# Design, Synthesis and Biological Evaluation Of 3-Acetylindole Derivatives

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***Abstract*—Indole derivatives, particularly 3-acetylindoles, are an important class of heterocyclic compounds with diverse pharmacological activities. In this study, a series of novel 3-acetylindole derivatives were rationally designed and synthesized using an efficient synthetic protocol under optimized reaction conditions, affording the target compounds in good to excellent yields. The structures of the synthesized derivatives were confirmed through spectroscopic analyses, including $^1$H NMR and GC-MS. The synthesized compounds were further evaluated for their biological activities using standard in vitro assays. Several derivatives exhibited significant biological activity, indicating that the substitution pattern on the indole nucleus plays a crucial role in modulating activity. These findings suggest that the synthesized 3-acetylindole derivatives may serve as promising lead compounds for further pharmacological and drug development studies.**

***Index Terms*—3-Acetylindole derivatives, Indole heterocycles, Heterocyclic synthesis, biological evaluation**

## I. INTRODUCTION

The fundamental skeleton of many compounds with biological and commercial significance is the indole nucleus.[1] The expanding amount of chemical literature on indole and its several derivatives in the fields of synthetic chemistry, natural products, agrochemicals, and pharmaceutical/medicinal chemistry [2–3] makes clear how important these compounds are.[5] The development of an effective and useful synthesis of substituted indoles is becoming more and more necessary due to the high importance of indole-based compounds. In order to create novel indole-based heterocycles, our research team is actively investigating the chemistry of substituted indoles. [6,7]

The delocalization of 10 π-electrons gives the indole core, a weakly basic molecule made up of a pyrrole ring joined to a benzene ring, its aromatic character. There are three tautomeric forms of indole: 1H-indole, 2H-indole, and 3H-indole [8]. These forms vary in where the hydrogen atom is located inside the ring structure. The chemical reactivity and biological interactions of indole derivatives can be affected by these tautomers. Because of their wide range of biological functions and potential for therapeutic use, indole derivatives have long captivated researchers [8–12]. Indoles are essential scaffolds in drug discovery and development since they are fundamental components of many medicines and natural compounds.

In continuation, synthesizing the derivatives of 1,1'-(1H-indole-1,3-diyl) substituted bis(ethan-1-one). This study aims to synthesized 1,1'-(1H-indole-1,3-diyl) substituted bis(ethan-1-one) understanding of substituted compounds as has promising biological properties. In future it may leads to synthesized new drug strategies.

## II. MATERIAL AND METHODS

All chemicals used in the experiments were of analytical reagent (AR) grade. Analytical thin-layer chromatography (TLC) was carried out on Merck pre-coated silica gel 60 F254 aluminium sheets. Proton nuclear magnetic resonance ($^1$H NMR) spectra were

recorded in $CDCl_3$ on a 500 MHz spectrometer with tetramethylsilane (TMS) serving as the internal standard.

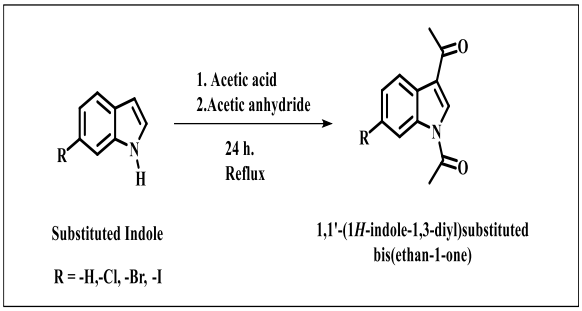
## III. CHARACTERIZATION TECHNIQUES

The structure of synthesized compounds was determined by chemical properties elemental analysis and spectral data. $^1$H-NMR spectra were recorded on Bruker Avance Neo 500 MHz spectrometer using $CDCl_3$ solvent and TMS as internal standards at SAIF, Punjab University, Chandigarh (India). Chemical shifts are expressed in ppm. Mass spectrums were recorded on Thermo Scientific TSQ 8000 Gas Chromatogram.

Experimental

General Reaction for synthesis of 1,1'-(1H-indole-1,3-diyl) substituted bis(ethan-1-one)

1,3- Di acetyl indole (I) 1 g (0.005) was suspended in ethanol (35 ml) and sodium hydroxide (10 ml) of 2 N was added. The mixture was stirred and warmed until the di acetyl indole had dissolved; the product after being precipitated by dilution with water, collected and crystallized from ethanol. The reaction was monitored by TLC using the same solvent system (Ethyl Ether/ n-Hexane; 7/5).




