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SYNTHESIS OF NEW PYRAZOLE CONTAINING 1, 4-DIHYDROQUINOXALINE-2-CARBOXYLATE MOIETY

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Abstract: A new series of pyrazole bearing 1**,** 4-dihydroquinoxaline-2-carboxylate moiety Compounds**4, 5, 6(a-d)** were preparedby reactions of chalcones**3a-d**with hydrazine hydrate and 4-chloro phenyl hydrazine via cyclocondensation reaction. Reaction of Ethyl 3-acetamido-1, 4-dihydroquinoxaline-2-carboxylate**2**andaromatic aldehydes (Benzaldehyde,p-chlorobenzaldhyde,p-methoxybenzaldyde, p-nitrobenzaldhyde)afford the corresponding chalcones**3a-d**, the reaction proceed via Condensation by Claisen-Schmidt method. The synthesized compounds expected to have biological activity.

Key words: Chalcones, pyrazol-1, 4-dihydroquinoxaline, acetylchloride, anticancer properties, pyrazoline derivatives.

Introduction

The biological importance of Chalconesdue to their properties as antioxidant agents [I], antiviral [II], anticancer [III, IV], and antimalarial [V]pyrazolinederivatives which obtained from chalcons inhibit heat shock proteins [VI], P-glycoprotein [VII], and cyclin-dependent kinase [VIII], anticancer properties [IX, X].This drives us to synthesis heterocyclic compounds especiallypyrazolinederivatives fromchalcones.Alsoquinoxaline derivatives play a vital role in medicinal chemistry organic synthesis [XI–XIV], Quinoxaline derivatives have wide biological activity like anticancer [XV– XVIII], antimicrobial [XIX–XXI], antimalarial [XXII], anti-inflammatory[XXIII,XXIV], antiviral [XXV], kinase inhibitors, antileishmanial and ant tubercular,[XXVI–XXIX],Also quinoxaline derivatives have many industrial application like chemically controllable switches [XXX], organic semiconductors [XXXI], dyes [XXXII],electron luminescent materials [XXXIII],quinazoline derivatives is considered as rigid subunits in macrocyclicreceptorsin molecular recognition [XXXIV].Also used in the synthesis of the synthesis of dehydoannulenes, cavitands, and anion [XXXV,XXXVI].Thus in our research project

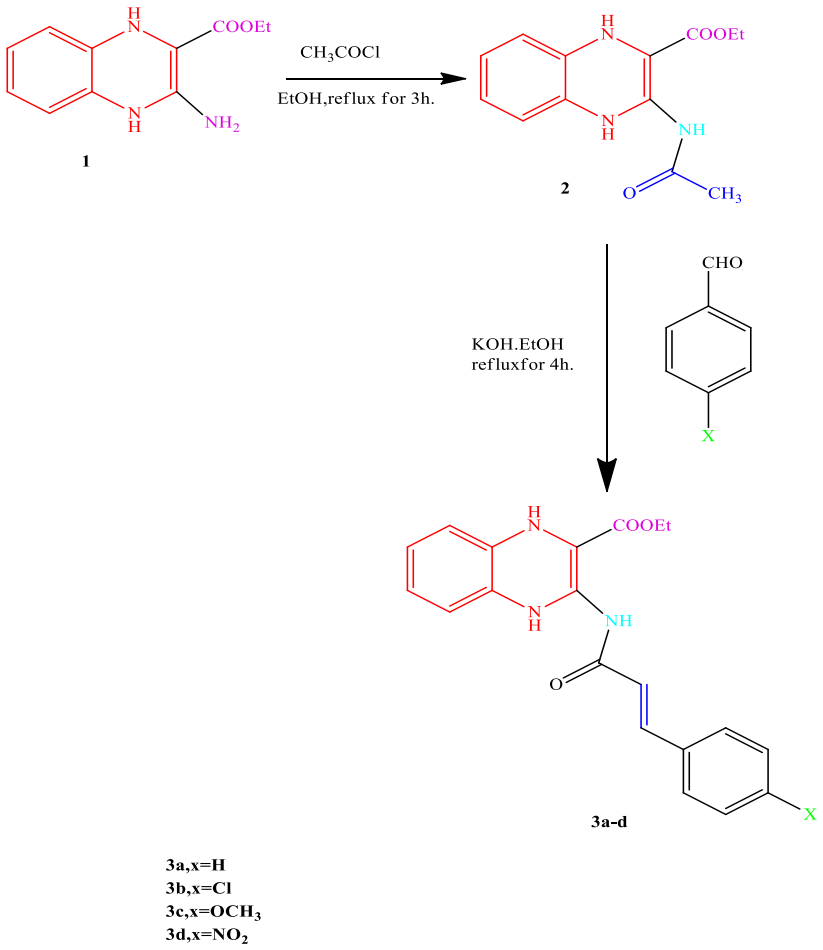
we aim to synthesis of new pyrazolinequinazoline derivatives which expected to have biological activity.

