Arati A. Narwade, 2025, 13:2
ISSN (Online): 2348-4098
ISSN (Print): 2395-4752

International Journal of Science, Engineering and Technology

An Open Access Journal

Synthesis and Characterization of Novel Pyrazoline Derivatives: Design, Development and Applications

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Abstract- The synthesis of a novel substituted pyrazoline compound, a derivative with significant , was accomplished through a series of chemical reactions starting from suitable precursor materials. The process began with the condensation of 2-hydroxyacetophenone and anisic acid under basic conditions, yielding the corresponding intermediate. Following this, a base-mediated BVT of the intermediate resulted in the formation of a flavanone derivative. This derivative was then reacted with hydrazine to produce the novel substituted pyrazoline derivative. The final product was characterized by various spectroscopic techniques, including NMR spectroscopy and mass spectrometry, to confirm both its structure and purity. This synthesis route offers a straightforward approach to obtaining the substituted pyrazoline derivative, which holds potential for further pharmacological exploration.

Keywords- novel pyrazoline, biological activity, hydrazine, pharmacological exploration , NMR spectroscopy , mass spectrometry.

I. INTRODUCTION

Pyrazoline derivatives are widely studied heterocyclic compounds due to their broad range of biological activities, including antimicrobial, anti-inflammatory, anticancer, antitubercular, and antioxidant properties[1][2]. These five-membered nitrogen-containing compounds are typically synthesized via the cyclization of chalcones (α,β-unsaturated carbonyl compounds) with hydrazine or its derivatives, often using base catalysts and polar solvents such as ethanol, DMSO, or methanol [3][4]. Emerging green chemistry approaches, including microwave-assisted synthesis, have been shown to enhance yields and reduce reaction times, making the process more environmentally friendly [5][6]Characterization of pyrazoline derivatives is essential for structural confirmation and purity assessment. Commonly used techniques include infrared (IR) spectroscopy, which identifies functional groups; nuclear magnetic resonance (^{1}H NMR and ^{13}C NMR) for structural elucidation; and mass spectrometry (MS) for molecular weight determination[7][8]. and elemental analysis verify purity[9].

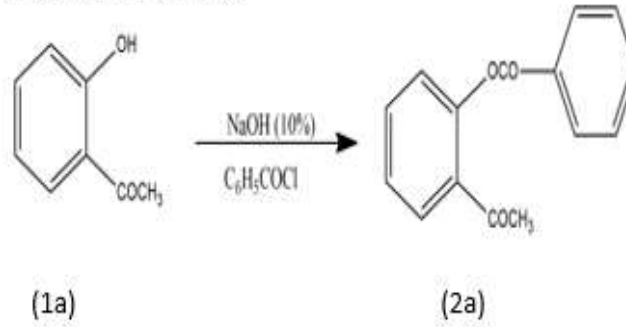
The ease of synthesis and biological relevance of pyrazoline derivatives make them an attractive focus of ongoing research, with their potential applications in various therapeutic areas being explored extensively.

II. EXPERIMENTAL SETUP

The synthesis of novel pyrazoline derivatives was achieved through a VBT of acetophenone derivatives (e.g., 2-hydroxyacetophenone) with aromatic aldehydes (e.g., anisic acid) to form chalcone intermediates, followed by cyclization with hydrazine hydrate. The products were characterized

using ^{1}H and ^{13}C NMR, mass spectrometry (HRMS), and infrared spectroscopy (IR) to confirm their structures. Physicochemical properties, such as solubility, thermal stability (via TGA), were evaluated. Thin-layer chromatography (TLC) was employed to monitor reactions, and melting points were measured using a digital melting point apparatus. This setup allowed for the efficient synthesis and detailed characterization of the pyrazoline derivatives.

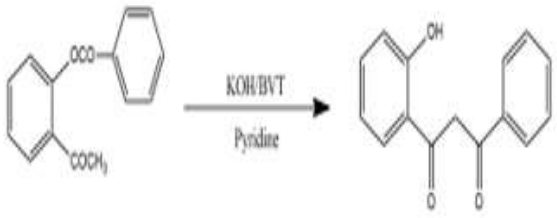
A. Preparation of 2-acetyl phenylbenzoate (2A):
A solution of 2-hydroxyacetophenone (0.04 mol) and benzoyl chloride (0.05 mol) was prepared in 30 mL of 10% NaOH. The reaction mixture was shaken for approximately 30 minutes. The resulting solid product was filtered and washed with water, followed by a wash with 10% sodium bicarbonate solution, and then rinsed again with water. The product was recrystallized from ethanol to yield 4-methoxyphenyl 2-acetylbenzoate (2A) with a melting point of 184°C and a yield of 76%



