
CAS-No.	1639843-35-8
Formula	$C_{31}H_{25}NO_5Se$
Mol. weight	570,49 g/mol



FAA8600 Fmoc-D-Sec(Xan)-OH

Fmoc-Se-xanthyl-D-selenocysteine

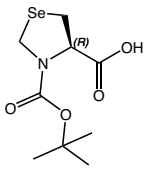
CAS-No.	2988660-46-2
Formula	$C_{31}H_{25}NO_5Se$
Mol. weight	570,49 g/mol



BAA4880 Boc-L-Sez-OH

Boc selenazolidine carboxylic acid

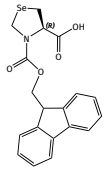
CAS-No.	1841180-44-6
Formula	$C_9H_{15}NO_4Se$
Mol. weight	280,19 g/mol



FAA8860 Fmoc-L-Sez-OH

Fmoc selenazolidine carboxylic acid

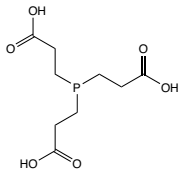
CAS-No.	1985651-74-8
Formula	$C_{19}H_{17}NO_4Se$
Mol. weight	402,31 g/mol



LS-3405 TCEP*HCl

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

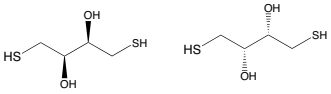
CAS-No.	51805-45-9
Formula	$C_9H_{15}O_6P*HCl$
Mol. weight	250,19*36,45 g/mol



RL-1020 DTT (racemic)

DL-Dithiothreitol

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



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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.

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.

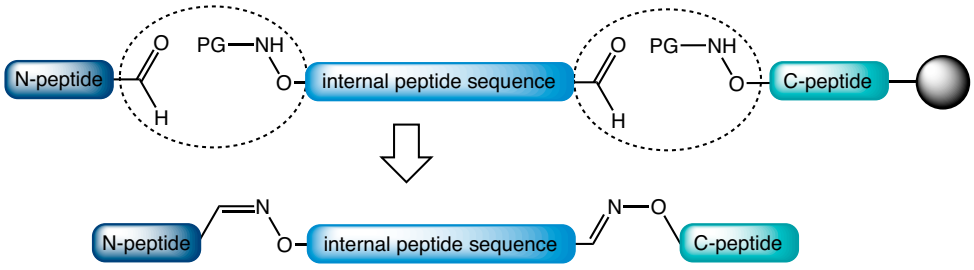


Fig. 12: Illustration of oxime ligation.

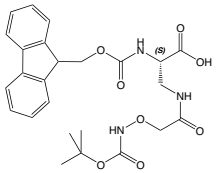
References:

- *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 α-amino-oxy-acids and α-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*

FAA1461 Fmoc-L-Dap(Boc-Aoa)-OH

N-alpha-(9-Fluorenylmethyloxycarbonyl)-N-beta-(*t*-butyloxycarbonyl-aminooxy-acetyl)-L-2,3-diaminopropionic acid

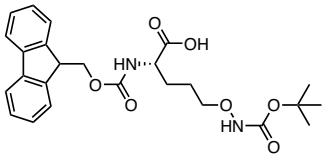
CAS-No.	600153-12-6
Formula	$C_{25}H_{29}N_3O_8$
Mol. weight	499,53 g/mol



FAA8445 Fmoc-Hcan(Boc)-OH (S)

(S)-2-(Fmoc-amino)-5-(Boc-aminoxy)pentanoic acid

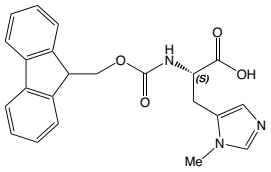
CAS-No.	204844-15-5
Formula	$C_{25}H_{30}N_2O_7$
Mol. weight	470,51 g/mol



FAA1995 Fmoc-L-His(3-Me)-OH

N-alpha-(9-Fluorenylmethyloxycarbonyl)-N_3-methyl-L-histidine

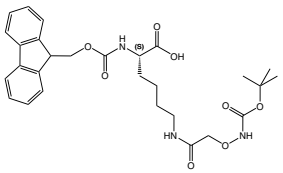
CAS-No.	252049-16-4
Formula	$C_{22}H_{21}N_3O_4$
Mol. weight	391,42 g/mol



