SYNTHESIS OF NEW LIGANDS CONTAINING THE SULFONYL GROUP AND ANTIMICROBIAL ACTIVITIES

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In this study firstly, the acylhydrazone compound named Ethyl-4-methylbenzene-sulfonyl-carbonyl-4-methyl-benzohydrazonate was synthesized by the condensation of ethyl-4-methyl-benzimidate hydrochloride with 4-methyl-benzene sulfonyl hydrazide. The treatment of the acylhydrazone compound with hydrazine hydrate afforded 4-amino-3-4-methylbenzene sulfonyl-2-yl-5-4-methyl-phenyl-1, 2, 4-triazole. The usage of this compound with various aromatic aldehydes resulted in the formation of 4-arylidenamino-3-4-methylbenzene sulfonyl-2-yl-5-4-methyl-phenyl-1,2,4-triazoles. Sodium borohydride reduction of 4-arylidenamino derivatives afforded 4-alkylamino-3-4-methylbenzene sulfonyl-2-yl-5-4-methyl-phenyl-1, 2, 4-triazoles. The obtained products were identified by FT-IR, ^{1}H-NMR, ^{13}C-NMR and elemental analysis data. A series of compounds have been evaluated for their antimicrobial activities. The results show that the synthesized new compounds had effective antimicrobial activities.

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Keywords: Sulfonyl Group, 1, 2, 4-triazoles, Arylidenamino Compounds, Antimicrobial Activities

1. Introduction

Compounds containing imino groups are an important field of study for various applications in optical communication and optical instruments, electronics, optoelectronics and photonics, and are expected to be suitable for future chemical development. The phenyl derivatives of Schiff bases have been used as corrosion inhibitors [1]. In recent years, many Schiff bases have been found that can be used in liquid crystal technology [2].

These compounds are of great importance in the case of supermolecular compounds. Schiff bases and complexes are used in medicine, plastics industry, water treatment, biochemical processes and many other areas due to their remarkable and important features [3]. Many catalysts used industrially are essentially coordination compounds. In addition, the working mechanisms of the enzymes [4] and the C=N double bond, that is, Schiff base formation, is also mentioned in the steps of visual processing [5]. Schiff bases have also been reported to be widely used as protective groups for the amino group in organic synthesis. Schiff bases with UV-Vis (solvakromic) spectra solvents have been reported to be suitable NLO (Non-Linear Optically Active) materials [6].

The metal complexes obtained from the groups of Schiff bases are used as pigment materials in the paint industry, especially in textile dyeing, since they are colored materials [7]. Some Schiff bases are also used in the construction of ion selective electrodes. In particular, the determination of the effectiveness of various metal complexes in living organisms over time has led to intensification of studies on these compounds [8]. Therefore, the clarification of structures of Schiff bases and complexes has become more important.

Schiff bases and biologically active complexes are known to be used as chelating ligands in dioxygen carrier, catalyst, model systems in biological macromolecules, cancer inhibiting radiopharmaceutical effects and coordination chemistry. It is known that Schiff bases and biologically active complexes are used as chelating ligands in dioxygen carrier, catalyst, model systems in biological macromolecules, cancer inhibiting radiopharmaceutical effects and

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coordination chemistry [9]. Previous studies have shown that Schiff bases with sulfur in their structure inhibit the growth of some bacteria in different amounts [10-13]. It is also known that they exhibit anticancer properties by inhibiting the proliferation of some viruses [14, 15].

Classical sulfonamides are broad-spectrum antibiotics, have been used in the treatment of many infections for many years due to their low cost and low toxicity [16]. Rapid spread of HIV virus, the emergence of new pathogenic bacteria such as SARS, bacteria gain resistance against existing drugs causes infectious diseases that threaten human health. Also the use of some bacteria for bioterrorism necessitated new studies on infectious diseases. Studies on this subject synthesize new drugs showing not only antimicrobial activity but also pathogenic bacteria in the form of detection of new target enzymes [17, 18]. In previous studies, methanesulfonic acid hydrazide and its sulfonyl hydrazones were synthesized and has shown activity against Bacillus macerans ATCC 2214 bacteria. Also, they have been shown to have antineoplastic effects against human melanoma cell SK-MEL 3 [19].

