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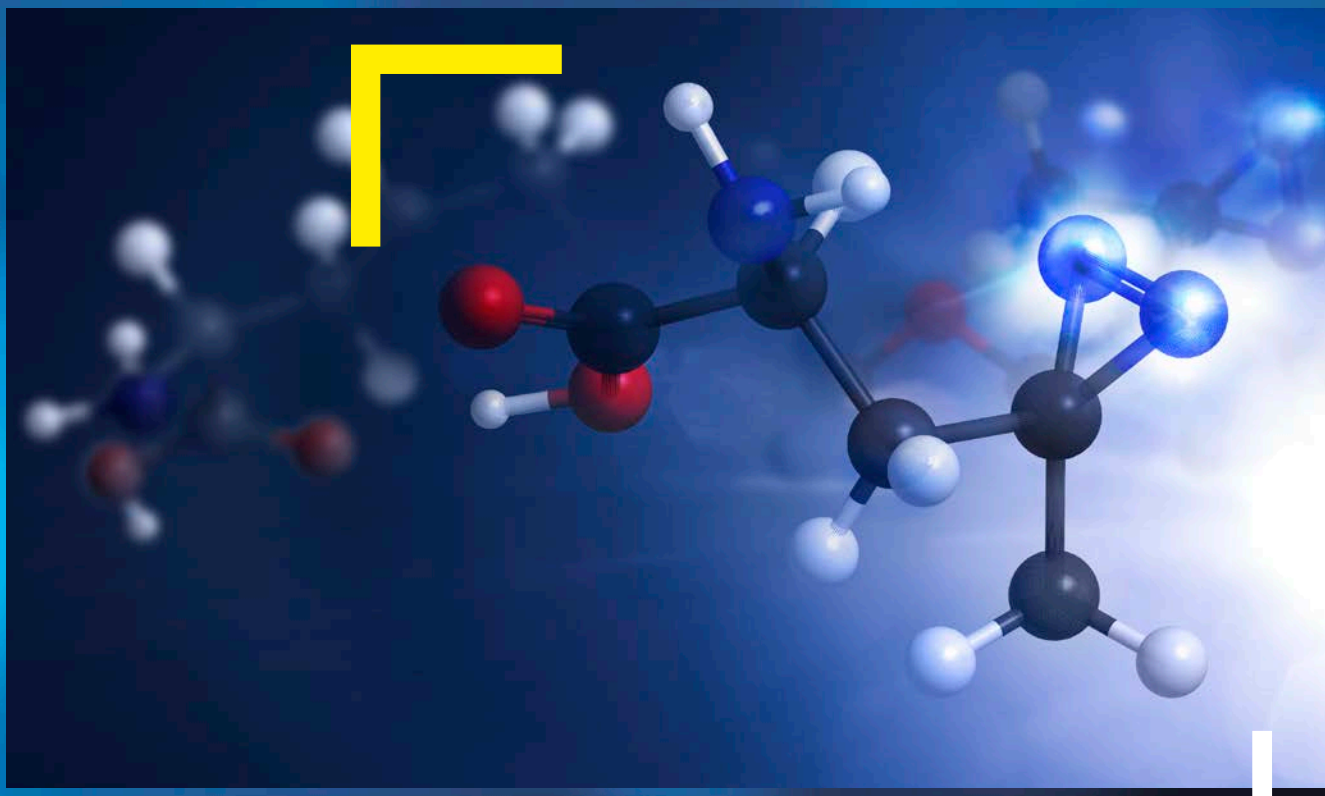

CHEMISTRY

PHOTOACTIVATED COMPOUNDS FOR PEPTIDE SYNTHESIS AND BIOCONJUGATION

Empowering Peptide Innovation

Photochemistry in Peptide Synthesis and Bioconjugation

The term photochemistry describes a group of chemical transformations initiated by irradiation with light. Photochemical reactions usually occur at room temperature and normal pressure, and mostly do not require additional reagents or catalysts, with the notable exception of some cases where the presence of a photosensitizer is necessary. Therefore, photochemical transformations are usually orthogonal to classical chemical transformations, a characteristic that renders them a valuable tool for chemists.

Consequently, the applications of photochemistry are numerous. Orthogonality is a trait often sought for in protecting groups and linkers, as it allows for their selective cleavage. Furthermore, photocleavage is a convenient method for selective removal of auxiliaries after their function has been served.
The typical moiety that is incorporated into protecting groups, linkers and auxiliaries to facilitate light-induced cleavage is an *o*-nitrobenzyl group, which undergoes a Norrish-type II reaction upon UV-irradiation.

Another common application of photochemistry is the labeling or crosslinking of biomolecules *in vitro* and *in vivo*. The latter is of particular interest as a photochemical reaction is one of the few chemical transformations that can be selectively initiated in living cells.

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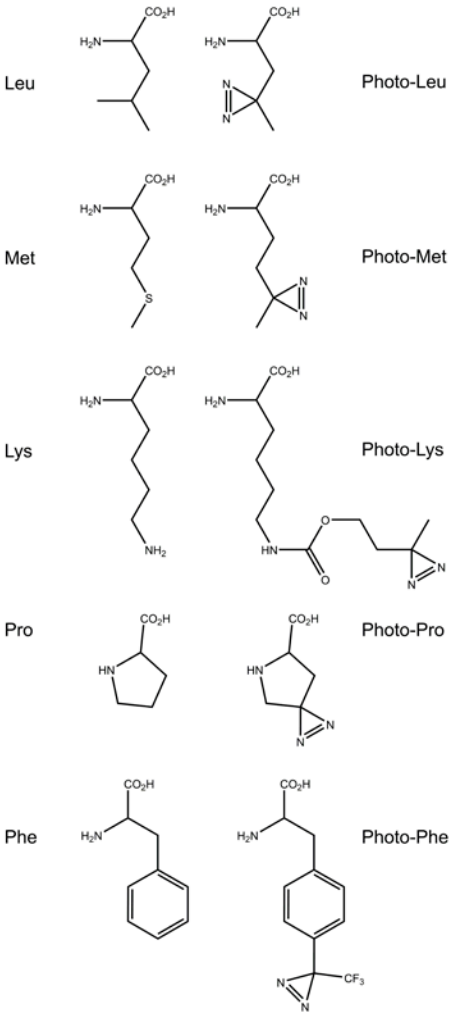
1. Diazirine Amino Acids for Photo-Crosslinkage in Living Cells

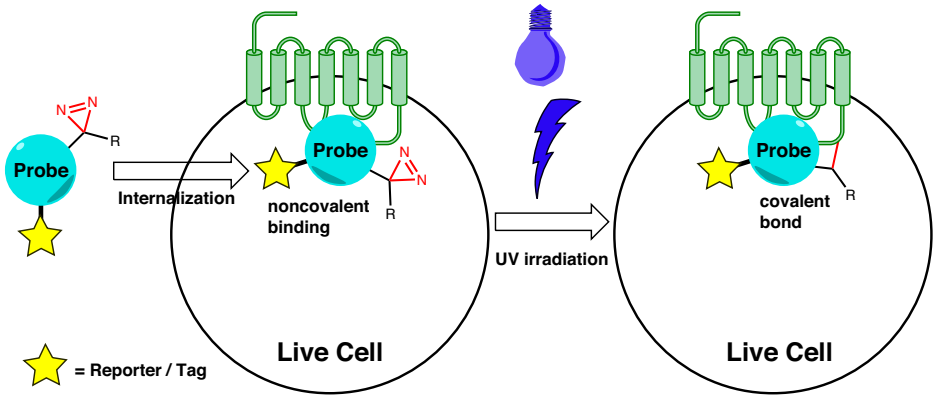
Iris Biotech introduces a comprehensive set of photo-crosslinking amino acids bearing the diazirine moiety. Irradiation of diazirines with UV light (ca. 350 nm – 360 nm) yields a highly reactive carbene species that can undergo insertions into C-C, CH, O-H and X-H (X = heteroatom) bonds of neighboring molecules to irreversibly form a covalent bond. The diazirine moiety is the smallest of all photophores, so introduction of a diazirinebearing amino acid into a peptide or protein usually does not impair its biological activity. Further advantages of diazirine crosslinkers are their stability at room temperature, as well as their relative stability to nucleophiles, and to both acidic and basic conditions.



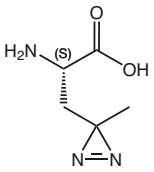
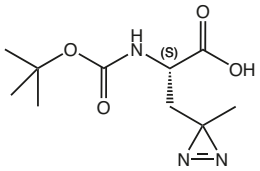
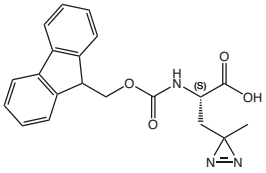
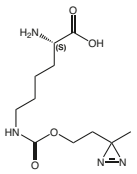
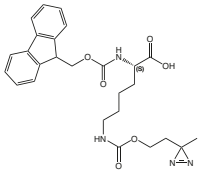
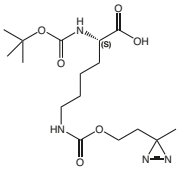
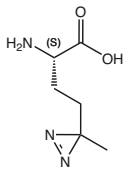
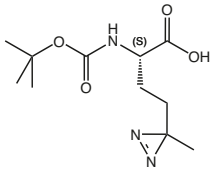
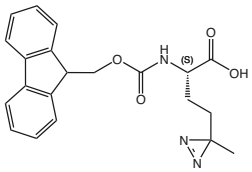
Applications:

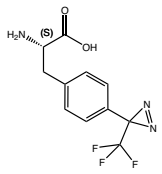
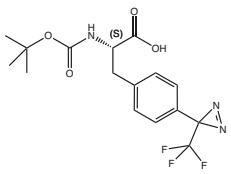
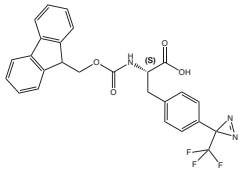
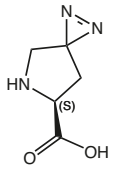
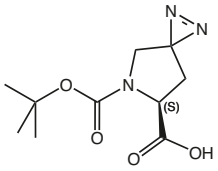
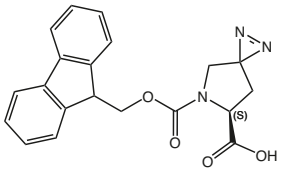
- Probing protein-protein and protein- peptide interactions by photo-crosslinking (e.g. site-specific incorporation of Photo-Lys into glutathione S-transferase allowing covalent crosslinking of the two subunits of the dimeric protein in E. coli)
- Probing protein- peptide interactions in order to identify cellular targets of peptides of interest
- Studying protein-drug interactions and identifying new drug targets
- By comparing results obtained from different proteomic setups (e.g. live cells and cell lysates), more putative targets can be identified.

