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Synthesis New and Novel Aryl Thiazole Derivatives Compounds

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ABSTRACT

Six new compounds of Thiazoles family was synthesis from condensation reaction of some compounds from pyrazolines. NMR, IR and elemental analysis was used for identification of these compounds. Position of aliphatic and aromatic hydrogens in pyrazolone and thiazole cycles had established proceeding of identification. Most of obtained compounds like aciform crystals, their color is white and yellow. Reaction time and yield of these compounds had shown better results as compared with other thiazole derivations.

Key words: Thiazoles, Synthesis, NMR, Elemental analysis.

INTRODUCTION

Thiazoles are 5-membered cyclic compounds that nitrogen and sulfur group at different situation[1]. This compound have a lot of derivations and because of its derivations type have a lot of application in various industries, medical science and pharmacy. In 1887, Hantzsch et al identified and established molecular structure of thiazoles[2]. In 1889, the first derivation of thiazoles identified by Prop et al and was named 2-amino thiazole [3]. After that until now, many derivations identified and reported[4-9]. However, identification of vitamin B1 and penicillin former components. It was found that thiazoles system including of S-C-N bound and have biological specifications. So, synthesis of thiazole derivations was become more important. Thiazoles are applicable in anti-fire and hard PVC stabilizer compounds. However, their derivations are applicable in anti-wart[10], anti-allergenic[11], anti-bacterial[12], anti-spasm[13], anti-paroxysm[14] and anti-fungal[15-17]. Derivations of this compounds like 2-mercapto-5-hydroxy ethyl-4-methyl thiazole was used for destroying of helminthes and parasites and 2-methyl mercapto-4,5-di-4-methoxy as a drug for treatment of rheumatic. 2-aryl mercaptos are applicable for treatment of phlegmasia, too. 5-nitro-2,2-thio bis thiazole was used as an anti bacterial compound. But quality of substitution mechanisms is different in thiazoles group[18]. For example, substitution of methyl group in thiazoles structures is done by

heteroatomic and hyper conjugation models. It is done by changing of pay electron. In this research, some new family of these compounds was produced that have many applications in medical science, pharmacy and industries.

EXPERIMENTAL

General method

All of chemical materials were purchased from Germany firm Merk. For this study, all of instruments that were used, are as following: microwave oven model LG-SOLARDOM LF-5901WCR, Japanese weighing with 0.100 g accuracy, model ANDGF-300, hitter and stirrer model Heidolphm Rn3004 Safty, Merk thin layer chromatography sheets Art no: 1:0554, Electro thermal melting point measurement apparatus, Memmert (oven) materials and glossy instruments desiccators (oven), vacuum pump Emerson model: C55-JJXH4205, Rmp: 1425/1725, Heidolph model: Labrota rotary solution. ^{1}H-NMR spectra studying done by Bruker Avance 300 spectrometer with processing software XWINNMR version 3.1. FT-IR by a Perkin Elmer spectrum 1420 spectrometer in the frequency range of 4000–400cm^{-1} using KBr discs are reported on 1 scale. The IR spectra were recorded at room temperature at the spectral resolution of 1 cm^{-1}. Used Glossy instruments are as follows: one and two ports round- bottom emery-top flasks species, simple, bubble and spiral radiator, Erlenmeyer flask, beakers, three and two ports, links, addition funnel, Buchner funnel, capillary tube and etc.

Synthesis

Synthesis methods and proceeding of this family from thiazoles was described at following. NMR, IR and elemental analysis was used for identification of these compounds.

Preparation of Ammonia gas

In the libratory, ammonium gas was prepared from reaction of ammonium chloride by sodium hydroxide. So, ammonium chloride and sodium hydroxide was heated. Sodium chloride salt, H_2O and ammonium gas was prepared. For elimination of moisture, Calcium oxide was put in the path of ammonia gas exodus.

Preparation of ammonium di-thio carbamate

100.0 ml 95% ethanol was poured in 250.0 ml Erlenmeyer. It was kept in the ice bath and then was transited ammonia gas until weight increasing approximately 39.0 g was obtained. 60.0 ml (1.0 mol) carbon disulfide and 200.0 ml diethyl ether was added to the solution and it was kept for 2-3 hours in the ice container and then for 1 day in the refrigerator. After passing this time, yellow crystals of ammonium di-thio carbamate was formed. Then content of container was strained and washed by ether (50.0 ml). 80.0 g ammonium di-thio carbamate was produced.

Synthesis of 4-Bromophenacylbromid structure (1a)

50.0 g (0.2 mol) 4-bromo acetophenone was solved in 100.0 ml pure acetic acid in the 250.0 ml Erlenmeyer and then 12.5 ml (0.2 mol) bromine was added slowly to obtained solution and during the mixing, temperature of reaction container was kept to less than 20°C. Aciform crystals were produced approximately 30 minutes after adding of bromine. Mixing was continued for 30 minutes later. Then content of Erlenmeyer was strained and dried. 50.0 g production by 80% yield was produced. Obtained precipitation was recrystallized by 95% ethanol for purification. 4-bromophenacylbromide was produced by 108-109 °C melting point. TLC chromatogram and comparison of its R_f by bromo acetophenone R_f was established forming of production and its purity. The residue was purified by thin layer chromatography on silica gel (8:2 cyclo hexane–acetone) to give (56.0 g , 80%); A white solid; Mp: 108-109; IR (KBr): 3065-2950-2064-1693-1180-644; ^{1}H-NMR (400 MHz, $CDCl_3$) δ 4.44(s, 2H, CH_2Br), 7.66-7.68 (d, 2H, 2-H, 6-H), 7.87-7.90 (J=9 Hz, d, 2H, 3-H, 5-H).

