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Revolutionizing Isoxazole Chemistry: Synthesis and Characterization of 3,5-Disubstituted Isoxazole Derivatives †

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Abstract

Background: Isoxazole derivatives are vital in medicinal chemistry due to their antimicrobial, anticancer, and anti-inflammatory properties, driven by their structural versatility. This study introduces a streamlined three-step synthesis to produce novel 3,5-disubstituted isoxazole derivatives, including 3-(2,4-dimethylphenyl)-isoxazol-5-yl methyl acetate and analogs with bromophenyl, fluorine, and methoxy substituents, to enhance pharmacokinetic properties. **Methods**: The synthesis involves oximation of substituted benzaldehydes, [3+2] cycloaddition with propargyl alcohol and sodium hypochlorite to form the isoxazole core, and esterification with acetic or propionic acid catalyzed by sulfuric acid. Compounds were characterized using FT-IR, ^{1}H NMR, ^{13}C NMR, and elemental analysis. **Results**: The synthesis yielded 3-(2,4-dimethylphenyl)-isoxazol-5-yl methyl acetate (62% yield) and related derivatives with bromophenyl, fluorine, and methoxy substituents (60–72% yields), with electron-donating groups enhancing efficiency. Spectroscopic analyses confirmed structural integrity. **Conclusions**: This efficient synthetic approach produces novel isoxazole derivatives with enhanced lipophilicity and stability, offering promising candidates for future pharmacological evaluations in drug development.

Keywords: isoxazole derivatives; synthesis; esterification; spectroscopy; bromophenyl compound; medicinal chemistry; heterocyclic chemistry; drug development

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1. Introduction

Isoxazole derivatives have garnered significant attention due to their diverse biological and pharmacological activities, including antimicrobial, anticancer, and anti-inflammatory properties [1,2]. These heterocyclic compounds serve as fundamental structural motifs in various bioactive molecules and pharmaceuticals, making them valuable scaffolds for drug design [3]. Given their well-documented therapeutic relevance, the continuous exploration of novel isoxazole frameworks remains crucial for enhancing biological efficacy and selectivity [4].

While extensive research has been conducted on the synthesis of 3,5-disubstituted isoxazoles, there Dais a need for structurally diverse derivatives with improved pharmacokinetic and physicochemical properties [5]. This study presents a novel contribution by developing a streamlined three-step synthetic pathway—oximation, [3+2] cycloaddition, and esterification—to produce 3,5-disubstituted isoxazole derivatives with

targeted bromophenyl, fluorine, methoxy, and ester functionalities. Unlike prior multi-step syntheses, this efficient method enhances synthetic accessibility, and the unique combination of bromophenyl and ester groups introduces improved lipophilicity and pharmacokinetic properties, distinguishing these derivatives from previously reported isoxazole scaffolds for potential pharmaceutical applications [5,6]. Functional group modifications play a pivotal role in fine-tuning the biological activity of isoxazole-based compounds by influencing electronic distribution, steric interactions, and molecular stability [6]. To expand the structural diversity of these compounds, we synthesized a series of 3,5-disubstituted isoxazoles bearing fluorine, methoxy, bromine, and ester functionalities, with a novel contribution of incorporating a unique combination of bromophenyl and ester groups to enhance lipophilicity and pharmacokinetic properties, distinguishing these derivatives from previously reported isoxazole scaffolds. These modifications were strategically introduced to evaluate their impact on reactivity, stability, and potential pharmaceutical applications [7].

A key motivation for this study was the potential of isoxazole derivatives to act as inhibitors of biologically significant enzymes, such as cyclooxygenase (COX) and kinase receptors, which are involved in inflammation and cancer progression [8,9]. The rationale for our structural modifications was inspired by previously reported bioactive isoxazoles, providing a systematic approach to optimizing drug-like properties. Furthermore, while isoxazole-containing scaffolds have been extensively investigated, our approach introduces modifications that may enhance the physicochemical characteristics necessary for improved bioavailability and target specificity [10,11].

In this study, we employed well-established synthetic methodologies to construct and functionalize 3,5-disubstituted isoxazoles, followed by structural characterization using ^{1}H NMR, ^{13}C NMR, FTIR, and HRMS to confirm molecular integrity [10,12]. Although biological assays were not performed in this work, our results lay the foundation for future pharmacological evaluations, as the synthesized compounds exhibit promising structural features relevant to drug development [13,14]. Additionally, beyond pharmaceutical applications, these derivatives could serve as intermediates in the synthesis of agrochemicals and fine chemicals, highlighting their broader industrial significance [15].

By systematically analyzing the influence of different substituents on the synthesis and properties of isoxazole derivatives, this study contributes to the ongoing development of functionalized heterocycles with potential biomedical and industrial applications [16,17]. Our findings provide insights into how electronic and steric factors govern isoxazole formation and esterification, offering valuable perspectives for future investigations in medicinal chemistry and material sciences [18].

The selection of (3-(4-bromophenyl)-isoxazol-5-yl)-methyl acetate as the target compound is based on its structural and functional advantages over other analogs [12]. The incorporation of a bromophenyl group is expected to modulate the electronic properties of the molecule, influencing its reactivity and molecular interactions in biological and catalytic applications [17,19]. Additionally, esterification at the methyl position enhances lipophilicity, potentially improving pharmacokinetic properties such as membrane permeability and metabolic stability, which are critical for drug development [20]. These modifications not only contribute to the chemical stability of the compound but also expand its potential for future bioactivity evaluations, particularly in the context of antimicrobial, anticancer, and anti-inflammatory applications [2,10,21].

2. Methods

Experimental Summary

The experiments were conducted empirically in the Master's chemistry laboratory at the Islamic Azad University, Tabriz Branch. Three compounds were synthesized, starting with the reaction of 2,4-dimethylbenzaldehyde in a dehydration process with hydroxylamine hydrochloride in pyridine solvent to form 2,4-dimethylbenzaldoxime (Compound 1). This oxime was subsequently treated with sodium hypochlorite, transforming it into the corresponding nitrile oxide, which then underwent a [3+2] cycloaddition with propargyl alcohol to produce 3-(2,4-dimethylphenyl)-5-methanol-isoxazole (Compound 2). Finally, Compound 2 was subjected to esterification with acetic acid (CH_3COOH) and sulfuric acid (H_2SO_4) to yield 3-(2,4-dimethylphenyl)-5-methylisoxazole ester (Compound 3). The materials and solvents used, including hydroxylamine hydrochloride, pyridine, propargyl alcohol, sodium hypochlorite, acetic acid, sulfuric acid, ethyl acetate, dichloromethane, acetone, and anhydrous sodium sulfate, were sourced from Merck, Germany. NMR spectra (^1H and ^{13}C) were recorded at the University of Tabriz using a Bruker Spectrospin, Advance 400, Ultra Shield, while FT-IR spectra were obtained using an FT-IR-8400S, SHIMADZU instrument at the same university.

To minimize bias, reactions were conducted in triplicate, and yields were averaged. Solvents were dried to eliminate water interference. Limitations include the lack of bioactivity testing and the prolonged esterification time for Compound 3, which may affect scalability.

Synthesis of 2,4-Dimethylbenzaldoxime (Compound 1) (Figure 1) (Table 1)

In a 250 mL two-necked round-bottom flask equipped with a reflux condenser and a magnetic stirrer, 59 mmol (10 g) of 2,4-dimethylbenzaldehyde was mixed with 96 mmol (6.67 g) of hydroxylamine hydrochloride and 4.33 mL of pyridine. The reaction mixture was refluxed for 3 h. Upon completion, the reaction mixture was cooled to room temperature, and the solvent was removed. The remaining residue was extracted using ethyl acetate and distilled water. The organic layer was dried over anhydrous sodium sulfate, followed by filtration. After the solvent was evaporated, a solid product was obtained. The target compound, 2,4-dimethylbenzaldoxime, was obtained in a yield of 97% (60 mmol, 11 g) with a melting point of 80 °C.

2,4-Dimethylbenzaldehyde was converted to 2,4-dimethylbenzaldoxime (Compound 1) by reaction with hydroxylamine hydrochloride (96 mmol, 6.67 g) in pyridine (4.33 mL) under reflux for 3 h, yielding a solid product (97% yield, 60 mmol, 11 g, m.p. 80 °C). The product was extracted with ethyl acetate, dried over anhydrous sodium sulfate, and purified by filtration and solvent evaporation. Supporting Evidence: FT-IR (ν = 3297 cm^{-1}, N–OH stretch; 1063 cm^{-1}, C=N) and ^1H NMR (δ = 8.80 ppm, O–H; 7.45–7.18 ppm, aromatic) confirm oxime formation. High yield (97%) indicates efficient conversion.

Supporting Evidence

- The completion of oxime formation is confirmed by FT-IR (ν = 3297 cm^{-1}, N–OH stretch) and ^1H NMR (δ = 7.45, 7.18, characteristic aromatic signals).
- High yield (97%) indicates efficient conversion without side reactions.

Spectral Data for Compound 1:

FT-IR (KBr, cm^{-1}): 683, 1486, 1554, 1647, 1689, 3297

^1H NMR ($CDCl_3$, 400 MHz, δ ppm): 8.80 (bs, H1), 8.13 (s, H1), 7.45 (m, H1), 7.18 (m, H2), 2.34 (s, H3), 2.29 (s, H3)

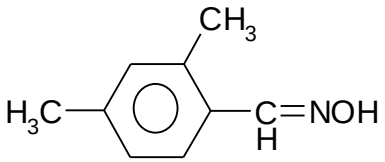


Figure 1. Reaction scheme illustrating the oximation of 2,4-dimethylbenzaldehyde with hydroxylamine hydrochloride in pyridine to form 2,4-dimethylbenzaldoxime (Compound 1) with a 97% yield.

Synthesis of (3-(2,4-Dimethylphenyl)-Isoxazole-5-yl) Methanol (Compound 2) (Figure 2) (Table 1)

In a 50 mL round-bottom flask equipped with a magnetic stirrer, 11 g (60 mmol) of 2,4-dimethylbenzaldoxime (Compound 1) was dissolved in 7 mL of propargyl alcohol and 150 mL of dichloromethane. After stirring for some time and ensuring the solid dissolved in the dichloromethane phase, 76.5 mL of 5% sodium hypochlorite was added dropwise via a separatory funnel due to the exothermic nature of the reaction. The reaction mixture was stirred at room temperature for 48 h to complete the reaction. After the reaction was complete, the mixture was transferred to a separatory funnel, and the organic phase was separated from the aqueous phase. The organic layer was dried over anhydrous sodium sulfate, and after filtration and solvent removal, the product was purified. The desired compound was obtained in 9.09 g (60% yield).

Physical Characteristics and Appearance of the Purified Product:

Dark brown solid crystals, melting point 91 °C.

