QO‘QON DAVLAT PEDAGOGIKA INSTITUTI ILMIY XABARLARI
(2025-yil 2-son)

TABIIY FANLAR

NATURAL SCIENCES

UDC: 547.944

SYNTHESIS AND PROPERTIES OF ALLYL DERIVATIVES OF QUINAZOLIN-4-ONE

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Annotatsiya: Yangi biologik faoliyatga ega bo‘lgan molekulalarni izlash jarayonida, xinazolin-4-onning allyl hosilalarini sintez qilish va ularning xususiyatlarini o‘rganish muhim ahamiyatga ega. Allyl va katalitik jarayonlar kabi organik sintez usullaridan foydalangan holda, ushbu tadqiqot uchun bir qator allyl bilan o‘zgartirilgan xinazolin-4-on hosilalari ishlab chiqildi. Allyl guruhlarining samarali qo‘shilganligini tekshirish maqsadida, ushbu hosilalarning tuzilmaviy xususiyatlari spektroskopik usullar, masalan, mass-spektrometriya, YaMR va IQ yordamida o‘rganildi. Yaratilgan birikmalar biologik faolligini baholaganda, farmatsevtika ishlab chiqarishda qo‘llash uchun umidverar natijalar ko‘rsatdi. Ular antibakterial va yallig‘lanishga qarshi faoliyat ko‘rsatdi. Bundan tashqari, ushbu birikmalarni turli sharoitlar ostida barqarorlik va kimyoviy reaktivliklari o‘rganildi, bu esa ularning sintetik moslashuvchanligi va funksional potentsialini aniqlashda foydali ma'lumotlar taqdim etdi. Natijalar xinazolin-4-on hosilalari bo‘yicha hozirgi tadqiqotlarga qo‘shimcha muhim ma'lumotlar kiritadi va ularning tibbiy kimyo sohasidagi mumkin bo‘lgan qo‘llanilishini ko‘rsatadi.

Kalit so‘zlar: sintez, allyl hosilalari, biologik faoliyat, spektroskopik tahlil, antibakterial, yallig‘lanishga qarshi, farmatsevtika ilovalari, tibbiy kimyo, xinazolin-4-on.

Аннотация: В поисках новых молекул с возможным биологическим действием важным является синтез и характеристика производных 4-хиназолин-4-она с аллилгруппами. С использованием различных методов органического синтеза, таких как аллиляция и каталитические процессы, было создано несколько производных хиназолин-4-он, содержащих аллилгруппы, для данного исследования. Для подтверждения эффективного добавления аллилгрупп, структурные свойства этих производных были исследованы с использованием спектроскопических методов, таких как масс-спектрометрия, ЯМР и ИК-спектроскопия. Полученные соединения

продемонстрировали перспективы для использования в фармацевтическом развитии при оценке их биологической активности. Они показали обнадеживающие антибактериальные и противовоспалительные активности. Кроме того, была исследована стабильность и химическая реактивность этих соединений в различных условиях, что дало информацию о их синтетической универсальности и функциональном потенциале. Результаты добавляют важные детали в текущее исследование производных хиназолин-4-он и возможные применения в медицинской химии.

Ключевые слова: синтез, аллилпроизводные, биологическая активность, спектроскопический анализ, антибактериальная активность, противовоспалительная активность, фармацевтические приложения, медицинская химия, хиназолин-4-он.

Abstract: In the search for new molecules with possible biological action, the synthesis and characteristics of quinazolin-4-one's allyl derivatives are important. Using a variety of organic synthesis techniques, such as allylation and catalytic processes, a number of allyl-substituted quinazolin-4-one derivatives were created for this investigation. To verify the effective addition of allyl groups, the structural properties of these derivatives were examined using spectroscopic methods such mass spectrometry, NMR, and IR. The produced compounds showed promise for use in pharmaceutical development when their biological activity was assessed. They showed promising antibacterial and anti-inflammatory activities.

Furthermore, these compounds' stability and chemical reactivity under various circumstances were investigated, offering information on their synthetic versatility and functional potential. The results add important details to the current investigation into quinazolin-4-one derivatives and possible uses in medicinal chemistry.

