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Synthesis And Characterization Of Some New Quinolin-2(1H)-Ones And Imidazoles Containing 1, 3, 4-Thiadiazoline Ring Derived From Thiosemicarbazone.

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ABSTRACT

A new derivatives of imidazoles and quinolin-2(1H)-ones were synthesized by many reaction steps. Firstly, thiosemicarbazones $[1]_{a,b}$ were prepared by the condensation of thiosemicarbazide with 4-bromobenzaldehyde or 4-bromoacetophenone then cyclized to get 2,4-diacetamido-1,3,4-thiadiazolines $[2]_{a,b}$. These compounds were converted to 2-amino-4-acetamido-1,3,4-thiadiazolines $[3]_{a,b}$ by hydrolysis of amide group (at position -2) to amino group using hydrazine hydrate/water. The reaction of 2-amino-1,3,4-thiadiazolines with different coumarine derivatives and (4-N,N-dimethylbenzaldehyde) in glacial acetic acid led to formation new 1H-quinolin-2-ones $[4]_{a-f}$ and Schiff bases $[5]_{a,b}$, respectively. Furthermore, Schiff bases $[5]_{a,b}$ were reacted with available acid chlorides to get N-acyl compounds $[6]_{a-d}$ which are converted to thiourea derivatives $[7]_{a-d}$, followed by cyclization reaction of thiourea derivatives with benzoin to yield new imidazole derivatives $[8]_{a-d}$. These synthesized compounds were characterized on the basis of IR, 1H-NMR, mass spectra and elemental analysis results.

Keywords: Imidazoles, Quinolin-2(1H)-ones, 1,3,4-Tiadiazolines, Thiosemicarbazones.

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INTRODUCTION

The heterocyclic products containing three heteroatoms in the five or six member rings have been reported in the past decades because of their wide range of pharmacological behaviors. Thiadiazolines belongs to the above category of heterocyclic compounds having broad spectrum of biological activity; such as anti-inflammatory[1,2], antimicrobial [3-6], and vitro cytotoxic activity [7] and technological applications [8]. Among the few general routes to obtain 1,3,4-thiadiazolines, one of the most employed is that of heterocyclization of thiosemicarbazones under acylation conditions (acetic anhydride and pyridine) [9-10]. Quinolines and imidazoles have been the subject of continued interest as several derivatives have been found to possess useful biological activities such as bactericidal [11]. Antimalarial [12], and anti-inflammatory [13,14] and antimicrobial activity [15-16]…etc. Synthetic imidazoles are present in many fungicides and antifungal [17,18], anticancer [19] and antihypertensive medications [20]. In the literature survey, many methods are available for the synthesis of quinolines. Skraup, Doebner-Von Miller, Pfitzinger, Conrad-Limpach and Combes procedures have been reported for the preparation of quinolines [21-23], nevertheless, Friedländer hetero-annulation is still one of the most simple and straight forward approaches for the preparation of poly-substituted quinolines [24-29]. New general method for the synthesis of medicinally important diversely functionalized imidazoles from N-acylated α-aminonitriles has been developed [30]. This new methodology was applied for the synthesis of new imidazole derivatives from the reaction of N-acylated α-aminonitriles with triphenylphosphine and carbon tetra-halide. Many of these syntheses can also be applied to different substituted imidazoles and thier derivatives simply by varying the functional groups on the reactants an α-aminoaldehyde and α-aminoacetal, resulting in the cyclization of an amidine to imidazole [31]. A simple reaction allow the synthesis of bis - {4- [α - (N-acetyl or anisoyl)-4-nitrobenzyl-2- thio -4,5-diphenylimidazoles]- anilines} substituted include the reaction of bis-{4-[α-(N-acetyl or ansoyl)-4'-nitrobenzyl-isothioureas]- anilines} substituted with benzoin in dry DMF to give good yields of substituted imidazoles [32]. As a part of our interest towards the development of novel heterocyclic compounds, we decided to synthesis new quinolin-2(1H)-ones and imidazoles containing 1,3,4-thiadiazoline ring derived from thiosemicarbazone using required agents.

EXPERIMENTAL

Material and methods

All the chemicals used were procured from Sigma–Aldrich and Fluka, and used without further purification. Uncorrected melting points were determined in open capillary on SMP30 Melting point (Stuart, Germany). Ractions were monitored by thin layer chromatography TLC was performed on plastic plates Silica Gel 60F254 (E. Merck, Darmstadt, Germany; layer thickness 0.2 mm). (TLC) on silica gel, plates were visualized with iodine. The IR spectra were recorded on FTIR 8400 s Shimadzu spectrophotometer. ^{1}HNMR were recorded on Bruker 300 MHz spectrophotometer , University of Al-albayt, Jordan using DMSO as a solvent with TMS as an internal standard. The mass spectra were recorded on Shimadzu model GCMS QP 1000 EX gas chromatography _MS apparatus made in japan at department of chemistry college of science, university of Al Mustansiriyah.

Chemical synthesis

Preparation of 7-hydroxy -4-methyl coumarin: This compound was prepared according to Pawar et al., [33].

Preparation of 4- bromobenzaldehyde-thiosemicarbazone [1]$_a$ and 4-bromoacetophenone thiosemicarbazone [1]$_b$: These two compounds were prepared according to Ayyash et al., [34].

