Original Article

A Convenient Routes For Synthesis Of New Series Of Spiro Five Heterocyclic Compounds Derived From Thiazoloquinazolinone

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Abstract

Dimedone, 2-amino thiazole and substituted benzaldehyde have been reacted through Biginelli reaction as a type of multicomponent reaction and accelerated by microwave irradiation in power (450 watt) in acidic media from boric acid to afford 8,8-dimethyl-5-aryl-8,9-dihydro thiazolo[3,2-a]quinazolin-6-one (B_{1-6}), these carbonyl compounds were later used as active synthon to prepare a new series of Schiff bases represented by compounds 8,8-dimethyl-5-aryl-8,9-dihydro thiazolo[3,2-a]quinazolin-6-thiocarbohydrazone (C_{1-6}) by its reaction with thiocarbohydrazide which in turn underwent intracyclization reaction with acetic anhydride to afford the titled compounds 8,8-dimethyl-5-aryl-8,9-dihydro thiazolo[3,2-a]quinazolin-6-spiro(3-acetyl-5-acetohydrazide)-1,3,4-triazoline (D_{1-6})

Keywords: Biginelli products, Fused heterocyclics, Spiro heterocyclics, Thiadiazoles, Schiff bases

1-INTRODUCTION

Most organic researches designed to prepared fused heterocyclic system which received a great interest in biological [1], agricultural[2-4], biological[5], medicinal [6,7] and industrial fields[8,9]. Actually , these researches designed to prepare selective products which could be used latter as active materials in different field and as active precursor in organic synthesis. Accordingly, the most important one is the Biginelli products, which involving the hetero fused cyclic system and additionally it occupied an importance applications as calcium-channel inhibitory properties[10] anticancer [11] ,antimicrobial [12], antioxidant [13], antimalarial [14], anti-inflammatory [15] and as good synthon in organic synthesis [16]. Furthermore it used to increasing applications in the development of materials such as renewable polymers [17], adhesives [18], fabric dyes [19] has been vastly explored , so in this presentation the Biginelli products were used as active synthon in order to prepare supreme type of heterocyclic compounds containing both fused and spiro system. Biginelli products represented by compounds (8,8-dimethyl-5-aryl-8,9-dihydro thiazolo [3,2-a] quinazolin-6-one) (B_{1-6}) were prepared firstly through one put multicomponent reaction between 2-amino thiazole, substituted benzaldehyde and dimedone in acidic media from boric acid and also accelerated by using microwave irradiation technique which reducing the reaction time and gave pure products and high yields. These products reacted later with thiocarbohydrazide to form unusual Schiff bases (8,8-dimethyl-5-aryl-8,9-di hydro thiazolo [3,2-a] quinazolin-6-thiocarbo hydrazone) (C_{1-6}) followed by intracycli -zation reaction in presence of acetic anhydride to afford the corresponding spiro derivatives represented by compounds (8,8-dimethyl-5-aryl-8,9-dihydro thiazolo [3,2-a] quinazolin-6-spiro(3-acetyl-5-aceto hydrazide)-1,3,4-triazoline) (D_{1-6}).

All prepared compound were illustrated by available physical and spectral methods such as M.P, T.L.C, U.V, FT-IR and ^{1}H-NMR.

2-MATERIALS AND METHODS

Melting points (M.P.) were measured on Electrothermal SMP30- Stuart melting point apparatus. ^{1}H-NMR spectra were recorded using England-Oxford (AS400 MHZ) with TMS as iternal standared and DMSO-d6 and $CDCl_3$ as solvents, [(s) singlet, (d) doublet, (m) multiplet], Turkish EGE University. Infrared (FT-IR) spectra were recorded as (KBr) disk using Bruker -Alpha platinum ATP (Germany) FT-IR, spectrophotometer. Ultraviolet (U.V) spectra were performed on T92+UV Spectrophotometer PG instruments using methanol as a solvent. The domestic microwave oven (LG,MS,192w) with (450 watts) power sitting was used for irradiation. Thin layer chromatography (TLC) were carried out on eastman chromatogram sheet (20x20) cm, 13181 silica gel with fluorescent indicator (No. 6060) using solvent system benzene: chloroform in ratio (8:2).

Synthesis of 8,8-dimethyl-5-aryl-8,9-dihy dro thiazolo[3,2-a]quinazolin-6-one (B_{1-6}):

Method A [20]: In round bottomed flask (100 ml) with condenser supplied with calcium chloride tube, a mixture of equimolar (0.002 mole) from substituted benzaldehyde,2-amino thiazole and dimidone with catalytic amounts of (20% mole) boric acid were dissolved in abs. ethanol (50ml) followed by reflux for (5hr.), cooling and poured in crushed-ice. The solid products thus separated out were filtered, and washed thoroughly with water followed by recrystallization from ethanol-water to yield compounds (B_{1-6}). The completion of the reaction was monitored by thin layer chromatography (T.L.C) .

