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Research Article

Synthesis And Antimicrobial Activity Of Some New2-(Substituted1H-Indol-2-Yl)-5-Phenyl-1,3,4-Thiadiazole Derivatives

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ARTICLE INFO **ABSTRACT**

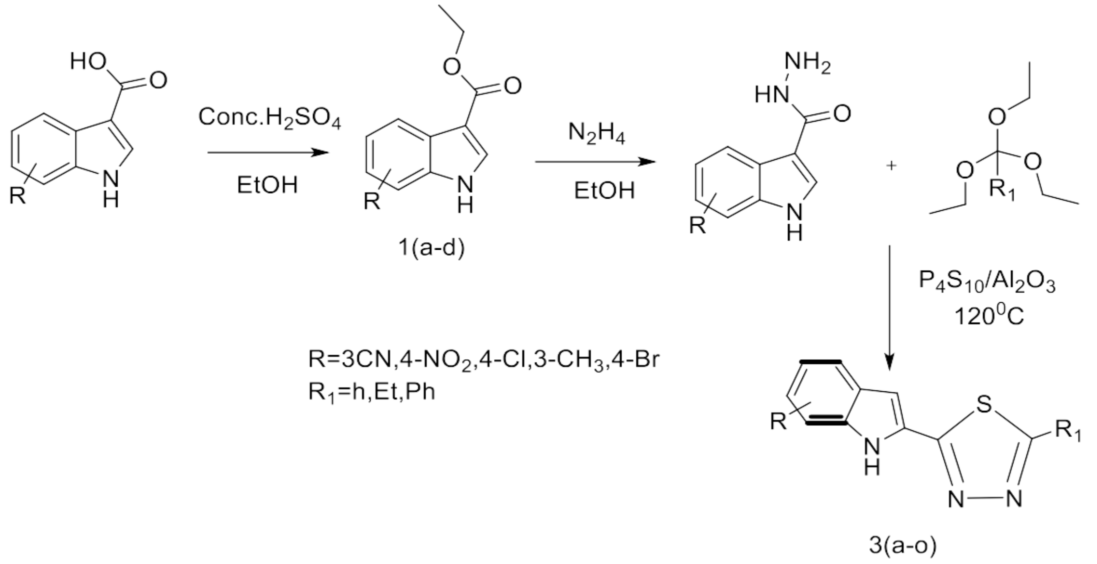
2-(Substituted 1H-indol-2-yl)-5-phenyl-1,3,4-thiadiazole was prepared by reacting Substituted 1H-indole-3-carbohydrazide with phosphorus pentasulfide thionating agent and solid- supported NafionNR50 to produce triethyl orthoformate, triethyl orthoproponate, and triethyl orthobenzoate. The reaction was catalyzed by phosphorus pentasulfide, as well as solid- supported NafionNR50. The products were then examined for their antimicrobial properties.Elements and spectrum analysis were used to determine the novel products' structure. It was investigated how the goods' structures related to how active they were againstspecific microbes, and encouraging findings were found.

Introduction

Recently, the chemistry of enaminones has received considerable attention due totheir utility as building blocks in heterocyclic synthesis [1–5]. On the other hand, 1,3,4-thiadiazole derivatives have attracted considerable interest owing to their wide spectrum of biological activity, including anti-microbial, anti-tuberculosis, anticonvulsant, anti-inflammatory, and antiulcer properties [6–10]. Recently, we published the antimicrobial activity results of a series of 2-(Substituted1H-indol-2-yl)-5-phenyl-1,3,4-thiadiazole , which showed promising activity [11]. Based on these findings, and in continuation of our interest in synthesis of bioactive compounds [12–16], we have now prepared a new series of 2-(Substituted1H- indol-2-yl)-5-phenyl-1,3,4-thiadiazole *via* reaction of Substituted 1H-indole-3- carbohydrazide triethyl orthoformate, triethyl orthoproponate, and triethyl orthobenzoate catalyzed by solid-supported NafionNR50 and thionating agent phosphorus pentasulfide in alumina to investigate the antimicrobial activity of theproducts and study their structure activity relationship (SAR) towards some microorganisms.

