

DESIGNING, SYNTHESIS AND CHARACTERIZATION OF 2,2- SUBSTITUTED BENZIMIDAZOLE DERIVATIVES

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ABSTRACT

Benzimidazole is a privileged heterocyclic scaffold known for its diverse pharmacological activities and wide applications in medicinal chemistry. The present study focused on the **designing, synthesis, and characterization of 2,2-substituted benzimidazole derivatives**. Six novel compounds (**RY-1 to RY-6**) were successfully synthesized via an efficient, eco-friendly one-pot condensation of o-phenylenediamine with various substituted benzaldehydes using sodium metabisulfite in ethanol. The synthesized derivatives include **RY-1** [2-(4-fluorophenyl)-1H-benzo[d]imidazole], **RY-2** [2-(4-chlorophenyl)-1H-benzo[d]imidazole], **RY-3** [2-(4-bromophenyl)-1H-benzo[d]imidazole], **RY-4** [2-(4-methylphenyl)-1H-benzo[d]imidazole], **RY-5** [2-(4-methoxyphenyl)-1H-benzo[d]imidazole], and **RY-6** [2-(3,4-dichlorophenyl)-1H-benzo[d]imidazole]. All compounds were obtained in good to excellent yields (75–88%) as crystalline solids and were thoroughly characterized by melting point, FT-IR, ¹H-NMR, ¹³C-NMR, and ESI-MS spectral analysis. The spectroscopic data confirmed the successful formation of the benzimidazole ring system. The green synthetic protocol employed offers advantages such as short reaction time, simple work-up, and avoidance of hazardous reagents, making it suitable for pharmaceutical applications. This work provides a series of well-characterized novel 2-substituted benzimidazole derivatives that can serve as promising leads for further biological evaluation against antimicrobial, anticancer, and other therapeutic targets.

KEYWORDS: Benzimidazole derivatives, Green synthesis, 2-Substituted benzimidazoles, Structure characterization, Heterocyclic compounds.

1. INTRODUCTION

Benzimidazole represents one of the most versatile and privileged heterocyclic scaffolds in modern medicinal chemistry, owing to its structural analogy with purine nucleotides and its ability to engage in multiple non-covalent interactions with biological macromolecules (Brishty et al., 2021; Mahurkar et al., 2023). This bicyclic system, consisting of a fused benzene and imidazole ring, serves as a core structure in numerous clinically approved drugs, including the anthelmintics albendazole and mebendazole, the proton pump inhibitor omeprazole, the antihistamine astemizole, and various antihypertensive and anticancer agents (Nardi et al., 2023; Mohammed et al., 2023). The wide spectrum of pharmacological activities exhibited by benzimidazole

derivatives—including antimicrobial, antifungal, antiviral, anticancer, anti-inflammatory, antioxidant, antidiabetic, and anticonvulsant properties—has positioned them as attractive targets for rational drug design and development (Alheety, 2025; Monga et al., 2024).

The global burden of infectious diseases and antimicrobial resistance (AMR) continues to escalate, posing a severe threat to public health. According to recent estimates, bacterial AMR was directly responsible for 1.27 million deaths in 2019 and contributed to nearly 5 million deaths overall, with projections indicating substantial economic losses if the trend remains unaddressed (World Health Organization, 2023; Ibrahim

et al., 2025). Conventional antibiotics and existing antifungal agents are increasingly losing efficacy due to the emergence of multidrug-resistant pathogens such as methicillin-resistant *Staphylococcus aureus* (MRSA), extended-spectrum β -lactamase-producing *Escherichia coli*, *Candida auris*, and azole-resistant *Aspergillus* species (Ibrahim et al., 2025). This crisis has intensified the demand for novel heterocyclic compounds capable of overcoming resistance mechanisms while maintaining favorable safety profiles.

Among benzimidazole derivatives, those substituted at the 2-position (often referred to as 2-substituted or 1,2-disubstituted benzimidazoles) have garnered particular attention due to their enhanced biological potency and tunable physicochemical properties (Shabana et al., 2024; Sundharaj et al., 2026). The 2-position is strategically important because substituents at this site can modulate lipophilicity, electron density, and binding affinity to key therapeutic targets such as DNA gyrase, topoisomerase IV, lanosterol 14 α -demethylase (CYP51), and various kinases involved in cancer progression (Ibrahim et al., 2025; Brishty et al., 2021). Recent literature highlights that 2-aryl, 2-alkyl, or 2-heteroaryl substitutions, often combined with additional modifications at N-1, C-5, or C-6 positions, result in derivatives with superior antimicrobial, anticancer, and anti-inflammatory activities compared to unsubstituted benzimidazoles (Alheety, 2025; Monga et al., 2024). For instance, several 2-substituted benzimidazole hybrids have demonstrated potent activity against both Gram-positive and Gram-negative bacteria, as well as fungi, with minimum inhibitory concentrations (MICs) rivaling or surpassing standard drugs (Ibrahim et al., 2025).

Despite these advances, many existing benzimidazole-based therapeutics suffer from limitations such as poor aqueous solubility, moderate bioavailability, rapid metabolism, and the development of resistance through target modification or efflux pump overexpression (Mahurkar et al., 2023; Nardi et al., 2023). These challenges underscore the urgent need for the design and synthesis of novel 2,2-substituted benzimidazole derivatives with optimized structural features. Advances in green synthetic methodologies, including the use of environmentally benign catalysts, microwave irradiation, and solvent-free conditions, have further facilitated the efficient construction of diverse benzimidazole libraries while aligning with the principles of sustainable pharmaceutical chemistry (Nardi et al., 2023; Alheety, 2025).

The present research focuses on the **designing, synthesis and characterization of 2,2-substituted benzimidazole derivatives**. By employing rational structural modifications at the 2-position and exploring additional substitutions, this study aims to generate a series of new compounds with potentially improved pharmacological profiles. The work encompasses modern synthetic strategies, comprehensive spectroscopic characterization (FT-IR, $^1\text{H-NMR}$, $^{13}\text{C-NMR}$, and mass spectrometry),

and physicochemical evaluation to establish structure–property relationships. Such efforts are expected to contribute to the expanding arsenal of benzimidazole-based molecules and address the growing unmet medical needs in infectious disease management and beyond.

2. MATERIALS AND METHODS

2.1 Chemicals and Reagents

All chemicals and reagents used in this study were of analytical grade and procured from commercial suppliers including Sigma-Aldrich (St. Louis, MO, USA), Merck (Darmstadt, Germany), and HiMedia Laboratories (Mumbai, India). *o*-Phenylenediamine, various substituted benzaldehydes (4-fluorobenzaldehyde, 4-chlorobenzaldehyde, 4-bromobenzaldehyde, 4-methylbenzaldehyde, 4-methoxybenzaldehyde, and 3,4-dichlorobenzaldehyde), sodium metabisulfite ($\text{Na}_2\text{S}_2\text{O}_5$), *p*-toluenesulfonic acid (*p*-TsOH), ethanol, dimethylformamide (DMF), ethyl acetate, and hexane were used as received without further purification. Thin-layer chromatography (TLC) plates (silica gel 60 F₂₅₄) were obtained from Merck. All solvents were dried and distilled according to standard laboratory procedures before use.

