Reductive Cleavage of the Peptide Bond

In many biological research efforts, long chain organic molecules are studied by breaking the large molecules into smaller components. One method of doing this is reductive cleavage of the peptide (amid) bond in molecules such as RCONHR to give an amine, NH_2R, and a variety of carbonyl products such as $(RCO)_2$ and RCHO.

A cleavage technique that has been of recent interest is the use of solvated electrons, e^-aq These are formed when aqueous solutions are bombarded with gamma radiation. The solvated electron is very reactive and can reduce most any species present, even to form free radicals.

One of the reactions which will occur in a gamma-ray bombarded aqueous solution of peptides is

$$e^-aq + RCONHR + H_20 \rightarrow R\dot{C}(OH)NR + OH^-$$

The peptide may also be attacked by OH and H radicals in the solution. The peptide free radicals combine with reductive cleavage of the amide linkage:

$$2\ R\dot{C}(OH)NHR \rightarrow R(C0)_2 + 2\ NH_2R$$

However, the yield of carbonyl products from this and other reactions occurring in the system is very small. This is thought to result from a preferential, competing, recombination reaction among the peptide free radicals.

It has been found that this back reaction may be blocked by the addition of certain labile organic compounds, especially thiols, RSH. The blocking occurs by virtue of the hydrogen atom transfer reaction:

$$R\dot{C}(OH)NHR + RSH \rightarrow RCHC(OH)NHR + R\dot{S}$$

which in turn leads to reductive cleavage of the amide linkage:

$$R\dot{C}H(OH)NHR \rightarrow RCHO + NH_2R$$

In this case the aldehyde appears as the major product. The thiol effectively blocks the back reaction.

Note:

Requests for further information may be directed to:

Technology Utilization Officer
Lawrence Berkeley Laboratory
University of California
Berkeley, California 94270
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NASA has decided not to apply for a patent.

Source: John Holian and
Warren M. Garrison
Lawrence Berkeley Laboratory
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Category 04