alfa-Aminopimelic acid

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summary

alfa-Aminopimelic acid, also known as Diaminopimelic acid (DAPA), is a non-proteinogenic amino acid that plays a critical role in the biosynthesis of various metabolites and the structural integrity of bacterial cell walls. With the molecular formula $C_7H_{14}N_2O_4$, this compound is distinguished by its heptanedioic acid backbone containing two amino groups at the 2nd and 6th positions. DAPA is not only pivotal for bacterial growth but also serves as a precursor in the biosynthesis of lysine and

other essential biomolecules, underscoring its importance in both prokaryotic and eukaryotic organisms.[1][2][3]

Alfa-aminopimelic acid is notable for its involvement in crucial metabolic pathways, particularly in bacteria, where it contributes to the formation of peptidoglycan, a vital component of the bacterial cell wall.[3][4] This amino acid's multifaceted roles extend beyond structural functions; it participates in various enzymatic reactions, such as those mediated by transaminases, that are fundamental to amino acid metabolism.[5] Given its widespread implications in both environmental and industrial applications, DAPA has attracted interest from researchers in fields ranging from biotechnology to agriculture.

The compound is primarily sourced from agricultural byproducts and microbial fermentation processes, with certain bacteria, including various strains of the genus, being capable of synthesizing DAPA under optimal conditions.[6][7] Furthermore, advances in biotechnology have enabled the use of recombinant host cells to enhance the production of alfa-aminopimelic acid, highlighting its potential for sustainable amino acid production in industrial settings.[2][8]

Despite its biological significance, alfa-aminopimelic acid presents safety risks that necessitate careful handling. Classified under various hazard categories, including eye and skin irritation, the compound's handling requires protective measures to mitigate potential exposure risks.[9] Regulatory agencies, such as the U.S. Food and Drug Administration (FDA) and the European Food Safety Authority (EFSA), impose stringent guidelines on its use, particularly in food and feed applications, to ensure safety and compliance with health standards.[10]

Chemical Structure

Alfa-Aminopimelic acid, also known as Diaminopimelic acid (DAPA), is a compound with the molecular formula C7H14N2O4, characterized by a heptanedioic acid backbone featuring two amino groups at the 2nd and 6th positions[1][11]. This structural arrangement classifies it as a difunctional C7 alkane, which can include both straight and branched forms, as well as saturated and unsaturated variants, with functional groups potentially located at various points along the hydrocarbon chain[2].

The compound's functional groups include amino groups (–NH2) and carboxylic acid groups (–COOH), which are pivotal for its biological roles. The presence of these functional groups influences the compound's reactivity and interactions in biochemical pathways, particularly in the synthesis of important metabolites such as biotin[1][2].

In addition to its basic structure, variations of alfa-aminopimelic acid may exist, including trifunctional derivatives where additional functional groups such as keto (C=O) or hydroxyl (–OH) groups are present, demonstrating the compound's versatility in biochemical applications[2].

Biological Role

Alfa-aminopimelic acid (DAP) is a vital component of the peptidoglycan layer of bacterial cell walls, playing a crucial role in maintaining the structural integrity and stability of bacterial cells.[3][4] As a non-proteinogenic amino acid, DAP functions as a bacterial metabolite and is essential for bacterial growth and interaction with other organisms.[3]

In addition to its structural role, DAP participates in various metabolic pathways within bacteria. For example, the lysine biosynthesis pathways IV and V utilize DAP as a precursor in a series of enzymatic reactions, contributing to the biosynthesis of lysine and related compounds.[2] These pathways involve multiple enzymes, such as homocitrate synthase and homoisocitrate dehydrogenase, which facilitate the transformation of ±ketoglutarate to ±ketoadipate, demonstrating the metabolic versatility of DAP in cellular processes.[2]

Moreover, DAP's importance extends beyond bacteria, as it is also implicated in the synthesis of other biomolecules. It serves as a substrate in enzymatic reactions catalyzed by transaminases, which play a fundamental role in amino acid metabolism by transferring amino groups between amino acids and ±keto acids.[5] This function underscores the broader biochemical significance of DAP within various biological systems, from prokaryotes to eukaryotes.

Natural Sources

Alfa-Aminopimelic acid, an essential amino acid, can be sourced from various biological materials, particularly those associated with agricultural byproducts and microbial fermentation processes.

Agricultural Byproducts

A variety of agricultural byproducts are rich in bioactive compounds, including amino acids. Notably, fruit and vegetable industry byproducts contain high levels of antioxidant components and amino acids, which are beneficial for health. For instance, the processing of fruits such as pistachio, pomegranate, and olive in Turkey results in substantial byproduct generation, which poses environmental challenges but also offers opportunities for amino acid extraction [6]. These byproducts can serve as alternative feed sources, especially in regions facing difficulties in traditional grain harvests due to climate change and environmental degradation [6][8].

Microbial Fermentation

In addition to agricultural sources, alfa-aminopimelic acid can be produced through microbial fermentation. Studies have shown that specific strains of bacteria, including various species of the Bacillus genus, can synthesize essential amino acids under optimal growth conditions [7]. For instance, the soil isolate Bacillus laterosporus has demonstrated the capacity to produce L-L-lysine, an amino acid related to alfa-aminopimelic acid, when cultured with specific carbon and nitrogen sources, highlighting the potential of using microbial processes for amino acid production [7].