Method B[21]: Equimolar (0.002) of 2-amino thiazole, substituted benzaldehyde and dimedone with catalytic amounts of (20% mole) boric acid were grinding thoroughly with mortar then put in beaker (50ml) and irradiated via microwave oven in power (450 watt) for (10min.), cooling with crushed-ice followed by filtration and washed thoroughly with water and recrystallized from ethanol-water to yield compounds (B_{1-6}).

8,8-dimethyl-5-phenyl-8,9-dihydro thiazolo [3,2-a]quinazolin-6-one(B_1)

Yield 81%, M.P (189-191°C), T.L.C (R_f): 0.566, UV λ_{max} (nm): 260&219, FT-IR (KBr) (ν cm^{-1}): 3300 (OH), 2958 & 2878 (CH_3), 1582 (C=O cycl.), 1500 (C=N), 1483 (C=C cycl.), 1366 (C-N-C), 773 (C-S-C). ^{1}H-NMR δ (ppm): (s,1.02,6H,2CH_3) ; (d,1.82,2H, CH_2-C-N); (s, 2.27,2H,CH_2-C=O); (d, 3.85,1H,CH-C=O); (dd,5.55,1H, N-CH=C);(dd,5.92,S-CH=C); (s,6.87,1H, CH-ph) ; (m,7.03-7.20,5H, Ar); (s,8.57, 1H, OH).

8,8-dimethyl-5-(4-chloro phenyl)-8,9-dihy -dro thiazolo [3,2-a]quinazolin-6-one (B_2)

Yield 75%, M.P (145-147°C), T.L.C (R_f): 0.278, UV λ_{max} (nm): 262&248, FT-IR (KBr) (ν cm^{-1}): 3281 (OH), 2957 & 2875 (CH_3), 1610 (C=O cycl.), 1584 (C=N), 1500 (C=C cycl.), 1369(C-N-C), 821 (C-S-C), 575(C-Cl). ^{1}H-NMR δ (ppm): (s,0.94,6H, 2CH_3) ; (d,2.46,2H, CH_2-C-N); (s,3.19,2H, CH_2-C=O) ; (d, 3.43,1H,CH-C=O); (dd, 5.52, 1H, N-CH=C); (dd,6.03,S-CH=C); AB system (dd,6.73-7.38,4H, Ar) ; (s,8.99,1H, CH-Ar) ; (s,9.99, 1H, OH).

8,8-dimethyl-5-(2-chloro phenyl)-8,9-di hydro thiazolo [3,2-a]quinazolin-6-one (B_3)

Yield 88%, M.P (135-137°C), T.L.C (R_f): 0.275, UV λ_{max} (nm): 258&206, FT-IR (KBr) (ν cm^{-1}): 3391 (OH), 2956 & 2873 (CH_3), 1592 (C=O cycl.), 1513 (C=N), 1467 (C=C cycl.), 1371(C-N-C), 749 (C-S-C), 702(C-Cl). ^{1}H-NMR δ (ppm): (s,1.01,6H, 2CH_3) ; (d,2.14,2H, CH_2-C-N); (s,2.37,2H, CH_2-C=O) ; (d, 3.43,1H,CH-C=O); (dd, 6.39,1H, N-CH=C); (dd,6.56,S-CH=C); (m, 7.16-7.61,4H, Ar) ; (s,9.59,1H,CH- Ar) ; (s, 10.33, 1H, OH).

8,8-dimethyl-5-(4-N,N-dimethyl amino phenyl)-8,9-dihydro thiazolo [3,2-a]quina -zolin-6-one (B_4)

Yield 67%, M.P (68-70°C), T.L.C (R_f): 0.368, UV λ_{max} (nm): 264&240, FT-IR (KBr) (ν cm^{-1}): 3476 (OH), 2951 & 2875 (CH_3), 1592 (C=O cycl.), 1518 (C=N), 1448 (C=C cycl.), 1362(C-N-C), 813 (C-S-C). ^{1}H-NMR δ (ppm): (s,1.01,6H,2CH_3) ; (d, 1.59,2H, CH_2-C-N) ; (s,2.60,6H,N,N-di CH_3); (s,2.80,2H,CH_2-C=O) ; (d, 3.37,1H, CH-C=O);(dd,5.42,,1H, N-CH=C); (dd,6.60, S-CH=C); AB system(dd,7.02-7.77,4H, Ar) ; (s,8.68,1H,CH- Ar) ; (s,9.65, 1H, OH).