Preparation of N-(4-acetyl-5-(4-bromophenyl)-4,5-dihydro-1,3,4-thia-diazol-2-yl)acetamide [2]$_a$,N-(4-acetyl-5-(4-bromophenyl)-5-methyl-4,5-dihydro-1,3,4-thiadiazol-2-yl)acetamide [2]$_b$ and their 4-acetyl-2-amino-5-(4-bromophenyl)-4,5-dihydro-1,3,4-thiadiazole [3]$_a$, 4-acetyl-2-amino-5-(4-bromophenyl)-5-methyl-4,5-dihydro-1,3,4-thiadiazoline[3]$_b$: These compounds were prepared according to Ayyash et al., [35].

General procedure for the synthesis of new -quinolin-2(1H) -one derivatives [4]$_{a-f}$:

A coumarine derivatives (0.01 mol) were treated with the solution of compound [3] (0.01mol) dissolved in glacial acetic acid (5mL), the reaction mixture was refluxed for 6hrs, and the solid was precipitate. The solid was obtained by evaporated of the solvent and recrystallized from ethanol.

1-[4-acetyl-5-(4-bromophenyl)-4,5-dihydro-1,3,4-thiadiazol-2-yl]-1H-quinolin-2(1H)-one [4]$_a$: Pale-yellow solid, yield: 53%; m.p: 152-153 ^{0}C; IR (KBr) ν, cm $^{-1}$: 3182 (CH=), 3078 (C–H arom),1680, 1656(C=O, amid), 1643 (C=N, endocyclic), 1610, 1589 (C=C); MS (SCI): m/z= 441 $[M]^+$, Calculated= 441.

1-[4-acetyl-5-(4-bromophenyl)-5-methyl-4,5-dihydro-1,3,4-thiadiazol-2-yl]-1H-quinolin-2(1H)-one [4]$_b$: Off-white solid, yield: 47%; m.p: 143-146 ^{0}C, IR (KBr) ν, cm $^{-1}$: 3155 (CH=), 3070 (C–H arom),1683, 1654(C=O, amid), 1640 (C=N, endocyclic), 1612, 1585 (C=C). ^{1}H NMR spectrum, δ, ppm: 2.04 (s, 3H,CH_3), 2.18 (s, 3H,$COCH_3$), 6.60 (d, *J*=5.6,1H, COCH=), 7.14–7.89 (m, 8H, H arom), 8.2 (d, 1H, *J*=5.4.4Hz, PhCH=); Anal. Calcd. for (C_{20} H_{16}Br N_3O_2S) (442.33g/mol): C,54.31; H, 3.65; N, 9.50; S, 7.25%. found:C,54.12; H, 3.22; N, 9.82; S, 7.15%.

1-[4-acetyl-5-(4-bromophenyl)-4,5-dihydro-1,3,4-thiadiazol-2-yl]-4-hydroxy-quinolin-2(1H)-one [4]$_c$: Yellow solid, yield: 54%; m.p: 218-221 ^{0}C; IR (KBr) ν, cm $^{-1}$: 3358(OH), 3180 (CH=), 3065 (C–H arom),1681, 1651(C=O, amid), 1645 (C=N, endocyclic), 1620, 1599 (C=C). ^{1}H NMR spectrum, δ, ppm: 2.28 (s, 3H,$COCH_3$), 5.59(s, 1H, CH at C5 of thiadiazoline ring), 5.86 (s, 1H, CH=), 7.29–7.92 (m, 8H, H arom), 10.29 (s, 1H, OH); Anal. Calcd. for (C_{19} H_{14}Br N_3O_3S) (444.30g/mol): C,51.36; H, 3.18; N, 9.46; S, 7.22%. found: C, 51.49; H, 3.09; N, 9. 18%; S, 7.42%.

1-[4-acetyl-5-(4-bromophenyl)-5-methyl-4,5-dihydro-1,3,4-thiadiazol-2-yl]-4-hydroxy-quinolin-2(1H)-one [4]$_d$: Off-white solid, yield: 48%; m.p: 158-162 ^{0}C; IR (KBr) ν, cm $^{-1}$: 3410(OH), 3192 (CH=), 3064 (C–H arom),1685, 1658(C=O, amid), 1638 (C=N, endocyclic), 1615, 1575 (C=C); ^{1}H NMR spectrum, δ, ppm: 2.02 (s, 3H,CH_3), 2.28 (s, 3H,$COCH_3$), 5.60 (s, 1H, CH=), 7.34–7.99 (m, 8H, H arom), 10.26 (s, 1H, OH); MS (SCI): m/z= 449 $[M]^+$, Calculated= 449.

1-[4-acetyl-5-(4-bromophenyl)-4,5-dihydro-1,3,4-thiadiazol-2-yl]7-hydroxy-4-methylquinolin-2(1H)-one [4]$_e$: Pale-yellow solid, yield: 67%; m.p: 116-118 ^{0}C; IR (KBr) ν, cm $^{-1}$: 3415(OH), 3180 (CH=), 3058 (C–H arom),1678, 1662(C=O, amid), 1635 (C=N, endocyclic), 1600, 1595 (C=C); Anal. Calcd. for (C_{19} H_{14}Br N_3O_3S) (458.33g/mol): C,52.41; H, 3.52; N, 9.17; S, 7.00%. found: C, 52.55; H, 3.68; N, 9. 08%; S, 7.12%.

1-[4-acetyl-5-(4-bromophenyl)-5-methyl-4,5-dihydro-1,3,4-thiadiazol-2-yl]7-hydroxy-4-methyl quinolin-2(1H)-one [4]$_f$: Brown solid, yield: 52%; m.p: 136-140 ^{0}C; IR (KBr) ν, cm $^{-1}$: 3410(OH), 3194 (CH=), 3054 (C–H arom),1674, 1666(C=O, amid), 1639 (C=N, endocyclic), 1610, 1588 (C=C); MS (SCI): m/z= 473 $[M+1]^+$, Calculated= 472.