FAA4370 Fmoc-L-Lys(Boc-Aoa)-OH

N-alpha-(9-Fluorenylmethyloxycarbonyl)-N-epsilon-(*t*-butyloxycarbonyl)aminooxyacetyl-L-lysine

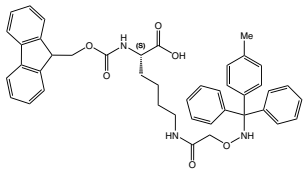
CAS-No.	757960-24-0
Formula	$C_{28}H_{35}N_3O_8$
Mol. weight	541,59 g/mol



FAA4700 Fmoc-L-Lys(Mtt-Aoa)-OH

N-alpha-(9-Fluorenylmethyloxycarbonyl)-N-epsilon-(4-methyltrityl)aminooxyacetyl-L-lysine

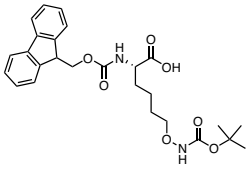
CAS-No.	2250436-45-2
Formula	$C_{43}H_{43}N_3O_6$
Mol. weight	697,82 g/mol



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



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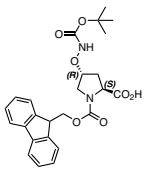
Product details

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

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

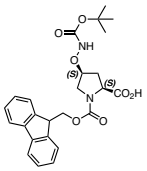
CAS-No.	1015426-45-5
Formula	$C_{25}H_{28}N_2O_7$
Mol. weight	468,50 g/mol



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



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 cysteine 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.

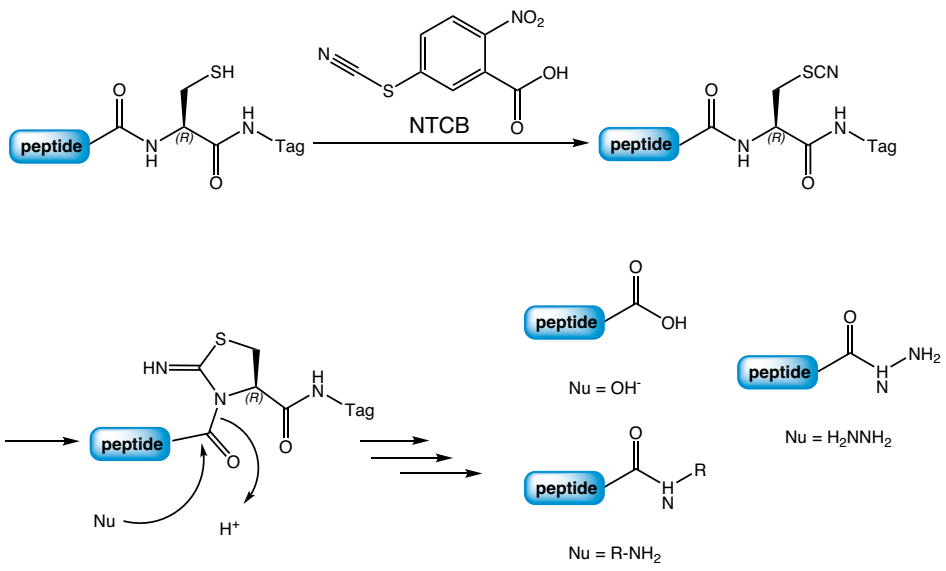
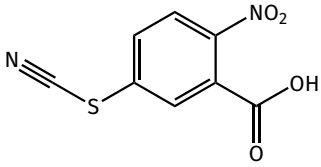


Fig. 13: Schematic illustration of the activated cysteine-based protein ligation.

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

3.6. Nitrile-Aminothiol Conjugation (NATC) as Biocompatible Ligation Technique

While nitriles in general may react with sulfhydryl groups (e.g., from cysteines) in a rather unspecific way, the advantage of α-cyanopyridines (2-picolinonitrils) is their strong selectivity for 1,2-aminothiols (e.g., provided as N-terminal cysteine, internally as non-canonical amino acid, or by conversion of thiazolidines). The so-called nitrile-aminothiol conjugation (NATC) proceeds rapidly under physiological pH conditions without the need for any added catalyst and leads to the formation of a thiazolidine ring.