8,8-dimethyl-5-(3,4-dimethoxy phenyl)-8,9 -dihydro thiazolo[3,2-a]quinazolin-6-one (B_5)

Yield 74%, M.P (107-110°C), T.L.C (R_f): 0.289, UV λ_{max} (nm): 352&260, FT-IR (KBr) (ν cm^{-1}): 3412 (OH), 2946 & 2872 (CH_3), 1591 (C=O cycl.), 1507 (C=N), 1457 (C=C cycl.), 1371(C-N-C),1131&1018(C-O-C), 753 (C-S-C). ^{1}H-NMR δ (ppm): (s,1.06,6H,2CH_3) ; (d,1.92,2H, CH_2-C-N); (s,2.38,2H,CH_2-C=O); (s,3.15,6H,2OCH_3) ; (d, 3.82,1H,CH-C=O); (dd,5.39,,1H, N-CH=C); (dd,6.12,S-CH=C); (m,7.10-7.75, 3H, Ar) ; (s,8.84,1H,CH- Ar) ; (s,9.82, 1H, OH).

8,8-dimethyl-5-(4-nitro phenyl)-8,9-dihy- dro thiazolo [3,2-a]quinazolin-6-one(B_6)

Yield 78%, M.P (176-178°C), T.L.C (R_f): 0.317, UV λ_{max} (nm): 380&264, FT-IR (KBr) (ν cm^{-1}): 3391 (OH), 2954 & 2874 (CH_3), 1589 (C=O cycl.), 1513 (C=N), 1449 (C=C cycl.), 1340(C-N-C),1253&1112 (NO_2), 843 (C-S-C). ^{1}H-NMR δ (ppm): (s,1.15,6H,2CH_3); (d,2.02,2H, CH_2-C-N) ; (s,2.26,2H,CH_2-C=O) ; (d, 3.69,1H,CH-C=O); (dd,5.64,,1H, N-CH=C); (dd,6.13,S-CH=C); AB system (dd,7.60-8.35,4H, Ar) ; (s,9.16,1H,CH- Ar) ; (s, 10.15, 1H, OH).

Synthesis of 8,8-dimethyl-5-aryl-8,9-dihy -dro thiazolo [3,2-a]quinazolin-6-thiocarbo hydrazone (C_{1-6}) [23]:

Ethanolic solution of thiocarbohydrazide (0.0007 mole / 10 ml) was added dropwise to an ethanolic solution of compound (B_{1-6}) (0.0007 mole / 10 ml) with catalytic amount of glacial acetic acid (2drops) . The reaction mixture stirred at room temperature for (30 min.) followed by reflux for (4 hrs.) .Cooling , filtration then washed with water thoroughly to remove the excess of acid and recrystallized from methanol to obtained compounds (C_{1-6}). The completion of the reaction was monitored by thin layer chromatography (T.L.C), Table (3).

8,8-dimethyl-5-phenyl-8,9-dihydro thiazolo[3,2-a]quinazolin-6-thiocarbo hydrazone (C_1)

Yield 53%, M.P (136-139°C), T.L.C (R_f): 0.429, UV λ_{max} (nm): 342&262, FT-IR (KBr) (ν cm^{-1}): 3429 (OH), 3320(NH_2), 3202(NH), 2950 & 2873 (CH_3), 1585 (C=N acycl.), 1456 (C=N cycl.), 1362(C-N-C),1235(C=S), 729 (C-S-C). ^{1}H-NMR δ (ppm): (s,1.02,6H,2CH_3); (d,1.49,2H,CH_2-C=N); (s,1.98,2H,CH_2-C-N); (s,2.04,2H, NH-NH_2); (s,4.50, 1H, NH-NH_2) ; (s,4.79, 1H,=N-NH-C=S) ; (d,5.91, 1H, CH-C=O); (dd,6.96,1H,N-CH=CH); (dd, 7.09,1H,S-CH=CH); (m,7.14-7.19,5H-Ar); (S,7.64, 1H,CH-ph) ; (s,7.75, 1H, OH).

