Original Research Article

Synthesis, Characterization and Biological Evaluation *N*-[5-(1*H*-indol-3-yl)-1,3,4-thiadiazol-2-yl]methanimine Derivatives.

Abstract

A new class of potentially biologically active new 1,3,4-thiadiazol derivatives were synthesised and its antioxidant properties were examined. It exhibited good activity, which had the highest *in vitro* anti oxidant properties against DPPH scavenging activity. All these derivatives were characterized by melting point, FTIR, HNMR and 13CNMR.

Keywords: 1,3,4-thiadiazol, Antioxidant property, FTIR, HNMR and 13CNMR.

1. Introduction

Thiazoles and pyrazoles have been reported to show pharmacological activities. Some of them are used as medicines[1]. According to literature survey, thiazoles were reported to possess antimicrobial[2-5],analgesic[6],antiinflammatory[7],anticonvulsant[8],cardiotonic[9], anticancer[10-11], antitubercular[12] and anthelmintic[13] activities. Antimicrobial activities of some substituted thiazoles are well established because it posses (S-C=N) toxophoric unit. Thiazoles have enhanced lipid solubility with hydrophilicity. Thiazoles are easily metabolized by routine biochemical reactions and are non-carcinogenic in nature[14]. In addition, pyrazoles are reported as antimicrobial[15-16],antiviral[18],antipyretic[19],anti-inflammatory[20], antidepressant[21],

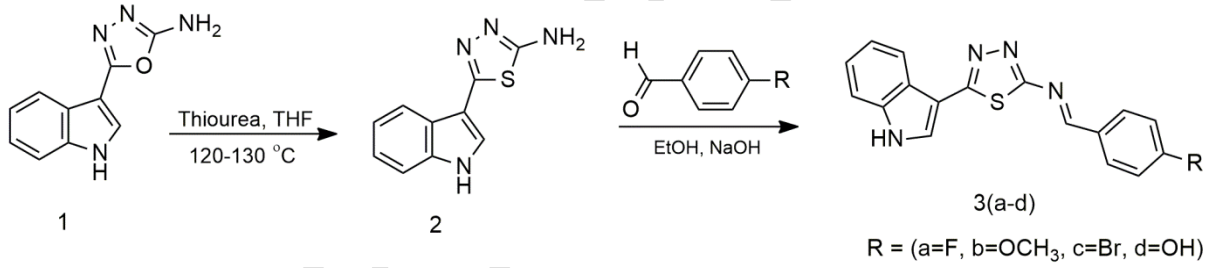
tranquillizing, anticancer, antihypertensive, antiarrhythmi, psychoanaleptic, anticonvulsant and antidiabetic activities.

2. Experimental

2.1 synthesis

Comopound was 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-3-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.

Scheme1:



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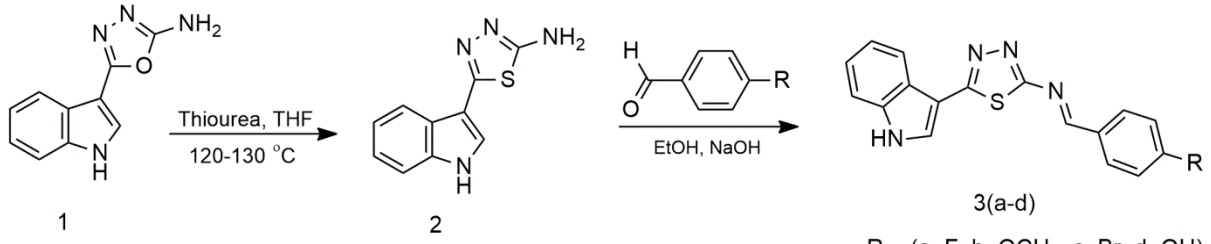
3. Result And Discussion

Condensation of Semicarbazide hydrochloride with sodium acetate results a compound. After this, an indole-3-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.