Results and Discussion

Reaction of Ethyl 3-amino-1,4-dihydroquinoxaline-2-carboxylate **1**[XXXVII] with acetyl chloride provide Ethyl 3-acetamido-1,4-dihydroquinoxaline-2-carboxylate **2** , elucidation structure of compound **2** was obtained by analysis(FTIR, 1H-NMR, ^{13}C-NMR and mass spectrometry).The IR spectrum of compound **2**shows absorption bands at 3400-3100, 1733, 1660-1665 cm^{-1}corresponding NH, and 2CO. the ^{1}H-NMR spectrum show signal at 3.55assigned for CH_3,The mass spectrum shows a molecular ion peak at m/z 261, which is in agreement with the structure proposed for**2.**

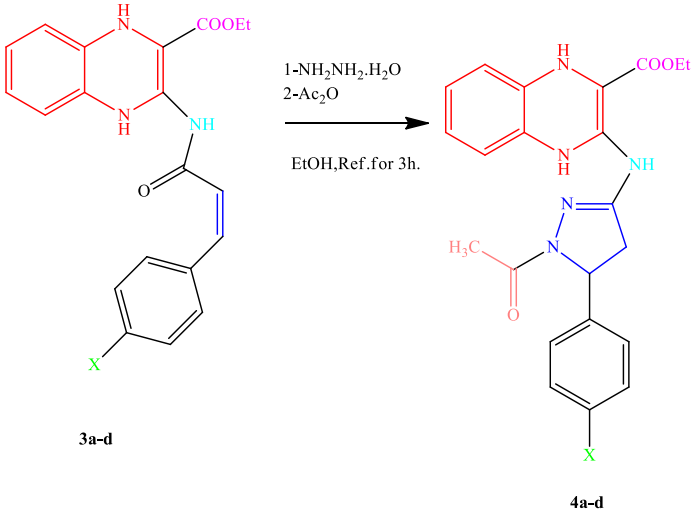
On the other hand treatment of compound **2** with different aromatic aldehyde (benzaldhyde, p-chlorobenzaldhyde, p-methoxybenzaldhyde, p-nitro benzaldhyde) and potassium hydroxide in presence of ethanol as solvent afford the corresponding chalcones**3a-d** .

The structure was established for compounds **3a**–**d**by analysis of their spectroscopic data (FTIR, ^{1}H-NMR, ^{13}C-NMR and mass spectrometry).From the series representative **3a-d** we discuss compound **3a**. The IR spectrum of compound **3a** shows absorption bands3400-3100 (NH), 1733(CO), 1665 (CO) cm^{-1}. The ^{1}H-NMR spectrum show the signals at 8.99, 9.41 assigned for CH=CH group. Themass spectrum shows a molecular ion peak at m/z 349, which is in agreement with the structure proposed for**3a**,**Scheme 1**.

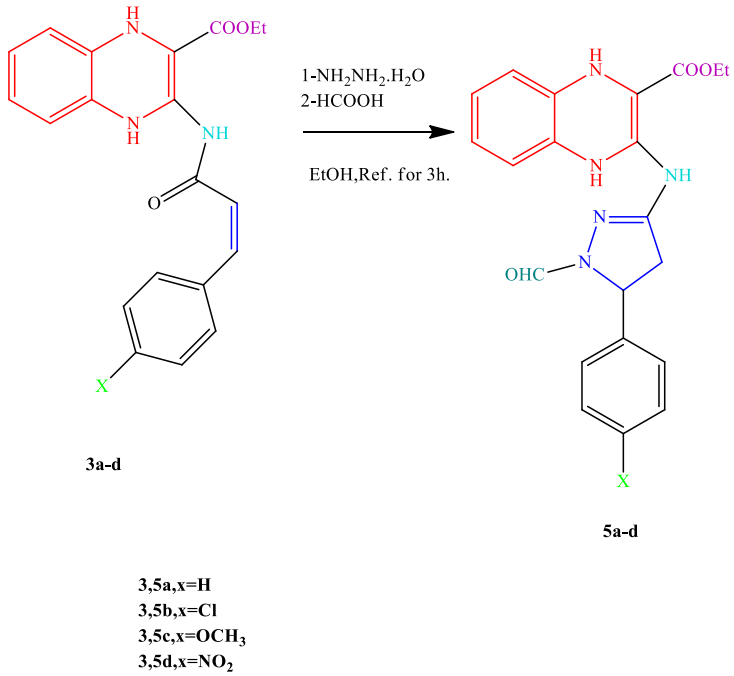


Scheme 1: Synthesis of compounds **3a-d**.

The target compounds **4, 5, 6(a-d)** was synthesized via 1, 2-dinucleophiliccyclocondensationreactions under different experimental conditions (**Scheme 2, 3, 4**). So, the N-acetylPyrazole 1, 4-dihydroquinoxaline-2-carboxylatederivatives**4a-d**and N-formylpyrazole1, 4-dihydroquinoxaline-2-carboxylatederivatives **5a**–**d**were obtained by reaction of chalcones**3a**–**d**with hydrazine monohydrate and their subsequent functionalization with acetic anhydride and formic acid, respectively, under refluxing in ethanol for 3-4 h, **Scheme2, 3**.