Today, sulfonamides are used in combination with pyriminamine (dihydrofolate reductase inhibitor) in the treatment of systemic infections. Co-trimethazole has an important role in the treatment of pneumonia (lung inflammation) in children [20]. Sulfisoxazole, sulfamethoxazole, sulfadiazine, sulfamethisole and Co-trimoxazole are widely used in the treatment of urinary tract infections. These compounds act in a short time and have high solubility [21]. Necordiosis is a disease that can lead to discharge of the skin, fluid accumulation in the chest cavity. Various sulfa drugs, especially Co-trimoxazole, are used in the treatmen [22]. “Sulfapiridine in throat and skin infections, Sulfacetamide used in eye infections. It is used as an alternative to amoxicillin in the treatment of sinusitis in patients with penicillin allergy [23, 24]. Sulphonamides and sulfones are enzyme inhibitors that inhibit the growth of microorganisms by inhibiting the folate metabolism of bacteria [25]. In our studies we have reported that 1,2 4-triazole ligands showed, ion extraction selectivity, fluorescent chemosensor and complex stability constant [26-28].

In our current work, we have synthesized some novel 1, 2, 4-triazole compounds containing a sulfonyl group. The synthesized compounds were evaluated for antimicrobial activity.

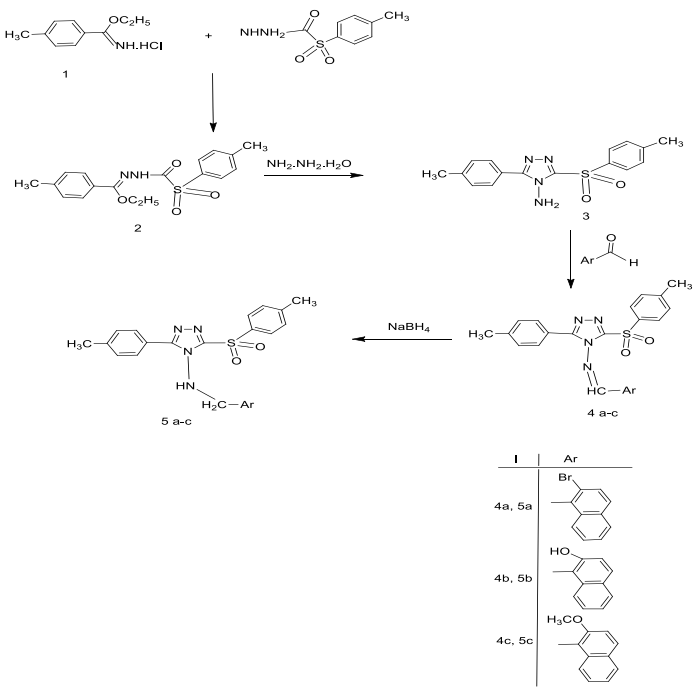

Fig. 1. General Synthetic pathway for the preparation of new compounds.

2. Experimental

The necessary chemicals were purchased from Merck and Fluka including 4-methyl-benzene sulfonylhydrazide, p-tolylnitrile, ethanol (99.9%), hydrazine hydrate (98%), 2-bromo-1-naphtaldehyde, 2-hydroxy-1-naphtaldehyde, 2-metoxy-1-naphtaldehyde, 2-propanol (99.5%), methanol (99.8%), glacial acetic acid and $NaBH_4$. All chemicals were used as received without further purification. Melting points were determined on a Barnstead Electrothermal melting point apparatus and were uncorrected. The IR spectra (υ, cm^{-1}) was obtained with a Perkin Elmer 1600 FTIR spectrometer in KBr pellets. ^{1}H-NMR and ^{13}C-NMR spectra (δ, ppm) were recorded on a Varian-Mercury 200 MHz spectrophotometer using tetramethylsilane as the internal reference. Combustion analysis was performed on a Carlo Erba 1106 elemental analyzer. All the compounds gave C, H, and N analysis results within ±0.6 % of the theoretical values.

Microbiology

Antibacterial activity

All test microorganisms were obtained from the Refik Saydam Hıfzıssıhha Institute (Ankara, Turkey), which included Escherichia coli ATCC 25922, Pseudomonas aeruginosa ATCC 10145, Yersinia pseudotuberculosis ATCC 911, Klepsiella pneumonia ATCC 13883, Enterococcus faecalis ATCC 29212, Staphylococcus aureus ATCC 25923, Bacillus cereus 709 ROMA, Candida albicans ATCC 60193, and Candida tropicalis ATCC 13803. The chemicals were weighed and dissolved in dimethylsulfoxide (DMSO) to prepare extract stock solutions of 10 mg/mL.