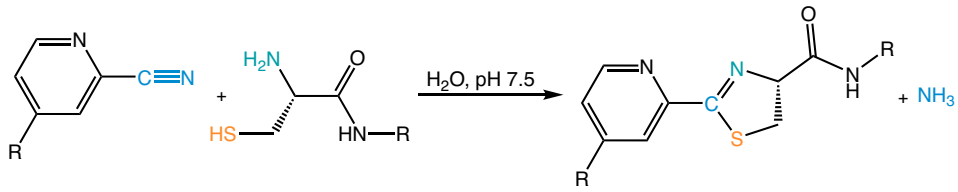
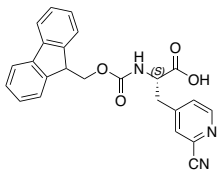


Fig. 14: The reaction between a 2-cyanopyridine and a 1,2-aminothiol forms a 2-thiazoline.

FAA9370 Fmoc-L-3-(2-cyano-4-pyridyl)-alanine

(S)-2-((((9H-fluoren-9-yl)methoxy)carbonyl)amino)-3-(2-cyanopyridin-4-yl)propanoic acid

CAS-No.	2245755-79-5
Formula	$C_{24}H_{19}N_3O_4$
Mol. weight	413,43 g/mol



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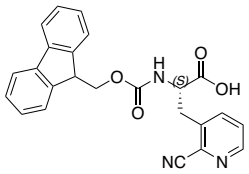
Product details

FAA9375 Fmoc-L-3-(2-cyano-3-pyridyl)-alanine

(S)-2-((((9H-fluoren-9-yl)methoxy)carbonyl)amino)-3-(2-cyanopyridin-3-yl)propanoic acid

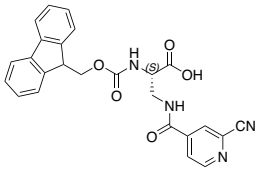
CAS-No.	2245755-77-3
Formula	$C_{24}H_{19}N_3O_4$
Mol. weight	413,43 g/mol



FAA9380 Fmoc-L-Dap(2-CINA)-OH

(S)-2-((((9H-fluoren-9-yl)methoxy)carbonyl)amino)-3-(2-cyanoisonicotinamido)propanoic acid

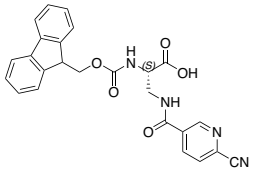
Formula	$C_{25}H_{20}N_4O_5$
Mol. weight	456,46 g/mol



FAA9385 Fmoc-L-Dap(6-CNA)-OH

(S)-2-((((9H-fluoren-9-yl)methoxy)carbonyl)amino)-3-(6-cyanonicotinamido)propanoic acid

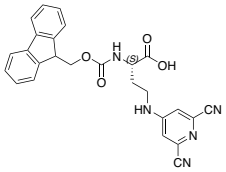
Formula	$C_{25}H_{20}N_4O_5$
Mol. weight	456,46 g/mol



FAA9390 Fmoc-L-Dab(2,6-DCP)-OH

(S)-2-((((9H-fluoren-9-yl)methoxy)carbonyl)amino)-4-((2,6-dicyanopyridin-4-yl)amino)butanoic acid

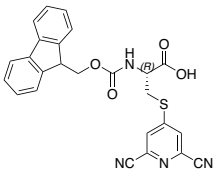
CAS-No.	2968514-51-2
Formula	$C_{26}H_{21}N_5O_4$
Mol. weight	467,49 g/mol



FAA9395 Fmoc-L-Cys(2,6-DCP)-OH

N-(((9H-fluoren-9-yl)methoxy)carbonyl)-S-(2,6-dicyano-pyridin-4-yl)-L-cysteine

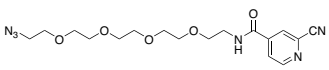
CAS-No.	2968514-50-1
Formula	$C_{25}H_{18}N_4O_4S$
Mol. weight	470,50 g/mol



RL-8625 N_3-PEG(4)-CINA

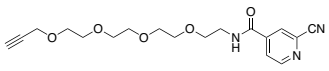
N-(14-azido-3,6,9,12-tetraoxatetradecyl)-2-cyanoisonicotinamide

