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RESEARCH ARTICLE

Synthesis, Characterization and Antimicrobial Evaluation of Mannich Bases of 4-(Furan-2-yl-methyleneamino)-3-(2-hydroxyphenyl)-1*H*-1,2,4-triazole-5-thione

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Abstract

Triazole nucleus has drawn much attention since the last decade because of its various potent biological activities. The pharmacological application of triazoles has been widely recognized and well documented. Schiff and Mannich bases are both considered as bioactive compounds, however, there are not much of documentation about the Mannich bases as their study has begun lately. The main aim of this study was to synthesize new Mannich bases from Schiff base bearing 1,2,4-triazole nucleus to access their antimicrobial activities. The newly synthesized compounds 1,2,4-triazole-5-thione, Schiff base (4) and Mannich bases (5a & 5b) were characterized by spectral techniques like UV, FT-IR, and NMR. Mannich bases were tested against various bacterial (gm +ve and gm –ve) as well as fungal strains. The synthesized Mannich bases showed good to moderate activities against the tested bacterial and fungal strains.

Keywords: 1,2,4-triazole-5-thione, Schiff base, Mannich base, antibacterial activity, antifungal activity

Introduction

Life on Earth relies exquisitely on heterocyclic compounds that play key roles in the biochemical reactions involved in fundamental activities such as metabolism, energy delivery, the replication of genetic material, nerve impulse transmission, etc. With their tunable properties available from the variety of structure, heterocyclic compounds allow for the design of new synthetic compounds for specific purposes like drugs, pesticides [1], detergents [2], dyes [3] polymers [4], and electronics [5]. The nitrogen-containing heterocyclic compounds have been utilized by many researchers because of their various potent biological activities, low toxicity and efficient selectivity [6]. One example of such nitrogen-containing heterocyclic compounds is Triazole containing a five-membered di-unsaturated ring structure composed of three nitrogen atoms and two carbon atoms at non-adjacent positions.

Triazoles exist as two isomers–1,2,3-triazoles and 1,2,4-triazoles [7]. The two tautomeric form of the 1,2,4-triazoles 1*H*- and 4*H*-1,2,4-triazoles are characterized by the position of hydrogen. In the substituted 1,2,4-triazoles, 3-mercapto-1,2,4-triazoles, the labile hydrogen may be attached either to the nitrogen or the sulphur atom and hence exist in two tautomeric forms – thione and thiol (Fig. 1) [8].

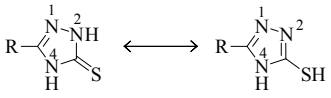


Figure 1: *Thione (a) and Thiol (b) tautomers of substituted 3-mercapto 1,2,4-triazole*

1, 2, 4- triazoles occupy a distinctive place in the field of medicinal and pharmaceutical chemistry [9], as well as in industry [10]. A large number of compounds containing 1,2,4-triazole nucleus as an important structural fragment have been reported to possess a wide range of biological activities such as antifungal [9], antibacterial [12-13], anticonvulsant [14], anti-tubercular [15], anti-inflammatory [9], anticancer [16-18], antioxidant [19] activities. Various drugs with 1,2,4-triazole ring have been introduced, for example, Rivabarin (antiviral agent) [20], Rizaptriptan (antimigraine agent) [21], Fluconazole, Itraconazole, (antimycotic agent) [22], Triazolam, Alprazolam, Estazolam (anticonvulsant drug) [23-24], Letrozole, Anastrozole, Vorozole (aromatase inhibitors) [25-26].

The properties and activity of a target compound such as Schiff base [14], Mannich base [27], thiourea [28], triazolothiadiazole [29] etc. can be changed simply by incorporating various substituents to the triazole ring on a different position. Mannich bases are the β-aminoketone that are generally obtained from Mannich reaction. The great synthetic relevance of the Mannich reaction is such that two different chemical moieties could be linked together in one step by means of methylene Bridge [30].