Agar well diffusion method

A simple susceptibility screening test using agar-well diffusion as adapted earlier **[30]** was used. Each microorganism was suspended in Mueller Hinton (Difco, Detroit, MI, USA) broth and diluted to ca. 106 colony forming units (cfu) per mL. They were flood-inoculated onto the surface of Mueller Hinton agar and Sabouraud dextrose agar (SDA) (Difco), which were then dried. For C. albicans and C. tropicalis, SDA was used. From the agar, 5-mm diameter wells were cut using a sterile cork-borer and 500 µg/50 µL (10 mg/mL) of the chemical substances were delivered into the wells. The plates were incubated for 18 h at 35 ◦C.

2.1. Ethyl-4-methylbenzene-sulfonyl-carbonyl-4-methyl-benzohydrazonate (2)

Ethyl-4-methyl-benzimidate hydrochloride (1) was synthesized using a published method **[29]**. Ethyl-4-methylbenzene-sulfonyl-carbonyl-4-methyl-benzohydrazonate (2) was obtained the solution of ethyl-4-methyl-benzimidate hydrochloride 1 (10 mmol) in absolute ethanol was added the solution of 4-methyl-benzene sulfonyl hydrazide (10 mmol) in absolute ethanol and the mixture was stirred at 0–5 °C for 6 h. Then, the precipitated ammonium chloride 35–40 °C under reduced pressure, a white solid was obtained. This dry product was recrystallized from alcohol and named compound 2 yield 64.00%. M.p. 122–123 °C; IR (KBr) cm^{-1} 3334 (ν NH), 1680 (ν C=O), 1625 (ν C=N), 1310 (ν SO_2), 809, 817 (1, 4-disubstitue arom. ring); ^{1}H-NMR (DMSO-d_6) δ (ppm) 1.34 (t, 3H, CH_3), 2.31 (t, 3H, Ar-CH_3), 2.34 (t, 3H, Ar-CH_3), 4.09 (q, 2H, CH_2), Ar–H [6.67 (d, 2H), 7.48 (d, 2H), 7.56 (d, 2H), 7.60 (d, 2H)], 10.24 (s, 1H, NH); ^{13}C-NMR (DMSO-d_6) δ(ppm) 166.41 (C=O), 162.28 (C=N), Ar–C [139.12 (2CH), 136.75 (2C), 132.88 (2CH), 128.49 (2CH), 128.04 (2CH), 118.41 (C), 114.63 (C)], 63.15 (OCH_2), 23.14 (Ar-CH_3), 21.48 (Ar-CH_3), 16.64 (CH_3). Anal.calcd. (%) for ($C_{18}H_{20}N_2SO_4$) 360.41 g/mol: C, 59.98; H, 5.59; N, 7.77. Found: C, 59.83; H, 5.44; N, 7.83.

2.2. 4-amino-3-4-methylbenzene sulfonyl-2-yl-5-4-methyl-phenyl-1,2,4-triazole (3)

A solution of hydrazine hydrate (0.01 mol) in 1-propanol (50 mL) was partly added to the compound **2** (0.005 mol), and the mixture was refluxed for 24 h. After the product was cooled, filtered and %. M.p. 166-167 °C; IR (KBr) cm^{-1} 3341-3234 (ν NH_2), 1628, 1616 (ν2C=N), 1316 (ν SO_2), 823, 809 (1, 4-disubstitue arom. ring); ^{1}H-NMR (DMSO-d_6) δ (ppm) 2.38 (t, 3H, Ar-CH_3), 2.41 (t, 3H, Ar-CH_3), 6.32 (s, 2H, NH_2), Ar–H [6.72 (d, 2H), 7.39 (d, 2H), 7.47 (d, 2H), 7.82 (d,

2H)]; ^{13}C-NMR (DMSO-d_6) δ (ppm) 154.15, 149.96 (2C, triazole C_3, C_5), Ar–C [145.67 (2CH), 144.91(C), 133.47 (2CH), 130.09 (2C), 128.11 (2CH), 126.31 (C), 114.89 (2CH)], 22.87 (Ar-CH_3), 21.62 (Ar-CH_3). Anal.calcd. (%) for ($C_{16}H_{16}N_4SO_2$) 328.36 g/mol: C, 58.52; H, 4.90; N, 17.06. Found: C, 58.61; H, 4.86; N, 17.13.

