EDITION 2020

Iris BIOTECH GMBH

LINKEROLOGY

Advanced Linker Technology for Antibody-Drug Conjugation (ADC) and other Bioconjugations

Empowering Peptide Innovation

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1. The Concept of Antibody-Drug Conjugation (ADC)

1.1. Technical and Market Background

Conjugating highly potent small molecules to vastly target specific biomolecules, like antibodies, has become a modern and sophisticated approach, particularly in the field of cancer therapy. The list of ADCs in clinics continues to grow, bolstered by the success of two pioneers in this field:

Adcetris® (Seattle Genetics) has been approved in 2011 for the treatment of Hodgkin's lymphoma and systemic anaplastic large cell lymphoma (ALCL) and reached $476.9 million sales per year in 2018. This drug is composed of a monoclonal antibody targeting CD30 conjugated to four molecules of monomethyl auristatin E *via* self-immolative linkage (Fig. 1). Reduction of interchain disulfide bonds provides reactive cysteine residues, which are then conjugated with maleimide payload linker systems yielding the final drug compound.

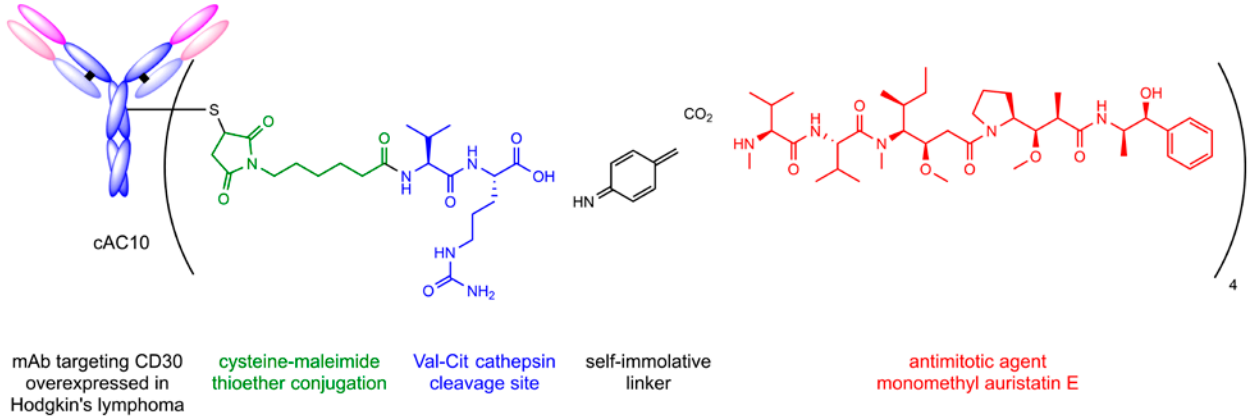


Fig. 1: Composition of Adcetris®, one of the first FDA-approved ADCs.

Kadcyla®, another pioneer in this field, has been approved in 2013 for the treatment of HER-2 positive metastatic breast cancer and reached $981 million sales per year in 2018. In this case payloads are conjugated to surface accessible lysines resulting in a heterogeneous modification of the core antibody.

Reference:

- Antibody-drug conjugates in tumor therapy; B. Sammet, C. Steinkuhler and N. Sewald; *Pharm Pat Anal* 2012; **1**: 65-73. https://doi.org/10.4155/ppa.12.4.

IC_{50}
Inhibitory Concentration
Concentration causing 50% of maximal inhibition of the desired activity.

EC_{50}
Effective Concentration
Concentration causing 50% of maximal response of the desired effect.

ED_{50}
Effective Dose
Dose causing the desired effect in 50% of individuals.

GI_{50}
Growth Inhibition
Concentration causing 50% inhibition of cell proliferation/cell growth.

TC_{50}
Toxic Concentration
Concentration causing a defined toxic effect in 50% of individuals.

TD_{50}
Toxic Dose
Dose causing a defined toxic effect in 50% of individuals.

CC_{50}
Cytotoxic Concentration
Concentration killing 50% of cells.

LC_{50}
Lethal Concentration
Concentration killing 50% of individuals.

LD_{50}
Lethal Dose
Dose killing 50% of individuals.

ADCs - Mode of Action

The typical mode of action of ADCs is shown in Figure 2. An ADC circulates in plasma until it reaches the target cell. The antibody portion of an ADC then nails onto a cell-surface antigen that is ideally specific to a cancer cell. Upon binding, the ADC-antigen protein complex becomes internalized into the cancer cell. When the complex is degraded, it releases the cytotoxin which then binds to its target to cause cancer cell apoptosis. The linker between antibody and payload is typically either permanent or clevable by hydrolases, like the protease cathepsin B, by glucoronidases or through reductive conditions and the presence of glutathion.

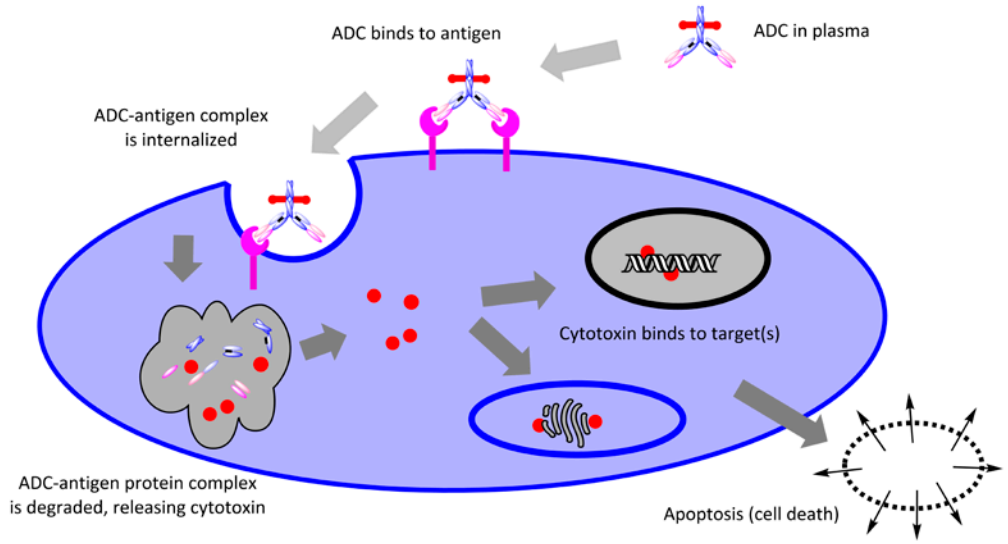


Fig. 2: Mode of action of ADCs.

This concept is a sophisticated approach combining high specificity of antibodies and high potency of (small) drug molecules. The disadvantages of antibodies, like low potency, as well as the drawbacks of small drug molecules, like low specificity accompanied by high toxicity through many side effects, are compensated by the advantages of the other counterpart. A smart synergistic combination of both enlarges significantly the narrow therapeutic window of a small drug molecule between minimum (efficacious) and maximum (toxic) dosage (Fig. 3). ADC drugs expand the therapeutic window, as they can increase efficacy and decrease toxicity in comparison to traditional chemotherapeutic cancer treatments. Specific delivery to cancer cells increases the amount of dosed drug reaching the tumor, thus lowering the minimum effective dose (MED). The maximum tolerated dose (MTD) is increased, as less drug reaches healthy, non-target tissues. Hence, the use of ADCs enlarges the therapeutic window.

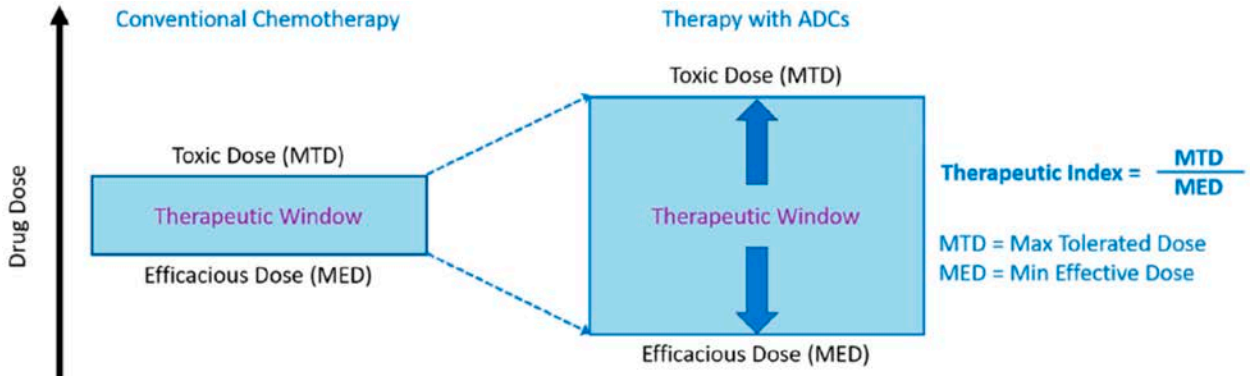


Fig. 3: The therapeutic window is significantly enlarged using ADCs compared to small-molecule drugs.

References:

- L. Anthony, (2019). ADC Landscape Review 2019 [PowerPoint slides]. Retrieved from http://worldadc-usa.com.
- Design and Synthesis of Tesirine, a Clinical Antibody-Drug Conjugate Pyrrolobenzodiazepine Dimer Payload; A. C. Tiberghien, J. N. Levy, L. A. Masterson, N. V. Patel, L. R. Adams, S. Corbett, D. G. Williams, J. A. Hartley and P. W. Howard; *ACS Med Chem Lett* 2016; **7**: 983-987. https://doi.org/10.1021/acsmedchemlett.6b00062.

In 2019 there have been some 100 ADCs in various phases of clinical development, of which some 20 ADCs were carrying auristatins, PBD derivatives, and maytansines, respectively (Fig. 4).

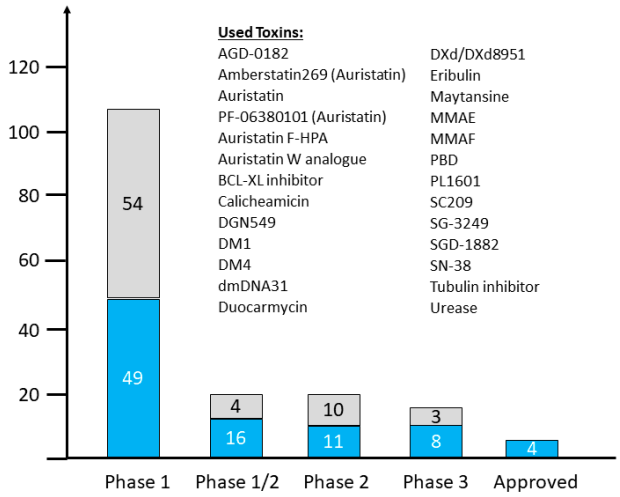


Fig. 4: ADCs in clinical phases (2019).

While initially only small molecules or short peptides have been used, the panel of conjugates has opened to chelators for radioactive nuclides and larger biomolecules, like toxic enzymes. Additional variations have been introduced on the antibody side by utilizing antibody fragment combinations or diabodies (Fig. 5).

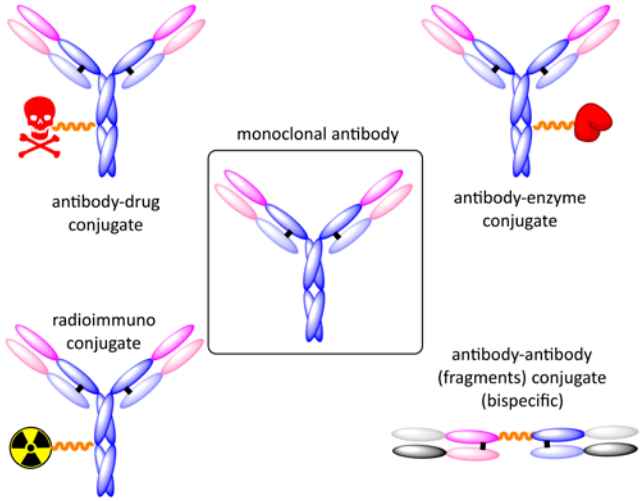


Fig. 5: The concept of antibody-drug conjugation can be extended from conjugations of small cytotoxic molecules to conjugation with chelators for radionuclides, proteins or with antibody fragments.

Points of conjugation are typically the thiol groups of cysteines, the amino functions of lysines or the N-terminus of a monoclonal antibody. Due to the inherent heterogeneity of conjugation to the multiple amines or cysteines found in mAbs, significant research efforts are directed toward the production of discrete, homogeneous ADC products, *via* site-specific conjugation. This may involve genetic engineering of the mAb to introduce discrete, available cysteines or non-natural amino acids with an orthogonally reactive functional handle such as an aldehyde, ketone, azido, or alkynyl tag. These site-specific approaches increase the homogeneity of ADCs and enable novel biorthogonal chemistries which utilize reactive moieties rather than thiol or amine. This broad diversity of applicable linkers can then be utilized leading to improved design in future generations of ADCs.

References:

- Site-specific antibody drug conjugates for cancer therapy; S. Panowski, S. Bhakta, H. Raab, P. Polakis and J. R. Junutula; *MAbs* 2014; **6**: 34-45. https://doi.org/10.4161/mabs.27022.
- Advances in Precision Oncology: Targeted Thorium-227 Conjugates As a New Modality in Targeted Alpha Therapy; U. B. Hagemann, K. Wickstroem, S. Hammer, R. M. Bjerke, S. Zitzmann-Kolbe, O. B. Ryan, J. Karlsson, A. Scholz, H. Hennekes, D. Mumberg and A. S. Cuthbertson; *Cancer Biother Radiopharm* 2020; **0**. https://doi.org/10.1089/cbr.2020.3568.

1.2. Linker Design, Connectivity, Degradability, and Drug-Antibody Ratio (DAR)

Antibody-drug conjugates (ADCs), which combine the specificity, favorable pharmacokinetics, and biodistribution of a monoclonal antibody (mAb) with the cytotoxic potency of a drug are promising new therapeutics for cancer. Along with the development of monoclonal antibodies (mAbs) and cytotoxic drugs, the design of the linker is essential, as it impacts the efficacy and tolerability of ADCs. The linker needs to provide sufficient stability during systemic circulation while providing rapid and efficient release of the cytotoxic drug in its active state inside the tumor cells.

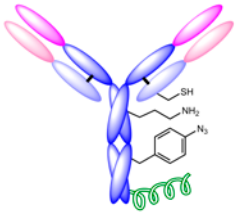
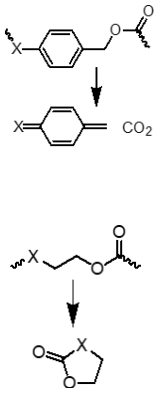
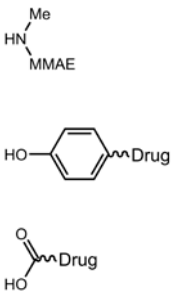
Antibody	Linker			Payload
Natural Connectivities: thiols (Cys) amines (Lys) 	Conjugation	Cleavable Part	Traceless Part	
	Chemically: maleimide disulfide acid/active ester Click tetrazine/TCO His-Tag specific acylation	**Hydrolases:** Val-Ala Val-Cit Phe-Lys Gly-Phe-Leu-Gly Ala-Leu-Ala-Leu cyclobutyl-Ala cyclobutyl-Cit glucuronic acid	 X = NH, S	
Artificial Connectivities: azides and alkynes peptides (ligases) His-Tag	**Enzymatically:** $(Gly)_3$-linker ligase substrate	**Oxidoreductases:** $-CH_2-S-S-CH_2-$ $-CH_2-S-S-CHMe-$ $-CH_2-S-S-CMe_2-$		

Fig. 6: Conceptual overview of antibody-drug conjugation.

The type of linkage between payload and biomolecule can basically be either permanent or cleavable under certain well-defined circumstances (Fig. 6). As payloads typically are highly cytotoxic, it would be fatal if they would be released from their carrier during circulation in plasma. Hence, the linker part should be stable to conditions like pH, redox potential, presence of proteases in plasma, and all other parameters of plasma. However, after internalization it is favorable that the linker is fragmentizing in order to release the drug molecule, ideally in a traceless manner.

Conjugations with the antibody can rather easily be achieved using active esters forming amide bonds with lysines, which are usually accessible in a high number on the surface. The resulting conjugate, hence, is rather heterogenic with different numbers of payloads attached at different positions.

A more and well-defined drug-antibody ratio (DAR) can be achieved by utilizing the disulfide bridges between heavy and light chains of the antibody. After reductive cleavage of the disulfide bonds, conjugation chemistry can be performed by different kinds of reactions like conventional maleimides or disulfide bond formation. Heterogeneity can be observed if heavy and light antibody chains do not recombine in the original manner.

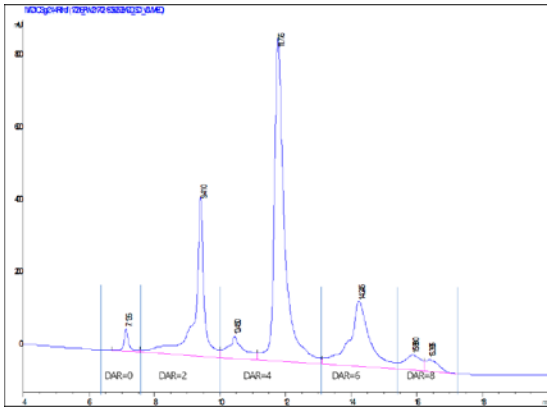


Fig. 7: Drug-antibody ratio (DAR) is an important parameter of ADC. Low DAR could reduce the antitumor efficacy, while high DAR may affect antibody structure, stability, and antigen binding etc. therefore causing loss of activity. DAR values are also important for the therapeutic index of ADCs. In most ADC drug candidates, the DAR values were maintained at about 2-4. Hence, controlling DAR during ADC preparation is a key procedure. Figure provided by Glycotope.

A highly accurate and specific DAR with well-defined connectivity can be achieved, if unnatural amino acids, e.g., *p*-azidophenylalanine, can recombinantly be introduced. Click chemistry or other Diels-Alder type reactions can be used to introduce linkers and payloads. In a similar manner certain peptide fragments can be added, which serve as substrates for ligases in order to conjugate to appropriate linker-payload conjugates.

Reference:

- Linker Technologies for Antibody-Drug Conjugates; B. Nolting; *Antibody-Drug Conjugates* L. Ducry 2013; **1045**: 71-100. https://doi.org/10.1007/978-1-62703-541-5_5.

Cleavage Mechanisms

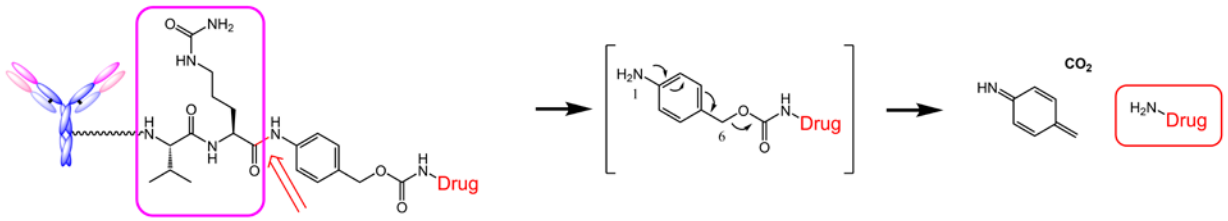


Fig. 8: Valyl-citrullyl dipeptide fragment serves as substrate for cathepsin and suffers cleavage by hydrolysis leading to a 1,6-elimination with fragmentation and traceless release of the drug molecule.

An ADC travels through plasma until it reaches the target cell. After internalization, the complex degrades and releases the payload even with a stable linker. However, release can be accelerated through implementation of moieties which fragmentize under certain conditions. One of the most commonly used spacers is the bifunctional *p*-aminobenzyl alcohol group, which is linked to the peptide through the amino group forming an amide bond, while amine containing cytotoxic drugs are attached through carbamate functionalities to the benzylic hydroxyl group of the linker. The resulting prodrugs are activated upon protease mediated hydrolysis and cleavage of the amide bond of citrulline to the *p*-aminobenzyl fragment, leading to a 1,6-elimination reaction releasing the unmodified drug, carbon dioxide, and remnants of the linker group (Fig. 8, Fig. 9).

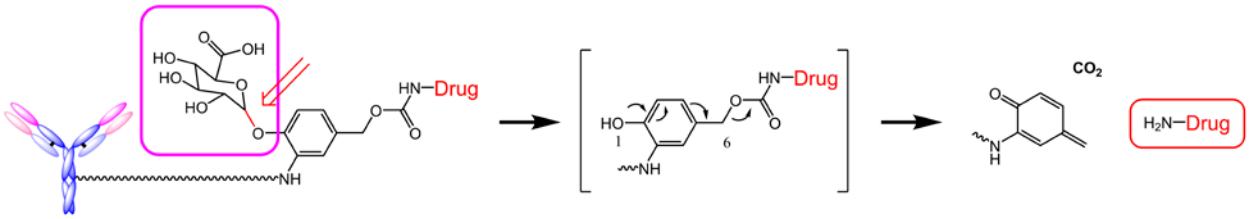


Fig. 9: Glucuronic acid capped p-aminobenzyl will be cleaved by glucuronidases resulting in 1,6-elmination, fragmentation, and traceless release of the drug molecule.

In an extension to the peptide-based linker strategies to provide high ADC stability, β-glucuronic acid-based linkers were developed. Facile release of the active drug is realized through cleavage of the β-glucuronide glycosidic bond by the lysosomal enzyme β-glucuronidase. This enzyme is abundantly present in lysosomes and overexpressed in some tumor types, while its activity outside cells is low. The linker is hydrophilic, stable against circulation, and provides ADCs that are highly active both *in vitro* and *in vivo*.

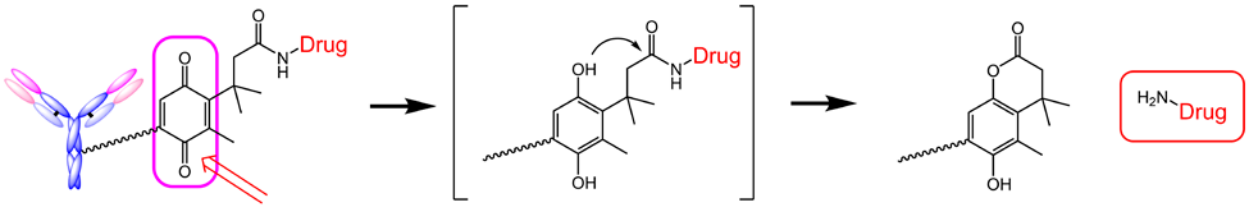
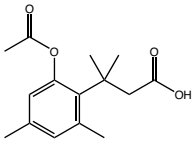
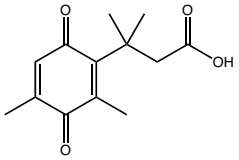
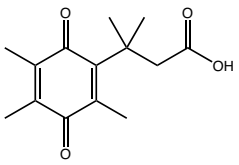
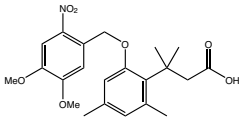
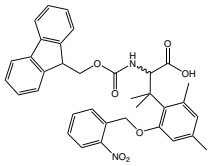
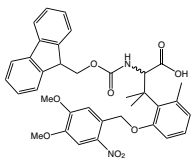


Fig. 10: Chinoidic variations of trimethyl locks are reduced to the corresponding diphenol followed by traceless release of a drug molecule via lacton formation.

Besides hydrolases, the presence of oxidoreductases in the lysosome is being utilized for the design of cleavable linkers. Cytochrome P450 oxidoreductase (CPR), nitroquinone oxidoreductase 1 (NQO1), and cellular reductants such as glutathione (GSH) transform reducible fragments like chinone or disulfide to self-immolative intermediates.

Trimethyl Lock

The sterical demand of three closely positioned methyl groups (Fig. 10) favors the cleavage of a carbonyl bond by lacton formation. The acidity of phenol is sufficient to accelerate lactonization at neutral pH and any residue carrying a hydroxyl or amino function will be unlocked, i.e. tracelessly released. The hydroxy group of phenol can be protected and released by a variety of methodologies. This reaction usually requires no elevated temperature. Hence, it will work nicely at physiological conditions.

		Article No.	Quantity	Price
RL-2960 Acetyl-Trimethyl-Lock 3-(2-Acetoxy-4,6-dimethylphenyl)-3-methylbutyric acid CAS-NO: 134098-68-3 FORMULA: $C_{15}H_{20}O_4$ MOLECULAR WEIGHT: 264,14 g/mol			please inquire!	
RL-2950 Fourmethyl-Lock 3-(2,4-dimethyl-3,6-dioxocyclohexa-1,4-dienyl)-3-methylbutanoic acid CAS-NO: 133544-77-1 FORMULA: $C_{13}H_{16}O_4$ MOLECULAR WEIGHT: 236,26 g/mol			please inquire!	
RL-2940 Fivemethyl-Lock 3-methyl-3-(2,4,5-trimethyl-3,6-dioxocyclohexa-1,4-dienyl)butanoic acid CAS-NO: 40662-29-1 FORMULA: $C_{14}H_{18}O_4$ MOLECULAR WEIGHT: 250,29 g/mol		RL-2940.0001	1 g	€ 1500,00
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			please inquire!	
FAA7190 Fmoc-Spr(oNB)-OH N-alpha-(9-Fluorenylmethyloxycarbonyl)-beta,beta-dimethyl-(2,4-dimethyl-6-(2-nitrobenzyloxy)phenyl)alanine (rac.) CAS-NO: 1032400-98-8 FORMULA: $C_{35}H_{34}N_2O_7$ MOLECULAR WEIGHT: 594,66 g/mol			please inquire!	
FAA7200 Fmoc-Spr(oNv)-OH N-alpha-(9-Fluorenylmethyloxycarbonyl)-beta,beta-dimethyl-(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			please inquire!	

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- Invention of stimulus-responsive peptide-bond-cleaving residue (Spr) and its application to chemical biology tools; A. Shigenaga, J. Yamamoto, T. Kohiki, T. Inokuma and A. Otaka; *J Pept Sci* 2017; **23**: 505-513. https://doi.org/10.1002/psc.2961.
- Trimethyl Lock: A Multifunctional Molecular Tool for Drug Delivery, Cellular Imaging, and Stimuli-Responsive Materials; O. A. Okoh and P. Klahn; *ChemBioChem* 2018; **19**: 1668-1694. https://doi.org/10.1002/cbic.201800269.

Disulfide Linkers

Disulfide linkers are likely first degraded in the lysosome to generate a cysteine-disulfide catabolite followed by disulfide reduction in the cytosol by cellular reductants such as GSH. The kinetics of reduction can be tailored by neighboring one to four methyl groups next to both sulfurs.

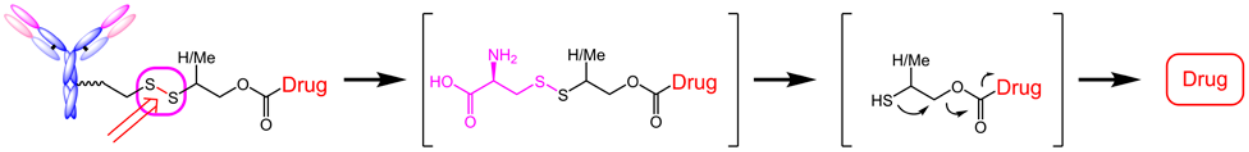

Fig. 11: Mechanism of disulfide bond cleavage in lysosomal compartments.

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- Modulating Therapeutic Activity and Toxicity of Pyrrolobenzodiazepine Antibody-Drug Conjugates with Self-Immolative Disulfide Linkers; T. H. Pillow, M. Schutten, S. F. Yu, R. Ohri, J. Sadowsky, K. A. Poon, W. Solis, F. Zhong, G. Del Rosario, M. A. T. Go, J. Lau, S. Yee, J. He, L. Liu, C. Ng, K. Xu, D. D. Leipold, A. V. Kamath, D. Zhang, L. Masterson, S. J. Gregson, P. W. Howard, F. Fang, J. Chen, J. Gunzner-Toste, K. K. Kozak, S. Spencer, P. Polakis, A. G. Polson, J. A. Flygare and J. R. Junutula; *Mol. Cancer. Ther.* 2017; **16**: 871-878. https://doi.org/10.1158/1535-7163.MCT-16-0641.
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- Expanded Utility of the beta-Glucuronide Linker: ADCs That Deliver Phenolic Cytotoxic Agents; S. C. Jeffrey, J. De Brabander, J. Miyamoto and P. D. Senter; *ACS Med Chem Lett* 2010; **1**: 277-80. https://doi.org/10.1021/ml100039h.

Multiple Payloads with one self-immolative Linker

p-Hydroxy- and *p*-amino-benzyl fragments will release payloads by a 1,6-elimination cascade resulting in chinoide intermediates. Under physiological conditions they readily add water to reform the aromatic ring structure. In case appropriate carbamate substitutions are also placed on position 2 and 2', a fragmentation will occur in a similar manner as by a 1,4-elimination and release any molecules at these positions.

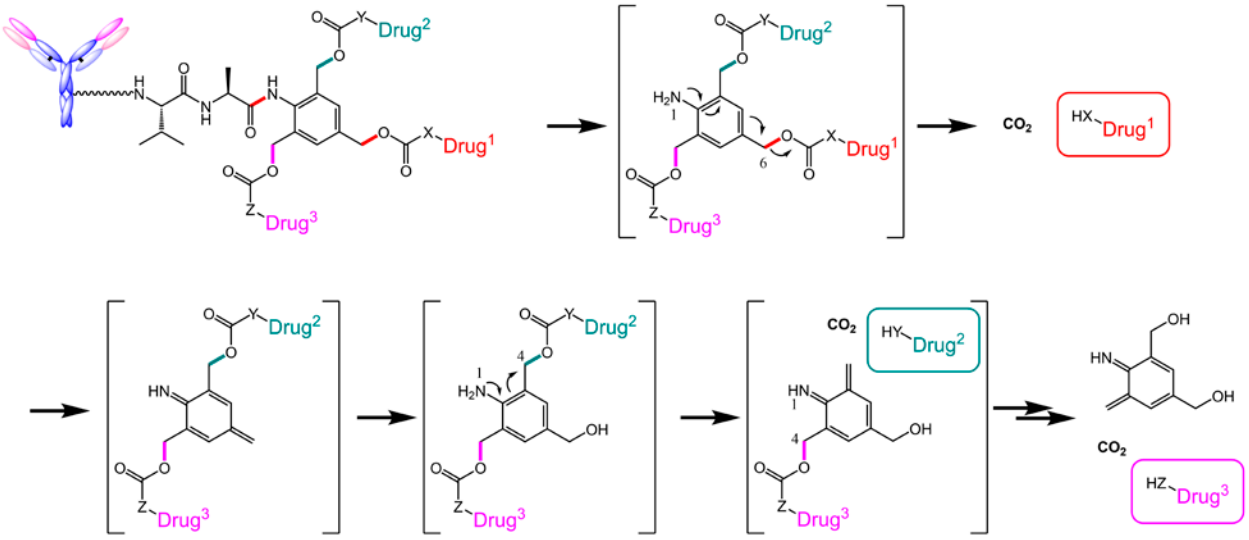

Fig. 12: Mechanism of multiple traceless release.

One of the major challenges related to anticancer chemotherapy is resistance against anticancer drugs. A strategy to revert the resistance of tumor cells is the combined use of different anticancer drugs.

References:

- A novel connector linkage applicable in prodrug design; P. L. Carl, P. K. Chakravarty and J. A. Katzenellenbogen; *J. Med. Chem.* 1981; **24**: 479-80. https://doi.org/10.1021/jm00137a001.
- The azaquinone-methide elimination: comparison study of 1,6- and 1,4-eliminations under physiological conditions; R. Erez and D. Shabat; *Org Biomol Chem* 2008; **6**: 2669-72. https://doi.org/10.1039/b808198k.
- Dendritic chain Dendritic chain reaction: responsive release of hydrogen peroxide upon generation and enzymatic oxidation of methanol; M. Avital-Shmilovici and D. Shabat; *Bioorg Med Chem* 2010; **18**: 3643-7. https://doi.org/10.1016/j.bmc.2010.02.038.
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It has been reported that payload release can be supported by introducing a *N,N'*-dimethylethane-1,2-diamine bridge between carbamate and payload. After release of carbon dioxide it will cyclize and form 1,3-dimethylimidazolidin-2-one and liberate the payload from the linker construction (Fig. 13).

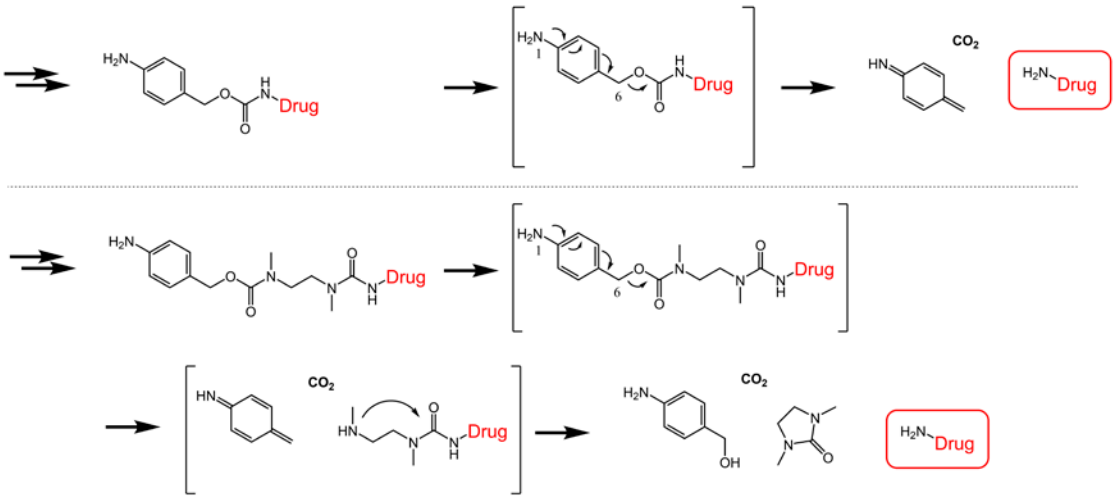


Fig. 13: Mechanism of assisted traceless release by N,N'-dimethylethane-1,2-diamine.