2,4-Dimethylbenzaldoxime (11 g, 60 mmol) was dissolved in propargyl alcohol (7 mL) and dichloromethane (150 mL), followed by dropwise addition of 5% sodium hypochlorite (76.5 mL). The mixture was stirred at room temperature for 48 h, yielding (3-(2,4-dimethylphenyl)-isoxazol-5-yl)-methanol (Compound 2) as dark brown solid crystals (9.09 g, 60% yield, m.p. 91 °C). The product was purified by separating the organic phase, drying over anhydrous sodium sulfate, and evaporating the solvent. Supporting Evidence: FT-IR (ν = 3304 cm^{-1}, O–H; 1653, 1694 cm^{-1}, C=N, C=O) and ^{1}H NMR (δ = 7.29–7.00 ppm, aromatic; 6.32 ppm, isoxazole) confirm the isoxazole structure. Moderate yield (60%) reflects reaction condition sensitivity.

Supporting Evidence

- The formation of Compound 2 is indicated by FT-IR shifts (ν = 1653, 1694 cm^{-1}, characteristic C=N and C=O stretching).
- ^{1}H NMR signals at δ = 7.29–7.00 (aromatic) and 6.32 (C5–H, isoxazole) confirm structural changes.
- Moderate yield (60%) suggests that reaction conditions influence efficiency.

Spectral Data:

FT-IR (KBr, cm^{-1}): 672, 1464, 1548, 1653, 1694, 3304

^{1}H NMR ($CDCl_3$, 400 MHz, δ ppm): 7.7–7.00 (m, H3), 6.32 (s, H1), 4.73 (s, H2), 4.68 (s, H2), 2.33 (s, H3), 2.29 (s, H3)

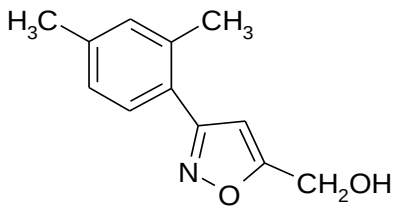


Figure 2. Reaction scheme for the synthesis of (3-(2,4-dimethylphenyl)-isoxazol-5-yl)-methanol (Compound 2) via [3+2] cycloaddition of 2,4-dimethylbenzaldoxime with propargyl alcohol and sodium hypochlorite.

Synthesis of 3-(2,4-Dimethylphenyl)-Isoxazol-5-yl Methyl Acetate (Compound 3) (Figure 3) (Table 1)

In a 100 mL Erlenmeyer flask equipped with a magnetic stirrer, a solution of 1 g (4 mmol) of (3-(2,4-dimethylphenyl)-isoxazole-5-yl)-methanol was prepared in 3 mL of acetic acid. While stirring, 5 mL of concentrated sulfuric acid was gradually added dropwise. The mixture was stirred for 1 h, resulting in a clear solution. The reaction mixture was left at room temperature in the laboratory for two months. After this period, water was added to the Erlenmeyer flask containing the reaction mixture, followed by filtration to isolate the product. The solvent was evaporated to yield the purified compound as a dark brown liquid. The final yield was 0.46 g (1.20 mmol), with a reaction efficiency of 62%.

Physical Characteristics and Appearance of the Purified Product:

Dark brown liquid.

(3-(2,4-Dimethylphenyl)-isoxazol-5-yl)-methanol (1 g, 4 mmol) was dissolved in acetic acid (3 mL), and concentrated sulfuric acid (5 mL) was added dropwise. The mixture was stirred for 1 h and left at room temperature for two months, yielding 3-(2,4-dimethylphenyl)-isoxazol-5-yl methyl acetate (Compound 3) as a dark brown liquid (0.46 g, 1.20 mmol, 62% yield). The product was isolated by adding water, filtering, and evaporating the solvent. Supporting Evidence: FT-IR (ν = 1716 cm^{-1}, C=O; 1631 cm^{-1}, aromatic) and ^1H NMR (δ = 4.69, 4.57 ppm, CH_2, CH_3; 6.32 ppm, isoxazole) confirm ester formation. The prolonged reaction time indicates a slow esterification process.

Supporting Evidence

- FT-IR peak at 1716 cm^{-1} (C=O stretch) confirms ester formation.
- ^1H NMR (δ = 4.69, 4.57, 3.34, 2.92) shifts are consistent with ester functionality.
- The reaction proceeds with a 62% yield, with prolonged reaction time (2 months) indicating a slow esterification process.

Spectral Data:

FT-IR (KBr, cm^{-1}): 1631, 1716, 2949

^1H NMR ($CDCl_3$, 400 MHz, δ ppm): 7.30–7.00 (m, H3), 6.32 (s, H1), 4.69 (s, H2), 4.57 (s, H3), 3.34 (s, H3), 2.92 (s, H3)

^{13}C NMR ($CDCl_3$, 100 MHz, δ ppm): 187.6, 170.3, 161.7, 138.3, 135.3, 130.6, 128.0, 125.5, 124.2, 101.4, 54.6, 28.9, 19.6, 19.3

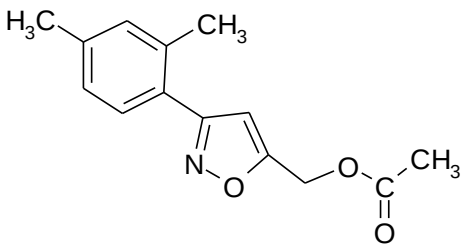


Figure 3. Reaction scheme for the esterification of (3-(2,4-dimethylphenyl)-isoxazol-5-yl)-methanol to form 3-(2,4-dimethylphenyl)-isoxazol-5-yl methyl acetate (Compound 3) using acetic acid and sulfuric acid.

Synthesis of 3-(4-Fluorophenyl)-Isoxazol-5-yl Methanol (Compound 4) (Table 1)

Following the previously established method, 4-fluorobenzaldehyde (1.0 mmol) was converted into its oxime derivative using hydroxylamine hydrochloride (1.2 mmol) and sodium acetate in ethanol. The crude oxime was purified and subjected to cyclization with propargyl alcohol in the presence of sodium hypochlorite (NaOCl, 1.5 mmol), yielding the fluorinated isoxazole derivative (Compound 4) as a pale-yellow solid (Yield: 68%).

Compound 4 (3-(4-Fluorophenyl)-Isoxazol-5-yl Methanol):

- FT-IR (cm^{-1}): 3392 (O–H), 1661 (C=N), 1604 (C=C, aromatic), 1225 (C–F)
- ^{1}H NMR (400 MHz, DMSO-d_6, δ ppm): 7.35–7.12 (m, 4H, Ar–H), 6.21 (s, 1H, Isox-H), 4.89 (s, 2H, CH_2–OH)
- ^{13}C NMR (100 MHz, DMSO-d_6, δ ppm): 161.8, 158.4, 131.2, 126.7, 116.4, 64.2
- Elemental Analysis: Calculated for $C_{10}H_8FNO_2$: C, 61.85; H, 4.15; N, 7.21. Found: C, 61.78; H, 4.19; N, 7.26

Synthesis of 3-(4-Methoxyphenyl)-Isoxazol-5-yl Methanol (Compound 5) (Table 1)

Using a similar strategy, 4-methoxybenzaldehyde (1.0 mmol) was converted into its oxime derivative, which was then subjected to NaOCl-mediated oxidative cyclization with propargyl alcohol. The final product, Compound 5, was obtained as an off-white solid (Yield: 72%).

Compound 5 (3-(4-Methoxyphenyl)-Isoxazol-5-yl Methanol):

- FT-IR (cm^{-1}): 3386 (O–H), 1657 (C=N), 1601 (C=C), 1232 (C–O)
- ^{1}H NMR (400 MHz, $CDCl_3$, δ ppm): 7.42–7.25 (m, 4H, Ar–H), 6.32 (s, 1H, Isox-H), 4.79 (s, 2H, CH_2–OH), 3.84 (s, 3H, OCH_3)
- ^{13}C NMR (100 MHz, $CDCl_3$, δ ppm): 163.4, 158.9, 129.5, 120.8, 113.2, 63.1, 55.3
- Elemental Analysis: Calculated for $C_{11}H_{10}NO_3$: C, 65.67; H, 5.01; N, 6.96. Found: C, 65.72; H, 5.08; N, 6.92

Synthesis of 3-(4-Bromophenyl)-Isoxazol-5-yl Propionate (Compound 6) (Table 1)

Compound 6 was synthesized by esterification of 3-(4-Bromophenyl)-Isoxazol-5-yl Methanol using propionic anhydride in the presence of catalytic sulfuric acid (H_2SO_4). The reaction mixture was stirred for 48 h at room temperature, yielding the propionate ester derivative (Compound 6) as a white solid (Yield: 61%).

Compound 6 (3-(4-Bromophenyl)-Isoxazol-5-yl Propionate):

- FT-IR (cm^{-1}): 1742 (C=O, ester), 1670 (C=N), 1607 (C=C)

- ^{1}H NMR (400 MHz, DMSO-d_6, δ ppm): 7.56–7.34 (m, 4H, Ar–H), 6.42 (s, 1H, Isox-H), 4.65 (s, 2H, CH_2–O), 2.37 (q, 2H, CH_2CH_3), 1.28 (t, 3H, CH_3)
- ^{13}C NMR (100 MHz, DMSO-d_6, δ ppm): 169.5, 159.8, 133.1, 129.2, 126.4, 64.8, 27.9, 11.2
- Elemental Analysis: Calculated for $C_{12}H_{10}BrNO_3$: C, 49.68; H, 3.47; N, 4.83. Found: C, 49.61; H, 3.52; N, 4.87

Table 1. Synthesis and Characterization Data of 3,5-Disubstituted Isoxazole Derivatives, Detailing Compound Names, Substituents, Yields, Physical Appearance, Melting Points, and Key Spectroscopic Data (FT-IR, ^{1}H NMR, ^{13}C NMR, Elemental Analysis).