Synthesis of 4-Methylphenacylbromid structure (2a)

50.0 g (0.2 mol) 4-bromo acetophenone was solved in 100.0 ml pure diethyl ether in the 250.0 ml Erlenmeyer and then 12.5 ml (0.2 mol) bromine was added slowly to obtained solution and during the mixing, temperature of reaction container was kept to less than 20 °C. White aciform crystals were produced approximately 30 minutes after

adding of bromine. Mixing was continued for 30 minutes later. Then content of Erlenmeyer was strained and dried. 48.0 g production by 83% yield was produced. Obtained precipitation was recrystallized by 95% ethanol for purification. Production was produced by 80-82 °C melting point. TLC chromatogram and comparison of its R_f by 4-methyl acetophenone R_f was established forming of production and its purity. The residue was purified by thin layer chromatography on silica gel (8:2 cyclo hexane–acetone) to give (48.0 g, 83%); A white solid; Mp: 80-82; ^{1}H-NMR (400 MHz, $CDCl_3$) δ 2.40 (s, 3H, CH3), 4.53 (s, 2H, CH_2Br), 7.53-7.54 (d, 2H, 3-H, 5-H), 8.174-8.177 (J=9Hz, d, 2H, 2-H, 6-H).

Synthesis of 4-(4′-Bromophenyl)-2-mercaptothiazole structure (3a)

12.5 g (0.04 mol) 4-bromo phenacyl bromide was solved in 212.5 ml ethanol and 9.3 g (0.08 mol) ammonium di-thio carbamate was added to it and was refluxed for 3 hours. After ejecting of solvent by rotary, the yellow solid was formed that was refluxed for 15 minutes by 125.0 ml benzene. Than obtained solution was become cold and crystal precipitation was formed. Finally, the precipitation was strained and dried. 18 g production, 74% yield and 218 °C melting point was produced. TLC chromatogram and comparison of its R_f by 4-bromo phenacyl bromide R_f was established forming of production and its purity. The residue was purified by thin layer chromatography on silica gel (8:2 cyclo hexane–acetone) to give (18 g, 74%); A pale yellow; Mp: 216-218; IR (KBr): 3128-3050-1628-1401-1259-1180-746; ^{1}H-NMR (400 MHz, $CDCl_3$) δ 3.46 (s, 1H, SH Aliphatic), 7.37 (s, 1H, H-5), 7.61-7.63 (d, 2H, 2′-H, 6′-H), 7.67-7.69 (J=9Hz, d, 2H, 3-H′, 5-H′).

Synthesis of 4-(4′-methylphenyl)-2-mercaptothiazole structure (4a)

12.50 g (0.04 mol) 4-bromo phenacyl bromide was solved in 212.5 ml ethanol and 9.3 g (0.08 mol) ammonium di-thio carbamate was added to it and was refluxed for 3 hours. After ejecting of solvent by rotary, the yellow solid was formed that was refluxed for 15 minutes by 125.0 ml benzene. Than obtained solution was become cold and crystal precipitation was formed. Finally, the precipitation was strained and dried. 18.0 g production, 86% yield and 191-193 °C melting point was produced. TLC chromatogram and comparison of its R_f by 4-methyl phenacyl bromide R_f was established forming of production and its purity. The residue was purified by thin layer chromatography on silica gel (85:15 cyclo hexane–acetone) to give (18g, 86%); A yellow solid; Mp: 191-193; ^{1}H-NMR (400 MHz, $CDCl_3$) δ 2.40 (s, 3H, CH_3), 3.16 (s, 1H, SH Aliphatic), 6.92 (s, 1H, H-5), 7.28-7.30 (J=9Hz, d, 2H, 3-H′¡5-H′), 7.48-7.49 (d, 2H, 2′-H¡6′-H).

Synthesis of 3-methyl-1-phenyl-2-pyrazolin-5-on structure (5a)

The production 5a was produced by three following method:

Method number one

In the round bottom balloon, 100.0 ml ethanol was added to mixture of 33.3 g (0.2 mol) ethyl thio acetate and 27.7 g (0.2 mol) phenyl hydrazine and was refluxed in the oil container at 130 °C for 3 hours. After cooling, reaction mixture was put at the room temperature until crystals was formed and was filtered by Buchner funnel. Finally, it was recrystallized in ethanol.

Method number two

In the round bottom balloon, 14.7 g (0.1 mol) ethyl acetate and 10.9 g (0.1 mol) phenyl hydrazine was heated for 2 hours on steam bath distillation instrument was used for controlling of gases and doing of reaction at constant press. Then, reaction mixture was gotten cold and was mixed by adding of 20.0 ml cold di ethyl ether and produced solid was filtered and was washed by cold ether (50.0 ml) and dried. Finally, it was recrystallized in ethanol.