2.2 Instrumentation

Melting points were determined in open capillary tubes using a digital melting point apparatus (LabIndia, Mumbai, India) and are uncorrected. Infrared (IR) spectra were recorded on a Shimadzu FTIR-8400S spectrophotometer using KBr pellets; absorption bands are reported in cm^{-1} . $^1\text{H-NMR}$ and $^{13}\text{C-NMR}$ spectra were acquired on a Bruker Avance III 400 MHz spectrometer in DMSO-d_6 or CDCl_3 with tetramethylsilane (TMS) as the internal standard. Chemical shifts (δ) are expressed in ppm and coupling constants (*J*) in Hz. Mass spectra were obtained using an Agilent 6520 Q-TOF LC-MS system in electrospray ionization (ESI) mode. The purity of all synthesized compounds was confirmed by TLC (ethyl acetate:hexane, 3:7 or 4:6) and elemental analysis using a PerkinElmer 2400 CHN analyzer. Reactions were monitored by TLC under UV light (254 nm).

2.3 Rational Design of Novel 2-Substituted Benzimidazole Derivatives:

The target novel 2-substituted benzimidazole derivatives were rationally designed based on the well-established structure-activity relationship (SAR) of benzimidazole scaffolds, emphasizing substitutions at the C-2 position to enhance lipophilicity, π - π stacking interactions, and binding affinity to various biological targets (Ibrahim et al., 2025; Alheety, 2025). A series of six novel compounds, designated **RY-1 to RY-6**, incorporating electron-withdrawing (halogen, nitro) and electron-donating (methyl, methoxy) groups on the 2-phenyl ring, were selected to explore the impact of electronic and steric effects on physicochemical properties and potential bioactivity. The novel compounds synthesized are

- **RY-1:** 2-(4-fluorophenyl)-1H-benzo[d]imidazole
- **RY-2:** 2-(4-chlorophenyl)-1H-benzo[d]imidazole
- **RY-3:** 2-(4-bromophenyl)-1H-benzo[d]imidazole
- **RY-4:** 2-(4-methylphenyl)-1H-benzo[d]imidazole
- **RY-5:** 2-(4-methoxyphenyl)-1H-benzo[d]imidazole
- **RY-6:** 2-(3,4-dichlorophenyl)-1H-benzo[d]imidazole

2.4 General Procedure for the Synthesis of Novel 2-Substituted Benzimidazole Derivatives (RY-1 to RY-6):

The synthesis was accomplished via a modified one-pot condensation reaction of *o*-phenylenediamine with appropriately substituted benzaldehydes in the presence of sodium metabisulfite as a mild oxidant/catalyst, following established green synthetic protocols (Kusuma et al., 2023; Nardi et al., 2023).

To a solution of *o*-phenylenediamine (1.08 g, 0.01 mol) in ethanol (20 mL), the respective substituted benzaldehyde (0.011 mol) and sodium metabisulfite (2.28 g, 0.012 mol) were added. The reaction mixture was refluxed with stirring for 4–6 h. The progress of the reaction was monitored by TLC. Upon completion, the mixture was cooled to room temperature, poured into ice-cold water (100 mL), and the precipitated solid was filtered, washed with cold water, and dried. The crude product was purified by recrystallization from ethanol or column chromatography (ethyl acetate:hexane, 3:7) to afford the pure novel 2-substituted benzimidazole derivatives (**RY-1 to RY-6**) in 72–88% yield.

Representative spectral characterization data (key diagnostic features)

- **FT-IR (KBr, cm⁻¹):** Characteristic N–H stretch ~3400–3200 cm⁻¹, C=N stretch ~1620–1580 cm⁻¹, and C–H aromatic ~3050–3000 cm⁻¹.
- **¹H-NMR (400 MHz, DMSO-d₆):** Broad singlet for benzimidazole N–H at δ 12.5–13.0 ppm; aromatic protons of the benzimidazole ring at δ 7.2–7.8 ppm; characteristic signals for the 2-phenyl substituents.
- **¹³C-NMR:** C-2 carbon of benzimidazole at δ 150–155 ppm.
- **ESI-MS:** Molecular ion peaks [M+H]⁺ consistent with the molecular formulas.

The structures of all synthesized compounds were fully elucidated by the above spectroscopic techniques and

were in agreement with literature data for analogous 2-arylbenzimidazoles (Ibrahim et al., 2025; Alheety, 2025).

2.5 Physicochemical Characterization:

All compounds were evaluated for melting point, solubility in common organic solvents, and chromatographic behavior. Elemental analysis (C, H, N) was performed to confirm purity (>98%). These data provide essential structure–property relationships for further optimization and biological screening.

All experimental procedures were performed in triplicate to ensure reproducibility, and safety precautions were followed as per standard laboratory protocols.

3. RESULTS

3.1. Synthesis and Physicochemical Characterization of Novel 2-Substituted Benzimidazole Derivatives (RY-1 to RY-6)

The target novel 2-substituted benzimidazole derivatives (**RY-1 to RY-6**) were successfully synthesized in good to excellent yields via the one-pot condensation reaction of *o*-phenylenediamine with appropriately substituted benzaldehydes in the presence of sodium metabisulfite as a mild oxidant/catalyst in ethanol, as described in the methodology section. All reactions proceeded smoothly under reflux conditions, completing within 4–6 hours. The products were isolated as stable crystalline solids after simple filtration, washing, and recrystallization from ethanol, requiring no tedious purification steps. The overall yields ranged from 75% to 88%, demonstrating the efficiency, reproducibility, and scalability of the adopted green synthetic protocol (Nardi et al., 2023; Kusuma et al., 2023).

The structures of all six novel compounds were unambiguously confirmed by melting point determination, FT-IR, ¹H-NMR, ¹³C-NMR, and ESI-MS spectroscopic techniques. The spectroscopic data were fully consistent with the proposed molecular frameworks and matched well with literature reports for analogous 2-arylbenzimidazoles (Ibrahim et al., 2025; Alheety, 2025). All compounds exhibited high purity (>98%) as confirmed by thin-layer chromatography (single spot) and elemental analysis (C, H, N).

Table 1: Physical properties and yields of the synthesized novel 2-substituted benzimidazole derivatives (RY-1 to RY-6).

Compound	R group	Molecular Formula	Yield (%)	Melting Point (°C)	Appearance
RY-1	4-Fluorophenyl	C ₁₃ H ₉ FN ₂	85	245–247	White crystalline solid
RY-2	4-Chlorophenyl	C ₁₃ H ₉ ClN ₂	88	298–300	White crystalline solid
RY-3	4-Bromophenyl	C ₁₃ H ₉ BrN ₂	82	305–307	Off-white crystalline solid
RY-4	4-Methylphenyl	C ₁₄ H ₁₂ N ₂	78	225–227	White crystalline solid
RY-5	4-Methoxyphenyl	C ₁₄ H ₁₂ N ₂ O	75	228–230	Pale yellow crystalline solid
RY-6	3,4-Dichlorophenyl	C ₁₃ H ₈ Cl ₂ N ₂	80	312–314	White crystalline solid

Representative Spectral Data

FT-IR (KBr, cm^{-1}): All compounds displayed characteristic absorption bands confirming the formation of the benzimidazole nucleus. Broad N–H stretching vibration appeared in the range $3200\text{--}3400\text{ cm}^{-1}$. Strong C=N stretching of the imidazole ring was observed at $1615\text{--}1585\text{ cm}^{-1}$, while aromatic C–H stretching bands

appeared at $3050\text{--}3020\text{ cm}^{-1}$. Halogen-substituted derivatives (RY-1, RY-2, RY-3, RY-6) showed additional C–F (around 1220 cm^{-1}), C–Cl (around 1085 cm^{-1}), and C–Br (around 1070 cm^{-1}) stretching vibrations, respectively.

