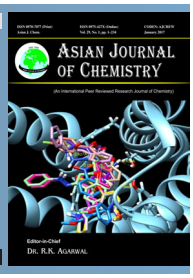
Asian Journal of Chemistry; Vol. 29, No. 12 (2017), 2794-2798

ASIAN JOURNAL OF CHEMISTRY

https://doi.org/10.14233/ajchem.2017.20925



Synthesis and Antimicrobial Activities of Some Novel 2,3-Substituted-1,3-Thiazolidin-4-ones Derived from 2-Amino-1,3-thiazole

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Received: 17 July 2017; *Accepted*: 22 September 2017; *Published online*: 30 October 2017; AJC-18635

New 2,3-substituted-1,3-thiazolidin-4-one (**6a-f**) were prepared by cyclocondensation of 2-[6-(4-chlorobenzyloxy)-2-naphthyliden]-4-(4-substituted phenyl)-5-methyl-1,3-thiazole (**5a-f**) and mercaptoacetic acid in benzene. The synthesized compounds were characterized on the basis of elemental analysis, ^{1}H NMR, ^{13}C NMR and FT-IR. The prepared compounds have been screened *in vitro* against two Gram-positive *Staphylococcus aureus*, *Staphylococcus epidermidis*, and two Gram-negative *Escherichia coli*, *Pseudomonas aernuginosa* for antibacterial activity and two fungal strains *Candida albicans*, *Candida krusei* for antifungal activity using ciprofloxacin, ampicillin and ketoconazole with minimal inhibitory concentration (MIC) value of 10 mcg/L in DMSO. Compounds **6a** and **6d** showed good antibacterial and antifungal activities compared to reference medications utilized within this study.

Keywords: Thiazolidin-4-one, 2-Naphthaldehyde, Schiff Bases, Antimicrobial activities.

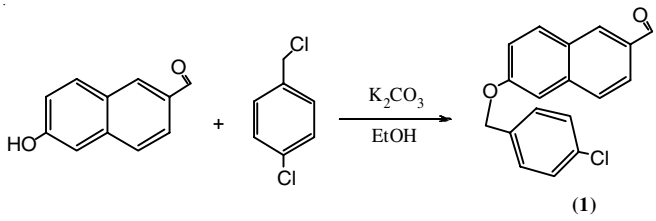
INTRODUCTION

The number of life threatening infections created toward multidrug-resistant has reached an alarming level in hospitals and community. Infections initiated toward these organisms pose a serious challenge to the scientific community and the need for an effective therapy has led to the search for novel medications. There are various naturally animated atoms which hold numerous hetero-atoms, continuously drawn the consideration about physicist over those quite some time mostly due to their living vitality. Thiazolidinones are thiazolidine subsidiaries have a place with a large portion every now and again examined moieties. Its vicinity in penicillin might have been those initial distinguishment about its event has did nature [1,2]. 4-Thiazolidinone platform will need to be offered clinched alongside an amount for clinically utilized medications. It needs to be accounted to show different physiological activities. They found uses as antitubercular [3], antimicrobial [4-8], antiinflammatory [9], anticancer [10], antihistamines [11], anticonvulsant [12] and as antiviral agents especially as anti-HIV agents[11,13,14]. It has been extensively reported that the antibacterial activity strongly depended on the nature of substituents at C2 and N3 of thiazolidinone ring. Several methods for the synthesis of 4-thiazolidinones are widely reported in the literature. The main synthetic routes to 1,3-thiazolidin-4-ones involve three components that are an amine, a carbonyl compound and a mercapto acid. The traditional methods reported can be either a one-pot three-component condensation [15] or in two-step transform. In the current study, 4-thiazolidinones have been synthesized in two steps, the first step included condensation of substituted-2-naphthaldehyde with various substituted aromatic amines and formation of an imine, which undergoes attack by generated sulfur nucleo-phile, followed by intramolecular cyclization on disposal of water in the second step [16-18].

EXPERIMENTAL

All the chemicals for the synthesis were purchased from approved venders of different make like Sigma-Aldrich and Merck. Melting point was obtained from Thermal Electro-Melting point apparatus 9300 using capillary tubes. Reactions were carried out under an argon atmosphere with dry solvents under anhydrous conditions. Thin layer chromatography (TLC): Merck Kiese gel 60 F254 on aluminum foil from Macherey-Nagel. Detection was carried out under UV light at 254 and 365 nm. FT-IR spectra were recorded using Perkin-Elmer 1420 (FT-IR) spectrometer. ^{1}H and ^{13}C NMR were recorded on Bruker ultra shield 400 MHZ. All NMR spectra present in this work were measured in $CDCl_3$ solution and TMS as the internal standard. The chemical shifts (δ) are expressed in ppm and Hz, respectively. Element analysis data were performed on a Perkin -Elmer 2400 and elemental analysis of all compounds were in good agreement with the calculated values.