These amino acids are available in Fmoc- as well as Boc-protected versions for their incorporation into synthetic peptides via standard coupling methods. Furthermore, the unprotected diazirine amino acids are also available for incorporation into expressed peptides and proteins by utilizing the appropriate aminoacyl-tRNA synthetase/tRNA pair. A combination of synthetic and recombinant approaches utilizing NCL has been demonstrated as well. Unnatural amino acids are frequently toxic to cells; however, these photo-amino acids are functional and nontoxic, which allows them to be a premium tool for studying mechanisms and interactions in living cells.



Identification of intracellular targets using a diazirine-bearing probe. By attaching a reporter group or tag to the probe, the target of the binding probe can be either identified using the reporter group, or isolated using the tag.

		Article No.	Quantity	Price
HAA3100 H-L-Photo-Leucine*HCl (S)-2-amino-3-(3-methyl-3H-diazirin-3-yl)propanoic acid hydrochloride CAS NO: 851960-91-3 FORMULA: $C_5H_9N_3O_2$*HCl MOLECULAR WEIGHT: 143,14*36,45 g/mol		HAA3100.0250 HAA3100.1000 HAA3100.5000	250 mg 1 g 5 g	€ 375,00 € 1.100,00 € 4.250,00
BAA3070 Boc-L-Photo-Leucine*DCHA CAS NO: 1000770-97-7 net FORMULA: $C_{10}H_{17}N_3O_4$*$C_{12}H_{23}N$ MOLECULAR WEIGHT: 243,26*181,34 g/mol		BAA3070.0100 BAA3070.0250 BAA3070.1000	100 mg 250 mg 1 g	€ 250,00 € 590,00 € 1.750,00
FAA4590 Fmoc-L-Photo-Leucine (S)-2-(((9H-fluoren-9-yl)methoxy)carbonylamino)-3-(3-methyl-3H-diazirin-3-yl)propanoic acid CAS NO: 1360651-24-6 FORMULA: $C_{20}H_{19}N_3O_4$ MOLECULAR WEIGHT: 365,38 g/mol		FAA4590.0100 FAA4590.0250 FAA4590.0001	100 mg 250 mg 1 g	€ 225,00 € 490,00 € 1.450,00
HAA3110 H-L-Photo-Lysine*HCl (S)-2-amino-6-((2-(3-methyl-3H-diazirin-3-yl)ethoxy)carbonylamino)hexanoic acid hydrochloride CAS NO: 1253643-88-7 FORMULA: $C_{11}H_{20}N_4O_4$*HCl MOLECULAR WEIGHT: 272,30*36,45 g/mol		HAA3110.0250 HAA3110.1000 HAA3110.5000	250 mg 1 g 5 g	€ 375,00 € 1.100,00 € 4.250,00
FAA4600 Fmoc-L-Photo-Lysine (S)-2-(((9H-fluoren-9-yl)methoxy)carbonylamino)-6-((2-(3-methyl-3H-diazirin-3-yl)ethoxy)carbonylamino)hexanoic acid FORMULA: $C_{26}H_{30}N_4O_6$ MOLECULAR WEIGHT: 494,54 g/mol		FAA4600.0250 FAA4600.1000 FAA4600.5000	250 mg 1 g 5 g	€ 375,00 € 1.100,00 € 4.250,00
BAA3080 Boc-L-Photo-Lysine (S)-2-(tert-butoxycarbonylamino)-6-((2-(3-methyl-3H-diazirin-3-yl)ethoxy)carbonylamino) hexanoic acid CAS NO: 1330088-06-6 FORMULA: $C_{16}H_{28}N_4O_6$ MOLECULAR WEIGHT: 372,42 g/mol		BAA3080.0250 BAA3080.1000 BAA3080.5000	250 mg 1 g 5 g	€ 375,00 € 1.100,00 € 4.250,00
HAA3120 H-L-Photo-Methionine*HCl (S)-2-amino-4-(3-methyl-3H-diazirin-3-yl)butanoic acid hydrochloride CAS NO: 851960-68-4 FORMULA: $C_6H_{11}N_3O_2$*HCl MOLECULAR WEIGHT: 157,17*36,45 g/mol		HAA3120.0250 HAA3120.1000 HAA3120.5000	250 mg 1 g 5 g	€ 375,00 € 1.100,00 € 4.250,00
BAA3090 Boc-L-Photo-Methionine (S)-2-(tert-butoxycarbonylamino)-4-(3-methyl-3H-diazirin-3-yl)butanoic acid CAS NO: 1002754-75-7 FORMULA: $C_{11}H_{19}N_3O_4$ MOLECULAR WEIGHT: 257,29 g/mol		BAA3090.0250 BAA3090.1000 BAA3090.5000	250 mg 1 g 5 g	€ 375,00 € 1.100,00 € 4.250,00
FAA4610 Fmoc-L-Photo-Methionine (S)-2-(((9H-fluoren-9-yl)methoxy)carbonylamino)-4-(3-methyl-3H-diazirin-3-yl)butanoic acid CAS NO: 945859-89-2 FORMULA: $C_{21}H_{21}N_3O_4$ MOLECULAR WEIGHT: 379,41 g/mol		FAA4610.0250 FAA4610.1000 FAA4610.5000	250 mg 1 g 5 g	€ 375,00 € 1.100,00 € 4.250,00

		Article No.	Quantity	Price
HAA3490 H-L-Photo-Phe-OH **4-(trifluoromethyldiazirin)-L-phenylalanine** CAS NO: **92367-16-3** FORMULA: $C_{11}H_{10}F_3N_3O_2$ MOLECULAR WEIGHT: **273,21 g/mol**		HAA3490.0050 HAA3490.0100	50 mg 100 mg	€ 910,00 € 1.410,00
BAA1530 Boc-L-Photo-Phe-OH **N-alpha-(t-Butyloxycarbonyl)-4-(trifluoromethyldiazirin)-L-phenylalanine** CAS NO: **92367-17-4** FORMULA: $C_{16}H_{18}F_3N_3O_4$ MOLECULAR WEIGHT: **373,33 g/mol**		BAA1530.0100 BAA1530.0250 BAA1530.0500	100 mg 250 mg 500 mg	€ 910,00 € 1.740,00 € 2.570,00
FAA5690 Fmoc-L-Photo-Phe-OH **N-alpha-(9-Fluorenylmethyloxycarbonyl)-4-(trifluoromethyldiazirin)-L-phenylalanine** CAS NO: **133342-64-0** FORMULA: $C_{26}H_{20}F_3N_3O_4$ MOLECULAR WEIGHT: **495,45 g/mol**		FAA5690.0100 FAA5690.0250 FAA5690.0500	100 mg 250 mg 500 mg	€ 740,00 € 1.410,00 € 2.070,00
HAA3130 H-L-Photo-Proline*HCl **(S)-1,2,5-triazaspiro[2.4]hept-1-ene-6-carboxylic acid** CAS NO: **1675206-55-9** FORMULA: $C_5H_7N_3O_2$*HCl MOLECULAR WEIGHT: **141,13*36,45 g/mol**		HAA3130.0250 HAA3130.1000 HAA3130.5000	250 mg 1 g 5 g	€ 375,00 € 1.100,00 € 4.250,00
BAA3100 Boc-L-Photo-Proline **(S)-5-(tert-butoxycarbonyl)-1,2,5-triazaspiro[2.4]hept-1-ene-6-carboxylic acid** CAS NO: **1266778-55-5** FORMULA: $C_{10}H_{15}N_3O_4$ MOLECULAR WEIGHT: **241,24 g/mol**		BAA3100.0250 BAA3100.1000 BAA3100.5000	250 mg 1 g 5 g	€ 375,00 € 1.100,00 € 4.250,00
FAA4620 Fmoc-L-Photo-Proline **(S)-5-(((9H-fluoren-9-yl)methoxy)carbonyl)-1,2,5-triazaspiro[2.4]hept-1-ene-6-carboxylic acid** CAS NO: **1266778-58-8** FORMULA: $C_{20}H_{17}N_3O_4$ MOLECULAR WEIGHT: **363,37 g/mol**		FAA4620.0250 FAA4620.1000 FAA4620.5000	250 mg 1 g 5 g	€ 375,00 € 1.100,00 € 4.250,00