Method number three

Red oily mixture was produced from reaction of β-keto ester, ethyl acetate and phenyl hydrazine (1:1) respectively 14.7 g (0.1 mol) and 10.9 g (0.1 mol) in presence of concentrated sulfuric acid (4-5 drops) for 15 minutes. After 1 day, obtained solid was converted to powder by using of mortar. Powdered solid was washed by cold di ethyl ether. Then obtained powder was washed by 10% aqueous sodium carbonate (200.0 ml). 21.2 g pyrazoline was produce by 83% yield and 125-126 °C melting point. TLC chromatogram and comparison of its R_f by ethyl aceto acetate and

phenyl hydrazine R_f was established forming of production and its purity. The residue was purified by thin layer chromatography on silica gel (8:2 cyclo hexane-acetone) to give (21.2 g, 83%); A yellow crystal; Mp: 125-126; ^{1}H-NMR (400 MHz, $CDCl_3$) δ 2.13 (s, 3H, CH_3), 3.37 (s, 2H, Pyrazoline), 7.11 (t, 1H, 4-H′), 7.29-7.32 (J=9Hz, t, 2H, 3-H′, 5-H′), 7.71-7.73 (J=9Hz, d, 2H, 2′-H, 6′-H).

Synthesis of 3-propyl-1-phenyl-2-pyrazolin-5-on structure (6a)

In the round bottom balloon, 5.1 g (0.2 mol) ethyl butyryl acetate and 9.6 g (0.8 mol) phenyl hydrazine was heated on the steam bath for 2 hours. After cooling, 20.0 ml ether was added to reaction mixture and filtered. Then it was washed by ether and finally, it was recrystallized by ethanol. 10.0 g production was produced by 71% yield and 111 °C melting point. TLC chromatogram and comparison of its R_f by ethyl aceto acetate and phenyl hydrazine R_f was established forming of production and its purity. The residue was purified by thin layer chromatography on silica gel (75:15 n-hexane-acetone) to give (10 g, 71%); A yellow solid; Mp: 111-113; ^{1}H-NMR (400 MHz, $CDCl_3$) δ 1.07 (J=9Hz, t, 3H, CH_3), 1.70 (J=9Hz, Sextet, 2H, CH_2), 2.5 (J=9Hz, t, 2H, CH_2), 3.46 (s, 2H, Pyrazoline), 7.22 (J=9Hz, t, 1H, 4-H′), 7.61-7.63 (J=9Hz, t, 2H, 3-H′¡5-H′), 7.90-7.92 (J=9Hz, d, 2H, 2′-H¡6′-H).

Synthesis of 1,3-diphenyl-2-pyrazolin-5-on structure (7a)

5.1 g (0.2 mol) ethyl benzoyl acetate and 9.6 g(0.8 mol) phenyl hydrazine was put in the round bottom balloon on the bath for 2 hours. After cooling, add 20.0 ml ether to reaction mixture and then filter the solid particles or wash them by ether. Finally, production was produced by 84% yield and then recrystallized by ethanol. TLC chromatogram and comparison of its R_f by ethyl benzoyl acetate R_f and phenyl hydrazine R_f was established forming of production and its purity. The residue was purified by thin layer chromatography on silica gel (25:75 n-hexane- acetone) to give (7.4 g , 84%); A yellow crystal; Mp: 112-115; ^{1}H-NMR (400 MHz, $CDCl_3$) δ 3.37 (s, 2H, CH_2), 7.10-7.11 (J=9Hz, t, 2H, 4′-H), 7.69-7.77 (j=9Hz, d, 4H, 3-H, 5-H), 7.82-7.90 (j=9Hz, t, 4H, 2-H, 6-H).

Synthesis of 4-bromo-3-methyl-1-phenyl-2-pyrazolin-5-on structure (8a)

1.2 ml (0.4 mol) bromine (15% solution in acetic acid) was added to 4.0 g (0.2 mol) 3-methyl-1-phenyl-2-pyrazoline-5-on solution in 20.0 ml acetic acid during the mixing for 30 minutes at less than 10 °C temperature. At first, was washed by 25% acetic acid solution and then by 10% acetic acid solution. Aciform crystals were produced by 94% yield. Melting point after recrystallization in acetic acid was obtained 128-130°C. TLC chromatogram and comparison of its R_f by 3-methyl-1-phenyl-2 pyrazoline-5-on R_f was established forming of production and its purity. The residue was purified by thin layer chromatography on silica gel (85:15 cyclo hexane-acetone) to give (6.1 g, 94%); A white crystal; Mp: 128-130; ^{1}H-NMR (400 MHz, $CDCl_3$) δ 2.12 (s, 3H, CH_3), 7.20-7.23 (d, 1H, 4-H), 7.42-7.45 (J=9Hz, d, 2H, 3-H, 5-H), 7.90-7.92 (t, 2H, 2-H, 6-H).