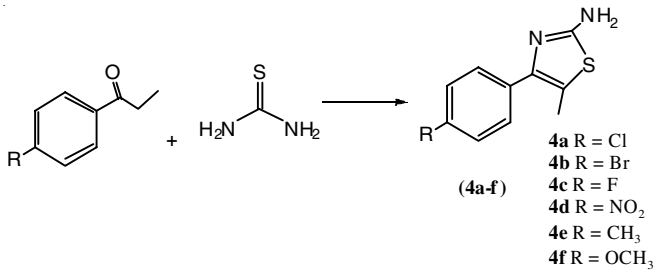
Synthesis of 6-(4-chlorobenzyloxy)-2-naphthaldehyde (1): A mixture of 6-hydroxy-2-naphthaldehyde (0.05 mol), 4-chlorobenzyl chloride (0.05 mol) and anhydrous K_2CO_3 (0.1 mol) in 100 mL absolute ethanol was refluxed with stirring for 7 h. The solution was poured into cold water. A solid product 6-(4-chlorobenzyloxy)-2-naphthaldehyde was immediately formed, filtered off, washed several times with water and cold ethanol, dried and recrystallized from absolute ethanol to obtain white crystals [19] (**Scheme-I**). Yield: 90 %; m.p. 113-115 °C; m.f. $C_{18}H_{13}O_2Cl$, m.w. = 296.5, IR (KBr, cm^{-1}, ν_{max}): 3077.60 (C-H arom), 1672.31 (C=O), 1250.33 (C-O-C); ^{1}H NMR ($CDCl_3$) δ ppm: 5.10 (s, 2H, -CH_2), 9.56 (s, 1H, ald.), 7.20-7.98 (m,10H, arom).



(1)

Scheme-I: Synthesis of 6-(4-chlorobenzyloxy)-2-naphthaldehyde (**1**)

Synthesis of 2-amino-4-(4'-substituted phenyl)-5-methyl-1,3-thiazole (4a-f): Thiourea (0.04 mol) and iodine (0.02 mol) were triturated and mixed with appropriate 4-substituted propiophenone (0.02 mol), the mixture was heated on a water bath at 70 °C with occasional stirring for 8 h. The solid product was triturated and mixed with ethyl ether to remove unreacted 4-substituted phenyl propiophenone, washed with aqueous thiosulphate (5 %) to remove excess iodine and finally with water. The crude product was dissolved in hot water, filtered to remove impurity and 2-amino-4-(4'-substituted phenyl)-5-methyl-1,3-thiazole (**Scheme-II**) was precipitated by addition of ammonia solution. The product was recrystallized from ethanol to give crystal of desired product [9].



(4a-f)

4a R = Cl
4b R = Br
4c R = F
4d R = NO_2
4e R = CH_3
4f R = OCH_3

Scheme-II: Synthesis of 2-amino-4-(4'-chloro phenyl)-5-methyl-1,3-thiazole (**4a-f**)

2-Amino-4-(4'-chlorophenyl)-5-methyl-1,3-thiazole (4a): ($C_{10}H_9N_2SCl$ m.w. = 244.5). Yield 84 %; m.p.: 141-143 °C; IR (KBr, ν_{max}, cm^{-1}): 3390-3298 (NH_2), 3060.10 (C-H arom), 2882 (C=N), 1631 (C=C), 688 (C-S-C); ^{1}H NMR ($CDCl_3$) δ ppm 1.82 (s.3H.-CH_3), 6.90 (s.2H.NH_2.), 7.18-7.98 (m.4H.arom). ^{13}C NMR ($CDCl_3$) δ 31.4 (C-4), 57.2 (C-3), 73.2 (C-2), 76.4 (C-1).118.24-132.67 (phenyl carbons).

2-Amino-4-(4'-bromophenyl)-5-methyl-1,3-thiazole (4b): ($C_{10}H_9N_2SBr$ m.w. = 269). Yield 80 %; m.p.: 126-124 °C; IR (KBr, ν_{max}, cm^{-1}): 3388-3277 (NH_2), 3066.10 (C-H arom), 2891 (C=N), 1635, 6 (C=C), 690.2 (C-S-C); ^{1}H NMR ($CDCl_3$) δ ppm 1.79 (s.3H.-CH_3), 6.78 (s.2H.NH_2.), 7.10-7.84 (m.4H.arom). ^{13}C NMR ($CDCl_3$) δ 32.13 (C-4), 58.00 (C-3), 73.24 (C-2), 76.48 (C-1).119.24-132.12 (phenyl carbons).