Formula	$C_{17}H_{24}N_6O_5$
Mol. weight	392,42 g/mol



RL-8630 Alkyne-PEG(4)-CINA

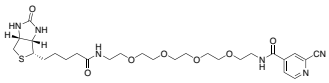
2-cyano-N-(3,6,9,12-tetraoxapentadec-14-yn-1-yl) isonicotinamide



Formula $C_{18}H_{23}N_3O_5$
Mol. weight 361,40 g/mol

RL-8635 Biotin-PEG(4)-CINA

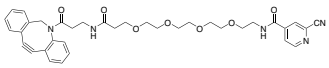
2-cyano-N-(16-oxo-20-((3aS,4S,6aR)-2-oxohexahydro-1H-thieno[3,4-d]imidazol-4-yl)-3,6,9,12-tetraoxa-15-azaicosyl)isonicotinamide



Formula $C_{27}H_{40}N_6O_7S$
Mol. weight 592,71 g/mol

RL-8640 DBCO-PEG(4)-CINA

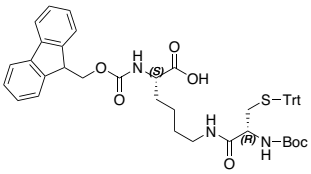
Dibenzoazacyclooctyne-tetra(ethylene glycol)-cyanoisonicotinamide



Formula $C_{36}H_{39}N_5O_7$
Mol. weight 653,74 g/mol

FAA9315 Fmoc-L-Lys(Boc-Cys(Trt))-OH

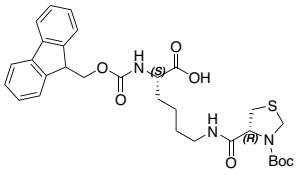
N2-(((9H-fluoren-9-yl)methoxy)carbonyl)-N6-(N-(*tert*-butoxycarbonyl)-S-trityl-L-cysteinyl)-L-lysine



CAS-No. 587854-43-1
Formula $C_{48}H_{51}N_3O_7S$
Mol. weight 814,01 g/mol

FAA9320 Fmoc-L-Lys(Boc-Thz)-OH

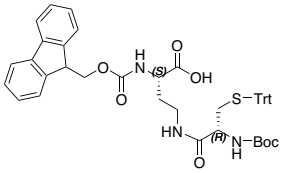
N2-(((9H-fluoren-9-yl)methoxy)carbonyl)-N6-((R)-3-(*tert*-butoxycarbonyl)thiazolidine-4-carbonyl)-L-lysine



Formula $C_{30}H_{37}N_3O_7S$
Mol. weight 583,70 g/mol

FAA9325 Fmoc-L-Dab(Boc-Cys(Trt))-OH

(S)-2-((((9H-fluoren-9-yl)methoxy)carbonyl) amino)-4-((R)-2-((*tert*-butoxycarbonyl)amino)-3-(tritylthio)propanamido)butanoic acid



CAS-No. 2968514-52-3
Formula $C_{46}H_{47}N_3O_7S$
Mol. weight 785,96 g/mol

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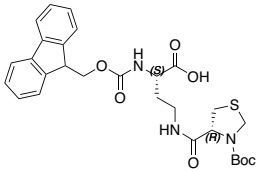
Product details

FAA9330 Fmoc-L-Dab(Boc-Thz)-OH

(S)-2-((((9H-fluoren-9-yl)methoxy)carbonyl) amino)-4-((R)-3-(*tert*-butoxycarbonyl)thiazolidine-4-carboxamido)butanoic acid

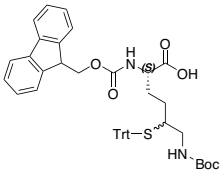
CAS-No.	2968514-54-5
Formula	$C_{28}H_{33}N_3O_7S$
Mol. weight	555,65 g/mol



FAA9335 Fmoc-L-Lys(5-STrt, Boc)-OH

(2S)-2-((((9H-fluoren-9-yl)methoxy)carbonyl) amino)-6-((*tert*-butoxycarbonyl)amino)-5-(tritylthio) hexanoic acid