Synthesis of 4-bromo-3-propyl-1-phenyl-2-pyrazolin-5-on structure (9a)

1.5 ml (0.5 mol) bromine (15% solution in acetic acid) was added to 4.0 g (0.02 mol) 1-phenyl-3-propyl-2-pyrazoline-5-on solution in 20.0 ml acetic acid during the mixing for 30 minutes at less than 10 °C temperature. At first, obtained solid was washed by 25% acetic acid solution and then by 10% acetic acid solution. 4.7 g aciform crystals were produced by 85% yield and 128-130 °C melting point. TLC chromatogram and comparison of its R_f by 1-phenyl-3-propyl-2-pyrazoline-5-on R_f was established forming of production and its purity. The residue was purified by thin layer chromatography on silica gel (80:20 cyclo hexane-acetone) to give (4.7 g, 85%); A yellow crystal; Mp: 122-123; ^{1}H-NMR (400 MHz, $CDCl_3$) δ 0.88 (J=9Hz, t, 3H, CH_3), 1.62 (m, 2H, CH_2), 2.64 (J=9Hz, t, 2H, CH_2), 5.82 (s, 1H, Pyrazoline), 7.30 (J=9Hz, t, 1H, 4-H), 7.40 (J=9Hz, d, 2H, 3-H, 5-H), 7.53 (J=9Hz, d, 2H, 2-H, 6-H).

Synthesis of 4-bromo-1,3-diphenyl-2-pyrazolin-5-on structure (10a)

1.5 ml (0.5 mol) bromine(15% solution in acetic acid) was added to 4.0 g (0.02 mol) 1,3-diphenyl-2-pyrazoline-5-on solution in 20.0 ml acetic acid during the mixing for 30 minutes at less than 10 °C temperature. At first, obtained solid was washed by 25% acetic acid solution and then by

10% acetic acid solution. 6.3 g white aciform crystals were produced by 84% yield. TLC chromatogram and comparison of its R_f by 1,3-diphenyl-2-pyrazoline-5-on R_f was established forming of production and its purity. The residue was purified by thin layer chromatography on silica gel (80:20 cyclo hexane–acetone) to give (6.3 g, 84%); A white crystal; Mp: 105-110; ^{1}H-NMR (400 MHz, $CDCl_3$) δ 7.40-7.55 (J=9Hz, t, 4H, 3-H, 5-H), 7.70 (t, 1H, 4-H), 8.10-8.20 (J=9Hz, d, 4H, 2-H, 6-H).

Synthesis of 2-(3-methyl-1-phenyl-4,5-dihydro-5-oxopyrazol)-4-thio-4-(4-bromophenyl)thiazol structure (11a)

10.0 g sodium hydroxide (powdered) was added to solution contains of 5.0 g (0.001 mol) 2-mercapto-(4-bromo-phenyl) thiazole in 250.0 ml absolute ethanol and was refluxed for 15 minutes. Then 6.0 g (0.002 mol) 4-bromo-3-methyl-1-phenyl-2-pyrazoline-5-on was added to obtained solution and reflux was continued for 45 minutes later. Then the solvent was separated by rotary. Some ice was added to residue solid and was washed by cool water. After drying, 7.5 g production by 84% yield was produced. It was recrystallized by absolute ethanol and finally white crystals were produced. TLC chromatogram and comparison of its R_f by 4-bromo-1,3-diphenyl-2-pyrazoline-5-on and 4-(4-bromo phenyl)-2-mercapto thiazole R_f was established forming of production and its purity. The residue was purified by thin layer chromatography on silica gel (80:20 cyclo hexane-acetone) to give (7.5 g, 84%); A white crystal; Mp: 128-135; ^{1}H-NMR (400 MHz, $CDCl_3$) δ 2.47 (s, 3H, CH_3), 4.92 (J=9Hz, s, 1H, Pyrazole), 7.50-7.56 (J=9Hz, dd, 4H, $2^{//}$-H, $6^{/}$-H Aromatic), 7.55-7.77 (m, 5H, Phenyl), 7.60 (s, 1H, 5-H), 7.75-7.77 (J=9Hz, dd, 4H, $3^{//}$-H, $5^{//}$-H Aromatic).

Synthesis of 2-(3-propyl-1-phenyl-4,5-dihydro-5-oxopyrazol)-4-thio-4-(4-bromophenyl)thiazol structure (12a)

9.0 g sodium hydroxide (powdered) was added to solution contains of 5.0 g (0.001mol) 2-mercapto-4-(4-bromo-phenyl) thiazole in 250.0 ml absolute ethanol and was refluxed for 15 minutes. Then 6.1 g (0.002 mol) 4-bromo-3-propyl-1-phenyl-2-pyrazoline-5-on was added to obtained solution and reflux was continued for 45 minutes later. Then the solvent was separated by rotary. Some ice was added to residue solid and was washed by cool water. After drying, 9.8 g light yellow scaly crystals by 86% yield was produced. It was recrystallized by absolute ethanol. TLC chromatogram, melting point and comparison of its R_f by 4-bromo-1-phenyl-3-propyl-2-pyrazoline-5-on and 4-(4-bromo phenyl)-2-mercapto thiazole Rf was established Forming of production and its purity. The residue was purified by thin layer chromatography on silica gel (80:20 cyclo hexane–acetone) to give (9.8 g, 86%); A yellow crystal; Mp: 140-145; ^{1}H-NMR (400 MHz, DMSO) δ 1.07-1.09 (J=7Hz, t, 3H, CH_3), 1.70-1.95 (J=7Hz, Sextet, 2H, Methylene), 2.83-3.00 (J=7Hz, t, 2H, CH_2), 4.73 (J=9Hz, d, 1H, Pyrazoline), 7.42-7.72 (J=9Hz, m, 5H, $3^{/}$-H, $5^{/}$-H), 7.58 (J=9Hz, s, 1H, 5-H), 7.65-7.67 (J=9Hz, dd, 4H, $2^{//}$-H, $6^{//}$-H Aromatic), 7.70-7.77 (J=9Hz, dd, 4H, $3^{//}$-H, $5^{//}$-H Aromatic).