Besides the benzyl system, other moieties have been used for fragmentation reactions. In Fig. 14 different methods are summarized, which have been studied and published. PG is the protecting group and LG the leaving group belonging to the payload to be released. X needs to be a strong electron-donating group, such as O, X or NH, in order to initiate the elimination cascade. While the 1,6-elimination of a benzyl system tends to be the most common system, *ortho*-benzyl undergoing a 1,4-elimination can alternatively be used, as well as styrene fragments (1,8-elimination). However, neither naphthalene rings nor biphenyl structures (1,10-elimination) work, even with a strongly donating amino group.

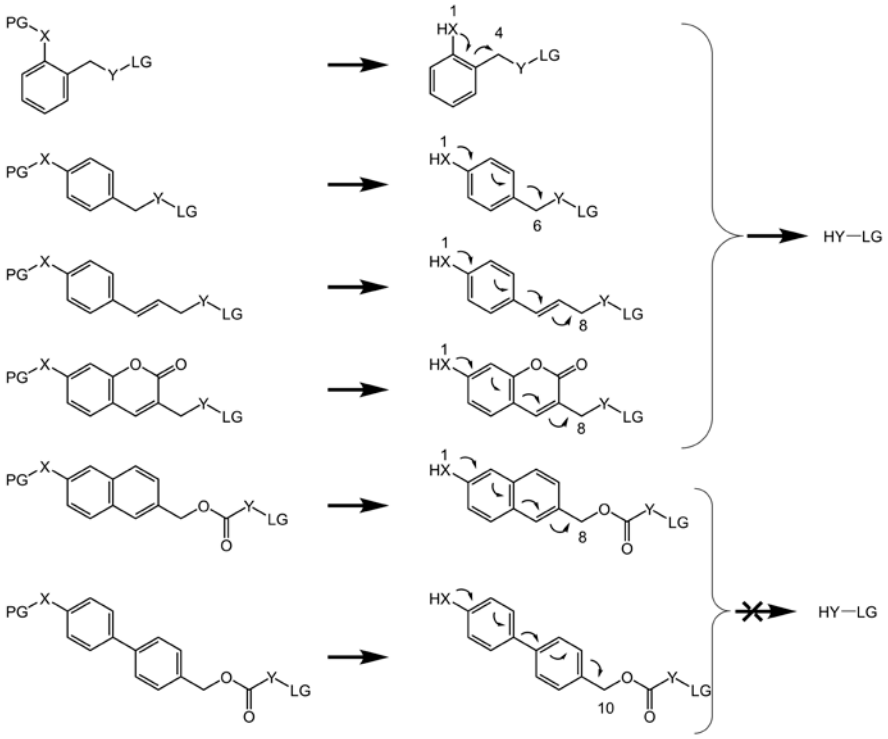


Fig. 14: Possible fragments enabling traceless release of payloads.

References:

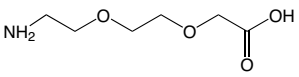
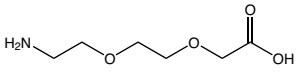
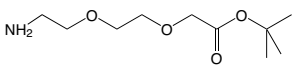
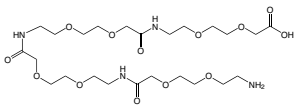
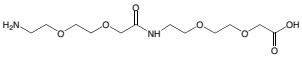
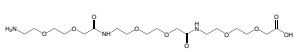
- Self-immolative spacers: kinetic aspects, structure-property relationships, and applications; A. Alouane, R. Labruere, T. Le Saux, F. Schmidt and L. Jullien; *Angew Chem Int Ed Engl* 2015; **54**: 7492-509. https://doi.org/10.1002/anie.201500088.
- Cleavable linkers in chemical biology; G. Leriche, L. Chisholm and A. Wagner; *Bioorg Med Chem* 2012; **20**: 571-82. https://doi.org/10.1016/j.bmc.2011.07.048.

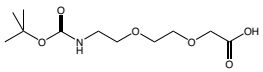
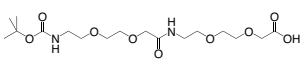
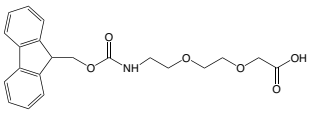
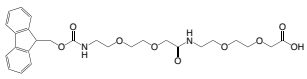
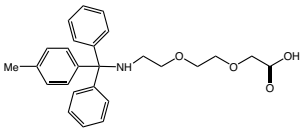
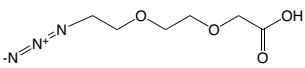
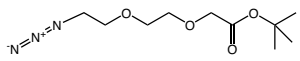
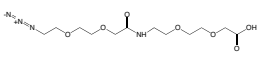
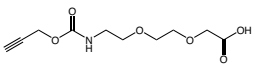
2. Permanent Linkers

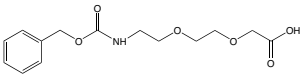
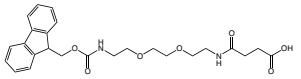
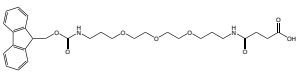
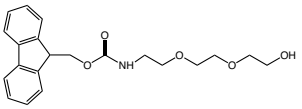
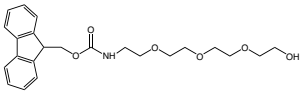
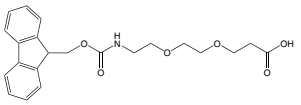
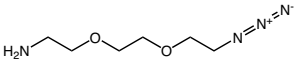
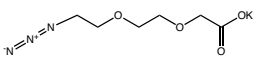
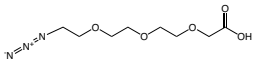
2.1. PEG-Based Spacer Molecules

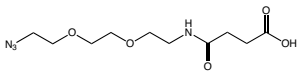
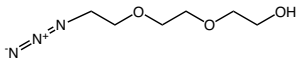
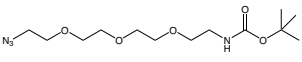
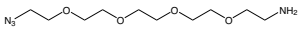
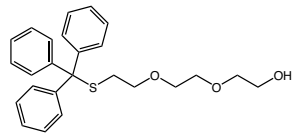
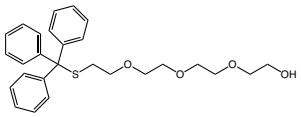
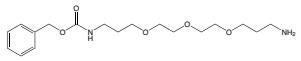
This class of linkers is considered non-cleavable, meaning linker cleavage and payload release do not depend on the differential properties between plasma and cytoplasmic compartments. Instead, the release of the cytotoxic drug is postulated to occur after internalization of the ADC *via* antigen-mediated endocytosis and delivery to lysosomal compartments, where the antibody is degraded to the level of amino acids through intracellular proteolytic degradation. This process releases a drug derivative, formed by the cytotoxic drug, the linker, and the amino acid residue to which the linker was covalently attached.

The following section displays examples of hetero-bifunctional PEG-based spacer molecules. As payloads are quite often rather hydrophobic, PEG fragments help to solubilize the linker-payload conjugate, which is essential to perform successful conjugation onto the antibody. It further helps to increase the solubility in physiological media and to improve the pharmacokinetic properties of the whole ADC construct.

		Article No.	Quantity	Price
PEG2420 H-O2Oc-OH [2-(2-aminoethoxy)ethoxy]acetic acid CAS-NO: 134978-97-5 FORMULA: $C_6H_{13}NO_4$ MOLECULAR WEIGHT: 163,17 g/mol		PEG2420.0001 PEG2420.0005 PEG2420.0025	1 g 5 g 25 g	€ 98,00 € 350,00 € 1400,00
PEG7940 H-O2Oc-OH*HCl 8-amino-3,6-dioxaoctanoic acid hydrochloride CAS-NO: 134979-01-4 FORMULA: $C_6H_{13}NO_4$*HCl MOLECULAR WEIGHT: 163,17*36,45 g/mol		PEG7940.0001 PEG7940.0005 PEG7940.0025 PEG7940.0100 PEG7940.0250	1 g 5 g 25 g 100 g 250 g	€ 80,00 € 250,00 € 1000,00 € 2500,00 € 4500,00
PEG2430 H-O2Oc-OtBu*HCl [2-(2-aminoethoxy)ethoxy]acetic acid tert-butyl ester*HCl CAS-NO: 2098500-69-5 FORMULA: $C_{10}H_{21}NO_4$*HCl MOLECULAR WEIGHT: 219,28*36,45 g/mol		PEG2430.0250 PEG2430.0500 PEG2430.0001 PEG2430.0005 PEG2430.0025	250 mg 500 mg 1 g 5 g 25 g	€ 80,00 € 108,00 € 168,00 € 600,00 € 2400,00
PEG8060 H-O2Oc-O2Oc-O2Oc-O2Oc-OH 8-amino-3,6-dioxaoctanoic acid tetramer FORMULA: $C_{24}H_{46}N_4O_{13}$ MOLECULAR WEIGHT: 598,64 g/mol		PEG8060.0100 PEG8060.0250 PEG8060.0500 PEG8060.1000 PEG8060.5000	100 mg 250 mg 500 mg 1 g 5 g	€ 170,00 € 280,00 € 510,00 € 785,00 € 2800,00
PEG1221 H-O2Oc-O2Oc-OH 17-Amino-10-oxo-3,6,12,15-tetraoxa-9-azaheptadecan-1-oic acid CAS-NO: 1143516-05-5 FORMULA: $C_{12}H_{24}N_2O_7$ MOLECULAR WEIGHT: 308,33 g/mol		PEG1221.9250 PEG1221.9500 PEG1221.0001 PEG1221.0005 PEG1221.0025 PEG1221.0100	250 mg 500 mg 1 g 5 g 25 g 100 g	€ 90,00 € 135,00 € 210,00 € 750,00 € 3000,00 € 7500,00
PEG2770 H-O2Oc-O2Oc-O2Oc-OH 26-amino-10,19-dioxo-3,6,12,15,21,24-hexaoxa-9,18-diazahexacosan-1-oic acid FORMULA: $C_{18}H_{35}N_3O_{10}$ MOLECULAR WEIGHT: 453,48 g/mol		PEG2770.0100 PEG2770.0250 PEG2770.0500 PEG2770.0001 PEG2770.0005	100 mg 250 mg 500 mg 1 g 5 g	€ 96,00 € 160,00 € 288,00 € 448,00 € 1600,00

		Article No.	Quantity	Price
PEG8080 Boc-O2Oc		PEG8080.0001	1 g	€ 70,00
(2-(2-(t-Butyloxycarbonylamino)ethoxy)ethoxy)acetic acid		PEG8080.0005	5 g	€ 250,00
CAS-NO: 108466-89-3		PEG8080.0025	25 g	€ 1000,00
FORMULA: $C_{11}H_{21}NO_6$		PEG8080.0100	100 g	€ 2800,00
MOLECULAR WEIGHT: 263,29 g/mol				
BAA1485 Boc-O2Oc-O2Oc-OH		BAA1485.0500	500 mg	€ 100,00
17-(t-Butyloxycarbonyl-amino)-9-aza-3,6,12,15-tetraoxa-10-on-heptadecanoic acid		BAA1485.0001	1 g	€ 150,00
CAS-NO: 1069067-08-8		BAA1485.0005	5 g	€ 500,00
FORMULA: $C_{17}H_{32}N_2O_9$		BAA1485.0025	25 g	€2000,00
MOLECULAR WEIGHT: 408,45 g/mol				
FAA1435 Fmoc-O2Oc-OH		FAA1435.0001	1 g	€ 56,00
8-(9-Fluorenylmethyloxycarbonyl-amino)-3,6-dioxaoctanoic acid		FAA1435.0005	5 g	€ 125,00
CAS-NO: 166108-71-0		FAA1435.0025	25 g	€ 500,00
FORMULA: $C_{21}H_{23}NO_6$		FAA1435.0100	100 g	€ 1500,00
MOLECULAR WEIGHT: 385,42 g/mol		FAA1435.0250	250 g	€ 2900,00
FAA1787 Fmoc-O2Oc-O2Oc-OH		FAA1787.0500	500 mg	€ 85,00
17-(9-Fluorenylmethyloxycarbonyl-amino)-9-aza-3,6,12,15-tetrao-xa-10-on-heptadecanoic acid		FAA1787.0001	1 g	€ 126,00
CAS-NO: 560088-89-3		FAA1787.0005	5 g	€ 450,00
FORMULA: $C_{27}H_{34}N_2O_9$		FAA1787.0025	25 g	€ 1800,00
MOLECULAR WEIGHT: 530,58 g/mol				
PEG4650 Mtt-O2Oc-OH*DEA		PEG4650.0500	500 mg	€ 126,00
N-(4-Methyltrity)-8-amino-3,6-dioxaoctanoic acid diethylamine		PEG4650.0001	1 g	€ 196,00
CAS-NO: 2098500-66-2		PEG4650.0005	5 g	€ 700,00
FORMULA: $C_{26}H_{29}NO_4*C_4H_{11}N$		PEG4650.0025	25 g	€ 2800,00
MOLECULAR WEIGHT: 419,51*73,14 g/mol				
PEG2780 N_3-O2Oc-OH*CHA		PEG2780.0500	500 mg	€ 90,00
[2-(2-azidoethoxy)ethoxy]acetic acid cyclohexylamine salt		PEG2780.0001	1 g	€ 140,00
CAS-NO: 2098500-94-6		PEG2780.0005	5 g	€ 500,00
FORMULA: $C_6H_{11}N_3O_4*C_6H_{13}N$		PEG2780.0025	25 g	€ 2000,00
MOLECULAR WEIGHT: 189,17*99,17 g/mol				
PEG5390 N_3-O2Oc-OtBu		PEG5390.0500	500 mg	€ 150,00
8-Azido-3,6-dioxaoctanoic acid t-butyl ester		PEG5390.0001	1 g	€ 225,00
CAS-NO: 251564-45-1		PEG5390.0005	5 g	€ 750,00
FORMULA: $C_{10}H_{19}N_3O_4$		PEG5390.0025	25 g	€ 3000,00
MOLECULAR WEIGHT: 245,28 g/mol				
PEG2790 N_3-O2Oc-O2Oc-OH		PEG2790.0250	250 mg	€ 120,00
8-(8-Azido-3,6-dioxaoctanoylamido)-3,6-dioxaoctanoic acid		PEG2790.0500	500 mg	€ 216,00
CAS-NO: 1254054-60-8		PEG2790.0001	1 g	€ 336,00
FORMULA: $C_{12}H_{22}N_4O_7$		PEG2790.0005	5 g	€ 1200,00
MOLECULAR WEIGHT: 334,33 g/mol				
PAA1050 Poc-O2Oc-OH*DCHA		PAA1050.0500	500 mg	€ 108,00
8-(Popargylyloxycarbonyl-amino)-3,6-dioxaoctanoic acid dicyclohe-xylamine		PAA1050.0001	1 g	€ 168,00
FORMULA: $C_{10}H_{15}NO_6*C_{12}H_{23}N$		PAA1050.0005	5 g	€ 600,00
MOLECULAR WEIGHT: 245,23*181,32 g/mol		PAA1050.0025	25 g	€ 2400,00

		Article No.	Quantity	Price
ZAA1186 Z-O2Oc-OH*DCHA 8-(Benzyloxycarbonyl-amino)-3,6-dioxaoctanoic acid dicyclohexyl-amine CAS-NO: 560088-84-8 FORMULA: $C_{14}H_{19}NO_6*C_{12}H_{23}N$ MOLECULAR WEIGHT: 297,31*181,32 g/mol		ZAA1186.0001 ZAA1186.0005 ZAA1186.0025 ZAA1186.0100	1 g 5 g 25 g 100 g	€ 60,00 € 200,00 € 800,00 € 3000,00
PEG4970 Fmoc-Ebes N-[8-(9-Fluorenylmethyloxycarbonyl)amino-3,6-dioxaoctyl]succi-namic acid CAS-NO: 613245-91-3 FORMULA: $C_{25}H_{30}N_2O_7$ MOLECULAR WEIGHT: 470,51 g/mol		PEG4970.0005 PEG4970.0025	5 g 25 g	€ 225,00 € 900,00
FAA1568 Fmoc-TTDS-OH [N_1-(9-Fluorenylmethoxycarbonyl)-1,13-diamino-4,7,10-trioxa-tridecan-succinamic acid CAS-NO: 172089-14-4 FORMULA: $C_{29}H_{38}N_2O_8$ MOLECULAR WEIGHT: 542,63 g/mol		FAA1568.0001 FAA1568.0005 FAA1568.0025	1 g 5 g 25 g	€ 70,00 € 250,00 € 1000,00
PEG5370 Fmoc-AEEE 2-(2-(2-(9-Fluorenylmethyloxycarbonyl)aminoethoxy)ethoxy)ethanol CAS-NO: 560088-66-6 FORMULA: $C_{21}H_{25}NO_5$ MOLECULAR WEIGHT: 371,43 g/mol		PEG5370.0500 PEG5370.0001 PEG5370.0005 PEG5370.0025	500 mg 1 g 5 g 25 g	€ 90,00 € 140,00 € 500,00 € 2000,00
PEG5380 Fmoc-AEEEE 2-(2-(2-(2-(9-Fluorenylmethyloxycarbonyl)aminoethoxy)ethoxy) ethoxy)ethanol CAS-NO: 868594-41-6 FORMULA: $C_{23}H_{29}NO_6$ MOLECULAR WEIGHT: 415,48 g/mol		PEG5380.0250 PEG5380.0500 PEG5380.0001 PEG5380.0005 PEG5380.0025	250 mg 500 mg 1 g 5 g 25 g	€ 108,00 € 180,00 € 270,00 € 900,00 € 3600,00
PEG1810 Fmoc-AEEP 3-(2-(2-(9-Fluorenylmethyloxycarbonyl)aminoethoxy)ethoxy)propa-noic acid CAS-NO: 872679-70-4 FORMULA: $C_{22}H_{25}NO_6$ MOLECULAR WEIGHT: 399,44 g/mol		PEG1810.0001 PEG1810.0005 PEG1810.0025	1 g 5 g 25 g	€ 85,00 € 300,00 € 1200,00
PEG4980 H_2N-PEG(2)-N_3*TosOH 2-[2-(2-Azidoethoxy)ethoxy]ethanaminium tosylat CAS-NO: 2173092-98-1 FORMULA: $C_7H_{14}N_4O_2*C_7H_8O_3S$ MOLECULAR WEIGHT: 174,20*172,20 g/mol		PEG4980.0001 PEG4980.0005 PEG4980.0025	1 g 5 g 25 g	€ 125,00 € 450,00 € 1800,00
PEG7950 N_3-AEEA-OK Potassium 8-azido-3,6-dioxaoctanoate CAS-NO: 882518-90-3 net FORMULA: $C_6H_{10}KN_3O_4$ MOLECULAR WEIGHT: 39,10*188,16 g/mol		PEG7950.0500 PEG7950.1000 PEG7950.5000 PEG7950.9025	500 mg 1 g 5 g 25 g	€ 150,00 € 225,00 € 750,00 € 3000,00
PEG5400 N_3-AEEEA*CHA 11-Azido-3,6,9-trioxaundecanoic acid cyclohexylamine FORMULA: $C_8H_{15}N_3O_5*C_6H_{13}N$ MOLECULAR WEIGHT: 233,22*99,17 g/mol		PEG5400.0500 PEG5400.0001 PEG5400.0005 PEG5400.0025	500 mg 1 g 5 g 25 g	€ 130,50 € 203,00 € 725,00 € 2900,00

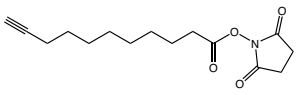
		Article No.	Quantity	Price
PEG5290 N_3-DOOA-Suc-OH 4-(2-(2-(2-azidoethoxy)ethoxy)ethylamino)-4-oxobutanoic acid CAS-NO: 1189096-56-7 FORMULA: $C_{10}H_{18}N_4O_5$ MOLECULAR WEIGHT: 274,27 g/mol		PEG5290.0500 PEG5290.0001 PEG5290.0005 PEG5290.0025	500 mg 1 g 5 g 25 g	€ 150,00 € 225,00 € 750,00 € 3000,00
PEG4900 N_3-EEEt-OH 2-[2-(2-Azidoethoxy)ethoxy]ethanol CAS-NO: 86520-52-7 FORMULA: $C_6H_{13}N_3O_3$ MOLECULAR WEIGHT: 175,19 g/mol		PEG4900.0001 PEG4900.0005 PEG4900.0025	1 g 5 g 25 g	€ 125,00 € 350,00 € 1400,00
PEG8160 N_3-PEG(3)-NH-Boc t-Butyl N-(2-(2-(2-azidoethoxy)ethoxy)ethoxy)ethyl)carbamate CAS-NO: 642091-68-7 FORMULA: $C_{13}H_{26}N_4O_5$ MOLECULAR WEIGHT: 318,37 g/mol		PEG8160.0001 PEG8160.0005 PEG8160.0025	1 g 5 g 25 g	€ 112,00 € 400,00 € 1600,00
PEG5320 N_3-PEG(4)-NH2 14-Azido-3,6,9,12-tetraoxatetradecan-1-amine CAS-NO: 951671-92-4 FORMULA: $C_{10}H_{22}N_4O_4$ MOLECULAR WEIGHT: 262,31 g/mol		PEG5320.0250 PEG5320.0500 PEG5320.0001 PEG5320.0005 PEG5320.0025	250 mg 500 mg 1 g 5 g 25 g	€ 108,00 € 180,00 € 270,00 € 900,00 € 3600,00
PEG7010 Trt-S-EEE S-Trityl-2-(2-(2-mercaptoethoxy)ethoxy)ethanol CAS-NO: 728033-15-6 FORMULA: $C_{25}H_{28}O_3S$ MOLECULAR WEIGHT: 408,55 g/mol		PEG7010.0250 PEG7010.0500 PEG7010.0001 PEG7010.0005	250 mg 500 mg 1 g 5 g	€ 90,00 € 165,00 € 255,00 € 900,00
PEG6730 Trt-S-EEEE S-Trityl-2-(2-(2-(2-mercaptoethoxy)ethoxy)ethoxy)ethanol CAS-NO: 125607-10-5 FORMULA: $C_{27}H_{32}O_4S$ MOLECULAR WEIGHT: 452,61 g/mol		PEG6730.0250 PEG6730.0500 PEG6730.0001 PEG6730.0005	250 mg 500 mg 1 g 5 g	€ 90,00 € 165,00 € 255,00 € 900,00
PEG1745 Z-TOTA 1-Benzyloxycarbonyl-4,7,10-trioxa-13-tridecaneamine CAS-NO: 220156-99-0 FORMULA: $C_{18}H_{30}N_2O_5$ MOLECULAR WEIGHT: 354,44 g/mol		PEG1745.0001 PEG1745.0005 PEG1745.0025	1 g 5 g 25 g	€ 126,00 € 450,00 € 1800,00

Find many more PEG-based spacers in our brochure Comprehensive Drug Delivery Survey or visit our website.

2.2. Hydrophobic Spacer Molecules

RL-3460 10-Undecynoyl-OSu

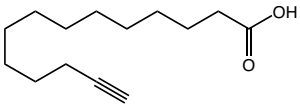
10-Undecynoic acid N-hydroxysuccinimide ester
CAS-NO: 1006592-57-9
FORMULA: $C_{15}H_{21}NO_4$
MOLECULAR WEIGHT: 279,34 g/mol



Article No.	Quantity	Price
RL-3460.0250	250 mg	€ 89,00
RL-3460.0500	500 mg	€ 160,00
RL-3460.0001	1 g	€ 250,00
RL-3460.0005	5 g	€ 890,00

RL-2055 Alkyne-myristic acid

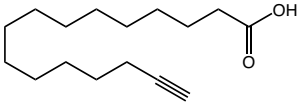
13-Tetradecynoic acid
CAS-NO: 82909-47-5
FORMULA: $C_{14}H_{24}O_2$
MOLECULAR WEIGHT: 224,34 g/mol



Article No.	Quantity	Price
RL-2055.0100	100 mg	€ 250,00
RL-2055.0500	500 mg	€ 960,00
RL-2055.1000	1 g	€ 1600,00

RL-2060 Alkyne-palmitic acid

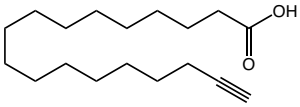
15-Hexadecynoic acid
CAS-NO: 99208-90-9
FORMULA: $C_{16}H_{28}O_2$
MOLECULAR WEIGHT: 252,39 g/mol



Article No.	Quantity	Price
RL-2060.0100	100 mg	€ 250,00
RL-2060.0500	500 mg	€ 960,00
RL-2060.1000	1 g	€ 1600,00

RL-2065 Alkyne-stearic acid

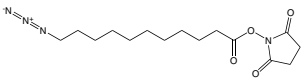
17-Octadecynoic acid
CAS-NO: 34450-18-5
FORMULA: $C_{18}H_{32}O_2$
MOLECULAR WEIGHT: 280,45 g/mol



Article No.	Quantity	Price
RL-2065.0500	500 mg	€ 1100,00
RL-2065.1000	1 g	€ 2000,00

RL-3170 11-azido-undecanoyl-OSu

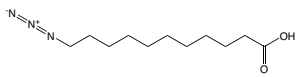
11-azidoundecanoic acid N-hydroxysuccinimide ester
CAS-NO: 850080-13-6
FORMULA: $C_{15}H_{24}N_4O_4$
MOLECULAR WEIGHT: 324,38 g/mol



Article No.	Quantity	Price
RL-3170.0250	250 mg	€ 100,00
RL-3170.0500	500 mg	€ 180,00
RL-3170.1000	1 g	€ 280,00
RL-3170.5000	5 g	€ 1000,00

RL-3200 11-Azidoundecanoic acid

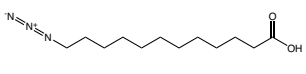
11-Azido-undecanoic acid
CAS-NO: 118162-45-1
FORMULA: $C_{11}H_{21}N_3O_2$
MOLECULAR WEIGHT: 227,30 g/mol



Article No.	Quantity	Price
RL-3200.0500	500 mg	€ 108,00
RL-3200.0001	1 g	€ 168,00
RL-3200.0005	5 g	€ 600,00
RL-3200.0025	25 g	€ 2400,00

RL-3210 12-Azidododecanoic acid

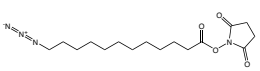
12-Azido-dodecanoic acid
CAS-NO: 80667-36-3
FORMULA: $C_{12}H_{23}N_3O_2$
MOLECULAR WEIGHT: 241,33 g/mol



Article No.	Quantity	Price
RL-3210.0500	500 mg	€ 108,00
RL-3210.0001	1 g	€ 168,00
RL-3210.0005	5 g	€ 600,00
RL-3210.0025	25 g	€ 2400,00

RL-3220 12-azido-dodecanoyl-OSu

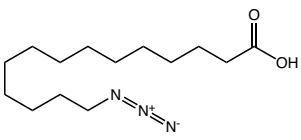
12-Azidododecanoic acid N-hydroxysuccinimide ester
FORMULA: $C_{16}H_{26}N_4O_4$
MOLECULAR WEIGHT: 338,40 g/mol



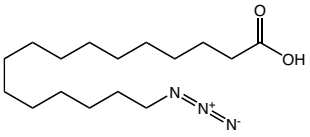
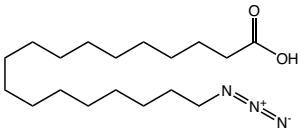
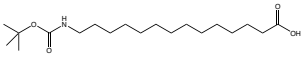
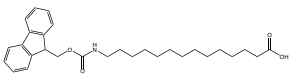
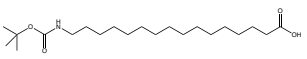
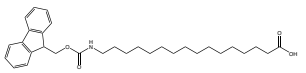
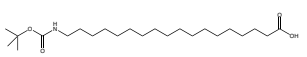
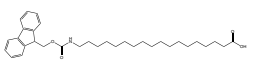
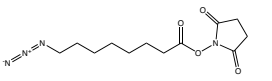
Article No.	Quantity	Price
RL-3220.0250	250 mg	€ 100,00
RL-3220.0500	500 mg	€ 180,00
RL-3220.0001	1 g	€ 280,00
RL-3220.0005	5 g	€ 1000,00

RL-3230 14-Azido-myristic acid

14-azidotetradecanoic acid
CAS-NO: 176108-61-5
FORMULA: $C_{14}H_{27}N_3O_2$
MOLECULAR WEIGHT: 269,38 g/mol



Article No.	Quantity	Price
RL-3230.0100	100 mg	€ 175,00
RL-3230.0500	500 mg	€ 600,00
RL-3230.0001	1 g	€ 1500,00

		Article No.	Quantity	Price
RL-3240 **16-Azido-palmitic acid** 16-azidohexadecanoic acid CAS-NO: 112668-54-9 FORMULA: $C_{16}H_{31}N_3O_2$ MOLECULAR WEIGHT: 297,44 g/mol			please inquire!	
RL-3250 **18-Azido-stearic acid** 18-azidooctadecanoic acid CAS-NO: 1529763-58-3 FORMULA: $C_{18}H_{35}N_3O_2$ MOLECULAR WEIGHT: 325,49 g/mol		RL-3250.0100 RL-3250.0250 RL-3250.0500 RL-3250.0001	100 mg 250 mg 500 mg 1 g	€ 375,00 € 750,00 € 1450,00 € 2400,00
BAA4240 **14-(Boc-amino)-myristic acid** 14-((t-Butyloxycarbonyl)amino)tetradecanoic acid CAS-NO: 2307778-46-5 FORMULA: $C_{19}H_{37}NO_4$ MOLECULAR WEIGHT: 343,51 g/mol		BAA4240.0100 BAA4240.0250 BAA4240.0001	100 mg 250 mg 1 g	€ 285,00 € 600,00 € 1800,00
FAA8160 **14-(Fmoc-amino)-myristic acid** 14-((9-Fluorenylmethyloxycarbonyl)amino)tetradecanoic acid CAS-NO: 1931109-55-5 FORMULA: $C_{29}H_{39}NO_4$ MOLECULAR WEIGHT: 465,63 g/mol		FAA8160.0100 FAA8160.0250 FAA8160.0001	100 mg 250 mg 1 g	€ 285,00 € 600,00 € 1800,00
BAA3900 **16-(Boc-amino)-palmitic acid** 16-((t-Butyloxycarbonyl)amino)hexadecanoic acid CAS-NO: 135747-73-8 FORMULA: $C_{21}H_{41}NO_4$ MOLECULAR WEIGHT: 371,55 g/mol		BAA3900.010 BAA3900.0500 BAA3900.0001	100 mg 500 mg 1 g	€ 285,00 € 1100,00 € 1800,00
FAA7460 **16-(Fmoc-amino)-palmitic acid** 16-((9-Fluorenylmethyloxycarbonyl)amino)hexadecanoic acid CAS-NO: 1356220-22-8 FORMULA: $C_{31}H_{43}NO_4$ MOLECULAR WEIGHT: 493,68 g/mol		FAA7460.0100 FAA7460.0500 FAA7460.0001	100 mg 500 mg 1 g	€ 285,00 € 1100,00 € 1800,00
BAA3910 **18-(Boc-amino)-stearic acid** 18-((t-Butyloxycarbonyl)amino)octadecanoic acid FORMULA: $C_{23}H_{45}NO_4$ MOLECULAR WEIGHT: 399,61 g/mol		BAA3910.0100 BAA3910.0500 BAA3910.0001	100 mg 500 mg 1 g	€ 285,00 € 1100,00 € 1800,00
FAA7450 **18-(Fmoc-amino)-stearic acid** 18-((9-Fluorenylmethyloxycarbonyl)amino)octadecanoic acid FORMULA: $C_{33}H_{47}NO_4$ MOLECULAR WEIGHT: 521,73 g/mol		FAA7450.0100 FAA7450.0500 FAA7450.0001	100 mg 500 mg 1 g	€ 285,00 € 1100,00 € 1800,00
RL-3480 **8-azido-octanoyl-OSu** 8-Azidodooctanoic acid N-hydroxysuccinimide ester FORMULA: $C_{12}H_{18}N_4O_4$ MOLECULAR WEIGHT: 282,30 g/mol		RL-3480.0250 RL-3480.0500 RL-3480.1000 RL-3480.5000	250 mg 500 mg 1 g 5 g	€ 120,00 € 216,00 € 336,00 € 1200,00

2.3. Permanent Linkers with Maleimide Function

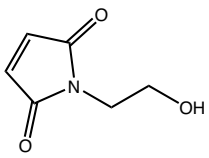
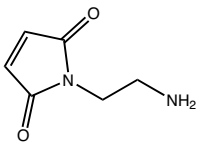
Michael addition of a thiol to a maleimide is commonly used for numerous bioconjugations. Several commercial constructs like Brentuximab vedotin, Trastuzumab emtansine, and Cimzia contain a thiol-maleimide adduct. However, this reaction is reversible. During the journey of an appropriate thioether containing drug through physiological media, this bond can break, and fragments are released which might contribute to certain unwanted or even toxic reactions.

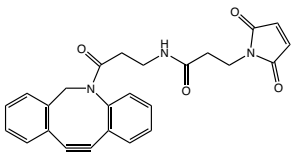
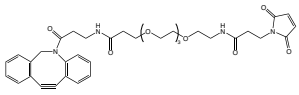
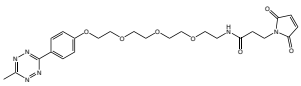
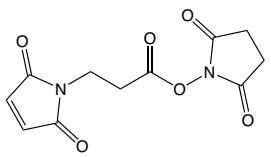
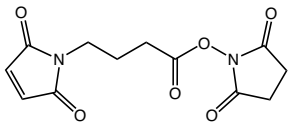
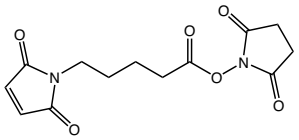
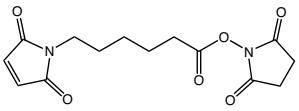
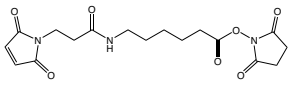
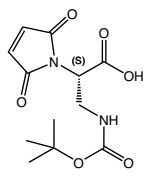
Fig. 15: Maleimides bind reversibly to thiols resulting in thioethers. This linkage turns stable once the maleimide ring is opened through hydrolysis.