General procedure for the preparation of the Schiff bases [5]$_{a,b}$ [35]:

A solution of the compound [3] (0.01 mol) in dry benzene (10 mL)was added to the solution of 4-N,N-dimethylbenzaldehyde (0.01 mol) dissolved in the same solvent (10mL) which acidified with glacial acetic acid (2-3 drops), then the mixture was heated under reflux for 4 hrs. The solvent was evaporated and the resulting precipitate was washed with water, dried and recrystallized from ethanol.

1-(2-(4-bromophenyl)-5-(4-(dimethylamino)benzylideneamino)-1,3,4-thiadiazol-3(2H)-yl)ethanone[5]$_a$: Orange solid, yield: 78%; m.p: 232-234 ^{0}C; IR (KBr) ν, cm^{-1}: 1683(C=O, amid), 1620 (C=N, exoocyclic), 1602 (C=C), 1344,1156,814(C-NMe_2); MS (SCI): m/z= 432 $[M+1]^+$, Calculated= 431.

1-(2-(4-bromophenyl)-5-(4-(dimethylamino)benzylideneamino)-2-methyl-1,3,4-thiadiazol-3 (2H)-yl)ethanone [5]$_b$: Orange-Yellowship solid, yield: 73%; m.p: 168-170 ^{0}C; IR (KBr) ν, cm^{-1}: 1681(C=O, amid), 1614 (C=N, exoocyclic), 1597 (C=C), 1348,1155,814(C-NMe_2); ^{1}H NMR spectrum, δ, ppm: 2.06 (s, 3H,CH_3), 2.33 (s, 6H,2$COCH_3$), 2.68 (s, 6H,N$(CH_3)_2$) , 6.89–7.45 (m, 8H, H arom), 8.29 (s, 1H, CH=N).

General procedure for the synthesis of N-(acetyl or anisoyl) derivatives [6]$_{a-d}$:

To a cold stirred solution of Schiff bases [5] (0.01mol) in 10 mL dry benzene was added drop-wise of acetyl or ansoyl chloride (0.01mol), afterward the reaction mixture was refluxed for 4hrs. The solvent was evaporated and the residue was washed with water for many times and recrystallized from ethyl acetate.

N-(4-acetyl)-5-(4-bromophenyl)-4,5-dihydro-1,3,4-thiadiazol-2-yl)-N-(chloro(4-dimethyl amino) phenyl) methyl) acetamide [6]$_a$: Brown solid, yield: 78%; m.p: 194-197 ^{0}C; IR (KBr) ν, cm^{-1}: 1691(C=O, amid), 1602(C=C), 1345,1152,815(C-NMe$_2$), 812(C-Cl); ^{1}H NMR spectrum, δ, ppm: 2.33 (s, 3H, COCH$_3$), 2.68 (s,6H, N(CH$_3$)$_2$), 5.44 (s, 1H, CH at C5 of thiadiazoline ring), 6.39 (s, 1H,CH-Cl), 6.88–7.40 (m, 8H, H arom).

N-(4-acetyl)-5-(4-bromophenyl)-5-methyl-4,5-dihydro-1,3,4-thiadiazol-2-yl)-N-(chloro(4-dimethylamino) phenyl) methyl) acetamide [6]$_b$: Red solid, yield: 60%; m.p: 200-202 ^{0}C; IR (KBr) ν, cm^{-1}: 1691(C=O, amid), 1597(C=C), 1345,1150,816(C-NMe$_2$), 817(C-Cl); ^{1}H NMR spectrum, δ, ppm: 2.24 (s, 3H,CH$_3$), 2.28 (s, 3H, COCH$_3$), 2.77 (s,6H, N(CH$_3$)$_2$), 5.86 (s, 1H,CH-Cl), 6.38–8.44 (m, 8H, H arom).

N-(4-acetyl)-5-(4-bromophenyl)-4,5-dihydro-1,3,4-thiadiazol-2-yl)-N-(chloro(4-dimethyl amino)phenyl)methyl)-4-methylbenzamide[6]$_c$: Brown solid; yield 62%; m.p 157-159 ^{0}C. IR (KBr) ν, cm^{-1}: 1695(C=O, amid), 1600(C=C), 1342,1159,810(C-NMe$_2$), 799(C-Cl); Anal. Calcd. for ($C_{27}H_{26}BrCl\ N_4O_3S$) (601.94g/mol): C,53.87; H, 4.35; N, 9.31; S, 5.33%. found: C, 53.69; H, 4.40; N, 9.42; S, 5.62%.

N-(4-acetyl)-5-(4-bromophenyl)-5-methyl-4,5-dihydro-1,3,4-thiadiazol-2-yl)-N-(chloro(4-di methylamino) phenyl) methyl)-4-methylbenzamide[6]$_d$: Red solid; yield 55%; m.p 177-179 ^{0}C. IR (KBr) ν, cm^{-1}: 1687(C=O, amid), 1595(C=C), 1342,1150,816(C-NMe$_2$), 817(C-Cl).); MS (SCI): m/z= 616 [M]$^+$, Calculated= 616.

General procedure for the synthesis of N-(acetyl or anisoyl) thiourea derivatives [7]$_{a-d}$:

A mixture of compound [6](0.01mol), thiourea (0.01mol) , anhydrous sodium carbonate (0.01mol) and (20mL) analar acetone was refluxed for 4 hrs with stirring. The reaction mixture was cooled and poured onto ice – water (200 mL). The precipitate was filtered off, dried and recrystallized from chloroform.

