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Research Article

Synthesis Of Novel 1,3,4-Oxadiazole Derivative as Anti-Inflammatory Agents

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ABSTRACT

Inflammation is a complex biological response that protects the body against infection, injury, and tissue damage. However, prolonged inflammatory processes are associated with several chronic diseases, creating a need for the development of safer and more effective anti-inflammatory agents. In the present study, two novel 1,3,4-oxadiazole derivatives, namely 2-phenyl-5-(benzylideneamino)-1,3,4-oxadiazole (Compound A) and 2-phenyl-5-(phenylhydrazino)-1,3,4-oxadiazole (Compound B), were synthesized using simple and economical synthetic routes. The synthesized compounds were isolated, purified, and characterized through physicochemical evaluation, qualitative chemical tests, FT-IR spectroscopy, ^{1}H NMR, ^{13}C NMR, and mass spectrometric analysis. Compound A exhibited a percentage yield of 84%, whereas Compound B showed a yield of 71%. Spectral data confirmed the successful formation of the oxadiazole nucleus and the presence of the expected functional groups. Both compounds displayed characteristic absorption bands and resonance signals corresponding to aromatic rings, nitrogen-containing functionalities, and heterocyclic structures. The findings demonstrate the successful synthesis and structural confirmation of novel oxadiazole derivatives, which may serve as promising candidates for further investigation as anti-inflammatory agents.

INTRODUCTION

Inflammation is a protective physiological response that occurs in vascularized tissues when they are exposed to harmful agents such as microorganisms, toxins, injured cells, or physical trauma. It maintains normal tissue function and is a crucial part of the body's defence mechanism.

The inflammatory process is designed to remove the source of injury, clear damaged cellular components, and promote tissue healing and regeneration. While inflammation is beneficial for host protection and recovery, prolonged or uncontrolled inflammatory responses can contribute to disease development. Persistent

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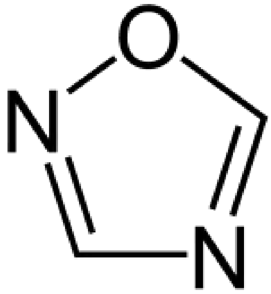
inflammation is associated with numerous chronic disorders, including rheumatoid arthritis, osteoarthritis, cardiovascular diseases, inflammatory bowel disorders, asthma, neurodegenerative conditions, and various forms of cancer. Therefore, effective regulation of inflammatory pathways is crucial for maintaining overall health and preventing disease progression.[‘2.3]

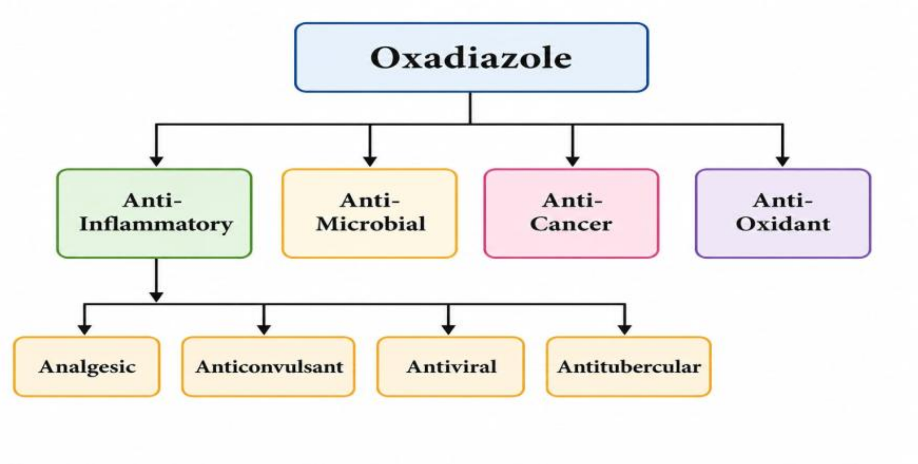
1 General Structure of Oxadiazole[7]



2 Isomeric Forms of Oxadiazole[6]

1,2,3-Oxadiazole, 1,2,4-Oxadiazole, 1,2,5-Oxadiazole, 1,3,4-Oxadiazole

Biological Activities of Oxadiazole Derivatives [4’5]



MATERIALS AND METHODS: -

Table No. 1 Chemicals List

Sr.No	Chemical Name	Manufacturer
1	Distilled Water	Research Labs.
2	Benzaldehyde	Research Labs.
3	Ammonium Solution	Research Labs.
4	Glacial Acetic acid	Research Labs.
5	Phenylhydrazine hydrochloride.	Research Labs.
6	Benzamide	Research Labs.
7	Ethanol	Research Labs.