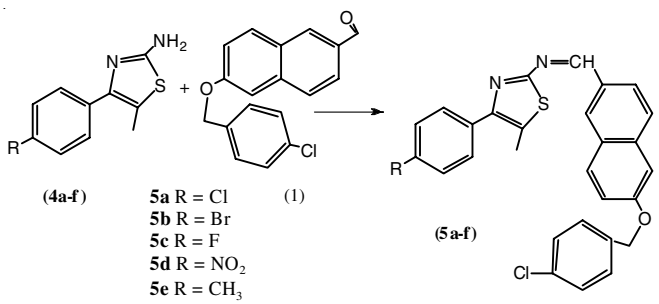
2-Amino-4-(4'-fluoro phenyl)-5-methyl-1,3-thiazole (4c): ($C_{10}H_9N_2SF$ m.w. = 208). Yield 84 %; m.p.: 124-122 °C; IR (KBr, ν_{max}, cm^{-1}): 3389-3268 (NH_2), 3049.20 (C-H arom), 2877 (C=N), 1620.5 (C=C), 683.3 (C-S-C); ^{1}H NMR ($CDCl_3$) δ ppm 1.80 (s.3H.-CH_3), 6.82 (s.2H.NH_2.), 7.10-7.88 (m.4H.arom). ^{13}C NMR ($CDCl_3$) δ 32.48 (C-4), 58.22 (C-3), 74.00 (C-2), 76.5 (C-1), 129.98-132.13 (phenyl carbons).

2-Amino-4-(4'-nitro phenyl)-5-methyl-1,3-thiazole (4d): ($C_{10}H_9O_2N_3S$ m.w. = 235). Yield 82 %; m.p.: 133-135 °C; IR (KBr, ν_{max}, cm^{-1}): 3392-3296 (NH_2), 3056.10 (C-H arom), 2888 (C=N), 1636 (C=C), 688 (C-S-C); ^{1}H NMR ($CDCl_3$) δ ppm 1.80 (s.3H.-CH_3), 6.90 (s.2H.NH_2.), 7.14-7.80 (m.4H.arom). ^{13}C NMR ($CDCl_3$) δ 33.08 (C-4), 58.25 (C-3), 73.90 (C-2), 76.48 (C-1).120.48-135.00 (phenyl carbons).

2-Amino-4-(4'-methyl phenyl)-5-methyl-1,3-thiazole (4e): ($C_{11}H_{12}N_2S$ m.w. = 204). Yield 79 %; m.p.: 162-164 °C; IR (KBr, ν_{max}, cm^{-1}): 3392-3293 (NH_2), 3069.33 (C-H arom), 2890 (C=N), 1639 (C=C), 698.3 (C-S-C); ^{1}H NMR ($CDCl_3$) δ ppm 1.74 (s.3H.-CH_3), 2, 30 (s.3H.CH_3-ph), 6.84 (s.2H.NH_2.), 7.10-7.88 (m.4H.arom). ^{13}C NMR ($CDCl_3$) δ 30.12 (C-4), 55.29 (C-3), 71.20 (C-2), 73.47 (C-1).118.24-130.34 (phenyl carbons).

2-Amino-4-(4'-methoxy phenyl)-5-methyl-1,3-thiazole (4f): ($C_{11}H_{12}ON_2S$ m.w. = 220). Yield 78 %; m.p.: 170-172 °C; IR (KBr, ν_{max}, cm^{-1}): 3383-3288 (NH_2), 3066.22 (C-H arom), 2874.4 (C=N), 1628.5 (C=C), 680.7 (C-S-C); ^{1}H NMR ($CDCl_3$) δ ppm 1.72 (s.3H.-CH_3), 2, 10 (s.3H.OCH_3), 6.82 (s.2H.NH_2.), 7.08-7.98 (m.4H.arom). ^{13}C NMR ($CDCl_3$) δ 31.00 (C-4), 56.57 (C-3), 71.25 (C-2), 74.11 (C-1).118.08-130.39 (phenyl carbons).

Synthesis of 2-[6-(4-chlorobenzyloxy)-2-naphthyliden-4-(4-substituted phenyl)]-5-methyl-1,3-thiazole (5a-f): in round bottom flask (0.01 mol) of appropriate 2-amino-4-(4'-substituted phenyl)-5-methyl-1,3-thiazole **(4a-f)** was dissolved in 40 mL of absolute ethanol, (0.01 mol) of 6-(4-chlorobenzyloxy)-2-naphthaldehyde **(1)** in 20 mL of absolute ethanol with few drops of glacial acetic acid was added. The reaction mixture was refluxed for 7 h. After completion of reaction which is controlled with TLC, the reaction mixture was cooled. The precipitated product was collected, filtered off and recrystallized from absolute ethanol [20] (**Scheme-III**).



