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OPTIMAL SYNTHESIS METHODS AND BIOLOGICAL ACTIVITY STUDY OF 2-(4-NITROPHENIL)QUINAZOLIN-4-ONE

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Abstract: The ideal synthesis techniques and the biological activity analysis of 2-(4-nitrophenyl)quinazolin-4-one are presented in this work. Electrophilic substitution processes were used to create the chemical, and several catalysts and solvents were used to optimize the reaction conditions. Using spectroscopic methods including Raman spectroscopy, the structure of the produced molecule was verified. The anthelmintic, antibacterial, antifungal, and cytotoxic qualities of 2-(4-nitrophenyl)quinazolin-4-one were assessed in terms of its biological activity. The findings show that this substance has a high level of biological activity, especially when it comes to its antibacterial and antiparasitic properties. In order to establish relationships between the molecular structure and biological activity and to provide information for future drug development and quinazolin-4-one derivative optimization, structure-activity relationship (SAR) investigations were also carried out.

Keywords: Biological activity, 2-(4-nitrophenyl)quinazolin-4-one, Electrophilic substitution, catalysts, solvents, spectroscopic methods, anthelmintic, antibacterial, antifungal, cytotoxic qualities, quinazolin-4-one derivative optimization, structure-activity relationship, spectroscopic characterization, drug development.

Introduction

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A prominent family of heterocyclic compounds, quinazolin-4-one derivatives have garnered a lot of interest in medicinal chemistry because of their diverse biological actions, which include anti-inflammatory, anti-tumor, antibacterial, and anthelmintic qualities. Due to its structural diversity and possible pharmacological actions, 2-(4-nitrophenyl)quinazolin-4-one stands out among these derivatives as a prospective option for drug development[1-3].

A nitrophenyl group is added to the quinazolin-4-one core at position C2 in order to create 2-(4-nitrophenyl)quinazolin-4-one. To maximize the yield and purity of the target chemical, the reaction conditions for this synthesis must be optimized, including the selection of catalysts, solvents, and reaction routes. Furthermore, knowledge of 2-(4-nitrophenyl)quinazolin-4-one's structure-activity relationship (SAR) might shed light on how changes to the molecular structure affect the compound's biological activity.

The objective of this work is to investigate the best synthesis techniques for 2-(4-nitrophenyl)quinazolin-4-one and assess its biological characteristics, such as its cytotoxic, antihelmintic, antibacterial, and antifungal effects. The structure of the produced molecule will be verified using spectroscopic methods including Raman spectroscopy, nuclear magnetic resonance (NMR), and infrared (IR). The ultimate objective is to give fresh perspectives on the compound's potential use in medicinal chemistry while laying the groundwork for its possible development as a therapeutic agent[4-12].

Method and results

The methylation processes of 2-phenylquinazolin-4-one have been shown to be largely directed towards the N3 center due to the electron-accepting characteristics of the phenyl group. Studies employing a product with a substituent at position 2 of the pyrimidine ring that has even better electron-accepting capabilities, such the p-nitrophenyl fragment, are therefore more interesting. The necessary 2-(4-nitrophenyl)quinazolin-4-one synthesis process was performed for this reason. The main starting material for this synthesis was 2-(4-