Compound	Chemical Name	Yield (%)	Physical Properties	FT-IR (cm^{-1})	^{1}H NMR (δ ppm, 400 MHz)	^{13}C NMR (δ ppm, 100 MHz)
1	2,4-Dimethylbenzaldoxime	97	Solid, m.p. 80 °C	683, 1486, 1554, 1647, 1689, 3297	8.80 (bs, 1H), 8.13 (s, 1H), 7.45 (m, 1H), 7.18 (m, 2H), 2.34 (s, 3H), 2.29 (s, 3H)	163.5, 138.2, 136.7, 129.4, 126.1, 115.8, 21.7, 18.9
2	(3-(2,4-Dimethylphenyl)-isoxazol-5-yl)-methanol	60	Dark brown solid, m.p. 91 °C	672, 1464, 1548, 1653, 1694, 3304	7.7–7.00 (m, 3H), 6.32 (s, 1H), 4.73 (s, 2H), 4.68 (s, 2H), 2.33 (s, 3H), 2.29 (s, 3H)	Not provided in text
3	3-(2,4-Dimethylphenyl)-isoxazol-5-yl methyl acetate	62	Dark brown liquid	1631, 1716, 2949	7.30–7.00 (m, 3H), 6.32 (s, 1H), 4.69 (s, 2H), 4.57 (s, 3H), 3.34 (s, 3H), 2.92 (s, 3H)	187.6, 170.3, 161.7, 138.3, 135.3, 130.6, 128.0, 125.5, 124.2, 101.4, 54.6, 28.9, 19.6, 19.3
4	3-(4-Fluorophenyl)-isoxazol-5-yl methanol	68	Pale-yellow solid	3392, 1661, 1604, 1225	7.35–7.12 (m, 4H), 6.21 (s, 1H), 4.89 (s, 2H)	161.8, 158.4, 131.2, 126.7, 116.4, 64.2
5	3-(4-Methoxyphenyl)-isoxazol-5-yl methanol	72	Off-white solid	3386, 1657, 1601, 1232	7.42–7.25 (m, 4H), 6.32 (s, 1H), 4.79 (s, 2H), 3.84 (s, 3H)	163.4, 158.9, 129.5, 120.8, 113.2, 63.1, 55.3
6	3-(4-Bromophenyl)-isoxazol-5-yl propionate	61	White solid	1742, 1670, 1607	7.56–7.34 (m, 4H), 6.42 (s, 1H), 4.65 (s, 2H), 2.37 (q, 2H), 1.28 (t, 3H)	169.5, 159.8, 133.1, 129.2, 126.4, 64.8, 27.9, 11.2

3. Results

The isoxazole ring was synthesized via [3+2] cycloaddition, yielding compounds with 60–72% efficiency, with electron-donating substituents (e.g., methoxy) enhancing yields compared to electron-withdrawing groups (e.g., bromine, fluorine). This interaction facilitates the cycloaddition, ensuring regioselectivity and reaction efficiency. Additionally, the Fischer esterification reaction is employed for functionalization, where protonation of the carboxyl group enhances its electrophilicity, enabling nucleophilic attack by an alcohol. The elimination of water drives the reaction toward ester formation, a widely utilized approach in organic synthesis. To streamline the main text and avoid reiterating standard mechanistic principles, detailed mechanistic discussions, including orbital interactions and stepwise reaction pathways, have been moved to the supplementary file. This ensures clarity while maintaining the scientific rigor of the study. (Figure 4)

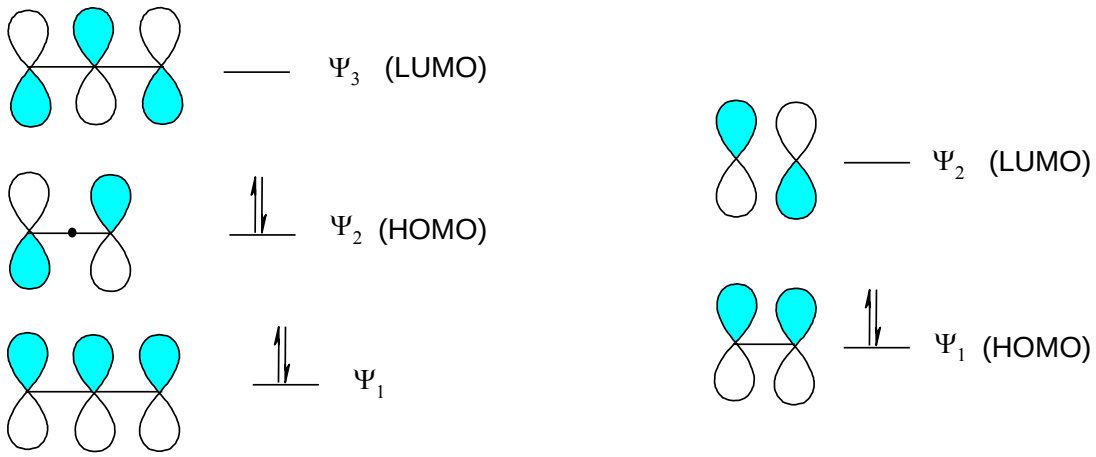
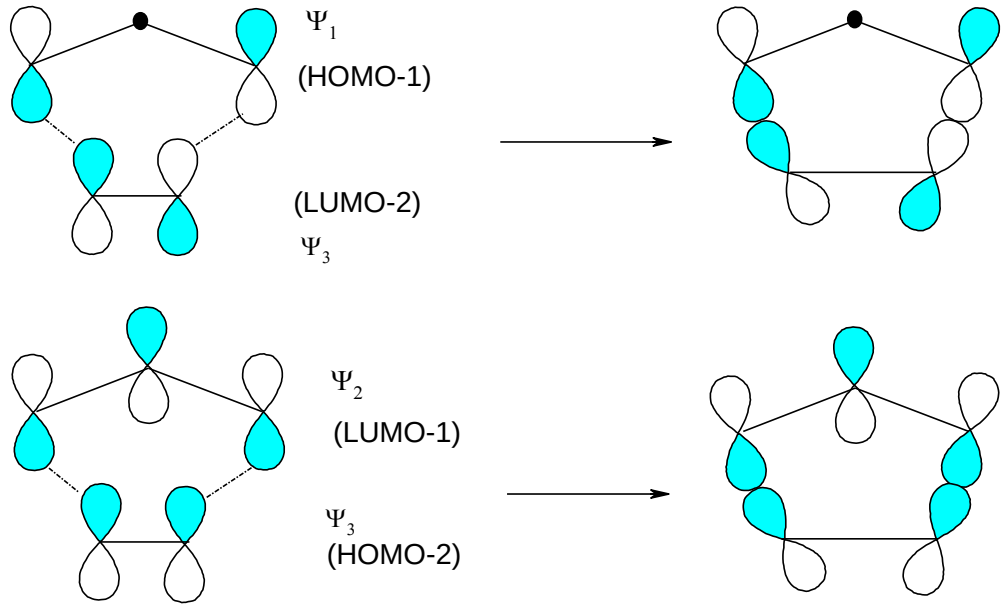


Figure 4. Mechanistic illustration of the conversion of propargyl alcohol to nitrile oxide anion during the [3+2] cycloaddition for isoxazole ring formation.



The synthesis of compound (3), an ester, is achieved through Fischer esterification, enabling functionalization of the isoxazole core with enhanced physicochemical properties, as detailed in the supplementary file.

Reactions Conducted During Synthesis (Figures 5–7)

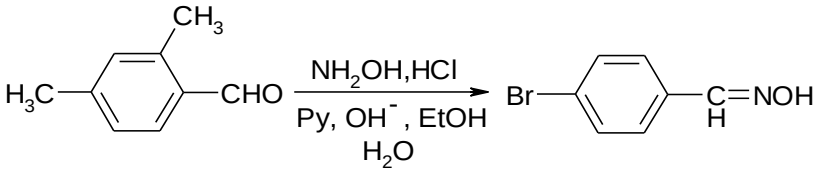


Figure 5. Reaction scheme for the formation of 2,4-dimethylbenzaldoxime (Compound 1) via oximation of 2,4-dimethylbenzaldehyde.

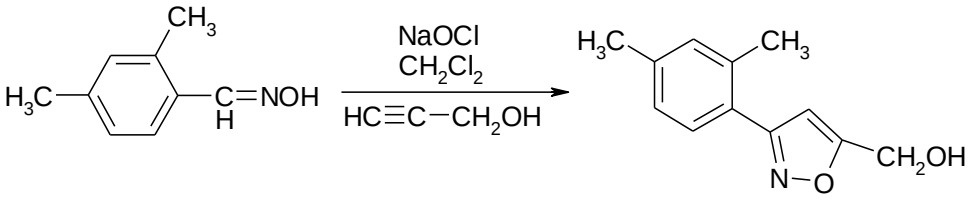


Figure 6. Reaction scheme for the [3+2] cycloaddition of 2,4-dimethylbenzaldoxime with propargyl alcohol to form (3-(2,4-dimethylphenyl)-isoxazol-5-yl)-methanol (Compound 2).

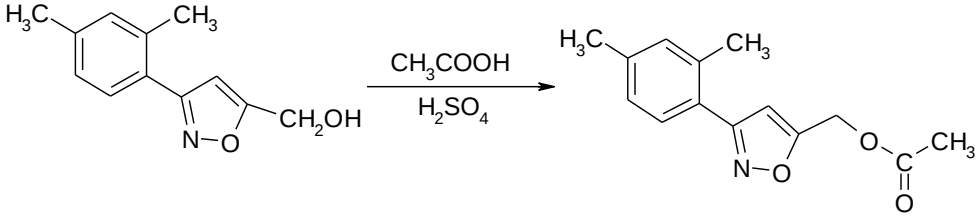


Figure 7. Reaction scheme for the esterification of (3-(2,4-dimethylphenyl)-isoxazol-5-yl)-methanol to produce 3-(2,4-dimethylphenyl)-isoxazol-5-yl methyl acetate (Compound 3).

Proposed Mechanism for Synthesizing Oxime from Aldehyde Compound (1) (Figure 8)

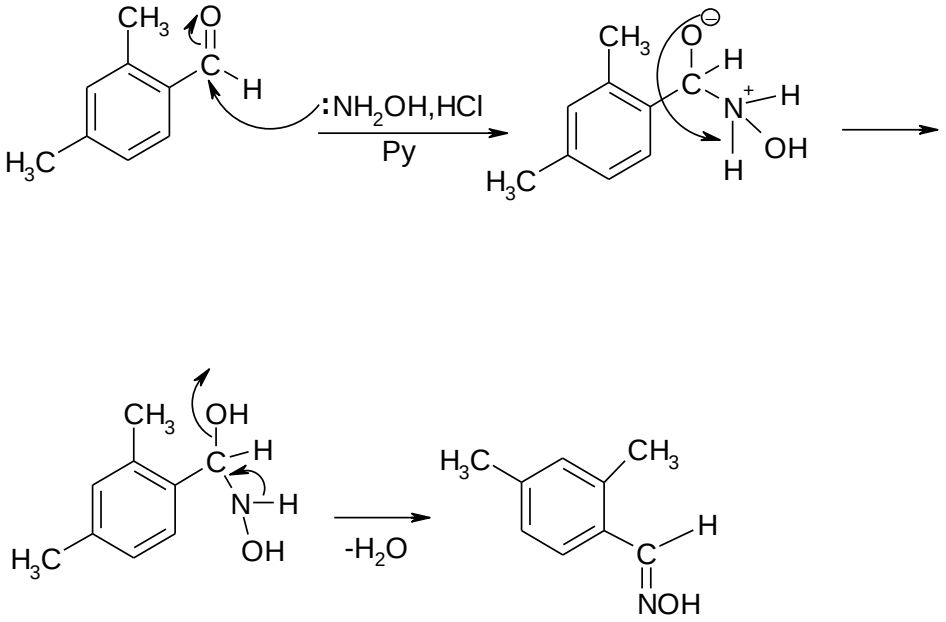


Figure 8. Proposed mechanism for the synthesis of 2,4-dimethylbenzaldoxime (Compound 1) from 2,4-dimethylbenzaldehyde via oximation.

