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Synthesis and Characterization of New Series of Thiazole Integrated Novel Pyrazoles

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ABSTRACT

A new series of of novel pyrazole derivatives i.e, 2-arylsulfanyl-1-(5-phenyl-3-thiazol-2-yl-4,5-dihydro-pyrazol-1-yl)-ethanone have been synthesized in good to excellent yields by employing 2-acetylthiazole and 3-phenyl-1-thiazol-2-yl-propenone, 2-(5-phenyl-4,5-dihydro-1H-pyrazol-3-yl)-thiazole and 2-chloro-1-(5-phenyl-3-thiazol-2-yl-4,5-dihydro-pyrazol-1-yl)-ethanone as reactive intermediates.

K**eywords**: Pyrazole; Thiazole and heterocyclic compounds

INTRODUCTION

The term pyrazole was given by Ludwig Knorr in 1883. The first natural pyrazole, 1-pyrazolyl-alanine was isolated from seeds of watermelons [1]. Pyrazoles are prominent nitrogen-containing heterocyclics and these have been found to possess useful biological activity such as antihyperglycemic [2], analgesic [3], anti-inflammatory [4], antipyretic [5], antibacterial [6], hypoglycemic [7], sedative-hypnotic activity [8], antimicrobial [9], central nervous system [10] and immunosuppressive [11].

Peng-cheng et al [12] synthesized a series of pyrazole derivatives and studied antiproliferative activity. Michael et al [13] synthesized a new series of the trisubtituted pyrazole derivatives and screened the compounds for anti-antiangiogenic activity. Ronghui Lin et al [14] synthesized 3, 4-disubstituted pyrazole derivatives. The analogues showed potent and selective cyclindependent kinase inhibitory activities and inhibited in vitro cellular proliferation in various human cells. Bonesi et al [15] prepared new class of pyrazole derivatives and investigated their potential activity as angiotensin-I-converting enzymes inhibitory activity by performing assay. Samir Bondock et al [16] synthesized a series of substituted pyrazole derivatives and found to exhibit the most potent in-vitro antifungal activity against A. fumigatus and F. oxysporum comparable. Smaail et al [17] synthesized novel pyrazole derivatives and were evaluated for their antimicrobial activity against different antimicrobial strains by agar plate diffusion method. Sahu et al [18] synthesized novel pyrazoline derivatives and these compounds were showed potent antimicrobial activity by agar diffusion cup-plate method against Staphylococcus aureus, Salmonella typhi, E. coli, Candida albicans and Aspergillus niger. Sridhar et al [19] synthesized pyrazole-3-carboxylate derivatives and screened for antibacterial activity.lora et al [20] synthesized and evaluated anti-inflammatory activity of a novel series of bis (3-aryl-4, 5-dihydro-1H pyrazole-1-thio carboxamide derivatives against carrageenan-induced rat paw edema test.

Adnan et al [20] synthesized thiazolyl and thaidiazolyl derivatives of 1H-pyrazole which showed significant anti-inflammatory activity. Burguete et al [21] synthesized substituted pyrazole derivatives and evaluated them for their anti-inflammatory activities against carrageenan induced rat paw edema test. Kelekc et al [22] synthesized novel pyrazole derivatives and studied anti-inflammatory activity using carrageenan induced paw edema method with no ulcerogenic effect. Osama et al [23] synthesized 4, 5-disubstituted pyrazole derivatives. These derivatives showed

the potent antiviral activity against a broad panel of viruses in different cell culture. Rashad et al [24] synthesized substituted pyrazole derivatives and performed promising antiviral activity against hepatitis A virus and Herpes Simplex virus type-1 using plaque infective assay.

Thiazole derivatives are of considerable interest from therapeutic point of view because of their utility as antimicrobial, antiphychotics [25], anti-inflammatory [26], analgesic [27], antitubercular [28], central nervous system (CNS) stimulate [29], anti-HIV [30], algicidol [31] and antimalarial [32] activity. Integration of pyrazole moiety with thiazole nucleus may enhance these activities.

