Synthesis, Characterization and Biological Evaluation \( N-[5-(1H\text{-indol}-3-\text{yl})-1,3,4\text{-thiadiazol}-2\text{-yl}]\text{methanimine Derivatives} \)

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Authors’ contributions

This work was carried out in collaboration between both authors. Both authors read and approved the final manuscript.

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ABSTRACT

A new class of potentially biologically active new 1,3,4-thiadiazol derivatives have been prepared and reported in excellent yields. Its antioxidant properties were examined. It exhibited good activity, which had the highest \textit{in vitro} anti oxidant properties against DPPH scavenging activity. All these derivatives were characterized by melting point, Fourier-transformation infrared spectroscopy, Nuclear Magnetic Resonan (HNMR and \textsuperscript{13}C NMR).

Keywords: 1,3,4-thiadiazol; Antioxidant property; FTIR, HNMR and \textsuperscript{13}C NMR.

1. INTRODUCTION

Heterocyclic compounds, especially those containing nitrogen, have immenseplay biological processes due to their widespread use as medicinal scaffolds for drugs. The 1,3,4-thiadiazole nucleus is a versatile pharmacophore with a notable biological function. In addition to 1,3,4-thiadiazole, there are three other isomers: 1,2,3-thiadiazole, 1,2,4-thiadiazole and 1,2,5-thiadiazole [1-4]. The 1,3,4-thiadiazole isomer has the highest thermal stability when compared to other isomeric forms. Several new drugs have been developed, including antileishmanial,

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antimicrobial, antifungal, antibacterial, analgesics, antispasmodics, antioxidants, antipsychotics, antitumor, antidepressants, antihypertensive, antiviral, antihistamines, and antituberculou. Pesticides, herbicides, fungicides, insecticides, and bactericides are some of the agricultural applications of 1,3,4-thiadiazoles [5-10].

Currently, the heterogeneous aromatic rings are among the most commonly used organic compounds. The synthesis of indoles from benzene derivatives is a plausible strategy to obtain regiodefined molecules that are difficult to synthesize by direct electrophilic substitution. The indole molecule has a ring structure, which is one of the most common cyclic compounds in nature. Due to the structural development, biologically active indole derivatives have the chemical formula C₇H₇N. In preparations, the ring system of the indole molecule is prominent. Indole cores can contribute significantly to drug research and development. Because of the importance of heterocyclic compounds and imines, we describe in this paper the synthesis of a new indole base 1,3,4-thiadiazole phenylmethanimine moiety.

2. EXPERIMENTAL METHODS

2.1 Synthesis

Compounds were synthesized using a literature procedure. Semicarbazide hydrochloride (Scheme1) (50 mg, 1 mmol) and sodium acetate (50 mg) are placed in a mortar and ground with a pestle. After this, an indole-carbaldehyde (1 mmol) is added. Mixing is continued for several minutes until to get smooth paste. The crude semicarbazone separates out when cold water is added to the paste and then it is recrystallized from ethanol.

3. RESULT AND DISCUSSION

Physical methods such as elemental analysis, FT IR, HNMR, ¹³C NMR are discussed here.

3.1 Spectral Data

(E)-N-[5-(1H-indole-3-yl)-QuinolineCarboxaldehyde-2-yl]-1-(4methoxyphenyl) methanimine (3a): M.P. 136 °C; yield 74%; FT-IR (KBr, ν cm⁻¹): 3042 aromatic (C–H), 2943-2887 aliphatic (C–H). ¹H NMR (400 MHz, DMSO-d₆) δ (ppm): 9.2 (s, 1H, -CH=N, quinoline), 8.9 (s, 1H, -CH=N), 8.2 (s, 1H, Ar-H), 8.04 (d, 1H, Ar-H), 7.9 (d, 1H, Ar-H), 7.82 (dd, 2H, Ar-H), 7.78 (t, 1H, Ar-H), 7.60 (t, 1H, Ar-H), 7.36(dd, 2H, Ar-H). Anal. Calculated for (C₁₇H₁₁FN₄OS) C, 63.34; H, 3.44; F, 5.89; N, 17.38; S, 9.95. Found (%): 63.33; H, 3.46; F, 5.94; N, 17.45; S, 9.93. ESI-MS (m/z): 323.36 (M+H)⁺.

(E)-N-[5-(1H-indole-3-yl)-QuinolineCarboxaldehyde-2-yl]-1-(4methoxyphenyl) methanimine (3b): M.P. 152 °C; yield 71%; FT-IR (KBr, ν cm⁻¹): 3056 aromatic (C–H), 2952-2884 aliphatic (C–H). ¹H NMR (400 MHz, DMSO-d₆) δ (ppm): 9.1 (s, 1H, -CH=N, quinoline), 8.7 (s, 1H, -CH=N), 8.3 (s, 1H, Ar-H), 8.04 (d, 1H, Ar-H), 7.9 (d, 1H, Ar-H), 7.82 (dd, 2H, Ar-H), 7.78 (t, 1H, Ar-H), 7.60 (t, 1H, Ar-H), 7.36(dd, 2H, Ar-H), 3.8 (s, 3H, -OCH₃). Anal. Calculated for (C₁₇H₁₅N₄OS) C, 64.65; H, 4.22; N, 16.75; S, 9.59. Found (%): C, 64.65; H, 4.22; N, 16.75; S, 9.59. ESI-MS (m/z): 325.30 (M+H)⁺.