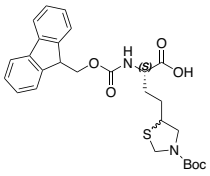
CAS-No.	1240666-29-8
Formula	$C_{45}H_{46}N_2O_6S$
Mol. weight	742,93 g/mol



FAA9340 Fmoc-L-Lys(4-Thz, Boc)-OH

(2S)-2-((((9H-fluoren-9-yl)methoxy)carbonyl) amino)-4-(3-(*tert*-butoxycarbonyl)thiazolidin-5-yl) butanoic acid

CAS-No.	1240666-28-7
Formula	$C_{27}H_{32}N_2O_6S$
Mol. weight	512,62 g/mol



References:

→ *Advancing Nitrile-Aminothiol Strategy for Dual and Sequential Bioconjugation; V. J. Thombare, Y. Wu, K. Pamulapati, M. Han, J. Tailhades, M. J. Cryle, K. D. Roberts, T. Velkov, J. Li, N. A. Patil;* ***Chem. Eur. J.*** *2024;* ***30(46)****: e202401674.* https://doi.org/10.1002/chem.202401674

→ *The Cyanopyridine-Aminothiol Click Reaction: Expanding Horizons in Chemical Biology; C. Nitsche;* ***SynLett.*** *2024;* ***35****: A-E.* https://dx.doi.org/10.1055/a-2214-7612

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.

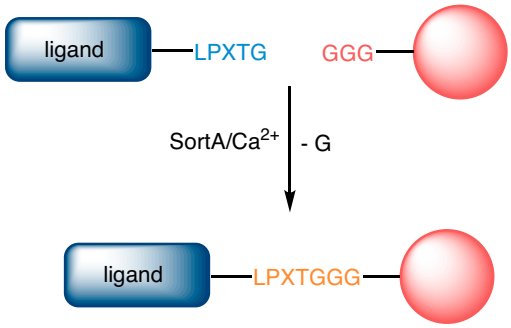
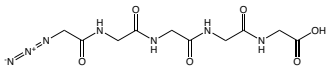


Fig. 15: Enzymatically supported conjugation utilizing sortase A.

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

Product details

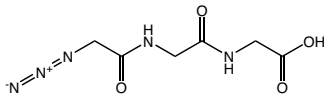
HAA2860 N_3-Gly-Gly-Gly-Gly-Gly-OH



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

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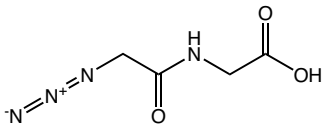
Product details

HAA2850 N_3-Gly-Gly-OH*DCHA

Azido-glycylglycine dicyclohexylamine

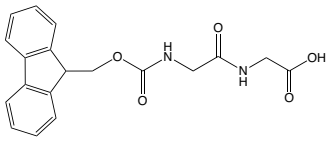
CAS-No.	855750-87-7 net
Formula	$C_4H_6N_4O_3$*$C_{12}H_{23}N$
Mol. weight	158,12*181,32 g/mol



FDP1030 Fmoc-Gly-Gly-OH

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

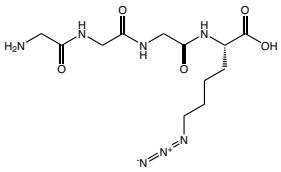
CAS-No.	35665-38-4
Formula	$C_{19}H_{18}N_2O_5$
Mol. weight	354,36 g/mol