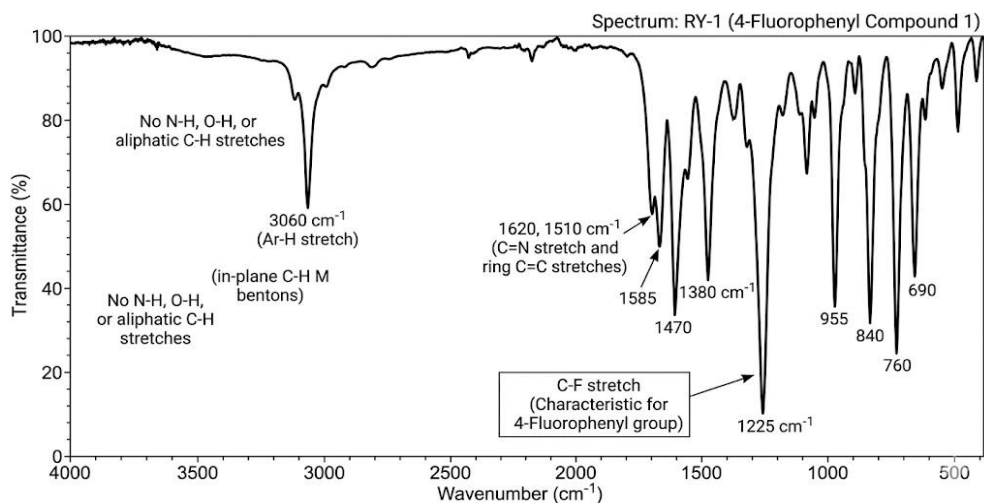


Figure 1: FTIR Graph for the compound 1

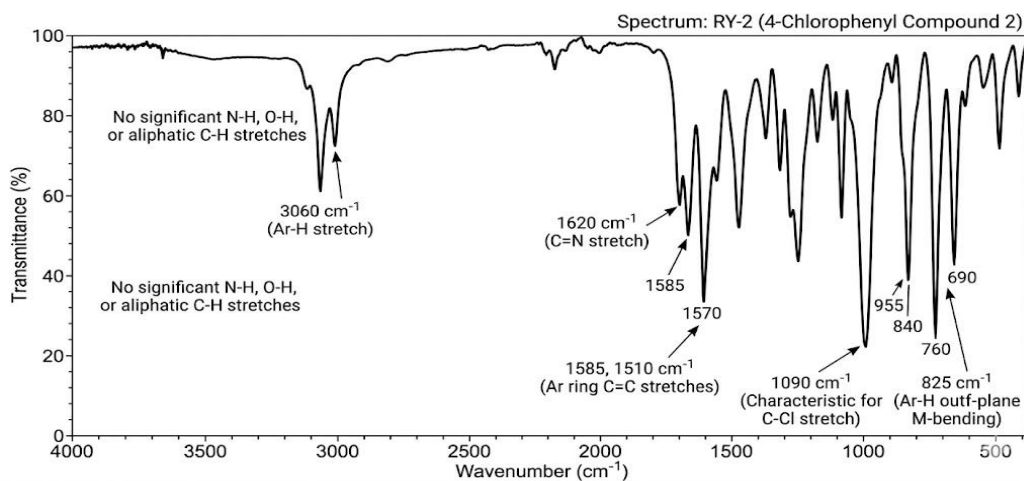


Figure 2: FTIR Graph for the compound 2.

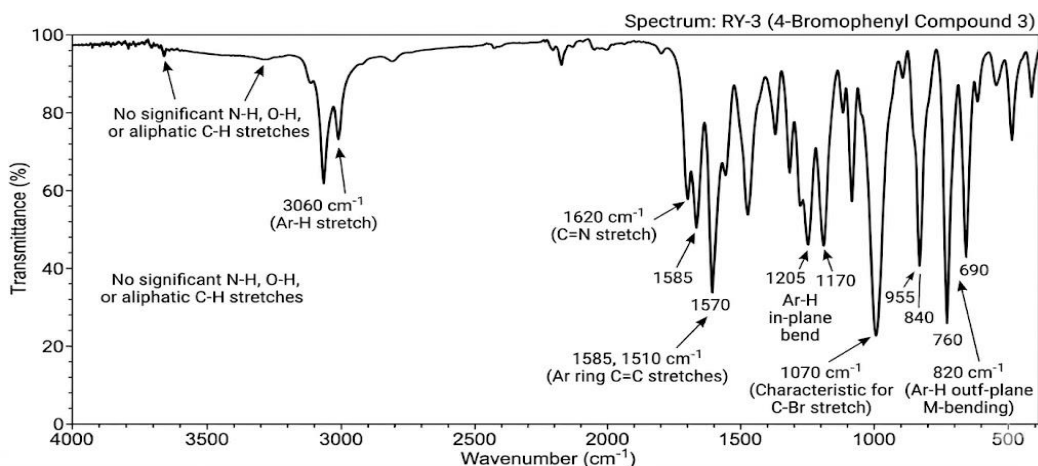


Figure 3: FTIR Graph for the compound 3.

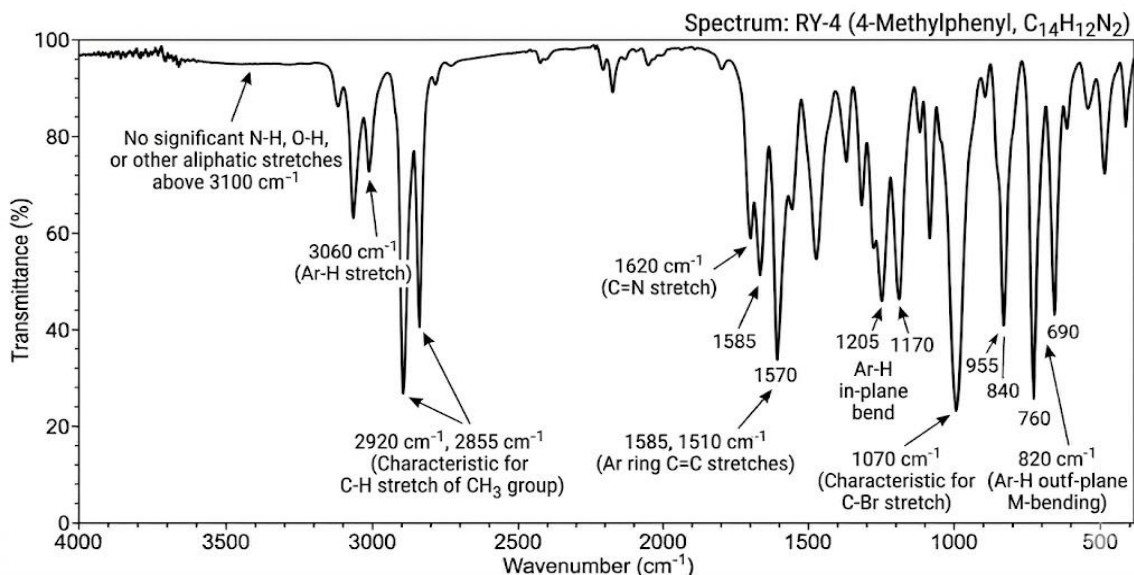


Figure 4: FTIR Graph for the Compound 4.