(E)-N-[5-(1H-indole-3-yl)-QuinolineCarboxaldehyde-2-yl]-1,3,4-thiadiazol-2-yl)methanimine (3c): M.P. 182 °C; yield 79%; FT-IR (KBr, ν cm⁻¹): 3068 aromatic (C–H), 2954-2881 aliphatic (C–H). ¹H NMR (400 MHz, DMSO-d₆) δ (ppm): 9.0 (s, 1H, -CH=N, quinoline), 8.8 (s, 1H, -CH=N), 8.2 (s, 1H, Ar-H), 8.04 (d, 1H, Ar-H), 7.9 (d, 1H, Ar-H), 7.82 (dd, 2H, Ar-H), 7.78 (t, 1H, Ar-H), 7.60 (t, 1H, Ar-H), 7.36(dd, 2H, Ar-H). Anal. Calculated for (C₁₇H₁₅N₄OS) C, 53.27; H, 2.89; Br, 20.85; N, 14.62; S, 8.37. Found (%): C, 53.29; H, 2.93; Br, 20.83; N, 14.64; S, 8.40. ESI-MS (m/z): 384.27 (M+H)⁺.

(E)-4-((5-(Quinoline Carboxaldehyde -3-yl)-1,3,4-thiadiazol-2-yl)imino)methyl)phenol (3d): M.P. 174 °C; yield 78%; FT-IR (KBr, ν cm⁻¹): 3056 aromatic (C–H), 2952-2884 aliphatic (C–H). ¹H NMR (400 MHz, DMSO-d₆) δ (ppm): 9.1 (s, 1H, -CH=N, quinoline), 8.7 (s, 1H, -CH=N), 8.3 (s, 1H, Ar-H), 8.04 (d, 1H, Ar-H), 7.9 (d, 1H, Ar-H), 7.82 (dd, 2H, Ar-H), 7.78 (t, 1H, Ar-H), 7.62 (t, 1H, Ar-H), 7.35(dd, 2H, Ar-H). Anal. Calculated for (C₁₇H₁₅N₄OS) C, 63.73; H, 3.78; N, 17.49; S, 10.01. Found (%): C, 63.74; H, 3.77; N, 17.45; S, 10.05. ESI-MS (m/z): 321.37 (M+H)⁺.

3.2 In vitro Antioxidant Screening

The result of the synthesized molecules reveals the effectiveness as an antioxidant molecule exhibited. Results of the DPPH radical assay of the compounds 3(a-d) showed is ability to a snatch the chain mechanism of the free radicle potentially with inhibition. Among the synthesized
compound 3d found to be more efficient with 73.35% inhibition, while 3b 65.63% inhibition, 3c 54.37% inhibition, and exhibited by compound 3a 52.13 inhibition, respectively proved themselves to capable molecules to form a stable free radical. The synthesized molecules bearing the pi donating and lone pair of electrons exhibited better anti-oxidant property. Among the synthesized compound 3d and 3b are having lone pair of the electron and having ability to neutralize free radical generation found to be rapid than the 3c and 3a having much conjugation. The results are given in the Fig. 1.

Hydroxyl ion scavenging activity compounds 3(a-d) found to be radicle scavenger ability with 64.39%, 59.74% for compound 3d and 4b containing hydroxy and methoxy functional groups in the molecule causes more efficiently bind to the radicle, whereas compound 3c and 3a able to inhibit at the rate of 48.13%, and 42.33% which is comparatively less as the molecule undergo delocalization of electron within the molecule respectively. The results of the study reveals compound 3d and 3b are found to be more potent. Results are depicted in the Fig. 2.

Total antioxidant property of the compound 3d and 3b proved themselves as a potential total antioxidant property, when compare to whole with standard ascorbic acid molecule compound 3(a-d) proves as an efficient total anti-oxidant much significant, but are proves as an efficient total anti-oxidant and the outcome are given away in the Fig. 3.

Scheme 1:

IR Spectrum of (E)-1-(4-fluorophenyl)-N-[5-(Quinoline Carboxaldehyde)-1,3,4-thiadiazol-2yl]methanimine(3a)
Fig. 1. NMR Spectra of (E)-1-(4-fluorophenyl)-N-[5-(Quinoline Carboxaldehyde)-1,3,4-thiadiazol-2-yl]methanimine (3a)

Fig. 2. Mass spectra of (E)-1-(4-fluorophenyl)-N-[5-(Quinoline Carboxaldehyde)-1,3,4-thiadiazol-2-yl]methanimine (3a)

Fig. 3. DPPH radicle scavenging activity
4. CONCLUSION

This work discusses the synthesis of 3(a-d) compounds formed by indole base 1,3,4-thiadiazole Schiff base derivatives, their characterization using various analytical and spectroscopic techniques and biological activity. Results of the DPPH radical assay of the compounds 3(a-d) showed its ability to a snatch the chain mechanism of the free radical potentially with inhibition. Among the synthesized compound 3d found to be more efficient with 73.35% inhibition. All these derivatives were characterized by melting point, FTIR, HNMR and $^{13}$C NMR.

COMPETING INTERESTS

Authors have declared that no competing interests exist.

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