2.3. Compounds 4a–4c (general procedure)

The selected aldehyde (0.01 mol) was added to a solution of Amino compound **3** (0.005 mol) in glacial acetic acid (30 mL), and the mixture was refluxed for 8 h. The mixture was cooled and poured into ice water in a beaker (100 mL). The precipitate formed was filtered. After drying in vacuo, the product was recrystallized from an appropriate solvent to give the desired compound **[29]**.

2.3.1. 3-4-methyl-phenyl-5-(4-methylbenzenesulfonyl-4yl)-4-(2-Bromo-1-phyliden-amino)-4H-1,2,4-Triazole (4a)

Yield 78.16%. M.p. 148-149 °C; IR (KBr) cm^{-1} 1594, 1566 (ν 2C=N), 1320 (ν SO_2), 820, 809 (1, 4-disubstitue arom. ring), 745 (1, 2-mono substitue arom. ring); ^{1}H-NMR (DMSO-d_6) δ (ppm) 2.35 (t, 3H, Ar-CH_3), 2.37 (t, 3H, Ar-CH_3), Ar–H [6.67 (d, 1H), 6.91 (d, 2H), 7.45 (d, 2H), 7.62-7.74 (m, 2H), 7.76 (d, 2H), 7.79–8.01 (m, 2H), 8.03 (d, 1H), 8.18 (d, 2H)], 8.84 (s, 1H, N=CH); ^{13}C-NMR (DMSO-d_6) δ (ppm) 171.06 (N=CH), 150.39, 143.82 (2C, triazole C_3, C_5), Ar–C [159.67 (C), 141.31 (2CH), 139.10 (C), 131.53 (2CH), 133.02 (CH), 131.84 (C), 130.64 (CH), 130.31 (2CH), 130.17 (2CH), 129.62 (2CH), 128.97 (CH), 128.26 (2C), 127.12 (CH), 125.43 (CH), (113.25 (CH), 112.66 (2C)], 21.12 (Ar-CH_3), 20.34 (Ar-CH_3). Anal.calcd. (%) for ($C_{27}H_{21}N_4BrSO_2$) 545.22 g/mol: C, 59.47; H, 3.88; N, 10.27. Found: C, 59.44; H, 3.74; N, 10.41.

2.3.2. 3-4-methyl-phenyl-5-(4-methylbenzenesulfonyl-4yl)-4-(2-Hydroxy-1-phyliden-amino)-4H-1,2,4-Triazole (4b)

Yield 76.94%. M.p. 154-155 °C; IR (KBr) cm^{-1} 3320 (ν OH), 1624, 1601 (ν 2C=N), 1320 (ν SO_2), 814, 807 (1, 4-disubstitue arom. ring), 748 (1, 2-di substitue arom. ring); ^{1}H-NMR (DMSO-d_6) δ (ppm) 2.33 (t, 3H, Ar-CH_3), 2.36 (t, 3H, Ar-CH_3), Ar–H [7.20 (d, 1H), 7.35 (d, 2H), 7.53 (d, 1H), 7.68 (d, 2H), 7.86 (d, 2H), 7.90–8.05 (m, 2H), 8.10 (d, 2H), 8-80-8.90 (m, 2H)], 9.02 (s, 1H, N=CH), 9.87 (s, 1H, OH); ^{13}C-NMR (DMSO-d_6) δ (ppm) 168.12 (N=CH), 152.79, 150.28 (2C, triazole C_3, C_5), Ar–C [160.80 (C), 152.16 (CH), 143.80 (2CH), 139.92 (C), 137.12 (2CH), 131.51 (C), 129.88 (2CH), 129.10 (CH), 128.91 (2CH), 128.15 (2C), 124.76 (CH), 124.18 (CH), 123.77 (C), 118.22 (CH), 116.14 (CH), 111.46 (C)], 23.17 (Ar-CH_3), 21.69 (Ar-CH_3). Anal.calcd. (%) for ($C_{27}H_{22}N_4SO_3$) 482.53 g/mol: C, 67.20; H, 4.59; N, 11.60. Found: C, 67.28; H, 4.53; N, 11.67.

