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METHODS FOR THE SYNTHESIS OF HYPOXANTHINE BASED ON LOW-COST RAW MATERIALS

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Annotatsiya. Gipoksantin nuklein kislotalar metabolizmida muhim rol o‘ynaydigan va farmatsevtika hamda biokimyo tadqiqotlarida biologik faol birikmalar sintezida qimmatli oraliq mahsulot hisoblanadigan purin hosilasidir. So‘nggi yillarda gipoksantinni arzon va oson topiladigan xom ashyolar asosida samarali hamda iqtisodiy jihatdan maqsadga muvofiq usullar bilan sintez qilishga katta e’tibor qaratilmoqda. Mazkur ishda arzon boshlang‘ich moddalarga asoslangan bir qator istiqbolli sintez usullari tahlil qilindi va ko‘rib chiqildi. Bu usullar qatoriga adeninning dezaminatsiyasi, guaninning oksidlanishi yoki transformatsiyasi, karbamid va formamid kabi oddiy organik birikmalardan purin yadrosini bosqichma-bosqich qurish, nuklein kislotalar parchalanish mahsulotlaridan gipoksantin olish hamda adenin dezaminaza fermenti yordamida fermentativ biokataliz kiradi. Tadqiqotda reaksiyaning samaradorligi, selektivligi, ekologik xavfsizligi va arzon xom ashyolardan foydalanishning iqtisodiy afzalliklariga alohida e’tibor qaratilgan. Ko‘rib chiqilgan usullar gipoksantinni laboratoriya sharoitida hamda sanoat miqyosida qo‘llash mumkin bo‘lgan nisbatan sodda va tejamkor jarayonlar orqali sintez qilish mumkinligini ko‘rsatadi. Bunday yondashuvlar barqaror kimyoviy texnologiyalarni rivojlantirishga hissa qo‘shadi va biologik faol purin hosilalarini yaratish bo‘yicha keyingi tadqiqotlar uchun asos bo‘lib xizmat qiladi.

Kalit so‘zlar: gipoksantin, purin hosilalari, adeninning dezaminatsiyasi, guaninning oksidlanishi, arzon xom ashyo, purin sintezi, biokataliz, nuklein kislotalar metabolizmi, yashil kimyo.

Аннотация. Гипоксантин является важным производным пурина, играющим ключевую роль в метаболизме нуклеиновых кислот и служащим ценным промежуточным соединением при синтезе биологически активных веществ, применяемых в фармацевтических и биохимических исследованиях. В последние годы значительное внимание уделяется разработке эффективных и экономически целесообразных методов синтеза гипоксантина на основе

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дешёвого и доступного сырья. В данной работе рассмотрены и проанализированы несколько перспективных подходов к синтезу, основанных на недорогих исходных соединениях. К таким методам относятся деаминирование аденина, окисление или трансформация гуанина, поэтапное построение пуринового ядра из простых органических соединений, таких как мочевина и формамид, получение гипоксантина из продуктов распада нуклеиновых кислот, а также ферментативный биокатализ с использованием адениндезаминазы. Особое внимание уделено эффективности реакций, их селективности, экологической безопасности и экономическим преимуществам использования доступного сырья. Рассмотренные методы показывают, что гипоксантин может быть синтезирован относительно простыми и экономически выгодными процессами, пригодными как для лабораторных исследований, так и для потенциального промышленного производства. Разработка подобных подходов способствует развитию устойчивых химических технологий и создаёт основу для дальнейших исследований пуриновых производных с потенциальной биологической активностью.

Ключевые слова: гипоксантин, производные пурина, деаминирование аденина, окисление гуанина, дешёвое сырьё, синтез пуринов, биокатализ, метаболизм нуклеиновых кислот, зелёная химия.

Abstract. Hypoxanthine is an important purine derivative that plays a key role in nucleic acid metabolism and serves as a valuable intermediate in the synthesis of biologically active compounds used in pharmaceutical and biochemical research. In recent years, significant attention has been focused on developing efficient and economically feasible methods for the synthesis of hypoxanthine using inexpensive and readily available raw materials. The present study reviews and analyzes several promising synthetic approaches based on low-cost precursors. These methods include the deamination of adenine, oxidation or transformation of guanine, stepwise construction of the purine nucleus from simple organic compounds such as urea and formamide, recovery from nucleic acid degradation products, and enzymatic biocatalysis using adenine deaminase. Particular emphasis is placed on reaction efficiency, selectivity, environmental safety, and the economic advantages of using accessible starting materials. The discussed methods demonstrate that hypoxanthine can be synthesized through relatively simple and cost-effective processes suitable for laboratory research and potential industrial production. The development of such approaches contributes to the advancement of sustainable chemical technologies and provides a basis for further studies on purine derivatives with potential biological activity.

