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REVIEW ARTICLE

Synthetic Strategies of Pyrazoline Derivatives for the Development of New Anticancer Agents: Recent Updates

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Abstract: ***Background*:** Pyrazoline is a heterocyclic compound with five members, two nitrogen atoms in a circle, and one endocyclic bond. Pyrazoline is a popular electron-rich nitrogen carrier that combines exciting electronic properties with the potential for dynamic applications. Pyrazine derivatives have been synthesized using a variety of methods, all of which have shown to have a strong biological effect.

***Objective*:** The study of the biological activity of pyrazoline derivatives has been a fascinating field of pharmaceutical chemistry. Pyrazolines are used in a wide range of applications. The pyrazoline derivatives described in the literature between 2000 and 2021 were the focus of this study. Pyazolines have been discussed in terms of their introduction, general synthetic method, and anticancer potential in the current review.

***Conclusion*:** Pyrazolines are well-known heterocyclic compounds. Pyrazoline is a five-membered ring containing three carbon and two nitrogen atoms nearby. The synthesis of pyrazolines has been described using a variety of methods. Anticancer activity has been discovered in a number of pyrazoline derivatives, which encourages further research. The use of pyrazoline to treat cancer has piqued researchers' interest in learning more about this moiety.

Keywords: Cancer, pyrazoline, anticancer potential, cell lines, receptors, synthetic methods.

1. INTRODUCTION

Pyrazoline is a heterocyclic compound with numerous biological uses. It's the most common fluorescent agent, absorbing light between 300 and 400 nm and emitting blue fluorescence in the process [1]. It's a five-membered ring with only one endocyclic bond and three carbon and two nitrogen atoms [2]. It's derivatives possess many biological activities like antimicrobial [3], antiviral [4], anti-tubercular [5], anti- HIV [6], molluscicides [7], and cerebroprotective [8]. Pyrazoline derivatives are electron-rich nitrogenous heterocycles that are also known as dihydropyrazoles, which are closely related to pyrazoles [9]. Sulfinpyrazone, a pyrazoline derivative, is a potent uricosuric drug that reduces uric acid levels while increasing urine volume. Pyrazolines were found to be cytotoxic to K562 and Jurkat cells. They were also cytotoxic to Daudi, murine melanoma (B16eF10), and nonneoplastic peripheral blood mononuclear cells (PBMC) [10]. This derivative is used clinically as cannabinoid CB1 receptor reverse agonist [11]. The main cytotoxicity of three human cancer cell lines, MCF-7 (breast cancer), K562 (leukemia), and HT-29 (colorectal adenocarcinoma), was examined using the MTT cell viability assay. Axitinib is a pyrazoline-containing VEGFR second-generation inhibitor used to treat renal cell carcinoma [12]. It works by binding to the intracellular tyrosine kinase domains of vascular endothelial growth factor receptors (VEGFRs) [13-15]. It reduces the amount of VEGF protein in the body, preventing angiogenesis and causing cell death [16]. GDC-0941 (pictilisib dimethane sulfonate), a selective p13k inhibitor, is a pyrazoline derivative. It's currently in phase 2 of a clinical trial, and it's an excellent anticancer drug [17]. Pyrazoline-fuses acridine rings (NSC-366140, pyrazinamide, 9-methoxy pyrazole acridine) were discovered as potential anticancer drug candidates in phase 2 clinical trials [18,19]. Li *et al.,* reported 2-pyrazoline derivatives as potential anticancer agents [20].

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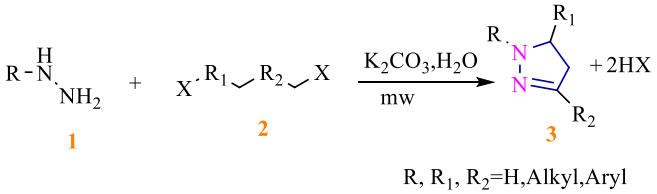
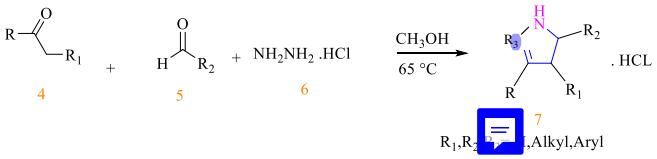
2. COMMON SYNTHETIC ROUTE OF PYRAZOLINE

Ju *et al.*, synthesized pyrazoline derivatives (**3**) from alkyl dihalides (**2**) that reacted with hydrazines (**1**) *via* efficient and straightforward cyclo condensation in an alkaline aqueous medium under microwave irradiation (Scheme **1**). This reaction has the advantages of a clean reaction and a high yield, but it also has the disadvantage of a long reaction time [21].



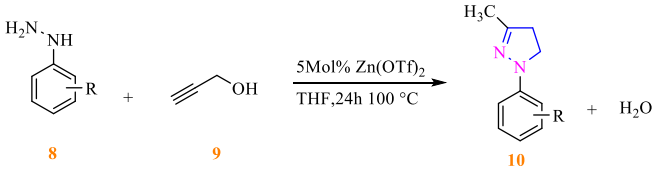
Scheme 1. Synthetic Scheme of nitrogen contains compound and pyrazoline derivatives.

Lellek *et al.*, reported the synthesis of pyrazoline derivatives (**7**) from various alkyl or aryl compounds (**4**)**,** ketones (**5**)**,** and hydrazine monohydrochloride (**6**) in the presence of methanol (Scheme **2**). The advantages of this reaction are its cleanliness and quickness, while the disadvantage is the lack of scope investigations for hydrazine [22].



Scheme 2. One-Pot three-component coupling in methanol to form pyrazoline derivatives

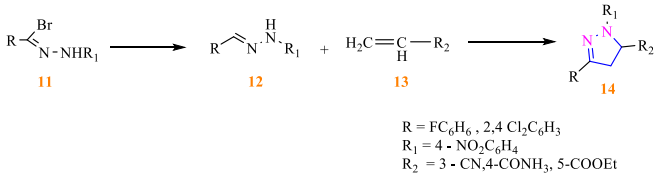
Alex *et al.*, reported that pyrazoline derivatives (**10**) were synthesized from arylhydrazines (**8**) that reacted regioselectively with 3-butynol (**9**) in the presence of a catalytic amount of zinc triflate to give aryl-substituted pyrazolines (Scheme **3**). Advantages of this reaction are regioselectivity and disadvantages of this reaction are the method not investigated for other hydrazines and butynols [23].



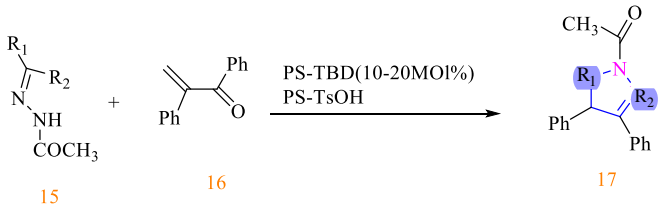
Scheme 3-Synthetic scheme of pyrazoline derivatives

Yusuf *et al.*, reported the synthesis of pyrazoline derivatives (**14**) from 1,3-diaryl-5-(cyano-, aminocarbonyl- and ethoxycarbonyl-)-2-pyrazoline, pyrrolo[3,4-c]pyrazole-4,6-dione and 1,3,4,5-tetraaryl-2-pyrazoline derivatives (Scheme **4**). The advantage of this reaction is its usefulness for the synthesis of 2-pyrazolines possessing an electron-withdrawing functional group on the N1 nitrogen [24].

Gembus *et al.*, investigated that pyrazoline derivatives (**17**) were synthesized from hydrazones (**15**) that reacted with terminal enones (**16**) in the presence of PS-TBD and PS-TsOH to form pyrazoline *via* base-catalyzed aza-Michael (Scheme **5**). The advantages of this reaction are an efficient method to access chiral 2-pyrazolines bearing a polar group on N1 (usually an electron-withdrawing group disadvantage of this reaction is limited scope for hydrazine [25].

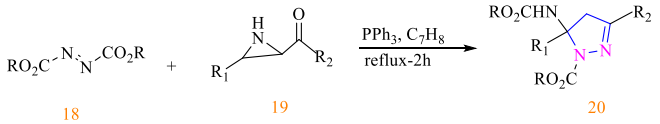


Scheme 4. Synthesis of 1,3-Diaryl-5(cyano-aminocarbonyl-andethoxycarbonyl-)-2-pyrazoline derivatives**.**



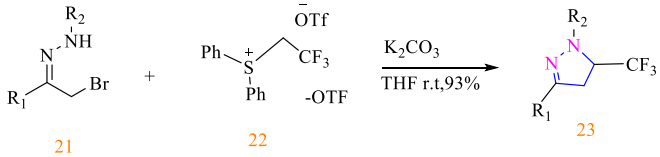
Scheme 5. Synthesis of pyrazoline derivatives from hydrazone

Cui *et al.*, reported the use of Huisgen zwitter ions to synthesise pyrazoline derivatives (**20**) from novel 2-pyrazolines and specific atom response of 2-acylaziridines (Scheme **6**). This reaction has the advantages of being low cost and safe due to the use of water as a solvent, as well as having a short reaction time [26].



Scheme 6. Synthesis 2-acylaziridines and pyrazoline derivatives**.**

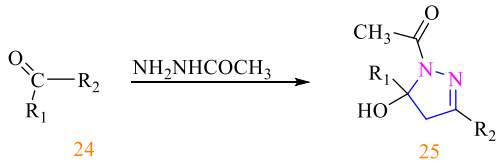
Wang *et al.*, reported the synthesis of pyrazoline derivatives (**23**) from 1,2-diaza-1,3-dienes (**21**) using informal [4 + 1]-annulation reactions with fluorinated sulphur ylides (**22**) to give 5-(trifluoromethyl) pyrazolines (Scheme **7**). Excellent yields are one of the benefits of this reaction. The long reaction timeis a disadvantage of this reaction [27].



Scheme 7. Synthesis of pyrazoline derivatives from 1-2-diaza-1,3-dines

Waldo *et al.* reported the synthesis of pyrazoline derivatives (**25**) from 2-alkyn-1-ones (**24**), various 1-acyl-5-hydroxy-4,5-dihydro-1*H*-pyrazoles are synthesized in high

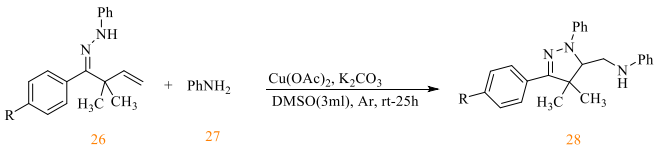
yields. In the presence of ICl and Li2CO3 at room temperature, the dihydropyrazoles undergo hydration and iodination, yielding 1-acyl-4-iodo-1H-pyrazoles (Scheme **8**). The advantage of this reaction process is very simple [28].



R_1= Ph, 2-naphthyl, P-FC_6H_4, P-ClC_6H_4, P-BrC_6H_4, P-$CF_3C_6H_4$, P-NCC_6H_4, P-t-BuC_6H_4, P-$Me_2C_6H_4$, O-MeC_6H_4
R_2=Ph, P-$EtO_2CC_6H_4$, n-Bu

Scheme 8. Synthesis of pyrazoline derivatives from 2-alkyn-1-ones

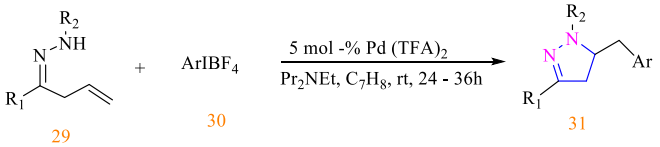
Chen *et al.* reported the synthesis of pyrazoline derivatives (**28**) from copper-catalyzed intramolecular/and intermolecular deamination of beta, gamma-unsaturated hydrazones (**26**) with simple amines (**27**) enable productive permission to various nitrogen-containing pyrazolines (Scheme **9**). The disadvantage of this reaction process is that it takes an excessive amount of time [29].



R= H, Br, Cl, CH3, OCH3, isopropyl, Ts, Ac

Scheme 9. Synthesis of pyrazoline derivatives from hydrazones and amines.

Yang *et al*., reported the synthesis of pyrazoline derivatives using an efficient and synchronous arrangement of C(sp3)- N and C(sp3)- C(sp2) derivatives under mellow conditions, a free-ligand, palladium-catalyzed aminoarylation of unactivated alkenes in beta-gamma-unsaturated hydrazones gives differently subbed dihydropyrazoles (Scheme **10**). The benefits of this reaction are high yields, but the disadvantages are that it takes a long time [30].



R_1=R_2=H, CH_3, Cl, Br, OCH_3, 4-ClC_6H_4, 2,4,6-MeC_6H_2
Ar = Ph, 4-CN-C_6H_4, 4-Br-C_6H_4, 2-Me-C_6H_4, 1-naphthyl

Scheme 10. Synthesis of pyrazoline derivatives from β, γ-unsaturated hydrazone

3. POTENTIAL TARGETS FOR PYRAZOLINE DERIVATIVES AND SYNTHETIC SCHEME

Kumar *et al.*, reported the synthesis of pyrazoline derivatives from 3-(4, 5-dihydro-1-phenyl-5-substituted phenyl-1H-pyrazol-3-yl)-2*H*-chromen-2-one (**35**). The synthesized compounds were screened for their anticancer activity against MDA-MB-231/ATCC, CAK-1, UO-31, NCI-H522. The 3-(4, 5-Dihydro-5-(4-hydroxyphenyl)-1-phenyl-1Hpyrazol-3-yl)-2H-chromen-2-one (**36**) showed potent activity due to the presence of electron-donating capacity of hydroxyl group as shown in Scheme **11** [31].

George *et al.*, reported synthesis of 4,5-dihydro-1-(4-phenylthiazol-2-yl)-1H-pyrazole derivatives (Scheme **12**) and their evaluation as anticancer agents against MCF-7, HELA, DLD1 cell lines. The 2-[5-(2-Chloro-6-methoxyquinolin-3-yl)-3-(p-tolyl)-4,5-dihydro1H-pyrazol-1-yl]-4-(4-fluorophenyl)thiazole (**38**) and 2-[5-(2-Chloro-6-methoxyquinolin-3-yl)-3-(p-tolyl)-4,5-dihydro1H-pyrazol-1-yl]-5-phenylcarbamoyl-4-methylthiazole (**39**) showed more potent activity in nanomolar concentration with (IC_{50} =31.8 and 42.52 nM, respectively) as EGFR inhibitors compared to gefitinib (IC_{50} = 29.16 nM) [32].

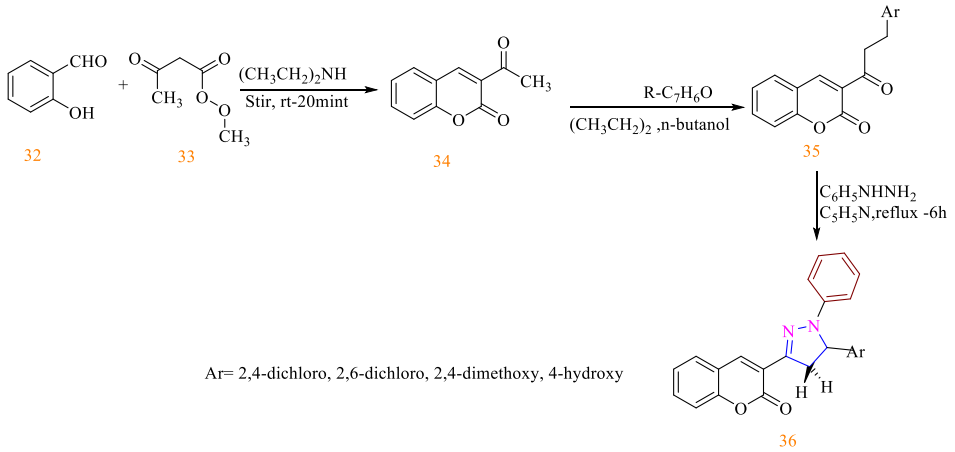
Abdel-Aziz *et al.*, reported the synthesis of 1-(3',4',5'-trimethoxybenzoyl)-3,5-diarylpyrazoline derivatives (**45**) (Scheme **13**). The pyrazoline derivatives were screened for their anti-tumor activity against CCRF-CEM, A549/ATCC, COLO205, SF-268, M14, IGROV1, MCF-7, MDA-MB-468, TK-10. 5-(4-Cyanophenyl)-4,5-dihydro-1-(3,4,5-trimethoxybenzoyl)-3-(3,4-dimethoxyphenyl)-1H-pyrazole (**45**) and 1-(3,4,5-trimethoxybenzoyl)-4,5-dihydro-5-(4- methoxyphenyl)-3-(3,4-dimethoxyphenyl)-1H-pyrazole (**45**) showed potent activity with excellent tubulin polymerization inhibitory activity with IC_{50} 17±2 and 40±2 µM [33].