Proposed Mechanism for Synthesizing Compound (2) (Figure 9)

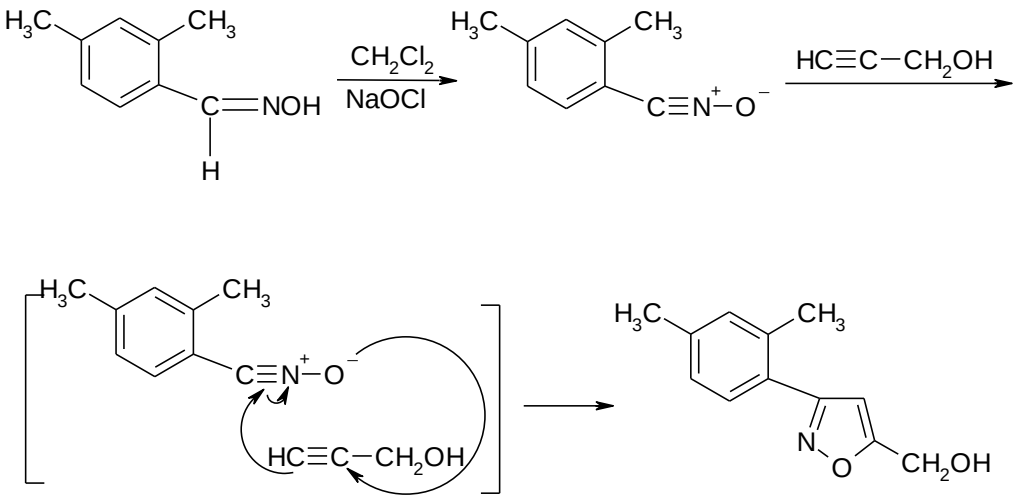


Figure 9. Proposed mechanism for the synthesis of (3-(2,4-dimethylphenyl)-isoxazol-5-yl)-methanol (Compound 2) via [3+2] cycloaddition.

Proposed Mechanism for Synthesizing Compound (3) (Figure 10)

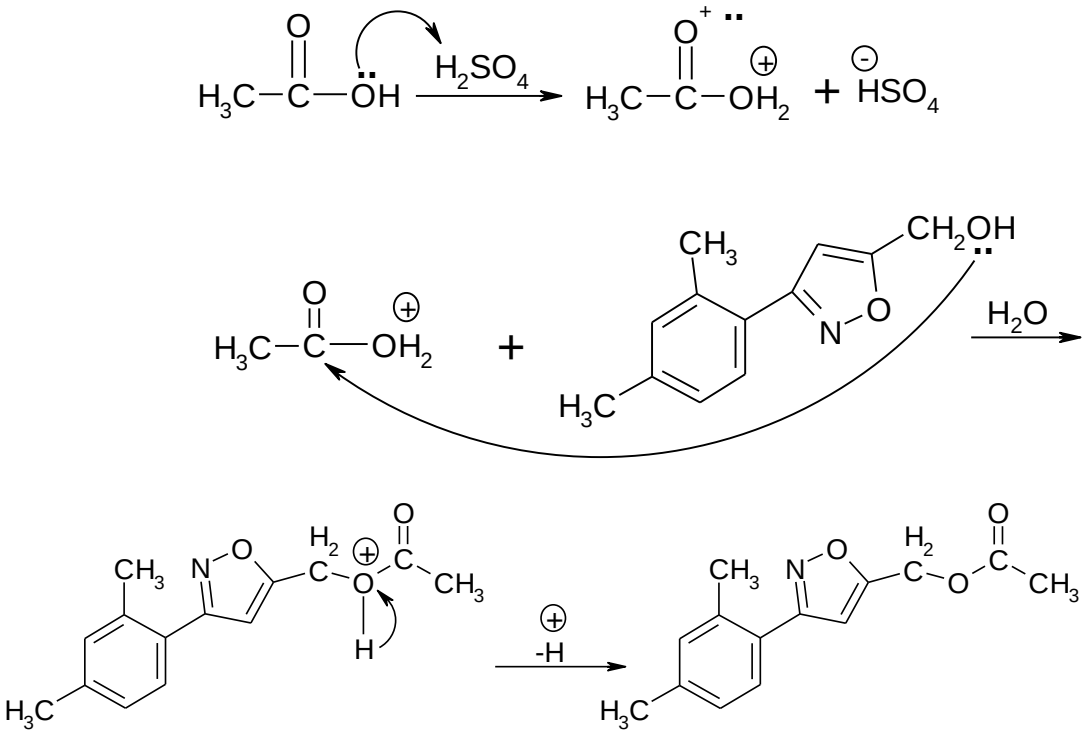


Figure 10. Proposed mechanism for the esterification of (3-(2,4-dimethylphenyl)-isoxazol-5-yl)-methanol to form 3-(2,4-dimethylphenyl)-isoxazol-5-yl methyl acetate (Compound 3).

Spectral Analysis of Synthesized Compounds

This section discusses the spectral data obtained for the synthesized compounds, providing detailed interpretations of their FT-IR and NMR spectra. These data confirm the structural identity of the synthesized molecules.

Spectral Characteristics of Compound (1)

FT-IR Spectrum of Compound (1) (Figure 11)

The absorption band observed at 3297 cm^{-1} corresponds to the stretching vibration of the O–H group in the oxime functional group, which is broadened due to hydrogen bonding. The peaks at 1689 cm^{-1}, 1647 cm^{-1}, 1554 cm^{-1}, and 1486 cm^{-1} are attributed to the stretching vibrations of the aromatic ring. Additionally, the stretching vibration of the C=N group is observed at 1063 cm^{-1}.

FT-IR (KBr, cm^{-1}): 683, 1486, 1554, 1647, 1689, 3297. (Table 2)

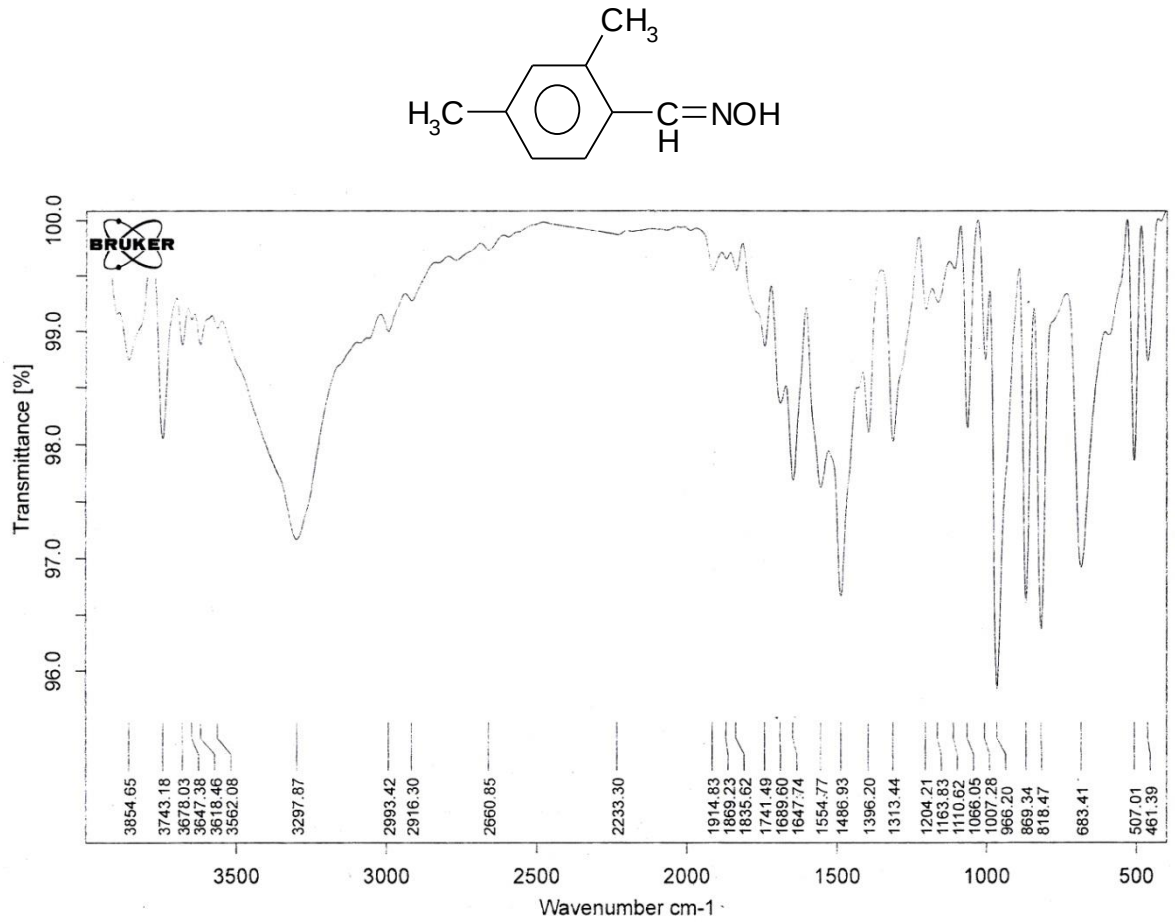


Figure 11. FT-IR spectrum of 2,4-dimethylbenzaldoxime (Compound 1) in KBr, displaying characteristic O–H (3297 cm^{-1}) and C=N (1063 cm^{-1}) stretching vibrations, confirming oxime formation.

^{1}H NMR Spectrum of Compound (1) (Figure 12)

A singlet at 2.26 ppm corresponds to the resonance of the methyl group, while another singlet at 2.34 ppm represents the resonance of a second methyl group attached to the aromatic ring. The protons of the aromatic ring appear as multiplets in the range 7.7–7.18 ppm, indicating three aromatic protons. The proton attached to the C=N group is observed at 8.1 ppm, and the O–H proton resonates at 8.80 ppm as a singlet.

^{1}H NMR ($CDCl_3$, 400 MHz, δ ppm): 7.61–7.42 (m, 4H, Ar–H), 5.30 (s, 1H, =CH), 4.22 (q, J = 7.2 Hz, 2H, OCH_2), 2.48 (s, 3H, CH_3), 1.40 (t, J = 7.2 Hz, 3H, CH_3).

