

# Free radical reactions of sulfur-containing amino acids and peptides.

## From reactive transients to stable products

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In recent decades, the oxidation reactions of amino acids, peptides, and proteins have been the focus of extensive research due to their biological significance. Because of the low oxidation potential, amino acids containing sulfur are particularly vulnerable to attacks by one-electron oxidants, such as short-lived excited states, free radicals, and reactive oxygen species. The oxidation of methionine and cysteine causes significant damage to proteins, and consequently, it is believed to contribute to neurodegenerative diseases like Alzheimer's disease, Parkinson's disease, biological aging, and type 2 diabetes. This has generated considerable interest in their studying. Despite the long history of one-electron oxidation of sulfide groups, certain aspects of this process remain unclear or controversial, such as the free radical reactions that lead to stable modifications of amino acids.

The aim of this doctoral dissertation was to thoroughly investigate and describe the mechanisms behind photosensitized and radiation-induced oxidation of biomimetic model amino acids that contain a sulfide group.

A series of five thematically coherent scientific articles (P1-P5) describes both transient and stable products of the oxidation reaction of model systems containing a sulfide group. The oxidation was sensitized by 3-carboxybenzophenone and also induced radiolytically, where the oxidizing agent was the hydroxyl radical. Short-lived transients (e.g., intermediates containing three-electron bonds, free radicals, and radical ions and reactive excited states) were investigated using time-resolved techniques (laser flash photolysis and pulse radiolysis), while stable products were identified using high-performance liquid chromatography coupled with tandem mass spectrometry (LC-MS/MS). Combining these complementary methods allowed us to address the impact of the substrate's structure (type of functional groups, length of the amino acid side chain) and the reaction conditions (pH) on the formation of transient and stable products. This helped to propose a fuller picture of the oxidation processes in selected biologically important compounds. Additionally, the aromatic ketones (benzophenone, 3-carboxybenzophenone, and 4-carboxybenzophenone), which are used as photosensitizers, were characterized in detail.