EXPERIMENTAL SECTION

All reagents and solvents were used as purchased without further purification. Melting points were determined on a Fisher–Johns melting point apparatus and are uncorrected. Crude products were purified by column chromatography on silica gel of 60–120 mesh. IR spectra were obtained on a PerkinElmer BX series FT-IR 5000 spectrometer using KBr pellet. ^{1}H & ^{13}C-NMR spectra were recorded on a Varian 300 MHz &100 MHz spectrometers respectively. The chemical shifts were reported as ppm down field using TMS as an internal standard. Mass spectra were recorded on a VG-Micromass 7070H spectrometer operating at 70 eV.

Preparation of 3-phenyl-1-thiazol-2-yl-propenone (2)
A homogenous solution of 2-acetylthiazole **(1)** (0.01 mol), benzaldehyde (0.01 mol) and sodium hydroxide solution (10%, 10 ml) in absolute ethanol (20 ml) was maintained at room temperature with constant stirring for 5 h. After completion of the reaction (monitored by the TLC), the reaction mixture was decanted into crushed ice (20 g). The generated solid was filtered, washed with cold-water, dried and recrystallized from ethanol to offer pure 3-phenyl-1-thiazol-2-yl-propenone **(2)**.

Preparation of 2-(5-phenyl-4,5-dihydro-1*H*-pyrazol-3-yl)-thiazole (3)
A mixture of 3-phenyl-1-thiazol-2-yl-propenone **(2)** (0.01 mol) and hydrazine hydrate (80%, 0.02 mol) in ethanol (20 ml) was heated at reflux temperature for 5 h with uniform stirring. After realization of the reaction (examined by the TLC), the reaction mixture was cooled to room temperature, then poured in ice-cold water and the resulted solid was filtered, dried and recrystallized from ethyl acetate to give 2-(5-phenyl-4,5-dihydro-1*H*-pyrazol-3-yl)-thiazole **(3)** in pure form.

Preparation of 2-chloro-1-(5-phenyl-3-thiazol-2-yl-4,5-dihydro-pyrazol-1-yl)-ethanone (4)
To a cold solution of 2-(5-phenyl-4,5-dihydro-1*H*-pyrazol-3-yl)-thiazole **(3)** (0.01 mol) and triethylamine (0.01 mol) in benzene (20 ml) was drop wise added chloroacetyl chloride (0.01 mol). The whole reaction mixture was stirred steadily at room temperature for about 2 h. After fulfilment of the reaction (scanned by the TLC), the solvent was evaporated under reduced pressure to get a solid residue and it was washed with cold water, dried and recrystallized from ethyl acetate to obtain 2-chloro-1-(5-phenyl-3-thiazol-2-yl-4,5-dihydro-pyrazol-1-yl)-ethanone **(4)** in pure form.

Preparation of 2-arylsulfanyl-1-(5-phenyl-3-thiazol-2-yl-4,5-dihydro-pyrazol-1-yl)-ethanone (5a-f)
A mixture of 2-chloro-1-(5-phenyl-3-thiazol-2-yl-4,5-dihydro-pyrazol-1-yl)-ethanone **(4)** (0.01 mol) and thiophenol or substituted thiophenol (0.01 mol) in absolute ethanol (20 ml) was allowed at room temperature for 7-9 h with consistent stirring. After realization of the reaction (investigated by the TLC), the solvent was evaporated to acquire crude product and it is washed with ice-cold water and recrystallized from ethanol to get corresponding pure 2-arylsulfanyl-1-(5-phenyl-3-thiazol-2-yl-4,5-dihydro-pyrazol-1-yl)-ethanone **(5a-f)**.

SPECTRAL AND PHYSICAL DATA

3-Phenyl-1-thiazol-2-yl-propenone (2)
White solid, Yield: 77%, mp: 125-127; IR (KBr, cm^{-1}): 3050 (C–H Ar), 1684 (C=O), 1652 (C=N), 1618, (C=C, Ar), 1224 (C-S); ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.62-7.15 (m, 5H, Ar–H), 7.68 (d, 1H, J = 7.6 Hz, CH), 7.45 (d, 1H, J = 6.9 Hz, CH), 7.35 (d, 1H, J = 6.9 Hz, CH), 6.89 (d, 1H, J = 7.6 Hz, CH); ^{13}C NMR (300 MHz, $CDCl_3$): δ: 173.5,

154.7, 147.7, 141.4, 132.8, 127.3, 125.8, 123.7, 120.5, 118.6; MS: *m/z* 215 (M^+); Elemental analysis: Calculated for $C_{12}H_9NOS$: C-66.95, H-4.21, N-6.51, O-7.43, S-14.90. Found: C-66.41, H-4.19, N-6.48, O-7.40, S-14.81.