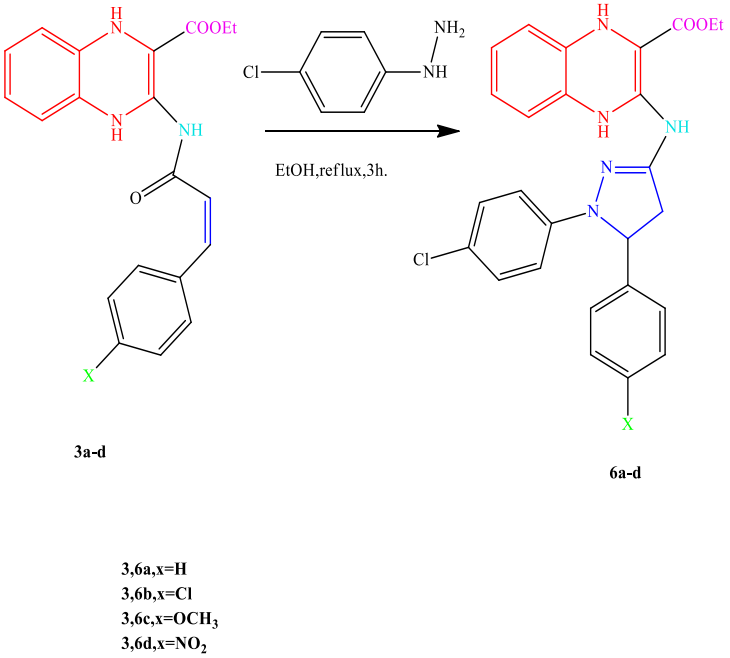


Scheme 2: Synthesis of compounds **4a-d**.



Scheme 3: Synthesis of compounds **5a-d**.

On theother hand, the treatment of chalcones**3a**–**d**with 4-chlorophenylhydrazine under reflux in ethanol for 3-4 h afforded the4-chlorophenylpyrazol-1, 4-dihydroquinoxaline-2-carboxylate derivatives **6a-d**, Scheme **4**.



Scheme 4: Synthesis of compounds **6a-d**.

The obtained Pyrazole 1, 4-dihydroquinoxaline-2-carboxylate derivatives**4a-d** and N-formylpyrazole 1, 4-dihydroquinoxaline-2-carboxylate derivatives**5a**–**d** showed wide FT-IR absorption bands in the Range of 1565–1655cm^{-1} assigned to C=N groups. The IR spectra of compound 4-chlorophenylpyrazol-1, 4-dihydroquinoxaline-2-carboxylate derivatives **6a-d**showed absorption bands at1510–1608 (C=C), 1565–1655(C=N) cm^{-1} assigned to C=C and C=N functiongroup, respectively, the structures of compounds **4a-d**, **5a-d** and **6a-d** were established by spectral analysis ^{1}HNMR, ^{13}CNMR and mass spectra (see experimental section).

Experimental Section

All melting points are uncorrected, the reactions were monitored and the purity of products was controlled by Thin Layer Chromatography (TLC) using silica gel aluminum sheets 60F254 (Merck, Germany). IR spectra were recorded as potassium bromide disks using Shimadzo infrared spectrophotometer central research laboratory, Jouf University ,^{1}H NMR spectra were recorded on Bruker AMX-250 spectrometer (Germany) at 250 MHz Mass spectra were recorded on Hewlett Packard MS 5988 Spectrometer (USA). Elemental microanalyses were carried out on CE 440 Elemental Analyzer- Automatic Injector (Exeter Analytical, Inc., USA) at Cairo University, Cairo, Egypt, Compound **1**was prepared according to the reported method [XXXVII]

Ethyl 3-acetamido-1, 4-dihydroquinoxaline-2-carboxylate2:

A mixture ofEthyl 3-amino-1, 4-dihydroquinoxaline-2-carboxylate **1**[XXXVII] **(**0.01mol**)** andethanol (20ml) was put in 250 ml round flask and the acetyl chloride **(**0.01mol**)** was added then the mixture was heated under reflux for 3h. The solid product formed poured into ice water, stirringwell, the precipitate formed filtered and recrystallized from ethanol to afford compound **2**.

Orange solid, yield 85%, mp.160-162°C. IR (KBr, cm^{-1}): 3400-3100 (NH), 1733(CO),1660-1665 (CO) cm^{-1};^{1}H NMR (400 MHz, DMSO-d_6)δ (ppm):1.27 (t, J = 7.54 Hz, 3H, CH_2CH_3), 4.19 (q, J = 7.54 Hz, 2H, CH_2CH_3), 3.55(s,3H,CH_3),8.58(s,1H,NH),12.35 (s, 1H, N-HAr), and 12.62 (s, 1H, N-HAr-),7.02-8.03(m,Ar-H,4H);^{13}C NMR (125 MHz, DMSO-d6): δ15.14(CH_3),24.12(CH_3),61.68(CH_2),119.82,120.61,90.43,125.34,165.32,170.82(2CO)ppm. MS (ESI): m/z 261.28(M+). Anal.Calcd. For: $C_{13}H_{15}N_3O_3$: C, 59.76; H, 5.79; N, 16.08. Found C, 59.83; H, 5.85; N, 16.12.