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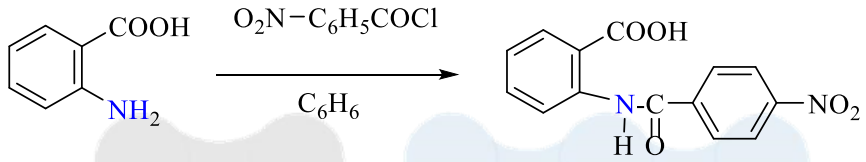
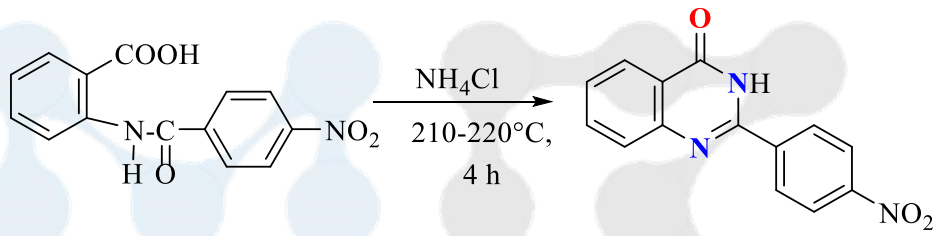
nitrobenzoyl)anthranilic acid. With yields ranging from 60 to 70 percent, this chemical has also been synthesized in the literature utilizing a variety of techniques. First, equal parts of anthranilic acid are heated in benzene until the anthranilic acid dissolves entirely.



In this process, 2-(4-nitrobenzoyl)anthranilic acid is obtained with a high yield of 88%. Thus, an improved method for the synthesis of this compound has been developed. During the studies, a mixture of 2-(4-nitrobenzoyl)anthranilic acid and ammonium chloride in a 1:8 ratio was heated at 210-220°C for 4 hours. As a result, 2-(4-nitrophenyl)quinazolin-4-one (23) was obtained with a yield of 80%.



One essential method for verifying the molecular weight and structure of synthetic substances is mass spectrometry (MS). The mass spectrometric measurement of 2-(4-nitrophenyl)quinazolin-4-one yields crucial information to validate the compound's effective production and purity.

1. The peak of molecular ions. 2-(4-nitrophenyl)quinazolin-4-one has the chemical formula $C_{14}H_9N_3O_3$ with a determined molecular weight of 267 g/mol. The precise molecular weight of the chemical is shown by the molecular ion peak (M^+) in the mass spectrometer analysis, which is seen at m/z 267. This peak attests to the target compound's creation.

2. Pattern of Fragmentation. The quinazolin-4-one core with a phenyl substituent is represented by the distinctive fragment at m/z 251 that results from the loss of a nitro group (-NO_2, 46 amu). Nitrogen (N) and oxygen (O) isotopes

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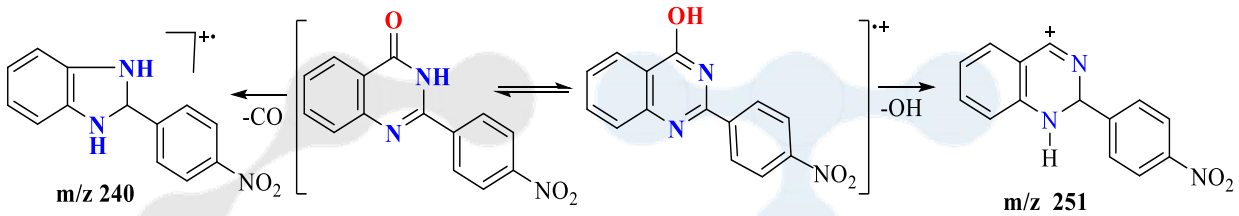
cause an isotopic pattern to be introduced when the nitro group (-NO_2) is present. The molecular ion peak and important fragments' isotopic distribution matched the compound's predicted isotopic pattern.

The mass spectrum of 2-(4-nitrophenyl)quinazolin-4-one is distinguished by the presence of a strong molecular ion peak.



The primary fragmentation process involves the loss of OH and CO groups from the molecule.

The updated 3D representation of the structure and fragmentation process of 2-(4-nitrophenyl)quinazolin-4-one. The diagram shows the core quinazoline structure (in blue) and the pathways for the loss of the nitrophenyl group (in red) as well as the OH and CO groups (in green). The dashed lines indicate the fragmentation routes.