HAA2870 H-$(Gly)_3$-Lys(N_3)-OH*HCl

Triglycyl-epsilon-azido-L-lysine hydrochloride

CAS-No.	2250437-45-5
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

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.*

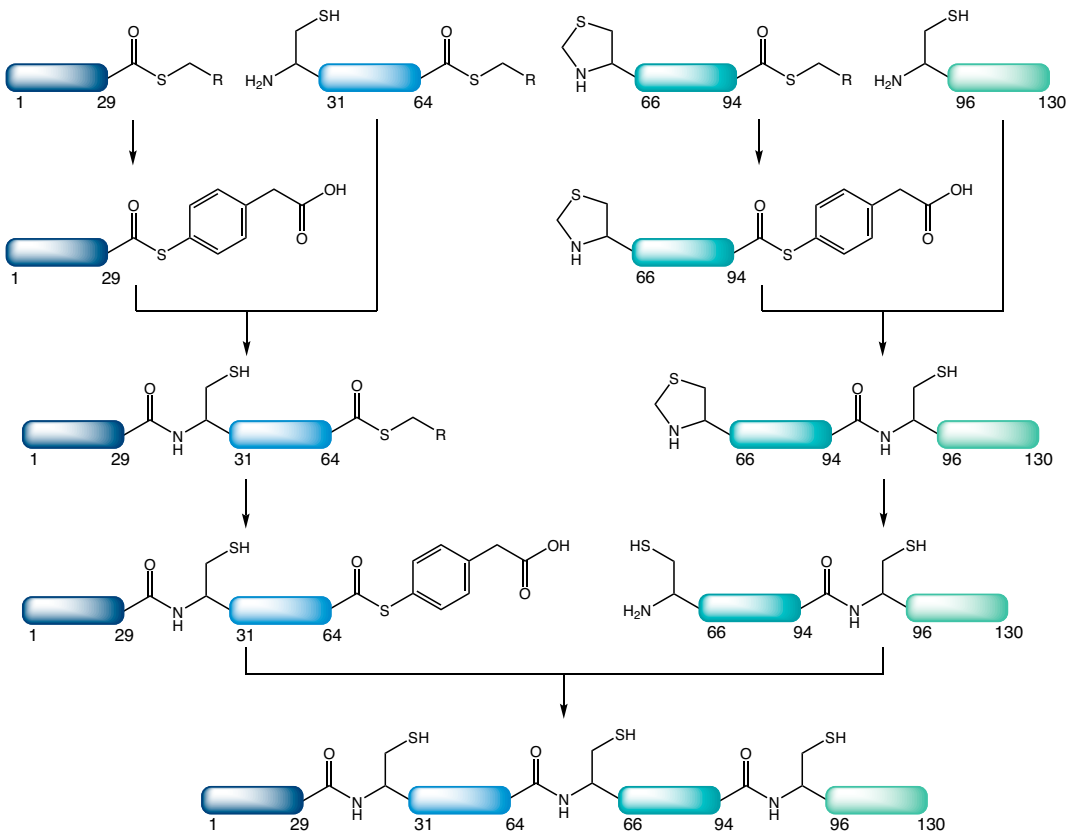


Fig. 16: Kinetically controlled four-fragment ligation.

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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.*

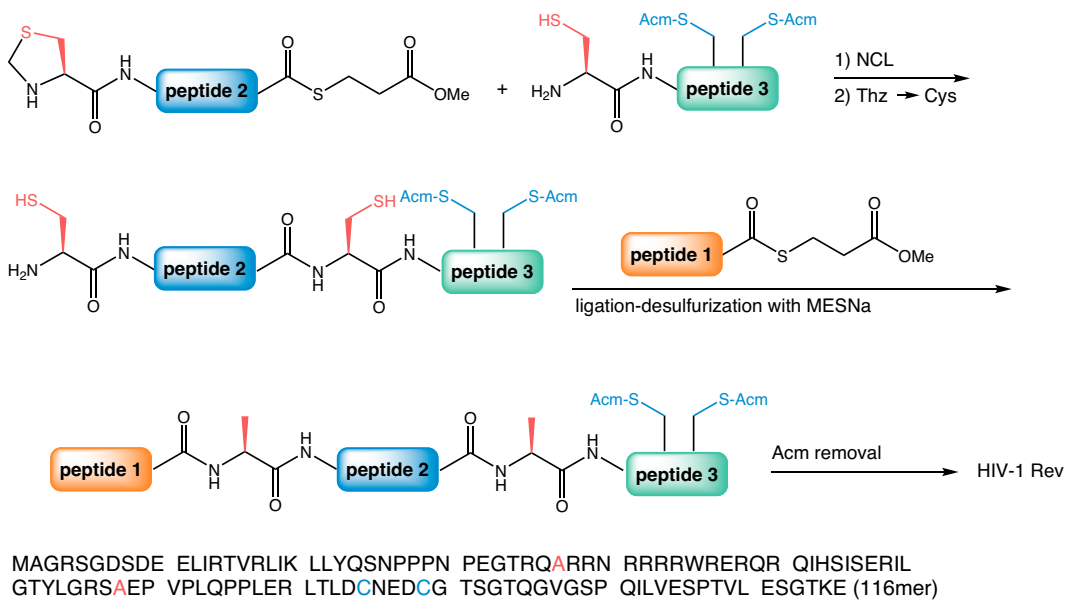

Fig. 17: Example of a synthesis of a peptide via ligation of three segments and thiazolidine as temporarily protected cysteine.