James *et al.*, reported the synthesis of pyrazoline derivatives started substituted aldehyde and substituted acetophenones in ethanol (Scheme **14**). The synthesized compounds were screened for their anti-tumor activity against EAC (Ehrlich-Lettre ascites carcinoma) cell lines using tryphan blue exclusion method. 5-(Anthracen-9-yl)-3-(4-bromophenyl)-1-tosyl-4,5-dihydro1*H*-pyrazole (**49**) showed potent activity on EAC cell lines [34].

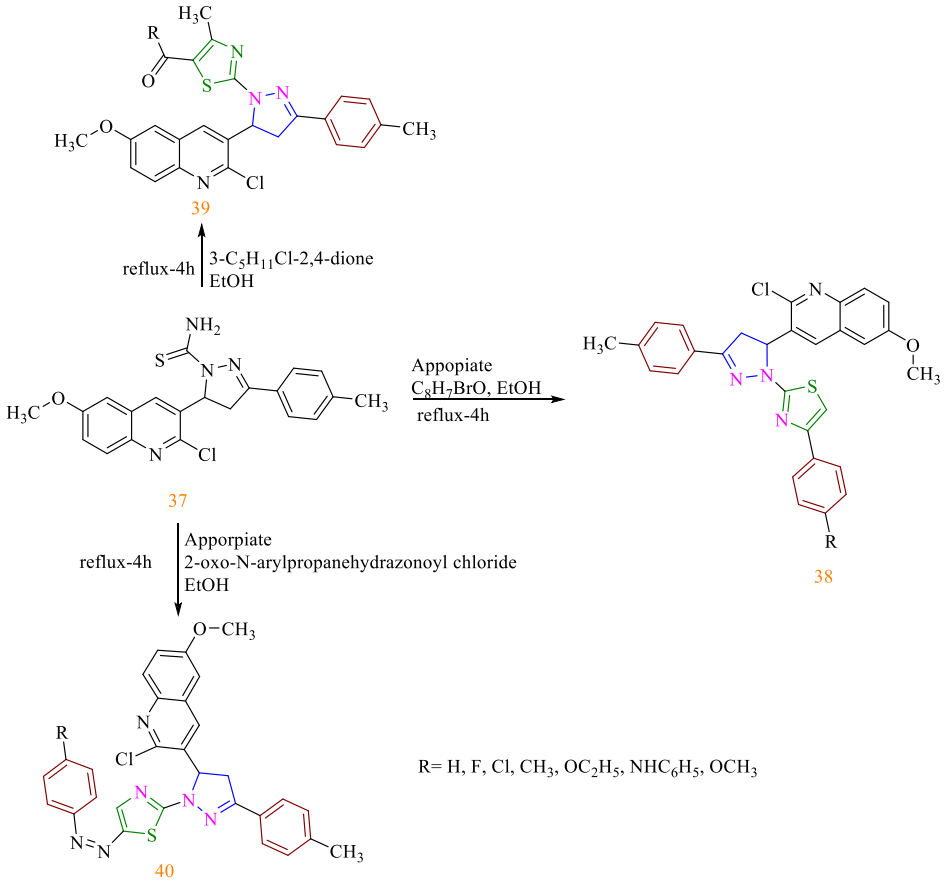
Taj *et al.*, reported the synthesis of pyrazoline derivatives from 3-[4-(5-aryl-4,5-dihydro-1H-pyrazol-3-yl)]phenylsydnone in the presence of concentrated hydrochloric acid, absolute alcohol, and addition of cyclohexanone by the cyclization process afforded the synthesis of 6,7,8,9-tetrahydro2-(4,5-dihydro-5-aryl-1H-pyrazol-3-yl)-5*H*-carbazoles (**51**) (Scheme **15**). The pyrazoline derivatives were screened for their anticancer activity A498, LC50, and TGI cell lines. The compounds substituted with R= P-hydroxyphenyl (**51**) showed significant activity [35].

Akhtar *et al.*, reported the synthesis of pyrazoline bearing benzimidazole derivatives by cyclocondensation reaction of 2-(1H-benzo[d]imidazole-2-yl)-1-(3,5-bis(4-substituted)-4,5-dihydro-1H-pyrazol-1-yl) ethenone (Scheme **16**). The synthesized compounds tested for their anticancer activity against five cancer cell lines like MCF-7, MDA-MB231, As49, HaCaT, and HePG2. The compound substituted with R= Cl group and R_1. Cl group (**55**) showed more potent activity against the lung cancer (A549) cell line with IC_{50} value of 2.2µM [36].

Shahryar *et al.*, reported the synthesis of pyrazoline bearing benzimidazole derivatives 2-{5-[(substituted) phenyl]-1-phenyl-4,5-dihydro-1H-3-pyrazolyl}-1H-benzimida-zole (**61b**) and 2-{5-[(substituted)phenyl]-4,5-dihydro-1H-3-pyrazolyl}-1H-benzoimidazole (**61a**) (Scheme-**17**). The synthesized compounds were tested for their anticancer activity



Scheme 11. Synthesis of pyrazoline from 3-(4,5-dihydro-1-phenyl-5-substituted phenyl-1*H*-pyrazol-3-yl)-2*H*-chromen-2-one derivatives**.**

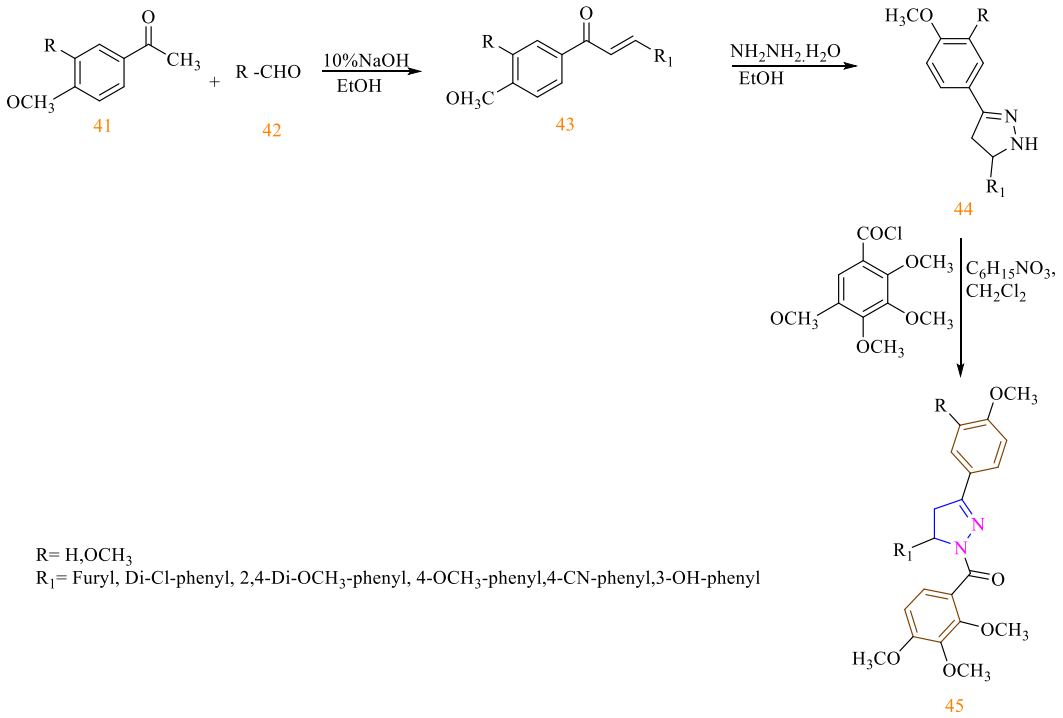


Scheme 12. Preparation of quinoline, thiazole, clubbed pyrazoline derivatives.

against CCRF-CEM, A549, Colon -205, SF-268, M14, MCF-7 cell lines. The 2-[5-(3,4-dimethoxyphenyl)-1-phenyl-4,5-dihydro-1*H*-3-pyrazolyl]-1H-benzimidazole (NSC-748326) (**61b**) showed significant anticancer activity [37].

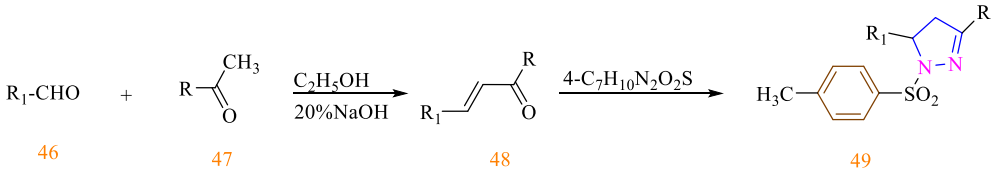
Havrylyuk *et al.*, reported the synthesis of 4-(5-aryl-3-phenyl-4,5-dihydro-1H-pyrazol-1-yl-1,3-thiazol-2(5*H*)-ones (Scheme **18**). The synthesized compounds were evaluated for their anticancer activity against rectal tumor cell lines, particularly at HT 29. 5-(4-Hydroxy-3,5-dimethoxybenzylidene)-2-[5-(2-hydroxyphenyl)-3-phenyl-4,5-dihydro-1*H*-pyrazol-1-yl]-1,3-thiazol-4(5H)-one (**64**) showed potent activity against colon cancer cell lines, particularly on HT 29 (log GI_{50}= -6.37) [38].

Karabacak *et al.*, reported the synthesis of 1-[(aryl)thioacetyl]-3-(2-thienyl)-5-(4-chlorophenyl)-2-pyrazoline derivatives (Scheme **19**). The synthesized compounds screened for their anticancer activity against AsPC-1 and U2 51 cancer Cell lines. 1-[((5-(4-methylphenyl)-1,3,4-oxadiazol-2-yl) thio) acetyl]-3-(2-thienyl)-5-(4-chlorophenyl)-2-pyrazoline (**69**) were found to be more potent compound against AsPC-1 and U2 51 cell lines with IC_{50} values of 16.8 and 11.9 µM respectively [39].



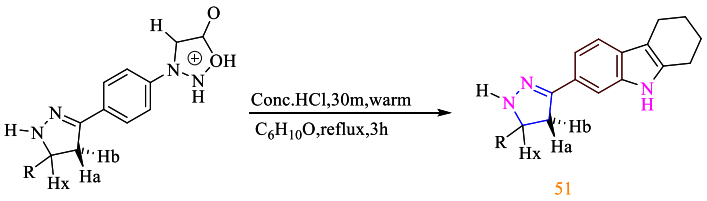
R= H,OCH_3
R_1= Furyl, Di-Cl-phenyl, 2,4-Di-OCH_3-phenyl, 4-OCH_3-phenyl,4-CN-phenyl,3-OH-phenyl

Scheme 13. Synthesis of novel pyrazoline derivatives.



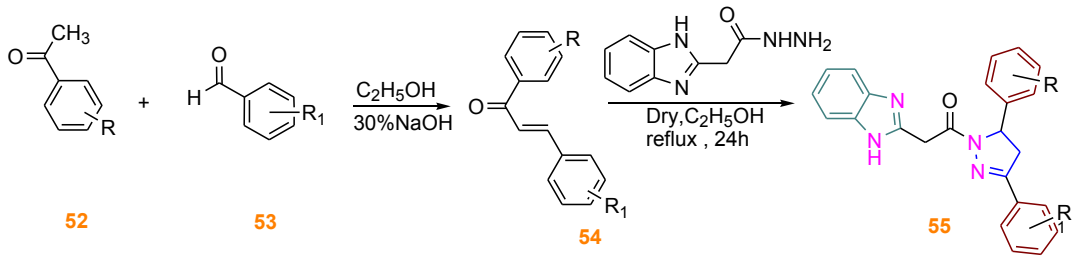
R= 4 - Cl -C_6H_4, 4 - Br -C_6H_4, 4 -F - C_6H_4, 4 -NH_2 -C_6H_4, 4 -OH - C_6H_4, 4 - NO_2 -C_6H_4, 4 -CH_3 - C_6H_4
R_1=Pyridine, Pyrolle, Anthraldehyde, Isoniazid, Streptomycin, 5-Fluorouracil

Scheme 14. Synthesis of pyrazoline derivatives**.**



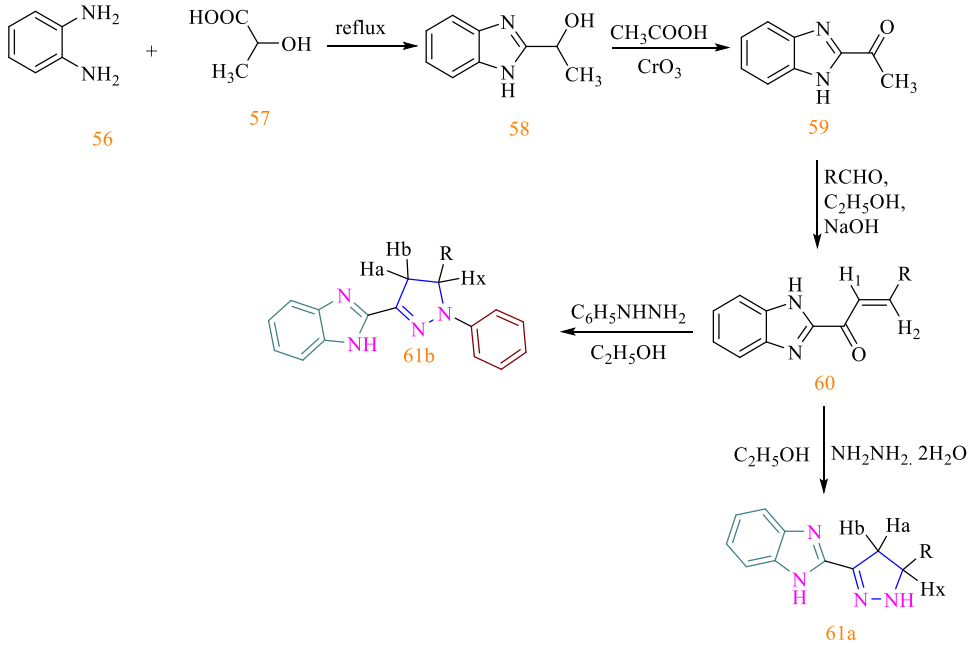
R=phenyl, o-chlorophenyl, m-chlorophenyl, p-chlorophenyl, p-nitrophenyl, o-hydroxyphenyl,p-hydroxyphenyl, styryl, methyl, p-anisyl, p-tolyl

Scheme 15. Synthesis of pyrazoline derivatives from tri-cyclic carbazoles sydnone



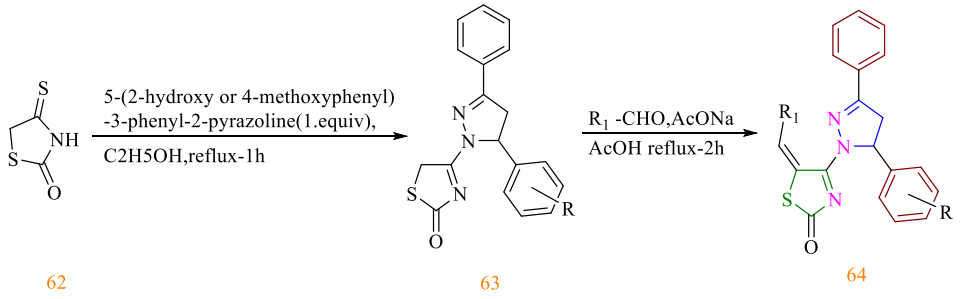
R= 4-Cl, 4-OCH_3, 4-CH_3, 4-OH
R_1= 4-Cl, 4-Br, 4-F

Scheme 16. Synthesis of pyrazoline bearing benzimidazole derivatives



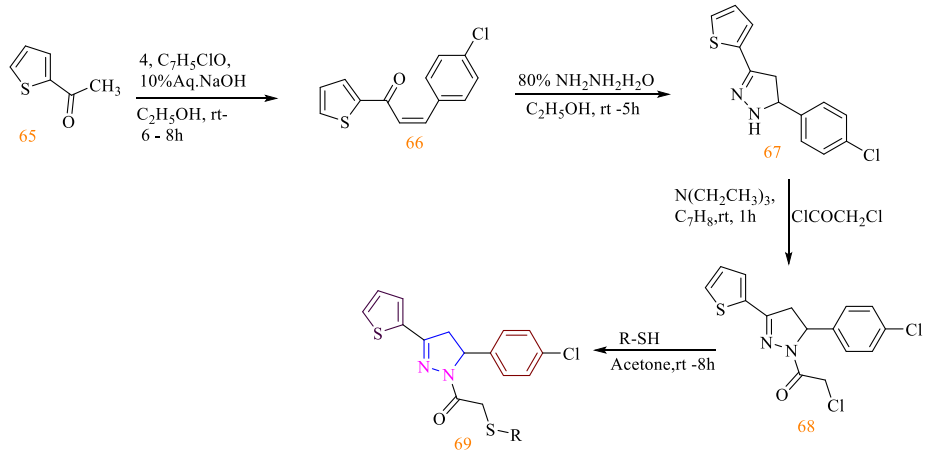
R = Phenyl, 4-methoxyphenyl, 4-chlorophenyl, 4-bromophenyl, 4-flurophenyl , 3,4-dimethoxyphenyl, 2,6-dichlorophenyl

Scheme 17. Synthesis of 2-acetyl pyrazoline bearing benzimidazole derivatives.