Microorganisms

Various microorganisms are utilized in the production of amino acids, with both prokaryotic and eukaryotic cells being applicable. Prokaryotic cells such as Escherichia coli and Bacillus spp., as well as eukaryotic cells like yeast (e.g., Saccharomyces and Yarrowia lipolytica), are commonly employed in fermentation processes to synthesize amino acids, including alfa-aminopimelic acid [2][8]. The selection of suitable strains and optimal growth media can significantly influence the yield and efficiency of amino acid production [2].

Synthesis

Overview of Synthesis Pathways

The synthesis of ±aminopimelic acid (±AP) involves various biosynthetic routes, which can include the use of radical chemistry for the production of ±amino acids and their derivatives. A notable method includes the radical synthesis of ±amino-adipic acids, which serve as precursors in the pathway to ±AP[12][13].

Biosynthetic Routes

One key biosynthetic strategy for the formation of ±AP involves the utilization of ±ketoglutaric acid as a precursor. This pathway is characterized by a series of reactions starting with a Claisen-Schmidt condensation between ±ketoglutaric acid and acetyl CoA, leading to the formation of ±aminoadipic acid[14]. Subsequent reactions including rearrangement, oxidation, and decarboxylation contribute to the production of the L isomer of ±aminoadipic acid, which is crucial for the synthesis of ±AP[14].

In the biosynthetic pathway specific to lysine in fungi, ±ketoglutaric acid is used instead of succinaldehydic acid, progressing through similar steps to yield ±AP[14]. The overall process is also influenced by the transformation of one-carbon groups, facilitated by coenzymes derived from folic acid, that ultimately contribute to the synthesis of methionine and other key amino acids, which are precursors in the pathway[14].

Use of Recombinant Host Cells

Recent advances in biotechnology have explored the use of recombinant host cells to enhance the synthesis of ±AP. These genetically modified cells express enzymes that catalyze critical steps in the biosynthesis of polymer monomers, including those that contribute to the formation of ±AP[2]. By integrating various enzymes such as acyl-CoA reductases, aminotransferases, and ±keto acid decarboxylases, researchers aim to optimize metabolic pathways for more efficient production of ±AP from renewable and non-renewable feedstocks[2].

Chemical Synthesis Methods

In addition to biological pathways, chemical synthesis techniques are employed to create ±AP and related compounds. This includes the synthesis of ±ketosuberate and ±ketopimelate, which are precursors in the production of ±AP[2]. Such methods often utilize reactions involving condensation, isomerization, and oxidative decarboxylation to achieve the desired compounds, allowing for a versatile approach to ±AP synthesis.

Applications

Industrial Applications

The compound is also investigated for its potential use in industrial biotechnology. It can be involved in the biosynthesis of various chemical intermediates, which are essential for the production of polymers and other industrial materials. For instance, ±AAD can serve as a precursor in the synthesis of polyamides, such as nylon-7, demonstrating its utility in producing environmentally friendly and sustainable materials from renewable feedstocks[2].

Agricultural Uses

Alpha-aminoadipic acid (±AAD) has significant implications in agriculture, particularly in animal husbandry. The rising demand for high-quality milk, particularly sheep milk, underscores the importance of optimizing feed resources. Given that the quality of feed directly influences animal health and milk production performance, ±AAD serves as a potential supplement to enhance the nutritional value of animal feed, particularly in regions like Southeast Turkey, where byproducts from fruit production can be utilized as alternative feed sources[6][15].

Biochemical Research

In biochemical research, ±aminoadipic acid is studied for its role as a metabolic intermediate. It is involved in the transamination process, which is crucial for the metabolism of amino acids. An elevation of ±aminoadipic acid in urine is often linked to vitamin B6 insufficiency, prompting research into its metabolic pathways and potential treatments, including supplementation with vitamin B6 and ±ketoglutarate to facilitate transamination reactions[15].

Nutraceuticals

In the field of nutraceuticals, ±aminoadipic acid's properties make it a candidate for dietary supplements aimed at improving metabolic health. Its role in amino acid metabolism can be leveraged to address deficiencies and enhance nutrient absorption in humans, particularly in populations with dietary restrictions or malnutrition[6].

Toxicity and Safety

2,6-Diaminopimelic acid, also known as alfa-aminopimelic acid, is a compound that poses certain safety risks and requires careful handling. It is classified under multiple hazard categories, including serious eye damage or eye irritation (Category 2), skin corrosion or irritation (Category 2), and specific target organ toxicity (Category 3) due to respiratory effects[9]. The compound can cause skin irritation (H315), serious eye irritation (H319), and may lead to respiratory irritation (H335) upon exposure[9].

In terms of safety measures, it is essential to wear protective gloves, clothing, and eye protection when handling 2,6-diaminopimelic acid. If contact occurs with the eyes, immediate action should be taken to rinse them cautiously with water for several minutes, removing any contact lenses if possible[9].

From an environmental perspective, 2,6-diaminopimelic acid is soluble in water, diluted acids, and alkali, but it is incompatible with strong oxidizing agents[9]. This chemical behavior necessitates careful consideration during its storage and disposal to prevent unintended reactions.

Furthermore, regulatory frameworks in various regions impose strict guidelines on the use of amino acids, including 2,6-diaminopimelic acid, especially in applications such as animal feed. For instance, the U.S. Food and Drug Administration (FDA) mandates that all food additives, including amino acids, must be proven safe and effective prior to market approval, thereby ensuring they meet safety and quality standards[10]. In the European Union, similar regulations require that all feed additives, including amino acids, are authorized, safe, and correctly labeled, with the European Food Safety Authority overseeing these compliance checks[10].

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