Experimental Section Materials and methods

Melting points were determined using an electrothermal Gallenkamp apparatus and are reported uncorrected. IR spectra were recorded in KBr using a Pye Unicam SP-1000 Spectrometer. ^{1}H-NMR spectra were recorded using DMSO- d_6 solutions on a Varian EM-300 MHz Spectrometer and chemical shifts are reported in ppm relative to that of TMS, which was used as an internal standard. Mass spectra were recorded using a AEI MS 30 mass spectrometer operating at 70 eV. Elemental analyses were carried out by using the Microanalytical Centerof mysore University, mysuru.



Scheme: Synthesis of 2-(Substituted1H-indol-2-yl)-5-phenyl-1,3,4-thiadiazole

Preparation for the Synthesis of ethyl Substituted-1H-indole-3- carboxylate.1(a-d)

Substituted indole-3-carboxylic acid (0.01 mole) in 20 mL of ethanol and 0.5 mLconc. sulfuric acid was refluxed for 12 hours and poured into ice. The product obtained was filtered through a sintered glass crucible and dried.

Preparation for the Synthesis of Substituted-1H-indole-3-carbohydrazide. 2(a-d)

A mixture of Indole Carboxylic ester (0.01mole) and hydrazine hydrate (0.6 mL, 0.01 mole) was heated for 9 hours in the presence of ethanol medium and poured into ice. The product was isolated and crystallized from ethanol.

Preparation for the Synthesis of 2-(Substituted -1H-indol-2-yl)-1,3,4- thiadiazole. 3(a-o)

Various aromatic and heterocyclic hydrazides(0.01mol) reacted efficiently with triethyl orthoformate(0.025), triethyl orthoproponate, and triethyl orthobenzoate catalyzed by solid-supported NafionNR50 and thionating agent phosphorus pentasulfide in alumina (P_4S_{10}/Al_2O_3) without any solvent, providing moderate togood yields of 1,3,4-thiadiazoles.

Table:01 Physiochemical Data of Synthesised Compound

CompoundNumber	R	R1	%Yield Melting point (^{0}C)
3a	3-CN	H	74 (190)
3b	3-CN	Et	77 (189)
3c	3-CN	Ph	80 (188)
3d	4-NO_2	H	85 (191)
3e	4-NO_2	Et	88 (190)
3f	4-NO_2	Ph	89 (191)
3g	4-Cl	H	90 (192)
3h	4-Cl	Et	76 (191)
3i	4-Cl	Ph	77 (190)
3j	3-CH_3	H	70 (188)
3k	3-CH_3	Et	69 (189)
3l	3-CH_3	Ph	67 (188)
3m	4-Br	H	66 (186)
3n	4-Br	Et	67 (187)
3o	4-Br	Ph	70 (188)

Spectral data of Synthesised CompoundsCompound 3a

^{1}H NMR: δ 7.51-7.75 (3H), 7.56 (t, *J* = 1.7Hz), 7.58 (d, *J* = 8.6Hz), 7.68 (d, *J* = 8.6 Hz)), 7.84 (1H, d, *J* = 1.8,Hz), 8.59 (1H, s), 8.71 (1H, s)

^{13}C NMR: δ 102.3 (1C, s), 119.3 (1C, s), 120.4 (1C, s), 128.2 (1C, s), 128.5 (1C, s), 133.7 (1C, s), 134.0 (1C, s), 136.3 (1C, s), 142.6 (1C, s), 143.2 (1C, s), 165.1(1C, s)
Mass (m/z):226(M^+)
FT-IR (cm^{-1}) υ_{maks}: 3282.01 (-NH stretching) , 3053.61 (aromatic C-H), 1590.51(C=N thiadiazole), 1600 (C=C) 695.56 (C-S-C)