8,8-dimethyl-5-(4-chloro phenyl)-8,9-di hydro thiazolo [3,2-a]quinazolin-6-thio carbo hydrazone (C_2)
Yield 57%, M.P (161-162°C), T.L.C (R_f): 0.250, UV λ_{max} (nm): 356&258, FT-IR (KBr) (ν cm^{-1}): 3455 (OH), 3328(NH_2), 3188(NH), 2956 & 2879 (CH_3), 1588 (C=N acycl.), 1481 (C=N cycl.), 1369(C-N-C),1254(C=S), 820 (C-S-C), 705(C-Cl). ^{1}H-NMR δ (ppm): (s,1.01,6H,2CH_3); (d,1.53, 2H,CH_2-C=N); (s,1.94,2H,CH_2-C-N); (s, 2.04,2H,NH-NH_2); (s, 4.48 , 1H, NH-NH_2); (s,5.58,1H, =N-NH-C=S); (d,5.91, 1H, CH-C=O) ; (dd,6.02,1H,N-CH=CH) ; (dd,6.95, 1H,S-CH=CH); AB system(dd,7.08-7.68, 4H-Ar) ; (s,8.00 ,1H,CH-ph) ; (s,8.58, 1H, OH).

8,8-dimethyl-5-(2-chloro phenyl)-8,9-dihy -dro thiazolo [3,2-a]quinazolin-6-thio carbohydrazone (C_3)
Yield 54%, M.P (127-129°C), T.L.C (R_f): 0.743, UV λ_{max} (nm): 348&258, FT-IR (KBr) (ν cm^{-1}): 3402 (OH), 3364(NH_2), 3156(NH), 2957 & 2874 (CH_3), 1600 (C=N acycl.), 1520 (C=N cycl.), 1276(C-N-C),1245 (C=S), 751 (C-S-C), 702(C-Cl). ^{1}H-NMR δ (ppm): (s,1.22,6H,2CH_3); (d,2.03, 2H,CH_2-C=N); (s,2.33,2H,CH_2-C-N); (s, 2.12,2H,NH-NH_2); (s, 4.56 ,1H, NH-NH_2) ; (d,5.59, 1H, CH-C=O) ; (s,5.70,1H,N-NH-C=S); (dd,6.70,1H,N-CH=CH) ; (dd,7.07, 1H,S-CH=CH); (m,7.25-7.52,4H-Ar) ; (s, 9.89,1H,CH-ph) ; (s,11.67, 1H, OH).

8,8-dimethyl-5-(4-N,N-dimethyl amino phenyl) -8,9-dihydro thiazolo [3,2-a]quina zolin-6-thiocarbohydrazone (C_4)
Yield 78%, M.P (170-171°C), T.L.C (R_f): 0.443, UV λ_{max} (nm): 374&260, FT-IR (KBr) (ν cm^{-1}): 3337 (OH), 3227(NH_2), 3111(NH), 2957 & 2875 (CH_3), 1599 (C=N acycl.), 1513 (C=N cycl.), 1360(C-N-C),1235 (C=S), 809 (C-S-C. ^{1}H-NMR δ (ppm): (s,1.02,6H,2CH_3); (d,1.21,2H,CH_2-C=N) ;(s,2.19,6H, N,N-diCH_3); (s,2.20, 2H, CH_2-C-N) ; (s,2.37,2H,NH-NH_2); (s, 2.87, 1H,NH-NH_2) ; (s,3.43,1H,=N-NH-C=S); (d, 6.13,1H, CH-C=O) ; (dd,6.59,1H,N-CH= CH) ; (dd,6.74,1H,S-CH=CH); AB system (dd,7.44-7.60,4H-Ar) ; (s, 7.85 ,1H,CH-ph) ; (s,7.94, 1H, OH).

8,8-dimethyl-5-(3,4-dimethixy phenyl)-8,9-dihydro thiazolo[3,2-a]quinazolin-6-thiocarbo hydrazone (C_5)
Yield 50%, M.P (175-176°C), T.L.C (R_f): 0.348, UV λ_{max} (nm): 218&208, FT-IR (KBr) (ν cm^{-1}): 3401 (OH), 3296(NH_2), 3201(NH), 2949 & 2873 (CH_3), 1598 (C=N acycl.), 1505(C=N cycl.), 1373(C-N-C), 1255 (C=S), 1135& 1019(C-O-C),706 (C-S-C. ^{1}H-NMR δ (ppm): (s,0.52,6H,2CH_3); (d, 1.96,2H,CH_2-C=N); (s,2.18,2H,NH-NH_2); (s,2.26,2H,CH_2-C-N); (s,2.42,6H, 2OCH_3); (s, 3.82 ,1H,NH-NH_2) ; (d,5.43, 1H, CH-C=O); (dd,5.46,1H,N-CH=CH) ; (s,6.20, 1H,N-NH-C=S); (dd,6.65,1H,S-CH=CH); (m,6.71-7.18,3H-Ar) ; (s,7.23,1H,CH-ph) ; (s,8.47, 1H, OH).

