

# Lanthionine

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## summary

Lanthionine, a sulfur-containing amino acid with the molecular formula  $C_6H_{12}N_2O_4S$ , plays a pivotal role in biochemical processes and is notable for its structural complexity as a bis-amino acid. This compound, classified as a heterocyclic amino acid within the 1,4-thiazine family, is characterized by its unique stereochemistry and is integral to the formation of lanthipeptides, which are essential in various biological functions, including protein synthesis and neurotransmission.[\[1\]\[2\]\[3\]](#)

Lanthionine is synthesized through multiple pathways, primarily involving the condensation of cysteine and serine, and has garnered attention for its neurobiological effects, particularly its interaction with the protein LanCL1, which is implicated in neurite outgrowth and synaptogenesis.[\[4\]\[5\]](#) The compound's significance extends beyond neurobiology, as it plays a critical role in metabolic processes and is being explored for applications in food biotechnology and metabolic engineering, particularly in lactic acid bacteria.[\[2\]\[6\]](#)

Controversies surrounding lanthionine primarily stem from its dual potential in therapeutic applications and the necessity for further research to clarify its safety and efficacy profiles, especially in treating neurodegenerative diseases and various cancers.[\[7\]\[8\]](#) As studies continue to reveal the compound's antioxidant and anti-inflammatory properties, its applications in medical formulations present promising avenues for future therapeutic interventions against conditions such as Alzheimer's disease, Parkinson's disease, and cancer.[\[7\]\[8\]](#)

## Structure

Lanthionine, with the molecular formula  $C_6H_{12}N_2O_4S$ , has a molecular weight of approximately 208.23 g/mol[\[1\]\[2\]](#). It is classified as a bis-amino acid, characterized by the presence of both lanthionine and methyllanthionine, which exhibit varying stereochemistry[\[3\]](#). The chemical structure includes a central carbon atom bonded to a hydrogen atom, a basic amino group, a carboxylic acid group, and a unique side chain known as the R group, which contributes to the distinct properties of this compound[\[9\]\[3\]](#).

In terms of its physical state, lanthionine is solid at room temperature and is recommended to be stored in a cool, dry place[\[10\]](#). The compound's stereochemistry is defined by its two stereocenters, influencing its interactions and biological activities[\[11\]](#). The structure of lanthionine is significant not only in its biochemical role but also in the formation of various lanthipeptides, which incorporate this amino acid as a key component in their peptide chains[\[3\]](#).

Lanthionine's classification as a heterocyclic compound further places it within the category of 1,4-thiazines, indicating its structural complexity that includes a sulfur atom in its cyclic formation[\[2\]](#). This complexity plays a critical role in its function within biological systems, particularly in the synthesis of proteins and other biomolecules[\[7\]\[2\]](#).

## Synthesis

Lanthionine can be synthesized through various biochemical pathways, notably from the precursor lanthionine and alpha-keto acids, such as pyruvate. A detailed synthesis process involves the formation of lanthionine ketimine (LK) through the spontaneous reaction of lanthionine with pyruvate, facilitated by the enzyme L-amino acid oxidase, or through other enzymatic mechanisms involving kynurenine amino transferase (KAT) which plays a critical role in the brain[\[7\]\[12\]](#).

## Reaction Mechanisms

The primary reaction pathway begins with the condensation of cysteine and serine, yielding lanthionine. Specifically, the conversion of serine and homocysteine into cystathionine and lanthionine involves cystathionine  $\beta$ -synthase (CS) and cystathionine  $\beta$ -lyase (CL), as illustrated in the classical transsulfuration pathway[\[12\]](#). Additionally, LK can be synthesized through the reaction of 3-bromopyruvate with cysteine in an aqueous solution, leading to a cyclization that retains stereochemical properties[\[13\]](#).

## Synthesis of LK Derivatives

Lanthionine ketimine derivatives can also be produced through similar synthetic routes, with variations in the starting materials and conditions. A common method involves mixing an aqueous solution of enantiomerically pure L-cysteine or its derivatives with an equimolar solution of a suitable ~~α~~ keto acid. This leads to the formation of a lanthionine intermediate, which subsequently cyclizes to yield LK or its derivatives, such as (R)-LKE1, in high yields[\[7\]\[14\]](#). Recovery of LK or its derivatives is typically achieved through crystallization, extraction, or distillation methods well-known to those skilled in synthetic organic chemistry[\[7\]\[13\]](#).