2-(5-Phenyl-4,5-dihydro-1*H*-pyrazol-3-yl)-thiazole (3)
Pale yellow solid, Yield: 72%, mp: 130-132; IR (KBr, cm^{-1}): 3138 ((N–H), 3045 (C–H Ar), 2962 (C–H, CH_2), 1650 (C=N), 1648 (C=C, Ar), 1214 (C-S); ^1H NMR (300 MHz, $CDCl_3$): δ 7.67-7.38 (m, 5H, Ar–H), 7.52 (d, 1H, J = 6.5 Hz ,CH), 7.41 (d, 1H, J = 6.5 Hz, CH), 6.39 (s, 1H, NH), 3.28 (t, 1H, J = 4.5 Hz, CH), 2.84 (d, 2H, J = 4.5 Hz, CH_2); ^{13}C NMR (300 MHz, $CDCl_3$): δ: 154.8, 150.7, 146.8, 142.2, 135.2, 128.1, 126.8, 118.8, 48.0, 42.0; MS: *m/z* 229 (M^+); Elemental analysis: Calculated for $C_{12}H_{11}N_3S$: C-62.86, H-4.84, N-18.33, S-13.98. Found: C-62.38, H-4.80, N-18.28, S-13.81.

2-Chloro-1-(5-phenyl-3-thiazol-2-yl-4,5-dihydro-pyrazol-1-yl)-ethanone (4)
Orange solid, Yield: 76%, mp: 148-150; IR (KBr, cm^{-1}): 3058 (C–H Ar), 2930 (C–H, CH_2), 1684 (C=O), 1632 (C=N), 1575 (C=C, Ar), 1226 (C-S), 1146 (C–O); ^1H NMR (300 MHz, $CDCl_3$): δ 7.74-7.52 (m, 5H, Ar–H), 7.50 (d, 1H, J = 6.6 Hz, CH), 7.37 (d, 1H, J = 6.6 Hz, CH), 4.24 (s, 2H, CH_2), 3.36 (t, 1H, J = 5.0 Hz, CH), 2.79 (d, 2H, J = 5.0 Hz, CH_2); ^{13}C NMR (300 MHz, $CDCl_3$): δ: 163.2, 154.9, 150.8, 145.3, 142.7, 135.2, 128.6, 123.7, 118.9, 49.0, 46.2, 42.0; MS: *m/z* 305 (M^+); Elemental analysis: Calculated for $C_{14}H_{12}ClN_3OS$: C-54.99, H-3.96, Cl-11.59, N-13.74, O-5.23, S-10.49. Found: C-54.10, H-3.94, Cl-11.51, N-13.68, O-5.21, S-10.42.

2-Phenylsulfanyl-1-(5-phenyl-3-thiazol-2-yl-4,5-dihydro-pyrazol-1-yl)-ethanone (5a)
Yellow solid, Yield: 78%, mp: 115-117; IR (KBr, cm^{-1}): 3048 (C–H Ar), 2932 (C–H, CH_2), 1675 (C=O), 1636 (C=N), 1572 (C=C, Ar), 1220 (C-S); ^1H NMR (300 MHz, $CDCl_3$): δ 7.75-7.38 (m, 10H, Ar–H), 7.55 (d, 1H, J = 7.2 Hz, CH), 7.40 (d, 1H, J = 7.2 Hz, CH), 4.31 (s, 2H, CH_2), 3.74 (t, 1H, J = 5.8 Hz, CH), 2.51 (d, 2H, J = 5.8 Hz, CH_2); ^{13}C NMR (300 MHz, $CDCl_3$): δ: 172.1, 157.4, 153.4, 144.0, 142.0, 137.0, 135.0, 132.1, 129.4, 128.0, 123.0, 120.0, 117.2, 48.0, 42.0, 39.0; MS: *m/z* 379 (M^+); Elemental analysis: Calculated for $C_{20}H_{17}N_3OS_2$: C-63.30, H-4.52, N-11.07, O-4.22, S-16.90. Found: C-62.98, H-4.50, N-10.95, O-4.20, S-16.79.