(4a-f) **(1)** **(5a-f)**

5a R = Cl
5b R = Br
5c R = F
5d R = NO_2
5e R = CH_3
5f R = OCH_3

Scheme-III: Synthesis of 2-{6-(4-chlorobenzyloxy)-2-naphthyliden)-4-(4-substituted phenyl}-5-methyl-1,3-thiazole (**5a-f**)

2-[6-(4-Chlorobenzyloxy)-2-naphthyliden-4-(4-chlorophenyl)]-5-methyl-1,3-thiazole (5a): ($C_{28}H_{20}N_2OSCl_2$. m.w. = 474). Yield 70 %; m.p.: 150-152 °C; IR (KBr, ν_{max}, cm^{-1}): 3066.22 (C-H arom), 1616.4 (-HC=N), 1540.5 (C=C), 1262 (-O-CH_2), 680.7 (C-S-C);^{1}H NMR ($CDCl_3$) δ ppm 1.92 (s.3H.-CH_3), 4.82 (s.2H.OCH_2), 7.08-7.98 (m.14H.arom). 9.2 (s.1H.-CH=N); ^{13}C NMR ($CDCl_3$) δ 33 (C-4), 61.4 (OCH_2), 72 (C-3), 75.4 (C-2, 1), 77 (C-5), 132-129.7 (phenyl carbons), 138.9-129.00 (naphthyl carbons).

2-[6-(4-Chlorobenzyloxy)-2-naphthyliden-4-(4-bromophenyl)]-5-methyl-1,3-thiazole (5b): ($C_{28}H_{20}N_2OSClBr$; m.w. = 518.5). Yield 72 %; m.p.: 156-158 °C; IR (KBr, ν_{max}, cm^{-1}): 3066.22 (C-H arom), 1616.4 (-HC=N), 1540.5 (C=C), 1262 (-O-CH_2), 680.7 (C-S-C);^{1}H NMR ($CDCl_3$) δ ppm 1.92 (s.3H.-CH_3), 4.82 (s.2H.OCH_2), 7.08-7.98 (m.14H.arom). 8.9 (s.1H.-CH=N); ^{13}C NMR ($CDCl_3$) δ 33.8 (C-4), 61.8 (OCH_2), 71.8 (C-3), 75.00 (C-2, 1), 77.5 (C-5), 131-129.2 (phenyl carbons), 138.9-129.80 (naphthyl carbons).

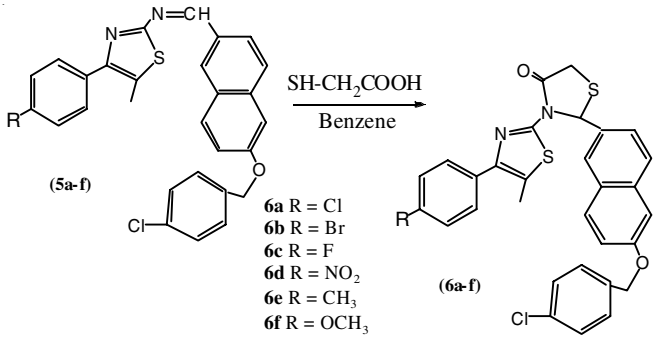
2-[6-(4-Chlorobenzyloxy)-2-naphthyliden-4-(4-fluorophenyl)]-5-methyl-1,3-thiazole (5c): ($C_{28}H_{20}N_2OSClF$; m.w. = 457.5). Yield 76 %; m.p.: 150-152 °C; IR (KBr, ν_{max}, cm^{-1}): 3065.2 (C-H arom), 1618.2 (-HC=N), 1542.3 (C=C), 1260 (-O-CH_2), 682 (C-S-C);^{1}H NMR ($CDCl_3$) δ ppm 1.90 (s.3H.-CH_3), 4.80 (s.2H.OCH_2), 7.08-8.02 (m.14H.arom). 8.98 (s.1H.-CH=N); ^{13}C NMR ($CDCl_3$) δ 34.2 (C-4), 62.8 (OCH_2), 71.6 (C-3), 73.7 (C-2, 1), 76.6 (C-5), 131-129.3 (phenyl carbons), 138.02-129.44 (naphthyl carbons).