The study of Mannich bases has increased significantly because of their ability to show biological activities as antitubercular [31-32], antimalarial [33], vasorelaxing [34], anticancer [16, 35], anti-inflammatory [36], antifilarial [37], antibacterial [38], antifungal [38], anticonvulsant [39], anthelmintic [40], analgesic [41], anti-HIV [32], antipsychotic [42], antiviral [43] activities and so forth. Besides the biological activities, Mannich bases find applications in a variety of ways including their use as fuel additives [44], resins [45], polymers [46], surfactants [47], as plant growth regulators [48-49]. In the present study, we synthesized Mannich bases following Mannich reaction by combining chemically different amines (diphenylamine and piperazine) with a pharmacologically compatible 1,2,4-triazole nucleus containing Schiff base and evaluated their antimicrobial activities.

Materials and Methods

Starting materials

Hydrazine hydrate was purchased form Qualigens, ethanol from Alpha Chemica, methyl salicylate, *conc.* sulphuric acid, furfuraldehyde, methanol, potassium hydroxide, and hydrochloric acid were purchased from Fischer scientific, carbon disulphide and diphenylamine from Merck, and piperazine from Loba Chemie.

Physical measurements

Melting points of the synthesized compounds were determined with electrothermal apparatus from Optics technology. TLC of synthesized compounds was performed on silica gel coated plates using *n*-hexane : ethyl acetate solvent system and the spots were visualized by iodine vapuors in an iodine chamber. UV-visible electronic spectra in DMSO were recorded on double beam UV-Visible spectrophotometer of Labtronics (Model LT-2802) in the region 1100-200 nm. FT-IR spectra were measured in the range of (4000-400) cm^{-1} using KBr on IR prestige-21, Shimadzu, Japan. ^{1}H-NMR and ^{13}C-NMR were recorded on Bruker AV III 500 MHz NMR using DMSO as the solvent and chemical shifts are expressed in δ ppm.

Synthesis and analyses

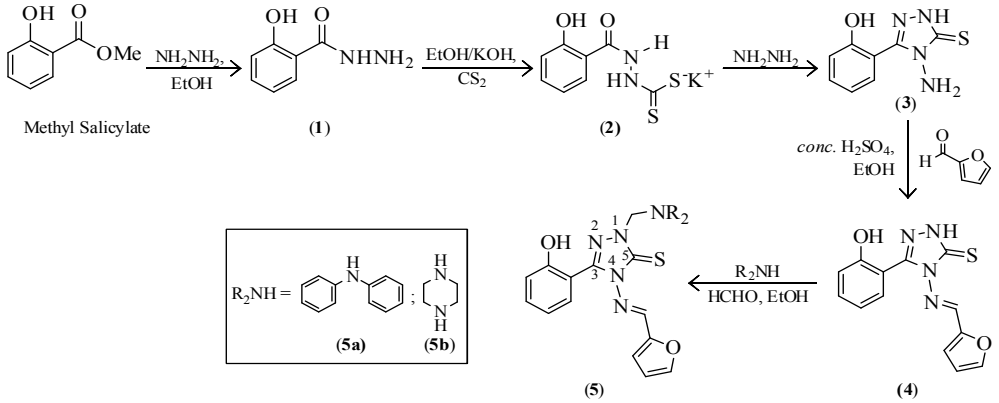
The compounds were synthesized from the starting materials as shown in the scheme1.

Synthesis of 2-hydroxybenzohydrazide (1)

2-Hydroxybenzohydrazide (1) was prepared by refluxing a mixture of hydrazine monohydrate (4.5 mL, 0.090 mol) and methyl salicylate (9.129 g, 0.060 mol) for 6 h [50]. The volume of the resulting solution was reduced to half by evaporation on a hot water bath and cooled. White crystalline solid separated out was filtered, washed with cold ethanol and recrystallized with absolute ethanol and was dried in a hot air oven at 50-60 °C. Yield - 79 % (7.228 g), white solid, mp 145-147 °C, R_f = 0.64 (*n*-hexane : ethyl acetate, 8:2).