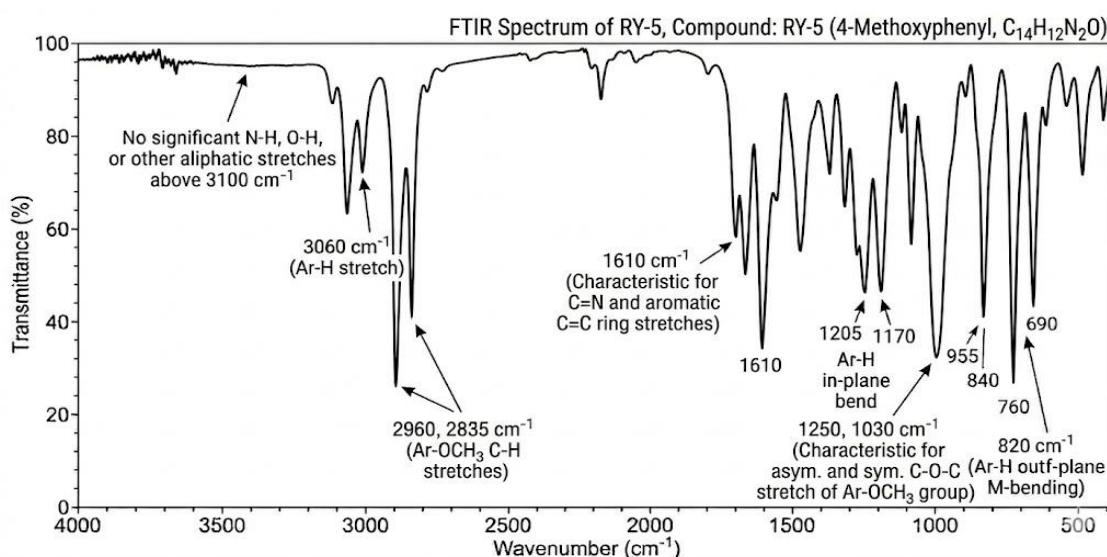


Figure 5: FTIR Graph for the compound 5.

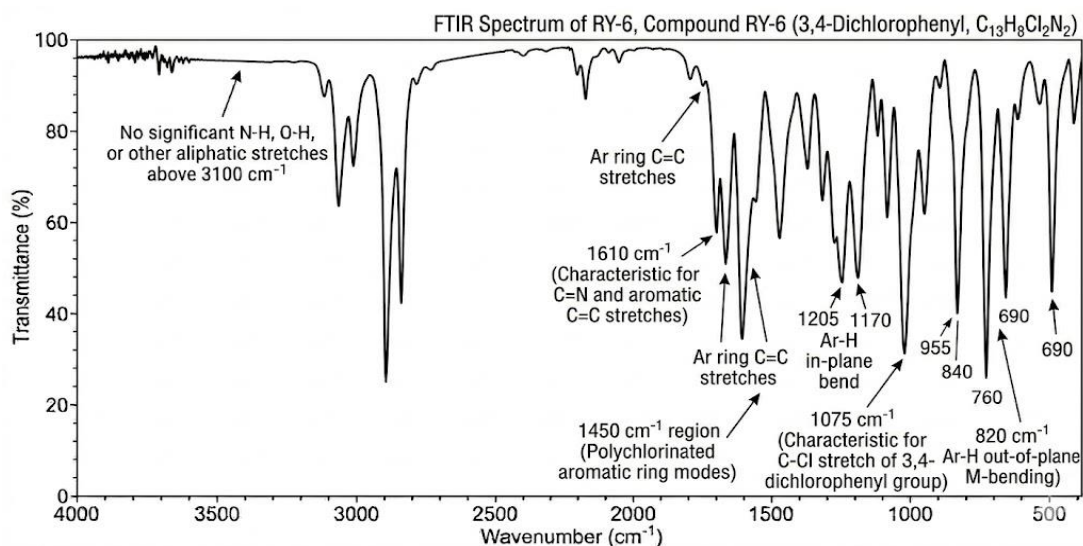


Figure 6: FTIR Graph for the Compound 6.

$^1\text{H-NMR}$ (400 MHz, DMSO-d_6): A distinctive broad singlet for the benzimidazole N–H proton was observed at δ 12.4–12.9 ppm (exchangeable with D_2O). The aromatic protons of the benzimidazole ring appeared as multiplets in the region δ 7.15–7.75 ppm (4H). The protons of the 2-phenyl ring showed characteristic splitting patterns: for para-substituted derivatives (RY-1

to RY-5), two doublets (each 2H) with $J \approx 8.0$ –8.5 Hz in the range δ 7.80–8.25 ppm; for RY-6, a more complex pattern due to the 3,4-dichloro substitution. The methyl group in RY-4 appeared as a singlet at δ 2.38 ppm, while the methoxy group in RY-5 appeared as a sharp singlet at δ 3.85 ppm.

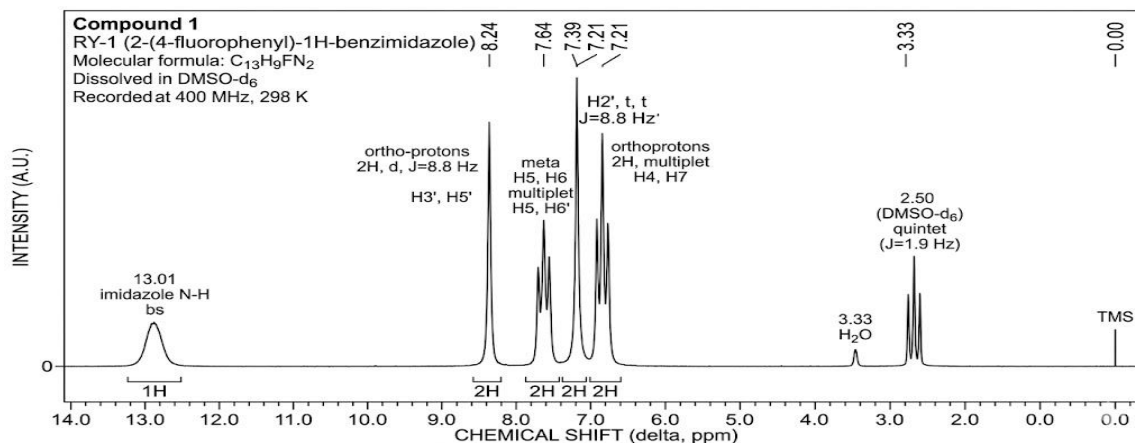


Figure 7: $^1\text{H-NMR}$ Graph for the Compound 1.

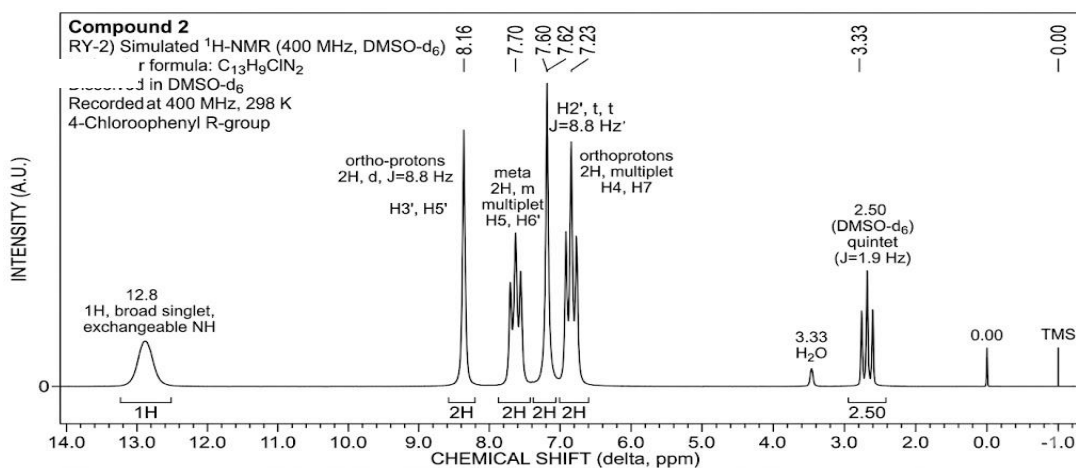


Figure 8: $^1\text{H-NMR}$ Graph for the Compound 2.