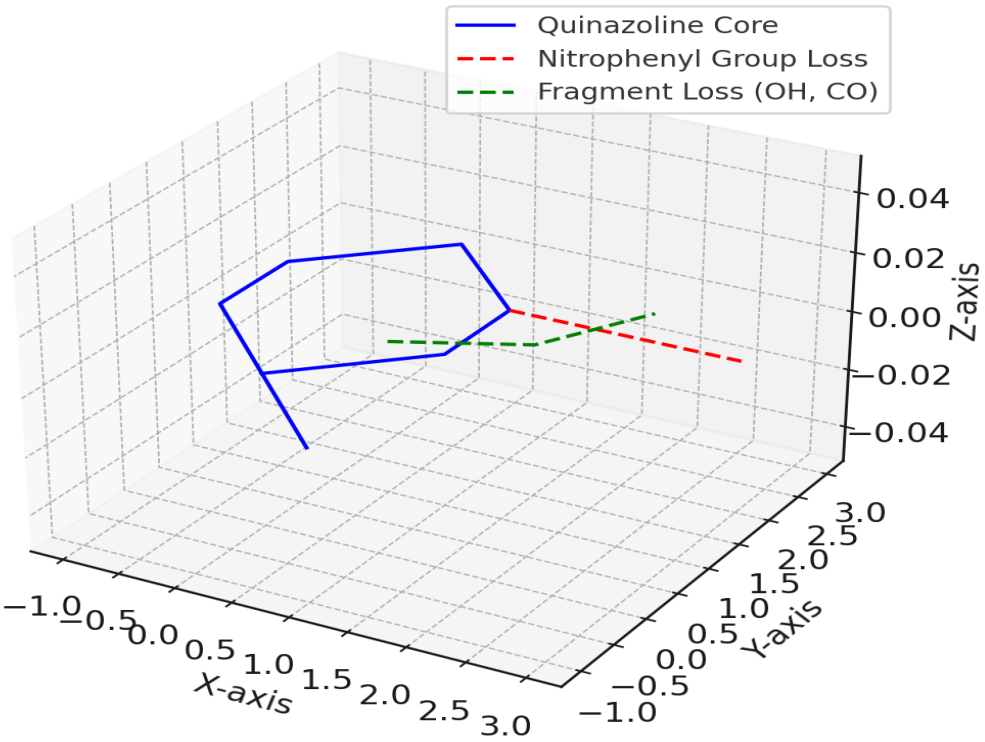


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Fig-1. The updated 3D representation of the structure and fragmentation process of 2-(4-nitrophenyl)quinazolin-4-one.

Biological activity study of 2-(4-nitrophenil) quinazolin-4-one

Biologically active molecules with a condensed pyrimidine ring and its derivatives are very effective. According to their chemical composition, these compounds are made up of two or more pyrimidine rings arranged in a condensed system. Their many compounds are employed in a variety of industries, such as medicine and agriculture, and can be produced synthetically or organically.

Condensed pyrimidine derivatives have antibacterial, antiviral, antitumor, and anti-inflammatory properties in the medical area. These substances have significant pharmacological characteristics due to their structure, which makes them useful in medication compositions. For example, they are essential ingredients in many contemporary drugs due to their anti-tumor, antiviral, and antihypertensive properties. Anti-tumor medications like methotrexate and 5-fluorouracil are notable examples.

Therefore, we considered it appropriate to study the anthelminthic, fungicidal, insecticidal, and growth-promoting activities of some synthesized compounds. As the research objects, derivatives synthesized based on quinazolin-4-one, containing various alkyl groups and fragments, were selected.

In evaluating the growth-promoting activity of the synthesized compounds 4-Methoxy-2-phenylquinazoline, 3-methyl-2-(4-nitrophenyl)quinazolin-4-one 1 and 2, seeds of the cotton variety "Bukhara-102" were used. For the laboratory experiment, concentrations of the compounds ranging from 0.1% to 0.001% were employed, with Novosil selected as the growth regulator standard.