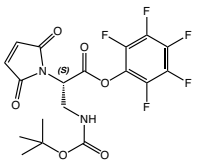
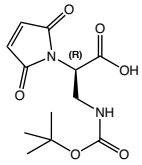
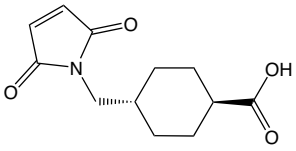
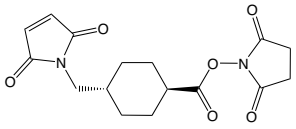
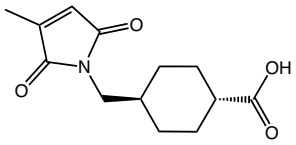
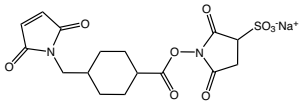
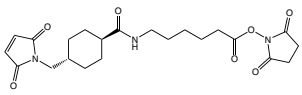
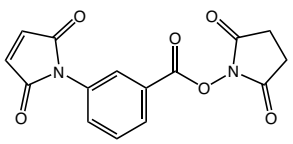
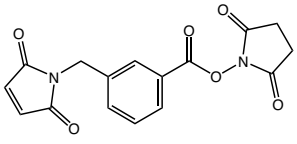
However, if the succinimide moiety of a maleimide-thiol conjugate is hydrolyzed, the ring-opened product is fully stabilized towards cleavage (Fig. 15). The rates of ring-opening hydrolysis are greatly accelerated by electron withdrawing N-substituents and good nucleophiles in the proximity of the carbonyl functions. Thus, conjugates made with nucleophilic side chains and electron-withdrawing maleimides may be purposefully hydrolyzed to their ring-opened counterparts and ensure good *in vivo* stability.

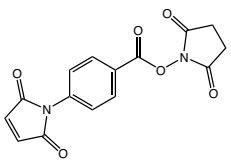
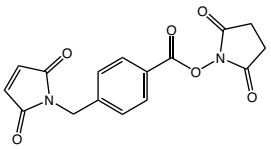
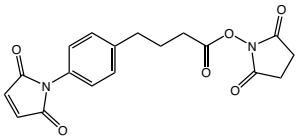
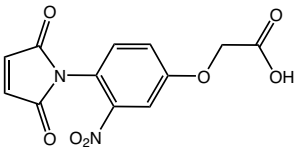
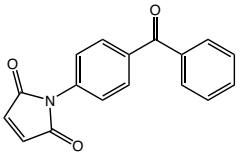
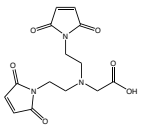
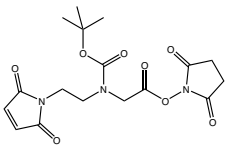
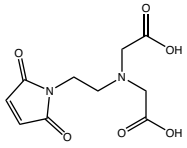
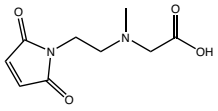
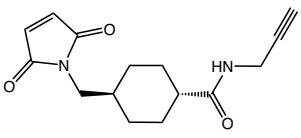
References:

- Covalent Modification of Biomolecules through Maleimide-Based Labeling Strategies; K. Renault, J. W. Fredy, P. Y. Renard and C. Sabot; *Bioconjug Chem* 2018; **29**: 2497-2513. https://doi.org/10.1021/acs.bioconjchem.8b00252.
- Optimisation of the dibromomaleimide (DBM) platform for native antibody conjugation by accelerated post-conjugation hydrolysis; M. Morais, J. P. M. Nunes, K. Karu, N. Forte, I. Benni, M. E. B. Smith, S. Caddick, V. Chudasama and J. R. Baker; *Org Biomol Chem* 2017; **15**: 2947-2952. https://doi.org/10.1039/c7ob00220c.
- Use of a next generation maleimide in combination with THIOMAB™ antibody technology delivers a highly stable, potent and near homogeneous THIOMAB™ antibody-drug conjugate (TDC); J. P. M. Nunes, V. Vassileva, E. Robinson, M. Morais, M. E. B. Smith, R. B. Pedley, S. Caddick, J. R. Baker and V. Chudasama; *RSC Advances* 2017; **7**: 24828-24832. https://doi.org/10.1039/c7ra04606e.
- Long-term stabilization of maleimide-thiol conjugates; S. D. Fontaine, R. Reid, L. Robinson, G. W. Ashley and D. V. Santi; *Bioconjug Chem* 2015; **26**: 145-52. https://doi.org/10.1021/bc5005262.
- Self-hydrolyzing maleimides improve the stability and pharmacological properties of antibody-drug conjugates; R. P. Lyon, J. R. Setter, T. D. Bovee, S. O. Doronina, J. H. Hunter, M. E. Anderson, C. L. Balasubramanian, S. M. Duniho, C. I. Leiske, F. Li and P. D. Senter; *Nat Biotechnol* 2014; **32**: 1059-62. https://doi.org/10.1038/nbt.2968.
- Mild method for succinimide hydrolysis on ADCs: impact on ADC potency, stability, exposure, and efficacy; L. N. Tumey, M. Charati, T. He, E. Sousa, D. Ma, X. Han, T. Clark, J. Casavant, F. Loganzo, F. Barletta, J. Lucas and E. I. Graziani; *Bioconjug Chem* 2014; **25**: 1871-80. https://doi.org/10.1021/bc500357n.

		Article No.	Quantity	Price
RL-3000 **Mal-Et-OH**		RL-3000.0001	1 g	€ 275,00
N-(2-Hydroxyethyl)maleimide CAS-NO: 1585-90-6 FORMULA: $C_6H_7NO_3$ MOLECULAR WEIGHT: 141,12 g/mol		RL-3000.0005	5 g	€ 900,00
RL-2780 **Mal-NH_2*HCl**		RL-2780.0250	250 mg	€ 75,00
2-Maleimidoethylamine hydrochloride CAS-NO: 134272-64-3 FORMULA: $C_6H_8N_2O_2$*HCl MOLECULAR WEIGHT: 140,14*36,45 g/mol		RL-2780.0001	1 g	€ 200,00
		RL-2780.0005	5 g	€ 800,00

		Article No.	Quantity	Price
RL-2490 DBCO-mal Dibenzoazacyclooctyne-maleimide CAS-NO: 1395786-30-7 FORMULA: $C_{25}H_{21}N_3O_4$ MOLECULAR WEIGHT: 427,45 g/mol		RL-2490.0025 RL-2490.0100 RL-2490.1000	25 mg 100 mg 1 g	€ 190,00 € 410,00 € 2070,00
RL-2500 DBCO-PEG(4)-mal Dibenzoazacyclooctyne-tetra(ethylene glycol)-maleimide CAS-NO: 1480516-75-3 FORMULA: $C_{36}H_{42}N_4O_9$ MOLECULAR WEIGHT: 674,74 g/mol		RL-2500.0010 RL-2500.0025 RL-2500.0100 RL-2500.0500	10 mg 25 mg 100 mg 500 mg	€ 170,00 € 295,00 € 675,00 € 2070,00
RL-2340 MeTz-PEG(4)-mal Methyltetrazine-PEG(4)-maleimide CAS-NO: 1802908-02-6 FORMULA: $C_{24}H_{30}N_6O_7$ MOLECULAR WEIGHT: 514,53 g/mol		RL-2340.0010 RL-2340.0025 RL-2340.0100	10 mg 25 mg 100 mg	€ 200,00 € 290,00 € 640,00
MAA1020 Mal-beta-Ala-OSu 3-(Maleimido)propionic acid N-succinimidyl ester CAS-NO: 55750-62-4 FORMULA: $C_{11}H_{10}N_2O_6$ MOLECULAR WEIGHT: 266,21 g/mol		MAA1020.0001 MAA1020.0005	1 g 5 g	€ 250,00 € 475,00
RL-2640 Mal-Bu-NHS 4-Maleimidobutyric acid-NHS ester CAS-NO: 80307-12-6 FORMULA: $C_{12}H_{12}N_2O_6$ MOLECULAR WEIGHT: 280,23 g/mol		please inquire!		
RL-2670 Mal-Pen-NHS 5-Maleimidopentanoic acid-NHS ester CAS-NO: 103750-03-4 FORMULA: $C_{13}H_{14}N_2O_6$ MOLECULAR WEIGHT: 294,26 g/mol		please inquire!		
RL-2660 Mal-Hx-NHS 6-Maleimidohexanoic acid-NHS ester CAS-NO: 55750-63-5 FORMULA: $C_{14}H_{16}N_2O_6$ MOLECULAR WEIGHT: 308,29 g/mol		RL-2660.0250 RL-2660.0001 RL-2660.0005	250 mg 1 g 5 g	€ 60,00 € 120,00 € 480,00
RL-2690 Mal-PrHx-NHS 6-(3-Maleimidopropionylamino)-hexanoic acid-NHS ester CAS-NO: 367927-39-7 FORMULA: $C_{17}H_{21}N_3O_7$ MOLECULAR WEIGHT: 379,36 g/mol		please inquire!		
MAA1040 Mal-L-Dap(Boc)-OH*DCHA N-alpha-MaleimidoN-beta-t-butyloxycarbonyl-L-2,3-diaminopropionic acid dicyclohexylamine CAS-NO: 2004724-16-5 FORMULA: $C_{12}H_{16}N_2O_6*C_{12}H_{23}N$ MOLECULAR WEIGHT: 284,27*181,32 g/mol		MAA1040.0250 MAA1040.0500 MAA1040.0001 MAA1040.0005 MAA1040.0025	250 mg 500 mg 1 g 5 g 25 g	€ 80,00 € 144,00 € 224,00 € 800,00 € 3200,00

		Article No.	Quantity	Price
MAA1080 Mal-L-Dap(Boc)-OPfp N-alpha-MaleimidoN-beta-t-butyloxycarbonyl-L-2,3-diaminopropionic acid pentafluorophenolate CAS-NO: 1887132-90-2 FORMULA: $C_{18}H_{15}F_5N_2O_6$ MOLECULAR WEIGHT: 450,31 g/mol		MAA1080.0250	250 mg	€ 95,00
		MAA1080.0500	500 mg	€ 170,00
		MAA1080.1000	1 g	€ 265,00
		MAA1080.5000	5 g	€ 950,00
		MAA1080.9025	25 g	€ 3800,00
MAA1060 Mal-D-Dap(Boc)-OH*DCHA N-alpha-MaleimidoN-beta-t-butyloxycarbonyl-D-2,3-diaminopropionic acid dicyclohexylamine CAS-NO: 2382651-11-6 net FORMULA: $C_{12}H_{16}N_2O_6*C_{12}H_{23}N$ MOLECULAR WEIGHT: 284,27*181,32 g/mol		MAA1060.0100	100 mg	€ 90,00
		MAA1060.0250	250 mg	€ 150,00
		MAA1060.0500	500 mg	€ 270,00
		MAA1060.1000	1 g	€ 420,00
		MAA1060.5000	5 g	€ 1500,00
MAA5400 Mal-AMCHC-OH trans-4-(maleimidomethyl)cyclohexane-1-carboxylic acid CAS-NO: 69907-67-1 FORMULA: $C_{12}H_{15}NO_4$ MOLECULAR WEIGHT: 237,25 g/mol		MAA5400.0001	1 g	€ 100,00
		MAA5400.0005	5 g	€ 400,00
		MAA5400.0025	25 g	€ 1600,00
		MAA5400.0100	100 g	€ 4800,00
MAA1000 Mal-AMCHC-OSu trans-N-Succinimidyl 4-(maleimidomethyl)cyclohexane-1-carboxylate CAS-NO: 71875-81-5 FORMULA: $C_{16}H_{18}N_2O_6$ MOLECULAR WEIGHT: 334,33 g/mol		MAA1000.0500	500 mg	€ 108,00
		MAA1000.0001	1 g	€ 168,00
		MAA1000.0005	5 g	€ 600,00
MAA1005 Mal(3-Me)-AMCHC trans-4-[(methylmaleimido)methyl]cyclohexane-1-carboxylic acid CAS-NO: 71738-82-4 FORMULA: $C_{13}H_{17}NO_4$ MOLECULAR WEIGHT: 251,28 g/mol		MAA1005.0250	250 mg	€ 90,00
		MAA1005.0500	500 mg	€ 162,00
		MAA1005.0001	1 g	€ 252,00
		MAA1005.0005	5 g	€ 900,00
		MAA1005.0025	25 g	€ 3600,00
MAA1050 Sulfo-SMCC 4-(N-Maleimidomethyl)cyclohexane-1-carboxylic acid 3-sulfo-N-hydroxysuccinimide ester sodium salt (cis/trans mixture) CAS-NO: 92921-24-9 FORMULA: $C_{16}H_{17}N_2NaO_9S$ MOLECULAR WEIGHT: 436,37 g/mol		MAA1050.0250	250 mg	€ 250,00
		MAA1050.0001	1 g	€ 750,00
		MAA1050.0005	5 g	€ 3000,00
RL-2650 Mal-cHxHx-NHS CAS-NO: 125559-00-4 FORMULA: $C_{22}H_{29}N_3O_7$ MOLECULAR WEIGHT: 447,48 g/mol		please inquire!		
RL-2600 3-Mal-Bz-NHS 3-Maleimidobenzoic acid-NHS ester CAS-NO: 58626-38-3 FORMULA: $C_{15}H_{10}N_2O_6$ MOLECULAR WEIGHT: 314,25 g/mol		please inquire!		
RL-2610 3-Mal-MBz-NHS 3-(Maleimidomethyl)-benzoic acid-NHS ester CAS-NO: 91574-36-6 FORMULA: $C_{16}H_{12}N_2O_6$ MOLECULAR WEIGHT: 328,28 g/mol		please inquire!		

		Article No.	Quantity	Price
RL-2620	**4-Mal-Bz-NHS**			
4-Maleimidobenzoic acid-NHS ester CAS-NO: 64191-06-6 FORMULA: $C_{15}H_{10}N_2O_6$ MOLECULAR WEIGHT: 314,25 g/mol		please inquire!		
RL-2630	**4-Mal-MBz-NHS**			
4-(Maleimidomethyl)-benzoic acid-NHS ester CAS-NO: 64987-84-4 FORMULA: $C_{16}H_{12}N_2O_6$ MOLECULAR WEIGHT: 328,28 g/mol		please inquire!		
RL-2680	**Mal-PhBu-NHS**			
4-(4-Maleimidophenyl)-butyric acid-NHS ester CAS-NO: 79886-55-8 FORMULA: $C_{18}H_{16}N_2O_6$ MOLECULAR WEIGHT: 356,33 g/mol		please inquire!		
MAA1070	**Mal-ANPA**			
4-maleimido-3-nitrophenoxyacetic acid FORMULA: $C_{12}H_8N_2O_7$ MOLECULAR WEIGHT: 292,20 g/mol		MAA1070.0250 MAA1070.0500 MAA1070.0001 MAA1070.0005 MAA1070.0025	250 mg 500 mg 1 g 5 g 25 g	€ 80,00 € 144,00 € 224,00 € 800,00 € 3200,00
LS-3350	**4-(N-Maleimido)benzophenone**			
1-(4-Benzoylphenyl)-1H-pyrrole-2,5-dione CAS-NO: 92944-71-3 FORMULA: $C_{17}H_{11}NO_3$ MOLECULAR WEIGHT: 277,28 g/mol		LS-3350.0100 LS-3350.0500	100 mg 500 mg	€ 175,00 € 375,00
RL-3380	**(Mal-CH_2CH_2)$_2$-N-CH_2-COOH**			
bis(2-(maleinimido)ethyl)glycine FORMULA: $C_{14}H_{15}N_3O_6$ MOLECULAR WEIGHT: 321,29 g/mol		please inquire!		
RL-3430	**Mal-N-Boc-Aeg-NHS**			
N-(t-butoxycarbonyl)-N-(2-(maleinimido)ethyl)glycine N-Hydroxysuccinimidyl ester FORMULA: $C_{17}H_{21}N_3O_8$ MOLECULAR WEIGHT: 395,37 g/mol		please inquire!		
RL-3450	**Mal-CH_2CH_2-N-(CH_2-COOH)$_2$**			
2,2'-((2-(maleinimido)ethyl)azanediyl)diacetic acid CAS-NO: 207612-92-8 FORMULA: $C_{10}H_{12}N_2O_6$ MOLECULAR WEIGHT: 256,21 g/mol		please inquire!		
RL-3400	**Mal-CH_2CH_2-N(Me)-CH_2-COOH**			
N-(2-(maleinimido)ethyl)-N-methylglycine FORMULA: $C_9H_{12}N_2O_4$ MOLECULAR WEIGHT: 212,21 g/mol		please inquire!		
MAA1100	**Mal-AMCHC-N-Propargylamide**			
trans-4-[(2,5-dioxo-2,5-dihydro-1H-pyrrol-1-yl)methyl]-N-(prop-2-yn-1-yl)cyclohexane-1-carboxamide CAS-NO: 2027476-42-0 FORMULA: $C_{15}H_{18}N_2O_3$ MOLECULAR WEIGHT: 274,32 g/mol		MAA1100.0250 MAA1100.0500 MAA1100.0001 MAA1100.0005	250 mg 500 mg 1 g 5 g	€ 120,00 € 216,00 € 336,00 € 1200,00

2.4. Photoactivatable Linkers

Irradiation of diazirines with UV light (ca. 350-360 nm) yields a highly reactive carbene species that can undergo insertions into C-C, C-H, O-H, and X-H (X = heteroatom) bonds of neighboring molecules to irreversibly form a covalent bond (Fig. 16). The diazirine moiety is the smallest of all photophores, so introduction of a diazirine-bearing 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 and their relative stability against nucleophiles as well as towards both acidic and basic conditions.

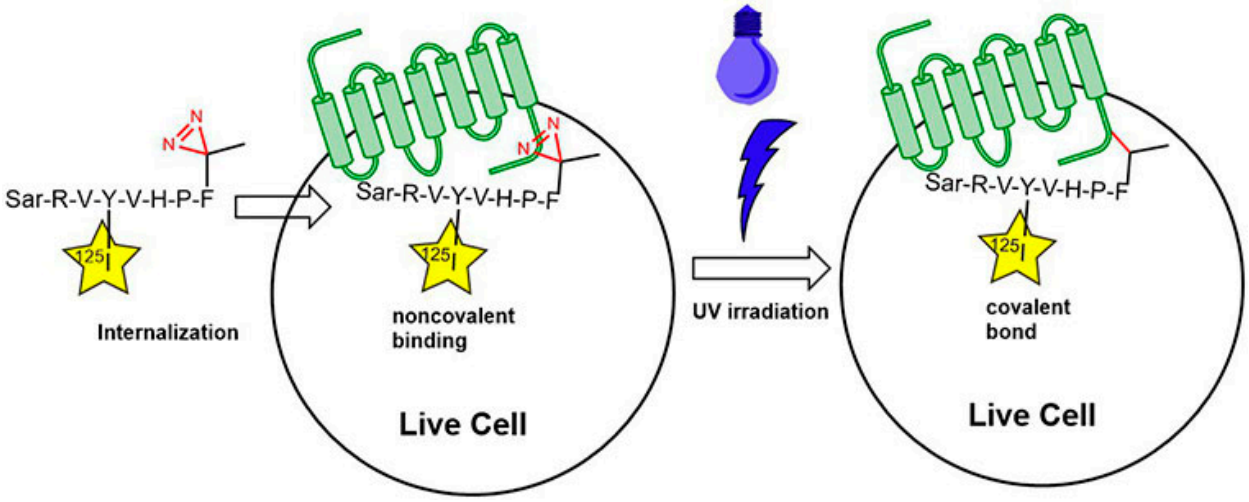


Fig. 16: Use of photo-phenylalanine for the identification of angiotensin-II receptor binding sites; ^{125}I is used as a radiotracer.

References:

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- Cell-based proteome profiling of potential dasatinib targets by use of affinity-based probes; H. Shi, C. J. Zhang, G. Y. Chen and S. Q. Yao; *J Am Chem Soc* 2012; **134**: 3001-14. https://doi.org/10.1021/ja208518u.
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- Proteome profiling reveals potential cellular targets of staurosporine using a clickable cell-permeable probe; H. Shi, X. Cheng, S. K. Sze and S. Q. Yao; *Chem Commun (Camb)* 2011; **47**: 11306-8. https://doi.org/10.1039/c1cc14824a.
- Direct interaction between an allosteric agonist pepducin and the chemokine receptor CXCR4; J. M. Janz, Y. Ren, R. Looby, M. A. Kazmi, P. Sachdev, A. Grunbeck, L. Haggis, D. Chinnapen, A. Y. Lin, C. Seibert, T. McMurry, K. E. Carlson, T. W. Muir, S. Hunt, 3rd and T. P. Sakmar; *J Am Chem Soc* 2011; **133**: 15878-81. https://doi.org/10.1021/ja206661w.
- Aliphatic diazirines as photoaffinity probes for proteins: recent developments; J. Das; *Chem Rev* 2011; **111**: 4405-17. https://doi.org/10.1021/cr1002722.
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- Photo-crosslinking of proteins in intact cells reveals a dimeric structure of cyclooxygenase-2 and an inhibitor-sensitive oligomeric structure of microsomal prostaglandin E2 synthase-1; P. O. Hetu, M. Ouellet, J. P. Falgueyret, C. Ramachandran, J. Robichaud, R. Zamboni and D. Riendeau; *Arch Biochem Biophys* 2008; **477**: 155-62. https://doi.org/10.1016/j.abb.2008.04.038.
- Covalent capture of phospho-dependent protein oligomerization by site-specific incorporation of a diazirine photo-cross-linker; M. Vila-Perello, M. R. Pratt, F. Tulin and T. W. Muir; *J Am Chem Soc* 2007; **129**: 8068-9. https://doi.org/10.1021/ja072013j.
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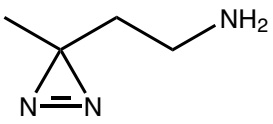
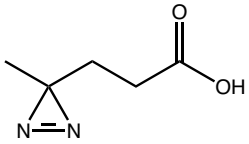
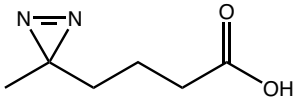
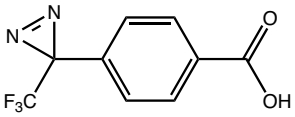
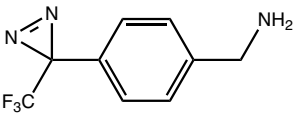
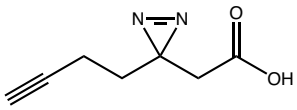
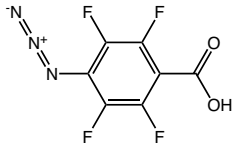
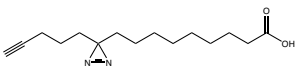
		Article No.	Quantity	Price
RL-2910	**Photo-Ethylamine*HCl**	RL-2910.0250	250 mg	€ 350,00
2-(3-methyl-3H-diazirin-3-yl)ethan-1-amine hydrochloride		RL-2910.0500	500 mg	€ 600,00
CAS-NO: 25055-95-2		RL-2910.0001	1 g	€ 1000,00
FORMULA: $C_4H_9N_3$*HCl				
MOLECULAR WEIGHT: 99,13*36,45 g/mol				
RL-2890	**Photo-Propanoic acid**	please inquire!		
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-2900	**Photo-Butyric acid**	please inquire!		
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-2920	**Photo-Benzoic acid**	RL-2920.0200	200 mg	€ 200,00
4-[3-(Trifluoromethyl)-3H-diazirin-3-yl]benzoic acid		RL-2920.1000	1 g	€ 600,00
CAS-NO: 85559-46-2				
FORMULA: $C_9H_5F_3N_2O_2$				
MOLECULAR WEIGHT: 230,14 g/mol				
RL-2930	**Photo-Benzylamine*HCl**	RL-2930.0200	200 mg	€ 250,00
4-[3-(Trifluoromethyl)-3H-diazirin-3-yl]benzylamine hydrochloride		RL-2930.1000	1 g	€ 700,00
CAS-NO: 1258874-29-1				
FORMULA: $C_9H_8N_3F_3$*HCl				
MOLECULAR WEIGHT: 215,18*36,45 g/mol				
RL-3410	**Propargyl-Photo-Propanoic acid**	please inquire!		
2-(3-(but-3-ynyl)-3H-diazirin-3-yl)acetic acid				
CAS-NO: 2049109-24-0				
FORMULA: $C_7H_8N_2O_2$				
MOLECULAR WEIGHT: 152,15 g/mol				
RL-2035	**ATFB**	RL-2035.0250	250 mg	€ 100,00
4-Azido-2,3,5,6-tetrafluorobenzoic acid		RL-2035.0500	500 mg	€ 180,00
CAS-NO: 122590-77-6		RL-2035.0001	1 g	€ 280,00
FORMULA: $C_7HF_4N_3O_2$		RL-2035.0005	5 g	€ 1000,00
MOLECULAR WEIGHT: 235,1 g/mol				
RL-3420	**10-Azirinpentadec-14-yneoic-acid**	please inquire!		
9-(3-(pent-4-ynyl)-3H-diazirin-3-yl)nonanoic acid				
CAS-NO: 1262788-55-5				
FORMULA: $C_7H_8N_2O_2$				
MOLECULAR WEIGHT: 264,36 g/mol				

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3. Cleavable Linkers

Peptidic bonds are expected to have a high serum stability, as lysosomal proteolytic enzymes show reduced activities in blood due to endogenous inhibitors and the unfavorably high pH value of blood compared to lysosomes. This was confirmed by preclinical *in vivo* studies which revealed half-lives of seven to ten days for peptide linkers. Release of a drug conjugated *via* a peptidyl linker to monoclonal antibodies (mAb) occurs specifically due to the action of lysosomal proteases (e.g., cathepsin and plasmin). These proteases may be present at even elevated levels in certain tumor tissues. Therefore, peptide linkers combine greater systemic stability with rapid enzymatic release of the drug in the target cell. Besides Val-Ala, Val-Cit and Phe-Lys, other sequences have been reported as lysosomally cleavable peptides, like Gly-Phe-Leu-Gly and Ala-Leu-Ala-Leu.

References:

- Star structure of antibody-targeted HPMA copolymer-bound doxorubicin: a novel type of polymeric conjugate for targeted drug delivery with potent antitumor effect; M. Kovar, J. Strohalm, T. Etrych, K. Ulbrich and B. Rihova; *Bioconjug Chem* 2002; **13**: 206-15. https://doi.org/10.1021/bc010063m.
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- Influence of a peptide linker on biodistribution and metabolism of antibody-conjugated benzyl-EDTA. Comparison of enzymatic digestion in vitro and in vivo; M. Studer, L. A. Kroger, S. J. DeNardo, D. L. Kukis and C. F. Meares; *Bioconjug Chem* 1992; **3**: 424-9. https://doi.org/10.1021/bc00017a012.

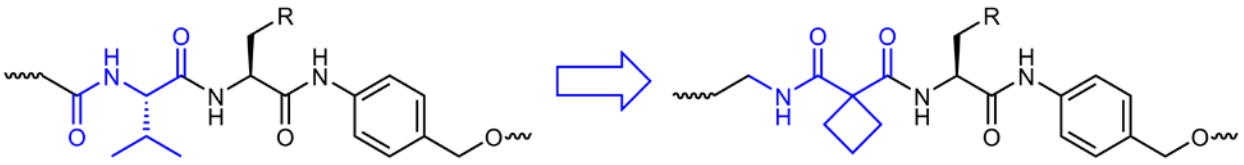


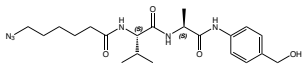
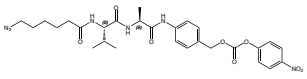
Fig. 17: Cyclobutane-1,1-dicarboxamide can replace valine in dipeptide linker systems, resulting in improved ADC selectivity.

Peptide-based ADC linkers, like Val-Cit or Val-Ala, that are cleaved by lysosomal proteases have shown sufficient stability in serum and effective payload-release in targeted cells. However, the use of peptide-based linkers limits the ability to modulate protease specificity. Furthermore, if the linker can preferentially be hydrolyzed by tumor-specific proteases only, safety margin may improve. In this context, a cyclobutane-1,1-dicarboxamide-containing linker replacing valine in other sequences has been invented which is hydrolyzed predominantly by cathepsin B, while the typical valine-citrulline dipeptide linker is rather less. ADCs bearing the nonpeptidic linker are as efficacious and stable *in vivo* as those with the dipeptide linker. Hence, the application of the peptidomimetic linker presents new opportunities for improving the selectivity of ADCs.

Reference:

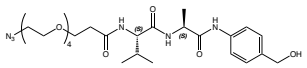
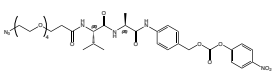
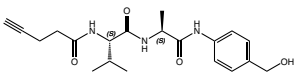
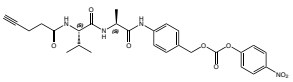
- Discovery of Peptidomimetic Antibody-Drug Conjugate Linkers with Enhanced Protease Specificity; B. Wei, J. Gunzner-Toste, H. Yao, T. Wang, J. Wang, Z. Xu, J. Chen, J. Wai, J. Nonomiya, S. P. Tsai, J. Chuh, K. R. Kozak, Y. Liu, S. F. Yu, J. Lau, G. Li, G. D. Phillips, D. Leipold, A. Kamath, D. Su, K. Xu, C. Eigenbrot, S. Steinbacher, R. Ohri, H. Raab, L. R. Staben, G. Zhao, J. A. Flygare, T. H. Pillow, V. Verma, L. A. Masterson, P. W. Howard and B. Safina; *Journal of medicinal chemistry* 2018; **61**: 989-1000. https://doi.org/10.1021/acs.jmedchem.7b01430.

3.1. Valine-Alanine-Based Enzymatically Cleavable Linkers

		Article No.	Quantity	Price
ADC1290 **6-Azidohexanoyl-Val-Ala-PAB** 6-azidohexanoyl-valyl-alanyl-(4-aminobenzyl alcohol) FORMULA: $C_{21}H_{32}N_6O_4$ MOLECULAR WEIGHT: 432,52 g/mol		ADC1290.0100	100 mg	€ 325,00
		ADC1290.0250	250 mg	€ 650,00
ADC1300 **6-Azidohexanoyl-Val-Ala-PAB-PNP** 6-azidohexanoyl-valyl-alanyl-(4-aminobenzyl)-(4-nitrophenyl)-carbonate FORMULA: $C_{28}H_{35}N_7O_8$ MOLECULAR WEIGHT: 597,62 g/mol		ADC1300.0100	100 mg	€ 375,00
		ADC1300.0250	250 mg	€ 750,00

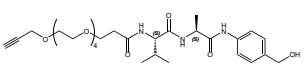
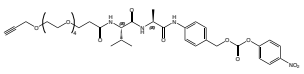
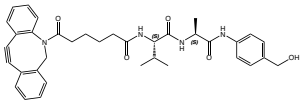
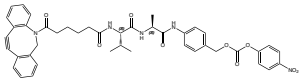
Reference:

- NKT cell-dependent glycolipid-peptide vaccines with potent anti-tumour activity; R. J. Anderson, B. J. Compton, C. W. Tang, A. Authier-Hall, C. M. Hayman, G. W. Swinerd, R. Kowalczyk, P. Harris, M. A. Brimble, D. S. Larsen, O. Gasser, R. Weinkove, I. F. Hermans and G. F. Painter; *Chem. Sci.* 2015; **6**: 5120-5127. https://doi.org/10.1039/c4sc03599b.

		Article No.	Quantity	Price
ADC1330 **Azido-PEG(4)-Val-Ala-PAB** azido-tetraethyleneglycol-propanoyl-valyl-alanyl-(4-aminobenzyl alcohol) FORMULA: $C_{26}H_{42}N_6O_8$ MOLECULAR WEIGHT: 566,65 g/mol		ADC1330.0100	100 mg	€ 450,00
		ADC1330.0250	250 mg	€ 900,00
ADC1340 **Azido-PEG(4)-Val-Ala-PAB-PNP** azido-tetraethyleneglycol-propanoyl-valyl-alanyl-(4-aminobenzyl)-(4-nitrophenyl)-carbonate FORMULA: $C_{33}H_{45}N_7O_{12}$ MOLECULAR WEIGHT: 731,75 g/mol		ADC1340.0100	100 mg	€ 500,00
		ADC1340.0250	250 mg	€ 1000,00
ADC1310 **4-Pentynoyl-Val-Ala-PAB** 4-pentynoyl-valyl-alanyl-(4-aminobenzyl alcohol) CAS-NO: 1956294-75-9 FORMULA: $C_{20}H_{27}N_3O_4$ MOLECULAR WEIGHT: 373,45 g/mol		ADC1310.0100	100 mg	€ 325,00
		ADC1310.0250	250 mg	€ 650,00
ADC1320 **4-Pentynoyl-Val-Ala-PAB-PNP** 4-pentynoyl-valyl-alanyl-(4-aminobenzyl)-(4-nitrophenyl)-carbonate CAS-NO: 1956294-76-0 FORMULA: $C_{27}H_{30}N_4O_8$ MOLECULAR WEIGHT: 538,55 g/mol		ADC1320.0100	100 mg	€ 375,00
		ADC1320.0250	250 mg	€ 750,00

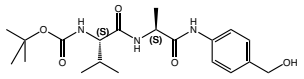
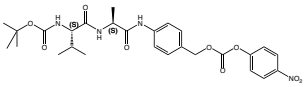
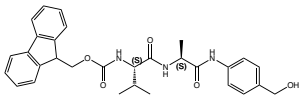
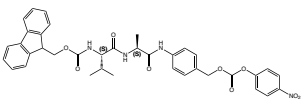
Reference:

- Integrin-Targeting Knottin Peptide-Drug Conjugates Are Potent Inhibitors of Tumor Cell Proliferation; N. Cox, J. R. Kintzing, M. Smith, G. A. Grant and J. R. Cochran; *Angew Chem Int Ed Engl* 2016; **55**: 9894-7. https://doi.org/10.1002/anie.201603488.