Synthesis of potassium 2-(2-hydroxybenzoyl) hydrazinecarbodithioate (2)

To the ice-cold ethanol solution (~20 mL) containing 2-hydroxybenzohydrazide (4.565 g, 0.030 mol) and potassium hydroxide (1.683 g, 0.030 mol), carbon disulphide (2.284 g, 0.030 mol) was added dropwise



Scheme 1: *Synthetic route for the synthesis of Mannich bases of 1,2,4-triazole*

with constant stirring. The solution was stirred for 21 hours at room temperature on a magnetic stirrer. Anhydrous diethyl ether (~20 mL) was added, the precipitated solid was washed twice with anhydrous diethyl ether and dried in a desiccator [51]. Yield - 62% (4.898 g), white solid, mp 240 °C, R_f = 0.58 (*n*-hexane : ethyl acetate, 8:2).

Synthesis of 4-amino-2-(2-hydroxyphenyl)-1H-1,2,4-triazole-5-thione (3)

A suspension of potassium 2-(2-hydroxybenzoyl) hydrazinecarbodithioate (4.680 g, 0.018 mol) and hydrazine monohydrate (1.5 mL) in distilled water (~5 mL) was refluxed for 5 h till the evolution of hydrogen sulphide gas was ceased. The reaction mixture was cooled, diluted with ice-cold water (~50 mL) and acidified with conc. HCl. The solid product was separated by filtration, washed twice with cold water (30 mL) and recrystallized with absolute ethanol [52]. Yield: 79 % (2.894 g, 0.014 mol), off white solid, m.p. 166-169 °C, R_f : 0.35 (n-hexane :ethyl acetate, 8:2). UV- Visible spectrum (λ_{max}) nm = 302, 309, 331, 353. IR spectrum (selected bands) cm^{-1} = 3287, 3186, 3063, 1612, 1543, 1296, 946. ^{1}H-NMR (500 MHz, DMSO- d_6) δ ppm = 13.86 (br s, 1H, NH), 10.36 (s, 1H, OH), 7.43-7.31 (m, 2H, Ar-H), 7.00 (d, J = 8.20 Hz, 1H, Ar-H), 6.93 (t, J = 7.57 Hz, 1H, Ar-H), 5.62 (br s, 2H, NH_2). ^{13}C- NMR (125 MHz, d_6) δ ppm = 166.54 (Triazole-C5), 156.53 (Ar-C), 149.62 (Triazole-C3), 132.6 (Ar-C), 131.32 (Ar-C), 119.5 (Ar-C), 116.67 (Ar-C), 113.52 (Ar-C).

Synthesis of Schiff's base 4-(furan-2-yl-methyleneamino)-3-(2-hydroxyphenyl)-1H-1,2,4-triazole-5-thione (4)

A hot ethanolic solution (~5 mL) of furfuraldehyde (1.922 g, 0.020 mol) and triazole thione (4.165 g, 0.020 mol) was refluxed for ~5 h in presence of 5 drops of *con*c. sulphuric acid. The solid mass obtained on cooling was filtered under suction, washed with cold ethanol and recrystallized with hot ethanol [53]. Yield: 65% (3.626 g, 0.013 mol), greyish black crystalline solid, m.p.161-163 °C, R_f : 0.74 (n-hexane: ethyl acetate, 8:2). UV- Visible spectrum (λ_{max}) nm = 302, 309, 331, 353. 394. IR spectrum (selected bands) cm^{-1} = 3356, 3225, 3093, 2931, 1614, 1540, 1236, 948. ^{1}H-NMR (500 MHz, DMSO- d_6) δ ppm = 14.09 (br s, 1H, triazole NH), 10.06 (s, 1H, OH), 9.42 (s, 1H, N=CH), 7.98 (br s, 1H, Furan-H), 7.39 (br s, 1H, Ar-H), 7.37 (br s, 1H, Ar-H), 7.31 (d, *J* = 3.15 Hz, 1H, Ar-H), 6.93-6.90 (m, 2H, Ar-H & Furan-H), 6.73 (dd, *J* = 1.89, 3.78 Hz, 1H, Furan-H), ^{13}C- NMR (125 MHz, d_6) δ ppm = 162.14 (N=CH), 156.66 (Triazole C5), 154.43 (Ar-C), 148.83 (Triazole C3), 148.35 (Furan-C), 147.67 (Furan-C), 132.82 (Ar-C), 131.61 (Ar-C), 120.93 (Ar-C), 119.37 (Furan-C), 116.46 (Ar-C), 113.42 (Ar-C), 113.39 (Furan-C).