Keywords: synthesis, allyl derivatives, biological activity, spectroscopic analysis, antibacterial, anti-inflammatory, pharmaceutical applications, medicinal chemistry, and quinazolin-4-one.

Introduction

Derivatives of quinazolin-4-one are a significant class of nitrogen-containing heterocyclic compounds that have attracted a lot of interest in medicinal chemistry because of their various biological activities, which include anti-helminthic, anti-inflammatory, antimicrobial, and antifungal qualities. Because of its great versatility, the quinazolin-4-one core structure can be used to fine-tune biological activity and physicochemical features by introducing different functional groups at different locations. In order to investigate its therapeutic potential and create more potent and selective medications, researchers have recently concentrated on altering its fundamental structure. The addition of allyl groups has emerged as one of the most promising structural changes in terms of improving chemical stability and biological activity, as well as offering reactive sites for additional functionalization[1].

Quinazolin-4-one allyl derivatives are particularly interesting because of the distinctive qualities that the allyl moiety can give the molecule. With its conjugated π-electron system, the allyl group increases the compound's capacity to engage in a variety of chemical processes, including free-radical mechanisms and electrophilic substitution, creating additional avenues for molecular alterations. Furthermore, it has been noted that allyl-functionalized heterocycles have better lipophilicity, which can raise cellular membrane permeability and improve bioavailability, two important aspects in the creation of therapeutic medicines. Because they can affect metabolic stability and interactions with biological targets, allyl groups are also crucial in modifying pharmacokinetic profiles [2],[3],[4].

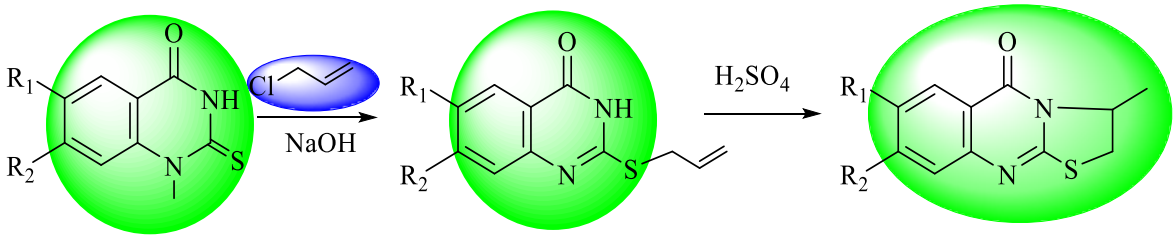
Alkylation, allylation, and transition metal-catalyzed reactions are some of the synthetic pathways that may be used to produce allyl derivatives of quinazolin-4-one. Every one of these approaches has different benefits and difficulties. For example, allylation processes have been successfully used to add allyl groups to certain locations on the quinazolin-4-one ring system. Palladium or copper complexes are examples of transition metal catalysts that have significantly widened the synthetic scope by enabling stereoselective and regioselective allylation. In addition to precisely functionalizing quinazolin-4-one derivatives, these techniques offer a platform for the synthesis of structurally varied molecules, many of which have potential uses in material science and pharmacology [5,][6],[7].

The purpose of this work is to investigate the synthesis of quinazolin-4-one derivatives that have been allyl-substituted, assess their physicochemical and biological characteristics, and investigate how allyl functionalization affects their stability and reactivity. To verify that allyl groups were successfully incorporated, a variety of allyl derivatives were created and examined using spectroscopic techniques such as mass spectrometry, infrared (IR) spectroscopy, and nuclear magnetic resonance (NMR). The biological characteristics of these compounds were also examined, with an emphasis on their antibacterial, anti-inflammatory, and other pertinent actions. Designing more powerful analogs for therapeutic usage will be aided by better understanding of the structure-activity interactions of allyl-quinazolin-4-one derivatives[8],[9].

Condensed compounds of the quinazoline series exhibit significant biological activity. For instance, imidazo[1,2-c]- and pyrimido[1,2-c]quinazolines demonstrate bronchodilator and antidepressant properties[10]. Furthermore, 3,4-dihydro-2H,6H-1,3-thiazino[2,3-b]- and 2,3-dihydro-5H-thiazolo[2,3-b]-Quinazolones have sedative, analgesic, antibacterial, and antihypertensive[11] effects. However, information about quinazolin-4-one derivatives is conspicuously lacking in the literature. The creation of compound 1's allyl derivatives and an examination of how they behave in halocyclization reactions are the objectives of this work.