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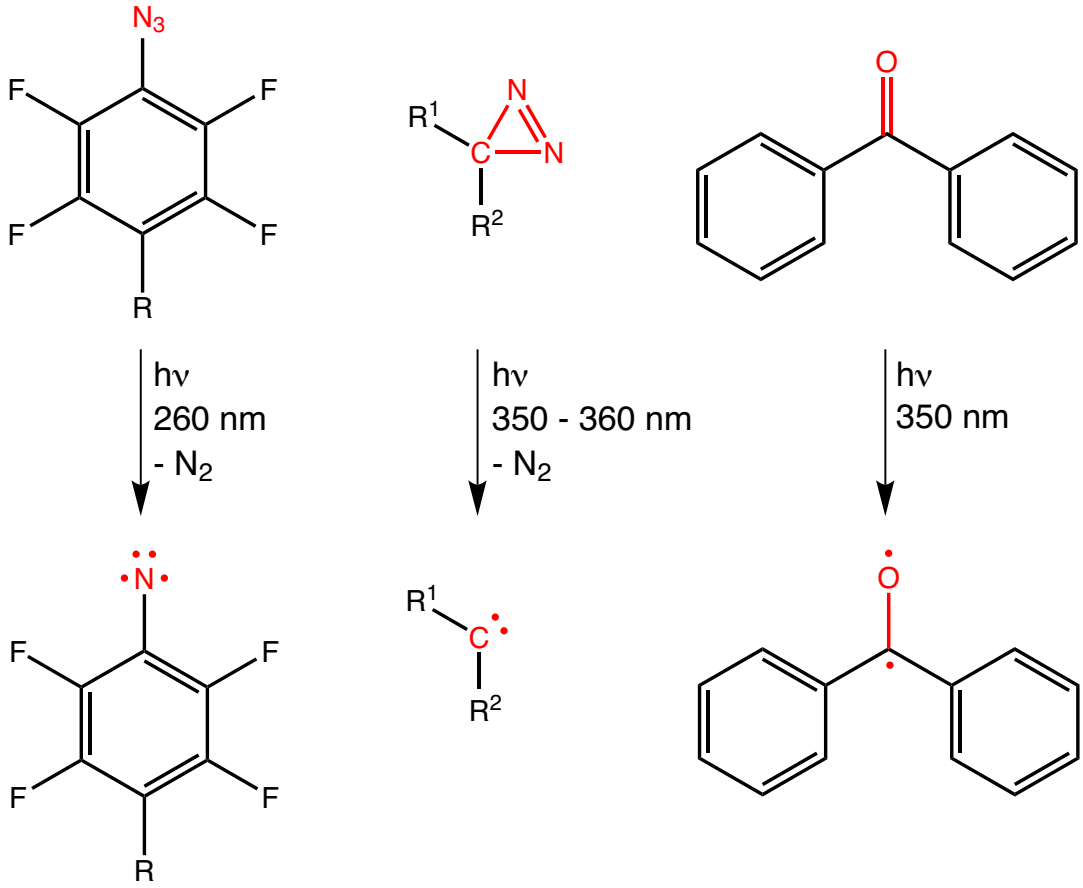
2. Photo-Crosslinkers for Various Applications

Many photo-crosslinkers for photoaffinity labeling rely on benzophenone as the crosslinking agent. However, these types of crosslinkers usually show low crosslinking yields and require relatively long irradiation times due to slow reaction rates, which may lead to non-specific labeling. Moreover, the irradiation conditions for benzophenones have been shown to lead to cell damage and cell death.

Conversely, diazirine- and perfluorophenyl-based crosslinkers generate a reactive species (carbene and nitrene, respectively) upon relatively short irradiation with UV light. Consequently, diazirine- and perfluorophenyl-crosslinkers are commonly used in molecular biology and biochemistry.

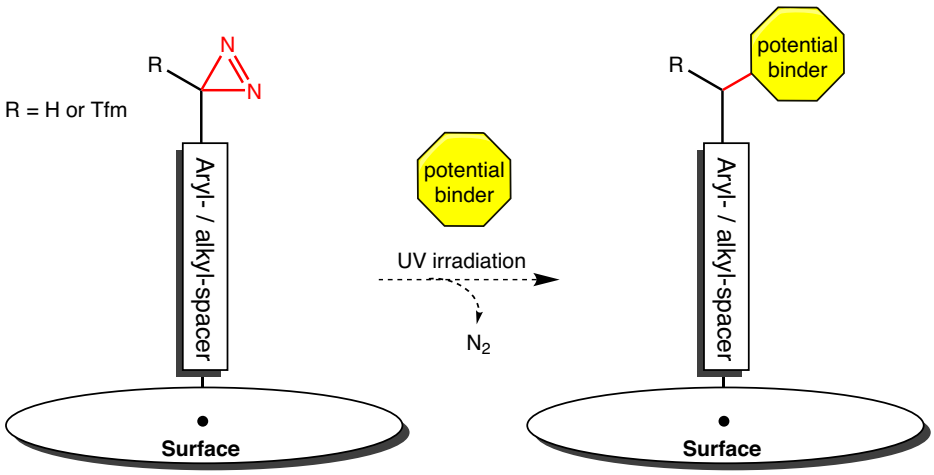


Three types of photophores: Perfluorophenyl azides, diazirines and benzophenones

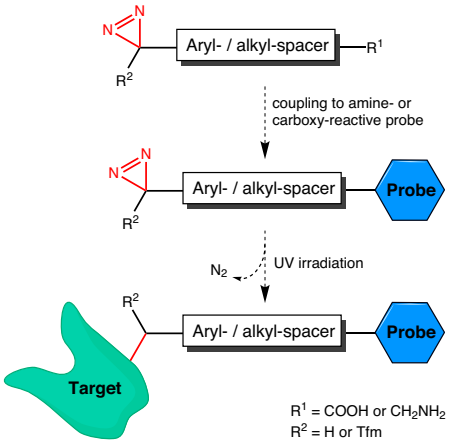
2.1. Photo-Crosslinkers for Various Applications

Diazirine-bearing crosslinkers are activated at wavelengths that cause little to no damage to cells. In addition to this, trifluoromethylaryl diazirines show a fast initial reaction rate and rapid termination of reaction. Consequently, they exhibit a highly ligand-dependent reactivity, which renders them ideal probes for ligand binding to low-affinity targets, e.g. for probing carbohydrate-lectin interactions. Moreover, the small size of the diazirine group minimizes the risk of impairing or altering the biological activity of a ligand. Our diazirine crosslinkers are functionalized to react with either carboxyl- or amine-reactive ligands, respectively.

Another application of diazirine photo crosslinkers is the surface immobilization of molecules of interest. The linker is bound to a surface through its carboxyl or amino functionality, leaving the diazirine group free to react with any type of molecule. Since this reaction takes place irrespective of available functional groups, it is not necessary to chemically modify molecules of interest prior to immobilization. This virtually ensures that molecules are immobilized without altering their binding properties. By using this approach, it is possible to easily create microarrays of whole libraries of small molecules for rapid screening.



Immobilization of molecules of interest on a surface (e.g. a glass slide) using a diazirine crosslinker.



Photoaffinity labeling of a target molecule by a diazirine-functionalized binding probe.

	Article No.	Quantity	Price
RL-2890 Photo-Propanoic acid **3-(3-methyl-3H-diazirin-3-yl)propanoic acid** CAS NO: **25055-86-1** FORMULA: $C_5H_8N_2O_2$ MOLECULAR WEIGHT: **128,13 g/mol**	RL-2890.0000	please inquire	
RL-2900 Photo-Butyric acid **4-(3-methyl-3H-diazirin-3-yl)butanoic acid** CAS NO: **16297-97-5** FORMULA: $C_6H_{10}N_2O_2$ MOLECULAR WEIGHT: **142,16 g/mol**	RL-2900.0000	please inquire	
RL-2920 Photo-Benzoic acid **4-[3-(Trifluoromethyl)-3H-diazirin-3-yl]benzoic acid** CAS NO: **85559-46-2** FORMULA: $C_9H_5F_3N_2O_2$ MOLECULAR WEIGHT: **230,14 g/mol**	RL-2920.0200 RL-2920.1000	200 mg 1 g	€ 200,00 € 600,00
RL-2910 Photo-Ethylamine*HCl **2-(3-methyl-3H-diazirin-3-yl)ethan-1-amine hydrochloride** FORMULA: $C_4H_9N_3$*HCl MOLECULAR WEIGHT: **99,13*36,45 g/mol**	RL-2910.0000	please inquire	
RL-2930 Photo-Benzylamine*HCl **4-[3-(Trifluoromethyl)-3H-diazirin-3-yl]benzylamine hydrochloride** CAS NO: **1258874-29-1** FORMULA: $C_9H_8N_3F_3$*HCl MOLECULAR WEIGHT: **215,18*36,45 g/mol**	RL-2930.0200 RL-2930.1000	200 mg 1 g	€ 250,00 € 700,00

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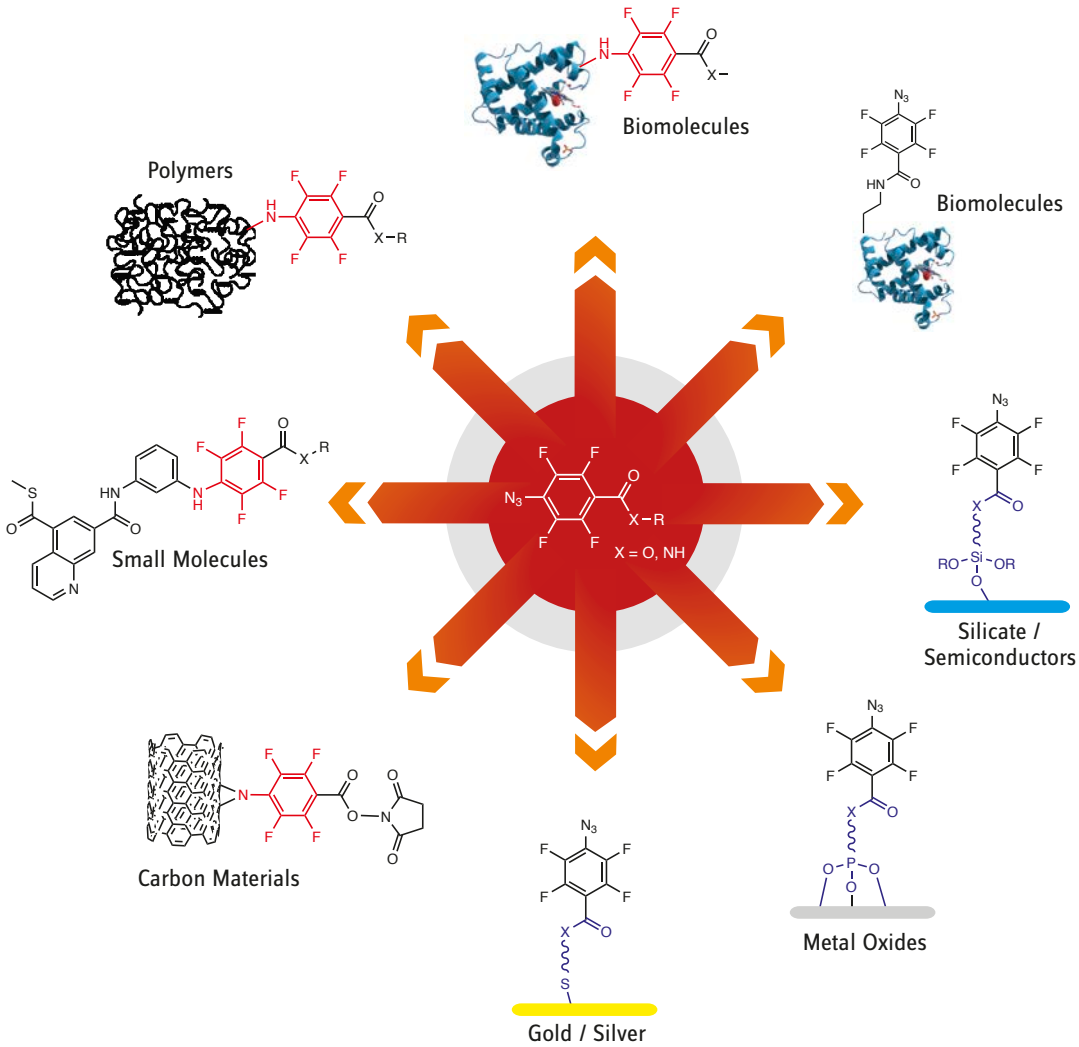
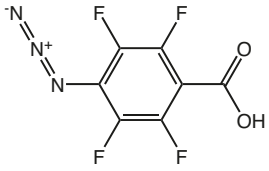
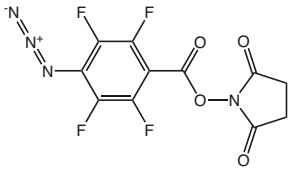
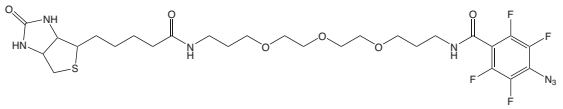
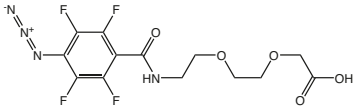
2.2. Tetrafluorophenyl-Azide-based Photo-Crosslinkers