Synthesis of Mannich's base 1-{(diphenylamino) methyl}-4-(furan-2-ylmethyleneamino)-3-(2-hydroxyphenyl)-1H-1,2,4-triazole-5-thione (5a)

A mixture 40% formaldehyde (0.3 mL, 0.01 mol), hot ethanolic solution of Schiff's base (1.432 g, 0.005 mol) and diphenylamine (0.846 g, 0.005 mol) was refluxed for 3 h. Excess amount of distilled water was added and the reaction mixture was left overnight. The precipitate was filtered under suction, washed with cold ethanol and recrystallized by absolute ethanol [53]. Yield: 66% (1.540 g, 0.033 mol), brownish black crystalline solid, m.p. 109-110 °C, R_f : 0.72 (*n*-hexane : ethyl acetate, 8:2). UV- Visible spectrum (λ_{max}) nm =302, 309, 339, 353, 393. IR spectrum (selected bands) cm^{-1} = 3217, 2932, 1605, 1497, 1234, 933.^{1}H-NMR (500 MHz, DMSO- d_6) δ ppm = 10.93 (s, 1H, OH), 9.32 (s, 1H, N=CH), 8.14 (br s, 1H. Ar-H), 8.00 (br s, 1H, Furan-H), 7.96-7.94 (dd, *J* = 8.20×(2), 1H, Ar-H), 7.51-7.44 (m, 1H, Ar-H), 7.37-7.29 (m,4H, Diphenylamine-H & Furan-H), 7.27-7.20 (m, 4H, Diphenylamine-H & Furan-H), 7.08 (d, *J*= 8.20, 1H, Ar-H), 6.82 (dd, *J* = 5.7 Hz, 1H, Furan –H), 6.16 (s, 2H, N-CH_2-N).^{13}C- NMR (125 MHz, d_6) δ ppm = 166.30 (Triazole C5), 159.02 (Ar-C), 148.57 (Triazole C3), 147.54 (Furan-C), 146.65 (2C, Diphenhylamine–C), 143.90 (2C, Furan-C), 134.55 (N=CH), 129.61 (4C, Diphenyl–C), 121.93 (2C, Diphenhylamine–C), 120.11 (Ar-C), 119.72 (Furan-C), 117.74 (4C, Diphenhylamine–C), 117.19 (Ar-H), 115.43 (2C, Furan-H), 113.44 (Ar-H), 88.61 (N-CH_2-N).

Synthesis of Mannich's base 4-(furan-2-ylmethylemeamino)-3-(2-hydroxyphenyl)-1-(piperazin-1-ylmethyl)-1H-1,2,4-triazole-5-thione(5b)

A mixture 40% formaldehyde (0.3 mL, 0.01 mol), hot ethanolic solution of Schiff's base (1.432 g, 0.005 mol) and piperazine (0.431 g, 0.005 mol) was refluxed for 3 h. Excess amount of distilled water was added and the reaction mixture was left overnight. The precipitate was filtered under suction, washed with cold ethanol and recrystallized by absolute ethanol. Yield: 78% (1.501 g, 0.004 mol), brown solid, m.p. 140-142 °C, R_f: 0.89 (*n*-hexane : ethyl acetate, 8:2). UV- Visible spectrum (λ_{max}) nm = 302, 309, 339,