1-(5-Phenyl-3-thiazol-2-yl-4,5-dihydro-pyrazol-1-yl)-2-*o*-tolylsulfanyl-ethanone (5b)
Yellow solid, Yield: 72%, mp: 125-127; IR (KBr, cm^{-1}): 3036 (C–H Ar), 2965 (C–H, CH_3), 1678 (C=O), 1638 (C=N), 1573 (C=C, Ar), 1212 (C-S); ^1H NMR (300 MHz, $CDCl_3$): δ 7.75-7.39 (m, 9H Ar–H), 7.55 (d, 1H, J = 6.2 Hz, CH), 7.41 (d, 1H, J = 6.2 Hz, CH), 4.23 (s, 2H, CH_2), 3.68 (t, 1H, J = 5.5 Hz, CH), 2.70 (s, 3H, CH_3), 2.47 (d, 2H, J = 5.5 Hz, CH_2); ^{13}C NMR (300 MHz, $CDCl_3$): δ: 174.6, 154.5, 151.4, 145.5, 142.4, 137.1, 135.0, 132.9, 129.7, 128.1, 126.4, 124.7, 122.7, 120.8, 116.4, 47.6, 43.4, 40.5, 12.0; MS: *m/z* 393 (M^+); Elemental analysis: Calculated for $C_{21}H_{19}N_3OS_2$: C-64.09, H-4.87, N-10.68, O-4.07, S-16.30. Found: C-63.68, H-4.85, N-10.62, O-4.05, S-16.01.

1-(5-Phenyl-3-thiazol-2-yl-4,5-dihydro-pyrazol-1-yl)-2-*p*-tolylsulfanyl-ethanone (5c)
White solid, Yield: 78%, mp: 135-137; IR (KBr, cm^{-1}): 3045 (C–H Ar), 2974 (C–H, CH_3), 1680 (C=O), 1644 (C=N), 1545 (C=C, Ar), 1220 (C-S); ^1H NMR (300 MHz, $CDCl_3$): δ 7.62-7.38 (m, 5H, Ar–H), 7.50 (d, 2H, J = 7.5 Hz, Ar–H), 7.48 (d, 1H, J = 6.0 Hz, CH), 7.42 (d, 2H, J = 7.5 Hz, Ar–H), 7.35 (d, 1H, J = 6.0 Hz, CH), 4.19 (s, 2H, CH_2), 3.59 (t, 1H, J = 5.4 Hz, CH), 2.84 (s, 3H, CH_3), 2.44 (d, 2H, J = 5.4 Hz, CH_2); ^{13}C NMR (300 MHz, $CDCl_3$): δ: 171.2, 154.8 152.3, 148.4, 143.2, 136.1, 134.9, 131.9, 129.4, 127.1, 125.3, 124.5, 119.5, 47.1, 45.3, 43.3, 14.0; MS: *m/z* 393 (M^+); Elemental analysis: Calculated for $C_{21}H_{19}N_3OS_2$: C-64.09, H-4.87, N-10.68, O-4.07, S-16.30. Found: C-63.68, H-4.85, N-10.62, O-4.05, S-16.01.

2-(4-Methoxy-phenylsulfanyl)-1-(5-phenyl-3-thiazol-2-yl-4,5-dihydro-pyrazol-1-yl)-ethanone (5d)
Orange solid, Yield: 73%, mp: 119-121; IR (KBr, cm^{-1}): 3048 (C–H Ar), 29768(C–H, CH_3), 1680 (C=O), 1642 (C=N), 1588 (C=C, Ar), 1218 (C-S), 1128 (C–O); ^1H NMR (300 MHz, $CDCl_3$): δ 7.80-7.58 (m, 5H, Ar–H), 7.52 (d, 1H, J = 6.3 Hz, CH), 7.44 (d, 2H, J = 7.0 Hz, Ar-H), 7.35 (d, 2H, J = 7.0 Hz, Ar-H), 7.29 (d, 1H, J = 6.3 Hz, CH), 4.35 (s, 3H, OCH_3), 4.15 (s, 2H, CH_2), 3.48 (t, 1H, J = 5.2 Hz, CH), 2.40 (d, 2H, J = 5.2 Hz, CH_2); ^{13}C NMR (300 MHz, $CDCl_3$): δ: 172.0, 156.7, 154.2, 152.0, 144.7, 142.0, 135.4, 132.7, 130.5, 128.3, 125.0, 122.4, 116.4, 52.2, 48.5, 46.3, 43.3; MS: *m/z* 409 (M^+); Elemental analysis: Calculated for $C_{21}H_{19}N_3O_2S_2$: C-61.59, H-4.68, N-10.26, O-7.81, S-15.66. Found: C-61.05, H-4.65, N-10.20, O-7.79, S-15.59.