Tetrafluorophenyl-azides follow a principle similar to diazirines. Upon irradiation with UV light (ca. 260 nm), a highly stabilized nitrene is formed. Nitrenes are the nitrogen analogs of carbenes (isoelectronic) and react in a comparable fashion. In terms of crosslinking yield and duration of irradiation, they compare favorably to benzophenones. Moreover, the azido group can also undergo classical copper-catalyzed azide-alkyne cycloadditions. Tetrafluorophenyl-azido crosslinkers are also available with a short PEG-spacer for increased solubility (PEG2065), and as Biotin-TEG-ATFBA (PEG5000) for applications such as surface functionalization with biotin, or the biotinylation of biomacromolecules.



		Article No.	Quantity	Price
RL-2035 ATFB-C004 **4-Azido-2,3,5,6-tetrafluorobenzoic acid** CAS NO: **122590-77-6** FORMULA: $C_7HF_4N_3O_2$ MOLECULAR WEIGHT: **235,1 g/mol**		RL-2035.0250	250 mg	€ 100,00
		RL-2035.0500	500 mg	€ 180,00
		RL-2035.0001	1 g	€ 280,00
		RL-2035.0005	5 g	€ 1.000,00
RL-2045 ATFB-NHS **N-Succinimidyl 4-azido-2,3,5,6-tetrafluorobenzoate** CAS NO: **126695-58-7** FORMULA: $C_{11}H_4F_4N_4O_4$ MOLECULAR WEIGHT: **332,17 g/mol**		RL-2045.0100	100 mg	€ 96,00
		RL-2045.0250	250 mg	€ 160,00
		RL-2045.0500	500 mg	€ 288,00
		RL-2045.1000	1 g	€ 448,00
		RL-2045.5000	5 g	€ 1.600,00
PEG2065 Biotin-TEG-ATFB **Biotin-triethylenglycol-(p-azido-tetrafluorobenzamide)** CAS NO: **1264662-85-2** FORMULA: $C_{27}H_{37}F_4N_7O_6S$ MOLECULAR WEIGHT: **663,68 g/mol**		PEG2065.0025	25 mg	€ 250,00
		PEG2065.0100	100 mg	€ 425,00
PEG5000 ATFB-O_2Oc **{2-[2-(4-Azido-2,3,5,6-tetrafluorobenzoyl-amino)ethoxy]ethoxy}acetic acid** FORMULA: $C_{13}H_{12}F_4O_5$ MOLECULAR WEIGHT: **380,25 g/mol**		PEG5000.0100	100 mg	€ 120,00
		PEG5000.0250	250 mg	€ 200,00
		PEG5000.0500	500 mg	€ 360,00
		PEG5000.1000	1 g	€ 560,00
		PEG5000.5000	5 g	€ 2.000,00

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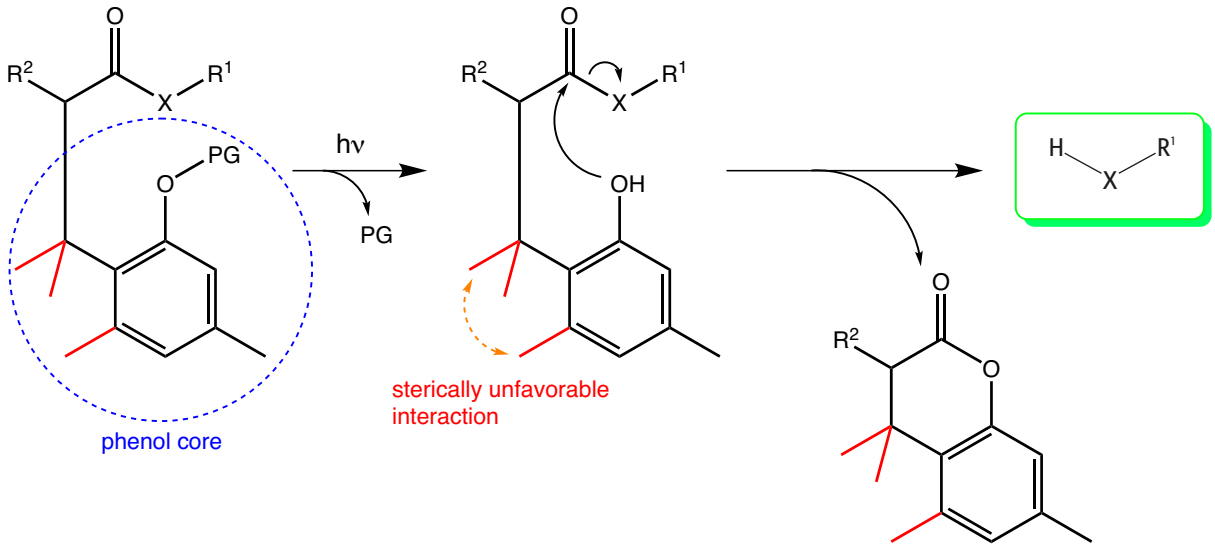
3. Photoactivated Self-Cleaving Linkers and Protecting Groups *via* Trimethyl Lock

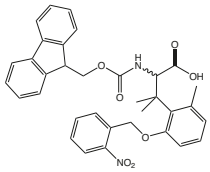
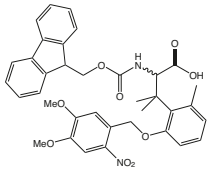
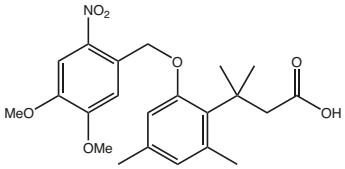
Iris Biotech introduces a series of self-immolative compounds that find application as protecting groups, linkers, or amino acid derivatives (Spr = stimulus-responsive peptide bond cleaving residue). The self-cleavage is induced by irradiation with UV light (ca. 350 – 365 nm) that leads to the unmasking of a hydroxyl group of a 2-alkyl-3,5-dimethyl phenol moiety. The photocleavable group is either *o*-nitrobenzyl or *o*-nitroveratryl, which can be cleaved at wavelengths > 350 nm. Since wavelengths above 350 nm tend to be unproblematic for biomacromolecules, this technique is especially interesting for cell-based systems.

The liberated OH-group serves as a nucleophile that intramolecularly cleaves ester (or amide) bonds at neutral pH and room temperature by cyclization via a six-membered transition state. This reaction is greatly accelerated since the sterically unfavorable interaction between the methyl group at the 3-position of the phenol core and the two geminal CH_3-groups on the alkyl chain (in β-position to the ester or amide carbonyl group) favor conformations that bring the phenolic OH-group and the neighboring carbonyl function into closer vicinity. This phenomenon is termed the gem-dialkyl effect, for which a theory was first proposed by Thorpe and Ingold in 1915 ("Thorpe-Ingold effect"). An alternative explanation for this effect was posited by Bruice and Pandit in 1960 ("reactive rotamer effect").



Principle of photoactivated trimethyl lock; PG = o-nitrobenzyl or o-nitroveratryl; X = O or NH; R¹-XH = target molecule; R² = H or NH-alkyl.

The applications for this approach are numerous. Incorporation of a Spr-residue into a peptide sequence enables the photoactivated self-cleavage of the peptide at the position of said residue. This technique allows for the intracellular removal of e.g. cell penetrating peptides or localization sequences from a bioactive molecule. The Spr-residue can also be used as a photolabile linker in order to reversibly connect a moiety such as biotin to a molecule of interest. Finally, while *o*-nitroveratryl itself is a valuable protecting group for sulfhydryl groups, the combination of *o*-Nv with a trimethyl lock moiety also allows for its use as a protecting group for hydroxyl and amino functions.