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Product code	Product name	Page
FAA8420	Fmoc-L-Cys(NDBF)-OH	29
FAA3970	Fmoc-L-Cys(*o*Nv)-OH	30
FAA6910	Fmoc-L-Cys(Phacm)-OH	30
FAA3180	Fmoc-L-Cys(S-DMP)-OH	28
FAA8495	Fmoc-L-Cys(SIT)-OH	30
FAA1575	Fmoc-L-Cys(S*t*Bu)-OH	30
FAA1716	Fmoc-L-Cys(*t*Bu)-OH	31
FAA4160	Fmoc-L-Cys(Thp)-OH	31
PSI1580	Fmoc-L-Cys(Trt)-L-Cys(Psi(Dmp,H)pro)-OH	33
PYV1140	Fmoc-L-Cys(Trt)-NHN=Pyv Resin	13
FAA1040	Fmoc-L-Cys(Trt)-OH	31
FAA5670	Fmoc-L-Cys(Trt)-OMe	32
FAA1980	Fmoc-L-Cys-NH_2	26
FAA1362	Fmoc-L-Cys-OH*H_2O	26
FAA9390	Fmoc-L-Dab(2,6-DCP)-OH	45
FAA9325	Fmoc-L-Dab(Boc-Cys(Trt))-OH	46
FAA9330	Fmoc-L-Dab(Boc-Thz)-OH	18, 47
FAA9380	Fmoc-L-Dap(2-CINA)-OH	45
FAA9385	Fmoc-L-Dap(6-CNA)-OH	45
FAA1461	Fmoc-L-Dap(Boc-Aoa)-OH	42
PYV1160	Fmoc-L-Gln(Trt)-NHN=Pyv Resin	13
PSI1490	Fmoc-L-Glu(*t*Bu)-L-Cys[PSI(Dmp,H)pro]-OH	33
PYV1150	Fmoc-L-Glu(*t*Bu)-NHN=Pyv Resin	13
FAA1995	Fmoc-L-His(3-Me)-OH	42
PYV1180	Fmoc-L-His(Trt)-NHN=Pyv Resin	14
PYV1190	Fmoc-L-Ile-NHN=Pyv Resin	14
PSI1510	Fmoc-L-Leu-L-Cys[PSI(Dmp,H)pro]-OH	33
PYV1200	Fmoc-L-Leu-NHN=Pyv Resin	14
FAA9340	Fmoc-L-Lys(4-Thz, Boc)-OH	19, 47
FAA9335	Fmoc-L-Lys(5-STrt, Boc)-OH	47
PSI1520	Fmoc-L-Lys(Boc)-L-Cys[PSI(Dmp,H)pro]-OH	34
PYV1210	Fmoc-L-Lys(Boc)-NHN=Pyv Resin	14
FAA4370	Fmoc-L-Lys(Boc-Aoa)-OH	42
FAA9315	Fmoc-L-Lys(Boc-Cys(Trt))-OH	46
FAA9320	Fmoc-L-Lys(Boc-Thz)-OH	18, 46
FAA4700	Fmoc-L-Lys(Mtt-Aoa)-OH	42
FAA6720	Fmoc-L-MeCys(Acm)-OH	27
FAA3340	Fmoc-L-MeCys(S-*t*Bu)-OH	31
FAA3570	Fmoc-L-MeCys(Trt)-OH	31
PYV1220	Fmoc-L-Met-NHN=Pyv Resin	14
PYV1230	Fmoc-L-Phe-NHN=Pyv Resin	15