8,8-dimethyl-5-(4-nitro phenyl)-8,9-dihydro thiazolo [3,2-a] quinazolin-6-thio carbohydrazone (C_6)
Yield 67%, M.P (162-164°C), T.L.C (R_f): 0.500, UV λ_{max} (nm): 384&260, FT-IR (KBr) (ν cm^{-1}): 3480 (OH), 3298(NH_2), 3193(NH), 2957 & 2872 (CH_3), 1591 (C=N acycl.), 1508(C=N cycl.), 1376(C-N-C), 1339& 1102(NO_2),1249 (C=S), 793 (C-S-C. ^{1}H-NMR δ (ppm): (s,1.01,6H,2CH_3); (d, 1.97,2H,CH_2-C=N); (s,3.31,2H,CH_2-C-N); (s,3.40,2H,NH-NH_2) ; (s,4.36,1H,NH-NH_2); (s,4.61,1H,N-NH-C=S); (dd,5.66, 1H,N-CH=CH); (dd,6.09,1H,S-CH=CH) ; (d,6.88, 1H, CH-C=O); AB system(dd,7.20-8.21,4H-Ar) ; (s,9.20,1H,CH-ph) ; (s,11.68, 1H, OH).

Synthesis of 8,8-dimethyl-5-aryl-8,9-dihydro thiazolo[3,2-a]quinazolin-6-spiro (3-acetyl-5-acetohydrazide)-1,3,4-triazoline (D_1-$_6$) [24]:
A mixture of compounds (C_1-$_6$) (0.00025 mole) and acetic anhydride (0.005 mole) was generally refluxed for (2 hrs.). Cooling then poured onto ice-water (10 ml) and the forming product filtered off ,washed thoroughly with water then dried to give compounds (D_1-$_6$). The completion of the reaction was monitored by thin layer chromatography (T.L.C), Table (5).

8,8-dimethyl-5-phenyl-8,9-dihydro thiazolo[3,2-a]quinazolin-6-spiro(3-acetyl-5-acetohydrazide) -1,3,4-triazoline (D_1)
Yield 67%, M.P (164-166°C), T.L.C (R_f): 0.291, UV λ_{max} (nm): 378&238, FT-IR (KBr) (ν cm^{-1}): 3559 (OH), 3138(NH), 2952 & 2880 (CH_3), 1657 (C=O), 1458(C=N cycl.), 1008(N-N), 696 (C-S-C. ^{1}H-NMR δ (ppm): (s,1.01,6H,2CH_3); (d,1.77,CH_2-C-N); (s,1.92,6H,,2CH_3-C=O); (s,2.07,2H,CH_2-C-spiro) ; (d,2.42, 1H, CH-C=O) ;(s,3.27, 1H,NH-C=N);(s,3.57,1H,NH-C=O); (dd, 4.81,1H,N-CH=CH); (dd,5.23,1H,S-CH= CH); (m,7.02-7.19,5H-Ar) ;(d,7.21,1H, CH-ph) ; (s,7.82,1H,NH-thiadiazole) ; (s,9.33, 1H, OH).

8,8-dimethyl-5-(4-chloro phenyl)-8,9-dihy -dro thiazolo [3,2-a]quinazolin-6-spiro (3-acetyl-5-acetohydrazide) -1,3,4-triazo line (D_2)
Yield 69%, M.P (90-93°C), T.L.C (R_f): 0.313, UV λ_{max} (nm): 372&236, FT-IR (KBr) (ν cm^{-1}): 3430 (OH), 3177(NH), 2949 & 2871 (CH_3), 1660 (C=O), 1481(C=N cycl.), 1010(N-N), 834 (C-S-C), 705(C-Cl). ^{1}H-NMR δ (ppm): (s,1.01,6H,2CH_3); (d, 1.73,CH_2-C-N); (s,1.98,6H,,2CH_3-C=O); (s, 2.42,2H,CH_2-C-spiro) ; (d,2.45, 1H, CH-C=O) ;(s,3.48,1H,NH-C=N);(s,3.55,1H,NH-C=O); (dd,4.62,1H,N-CH=CH); (dd, 5.67 ,1H,S-CH=CH); AB system (dd,7.02-7.21,4H-Ar) ;(d, 8.87,1H,CH-ph)); (s, 10.93,1H, NH-thiadiazole) ; (s,11.83, 1H, OH).