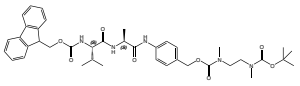
		Article No.	Quantity	Price
ADC1350	**Alkyne-PEG(4)-Val-Ala-PAB**	ADC1350.0100	100 mg	€ 450,00
propargyl-tetraethyleneglycol-propanoyl-valyl-alanyl-(4-aminobenzyl alcohol) FORMULA: $C_{29}H_{45}N_3O_9$ MOLECULAR WEIGHT: 579,68 g/mol		ADC1350.0250	250 mg	€ 900,00
ADC1360	**Alkyne-PEG(4)-Val-Ala-PAB-PNP**	ADC1360.0100	100 mg	€ 500,00
propargyl-tetraethyleneglycol-propanoyl-valyl-alanyl-(4-aminobenzyl)-(4-nitrophenyl)-carbonate FORMULA: $C_{36}H_{48}N_4O_{13}$ MOLECULAR WEIGHT: 744,79 g/mol		ADC1360.0250	250 mg	€ 1000,00
ADC1420	**DBCO-C6-Val-Ala-PAB**	ADC1420.0100	100 mg	€ 450,00
6-dibenzoazacyclooctyne-6-oxohexanoyl-valyl-alanyl-(4-amino-benzyl alcohol) FORMULA: $C_{36}H_{40}N_4O_5$ MOLECULAR WEIGHT: 608,73 g/mol		ADC1420.0250	250 mg	€ 900,00
ADC1430	**DBCO-C6-Val-Ala-PAB-PNP**	ADC1430.0100	100 mg	€ 500,00
6-dibenzoazacyclooctyne-6-oxohexanoyl-valyl-alanyl-(4-amino-benzyl)-(4-nitrophenyl)-carbonate FORMULA: $C_{43}H_{43}N_5O_9$ MOLECULAR WEIGHT: 773,83 g/mol		ADC1430.0250	250 mg	€ 1000,00

References:

- Exploration of the carmaphycins as payloads in antibody drug conjugate anticancer agents; J. Almaliti, B. Miller, H. Pietraszkiewicz, E. Glukhov, C. B. Naman, T. Kline, J. Hanson, X. Li, S. Zhou, F. A. Valeriote and W. H. Gerwick; *Eur J Med Chem* 2019; **161**: 416-432. https://doi.org/10.1016/j.ejmech.2018.10.024.
- Design and synthesis of novel dual-cyclic RGD peptides for alphavbeta3 integrin targeting; J. Liu, X. Cheng, X. Tian, D. Guan, J. Ao, Z. Wu, W. Huang and Z. Le; *Bioorg Med Chem Lett* 2019; **29**: 896-900. https://doi.org/10.1016/j.bmcl.2019.01.043.

		Article No.	Quantity	Price
ADC1040	**Boc-Val-Ala-PAB**	ADC1040.0250	250 mg	€ 225,00
t-Butyloxycarbonyl-valyl-alanyl-4-aminobenzylalcohol CAS-NO: 1884577-99-4 FORMULA: $C_{20}H_{31}N_3O_5$ MOLECULAR WEIGHT: 393,48 g/mol		ADC1040.1000	1 g	€ 650,00
ADC1050	**Boc-Val-Ala-PAB-PNP**	ADC1050.0100	100 mg	€ 125,00
t-Butyloxycarbonyl-valyl-alanyl-(4-aminobenzyl)-(4-nitrophenyl) carbonate CAS-NO: 1884578-00-0 FORMULA: $C_{27}H_{34}N_4O_9$ MOLECULAR WEIGHT: 558,58 g/mol		ADC1050.0250	250 mg	€ 250,00
		ADC1050.1000	1 g	€ 750,00
ADC1060	**Fmoc-Val-Ala-PAB**	ADC1060.0250	250 mg	€ 225,00
9-Fluorenylmethyloxycarbonyl-valyl-alanyl-4-aminobenzylalcohol CAS-NO: 1394238-91-5 FORMULA: $C_{30}H_{33}N_3O_5$ MOLECULAR WEIGHT: 515,61 g/mol		ADC1060.1000	1 g	€ 650,00
ADC1070	**Fmoc-Val-Ala-PAB-PNP**	ADC1070.0100	100 mg	€ 125,00
9-Fluorenylmethyloxycarbonyl-valyl-alanyl-(4-aminobenzyl)-(4-nitro-phenyl)carbonate CAS-NO: 1394238-92-6 FORMULA: $C_{37}H_{36}N_4O_9$ MOLECULAR WEIGHT: 680,71 g/mol		ADC1070.0250	250 mg	€ 250,00
		ADC1070.1000	1 g	€ 750,00

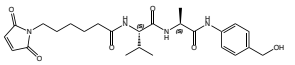
	Article No.	Quantity	Price
ADC1410 Fmoc-Val-Ala-PAB-NMeCH$_2$CH$_2$NMe-Boc	ADC1410.0100	100 mg	€ 175,00
9-Fluorenylmethyloxycarbonyl-valyl-alanyl-4-aminobenzyloxycarbonyl-((t-buytl methyl(2-methylamino)ethyl)carbamate)	ADC1410.0250	250 mg	€ 350,00
CAS-NO: 1691196-82-3	ADC1410.0001	1 g	€ 1000,00
FORMULA: $C_{40}H_{51}N_5O_8$			
MOLECULAR WEIGHT: 729,86 g/mol			



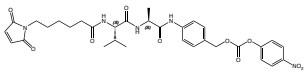
References:

- Multivalency Increases the Binding Strength of RGD Peptidomimetic-Paclitaxel Conjugates to Integrin alphaV beta3; A. Raposo Moreira Dias, A. Pina, A. Dal Corso, D. Arosio, L. Belvisi, L. Pignataro, M. Caruso and C. Gennari; *Chemistry* 2017; **23**: 14410-14415. https://doi.org/10.1002/chem.201703093.
- Synthesis and biological evaluation of RGD peptidomimetic-paclitaxel conjugates bearing lysosomally cleavable linkers; A. Dal Corso, M. Caruso, L. Belvisi, D. Arosio, U. Piarulli, C. Albanese, F. Gasparri, A. Marsiglio, F. Sola, S. Troiani, B. Valsasina, L. Pignataro, D. Donati and C. Gennari; *Chemistry* 2015; **21**: 6921-9. https://doi.org/10.1002/chem.201500158.
- Elongated multiple electronic cascade and cyclization spacer systems in activatible anticancer prodrugs for enhanced drug release; F. M. de Groot, W. J. Loos, R. Koekkoek, L. W. van Berkom, G. F. Busscher, A. E. Seelen, C. Albrecht, P. de Bruijn and H. W. Scheeren; *J Org Chem* 2001; **66**: 8815-30. https://doi.org/10.1021/jo0158884.

	Article No.	Quantity	Price
ADC1270 MC-Val-Ala-PAB	ADC1270.0100	100 mg	€ 150,00
6-maleimidohexanoyl-valyl-alanyl-(4-aminobenzyl alcohol)	ADC1270.0250	250 mg	€ 300,00
CAS-NO: 1870916-87-2	ADC1270.0001	1 g	€ 900,00
FORMULA: $C_{25}H_{34}N_4O_6$			
MOLECULAR WEIGHT: 486,56 g/mol			



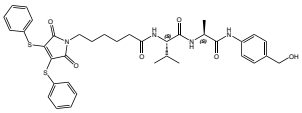
ADC1280 MC-Val-Ala-PAB-PNP	ADC1280.0100	100 mg	€ 175,00
6-maleimidohexanoyl-valyl-alanyl-(4-aminobenzyl)-(4-nitrophenyl)-carbonate	ADC1280.0250	250 mg	€ 350,00
CAS-NO: 1639939-40-4	ADC1280.0001	1 g	€ 1000,00
FORMULA: $C_{32}H_{37}N_5O_{10}$			
MOLECULAR WEIGHT: 651,66 g/mol			



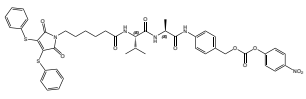
Reference:

- Improved Methodology for the Synthesis of a Cathepsin B Cleavable Dipeptide Linker, Widely Used in Antibody-Drug Conjugate Research; D. Mondal, J. Ford and K. G. Pinney; *Tetrahedron Lett* 2018; **59**: 3594-3599. https://doi.org/10.1016/j.tetlet.2018.08.021.

	Article No.	Quantity	Price
ADC1540 DTM-C6-Val-Ala-PAB			
6-(3,4-bisphenylthiomaleimido)hexanoyl-valyl-alanyl-(4-aminobenzyl alcohol)			please inquire!
FORMULA: $C_{37}H_{42}N_4O_6S_2$			
MOLECULAR WEIGHT: 702,88 g/mol			



ADC1550 DTM-C6-Val-Ala-PAB-PNP			
6-(3,4-bisphenylthiomaleimido)hexanoyl-valyl-alanyl-(4-aminobenzyl)-(4-nitrophenyl)-carbonate			please inquire!
FORMULA: $C_{44}H_{45}N_5O_{10}S_2$			
MOLECULAR WEIGHT: 867,99 g/mol			



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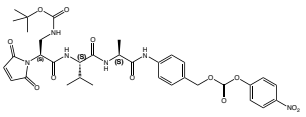
- Next generation maleimides enable the controlled assembly of antibody-drug conjugates via native disulfide bond bridging; F. F. Schumacher, J. P. Nunes, A. Maruani, V. Chudasama, M. E. Smith, K. A. Chester, J. R. Baker and S. Caddick; *Org Biomol Chem* 2014; **12**: 7261-9. https://doi.org/10.1039/c4ob01550a.
- Site-Specific Conjugation of Auristatins onto Engineered scFv Using Second Generation Maleimide to Target HER2-positive Breast Cancer in Vitro; N. Aubrey, E. Allard-Vannier, C. Martin, F. Bryden, S. Letast, C. Colas, Z. Lakhrif, N. Collinet, I. Dimier-Poisson, I. Chourpa, M. C. Viaud-Massuard and N. Joubert; *Bioconjug Chem* 2018; **29**: 3516-3521. https://doi.org/10.1021/acs.bioconjchem.8b00668.
- Impact of cathepsin B-sensitive triggers and hydrophilic linkers on in vitro efficacy of novel site-specific antibody-drug conjugates; F. Bryden, C. Martin, S. Letast, E. Lles, I. Vieitez-Villemin, A. Rousseau, C. Colas, M. Brachet-Botineau, E. Allard-Vannier, C. Larbouret, M. C. Viaud-Massuard and N. Joubert; *Org Biomol Chem* 2018; **16**: 1882-1889. https://doi.org/10.1039/c7ob02780j.

	Article No.	Quantity	Price
ADC1080 Mal-Dap(Boc)-Val-Ala-PAB-PNP	ADC1080.0250	250 mg	€ 750,00

N-alpha-Maleimido-N-beta-t-butyloxycarbonyl-L-2,3-diaminopropionyl-valyl-alanyl-(4-aminobenzyl)-(4-nitrophenyl)-carbonate
FORMULA: $C_{34}H_{40}N_6O_{12}$
MOLECULAR WEIGHT: 721,71 g/mol



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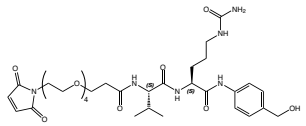
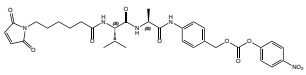
- Linker Technologies for Antibody-Drug Conjugates; B. Nolting; *Antibody-Drug Conjugates L. Ducry* 2013; **1045**: 71-100. https://doi.org/10.1007/978-1-62703-541-5_5.
- Self-hydrolyzing maleimides improve the stability and pharmacological properties of antibody-drug conjugates; R. P. Lyon, J. R. Setter, T. D. Bovee, S. O. Doronina, J. H. Hunter, M. E. Anderson, C. L. Balasubramanian, S. M. Duniho, C. I. Leiske, F. Li and P. D. Senter; *Nat Biotechnol* 2014; **32**: 1059-62. https://doi.org/10.1038/nbt.2968.
- Self-Stabilizing Linker Conjugate; Lyon R., Doronina S., Bovee T.; Seattle Genetics, Inc.; *U.S. Patent No. 9,504,756*, 2013.

	Article No.	Quantity	Price
ADC1370 Mal-PEG(4)-Val-Ala-PAB	ADC1370.0100	100 mg	€ 450,00
	ADC1370.0250	250 mg	€ 900,00
ADC1280 MC-Val-Ala-PAB-PNP	ADC1280.0100	100 mg	€ 175,00
	ADC1280.0250	250 mg	€ 350,00
	ADC1280.0001	1 g	€ 1000,00

maleimido-tetraethyleneglycol-propanoyl-alanyl-citrullyl-(4-amino-benzyl alcohol)
FORMULA: $C_{33}H_{50}N_6O_{11}$
MOLECULAR WEIGHT: 706,78 g/mol



6-maleimidohexanoyl-valyl-alanyl-(4-aminobenzyl)-(4-nitrophenyl)-carbonate
CAS-NO: 1639939-40-4
FORMULA: $C_{32}H_{37}N_5O_{10}$
MOLECULAR WEIGHT: 651,66 g/mol

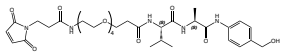


Reference:

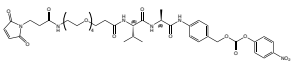
- In Vivo Antitumor Activity of a Novel Acetazolamide-Cryptophycin Conjugate for the Treatment of Renal Cell Carcinomas; S. Cazzamalli, E. Figueras, L. Petho, A. Borbely, C. Steinkuhler, D. Neri and N. Sewald; *ACS Omega* 2018; **3**: 14726-14731. https://doi.org/10.1021/acsomega.8b02350.

	Article No.	Quantity	Price
ADC1390 Mal-beta-Ala-PEG(4)-Val-Ala-PAB	ADC1390.0100	100 mg	€ 450,00
	ADC1390.0250	250 mg	€ 900,00
ADC1400 Mal-beta-Ala-PEG(4)-Val-Ala-PAB-PNP	ADC1400.0100	100 mg	€ 500,00
	ADC1400.0250	250 mg	€ 1000,00

maleimido-beta-alanyl-tetraethyleneglycol-propanoyl-valyl-alanyl-(4-aminobenzyl alcohol)
FORMULA: $C_{33}H_{49}N_5O_{11}$
MOLECULAR WEIGHT: 691,77 g/mol



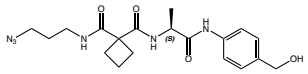
maleimido-beta-alanyl-tetraethyleneglycol-propanoyl-valyl-alanyl-(4-aminobenzyl)-(4-nitrophenyl)-carbonate
FORMULA: $C_{40}H_{52}N_6O_{15}$
MOLECULAR WEIGHT: 856,87 g/mol



Article No.	Quantity	Price

ADC1580 Azido-cyclobutane-1,1-dicarboxamide-Ala-PAB

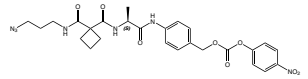
3-azidopropyl-cyclobutane-1,1-dicarboxamide-alanyl-(4-aminobenzyl alcohol)
FORMULA: $C_{19}H_{26}N_6O_4$
MOLECULAR WEIGHT: 402,45 g/mol



please inquire!

ADC1590 Azido-cyclobutane-1,1-dicarboxamide-Ala-PAB-PNP

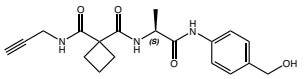
3-azidopropyl-cyclobutane-1,1-dicarboxamide-alanyl-(4-amino-benzyl)-(4-nitrophenyl)-carbonate
FORMULA: $C_{26}H_{29}N_7O_8$
MOLECULAR WEIGHT: 567,55 g/mol



please inquire!

ADC1600 Propargyl-cyclobutane-1,1-dicarboxamide-Ala-PAB

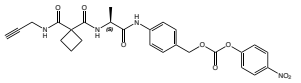
propargyl-cyclobutane-1,1-dicarboxamide-alanyl-(4-aminobenzyl alcohol)
FORMULA: $C_{19}H_{23}N_3O_4$
MOLECULAR WEIGHT: 357,40 g/mol



please inquire!

ADC1610 Propargyl-cyclobutane-1,1-dicarboxamide-Ala-PAB-PNP

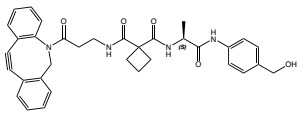
propargyl-cyclobutane-1,1-dicarboxamide-alanyl-(4-aminobenzyl)-(4-nitrophenyl)-carbonate
FORMULA: $C_{26}H_{26}N_4O_8$
MOLECULAR WEIGHT: 522,51 g/mol



please inquire!

ADC1620 DBCO-cyclobutane-1,1-dicarboxamide-Ala-PAB

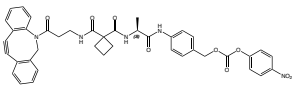
dibenzoazacyclooctyne-cyclobutane-1,1-dicarboxamide-alanyl-(4-aminobenzyl alcohol)
FORMULA: $C_{34}H_{34}N_4O_5$
MOLECULAR WEIGHT: 578,66 g/mol



please inquire!

ADC1630 DBCO-cyclobutane-1,1-dicarboxamide-Ala-PAB-PNP

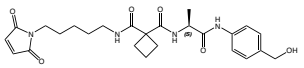
dibenzoazacyclooctyne-cyclobutane-1,1-dicarboxamide-alanyl-(4-aminobenzyl)-(4-nitrophenyl)-carbonate
FORMULA: $C_{41}H_{37}N_5O_9$
MOLECULAR WEIGHT: 743,76 g/mol



please inquire!

ADC1560 Mal-cyclobutane-1,1-dicarboxamide-Ala-PAB

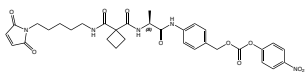
5-maleimidopentyl-cyclobutane-1,1-dicarboxamide-alanyl-(4-amino-benzyl alcohol)
FORMULA: $C_{25}H_{32}N_4O_6$
MOLECULAR WEIGHT: 484,54 g/mol



please inquire!

ADC1570 Mal-cyclobutane-1,1-dicarboxamide-Ala-PAB-PNP

5-maleimidopentyl-cyclobutane-1,1-dicarboxamide-alanyl-(4-aminobenzyl)-(4-nitrophenyl)-carbonate
FORMULA: $C_{32}H_{35}N_5O_{10}$
MOLECULAR WEIGHT: 649,65 g/mol

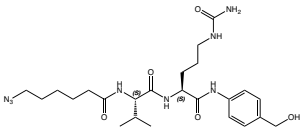
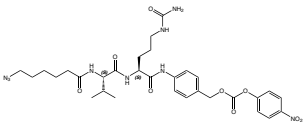


please inquire!

Reference:

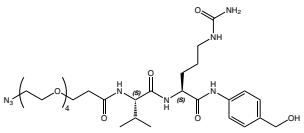
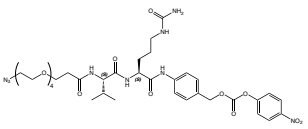
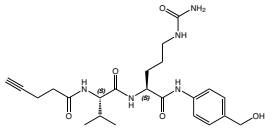
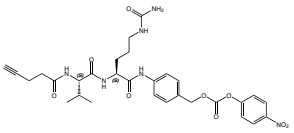
- Discovery of Peptidomimetic Antibody-Drug Conjugate Linkers with Enhanced Protease Specificity; B. Wei, J. Gunzner-Toste, H. Yao, T. Wang, J. Wang, Z. Xu, J. Chen, J. Wai, J. Nonomiya, S. P. Tsai, J. Chuh, K. R. Kozak, Y. Liu, S. F. Yu, J. Lau, G. Li, G. D. Phillips, D. Leipold, A. Kamath, D. Su, K. Xu, C. Eigenbrot, S. Steinbacher, R. Ohri, H. Raab, L. R. Staben, G. Zhao, J. A. Flygare, T. H. Pillow, V. Verma, L. A. Masterson, P. W. Howard and B. Safina; *J. Med. Chem.* 2018; **61**: 989-1000. https://doi.org/10.1021/acs.jmedchem.7b01430.

3.2. Valine-Citrulline-Based Enzymatically Cleavable Linkers

		Article No.	Quantity	Price
ADC1120	**6-Azidohexanoyl-Val-Cit-PAB**	ADC1120.0100	100 mg	€ 325,00
6-azidohexanoyl-valyl-citrullyl-(4-aminobenzyl alcohol) CAS-NO: 1613321-02-0 FORMULA: $C_{24}H_{38}N_8O_5$ MOLECULAR WEIGHT: 518,61 g/mol		ADC1120.0250	250 mg	€ 650,00
ADC1130	**6-Azidohexanoyl-Val-Cit-PAB-PNP**	ADC1130.0100	100 mg	€ 375,00
6-azidohexanoyl-valyl-citrullyl-(4-aminobenzyl)-(4-nitrophenyl)-carbonate CAS-NO: 1613321-01-9 FORMULA: $C_{31}H_{41}N_9O_9$ MOLECULAR WEIGHT: 683,71 g/mol		ADC1130.0250	250 mg	€ 750,00

Reference:

- NKT cell-dependent glycolipid-peptide vaccines with potent anti-tumour activity; R. J. Anderson, B. J. Compton, C. W. Tang, A. Authier-Hall, C. M. Hayman, G. W. Swinerd, R. Kowalczyk, P. Harris, M. A. Brimble, D. S. Larsen, O. Gasser, R. Weinkove, I. F. Hermans and G. F. Painter; *Chem. Sci.* 2015; **6**: 5120-5127. https://doi.org/10.1039/c4sc03599b.

		Article No.	Quantity	Price
ADC1160	**Azido-PEG(4)-Val-Cit-PAB**	ADC1160.0100	100 mg	€ 450,00
azido-tetraethyleneglycol-propanoyl-valyl-citrullyl-(4-aminobenzyl alcohol) CAS-NO: 2055024-64-9 FORMULA: $C_{29}H_{48}N_8O_9$ MOLECULAR WEIGHT: 652,74 g/mol		ADC1160.0250	250 mg	€ 900,00
ADC1170	**Azido-PEG(4)-Val-Cit-PAB-PNP**	ADC1170.0100	100 mg	€ 500,00
azido-tetraethyleneglycol-propanoyl-valyl-citrullyl-(4-aminobenzyl)-(4-nitrophenyl)-carbonate CAS-NO: 1869126-60-2 FORMULA: $C_{36}H_{51}N_9O_{13}$ MOLECULAR WEIGHT: 817,84 g/mol		ADC1170.0250	250 mg	€ 1000,00
ADC1140	**4-Pentynoyl-Val-Cit-PAB**	ADC1140.0100	100 mg	€ 325,00
4-pentynoyl-valyl-citrullyl-(4-aminobenzyl alcohol) FORMULA: $C_{23}H_{33}N_5O_5$ MOLECULAR WEIGHT: 459,54 g/mol		ADC1140.0250	250 mg	€ 650,00
ADC1150	**4-Pentynoyl-Val-Cit-PAB-PNP**	ADC1150.0100	100 mg	€ 375,00
4-pentynoyl-valyl-citrullyl-(4-aminobenzyl)-(4-nitrophenyl)-carbonate FORMULA: $C_{30}H_{36}N_6O_9$ MOLECULAR WEIGHT: 624,64 g/mol		ADC1150.0250	250 mg	€ 750,00

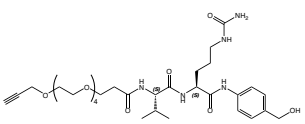
Reference:

- Integrin-Targeting Knottin Peptide–Drug Conjugates Are Potent Inhibitors of Tumor Cell Proliferation. N. Cox, J. R. Kintzing, M. Smith, G. A. Grant, J. R. Cochran; *Angew. Chem. Int. Ed.* 2016; **55(34)**: 9894-9897. https://doi.org/10.1002/anie.201603488.

	Article No.	Quantity	Price

ADC1180 Alkyne-PEG(4)-Val-Cit-PAB

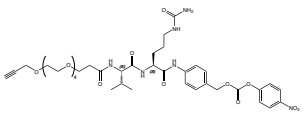
propargyl-tetraethyleneglycol-propanoyl-valyl-citrullyl-(4-aminobenzyl alcohol)
FORMULA: $C_{32}H_{51}N_5O_{10}$
MOLECULAR WEIGHT: 665,77 g/mol



Article No.	Quantity	Price
ADC1180.0100	100 mg	€ 450,00
ADC1180.0250	250 mg	€ 900,00

ADC1190 Alkyne-PEG(4)-Val-Cit-PAB-PNP

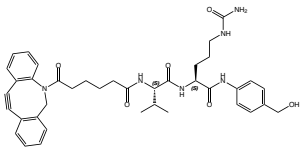
propargyl-tetraethyleneglycol-propanoyl-valyl-citrullyl-(4-aminobenzyl)-(4-nitrophenyl)-carbonate
FORMULA: $C_{39}H_{54}N_6O_{14}$
MOLECULAR WEIGHT: 830,88 g/mol



Article No.	Quantity	Price
ADC1190.0100	100 mg	€ 500,00
ADC1190.0250	250 mg	€ 1000,00

ADC1250 DBCO-C6-Val-Cit-PAB

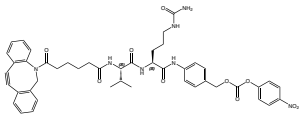
6-dibenzoazacyclooctyne-6-oxohexanoyl-valyl-citrullyl-(4-aminobenzyl alcohol)
FORMULA: $C_{39}H_{46}N_6O_6$
MOLECULAR WEIGHT: 694,82 g/mol



Article No.	Quantity	Price
ADC1250.0100	100 mg	€ 600,00
ADC1250.0250	250 mg	€ 1200,00

ADC1260 DBCO-C6-Val-Cit-PAB-PNP

6-dibenzoazacyclooctyne-6-oxohexanoyl-valyl-citrullyl-(4-aminobenzyl)-(4-nitrophenyl)-carbonate
FORMULA: $C_{46}H_{49}N_7O_{10}$
MOLECULAR WEIGHT: 859,92 g/mol



Article No.	Quantity	Price
ADC1260.0100	100 mg	€ 900,00
ADC1260.0250	250 mg	€ 1800,00

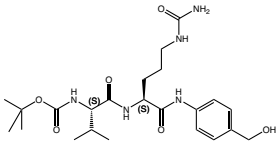
References:

- Exploration of the carmaphycins as payloads in antibody drug conjugate anticancer agents. J. Almaliti, B. Miller, H. Pietraszkiewicz, E. Glukhov, C. B. Naman, T. Kline, J. Hanson, X. Li, S. Zhou, F. A. Valeriote, W. H. Gerwick; Eur J Med Chem. 2019; 161: 416-432. https://doi.org/10.1016/j.ejmech.2018.10.024.
- Design and synthesis of novel dual-cyclic RGD peptides for -v-3 integrin targeting. J. Liu, X. Cheng, X. Tian, D. Guan, J. Ao, Z. Wu, W. Huang, Z. Le; Bioorg Med Chem Lett. 2019; 29(7): 896-900. https://doi.org/10.1016/j.bmcl.2019.01.043.

	Article No.	Quantity	Price

ADC1020 Boc-Val-Cit-PAB

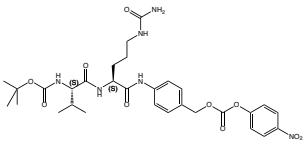
t-Butyloxycarbonyl-valyl-citrullyl-4-aminobenzylalcohol
CAS-NO: 870487-09-5
FORMULA: $C_{23}H_{37}N_5O_6$
MOLECULAR WEIGHT: 479,59 g/mol



Article No.	Quantity	Price
ADC1020.0250	250 mg	€ 225,00
ADC1020.1000	1 g	€ 650,00
ADC1020.5000	5 g	€ 2500,00

ADC1010 Boc-Val-Cit-PAB-PNP

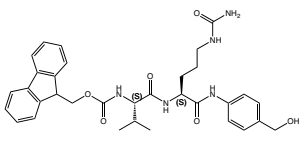
t-Butyloxycarbonyl-valyl-citrullyl-(4-aminobenzyl)-(4-nitrophenyl) carbonate
CAS-NO: 870487-10-8
FORMULA: $C_{30}H_{40}N_6O_{10}$
MOLECULAR WEIGHT: 644,67 g/mol



Article No.	Quantity	Price
ADC1010.0100	100 mg	€ 125,00
ADC1010.0250	250 mg	€ 250,00
ADC1010.1000	1 g	€ 750,00

ADC1030 Fmoc-Val-Cit-PAB

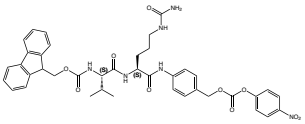
9-Fluorenylmethyloxycarbonyl-valyl-citrullyl-4-aminobenzylalcohol
CAS-NO: 159858-22-7
FORMULA: $C_{33}H_{39}N_5O_6$
MOLECULAR WEIGHT: 601,29 g/mol



Article No.	Quantity	Price
ADC1030.0250	250 mg	€ 225,00
ADC1030.1000	1 g	€ 650,00
ADC1030.5000	5 g	€ 2500,00

ADC1000 Fmoc-Val-Cit-PAB-PNP

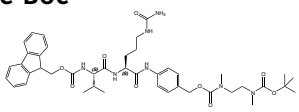
9-Fluorenylmethyloxycarbonyl-valyl-citrullyl-(4-aminobenzyl)-(4-nitrophenyl)carbonate
CAS-NO: 863971-53-3
FORMULA: $C_{40}H_{42}N_6O_{10}$
MOLECULAR WEIGHT: 766,80 g/mol



Article No.	Quantity	Price
ADC1000.0100	100 mg	€ 125,00
ADC1000.0250	250 mg	€ 250,00
ADC1000.1000	1 g	€ 750,00

ADC1240 Fmoc-Val-Cit-PAB-NMeCH$_2$CH$_2$NMe-Boc

9-Fluorenylmethyloxycarbonyl-valyl-citrullyl-4-aminobenzyloxycarbonyl-((t-buytl methyl(2-methylamino)ethyl)carbamate)
CAS-NO: 1802297-96-6
FORMULA: $C_{43}H_{57}N_7O_9$
MOLECULAR WEIGHT: 815,95 g/mol



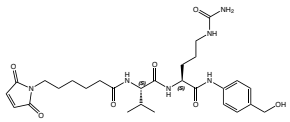
Article No.	Quantity	Price
ADC1240.0100	100 mg	€ 175,00
ADC1240.0250	250 mg	€ 350,00
ADC1240.0001	1 g	€ 1000,00

References:

- Multivalency Increases the Binding Strength of RGD Peptidomimetic-Paclitaxel Conjugates to Integrin αVβ3. A. R. M. Dias, A. Pina, A. Dal Corso, D. Arosio, L. Belvisi, L. Pignataro, M. Caruso, C. Gennari; *Chem. Eur. J.* 2017; **23(58)**: 14410-14415. https://doi.org/10.1002/chem.201703093.
- Synthesis and Biological Evaluation of RGD Peptidomimetic-Paclitaxel Conjugates Bearing Lysosomally Cleavable Linkers. A. D. Corso, M. Caruso, L. Belvisi, D. Arosio, U. Piarulli, C. Albanese, F. Gasparri, A. Marsiglio, F. Sola, S. Troiani, B. Valsasina, L. Pignataro, D. Donati, C. Gennari; *Chem. Eur. J.* 2015; **21(18)**: 6921-6929. https://doi.org/10.1002/chem.201500158.
- Elongated Multiple Electronic Cascade and Cyclization Spacer Systems in Activatible Anticancer Prodrugs for Enhanced Drug Release. F. M. H. de Groot, W. J. Loos, R. Koekkoek, L. W. A. van Berkom, G. F. Busscher, A. E. Seelen, C. Albrecht, P. Bruijn, H. W. Scheeren. *J. Org. Chem.* 2001; **66(26)**: 8815-8830. https://doi.org/10.1021/jo0158884.

ADC1100 MC-Val-Cit-PAB

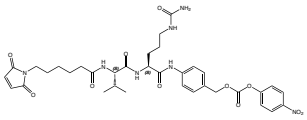
6-maleimidohexanoyl-valyl-citrullyl-(4-aminobenzyl alcohol)
CAS-NO: 159857-80-4
FORMULA: $C_{28}H_{40}N_6O_7$
MOLECULAR WEIGHT: 572,65 g/mol



Article No.	Quantity	Price
ADC1100.0250	250 mg	€ 300,00
ADC1100.0001	1 g	€ 900,00

ADC1110 MC-Val-Cit-PAB-PNP

6-maleimidohexanoyl-valyl-citrullyl-(4-aminobenzyl)-(4-nitrophenyl)-carbonate
CAS-NO: 159857-81-5
FORMULA: $C_{35}H_{43}N_7O_{11}$
MOLECULAR WEIGHT: 737,76 g/mol



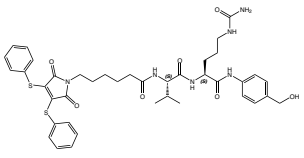
Article No.	Quantity	Price
ADC1110.0100	100 mg	€ 175,00
ADC1110.0250	250 mg	€ 350,00
ADC1110.0001	1 g	€ 1000,00

Reference:

- Improved Methodology for the Synthesis of a Cathepsin B Cleavable Dipeptide Linker, Widely Used in Antibody-Drug Conjugate Research. D. Mondal, J. Ford, K. G. Pinney; *Tetrahedron Lett.* 2018; **59(40)**: 3594-3599. https://doi.org/10.1016/j.tetlet.2018.08.021.

ADC1440 DTM-C6-Val-Cit-PAB

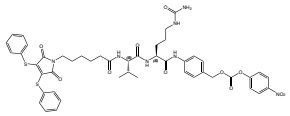
6-(3,4-bisphenylthiomaleimido)hexanoyl-valyl-citrullyl-(4-aminobenzyl alcohol)
CAS-NO: 1454662-44-2
FORMULA: $C_{40}H_{48}N_6O_7S_2$
MOLECULAR WEIGHT: 788,98 g/mol



Article No.	Quantity	Price
please inquire!		

ADC1450 DTM-C6-Val-Cit-PAB-PNP

6-(3,4-bisphenylthiomaleimido)hexanoyl-valyl-citrullyl-(4-aminobenzyl)-(4-nitrophenyl)-carbonate
CAS-NO: 1659319-42-2
FORMULA: $C_{47}H_{51}N_7O_{11}S_2$
MOLECULAR WEIGHT: 957,08 g/mol



Article No.	Quantity	Price
please inquire!		