Synthesis of 2-(1,3-diphenyl-4,5-dihydro-5-oxopyrazol)-4-thio-4-(4-bromophenyl)thiazol structure (13a)

10.0 g sodium hydroxide (powdered) was added to solution contains of 5.0 g (0.001mol) 2-mercapto-4-(4-bromo-phenyl) thiazole in 250.0 ml absolute ethanol and was refluxed for 15 minutes. Then 6.1 g (0.002mol) 4-bromo-1,3-diphenyl-2-pyrazoline-5-on was added to obtained solution and reflux was continued for 45 minutes later. Then the solvent was separated by rotary. Some ice was added to residue solid and was washed by cool water. After drying, 8.6 g production by 91% yield was produced. It was recrystallized by absolute ethanol and finally yellow crystals were produced. TLC chromatogram and comparison of its R_f by 4-bromo-1,3-diphenyl-2-pyrazoline-5-on and 4-(4-bromo phenyl)-2-mercapto thiazole R_f was established forming of production and its purity. The residue was purified by thin layer chromatography on silica gel (25:75 n-hexane- acetone) to give (8.6 g, 95%); A pale yellow crystal; Mp: 132-135; ^{1}H-NMR (400 MHz, $CDCl_3$) δ 4.30 (s, 1H, Pyrazolone), 7.38 (s, 1H, 5-H), 5.47-5.48 (J=9HZ, dd, 4H, $2^{//}$-H, $6^{/}$-H Aromatic), 7.48-7.50 (J=9HZ, dd, 4H, $3^{//}$-H, $5^{//}$-H Aromatic), 7.38-7.86 (m, 10H, Aromatic), 7.58 (J=9Hz, d, 2H, $2^{/}$-H, $6^{/}$-H), 7.67(J=9Hz, d, 2H, $2^{//}$-H, $6^{//}$-H).

Synthesis of 2-(3-methyl-1-phenyl-4,5-dihydro-5-oxopyrazol)-4-thio-4-(4-methylphenyl)thiazol structure (14a)

10.0 g sodium hydroxide (powdered) was added to solution contains of 5.0 g (0.001mol) 2-mercapto-4-(4-bromo-phenyl) thiazole in 250.0 ml absolute ethanol and was refluxed for 15 minutes. Then 6.1 g (0.002mol) 4-bromo-3-methyl-1-phenyl-2-pyrazoline-5-on was added to obtained solution and reflux was continued for 45 minutes later. Then the solvent was separated by rotary. Some ice was added to residue solid and was washed by cool water. After drying, 7.5 g production by 84% yield was produced. It was recrystallized by absolute ethanol and finally gray scaly crystals were produced. TLC chromatogram and comparison of its R_f by 4-bromo-3-methyl-1-phenyl-2-pyrazoline-5-on and 4-(4-methyl phenyl)-2-mercapto thiazole R_f was established forming of production and its purity. The residue was purified by thin layer chromatography on silica gel (25:75 n-hexane-acetone) to give (7.8 g, 86%); A black crystal; Mp: 120-125; ^{1}H-NMR (400 MHz, DMSO) δ 2.38 (s, 3H, CH_3 Phenyl), 2.42 (s, 3H, CH_3 Pyrazole), 4.42 (s, 1H, Pyrazolone), 7.35-7.85 (J=9Hz, m, Phenyl), 7.36 (s, 1H, 5-H), 7.52-7.60 (J=9Hz, dd, 4H, $2^{//}$-H, $6^{//}$-H Aromatic), 7.81-7.85 (J=9Hz, dd, 4H, $3^{//}$-H¡$5^{//}$-H Aromatic).

Synthesis of 2-(3-propyl-1-phenyl-4,5-dihydro-5-oxopyrazol)-4-thio-4-(4-methylphenyl)thiazol structure (15a)

10.0 g sodium hydroxide (powdered) was added to solution contains of 5.0 g (0.001mol) 2-mercapto-4-(4-methyl-phenyl) thiazole in 250.0 ml absolute ethanol and was refluxed for 15 minutes. Then 6.1 g (0.002mol) 4-bromo-1,3-diphenyl-2-pyrazoline-5-on was added to obtained solution and reflux was continued for 45 minutes later. Then the solvent was separated by rotary. Some ice was added to residue solid and was washed by cool water. After drying, 7.5 g production by 84% yield was produced. It was recrystallized by absolute ethanol and finally white scaly crystals were produced. TLC chromatogram and comparison of its R_f by 4-bromo-1,3-diphenyl-2-pyrazoline-5-on and 4-(4-methyl- phenyl)-2-mercapto thiazole R_f was established forming of production and its purity. The residue was purified by thin layer chromatography on silica gel (25:75 ethyl acetate-CCl_4) to give (8.4 g, 86%); A white crystal; Mp: 123-125; ^{1}H-NMR (400 MHz, DMSO) δ 1.05-1.08 (J=7Hz, t, 3H, CH_3), 1.69-1.72 (J=7Hz, Sextet, 2H, CH_2), 2.73-2.93 (J=7Hz, t, 2H, CH_2), 2.78 (s, 3H, CH_3), 4.57 (s, 1H, Pyrazoline), 4.58 (s, 1H, 5-H), 7.42-7.72 (m, 5H, Phenyl), 7.60-7.61 (J=7Hz, dd, 4H, $3^{//}$-H, $5^{//}$-H Aromatic), 7.61-7.62 (J=7Hz, dd, 4H, $2^{//}$-H, $6^{//}$-H Aromatic).