(N-(4-acetyl)-5-(4-bromophenyl)-4,5-dihydro-1,3,4-thiadiazol-2-yl)acetamido)(4-dimethyl amino)phenyl)methyl carbamimidothioate [7]$_a$:

Yellow solid, yield: 54%; m.p: 227-230 ^{0}C; IR (KBr) ν, cm^{-1}: 3410-3275(NH$_2$ asy,sy, NH),1678(C=O, amid), 1604(C=C), 1348,1152,81(C-NMe$_2$), 744(C-S); MS (SCI): m/z= 550 [M+1]$^+$, Calculated= 549.

(N-(4-acetyl)-5-(4-bromophenyl)-5-mehyl-4,5-dihydro-1,3,4-thiadiazol-2-yl)acetamido)(4-dimethylamino)phenyl) methyl carbamimidothioate [7]$_b$:

Brown solid, yield: 82%; m.p: 118-120 ^{0}C; IR (KBr) ν, cm^{-1}: 3442-3385(NH$_2$ asy,sy, NH),1695(C=O, amid), 1602(C=C), 1349,1154,810(C-NMe$_2$), 742(C-S); ^{1}H NMR spectrum, δ, ppm: 2.05 (s, 3H,CH$_3$), 2.19(s, 6H,2COCH$_3$), 2.75 (s, 6H,N(CH$_3$)$_2$), 5.54(s, 1H, CH-S), 6.62-6.69(broad, 2H, NH$_2$), 6.82–7.48(m, 18H, H arom), 9.54 (s, 1H, NH).

(N-(4-acetyl)-5-(4-bromophenyl)-4,5-dihydro-1,3,4-thiadiazol-2-yl)-4-methylbenzamido)(4-di methylamino)phenyl) methyl carbamimidothioate [7]$_c$: Orange-yellowship solid, yield: 74%; m.p: 198-201 ^{0}C; IR (KBr) ν, cm^{-1}: 3387-3261(NH$_2$ asy,sy, NH), 1668(C=O, amid), 1600(C=C), 1345,1150,810(C-NMe$_2$), 742(C-S); Anal. Calcd. for ($C_{28}H_{29}BrN_6O_3S_2$) (641.60g/mol): C,52.42; H, 4.56; N, 13.10; S, 10.00%. found: C, 52.58; H, 4.40; N, 13.42; S, 9.85%.

(N-(4-acetyl)-5-(4-bromophenyl)-5-mehyl-4, 5-dihydro-1,3,4-thiadiazol-2-yl)-4-methylbenz amido) (4-dimethyl amino) phenyl) methyl carbamimidothioate [7]$_d$:

Brown solid, yield: 68%; m.p:140-142 ^{0}C; IR (KBr) ν, cm^{-1}: 3454-3232(NH$_2$ asy,sy, NH), 1675(C=O, amid), 1598(C=C), 1349,1154,819(C-NMe$_2$), 752(C-S); Anal. Calcd. for ($C_{29}H_{31}BrN_6O_3S_2$) (655.63g/mol): C,53.13; H, 4.77; N, 12.82; S, 9.78%. found: C, 53.39; H, 4.89; N, 12.52; S, 9.65%.

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General procedure for the synthesis of new imidazole derivatives [8]$_{a-d}$:

To a stirred solution of compound [7] (0.01mol) in dry DMF (10 mL), the benzoin (0.01mol) was added . The reaction mixture was refluxed for 5hrs. After cooling, few drops of water was added with stirring until a precipitate separated out. The precipitate was filtered off, dried and recrystallized from ethanol.

N-(4-acetyl)-5-(4-bromophenyl)-4,5-dihydro-1,3,4-thiadiazol-2-yl))-N-((4-di-methylamino) phenyl)(4,5-diphenyl-1H-imidazol-2-ylthio)methyl)acetamide [8]$_a$:

Orange solid, yield: 76%; m.p: 118-120 ^{0}C; IR (KBr) ν, cm^{-1}: 3454(NH), 1672(C=O, amid), 1656(C=N), 1593(C=C), 1349,1152,85(C-NMe$_2$); ^{1}H NMR spectrum, δ, ppm: 2.22(s, 6H,2COCH$_3$), 2.76 (s, 6H,N(CH$_3$)$_2$), 5.46(s, 1H, CH at C5 of thiadiazoline ring), 6.49(s, 1H, CH-S), 6.79–7.48 (m, 18H, H arom), 11.39 (s, 1H, NH); Anal. Calcd. for ($C_{36}H_{33}BrN_6O_2S_2$) (725.72g/mol): C, 59.58; H, 4.58; N, 11.58; S, 8.84%. found: C, 59.42; H, 4.68; N, 11.65; S, 8.68%.

N-(4-acetyl)-5-(4-bromophenyl)-5-mehyl-4,5-dihydro-1,3,4-thiadiazol-2-yl))-N-((4-dimethyl amino)phenyl)(4,5-diphenyl-1H-imidazol-2-ylthio)methyl)acetamide [8]$_b$:

Yellow solid; yield 69%; m.p 132-134 ^{0}C. IR (KBr) ν, cm^{-1}: 3415(NH),1680(C=O, amid), 1620(C=N), 1590(C=C), 1348,1152,84(C-NMe$_2$). ^{1}H NMR spectrum, δ, ppm: 2.03 (s, 3H,CH$_3$), 2.16(s, 6H,2COCH$_3$), 2.84 (s, 6H,N(CH$_3$)$_2$), 6.61(s, 1H, CH-S), 6.77–7.58(m, 18H, H arom), 11.47 (s, 1H, NH); Anal. Calcd. for ($C_{37}H_{35}BrN_6O_2S_2$) (739.75g/mol): C, 60.07; H, 4.77; N, 11.36; S, 8.67%. found: C, 60.22; H, 4.65; N, 11.54; S, 8.86%.