References:

- Next generation maleimides enable the controlled assembly of antibody-drug conjugates via native disulfide bond bridging. F. F. Schumacher, J. P. M. Nunes, A. Maruani, V. Chudasama, M. E. B. Smith, K. A. Chester, J. R. Baker, S. Caddick; *Org. Biomol. Chem.* 2014; **12**: 7261-7269. https://doi.org/10.1039/C4OB01550A.
- Site-Specific Conjugation of Auristatins onto Engineered scFv Using Second Generation Maleimide to Target HER2-positive Breast Cancer in Vitro. N. Aubrey, E. Allard-Vannier, C. Martin, F. Bryden, S. Letast, C. Colas, Z. Lakhrif, N. Collinet, I. Dimier-Poisson, I. Chourpa, M. Viaud-Massuard, N. Joubert; *Bioconjugate Chem.* 2018; **29(11)**: 3516-3521.https://doi.org/10.1021/acs.bioconjchem.8b00668.

- Impact of cathepsin B-sensitive triggers and hydrophilic linkers on in vitro efficacy of novel site-specific antibody–drug conjugates. F. Bryden, C. Martin, S. Letast, E. Lles, I. Viéitez-Villemin, A. Rousseau, C. Colas, M. Brachet-Botineau, E. Allard-Vannier, C. Larbouret, M. Viaud-Massuard, N. Joubert; *Org. Biomol. Chem.* 2018; **16**: 1882-1889. https://doi.org/10.1039/C7OB02780J.

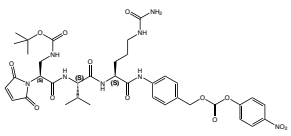
	Article No.	Quantity	Price

ADC1090 Mal-Dap(Boc)-Val-Cit-PAB

N-alpha-Maleimido-N-beta-t-butyloxycarbonyl-L-2,3-diaminopropionyl-valyl-citrullyl-(4-aminobenzyl)-(4-nitrophenyl)-carbonate

FORMULA: $C_{37}H_{46}N_8O_{13}$

MOLECULAR WEIGHT: 810,81 g/mol



ADC1090.0100	100 mg	€	750,00

References:

- Laurent Ducry (ed.), Antibody-Drug Conjugates, Methods in Molecular Biology, vol. 1045, DOI 10.1007/978-1-62703-541-5_5, # Springer Science+Business Media, LLC 2013.
- Self-hydrolyzing maleimides improve the stability and pharmacological properties of antibody-drug conjugates; R. P. Lyon, J. R. Setter, T. D. Bovee, S. O. Doronia, J. H. Hunter, M. E. Anderson, C. L. Balasubramanian, S. M. Duniho, C. I. Leiske, F. Li, P. D. Senter; *Nat. Biotechnol.* 2014; **32(10)**: 1059-1062. https://doi.org/10.1038/nbt.2968.
- Self-Stabilizing Linker Conjugates. Seattle Genetics, Inc. R. Lyon, S. Doronina, T. Bovee; WO 2013/173337 A2.

	Article No.	Quantity	Price

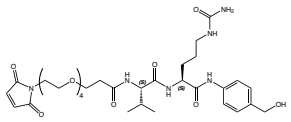
ADC1200 Mal-PEG(4)-Val-Cit-PAB

maleimido-tetraethyleneglycol-propanoyl-valyl-citrullyl-(4-aminobenzyl alcohol)

CAS-NO: 2055041-39-7

FORMULA: $C_{33}H_{50}N_6O_{11}$

MOLECULAR WEIGHT: 706,78 g/mol



ADC1200.0100	100 mg	€	500,00
ADC1200.0250	250 mg	€	1000,00

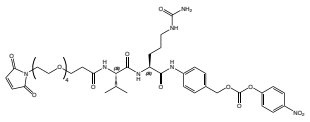
ADC1210 Mal-PEG(4)-Val-Cit-PAB-PNP

maleimido-tetraethyleneglycol-propanoyl-valyl-citrullyl-(4-aminobenzyl)-(4-nitrophenyl)-carbonate

CAS-NO: 2112738-09-5

FORMULA: $C_{40}H_{53}N_7O_{15}$

MOLECULAR WEIGHT: 871,89 g/mol



ADC1210.0100	100 mg	€	750,00
ADC1210.0250	250 mg	€	1500,00

Reference:

- In Vivo Antitumor Activity of a Novel Acetazolamide–Cryptophycin Conjugate for the Treatment of Renal Cell Carcinomas. S. Cazzamalli, E. Figueras, L. Pethő, A. Borbély, C. Steinkühler, D. Neri, N. Sewald; *ACS Omega* 2018; **3(11)**: 14726-14731. https://doi.org/10.1021/acsomega.8b02350.

	Article No.	Quantity	Price

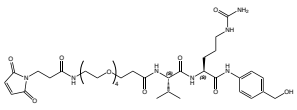
ADC1220 Mal-beta-Ala-PEG(4)-Val-Cit-PAB

maleimido-beta-alanyl-tetraethyleneglycol-propanoyl-valyl-citrullyl-(4-aminobenzyl alcohol)

CAS-NO: 1949793-41-2

FORMULA: $C_{36}H_{55}N_7O_{12}$

MOLECULAR WEIGHT: 777,86 g/mol



ADC1220.0100	100 mg	€	450,00
ADC1220.0250	250 mg	€	900,00

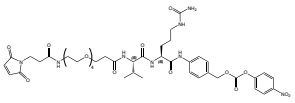
ADC1230 Mal-beta-Ala-PEG(4)-Val-Cit-PAB-PNP

maleimido-beta-alanyl-tetraethyleneglycol-propanoyl-valyl-citrullyl-(4-aminobenzyl)-(4-nitrophenyl)-carbonate

CAS-NO: 2003260-12-4

FORMULA: $C_{43}H_{58}N_8O_{16}$

MOLECULAR WEIGHT: 942,96 g/mol

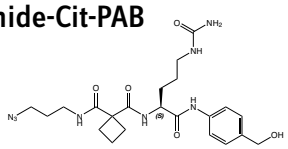


ADC1230.0100	100 mg	€	500,00
ADC1230.0250	250 mg	€	1000,00

	Article No.	Quantity	Price

ADC1480 Azido-cyclobutane-1,1-dicarboxamide-Cit-PAB

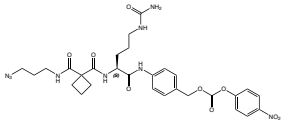
3-azidopropyl-cyclobutane-1,1-dicarboxamide-citrullyl-(4-aminobenzyl alcohol)
FORMULA: $C_{22}H_{32}N_8O_5$
MOLECULAR WEIGHT: 488,54 g/mol



please inquire!

ADC1490 Azido-cyclobutane-1,1-dicarboxamide-Cit-PAB-PNP

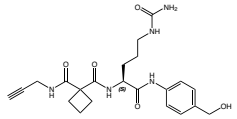
3-azidopropyl-cyclobutane-1,1-dicarboxamide-citrullyl-(4-aminobenzyl)-(4-nitrophenyl)-carbonate
FORMULA: $C_{29}H_{35}N_9O_9$
MOLECULAR WEIGHT: 653,64 g/mol



please inquire!

ADC1500 Propargyl-cyclobutane-1,1-dicarboxamide-Cit-PAB

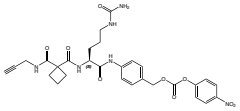
propargyl-cyclobutane-1,1-dicarboxamide-citrullyl-(4-aminobenzyl alcohol)
FORMULA: $C_{22}H_{29}N_5O_5$
MOLECULAR WEIGHT: 443,50 g/mol



please inquire!

ADC1510 Propargyl-cyclobutane-1,1-dicarboxamide-Cit-PAB-PNP

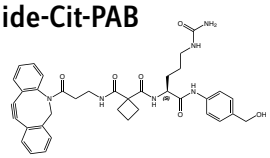
propargyl-cyclobutane-1,1-dicarboxamide-citrullyl-(4-aminobenzyl)-(4-nitrophenyl)-carbonate
FORMULA: $C_{29}H_{32}N_6O_9$
MOLECULAR WEIGHT: 608,60 g/mol



please inquire!

ADC1520 DBCO-cyclobutane-1,1-dicarboxamide-Cit-PAB

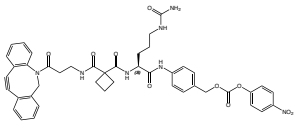
dibenzoazacyclooctyne-cyclobutane-1,1-dicarboxamide-citrullyl-(4-aminobenzyl alcohol)
FORMULA: $C_{37}H_{40}N_6O_6$
MOLECULAR WEIGHT: 664,75 g/mol



please inquire!

ADC1530 DBCO-cyclobutane-1,1-dicarboxamide-Cit-PAB-PNP

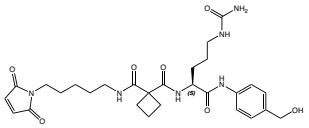
dibenzoazacyclooctyne-cyclobutane-1,1-dicarboxamide-citrullyl-(4-aminobenzyl)-(4-nitrophenyl)-carbonate
FORMULA: $C_{44}H_{43}N_7O_{10}$
MOLECULAR WEIGHT: 829,85 g/mol



please inquire!

ADC1460 Mal-cyclobutane-1,1-dicarboxamide-Cit-PAB

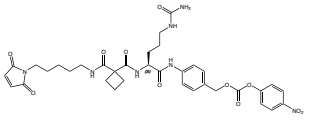
5-maleimidopentyl-cyclobutane-1,1-dicarboxamide-citrullyl-(4-aminobenzyl alcohol)
CAS-NO: 1799663-03-8
FORMULA: $C_{28}H_{38}N_6O_7$
MOLECULAR WEIGHT: 570,64 g/mol



please inquire!

ADC1470 Mal-cyclobutane-1,1-dicarboxamide-Cit-PAB-PNP

5-maleimidopentyl-cyclobutane-1,1-dicarboxamide-citrullyl-(4-aminobenzyl)-(4-nitrophenyl)-carbonate
CAS-NO: 2204228-34-0
FORMULA: $C_{35}H_{41}N_7O_{11}$
MOLECULAR WEIGHT: 735,74 g/mol



please inquire!

Reference:

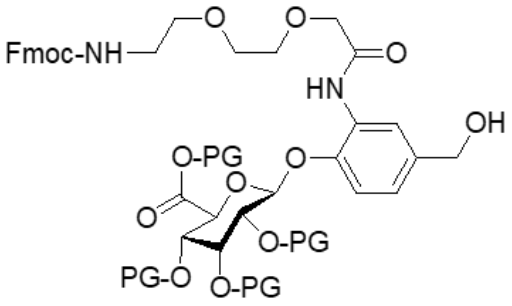
- Discovery of Peptidomimetic Antibody–Drug Conjugate Linkers with Enhanced Protease Specificity. B. Wei, J. Gunzner-Toste, H. Yao, T. Wang, J. Wang, Z. Xu, J. Chen, J. Wai, J. Nonomiya, S. Ping Tsai, J. Chuh, K. R. Kozak, Y. Liu, S. Yu, J. Lau, G. Li, G. D. Phillips, D. Leipold, A. Kamath, D. Su, K. Xu, C. Eigenbrot, S. Steinbacher, R. Ohri, H. Raab, L. R. Staben, G. Zhao, J. A. Flygare, T. H. Pillow, V. Verma, L. A. Masterson, P. W. Howard, B. Safina; *J. Med. Chem.* 2018; **61(3)**: 989-1000. https://doi.org/10.1021/acs.jmedchem.7b01430.

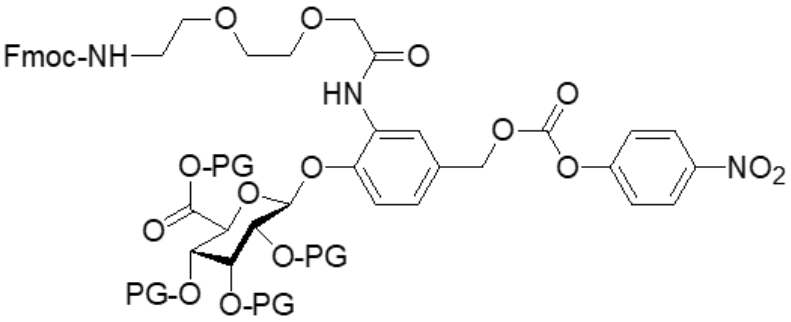
3.3. β-Glucuronide Enzymatically Cleavable Linkers

As extension of the linkerology toolbox the design of linkers with improved stability during systemic circulation is highly desired. As the drug-releasing lysosomal enzyme β-glucuronidase is abundantly present within lysosomes and overexpressed in some tumor types but low outside cells, β-glucuronic acid-based linkers provide the potential for high ADC stability in the systemic circulation and selective intracellular drug release. Especially for ADCs based on highly hydrophobic drugs, the incorporation of the highly hydrophilic β-glucuronides may circumvent the tendency of aggregation.

For example, a drug-linker consisting of a β-glucuronide linked to auristatin MMAF was prepared. Rat plasma stability analysis revealed an extrapolated half-life of 81 days compared with about 6 days for the corresponding valine-citrulline dipeptide-linked MMAF.

Interested in β-Glucuronide Enzymatically Cleavable Linkers?





→ Please contact our Custom Synthesis for more details on your derivative of choice!

References:

- Expanded Utility of the β-Glucuronide Linker: ADCs That Deliver Phenolic Cytotoxic Agents; S. C. Jeffrey, J. De Brabander, J. Miyamoto, and P. D. Senter; ACS Med. Chem. Lett. 2010; 1: 277-280. https://doi.org/10.1021/ml100039h.
- Development and Properties of β-Glucuronide Linkers for Monoclonal Antibody-Drug Conjugates; S. C. Jeffrey, J. B. Andreyka, S. X. Bernhardt, K. M. Kissler, T. Kline, J. S. Lenox, R. F. Moser, M. T. Nguyen, N. M. Okeley, I. J. Stone, X. Zhang, P. D. Senter; Bioconjugate Chem. 2006, 17: 831-840. https://doi.org/10.1021/bc0600214.
- Linker Technologies for Antibody-Drug Conjugates; B. Nolting; Antibody-Drug Conjugates L. Ducry 2013; 1045: 71-100. https://doi.org/10.1007/978-1-62703-541-5_5.

3.4. Disulfide-Based (Self-Immolative) Linkers

Another chemically labile linkage extensively exploited in the development of antibody-drug conjugates are disulfides. They are stable at physiological pH and are designed to release the drug upon internalization inside cells. The cytosol provides a significantly more reducing environment compared to the extracellular milieu and the presence of cytoplasmic thiol cofactor, such as reduced glutathione (GSH). Additionally, the intracellular enzyme protein disulfide isomerase, or similar enzymes capable of cleaving disulfide bonds, may also contribute to the preferential cleavage of disulfide bonds inside cells. GSH is reported to be present in cells in the concentration range of 0.5-10 mM compared with a significantly lower concentration of GSH or cysteine in plasma at approximately 5 µM. This is especially true for tumor cells, where irregular blood flow leads to a hypoxic state, resulting in enhanced activity of reductive enzymes and therefore in even higher glutathione concentrations.

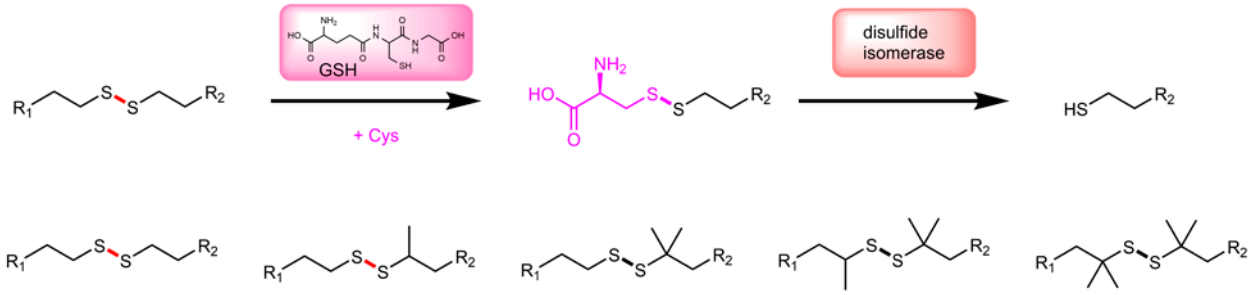


Fig. 18: The stability of disulfide linkers can be finetuned by neighboring methylation.

The stability of disulfide bridges can be fine-tuned by adjacent residues (Fig. 18). Methyl groups are bulky enough to have a significant influence on the thermodynamic stability of the disulfide bridge. While one additional methyl group already enhances the stability drastically, two methyl groups make the disulfide bond practically stable towards reductive cleavage. A methylation number of three or four will completely lock the disulfide bridge towards further modifications.

As the direct conjugation of cleavable triggers to bioactive agents through disulfide bridges suffers from ineffective cleavage in case of bulky moieties and resulting steric hindrance as well as restricted possibilities for trigger-drug combinations, disulfide based self-immolative linkers (DSILs) provide a robust strategy for selective activation upon disulfide cleavage in the reductive cytoplasmic milieu.

Disulfide-based self-immolative linkers benefit of the reversibility of disulfide-bond formation. Upon oxidation, free thiols form less nucleophilic disulfide bonds preventing self-immolative fragmentation. However, this process can be reversed in the presence of reducing agents, such as GSH. Those specifications allow for sufficient stability in the extracellular milieu but spontaneous self-immolative reaction within the cytosol upon GSH-mediated disulfide cleavage.

Variations in the linker's chemical composition (disulfide ethoxycarbonyl (SSE) vs. disulfide benzyloxycarbonyl (SSB)) result in chemically tunable kinetics of the self-immolative cleavage due to different response rates towards GSH, showing higher rates for SSB-based DSILs compared to SSE-based ones. Thus, the choice of the linker allows for fine-tuning of the cleavage speed and payload release.

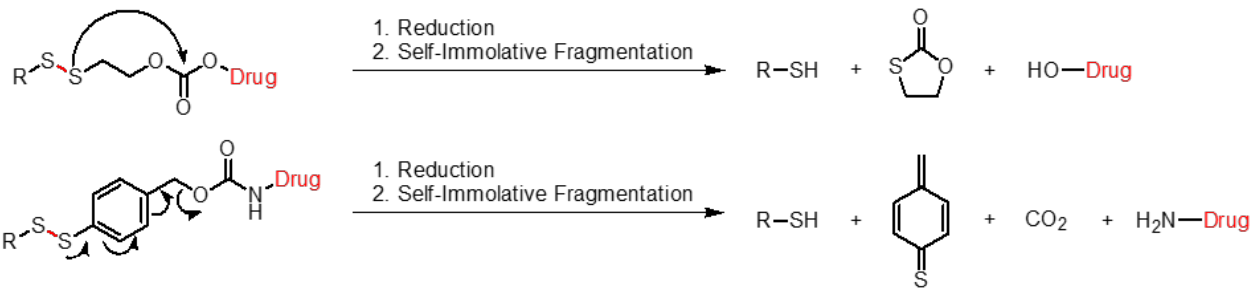
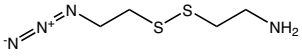


Fig. 19: Disulfide-based self-immolative linkers either based on an intramolecular cyclization cascade mechanism or on an 1,6-elimination.

HNN1090 N_3-Cystamine*HCl

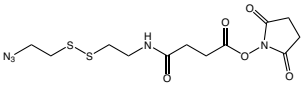
Azido-cystamine hydrochloride
CAS-NO: 1807512-40-8 net
FORMULA: $C_4H_{10}N_4S_2$*HCl
MOLECULAR WEIGHT: 178,28*36,45 g/mol



Article No.	Quantity	Price
HNN1090.0100	100 mg	€ 90,00
HNN1090.0250	250 mg	€ 150,00
HNN1090.0500	500 mg	€ 280,00
HNN1090.0001	1 g	€ 420,00
HNN1090.0005	5 g	€ 1500,00

HAA2255 N_3-Cystamine-Suc-OSu

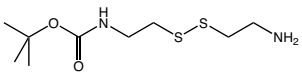
4-(2-((2-Azidoethyl)disulfanyl)ethylamino)-4-oxobutanoic acid succinimidyl ester
FORMULA: $C_{12}H_{17}N_5O_5S_2$
MOLECULAR WEIGHT: 375,42 g/mol



Article No.	Quantity	Price
HAA2255.0100	100 mg	€ 200,00
HAA2255.0250	250 mg	€ 400,00
HAA2255.0500	500 mg	€ 750,00
HAA2255.1000	1 g	€ 1200,00

BNN1170 Boc-Cystamine

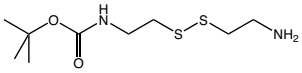
2-(t-Butyloxycarbonylamino)ethyldithio-2'-ethylamine
CAS-NO: 485800-26-8
FORMULA: $C_9H_{20}N_2O_2S_2$
MOLECULAR WEIGHT: 252,40 g/mol



Article No.	Quantity	Price
BNN1170.0500	500 mg	€ 81,00
BNN1170.0001	1 g	€ 126,00
BNN1170.0005	5 g	€ 450,00
BNN1170.0025	25 g	€ 1800,00

BNN1063 Boc-Cystamine*HCl

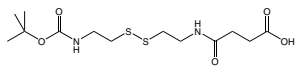
2-(t-Butyloxycarbonylamino)ethyldithio-2'-ethylamine hydrochloride
CAS-NO: 93790-49-9
FORMULA: $C_9H_{20}N_2O_2S_2$*HCl
MOLECULAR WEIGHT: 252,40*36,45 g/mol



Article No.	Quantity	Price
BNN1063.0001	1 g	€ 90,00
BNN1063.0005	5 g	€ 350,00
BNN1063.0025	25 g	€ 1400,00

BAA2180 Boc-Cystamine-Suc-OH

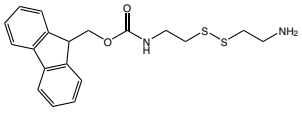
4-(2-((2-t-Butyloxycarbonylaminoethyl)disulfanyl)ethylamino)-4-oxobutanoic acid
CAS-NO: 946849-79-2
FORMULA: $C_{13}H_{24}N_2O_5S_2$
MOLECULAR WEIGHT: 352,47 g/mol



Article No.	Quantity	Price
BAA2180.0001	1 g	€ 145,00
BAA2180.0005	5 g	€ 450,00
BAA2180.0025	25 g	€ 1800,00

RL-3370 Fmoc-cystamine*HCl

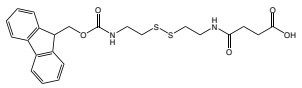
2-((9-Fluorenylmethyloxycarbonylamino)ethyl)disulfanyl-(2-aminoethane) hydrochloride
FORMULA: $C_{19}H_{22}N_2O_2S_2$*HCl
MOLECULAR WEIGHT: 374,52*36,45 g/mol



Article No.	Quantity	Price
RL-3370.0001	1 g	€ 126,00
RL-3370.0005	5 g	€ 450,00
RL-3370.0025	25 g	€ 1800,00

RL-3310 Fmoc-Cystamine-Suc

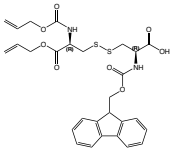
4-(2-((2-(9-Fluorenylmethyloxycarbonylamino)ethyl)disulfanyl) ethylamino)-4-oxobutanoic acid
CAS-NO: 946849-80-5
FORMULA: $C_{23}H_{26}N_2O_5S_2$
MOLECULAR WEIGHT: 474,59 g/mol



Article No.	Quantity	Price
RL-3310.0500	500 mg	€ 99,00
RL-3310.0001	1 g	€ 145,00
RL-3310.0005	5 g	€ 550,00
RL-3310.9025	25 g	€ 2200,00

FAA5550 Fmoc-L-Cys(Alloc-L-Cys-OAll)-OH

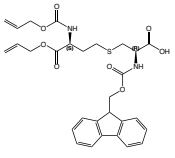
N-alpha-(9-Fluorenylmethyloxycarbonyl)-S-(N-alpha-allyloxycarbonyl)-L-cysteine allyl ester)-L-cysteine
FORMULA: $C_{28}H_{30}N_2O_8S_2$
MOLECULAR WEIGHT: 586,68 g/mol



please inquire!

FAA5560 Fmoc-L-Cys(Alloc-L-2Abu-OAll)-OH

N-alpha-(9-Fluorenylmethyloxycarbonyl)-S-(N-alpha-allyloxycarbonyl)-L-2-aminobutyric allyl ester)-L-cysteine
CAS-NO: 1309975-45-8
FORMULA: $C_{29}H_{32}N_2O_8S$
MOLECULAR WEIGHT: 568,64 g/mol

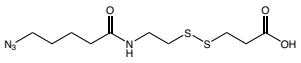


please inquire!

	Article No.	Quantity	Price

RL-3320 Azido-SS-COOH

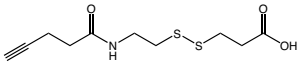
3-((2-(5-azidopentanamido)ethyl)disulfanyl)propanoic acid
FORMULA: $C_{10}H_{18}N_4O_3S_2$
MOLECULAR WEIGHT: 306,40 g/mol



please inquire!

RL-3330 Alkyne-SS-COOH

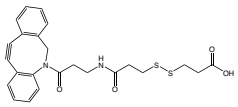
3-((2-pent-4-ynamidoethyl)disulfanyl)propanoic acid
FORMULA: $C_{10}H_{15}NO_3S_2$
MOLECULAR WEIGHT: 261,36 g/mol



please inquire!

RL-3340 DBCO-SS-COOH

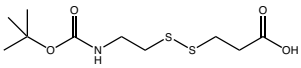
3-((3-(3-(azadibenzocyclooctyn-1-yl)-3-oxopropylamino)-3-oxopropyl) disulfanyl)propanoic acid
FORMULA: $C_{24}H_{24}N_2O_4S_2$
MOLECULAR WEIGHT: 468,59 g/mol



please inquire!

RL-2190 Boc-SS-COOH

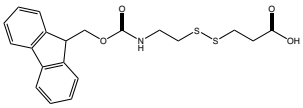
3-((2-(tert-butoxycarbonylamino)ethyl)disulfanyl)propanoic acid
FORMULA: $C_{10}H_{19}NO_4S_2$
MOLECULAR WEIGHT: 281,39 g/mol



RL-2190.0001	1 g	€	500,00
RL-2190.0005	5 g	€	2000,00

RL-2200 Fmoc-SS-COOH

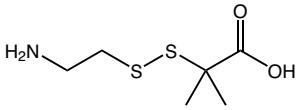
3-((2-(((9H-fluoren-9-yl)methoxy)carbonylamino)ethyl)disulfanyl) propanoic acid
FORMULA: $C_{20}H_{21}NO_4S_2$
MOLECULAR WEIGHT: 403,52 g/mol



RL-2200.0001	1 g	€	625,00
RL-2200.0005	5 g	€	2500,00

RL-2220 Stable Disulfide Linker

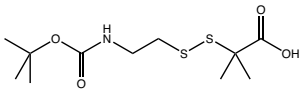
2-((2-aminoethyl)disulfanyl)-2-methylpropanoic acid
FORMULA: $C_6H_{13}NO_2S_2$
MOLECULAR WEIGHT: 195,30 g/mol



please inquire!

RL-2810 Boc-AEDI-OH

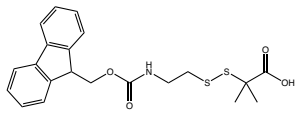
2-((2-(t-Butyloxycarbonylamino)ethyl)disulfanyl)-2-methylpropanoic acid
FORMULA: $C_{11}H_{21}NO_4S_2$
MOLECULAR WEIGHT: 295,42 g/mol



RL-2810.0001	1 g	€	350,00
RL-2810.0005	5 g	€	1300,00

RL-2800 Fmoc-AEDI-OH

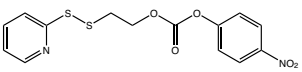
2-((2-((9-Fluorenylmethyloxycarbonyl)amino)ethyl)disulfanyl)-2-methylpropanoic acid
FORMULA: $C_{21}H_{23}NO_4S_2$
MOLECULAR WEIGHT: 417,54 g/mol



RL-2800.0001	1 g	€	750,00
RL-2800.0005	5 g	€	2750,00

RL-3500 OPSS-OpNC

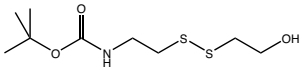
2-(2-Pyridithio)ethyl-p-nitrophenylcarbonate
CAS-NO: 874302-76-8
FORMULA: $C_{14}H_{12}N_2O_5S_2$
MOLECULAR WEIGHT: 352,38 g/mol



RL-3500.0250	250 mg	€	275,00
RL-3500.1000	1 g	€	800,00

RL-3510 Boc-NH-SS-OH

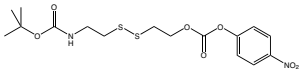
2-((2-(t-Butyloxycarbonylamino)ethyl)disulfaneyl)ethan-1-ol
CAS-NO: 877864-07-8
FORMULA: $C_9H_{19}NO_3S_2$
MOLECULAR WEIGHT: 253,38 g/mol



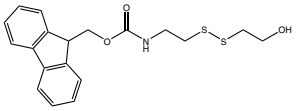
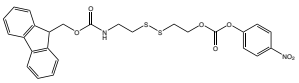
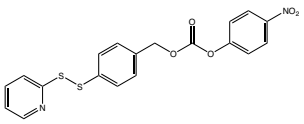
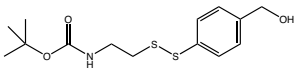
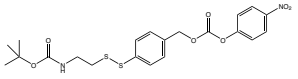
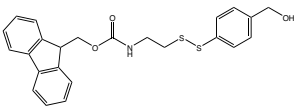
RL-3510.0250	250 mg	€	275,00
RL-3510.1000	1 g	€	800,00

RL-3520 Boc-NH-SS-OpNC

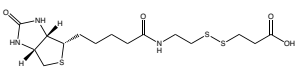
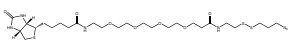
2-((2-(t-Butyloxycarbonylamino)ethyl)disulfaneyl)ethan-1-yl p-nitrophenylcarbonate
CAS-NO: 2040301-00-4
FORMULA: $C_{16}H_{22}N_2O_7S_2$
MOLECULAR WEIGHT: 418,48 g/mol

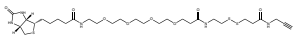
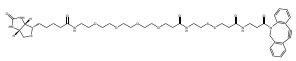
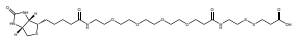
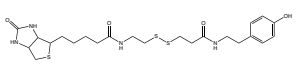


RL-3520.0100	100 mg	€	175,00
RL-3520.0250	250 mg	€	350,00
RL-3520.1000	1 g	€	1000,00

		Article No.	Quantity	Price
RL-3530 **Fmoc-NH-SS-OH**		RL-3530.0250	250 mg	€ 275,00
2-((2-((9-Fluorenylmethyloxycarbonyl)amino)ethyl)disulfaneyl) ethan-1-ol FORMULA: $C_{19}H_{21}NO_3S_2$ MOLECULAR WEIGHT: 375,50 g/mol		RL-3530.1000	1 g	€ 800,00
RL-3540 **Fmoc-NH-SS-OpNC**		RL-3540.0100	100 mg	€ 175,00
2-((2-((9-Fluorenylmethyloxycarbonyl)amino)ethyl)disulfaneyl) ethan-1-yl p-nitrophenylcarbonate FORMULA: $C_{26}H_{24}N_2O_7S_2$ MOLECULAR WEIGHT: 540,61 g/mol		RL-3540.0250	250 mg	€ 350,00
		RL-3540.1000	1 g	€ 1000,00
RL-3550 **OPSS-SS-Bzl-OpNC**		please inquire!		
(4-(pyridin-2-yldisulfaneyl)benzyl) p-nitrophenylcarbonate FORMULA: $C_{19}H_{14}N_2O_5S_2$ MOLECULAR WEIGHT: 414,45 g/mol				
RL-3560 **Boc-NH-SS-Bzl-OH**		please inquire!		
4-((2-(t-Butyloxycarbonylamino)ethyl)disulfaneyl)benzylalcohol FORMULA: $C_{14}H_{21}NO_3S_2$ MOLECULAR WEIGHT: 315,45 g/mol				
RL-3570 **Boc-NH-SS-Bzl-OpNC**		please inquire!		
4-((2-(t-Butyloxycarbonylamino)ethyl)disulfaneyl)benzyl p-nitrophenylcarbonate FORMULA: $C_{21}H_{24}N_2O_7S_2$ MOLECULAR WEIGHT: 480,55 g/mol				
RL-3580 **Fmoc-NH-SS-Bzl-OH**		please inquire!		
4-((2-((9-Fluorenylmethyloxycarbonyl)amino)ethyl)disulfaneyl) benzylalcohol CAS-NO: 2064282-26-2 FORMULA: $C_{24}H_{23}NO_3S_2$ MOLECULAR WEIGHT: 437,57 g/mol				

Find Biotin linkers with disulfide bridge in our Biotinylation brochure or visit our website.