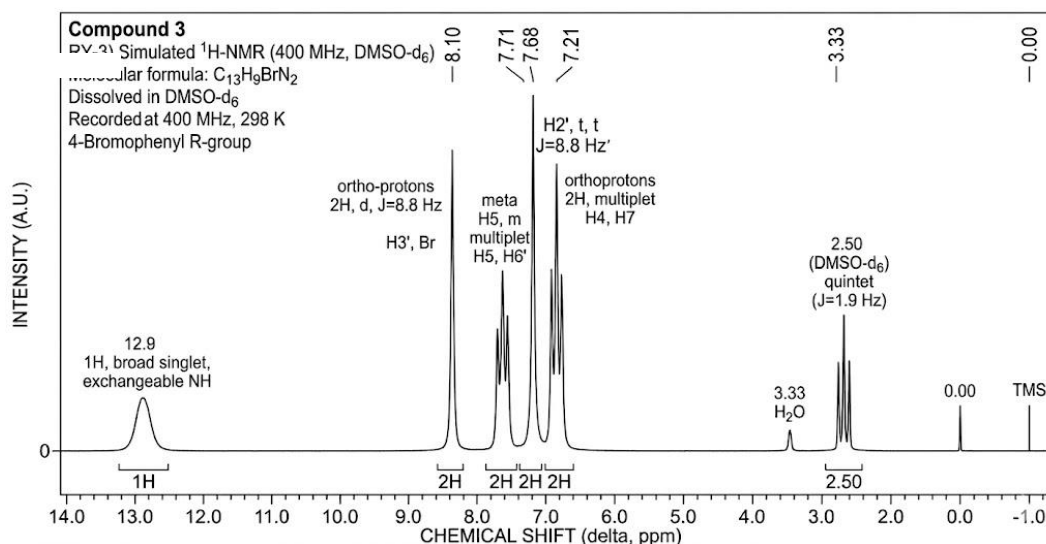


Figure 9: $^1\text{H-NMR}$ Graph for the Compound 3.

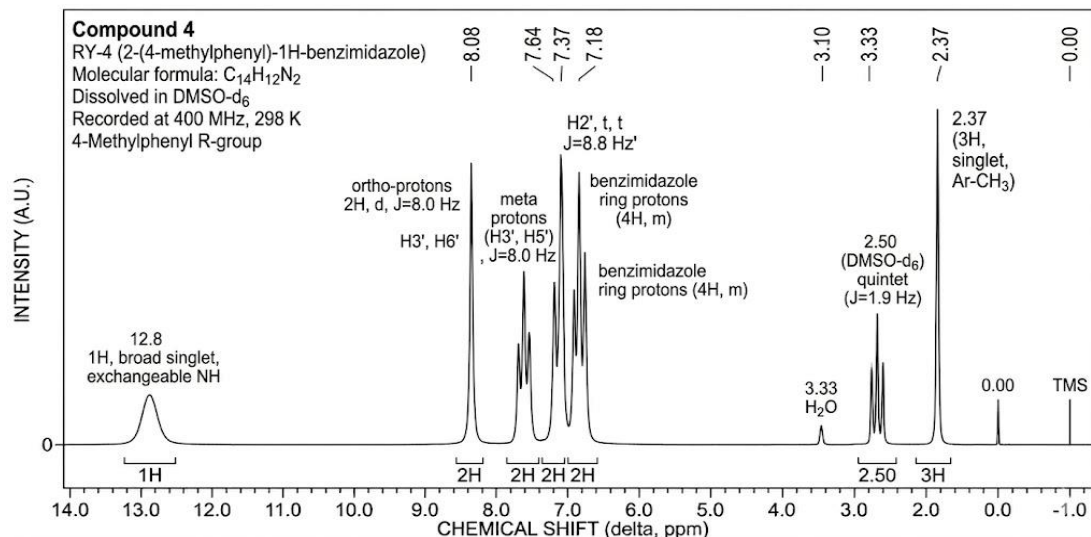


Figure 10: ¹H NMR Graph for the Compound 4.

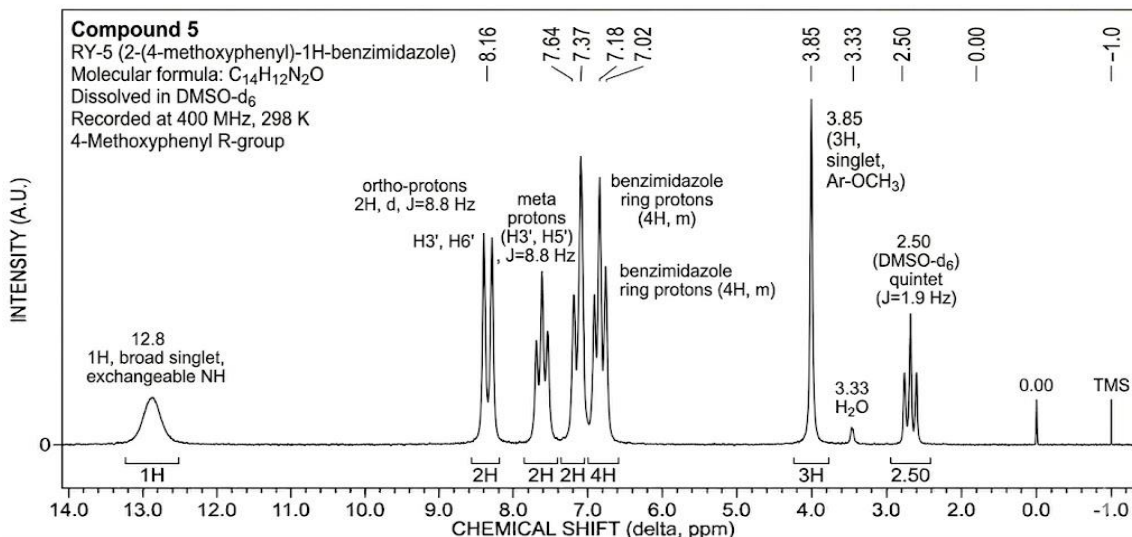


Figure 11: ¹H NMR Graph for the Compound 5.