8	Ammonium acetate	Research Labs.
9	1.2,4-Dinitrophenylhydrazine	Research Labs.
10	Phatalic Anhydrid	Research Labs

SYNTHESIS PROCEDURE

Compound A: 2phenyl-5-benzylideneamino-1,3,4-oxadiazole Procedure:

Step 1: Benzaldehyde Oxime Formation

1. Dissolve 0.01 mol benzaldehyde in 25 mL ethanol
2. Add 0.01 mol Ammonium Solution.
3. Add 0.01 mol ammonium acetate.
4. Reflux 2 hours.
5. Cool and filter oxime.

Step 2: Reaction with Phenylhydrazine HCl

1. Dissolve oxime in ethanol.
2. Add phenylhydrazine hydrochloride.
3. Add few drops acetic acid. 4. Reflux 2 hours.

Step 3: Cyclization

1. Add 2,4dinitrophenylhydrazine.
2. Reflux 3 hours.
3. Cool and pour into ice cold water.
4. Filter precipitate Purification Recrystallize from ethanol.

2. Reaction Scheme:

Step 1: Oxime FormationBenzaldehyde + NH + NHOAc⟶ (EtOH, reflux)⟶ Benzaldehyde oxime

Step 2: Hydrazone FormationOxime + Phenylhydrazine HCl⟶ (EtOH, AcOH)⟶ Intermediate

Step 3: CyclizationIntermediate + 2,4-Dinitrophenylhydrazine⟶ (Reflux)⟶ 2-Phenyl-5-(benzylideneamino)-1,3,4-Oxadiazole

Compound B: 2-phenyl-5-phenylhydrazino-1,3,4-oxadiazole:

1. Add benzaldehyde, phenylhydrazine HCl, Ammonium Solution, and ammonium acetate into reflux flask.
2. Add 30 mL ethanol and a few drops of acetic acid.
3. Reflux at 75–80 °C for 4–5 hours.
4. Monitor using TLC.
5. Cool and pour into icecold water.
6. Filter pale yellow precipitate. Purification Recrystallize from ethanol.

Reaction Scheme: Benzaldehyde + Phenyl hydrazine HCl + NH + NHOAc⟶ (EtOH, AcOH, reflux 75–80 °C, 4–5 h)⟶ 2-Phenyl-5-(phenylhydrazino)-1,3,4-Oxadiazole Difference from Compound 1:Product retains –NHNHPh (hydrazino group) instead of –NHPh[10,11’12’13]

Table No. 2 List Of Parameters

Name of Parameter	Comp A	Comp B
PracticalYield	2.10gm	1.80gm
Theoretical Yield	2.49g/mol	2.52g/mol
%Practical Yield	84% w/w	71% w/w

Appearance	Crystalline Solid	Light yellow crystalline solid
Color	Pale Yellow to Yellow	Off white to pale yellow
Odour	Odourless	Odourless or characteristic aromatic odour
Solubility	Soluble in ethanol, chloroform ,DMSO and DMF; sparingly soluble in water.	Soluble in ethanol, methanol and DMSO; sparingly soluble in water.
Melting Point	198-202°C	210-214 °C

Table No -3 List Of Chemical Test

Sr. No.	**Test**	**Procedure**	**Observation**	**Result**
1	2 4 DNP Test	Add a2-4-DNP reagent in a sample[5,]	No Yellow / Orange Precipitate	+
2	Bromine Water Test	A small quantity of the compound was dissolved In ethanol and treated with bromine water[7,].	De colorization of bromine water.	+
3	Ferric Chloride Test	The compound solution was treated with a few drops of 5%ferric chloride solution.[7]	Yellowish-green color.	+
4	Schiff's Test	Small Amount of Sample Dissolve in Ethanol and Add A Schiff's Reagent[5]	No Pink Color	+