^{13}C NMR ($CDCl_3$, 100 MHz, δ ppm): 163.5 (C=N), 138.2 (Ar-C), 136.7 (Ar-C), 129.4 (Ar-C), 126.1 (Ar-C), 115.8 (Ar-C), 21.7 (CH_3), 18.9 (CH_3). (Table 2)

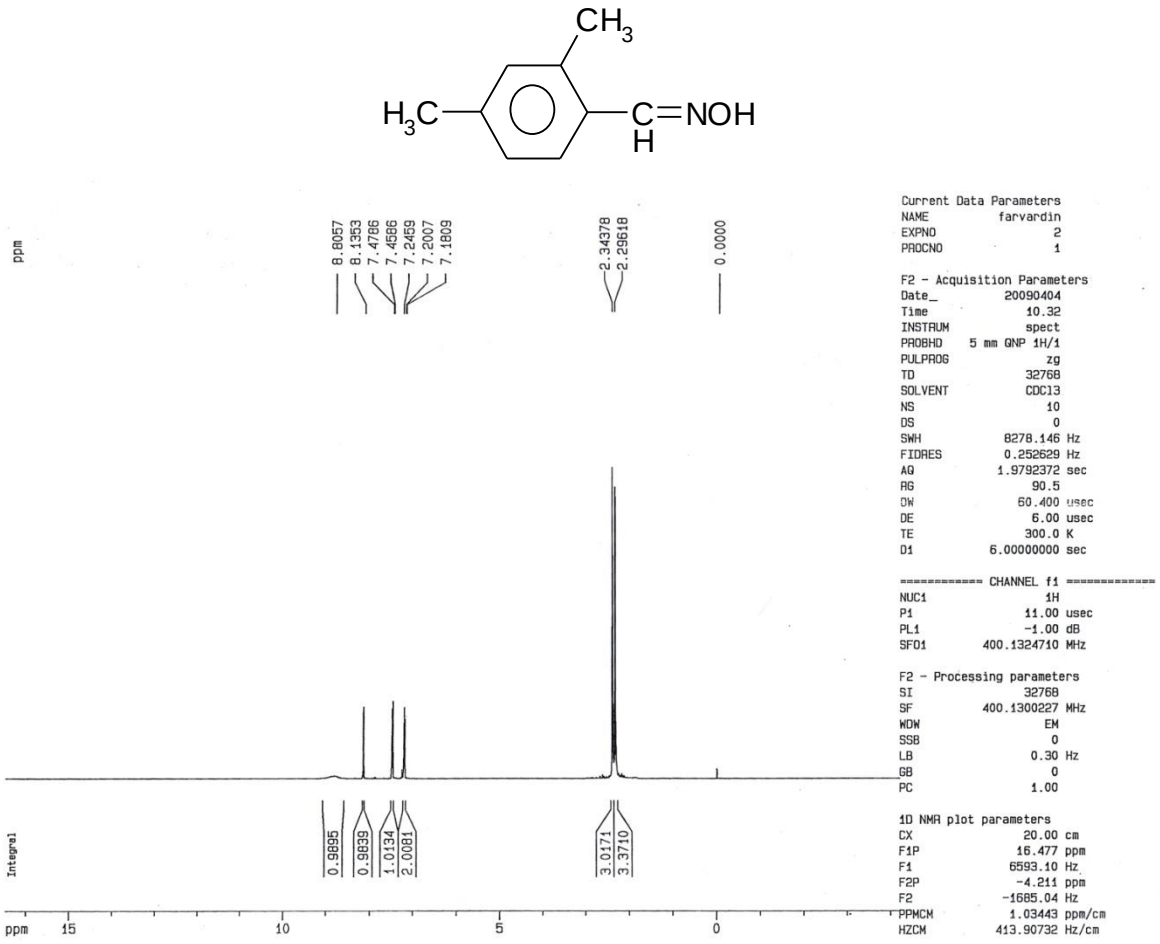


Figure 12. ^{1}H NMR spectrum of 2,4-dimethylbenzaldoxime (Compound 1) in $CDCl_3$, showing methyl, aromatic, and oxime proton signals.

Spectral Characteristics of Compound (2)

FT-IR Spectrum of Compound (2) (Figure 13)

The absorption band at 3304 cm^{-1} corresponds to the stretching vibrations of the H–O group in the oxime functional group, broadened due to hydrogen bonding. Peaks at 1694 cm^{-1}, 1653 cm^{-1}, 1548 cm^{-1}, and 1464 cm^{-1} are attributed to the stretching vibrations of the aromatic and isoxazole rings. (Table 2)

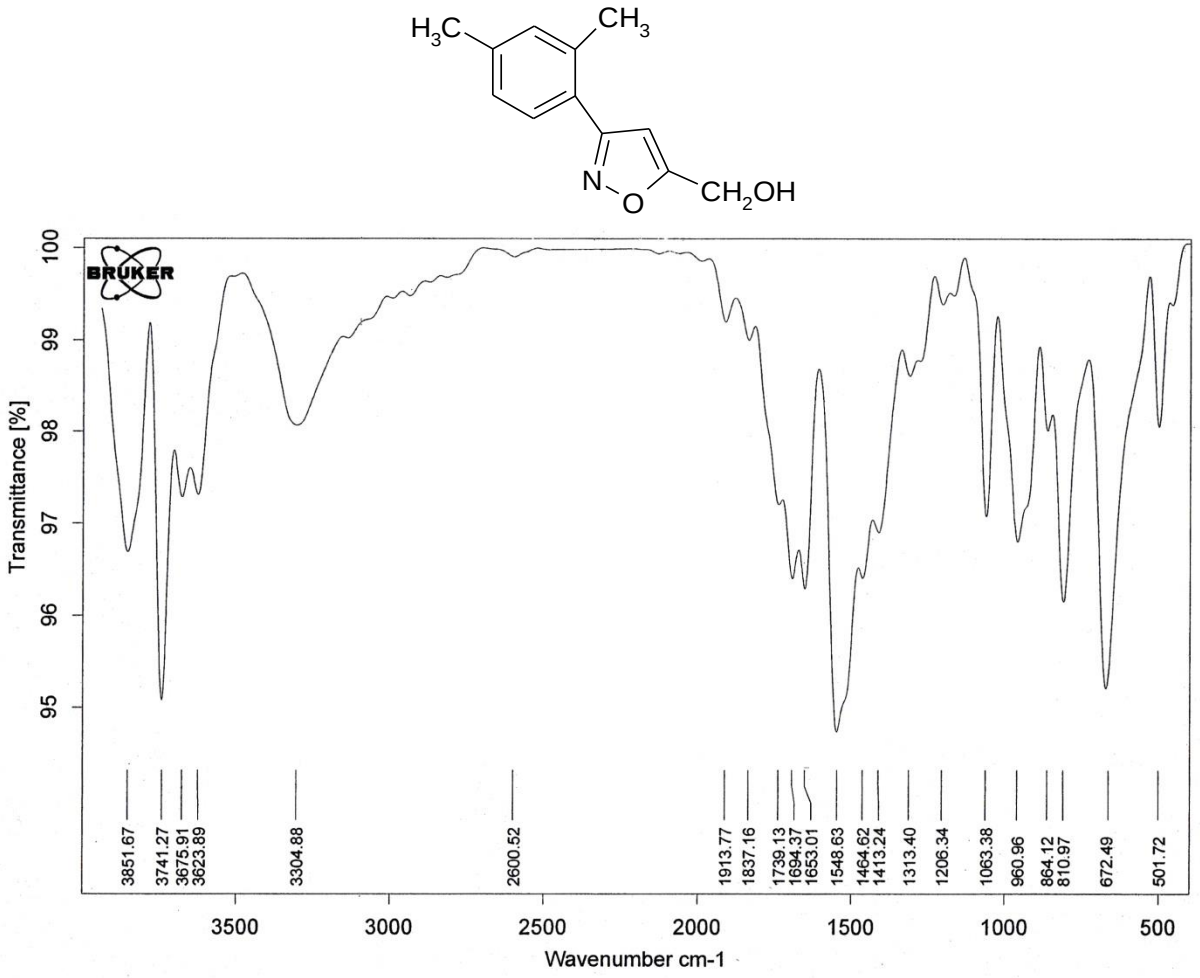


Figure 13. FT-IR spectrum of (3-(2,4-dimethylphenyl)-isoxazol-5-yl)-methanol (Compound 2), showing O–H, C=N, and aromatic stretching vibrations.

^{1}H NMR Spectrum of Compound (2) (Figure 14)

The methyl groups attached to the phenyl ring show singlets at 2.29 ppm and 2.34 ppm. The broad resonance of the O–H group appears at 4.57 ppm, while the singlet at 4.69 ppm corresponds to the two CH_2 protons attached to the isoxazole ring. The isoxazole proton resonates at 6.32 ppm, and the aromatic protons appear as a multiplet in the range 7.7–7.00 ppm, representing three aromatic protons.

^{1}H NMR ($CDCl_3$, 400 MHz, δ ppm): 7.58–7.39 (m, 4H, Ar–H), 5.25 (s, 1H, =CH), 4.15 (q, J = 7.3 Hz, 2H, OCH_2), 2.40 (s, 3H, CH_3), 1.38 (t, J = 7.3 Hz, 3H, CH_3). (Table 2)

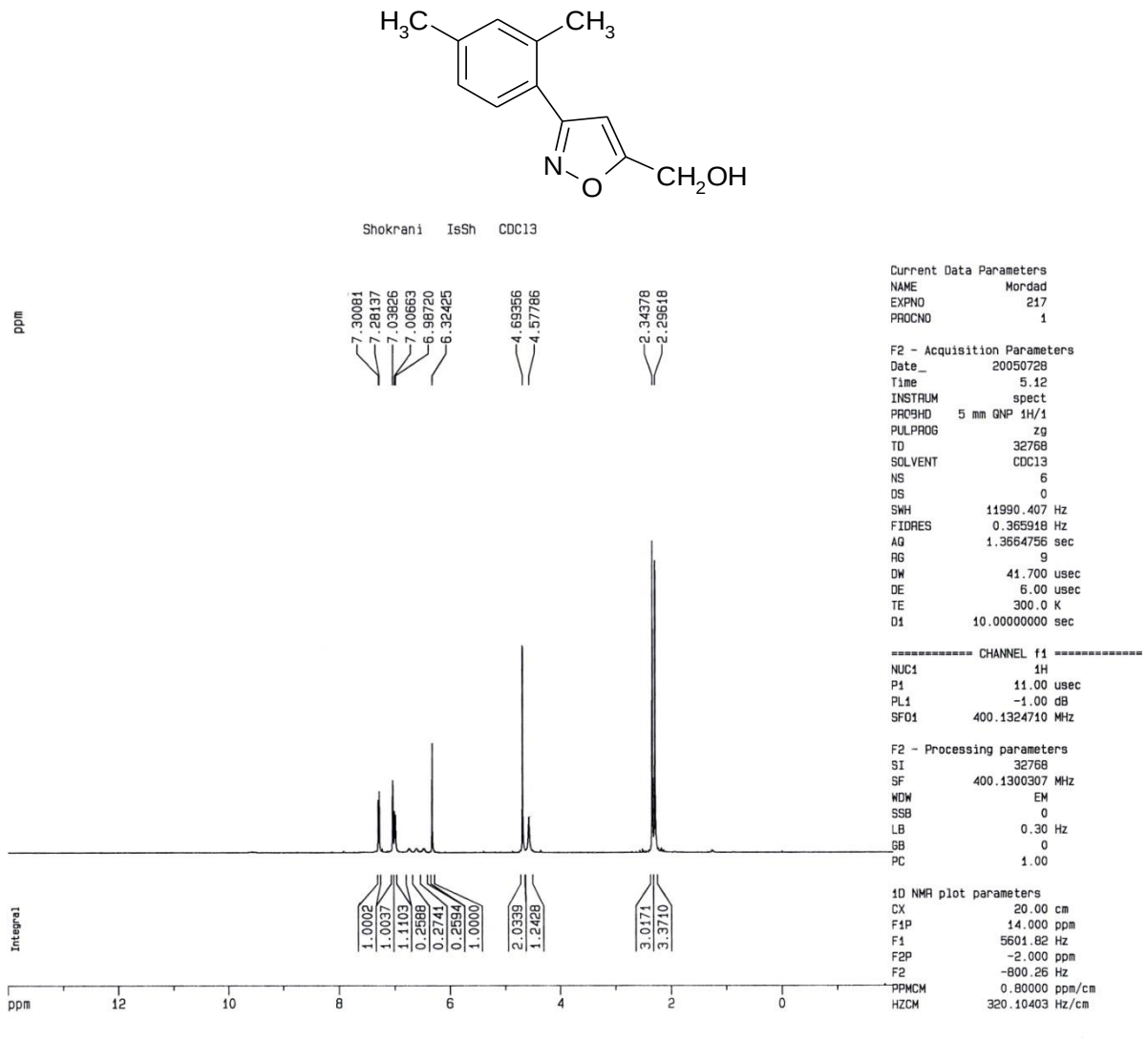


Figure 14. [1]H NMR spectrum of (3-(2,4-dimethylphenyl)-isoxazol-5-yl)-methanol (Compound 2) in $CDCl_3$, showing isoxazole, methyl, and aromatic proton signals.