N-(4-acetyl)-5-(4-bromophenyl)-4,5-dihydro-1,3,4-thiadiazol-2-yl))-N-((4-dimethylamino) phenyl)(4,5-diphenyl-1H-imidazol-2-ylthio)methyl) benzamide[8]$_c$:

Orange solid; yield 74%; m.p 162-165 ^{0}C. IR (KBr) ν, cm^{-1}: 3456(NH),1672(C=O, amid), 1620(C=N), 1595(C=C), 1345,1159,84(C-NMe$_2$). ^{1}H NMR spectrum, δ, ppm: 2.25(s, 3H,COCH$_3$), 2.69 (s, 6H,N(CH$_3$)$_2$), 3.76(s, 3H, OCH$_3$), 5.49(s, 1H, CH at C5 of thiadiazoline ring), 5.94(s, 1H, CH-S), 6.82–7.49(m, 22H, H arom), 11.2 (s, 1H, NH); Anal. Calcd. for ($C_{42}H_{37}BrN_6O_3S_2$) (817.82g/mol): C, 61.68; H, 4.56; N, 10.28; S, 7.84%. found: C, 61.84; H, 4.42; N, 10.42; S, 7.69%.

N-(4-acetyl)-5-(4-bromophenyl)-5-mehyl-4,5-dihydro-1,3,4-thiadiazol-2-yl))-N-((4-dimethyl amino)phenyl)(4,5-diphenyl-1H-imidazol-2-ylthio)methyl)benzamide [8]$_d$:

Brown solid; yield 68%; m.p 175-178 ^{0}C. IR (KBr) ν, cm^{-1}: 3415(NH),1670(C=O, amid), 1625(C=N), 1605(C=C), 1348,1156,89(C-NMe$_2$). ^{1}H NMR spectrum, δ, ppm: 2.02 (s, 3H,CH$_3$), 2.22(s, 3H,COCH$_3$), 2.68 (s, 6H,N(CH$_3$)$_2$), 3.79(s, 3H, OCH$_3$), 5.99(s, 1H, CH-S), 6.82–7.54 (m, 22H, H arom), 11.40(s, 1H, NH); Anal. Calcd. for ($C_{43}H_{39}BrN_6O_3S_2$) (831.84g/mol): C, 62.09; H, 4.73; N, 10.10; S, 7.71%. found: C, 62.38; H, 4.82; N, 10.19; S, 7.56%.

RESULTS AND DISCUSSION

In the present paper, we reported the synthesis of some new quinolin-2(1H)-ones and imidazoles containing 1,3,4-thiadiazoline ring [4]$_{a-d}$ and [8]$_{a-d}$, respectively. Starting from the 4-bromoacetophenon or 4-bromobenzaldehyde and thiosemi-carbazide, the good quantities yields of thiosemicarbazones [1]$_{a,b}$ were synthesized (Scheme 1). The synthesized thiosemicarbazone compounds [1]$_{a,b}$ were converted to N-(4-acetyl-5-(4-bromophenyl)-5-methyl(H)-4,5-dihydro-1,3,4-thiadiazol-2-yl)acetamide [2]$_{a,b}$ under acylation conditions according to the general procedure that mentioned in reference [34]. A third step of outlined in Scheme (1) involves convert amido group to amino group at the position -2 of the 1,3,4-thiadiazoline ring by hydrolysis of compound [2] in hydrazine hydrate in water at room temperature [35] to give 4-acetyl-2-amino-5-(4-bromophenyl)-5-methyl(H)-4,5-dihydro-1,3,4-thiadiazole [3]$_{a,b}$. The one mole of compound [3] was reacted with one mole of different

FT-IR , ^{1}HNMR, Mass spectra and C.H.N.S analysis are confirmed the approach to the target compounds. FT-IR data showed the disappearance absorption bands of the amino group and appearance the new bands in the region (1685-1674cm^{-1}) that may be attributed to the stretching of C=O group. The ^{1}HNMR

spectrum of compound $[4]_d$ showed disappeared the signal for NH_2 protons together with appeared a new signal around δ(5.60 ppm) for (=CH) proton, besides to all signals assigned to these compounds. The mass spectrum of compound $[4]_e$ (as example) showed a characteristic fragmentation of this compound, which are illustrated in Scheme (2). These fragmentation support the suggested structure given for this compound such as several peaks at m/z = 147, 119, 103, 91 attributed to the presence of quinoline unit, while the thiadiazoline ring fragmentation appears at m/z = 198,183 (base peak), 104, and 89. These results in agreement with that observed for quinoline-2-one and 1,3,4-thiadiazoline moieties [36,37].

On the other hand, compounds $[3]_{a.b}$ were reacted with (4-N,N-dimethylaminobenzaldehyde) in presence of a few drops of glacial acetic acid to get new Schiff bases $[5]_{a,b}$, then refluxed with different acid chlorides to get N-(acyl / ansoyl) compounds $[6]_{a-d}$. FTIR data exhibited the disappearance of stretching band of C=N group of Schiff bases and appearing some new bands due to C-Cl and C=O(amid) at (799-817) cm^{-1} and (1687-1695) cm^{-1}, respectively. The spectroscopic data for these compounds were in a good agreement with this proposed structure, IR should show no great difference, while the electron ionization mass spectrum was consistent with the expected molecular mass for the proposed structure. Furthermore, the ^{1}H-NMR spectrum displayed a new signal at around δ 5.86 ppm attributable to one proton ofCH-Cl group in new N-acyl compounds[6].