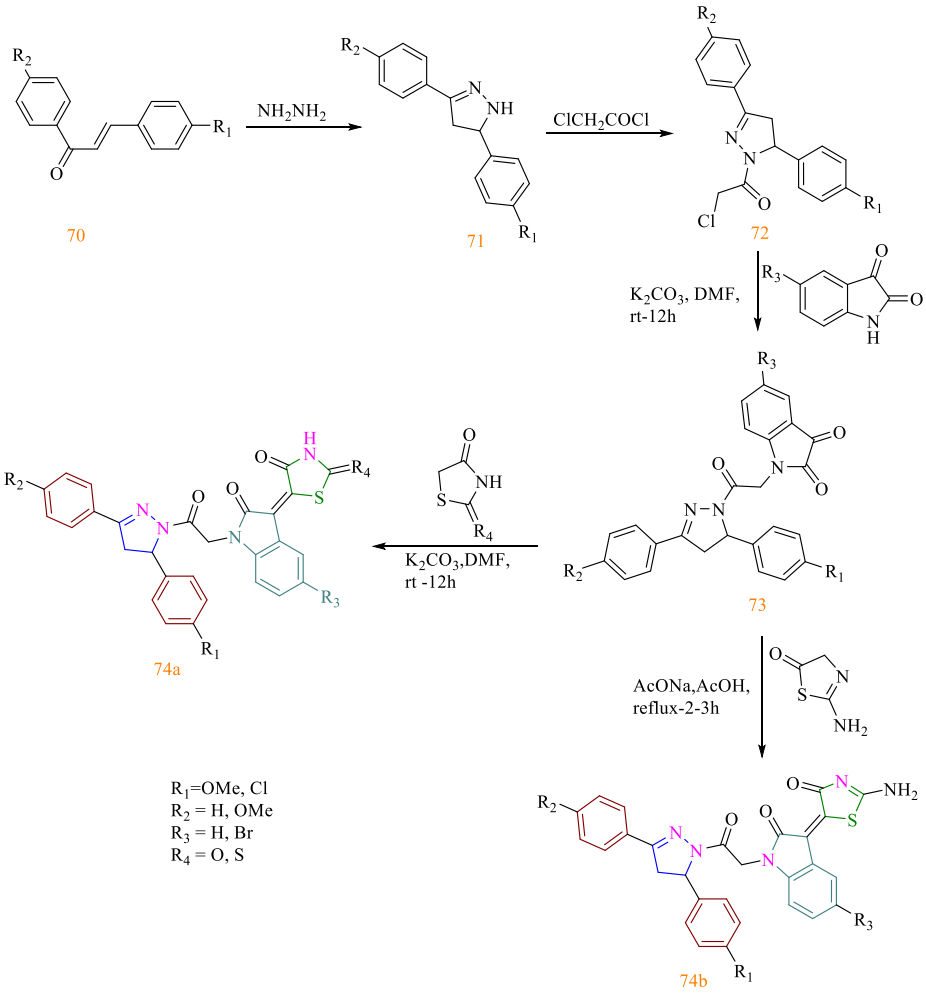
R= 2-OH, 4-OMe
R_1=Ph, 4-Cl-C_6H_4, 4-Br-C_6H_4, 4-OH-C_6H_4, 4-OMe-C_6H_4, 4-NMe_2-C_6H_4, 4-NO_2-C_6H_4, 2-Cl-C_6H_4, 3-Br-C_6H_4

Scheme 18. Prepration of novel 4-(5-aryl-3-phenyl-4,5-dihydro-1H-pyrazol-1-yl-1,3-thiazol-2(5*H*)-ones.



R=4-methyl-4H-1,2, 4-triazole, 1-methyl-1H-tetrazole, 1-phenyl-1H-tetrazole, 4-(1H-tetrazol-1-yl)phenol, N,N-dimethyl-2-(1H-tetrazol-1-yl)ethanamine, 2-methyl-1,3,4-thiadiazole, pyrimidine, 2-phenyl-1,3,4-oxadiazole, 3-(1,3,4-oxadiazol-2-yl)pyridine, 2-(4-chlorophenyl)-1,3,4-oxadiazole, 2-(4-methylphenyl)-1,3,4-oxadiazole, 2-(4-methylphenyl)-1,3,4-oxadiazole

Scheme 19. Synthesis of pyrazoline derivatives.



Scheme 20. 1,3-Dhydroindol-2-one conjugates with 3,5-diaryl-4,5-dihydropyrazole and thiazolidinone Derivatives.

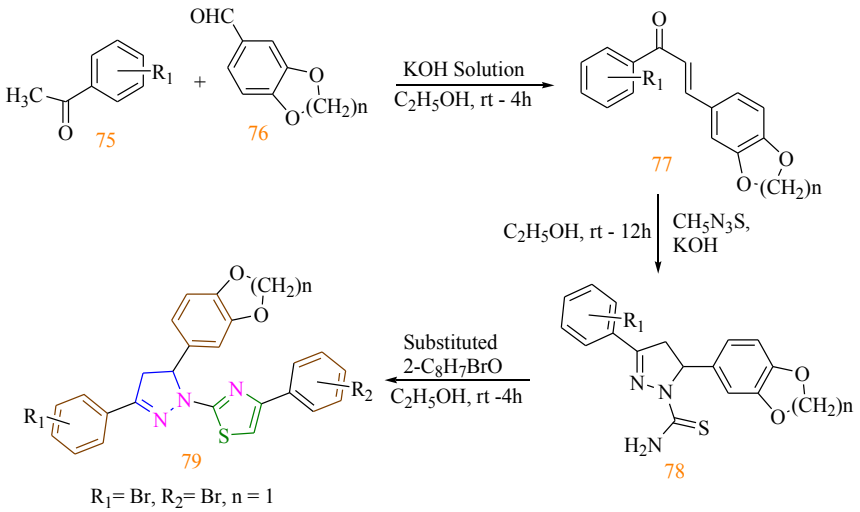
Havrylyuk *et al.*, synthesized pyrazoline derivatives clubbed novel 1,3-dihydroindol-2-one conjugates with 3,5-diaryl-4,5-dihydropyrazole and thiazolidinone derivatives (Scheme **20**) and evaluated their *in-vitro* anticancer activity against leukemia, and MCF-7 cell lines. 5-Bromo-1-{2-[5-(4-chlorophenyl)-3-(4-methoxyphenyl)-4,5-dihydropyrazol-1-yl]-2-oxoethyl}-1H-indole-2,3-dione (**73**) showed the most potent activity among the series of compounds against on leukemia cell line with GI_{50} value range of 0.69-3.35 µM [40].

Wang *et al.,* reported the synthesis of pyrazoline derivatives by thiazolyl- pyrazoline containing benzodioxole (Scheme **21**). The synthesized derivatives were screened for their anti-tumor activity against MCF-7 and B16-F10. 2-(5-(Benzo[d][1,3]dioxol-5-yl)-3-(4-bromophenyl)-4,5-dihydro-1*H*-pyrazol-1-yl)-4-(4-bromophenyl)thiazole (**79**) showed significant activity against MCF-7 and B16- F10 with IC_{50} value of 0.09 and 0.12 µM [41] .

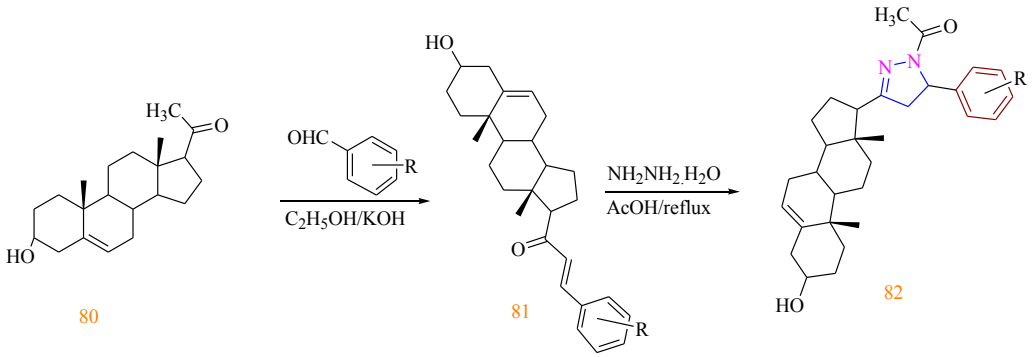
Banday *et al.,* reported the synthesis of pyrazoline derivatives vis formation of chalcone from carbonyl containing steroidal ring with aromatic aldehydes (Scheme **22**). The synthesized derivatives were evaluated for their anticancer activity against HT-29, HCT-15,502713, HOP-62, A-545, MCF-7, SF-295 cell lines. 1-(5-(2-Chlorophenyl)-4,5-dihydro-3-((10R,13S)- 2,3,4,7,8,9,10,11,12,13,14,15,16,17-tetradecahydro-3-hydroxy-10,13-dimethyl-1*H*-cyclopenta[a] phenanthren-17-yl)pyrazol-1-yl)ethenone (**82**) showed potent activity particularly against HT-29 and HCT-15, 502713 cell lines [42].

Al-Abdullah *et al.*, investigated that pyrazoline derivatives were synthesized *via* chalcone fromed from 1-(5,6,7,8-tetrahydronaphthalen-2-yl) ethenone with aromatic aldehyde in the presence of sodum hydroxide in ethanol (Scheme **23**). The synthesized compounds were screened for their anti-tumor activity against Hela and breast tumor cell lines. 3-(2,6-Dichlorophenyl)-1-(1,2,3,4-tetrahydronaphthalen-6-yl)prop-2-en-1-ones (**85**) showed more potent activity against Hela and MCF-7 with IC_{50}=3.5 and 4.5µg/ml [43].

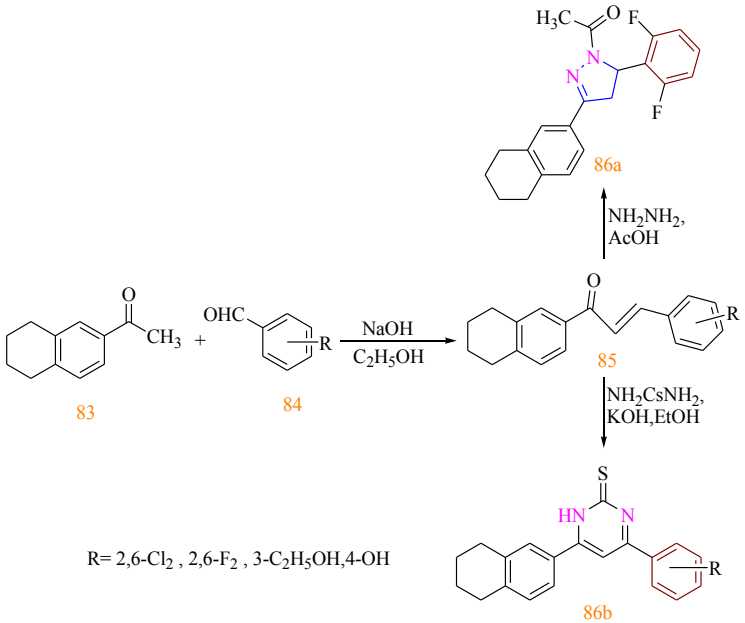
Lv *et al.,* reported the synthesis of pyrazoline derivatives *via* formation of chalcone from substituted acetophenone with a substituted aromatic aldehyde in the presence of sodium hydroxide to form chalcone derivatives (Scheme **24**). The synthesized compounds were screened for their anticancer activity against the MCF7 cell line. It was observed that constituents substituted with R_1=3,4-2CH_3, R_2=4-F, R_3=4-Cl showed potent activity against MCF-7 with IC_{50} value of 0.07 µM [44].



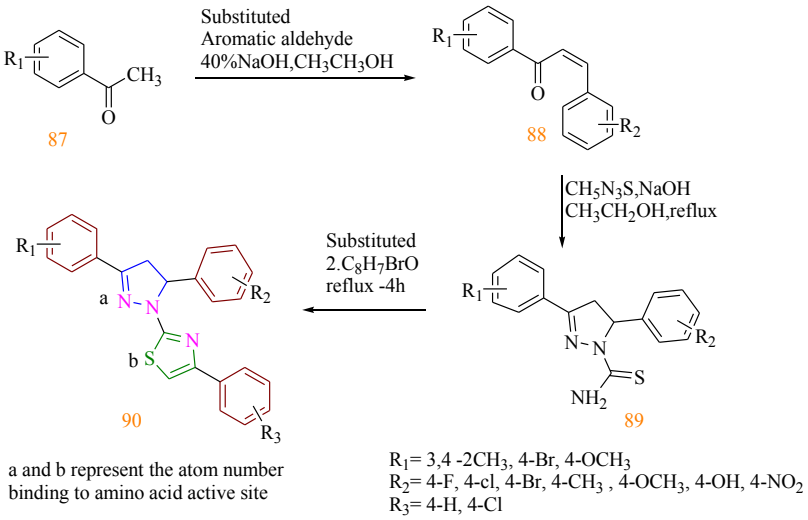
Scheme 21. Syntheis of thiazolyl pyrazoline derivatives.



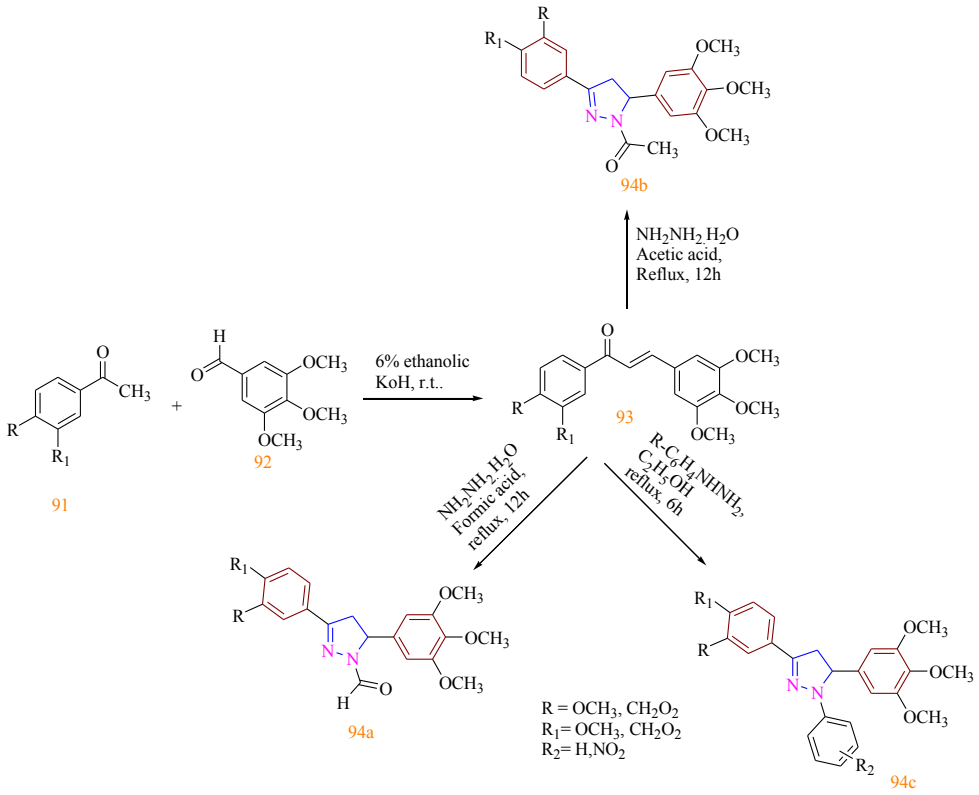
Scheme 22. Synthesis of D-ring substituted steroidal pyrazoline.