Compound 3b
^{1}H NMR: δ 1.22 (3H, t, J = 7.4 Hz), 3.04 (2H, q, J = 7.4 Hz), 7.50-7.73 (3H), 7.56 (d, J = 8.7Hz), 7.57 (d, J = 1.6Hz), 7.67 (d, J = 8.7Hz)), 7.83 (1H, t, J = 1.8Hz), 8.59 (1H, s)
^{13}C NMR: δ 13.1 (1C, s), 27.0 (1C, s), 102.3 (1C, s), 119.3 (1C, s), 120.4 (1C, s), 128.2 (1C, s), 128.5 (1C, s), 133.7 (1C, s), 134.0 (1C, s), 136.3 (1C, s), 143.2 (1C,s), 156.8 (1C, s), 165.1 (1C, s)
Mass (m/z):254(M^{+})
FT-IR (cm^{-1}) υ_{maks}: 3280.01 (-NH stretching) , 3052.61 (aromatic C-H), 1590.51(C=N thiadiazole), 1600 (C=C) 690.56 (C-S-C)

Compound 3c
^{1}H NMR: δ 7.49-7.81 (6H), 7.56 (t, J = 7.4Hz), 7.58 (d, J = 7.8Hz), 7.59 (t, J = 1.3 Hz), 7.63 (d, J = 8.6, Hz), 7.75 (d, J = 8.6Hz)), 7.99-8.13 (3H), 8.05 (d, J = 7.8Hz), 8.08 (d, J = 1.8 Hz)), 8.70 (1H, s).
^{13}C NMR: δ 102.3 (1C, s), 119.3 (1C, s), 120.4 (1C, s), 126.7 (2C, s), 127.8 (1C, s), 128.2 (1C, s), 128.3-128.6 (3C, 128.4 (s), 128.5 (s)), 131.9 (1C, s), 133.7 (1C, s), 134.0 (1C, s), 136.3 (1C, s), 143.2 (1C, s), 165.0-165.2 (2C, 165.1 (s), 165.1(s).
Mass (m/z):302(M^{+})
FT-IR (cm^{-1}) υ_{maks}: 3271.01 (-NH stretching) , 3054.61 (aromatic C-H), 1596.51(C=N thiadiazole), 1612 (C=C) 696.56 (C-S-C)

Compound 3d
^{1}H NMR: δ 6.67 (1H, d, J = 8.1 Hz), 7.18 (1H, d, J = 1.8Hz), 7.35-7.62 (4H, 7.41 (d, J = 8.1Hz), 7.47 (t, J = 7.7Hz), 7.54 (d, J = 7.8, Hz)), 7.84 (1H, d, J = 1.8 Hz),7.95 (2H, d, J = 7.8 Hz)
^{13}C NMR: δ 102.3 (1C, s), 103.2 (1C, s), 111.3 (1C, s), 114.1 (1C, s), 126.7 (2C, s), 127.8 (1C, s), 128.2 (1C, s), 128.4 (2C, s), 131.9 (1C, s), 133.7 (1C, s), 136.3 (1C, s), 146.6 (1C, s), 165.0-165.2 (2C, 165.1 (s), 165.1 (s)
Mass (m/z):246(M^{+})
FT-IR (cm^{-1}) υ_{maks}: 3271.01 (-NH stretching) , 3054.61 (aromatic C-H), 1596.51(C=N thiadiazole), 1612 (C=C) 696.56 (C-S-C)

Compound 3e
^{1}H NMR: δ 1.17 (3H, t, J = 7.4 Hz), 2.98 (2H, q, J = 7.4 Hz), 6.56 (1H, d, J = 8.2Hz), 7.17 (1H, d, J = 1.5 Hz), 7.51 (1H, d, J = 8.2,Hz), 7.64 (1H, d, J = 1.5 Hz)
^{13}C NMR: δ 13.1 (1C, s), 27.0 (1C, s), 102.3 (1C, s), 103.2 (1C, s), 111.3 (1C, s), 114.1 (1C, s), 128.2 (1C, s), 133.7 (1C, s), 136.3 (1C, s), 146.6 (1C, s), 156.8 (1C,s), 165.1 (1C, s)
Mass (m/z):274(M^{+})
FT-IR (cm^{-1}) υ_{maks}: 3285.01 (-NH stretching), 3055.61 (aromatic C-H), 1597.51(C=N thiadiazole), 1610 (C=C) 698.56 (C-S-C)