		Article No.	Quantity	Price
FAA7190 **Fmoc-Spr(oNB)-OH** **N-alpha-(9-Fluorenylmethyloxycarbonyl)-beta,beta-dimethyl-(2-methyl-6-(2-nitrobenzyl-oxy)phenyl)alanine (rac.)** CAS NO: **1032400-98-8** FORMULA: $C_{34}H_{32}N_2O_7$ MOLECULAR WEIGHT: **580,63 g/mol**		FAA7190.0000	please inquire	
FAA7200 **Fmoc-Spr(oNv)-OH** **N-alpha-(9-FluorenylmethyloN-alpha-(9-Fluorenylmethyloxycarbonyl)-beta,beta-di-methyl-(2-methyl-6-(2-nitroveratryl)phenyl)alanine (rac.)xycarbonyl)-beta,beta-dimet-hyl-(2-methyl-6-(2-nitroveratryl)phenyl)alanine (rac.)** CAS NO: **1228829-20-6** FORMULA: $C_{36}H_{36}N_2O_9$ MOLECULAR WEIGHT: **640,68 g/mol**		FAA7200.0000	please inquire	
RL-2970 **Photo-Trimethyl-Lock** **3-(2-Nitroveratryl-4,6-dimethylphenyl)-3-methylbutyric acid** CAS NO: **2095134-25-9** FORMULA: $C_{22}H_{27}NO_7$ MOLECULAR WEIGHT: **417,45 g/mol**		RL-2970.0000	please inquire	

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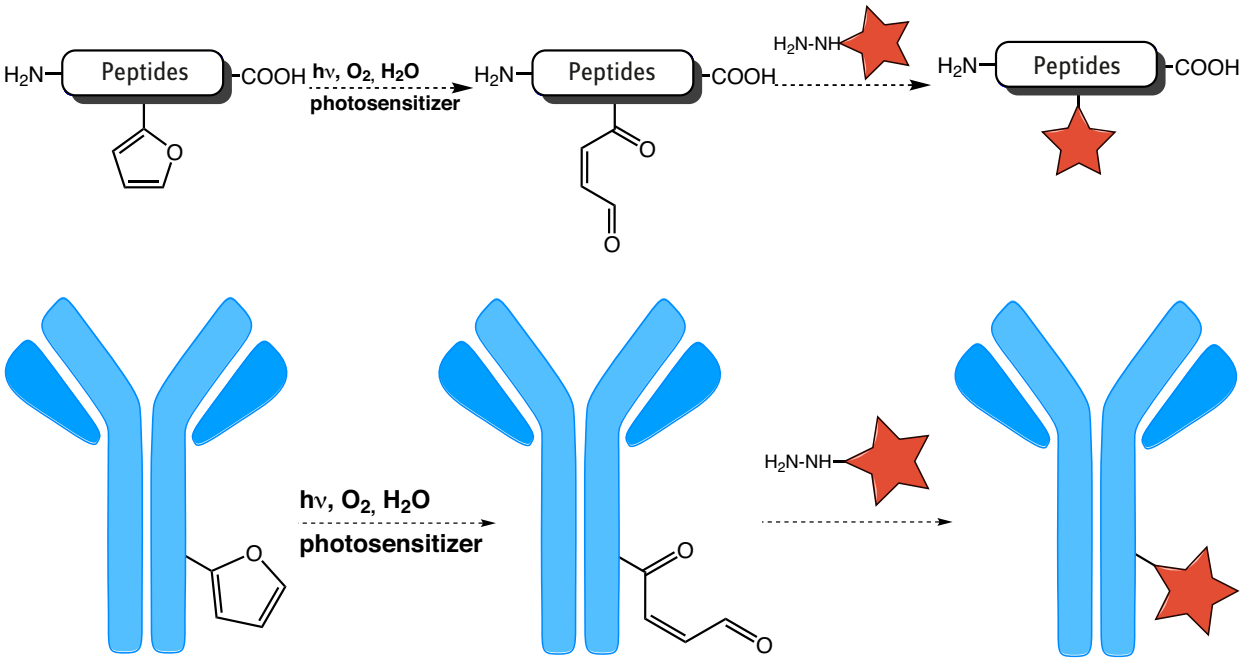
4. Furfuryl-Alanine for Side Chain Modification and Bioconjugation

2-Furyl-alanine can be incorporated into peptides *via* SPPS or by using enzymatic approaches. UV-irradiation in the presence of oxygen and a photosensitizer converts furyl-alanine to an intermediate that selectively reacts with certain nucleophiles. This property can be employed for site-specific labeling of peptides and proteins.

Labeling with different tags and reporter groups is a pivotal technique for the elucidation of peptide and protein function.

A novel and innovative approach is the site-specific labeling using the unnatural amino acid 2-furyl-alanine. UV-irradiation in the presence of oxygen and a photosensitizer converts furyl-alanine to an unsaturated dicarbonyl compound. This intermediate selectively reacts with certain nucleophiles such as hydrazine derivatives of dyes or fluorescent labels. This reaction can be used for the site-specific labeling of peptides and proteins and can be carried out in aqueous solution.



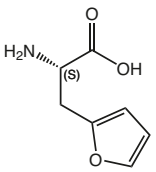
Site-specific labeling of peptides and proteins using 2-Furyl-alanine.

Iris Biotech offers Fmoc-L-Ala(2-Furyl)-OH suitable for SPPS, as well as H-L-Ala(2-Furyl)-OH which can be incorporated into proteins using the amber suppression methodology.

Article No.	Quantity	Price
HAA2930.0250	250 mg	€ 250,00
HAA2930.0001	1 g	€ 750,00
HAA2930.0005	5 g	€ 2.000,00

HAA2930 H-L-Ala(2-Furyl)-OH

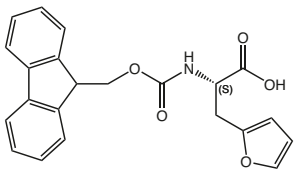
3-(2-Furyl)-L-alanine
CAS NO: **127682-08-0**
MOLECULAR WEIGHT: **155,15 g/mol**



Article No.	Quantity	Price
FAA4250.0250	250 mg	€ 95,00
FAA4250.0001	1 g	€ 250,00
FAA4250.0005	5 g	€ 900,00

FAA4250 Fmoc-L-Ala(2-Furyl)-OH

N-alpha-(9-Fluorenylmethyloxycarbonyl)-3-(2-furyl)-L-alanine
CAS NO: **159611-02-6**
FORMULA: **$C_{22}H_{19}NO_5$**
MOLECULAR WEIGHT: **377,39 g/mol**



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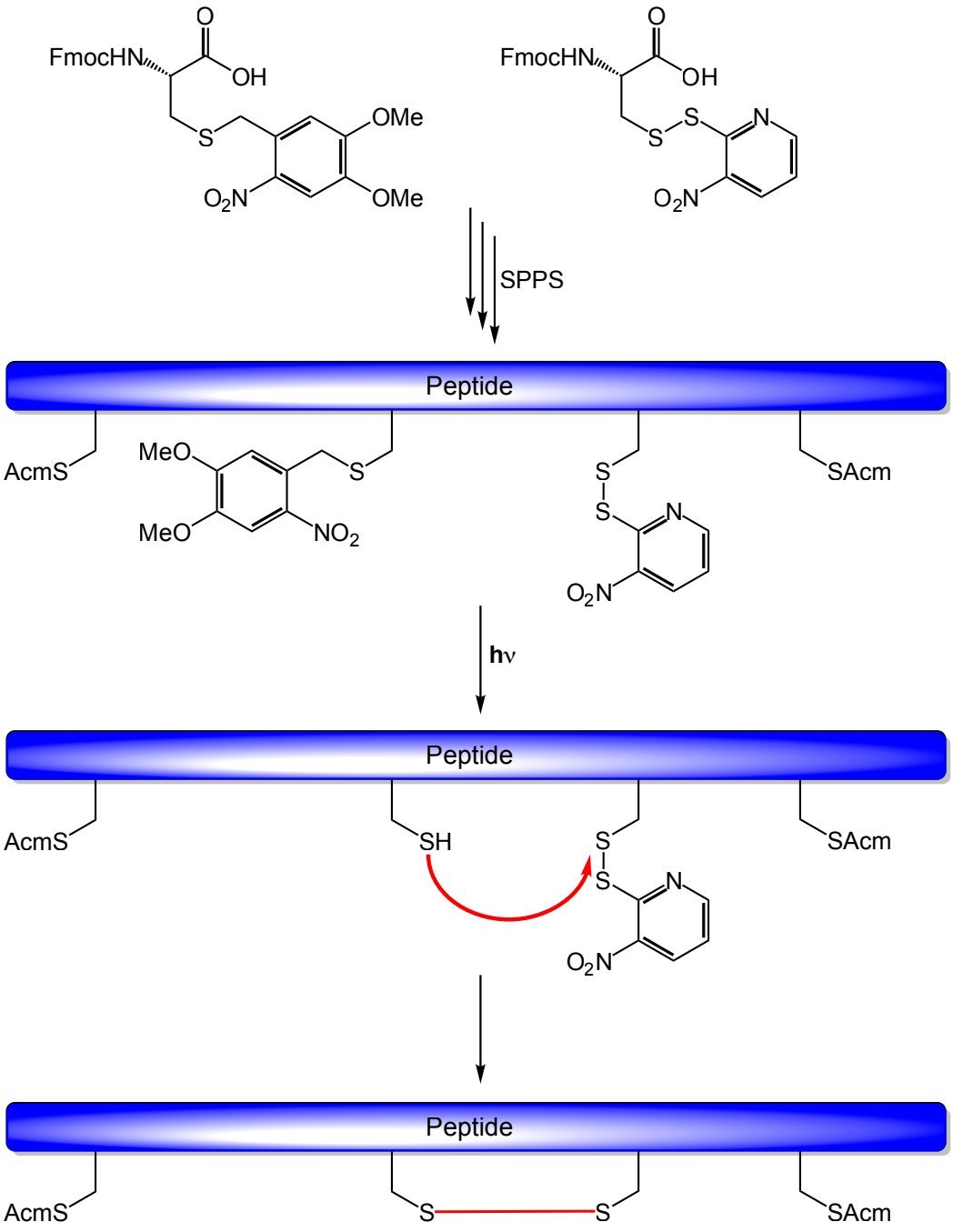
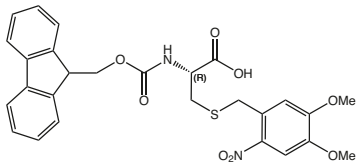
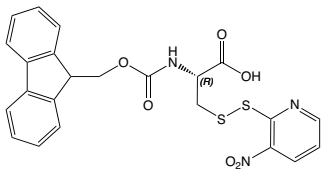
5. *o*-Nitroveratryl Protected Cysteine for Disulfide Bridge Formation

2-Nitroveratryl (oNv) is a photolabile orthogonal protecting group that is compatible with SPPS protocols and can be cleaved by irradiation with UV light (350 nm) under ambient conditions. Combination with S-pyridinesulfenyl activation allows for rapid *in situ* disulfide bond formation. In order to demonstrate the versatility of this approach, it was applied to the synthesis of a number of model peptides: oxytocin, alpha-conotoxin ImI, and human insulin.