Scheme 23. Synthesis of tetrahydronaphthalenes thioxopyrimidine oxopyradine and pyrazoline derivatives



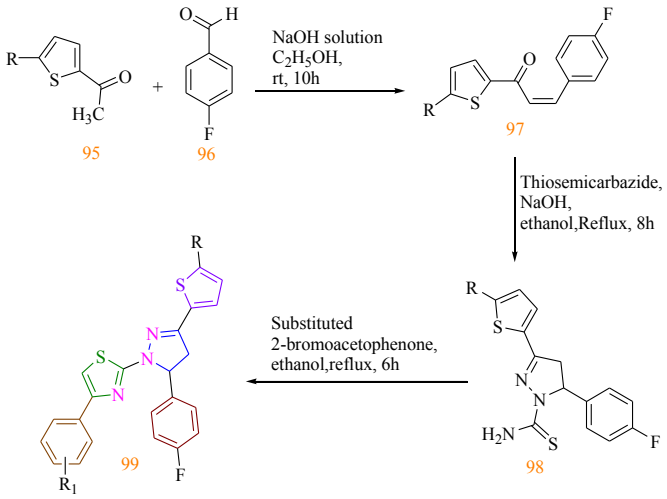
Scheme 24. Synthesis of thiazolyl pyrazoline derivatives.



Scheme 25. Synthesis of polymethoxy chalcones and pyrazoline derivatives

Rostom *et al.,* investigated the synthesis of pyrazoline derivatives vis the formation of chalcone from 1-phenylethanone with 3,4,5-trimethoxybenzaldehyde in the presence of ethanolic/potassium hydroxide to form (2*E*)-1-phenyl-3-(3,4,5-trimethoxyphenyl) prop-2-en-1-one (Scheme **25**). The synthesized derivatives evaluated for their anti-cancer activity against MG-MID and TGI-MG-MID cell lines. 3-(Benzo[1,3]dioxol-5-yl)-5-(3,4,5-trimethoxyphenyl)-4,5-dihydropyrazole-1-carbaldehyde (**94a**) and 1-(3-(benzo [1,3] dioxol-5-yl)-5-(3,4,5-trimethoxyphenyl)-4,5-dihydro-pyrazol-1-1-yl) ethenone (**94b**) showed remarkable growth inhibitory activities with GI50 MG-MID values of 2.10 and 1.38 µM respectively [45].

Altintop *et al.,* investigated the synthesis of pyrazoline *via* formation of chalcone from 1-thiophen -2-yl-ethanone react with 4-F-benzaldehyde in the presence of sodium hydroxide in ethanol (Scheme **26**). The synthesized compounds were screened for their anticancer activity against A549, NIH/3T3 cancer cell lines. The 2-[5-(4-fluorophenyl)-3-(5-chlorothiophen-2-yl)-4,5-dihydro-1H-yl]-4-(4-bromophenyl) thiazole (99) was found to be a more potent anticancer agent against A549 cells with IC_{50} value of 62.5 µM [46].



R= 4-F-phenyl
R_1= 4-chlorophenyl, 4-bromophenyl, 4-nitrophenyl, 4-cyanophenyl, 4-methylsulfonylphenyl, 4-methylphenyl, 1,3-benzodioxol, 4-trifluoromethylphenyl

Scheme 26. Synthesis of thiazolyl pyrazoline derivatives.

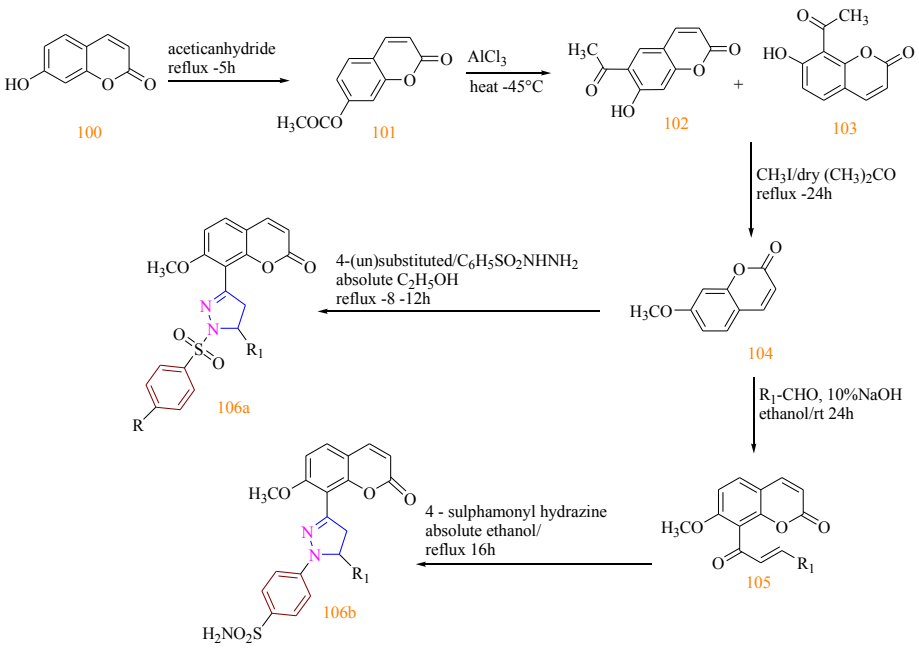
Amin *et al.,* synthesized that pyrazoline derivatives were synthesized from two groups of coumarin with acetic anhydride (Scheme **27**). The synthesized compounds were screened for their anticancer activity against CCRF-CEM, A549, HCT-116, SNB-19, M-14, OVCAR-3, UO-31, PC-3, MCF-7, P13K(p110/p81). 8-[1-(4-Chlorophenylsulfonyl)-5-phenyl-4,5-dihydro-1H-pyrazol-3-yl]-7-methoxy-2H-chromen-2-one (**106a**) showed potent activity against MCF-7 and HCT-116 with IC_{50} value of 0.01µM [47].

Garazd *et al.,* reported the synthesis of pyrazoline derivatives from coumarins derivatives with acetic anhydride (Scheme **28**). The synthesized compounds were tested for their anticancer activity against CCRF-CEM, A549, HCT-116, SNB-19, M-14, OVCAR-3, UO-31, PC-3, MCF-7, and MOLT-4 cell lines. 1-Hydroxy-2-[5-(4-hydroxy-3-methoxyphenyl)-4,5-dihydropyrazol-3-yl]-3-methyl-7,8,9,10-tetrahydrobenzo[c]chromen-6-one (**111**) showed the most potent activity against CCRF-CEM and MOLT-4 with IC_{50}/TGT value of 1.88/5.06µM and 1.92/4.04µM respectively [48].

Mansour *et al.,* reported the synthesis of pyrazoline derivatives 2-(5-(Benzo[d][1,3]dioxol-5-yl)-3-(naphthalen-1-yl)-4,5-dihydro-1H-pyrazol-1-yl)-4-(4-substituted phenyl)thiazole (Scheme **29**). The synthesized compounds were evaluated for their anticancer activity against HCT-116, BHK, HEP-G2, MCF-7. 2-(5-(Benzo[d][1,3]dioxol-5-yl)-3-(naphthalen-2-yl)-4,5-dihydro1H-pyrazol-1-yl)-4-(4-chlorophenyl) thiazole (**117**) was found to be more potent against HCT-116 cell line with an IC_{50} value of 6.19µM [49].

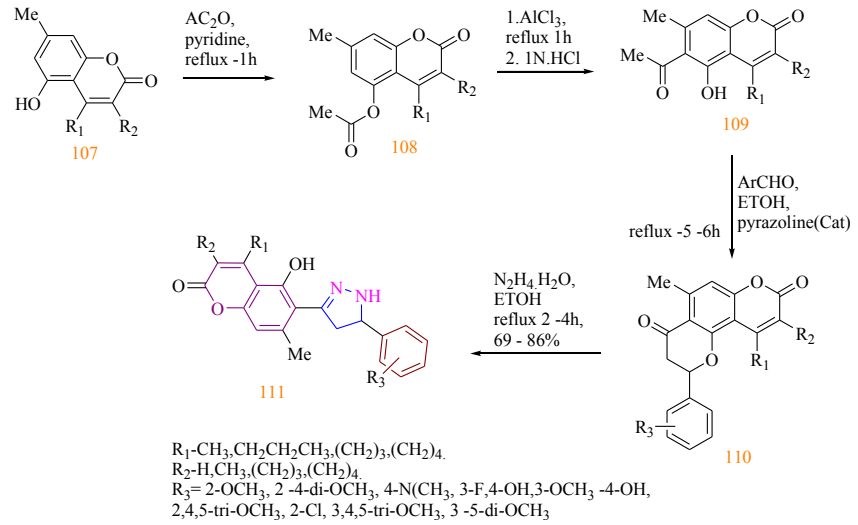
Saleem *et al.,* investigated the synthesis of pyrazoline derivatives *via* chalcone formation from 1-(4-fluorophenyl)ethanone with 4-chlorobenzaldehyde in the presence of methanolic sodium hydroxide (Scheme **30**). The synthesized compounds were evaluated for their anticancer activity against MCF-7 cell lines. (5-(4-Chlorophenyl)-3-(4-flurophenyl)-4,5-dihydro-1*H*-pyrazoline-1-carbothioamide showed significant activity against MCF-7 cell line [50].

Ravula *et al.,* investigated the synthesis of pyrazoline derivatives from dimethyl triazene that incorporated thiazolyl pyrazoline (Scheme **31**). The synthesized compounds were evaluated for their anti-tumor activity against human genus cancer (MCF-7) and colon cancer (HT-29) cell lines. (*E*)-4-(4-Chlorophenyl)-2-(3-(4-(3,3-dimethyltriaz-1-enyl) phenyl)-5-(4-methoxyphenyl)-4,5-dihydro-1H-pyrazol-1-yl) thiazole (**127**) showed potent activity against MCF-7 and HT-29 cell lines [51].

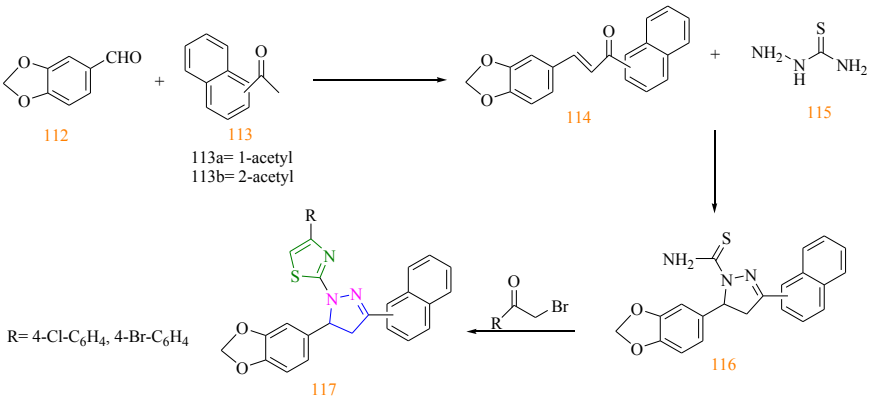


R= H, CH_3, Cl
R_1= 5-CH_3-C_4H_2O, C_4H_3S, C_6H_5, 4-CH_3-C_6H_4, 4-CF_3-C_6H_4, 4-SCH_3-C_6H_4, 5-CH_3-C_4H_2O,

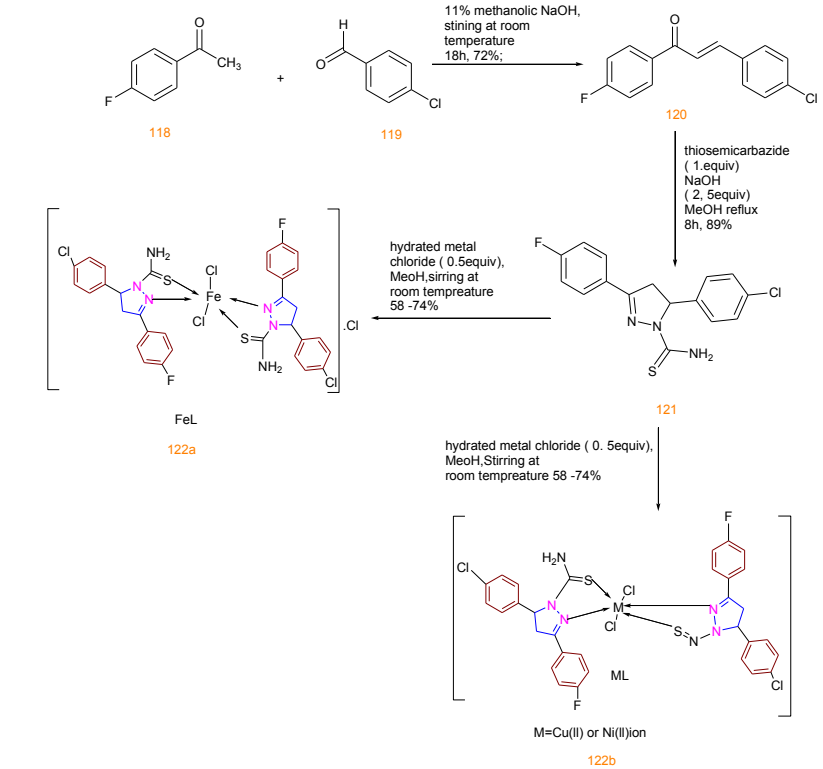
Scheme 27. Synthesis of coumarin clubbed pyrazoline derivatives



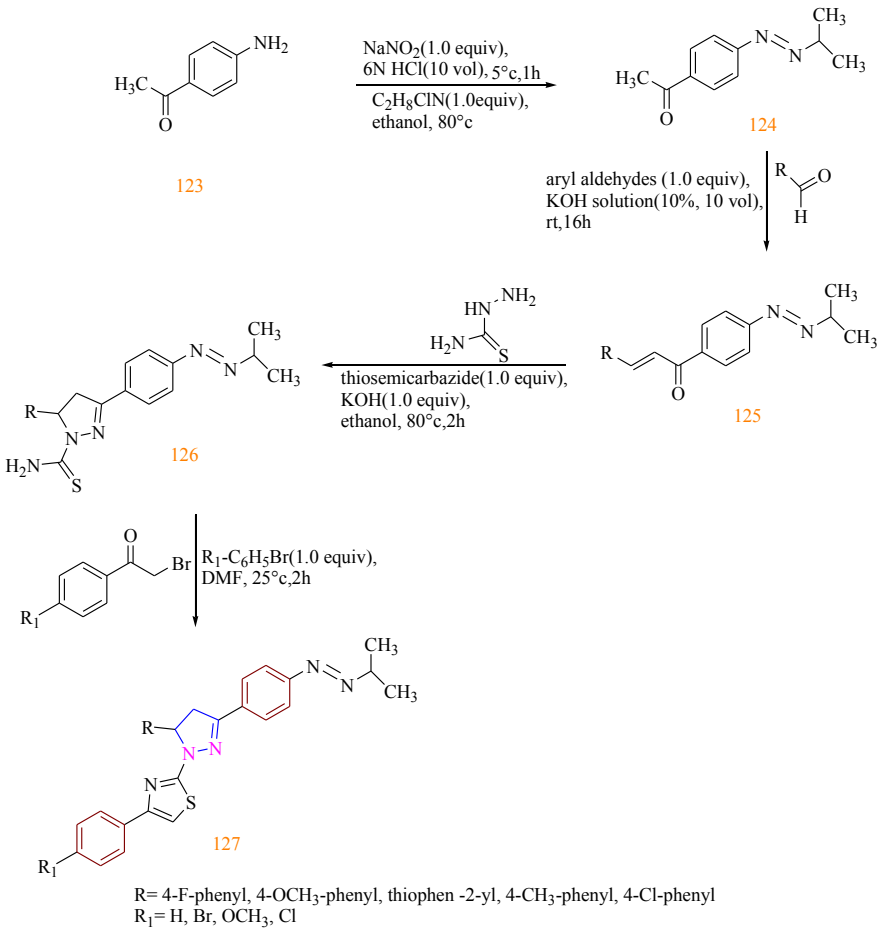
Scheme 28. Synthesis of 6-pyrazolinylcoumarins derivatives.



Scheme 29. Synthesis of thiazolyl pyrazoline derivatives.



Scheme 30. Synthesis of metal complexed pyrazoline derivatives.



Scheme 31. Synthesis of thiazolyl pyrazoline derivatives.