Compound 3f
^{1}H NMR: δ 6.67 (1H, d, J = 8.1Hz), 7.18 (1H, d, J = 1.8Hz), 7.35-7.62 (4H, 7.41 (t, J = 8.1Hz), 7.47 (d, J = 7.7Hz), 7.54 (d, J = 7.8 Hz)), 7.84 (1H, d, J = 1.8 Hz),7.95 (2H, d, J = 7.8, 1.5Hz)
^{13}C NMR: δ 102.3 (1C, s), 103.2 (1C, s), 111.3 (1C, s), 114.1 (1C, s), 126.7 (2C, s), 127.8 (1C, s), 128.2 (1C, s), 128.4 (2C, s), 131.9 (1C, s), 133.7 (1C, s), 136.3 (1C, s), 146.6 (1C, s), 165.0-165.2 (2C, 165.1 (s), 165.1 (s)
Mass (m/z):322(M^{+})
FT-IR (cm^{-1}) υ_{maks}: 3282.01 (-NH stretching), 3053.61 (aromatic C-H), 1592.51(C=N thiadiazole), 1611(C=C) 692.56 (C-S-C)

Compound 3g
^{1}H NMR: δ 7.29 (1H, d, J = 1.5, Hz), 7.53 (1H, d, J = 8.2 Hz), 7.60-7.75 (2H, 7.66 (t, J = 8.2, 0.5 Hz), 7.70 (d, J = 1.8Hz)), 8.66 (1H, s).
^{13}C NMR: δ 102.3 (1C, s), 112.9 (1C, s), 121.8 (1C, s), 128.4 (1C, s), 128.9 (1C, s), 130.4 (1C, s), 133.7 (1C, s), 136.3 (1C, s), 142.6 (1C, s), 165.1 (1C, s)
Mass (m/z):235(M^{+}),237(M+2)
FT-IR (cm^{-1}) υ_{maks}: 3282.01 (-NH stretching), 3053.61 (aromatic C-H), 1592.51(C=N thiadiazole), 1611(C=C) 692.56 (C-S-C)

Compound 3h
^{1}H NMR: δ 7.29 (1H, d, J = 1.5 Hz), 7.53 (1H, d, J = 8.2 Hz), 7.60-7.75 (2H, 7.66 (d, J = 8.2,Hz), 7.70 (d, J = 1.8, Hz)), 8.66 (1H, s)

^{13}C NMR: δ 13.1 (1C, s), 27.0 (1C, s), 102.3 (1C, s), 112.9 (1C, s), 121.8 (1C, s), 128.4 (1C, s), 128.9 (1C, s), 130.4 (1C, s), 133.7 (1C, s), 136.3 (1C, s), 156.8 (1C,s), 165.1 (1C, s).

Mass (m/z):263(M$^+$),265(M+2)

FT-IR (cm^{-1}) υ$_{maks}$: 3282.01 (-NH stretching), 3053.61 (aromatic C-H), 1592.51(C=N thiadiazole), 1611(C=C) 692.56 (C-S-C)

Compound 3i

^{1}H NMR: δ 7.18 (1H, d, *J* = 1.5 Hz), 7.44-7.76 (6H, 7.51 (d, *J* = 8.4 Hz), 7.55 (d, *J* = 7.8 Hz), 7.55 (t, *J* = 7.4 Hz), 7.64 (d, *J* = 8.4, 0.5 Hz), 7.71 (d, *J* = 1.8 Hz)),8.03 (2H, d, *J* = 7.8Hz)

^{13}C NMR: δ 102.3 (1C, s), 112.9 (1C, s), 121.8 (1C, s), 126.7 (2C, s), 127.8 (1C, s), 128.3-128.5 (3C, 128.4 (s), 128.4 (s)), 128.9 (1C, s), 130.4 (1C, s), 131.9 (1C, s), 133.7 (1C, s), 136.3 (1C, s), 165.0-165.2 (2C, 165.1 (s), 165.1 (s)Mass (m/z):311(M$^+$), 313(M+2)