Selective deprotection of 2-nitroveratryl in the presence of other cysteine protecting groups, and subsequent disulfide bond formation with an Npys-functionalized cysteine.

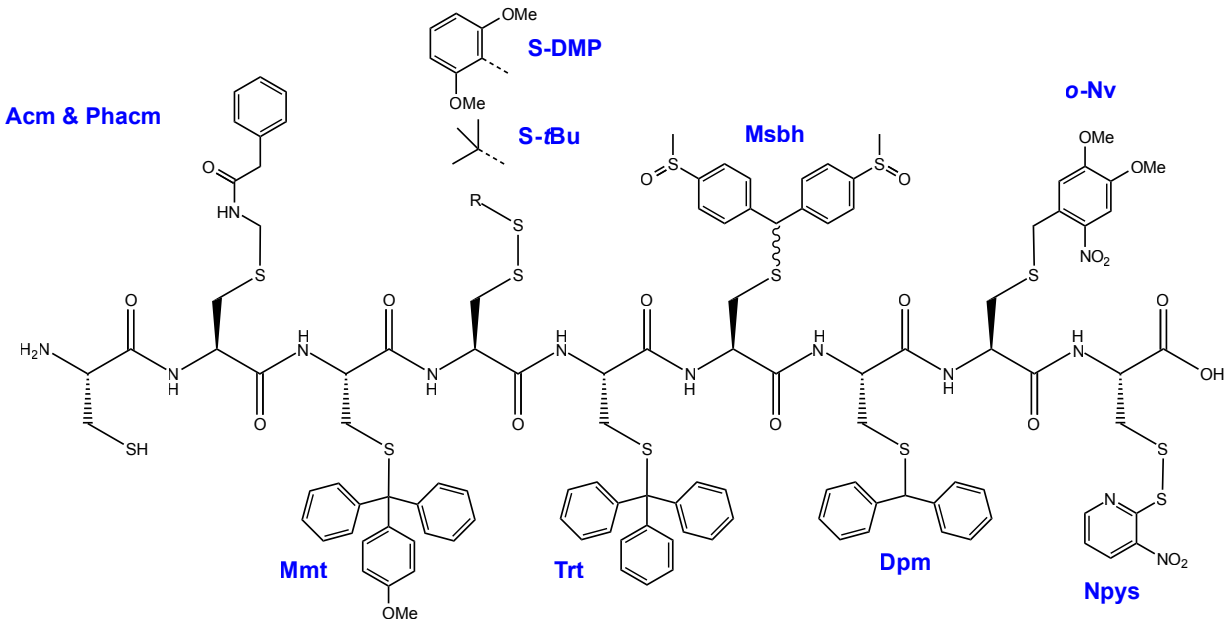
		Article No.	Quantity	Price
FAA3970	**Fmoc-L-Cys(oNv)-OH**	FAA3970.0250	250 mg	€ 475,00
N-alpha-(9-Fluorenylmethyloxycarbonyl)-S-(2-nitroveratryl)-L-cysteine		FAA3970.1000	1 g	€ 1.400,00
CAS NO: **214633-71-3**				
FORMULA: $C_{27}H_{26}N_2O_8S$				
MOLECULAR WEIGHT: **538,57 g/mol**				
FAA1975	**Fmoc-L-Cys(Npys)-OH**	FAA1975.0001	1 g	€ 275,00
N-alpha-(9-Fluorenylmethyloxycarbonyl)-S-(3-nitro-2-pyridylthio)-L-cysteine		FAA1975.0005	5 g	€ 850,00
FORMULA: $C_{23}H_{19}N_3O_6S_2$				
MOLECULAR WEIGHT: **497,54 g/mol**				

References:

- Karas J.A., Scanlon D.B., Forbes B.E., Vetter I., Lewis R.J., Gardiner J., Separovic F., Wade J.D., Hossain M.A.; 2-Nitroveratryl as a Photocleavable Thiol-Protecting Group for Directed Disulfide Bond Formation in the Chemical Synthesis of Insulin; *Chem. Eur. J.* 2014; **20:** 9549-9552. DOI: 10.1002/chem.201403574

Is one set of orthogonal side chain protecting groups for Cysteine not enough?

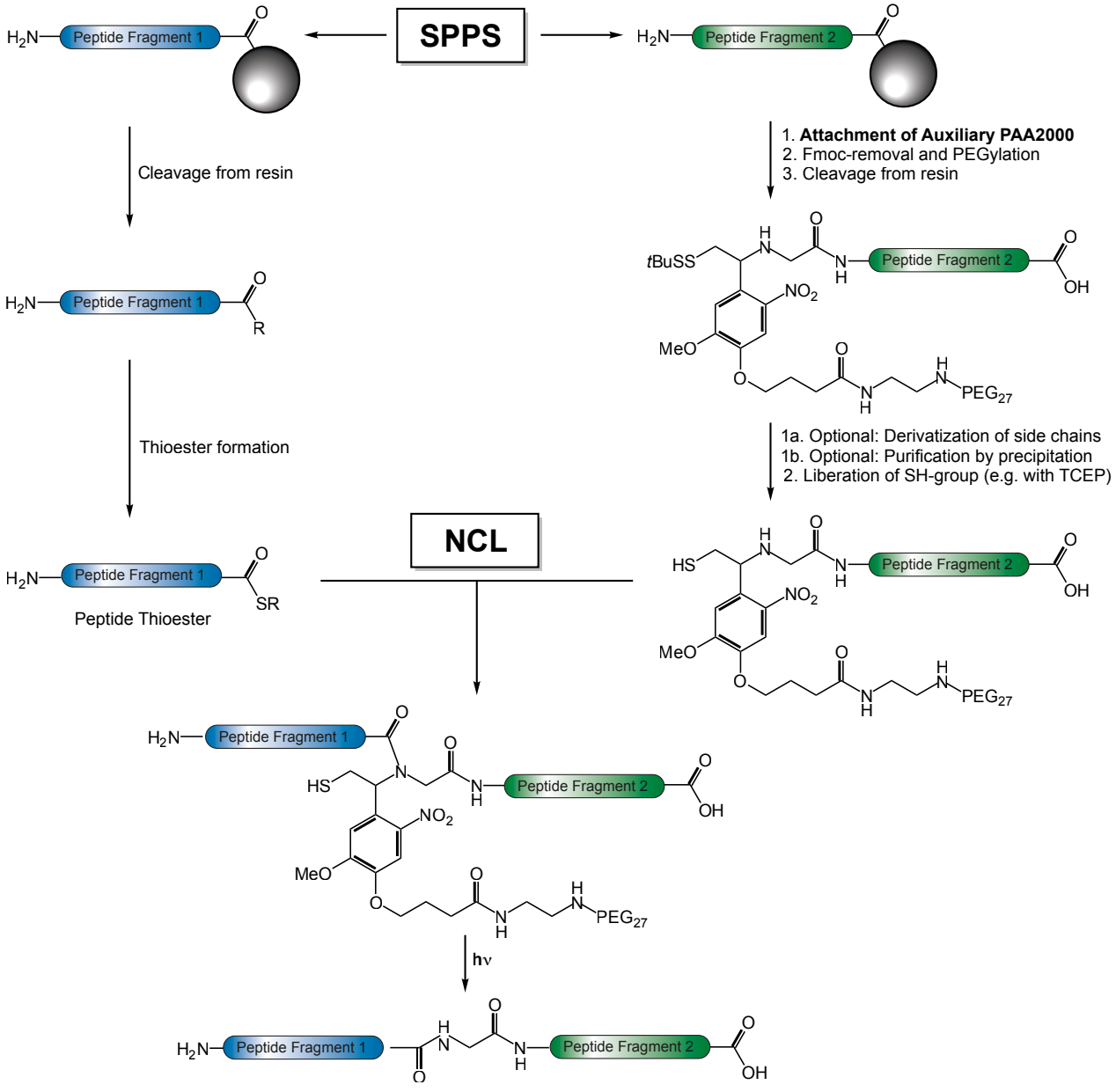
Iris Biotech offers a whole range of Cys protecting groups for disulfide bond formation:



6. Photocleavable Auxiliary Reagent for Native Chemical Ligation

Native Chemical Ligation is one of the most powerful tools for the preparation of complex peptides and small proteins. However, the classical variant of NCL requires an N-terminal cysteine at the ligation site. Iris Biotech presents an innovative auxiliary reagent for NCL that can be incorporated in place of a glycine residue.

Since glycine usually occurs several times in a peptide sequence, this approach significantly increases variability regarding the choice of possible ligation sites. In Native Chemical Ligation, the auxiliary's SH-group mimics the action of an N-terminal cysteine's sulfhydryl group.



Native Chemical Ligation utilizing the photocleavable NCL-auxiliary glycine building block (PAA2000).

Following SPPS, the auxiliary 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 monodisperse PEG. PEGylation is useful for increasing the solubility of peptide fragments, and for facilitating their purification by precipitation with EtOH/Et_2O. These properties are especially valuable if the peptide's amino acid side chains are supposed to be further derivatized post-SPPS, for example by enzymatic glycosylation. Following NCL, the auxiliary can be conveniently removed by irradiation with UV-light (10 min in water or water/acetonitrile). This method is particularly useful for the synthesis of sophisticated peptides such as glycopeptides, where cost- and labor-intensive short sequences can be prepared separately, and subsequently conjugated to long fragments synthesized in a standard manner.