General Procedure for the Synthesis of3a-d:

A mixture of compound **2**(3mmol), and substituted benzaldehyde (benzaldhyde, p-chlorobenzaldhyde, p-methoxybenzaldhyde, p-nitro benzaldhyde) (3.0 mmol) andPotassiumhydroxide (100 mg) in ethanol (7 mL) was heated under reflux for4 h. The solidformed was filtered and washed with ethanoland recrystallized from ethanol.

Ethyl 3-cinnamamido-1,4-dihydroquinoxaline-2-carboxylate3a

Pallyellow solid, yield 66%, mp.190-192°C. IR (KBr, cm^{-1}): 3400-3100 (NH), 1733(CO),1665 (CO) cm^{-1};^{1}H NMR (400 MHz, DMSO-d_6)δ (ppm):1.27 (t, J = 7.54 Hz, 3H, CH_2CH_3), 4.19 (q, J = 7.54 Hz, 2H, CH_2CH_3), 7.02-8.03(m,Ar-H,9H),8.58(s,1H,NH),8.99 (s, 1H,CH), 9.41 (s, 1H,CH), 12.35 (s, 1H, N-HAr), and 12.62 (s, 1H, N-HAr-); ^{13}C NMR (125 MHz, DMSO-d6): δ15.14(CH_3),24.12(CH_3),61.68 (CH_2),119.82, 120.61,90.43,125.34(C=C),165.32,170.82(2CO) ppm.MS (ESI): m/z 349.38 (M+). Anal.Calcd. For: $C_{20}H_{19}N_3O_3$: C, 68.75; H,5.48; N, 12.03. Found C, 68.79; H, 5.52; N, 12.08.

Ethyl 3-(3-(4-chlorophenyl) acrylamide)-1,4-dihydroquinoxaline-2-carboxylate3b

Reddish brown solid, yield 66%, mp.205-207°C. IR (KBr, cm^{-1}): 3400-3100 (NH), 1735(CO), 1665 (CO) cm^{-1}; ^{1}H NMR (400 MHz, DMSO-d_6)δ (ppm):1.32 (t, J = 7.56 Hz, 3H, CH_2CH_3), 4.39 (q, J = 7.58 Hz, 2H, CH_2CH_3), 7.02-8.03(m,Ar-H,8H),8.62(s,1H,NH),9.09 (s, 1H,CH), 9.51 (s, 1H,CH), 12.35 (s, 1H, N-HAr), and 12.62 (s, 1H, N-HAr-);^{13}C NMR (125 MHz, DMSO-d6):δ15.25(CH_3),24.19(CH_3),61.84(CH_2),119.82,120.61,90.51,125.37(C=C),131.22,165.32,170.82(2CO)ppm;MS (ESI): m/z 383.83 (M+).Anal.Calcd. For: $C_{20}H_{18}ClN_3O_3$: C, 62.58; H, 4.73; Cl, 9.24; N, 10.95%. Found: C, 62.58; H, 4.73; Cl, 9.24; N, 10.95%.

Ethyl 3-(3-(4-methoxyphenyl) acrylamide)-1,4-dihydroquinoxaline-2-carboxylate3c

Red solid, yield 74%, mp.219-221°C. IR (KBr, cm^{-1}): 3400-3100 (NH), 1735(CO), 1665 (CO) cm^{-1}; ^{1}H NMR (400 MHz, DMSO-d_6)δ (ppm):1.29 (t, J = 7.54 Hz, 3H, CH_2CH_3), 4.32 (q, J = 7.55 Hz, 2H, CH_2CH_3), 3.68 (s,3H,CH_3), 7.02-8.03(m,Ar-H,8H),8.71(s,1H,NH),8.99 (s, 1H,CH), 9.43 (s, 1H,CH), 12.35 (s, 1H, N-HAr), and 12.62 (s, 1H, N-HAr-);^{13}C NMR (125 MHz, DMSO-d6): δ15.16(CH_3) ,24.15(CH_3),61.70 (CH_2),119.82, 120.61,90.41,125.33(C=C), 131.22,165.32,170.82(2CO) ppm.MS (ESI): m/z 379.41(M+). Anal.Calcd. For: $C_{21}H_{21}N_3O_4$: C, 66.48; H, 5.58; N, 11.08 %. Found: C, 66.48; H, 5.58; N, 11.08%.

Ethyl 3-(3-(4-nitrophenyl) acrylamide)-1,4-dihydroquinoxaline-2-carboxylate3d

Red solid yield 69%, mp.243-245°C. IR (KBr, cm^{-1}): 3400-3100 (NH), 1733(CO), 1665 (CO) cm^{-1}; 1.28 (t, J = 7.54 Hz, 3H, CH_2CH_3), 4.27 (q, J = 7.54 Hz, 2H, CH_2CH_3), 7.02-8.03(m,Ar-H,8H),8.56(s,1H,NH),8.99 (s, 1H,CH), 9.43 (s, 1H,CH), 12.35 (s, 1H, N-HAr), and 12.62 (s, 1H, N-HAr-);^{13}C NMR (125 MHz, DMSO-d6): δ15.21CH_3) ,24.18(CH_3),61.73 (CH_2),119.82, 120.61,90.41,125.33(C=C), 131.22,165.32,170.82(2CO) ppm.MS (ESI): m/z 394.38 (M+). Anal.Calcd. For: $C_{20}H_{18}N_4O_5$: C, 60.91; H, 4.60; N, 14.21%. Found: C, 60.91; H, 4.60; N, 14.21%.