2-[6-(4-Chlorobenzyloxy)-2-naphthyliden-4-(4-nitrophenyl)]-5-methyl-1,3-thiazole (5d): ($C_{28}H_{20}N_3O_3SCl$; m.w. = 484.5). Yield 76 %; m.p.: 170-172 °C; IR (KBr, ν_{max}, cm^{-1}): 3069.2 (C-H arom), 1620 (-HC=N), 1542.8 (C=C), 1264 (-O-CH_2), 687 (C-S-C), 1521-1344 (N-O);^{1}H NMR ($CDCl_3$) δ ppm 1.98 (s.3H.-CH_3), 4.86 (s.2H.OCH_2), 7.08-8.12 (m.14H.arom). 9.1 (s.1H.-CH=N); ^{13}C NMR ($CDCl_3$) δ 33.80 (C-4), 61.2 (OCH_2), 73.4 (C-3), 76.1 (C-2, 1), 78 (C-5), 134-129.7 (phenyl carbons), 138.2-129.09 (naphthyl carbons).

2-[6-(4-Chlorobenzyloxy)-2-naphthyliden-4-(4-methylphenyl)]-5-methyl-1,3-thiazole (5e): ($C_{29}H_{23}N_2OSCl$; m.w. = 453.5). [Yield 78 %; m.p.: 155-157 °C; IR (KBr, ν_{max}, cm^{-1}): 3064 (C-H arom), 1613 (-HC=N), 1536 (C=C), 1256 (-O-CH_2), 678 (C-S-C);^{1}H NMR ($CDCl_3$) δ ppm 1.92 (s.3H.-CH_3), 2.32 (s.3H.CH_3-ph), 4.66 (s.2H.OCH_2), 7.12-8.12 (m.14H.arom). 9.00 (s.1H.-CH=N); ^{13}C NMR ($CDCl_3$) δ 31.60 (C-4), 60.6 (OCH_2), 70.60 (C-3), 73.20 (C-2, 1), 75.76 (C-5), 130-128.02 (phenyl carbons), 137.80-128.54 (naphthyl carbons).

2-[6-(4-Chlorobenzyloxy)-2-naphthyliden-4-(4-methoxyphenyl)]-5-methyl-1,3-thiazole (5f): ($C_{29}H_{23}N_2O_2SCl$; m.w. = 469.5). Yield 71 %; m.p.: 177-179 °C; IR (KBr, ν_{max}, cm^{-1}): 3068 (C-H arom), 1611 (-HC=N), 1526 (C=C), 1258 (-O-CH_2), 688 (C-S-C);^{1}H NMR ($CDCl_3$) δ ppm 1.88 (s.3H.-CH_3), 2.30 (s.3H.CH_3-O), 4.46 (s.2H.OCH_2), 7.1-8.10 (m.14H.arom). 9.10 (s.1H.-CH=N); ^{13}C NMR ($CDCl_3$) δ 30.78 (C-4), 60.00 (OCH_2), 70.65 (C-3), 73.14 (C-2, 1), 75.24 (C-5), 130-127.25 (phenyl carbons), 138.34-129.37 (naphthyl carbons).

Synthesis of 2-[6-(4-chlorobenzyloxy)naphthyl-3-(4-substituted phenyl)-5-methyl-1,3-thiazol-2-yl]thiazolidin-4-one (6a-f): (6m mol) of mercaptoacetic acid was added slowly with stirring to the solution of (5 mmol) in 25 mL benzene compound (**5a-f**). The mixture was refluxed (18-20) h. After completion of the reaction, the product was cooled to room temperature and the benzene was removed under vacuum [21]. The whole mass treated with saturated solution of sodium bicarbonate until carbon dioxide evolution. The formed product was filtered off and washed several times with water. The product thus obtained was recrystallized from absolute ethanol to get pure crystal of **6a-f** (**Scheme-IV**).



Scheme-IV: Synthesis of 2-{6-(4-chlorobenzyloxy)naphthyl)-3-[(4-substituted phenyl)-5-methyl-1,3-thiazol-2-yl}thiazolidine-4-one (**6a-f**)