Kuthyala *et al.,* reported the synthesis of pyrazoline derivatives from a combination of Imidazopyridine-connected pyrazoline analogs (Scheme **32**). The synthesized compounds screened for their anticancer activity against A549 cell lines. The compound substituted with R= methyl-Pyr, R_1=3-Cl-C_6H_5, R_2= $CH_3CH_2CH_2CO$ (131) showed potent activity against the A549 cell line [52].

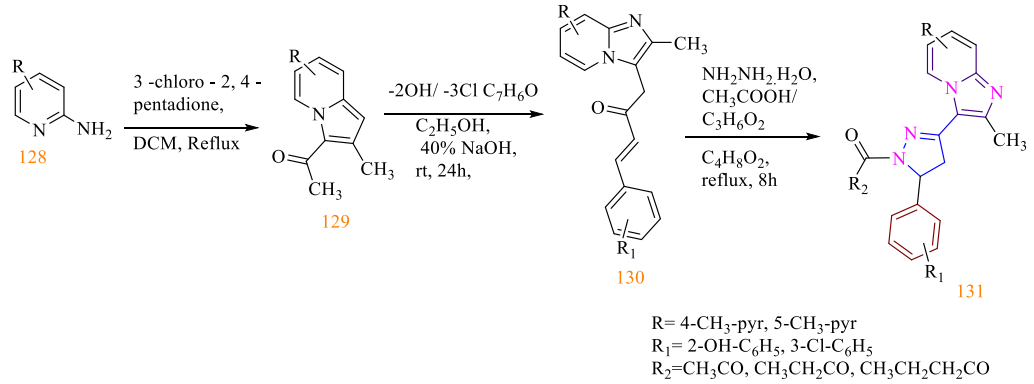
Havryluk *et al.,* reported the synthesis of pyrazoline derivatives clubbed with 4-thiazolidinone ring (Scheme **33**). The synthesized compounds were evaluated for their anticancer activity against NC160 cell line. 5-{2-[5-(4-Chlorophenyl)-3-napthalen-2-yl-4,5-dihydropyrazol-1-yl]-2-oxoethylidene}-thiazolidine-2,4-dione (**134a**) and 5-{2-[5-(2-hydroxyphenyl)-3-(4-methoxyphenyl)-4,5-dihydropyrazol-1-yl]-2-oxoethylidene}-thiazolidine-2,4-dione (**134b**) showed significant activity against leukemia subpanel tumor with GI_{50} value range of 2.12-4.58 and 1.64-3.20 µM respectively [53].

Khanum *et al.,* reported the synthesis of 2`-2``,4``-dinitrophenyl)-5α-cholestano[5,7-c d]pyrazolines (Scheme **34**). The synthesized compounds were screened for their anticancer activity against SW480, A549, HepG2, HeLa, HL60 cell lines. The 3β-Chloro-2`(2``,4``-dinitro-phenyl)-5α-cholestano[5,7-c d]pyrazoline (**136**) showed potent activity against HL60 cell line with IC_{50} value of 15.39 [54].

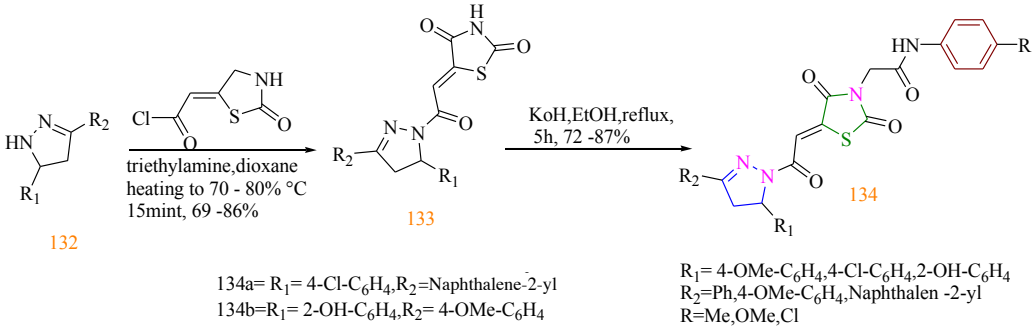
Stefanos *et al.,* reported the synthesis of pyrazoline derivatives from 1-(3,4,5-trimethoxyphenyl)ethanone react with benzaldehyde derivatives in the presence of potassium hydroxide (Scheme **35**). The synthesized compounds were evaluated for their anticancer activity against leukemic cells, and other cancer cell lines like K562, Jurkat, Daudi, B16-F10 neoplastic cell were some of the cell lines. The compounds substituted with R= 4-Br showed more potent activity against Jurkat and K562 cell lines [55].

Wang *et al.,* reported the synthesis of pyrazoline derivatives *via* chalcone formation from benzaldehyde derivatives with 1-phenylethanone in the presence of sodium hydroxide (Scheme **36**). The synthesized compounds were evaluated for their anticancer activity against liver cancer, Hela, HepG-2, A549, and the NIH/3T3 cell lines. 3-(4-Fluorophenyl)-5-(34,5-trimethoxythiophenyl)-4,5-dihydro-1H-pyrazole-1-carbothioamide (**144**) showed potent activity against HepG-2 and Hela cell line with an IC_{50} value of 6.78 µM [56].

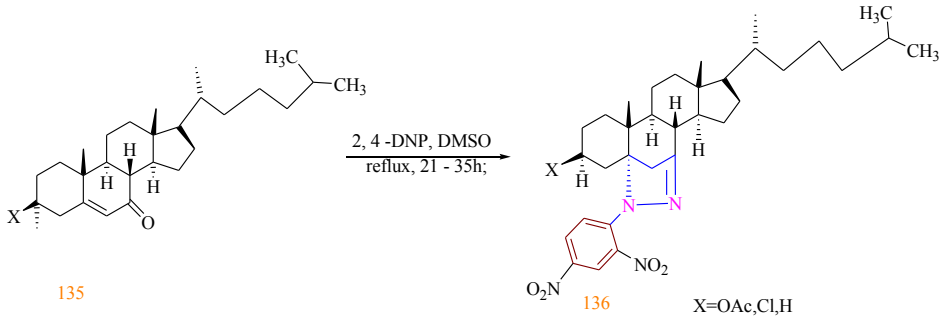
Xu *et al.* reported the synthesis of pyrazoline derivatives from benzaldehyde derivatives reacted with 1-phenyl-ethanone in the presence of phenylacetaldehyde (Scheme **37**). The synthesized compounds were evaluated for their anticancer activity against the HepG-2 cell line and primary hepatocytes. (Benzo[b]thiophen-2-yl-[5-(4-hydroxy-3,5-dimethoxy-phenyl)-3-(2-hydroxy-phenyl)-4,5-dihydo-pyrazol-1-yl]-methanone (**149**) were found to be more potent activity against HepG-2 cell line with IC_{50} value of 3.57 µM [57].



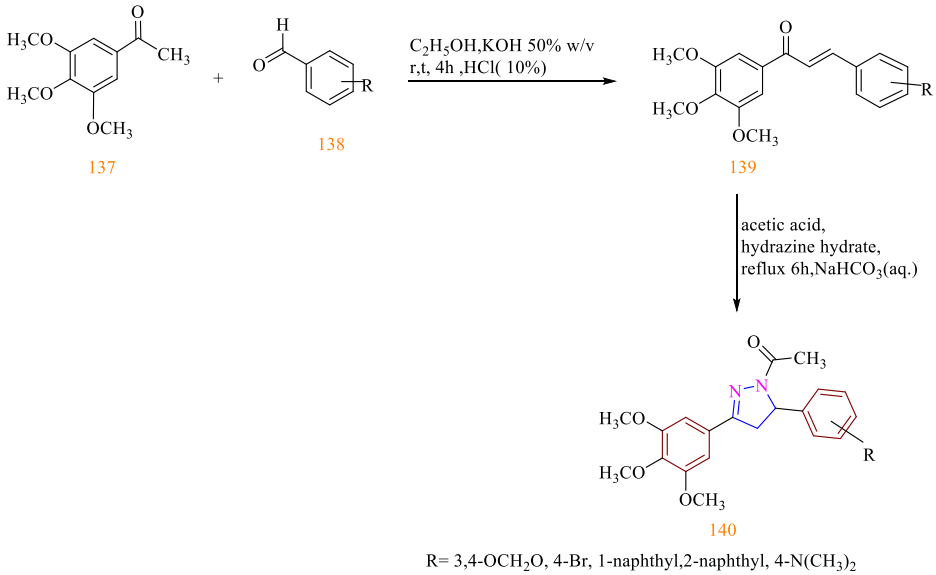
Scheme 32. Synthesis of imidazopyridine pyrazoline derivatives.



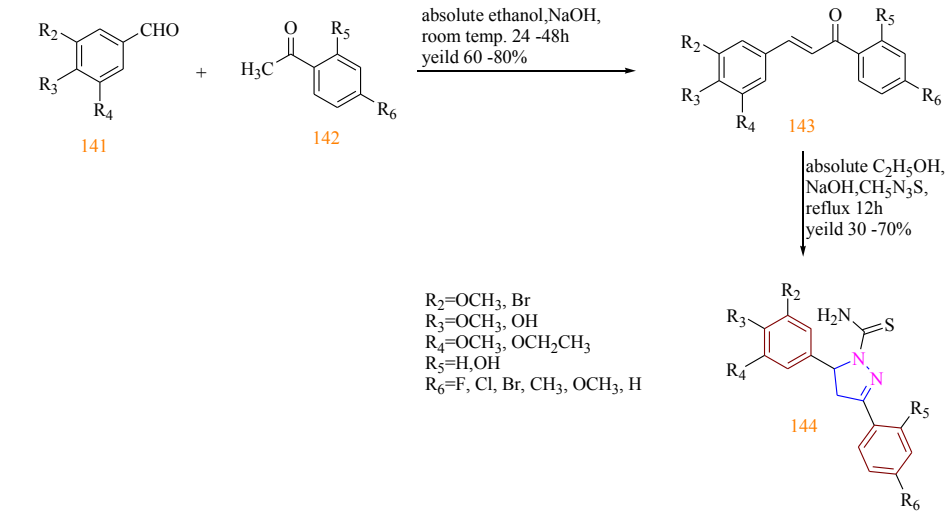
Scheme 33. Synthesis of 4-thiazolidinones clubbed 4-pyrazoline derivatives.



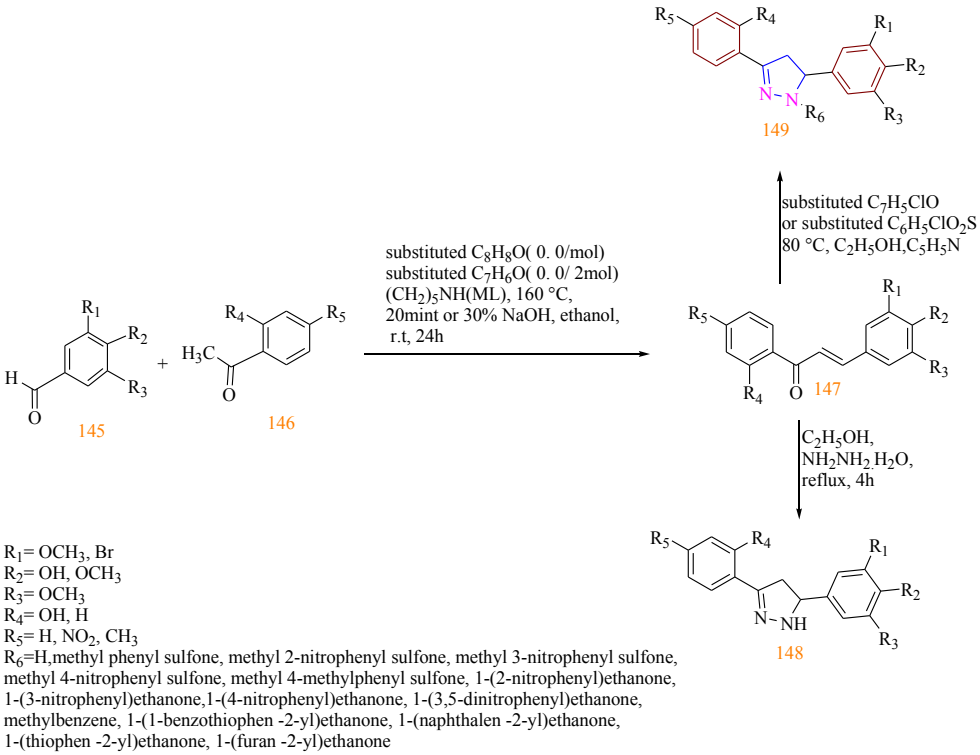
Scheme 34. Synthesis of the steroidal pyrazoline derivatives.



Scheme 35. Synthesis of novel pyrazoline derivatives.



Scheme 36. Synthesis of pyrazoline derivatives.

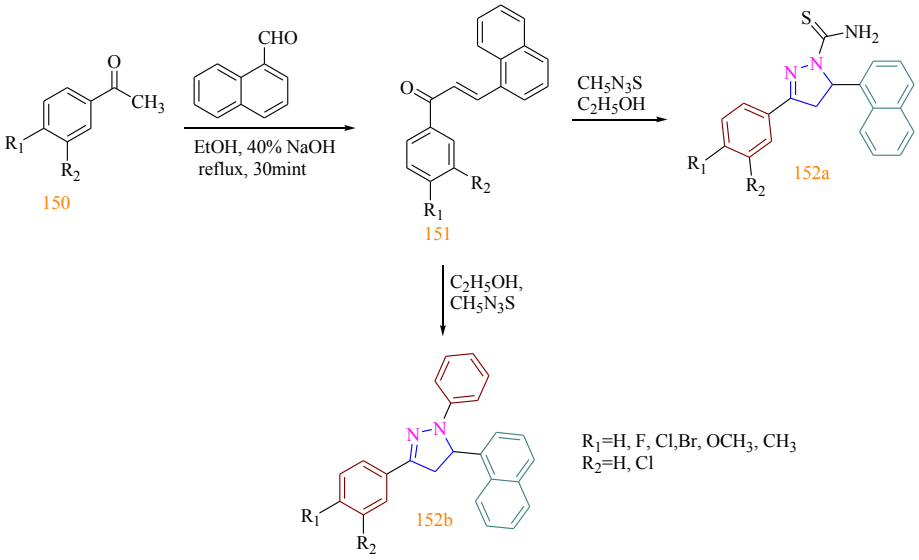


Scheme 37. Synthesis of pyrazoline derivatives.

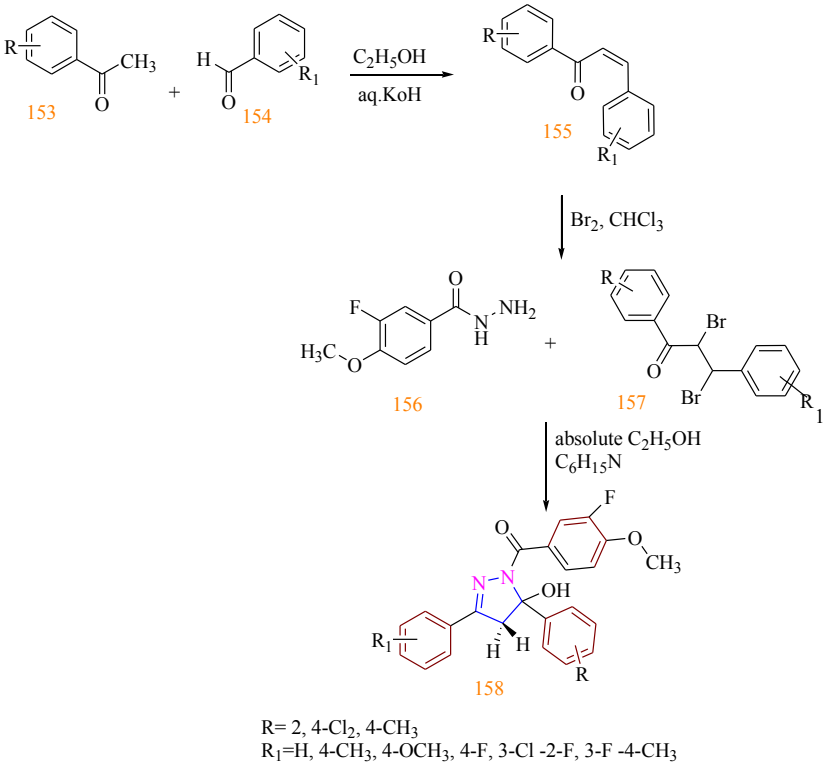
Yang *et al.,* reported the synthesis of pyrazoline derivatives from naphthalin connected with pyrazoline subordinates (Scheme **38**). The synthesized derivatives were screened for their anti-tumor activity against EGFR, HER-2, A549, MCF-7, and HER-2/EGFR cell lines. 3-(3,4-Dichlorophenyl)-5-(naphthalen-2-yl)-1-phenyl-4,5-dihydro-1H-pyrazole (**152b**) showed potent anti-tumor activity against EGFR and A549 cell line with an IC_{50} value of 0.05 µM and GI_{50} value of 0.11 µM [58].