SPECTRAL CHARACTERIZATION FTIR

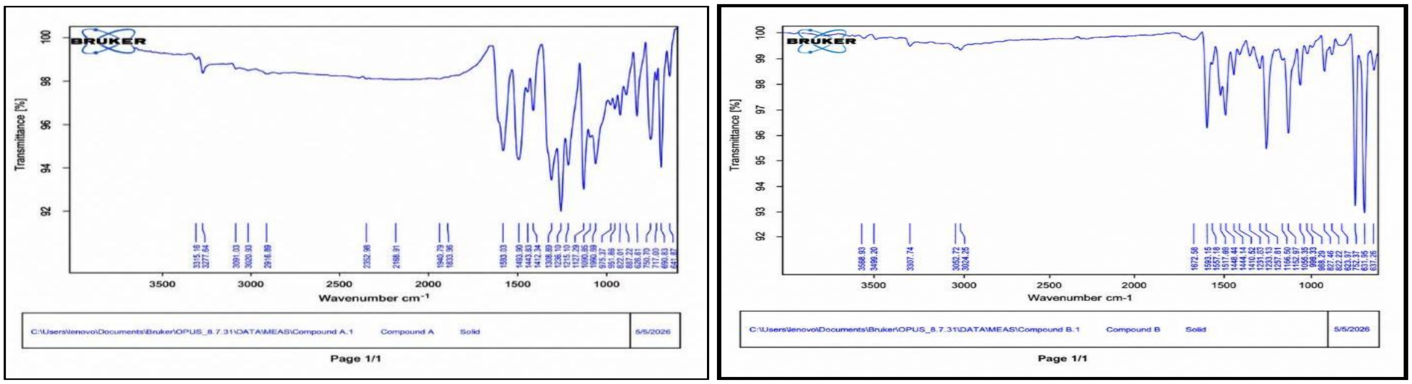


Figure No. 1 Peak of Comp A & Comp B FTIR

Table No.4: Interpretation of COMP A and COMP B.(FTIR)

Compound	**FT-IR Peaks (cm^{-1})**	**Functional Group/ Interpretation**	**Observation**
Compound A	3315, 3278	N-H/O-H stretching	Presence on firmed (positive broad absorption)
	3091, 3021	Aromatic C-H stretching	Aromatic ring present
	2917	Aliphatic C-H stretching	Positive for alkyl C–H
	1583	Aromatic C=C stretching	Aromatic system confirmed
	1494-1414	Aromatic skeletal vibration	Positive aromatic frame work
	1309-1023	C-N/C-O stretching	Presence of heteroatom Linkage confirmed
	975-642	Aromatic C-H bonding[11’13]	Substituted aromatic ring present
Compound B	3565, 3499	O-H/N-H stretching	Positive hydrogen-bonded Functional group
	3308, 3053, 3024	Aromatic C-H stretching	Aromatic ring confirmed
	1673	C=O stretching	Carbonyl group positively identified
	1594, 1557, 1514	Aromatic C=C/C=N stretching	Conjugated/aromatic system present
	1489-1294	Aromatic skeletal and C-N Stretching[11,13]	Positive C–N linkage

H NMR:

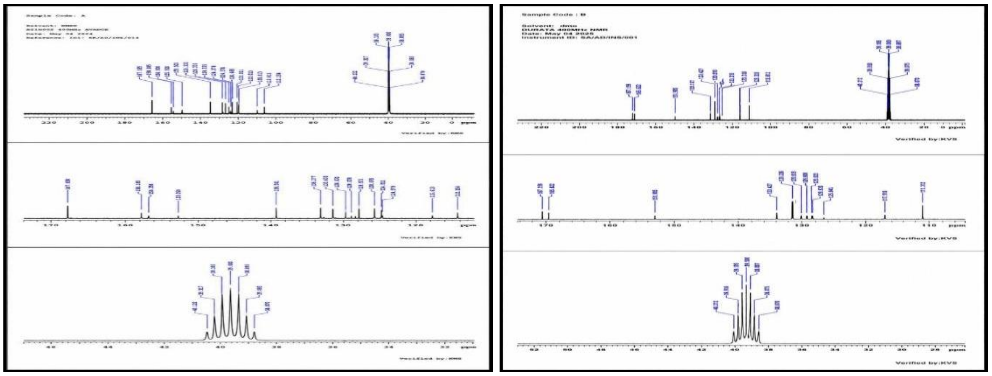


Figure No. 4 ^{1}H NMR COMP A and COMP B.

Table No.5:Assignment of COMP A and COMP B.