354, 405. IR spectrum (selected bands) cm^{-1} = 3240, 2939, 2831, 1705, 1551, 1304, 934. ^{1}H-NMR (500 MHz, DMSO- d_6) δ ppm = 10.13 (s, 1H, OH), 9.39 (s, 1H, N=CH), 8.12 (br s, 1H, Ar-H), 8.00 (br s, 1H, Furan-H), 7.93 (dd, *J* = 8.20 Hz×(2), 1H, Ar-H), 7.51-7.42 (m, 1H, Ar-H), 7.13 (d, *J* = 8.20, 1H, Ar-H), 5.13 (s, 2H, N-CH_2-N), 3.87 (br s, 4H, Piperazine-C), 3.82 (br s, 4H, Piperazine-C), 2.79 (br s, 1H, NH-Piperazine). ^{13}C- NMR (125 MHz, d_6) δ ppm = 166.13 (Triazole C5), 159.05 (Ar-C), 148.57 (Triazole C3), 147.22 (Furan-C), 145.55 (Furan-C), 134.55 (N=CH), 129.27 (Ar-C), 125.60 (Ar-C), 121.58 (Ar-C), 119.63 (Furan-C), 117.73 (Ar-C), 113.15 (Furan-C), 77.33 (N-CH2-N), 53.90 (2C, Piperzine-C), 44.22 (2C, Piperzine-C).

Antimicrobial (antibacterial and antifungal) screening

The antimicrobial activities of the newly synthesized Mannich bases were screened against different gram-positive bacterial strains – *Bacillus subtilis, Enterococcus faecalis, Staphylococcus aureus, and Staphylococcus epidermis*; gram-negative bacterial strains – *Escherichia coli, Klebsiella pneumonia, Proteus vulgaris, Pseudomonas aeruginosa, Shigella dysenteriae,* and fungal strains – *Candida albicans, Saccharomyces cerevisiae* according to agar well diffusion methods as described by Perez *et al*, [54]. The overnight culture of bacterial and fungal strains from nutrient agar and potato dextrose agar respectively was adjusted to 0.5 Mc Farland standards over the appropriate medium Muller-Hinton Agar (MHA) for bacteria and Muller-Hinton Agar with Glucose and Methylene Blue (MHA, GMB) for fungi by using a sterile swab. On each agar plate wells of 6 mm diameter suitably separated were loaded with 50 µL of the test solution of the samples and solvent as a negative control. Chloramphenicol (60 $mcg.mL^{-1}$) and Clotrimazole (200 $mcg.mL^{-1}$) were used as reference antibacterial and antifungal respectively. The inoculated plates were kept at a suitable temperature (35±2 °C for bacteria and 25±2 °C for fungi). After proper incubation (18-24 h for bacteria, 24-48 h for fungi) the plates were examined for zone of inhibition (ZOI) around the well which is suggested by clear area with no growth of organisms.

Results and Discussion

Chemistry

Mannich base 5a & 5b were synthesized from the Schiff base containing 1,2,4-triazole-5-thione nucleus according to the scheme 1. Methyl salicylate was refluxed with hydrazine hydrate and ethanol to yield acid hydrazide (1). Treatment of (1) with alcoholic potassium hydroxide and carbon disulphide resulted in the formation of dithiocarbazinate (2). The ring closure of compound (2) in presence of excess hydrazine hydrate in ethanol gave 4-amino-2-(2-hydroxyphenyl)-1*H*-1,2,4-triazole-5-thione (3). Condensation of 1,2,4-triazole (3) with furfuraldehyde and refluxed with ethanol along with *conc*. H_2SO_4 as catalyst gave 4-(furan-2-yl-methyleneamino)-3-(2-hydroxyphenyl)-1*H*-1,2,4-triazole-5-thione (4). Mannich bases were synthesized finally by refluxing formaldehyde, ethanolic solution of Schiff base (4) and diphenylamine to form (5a), whereas (5b) is formed when piperazine is used instead of diphenylamine.

Spectroscopic studies

The structure of the 1,2,4-triazole-5-thione, Schiff base and Mannich bases were confirmed by UV, FT-IR, ^{1}H-NMR and ^{13}C-NMR spectral techniques.