Dinesha *et al.,* reported the synthesis of pyrazoline derivatives from 1-phenylethanone react with benzaldehyde in the presence of ethanol, potassium hydroxide (Scheme **39**). The synthesized compounds were evaluated for their anticancer activity against breast cancer, triple-negative breast cancer, and VERO cell lines. (3-Fluoro-4-methoxyphenyl) (5-hydroxy-3-(4- methoxyphenyl)-5-p-tolyl-4,5-dihydropyrazol-1-yl)methanone (**158**) showed significant activity against MCF-7 cell line [59].

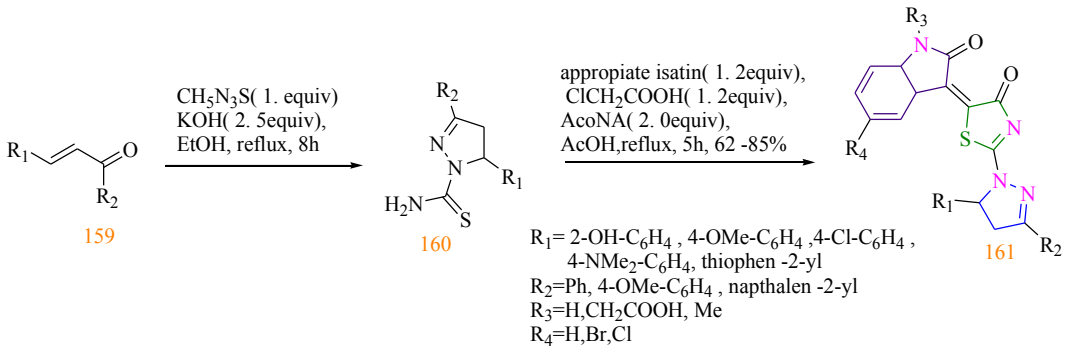
Havrylyuk *et al.,* prepared pyrazoline derivatives 3-[2-(3,5-diaryl-4,5-dihydropyrazol-1-yl)-4-oxo-4,5-dihydro-1,3-thiazol-5-ylidene]-2,3-dihydro-1H-indole-2-ones (**161**) (Scheme **40**) and evaluated for their antiproliferative activity on five different cancer cell lines against HOP-92, HCT-116, SNB-75, NCI/ADR-RES, RXF-393. 5-Bromo-3{2-[5-(4-methoxyphenyl)-3-naphthalen-2-yl-4,5-dihydro-pyrazol-1-yl]-4-oxo-4,5-dihydro-1,3-thiazol-5-ylidene}-2,3-dihydro-1H-indole-2-one (**161**) was found to be most potent activity agent against HOP-92 with GI_{50} value of <0.01 µM [60].



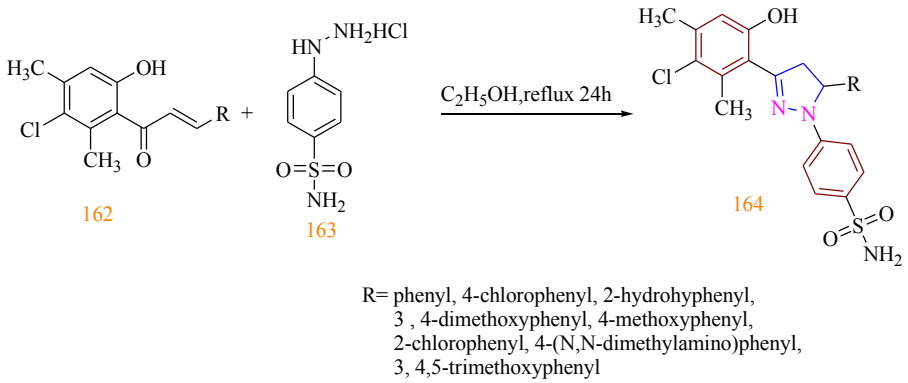
Scheme 38. Synthesis of naphthalin and pyrazoline derivatives.



Scheme 39. Synthesis of 1,3,5-trisubstituted aryl-5-hydroxypyrazolines derivatives.



Scheme 40. Synthesis of pyrazoline, thiazolidine, isatin derivatives.



Scheme 41. Synthesis of 3,5-diaryl-1-(p-sulfamylphenyl)-2-pyrazolines.

Bano *et al.,* prepared pyrazoline derivatives, 3,5-diaryl-1-(p-sulfamylphenyl)-2-pyrazolines derivatives (Scheme **41**). The synthesized compounds were screened for their anti-cancer activity against MOLT-4, SR, and EKVX, COLO-205 cell lines. (5`-Chloro-2`-hydroxy-4`,6`-dimethylphenyl)-5-(4-(*N*,*N*-dimethyl amino) phenyl)-1-(p-sulfanylphenol)-Δ2-pyrazoline (**164**) found to be more promising activity against MOLT-4, SR, EKVX, and COLO-205 with GI_{50} value of 1.94, 1.28, 1.88, and 1.69 µM respectively [61].

Chen *et al.,* prepared pyrazoline derivatives *N*-aryl methylene-3,3-ethylenedioxy-5-androstone-17-hydrazone derivatives (Scheme **42**). The synthesized compounds were screened for their anticancer activity against ECA-109, 446, and AGS cell lines. 3,3-Ethylenedioxy-5-androstene[17,16-C]-1`H-5`-phenyl pyrazoline (**167**) showed potent activity against ECA-109, 446 , AGS cell lines with an IC_{50} value of 17.5, 25.3, 27.4 µM [62].

Elmeligie *et al.,* prepared a new series of pyrazoline derivatives from benzaldehyde derivatives reacted with 1-(3,4,5-trimethoxyphenyl)ethanone in the presence of potassium hydroxide (Scheme **43**). The synthesized compounds were evaluated for their anticancer activity against MCF-7 and HCT-116 cell lines. 5-(4-Dimethylaminophenyl)-3-(3,4,5-trimethoxyphenyl)- 4,5-dihydro-1H-pyrazole-1-carbothioamide (**171b**) showed significant activity against MCF-7, HCT-116 cell lines with IC_{50} value of 6.85, and 9.64 µM respectively [63].

Fahmy *et al.,* syntheisized a novel series of pyrazoline derivatives from 1-[1-(3-chlorophenyl)-3-(3-methoxyphenyl)-4,5-dihydro-1*H*-pyrazol-4-yl]ethanone presence of 1-(thiophen-2-yl)ethenone (Scheme **44**). The synthesized compounds were evaluated for their anticancer activity against the MG-MID cell line. 6-(1-(3-Chlorophenyl)-3-(4-methoxy phenyl)-1H-pyrazol-4-yl)-4-(thiophen-2-yl) pyrimidine-2-(1H)-thione (**174c**) was found to be more potent activity against MG-MID cell line with GI_{50} value of 3.59 µM [64].

Edress *et al.,* reported the syhthesis of pyrazoline derivatives from 5-(3,5-dichlorophenyl)-3-(thiophen-2-yl)-4,5-dihydro-1*H*-pyrazole-1-carboxamide react and 1-bromopropan-2-one in the presence of grinding HBr *via* one-pot Synthesis (Scheme **45**). The synthesized compounds evaluated for their anticancer activity against the HePG-2 cell line. 2-(5-(2,4-Dichlorophenyl)-3-(thiophen-2-yl)-4,5-dihydro-H-pyrazol-1-yl)-4-(4-fluorophenyl) thiazole (**178**) showed significant activity against HepG-2 cell line with an IC_{50} value of 1.70 ± 8.2 µM [65].

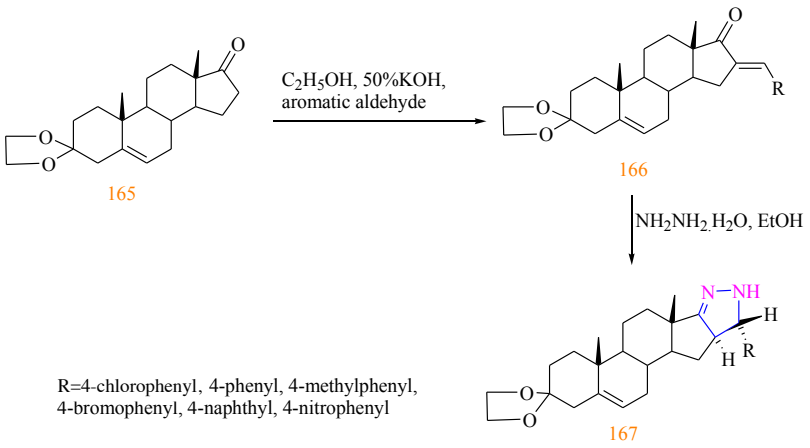
Farghaly *et. al.* reported the synthesis of a novel of pyrazoline derivatives from(1*Z*,2*E*)-*N*,3-diphenylprop-2-enehydrazonoyl chloride in the presence of triethanolamine and sodium carbonate (Scheme **46**). The synthesized compounds were evaluated for their Colon cancer cell line. 1,3-Diphenyl-4-(4-fluorophenyl)-5-(4-fluorobenzoyl)-pyr-azoline (**182a** and IC50 value 0.086 µm) and 4-(4-fluorophenyl)-5-(4-methoxybenzoyl)-1-phenyl-3-(styryl)-pyrazoline (**182b**) showed potent activity against HT-29 cell line with an IC_{50} value of 0.113µM [66].

Demirayak *et al.,* reported the synthesis of pyrazoline derivatives from 2-amino-1-(4-methylphenyl)ethanone react with isothiocyanatobenzene derivatives react with pyridine (Scheme **47**). The synthesized compounds were evaluated for their anticancer activity against MCF7, MG-MID, SF-268, NCI-H460 cell lines. The derivatives substituted with R= OCH_3, R_1=H(187) showed significant activity against MG-MID cell line with GI_{50} value of 4.39 µM [67].

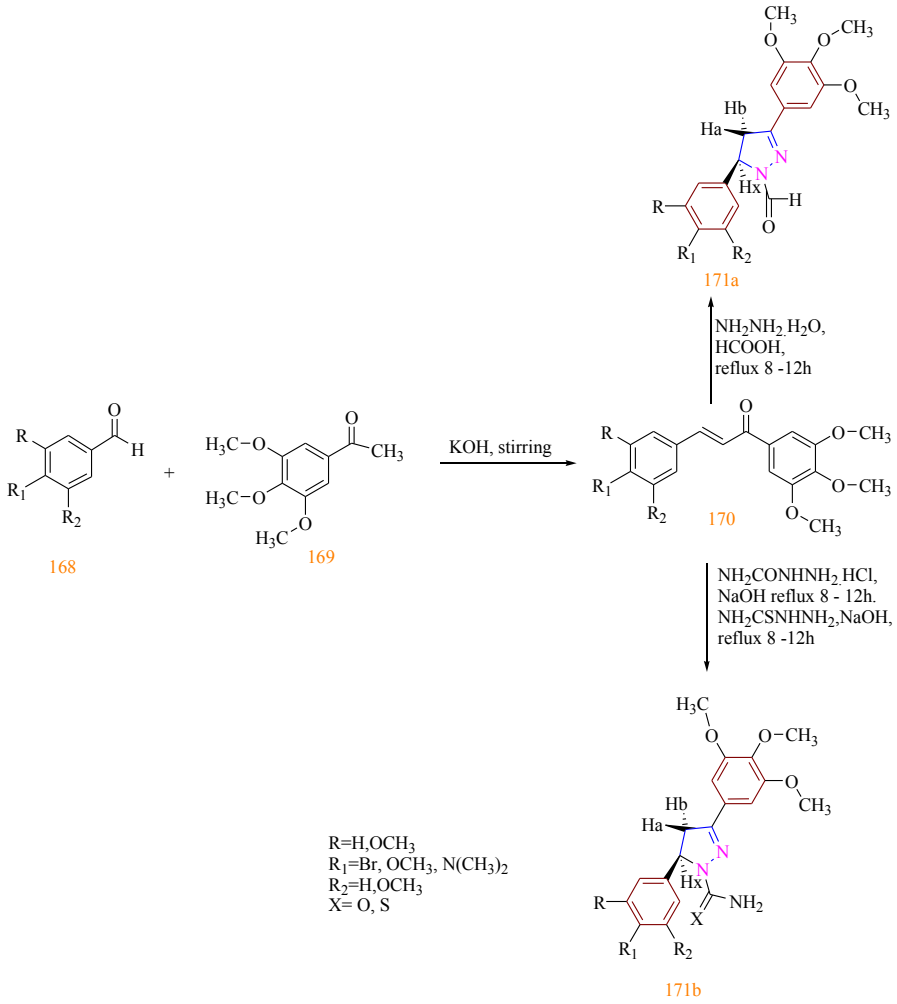
Gangarapu *et al.,* syntheiszed a series of novel pyrazoline derivatives from 1*H*-indole-2,3-dione react with benzaldehyde in the presence of dimethylamine and glacial acetic acid (Scheme **48**). The synthesized compounds were screened for their anticancer activity against CCRF-CEMa, HOP-92b, NCI-522b, HCT-116c, SF-295d, SNB-75d, MDA-MB-435e, OVCAR-3f, A498g, PC-3h, and BT-549i cell lines. 2-Phenyl-2-((5-phenyl-1,3,4-thiadiazol-2-yl) imino) ethylidene) indolin-2-one (**191b**) and 5-bromo-5′-phenyl-2′,4′-dihydrospiro [indoline-3,3′- pyrazol]-2-one (**191a**) showed significant activity against MG-MID with GI_{50} value of 0.65 and 0.72 µM [68].

Amin *et al.,* reported the synthesis of pyrazoline derivatives from coumarin in the presence of acetic anhydride (Scheme **49**). The synthesized compounds were evaluated for their anticancer activity against the HepG2 cell line. 7-Methoxy-8-{5-[4-(methylthio)phenyl]-4,5-dihydro-1H-pyrazol-3-yl}-2H-chromen2-one (**198**) showed potent activity against HepG2 cell line [69].

George *et al.,* reported the synthesis of a series of novel pyrazoline derivatives from novel 3-hydrazinyl-6-phenylpyridazidazine (Scheme **50**). The synthesized compounds were screened for their anticancer activity against A549, HepG-2, MCF-7, CaCo-2 cell lines. 3-{3-[4-



Scheme 42. Synthesis of *N*-aryl methylene-3,3-ethylenedioxy-5-androstone-17-hydrazone derivatives.

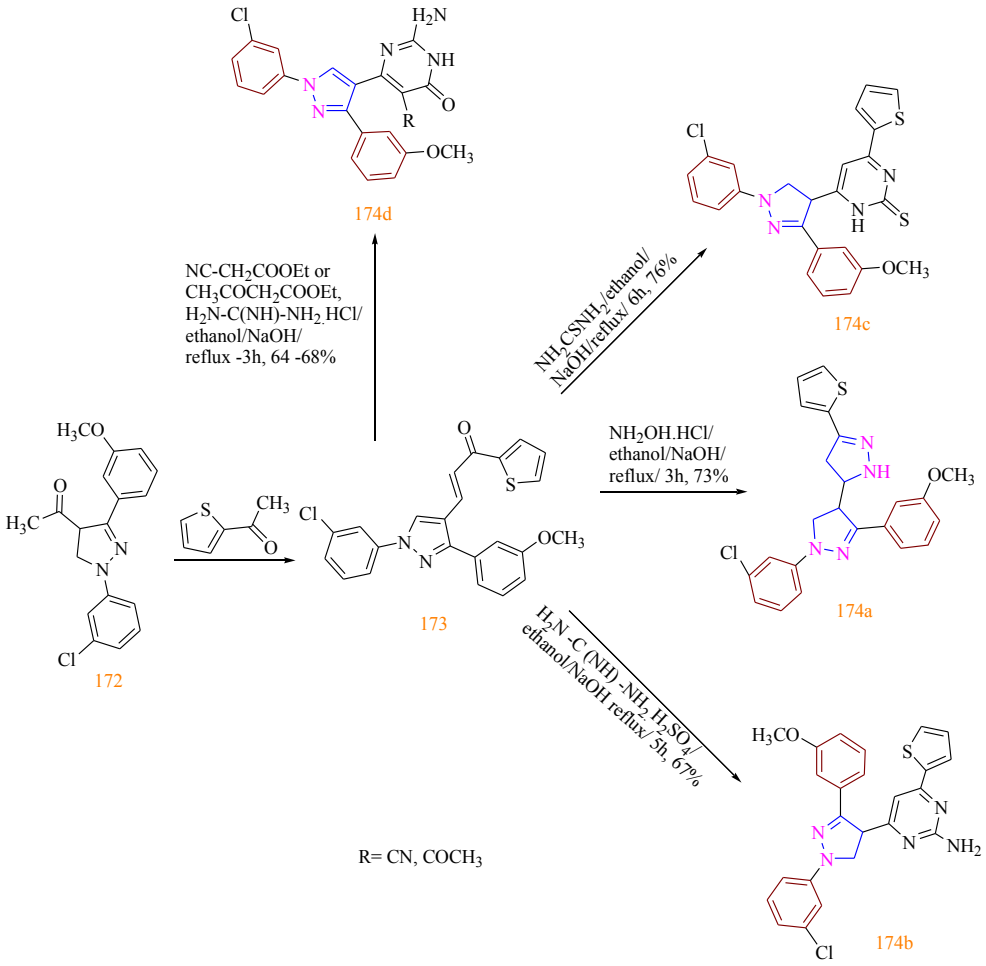


Scheme 43. Synthesis of combretastatin and pyrazoline derivatives.