2-[6-(4-Chlorobenzyloxy)naphthyl-3-(4-chloride-phenyl)-5-methyl-1,3-thiazol-2-yl]thiazolidin-4-one (6a): Pale yellow solid; [Yield 65 %]; m.p.: 145-147 °C; IR (KBr, ν_{max}, cm^{-1}): 3042 (C-H arom), 1704 (C=O), 1540 (C=C), 1330 (-C-N), 1234 (-O-CH_2), 680 (C-S-C); ^{1}H NMR ($CDCl_3$) δ ppm 1.84 (s.3H.-CH_3), 3.94-4.10 (dd.2H.CH_2), 4.46 (s.2H.OCH_2), 5.9 (s.1H.S-CH-N), 7.2-8.20 (m.14H.arom); ^{13}C NMR ($CDCl_3$) δ 31.2 (C-4, 6), 59 (OCH_2), 62 (C-5, 3, 2), 73 (C-1), 114.5-115.8 (phenyl Carbons), 130.4-122.4 (naphthyl carbons)171 (C-7). Elemental analysis of ($C_{30}H_{22}N_2O_2S_2Cl_2$ m.w. = 577) Calcd.. C, 62.35, H, 3.81, O, 5.55, N, 4.85, S, 11.09 found C, 62, 98, H.4.4, O, 6.1, N, 4.01, S, 10.42.

2-[6-(4-Chlorobenzyloxy)naphthyl-3-(4-bromo-phenyl)-5-methyl-1,3-thiazol-2-yl]thiazolidin-4-one (6b): Pale yellow solid; [Yield 60 %]; m.p.: 149-151 °C; IR (KBr, ν_{max}, cm^{-1}): 3052 (C-H arom), 1694 (C=O), 1530 (C=C), 1329 (-C-N), 1238 (-O-CH_2), 687 (C-S-C); ^{1}H NMR ($CDCl_3$) δ ppm 1.86 (s.3H.-CH_3), 3.80-3.99 (dd.2H.CH_2), 4.50 (s.2H.OCH_2), 6.1 (s.1H.S-CH-N), 7.12-8.20 (m.14H.arom); ^{13}C NMR ($CDCl_3$) δ 31.5 (C-4, 6), 59.2 (OCH_2), 61.1 (C-5, 3, 2), 72.8 (C-1), 114.2-115.6 (phenyl Carbons), 129.8-122.3 (naphthyl carbons)170 (C-13). Elemental analysis of ($C_{30}H_{22}N_2O_2S_2ClBr$ m.w. = 621.5) Calcd.. C, 57.9, H, 3.54, O, 5.15, N, 4.51, S, 10.3 found C, 60.88, H.4.44, O, 6.03, N, 4.22, S, 10.62.

2-[6-(4-Chlorobenzyloxy)naphthyl-3-(4-fluoro-phenyl)-5-methyl-1,3-thiazol-2-yl]thiazolidin-4-one (6c): Pale yellow solid; [Yield 58 %]; m.p.: 140-142 °C; IR (KBr, ν_{max}, cm^{-1}): 3082 (C-H arom), 1702 (C=O), 1522 (C=C), 1321 (-C-N), 1232 (-O-CH_2), 686 (C-S-C); ^{1}H NMR ($CDCl_3$) δ ppm 1.81 (s.3H.-CH_3), 3.77-3.87 (dd.2H.CH_2), 4.40 (s.2H.OCH_2), 6.0 (s.1H.S-CH-N), 7.12-8.20 (m.14H.arom); ^{13}C NMR ($CDCl_3$) δ 31.00 (C-4, 6), 58.2 (OCH_2), 61.4 (C-5, 3, 2), 72.9 (C-1), 114.4-115.8 (phenyl Carbons), 129.2-122.00 (naphthyl carbons)170.4 (C-13). Elemental analysis of ($C_{30}H_{22}N_2O_2S_2ClF$ m.w. = 559.5) Calcd.. C, 64.34, H, 3.96, O, 5.72, N, 5.00, S, 11.44 found C, 63.66, H.4.92, O, 6.45, N, 4.11, S, 10.64.

2-[6-(4-Chlorobenzyloxy)naphthyl-3-(4-nitro-phenyl)-5-methyl-1,3-thiazol-2-yl]thiazolidin-4-one (6d): Deep yellow solid; [Yield 54 %]; m.p.: 169-171 °C; IR (KBr, ν_{max}, cm^{-1}): 3022 (C-H arom), 1688 (C=O), 1513 (C=C), 1312 (-C-N), 1218 (-O-CH_2), 682 (C-S-C); ^{1}H NMR ($CDCl_3$) δ ppm 1.96 (s.3H.-CH_3), 3.96-4.10 (dd.2H.CH_2), 4.59 (s.2H.OCH_2), 6.0 (s.1H.S-CH-N), 7.12-8.20 (m.14H.arom); ^{13}C NMR ($CDCl_3$) δ 32.00 (C-4, 6), 61.1 (OCH_2), 62.5 (C-5, 3, 2), 73.9 (C-1), 114.9-116.6 (phenyl Carbons), 131.2-123.6 (naphthyl carbons)172.8 (C-13). Elemental analysis of ($C_{30}H_{22}N_3O_4S_2Cl$ m.w. = 587.5) Calcd.. C, 61.28, H, 3.74, O, 10.89, N, 7.15, S, 10.89 found C, 61.88, H.4.62, O, 11.11, N, 7.92, S, 10.56.