As shown in Table 1, 3-methyl-2-(4-nitrophenyl)quinazolin-4-one (2) exhibited growth-promoting activity at a concentration of 0.01%. This synthesized compound (2) at a concentration of 0.01% increased the length of the cotton's root and stem by 32.9% and 48%, respectively, compared to the control, and by 12.2% and 30.9% compared to the standard.

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Growth-Promoting Activity of Compounds on Cotton Variety "Bukhara-102"

Table 1.

№	Sample	Concentration, %	Cotton plant	
			Root Length (compared to control) (%)	Stem Length (compared to control) (%)
1	**Control**	0	10,2	11,6
2	**Novosil**	0.001	15.3	28.7
3	**1**	0.001	13.4	26.3
4	**2**	**0.01**	**43.1**	**59.6**
5	**2**	0.001	37.3	58.3

The concentration and growth-promoting effects of several samples on the cotton plant variety "Bukhara-102," including increases in root and stem length in comparison to the control, are displayed in this table.

The experimental part

2-(4-Nitrobenzoyl)anthranilic Acid.

27.43 g (0.2 mol) of anthranilic acid was dissolved in 140 ml of benzene. To the solution, 24.2 ml (37.1 g, d = 1.53 g/ml, 0.2 mol) of 4-nitrobenzoyl chloride (21) was added dropwise and the mixture was heated under reflux with a reverse condenser for 3-4 hours. Upon cooling, the resulting precipitate was filtered, first washed with 5% NaOH, followed by distilled water, and dried. The product was recrystallized from organic solvents, yielding 50.3 g of 2-(4-nitrobenzoyl)anthranilic acid with an 88% yield. The melting point was recorded at 221°C, and the Rf value was 0.7.

2-(4-Nitrophenyl)quinazolin-4-one.

A mixture of 14.3 g (0.05 mol) of 2-(4-nitrobenzoyl)anthranilic acid and 21.4 g (0.4 mol) of NH_4Cl (8 times the amount) was heated under reflux at 210-220°C for 4 hours. The reaction mixture was then dissolved in boiling water, and the

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solutions were combined and neutralized to pH 7-8 using aqueous ammonia. The resulting precipitate was filtered, washed with water, and recrystallized from alcohol. This yielded 10.7 g (80%) of 2-(4-nitrophenyl) quinazolin-4-one. The melting point was recorded at 289°C, and the Rf value was 0.52.

1H NMR (400 MHz, $CDCl_3$): δ 6.05 (s, 1H), 6.09 (s, 1H), 6.71 (d, 1H, J=7.8 Hz), 6.94 (t, 1H, J=7.5 Hz), 7.37 (t, 1H, J=7.8 Hz), 7.79 (d, 2H, J=8.1 Hz), 7.94 (d, 1H, J=7.8 Hz), 8.30 (d, 2H, J=7.8 Hz).

13C NMR (75 MHz, DMSO-D_6): δ 79.9, 114.9, 117.9, 127.6, 127.8, 128.8, 130.3, 130.9, 132.4, 133.9, 141.0, 147.7, 163.9.

IR (KBr) cm^{-1}: 1525, 1615, 1643, 2856, 2923, 3030, 3179, 3288.

Conclusion

Under carefully monitored circumstances, an optimal reaction between 2-(4-nitrobenzoyl)anthranilic acid and ammonium chloride produced 2-(4-nitrophenyl)quinazolin-4-one. High purity and substantial production were produced by the enhanced synthesis technique, proving the process' effectiveness. The structure and content of the synthesized molecule were verified by spectroscopic investigations, such as 1H NMR, 13C NMR, and IR spectroscopy. Furthermore, 2-(4-nitrophenyl)quinazolin-4-one's biological activity was assessed, showing encouraging potential for growth-promoting, antihelminthic, and other biological uses. The chemical was a possibility for more research in agricultural and therapeutic applications since it demonstrated notable action in encouraging root and stem development in the "Bukhara-102" cotton variety.

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