Scheme 1. 1,1'-(1H-indole-1,3-diyl) substituted bis(ethan-1-one)

Table 1. Scope of Substituted indole

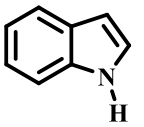
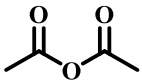
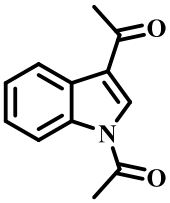
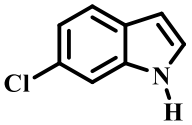
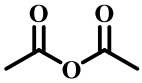
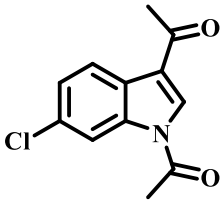
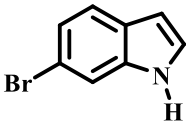
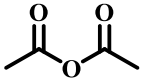
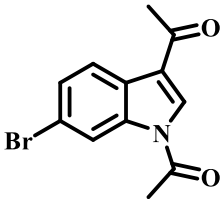
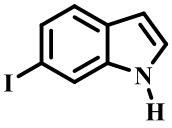
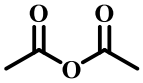
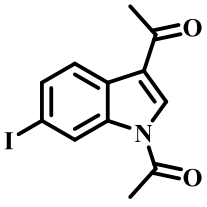
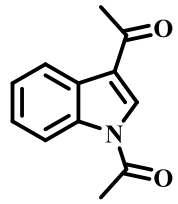
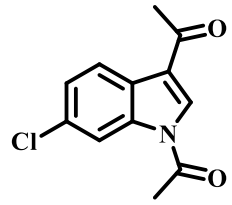
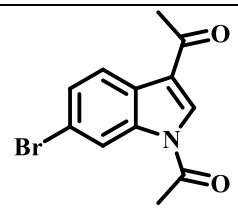
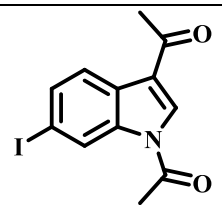
| Sr.No | Substrate | Reagent | Product | Time in Hrs. | Yield |
|---|---|---|---|---|---|
| 1 |  |  |  | 24 | 81 |
| 2 |  |  |  | 24 | 84 |
| 3 |  |  |  | 24 | 87 |
| 4 |  |  |  | 24 | 88 |

Table 2. Structural Analysis

| Sr. No | Structure of Products | Structural analysis by $^1$HNMR and GCMS |
|---|---|---|
| 1 |  (a) | $^1$HNMR (500MHz, $CDCl_3$):δ 8.94-7.30 (m, 5H), 2.65 (s,3 H), 2.50 (s,3H)<br>GCMS: Cal m/z: 201.22 Found m/z: 201.20 |
| 2 |  (b) | $^1$HNMR (500MHz, $CDCl_3$):δ 8.59-7.01 (m, 4H), 2.66 (s,3H), 2.50 (s,3H)<br>GCMS: Cal m/z: 235.67 Found m/z: 235.60 |
| 3 |  (c) | $^1$HNMR (500MHz, $CDCl_3$):δ 8.73-7.55 (m,4H), 2.64 (s,3H), 2.50 (s,3H)<br>GCMS: Cal m/z: 280.12 Found m/z: 280.10 |
| 4 |  (d) | $^1$HNMR (500MHz, $CDCl_3$):δ 8.59- 7.78 (m,4H), 2.63 (s, 3H), 2.50 (s,3 H)<br>GCMS: Cal m/z: 327.12 Found m/z: 327.10 |

Biological Investigation of (1,1'-(1H-indole-1,3-diyl) substituted bis(ethan-1-one) (compound 3a-d)

Antioxidant activity

Method: DPPH Free Radical Scavenging Assay

Preparation of Sample:

The free-radical scavenging activity was estimated by DPPH assay. The reaction mixture contained 10 µl of test sample and positive control ascorbic acid with 10 mg concentration and 190 µl of methanolic solution of 0.1 mM DPPH radical. The mixture was then shaken vigorously and incubated at 38 °C for 6 min. The absorbance was measured at 518 nm on ELISA plate reader indicated higher free radical scavenging activity, which was calculated using the following equation:

$$\text{(\%)Free radical scavenging effect} = \frac{[\text{Absorbance of control (Ac)- Absorbance of sample(As)}]}{\text{Absorbance of control (Ac)}} \times 100$$

Antioxidant Potential of synthetic compounds

The antioxidant activities were successfully performed 1,1'-(1H-indole-1,3-diyl) substituted bis(ethan-1-one) (compound 3a-d) free radical scavenging assay. The results are shown in the picture and table below;

Antioxidant activity of 1,1'-(1H-indole-1,3-diyl) substituted bis(ethan-1-one) (compound 3a-d)

Table 3. % Antioxidant Potential Using DPPH Assay Method (Conc. used 1 mg)

| Compound Code | Antioxidant Potential (%) (Mean±SD) | |
|---|---|---|
| | R | |
| a | -H | 30.260±1.31 |
| b | -Cl | 33.557±1.56 |
| c | -Br | 37.209±2.16 |
| d | -I | 37.209±2.28 |
| Standard | 88.76±2.16 | |

## IV. CONCLUSION

In present work, synthesized the series of 1,1'-(1H-indole-1,3-diyl) substituted bis (ethan-1-one) (compound 3a-d) structure is promising moiety that are able to shows the strong biological activity. Furthermore, the benzo ring inflection of the structure intentionally incorporation of chloro, bromo (-Cl, -Br) and iodo (-I) group over the ring. Which shows the promising and the strong biological activities. As a conclusion, our results revels and participate significantly to create a structural moiety and interactive relationship shows strong activity against microbes. Which is useful in drug design strategy in future.

Conflict of Interest:
Authors have declared that no competing interests exist.

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