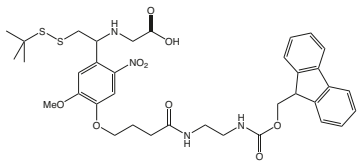
Article No.	Quantity	Price
PAA2000.0025	25 mg	€ 300,00
PAA2000.0100	100 mg	€ 750,00

PAA2000 tBu-SS-Photo(Fmoc)-Gly-OH

Photocleavable-NCL-auxiliary-Gly-OH

FORMULA: $C_{36}H_{44}N_4O_9S_2$

MOLECULAR WEIGHT: **740,89 g/mol**



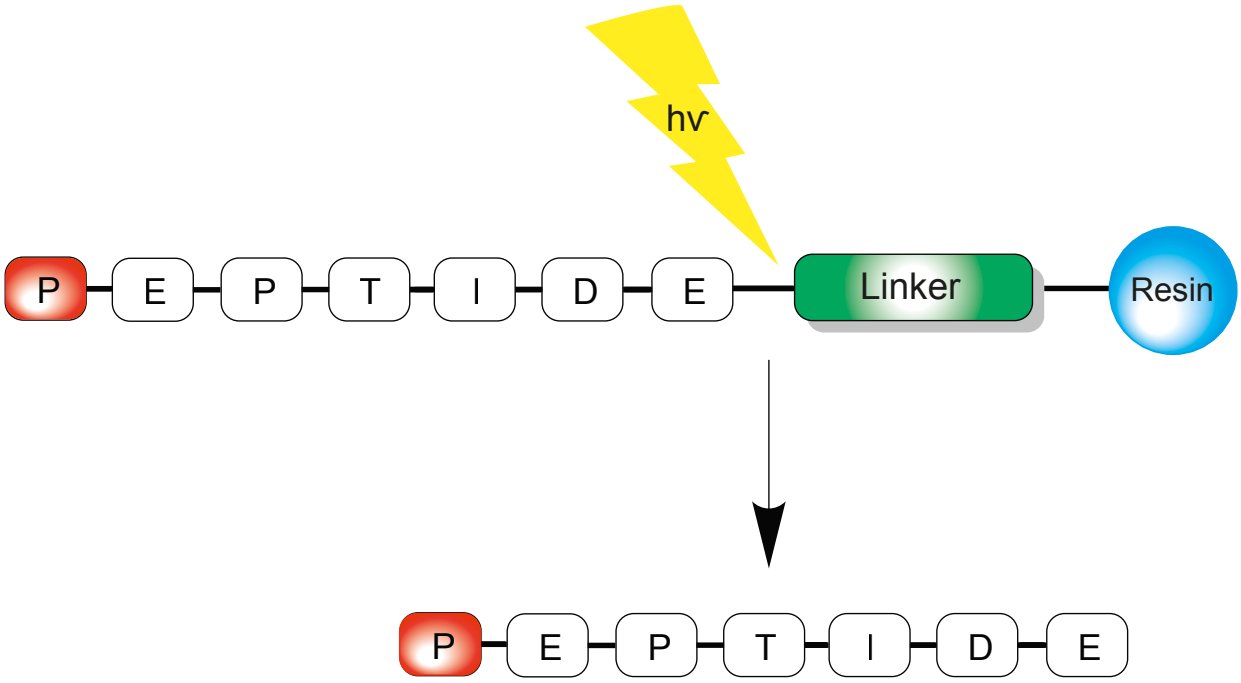
References:

- Ein PEGyliertes, lichtspaltbares Auxiliar für die sequenzielle enzymatische Glykosylierung und native chemische Ligation von Peptiden; Claudia Bello, Shuo Wang, Lu Meng, Kelly W. Moremen, Christian Becker; *Angew. Chem.* 2015; **127:** 7823-7828; DOI:10.1002/ange.201501517.
- A PEGylated Photocleavable Auxiliary Mediates the Sequential Enzymatic Glycosylation and Native Chemical Ligation of Peptides; Claudia Bello, Shuo Wang, Lu Meng, Kelly W. Moremen, Christian Becker; *Angew. Chem. Int. Ed.* 2015; **54:** 7711-7715; DOI:10.1002/anie.201501517.

Notes

7. Photo-Linker for Solid Phase Synthesis of Peptide Amides and Acids

Peptide linkers are usually cleaved under acidic conditions or using two-step procedures. Photocleavage proceeds under neutral conditions using UV light and can either be performed in batch or using flow chemistry.



Furthermore, photolabile linkers are orthogonal to standard peptide chemistry reaction conditions, thus enabling the use of a wide variety of amino acid protecting groups. Two different photolabile linkers are available for your convenience:

Photo-linker for the synthesis of C-terminal carboxylic acids

Article No.	Quantity	Price
RL-2150.0250	250 mg	€ 175,00
RL-2150.1000	1 g	€ 350,00
RL-2150.5000	5 g	€ 1.400,00

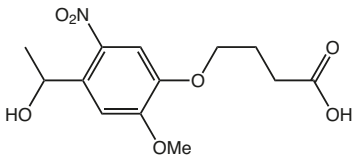
RL-2150 **Acid-Photo-Linker**

4-(4-(1-hydroxyethyl)-2-methoxy-5-nitrophenoxy)butanoic acid

CAS NO: **175281-76-2**

FORMULA: $C_{13}H_{17}NO_7$

MOLECULAR WEIGHT: **299,28 g/mol**



Fmoc-amino photo-linker for the synthesis of peptide amides

Article No.	Quantity	Price
RL-1026.0001	1 g	€ 250,00
RL-1026.0005	5 g	€ 900,00

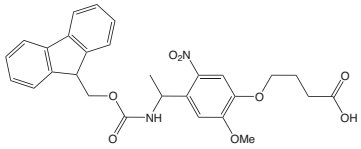
RL-1026 **Fmoc-Photo-Linker**

4-{4-[1-(9-Fluorenylmethyloxycarbonylamino)ethyl]-2-methoxy-5-nitrophenoxy}butanoic acid

CAS NO: **162827-98-7**

FORMULA: $C_{28}H_{28}N_2O_8$

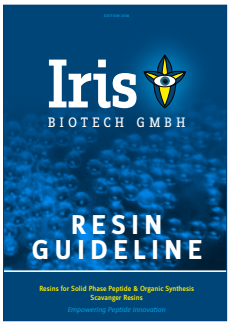
MOLECULAR WEIGHT: **520,56 g/mol**

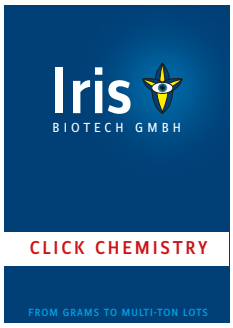


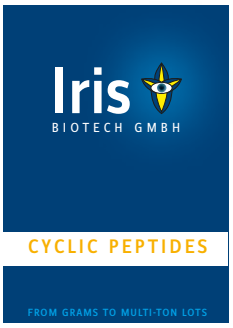
References:

- Continuous Photochemical Cleavage of Linkers for Solid-Phase Synthesis; M. Hurevich, J. Kandasamy, B. M. Ponnappa, M. Collot, D. Kopetzki, D. T. McQuade and P. H. Seeberger; *Organic Letters* 2014; **16:** 1794-1797. doi:10.1021/ol500530q
- Photolytic Mass Laddering for Fast Characterization of Oligomers on Single Resin Beads; K. Burgess, C. I. Martinez, D. H. Russell, H. Shin and A. J. Zhang; *The Journal of Organic Chemistry* 1997; **62:** 5662-5663. doi:10.1021/jo970866w
- Direct Monitoring of Organic Reactions on Polymeric Supports; M. R. Carrasco, M. C. Fitzgerald, Y. Oda and S. B. H. Kent; *Tetrahedron Letters* 1997; **38:** 6331-6334. doi:http://dx.doi.org/10.1016/S0040-4039(97)01456-1

Available Booklets:







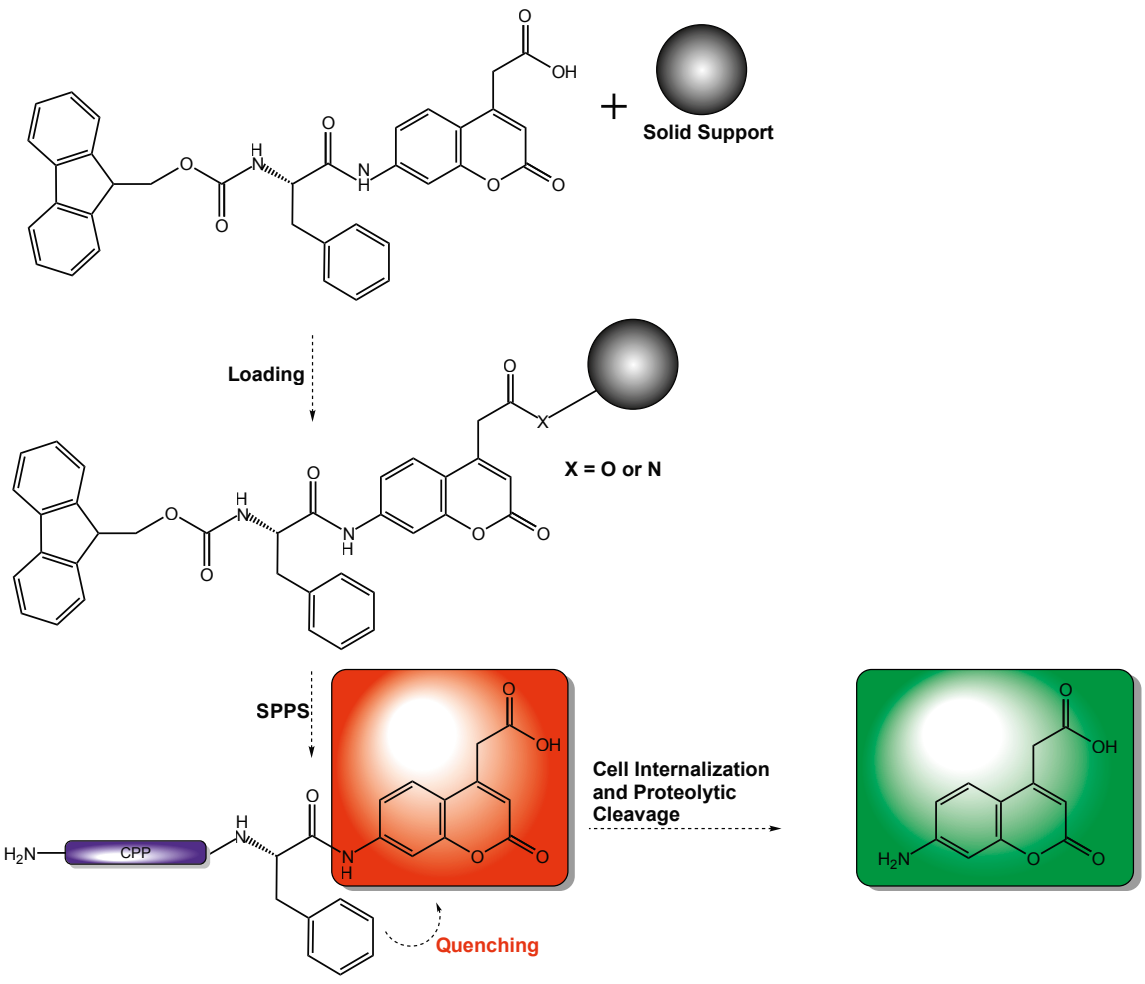
Order our Free Iris Booklets here:

8. Related Products

8.1. Fmoc-Phe-Aca: Fluorescent Internalization Reporter for Cell Penetrating Peptides (CPPs)

The unnatural amino acid Aca (7-amino-coumarin-4-acetic acid) is a coumarin derivative and thus exhibits fluorescence. When incorporated into a peptide C-terminally of phenylalanine, Aca is a useful reporter group for the successful internalization of CPPs. The phenyl moiety of Phe quenches the fluorescence of Aca. Internalization of the CPP containing Phe-Aca leads to proteolytic cleavage of the Phe-Aca bond and thus to fluorescence.

However, the peptide bond formation between Phe and Aca is considered to be a difficult coupling and often leads to low coupling yields. For your convenience, Iris Biotech offers Fmoc Phe-Aca as building block suitable for SPPS. This pseudodipeptide can be coupled to the resin of your choice and subsequently elongated to prepare your target cell penetrating peptides.



Loading of a solid support, subsequent elongation to CPPs and function as a reporter group for successful CPP internalization.

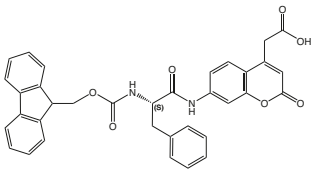
Article No.	Quantity	Price
FDP1240.0100	100 mg	€ 195,00
FDP1240.0001	1 g	€ 1.250,00

FDP1240 Fmoc-L-Phe-Aca-OH

7-[N-alpha-(9-Fluorenylmethyloxycarbonyl)-L-phenylalaninyl-amido]-coumarin-4-acetic acid

FORMULA: $C_{35}H_{28}N_2O_7$

MOLECULAR WEIGHT: **588,61 g/mol**

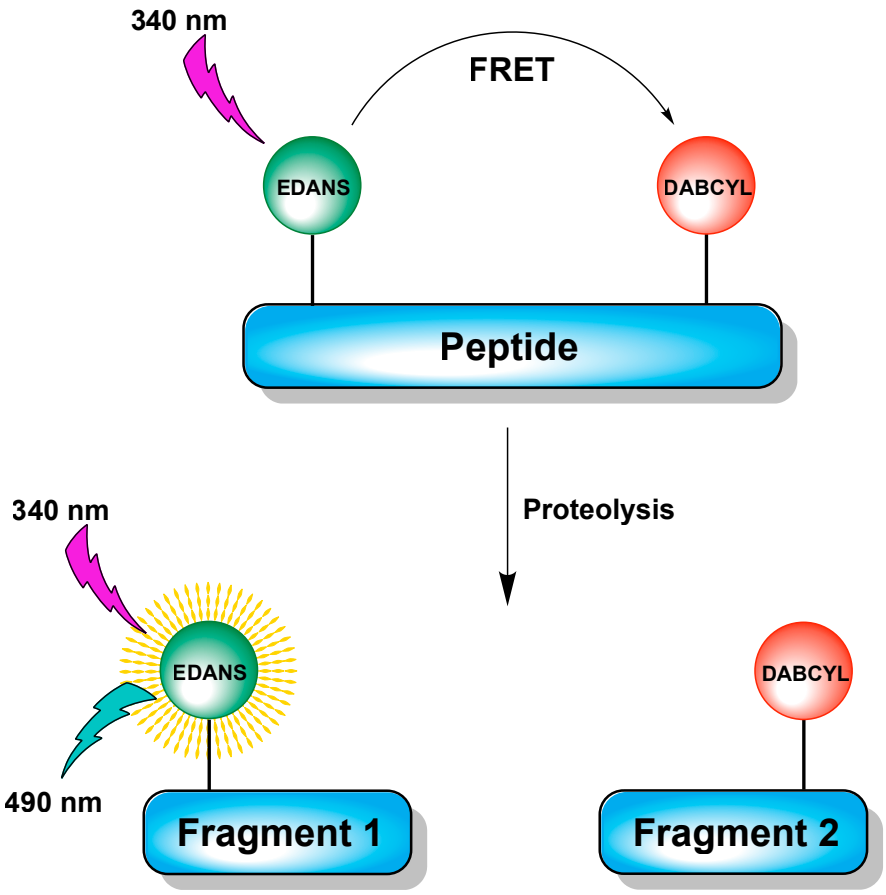


References:

- Rapid and general profiling of protease specificity by using combinatorial fluorogenic substrate libraries; J. L. Harris, B. J. Backes, F. Leonetti, S. Mahrus, J. A. Ellman and C. S. Craik; *Proceedings of the National Academy of Sciences* 2000; **97:** 7754-7759. doi:10.1073/pnas.140132697
- Expedient Solid-Phase Synthesis of Fluorogenic Protease Substrates Using the 7-Amino-4-carbamoylmethylcoumarin (ACC) Fluorophore; D. J. Maly, F. Leonetti, B. J. Backes, D. S. Dauber, J. L. Harris, C. S. Craik and J. A. Ellman; *The Journal of Organic Chemistry* 2002; **67:** 910-915. doi:10.1021/jo016140o

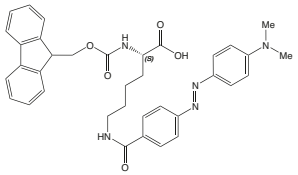
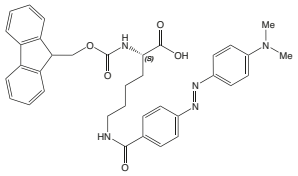
8.2. Building Blocks for the SPPS of FRET-based fluorogenic protease substrates

The classic FRET pair EDANS and DABCYL is now available linked to Fmoc amino acid building blocks that can be readily used in SPPS. Conveniently synthesize your own custom protease substrates!



Screening of protease activity using FRET-based fluorogenic protease substrates

Traditionally, fluorogenic protease substrates for the screening of protease activity are prepared by peptide synthesis and subsequent regioselective deprotection and functionalization with a fluorophore/quencher pair such as EDANS and DABSYL. For your convenience, we now offer a glutamate and a lysine building block functionalized with EDANS and DABSYL, respectively. Those building blocks are suitable for peptide synthesis using the Fmoc strategy and will allow you to prepare custom protease substrates without additional tedious and yield-reducing functionalization steps post-SPPS.

		Article No.	Quantity	Price
FAA1498 Fmoc-L-Lys(Dabcyl)-OH **N-alpha-(9-Fluorenylmethyloxycarbonyl)-N-epsilon-4-[4'-(dimethylamino)phenylazo] benzoyl-L-lysine** CAS NO: **146998-27-8** FORMULA: $C_{36}H_{37}N_5O_5$ MOLECULAR WEIGHT: **619,73 g/mol**		FAA1498.0500 FAA1498.0001 FAA1498.0005 FAA1498.0025	500 mg 1 g 5 g 25 g	€ 108,00 € 168,00 € 600,00 € 2.400,00
FAA1498 Fmoc-L-Lys(Dabcyl)-OH **N-alpha-(9-Fluorenylmethyloxycarbonyl)-N-epsilon-4-[4'-(dimethylamino)phenylazo] benzoyl-L-lysine** CAS NO: **146998-27-8** FORMULA: $C_{36}H_{37}N_5O_5$ MOLECULAR WEIGHT: **619,73 g/mol**		FAA1498.0500 FAA1498.0001 FAA1498.0005 FAA1498.0025	500 mg 1 g 5 g 25 g	€ 108,00 € 168,00 € 600,00 € 2.400,00

References:

- Enzymatic activity characterization of SARS coronavirus 3C-like protease by fluorescence resonance energy transfer technique; S. Chen, L.-l. Chen, H.-b. Luo, T. Sun, J. Chen, F. Ye, J.-h. Cai, J.-k. Shen, X. Shen and H.-l. Jiang; *Acta Pharmacol Sin* 2005; **26:** 99-106.
- Synthesis and evaluation of fluorescent probes for the detection of calpain activity; S. Mittoo, L. E. Sundstrom and M. Bradley; *Analytical Biochemistry* 2003; **319:** 234-238. doi:http://dx.doi.org/10.1016/S0003-2697(03)00324-5
- A general method for the preparation of internally quenched fluorogenic protease substrates using solid-phase peptide synthesis; L. L. Maggiora, C. W. Smith and Z. Y. Zhang; *Journal of Medicinal Chemistry* 1992; **35:** 3727-3730. doi:10.1021/jm00099a001
- Novel fluorogenic substrates for assaying retroviral proteases by resonance energy transfer; E. Matayoshi, G. Wang, G. Krafft and J. Erickson; *Science* 1990; **247:** 954-958. doi:10.1126/science.2106161
- Design and synthesis of new fluorogenic HIV protease substrates based on resonance energy transfer; G. T. Wang, E. Matayoshi, H. Jan Huffaker and G. A. Krafft; *Tetrahedron Letters* 1990; **31:** 6493-6496. doi:http://dx.doi.org/10.1016/S0040-4039(00)97099-0

Notes

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 the product 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.

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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 2010 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.

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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.

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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.

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General

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

Notes

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