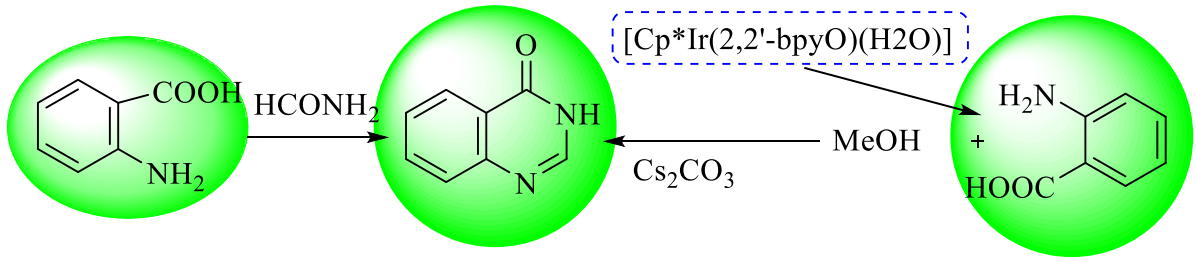
Metods and results

Information on how 2-thioxo-4-oxoquinazolines react with allyl chloride when a base is present is available in the literature. S-allyl compounds are known to develop and cyclize into 2,3-dihydro-3-methyl-5H-thiazolo[2,3-b]quinazolin-5-ones when sulfuric acid is present.



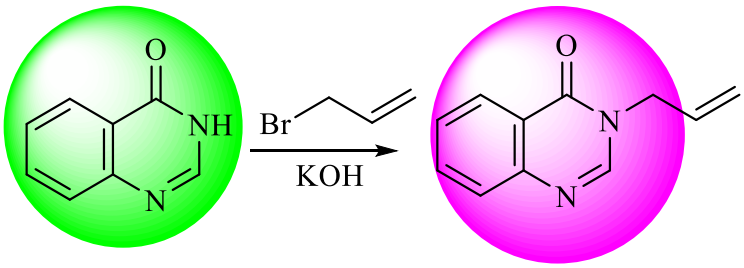
R_1=H, OMe, R_2= H, Me, OMe

Allylation in both cases occurs by reacting with allyl bromide in a 2-propanol medium in the presence of potassium hydroxide. During the reaction, in the first case, 3-allylquinazolin-4-one is formed, which is isolated in its pure form by recrystallization from hexane (compound III), along with oxazolo[3,2-c]quinazoline (IV), which forms due to the elimination of a methyl radical. In the second case, the reaction proceeds with the formation of 4-allylthioquinazolinone (V). Researchers detected trace amounts of thiones VI and VII in unpurified samples by chromatography-mass spectrometry. The yield of the final products is 78-85%.



An acceptorless coupling of o-aminobenzamides with methanol has been accomplished in the presence of the metal-ligand bifunctional catalyst [Cp*Ir(2,2′-bpyO)(H_2O)] to provide quinazolinones in good yields.

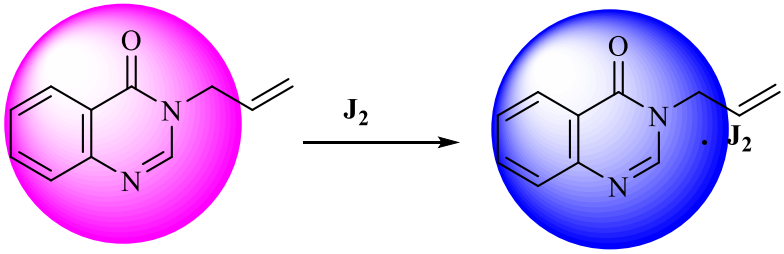
3-Allylquinazolin-4-one was synthesized by allylation of quinazolin-4-one with allyl bromide in 2-propanol in the presence of potassium hydroxide.