2-(4-Chloro-phenylsulfanyl)-1-(5-phenyl-3-thiazol-2-yl-4,5-dihydro-pyrazol-1-yl)-ethanone (5e)

Pale yellow solid, Yield: 78%, mp: 144-146; IR (KBr, cm^{-1}): 3045 (C–H Ar), 2958 (C-H, CH_2), 1640 (C=N), 1658 (C=O), 1578 (C=C, Ar), 1215 (C-S), 1124 (C–O); ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.79-7.58 (m, 5H, Ar-H), 7.54 (d, 1H, J = 6.5 Hz, CH), 7.42 (d, 2H, J = 7.2 Hz, Ar-H), 7.39 (d, 2H, J = 7.2 Hz, Ar-H), 7.39 (d, 1H, J = 6.9 Hz, CH), 4.22 (s, 2H, CH_2), 3.51 (t, 1H, J = 5.5 Hz, CH), 2.44 (d, 2H, J = 5.5 Hz, CH_2); ^{13}C NMR (300 MHz, $CDCl_3$): δ: 171.3, 154.2, 152.7, 150.4, 147.3, 143.1, 137.1, 134.9, 128.4, 126.9, 125.0, 116.2, 47.6, 45.3, 42.8, 40.5; MS: *m/z* 413 (M^+); Elemental analysis: Calculated for $C_{20}H_{16}ClN_3OS_2$: C-58.03, H-3.90, Cl-8.56, N-10.15, O-3.87, S-15.49. Found: C-57.89, H-3.88, Cl-8.54, N-10.00, O-3.85, S-15.39.

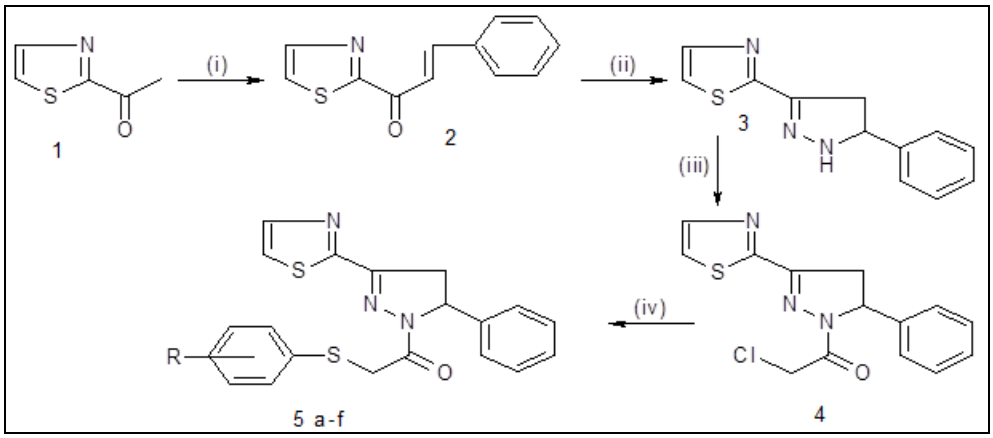
2-(4-Bromo-phenylsulfanyl)-1-(5-phenyl-3-thiazol-2-yl-4,5-dihydro-pyrazol-1-yl)-ethanone (5f)
Yellow solid, Yield: 77%, mp: 136-138; IR (KBr, cm^{-1}): 3054 (C–H Ar), 2965 (C-H, CH_2), 1665 (C=O), 1636 (C=N), 1586 (C=C, Ar), 1236 (C–S); ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.68-7.58 (m, 5H, Ar–H), 7.52 (d, 2H, J = 7.8 Hz, Ar-H), 7.43 (d, 1H, J = 6.6 Hz, CH), 7.38 (d, 2H, J = 7.8 Hz, Ar-H), 7.30 (d, 1H, J = 6.6 Hz, CH), 4.28 (s, 2H, CH_2), 3.55 (t, 1H, J = 5.7 Hz, CH), 2.49 (d, 2H, J = 5.7 Hz, CH_2); ^{13}C NMR (300 MHz, $CDCl_3$): δ: δ 172.0, 156.1, 153.7, 152.2, 143.1, 140.6, 134.6, 129.2, 126.8, 125.0, 117.4, 114.2, 116.3, 46.3, 45.9, 43.0, 41.8; MS: *m/z* 458 (M^+); Elemental analysis: Calculated for $C_{20}H_{16}BrN_3OS_2$: C-52.40, H-3.52, Br-17.43, N-9.17, O-3.49, S-13.99. Found: C-51.98, H-3.50, Br-17.28, N-9.14, O-3.46, S-13.89.