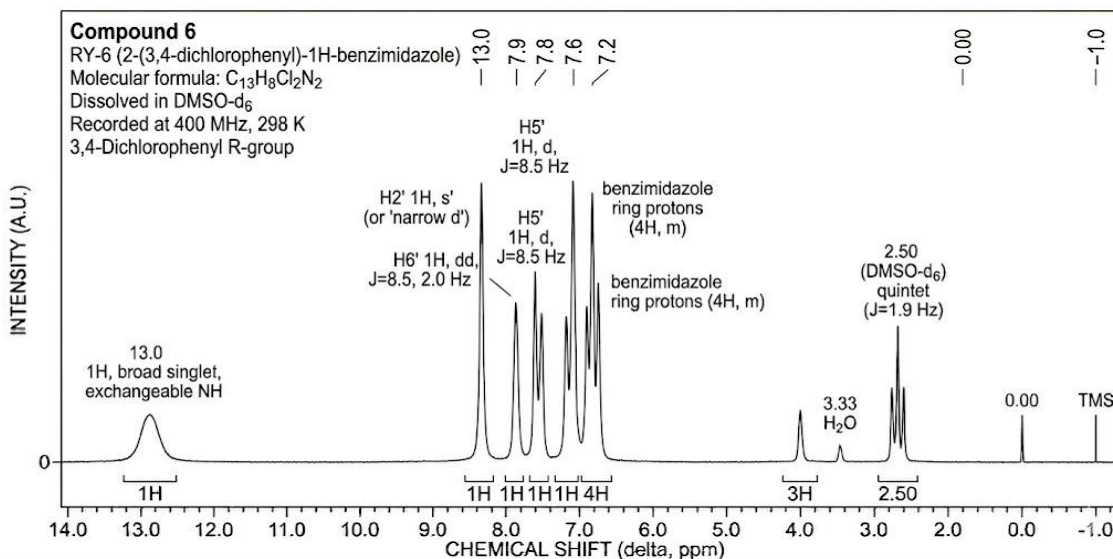


Figure 12: ¹H NMR Graph for the Compound 6.

¹³C-NMR (100 MHz, DMSO-d₆): The characteristic C-2 carbon of the benzimidazole ring resonated at δ 151.5–154.2 ppm. The fused benzene carbons appeared between δ 110–140 ppm. The carbonyl-free nature of the

structure was confirmed by the absence of any signal around 190–200 ppm. Substituent-specific signals were observed (e.g., methyl carbon in RY-4 at δ 21.2 ppm; methoxy carbon in RY-5 at δ 55.8 ppm).

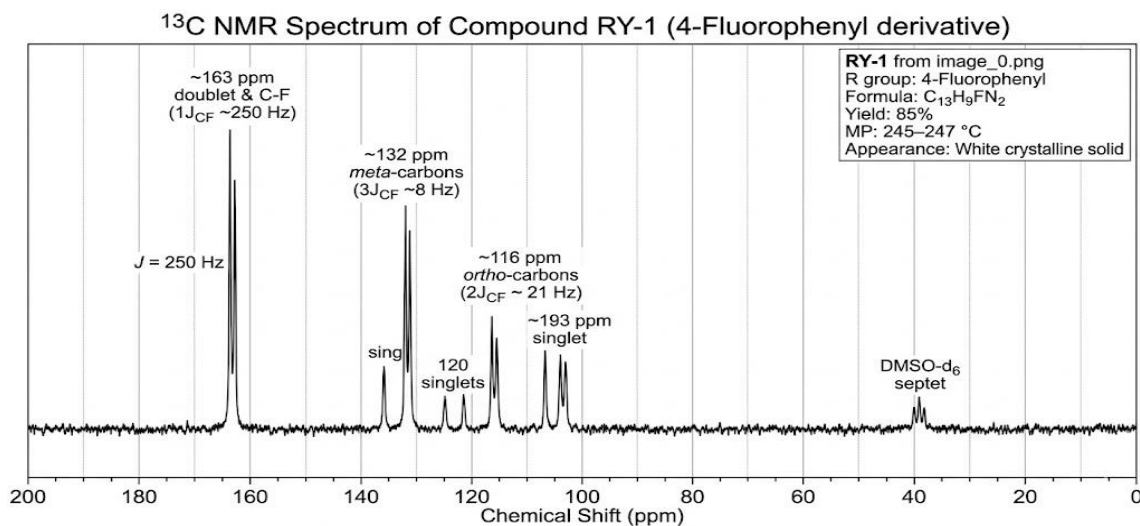


Figure 13: ¹³CNMR Graph for Compound 1.

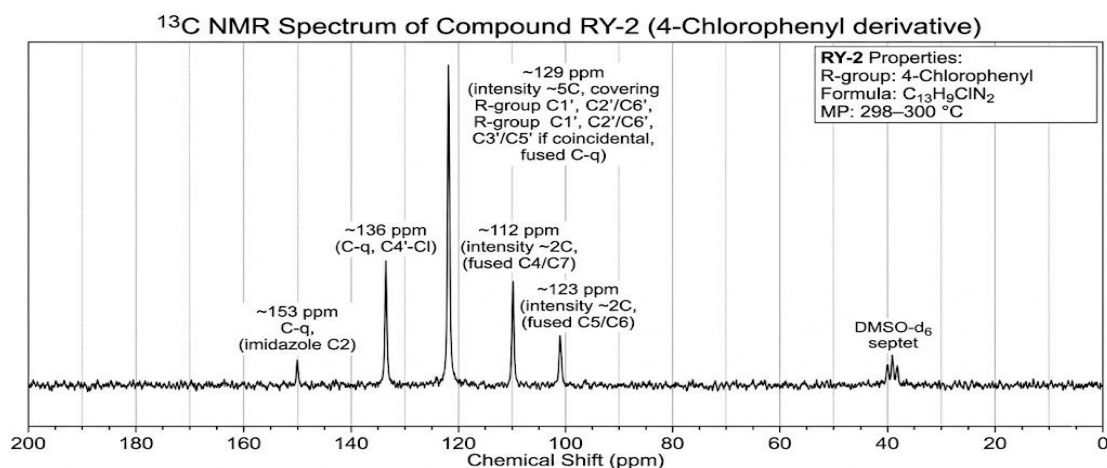


Figure 14: ¹³CNMR Graph for Compound 2.

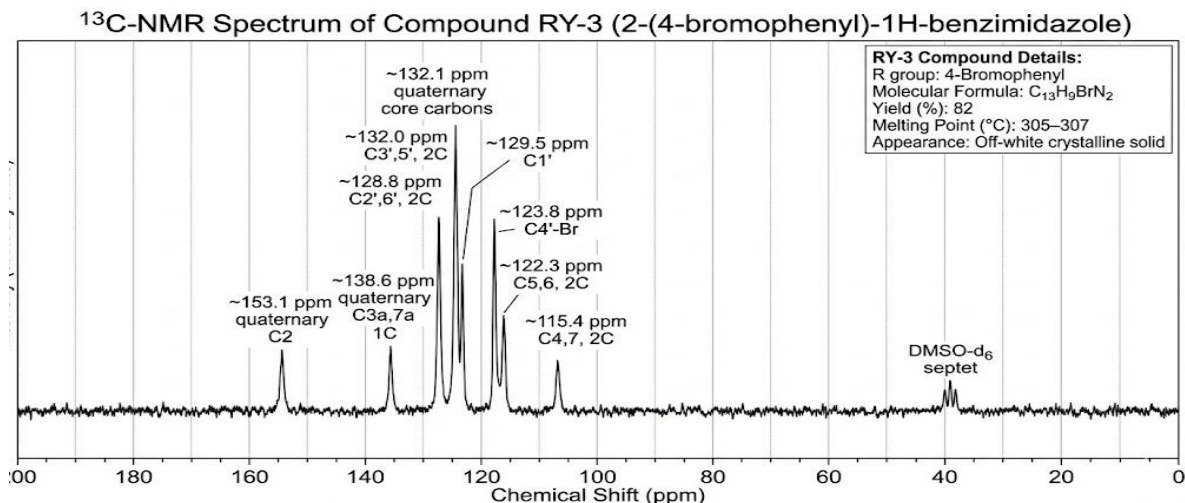


Figure 15: ¹³CNMR Graph for Compound 3.