FT-IR (cm^{-1}) υ$_{maks}$: 3282.01 (-NH stretching), 3053.61 (aromatic C-H), 1592.51(C=N thiadiazole), 1611(C=C) 692.56 (C-S-C)

Compound 3j

^{1}H NMR: δ 2.29 (3H, s), 6.94 (1H, d, *J* = 8.2, 1.6Hz), 7.17 (1H, t, *J* = 1.1, 0.5 Hz), 7.49 (1H, t, *J* = 1.6, 0.5 Hz), 7.79 (1H, d, *J* = 8.2, 1.1 Hz), 8.05 (1H, s).

^{13}C NMR: δ 21.3 (1C, s), 102.3 (1C, s), 109.8 (1C, s), 120.4 (1C, s), 128.2 (1C, s), 129.1 (1C, s), 133.6-133.8 (2C, 133.7 (s), 133.7 (s)), 136.3 (1C, s), 142.6 (1C,s), 165.1 (1C, s).

Mass (m/z):215(M$^+$).

FT-IR (cm^{-1}) υ$_{maks}$: 3282.01 (-NH stretching), 3053.61 (aromatic C-H), 1592.51(C=N thiadiazole), 1611(C=C) 692.56 (C-S-C)

Compound 3k

^{1}H NMR: δ 1.17 (3H, t, *J* = 7.4 Hz), 2.29 (3H, s), 3.02 (2H, q, *J* = 7.4 Hz), 6.92 (1H, d, *J* = 8.0, 1.6, Hz), 7.17 (1H, d, *J* = 1.1, 0.5 Hz), 7.48 (1H, d, *J* = 1.6, 0.5Hz), 7.77 (1H, d, *J* = 8.0, 1.1Hz)

^{13}C NMR: δ 13.1 (1C, s), 21.3 (1C, s), 27.0 (1C, s), 102.3 (1C, s), 109.8 (1C, s), 120.4 (1C, s), 128.2 (1C, s), 129.1 (1C, s), 133.6-133.8 (2C, 133.7 (s), 133.7 (s)), 136.3 (1C, s), 156.8 (1C, s), 165.1 (1C, s)

Mass (m/z):243(M$^+$).

FT-IR (cm^{-1}) υ$_{maks}$: 3282.01 (-NH stretching), 3053.61 (aromatic C-H), 1592.51(C=N thiadiazole), 1611(C=C) 692.56 (C-S-C)

Compound 3l

^{1}H NMR: δ 2.22 (3H, s), 7.04-7.24 (2H, 7.11 (d, *J* = 8.3, 1.9 Hz), 7.19 (d, *J* = 1.4, 0.5 Hz), 7.48-7.62 (3H, 7.54 (d, *J* = 7.4, 1.5 Hz), 7.55 (d, *J* = 7.8, 7.4, Hz), 7.74-8.02 (4H), 7.80 (d, *J* = 8.3, 1.4Hz), 7.88 (d, *J* = 1.9, 0.5 Hz), 7.96 (d, *J* = 7.8, 1.5Hz).

^{13}C NMR: δ 21.3 (1C, s), 102.3 (1C, s), 109.8 (1C, s), 120.4 (1C, s), 126.7 (2C, s), 127.8 (1C, s), 128.2 (1C, s), 128.4 (2C, s), 129.1 (1C, s), 131.9 (1C, s), 133.6-133.8 (2C, 133.7 (s), 133.7 (s)), 136.3 (1C, s), 165.0-165.2 (2C, 165.1 (s), 165.1 (s)

Mass (m/z):292(M$^+$).

FT-IR (cm^{-1}) υ$_{maks}$: 3282.01 (-NH stretching), 3053.61 (aromatic C-H), 1592.51(C=N thiadiazole), 1611(C=C) 692.56 (C-S-C)

Compound 3m

^{13}C NMR: δ 102.3 (1C, s), 112.8 (1C, s), 118.4 (1C, s), 124.0 (1C, s), 128.2 (1C, s), 131.7 (1C, s), 133.7 (1C, s), 136.3 (1C, s), 142.6 (1C, s), 165.1 (1C, s).