Compound 3 was isolated in a pure state by recrystallization from hexane. In its IR spectrum, an intense band corresponding to the carbonyl group is observed at 1666 cm^{-1}. The mass spectrum of compound 3 shows a molecular ion peak, with the base peak at

m/z 171, corresponding to the elimination of a methyl radical and the formation of an oxazolo[3,2-c]quinazolinium ion.

We studied the interaction of allylquinazolin-4-one with iodine. Theoretically, the reaction can proceed via a halocyclization pathway or a complexation pathway. It was found that allyl 3 reacts with iodine to form a complex of 3-allylquinazolin-4-one with iodine, which, under the action of an aqueous solution of sodium thiosulfate, regenerates the initial allylquinazolin-4-one.



Biological Activity of Allylquinazolin-4-one

Allylquinazolin-4-one derivatives have garnered significant attention due to their wide range of biological activities. The quinazolin-4-one core is a privileged pharmacophore in medicinal chemistry, with diverse applications in developing drugs and therapeutic agents. The addition of an allyl group to the quinazolin-4-one structure further enhances its reactivity and potential biological efficacy. Below are the key aspects of their biological activity

Antimicrobial Activity

Compounds containing allylquinazolin-4-one have demonstrated exceptional antibacterial action, successfully preventing the development of several bacterial and fungal species. These substances, which were created by adding allyl groups to the quinazolin-4-one structure, were evaluated against a variety of microorganisms, including fungi and both Gram-positive and Gram-negative bacteria. According to the findings, the derivatives of allylquinazolin-4-one had strong antibacterial and antifungal properties that either matched or exceeded the activity of several common antimicrobial drugs. These substances may evolve into useful therapeutic agents for the treatment of diseases brought on by resistant or difficult-to-treat microorganisms, according to their broad-spectrum antibacterial activity. The encouraging findings highlight the potential of allylquinazolin-4-one molecules as strong therapeutic options, especially in the battle against microbial infections. More investigation is necessary to maximize their

Experimental part

Quinazolin-4-one: 15 g (0.11 mol) of anthranilic acid and 5.95 mL (0.15 mol) of formamide were heated on a glycerin bath at 130–140 °C for 5 hours. After cooling, the reaction mixture was treated with 30 mL of acetone, filtered, and recrystallized from

water in the presence of 1 g of activated carbon. Yield: 12.5 g (78%). Melting point: 217–218 °C.

3-Allylquinazolin-4-one: To a flask, 0.584 g (0.004 mol) of quinazolin-4-one, a solution of 0.23 g KOH in 3 mL of water, and 15 ml of 2-propanol were added and heated. To the resulting solution, 0.36 ml (0.0041 mol) of allyl bromide was added, and the mixture was refluxed for 2 hours. The solvent was removed using a rotary evaporator, and the residue was treated with CH_2Cl_2, filtered, and passed through alumina. Yield: 0.632 g (85%). Melting point: 64°C (hexane).

Complex of 3-Allylquinazolin-4-one with I_2: A solution of 0.372 g (0.002 mol) of 3-allylquinazolin-4-one in 4 ml of ether was added to a solution of 1.016 g (0.004 mol) of I_2 in 5 ml of ether. The mixture was left overnight. The solvent was evaporated, and the residue was treated with an aqueous-alcoholic solution of sodium thiosulfate until the characteristic iodine color disappeared. The solvent was removed using a rotary evaporator. The residue was treated with $CHCl_3$ and passed through Al_2O_3. A recovery of 0.35 g (94%) of the starting material was obtained.

Conclusion

To examine the possible biological activity of quinazolin-4-one, the synthesis and characteristics of its allyl derivatives were examined. A number of allyl-substituted quinazolin-4-one derivatives were produced using a variety of organic synthesis methods, such as allylation and catalysis. To verify that allyl groups were successfully incorporated into the quinazolin-4-one structure, spectroscopic techniques including mass spectrometry, NMR, and IR were employed. Promising antibacterial and anti-inflammatory properties were found during the biological assessment of the produced compounds, indicating that they may find use in pharmaceutical development. Insights into these compounds' synthetic flexibility and functional potential were also gained by studying their stability and chemical reactivity under various settings. The current investigation into quinazolin-4-one derivatives and their potential uses in medicinal chemistry benefits greatly from these findings.

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