UV-Visible spectral analysis

The UV-visible electronic spectra of the compounds were studied in DMSO. All the synthesized compounds showed the absorbance at 302 and 309 nm which corresponds to the aromatic C=C and azomethine C=N (π→π*) of triazole ring. Compound (3) also exhibited absorptions at 331 nm due to (*n*→π*) transitions associated with the nonbonding electron pair of the nitrogen atom of triazole C=N and sulphur atom of C=S. The absorption at 353 nm is attributable to (*n*→π*) transitions associated with *o*-hydroxy group. Compound (4) also showed three other bands at 339 nm, 353 nm and 394 nm associated (*n*→π*) C=N and C=S, (*n*→π*) transitions of *o*-hydroxy group and (*n*→π*) transitions of azomethine group C=N respectively [55]. Compound (5a) & (5b) exhibited three other electronic transitions - one at 339 nm because of the (*n*→π*) electronic transitions of triazole C=N and sulphur atom of C=S, another at 353 & 354 nm (Mannich base 5a & 5b respectively) associated with (n→π*) transitions of o-hydroxy group, and the next band at 393 and 405 nm respectively due to (n→π*) transitions of azomethine group C=N.

FT-IR spectral analysis

The formation of triazole (3) is confirmed by the presence of a medium band at 1296 cm^{-1} and strong band at 946 cm^{-1} corresponding to N-C=S thioamide II and C=S thioamide IV. Moreover, no absorption bands were detected about 1651-1707 cm^{-1} indicating

the absence of C=O group of the compound which is the evidence for the conversion of dithiocarbazinate to triazoles [56]. The absence of band at 1700 cm^{-1} clearly indicates the amino condensation and hence the formation of Schiff bases [53]. The absence of medium intensity bands in the region of 3500-3200 cm^{-1} attributable to $–NH_2$ protons demonstrates the formation of Schiff bases [57]. Further, absence of an absorption band in the region of 2300-2600 cm^{-1} region cited for the –SH group clearly states that, in the solid-state, the compound exists predominantly in the thionic form [58-59]. The formation of Mannich bases (5a) & (5b) is supported by the presence of medium absorption band at 1234 cm^{-1} and weak absorption band at 1304 cm^{-1} respectively due to N-C=S group and also the absence of absorption band at 2550cm^{-1} due to S-H structure, hence, supporting the formation of N- Mannich bases but not S- Mannich bases [53].

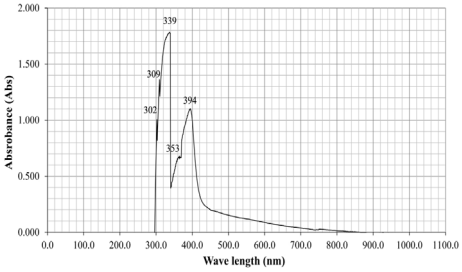


Figure 2: *UV-Visible spectrum of compound 4*

[1]H-NMR spectral analysis

In ^{1}H-NMR spectrum of compound (3), the broad singlet at 13.86 ppm is attributed to the hydrogen attached to the nitrogen which suggests the formation of thione based triazole [60] which is equally supported by the absence of IR absorption band at 2600 cm^{-1} due to thiol group. The ^{1}H-NMR spectrum of Schiff base showed a singlet at 9.42 due to presence of –N=CH group and absence of signals approximately at 5.76 ppm (NH_2) in the molecule confirming the formation of Schiff bases. The absence of exchangeable -SH signals c.a. 4.0 ppm indicated the predominance of the thione tautomer in DMSO-d_6 [61]. The singlets found at 6.16 ppm and 5.13 ppm due to N-CH_2-N group confirms the formation of Mannich bases (5a & 5b) from Schiff base. Moreover, the absence of a peak at 11.5 ppm clearly suggests the absence of thiol group in the structure instead thione based Mannich base is formed [53].

[13]C-NMR spectral analysis

The typical carbon resonance at δ162.57-167.67 ppm was indicative of triazole C5, i.e., C=S group [62].