General Procedure for the Synthesis of 4a-d:

A mixture of chalcone**3a-d** (0.01mmol) and hydrazine monohydrate (0.01mmol) in ethanol (10 mL) was stirred at reflux for 1h. Subsequently, acetic anhydride was added (1.5 mL) and the solution was refluxed for 3 h. The solid obtained was filtered and washed with water. The product was purified by method of column chromatography by using EtOH/CH_2Cl_2 (1:3) as eluent.

Ethyl 3-((1-acetyl-5-phenyl-4, 5-dihydro-1H-pyrazol-3-yl) amino)-1, 4-dihydroquinoxaline-2-carboxylate4a

Redsolid, yield 69%, mp.243-245°C. IR (KBr, cm^{-1}): 3400-3100 (NH), 1733(CO),1660- 1665 (CO),1565–1655(C=N) cm^{-1}; ^{1}H NMR (400 MHz, DMSO-d_6)δ (ppm):1.25 (t, J = 7.54 Hz, 3H, CH_2CH_3), 4.17 (q, J = 7.54 Hz, 2H, CH_2CH_3),3.22(s,3H,CH_3),4.32(d,2H,CH_2), 5.26(t,1H,$CH_{pyrazole}$), 7.02-8.03(m,Ar-H,9H),8.58(s,1H,NH), 12.35 (s, 1H, N-HAr), and 12.62 (s, 1H, N-HAr-);^{13}C NMR (125 MHz, DMSO-d6): δ15.14(CH_3),23.61(CH_3),37.97(CH_2 pyrazole),61.68(CH_2),62.77(CHpyrazole),119.82,152.98(C=N),120.61,127.11,129.33,141.93,88 .25,136.21(C=C),165.32,169.33 (2CO) ppm; MS (ESI): m/z 405.45 (M+). Anal.Calcd. For: $C_{22}H_{23}N_5O_3$: C, 65.17; H, 5.72; N, 17.27 %. Found: C, 65.21; H, 5.76; N, 17.31%.

Ethyl 3-((1-acetyl-5-(4-chlorophenyl)-4, 5-dihydro-1H-pyrazol-3-yl) amino)-1, 4-dihydroquinoxaline-2-carboxylate 4b

Green solid, yield 71%, mp.265-267°C. IR (KBr, cm^{-1}): 3400-3100 (NH), 1735(CO), 1660-1665(CO), 1565–1655(C=N) cm^{-1}; ^{1}H NMR (400 MHz, DMSO-d_6)δ (ppm):1.32 (t, J = 7.56 Hz, 3H, CH_2CH_3), 4.39 (q, J = 7.58 Hz, 2H, CH_2CH_3), 3.25(s,3H,CH_3),4.34(d,2H,CH_2), 5.28(t,1H,$CH_{pyrazole}$),7.02-8.03(m,Ar-H,8H),8.62(s,1H,NH), 12.35 (s, 1H, N-HAr), and 12.62 (s, 1H, N-HAr-);^{13}C NMR (125 MHz, DMSO-d6): δ15.28(CH_3) , 23.99(CH3),37.99(CH_2 pyrazole),61.71(CH_2),62.79(CHpyrazole),152.98(C=N),119.82,120.61,127.11,129.33,141.93, 88.25,136.21(C=C),165.32,169.52(2CO)ppm;MS (ESI): m/z 439.89 (M+). Anal.Calcd. For: $C_{22}H_{22}ClN_5O_3$: C, 60.07; H, 5.04; Cl, 8.06; N, 15.92. %. Found: C, 60.12; H, 5.13; Cl, 8.14; N, 15.99%.

Ethyl3-((1-acetyl-5-(4-methoxyphenyl)-4, 5-dihydro-1H-pyrazol-3-yl) amino)-1 , 4-dihydroquinoxaline-2-carboxylate 4c

Orange solid, yield 67%, mp.257-259°C. IR (KBr, cm^{-1}): 3400-3100 (NH), 1735(CO), 1665 (CO), 1565–1655(C=N) cm^{-1}; ^{1}H NMR (400 MHz, DMSO-d_6)δ (ppm):1.29 (t, J = 7.54 Hz, 3H, CH_2CH_3), 4.32 (q, J = 7.55 Hz, 2H, CH_2CH_3), 3.68 (s,3H,CH_3), 3.23(s,3H,CH_3),4.34(d,2H,CH_2), 7.02-8.03(m,Ar-H,8H),8.71(s,1H,NH), 12.35 (s, 1H, N-HAr), and 12.62 (s, 1H, N-HAr-);^{13}C NMR (125 MHz, DMSO-d6): δ15.16(CH_3) ,24.15(CH_3), 37.99(CH_2 pyrazole),61.71 (CH_2),62.79 ($CH_{pyrazole}$),152.98(C=N),119.82,120.61,127.11,129.33,141.93,88.25,136.21(C=C),165.32,16 9.52(2CO) ppm.MS (ESI): m/z 435.48 (M+). Anal.Calcd. For: $C_{23}H_{25}N_5O_4$: C, 63.44; H, 5.79; N, 16.08%. Found: C, 63.44; H, 5.79; N, 16.08%.