8,8-dimethyl-5-(2-chloro phenyl)-8,9-di hydro thiazolo [3,2-a] quinazolin-6-spiro (3-acetyl-5-acetohydrazide) -1,3,4-triazo-line (D_3)
Yield 77%, M.P (70-72°C), T.L.C (R_f): 0.272, UV λ_{max} (nm): 354&236, FT-IR (KBr) (ν cm^{-1}): 3423 (OH), 3181(NH), 2954 & 2870 (CH_3), 1667 (C=O), 1564(C=N cycl.), 1021(N-N), 748 (C-S-C), 703(C-Cl). ^{1}H-NMR δ (ppm):

(s,1.01,6H,2CH_3); (d, 1.89,CH_2-C-N); (s,2.22,6H,,2CH_3-C=O); (s, 2.04,2H,CH_2-C-spiro) ; (d,2.36, 1H, CH-C=O) ;(s,3.35,1H,NH-C=N);(s,4.80,1H, NH -C=O); (dd,4.90,1H,N-CH=CH); (dd,5.85, 1H,S-CH=CH); (m,6.93-7.51,5H-Ar) ;(d, 8.94,1H,CH-ph); (s,9.19,1H,NH-thiadiazole) ; (s,10.93, 1H, OH).

8,8-dimethyl-5-(4-N,N-dimethyl amino phenyl)-8,9-dihydro thiazolo[3,2-a]quina zolin-6-spiro(3-acetyl-5-acetohydrazide)-1,3,4-triazoline (D_4)

Yield 53%, M.P (82-85°C), T.L.C (R_f): 0.275, UV λ_{max} (nm): 360&258, FT-IR (KBr) (ν cm^{-1}): 3488 (OH), 3202(NH), 2950 & 2874 (CH_3), 1660 (C=O), 1520(C=N cycl.), 1047(N-N), 814 (C-S-C). ^{1}H-NMR δ (ppm): (s,1.01,6H,2CH_3); (d,1.85,CH_2-C-N); (s,1.98,6H,,2CH_3-C=O); (s,2.02,2H,CH_2-C-spiro); (s,2.64,6H,2CH_3) ; (d,2.96, 1H, CH-C=O) ;(s,3.30,1H,NH-C=N);(s,3.64,1H,NH-C=O);(dd,6.62,1H,N-CH=CH); (dd,6.76,1H, S-CH=CH); AB system (dd,7.05-7.07,4H-Ar) ; (d, 7.68,1H,CH-ph); (s,8.02,1H, NH-thiadiazole); (s, 9.65, 1H, OH).

8,8-dimethyl-5-(3,4-dimethoxy phenyl)-8,9 -dihydro thiazolo[3,2-a]quinazolin-6-spiro (3-acetyl-5-acetohydrazide) -1,3,4-triazo -line (D_5)

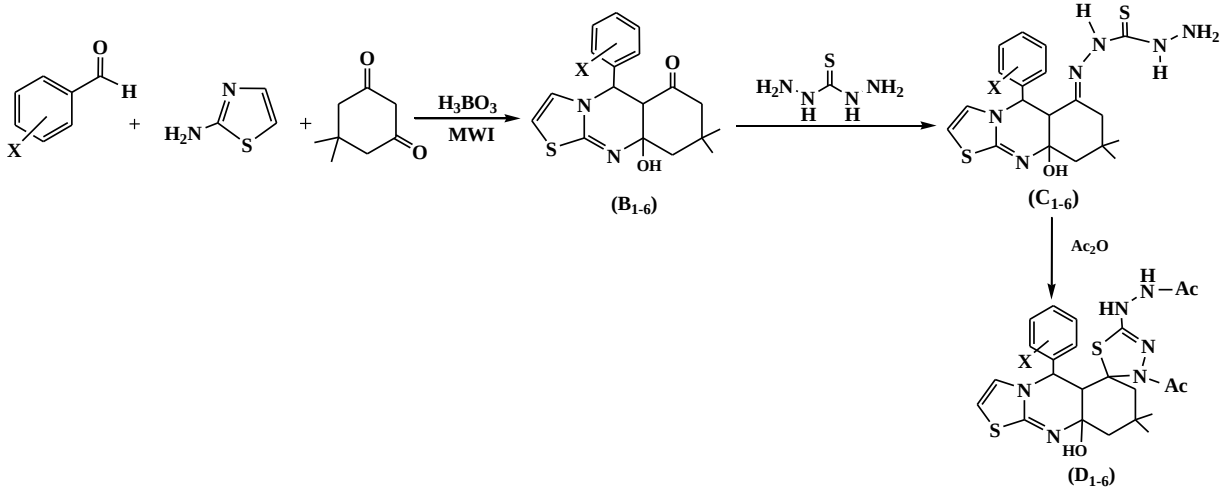
Yield 70%, M.P (83-84°C), T.L.C (R_f): 0.288, UV λ_{max} (nm): 294&266, FT-IR (KBr) (ν cm^{-1}): 3402 (OH), 3200(NH), 2956 & 2879 (CH_3), 1662 (C=O), 1510(C=N cycl.),1245&1135(C-O-C), 1015(N-N), 753 (C-S-C). ^{1}H-NMR δ (ppm): (s,1.03, 6H,2CH_3); (d,1.74,CH_2-C-N); (s,2.02, 6H,,2CH_3-C=O); (s,2.27,2H,CH_2-C-spiro) ; (s,3.51,6H,OCH_3); (d,2.27, 1H, CH-C=O); (s,3.67,1H,NH-C=N);(s,3.83,1H,NH-C=O); (dd,5.39,1H,N-CH=CH); (dd,6.11,1H,S-CH =CH); (m,6.66-7.07,3H-Ar)); (d,8.10,1H, CH-ph) ; (s,9.83,1H, NH-thiadiazole) ; (s, 11.83, 1H, OH).