2.3.3. 3-4-methyl-phenyl-5-(4-methylbenzenesulfonyl-4yl)-4-(2-Methoxy-1-Naphthyliden-amino)-4H-1,2,4-Triazole (4c)

Yield 77.04%. M.p. 161–162 °C; IR (KBr) cm^{-1} 1589, 1566 (ν 2C=N), 1320 (ν SO_2), 818, 807 (1,4 disubstitue arom. ring), 743 (mono substitue arom. ring); ^{1}H-NMR (DMSO-d_6) δ (ppm) 2.35 (t, 3H, Ar-CH_3), 2.38 (t, 3H, Ar-CH_3), 3.82 (s, 3H, OCH_3), Ar–H [6.69 (d, 1H), 6.94 (d, 1H), 7.12 (d, 2H), 7.36–7.40 (m, 2H), 7.54– 7.67 (m, 2H), 7.73 (d, 2H), 7.85 (d, 2H), 7.90 (d, 2H)], 8.79 (s, 1H, N=CH); ^{13}C-NMR (DMSO-d_6) δ (ppm) 168.06 (N=CH), 149.18, 148.96 (2C, triazole C_3, C_5), Ar–C [164.02 (C), 136.17 (2CH), 136.01 (2C), 135.12 (CH), 134.99 (2C), 131.83 (2CH), 130.04 (2CH), 129.53 (CH), 126.56 (C), 124.97 (2C), 123.16 (2CH), 122.04 (CH), 119.40 (CH), 115.48 (2CH)], 56.72 (OCH_3), 22.55 (Ar-CH_3), 21.00 (Ar-CH_3). Anal.calcd. (%) for ($C_{28}H_{24}N_4SO_3$) 496.56 g/mol: C, 67.72; H, 4.87; N, 11.28. Found: C, 67.75; H, 4.81; N, 11.22.

2.4. Compounds 5a–5c (general procedure)

First the Arylidenamino compounds **(4a–c)** (0.005 mol) were dissolved in dried methanol (50 mL), and NaBH4 (0.01 mol) was added to the solution in small particles. The mixture was refluxed for 20 min and then left to cool. After evaporation at 30–35 °C under reduced pressure, the solid residue was washed with cold water. After drying in vacuo, the solid product was recrystallized from an appropriate solvent to afford the desired compound **[29]**.

2.4.1. 3-4-methyl-phenyl-5-(4-methylbenzenesulfonyl-4yl)-4-(2-Bromo-1-Naphthylmethyl-amino)-4H-1, 2, 4-Triazole (5a)

Yield 88.41%. M.p. 144-145 °C; IR (KBr) cm^{-1} 3290 (ν NH), 1599, 1558 (ν 2C=N), 1314 (ν SO2), 816, 811 (1,4 di substitue arom. ring), 753 (mono substitue arom. ring); ^{1}H-NMR (DMSO-d_6) δ (ppm) 2.38 (t, 3H, Ar-CH_3), 2.41 (t, 3H, Ar-CH_3), 3.96 (d, 2H, CH_2), 6.70 (t, 1H, NH), Ar–H [6.95 (d, 1H), 7.03 (d, 2H), 7.17 (d, 2H), 7.25 (d, 1H), 7.54-7.65 (m, 2H), 7.80–7.87 (m, 2H), 7.90 (d, 2H), 7.96 (d, 2H)]; ^{13}C-NMR (DMSO-d_6) δ (ppm) 149.75, 148.49 (2C, triazole C_3, C_5), Ar–C [163.54 (C), 135.15 (2CH), 131.42 (2C), 131.39 (2CH), 130.72 (2CH), 130.24 (CH), 130.10 (2C), 130.00 (2CH), 129.80 (C), 129.63 (2CH), 127.90 (CH), 126.41 (2C), 124.62 (CH), 116.89 (CH)], 51.77 (CH_2), 21.32 (Ar-CH_3), 20.87 (Ar-CH_3). Anal.calcd. (%) for ($C_{27}H_{23}N_4BrSO_2$) 547.23 g/mol: C, 59.26; H, 4.23; N, 10.23. Found: C, 59.31; H, 4.18; N, 10.27.