Ethyl3-((1-acetyl-5-(4-nitrophenyl)-4, 5-dihydro-1H-pyrazol-3-yl) amino)-1, 4-dihydroquinoxaline-2-carboxylate 4d

Red solid, yield 69%, mp.243-245°C. IR (KBr, cm^{-1}): 3400-3100 (NH), 1733(CO), 1665 (CO) , 1565–1655(C=N)cm^{-1}; 1.28 (t, J = 7.54 Hz, 3H, CH_2CH_3), 4.27 (q, J = 7.54 Hz, 2H, CH_2CH_3), 3.23(s,3H,CH_3),4.34(d,2H,CH_2), 7.02-8.03(m,Ar-H,8H),8.56(s,1H,NH), 12.35 (s, 1H, N-HAr), and 12.62 (s, 1H, N-HAr-);^{13}C NMR (125 MHz, DMSO-d6): δ15.21CH_3) ,24.18(CH_3), 37.99($CH_{2pyrazole}$),61.71 (CH_2),62.79 ($CH_{pyrazole}$) ,152.98 (C=N),119.82, 120.61,127.11,129.33,141.93,88.25,136.21(C=C),165.32,169.52(2CO) ppm.MS (ESI): m/z 450.45 (M+). Anal.Calcd. For: $C_{22}H_{22}N_6O_5$: C, 58.66; H, 4.92; N, 18.66 %. Found: C, 58.66; H, 4.92; N, 18.66 %.

General Procedure for the Synthesis of 5a-d:

A mixture of chalcone**3a-d** (0.01mmol) and hydrazine monohydrate (0.01mmol) in ethanol (10 mL)was stirred at reflux for 1h.. Subsequently, formic acid was added (1.5 mL) and the solution was refluxed for 3 h. The solid product was filtered and washedwith water and recrystallized from ethanol.

Ethyl 3-((1-formyl-5-phenyl-4, 5-dihydro-1H-pyrazol-3-yl) amino)-1, 4-dihydroquinoxaline-2-carboxylate5a

Brown solid, yield 66%, mp.284-286°C. IR (KBr, cm^{-1}): 3400-3100 (NH), 1733(CO),1660-1665(CO), 1565–1655(C=N) cm^{-1}; ^{1}H NMR (400 MHz, DMSO-d_6)δ (ppm):1.25 (t, J = 7.54 Hz, 3H, CH_2CH_3), 4.17 (q, J = 7.54 Hz, 2H, CH_2CH_3) ,4.32(d,2H,CH_2), 5.24(t,1H,CHpyrazole),7.02-8.03(m,Ar-H,9H),8.58(s,1H,NH), 10.06(s,1H,CHO),12.35 (s, 1H, N-HAr), and 12.62 (s, 1H, N-HAr-);^{13}C NMR (125 MHz, DMSO-d6): δ15.14(CH_3),37.97($CH_{2\ pyrazole}$),61.68 (CH_2),62.77 ($CH_{pyrazole}$),119.82,152.98(C=N),120.61,127.11,129.33,141.93,88.25,136.21(C=C),165.32,169.33 (2CO) ppm. MS (ESI): m/z 391.42(M+). Anal.Calcd. For: $C_{21}H_{21}N_5O_3$: C, 64.44; H, 5.41; N, 17.89%. Found: C, 64.47; H, 5.45; N, 17.92%.

Ethyl3-((5-(4-chlorophenyl)-1-formyl-4, 5-dihydro-1H-pyrazol-3-yl) amino)-1, 4-Dihydroquinoxaline-2-carboxylate 5b

Yellow solid, yield 71%, mp.297-299°C. IR (KBr, cm^{-1}): 3400-3100 (NH), 1735(CO), 1660-1665(CO) , 1565–1655(C=N)cm^{-1}; ^{1}H NMR (400 MHz, DMSO-d_6)δ (ppm):1.32 (t, J = 7.56 Hz, 3H, CH_2CH_3), 4.39 (q, J = 7.58 Hz, 2H, CH_2CH_3), 4.34(d,2H,CH_2), 5.28(t,1H,CHpyrazole),7.02-8.03(m,Ar-H,8H),8.62(s,1H,NH), 10.16(s,1H,CHO),12.35 (s, 1H, N-HAr), and 12.62 (s, 1H, N-HAr-);^{13}C NMR (125 MHz, DMSO-d6): δ15.28(CH_3) , 37.99($CH_{2pyrazole}$),61.71 (CH_2),62.79 ($CH_{pyrazole}$),152.98(C=N),119.82,120.61,127.11,129.33,141.93,88.25,136.21(C=C),165.32,169.52(2CO)ppm;MS (ESI): m/z 425.87 (M+). Anal.Calcd. For: $C_{21}H_{20}ClN_5O_3$: C, 59.23; H, 4.73; Cl, 8.32; N, 16.44 %. Found: C, 59.28; H, 4.76; Cl, 8.37; N, 16.49%.