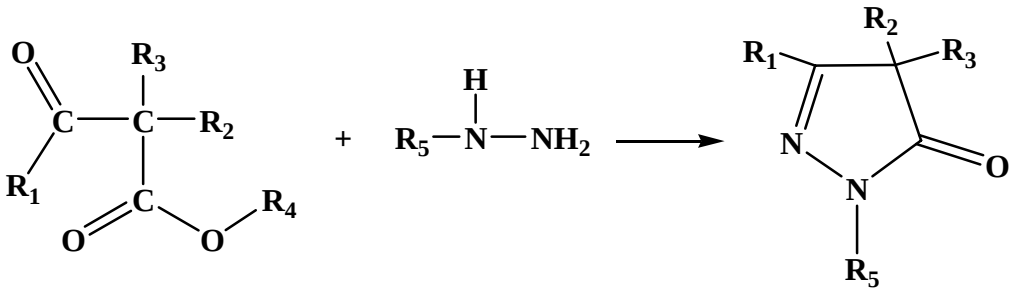
Synthesis of 2-(1,3-diphenyl-4,5-dihydro-5-oxopyrazol)-4-thio-4-(4-methylphenyl)thiazol (16a)

9.0 g sodium hydroxide (powdered) was added to solution contains of 5.0 g (0.001mol) 2-mercapto-4-(4-methyl-phenyl) thiazole in 250.0 ml absolute ethanol and was refluxed for 15 minutes. Then 6.0 g (0.002 mol) 4-bromo-3-methyl-1-phenyl-2-pyrazoline-5-on was added to obtained solution and reflux was continued for 45 minutes later. Then the solvent was separated by rotary. Some ice was added to residue solid and was washed by cool water. After drying, 8.6 g production by 91% yield was produced. It was recrystallized by absolute ethanol and finally brown scaly crystals were produced. TLC chromatogram and comparison of its R_f by 4-bromo-1,3-diphenyl-2-pyrazoline-5-on and 4-(4-methyl- phenyl)-2-mercapto thiazole R_f was established forming of production and its purity. The residue was purified by thin layer chromatography on silica gel (25:75 ethyl acetate-CCl_4) to give (8.6 g, 91%); A brown crystal; Mp: 121-123; ^{1}H-NMR (400 MHz, $CDCl_3$) δ 2.42 (s, 3H, CH_3), 4.32 (s, 1H, Pyrazlone), 7.38-7.72 (m, 10H, Phenyl), 7.39 (s, 1H, 5-H), 7.55-7.63 (J=9Hz, dd, 4H, $2^{//}$-H, $6^{//}$-H Aromatic), 7.70-7.72 (J=9HZ, dd, 4H, $3^{//}$-H, $5^{//}$-H Aromatic).

RESULTS AND DISCUSSION

At first, a group of pyrazolines of was produced by using of beta ceto esters condensation reaction by hydrazine group, and then by using of aryl thiazoles bromination. Finally, intended production was produced from synthesis compounds. Some methods like NMR, elemental analysis and IR was used for identification of this compounds. TLC method, melting point and comparison of its R_f by other same compounds R_f was used for identification of purity degree. 4-bromo phenyl-2-mercapto thiazole was synthesized from

reaction of ammonium di thio carbomate and N-bromo phenyl-5-pyrazolone synthesizes. From reaction of beta keto esters by phenyl hydrazine (see fig 1)

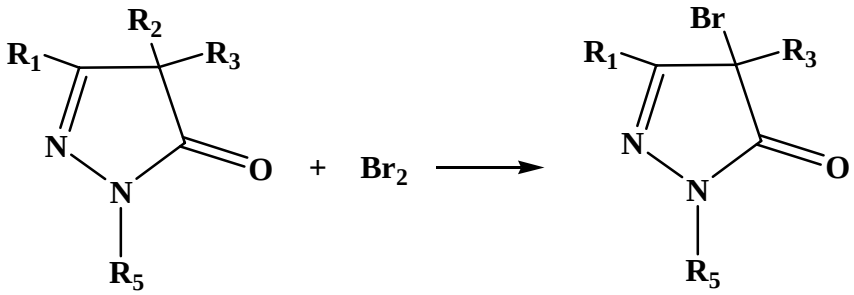


R1, R4, R5 = H, Aryl, Alkyl, Hetrocycle groups

R2, R3= H

Fig. 1. Synthetic route for the 2-pyrazolin-5-on derivatives.

Pyrazolone and thiazole residues was joint to each other by sulfide bridge from condensation of 4-bromo-2-pyrazoline-5-on with 2-mercapto thiazoles by elimination of HBr (see fig 2-4)



R1, R4, R5 = H, Aryl, Alkyl, Hetrocycle groups

R2, R3= H

Fig. 2. Synthetic route for the 4-Bromo-2-pyrazolin-5-on structure.