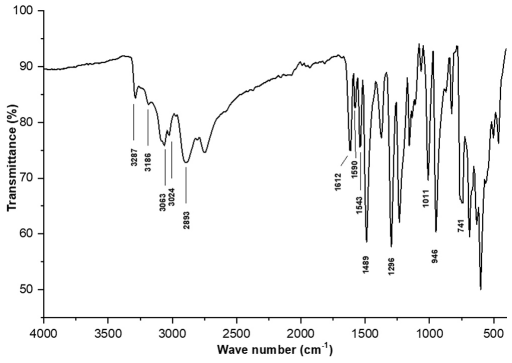


Figure 3: *IR spectrum of compound 3*

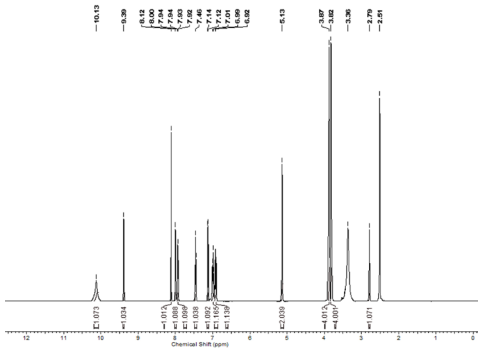


Figure 4: *[1]H NMR spectrum of compound 5b*

The compounds 3, 4, 5a & 5b consists of a peak at 166.54, 162.14, 166.30 and 166.13 ppm respectively. The signal of C=N is observed at 149.62, 148.83, 148.57 and 148.57 ppm for compounds 3, 4, 5a & 5b respectively. The peak found at 156.66 ppm due to the azomethine carbon confirms the formation of Schiff base [63]. In compound 5a, the aromatic carbons of diphenyl group were found in the region of 146.65-117.74 ppm whereas the piperazine carbon (5b) was found in the region of 53.90 & 44.22 ppm [62]. The formation of Mannich bases (5a & 5b) were confirmed by the presence of peak at 88.61 ppm and 77.33 ppm respectively.

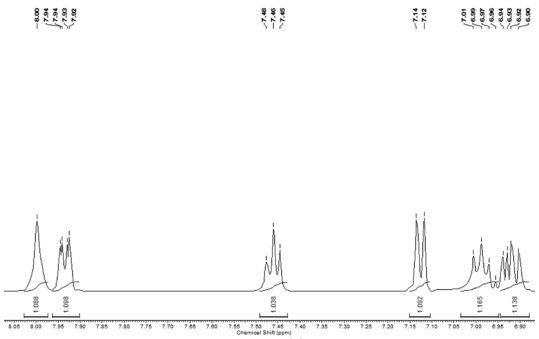


Figure 5: *Expanded [1]H NMR spectrum of compound 5b*

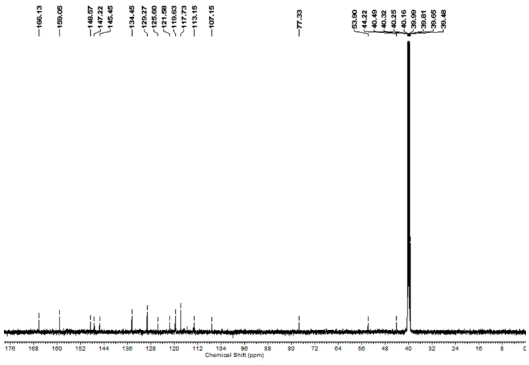


Figure 6: *^{13}C NMR spectrum of compound 5b*

Antimicrobial screening

The antimicrobial screening revealed that the compounds showed moderate activity against bacterial strains and good activity against fungi. Compound 5a with diphenylamine appeared more active against gram –ve bacteria than gram +ve bacteria, while compound 5b with piperazine was found to be more effective against gram +ve bacteria than gram –ve. Compound 5a showed better activity against gram-negative bacterial strain of *Proteus vulgaris* than any other bacterial strain whereas 5b showed the greatest activity against gram-positive bacterial strain *Staphylococcus aureus* against which 5a was ineffective. Compound 5a exhibited remarkable activity against the bacterial strains *P. vulgaris* and *P. aeruginosa* towards which the standard antibacterial chloramphenicol showed no activity. Likewise, compound 5b was also found to be effective against *P. vulgaris*. Both Mannich bases were ineffective against *B. subtilis,* and *S. epidermidis*.