Ethyl3-((1-formyl-5-(4-methoxyphenyl)-4,5-dihydro-1H-pyrazol-3-yl)amino)-1,4-dihydroquinoxaline-2-carboxylate5c

Orange solid, yield 67%, mp.228-230°C. IR (KBr, cm^{-1}): 3400-3100 (NH), 1735(CO), 1665 (CO), 1565–1655(C=N) cm^{-1}; ^{1}H NMR (400 MHz, DMSO-d_6)δ (ppm):1.29 (t, J = 7.54 Hz, 3H, CH_2CH_3), 4.32 (q, J = 7.55 Hz, 2H, CH_2CH_3),3.68(s,3H,CH_3),4.34(d,2H,CH_2), 5.26(t,1H,CHpyrazole),7.02-8.03(m,Ar-H,8H),8.71(s,1H,NH),10.04(s,1H,CHO), 12.35 (s, 1H, N-HAr), and 12.62 (s, 1H, N-HAr-);^{13}C NMR (125 MHz, DMSO-d6): δ15.16(CH_3) , 37.99($CH_{2\ pyrazole}$),61.71(CH_2),62.79($CH_{pyrazole}$),152.98(C=N),119.82,120.61,127.11,129.33,141.93,88.25 ,136.21(C=C),165.32,169.52(2CO) ppm.MS (ESI): m/z 421.45 (M+). Anal.Calcd. For: $C_{22}H_{23}N_5O_4$: C, 62.70; H, 5.50; N, 16.62%. Found: C, 62.76; H, 5.57; N, 16.65%.

Ethyl 3-((1-formyl-5-(4-nitrophenyl)-4, 5-dihydro-1H-pyrazol-3-yl) amino)-1, 4-dihydroquinoxaline-2-carboxylate5d

Red solid, yield 69%, mp.272-274°C. IR (KBr, cm^{-1}): 3400-3100 (NH), 1733(CO), 1665 (CO), 1565–1655(C=N) cm^{-1}; 1.28 (t, J = 7.54 Hz, 3H, CH_2CH_3), 4.27 (q, J = 7.54 Hz, 2H, CH_2CH_3), 4.34(d,2H,CH_2),5.28(t,1H,CHpyrazole),7.02-8.03(m,Ar-H,8H),8.56(s,1H,NH), 10.08(s,1H,CHO), 12.35 (s, 1H, N-HAr), and 12.62 (s, 1H, N-HAr-) ;^{13}C NMR (125 MHz, DMSO-d6): δ15.21(CH_3) , 37.99($CH_{2\ pyrazole}$),61.71 (CH_2),62.79 ($CH_{pyrazole}$) ,152.98 (C=N),119.82, 120.61,127.11,129.33,141.93,88.25,136.21(C=C),165.32,169.52(2CO) ppm.MS (ESI): m/z 436.42 (M+). Anal.Calcd. For: $C_{21}H_{20}N_6O_5$: C, 57.79; H, 4.62; N, 19.26%. Found: C, 57.82; H, 4.66; N, 19.29%.

General Procedure for the Synthesis of 6a-d

A mixture of chalcone**3a-d** (0.01mmol) and 4-chlorophenylhydrazine (0.01mmol) in ethanol (10 mL) was refluxed for 3 h. The solid product was filtered and recrystallized from ethanol.

Ethyl 3-((1-(4-chlorophenyl)-5-phenyl-4, 5-dihydro-1H-pyrazol-3-yl) amino)-1, 4-dihydroquinoxaline-2-carboxylate6a

Brown solid, yield 66%, mp.233-235°C. IR (KBr, cm^{-1}): 3400-3100 (NH), 1733(CO),1510–1608 (C=C),1565–1655(C=N) cm^{-1}; ^{1}H NMR (400 MHz, DMSO-d_6)δ (ppm):1.25 (t, J = 7.54 Hz, 3H, CH_2CH_3), 4.17 (q, J = 7.54 Hz, 2H, CH_2CH_3) ,4.32(d,2H,CH_2), 5.24(t,1H,CHpyrazole),7.02-8.03(m,Ar-H,13H),8.58(s,1H,NH), 12.35 (s, 1H, N-HAr), and 12.62 (s, 1H, N-HAr-);^{13}C NMR (125 MHz, DMSO-d6): δ15.14(CH_3),37.97($CH_{2\ pyrazole}$),61.68 (CH_2),62.77 ($CH_{pyrazole}$),119.82, 152.98 (C=N),120.61,127.11,129.33,141.93,88.25,136.21(C=C),165.32,169.33 (2CO) ppm.MS (ESI): m/z 473.95 (M+). Anal.Calcd. For: $C_{26}H_{24}ClN_5O_2$: C, 65.89; H, 5.10; Cl, 7.48; N, 14.78%. Found: C, 65.93; H, 5.15; Cl, 7.52; N, 14.84%.