^{1}H NMR: δ 7.23 (1H, dd, *J* = 1.5, 0.5 Hz), 7.43-7.69 (3H, 7.49 (d, *J* = 8.3, 1.8 Hz), 7.58 (d, *J* = 1.8, 1.5 Hz), 7.63 (d, *J* = 8.3, 0.5 Hz)), 8.66 (1H, s).Mass (m/z):279(M$^+$),281(M+2)

FT-IR (cm^{-1}) υ$_{maks}$: 3282.01 (-NH stretching), 3053.61 (aromatic C-H), 1592.51(C=N thiadiazole), 1611(C=C) 692.56 (C-S-C)

Compound 3n

^{1}H NMR: δ 1.18 (3H, t, *J* = 7.4 Hz), 3.03 (2H, q, *J* = 7.4 Hz), 7.23 (1H, d, *J* = 1.5,Hz), 7.41-7.64 (3H, 7.47 (d, *J* = 8.3, 1.8 Hz), 7.55 (d, *J* = 1.8,Hz), 7.58 (d, *J* = 8.3, 0.5 Hz).

^{13}C NMR: δ 13.1 (1C, s), 27.0 (1C, s), 102.3 (1C, s), 112.8 (1C, s), 118.4 (1C, s), 124.0 (1C, s), 128.2 (1C, s), 131.7 (1C, s), 133.7 (1C, s), 136.3 (1C, s), 156.8 (1C,s), 165.1 (1C, s).

Mass (m/z):308(M$^+$).

FT-IR (cm^{-1}) υ$_{maks}$: 3282.01 (-NH stretching), 3053.61 (aromatic C-H), 1592.51(C=N thiadiazole), 1611(C=C) 692.56 (C-S-C)

Compound 3o

^{1}H NMR: δ 7.25-7.38 (2H, 7.30 (d, *J* = 1.8, 0.5 Hz), 7.32 (d, *J* = 8.3, 1.8 Hz)), 7.47-7.75 (5H), 7.53 (t, *J* = 7.4, Hz), 7.55 (d, *J* = 7.8 Hz), 7.63 (d, *J* = 8.3, Hz), 7.70 (d, *J* = 1.8 Hz)), 8.03 (2H, d, *J* = 7.8Hz)

^{13}C NMR: δ 102.3 (1C, s), 112.8 (1C, s), 118.4 (1C, s), 124.0 (1C, s), 126.7 (2C, s), 127.8 (1C, s), 128.2 (1C, s), 128.4 (2C, s), 131.7 (1C, s), 131.9 (1C, s), 133.7 (1C, s), 136.3 (1C, s), 165.0-165.2 (2C, 165.1 (s), 165.1 (s)Mass (m/z):354(M^{+}), 356(M+2)

FT-IR (cm^{-1}) υ_{maks}: 3282.01 (-NH stretching), 3053.61 (aromatic C-H), 1592.51(C=N thiadiazole), 1611(C=C) 692.56 (C-S-C)

Pharmacological activities

Antimicrobial Activity

Using cultures of four fungal strains—Aspergillus fumigatus (RCMB 002003) (AF), Pseudomonas aeruginosa (RCMB 005003, PI), Geotrichum candidum (RB 052006, GC), and Candida albicans (RCMB 005002, CA)—as well as four bacterial species—Gram positive bacteria, Staphylococcus aureus (RCMB 000106, SA) and Bacillus subtilis (RCMB 000107, BS), Gram negative bacteria, Pseudomonas aeruginosa (RCMB 000102, PA), and Escherichiacoli (RCMB 000103, EC)—in vitro antimicrobial screening of compounds were prepared in this study was conducted. To assess the efficacy of the tested compounds under the same.