Scheme2:



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3.1 Spectral data

(E)-1-(4-fluorophenyl)-N-[5-(Quinoline Carboxaldehyde)-1,3,4-thiadiazol-2-yl]methanimine (3a):

M.P. 136 °C; yield 74%; FT-IR (KBr, ν cm^{-1}): 3042 aromatic (C–H), 2943-2887 aliphatic (C–H). ^{1}H NMR (400 MHz, DMSO-d_6) 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 ($C_{17}H_{11}FN_4S$) 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)-Quinoline Carboxaldehyde -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). ^{1}H NMR (400 MHz, DMSO-d_6) 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, -O-CH_3). Anal. Calculated for ($C_{18}H_{14}N_4OS$) 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): 335.40 $(M+H)^+$

(E)-1-(4-bromophenyl)-N-[5-(Quinoline Carboxaldehyde -3-yl)-1,3,4-thiadiazol-2-yl]methanimine (3c):

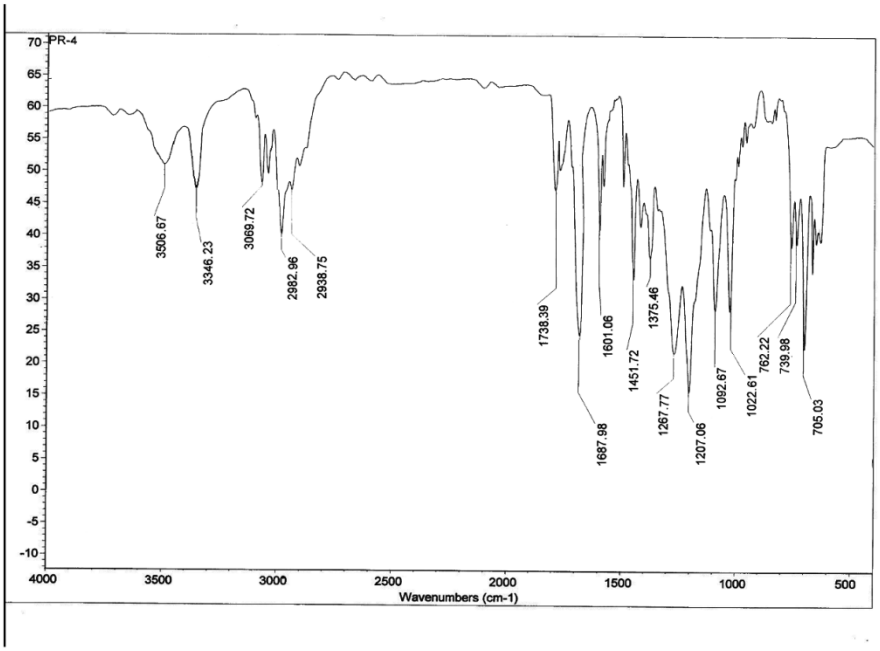
M.P. 182 °C; yield 79%; FT-IR (KBr, ν cm^{-1}): 3068 aromatic (C–H), 2954-2881 aliphatic (C–H). ^{1}H NMR (400 MHz, DMSO-d_6) δ (ppm): 9.0 (s, 1H, -CH=N, quinoline), 8.8 (s, 1H, -CH=N), 8.2 (s, 1H, Ar-H), 8.04 (d, 1H, Ar-H), 7.9 (d, 1H, Ar-H), 7.82 (dd, 2H, Ar-H), 7.78 (t, 1H, Ar-H), 7.60 (t, 1H, Ar-H), 7.36(dd, 2H, Ar-H). Anal. Calculated for ($C_{17}H_{11}ClN_4S$) 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). ^{1}H NMR (400 MHz, DMSO-d_6) 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), 5.4 (s, 1H, -OH). Anal. Calculated for ($C_{17}H_{12}N_4OS$) 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 $(M+H)^+$