(1a) (2a)

Scheme 1

B. Preparation of 1-(2-hydroxyphenyl)-3-phenylpropane-1,3-dione (3a):
2-acetyl phenylbenzoate (2a) (0.05 mol) was dissolved in 40 mL of dry pyridine. The solution was heated to 60°C, and pulverized KOH (15 g) was gradually added with constant stirring. After 4 hours of heating, the reaction mixture was acidified by adding ice-cold diluted HCl (1:1). The resulting brownish-yellow solid was filtered, washed with 10% sodium bicarbonate solution, and then rinsed with water. The product was recrystallized from a mixture of ethanol and acetic acid to obtain 1-(2-hydroxyphenyl)-3-phenylpropane-1,3-dione (3a), with a melting point of 252°C and a yield of 73%.

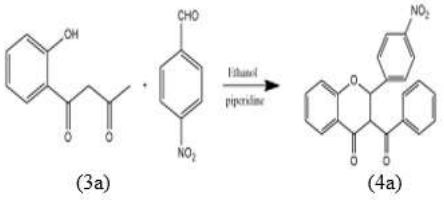


(2a) (3a)

Scheme 2

C.Preparationof3-benzoyl-2-(4-nitrophenyl) chroman-4-one (4a):A mixture of 1-(2-hydroxyphenyl)-3-phenylpropane-1,3-dione (3a) (0.01 mol) and 4-nitrobenzaldehyde (0.012 mol) was refluxed in 25 mL of ethanol along with 0.5 mol of piperidine for 15-20 minutes.

After cooling, the reaction mixture was acidified with dil HCl (1:1) and the product thus separated, was crystallized from ethanol-acetic acid mixture to get the compound 3-benzoyl-2-(4-nitrophenyl) chroman-4-one (4a) m.p.175oC yield 72%.

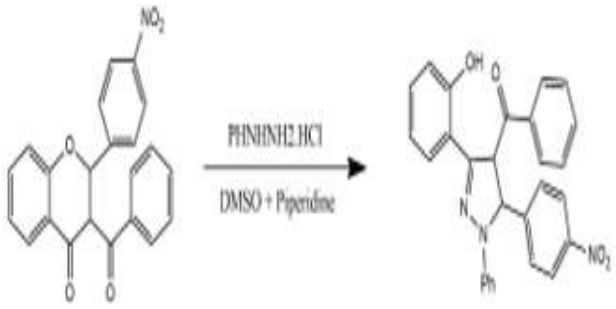


(3a) (4a)

Scheme 3

D.Synthesis of 3-(2-hydroxy-phenyl)-4-anisoyl-5-(3-nitrophenyl)-1-phenyl-‧2-pyrazoline (5a):

A solution of 3-benzoyl-2-(4-nitrophenyl)chroman-4-one (4a) (0.01 mol) and phenylhydrazine hydrochloride (0.02 mol) was refluxed in 20 ml of DMSO with a few drops of piperidine for 1.5 hours. After cooling the mixture was diluted with water. The product thus separated was filtered and crystallized from ethanol-acetic acid mixture to afford crystals of compound (3-(2-hydroxyphenyl)-5-(4-nitrophenyl)-1-phenyl-4,5-dihydro-1H-pyrazol-4-yl)(phenyl)methanone (5a) with a melting point of 162°C and a yield of 70%.



(4a) (5a)

Scheme 4

III. RESULTS AND DISSCUSIONS

Keeping in view the biological activity and medical importance of pyrazoline compounds 2-acetylphenylbenzoate (2a) was prepeard using the reported method [10][11], starting from 2-hydroxy acetophenone which on usual reaction with benzoyl chloride convertd to compund (2a) as shown in scheme 1.

We have synthesized compound (3a) from compound (2a) by using method [12][13] also the solvents used in synthesis reported by method [14]. The use of aprotic solvent by method [15]. The reaction undergoes BVT [14].

To synthesize novel pyrazoline derivative have to synthesize the flavanone(4a) from compound(3a) via method [16]. The compound (4a) undergoes reaction with phenylhydrazine to synthesized some new pyrazoline derivatives via method [17].[18] [19] The structure of target compounds was confirmed by physical properties which are listed in table I ,II,II.While the spectral data are listed in table II and III.