Ethyl 3-((1, 5-bis (4-chlorophenyl)-4, 5-dihydro-1H-pyrazol-3-yl) amino)-1, 4-dihydroquinoxaline-2-carboxylate6b

Yellow solid, yield 71%, mp.255-257-299°C. IR (KBr, cm^{-1}): 3400-3100 (NH), 1735(CO), 1510–1608 (C=C),1565–1655(C=N) cm^{-1}; ^{1}H NMR (400 MHz, DMSO-d_6)δ (ppm):1.32 (t, J = 7.56 Hz, 3H, CH_2CH_3), 4.39 (q, J = 7.58 Hz, 2H, CH_2CH_3), 4.34(d,2H,CH_2), 5.28(t,1H,CHpyrazole)7.02-8.03(m,Ar-H,12H),8.62(s,1H,NH),12.35 (s, 1H, N-HAr), and 12.62 (s, 1H, N-HAr-);^{13}C NMR (125 MHz, DMSO-d6): δ15.28(CH_3) , 37.99($CH_{2\ pyrazole}$),61.71 (CH_2),62.79($CH_{pyrazole}$),152.98(C=N),119.82,120.61,127.11,129.33,141.93,88.25,136.21(C=C),165.32,169.52(2CO)ppm;MS (ESI): m/z 508.40 (M+). Anal.Calcd. For: $C_{26}H_{23}Cl_2N_5O_2$: C, 61.42; H, 4.56; Cl, 13.95; N, 13.78%. Found: C, 61.45; H, 4.61; Cl, 13.99; N, 13.82%.

Ethyl 3-((1-(4-chlorophenyl)-5-(4-methoxyphenyl)-4,5-dihydro-1H-pyrazol-3-yl)amino)-1,4-dihydroquinoxaline-2-carboxylate6c

Green solid, yield 60%, mp.270-272°C. IR (KBr, cm^{-1}): 3400-3100 (NH), 1735(CO),1510–1608 (C=C),1565–1655(C=N) cm^{-1}; ^{1}H NMR (400 MHz, DMSO-d_6)δ (ppm):1.29 (t, J = 7.54 Hz, 3H, CH_2CH_3), 4.32 (q, J = 7.55 Hz, 2H, CH_2CH_3),3.68(s,3H,CH_3),4.34(d,2H,CH_2), 5.23(t,1H,CHpyrazole),7.02-8.03(m,Ar-H,12H),8.71(s,1H,NH), 12.35 (s, 1H, N-HAr), and 12.62 (s, 1H, N-HAr-);^{13}C NMR (125 MHz, DMSO-d6): δ15.16(CH_3) , 37.99($CH_{2\ pyrazole}$),61.71 (CH_2),62.79($CH_{pyrazole}$),152.98(C=N),119.82,120.61,127.11,129.33,141.93,88.25,136.21(C=C),165.32,169.52(2CO) ppm.MS (ESI): m/z 503.98(M+). Anal.Calcd. For: $C_{27}H_{26}ClN_5O_3$: C, 64.35; H, 5.20; Cl, 7.03; N, 13.90%. Found: C, 64.38; H, 5.27; Cl, 7.08; N, 13.95%.

Ethyl 3-((1-(4-chlorophenyl)-5-(4-nitrophenyl)-4, 5-dihydro-1H-pyrazol-3-yl) amino)-1, 4-dihydroquinoxaline-2-carboxylate6d

Reddish brown solid, yield 64%, mp.224-226°C. IR (KBr, cm^{-1}): 3400-3100 (NH), 1733(CO), 1510–1608 (C=C),1565–1655(C=N)cm^{-1}; 1.28 (t, J = 7.54 Hz, 3H, CH_2CH_3), 4.27 (q, J = 7.54 Hz, 2H, CH_2CH_3), 4.34(d,2H,CH_2), 5.28(t,1H,CHpyrazole),7.02-8.03(m,Ar-H,8H),8.56(s,1H,NH), 12.35 (s, 1H, N-HAr), and 12.62 (s, 1H, N-HAr-) ;^{13}C NMR (125 MHz, DMSO-d6): δ15.21CH_3) , 37.99($CH_{2\ pyrazole}$),61.71 (CH_2), 62.79 ($CH_{pyrazole}$) ,152.98 (C=N),119.82, 120.61,127.11,129.33,141.93, 88.25,136.21 (C=C), 165.32, 169.52(2CO) ppm.MS (ESI): m/z 518.95(M+). Anal.Calcd. For: $C_{26}H_{23}ClN_6O_4$: C, 60.17; H, 4.47; Cl, 6.83; N, 16.19%. Found: C, 60.21; H, 4.52; Cl, 6.87; N, 16.26%.

Conclusions

The starting material **2** was obtained in good yield and reacted with different aromatic aldehyde to afford chalcones**3a-d**, pyazoloe 1, 4-dihydroquinoxaline-2-carboxylatederivatives **4,5,6(a-d)** were prepared from reaction of chalcons with substituted hydrazine .these compounds expected to have biological activity .

Conflicts of Interest: The authors declare no conflicts of interest.

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