Proteax 3.0 – crosslinks

The upcoming version of Proteax will have support for crosslinking peptides via a new type of modification structure. The two literature examples shown here demonstrate binary crosslinks, with only two endpoints (a and b).

Higher-order crosslinks are supported, currently limited to six endpoints to keep things sane. The software itself does not have a technical limit on the number of endpoints.

Example 1 – stapled peptide

Chimia 2013, 67, nr. 12, p. 902.

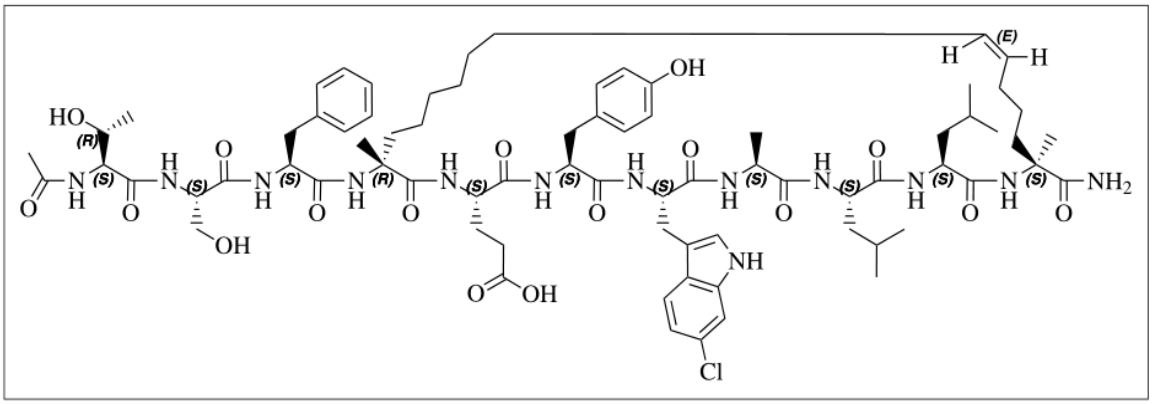
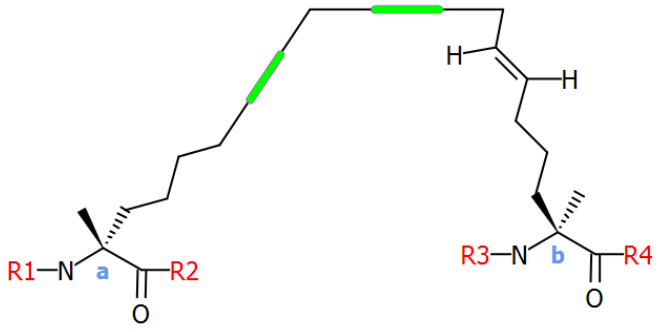


Fig. 5. Structure of the cellular active Hdm2-binding stapled peptide (*trans* isomer).[23]

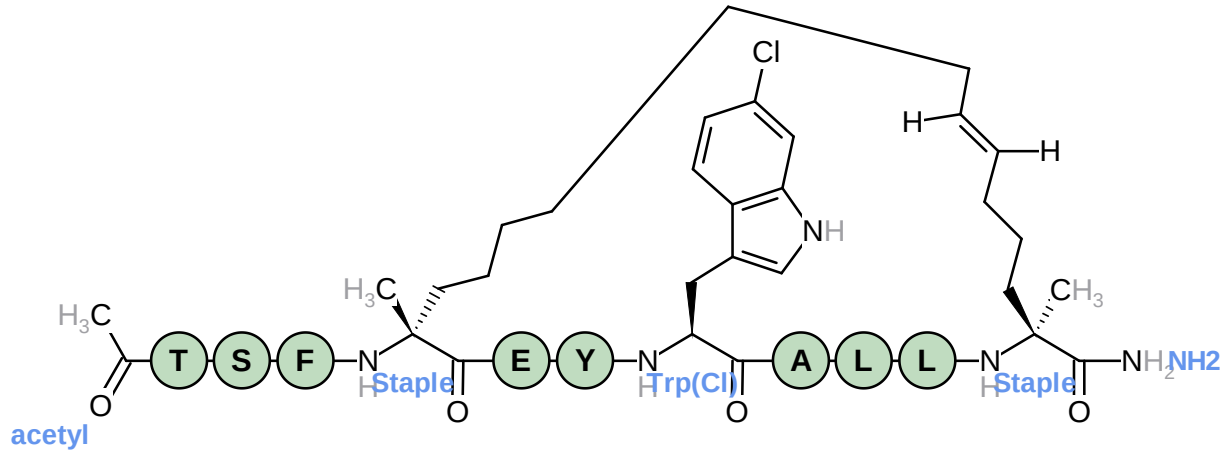
In Proteax 3.0 the peptide can be expressed in PLN, crosslink highlighted:

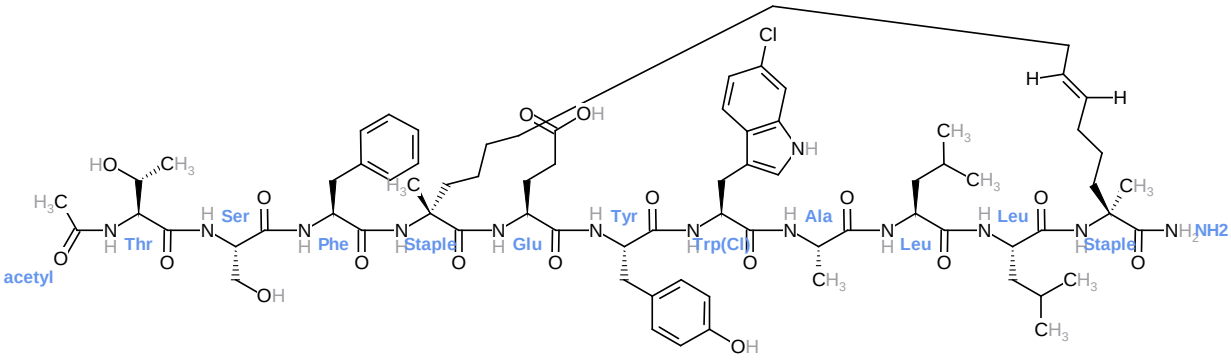
`[acetyl]-TSF[staple](1@a)EY[Trp(Cl)]ALL[staple](1@b)-[NH2]`

The “staple” modification is defined via the structure below. Endpoints “a” and “b” are defined via the “R1-R2” and “R3-R4” pairs. The green-marked bonds separate the parts belonging to the endpoints from the parts that will be placed between the endpoints when the final structure is generated.



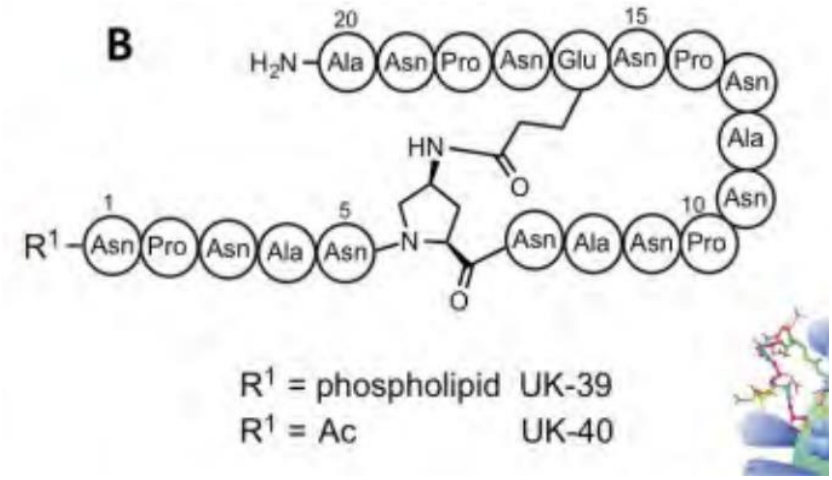
Resulting chemical structure, condensed and full structure renderings:





Example 2 – crosslinked peptide

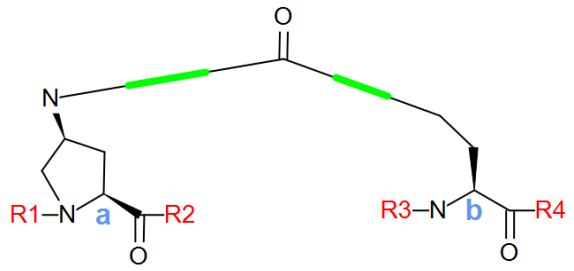
Chimia 2013, 67, nr. 12 p. 887.



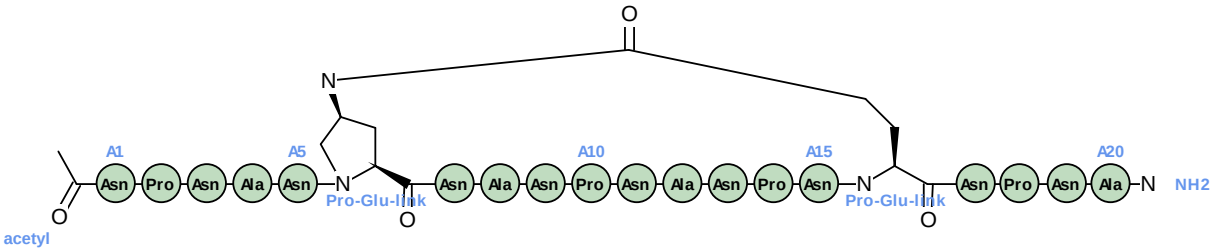
The UK-40 variant can be expressed in PLN like this, crosslink highlighted:

```
[acetyl]-Asn-Pro-Asn-Ala-Asn-[Pro-Glu-link](1@a)-Asn-Ala-Asn-Pro-Asn-
Ala-Asn-Pro-Asn-[Pro-Glu-link](1@b)-Asn-Pro-Asn-Ala-[NH2]
```

The “Pro-Glu-link” crosslink structure is, assuming that the sidechain connecting to the “Glu” in the Chimia figure is the Glu residue sidechain:



Generated chemical structure:


O
N
A1
A5
A10
A15
A20
Asn
Pro
Asn
Ala
Asn
N
Pro-Glu-link
O
Asn
Ala
Asn
Pro
Asn
Ala
Asn
Pro
Asn
N
Pro-Glu-link
O
Asn
Pro
Asn
Ala
N
NH2
O
acetyl