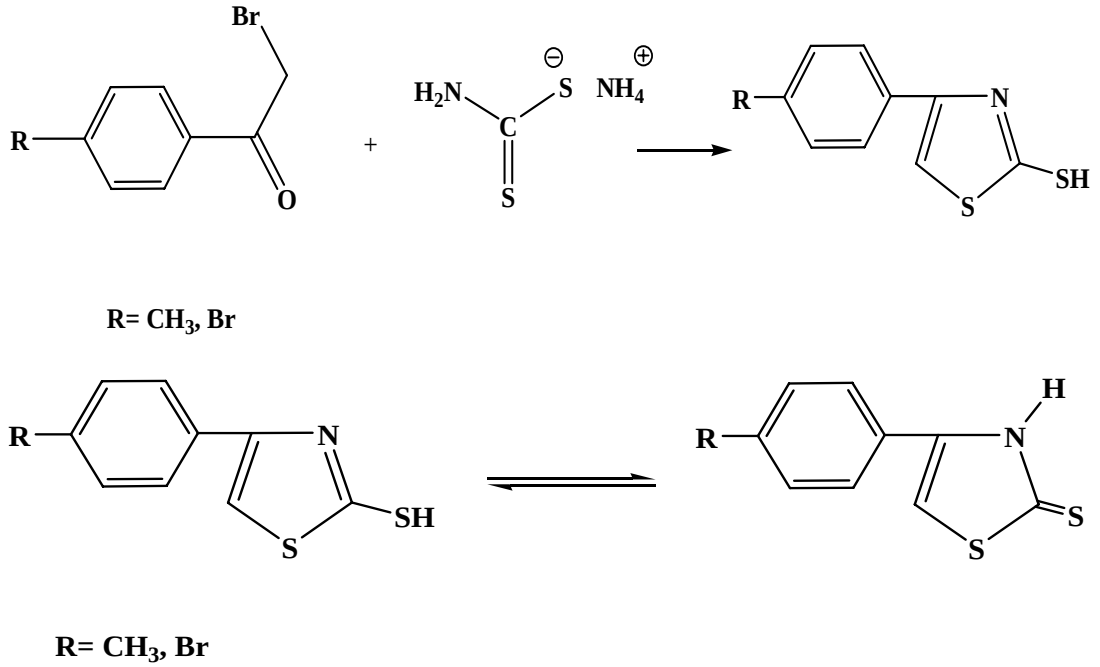


Fig. 3. Synthetic route for the 4-phenyl-2mercapto thiazol structure.

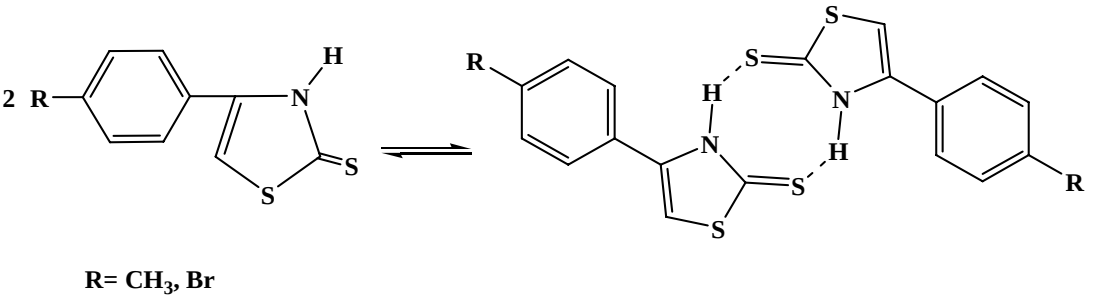


Fig. 4. Different reaction of the 4-phenyl-2mercapto thiazol structure.

Reactant, yield and reaction time had shown at table 1. However, color of aciform crystals had described at another column.

CONCLUSION

Mechanisms and synthesis of 6 new structures of thiazoles family had shown that substitution of hydrogen atom by methyl group was caused to decreasing of pay and sigma electron density in carbon atom of the cycle. But there is small increasing in electron density when hydrogen atom is substituted by sulfur atom. As results had shown electron density of carbonic group decreased by substitution of chlorine group by NH_2. Overall, obtained results had shown highest yield at all of mechanisms as compared with the same reactions and reaction rate is good and suitable.

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Table 1. Yields and reaction conditions of the synthesized compounds.

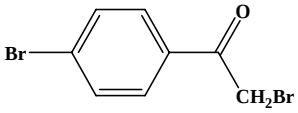
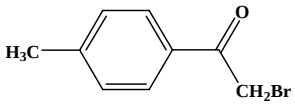
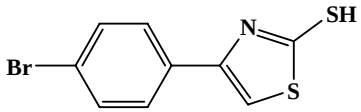
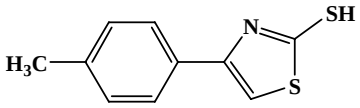
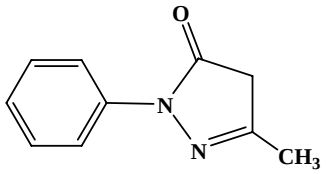
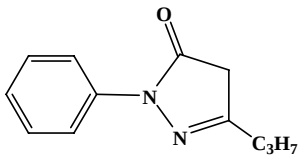
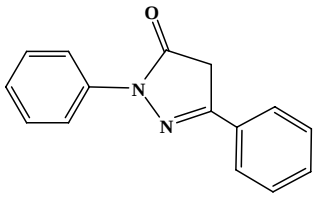
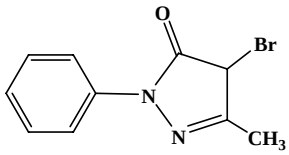
Entry	Products	Color	Time (min)	Yield (%)	m.p. (°C)
1a		white	30	80	109
2a		white	30	83	82
3a		yellow	195	74	218
4a		yellow	195	86	192
5a		yellow	120	83	126
6a		yellow	120	71	111
7a		white	130	84	112
8a		white	30	94	129