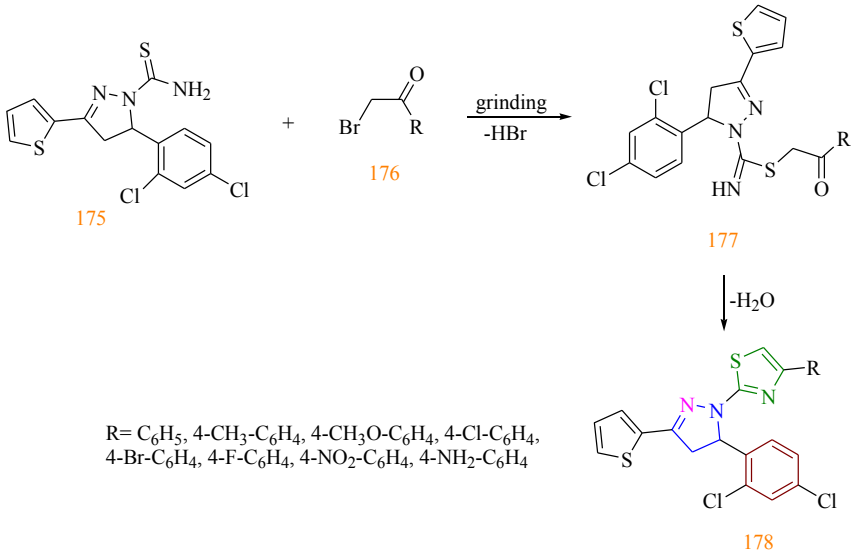
chlorophenyl]-5-[4-(trifluoromethyl)phenyl]-4,5-dihydropyrazol-1-yl}-6-phenylpyridazine (**201**) showed potent activity against HepG-2, MCF-7 and CaCo-2 with IC_{50} value of 8.33,1.67 and 10 µM respectively [70].

Tilekar *et al.,* reported the synthesis of a series of novel pyrazoline substituted pyrrolidine-2,5-dione (Scheme **51**). The synthesized compounds were screened for their anticancer activity against MCF-7, HT29, and K562 cell lines. 1-(2-(3-(4-Fluorophenyl)-5-(p-tolyl)-4,5-dihydro-1H-pyrazol-1-yl)-2-oxoethyl)pyrrolidine-2,5dione (**207**) showed potent activity against MCF-7 with an IC_{50} value of 0.78±0.01µM [71].

Sable *et al.,* reported the synthesis of pyrazoline derivatives from substituted acetophenone reacted with substituted benzaldehyde in the presence of ethanolic sodium hydroxide (Scheme **52**). The synthesized compounds were evaluated



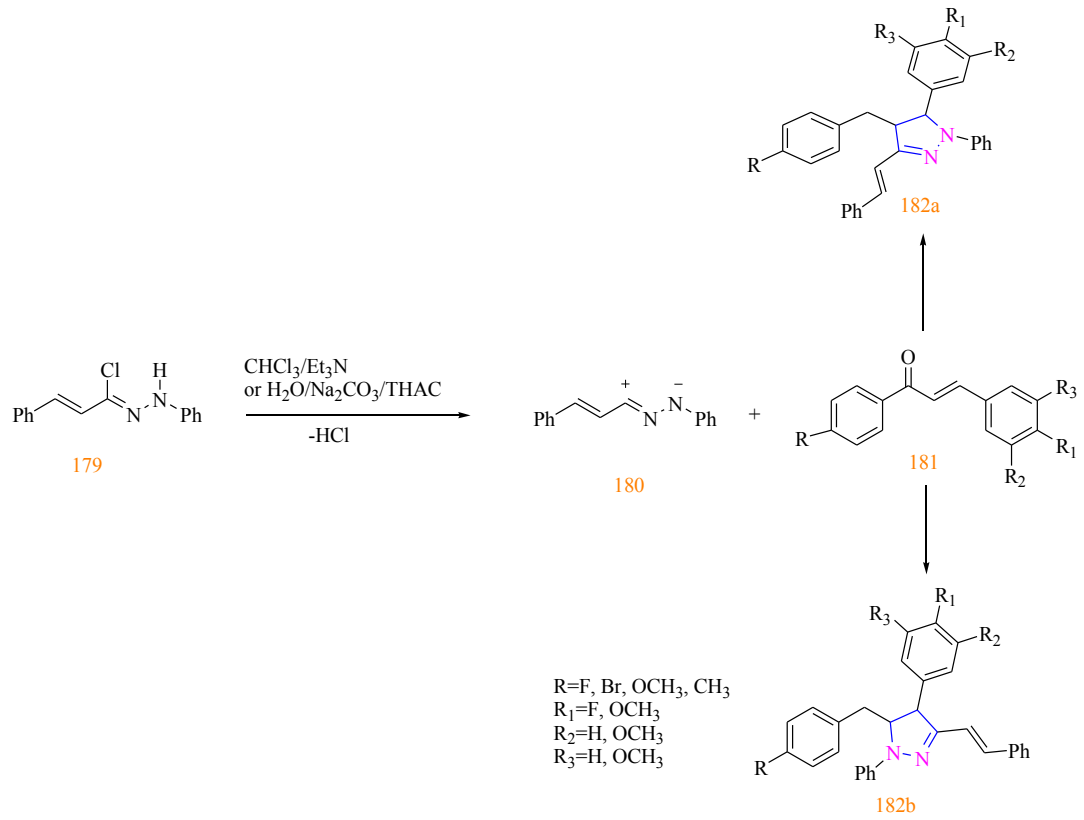
Scheme 44. Synthesis of trisubstituted pyrazoline derivatives.



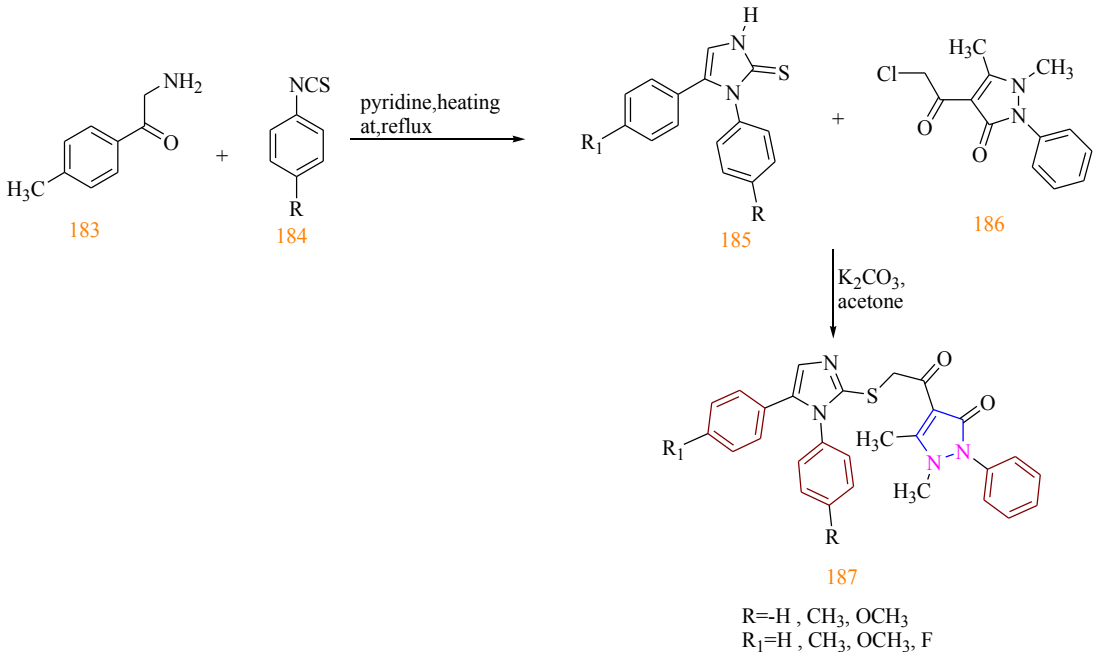
Scheme 45. Synthesis of thiazole and pyrazoline derivatives.

for their anticancer activity against the MCF-7 cell line determined by SRB analysis. 1-(5-(4-Chlorophenyl)-3-(4-ethoxyphenyl)-4,5-dihydropyrazol-1-yl) ethanone (**210**) showed potent activity having IC_{50} value of 0.010 µM [72].

Insuasty *et al.,* reported the synthesis of pyrazoline derivatives from (2*E*)-1-{4-[(7-chloroquinolin-4-yl)amino]-phenyl}-3-phenylprop-2-en-1-one derivatives in the presence of hydrazine hydrate and acetic acid (Scheme **53**). The synthesized compounds were screened for their anticancer activity against leukemia, non-small cell lung cancer, colon cancer, melanoma, ovarian cancer, kidney cancer, prostate cancer, and breast cancer cell lines. 5-(4-Chlorophenyl)-3-[4-(7-



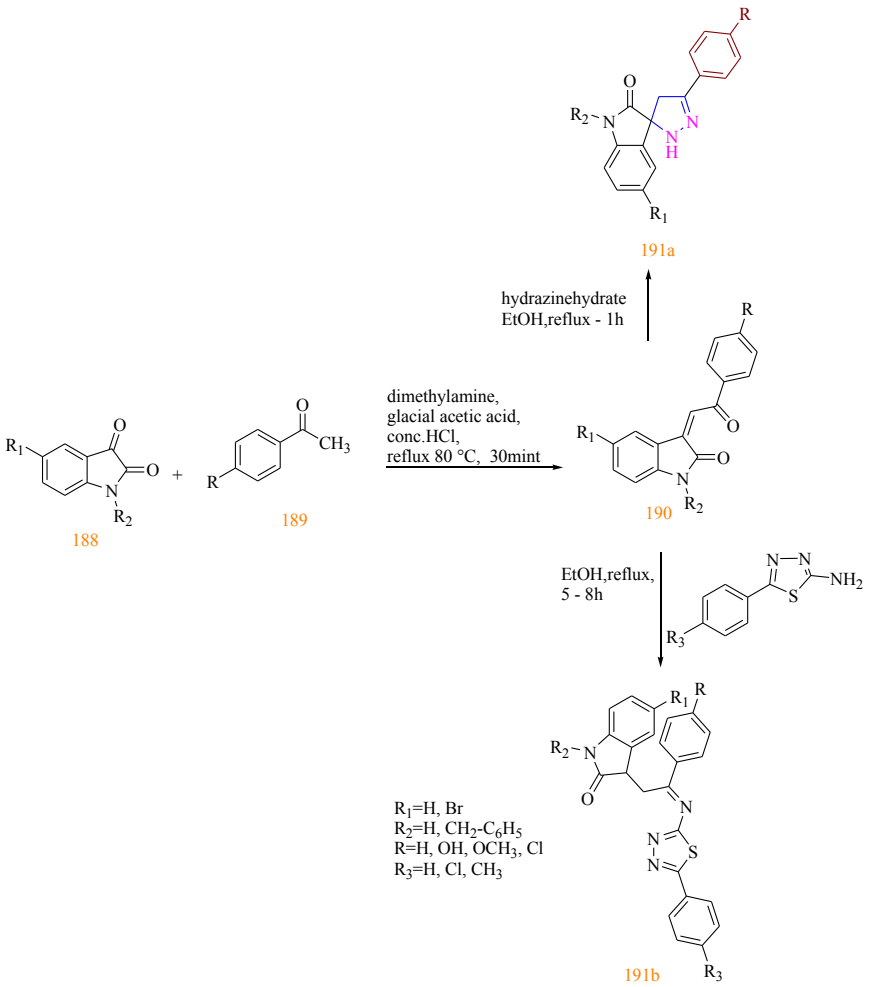
Scheme 46. Synthesis of pyrazoline derivatives.



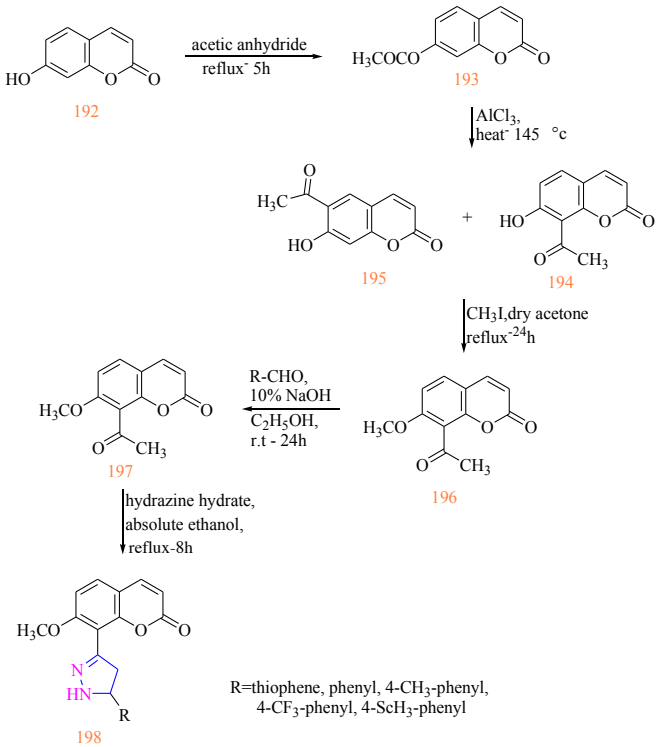
Scheme 47. Synthesis of imidazolyl-thioacetyl and pyrazoline derivatives.

c.hloroquinolin-4-ylamino)phenyl]-4,5-dihydro-1*H*-pyrazole-1-carbaldehyde (**215**) showed potent activity against all cancer cell lines with GI_{50} values ranging from 0.13 to 0.99µM [73].

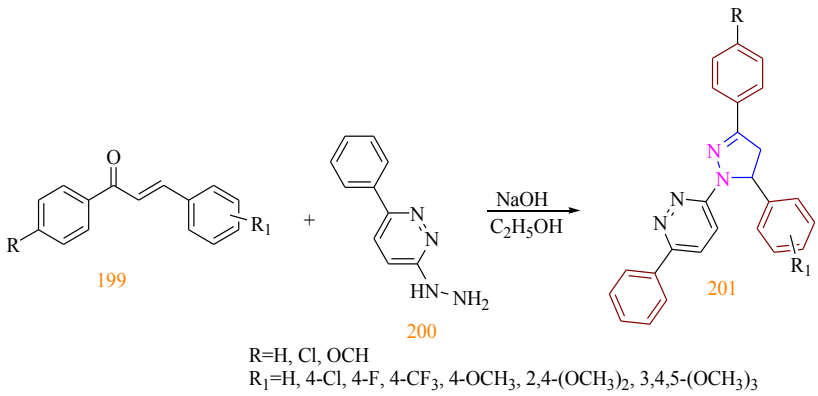
Jainey *et al.,* investigated the synthesis pyrazoline derivatives from 1-(thiophen-2-yl)ethanone react with benzaldehyde derivatives in the presence of ethanolic sodium hydroxide (Scheme **54**). The synthesized compounds were evaluated for their anticancer activity against Ehrlich cancer cell lines and heights cytotoxicity concentration of 80% at 20µg/ml. 3-(4-Fluorophenyl)-1-(thiopben-2-yl) prop-2-en-1-one (**219a**) and 3-(4-chlorophenyl)-1-(thiopben-2-yl) prop-2-en-1-one (**219b**) showed potent activity against EAC cell lines [74].