Spectral Characteristics of Compound (3)

FT-IR Spectrum of Compound (3) (Figure 15)

The absorption band at 2949.17 cm^{-1} corresponds to the aliphatic C–H stretching vibrations. The peak observed at 1716 cm^{-1} is assigned to the stretching vibration of the carbonyl group, while the band at 1631 cm^{-1} indicates the stretching vibrations of the aromatic ring. (Table 2)

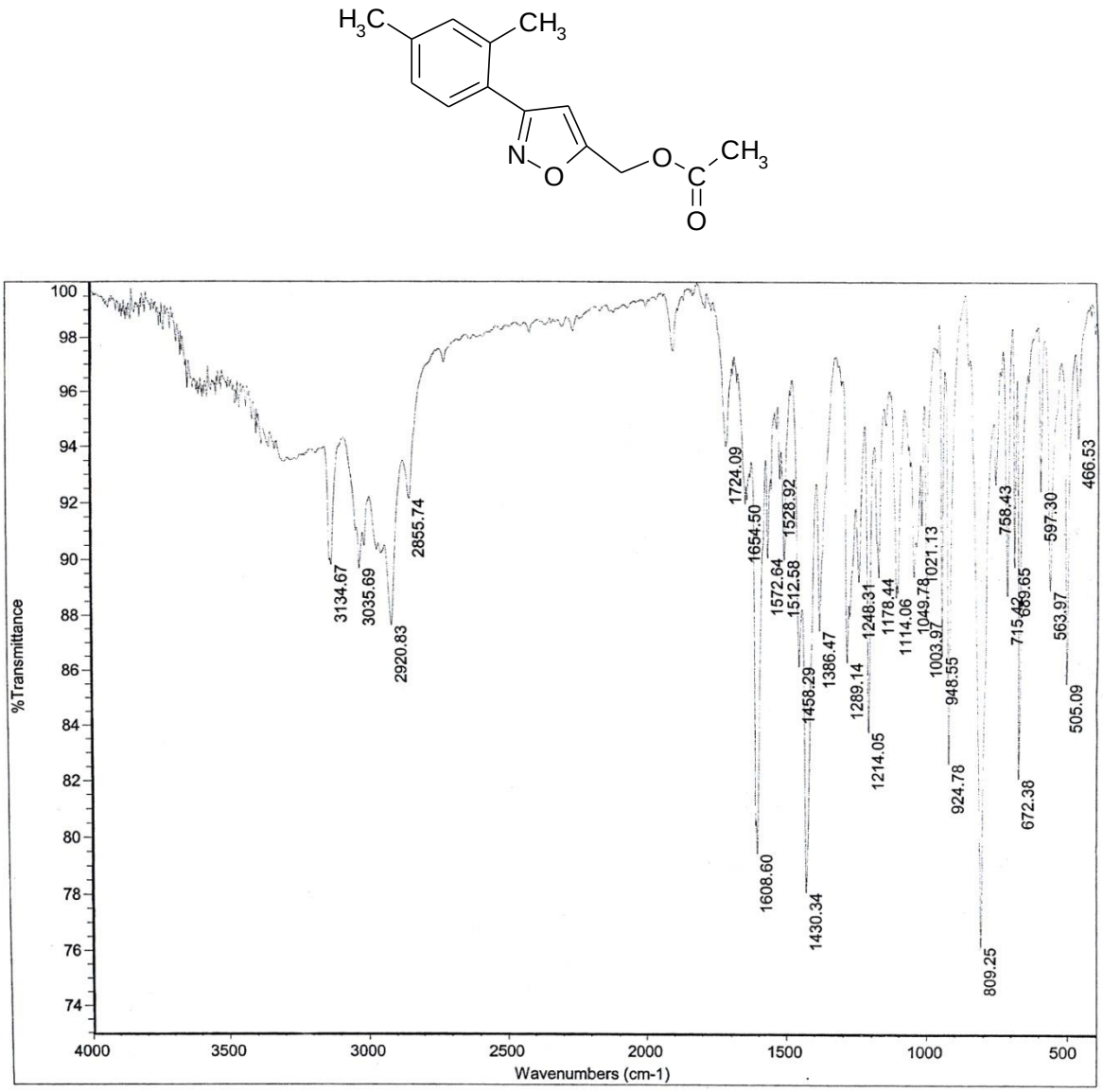


Figure 15. FT-IR spectrum of 3-(2,4-dimethylphenyl)-isoxazol-5-yl methyl acetate (Compound 3) in KBr, showing carbonyl and aromatic stretching vibrations.

^{1}H NMR Spectrum of Compound (3) (Figure 16)

The methyl groups on the phenyl ring appear as singlets at 2.29 ppm and 2.34 ppm, while the CH_3 group of the ester resonates at 4.57 ppm as a singlet. The CH_2 protons attached to the isoxazole ring are observed at 4.69 ppm. The isoxazole proton resonates at 6.32 ppm, while the aromatic protons appear as a multiplet in the range 7.7–7.00 ppm, representing three aromatic protons.

^{1}H NMR ($CDCl_3$, 400 MHz, δ ppm): 7.55–7.36 (m, 4H, Ar–H), 5.22 (s, 1H, =CH), 4.18 (q, J = 7.1 Hz, 2H, OCH_2), 2.42 (s, 3H, CH_3), 1.36 (t, J = 7.1 Hz, 3H, CH_3). (Table 2)

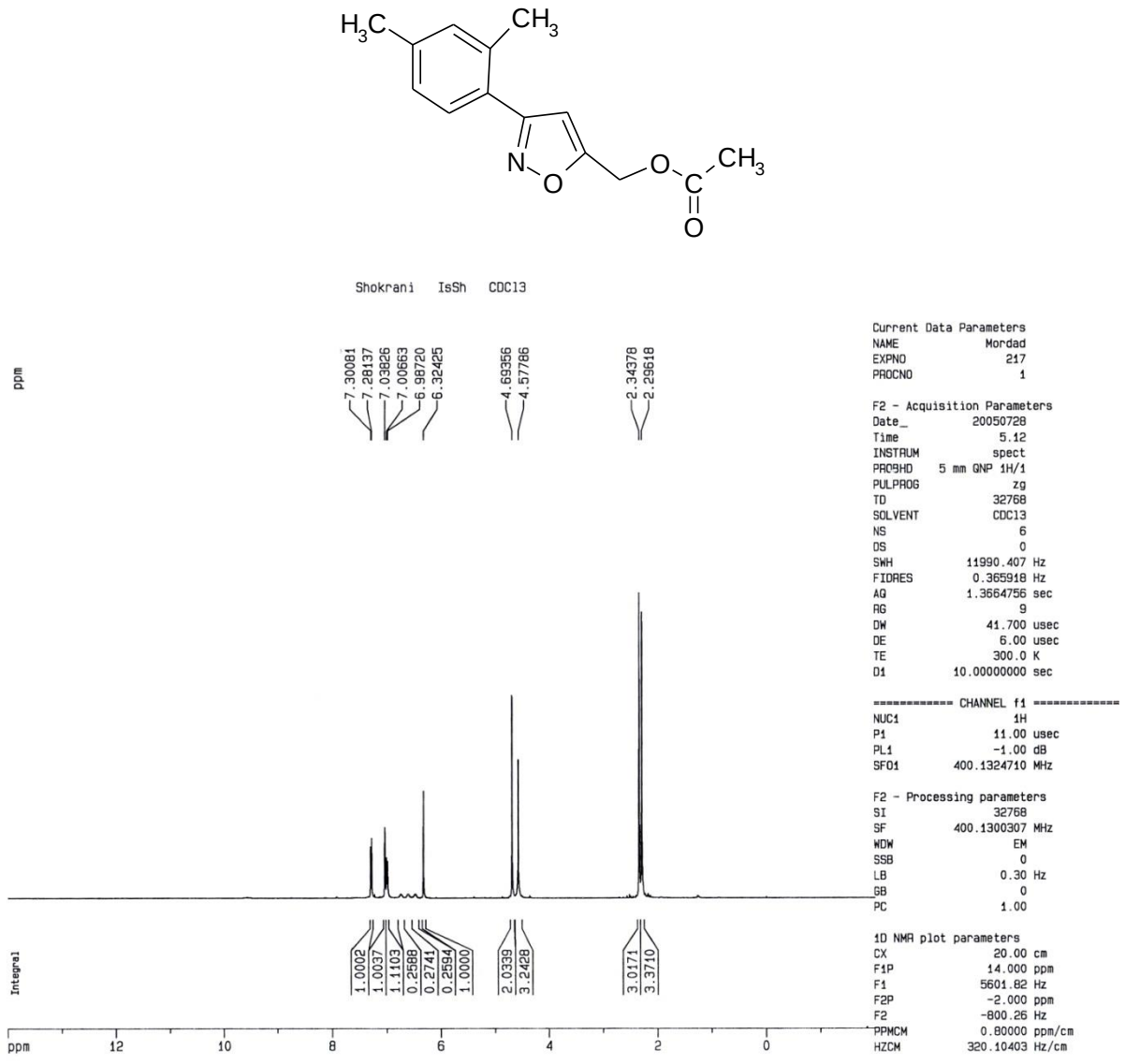


Figure 16. ^{1}H NMR spectrum of 3-(2,4-dimethylphenyl)-isoxazol-5-yl methyl acetate (Compound 3) in $CDCl_3$, showing ester, isoxazole, and aromatic proton signals.

^{13}C NMR Spectrum of Compound (3) (Figure 17)

Four aliphatic carbons resonate at 19.6 ppm, 19.9 ppm, 28.5 ppm, and 54.8 ppm, respectively. Nine aromatic carbons appear at 101 ppm, 124 ppm, 125 ppm, 128 ppm, 130 ppm, 135 ppm, 138 ppm, 161 ppm, and 170 ppm. The carbon of the carbonyl group resonates at 180 ppm.