Table 1. Continues

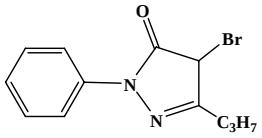
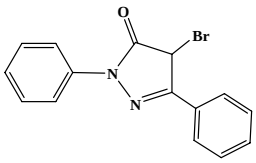
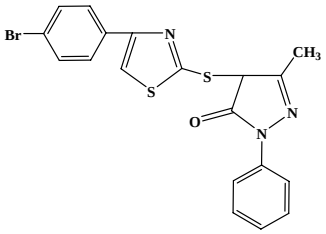
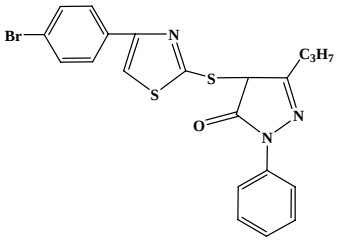
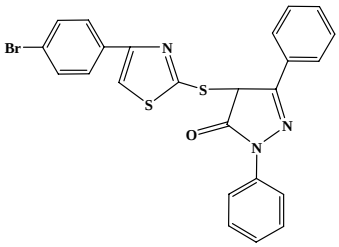
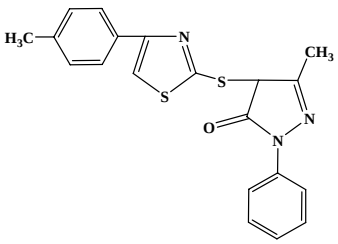
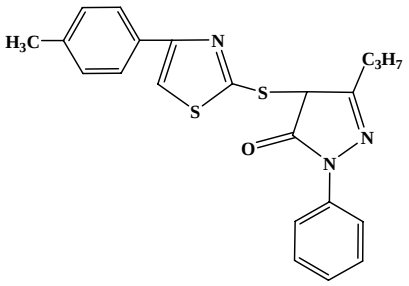
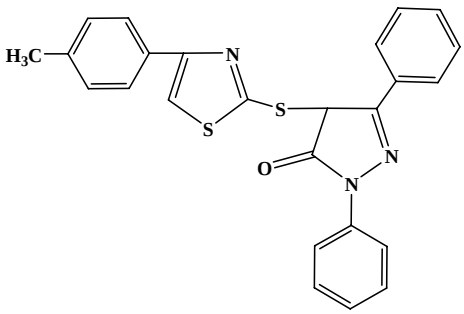
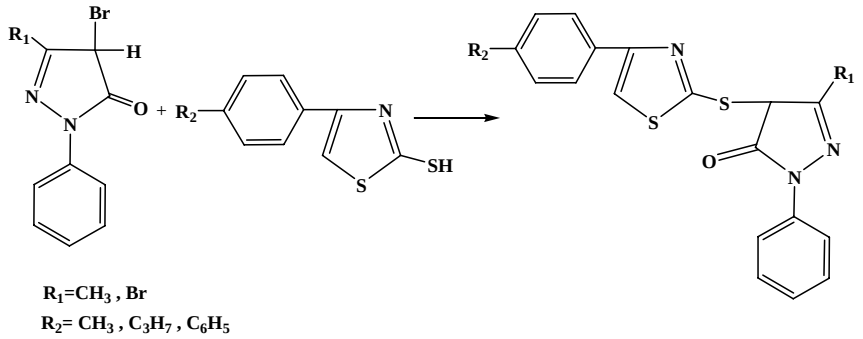
9a		yellow	60	85	123
10a		white	30	84	110
11a		white	60	84	130
12a		yellow	60	86	140
13a		yellow	65	95	135
14a		black	65	86	132

Table 1. Continues

15a		white	55	86	125
16a		brown	60	91	123



R_1=CH_3 , Br

R_2= CH_3 , C_3H_7 , C_6H_5

Fig. 5. Synthetic route for the 4-(4-methylphenyl)-2-mercaptothiazole structure.

$$NH_4Cl + NaOH \longrightarrow NaCl + H_2O + NH_3$$

Fig 6.

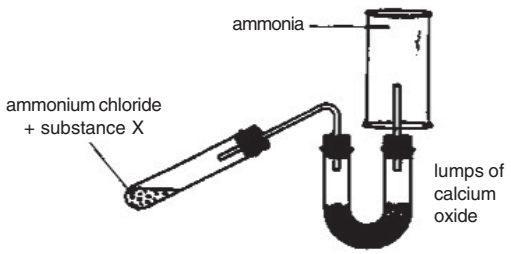


Fig 7.

$$CS_2 + 2NH_3 \xrightarrow[\text{Et OH}]{(Et)_2\ O} \ominus S \quad \oplus NH_4 \quad S \quad H_2N$$

Fig 8.

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