RESULTS AND DISCUSSION

In view of these previous findings and in continuation of our interest to synthesize different heterocyclic compounds, we report herein on the synthesis of some novel pyrazole derivatives containing thiazole with potential antibacterial activity. Thus the target compounds, 2-arylsulfanyl-1-(5-phenyl-3-thiazol-2-yl-4,5-dihydro-pyrazol-1-yl)-ethanone (5a-f) have been synthesized in good to excellent yields by employing 2-acetylthiazole (1) as raw material and 3-phenyl-1-thiazol-2-yl-propenone (2), 2-(5-phenyl-4,5-dihydro-1*H*-pyrazol-3-yl)-thiazole (3) and 2-chloro-1-(5-phenyl-3-thiazol-2-yl-4,5-dihydro-pyrazol-1-yl)-ethanone (4) as reactive intermediates (Scheme 1). The chemical structures of all compounds were confirmed by the examination of their IR, ^{1}H & ^{13}C NMR, Maas spectral data and elemental analysis.

The commercially accessible starting compound 2-acetylthiazole (1) was condensed with benzaldehyde in alkaline condition in presence of ethanol solvent at room temperature under uniform stirring for 5 h to produce the initial intermediate, 3-phenyl-1-thiazol-2-yl-propenone (2) in 77% of yield. The formation of compound 2 was confirmed by its spectral analysis. The IR spectrum of compound 2 showed absorption bands at 3050 (C–H Ar), 1684 (C=O), 1652 (C=N), 1618, (C=C, Ar) and 1224 (C-S) cm^{-1}. The proton NMR spectrum of 2 showed signals between δ 7.62-7.15 ppm as a multiplet for five protons corresponding to aromatic ring. Two signals at δ 7.68 ppm and 6.89 pm as doublets for one proton each with same coupling constant (J) 7.6 Hz are associated with two C-H groups of alkene. The rest of two signals at δ 7.45 ppm and 7.35 ppm as expected doublets with same coupling constant (J) 6.9 Hz are assigned to C-H proton of thiazole ring. The ^{13}C NMR spectrum of this compound exhibited signals at different chemical shifts 173.5, 154.7, 147.7, 141.4, 132.8, 127.3, 125.8, 123.7, 120.5 and 118.6 ppm associated for various carbons. Mass spectrum showed peak at m/z 215 (M^+), thus confirming the structure of 2.
Cyclization reaction of compound 2 with hydrazine hydrate in ethanol solvent under reflux on constant stirring for 6 h afforded the next intermediate, 2-(5-phenyl-4,5-dihydro-1*H*-pyrazol-3-yl)-thiazole (3) in 72% of yield. The emerging of compound 3 was confirmed by its spectral analysis. The IR spectrum of compound 3 showed absorption bands at 3138 ((N–H), 3045 (C–H Ar), 2962 (C–H, CH_2), 1650 (C=N), 1648 (C=C, Ar), and 1214 (C-S) cm^{-1}. The proton NMR spectrum of 3 showed a signal between δ 7.67-7.38 ppm as a multiplet integrating for five protons is assigned to aromatic protons. The δ-chemical shifts at 7.52 ppm and 7.41 ppm as doublets for one proton each with same coupling constants (J = 6.5 Hz) corresponding to both CH groups. The only one singlet signal of NH group as singlet is appeared at δ-chemical shift 6.39 ppm. The combination of triplet and doublet signals for each proton with uniform coupling constant (J = 4.5 Hz) of this compound at δ 3.28 ppm and 2.84 ppm are related to the CH and CH2 groups. The ^{13}C NMR spectrum of this compound performed various signals at different chemical shifts such as 154.8, 150.7, 146.8, 142.2, 135.2, 128.1, 126.8, 118.8, 48.0 and 42.0 ppm associated for related to different carbons. Mass spectrum showed peak at m/z 229 (M^+), thus confirming the structure of 3.
Further, the substitution reaction of compound 3 with chloroacetyl chloride in triethyl amine in the existence of benzene solvent at ambient temperature on steady stirring for 2 h furnished the final intermediate, 2-chloro-1-(5-phenyl-3-thiazol-2-yl-4,5-dihydro-pyrazol-1-yl)-ethanone (4) in 76% of yield. The emerging of compound 4 was