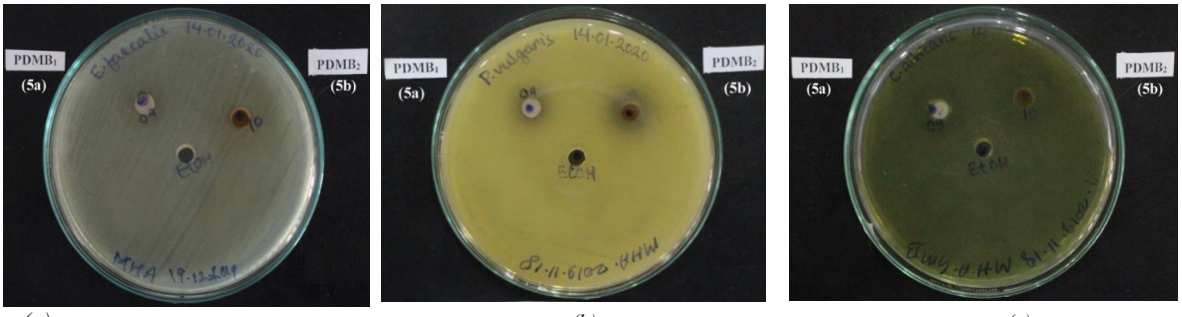
Both 5a and 5b exhibited remarkable activity against the fungal strains *C. albicans* and *S. crevisiae* comparable to that of the standard drug clotrimazole. The piperizinyl derivative 5b exhibited more potent antifungal activity than the diphenylamine derivative 5a.

Compound 5b showed better antifungal activity than compound 5a for both fungal strains.

Table 1: *Inhibition zones showing antimicrobial activities of Mannich bases and reference antibiotic*

Microbial Strain	Diameter of Zone of Inhibition (mm)			
	Compound (5a)	Compound (5b)	Chloramphenicol Conc^{n} (60 mcg.mL^{-1})	Clotrimazol Conc^{n} (200 mcg.mL^{-1})
Bacillus subtilis[a]	-	-	26.6	NT
Enterococcus faecalis[a]	7.0	8.0	20.9	NT
Staphylococcus aureus[a]	-	14.5	28.4	NT
Staphylococcus epidermidis[a]	-	-	31.7	NT
Escherichia coli[b]	7.8	7.3	20.9	NT
Klebsiella pneumoniae[b]	7.7	-	12.3	NT
Proteus vulgaris[b]	9.7	12.2	-	NT
Pseudomonas aeruginosa[b]	8.5	-	-	NT
Shigella dysenteriae[b]	7.0	-	29.0	NT
Candida albicans[f]	18.1	21.7	NT	32.3
Saccharomyces cerevisiae[f]	12.5	19.4	NT	24.4

'-' No activity; [a] Gram positive bacteria; [b] Gram negative bacteria; [f] fungi, NT = not tested



(a) *(b)* *(c)*

Figure 7: *Antimicrobial activity of Mannich bases against (a) Enterococcus faecalis (Gram +ve bacteria) (b) Proteus vulgaris (Gram –ve bacteria) and (c) Candida albicans (Fungi)*

Conclusion

A new Schiff base 4-(furan-2-yl-methyleneamino)-3-(2-hydroxyphenyl)-1H-1,2,4-triazole-5-thione and two new Mannich bases viz. 1-{(diphenylamino)methyl}-4-(furan-2-ylmethyleneamino)-3-(2-hydroxyphenyl)-1H-1,2,4-triazole-5-thione and 4-(furan-2-ylmethylemeamino)-3-(2-hydroxyphenyl)-1-(piperazin-1-ylmethyl)-1H-1,2,4-triazole-5-thione were prepared. These synthesized compounds were characterized by spectroscopic techniques (UV, FT-IR, ^{1}H-NMR and ^{13}C-NMR). The Mannich 5a with diphenylamine exhibited broad-spectrum against gram-negative bacterial strain than compound 5b with piperazine. However, compound 5b was found to be more potent in bacterial as well as fungal inhibition than 5a. 1,2,4-Triazole Mannich bases exhibit more promising antifungal activity than antibacterial activity.

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