2-[6-(4-Chlorobenzyloxy)naphthyl-3-(4-methyl-phenyl)-5-methyl-1,3-thiazol-2-yl]thiazolidin-4-one (6e): Brown solid; [Yield 65 %]; m.p.: 132-134 °C; IR (KBr, ν_{max}, cm^{-1}): 3042 (C-H arom), 1702 (C=O), 1540 (C=C), 1330 (-C-N), 1234 (-O-CH_2), 680 (C-S-C); ^{1}H NMR ($CDCl_3$) δ ppm 1.84 (s.3H.-CH_3), 2.32 (s.3H.CH_3-ph), 3.80-3.98 (dd.2H.CH_2), 4.36 (s.2H.OCH_2), 5.88 (s.1H.S-CH-N), 7.2-8.20 (m.14H. arom); ^{13}C NMR ($CDCl_3$) δ 31.2 (C-4, 6), 55.2 (-CH_3), 57.2 (OCH_2), 61 (C-5, 3, 2), 71.9 (C-1), 114.1-115.8 (phenyl carbons), 129.2-121.4 (naphthyl carbons)170.3 (C-13). Elemental analysis of ($C_{31}H_{25}N_2O_2S_2Cl$ m.w. = 597.5) Calcd.. C, 62.26, H, 4.18, O, 5.36, N, 4.69, S, 10.71 found C, 62.91, H.4.77, O, 6.14, N, 4.22, S, 10.13.

2-[6-(4-Chlorobenzyloxy)naphthyl-3-(4-methoxy-phenyl)-5-methyl-1,3-thiazol-2-yl]thiazolidin-4-one (6a-f): Deep yellow [Yield 55 %]; m.p.: 162-164 °C; IR (KBr, ν_{max}, cm^{-1}): 3024 (C-H arom), 1700 (C=O), 1532 (C=C), 1330 (-C-N), 1224 (-O-CH_2), 686 (C-S-C); ^{1}H NMR ($CDCl_3$) δ ppm 1.83 (s.3H.-CH_3), 3.32 (s.3H.-O-CH_3), 3.78-3.98 (dd.2H.CH_2), 4.44 (s.2H.OCH_2), 6.0 (s.1H.S-CH-N), 7.1-8.18 (m.14H.arom); ^{13}C NMR ($CDCl_3$) δ 31.2 (C-4, 6), 55.0 (-OCH_3), 57.8 (OCH_2), 61.2 (C-5, 3, 2), 71.5 (C-1), 114.2-115.7 (phenyl Carbons), 129.2-121.1 (naphthyl carbons)170 (C-13). Elemental analysis of ($C_{31}H_{25}O_3S_2N_2Cl$ m.w. = 613.5) Calcd. C, 60.64, H, 4.07, O, 7.82, N, 4.56, S, 10.43 found C, 61.60, H.4.72, O, 7.08, N, 4.98, S, 10.93.

Antimicrobial activity: The antimicrobial activity of the synthesized compounds (**6a-f**) was carried out using disc agar diffusion method [22] by measuring the inhibition zone in mm at the concentration of 10 µg. The synthesized compounds (**6a-f**) are screened against *S. aureus*, *S. epidermidis*, *E. coli*, *P. aernuginosa* for antibacterial activity and *Candida albicans, Candida krusei* for antifungal activity. All compounds were tested *in vitro* for their antimicrobial activities.

RESULTS AND DISCUSSION

Synthesis of 4-thiazolidinones (**6a-f**) from 6-(4-benzyl-oxy)-2-naphthaldehyde (**1**) with different amines (**5a-f**) in the presence of thioglycolic acid in benzene. The structure of synthesized compound **1** was supported by spectral analysis. In IR spectra the disappearance of a broad band at (3500-3400) cm^{-1} for (-OH) group which exists in start material and followed the appearance of singlet signal at δ 5.10 ppm for tow protons of (-OCH_2-) in ^{1}H NMR spectra of compound **1**.