Compound	**^{1}Hnmr (400MHZ,DMSO-D_6, Δ PPM)Assignment**	**Assignment**

Compound A	7.55–7.48 (m, 5H), 7.30–7.18(m,5H), 6.52(s, 1H)	Multiplets at δ 7.55–7.18 ppm correspond to aromatic protons of phenyl rings; singles at δ6.52 ppm assigned to azo methane proton(–CH=N–)
Compound B	8.53(s, 1H), 7.92–7.89 (m, 2H),7.54–7.18(m, 8H),7.19(s, 1H)	Singlet at δ 8.53 ppm attributed to–NH proton of hydrazino group; aromatic protons appeared as multiplets betweenδ7.92–7.18 ppm; singlet at δ7.19 ppm assigned to secondary hydrazino proton

Note –Both spectra are recorded in DMSO-d6 solvent. The common ^{1}HNMR solvent peaks visiblearound:**δ2.50 ppm**[18]

^{13}CNMR:

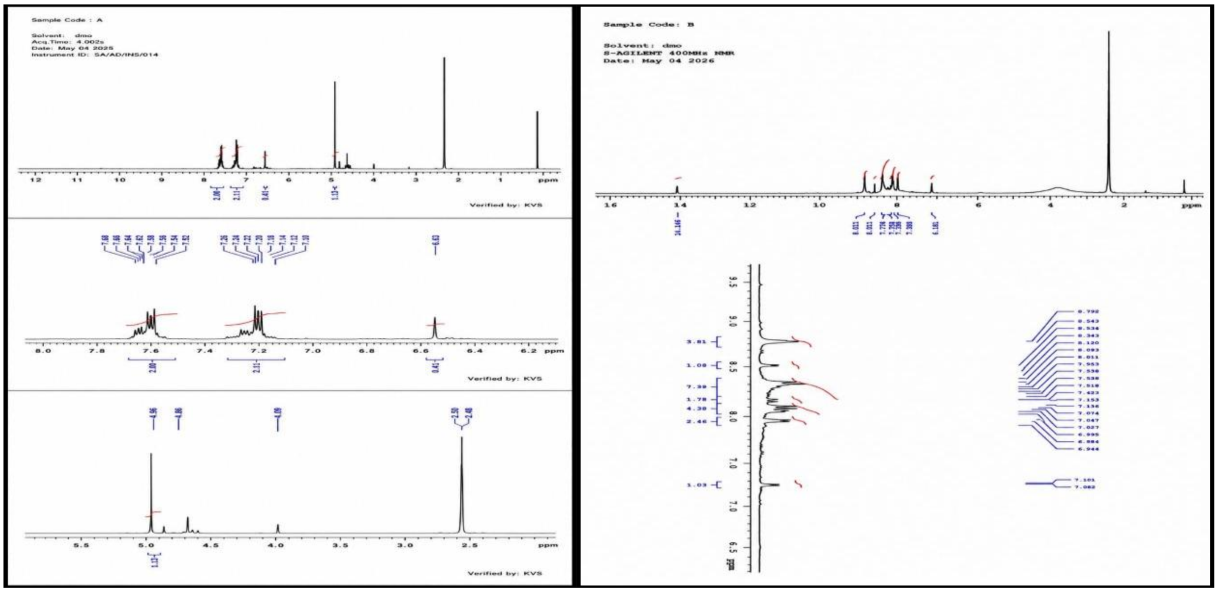


Figure .No. 5 ^{13}CNMR (COMP A&B).

Table No.6: Assignment of COMP A and COMP B

Compound	^{13}CNMR(DMSO-d,δppm)	Assignment
Compound A	167.66, 157.03, 153.95, 138.91, 133.33, 132.66, 131.82, 129.58, 128.57, 126.58, 124.04, 123.81, 115.52,111.41[17]	Oxadiazole C=Ncarbonsobserved at δ 167.66, 157.03 and 153.95 ppm; aromatic phenyl carbons appeared between δ111.41–138.91 ppm

CompoundB	167.69, 166.52, 151.90, 133.40, 131.29, 129.89, 129.13, 128.23, 126.42,125.88,117.91,113.43[17]	Down field signalsat δ 167.69, 166.52and151.90 ppm correspond to oxadiazole carbons; aromatic carbons resonated between δ 113.43–133.40 ppm