The treatment of N-acyl compounds [6] with thiourea and anhydrous sodium carbonate led to formation N-(acetyl / anisoyl) thiourea derivatives $[7]_{a-d}$. FTIR spectra of compounds $[7]_{a-d}$, showed the disappearance of stretching band of C-Cl group of and appearing some new bands in the region (3422-3232 cm^{-1}) belonging to the stretching vibration of NH_2 and NH groups. The mass spectrum of compound $[7]_a$ showed the molecular ion peaks at the expected *m/z* values, 550(M+1), 342, 258, 215, 208, 182, 136, 103 and 87.

Finally, imidazole derivatives $[8]_{a-d}$ were obtained when the compounds $[7]_{a-d}$ reacted with benzoin in DMF. The reaction proceeds through nucleophilic substitution followed by cyclocondensation. The structural assignment of these compounds was based on spectral evidence and microanalyses. FTIR spectra showed the peak around (1625) cm^{-1} due to new stretching vibration of C=N (endocyclic) and disappearance the peaks of NH_2 group of compounds $[7]_{a-d}$. Furthermore, ^{1}HNMR spectrum of compounds $[8]_{a-d}$ reveals a singlet signal at δ (11.40 ppm) for NH proton, and a singlet signal around δ 6.00ppm due to CH-S proton coumarine derivatives to give new quinolin-2(1H)-ones$[4]_{a-f}$.

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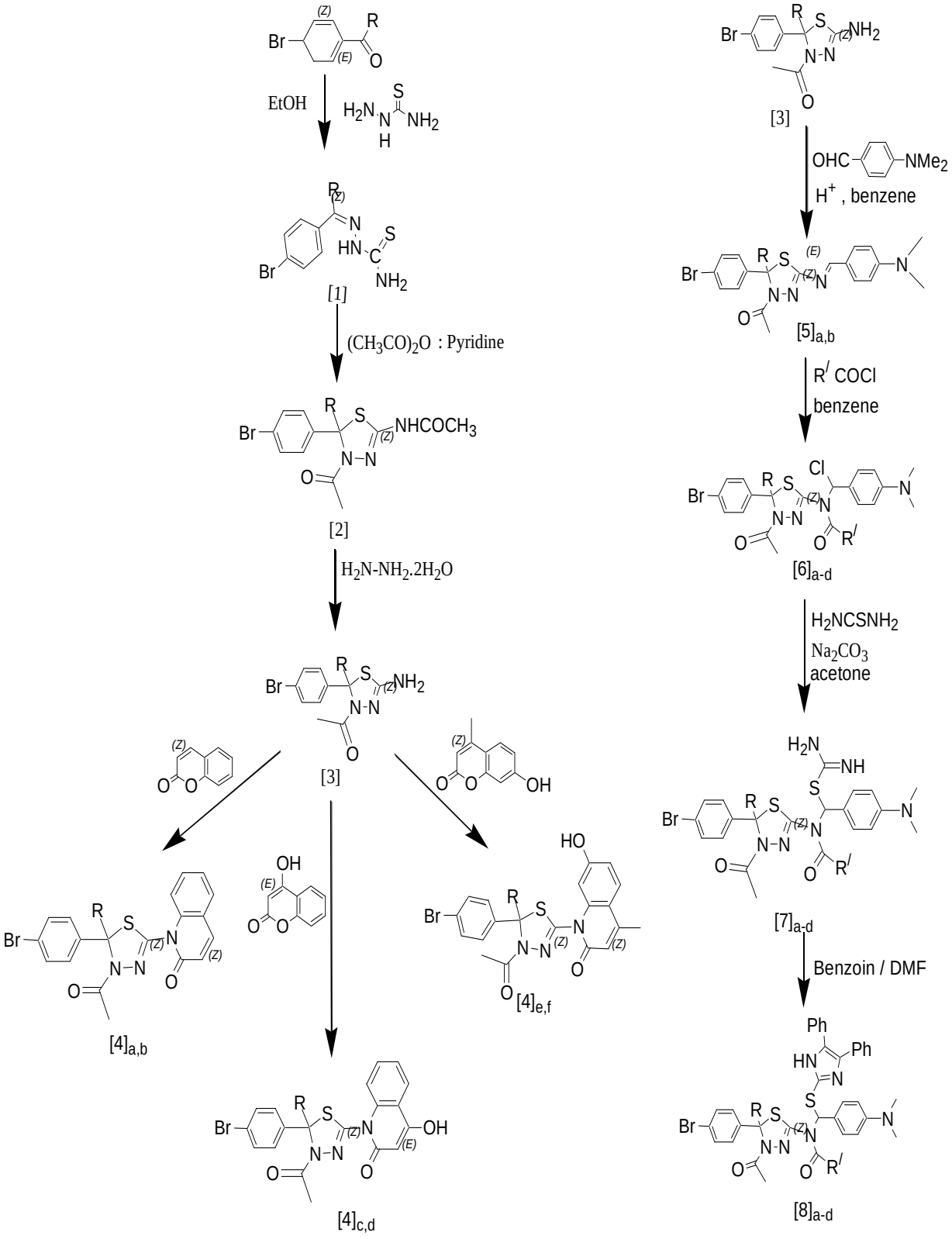

R= H , CH_3

$R^{/}$ = CH_3 , 4-$CH_3OC_6H_4$

Scheme 1: Synthetic route to synthesis new quinolines[4]a-f and imidazoles[8]a-f containing 1,3,4-thiadiazoline ring.