The second step includes synthesis of 2-amino-4-(4'-substituted phenyl)-5-methyl-1,3-thiazole (**4a-f**) from the reaction of 4-substituted propiophenone (**3a-f**) with thiourea in the presence of iodine. The structures of the synthesized compounds were supported by spectral analysis. In IR spectra the strong band at 1680 cm^{-1}, which belongs to carbonyl group of propiophenone disappeared and two new bands at 3388-3277 cm^{-1} relating with NH_2 exten-ding seemed which affirmed that cyclization of thiazole [23]. In ^{1}H NMR spectra of synthesized compounds (**4a-f**) show singlet signal at δ 6.90 ppm for two protons of NH_2 [24] and ^{13}C NMR spectra show ten peaks for ten different carbon atoms in compounds (**4a-c**) and eleven carbon peaks for compounds (**4d-f**).

Condensation of 2-amino-1,3-thiazole derivatives (**4a-f**) with 6-(4-chlorobenzyloxy)-2-naphthaldehyde (**1**) produced Schiff bases (**5a-f**). In IR spectra of these compounds, there are two shreds of evidences affirmed producing Schiff bases, the first, the two bands of an amino group -NH_2 at 3400-3300 cm^{-1} in all spectra disappeared, the second one is the absence of a band at 1690 cm^{-1} which is a characteristic band of aldehydic carbonyl group [25]. From ^{1}H NMR spectra of compounds **5a-f**, the singlet signal of proton of (-CH=N-) observed at δ (9.1-9.8) ppm. In ^{13}C NMR of all compounds, the imported signal is the appearance of C_{12} carbon atom of imines (-CH=N-) at δ (163-172) ppm.

2-Substituted thiazolidin-4-one derivatives (**6a-f**) were prepared by reaction of Schiff bases (**5a-f**) with mercaptoacetic acid in benzene. The formation of new synthesized thiazolidin-4-one derivatives (**6a-f**) is confirmed from their characteristic FT-IR, ^{1}H, ^{13}C NMR spectroscopic data and elemental analysis.

TABLE-1
ANTIMICROBIAL ACTIVITY OF THE PREPARED COMPOUNDS **6a-f**

Compd. No.	Antibacteiral activity				Antifungal activity	
	Diameter of zone of inhibition (mm)				Inhibition (%)	
	Gram-negative		Gram-positive			
	Escherichira coli	*Pesudomonas aernuginosa*	*Staphylococcus aureus*	*Staphylococcus epidermidis*	*Candida albicans*	*Candida krusei*
6a	21	20	17	17	65.00	62.32
6b	18	17	18	16	32.14	34.33
6c	16	17	18	16	44.12	22.60
6d	22	21	19	19	66.56	63.21
6e	19	18	17	16	36.52	32.02
6f	19	19	16	15	20.14	30.40
Ciprofloxacin	25	24	24	23	–	–
Ampicillin	27	27	26	15	–	–
Ketoconazole	–	–	–	–	75	72

In IR spectra of all compounds **6a-f** observed strong sharp band at 1702-1688 cm^{-1} which is a characteristic band of a carbonyl group of thiazolidinone [26]. The ^1H NMR spectra of **6a-f**, showed two doublets signals at 3.77-4.10 ppm due to non-equivalent geminal protons assigned for cyclic -S-CH_2- and the disappearance of imine -CH=N- signals at δ 9 ppm are good evidence for obtaining thiazolidin-4-one cycle.

Antimicrobial activities: It is evident from Table-1 that compounds **6e**, **6b**, **6c** and **6f** are moderately active while **6a** and **6d** are maximum active against bacterial compared with reference drugs ciprofloxacin and ampicillin. The antibacterial activity of the compounds depended on the nature and position of the substituents at aryl moiety attached with thiazolidinone. However, few derivatives with C_2 and N_3 substituted positions and the presence of electron-withdrawing substituents on the aromatic ring on C_2 of 4-thiazolinone presenting varying degrees of inhibition against Gram-positive and Gram-negative bacteria showing inhibition as good as to the standard drugs used [27]. Studies have revealed that the presence of electro-withdrawing groups at *para*-position of aryl moiety encourages the activity profile [28].

The compounds **6a** and **6d** showed more effective on Gram-negative bacteria *E. coli* and *P. aernuginosa* as compared to Gram-positive *S. aureus* and *S. epidermidis*. The synthesized compounds were evaluated against *Candida albicans* and *Candida krusei* for their antifungal activity, the results showed that the tested compounds **6a-6f** possessed weak antifungal activity [19] compared to ketoconazole as reference drug used in this study (Table-1).

Conclusion

In this work, new 4-thiazolidinones (**6a-6f**) derived from condensation of 2-[6-(4-chlorobenzyloxy)-2-naphthyliden]-4-(4-substituted phenyl)-5-methyl-1,3-thiazole with thioglycolic acid in benzene were synthesized and characterized. The synthesized compounds were evaluated for their antimicrobial activity and exhibited considerable antibacterial activity and weak antifungal activity.

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