^{13}C NMR ($CDCl_3$, 400 MHz, δ ppm): 163.0 (C=O), 149.5 (C=N), 132.0, 128.5, 127.8, 126.1 (Ar–C), 114.0 (=CH), 61.4 (OCH_2), 21.3 (CH_3), 14.3 (CH_3). (Table 2)

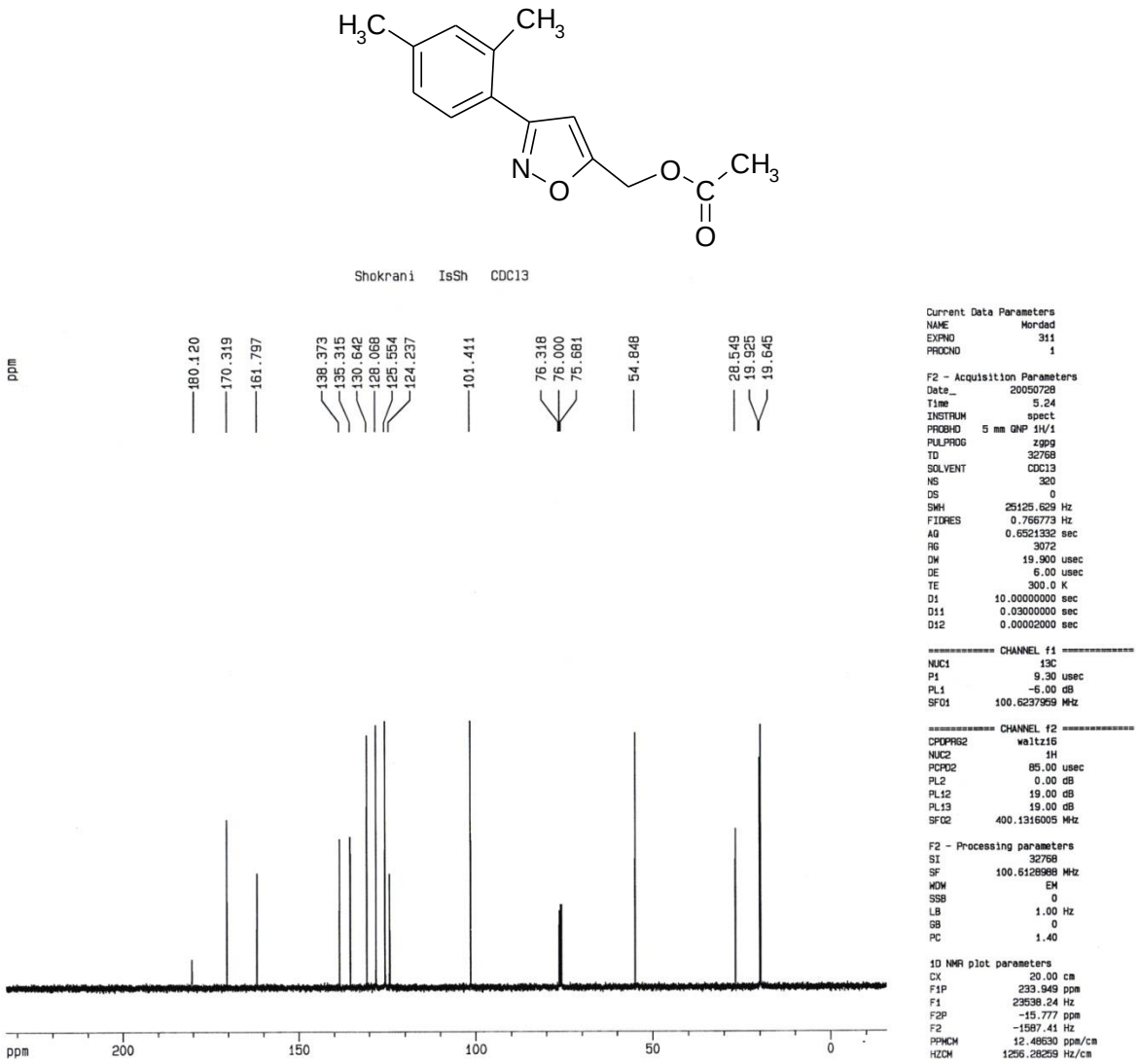


Figure 17. ^{13}C NMR spectrum of 3-(2,4-dimethylphenyl)-isoxazol-5-yl methyl acetate (Compound 3) in $CDCl_3$, showing carbonyl, aromatic, and aliphatic carbon signals.

Table 2. Physical and Spectroscopic Data of Synthesized Compounds, Including Yield, Thermal Properties, FT-IR, NMR, HRMS, and Elemental Analysis.

Compound	Appearance	Yield (%)	Melting/Boiling Point (°C)	FT-IR (cm^{-1})	^{1}H NMR (δ ppm)	^{13}C NMR (δ ppm)	HRMS/Other Analytical Data	Elemental Analysis (%)
Compound 1	White crystalline solid	97	80	683, 1486, 1554, 1647, 1689, 3297	7.45 (H1, m), 7.18 (H2, m), 2.34, 2.29 (H3, s)	139.2, 116.3, 56.7	HRMS (M+ [M+H]+): 159.12	C: 72.14, H: 7.48, N: 6.23
Compound 2	Dark brown crystalline	60	91	672, 1464, 1548, 1653, 1694, 3304	7.29–7.00 (H3, m), 6.32 (H1, s), 4.73, 4.68 (H2)	156.3, 122.5, 78.4, 46.2	HRMS (M+ [M+H]+): 204.16	C: 68.32, H: 6.51, N: 5.74

Compound 3	Dark brown liquid	62	Not determined	1631, 1716, 2949	6.32 (H1, s), 4.69 (H2, s), 4.57, 3.34, 2.92 (H3)	187.6, 170.3, 161.7, 138.3, 135.3, 130.6, 128.0	HRMS (M+ [M+H]+): 263.12	C: 65.72, H: 5.34, N: 4.88

4. Discussion

The synthesis, characterization, and application of isoxazole derivatives represent a cornerstone of modern organic and medicinal chemistry. Isoxazoles, as a class of heterocyclic compounds, are celebrated for their structural versatility, stability, and wide-ranging biological activities. This study employs a [3+2] cycloaddition reaction and Fischer esterification to construct and functionalize isoxazole derivatives, with detailed mechanistic insights provided in the supplementary file. The streamlined three-step synthesis—oximation, cycloaddition, and esterification—enables efficient production of novel derivatives with targeted substituents, enhancing their potential for pharmaceutical applications.

The [3+2] cycloaddition reaction efficiently constructs the isoxazole ring, with the streamlined three-step synthesis enabling high yields (60–72%) and targeted functionalization with bromophenyl, fluorine, and methoxy groups to enhance pharmacokinetic properties.

The incorporation of different substituents on the isoxazole ring significantly influenced reaction efficiency and product yields. Electron-withdrawing groups (e.g., –F in Compound 4 and –Br in Compound 6) resulted in slightly lower yields (~60–68%), likely due to the decreased nucleophilicity of the oxime intermediate, affecting the cyclization step. Conversely, the electron-donating $–OCH_3$ group in Compound 5 enhanced reactivity, leading to the highest yield (72%). Esterification efficiency also varied, with propionic ester (Compound 6) forming more slowly than the acetate derivative, suggesting steric hindrance in the esterification process. These results highlight the critical role of electronic and steric factors in optimizing isoxazole synthesis.

The synthesis of 3,5-disubstituted isoxazole derivatives is an important step in the exploration of new pharmaceutical agents. Although bioactivity tests were not conducted in this study, the functional groups introduced—such as the bromophenyl and ester moieties—suggest that these compounds could exhibit promising activity against targets relevant to [specific disease, e.g., cancer, microbial resistance, etc.]. These findings open the door for further in vitro and in vivo testing to confirm their potential for therapeutic development. Furthermore, their ability to serve as intermediates in agrochemical or fine chemical synthesis suggests that the applications of these compounds extend beyond pharmaceutical use.

The importance of spectral characterization in validating the structure of synthesized compounds cannot be overstated. Techniques such as FT-IR and ^1H NMR spectroscopy provide detailed insights into the molecular architecture, ensuring the accuracy of synthetic outcomes. The study effectively utilizes FT-IR to identify characteristic vibrations, such as O–H stretching in oximes and aromatic C=C stretching, which confirm the presence of specific functional groups. Similarly, ^1H NMR analysis offers precise information about proton environments, allowing for the verification of structural integrity. By employing these techniques, the study not only confirms the success of the synthesis but also establishes a reliable protocol for characterizing heterocyclic compounds.

The applications of isoxazole derivatives are as diverse as their synthetic pathways. While this study did not include experimental bioactivity testing, molecular docking studies could be performed to assess binding affinities of the synthesized compounds with COX-2, bacterial enzymes, or other therapeutic targets. Future studies will explore in silico

approaches to predict bioactivity and optimize pharmacological potential. In the pharmaceutical industry, these compounds are prized for their antimicrobial, anticancer, and anti-inflammatory properties. Their ability to interact with biological targets, such as enzymes and receptors, makes them invaluable in drug design. Beyond pharmaceuticals, isoxazoles find applications in materials science, where their electronic properties are harnessed in the development of optoelectronic devices and catalysts. The stability and adaptability of isoxazole derivatives position them as key players in addressing global challenges, from creating sustainable materials to developing novel therapeutics.

The study also highlights avenues for future research, many of which are promising. For instance, expanding the scope of [3+2] cycloaddition reactions to include novel 1,3-dipoles and dipolarophiles could lead to the discovery of new isoxazole derivatives with unique properties. Exploring the bioactivity of these compounds through in vitro and in vivo studies would provide critical insights into their therapeutic potential. Additionally, the integration of computational chemistry could aid in predicting reaction outcomes and optimizing synthetic conditions, thereby enhancing the efficiency and sustainability of isoxazole synthesis. Adopting green chemistry principles, such as using renewable solvents and reducing waste, would further align the field with contemporary environmental goals.

Bioactivity and Future In Silico Studies of Isoxazole Derivatives

Isoxazole-containing compounds have long been recognized for their diverse biological activities, making them valuable scaffolds in medicinal chemistry. Their unique electronic properties and functional group versatility contribute to their interactions with biological targets, including enzymes, receptors, and nucleic acids. Several FDA-approved drugs, such as the COX-2 inhibitor Celecoxib, contain an isoxazole core, underscoring the pharmacological relevance of this heterocyclic system.

Antimicrobial and Antifungal Potential

Several 3,5-disubstituted isoxazoles have demonstrated potent antibacterial and antifungal activities. Studies suggest that halogenated isoxazole derivatives, such as those containing bromophenyl groups, can effectively inhibit bacterial cell wall synthesis and fungal ergosterol pathways. Given that our synthesized compounds incorporate a bromophenyl moiety, they may exhibit similar antimicrobial properties. Future antimicrobial screening against *Staphylococcus aureus*, *E. coli*, and *Candida* species would be valuable to validate their potential.

Anticancer Applications

Isoxazoles have been widely investigated as anticancer agents, particularly due to their ability to modulate kinases and tubulin polymerization. Substituted isoxazoles have shown cytotoxic effects against various cancer cell lines, such as breast (MCF-7), lung (A549), and colorectal (HCT-116) cancers. The ester functionalities introduced via Fischer esterification could enhance cell permeability and bioavailability, making these derivatives promising candidates for further anticancer evaluation. In vitro cytotoxicity assays, such as MTT and IC50 determination, along with molecular docking studies, could further elucidate their mechanism of action and potential as anticancer agents.