		Article No.	Quantity	Price
RL-3300 **Biotin-SS-COOH**		RL-3300.0250	250 mg	€ 325,00
3-((2-(5-((3aS,4S,6aR)-2-oxohexahydro-1H-thieno[3,4-d]imidazol-4-yl) pentanamido)ethyl)disulfanyl)propanoic acid FORMULA: $C_{15}H_{25}N_3O_4S_3$ MOLECULAR WEIGHT: 407,57 g/mol		RL-3300.0001	1 g	€ 950,00
PEG8100 **Biotin-PEG(4)-SS-Azide**		PEG8100.0025	25 mg	€ 225,00
N-(2-((3-azidopropyl)disulfanyl)ethyl)-1-(5-((3aS,4S,6aR)-2-oxohexahydro-1H-thieno[3,4-d]imidazol-4-yl)pentanamido)-3,6,9,12-tetraoxapentadecan-15-amide FORMULA: $C_{26}H_{47}N_7O_7S_3$ MOLECULAR WEIGHT: 665,89 g/mol		PEG8100.0100	100 mg	€ 650,00
		PEG8100.0500	500 mg	€ 2600,00

		Article No.	Quantity	Price
PEG8110 **Biotin-PEG(4)-SS-Alkyne**		PEG8110.0025	25 mg	€ 225,00
N-(2-((3-oxo-3-(prop-2-ynylamino)propyl)disulfanyl)ethyl)-1-(5-((3aS,4S,6aR)-2-oxohexahydro-1H-thieno[3,4-d]imidazol-4-yl) pentanamido)-3,6,9,12-tetraoxapentadecan-15-amide		PEG8110.0100	100 mg	€ 650,00
FORMULA: $C_{29}H_{49}N_5O_8S_3$		PEG8110.0500	500 mg	€ 2600,00
MOLECULAR WEIGHT: 691,92 g/mol				
PEG8120 **Biotin-PEG(4)-SS-DBCO**		PEG8120.0025	25 mg	€ 225,00
N-(2-((3-(3-(azadibenzocyclooctyn-1-yl)-3-oxopropylamino)-3-oxopropyl)disulfanyl)ethyl)-1-(5-((3aS,4S,6aR)-2-oxohexahydro-1H-thieno[3,4-d]imidazol-4-yl)pentanamido)-3,6,9,12-tetrao xapentade-can-15-amide		PEG8120.0100	100 mg	€ 650,00
FORMULA: $C_{44}H_{60}N_6O_9S_3$		PEG8120.0500	500 mg	€ 2600,00
MOLECULAR WEIGHT: 913,18 g/mol				
PEG8090 **Biotin-PEG(4)-SS-COOH**		PEG8090.0100	100 mg	€ 145,00
9,25-dioxo-29-((3aS,4S,6aR)-2-oxohexahydro-1H-thieno[3,4-d] imidazol-4-yl)-12,15,18,21-tetraoxa-4,5-dithia-8,24-diazanonacosan-1-oic acid		PEG8090.0250	250 mg	€ 350,00
CAS-NO: 1380166-80-2		PEG8090.0001	1 g	€ 1000,00
FORMULA: $C_{26}H_{46}N_4O_9S_3$				
MOLECULAR WEIGHT: 654,86 g/mol				
LS-3570 **Biotin-SS-Tyramide**		LS-3570.0250	250 mg	€ 350,00
N-(2-((3-(4-hydroxyphenethylamino)-3-oxopropyl)disulfanyl)ethyl)-5-(2-oxohexahydro-1H-thieno[3,4-d]imidazol-4-yl)pentanamide		LS-3570.0001	1 g	€ 1000,00
CAS-NO: 678975-20-7		LS-3570.0005	5 g	€ 4000,00
FORMULA: $C_{23}H_{34}N_4O_4S_3$				
MOLECULAR WEIGHT: 526,74 g/mol				

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- Engineering Intracelular Delivery Nanocarriers and Nanoreactors from Oxidation-Responsive Polymersomes via Synchronized Bilayer Cross-Linking and Permeabilizing Inside Live Cells; Z. Deng, Y. Qian, Y. Yu, G. Liu, J. Hu, G. Zhang, and S. Liu; *J. Am. Chem. Soc.* 2016; **138**: 10452-10466. https://doi.org/10.1021/jacs.6b04115.

3.5. Dde-Based Linkers

The Dde [*N*-1-(4,4-dimethyl-2,6-dioxocyclohex-1-ylidene)-3-ethyl] protection group is commonly utilized to protect the sidechain amine groups of lysine, ornithine, 2,4-diaminobutyric acid, and 2,3-diaminoproionic acid. Dde shows orthogonal cleavage conditions to Fmoc (piperidine or DBU) and ^{t}Bu (TFA) deprotecting protocols and is stable to denaturing washing conditions, while allowing for a mild and selective removal in the presence of other protecting groups using a buffered aqueous solution of hydrazine or hydroxylamine, thus representing a versatile tool for the site-specific modification of peptides. Advantageously, the cleavage can be followed spectrophotometrically since the reaction product of Dde with hydrazine is a chromophoric derivative.

Placing Dde as one terminal group of a linker and a functional group prone for conjugation as the other, or using Dde as the central connective portion of a linker, allows for the creation of new bifunctional linkers that can be selectively and temporarily attached to:

- Appropriately modified biomolecules for binding to streptavidin (with terminal biotin) (Fig. 20 (A)), or conjugation to any solid supports, e.g. *via* Click reaction (Fig. 20 (B)).
- Solubilizing tags, e.g. hexa-lysin ("helping-hand linkers", Fig. 20 (C)), oligo-arginine, PEGs (Fig. 20 (D)) or other hydrophilic groups improving solubility of hydrophobic peptides or other compounds when being attached to either the N-terminus or any lysine side chain within a peptide sequence.
- Dyes and any other conjugate for monitoring, diagnostics, targeting or other purposes.

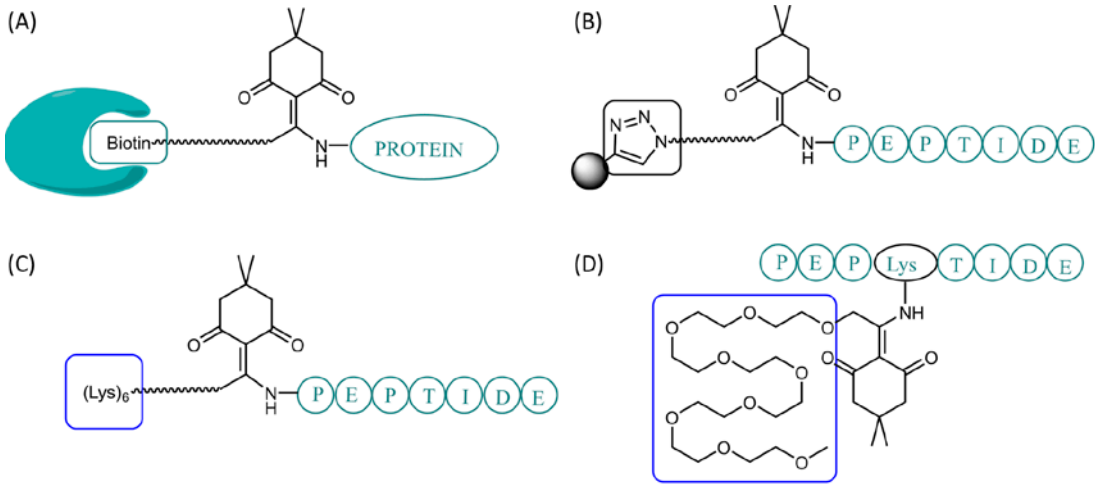


Fig. 20: Dde-based linkers can be utilized for various applications: Attachment of a cleavable biotin tag to proteins for catch-and-release affinity purification over Streptavidin beads (A), reversible labeling or conjugation to other biomolecules, or reversible immobilization on solid supports via Click chemistry (B), temporary attachment of solubilizing tags like oligo-lysine (C) or PEGs (D).

Dde/ivDde linkers are implemented in simple and nearly quantitative steps:

1. Orthogonal deprotection of lysine residues in a peptide or N-terminus or any other amino function of a hydrophobic compound.
2. On-resin incorporation of the linker.
3. Fmoc-SPPS elongation.
4. Cleavage of the peptide from the resin and removal of all side chain protecting groups.
5. The tagged peptide can be separated from truncated sequences.
6. In-solution cleavage using mild aqueous hydrazine to cleave the Dde linker after purification, streptavidin attachment, NCL-based assembly or another reaction step. The cleavage can be monitored spectroscopically as the resulting pyrazole shows a strong absorption at 290 nm.

Dde/ivDde becomes particularly useful for handling and purification of insoluble and aggregation-prone peptides, as any appropriate solubilizing promoting group can be attached to create so-called "helping-hand" linkers that can be removed in a traceless manner (Fig. 21).

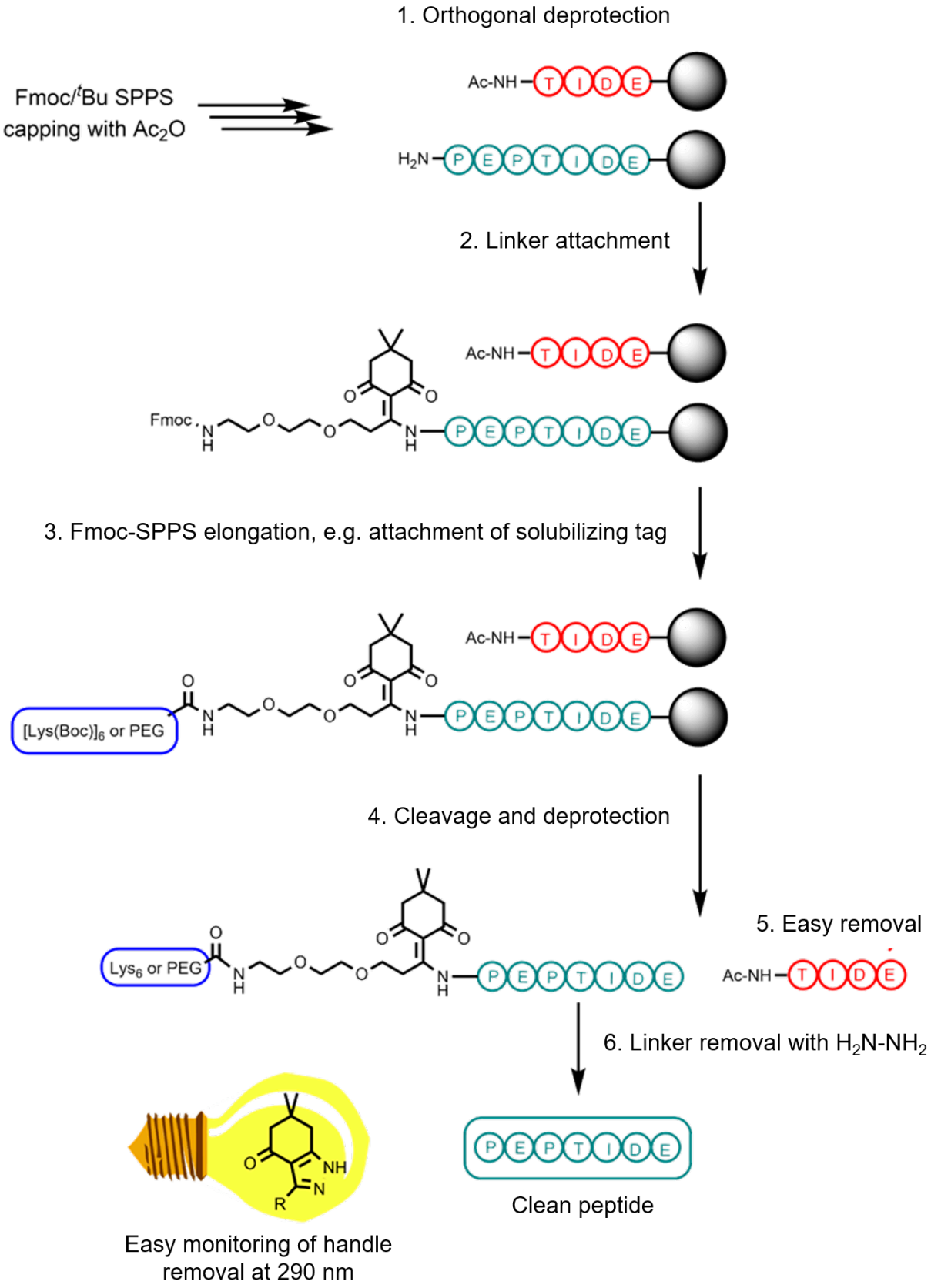


Fig. 21: Dde-based "helping-hand" linkers improve the solubility and allow for the purification of hydrophobic peptides. Removal of the handle can be easily monitored spectroscopically at 290 nm.

Procedure for Removing Helping-Hands from Peptides (adapted from Jacobsen *et al.*, *J Am Chem Soc* 2016)**:**

10 mL of 2 M hydrazine stock solution (pH 7.5) is being prepared as follows:

1. Weigh 5.7 g Guanidinium chloride and 75 mg DTT into 15 mL Falcon tube.
2. Add 1 mL of 1 M NaH_2PO_4.
3. Add 2 mL of 10 M hydrazine in water.
4. Add 0.5 mL of 12 M HCl.
5. Dissolve solution by thorough vortexing.
6. Adjust pH to 7.5 by adding concentrated HCl.
7. Fill to a final volume of 10 mL with water.
8. Filter solution using 0.2 µm syringe filter.

Cleavage of the helping-hand can be triggered by equivolume addition of 2 M hydrazine stock solution into the solution of the peptide. After adding the hydrazine solution, subtle adjustment may be necessary to achieve a final solution pH of 7.5. The reaction is normally completed within minutes. Deprotection can be monitored spectrophotometrically at 290 nm.

Despite its widespread use, the biotinylation of proteins for subsequent purification *via* Streptavidin beads bears certain hurdles, e.g. concerning the removal of the proteins from the beads due to the strong binding. One possible improvement is represented by the use of appropriately derivatized Dde-linkers. The connection of such a bifunctional linker with a biotin moiety on the one end, and a clickable group (alkyne, e.g. DBCO) or tyramide on the other, allows for the selective attachment to appropriately modified biomolecules, as well as the mild release of captured proteins from the beads after purification (Fig. 22).

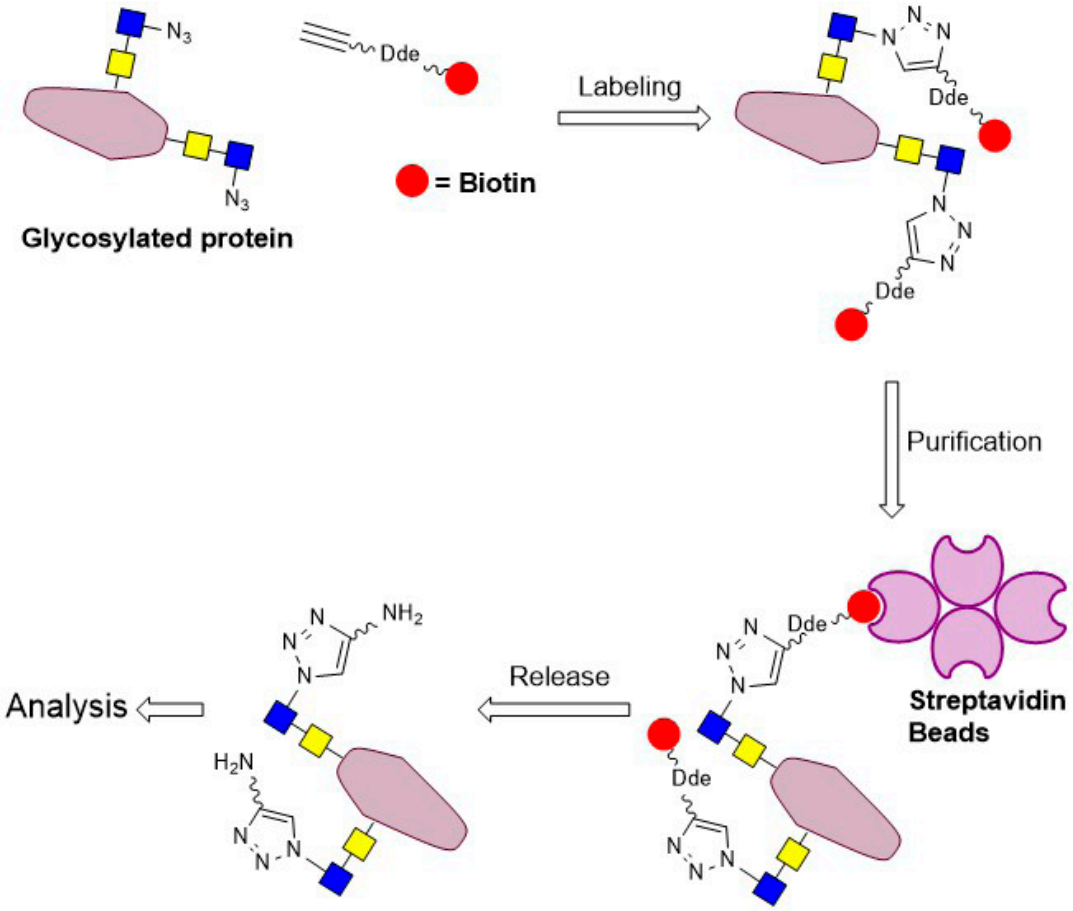
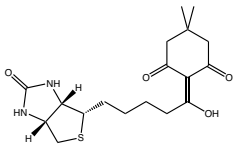
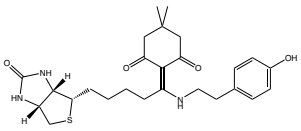
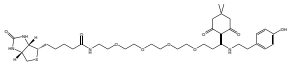
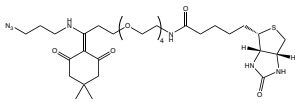
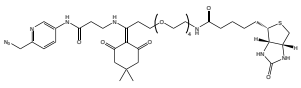
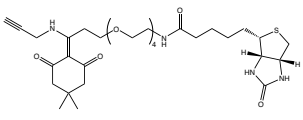


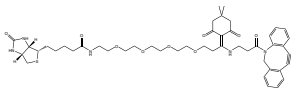
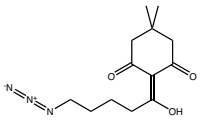
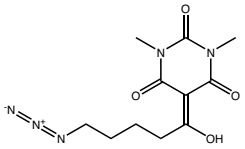
Fig. 22: Biotinylation of an azide-bearing glycoprotein using Click chemistry, followed by purification of the labelled protein over Streptavidin beads, release of the protein by hydrazinolysis of the Dde-group, and analysis of the isolated glycoprotein (adapted from Griffin et al. Mol. Biosys. 2016).

Aside from the commonly used cleavage solution for Dde consisting of 2% hydrazine monohydrate in H_2O, the following procedure may be used in order to ensure full orthogonality between Dde and Fmoc.

Selective Removal of Dde/ivDde using hydroxylamine (adapted from Díaz-Mochón *et al.*, *Org. Lett.* 2004)**:**

1.25 g (1.80 mmol) of $NH_2OH{\cdot}HCl$ and 0.918 g (1.35 mmol) of Imidazole were suspended in 5 mL NMP, and the mixture sonicated until complete dissolution. This solution can be stirred for at least 2 weeks at -20 °C. Just before reaction, five volumes of this solution were diluted with one volume of alternatively DCM or DMF.

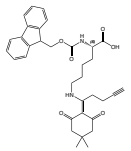
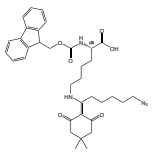
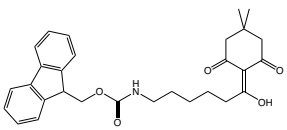
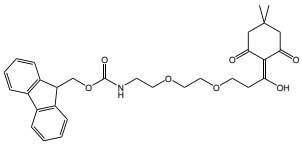
		Article No.	Quantity	Price
LS-4020 Biotin-Dde 2-(1-hydroxy-5-((3aS,4S,6aR)-2-oxohexahydro-1H-thieno[3,4-d] imidazol-4-yl)pentylidene)-5,5-dimethylcyclohexane-1,3-dione CAS-NO: 194038-08-9 FORMULA: $C_{18}H_{26}N_2O_4S$ MOLECULAR WEIGHT: 366,48 g/mol		LS-4020.0250 LS-4020.0001 LS-4020.0005	250 mg 1 g 5 g	€ 125,00 € 350,00 € 1400,00
LS-4000 Biotin-Dde-Tyramide 2-(1-(4-hydroxyphenethylamino)-5-((3aS,4S,6aR)-2-oxohexahydro-1H-thieno[3,4-d]imidazol-4-yl)pentylidene)-5,5-dimethylcyclohexane-1,3-dione FORMULA: $C_{26}H_{35}N_3O_4S$ MOLECULAR WEIGHT: 485,64 g/mol		please inquire!		
PEG8130 Biotin-PEG(4)-Dde-Tyramide N-(15-(4,4-dimethyl-2,6-dioxocyclohexylidene)-18-(4-hydroxyphenyl)-3,6,9,12-tetraoxa-16-azaoctadecyl)-5-((3aS,4S,6aR)-2-oxohexahydro-1H-thieno[3,4-d]imidazol-4-yl)pentanamide FORMULA: $C_{34}H_{56}N_4O_9S$ MOLECULAR WEIGHT: 732,93 g/mol		please inquire!		
PEG7960 Biotin-PEG(4)-Dde-N_3 N-(19-azido-15-(4,4-dimethyl-2,6-dioxocyclohexylidene)-3,6,9,12-tetraoxa-16-azanonadecyl)-5-((3aS,4S,6aR)-2-oxohexahydro-1H-thieno[3,4-d]imidazol-4-yl)pentanamide CAS-NO: 1802907-93-2 FORMULA: $C_{32}H_{53}N_7O_8S$ MOLECULAR WEIGHT: 695,87 g/mol		PEG7960.0010 PEG7960.0025 PEG7960.0100	10 mg 25 mg 100 mg	€ 250,00 € 415,00 € 1250,00
PEG7970 Biotin-PEG(4)-Dde-Picolyl-N_3 N-(6-(azidomethyl)pyridin-3-yl)-15-(4,4-dimethyl-2,6-dioxocyclohexylidene)-1-(5-((3aS,4S,6aR)-2-oxohexahydro-1H-thieno[3,4-d]imidazol-4-yl)pentanamido)-3,6,9,12-tetraoxa-16-azanona decan-19-amide CAS-NO: 2055048-42-3 FORMULA: $C_{38}H_{57}N_9O_9S$ MOLECULAR WEIGHT: 815,98 g/mol		PEG7970.0005 PEG7970.0010 PEG7970.0100	5 mg 10 mg 100 mg	€ 195,00 € 300,00 € 1450,00
PEG7980 Biotin-PEG(4)-Dde-Alkyne N-(15-(4,4-dimethyl-2,6-dioxocyclohexylidene)-3,6,9,12-tetraoxa-16-azanonadec-18-ynyl)-5-((3aS,4S,6aR)-2-oxohexahydro-1H-thieno[3,4-d]imidazol-4-yl)pentanamide CAS-NO: 1802908-00-4 FORMULA: $C_{32}H_{50}N_4O_8S$ MOLECULAR WEIGHT: 650,83 g/mol		PEG7980.0010 PEG7980.0025 PEG7980.0100	10 mg 25 mg 100 mg	€ 250,00 € 415,00 € 1250,00

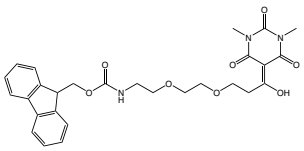
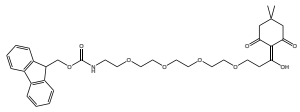
		Article No.	Quantity	Price
PEG8140 Biotin-PEG(4)-Dde-DBCO N-(15-(4,4-dimethyl-2,6-dioxocyclohexylidene)-19-oxo-19-(azadibenzocyclooctyn-1-yl)-3,6,9,12-tetraoxa-16-azanonadecyl)-5-((3aS,4S,6aR)-2-oxohexahydro-1H-thieno[3,4-d]imidazol-4-yl) pentanamide FORMULA: $C_{47}H_{61}N_5O_9S$ MOLECULAR WEIGHT: 872,08 g/mol			please inquire!	
RL-3280 N_3-Pen-Dde 2-(5-azido-1-hydroxypentylidene)-5,5-dimethylcyclohexane-1,3-dione FORMULA: $C_{13}H_{19}N_3O_3$ MOLECULAR WEIGHT: 265,31 g/mol		RL-3280.0250 RL-3280.0001 RL-3280.0005	250 mg 1 g 5 g	€ 125,00 € 350,00 € 1400,00
RL-3290 N_3-Pen-Dtpp 5-(5-azido-1-hydroxypentylidene)-1,3-dimethylpyrimidine-2,4,6(1H,3H,5H)-trione CAS-NO: 1867129-42-7 FORMULA: $C_{11}H_{15}N_5O_4$ MOLECULAR WEIGHT: 281,27 g/mol		RL-3290.0250 RL-3290.0001 RL-3290.0005	250 mg 1 g 5 g	€ 125,00 € 350,00 € 1400,00

The Dde derived linker might cleave under mildly acidic and even neutral conditions in the one or the other case. The DTPM derived linker is totally stable under acidic conditions as well as to a wide range of chemical treatments including particularly harsh sodium methoxide-based deacetylation of chemically introduced glycans.

Reference:

- Combining triazole ligation and enzymatic glycosylation on solid phase simplifies the synthesis of very long glycoprotein analogues; M. Galibert, V. Piller, F. Piller, V. Aucagne and A. F. Delmas; *Chem. Sci.* 2015; **6**: 3617-3623. https://doi.org/10.1039/c5sc00773a.

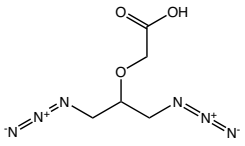
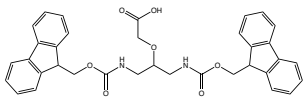
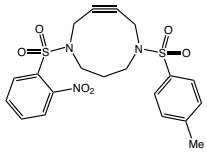
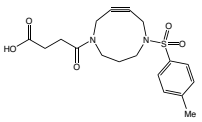
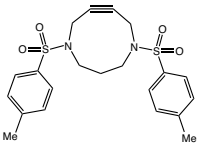
		Article No.	Quantity	Price
FAA8115 Fmoc-L-Lys(Pentynoyl-DIM)-OH N-alpha-(9-Fluorenylmethyloxycarbonyl)-N-epsilon-[1-(4,4-dimethyl-2,6- dioxocyclohexylidene)pent-4-yn-1-yl]-L-lysine CAS-NO: 2408993-33-7 FORMULA: $C_{34}H_{38}N_2O_6$ MOLECULAR WEIGHT: 570,69 g/mol		FAA8115.0250 FAA8115.0500 FAA8115.0001 FAA8115.0005	250 mg 500 mg 1 g 5 g	€ 180,00 € 324,00 € 504,00 € 1800,00
FAA8145 Fmoc-L-Lys(N_3-Aca-DIM)-OH N-alpha-(9-Fluorenylmethyloxycarbonyl)-N-epsilon-[6-azido-1-(4,4-dimethyl-2,6- dioxocyclohexylidene)hexyl]-L-lysine CAS-NO: 2408993-39-3 FORMULA: $C_{35}H_{43}N_5O_6$ MOLECULAR WEIGHT: 629,76 g/mol		FAA8145.0100 FAA8145.0250 FAA8145.0500 FAA8145.0001 FAA8145.0005	100 mg 250 mg 500 mg 1 g 5 g	€ 120,00 € 200,00 € 360,00 € 560,00 € 2000,00
RL-3260 Fmoc-Aca-DIM 6-((9-Fluorenylmethyl)oxycarbonylamino)-1-(4,4-dimethyl-2,6-dioxocyclohexylidene)-hexan-1-ol CAS-NO: 2379561-08-5 FORMULA: $C_{29}H_{33}NO_5$ MOLECULAR WEIGHT: 475,58 g/mol		RL-3260.0250 RL-3260.0500 RL-3260.0001 RL-3260.0005	250 mg 500 mg 1 g 5 g	€ 120,00 € 216,00 € 336,00 € 1200,00
RL-3270 Fmoc-AEEP-DIM 3-(2-(2-(9-Fluorenylmethyl)oxycarbonylaminoethoxy)ethoxy)-1-(4,4-dimethyl-2,6-dioxocyclohexylidene)-propan-1-ol CAS-NO: 1988771-96-5 FORMULA: $C_{30}H_{35}NO_7$ MOLECULAR WEIGHT: 521,60 g/mol		RL-3270.0250 RL-3270.0500 RL-3270.0001 RL-3270.0005	250 mg 500 mg 1 g 5 g	€ 140,00 € 255,00 € 395,00 € 1400,00

		Article No.	Quantity	Price
RL-3470 **Fmoc-AEEP-DMB**		RL-3470.0250	250 mg	€ 120,00
(9-Fluorenylmethyloxycarbonyl)amino-PEG(2)-Dtpp		RL-3470.0500	500 mg	€ 216,00
FORMULA: $C_{28}H_{31}N_3O_8$		RL-3470.1000	1 g	€ 336,00
MOLECULAR WEIGHT: 537,57 g/mol		RL-3470.5000	5 g	€ 1200,00
PEG8150 **Fmoc-PEG(4)-Dde**		PEG8150.0250	250 mg	€ 125,00
1-(9H-Fluorenylmethyloxycarbonylamino)-15-(4,4-dimethyl-2,6-dioxocyclohexylidene)-3,6,9,12-tetraoxapentadecyl-15-ol		PEG8150.0001	1 g	€ 350,00
CAS-NO: 2093409-87-9		PEG8150.0005	5 g	€ 1400,00
FORMULA: $C_{34}H_{43}NO_9$				
MOLECULAR WEIGHT: 609,71 g/mol				

References:

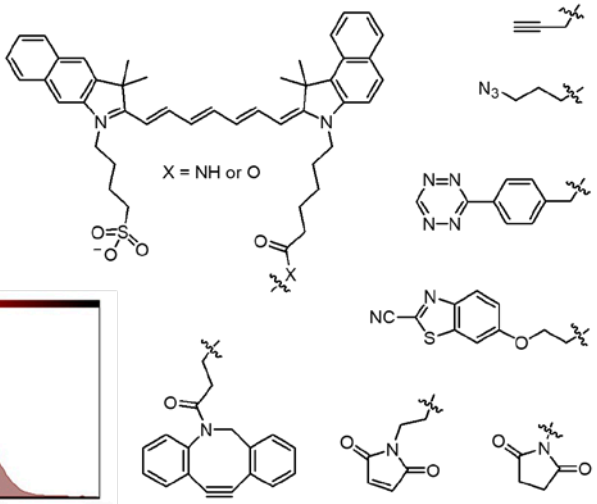
- Synthesis of hydrophobic insulin-based peptides using a helping hand strategy; M. M. Disotuar, M. E. Petersen, J. M. Nogueira, M. S. Kay and D. H. Chou; *Org Biomol Chem* 2019; **17**: 1703-1708. https://doi.org/10.1039/c8ob01212a.
- Chemical synthesis of Shiga toxin subunit B using a next-generation traceless "helping hand" solubilizing tag; J. M. Fulcher, M. E. Petersen, R. J. Giesler, Z. S. Cruz, D. M. Eckert, J. N. Francis, E. M. Kawamoto, M. T. Jacobsen and M. S. Kay; *Org Biomol Chem* 2019; **17**: 10237-10244. https://doi.org/10.1039/c9ob02012h.
- Mapping the Binding Site of BMS-708163 on gamma-Secretase with Cleavable Photoprobes; N. Gertsik, C. W. Am Ende, K. F. Geoghegan, C. Nguyen, P. Mukherjee, S. Mente, U. Seneviratne, D. S. Johnson and Y. M. Li; *Cell Chem Biol* 2017; **24**: 3-8. https://doi.org/10.1016/j.chembiol.2016.12.006.
- A Helping Hand to Overcome Solubility Challenges in Chemical Protein Synthesis; M. T. Jacobsen, M. E. Petersen, X. Ye, M. Galibert, G. H. Lorimer, V. Aucagne and M. S. Kay; *J Am Chem* Soc 2016; **138**: 11775-82. https://doi.org/10.1021/jacs.6b05719.
- Compounds and methods for purifying peptides produced by solid phase peptide synthesis; Aucagne V., Delmas A.; CNRS; *U.S. Patent No. 9,073,969*, 2015.
- Cleavable trifunctional biotin reagents for protein labelling, capture and release; Y. Yang and S. H. Verhelst; *Chem Commun (Camb)* 2013; **49**: 5366-8. https://doi.org/10.1039/c3cc42076k.
- Investigation on the stability of the Dde protecting group used in peptide synthesis: migration to an unprotected lysine; K. Augustyns, W. Kraas and G. Jung; *J Pept Res* 1998; **51**: 127-33. https://doi.org/10.1111/j.1399-3011.1998.tb00630.x.
- Full Orthogonality between Dde and Fmoc: The Direct Synthesis of PNA-Peptide Conjugates; J. J. Díaz-Mochón, L. Bialy, and M. Bradley; *Org. Lett.* 2004; **7**: 1127-1129. https://doi.org/10.1021/ol049905y

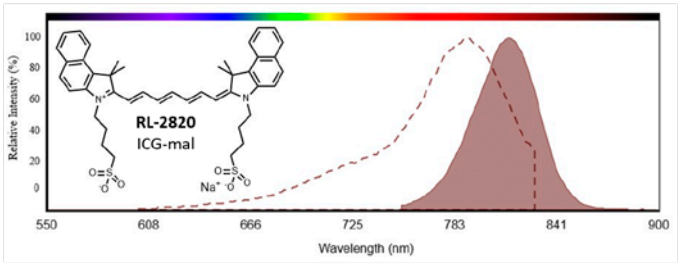
4. Trifunctional Linkers

		Article No.	Quantity	Price
AAA2190	**DAPOA*DCHA**	AAA2190.0250	250 mg	€ 120,00
2-(1,3-diazidopropan-2-yloxy)acetic acid dicyclohexylamine CAS-NO: 2389064-43-9 net FORMULA: $C_5H_8N_6O_3$*$C_{12}H_{23}N$ MOLECULAR WEIGHT: 200,16*181,32 g/mol		AAA2190.0500	500 mg	€ 216,00
		AAA2190.1000	1 g	€ 336,00
		AAA2190.5000	5 g	€ 1200,00
FAA7570	**Fmoc2-DAPOA**	FAA7570.0250	250 mg	€ 100,00
2-((1,3-bis((9-fluorenylmethyloxycarbonyl)amino)propan-2-yl)oxy) acetic acid CAS-NO: 688350-01-8 FORMULA: $C_{35}H_{32}N_2O_7$ MOLECULAR WEIGHT: 592,64 g/mol		FAA7570.0500	500 mg	€ 180,00
		FAA7570.1000	1 g	€ 280,00
		FAA7570.5000	5 g	€ 1000,00
RL-2710	**DACN(Tos,Ns)**	RL-2710.0025	25 mg	€ 275,00
N-(o-nitrobenzenesulfonyl)-N'-(p-toluenesulfonyl)-4,8-diazacyclononyne CAS-NO: 1797508-58-7 FORMULA: $C_{20}H_{21}N_3O_6S_2$ MOLECULAR WEIGHT: 463,53 g/mol		RL-2710.0100	100 mg	€ 375,00
RL-2720	**DACN(Tos,Suc-OH)**	RL-2720.0025	25 mg	€ 295,00
N-succinoyl-N'-(p-toluenesulfonyl)-4,8-diazacyclononyne FORMULA: $C_{18}H_{22}N_2O_5S$ MOLECULAR WEIGHT: 378,44 g/mol		RL-2720.0100	100 mg	€ 550,00
RL-2730	**DACN(Tos2)**	RL-2730.0025	25 mg	€ 265,00
N,N'-bis(p-toluenesulfonyl)-4,8-diazacyclononyne CAS-NO: 1797508-57-6 FORMULA: $C_{21}H_{24}N_2O_4S_2$ MOLECULAR WEIGHT: 432,56 g/mol		RL-2730.0100	100 mg	€ 350,00

Indocyanine Green (ICG) Dyes

ICG, a material approved by the FDA for various applications is a powerful tool for imaging in live cells an tissues. ICG exhibits an absorption maximum in the near infrared region (NIR). The emission maximum is at 810 nm. Iris Biotech offers a series of ICG dyes equipped with different popular functional groups, e.g. maleimide, NHS ester, as well as various clickable moieties.