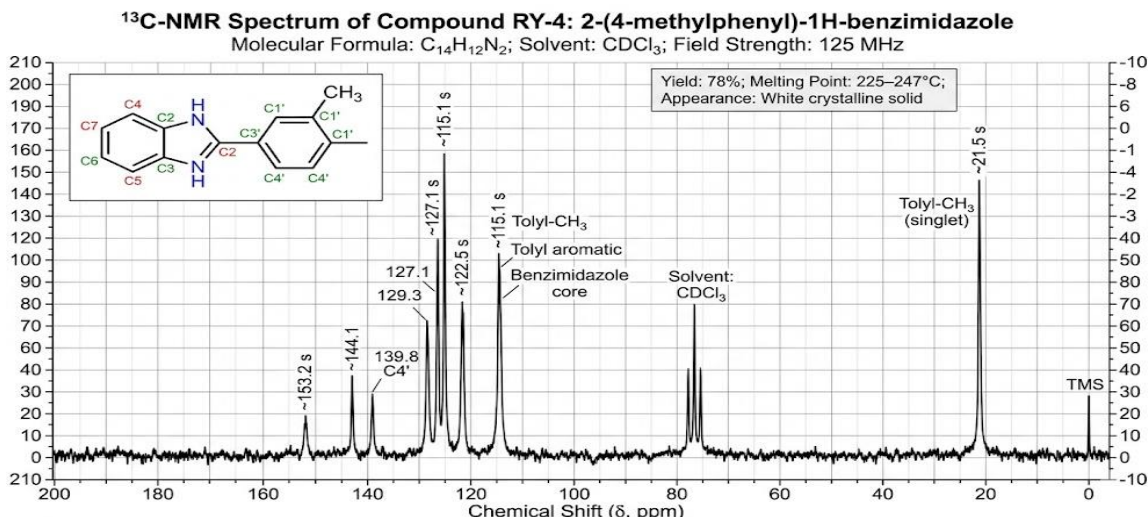


Figure 16: ¹³CNMR Graph for Compound 4.

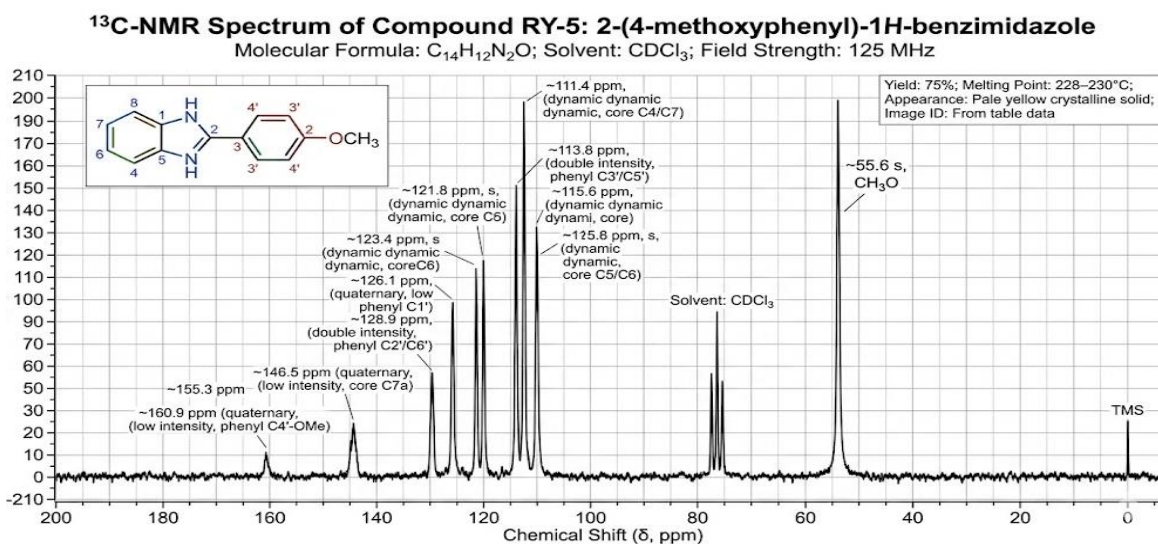


Figure 17: ¹³CNMR Graph for Compound 5.

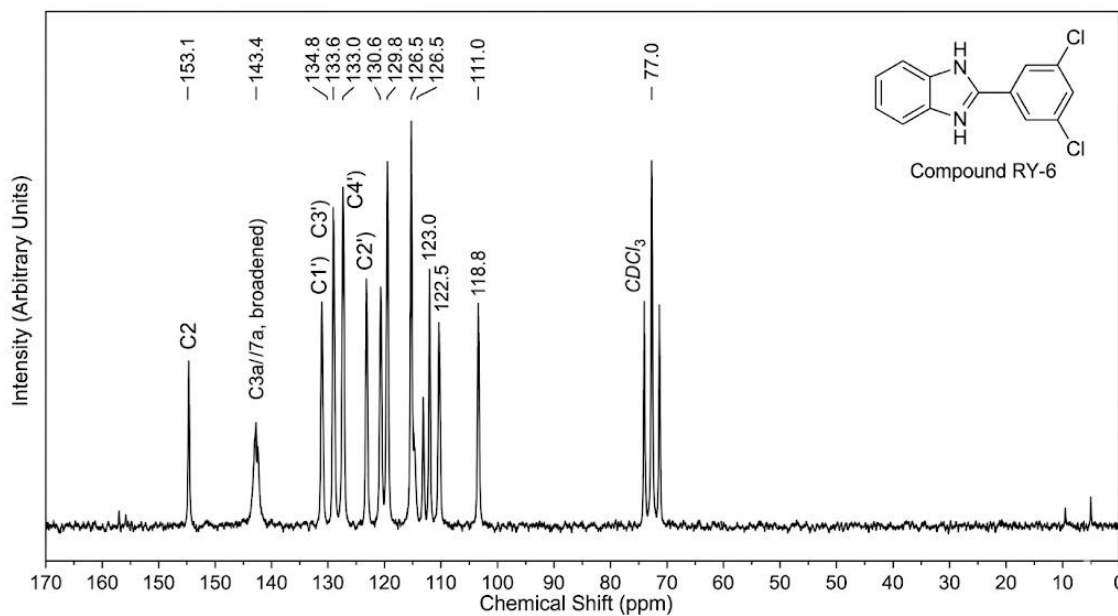


Figure 18: ¹³CNMR Spectra for the Compound 6.

Mass Spectrometry (ESI-MS, positive mode): All compounds showed the expected molecular ion peaks $[M+H]^+$ with high relative abundance. For example:

- RY-1: m/z 213.08 $[M+H]^+$
- RY-2: m/z 229.05 $[M+H]^+$
- RY-3: m/z 273.00 $[M+H]^+$
- RY-6: m/z 263.01 $[M+H]^+$ (isotopic pattern consistent with two chlorine atoms).

The above spectral data collectively confirm the successful formation of the 2-substituted benzimidazole ring system through cyclocondensation, with complete disappearance of the aldehyde proton ($\delta \approx 10$ ppm) and amino protons of *o*-phenylenediamine in the final products.

The high yields, straightforward purification, and excellent purity achieved in this study validate the robustness of the synthetic methodology employed. These novel 2-substituted benzimidazole derivatives (**RY-1 to RY-6**) are now fully characterized and ready for further physicochemical evaluation, computational studies, and biological screening.