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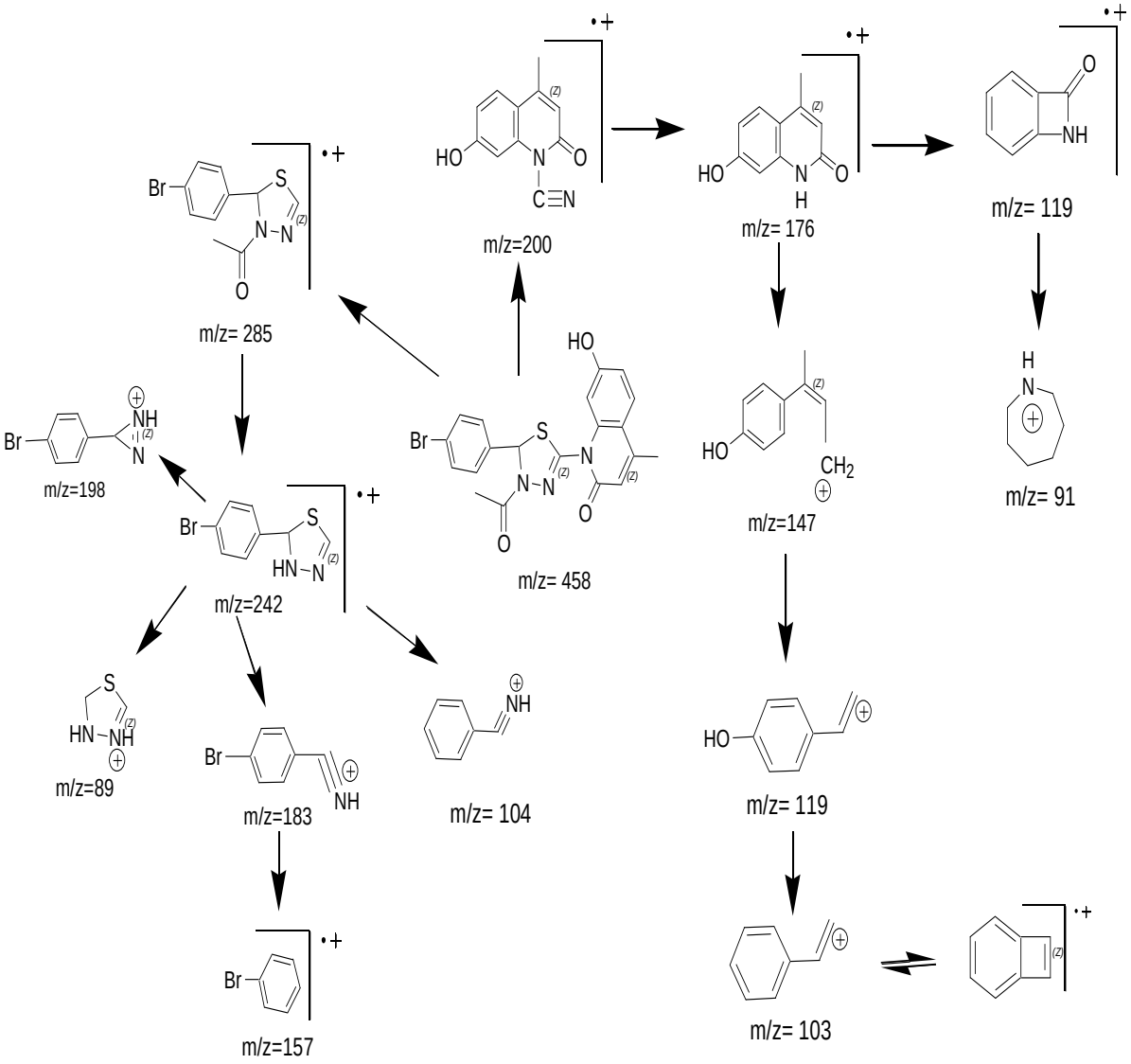

Scheme 2: The suggested fragmentation pattern of compound [F5]

CONCLUSIONS

In this paper, a simple method for the synthesis of new quinolin-2(1H) -one derivatives[4]$_{a\text{-}f}$ have been mentioned by the reactions of 4-acetyl-2-amino-5-(4-bromophenyl)-5-methyl(H)-4,5-dihydro-1,3,4-thiadiazoline[3] and different coumarine derivatives in glacial acetic acid. Imidazole derivatives have been synthesized in three steps. The first step includes synthesis of N-acyl compounds [6] by addition reaction of acid chloride to imine group of Schiff bases[5], while the second step was the reaction of thiourea with N-acyl derivatives in weak basic medium to yield thiourea derivatives[7]. The third step represents the synthesis of imidazoles [8] by cycloaddition reaction of the resulted thiourea derivatives with benzoin in good yields. The methods which are using for the synthesis these compounds are very simple, efficient and fast.

REFERENCES

[1] Kadi AA, Al-Abdullah ES, Shehata IA, Habib EE, Ibrahim TM, El-Emam A. A., *Eur J Med Chem.,* **2010**; 45(11): 5006-5011.
[2] Rostom SA, El-Ashmawy IM, El Razik HA, Badr MH, Ashour HMA. *Bioorg Med Chem.,* 2009; 17:882-895.
[3] Karegoudar P, Karthikeyan MS, Prasad DJ, Mahalinga M, Holla BS. Synthesis of some novel 2,4-disubstituted thiazoles as possible antimicrobial agents KumariNS. *Eur J Med Chem.,* 2008; 43:261-267.