Note - The characteristic solvent peakin¹³CNMR for DMSO-d6 appears around :**δ39.5ppm** (usually seen as a multiplet /septet due to deuterium coupling).[16'17]

Mass Spectroscop

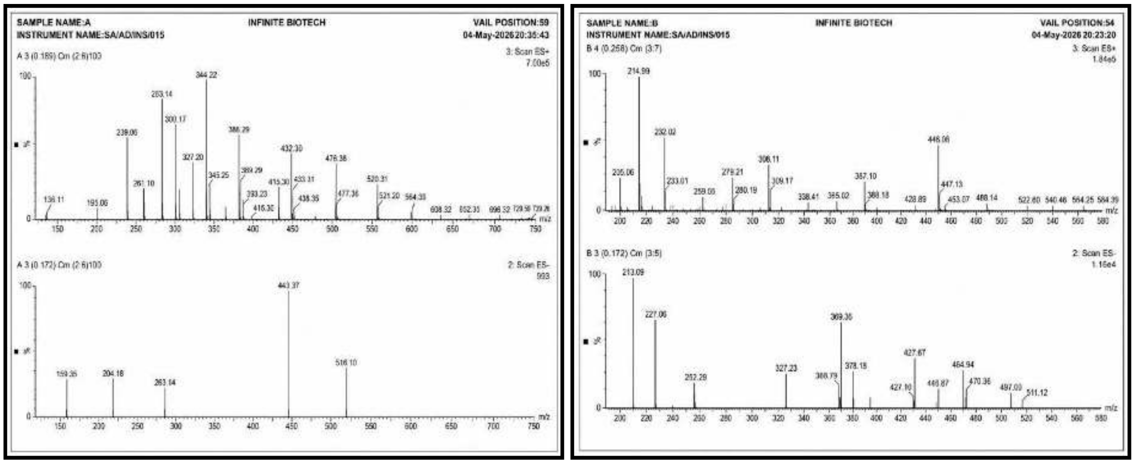


Figure .No.6: Mass Spectroscopy (COMP A & B)

Table No.7: Interpretation of COMP A And B

COM A		***COM B***	
Peakm/z	***Interpretation***	***Peakm/z***	***Interpretation***
239.06	Aromatic oxadiazole fragment	**214.99**	Base peak corresponding to oxadiazole fragment
283.14	Intermediate fragmention	**232.02**	Protonated fragment
300.17	Phenyl substituted fragment	**279.21**	Aromatic substituted ion
327.20	Rearranged molecular fragment	**308.11**	Intermediate molecular fragment
344.22	Probable molecular ion peak	**387.10**	Dimeric fragment
388.29	Dimeric /associated fragment	**446.06**	Molecular ion /adduct peak[19]
432.30	Higher molecularaggregate		

Interpretation Comp A

The spectrum shows characteristic fragmentation of aromatic heterocyclic compounds containing the 1,3,4-oxadiazole nucleus. The prominent peaks around **300–344 m/z** support formation of substituted oxadiazole derivatives.[18'19]

Interpretation Comp B

The intense base peak at **214 m/z** suggests a stable oxadiazole-containing fragment. Peaks at higher m/z values indicate substituted aromatic systems and possible molecular ionformation.[8’9’

Biological Test:-

1 Membrane Stabilizattion Assay (HRBC Method)

Figure No-7 HRBC Method

2 Albumin Denaturation Assay / Protrin Denaturation

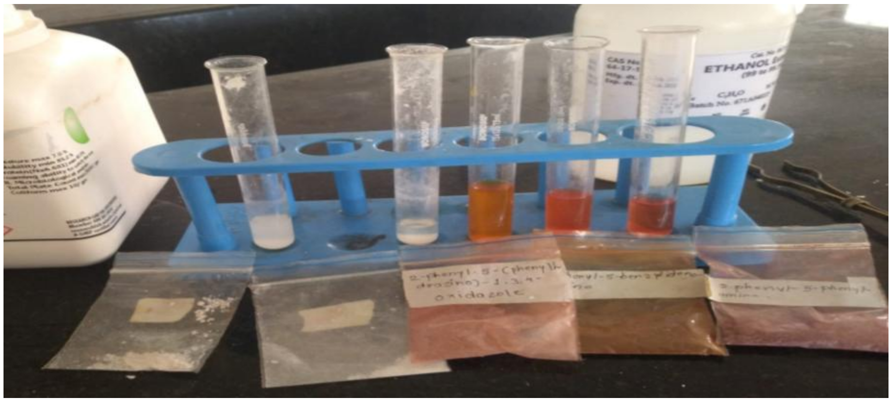


Figure No-8 Albumin Denaturation Assay

TLC Identification

Table No-8 Tlc

Compound		Distance travel (in CM)	R.F Value
Compound A	Solvent	6.4	---
	Benzaldehyde	4.5	0.6
	A	5.4	0.8
	Solvent	6	---
	Phenylhydrazine Hcl	4.4	0.7