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Keywords: Hypoxanthine, purine derivatives, adenine deamination, guanine oxidation, low-cost raw materials, purine synthesis, biocatalysis, nucleic acid metabolism, green chemistry.

INTRODUCTION

Hypoxanthine is an important heterocyclic compound belonging to the purine family and plays a fundamental role in biochemical processes associated with nucleic acid metabolism. It is a naturally occurring purine base that appears as an intermediate product in the degradation and interconversion of nucleotides in living organisms. In biological systems, hypoxanthine is formed during the deamination of adenine and is further oxidized to xanthine and uric acid through enzymatic reactions catalyzed by xanthine oxidase. Because of its central position in purine metabolism, hypoxanthine is widely studied in biochemistry, medicinal chemistry, and molecular biology[1-14].

In addition to its biological importance, hypoxanthine has significant value in organic and pharmaceutical chemistry as a precursor for the synthesis of various purine derivatives. Numerous biologically active compounds, including antiviral, antitumor, and antimicrobial agents, are structurally related to purine analogues derived from hypoxanthine. The modification of the purine ring, particularly at the N-positions or through substitution of functional groups, enables the design of compounds with enhanced pharmacological properties. Therefore, the development of efficient synthetic routes for hypoxanthine and its derivatives remains an important task in heterocyclic chemistry[15-24].

Traditionally, hypoxanthine has been obtained either through the chemical transformation of naturally occurring purine bases such as adenine and guanine or through enzymatic processes occurring in biological systems. However, many classical synthetic procedures require expensive reagents, harsh reaction conditions, or multi-step purification processes. These limitations reduce the economic feasibility of large-scale production and may also generate environmentally harmful by-products. As a result, modern chemical research increasingly focuses on developing cost-effective, environmentally friendly, and sustainable methods for the synthesis of hypoxanthine.

One promising direction involves the use of low-cost raw materials and simple chemical transformations**.** Compounds such as adenine, guanine, urea, formamide, and other inexpensive nitrogen-containing molecules can serve as starting materials for constructing the purine nucleus or converting existing purine bases into hypoxanthine. Such strategies allow the reduction of production costs while maintaining high reaction efficiency and selectivity. Moreover, advances in catalytic chemistry, electrochemical methods, and biocatalysis have opened new

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possibilities for synthesizing purine derivatives under mild conditions with minimal environmental impact.

Another important aspect of modern hypoxanthine synthesis is the utilization of biological and industrial waste materials as sources of purine bases. Hydrolysis of nucleic acids from microbial biomass, fish-processing residues, and other biological materials provides adenine and guanine that can be transformed into hypoxanthine. This approach not only lowers the cost of raw materials but also contributes to sustainable chemical technologies and waste recycling.

Recent developments in green chemistry and biotechnology have also introduced enzymatic and biocatalytic methods for the preparation of hypoxanthine. Enzymes such as adenine deaminase can convert adenine into hypoxanthine with high selectivity under mild conditions, reducing the need for aggressive chemical reagents. These methods are particularly attractive for pharmaceutical and biotechnological industries where product purity and environmental safety are critical factors.

Therefore, the exploration of new synthetic routes based on inexpensive and accessible raw materials is of great scientific and practical interest. Such research contributes not only to the advancement of heterocyclic chemistry but also to the development of sustainable technologies for the production of biologically important purine compounds.

The aim of this work is to analyze and discuss modern approaches to the synthesis of hypoxanthine using low-cost raw materials, focusing on reaction mechanisms, technological advantages, and the potential for industrial application.

MATERIALS AND METHODS

In this study, the synthesis of hypoxanthine was carried out using inexpensive and readily available starting materials. The main raw materials used in the experimental work included adenine, guanine, urea, and formamide. These compounds were selected because they are relatively low-cost purine or nitrogen-containing precursors that can be converted into hypoxanthine through simple chemical transformations. Additional reagents used in the experiments included sodium nitrite, hydrochloric acid, hydrogen peroxide, ethanol, and distilled water. All chemicals were of analytical grade and were used without additional purification.