2.4.2. 3-4-methyl-phenyl-5-(4-methylbenzenesulfonyl-4yl)-4-(2-Hydroxy-1-Naphthyl-methylamino)-4H-1, 2, 4-Triazole (5b)

Yield 82.93%. M.p. 164–165 °C; IR (KBr) cm^{-1} 3318 (ν OH), 3264 (ν NH), 1626, 1598 (ν 2C=N), 1318 (ν SO_2), 818, 809 (1, 4 di substitue arom. ring), 746 (1,2 di substitue arom. ring); ^{1}H-NMR (DMSO-d_6) δ (ppm) 2.41 (t, 3H, Ar-CH_3), 2.43 (t, 3H, Ar-CH_3), 4.23 (d, 2H, CH_2), 6.81 (t, 1H, NH), Ar–H [7.03 (d, 1H), 7.24 (d, 2H), 7.29 (d, 1H), 7.31-7.36 (m, 2H), 7.62 (d, 2H), 7.69-7.74 (m, 2H), 7.77 (d, 2H), 7.82 (d, 2H)], 9.86 (s, 1H, OH); ^{13}CNMR (DMSO-d_6) δ (ppm) 154.20, 153.92 (2C, triazole C_3, C_5), Ar–C [159.33 (C), 135.08 (2CH), 134.00 (C), 132.66 (2CH), 130.55 (CH), 129.48 (2CH), 128.98 (CH), 128.00 (2CH), 127.12 (2C), 126.44 (CH), 124.81 (C), 123.46 (CH), 122.00 (2C), 117.25 (CH), 116.57 (CH), 113.89 (C)], 55.07 (CH_2), 21.14 (Ar-CH_3), 20.06 (Ar-CH_3). Anal.calcd. (%) for ($C_{27}H_{24}N_4SO_3$) 484.54 g/mol: C, 66.87; H, 4.99; N, 11.56. Found: C, 66.82; H, 4.95; N, 11.62.

2.4.3. 3-4-methyl-phenyl-5-(4-methylbenzenesulfonyl-4yl)-4-(2-Methoxy-1-Naphthyl-methylamino)-4H-1, 2, 4-Triazole (5c)

Yield 84.75%. M.p. 147–148 °C; IR (KBr) cm^{-1} 3296 (ν NH), 1611, 1560 (ν 2C=N), 1322 (ν SO_2), 818, 800 (1, 4 di 33ubstitute arom. Ring), 755 (mono 33ubstitute arom. Ring); ^{1}H-NMR (DMSO-d_6) δ (ppm) 2.40 (t, 3H, Ar-CH_3), 2.43 (t, 3H, Ar-CH_3), 3.60 (s, 3H, OCH_3), 3.94 (d, 2H, CH_2), 6.36 (t, 1H, NH), Ar–H [6.90 (d, 1H), 7.02 (d, 2H), 7.18 (d, 1H), 7.30 (d, 2H), 7.60–7.75 (m, 2H), 7.81 (d, 2H), 7.90–8.00 (m, 2H), 8.02 (d, 2H)]; ^{13}C-NMR (DMSO-d_6) δ (ppm) 151.32, 149.00 (2C, triazole C_3, C_5), Ar–C [159.53 ©, 134.96 2CH), 133.09 (2C), 132.19 (2CH), 130.55 (CH), 129.11 (2CH), 128.24 (CH), 128.64 (2CH), 127.10 (2C), 126.00 ©, 124.31 (2CH), 122.66 (2C), 118.41 (CH), 113.77 (CH)], 56.12 (OCH_3), 54.89 (CH_2), 20.35 (Ar-CH_3), 19.98 (Ar-CH_3). Anal.calcd. (%) for ($C_{28}H_{26}N_4SO_3$) 498.57 g/mol: C, 67.39; H, 5.25; N, 11.23. Found: C, 67.44; H, 5.18; N, 11.32.

3. Results

In this study, a convenient method was established for the synthesis in good yields of new triazole Schiff bases.

Table 1. Antimicrobial activities of the synthesized compounds in DMSO (dimethylsulfoxide) solvent (10 mg/mL).

Compound no	Microorganisms and inhibition zone (mm)								
	E	Pa	Yp	Kp	Ef	Sa	Bc	Ca	Ct
2	5	5	5	5	5	**12**	5	5	5
3	5	5	5	5	5	**14**	5	5	5
4a	5	**15**	5	5	5	**14**	5	5	5
4b	5	5	5	5	5	**11**	5	**22**	**20**
4c	5	5	5	5	5	5	5	5	**11**
5a	5	**25**	5	**13**	5	5	5	**16**	**11**
5b	5	5	5	5	5	5	5	5	**12**
5c	5	**12**	5	5	5	5	5	5	**14**
DMSO	5	5	5	5	5	11	5	5	**5**
Ampicilin	9	5	5	5	10	15	13	5	5
Triflucan								**25**	**25**

Results were interpreted in terms of the diameter of the inhibition zone (5 mm: no antimicrobial activity; > 5 mm: positive antimicrobial activity). Ec: Escherichia coli ATCC 25922; Pa: Pseudomonas aeruginosa ATCC 10145; Yp: Yersinia pseudotuberculosis ATCC 911; Kp: Klebsiella pneumonia ATCC 13883; Ef: Enterococcus faecalis ATCC 29212; Sa: Staphylococcus aureus ATCC 25923; Bc: Bacillus cereus 709 ROMA; Ca: Candida albicans ATCC 60193; Ct: Candida tropicalis ATCC 13803.