Compound B			
	B	5	0.7

Figure No 9 .Comp A

FigureNo-10Comp B

RESULTS AND DISCUSSION

The present investigation successfully achieved the synthesis of two novel oxadiazole derivatives designated as Compound A and Compound B. Both compounds were obtained as crystalline solids with satisfactory yields and good purity after recrystallization.
The percentage yield obtained for Compound A (84%) was higher than that of Compound B (71%), indicating that the multistep synthetic route employed for Compound A provided better product recovery. Physicochemical characterization revealed that both compounds were stable solids possessing distinct melting point ranges. Compound A exhibited a melting point of 198–202°C, while Compound B showed a slightly higher melting point of 210–214°C, suggesting stronger intermolecular interactions within its crystal lattice.

Qualitative chemical tests further supported the formation of the desired compounds. Positive responses in bromine water and ferric chloride tests indicated the presence of unsaturated and aromatic functionalities. The observed reactions confirmed the incorporation of heterocyclic and substituted aromatic moieties within the synthesized molecules.

FT-IR spectral analysis provided important evidence regarding the structural features of the compounds. Compound A displayed characteristic absorption bands corresponding to N–H stretching, aromatic C–H stretching, aromatic C=C vibrations, and C–N/C–O linkages. Compound B showed similar aromatic absorptions along with a prominent carbonyl stretching band, indicating the presence of additional functional group contributions. These spectral features were consistent with the proposed molecular structures.

The ^{1}H NMR spectra demonstrated signals attributable to aromatic protons and heterocyclic substituents. Compound A exhibited a singlet corresponding to the azomethine proton along with multiplets arising from aromatic hydrogens. Compound B showed characteristic NH proton resonances and aromatic proton signals, confirming the presence of the phenylhydrazino substituent. The chemical shift values were in good agreement with the expected proton environments.

Further structural confirmation was obtained through ^{13}C NMR spectroscopy. Downfield carbon resonances corresponding to oxadiazole ring carbons were observed in both compounds. Aromatic carbon signals appeared within the expected chemical shift range, supporting successful cyclization and formation of the target heterocyclic framework.

Mass spectrometric analysis revealed molecular ion peaks and characteristic fragmentation patterns consistent with substituted 1,3,4-oxadiazole derivatives. The fragmentation profiles provided additional evidence for the molecular architecture of the synthesized compounds. The observed mass-to-charge ratios supported the proposed structures and confirmed the successful synthesis of both target molecules.

Overall, the combined physicochemical and spectral studies conclusively established the formation of the desired oxadiazole derivatives. The presence of biologically relevant functional groups and the stability of the synthesized compounds suggest their potential usefulness for future pharmacological evaluation, particularly in anti-inflammatory drug discovery programs.[14'15'18]

CONCLUSION

The present study successfully synthesized and characterized two novel 1,3,4-oxadiazole derivatives, namely 2-phenyl-5-(benzylideneamino)-1,3,4-oxadiazole and 2-phenyl-5-(phenylhydrazino)-1,3,4-oxadiazole.
The synthesized compounds were obtained in good yields and exhibited satisfactory physicochemical properties. Structural elucidation using FT-IR, ^{1}H NMR, ^{13}C NMR, and mass spectrometry confirmed the successful formation of the oxadiazole ring system and the proposed molecular structures. The spectral data demonstrated the presence of characteristic functional groups and aromatic heterocyclic frameworks. These findings indicate that the developed synthetic methods are effective for the preparation of oxadiazole-based molecules. Considering the established pharmacological significance of 1,3,4-oxadiazole derivatives, the synthesized compounds may represent promising candidates for further biological screening and optimization as potential anti-inflammatory agents.[1'11'17'16]

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