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5. Cross-Linkers for other Bio Applications

5.1. Haloalkane Dehalogenase Substrate

	Article No.	Quantity	Price
RL-3180 Haloalkane Dehalogenase Substrate	RL-3180.0100	100 mg	€ 95,00
4-((2-(2-((6-chlorohexyl)oxy)ethoxy)ethyl)amino)-4-oxobutanoic acid	RL-3180.0250	250 mg	€ 175,00
CAS-NO: 1488363-39-8	RL-3180.0001	1 g	€ 400,00
FORMULA: $C_{14}H_{26}ClNO_5$	RL-3180.0005	5 g	€ 1600,00
MOLECULAR WEIGHT: 323,81 g/mol			

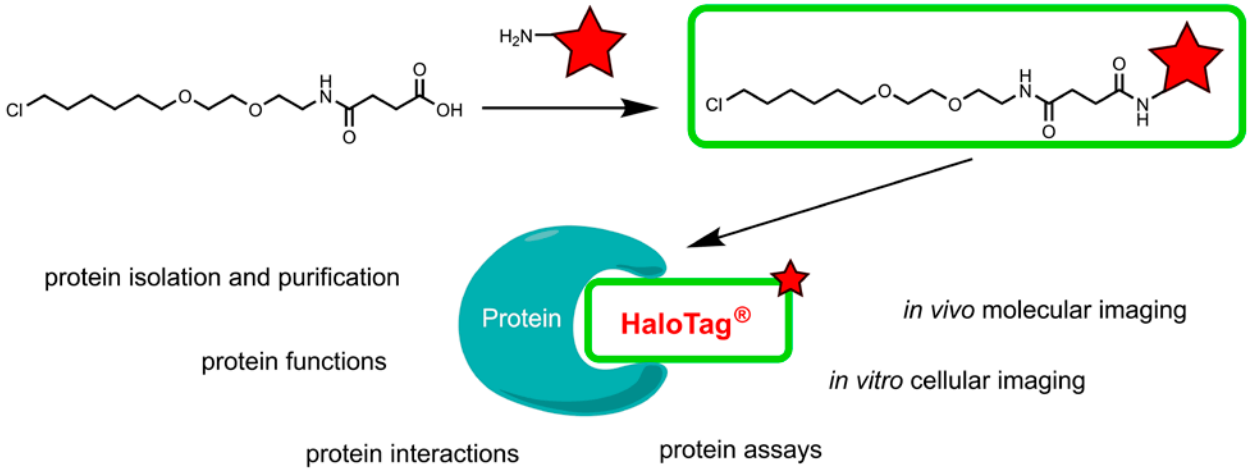


Fig. 23: The Haloalkane Dehalogenase Substrate can be utilized for a range of applications.

The shown chloroalkane linker (Fig. 23) is a ligand for a specific modified bacterial haloalkane dehalogenase, also known as HaloTag®. The linker can be used for the chloroalkane penetration assay (CAPA), a quantitative and compartment-specific cell penetration assay for peptides and other potential biotherapeutics.

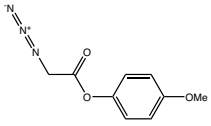
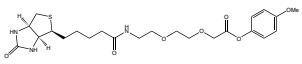
Further applications of the HaloTag® technology include cellular and molecular imaging, protein immobilization study of protein functions, protein-protein interactions and it can be used for protein isolation and protein purification.

Those applications can be accessed *via* an appropriate modification of the linker's carboxyl terminus, e.g., with an amine-functionalized fluorophore.

References:

- Bifunctional Molecules beyond PROTACs; S. J. Conway; *J. Med. Chem.* 2020; **63**: 2802-2806. https://doi.org/10.1021/acs.jmedchem.0c00293.
- Cell Penetration Profiling Using the Chloroalkane Penetration Assay; L. Peraro, K. L. Deprey, M. K. Moser, Z. Zou, H. L. Ball, B. Levine and J. A. Kritzer; *J Am Chem Soc* 2018; **140**: 11360-11369. https://doi.org/10.1021/jacs.8b06144.
- HaloTag technology: a versatile platform for biomedical applications; C. G. England, H. Luo and W. Cai; *Bioconjug Chem* 2015; **26**: 975-86. https://doi.org/10.1021/acs.bioconjchem.5b00191.
- HaloTag: a novel protein labeling technology for cell imaging and protein analysis; G. V. Los, L. P. Encell, M. G. McDougall, D. D. Hartzell, N. Karassina, C. Zimprich, M. G. Wood, R. Learish, R. F. Ohana, M. Urh, D. Simpson, J. Mendez, K. Zimmerman, P. Otto, G. Vidugiris, J. Zhu, A. Darzins, D. H. Klaubert, R. F. Bulleit and K. V. Wood; *ACS Chem Biol* 2008; **3**: 373-382. https://doi.org/10.1021/cb800025k.
- The HaloTag™; G. V. Los and K. Wood; *High Content Screening: A Powerful Approach to Systems Cell Biology and Drug Discovery* D. L. Taylor, J. R. Haskins and K. A. Giuliano 2006; 195-208. https://doi.org/10.1385/1-59745-217-3:195.

5.2. Specific His-Tag Acylation

		Article No.	Quantity	Price
RL-3010 **N_3Ac-OPhOMe**		RL-3010.0250	250 mg	€ 225,00
4-Methoxyphenyl 2-azidoacetate		RL-3010.1000	1 g	€ 625,00
FORMULA: $C_9H_9N_3O_3$		RL-3010.5000	5 g	€ 2500,00
MOLECULAR WEIGHT: 207,19 g/mol				
RL-3100 **Biotin-AEEA-OPhOMe**		RL-3100.0250	250 mg	€ 585,00
2-(2-(2-(Biotinamido)ethoxy)ethoxy)acetic acid 4-methoxyphenyl ester		RL-3100.0001	1 g	€ 1750,00
FORMULA: $C_{23}H_{33}N_3O_7S$				
MOLECULAR WEIGHT: 495,59 g/mol				

A methodology for highly selective N-terminal chemical acylation of expressed proteins. This 4-methoxyphenyl ester adds selectively to Gly-His-tags of proteins, while it does not react with epsilon amino functions of surface accessible lysines. Therefore, it expresses a unique possibility to label proteins regiospecifically at the Gly-His-tag position, enabling a wide application for chemical biology and biopharmaceuticals (Fig. 24).

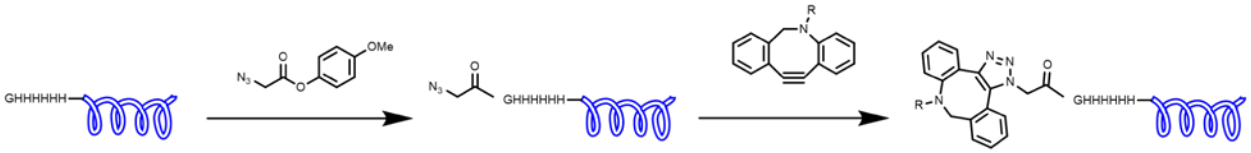


Fig. 24: 4-Methoxyphenyl 2-azidoacetate binds specifically to the N-terminus of the His-tag while other amino functions, e.g., from lysine side chains remain untouched.

General Conjugation Protocol:

A 35 µM solution of GH6-protein in 200 mM HEPES buffer at pH 7.5 is incubated with 40 equiv. of azidoacetyl 4-methoxyphenyl ester for 24 h at 4 °C. The formation of the mono-functionalized product can be observed by ESI-MS and can reach 70% to 90% conversion. A higher conversion rate can be achieved by the addition of two aliquots of 10 equiv. of the acylating agent in the next two days.

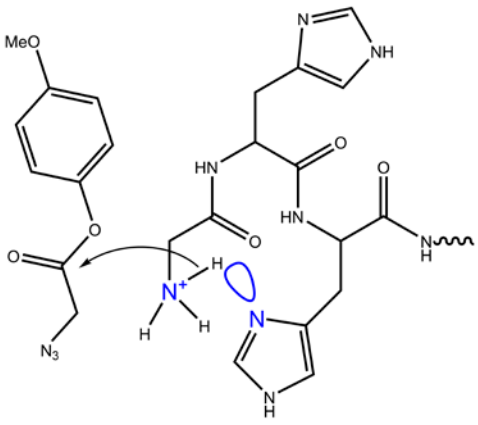


Fig. 25: Imidazole rings of neighboring histidines in a His-tag catalyze acylation of the N-terminus of glycine via a base catalyzed mechanism.

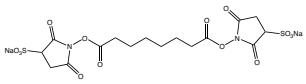
Mechanistic studies indicate that the very high selectivity of the His-tag acylation is based on specific base catalysis, in which a His side-chain assists deprotonation during the direct acylation of the Gly α-amine (Fig. 25). The ester reacts preferentially with assistance from His side-chain imidazoles since they are not protonated (pK_a ~ 6.0) at the pH of the reaction, in contrast to the N-terminal α-amine (pK_a ~ 7.6-8.0) and Lys side-chains (pK_a ~ 10.5). The presence of the additional five His residues in the His-tag may serve to modulate the basicity of the imidazole nitrogen of the catalytic residue. A recent study has shown that the pK_a values of individual His side-chains in a His_6-tag span a range from 4.8-7.5.

Reference:

- Selective N-terminal acylation of peptides and proteins with a Gly-His tag sequence; M. C. Martos-Maldonado, C. T. Hjuler, K. K. Sorensen, M. B. Thygesen, J. E. Rasmussen, K. Villadsen, S. R. Midtgaard, S. Kol, S. Schoffelen and K. J. Jensen; *Nat Commun* 2018; **9**: 3307. https://doi.org/10.1038/s41467-018-05695-3.

5.3. Bifunctional Protein Cross-Linkage

	Article No.	Quantity	Price
RL-2770 BSSS	RL-2770.0250	250 mg	€ 150,00
Bis(sulfosuccinimidyl) suberate sodium salt	RL-2770.0001	1 g	€ 500,00
CAS-NO: 82436-77-9	RL-2770.0005	5 g	€ 1500,00
FORMULA: $C_{16}H_{18}N_2Na_2O_{14}S_2$	RL-2770.0025	25 g	€ 2500,00
MOLECULAR WEIGHT: 572,43 g/mol			



This molecule (Fig. 26) carries amino reactive sulfo-NHS esters on both ends and is a water soluble, homo-bifunctional protein cross-linker (spacer length: 11.4 Å). Due to its water solubility, conjugation reactions can conveniently take place at physiological conditions. This 8-atom spacer is non-cleavable and the molecule is not cell membrane permeable. It can be used to prepare antibody-protein conjugates, for crosslinking cell surface proteins, and for covalently binding an antibody to an immobilized Protein A or Protein G resin.

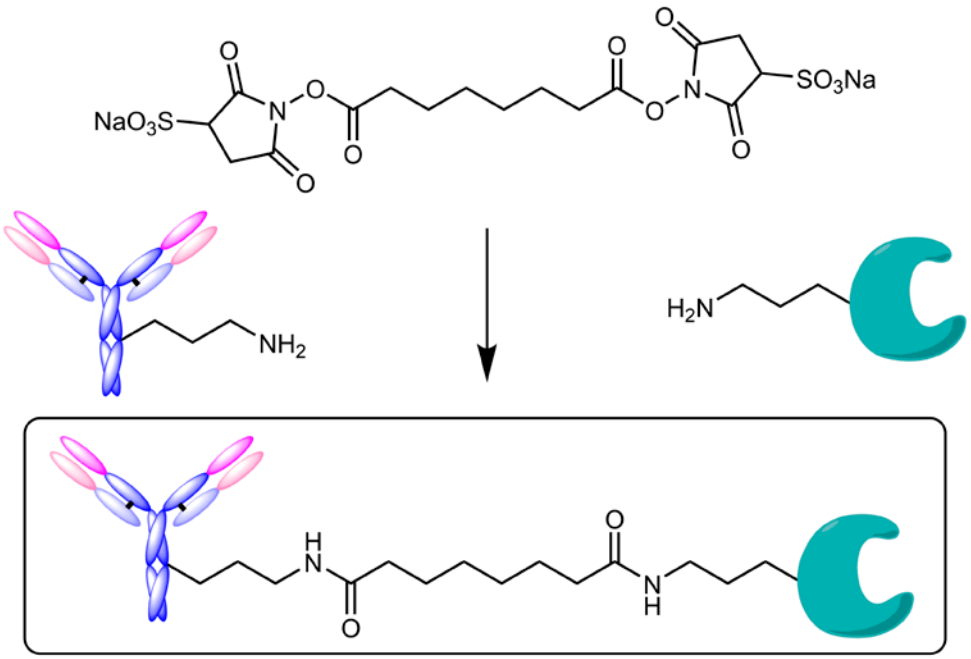


Fig. 26: BSSS can be used for cross-linkage of different biomolecules.

General BSSS Cross-Linking Protocol:

1. Allow vial of BSSS to fully equilibrate to ambient temperature before opening to prevent condensation inside the vial (BSSS is moisture-sensitive).
4. Immediately before use, prepare a 50 mM solution of BSSS, by dissolving 10 mg BSSS in 350 mL of 25 mM sodium phosphate, pH 7.4 (do not use amine containing buffers for the conjugation reaction).
5. Add BSSS solution (20-fold excess cross-linker to protein) to the protein sample so that the final concentration is between 0.5 to 5 mM.
6. Allow the sample to react at room temperature for 45 minutes to 1 hour. Allow slightly longer if reaction must be done on ice (the reaction rate is only slightly slower at low temperatures).
7. Quench any unreacted BSSS with 25 mM to 60 mM Tris and allow to react for 10-15 minutes at room temperature.
8. Desalt sample to remove unreacted BSSS, i.e., by gel filtration, dialysis, etc.

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5.4. Proteolysis Targeting Chimeras (PROTACs®)

Targeted protein degradation *via* proteolysis-targeting chimeras (PROTACs) is an emerging attempt to cure diseases caused by the irregular expression of certain disease-causing proteins. Such protein degraders act as bifunctional linkers and allow to feed the protein of interest (POI) to the cell's Ubiquitin-Proteasome system, thus, to eliminate the malexpressed proteins. These PROTACs consist of three components: one ligand with high affinity for E3 ubiquitin ligase, another one with high affinity for the protein of interest (POI) and an appropriate cross-linker joining both ligands. This linker can also be used to increase the solubility, if needed, e.g. by incorporation of PEGs. The resulting proximity of both, the recruited POI and the E3 ligase, allows the polyubiquitination of the POI by the E3 associated E2 enzyme. This leads to a labeling of the POI for degradation through the proteasome.

Mode of action:

1) A cross-linker unites the POI ligand and E3 ligase ligand = PROTAC.

2) The three-component PROTAC recruits the POI and the E2-associated E3 ligase *via* the respective ligands = Ternary complex.

3) Several Ubiquitins are added to Lys residues of the POI = Polyubiquitination.

4) The ubiquitinated POI is degraded by the proteasome.

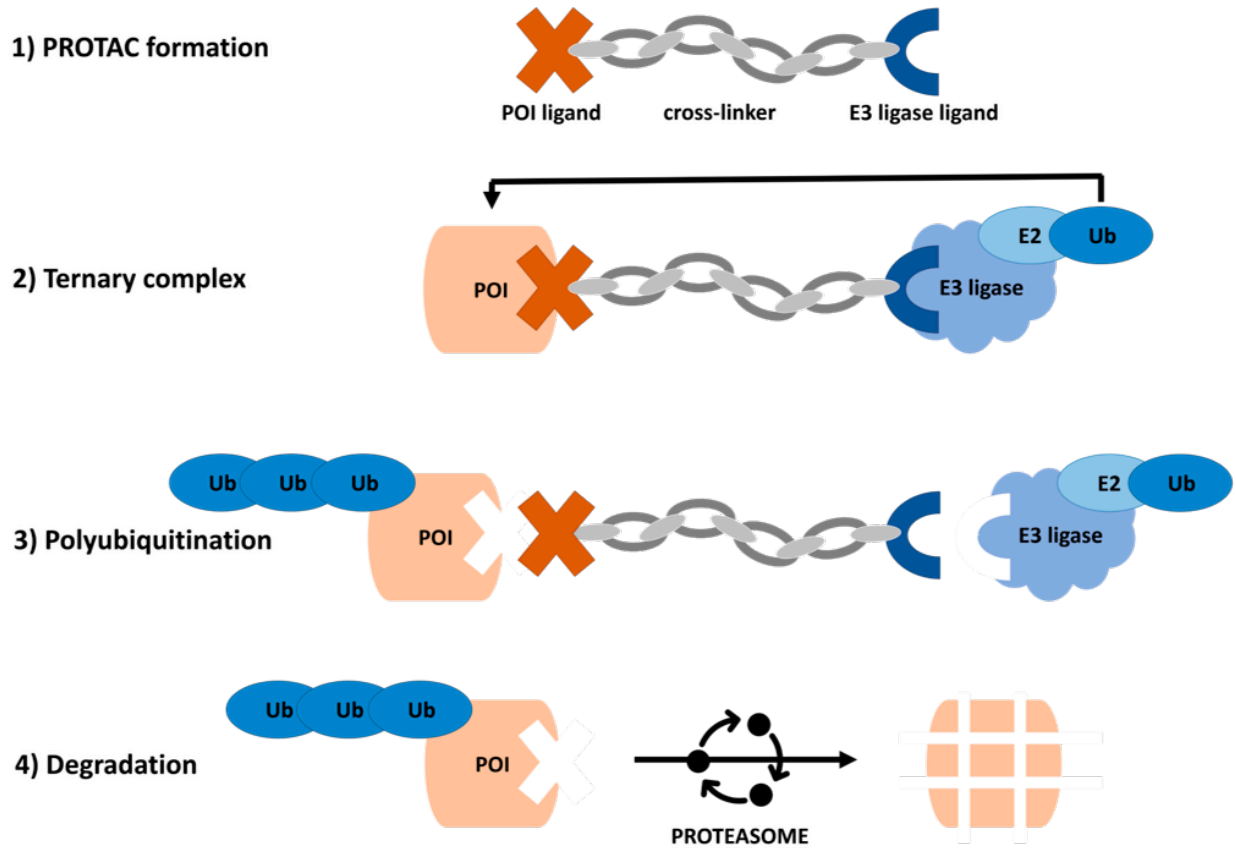
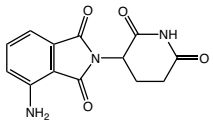
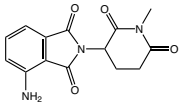
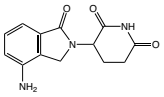
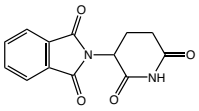
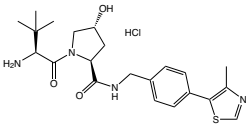
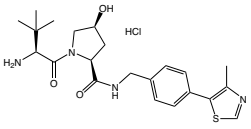
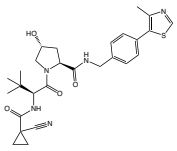
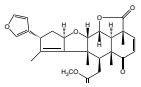
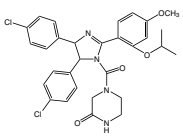


Fig. 27: Targeted protein degradation via proteolysis-targeting chimeras.

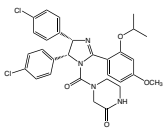
To construct a suitable PROTAC, we provide a variety of E3 ubiquitin ligase ligands in combination with linkers of various length and an elective amino-, carboxyl-, click- or thiol-reactive end ("Partial PROTACs").

E3-Ligase Ligands & Negative Controls

		Article No.	Quantity	Price
PTC1000 **Pomalidomide** 1,3-dioxo-2-(2,6-dioxopiperidin-3-yl)-4-aminoisoindoline, CAS-NO: 19171-19-8 FORMULA: $C_{13}H_{11}N_3O_4$ MOLECULAR WEIGHT: 273,24 g/mol		PTC1000.0025	25 mg	€ 520,00
PTC1010 **N-Methylated pomalidomide** 4-Amino-2-(1-methyl-2,6-dioxopiperidin-3-yl)isoindoline-1,3-dione CAS-NO: 1352827-50-9 FORMULA: $C_{14}H_{13}N_3O_4$ MOLECULAR WEIGHT: 287,27 g/mol		PTC1010.0025	25 mg	€ 405,00
PTC1020 **Lenalidomide** 1-Oxo-4-amino-2-(2,6-dioxopiperidin-3-yl)isoindole CAS-NO: 191732-72-6 FORMULA: $C_{13}H_{13}N_3O_3$ MOLECULAR WEIGHT: 259,26 g/mol		PTC1020.1000	1 g	€ 295,00
PTC1030 **(±)-Thalidomide** (±)-2-(2,6-Dioxo-3-piperidinyl)-1H-isoindole-1,3(2H)-dione CAS-NO: 50-35-1 FORMULA: $C_{13}H_{10}N_2O_4$ MOLECULAR WEIGHT: 258,23 g/mol		PTC1030.0100	100 mg	€ 180,00
PTC1040 **(S,R,S)-AHPC hydrochloride** (2S,4R)-1-((S)-2-Amino-3,3-dimethylbutanoyl)-4-hydroxy-N-(4-(4-methylthiazol-5-yl)benzyl)pyrrolidine-2-carboxamide hydrochloride CAS-NO: 1448189-80-7 FORMULA: $C_{22}H_{30}N_4O_3S$*xHCl MOLECULAR WEIGHT: 430,56 g/mol (free base)		PTC1040.0100	100 mg	€ 405,00
PTC1050 **(S,S,S)-AHPC hydrochloride** (2S,4S)-1-((S)-2-Amino-3,3-dimethylbutanoyl)-4-hydroxy-N-(4-(4-methylthiazol-5-yl)benzyl)pyrrolidine-2-carboxamide hydrochloride CAS-NO: 2115897-23-7 FORMULA: $C_{22}H_{30}N_4O_3S$*xHCl MOLECULAR WEIGHT: 430,56 g/mol (free base)		PTC1050.0010	10 mg	€ 505,00
PTC1060 **VH298** (2S,4R)-1-((S)-2-(1-Cyanocyclopropanecarboxamido)-3,3-dimethylbutanoyl)-4-hydroxy-N-(4-(4-methylthiazol-5-yl)benzyl) pyrrolidine-2-carboxamide CAS-NO: 2097381-85-4 FORMULA: $C_{27}H_{33}N_5O_4S$ MOLECULAR WEIGHT: 523,65 g/mol		PTC1060.0005	5 mg	€ 195,00
PTC1070 **Nimbolide** CAS-NO: 25990-37-8 FORMULA: $C_{27}H_{30}O_7$ MOLECULAR WEIGHT: 466,52 g/mol		PTC1070.0005	5 mg	€ 520,00
PTC1080 **Nutlin-3** (±)-4-[4,5-Bis(4-chlorophenyl)-2-(2-isopropoxy-4-methoxy-phenyl)-4,5-dihydro-imidazole-1-carbonyl]-piperazin-2-one CAS-NO: 548472-68-0 FORMULA: $C_{30}H_{30}Cl_2N_4O_4$ MOLECULAR WEIGHT: 581,49 g/mol		PTC1080.0005	5 mg	€ 480,00

PTC1090	**Nutlin-3a**		PTC1090.0005	5 mg	€ 320,00

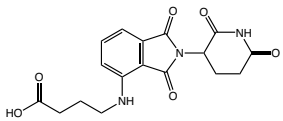
(-)-4-(4,5-Bis(4-chlorophenyl)-2-(2-isopropoxy-4-methoxyphenyl)-4,5-dihydro-1H-imidazole-1-carbonyl)piperazin-2-one
CAS-NO: 675576-98-4
FORMULA: $C_{30}H_{30}Cl_2N_4O_4$
MOLECULAR WEIGHT: 581,49 g/mol



Amino Reactive Partial PROTACs

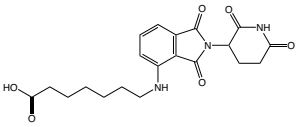
		Article No.	Quantity	Price
PTC1100	**Pomalidomide-C3-COOH**	PTC1100.0050	50 mg	€ 320,00

4-((2-(2,6-Dioxopiperidin-3-yl)-1,3-dioxoisoindolin-4-yl)amino) butanoic acid
CAS-NO: 2225940-47-4
FORMULA: $C_{17}H_{17}N_3O_6$
MOLECULAR WEIGHT: 359,33 g/mol



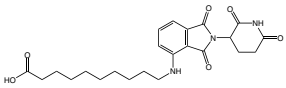
PTC1110	**Pomalidomide-C6-COOH**	PTC1110.0050	50 mg	€	320,00

7-((2-(2,6-Dioxopiperidin-3-yl)-1,3-dioxoisoindolin-4-yl)amino) heptanoic acid
CAS-NO: 2225940-50-9
FORMULA: $C_{20}H_{23}N_3O_6$
MOLECULAR WEIGHT: 401,41 g/mol



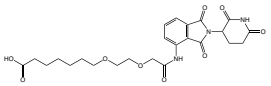
PTC1120	**Pomalidomide-C9-COOH**	PTC1120.0050	50 mg	€	320,00

10-((2-(2,6-Dioxopiperidin-3-yl)-1,3-dioxoisoindolin-4-yl)amino) decanoic acid
CAS-NO: 2243000-24-8
FORMULA: $C_{23}H_{29}N_3O_6$
MOLECULAR WEIGHT: 443,5 g/mol



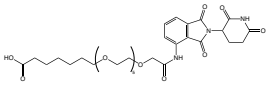
PTC1130	**Pomalidomide-PEG2-butyl COOH**	PTC1130.0050	50 mg	€	495,00

7-(2-(2-((2-(2,6-Dioxopiperidin-3-yl)-1,3-dioxoisoindolin-4-yl)amino)-2-oxoethoxy)ethoxy)heptanoic acid
FORMULA: $C_{24}H_{29}N_3O_9$
MOLECULAR WEIGHT: 503,5 g/mol



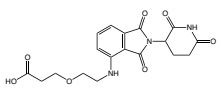
PTC1140	**Pomalidomide-PEG6-butyl COOH**	PTC1140.0050	50 mg	€	540,00

1-((2-(2,6-Dioxopiperidin-3-yl)-1,3-dioxoisoindolin-4-yl)amino)-1-oxo-3,6,9,12,15,18-hexaoxapentacosan-25-oic acid
FORMULA: $C_{32}H_{45}N_3O_{13}$
MOLECULAR WEIGHT: 679,71 g/mol



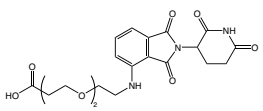
PTC1150	**Pomalidomide-PEG1-COOH**	PTC1150.0050	50 mg	€	520,00

3-(2-((2-(2,6-Dioxopiperidin-3-yl)-1,3-dioxoisoindolin-4-yl)amino) ethoxy)propanoic acid
CAS-NO: 2139348-60-8
FORMULA: $C_{18}H_{19}N_3O_7$
MOLECULAR WEIGHT: 389,36 g/mol



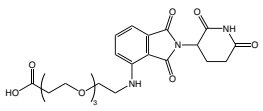
PTC1160	**Pomalidomide-PEG2-COOH**	PTC1160.0050	50 mg	€	520,00

3-(2-(2-((2-(2,6-Dioxopiperidin-3-yl)-1,3-dioxoisoindolin-4-yl)amino) ethoxy)ethoxy)propanoic acid
CAS-NO: 2140807-17-4
FORMULA: $C_{20}H_{23}N_3O_8$
MOLECULAR WEIGHT: 433,42 g/mol



PTC1170	**Pomalidomide-PEG3-COOH**	PTC1170.0050	50 mg	€	520,00

3-(2-(2-(2-((2-(2,6-Dioxopiperidin-3-yl)-1,3-dioxoisoindolin-4-yl) amino)ethoxy)ethoxy)ethoxy)propanoic acid
CAS-NO: 2138440-82-9
FORMULA: $C_{22}H_{27}N_3O_9$
MOLECULAR WEIGHT: 477,46 g/mol



	Article No.	Quantity	Price
PTC1180 Pomalidomide-PEG4-COOH 1-((2-(2,6-Dioxopiperidin-3-yl)-1,3-dioxoisoindolin-4-yl)amino)-3,6,9,12-tetraoxapentadecan-15-oic acid CAS-NO: 2138440-81-8 FORMULA: $C_{24}H_{31}N_3O_{10}$ MOLECULAR WEIGHT: 521,52 g/mol	PTC1180.0050	50 mg	€ 440,00
PTC1190 Pomalidomide-PEG5-COOH 1-((2-(2,6-Dioxopiperidin-3-yl)-1,3-dioxoisoindolin-4-yl)amino)-3,6,9,12,15-pentaoxaoctadecan-18-oic acid CAS-NO: 2139348-63-1 FORMULA: $C_{26}H_{35}N_3O_{11}$ MOLECULAR WEIGHT: 565,57 g/mol	PTC1190.0050	50 mg	€ 440,00
PTC1200 Pomalidomide-PEG6-COOH 1-((2-(2,6-Dioxopiperidin-3-yl)-1,3-dioxoisoindolin-4-yl)amino)-3,6,9,12,15,18-hexaoxahenicosan-21-oic acid CAS-NO: 2225148-49-0 FORMULA: $C_{28}H_{39}N_3O_{12}$ MOLECULAR WEIGHT: 609,62 g/mol	PTC1200.0050	50 mg	€ 440,00
PTC1210 (S,R,S)-AHPC-C6-COOH hydrochloride 7-(((S)-1-((2S,4R)-4-Hydroxy-2-((4-(4-methylthiazol-5-yl)benzyl) carbamoyl)pyrrolidin-1-yl)-3,3-dimethyl-1-oxobutan-2-yl)amino) heptanoic acid FORMULA: $C_{29}H_{42}N_4O_5S$*xHCl MOLECULAR WEIGHT: 558,73 g/mol (free base)	PTC1210.0050	50 mg	€ 330,00
PTC1220 (S,R,S)-AHPC-PEG2-butyl COOH (S,R,S)-AHPC-2-2-6-acid, 7-(2-(2-(((S)-1-((2S,4R)-4-Hydroxy-2-((4-(4-methylthiazol-5-yl)benzyl)carbamoyl)pyrrolidin-1-yl)-3,3-dimethyl-1-oxobutan-2-yl)amino)-2-oxoethoxy)ethoxy)heptanoic acid FORMULA: $C_{33}H_{48}N_4O_8S$ MOLECULAR WEIGHT: 660,82 g/mol	PTC1220.0050	50 mg	€ 520,00

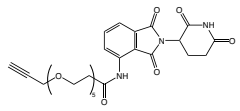
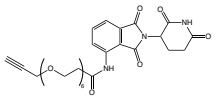
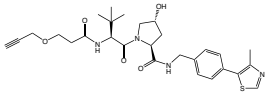
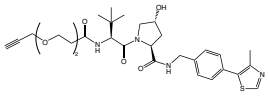
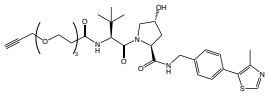
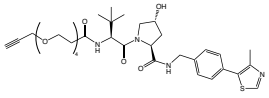
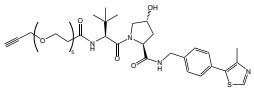
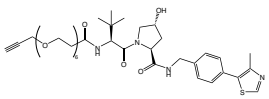
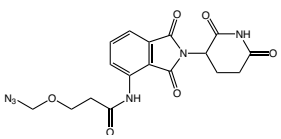
Carboxy Reactive Partial PROTACs

	Article No.	Quantity	Price
PTC1230 Pomalidomide-PEG1-NH_2 hydrochloride 2-(2-Aminoethoxy)-N-(2-(2,6-dioxopiperidin-3-yl)-1,3-dioxoisoindolin-4-yl)acetamide hydrochloride FORMULA: $C_{17}H_{18}N_4O_6$*xHCl MOLECULAR WEIGHT: 374,35 g/mol (free base)	PTC1230.0050	50 mg	€ 335,00
PTC1240 Pomalidomide-PEG2-NH_2 hydrochloride 2-(2-(2-Aminoethoxy)ethoxy)-N-(2-(2,6-dioxopiperidin-3-yl)-1,3-dioxoisoindolin-4-yl)acetamide hydrochloride FORMULA: $C_{19}H_{22}N_4O_7$*xHCl MOLECULAR WEIGHT: 418,40 g/mol (free base)	PTC1240.0050	50 mg	€ 335,00
PTC1250 Pomalidomide-PEG3-NH_2 hydrochloride 2-(2-(2-(2-Aminoethoxy)ethoxy)ethoxy)-N-(2-(2,6-dioxopiperidin-3-yl)-1,3-dioxoisoindolin-4-yl)acetamide hydrochloride FORMULA: $C_{21}H_{26}N_4O_8$*xHCl MOLECULAR WEIGHT: 462,45 g/mol (free base)	PTC1250.0050	50 mg	€ 335,00