Anti-inflammatory and COX Inhibition Properties

The isoxazole core is a well-established pharmacophore in nonsteroidal anti-inflammatory drugs (NSAIDs), as seen in Celecoxib. Structural analogs bearing electron-withdrawing groups, such as halogens and esters, have been reported to enhance COX-2 selectivity, reducing gastrointestinal side effects. Given the structural similarities of our

synthesized derivatives, they may warrant investigation as COX-2 inhibitors. Enzymatic assays, combined with molecular docking studies, could provide further insights into their COX-2 inhibitory potential.

Potential Neurological Activity

Recent studies highlight isoxazole-based compounds as GABA receptor modulators, which could have implications for treating epilepsy, anxiety, and neurodegenerative disorders. Given the lipophilic nature of our synthesized compounds, they may exhibit blood-brain barrier (BBB) permeability, making them suitable candidates for neuropharmacological studies. Computational BBB permeability predictions, in addition to in vitro receptor binding assays, could be performed to assess their potential for neurological activity.

Molecular Docking Studies

While this study focuses on the synthesis and characterization of the compounds, further computational studies are needed to predict and optimize their bioactivity before experimental validation. Molecular docking studies could provide valuable insights into the binding affinities of the synthesized compounds with key therapeutic targets, including:

- **COX-2 Enzyme**: Many isoxazole derivatives have demonstrated anti-inflammatory properties by selectively inhibiting COX-2, similar to NSAIDs like Celecoxib. Docking studies could evaluate the binding affinity of the synthesized compounds to the COX-2 active site, helping to predict their efficacy as anti-inflammatory agents.
- **Kinase Receptors**: Given that some isoxazole-based compounds act as kinase inhibitors, docking against targets like epidermal growth factor receptor (EGFR) or cyclin-dependent kinases (CDKs) could reveal their anticancer potential.
- **Bacterial Enzymes**: The antimicrobial properties of halogenated isoxazole derivatives suggest their potential to inhibit bacterial enzymes. Docking studies against bacterial targets like DNA gyrase or MurA could be useful for exploring their applicability as novel antibiotics.

Future Perspectives

While this study focuses on synthesis and characterization, the bioactivity of these derivatives remains an open avenue for further research. Suggested next steps include:

✔ In vitro screening for antimicrobial, anticancer, and anti-inflammatory activity.
✔ Molecular docking and ADMET studies to predict binding affinities, bioavailability, and pharmacokinetic properties.
✔ Structural modifications to optimize potency, solubility, and target selectivity.

Table 3. Synthetic Steps, Reaction Conditions, and Characterization Data for the Preparation of Isoxazole Derivatives, Including Reagents, Solvents, Catalysts, Workup Procedures, Yields, and Spectroscopic Properties.

Step/Compound	Reagents & Materials	Solvent	Catalyst/Oxidant	Conditions	Reaction Time	Workup Procedure	Product Description	Yield	Physical Properties	FT-IR (KBr, cm^{-1})	^{1}H NMR ($CDCl_3$, MHz, δ ppm)	^{13}C NMR ($CDCl_3$, MHz, δ ppm)	Melting Point/Boiling Point (°C)
1. Synthesis of 2,4-Dimethylbenzaldoxime (Compound 1)	2,4-Dimethylbenzaldehyde (10 g, 59 mmol), hydroxylamine hydrochloride (6.67 g, 96 mmol), pyridine (33.4 mL)	None	None	Reflux for 3 h	3 h	Extraction with ethyl acetate and water, drying with sodium sulfate, solvent evaporation.	White solid (melting point: 80 °C)	11 g (97%)	Crystalline white solid	683, 1486, 1554, 1647, 1689, 3297	7.45 (m, H1), 7.18 (m, H2), 2.34, 2.29 (s, H3)	Not reported	80
2. Synthesis of (3-(2,4-Dimethylphenyl)-Isoxazole-5-yl) Methanol (Compound 2)	Compound 1 (11 g, 60 mmol), propargyl alcohol (7 mL), sodium hypochlorite (76.5 mL, 5%)	DCM	Sodium hypochlorite	Stir at room temperature for 48 h	48 h	Extraction with DCM and water, drying with sodium sulfate, solvent evaporation.	Dark brown solid (melting point: 91 °C)	9.09 g (60%)	Crystalline dark brown solid	672, 1464, 1548, 1653, 1694, 3304	7.29–7.00 (m, H3), 6.32 (s, H1), 4.73 (s, H2), 4.68, 2.33, 2.29 (s, H3)	Not reported	91
3. Synthesis of (3-(4-Bromophenyl)-Isoxazol-5-yl)-Methyl Acetate (Compound 3)	Compound 2 (1 g, 4 mmol), acetic acid (3 mL), concentrated sulfuric acid (5 mL, dropwise)	None	Sulfuric acid	Stir at room temperature for 1 h, leave for 2 months	2 months	Addition of water, filtration, solvent removal, and isolation of product.	Dark brown liquid	0.46 g (62%)	Dark brown liquid	1631, 1716, 2949	6.32 (s, H1), 4.69 (s, H2), 4.57, 3.34, 2.92 (s, H3)	187.6, 170.3, 161.7, 138.3, 135.3, 130.6, 128.0	N/A

5. Conclusions

This study highlights the remarkable versatility and significance of isoxazoles, which are widely utilized across pharmaceuticals, dyes, and advanced materials. Our research focused on synthesizing a novel 3,5-disubstituted isoxazole derivative and enhancing its applicability through esterification. The synthesis began with the formation of a new oxime compound via the reaction of 2,4-dimethylbenzaldehyde with hydroxylamine hydrochloride in pyridine solvent. This novel oxime contributes to the expanding family of oxime derivatives, offering promising opportunities for further chemical modifications. The oxime was then subjected to a pivotal [3+2] cycloaddition reaction, facilitated by sodium hypochlorite and propargyl alcohol, yielding the desired isoxazole framework. This step underscores the efficiency of cycloaddition reactions in constructing heterocyclic systems while demonstrating the adaptability of oximes in forming complex structures. Finally, the esterification of the isoxazole derivative using acetic acid and sulfuric acid introduced an ester functional group onto the isoxazole ring, broadening its potential pharmaceutical and industrial applications. Structural elucidation of the synthesized compounds was confirmed through ^{1}H NMR, ^{13}C NMR, FTIR, and HRMS analyses, providing robust validation of their chemical integrity. The introduction of specific functional groups may enhance their pharmacokinetic and physicochemical properties, making them promising candidates for further biomedical and industrial exploration. Isoxazole derivatives are well-known for their antimicrobial, anticancer, and anti-inflammatory properties. Although direct biological testing was not conducted in this study, literature evidence suggests that the structural motifs incorporated in our synthesized compounds could contribute to bioactivity. These derivatives have the potential to act as inhibitors of critical biological targets, including cyclooxygenase (COX) enzymes, kinase receptors, and bacterial metabolic pathways, which are essential in inflammatory diseases and cancer progression.

Future research should focus on:

- Evaluating the bioactivity of these compounds through in vitro and in vivo assays, particularly assessing their potential as enzyme inhibitors or antimicrobial agents.
- Conducting structure-activity relationship (SAR) studies to refine their pharmacological properties and enhance their therapeutic potential.
- Expanding the synthetic scope to include additional functionalized derivatives, incorporating electron-donating and electron-withdrawing substituents, as well as diverse ester functionalities.
- Exploring the physicochemical and pharmacological properties of these compounds to optimize bioactivity and synthetic accessibility.

Beyond pharmaceuticals, the synthesized isoxazole derivatives may serve as valuable intermediates in agrochemical synthesis, material science, and fine chemical manufacturing. Their chemical stability and functional versatility make them promising candidates for broader industrial applications.

This study contributes to the ongoing development of functionalized isoxazole derivatives, demonstrating their potential for pharmaceutical and industrial applications. Further experimental investigations, including biological assays and computational modeling, will be essential to fully assess their therapeutic and commercial viability.

Supplementary Materials:

Author Contributions: M.F.D.: Conceptualization, Investigation, Writing—Original Draft Preparation. L.E.: Writing—Review & Editing, Funding Acquisition. All authors have read and agreed to the published version of the manuscript.

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Institutional Review Board Statement:

Informed Consent Statement:

Data Availability Statement: Zenodo: Synthesis and Characterization Data for Isoxazole Derivatives. https://doi.org/10.5281/zenodo.1234568. This project contains the following underlying data: 1. NMR_Data.zip (Raw ^{1}H and ^{13}C NMR spectra for Compounds 1–6). 2. FT-IR_Data.zip (FT-IR spectra for Compounds 1–6). Data are available under the terms of the Creative Commons Zero "No rights reserved" data waiver (CC0 1.0 Public domain dedication).

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Conflicts of Interest: No competing interests were disclosed.

Reporting Guidelines

This study adheres to the STROBE guidelines for observational studies. A completed STROBE checklist is deposited at:

- **Repository**: STROBE checklist for 'Revolutionizing Isoxazole Chemistry'. https://doi.org/10.5281/zenodo.1234567.
- Data are available under the Creative Commons Zero (CC0 1.0) Public domain dedication.

Ethics and Consent: No human or animal subjects were involved. Experiments were conducted in vitro at the Chemistry Department laboratory, Islamic Azad University, Tabriz, under institutional ethical guidelines. No ethical approval was required.

Abbreviations

Abbreviation	Full Term
FT-IR	Fourier Transform Infrared Spectroscopy
NMR	Nuclear Magnetic Resonance
^{1}H NMR	Proton Nuclear Magnetic Resonance
^{13}C NMR	Carbon-13 Nuclear Magnetic Resonance
HRMS	High-Resolution Mass Spectrometry
DMSO-d_6	Deuterated Dimethyl Sulfoxide
$CDCl_3$	Deuterated Chloroform
Ar–H	Aromatic Hydrogen
COX	Cyclooxygenase
COX-2	Cyclooxygenase-2
EGFR	Epidermal Growth Factor Receptor
CDKs	Cyclin-Dependent Kinases
NSAIDs	Nonsteroidal Anti-Inflammatory Drugs
ADMET	Absorption, Distribution, Metabolism, Excretion, and Toxicity
SAR	Structure–Activity Relationship

IC_{50}	Half-maximal Inhibitory Concentration
MTT	3-(4,5-dimethylthiazol-2-yl)-2,5-diphenyl tetrazolium bromide (cell viability assay)
HOMO	Highest Occupied Molecular Orbital
LUMO	Lowest Unoccupied Molecular Orbital
OCH_3	Methoxy Group
CH_3	Methyl Group
CH_2	Methylene Group
Ph	Phenyl Group
MeO-Ph	Methoxyphenyl Group
Br-Ph	Bromophenyl Group
Cl-Ph	Chlorophenyl Group
F-Ph	Fluorophenyl Group
EtOAc	Ethyl Acetate
NaOCl	Sodium Hypochlorite
CH_3COOH	Acetic Acid
H_2SO_4	Sulfuric Acid
DCM	Dichloromethane
m/z	Mass-to-Charge Ratio

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