Antimicrobial Activity Screening and Structure Activity Relationship

The results of antimicrobial activities for some of the newly synthesized compounds showed promising effects compared to control drugs (see Table 1). Compounds **3a** and **3b** have high potency as antifungals except for the fungus *Candida albicans* (CA). Replacing the substituent in the position 3 and 4 of the indole substituted moiety in compounds with electron withdrawing groups, e.g., X = Cl, NO2, as in **3c** and **3g**, leads to a decrease in the antifungal activity to zero (Table 1). The results also showed that compounds **3a** and **3b** have high potency towards Gram positive bacteria *SA* and *BS* and Gram negative bacteria *PA*. Their antibacterial activity is high compared with compounds **3c**,**d**, which is in agreement with what was mentioned before. On the other hand, compounds **3c** and **3d** have higher potency against all tested fungi except *CA* than compound **3a**.

Compound **3b** has no activity towards any of the tested fungi. In addition, compounds **3a**, **3c** and **3d** have high activity against almost all bacteria used, while compound **3b** has no activity against any of the tested bacteria. This indicates thatchanging position at 3 and 4 of indole moiety having 1,3,4-thiadiazole moiety in compounds with an electron donating group decreased the activity of these compounds towards all tested microorganisms. In addition, the results depicted in Table 1 revealed the high potency of compounds **3j** towards all tested microorganisms, except fungus *CA* and Gram negative bacteria *PA*. The order of decreasing reactivity towards tested fungi and bacteria is as follows:**3b** > **3c** > **3a**.

Furthermore, the results of Table 1 indicated that compounds **3a** and **3b** have high potency towards all tested fungi except fungus *CA* and Gram negative bacteria *PA*. The activity of compounds **3a**,**b** can be attributed to the presence of indole ring and the small size of the molecules.

Table 1. Antimicrobial activity expressed as inhibition diameter zones in millimeter (mm)of compounds against the pathological strains based on well diffusion as assay

npoundNo.	**Fungi**				**am positivebacteria**		**m negativebacteri**	
	A. fumigatus	***P. italicum***	***C. albicans***	***G. candidum***	***S. aureu***	***B. subtilis***	***P. aeruginosa***	***E. col***
3a	15.6 (±0.19)	16.3 (±0.24)	N.A	19.8	17.9 (±0.27	20.2 (±0.14)	N.A.	10.9
3b	19.6 (±0.13)	20.3 (±0.22)	N.A.	22.4 (±0.14)	22.8 (±0.25	25.8 (±0.31)	N.A.	17.6 ±0.25
3c	10.3 (±0.12)	N.A.	N.A.	N.A.	12.0 (±0.21	12.3 (±024)	N.A	8.4 (±0.12
3d	N.A.	N.A.	N.A.	N.A.	13.6 (±0.17	15.4 (±0.33)	N.A.	N.A.
3e	13.9 (±0.25)	16.7 (±0.19)	N.A	19.8 (±0.35)	11.7 (±0.14	14.6 (±0.67)	N.A.	N.A.
3f	N.A	N.A	N.A	N.A	N.A	N.A	N.A	N.A
3g	18.5 (±0.15)	19.2 (±0.11)	N.A	20.9 (±0.26)	18.3 (±0.19	19.2 (±0.21)	N.A.	12.2 (±0.13
3h	14.8 (±0.13)	12.6 (±0.21)	N.A	16.8 (±0.22)	15.0 (±0.18	11.2 (±0.12)	N.A.	11.3 (±0.31
3i	14.3 (±0.21)	15.2 (±0.23)	N.A.	11.7 (±0.15)	15.8 (±0.31	18.6 (±0.21)	N.A.	N.A.
3j	20.4 (±0.19)	21.6 (±0.12)	N.A.	25.8 (±0.37)	23.9 (±0.27	26.7 (±0.14)	N.A.	19.8 (±0.10
3k	16.9 (±0.13)	17.8 (±0.24)	N.A.	21.4 (±0.17)	19.4 (±0.27	20.4 (±0.14)	N.A.	10.6 (±0.31