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

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



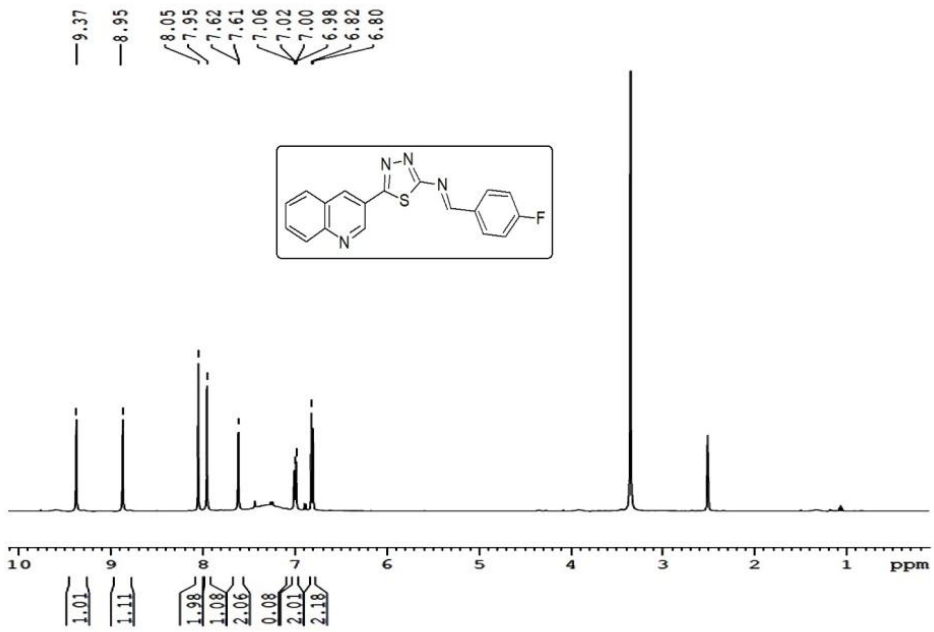


Fig 1: NMR Spectra of (E)-1-(4-fluorophenyl)-N-[5-(Quinoline Carboxaldehyde)-1,3,4-thiadiazol-2-yl]methanimine (3a):

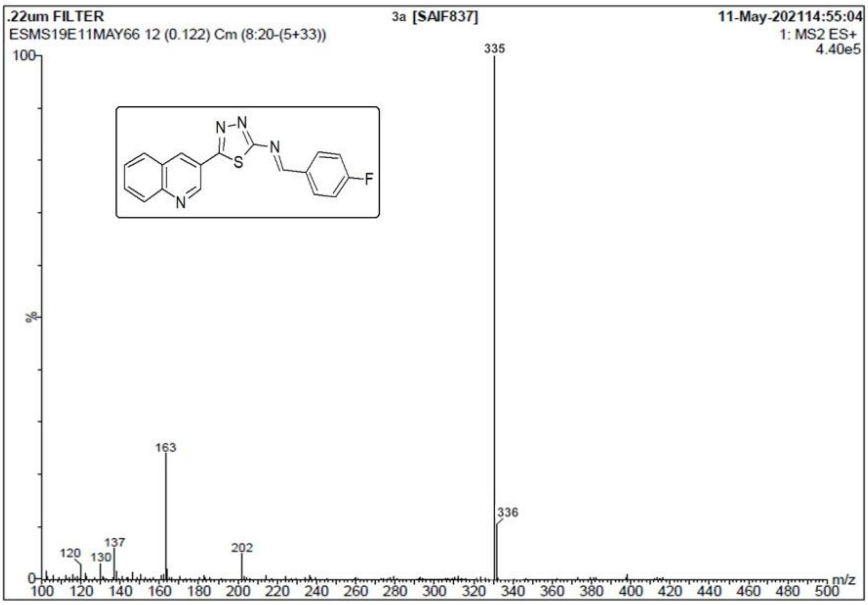


FIG 2: Mass spectra of (E)-1-(4-fluorophenyl)-N-[5-(Quinoline Carboxaldehyde)-1,3,4-thiadiazol-2-yl]methanimine (3a):

3.2 In vitro antioxidant screening

The result of the synthesized molecules reveals the efficiency 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 4c and 4a having much conjugation. The results are shown in the **Figure 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 revels compound **3d** and **3b** are found to be more potent. Results are depicted in the **Figure2**. 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 results are shown in the **Figure3**.

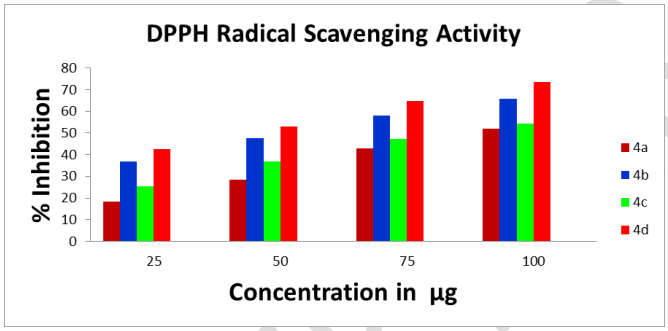


Figure 3. DPPH Radicle Scavenging Activity

4.Conclusion

This work describes simple reactions for the synthesis of new biologically heterocyclic compounds. 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. All these derivatives were characterized by melting point, FTIR, HNMR and 13CNMR.

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