[4] Ionut I, Tiperciuc B, Oniga O., *J Chromatogr Sci.,* 2017; 55 (4): 411-416.
[5] Saoji MB, Deshmukh Sh.P., *Der Pharma Chemica.* 2015; 7(4): 185-189.
[6] Al-Hamdani, A. A. S and Al-Zoubi, W. Spectrochimica Acta Part A: Mole. and Biomol. Spect.2015,137:75-89.
[7] Zivkovi MB, Mati IZ, Rodi´ MV, Novakovi´ IT, Sladi´ Du˘M, Krsti´ NM., *Royal Society of Chemistry Adv*., 2016; 6: 34333.
[8] Al Zoubi, W., A. A. S. Al-Hamdani, S. D. Ahmed and Y. G. Ko, J. Phys. Org. Chem., 2018, 31, 3752.
[9] Winter RW, Kelly JX, Smilkstein MJ, Dodean R, Hinrichs D, Riscoes MK. Antimalarial quinolones. *Exp. Parasitology*. 2008; 118; 487-497.
[10] Rani M, Ramachandran R, Kabilan S . Efficient Synthesis of Novel 2,4-[Diaryl-3-azabicyclo[3.3.1]nonan-9-yl]-5-spiro-4-acetyl-2-(acetyl amino)-1,3,4-thiadiazolines. *Journal Synthetic Communications*. 2010; 40: 1694-1700.
[11] Som S. Derivatives of 2-quinolones., *WJPPS Journal.* 2015; 4(4): 1368-1376.
[12] Al Zoubi, W. Al-Hamdani, A. A. S. Gun, Y. K. Separation science and technology. 2017:1-18.
[13] Chen YL, Chen IL, Lu CM, Treng CC, Tsao LT, Wang JP. , *Bioorg. Med. Chem.,* 2003; 11; 3921- 3927.
[14] Boyarshinov VD, Mikhalev AI, Yushkova TA, Ukhov SV, Kon'shina TM., *Pharmaceutical Chemistry Journal.* 2017; 51; 351–354.
[15] Tomma JH, Hussein DF, Jamel NM. Synthesis*., Iraqi Journal of Science*. 2016; 57(2C): 1316-1332.
[16] Lakshmanan B, Mazumder PM, Sasmal D, Ganguly S. , *Der Pharmacia Lettre.* 2010; 2(4): 82-89.
[17] Rezaei Z, Khabnadideh S, Zomorodian K, Pakshir K, Kashi G, Sanagoei N. Design., *Archiv der Pharmazie.* 344 (2011) 658–665.
[18] Rambabu R, Subbarao J, Kumar PP., *Int J Pharm Sci Res.,* 2015; 6(4): 1761-65.
[19] Li WT, Hwang DR, Song JS, Chen CP, Chuu JJ, Hu CB., *J. Med. Chem.,* 2010; 53(6): 2409-2417.
[20] Suvarna AS*., Res. J. Chem. Sci.,* 2015; 5(10): 67-72.
[21] Jiang B, Si YC*., J. Org. Chem.,* 2002; 67(26): 9449-9451.
[22] Linderman RJ, Kirollos SK., *Tetrahedron Lett.,* 1990; 31: 2689-2992.
[23] Geng X, Li Sh, Bian X, Xie Z, Wang C., *ARKIVOC*. 2008; xiv: 50-57.
[24] Soleimani E., Khodaei M. M., Batooie N., Samadi S.,*Chem. Pharm. Bull.,* 2010; 58(2): 212-213.
[25] Gladiali S, Chelucci G, Mudadu MS, Gastaut MA, Thumme RP. Friedländer., *J. Org. Chem.,* 2001; 66(2): 400-405.
[26] Narasimhulu M, Reddy TS, Mahesh KC, Prabhakar P, Rao CB, enkateswarlu YV. Silica., *J. Mol. Catal. A: Chem*., 2007; 266:114.
[27] Desai UV, Mitragotri SD, Thopate TS, Pore DM, Wadgaonkar PP.,. *ARKIVOC*. 2006; xv: 198-204.
[28] Das B, Damodar K, Chowdhury N, Kumar R.A., *J. Mol.Catal. A. Chem.*, 2007;274: 148-152.
[29] Muscia GC, Bollini M, Carnevale JP, Bruno AM, Asis SE.,*Tetrahedron Lett.,* 2006; 47: 8811-8815.
[30] Yongli Z, Jaemoon LA, David A., *Org. Lett.*, 2004; 6 (6): 929–931.
[31] David RH, Jessica LC, Zile JL, Barker KH., *J. Chem. Educ.,* 2006;83: 1658.
[32] Tomma JH*., J. for Pure & Appl. Sci.,* 2010; 23 (3): 134-151.
[33] Pawar P, Mane B, Salve M, Bafana S., *International Journal of Drug Research and Technology.* 2013; 3(3): 60-66.
[34] Ayyash AN, Jaffer HJ, Tomma JH., *American Journal of Organic Chemistry.* 2014; 4(2): 52-62.
[35] Ayyash AN, Tomma JH, Jaafer H. J. *International Journal of Applied and Natural Sciences.* 2014; 3: 61-66.
[36] Al-Hamdani, A. A. S. Research J. of Pharmaceutical, Biological and Chem. Sci. 2017, 8(3): 2119-2132.
[37] Porter N. Mass spectrometry of heterocyclic compounds, 2nd ed., A Wiley-Interscince Publication, John Wiley Sons, New York,1984; p. 932.