Product code	Product name	Page
PYV1240	Fmoc-L-Pro-NHN=Pyv Resin	15
FAA8705	Fmoc-L-Sec(Mob)-OH	39
FAA8760	Fmoc-L-Sec(Mob)-OPfp	39
FAA8465	Fmoc-L-Sec(Xan)-OH	40
PYV1250	Fmoc-L-Ser(*t*Bu)-NHN=Pyv Resin	15
FAA8860	Fmoc-L-Sez-OH	40
PYV1260	Fmoc-L-Thr(*t*Bu)-NHN=Pyv Resin	15
FAA9200	Fmoc-L-Thz(Dmp)-OH	18
FAA1437	Fmoc-L-Thz(Me2)-OH	18
FAA1427	Fmoc-L-Thz-OH	18
FAA8455	Fmoc-L-*trans*-Hyp(NHBoc)-OH	43
PYV1270	Fmoc-L-Trp(Boc)-NHN=Pyv Resin	15
PSI1560	Fmoc-L-Tyr(*t*Bu)-L-Cys[PSI(Dmp,H)pro]-OH	34
PYV1280	Fmoc-L-Tyr(*t*Bu)-NHN=Pyv Resin	15
PSI1570	Fmoc-L-Val-L-Cys[PSI(Dmp,H)pro]-OH	34
PYV1290	Fmoc-L-Val-NHN=Pyv Resin	16
FAA3166	Fmoc-MeDbz-OH	9
S-30091	Fmoc-MeDbz-RAM TG S	9
PYV1000	Fmoc-NHN=Pyv Resin	12
BR-5279	Fmoc-NHNH-2CT Resin	12
BR-5280	Fmoc-NHNH-Trt-PEG Resin	12
PEG8260	Fmoc-NHNH-Trt-PEG Resin HL	12
PEG8265	Fmoc-NHNH-Trt-PEG Resin XV	12
HAA2870	H-(Gly)3-Lys(N_3)-OH*HCl	49
HAA6110	H-D-Cys(Bzl)-OH	19
HAA3500	H-D-Cys(Mmt)-OH	20
HAA6120	H-D-Cys(Trt)-OH	21
HAA3520	H-D-Cys(Trt)-OMe*HCl	21
HAA2100	H-D-Cys(Trt)-O*t*Bu*HCl	21
HAA1017	H-D-Cys-OH*HCl*H_2O	19
HAA6070	H-L-Cys(Acm)-OH*HCl	19
HAA1574	H-L-Cys(Bzl)-OH	19
HAA6080	H-L-Cys(Bzl)-OMe*HCl	20
HAA6090	H-L-Cys(MBzl)-OH	20
HAA9270	H-L-Cys(MDNPE)-OH	20
HAA6100	H-L-Cys(Mob)-OH	20
HAA3510	H-L-Cys(Npys)-OH*HCl	20
HAA9320	H-L-Cys(*o*Nv)-OH	22
HAA6140	H-L-Cys(S*t*Bu)-OH	22
HAA6150	H-L-Cys(*t*Bu)-OH*HCl	22
HAA1560	H-L-Cys(Trt)-NH_2	21

Product code	Product name	Page
HAA6160	H-L-Cys(Trt)-OH	21
HAA1995	H-L-Cys(Trt)-O*t*Bu*HCl	21
HAA3530	H-L-Cys-NH_2*HCl	19
HAA3840	H-L-MeAla(4-Thz)-OH	17
HAA9230	H-L-Sec(MDNPE)*TFA	38
HAA9360	H-L-Sec(MDNPE)-OH	38
HAA9475	H-L-Sec(NPE)-OH*HCl	38
HAA9465	H-L-Sec(oNB)-OH*HCl	38
HAA9255	H-L-Sec(*o*Nv)-OH*TFA	38
HAA1132	H-L-Thz-OH	17
HAA2860	N_3-Gly-Gly-Gly-Gly-Gly-OH	48
HAA2840	N_3-Gly-Gly-Gly-OH	48
HAA2850	N_3-Gly-Gly-OH*DCHA	49
HAA2810	N_3-L-Cys(Trt)-OH*CHA	22
RL-8625	N_3-PEG(4)-CINA	45
RL-4080	NTCB	44
SAA1110	Smoc-L-Cys(Trt)-OH	34
PAA2000	*t*Bu-SS-Photo(Fmoc)-Gly-OH	35
LS-3405	TCEP*HCl	40
ZAA1161	Z-L-Cys(Bzl)-OH	32
ZAA1310	Z-L-Cys(Trt)-OH	32

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Notes

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.

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.

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.

Get in Contact

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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:

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