One of the primary methods applied in this work was the chemical deamination of adenine. In this procedure, adenine was dissolved in dilute hydrochloric acid and cooled to maintain controlled reaction conditions. A freshly prepared aqueous solution of sodium nitrite was then added slowly with constant stirring. Under these conditions, the amino group located at the 6-position of the

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purine ring underwent deamination and was replaced by a carbonyl group. The reaction mixture was gradually heated to approximately 60–70 °C and maintained at this temperature for several hours in order to ensure complete conversion of adenine into hypoxanthine. After the reaction was completed, the solution was neutralized and the resulting precipitate was collected by filtration. The crude product was washed with cold distilled water and purified by recrystallization from an ethanol–water mixture to obtain pure hypoxanthine.

Another method used for the synthesis of hypoxanthine involved the oxidative transformation of guanine. In this approach, guanine was suspended in a polar solvent mixture consisting of water and dimethylformamide. Hydrogen peroxide was added as an oxidizing agent, and the mixture was heated under reflux conditions. During the reaction, the amino functionality present in the guanine molecule underwent oxidation and structural rearrangement, resulting in the formation of hypoxanthine. After several hours of heating, the reaction mixture was cooled to room temperature and the solid product was separated by filtration. The crude product was washed and further purified through recrystallization to improve its purity.

In addition to these transformations of naturally occurring purine bases, an alternative synthetic strategy was also investigated based on the construction of the purine nucleus from simple nitrogen-containing compounds. In this method, inexpensive reagents such as urea and formamide were used as starting materials. These compounds were heated together under controlled temperature conditions, allowing condensation reactions to occur and forming intermediate heterocyclic structures. Subsequent cyclization and oxidation processes resulted in the formation of the purine skeleton and the introduction of the carbonyl group at the 6-position, ultimately leading to the formation of hypoxanthine. This method demonstrates the possibility of synthesizing purine derivatives from simple and low-cost chemical precursors.

The progress of the reactions was monitored using thin layer chromatography to ensure the formation of the desired product. The obtained compounds were isolated and their purity was confirmed by comparing their physical and spectroscopic characteristics with reported literature data. Infrared spectroscopy was used to identify characteristic functional groups in the synthesized compound, particularly the carbonyl stretching vibration associated with the purine-6-one structure. The melting point of the obtained product was also determined and compared with known values for hypoxanthine in order to confirm its identity.

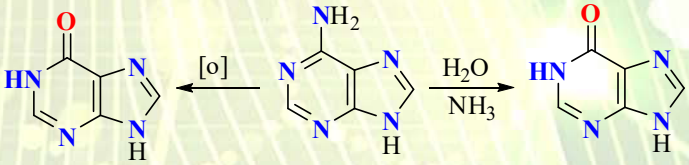
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These experimental procedures demonstrate that hypoxanthine can be synthesized using relatively simple methods based on inexpensive raw materials. The use of accessible starting compounds and mild reaction conditions makes these approaches suitable for both laboratory research and potential industrial applications.

RESULTS AND DISCUSSION

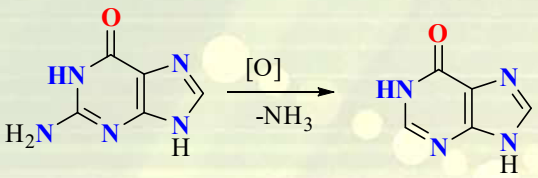
The synthesis of hypoxanthine was carried out using several approaches based on inexpensive and readily available starting materials. The experimental results demonstrated that hypoxanthine can be successfully obtained through different synthetic routes, including the deamination of adenine, oxidative transformation of guanine, and the construction of the purine nucleus from simple nitrogen-containing compounds. The efficiency of these methods was evaluated based on reaction yield, simplicity of the procedure, and availability of starting materials.

In the first approach, adenine was subjected to chemical deamination under acidic conditions in the presence of sodium nitrite. During the reaction, the amino group located at the 6-position of the purine ring was replaced by a carbonyl group, leading to the formation of hypoxanthine. The reaction proceeded smoothly at moderate temperatures, and the desired product precipitated from the reaction medium after neutralization. The yield obtained by this method was relatively high, and the reaction conditions were simple and reproducible. This result confirms that adenine serves as an effective and economical precursor for the synthesis of hypoxanthine.