The FT-IR spectra for compound (5a) manifests a strong absorption band and at (1680 ,1647cm1)due to stretching vibration of C=O , C=N group and at(1680) due to carbonyl group in compound (5a) as final product. Compound (5a) shows a strong absorption band at (1023cm1) due to stretching vibration of N-N group of pyrazoline derivative also the final compound (5a)shows strong band at (1555cm-1) due to asymmetric stretching of NO2 and at (1353cm-1) due to symmetric stretching.The elemental analysis of all compounds also shows the comformation of molecules in table IV.

Table I: Physical properties of compounds

Compound no.	Melting point (°C.)	yield
2a	184	76%
3a	252	73%
4a	175	72%
5a	162	70%

Table II: Mass and IR Spectral data of compounds

Comp. No..	m/z	IR. υ(cm-1 UV , KBr)			
		C=O	N-N	C=N	OH
2a	240.08 (100.0%), 241.08 (16.5%), 242.09 (1.3%)	1653	------	-------	----------
3a	m/z: 240.08 (100.0%), 241.08 (16.5%), 242.09 (1.3%)	1676	-------	-------	3419
4a	m/z: 373.10 (100.0%), 374.10 (24.2%), 375.10 (3.9%)	1678	--------	---------	----------
5a	m/z: 463.15 (100.0%), 464.16 (30.7%), 465.16 (5.4%), 464.15 (1.1%)	1680	1023	1647	----------

Com No.	1H-NMR δ (ppm)	13C-NMR δ (ppm)
2a	8.22(S,2H,ArCH),7.60 (S,2H,ArCH), 7.70(S,1H,ArCH),7.89 (S,1H,ArCH), 7.71(S,1H,ArCH),7.46 (S,1H,ArCH), 7.55(S,1H,ArCH),2.50 (S,3H,CH_3)	26.3, 196.8, 140.7, 127.6, 125.4, 133.5, 119.9,152.5, 165.2, 150.2, 150.3, 128.6, 133.9
3a	5.35(S,1H,OH),3.81(S ,2H,CH_2), 7.94(S,2H,ArCH),7.56 (S,2H,ArCH), 7.64(S,1H,ArCH,7.31(S,1H,ArCH), 7.12(S,1H,ArCH),7.47 (S,1H,ArCH), 6.88(S,1H,ArCH)	190.4, 136.7, 128.8, 128.6, 133.1, 51.1, 200.6, 121.8, 162.5, 117.6, 128.6, 121.2, 134.5
4a	6.04,(d,1H,CH),5.38(d,1H,CH), 7.07(S,1H,ArCH),7.52 (S,1H,ArCH), 7.09(S,1H,ArCH),7.40 (S,1H,ArCH), 7.97(S,2H,ArCH),7.52 (S,2H,ArCH), 7.63(S,1H,ArCH),7.62 (S,2H,ArCH), 8.19(S,2H,ArCH)	124.1,146.8, 124.1, 128.0, 128.0, 140.2, 85.5, 59.6, 195.2, 135.5, 128.8, 128.6, 133.1, 189.9, 120.3, 160.1, 118.9, 127.8, 120.2, 133.7
5a	5.6 (S,1H,CH), 4.9(d,1H, CH),5.35 (S,1H,OH),7.01(S,1H, ArCH), 7.50(S,1H,ArCH),7.43 (S,1H,ArCH), 7.91(S,1H,ArCH),7.98 (S,1H,ArCH), 7.52(S,1H,ArCH),7.62 (S,1H,ArCH), 7.52(S,1H,ArCH),7.53 (S,1H,ArCH), 7.98(S,1H,ArCH),8.21 (S,1H,ArCH), 8.2(S,1H,ArCH),7.55(S,1H,ArCH), 6.82(S,1H,ArCH),7.23 (S,1H,ArCH) ,6.77(S,1H,ArCH),7.2 1(S,1H,ArCH) ,6.82(S,1H,ArCH)	128.8, 128.6, 133.1, 123.7, 123.4, 135.5, 195.2, 56.7, 149.6, 128.8, 128.6, 145.9, 123.7, 123.4, 143.8, 116.7, 129.5, 129.5, 56.4, 149.6, 118.8, 162.5, 132.1, 121.4, 132.4, 117.8

Table III: 1H-NMR13C-NMRspectrum data of compounds

V. CONCLUSION

In this study, a series of pyrazole derivatives were successfully synthesized using various methodologies, including conventional and green chemistry approaches. The structural characterization of the compounds was confirmed through spectroscopic techniques such as NMR, IR, and mass spectrometry. The results demonstrated that the adopted synthetic strategies were efficient, yielding the desired derivatives in good to excellent yields Future studies will focus on the drug design

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