## Considerations in Synthesis

When synthesizing LK or its derivatives, particular attention must be given to the structural elements of the compounds, as certain groups (e.g., R1 and R2) can significantly influence the properties and activities of the resulting molecules. Variations in R1 and R2 can include alkoxy, alkenylamino, or amido groups, which may affect the bioavailability and pharmacological efficacy of the synthesized compounds[\[12\]\[13\]](#). Furthermore, the synthesis is designed to produce predominantly one enantiomer, thus enhancing the potential therapeutic applications of the resulting LK derivatives in treating conditions such as mood disorders and neurochemical imbalances[\[7\]\[12-14\]](#).

## Biological Role

Lanthionine (LK) plays significant roles in various biological processes, particularly in the central nervous system. One of the key findings is its selective binding to LanCL1, a protein implicated in neurite outgrowth, synaptogenesis, and neurotransmission. This suggests a functional relationship between LK and LanCL1, rather than a mere coincidence of nomenclature[\[4\]](#). The proteins CRMP2, STXBP1, and LanCL1 are recognized for their contributions to neuronal growth and polarization, critical during embryonic neurogenesis[\[4\]](#). The involvement of CRMP2 and LanCL1 in neuritogenesis indicates that LK may exert neurotrophic or neuritogenic effects[\[4\]](#).

Proteomic studies have further highlighted the association of LK-interacting proteins with neurological conditions, such as schizophrenia, where proteins like myelin basic protein (MBP) and CRMP2/DPYSL2 have been found to be differentially expressed in affected brain tissue[\[4\]\[5\]](#). This underscores the importance of sulfur-containing amino acids, such as cysteine and methionine, which are integral to structural, catalytic, and metabolic functions within biological systems[\[4\]](#).

In addition, free sulfurous amino acids and small peptides are vital for maintaining homeostasis and facilitating signal transduction in organisms inhabiting oxidizing environments. For example, glutathione plays a crucial role in maintaining a reduced intracellular environment, aiding in amino acid transport, and transducing signals via reversible glutathionylation[\[4\]\[2\]](#). The evolutionary significance of sulfur reactivity extends to anabolic pathways, such as those involving S-adenosyl methionine (SAM),

further highlighting the biological relevance of lanthionine and related compounds in metabolic processes[4][5].

Moreover, the biological roles of lanthionine extend beyond neurobiology; metabolic engineering applications have been explored, particularly concerning lactic acid bacteria. These organisms are noted for their protein degradation capabilities and production of beneficial metabolites, which are significant for food biotechnology[2][6]. Such metabolic characteristics illustrate the multifunctional nature of compounds like lanthionine in both health and industry contexts.

## Applications

Lanthionine and its derivatives, particularly lanthionine ketimine (LK) and thiomorpholine dicarboxylic acid (TMDCA), have significant applications in the medical field, especially concerning the treatment and prevention of various diseases. These compounds exhibit properties that are beneficial for neuroprotection and have potential therapeutic roles in conditions affecting the central nervous system (CNS) [7][8].

### Neurodegenerative Diseases

Lanthionine derivatives are being investigated for their efficacy in treating neurodegenerative diseases such as Alzheimer's disease (AD), Parkinson's disease (PD), amyotrophic lateral sclerosis (ALS), and multiple sclerosis (MS). These conditions are often associated with neuroinflammation and oxidative stress, where lanthionine compounds may play a crucial role due to their anti-oxidant and anti-neuroinflammatory activities [7][8]. For instance, LK has been shown to pass through cellular membranes, including the blood-brain barrier, enhancing its potential for CNS applications [7].

### Cancer Treatment

The compounds derived from lanthionine are also being explored for their anticancer properties. Research indicates that LK and its synthetic ethyl ester (R)-LKE1 exhibit antiproliferative effects on tumor cells, suggesting that they could serve as single agents or in combination with other therapies to inhibit cancer cell proliferation and induce apoptosis in various cancer types, including breast, prostate, and lung cancers [7][8]. Additionally, the compounds may improve the efficacy of existing cancer treatments by enhancing the sensitivity of hyperproliferative cells to apoptotic inducers [7].

### Formulations and Administration

Lanthionine derivatives can be formulated into various pharmaceutical compositions suitable for multiple routes of administration, including oral, topical, and parenteral applications. These formulations may include tablets, capsules, ointments, and injectable solutions, designed to ensure stability and bioavailability of the active

compounds [7]. The use of a pharmaceutically acceptable carrier is crucial, as it allows for effective delivery while minimizing adverse reactions [7][8].

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