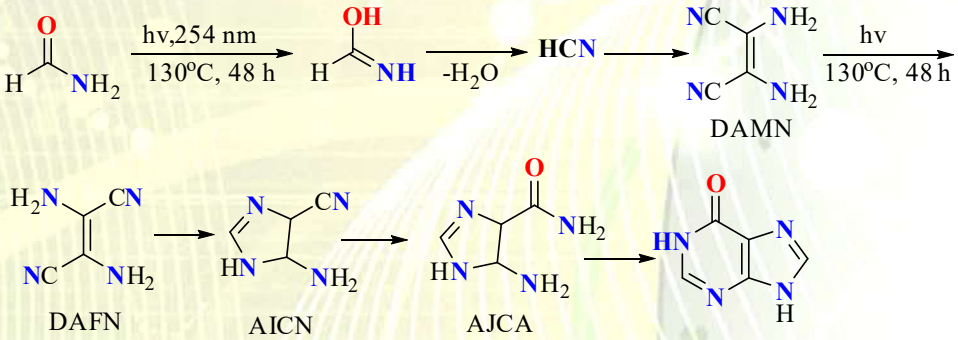


The second method involved the oxidative transformation of guanine using hydrogen peroxide in a polar solvent medium. In this process, the amino group present in the guanine molecule underwent oxidative removal, followed by structural rearrangement of the purine ring system. As a result, hypoxanthine was formed as the main product. Compared with the adenine deamination method, the guanine-based synthesis required a slightly longer reaction time, but it also produced satisfactory yields. Since guanine can be obtained from biological sources such as nucleic acid hydrolysis products, this method may provide an additional route for hypoxanthine production from natural raw materials.

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Another approach investigated in this study was the construction of the purine nucleus from simple nitrogen-containing precursors such as urea and formamide. Although this method involves several reaction stages, it demonstrates the possibility of synthesizing purine compounds from inexpensive and widely available starting materials. The formation of intermediate heterocyclic compounds followed by cyclization and oxidation ultimately resulted in the formation of the hypoxanthine structure. This strategy is particularly interesting from a theoretical perspective because it illustrates the possibility of assembling the purine skeleton through stepwise condensation reactions.



The obtained products were analyzed and compared with literature data to confirm their identity. The characteristic physical and spectroscopic properties of the synthesized compound corresponded well with those reported for hypoxanthine. In particular, the presence of the carbonyl functional group in the purine ring structure confirmed the successful conversion of the amino group during the reaction. Thin layer chromatography indicated that the isolated product was obtained with a satisfactory level of purity after recrystallization.

Comparative analysis of the investigated methods showed that the deamination of adenine provides the most convenient and efficient route for the preparation of hypoxanthine. This method combines relatively high yield, simple reaction conditions, and the use of inexpensive reagents. The guanine oxidation method also represents a viable alternative, especially when guanine is available from biological sources. In contrast, the stepwise construction of the purine nucleus requires more complex reaction conditions but offers flexibility for the synthesis of modified purine derivatives.

Overall, the experimental results demonstrate that hypoxanthine can be synthesized effectively using low-cost raw materials and relatively simple chemical transformations. These findings highlight the potential of economical synthetic

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strategies for the preparation of purine derivatives that are important in biochemical and pharmaceutical research.

CONCLUSION

In this study, several approaches for the synthesis of hypoxanthine (1,9-dihydro-6H-purin-6-one) were analyzed with particular emphasis on methods based on inexpensive and accessible starting materials. Hypoxanthine is an important purine derivative that plays a key role in nucleic acid metabolism and serves as a valuable intermediate in the synthesis of biologically active compounds. Therefore, the development of efficient and economically feasible synthetic routes for this compound is of considerable importance in modern heterocyclic and pharmaceutical chemistry.

The results show that hypoxanthine can be successfully synthesized through different chemical pathways, including the deamination of adenine, oxidative transformation of guanine, and the formation of the purine nucleus from simple nitrogen-containing compounds such as formamide and related intermediates. Among these approaches, the transformation of readily available purine bases such as adenine and guanine provides relatively simple reaction conditions and satisfactory product yields. In addition, the formation of purine derivatives from formamide under thermal or photochemical conditions demonstrates the possibility of constructing the purine framework from small and inexpensive molecules.

The use of low-cost raw materials and relatively simple reaction conditions makes these synthetic strategies attractive for both laboratory research and potential industrial applications. Moreover, such methods contribute to the development of sustainable chemical technologies by reducing the dependence on expensive reagents and complex synthetic procedures.

Overall, the investigated approaches confirm that hypoxanthine can be obtained efficiently through different synthetic routes, and further optimization of reaction conditions may improve the yield and selectivity of the process. These findings provide a useful basis for future studies aimed at the synthesis of new purine derivatives with potential biological and pharmacological activity.

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