	Article No.	Quantity	Price
PTC1260 Pomalidomide-PEG4-NH_2 hydrochloride 14-Amino-N-(2-(2,6-dioxopiperidin-3-yl)-1,3-dioxoisoindolin-4-yl)-3,6,9,12-tetraoxatetradecanamide hydrochloride FORMULA: $C_{23}H_{30}N_4O_9$*xHCl MOLECULAR WEIGHT: 506,41 g/mol (free base)	PTC1260.0050	50 mg	€ 450,00
PTC1270 Pomalidomide-PEG5-NH_2 hydrochloride 17-Amino-N-(2-(2,6-dioxopiperidin-3-yl)-1,3-dioxoisoindolin-4-yl)-3,6,9,12,15-pentaoxaheptadecanamide hydrochloride FORMULA: $C_{25}H_{34}N_4O_{10}$*xHCl MOLECULAR WEIGHT: 550,56 g/mol (free base)	PTC1270.0050	50 mg	€ 440,00
PTC1280 Pomalidomide-PEG6-NH_2 hydrochloride 20-Amino-N-(2-(2,6-dioxopiperidin-3-yl)-1,3-dioxoisoindolin-4-yl)-3,6,9,12,15,18-hexaoxaicosanamide hydrochloride FORMULA: $C_{27}H_{38}N_4O_{11}$*xHCl MOLECULAR WEIGHT: 594,61 g/mol (free base)	PTC1280.0050	50 mg	€ 495,00
PTC1290 Pomalidomide-C6-PEG3-butyl-NH_2 hydrochloride 6-(2-(2-((6-Aminohexyl)oxy)ethoxy)ethoxy)-N-(2-(2,6-dioxopiperidin-3-yl)-1,3-dioxoisoindolin-4-yl)hexanamide FORMULA: $C_{29}H_{42}N_4O_8$*xHCl MOLECULAR WEIGHT: 574,67 g/mol (free base)	PTC1290.0050	50 mg	€ 495,00
PTC1300 Pomalidomide-PEG6-butyl-NH_2 hydrochloride 4-Amino-N-(2-(2,6-dioxopiperidin-3-yl)-1,3-dioxoisoindolin FORMULA: $C_{31}H_{46}N_4O_{11}$*xHCl MOLECULAR WEIGHT: 650,72 g/mol (free base)	PTC1300.0050	50 mg	€ 495,00
PTC1310 (S,R,S)-AHPC-PEG1-NH_2 hydrochloride (2S,4R)-1-((S)-2-(2-(2-Aminoethoxy)acetamido)-3,3-dimethylbutanoyl)-4-hydroxy-N-(4-(4-methylthiazol-5-yl)benzyl) pyrrolidine-2-carboxamide hydrochloride- FORMULA: $C_{26}H_{37}N_5O_5S$*xHCl MOLECULAR WEIGHT: 531,67 g/mol (free base)	PTC1310.0050	50 mg	€ 370,00
PTC1320 (S,R,S)-AHPC-PEG2-NH_2 hydrochloride (2S,4R)-1-((S)-2-(2-(2-(2-Aminoethoxy)ethoxy)acetamido)-3,3-dimethylbutanoyl)-4-hydroxy-N-(4-(4-methylthiazol-5-yl)benzyl) pyrrolidine-2-carboxamide hydrochloride CAS-NO: 2097973-72-1 FORMULA: $C_{28}H_{41}N_5O_6S$*xHCl MOLECULAR WEIGHT: 575,72 g/mol (free base)	PTC1320.0050	50 mg	€ 370,00
PTC1330 (S,R,S)-AHPC-PEG3-NH_2 hydrochloride (2S,4R)-1-((S)-14-Amino-2-(tert-butyl)-4-oxo-6,9,12-trioxa-3-azatetradecanoyl)-4-hydroxy-N-(4-(4-methylthiazol-5-yl)benzyl) pyrrolidine-2-carboxamide hydrochloride FORMULA: $C_{30}H_{45}N_5O_7S$*xHCl MOLECULAR WEIGHT: 619,77 g/mol (free base)	PTC1330.0050	50 mg	€ 370,00
PTC1340 (S,R,S)-AHPC-PEG4-NH_2 hydrochloride (2S,4R)-1-((S)-17-Amino-2-(tert-butyl)-4-oxo-6,9,12,15-tetra-oxa-3-azaheptadecanoyl)-4-hydroxy-N-(4-(4-methylthiazol-5-yl) benzyl)pyrrolidine-2-carboxamide hydrochloride FORMULA: $C_{32}H_{49}N_5O_8S$*xHCl MOLECULAR WEIGHT: 663,83 g/mol (free base)	PTC1340.0050	50 mg	€ 580,00

Click Reactive Partial PROTACs

		Article No.	Quantity	Price
PTC1350	**(S,R,S)-AHPC-PEG5-NH_2 hydrochloride** (2S,4R)-1-((S)-20-Amino-2-(tert-butyl)-4-oxo-6,9,12,15,18-pentaoxa-3-azaicosanoyl)-4-hydroxy-N-(4-(4-methylthiazol-5-yl)benzyl) pyrrolidine-2-carboxamide hydrochloride FORMULA: $C_{34}H_{53}N_5O_9S$*xHCl MOLECULAR WEIGHT: 707,88 g/mol (free base)	PTC1350.0050	50 mg	€ 480,00
PTC1360	**(S,R,S)-AHPC-PEG6-NH_2 hydrochloride** (2S,4R)-1-((S)-23-Amino-2-(tert-butyl)-4-oxo-6,9,12,15,18,21-hexaoxa-3-azatricosanoyl)-4-hydroxy-N-(4-(4-methylthiazol-5-yl)benzyl) pyrrolidine-2-carboxamide hydrochloride FORMULA: $C_{36}H_{57}N_5O_{10}S$*xHCl MOLECULAR WEIGHT: 751,93 g/mol (free base)	PTC1360.0050	50 mg	€ 480,00
PTC1370	**(S,R,S)-AHPC-PEG2-butyl-NH_2 hydrochloride** (2S,4R)-1-((S)-2-(2-(2-((6-Aminohexyl)oxy)ethoxy)acetamido)-3,3-dimethylbutanoyl)-4-hydroxy-N-(4-(4-methylthiazol-5-yl)benzyl) pyrrolidine-2-carboxamide FORMULA: $C_{32}H_{49}N_5O_6S$*xHCl MOLECULAR WEIGHT: 631,83 g/mol (free base)	PTC1370.0050	50 mg	€ 480,00
PTC1380	**(S,R,S)-AHPC-C6-PEG3-butyl-NH_2 hydrochloride** (2S,4R)-1-((S)-22-Amino-2-(tert-butyl)-4-oxo-10,13,16-trioxa-3-azadocosanoyl)-4-hydroxy-N-(4-(4-methylthiazol-5-yl)benzyl) pyrrolidine-2-carboxamide FORMULA: $C_{38}H_{61}N_5O_7S$*xHCl MOLECULAR WEIGHT: 731,99 g/mol (free base)	PTC1380.0050	50 mg	€ 480,00
PTC1390	**(S,R,S)-AHPC-PEG6-butyl-NH_2 hydrochloride** (2S,4R)-1-((S)-27-Amino-2-(tert-butyl)-4-oxo-6,9,12,15,18,21-hexaoxa-3-azaheptacosanoyl)-4-hydroxy-N-(4-(4-methylthiazol-5-yl)benzyl) pyrrolidine-2-carboxamide FORMULA: $C_{40}H_{65}N_5O_{10}S$*xHCl MOLECULAR WEIGHT: 808,04 g/mol (free base)	PTC1390.0050	50 mg	€ 480,00
PTC1400	**Pomalidomide-PEG1-Alkyne** N-(2-(2,6-Dioxopiperidin-3-yl)-1,3-dioxoisoindolin-4-yl)-3-(prop-2-yn-1-yloxy)propanamide FORMULA: $C_{19}H_{17}N_3O_6$ MOLECULAR WEIGHT: 383,35 g/mol	PTC1400.0050	50 mg	€ 480,00
PTC1410	**Pomalidomide-PEG2-Alkyne** N-(2-(2,6-Dioxopiperidin-3-yl)-1,3-dioxoisoindolin-4-yl)-3-(2-(prop-2-yn-1-yloxy)ethoxy)propanamide FORMULA: $C_{21}H_{21}N_3O_7$ MOLECULAR WEIGHT: 427,41 g/mol	PTC1410.0050	50 mg	€ 480,00
PTC1420	**Pomalidomide-PEG3-Alkyne** N-(2-(2,6-Dioxopiperidin-3-yl)-1,3-dioxoisoindolin-4-yl)-3-(2-(2-(prop-2-yn-1-yloxy)ethoxy)ethoxy)propanamide FORMULA: $C_{23}H_{25}N_3O_8$ MOLECULAR WEIGHT: 471,46 g/mol	PTC1420.0050	50 mg	€ 480,00
PTC1430	**Pomalidomide-PEG4-Alkyne** N-(2-(2,6-Dioxopiperidin-3-yl)-1,3-dioxoisoindolin-4-yl)-4,7,10,13-tetraoxahexadec-15-ynamide FORMULA: $C_{25}H_{29}N_3O_9$ MOLECULAR WEIGHT: 515,51 g/mol	PTC1430.0050	50 mg	€ 370,00

		Article No.	Quantity	Price
PTC1440	**Pomalidomide-PEG5-Alkyne** N-(2-(2,6-Dioxopiperidin-3-yl)-1,3-dioxoisoindolin-4-yl)-4,7,10,13,16-pentaoxanonadec-18-ynamide FORMULA: $C_{27}H_{33}N_3O_{10}$ MOLECULAR WEIGHT: 559,57 g/mol		PTC1440.0050	50 mg	€ 370,00
PTC1450	**Pomalidomide-PEG6-Alkyne** N-(2-(2,6-Dioxopiperidin-3-yl)-1,3-dioxoisoindolin-4-yl)-4,7,10,13,16,19-hexaoxadocos-21-ynamide FORMULA: $C_{29}H_{37}N_3O_{11}$ MOLECULAR WEIGHT: 603,62 g/mol		PTC1450.0050	50 mg	€ 370,00
PTC1460	**(S,R,S)-AHPC-PEG1-Alkyne** (2S,4R)-1-((S)-3,3-Dimethyl-2-(3-(prop-2-yn-1-yloxy)propanamido) butanoyl)-4-hydroxy-N-(4-(4-methylthiazol-5-yl)benzyl)pyrrolidine-2-carboxamide FORMULA: $C_{28}H_{36}N_4O_5S$ MOLECULAR WEIGHT: 540,67 g/mol		PTC1460.0050	50 mg	€ 480,00
PTC1470	**(S,R,S)-AHPC-PEG2-Alkyne** (2S,4R)-1-((S)-3,3-Dimethyl-2-(3-(2-(prop-2-yn-1-yloxy)ethoxy)propanamido)butanoyl)-4-hydroxy-N-(4-(4-methylthiazol-5-yl)benzyl) pyrrolidine-2-carboxamide FORMULA: $C_{30}H_{40}N_4O_6S$ MOLECULAR WEIGHT: 584,73 g/mol		PTC1470.0050	50 mg	€ 520,00
PTC1480	**(S,R,S)-AHPC-PEG3-Alkyne** (2S,4R)-1-((S)-2-(tert-Butyl)-4-oxo-7,10,13-trioxa-3-azahexadec-15-ynoyl)-4-hydroxy-N-(4-(4-methylthiazol-5-yl)benzyl) pyrrolidine-2-carboxamide CAS-NO: 2374122-30-0 FORMULA: $C_{32}H_{44}N_4O_7S$ MOLECULAR WEIGHT: 628,78 g/mol		PTC1480.0050	50 mg	€ 480,00
PTC1490	**(S,R,S)-AHPC-PEG4-Alkyne** (2S,4R)-1-((S)-2-(tert-Butyl)-4-oxo-7,10,13,16-tetraoxa-3-azanonadec-18-ynoyl)-4-hydroxy-N-(4-(4-methylthiazol-5-yl)benzyl) pyrrolidine-2-carboxamide FORMULA: $C_{34}H_{48}N_4O_8S$ MOLECULAR WEIGHT: 672,83 g/mol		PTC1490.0050	50 mg	€ 480,00
PTC1500	**(S,R,S)-AHPC-PEG5-Alkyne** (2S,4R)-1-((S)-2-(tert-Butyl)-4-oxo-7,10,13,16,19-pentaoxa-3-azadocos-21-ynoyl)-4-hydroxy-N-(4-(4-methylthiazol-5-yl)benzyl)pyrrolidine-2-carboxamide FORMULA: $C_{36}H_{52}N_4O_9S$ MOLECULAR WEIGHT: 716,88 g/mol		PTC1500.0050	50 mg	€ 480,00
PTC1510	**(S,R,S)-AHPC-PEG6-Alkyne** (2S,4R)-1-((S)-2-(tert-Butyl)-4-oxo-7,10,13,16,19,22-hexaoxa-3-azapentacos-24-ynoyl)-4-hydroxy-N-(4-(4-methylthiazol-5-yl)benzyl) pyrrolidine-2-carboxamide FORMULA: $C_{38}H_{56}N_4O_{10}S$ MOLECULAR WEIGHT: 760,94 g/mol		PTC1510.0050	50 mg	€ 480,00
PTC1520	**Pomalidomid- PEG1-N_3** 2-(2-Azidoethoxy)-N-(2-(2,6-dioxopiperidin-3-yl)-1,3-dioxoisoindolin-4-yl)acetamide CAS-NO: 2133360-04-8 FORMULA: $C_{17}H_{16}N_6O_6$ MOLECULAR WEIGHT: 400,35 g/mol		PTC1520.0050	50 mg	€ 450,00

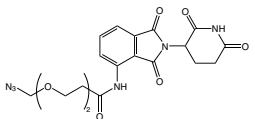
	Article No.	Quantity	Price

PTC1530 Pomalidomid- PEG2-N_3

2-(2-(2-Azidoethoxy)ethoxy)-N-(2-(2,6-dioxopiperidin-3-yl)-1,3-dioxoisoindolin-4-yl)acetamide

FORMULA: $C_{19}H_{20}N_6O_7$

MOLECULAR WEIGHT: 444,4 g/mol



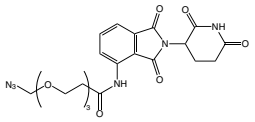
PTC1530.0050 | 50 mg | € 450,00

PTC1540 Pomalidomid- PEG3-N_3

2-(2-(2-(2-azidoethoxy)ethoxy)ethoxy)-N-(2-(2,6-dioxopiperidin-3-yl)-1,3-dioxoisoindolin-4-yl)acetamide

FORMULA: $C_{21}H_{24}N_6O_8$

MOLECULAR WEIGHT: 488,45 g/mol



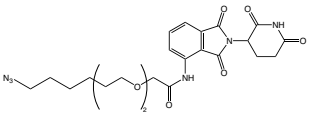
PTC1540.0050 | 50 mg | € 450,00

PTC1550 Pomalidomid-PEG2-butyl-N_3

2-(2-((6-Azidohexyl)oxy)ethoxy)-N-(2-(2,6-dioxopiperidin-3-yl)-1,3-dioxoisoindolin-4-yl)acetamide

FORMULA: $C_{23}H_{28}N_6O_7$

MOLECULAR WEIGHT: 500,5 g/mol



PTC1550.0050 | 50 mg | € 470,00

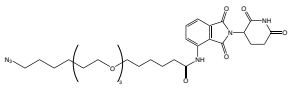
PTC1560 Pomalidomid-C6-PEG3-butyl-N_3

6-(2-(2-((6-Azidohexyl)oxy)ethoxy)ethoxy)-N-(2-(2,6-dioxopiperidin-3-yl)-1,3-dioxoisoindolin-4-yl)hexanamide

CAS-NO: 2300178-66-7

FORMULA: $C_{29}H_{40}N_6O_8$

MOLECULAR WEIGHT: 600,66 g/mol



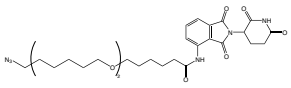
PTC1560.0050 | 50 mg | € 470,00

PTC1570 Pomalidomid-C6-PEG1-C3-PEG1-butyl-N_3

6-((5-((6-Azidohexyl)oxy)pentyl)oxy)-N-(2-(2,6-dioxopiperidin-3-yl)-1,3-dioxoisoindolin-4-yl)hexanamide

FORMULA: $C_{30}H_{42}N_6O_7$

MOLECULAR WEIGHT: 598,69 g/mol



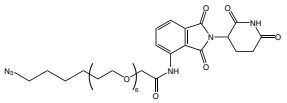
PTC1570.0050 | 50 mg | € 470,00

PTC1580 Pomalidomid-PEG6-butyl-N_3

4-azido-N-(2-(2,6-dioxopiperidin-3-yl)-1,3-dioxoisoindolin-4-yl)-3,6,9,12,15,18-hexaoxatetracosanamide

FORMULA: $C_{31}H_{44}N_6O_{11}$

MOLECULAR WEIGHT: 676,71 g/mol



PTC1580.0050 | 50 mg | € 470,00

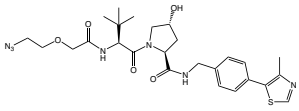
PTC1590 (S,R,S)-AHPC-PEG1-N_3

(2S,4R)-1-((S)-2-(2-(2-Azidoethoxy)acetamido)-3,3-dimethylbutanoyl)-4-hydroxy-N-(4-(4-methylthiazol-5-yl)benzyl)pyrrolidine-2-carboxamide

CAS-NO: 2101200-09-1

FORMULA: $C_{26}H_{35}N_7O_5S$

MOLECULAR WEIGHT: 557,67 g/mol



PTC1590.0050 | 50 mg | € 470,00

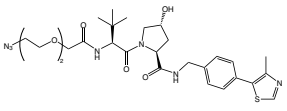
PTC1600 (S,R,S)-AHPC-PEG2-N_3

(2S,4R)-1-((S)-2-(2-(2-(2-Azidoethoxy)ethoxy)acetamido)-3,3-dimethylbutanoyl)-4-hydroxy-N-(4-(4-methylthiazol-5-yl)benzyl) pyrrolidine-2-carboxamide

CAS-NO: 2010159-45-0

FORMULA: $C_{28}H_{39}N_7O_6S$

MOLECULAR WEIGHT: 601,72 g/mol



PTC1600.0050 | 50 mg | € 470,00

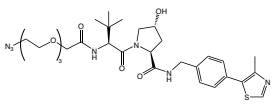
PTC1610 (S,R,S)-AHPC-PEG3-N_3

(2S,4R)-1-((S)-14-azido-2-(tert-butyl)-4-oxo-6,9,12-trioxa-3-azatetradecanoyl)-4-hydroxy-N-(4-(4-methylthiazol-5-yl)benzyl) pyrrolidine-2-carboxamide

CAS-NO: 1797406-80-4

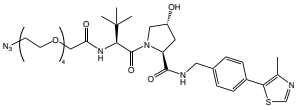
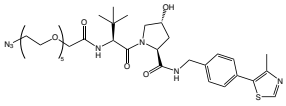
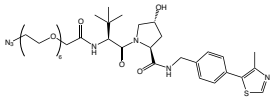
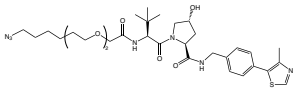
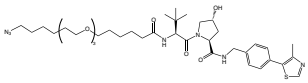
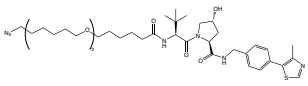
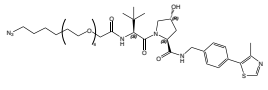
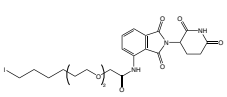
FORMULA: $C_{30}H_{43}N_7O_7S$

MOLECULAR WEIGHT: 645,77 g/mol



PTC1610.0050 | 50 mg | € 470,00

Thiol Reactive Partial PROTACs

		Article No.	Quantity	Price
PTC1620 **(S,R,S)-AHPC-PEG4-N_3**		PTC1620.0050	50 mg	€ 470,00
(2S,4R)-1-((S)-17-Azido-2-(tert-butyl)-4-oxo-6,9,12,15-tetra-oxa-3-azaheptadecanoyl)-4-hydroxy-N-(4-(4-methylthiazol-5-yl) benzyl)pyrrolidine-2-carboxamide CAS-NO: 1797406-81-5 FORMULA: $C_{32}H_{47}N_7O_8S$ MOLECULAR WEIGHT: 689,82 g/mol				
PTC1630 **(S,R,S)-AHPC-PEG5-N_3**		PTC1630.0050	50 mg	€ 470,00
(2S,4R)-1-((S)-20-Azido-2-(tert-butyl)-4-oxo-6,9,12,15,18-pentaoxa-3-azaicosanoyl)-4-hydroxy-N-(4-(4-methylthiazol-5-yl)benzyl) pyrrolidine-2-carboxamide FORMULA: $C_{34}H_{51}N_7O_9S$ MOLECULAR WEIGHT: 733,88 g/mol				
PTC1640 **(S,R,S)-AHPC-PEG6-N_3**		PTC1640.0050	50 mg	€ 470,00
(2S,4R)-1-((S)-23-Azido-2-(tert-butyl)-4-oxo-6,9,12,15,18,21-hexaoxa-3-azatricosanoyl)-4-hydroxy-N-(4-(4-methylthiazol-5-yl)benzyl) pyrrolidine-2-carboxamide FORMULA: $C_{36}H_{55}N_7O_{10}S$ MOLECULAR WEIGHT: 777,93 g/mol				
PTC1650 **(S,R,S)-AHPC-PEG2-butyl-N_3**		PTC1650.0050	50 mg	€ 470,00
(2S,4R)-1-((S)-2-(2-(2-((6-Azidohexyl)oxy)ethoxy)acetamido)-3,3-dimethylbutanoyl)-4-hydroxy-N-(4-(4-methylthiazol-5-yl)benzyl) pyrrolidine-2-carboxamide FORMULA: $C_{32}H_{47}N_7O_6S$ MOLECULAR WEIGHT: 657,82 g/mol				
PTC1660 **(S,R,S)-AHPC-C6-PEG3-butyl-N_3**		PTC1660.0050	50 mg	€ 470,00
(2S,4R)-1-((S)-22-Azido-2-(tert-butyl)-4-oxo-10,13,16-trioxa-3-azadocosanoyl)-4-hydroxy-N-(4-(4-methylthiazol-5-yl)benzyl) pyrrolidine-2-carboxamide CAS-NO: 2300155-90-0 FORMULA: $C_{38}H_{59}N_7O_7S$ MOLECULAR WEIGHT: 757,98 g/mol				
PTC1670 **(S,R,S)-AHPC-C6-PEG1-C3-PEG1-butyl-N_3**		PTC1670.0050	50 mg	€ 470,00
(2S,4R)-1-((S)-2-(6-((5-((6-Azidohexyl)oxy)pentyl)oxy) hexanamido)-3,3-dimethylbutanoyl)-4-hydroxy-N-(4-(4-methylthia-zol-5-yl)benzyl)pyrrolidine-2-carboxamide FORMULA: $C_{39}H_{61}N_7O_6S$ MOLECULAR WEIGHT: 756,01 g/mol				
PTC1680 **(S,R,S)-AHPC-PEG6-butyl-N_3**		PTC1680.0050	50 mg	€ 470,00
(2S,4R)-1-((S)-27-Azido-2-(tert-butyl)-4-oxo-6,9,12,15,18,21-hexaoxa-3-azaheptacosanoyl)-4-hydroxy-N-(4-(4-methylthiazol-5-yl)benzyl) pyrrolidine-2-carboxamide FORMULA: $C_{40}H_{63}N_7O_{10}S$ MOLECULAR WEIGHT: 834,03 g/mol				
PTC1690 **Pomalidomid-PEG2-butyl-I**		PTC1690.0050	50 mg	€ 470,00
N-(2-(2,6-Dioxopiperidin-3-yl)-1,3-dioxoisoindolin-4-yl)-2-(2-((6-iodo-hexyl)oxy)ethoxy)acetamide CAS-NO: 1835705-72-0 FORMULA: $C_{23}H_{28}IN_3O_7$ MOLECULAR WEIGHT: 585,39 g/mol				

		Article No.	Quantity	Price
PTC1700	**Pomalidomid-C6-PEG3-butyl-I** N-(2-(2,6-Dioxopiperidin-3-yl)-1,3-dioxoisoindolin-4-yl)-6-(2-(2-((6-iodohexyl)oxy)ethoxy)ethoxy)hexanamide CAS-NO: 1835705-70-8 FORMULA: $C_{29}H_{40}IN_3O_8$ MOLECULAR WEIGHT: 685,55 g/mol	PTC1700.0050	50 mg	€ 420,00
PTC1710	**Pomalidomid-C6-PEG1-C3-PEG1-butyl-I** N-(2-(2,6-Dioxopiperidin-3-yl)-1,3-dioxoisoindolin-4-yl)-6-((5-((6-iodohexyl)oxy)pentyl)oxy)hexanamide CAS-NO: 1835705-76-4 FORMULA: $C_{30}H_{42}IN_3O_7$ MOLECULAR WEIGHT: 683,57 g/mol	PTC1710.0050	50 mg	€ 470,00
PTC1720	**Pomalidomid-PEG6-butyl-I** N-(2-(2,6-Dioxopiperidin-3-yl)-1,3-dioxoisoindolin-4-yl)-24-iodo-3,6,9,12,15,18-hexaoxatetracosanamide FORMULA: $C_{31}H_{44}IN_3O_{11}$ MOLECULAR WEIGHT: 761,6 g/mol	PTC1720.0050	50 mg	€ 470,00
PTC1730	**(S,R,S)-AHPC-PEG2-butyl-Cl** (2S,4R)-1-((S)-2-(2-(2-((6-Chlorohexyl)oxy)ethoxy)acetamido)-3,3-dimethylbutanoyl)-4-hydroxy-N-(4-(4-methylthiazol-5-yl)benzyl) pyrrolidine-2-carboxamide FORMULA: $C_{32}H_{47}ClN_4O_6S$ MOLECULAR WEIGHT: 651,26 g/mol	PTC1730.0050	50 mg	€ 470,00
PTC1740	**(S,R,S)-AHPC-PEG6-butyl-Cl** (2S,4R)-1-((S)-2-(tert-Butyl)-27-chloro-4-oxo-6,9,12,15,18,21-hexaoxa-3-azaheptacosanoyl)-4-hydroxy-N-(4-(4-methylthiazol-5-yl)benzyl) pyrrolidine-2-carboxamide CAS-NO: 1835705-59-3 FORMULA: $C_{40}H_{63}ClN_4O_{10}S$ MOLECULAR WEIGHT: 827,47 g/mol	PTC1740.0050	50 mg	€ 470,00
PTC1750	**(S,R,S)-AHPC-C6-PEG3-butyl-Cl** (2S,4R)-1-((S)-2-(tert-Butyl)-22-chloro-4-oxo-10,13,16-trioxa-3-azadocosanoyl)-4-hydroxy-N-(4-(4-methylthiazol-5-yl)benzyl) pyrrolidine-2-carboxamide CAS-NO: 1835705-55-9 FORMULA: $C_{38}H_{59}ClN_4O_7S$ MOLECULAR WEIGHT: 751,42 g/mol	PTC1750.0050	50 mg	€ 470,00
PTC1760	**(S,R,S)-AHPC-C6-PEG1-C3-PEG1-butyl-Cl** (2S,4R)-1-((S)-2-(6-((5-((6-Chlorohexyl)oxy)pentyl)oxy) hexanamido)-3,3-dimethylbutanoyl)-4-hydroxy-N-(4-(4-methylthiazol-5-yl)benzyl)pyrrolidine-2-carboxamide CAS-NO: 1835705-61-7 FORMULA: $C_{39}H_{61}ClN_4O_6S$ MOLECULAR WEIGHT: 749,44 g/mol	PTC1760.0050	50 mg	€ 470,00

In addition to these pre-designed building blocks, we offer custom synthesis of your required ligand-linker combination or "complete PROTAC". This allows to design a library of slightly different PROTACs in order to find the best combination for your application, as even small changes in ligands and cross-linkers might affect the efficiency of the formation of the ternary complex.

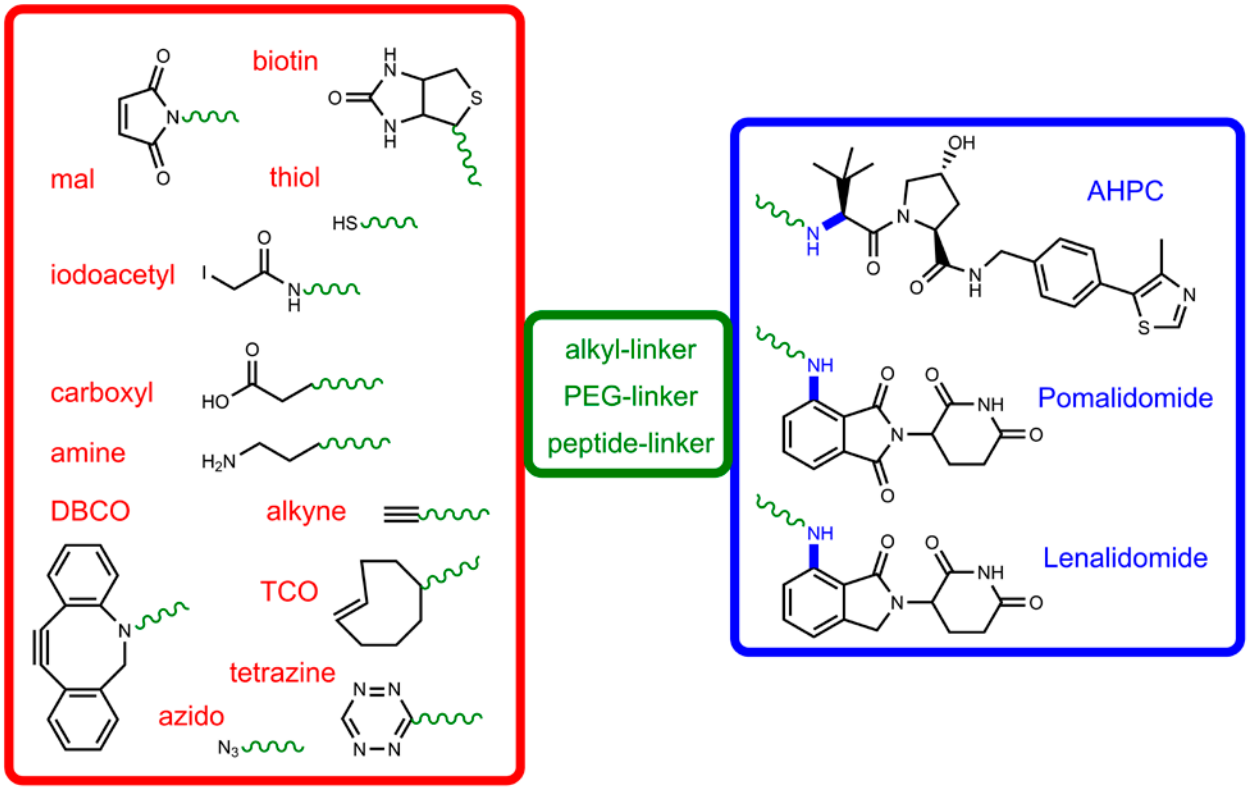


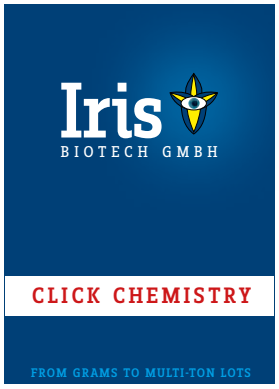
Fig. 28: Possibilities of PROTAC design. Above displayed options for linker constructs can be conjugated to substrates of the protein of interest, in order to create the desired PROTAC®.

Please contact us for Custom Synthesis of the PROTAC® linker fragment of your choice or complete functional PROTAC®.

References:

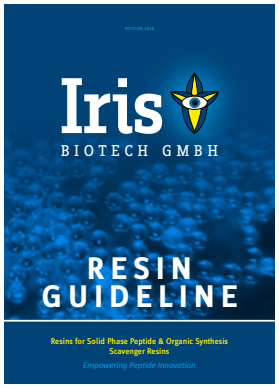
- Bifunctional Molecules beyond PROTACs; S. J. Conway; *J. Med. Chem.* 2020; **63**: 2802-2806. https://doi.org/10.1021/acs.jmedchem.0c00293.
- Targeted protein degradation by PROTACs; T. K. Neklesa, J. D. Winkler and C. M. Crews; *Pharmacol Ther* 2017; **174**: 138-144. https://doi.org/10.1016/j.pharmthera.2017.02.027.
- Targeted Protein Degradation: from Chemical Biology to Drug Discovery; P. M. Cromm and C. M. Crews; *Cell Chem Biol* 2017; **24**: 1181-1190. https://doi.org/10.1016/j.chembiol.2017.05.024.
- Targeted Protein Degradation by Small Molecules; D. P. Bondeson and C. M. Crews; *Annu Rev Pharmacol Toxicol* 2017; **57**: 107-123. https://doi.org/10.1146/annurev-pharmtox-010715-103507.
- Small-Molecule PROTACS: New Approaches to Protein Degradation; M. Toure and C. M. Crews; *Angew Chem Int Ed Engl* 2016; **55**: 1966-73. https://doi.org/10.1002/anie.201507978.
- Impact of linker length on the activity of PROTACs; K. Cyrus, M. Wehenkel, E. Y. Choi, H. J. Han, H. Lee, H. Swanson and K. B. Kim; *Mol Biosyst* 2011; **7**: 359-64. https://doi.org/10.1039/c0mb00074d.

Other publications from Iris Biotech:



Click Chemistry

Our Brochure for Click Chemistry with hundreds of different Azido and Alkyne Compounds. Find our possibilities for Copper-free Click Conjugation and our related Custom Synthesis capabilities.



Resin Guideline

Our comprehensive guideline on resins for solid-supported peptide synthesis. Complete with protocols for resin loading and linker cleavage, standard protocols for peptide chemistry, as well as a current product list of our solid supports. It also includes latest resin developments, e.g. SEA and Hydrazon resins, very useful tools for the synthesis of long peptides via native chemical ligation (NCL).

Betulin Derivatives

Betulin and its derivatives are pentacyclic triterpenoids of the lupane-type. They are natural products that occur as secondary metabolites in over 200 different plants. Betulinic acid, the oxidized derivative, is connected to various types of anti-cancer effects. Iris Biotech now offers natural betulin and betulinic acid, as well as an array of various derivatives.

ICG-Mal

Indocyanine green (ICG) is a near-infrared fluorescence imaging dye. Absorption maximum is at 800 nm and there is slight absorption in the visible range, which results in low auto-fluorescence and tissue absorbance. Emission maximum is at 810 nm. ICG has been approved by the FDA and has been found in numerous applications in therapeutics and diagnostics.

For more brochures visit our website: **www.iris-biotech.de**

6. 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 is respected.

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.

7. 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.

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 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.

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.

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