8,8-dimethyl-5-(4-nitro phenyl)-8,9-di hydro thiazolo [3,2-a]quinazolin-6-spiro (3-acetyl-5-acetohydrazide) -1,3,4-triazo line (D_6)

Yield 67%, M.P (99-202°C), T.L.C (R_f): 0.175, UV λ_{max} (nm): 356&266, FT-IR (KBr) (ν cm^{-1}): 3401 (OH), 3207(NH), 2959& 2872 (CH_3), 1661 (C=O), 1562(C=N cycl.),1517&1346(NO_2), 1012(N-N), 700 (C-S-C). ^{1}H-NMR δ (ppm): (s,1.10,6H, 2CH_3); (d,2.09,CH_2-C-N); (s,2.17,6H,2CH_3-C=O); (s,2.29,2H,CH_2-C-spiro) ; (d,2.17, 1H, CH-C=O);(s, 3.32 ,1H,NH-C=N); (s, 4.61 ,1H,NH-C=O) ;(dd,5.82,1H,N-CH= CH); (dd,6.23,1H,S-CH=CH); AB system (dd,7.12-8.16,4H-Ar) ;(d,9.10 ,1H,CH-ph); (s, 10.25,1H, NH-thiadiazole) ; (s, 11.97, 1H, OH).

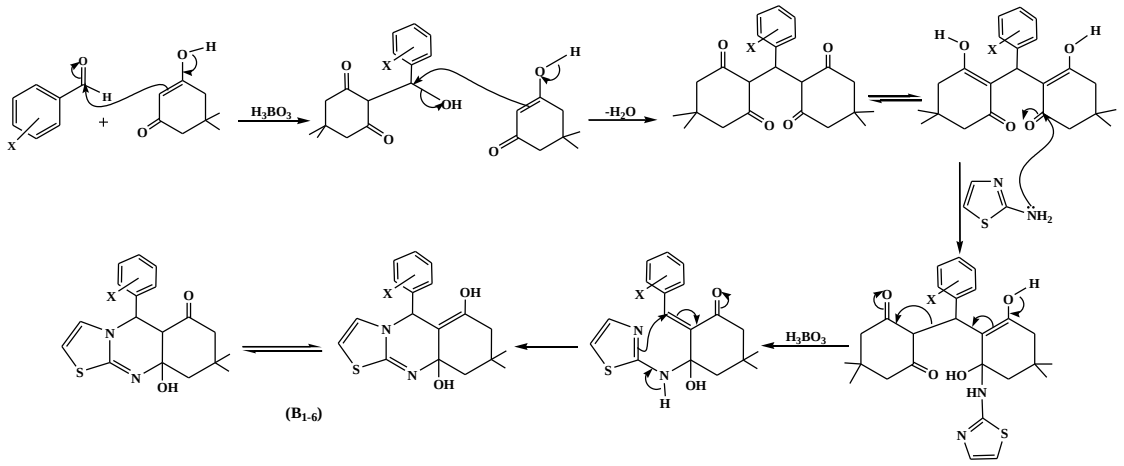
3-RESULTS AND DISCUSSION

The prepared compounds were obtained according to the general synthetic pathway bellow:



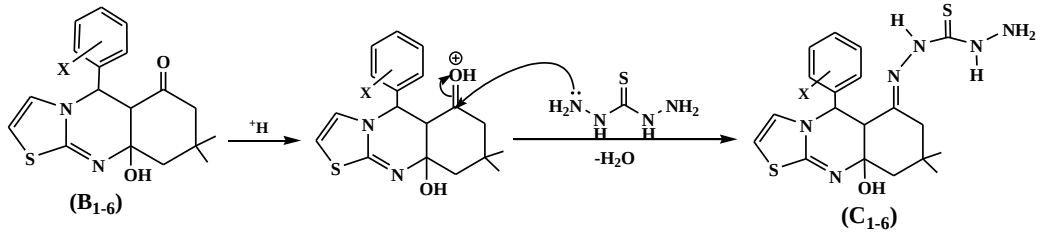
Scheme (1): General synthetic pathway of compounds (D_{1-6})

First of all, 2-amino thiazole, substituted benzaldehyde and dimedone underwent Biginelli reaction as a multicomponent reaction in presence of catalytic amount of boric acid to afford the Biginelli products represented by compounds (B_{1-6}). These compounds were achieved under microwave irradiation technique and conventional method as shown in the following mechanism, Scheme (2) [21,22]:



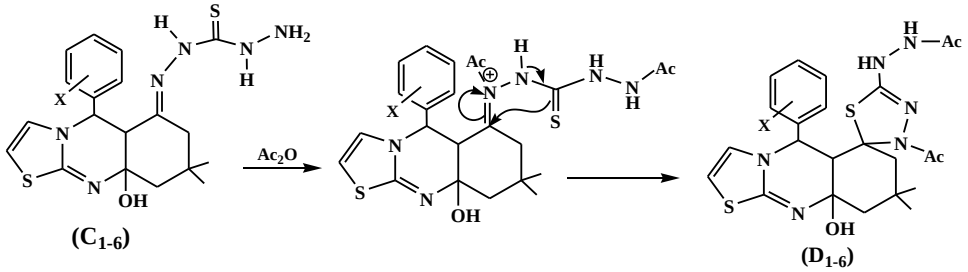
Scheme (2): Synthesis of compounds (B_{1-6})

Actually, and according to the ^{1}H-NMR spectroscopic data the suggested mechanism in Scheme (2) is seemed to be the right one because it gave and absorption bands between (δ ppm) (8.57-10.33) which refer to the hydroxy protons in position (10) ,additionally to the other functional groups absorptions which support the suggested structure as listed in thre experimental section . While in FT-IR spectroscopy they gave absorption bands at cm^{-1} (1582-1610) refer to cyclic ketone group (C=O) additionally to the absorption bands at cm^{-1} (1500-1584) refer to the cyclic alkene (C=C). On the other hand, the absence of primary amine (NH_2) absorption bands and the presence of hydroxyl (OH) absorption bands at cm^{-1} (3281-3476) and imine(C=N) absorption bands at cm^{-1} (1448-1500) gave an indication about the formation of fused cyclic system involving nitrogen atoms.The carbonyl group at position (6) in quinazoline ring used as active group to form Schiff bases via its reaction with thiocarbo hydrazide through acidic condensation reaction in presence of catalytic amount of glacial acetic acid [25], Scheme (3) :



Scheme (3): Synthesis of compounds (C_{1-6})

The structure of the formed Schiff bases were provided via the spectral methods, so ,in ^{1}H-NMR spectroscopy ,it's spectra shown clearly the absorption peaks for NH and NH_2 functional groups. Whereas, in FT-IR , the absence of carbonyl absorption bands and the appearance of the NH_2 , NH and C=N acycl. absorption band at cm^{-1}(3227-3364), (3111-3202) and (1585-1600) respectively supporting the suggested structure. Finally, these Schiff bases underwent intracyclization reaction in presence of catalytic amounts of acetic anhydride to form the corresponding spiro fused heterocyclic compounds represented by compounds (D_{1-6}) as summarized in Scheme (4) [26]:



Scheme (4): Synthesis of compounds (D_{1-6})

The chemical structure of (D_{1-6}) were confirmed by ^{1}H-NMR, FT-IR and UV spectroscopy. The FT-IR spectra showed stretching vibration bands at cm^{-1}(1657-1667) and (3138-3207) refer to the acetyl and NH-NH groups respectively, additionally to the other spectral data in the experimental section. On the other hand, in ^{1}H-NMR spectra they shown absorption peaks for acetyl and secondary amine and amide respectively which came in agreement with the assigned structures.

4-CONCLUSION

(20%mole) Boric acid was seemed to be the must suitable acid catalyst for the Biginelli reaction especially in dry conditions and also when it accelerated by MWI in power (450 watt) for (10 min.). Furthermore, the spiro derivatives

(D_{1-6}) were prepared directly, easily and high purity. Finally, we found that benzene: chloroform in ratio (8:2) as suitable solvent system in thin layer chromatography measurements.

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