3l	20.3 (±0.31)	N.A.	N.A.	22.6 (±0.22)	23.7 (±0.31	25.9 (±0.22)	N.A.	15.9 (±0.38
3m	21.6 (±0.22)	20.8 (±0.12).	N.A.	26.2 (±025)	22.0 (±0.23	21.4 (±012)	N.A.	18.9 (±0.26
Amphoterici B	23.7 (±0.10)	21.9 (±0.12)	19.8 (±0.20)	28.7 (±0.22)	N.A.	N.A.	N.A.	N.A.
Ampicillin	N.A.	N.A.	N.A.	N.A.	27.4 (±0.18	32.4 (±0.10)	N.A.	N.A.
Gentamicin	N.A.	N.A.	N.A.	N.A.	N.A.	N.A.	17.3 (±0.15)	22.3 (±0.18

The experiment was carried out in triplicate and average zone of inhibition was calculated (100µL was tested) (N.A. = no activity), data are expressed in the form of mean ± SD.

Minimum Inhibitory Concentration (MIC)

The minimum inhibitory concentration (MIC) of the synthesized compounds against highly inhibited organisms is reported in Table 2.. Compounds **3c** and **3a** exhibited a low MIC value of 0.12 µg/mL against Gram positive bacteria (BS), while compound **3b** revealed a MIC of
7.81 µg/mL against PI

Table 2. Minimum inhibitory concentration (µg/mL) against the pathological strains.

Compound No.	**Fungi**				**ram positivebacteria**		**ramnegativebacteria**	
	A. fumigatus	***P. italicum***	***C. albicans***	***G. candidum***	***S. aureus***	***B. subtilis***	***P. aeruginosa***	***E. coli***
3a	125	125	NA	31.25	62.5	15.63	N.A.	500
3c	31.3	15.6	NA	3.9	1.95	0.12	N.A.	62.5
3d	31.3	15.6	NA	7.81	62.5	31.3	N.A.	500
3e	15.6	7.8	NA	0.12	1.95	0.06	N.A.	31.3
3f	125	62.5	NA	7.81	15.6	7.8	N.A.	500
3h	14.1	N.A.	NA	0.11	1.75	0.12	N.A.	26.5
photericinB	0.49	1.95	15.63	0.015	N.A.	N.A	N.A.	N.A
Ampicillin	N.A.	N.A.	NA	NA	0.02	0.007	N.A	N.A
Gentamicin	N.A.	N.A.	NA	NA	N.A.	N.A.	62.5	0.98

Microbiological Studies

Antimicrobial Activity Determination Using the Agar Diffusion Well Method Using sterile cotton swabs, the microorganism inoculums were evenly distributed over a sterile Petri dish that contained nutrition agar for bacteria and malt extract agar for fungus. Each well(6 mm diameter holes punched in the agar gel, 20 mm apart from one another) received 100 µL of each sample. The systems were cultured at 37 °C for bacteria and 28 °C for fungi for a duration of 24 to 48 hours. Following incubation, the proliferation of microorganisms was noted. The amount of bacterial and fungal growth inhibition was expressed in millimetres The tests were run three times.
.[22]

Minimal Inhibitory Concentration (MIC) Measurement

Using the two fold serial dilution approach, the bacteriostatic activity of the active compounds (with inhibition zones (IZ) ≥ 16 mm) was then assessed. Using the appropriate nutritional broth, two fold serial dilutions of the investigated chemical solutions were made. The solutions' ultimate concentrations were 132, 66, 33, 16.5, and 8.25 mg/mL. Following the inoculation of the tubes with the test organisms, the bacteria were cultured in their appropriate broth at 37 °C for 24 hours (about 1 × 108 CFU/mL). Each 5 mL was then filled with 0.1 mL of the aforementioned inoculum and incubated for 24 hours at 37 °C. The minimum inhibitory concentration (MIC) was determined as the lowest concentration at which no growth was observed.

Conclusions

By reacting hydrazides with triethyl orthoformate, triethyl orthoproponate, and triethyl orthobenzoate, solid-supported NafionNR50 and phosphorus pentasulfide in alumina acted as catalysts to create a new family of 1,3,4-thiadiazoles with an indole moiety. Spectral analysis was used to establish the novel goods' structure. Results of the products' antibacterial activity suggested that some of the recently synthesized compounds have potential efficacy.

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