Antimicrobial activity was evaluated by measuring the zone of inhibition against the test organism. Ampicillin (10 µg/50 µL) served as the control antibiotic. Triflucan (5 µg/50 µL) served as the control fungicide. DMSO served as the solvent control. The results are shown in the Table 1.

Compound (2) was synthesized from the reaction of corresponding iminoester hydrochloride with acyl hydrazine and compound (3) was obtained by treatment of compound (2) with hydrazine hydrate, which was obtained by a literature method [29]. The reaction was carried out in 1-propanol at refluxing temperature for 24 h and the desired 4-amino-3,5-dialkyl-1,2,4-triazole (3) was yielded. Compound (3) was treated with some aromatic aldehydes such as 2-Bromo-1-Naphthaldehyde, 2-Hydroxy-1-Naphthaldehyde and 2-Metoxy-1-Naphthaldehyde); thus, Schiff base derivatives (4a-c) were obtained. In the last part of the synthesis reactions, compounds 4(a-c) were treated with sodium borohydride; Finally, Arylmethylamino types of compounds (5a-c) were obtained (Fig. 1).

4. Discussions

4-Amino-1, 2, 4- triazole (3) was converted to their Schiff bases (4a-c) by refluxing with 2-bromo-1-naphtaldehyde, 2-hydroxy-1-naphtaldehyde and 2-metoxy-1-naphtaldehyde in acetic acid. Previously, we obtained the Schiff bases of 1, 2, 4-triazole derivatives. The synthesis of compounds (5a-c) were performed by the reduction of only the exocyclic azomethine bond of the Schiff bases 4(a-c) (Fig. 1). These reduction reactions were conducted in considerably milder

conditions. The structures of these compounds were confirmed on the basis of FT-IR, ^{1}H-NMR, ^{13}C-NMR spectroscopic methods. In the IR spectra of compounds (4a-c) the characteristic absorption bands appeared at around 1624-1566 cm^{-1} attributed to the C=N groups. In the ^{1}H-NMR spectra of (4a-c), the signal derived from NH_2 group disappeared; instead, new signals originated from aldehyde moiety were recorded at the related chemical shift values in the ^{1}H-NMR and ^{13}C-NMR spectra. The ^{1}H-NMR signals for the N=CH group were observed between δ 8.79-9.02 ppm. The ^{13}C-NMR signals for the – N=CH- group were recorded at δ 168-171 ppm.

Reduced compounds (5a-c) showed IR absorption bands around 3264-3296 cm-1 (υNH). The ^{1}H-NMR signals for the -$NHCH_2$- group of these compounds were observed as a doublet at around δ 3.94-4.23 ppm and the proton signals of –NH-CH_2- groups were recorded as a triplet or strong singlet between δ 6.36-6.81 ppm. In the ^{13}C-NMR the triazole C_3 and C_5 of the Schiff base derivatives (4a-c) were observed between δ 152.79-143.82 ppm and the triazole C_3 and C_5 signals of the reduced compounds (5a-c) were observed between δ 154.20-148.49 ppm. The NH-CH_2-carbon signals of these compounds were recorded between δ 52-55.

5. Conclusions

In this study, a convenient method has been established for the synthesis in good yields of new triazole Schiff bases (4a-c) and corresponding amino triazole compounds (5a-c). Eight new 4H-1, 2, 4-triazole derivatives synthesized in the study exhibit some biological activities and these results are reported. The best activity was observed against C. albicans ATCC 60193 by compound 4b. Compound 4a was effective on both P. aeruginosa ATCC 10145 and S. aureus ATCC 25923. Compounds 4c, and 5b showed good antifungal activity only against yeastlike fungi, while compounds 5a, 5c showed antimicrobial activity against bacteria and yeast-like fungi. Compounds 2, and 3 were only effective on the gram-positive bacteria, S. aureus ATCC 25923.

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