confirmed by its different spectral study. The IR spectrum of compound 4 showed absorption bands at 3058 (C–H Ar), 2930 (C–H, CH_2), 1684 (C=O), 1632 (C=N), 1575 (C=C, Ar), 1226 (C-S) and 1146 (C–O) cm^{-1}. The proton NMR spectrum of compound 4 showed a signal at δ 7.74-7.52 as multiplet for five protons corresponding to aromatic group. The two signals at δ 7.50 ppm and δ 7.37 ppm for one proton each as both doublets with same coupling constant (J = 6.6 Hz) are assigned to two adjacent CH groups. The CH_2 group protons at δ 4.24 ppm are appeared as singlet. The signals as triplet for one and doublet for two proton at δ 3.36 ppm and δ 2.79 ppm respectively with same coupling constant (J = 5.0 Hz) are assigned to CH and CH_2 groups respectively. The ^{13}C NMR spectrum of this compound exhibited signals at different chemical shifts 163.2, 154.9, 150.8, 145.3, 142.7, 135.2, 128.6, 123.7, 118.9, 49.0, 46.2 and 42.0 ppm associated for various carbons. The mass spectrum of compound 4 showed m/z value at 305 confirmed the structure of compound 4.



Scheme 1: (i) C_6H_5CHO, NaOH, EtOH, 5 h; (ii) $NH_2NH_2.H_2O$, EtOH, reflux, 6 h; (iii) $ClCOCH_2Cl$, TEA, benzene, 2 h; (iv) Thiophenol/Substituted thiophenol, EtOH, 7-9h. 5a-f R (a) = H; (b) = 2-CH_3; (c) = 4-CH_3; (d) = 4-OCH_3; (e) = 4-Cl; (f) = 4-Br

Finally, treatment of compound 4 on substitution reaction with thiophenol or substituted thiophenol in absolute ethanol at room temperature under stable stirring for 7-9 h granted the corresponding target compounds, 2-arylsulfanyl-1-(5-phenyl-3-thiazol-2-yl-4,5-dihydro-pyrazol-1-yl)-ethanone (5a-f)) in 72-78% of yields. Formation of the compound 5a was confirmed by its spectral analysis. In the IR spectrum of compound 5a, the absorption bands are appeared at 3048 (C–H Ar), 2932 (C–H, CH_2), 1675 (C=O), 1636 (C=N), 1572 (C=C, Ar) and 1220 (C-S) cm^{-1}. Additional support was obtained from the ^1H NMR spectra. Ten protons of the aromatic ring are appeared between δ7.75-7.38 ppm as multiplet. One proton at δ 7.55 ppm as a doublet signal and another proton at δ 7.40 ppm as a doublet signal with uniform coupling constant (J = 7.2 Hz) singlet is assigned to both CH groups. The CH_2 group protons appeared at δ 4.31 ppm as singlet. The signal at δ 3.74 ppm as triplet for one proton is corresponding to the CH group and another signal at δ 2.51 ppm as doublet for two protons is assigned to the CH_2 group. The ^{13}C NMR spectrum of this compound performed various signals at different chemical shifts 172.1, 157.4, 153.4, 144.0, 142.0, 137.0, 135.0, 132.1, 129.4, 128.0, 123.0, 120.0, 117.2, 48.0, 42.0 and 39.0 ppm associated for related to different carbons. The mass spectrum of compound 5a showed m/z value at 379 confirmed the structure of compound 5a. Moreover, all the newly synthesized title compounds, 2-arylsulfanyl-1-(5-phenyl-3-thiazol-2-yl-4,5-dihydro-pyrazol-1-yl)-ethanone (5a-f)) were screened for their antibacterial activity and some of them were found to possess moderate to good antibacterial activity.

CONCLUSION

A new series of novel pyrazole derivatives containing thiazole with potential antibacterial activity have been synthesized.

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