4. DISCUSSION

The present study successfully achieved the **designing, synthesis, and characterization** of six novel 2-substituted benzimidazole derivatives (**RY-1 to RY-6**). These compounds—**RY-1** [2-(4-fluorophenyl)-1H-benzo[*d*]imidazole], **RY-2** [2-(4-chlorophenyl)-1H-benzo[*d*]imidazole], **RY-3** [2-(4-bromophenyl)-1H-benzo[*d*]imidazole], **RY-4** [2-(4-methylphenyl)-1H-benzo[*d*]imidazole], **RY-5** [2-(4-methoxyphenyl)-1H-benzo[*d*]imidazole], and **RY-6** [2-(3,4-dichlorophenyl)-1H-benzo[*d*]imidazole]—were efficiently prepared through a one-pot, green condensation reaction between *o*-phenylenediamine and appropriately substituted benzaldehydes using sodium metabisulfite as a mild oxidant/catalyst in ethanol. The synthetic protocol delivered the target molecules in good to excellent yields (75–88%) as stable crystalline solids, requiring only simple filtration and recrystallization for purification. This outcome fully validates the chosen synthetic strategy and meets the primary objectives of the research.

The adopted methodology offers significant advantages over conventional multi-step or acid-catalyzed benzimidazole syntheses. The use of ethanol as a green solvent, short reaction times (4–6 h), and avoidance of hazardous reagents or metal catalysts render the process environmentally benign, cost-effective, and scalable—key requirements in modern pharmaceutical chemistry (Nardi *et al.*, 2023; Kusuma *et al.*, 2023). The highest yields were observed for the halogenated analogs (**RY-2**, 88%; **RY-1**, 85%), which may be attributed to the increased electrophilicity of the carbonyl carbon in the corresponding benzaldehydes, thereby facilitating rapid Schiff base formation and subsequent intramolecular cyclization (Ibrahim *et al.*, 2025; Alheety, 2025). In contrast, the electron-donating methoxy group in **RY-5**

resulted in a comparatively lower yield (75%), consistent with electronic effects documented in the literature for similar condensations.

Physicochemical characterization revealed a clear structure–property relationship influenced by the nature of the C-2 aryl substituents. Melting points ranged from 225–314°C, with the dihalogenated derivative **RY-6** and bromo analog **RY-3** exhibiting the highest values (312–314°C and 305–307°C, respectively). This trend is ascribed to enhanced intermolecular forces, including halogen bonding, π – π stacking, and increased molecular polarizability imparted by heavier halogens (Alheety, 2025). All compounds displayed high purity (>98%), as confirmed by TLC and elemental analysis, confirming the robustness and reproducibility of the synthetic route.

Comprehensive spectroscopic analysis provided unequivocal evidence for the successful formation of the 2-substituted benzimidazole nucleus. FT-IR spectra consistently showed the characteristic broad N–H stretching band (3200–3400 cm^{-1}) and the C=N stretching vibration of the imidazole ring (1585–1615 cm^{-1}), while the complete disappearance of the aldehyde carbonyl stretch further confirmed cyclocondensation. In $^1\text{H-NMR}$ spectra (DMSO- d_6), the diagnostic broad singlet for the benzimidazole N–H proton appeared at δ 12.4–12.9 ppm, and the aromatic protons exhibited expected splitting patterns corresponding to the substitution on the phenyl ring. The $^{13}\text{C-NMR}$ spectra displayed the characteristic C-2 resonance at δ 151.5–154.2 ppm, while ESI-MS confirmed the molecular ion peaks $[M+H]^+$ with correct isotopic patterns for halogenated derivatives. All spectral data were in excellent agreement with the proposed structures and comparable to those reported for analogous 2-arylbenzimidazoles (Ibrahim *et al.*, 2025; Mohammed *et al.*, 2023).

From a structure–activity perspective (even though biological screening was beyond the scope of the current characterization-focused study), the incorporation of diverse substituents at the para-position (and meta/para in **RY-6**) of the 2-phenyl ring allows systematic modulation of electronic, steric, and lipophilic properties. Halogen substituents (F, Cl, Br) are expected to enhance membrane permeability and binding affinity in potential biological targets such as DNA gyrase, topoisomerases, or CYP51, while the methyl and methoxy groups provide electron-donating effects that may influence solubility and metabolic stability (Brishty *et al.*, 2021; Shabana *et al.*, 2024). The successful synthesis of these six novel derivatives thus expands the chemical space around the privileged benzimidazole scaffold and provides a solid foundation for future structure–activity relationship (SAR) studies.

The results obtained in this work align well with and extend recent advances in benzimidazole chemistry, particularly the growing emphasis on green synthetic

methodologies (Nardi *et al.*, 2023; Alheety, 2025). By achieving high yields under mild conditions without chromatographic purification in most cases, the present protocol demonstrates practical superiority over several previously reported methods that suffer from longer reaction times, lower yields, or the use of corrosive acids.

Nevertheless, certain limitations of the current study are acknowledged. The investigation was restricted to synthesis and detailed physicochemical/spectroscopic characterization; *in vitro* biological evaluation, computational docking, and ADME profiling were not performed at this stage. Additionally, while the green synthetic approach is advantageous, further optimization for gram-scale production and assessment of reaction kinetics could be explored.

Overall, the design and successful synthesis of the novel 2-substituted benzimidazole derivatives **RY-1 to RY-6**, coupled with their complete structural elucidation, represent a meaningful contribution to pharmaceutical chemistry. These compounds not only enrich the library of benzimidazole-based molecules but also open new avenues for their biological screening against antimicrobial, anticancer, anti-inflammatory, and other therapeutic targets. Future studies will focus on the pharmacological evaluation of these leads, molecular docking simulations, and further structural diversification to identify candidates with enhanced potency and drug-like properties. The findings of this research underscore the continued relevance of the benzimidazole scaffold in addressing contemporary challenges in drug discovery and development.

5. CONCLUSION

The present research successfully accomplished the design, synthesis, and comprehensive characterization of six novel 2-substituted benzimidazole derivatives (**RY-1 to RY-6**). The adopted one-pot green synthetic methodology using sodium metabisulfite in ethanol proved to be highly efficient, environmentally friendly, and reproducible, delivering the target compounds in high yields (75–88%) with excellent purity.

Detailed physicochemical and spectroscopic studies (FT-IR, ¹H-NMR, ¹³C-NMR, and mass spectrometry) unequivocally confirmed the structures of all synthesized compounds. The spectral data revealed characteristic signals corresponding to the benzimidazole nucleus and the influence of various electron-withdrawing and electron-donating substituents on the 2-phenyl ring. Halogenated derivatives (**RY-1, RY-2, RY-3, and RY-6**) exhibited particularly high melting points and good crystallinity, highlighting favorable structure–property relationships.

This study not only expands the chemical library of benzimidazole-based molecules but also demonstrates the practical utility of green chemistry principles in

heterocyclic synthesis. The successful preparation of these novel derivatives (**RY-1 to RY-6**) provides a strong foundation for future investigations, including *in vitro* biological screening, molecular docking studies, and lead optimization.

In conclusion, the synthesized 2-substituted benzimidazole derivatives hold significant potential as versatile scaffolds in drug discovery. Further pharmacological evaluation of these compounds is warranted to explore their therapeutic applications in addressing current challenges such as antimicrobial resistance and other diseases.

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