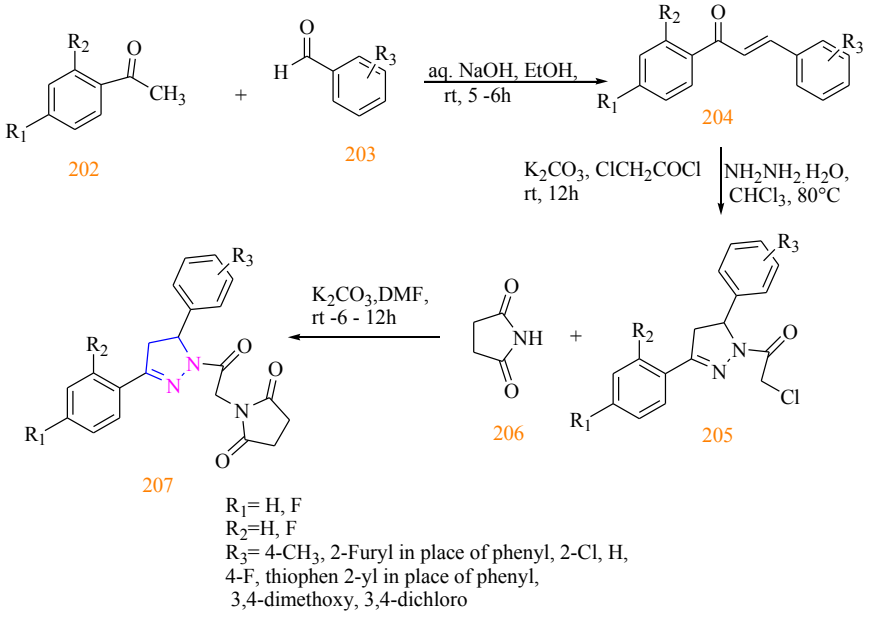
Scheme 48. Synthesis of isatin-based pyrazoline and thiadiazolines derivatives.



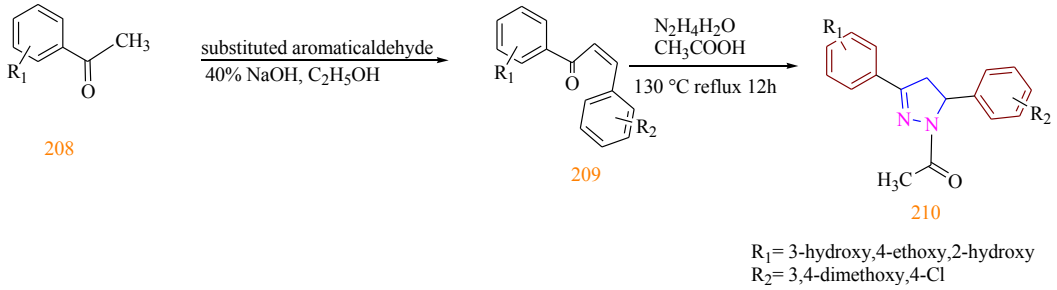
Scheme 49. Synthesis of coumarin and pyrazoline derivatives.



Scheme 50. Synthesis of chalcone with 3-hydrazinyl-6-phenylpyridazine to form pyrazoline derivatives.



Scheme 51. Synthesis of pyrazoline derivatives.

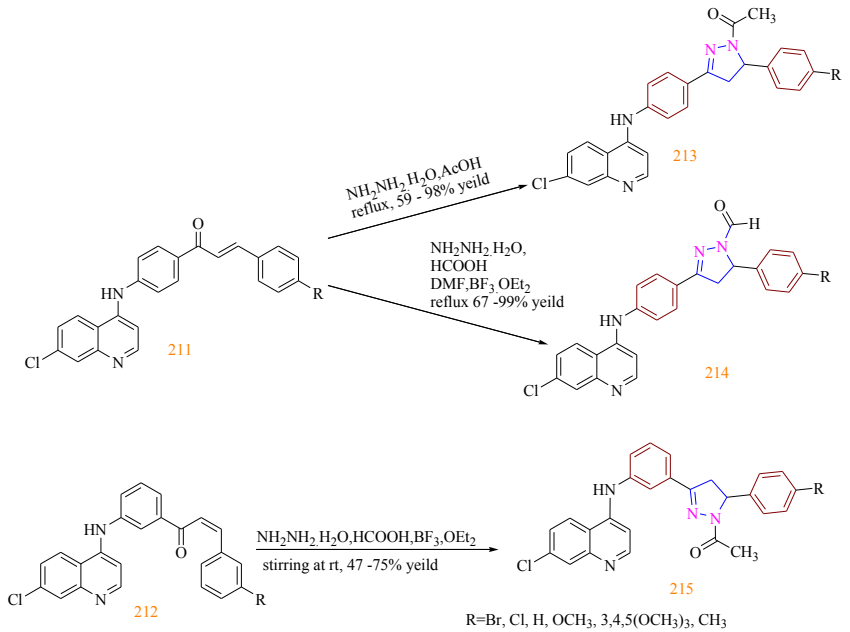


Scheme 52. Synthesis of chalcone and pyrazoline derivatives.

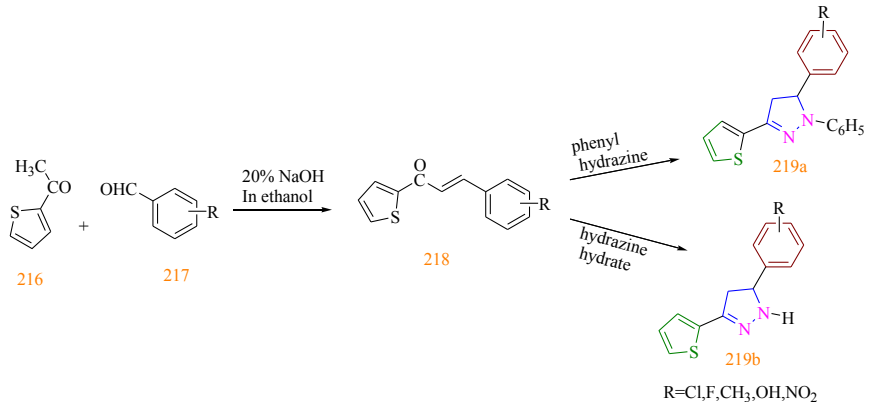
Khalil *et al.,* reported the synthesis of pyrazoline derivatives by the 5-arylidene-2-(3,5-diaryl-4,5-dihydro-1*H*-pyrazol-1-yl)-1,3-thiazol-4(5*H*)-ones (Scheme **55**). The synthesized compounds were screened for their anticancer activity against the breast melanoma cell line. 2-[3,5-Bis(4-chlorophenyl)-4,5-dihydro-1*H*-pyrazol-1-yl]-5-(2-methoxybenzylidine)-1,3-thiazol-4(5*H*)-one (**223**) showed significant activity against MCF-7 cell line with an IC_{50} value of 1.4µM [75].

Choudhary *et al.,* reported that pyrazoline derivatives were synthesized from novel pregnenolone in the presence of ethanol and sodium hydroxide (Scheme **56**). The synthesized compounds were screened for their anticancer activity against Hela and Breast tumor cell lines. The compounds substituted with R_1=furyl, R_2=phenyl (226) showed potent activity against MDA-MB-230 cell lines with an IC_{50} value of 0.91 µM [76].

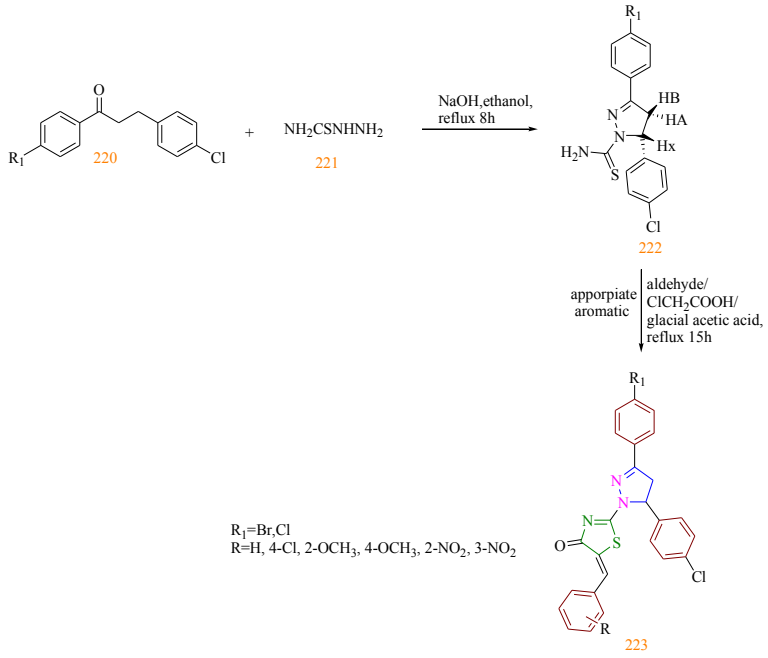
Kadasi. *et al.* reported the synthesis of pyrazoline derivatives N-pyridoyl-Δ2-pyrazoline (Scheme **57**). The synthesized compounds were screened for their anticancer activity against MDA-MB-468b and A375c. The compound substituted with R_1=H, R_2=H (230) showed more potent activity against the MCF-7 cancer cell line [77].



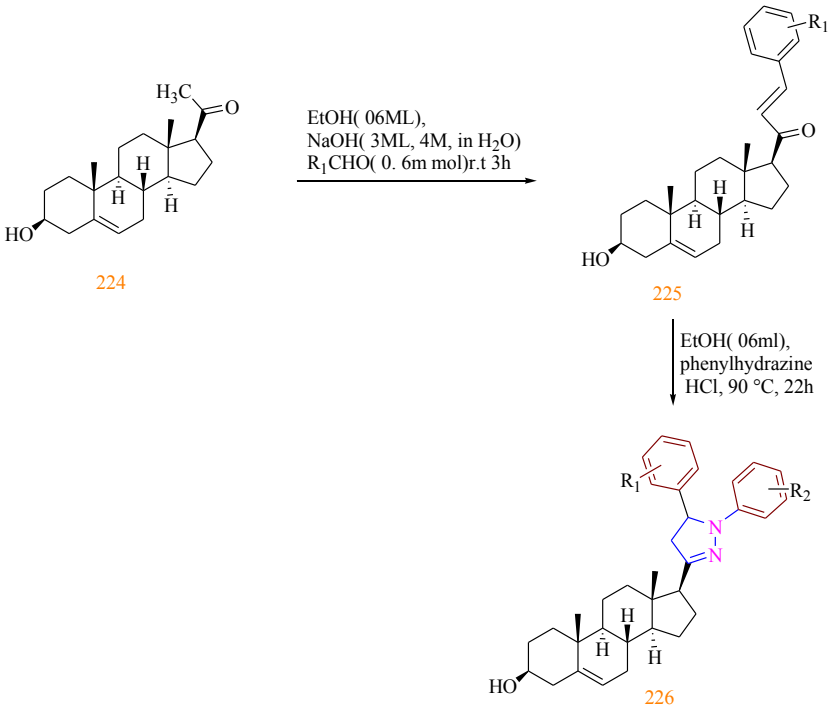
Scheme 53. Synthesis of N-acetyl and N-formyl pyrazolines derivatives.



Scheme 54. Synthesis of intermediate chalcone and pyrazoline derivatives.

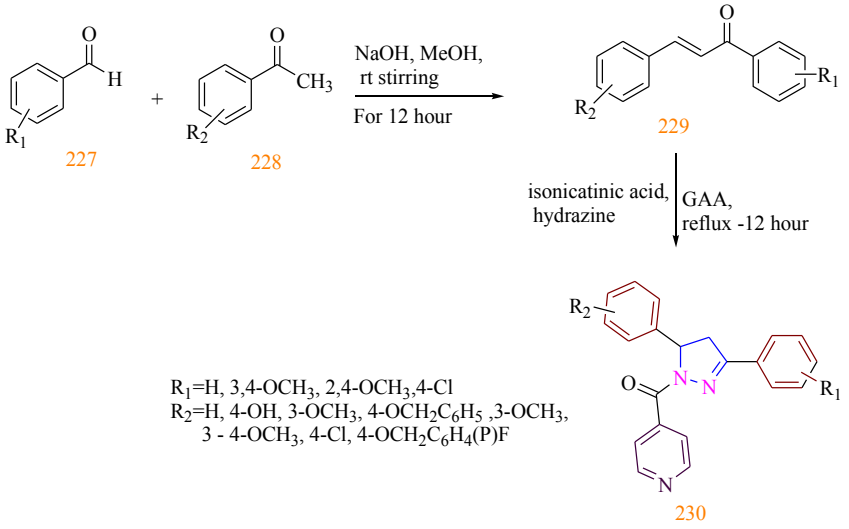


Scheme 55. Synthesis of thiazolone and pyrazoline derivatives.



R_1=Ph, 4-phenoxyphenyl, 4-methylphenyl, 3-nitrophenyl, 4-methoxyphenyl, 3-chlorophenyl, 2-furyl, 2-naphthalenyl, 2-thienyl, 3,4,5-trimethoxyphenyl, 4-ethoxyphenyl, 2-chlorophenyl, 3-4-Difluorophenyl, 3,4-dichlorophenyl, 2,-dichlorophenyl, 2-pyridinyl.
R_2= 4-Bromophenyl, 4-chlorophenyl, 2-Bromophenyl, 4-fluorophenyl, 2-chlorophenyl, phenyl, 2-nitrophenyl, 2,4-dichlorophenyl, 4-methylphenyl, 4-methoxyphenyl, 2-ethylphenyl

Scheme 56. Synthesis of pregnenolone, furyl, and pyrazoline derivatives.

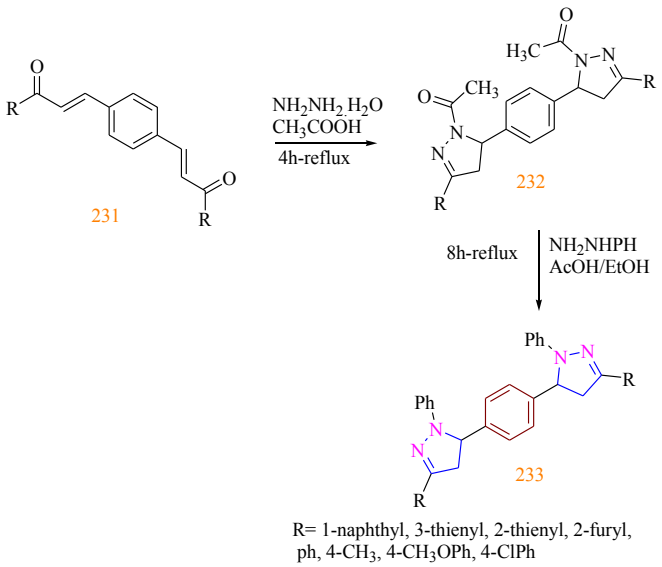


R_1=H, 3,4-OCH_3, 2,4-OCH_3,4-Cl
R_2=H, 4-OH, 3-OCH_3, 4-$OCH_2C_6H_5$,3-OCH_3, 3 - 4-OCH_3, 4-Cl, 4-$OCH_2C_6H_4$(P)F

Scheme 57. Synthesis of N-pyridoyl-Δ2-pyrazoline derivatives.

Gurdere *et al.,* reported the synthesis of pyrazoline derivatives bis-*N*-acetyl and bis-*N*-phenyl pyrazoline derivatives (Scheme **58**). The synthesized compounds were evaluated for their anticancer activity against human uterus carcinoma and rat brain cancer cell line. 1,4-Bis(1-phenyl-3-(thiophen-2-yl)-4,5-dihydro-1H-pyrazol-5-yl) benzene (**233**) showed potent activity against C6 cells with an IC_{50} value of 23.88 µM [78].

Dawood *et al.,* reported the synthesis of pyrazoline derivatives from 3-(3-nitrophenyl)-1-phenyl-1*H*-pyrazole-4-carbaldehyde react with propan-2-one in the presence of sodium methanolate methanol (Scheme **59**).The synthesized compounds were evaluated for their anticancer activity against VEGFR-2 side by side in the breast tumor cell lines. 1-(3-(Furan-2-yl)-4,5-dihydro-5-(3-(3-nitrophenyl)-1-phenyl-1H-pyrazol-4- yl) pyrazol-1-yl) ethenone (**240**) and 4-(3-(Furan-2-yl)-4,5-dihydro-1-phenyl-1H-pyrazol-5-yl)-3-(3-nitrophenyl)-1-phenyl-1H-pyrazole (**239**) showed potent activity against VEGFR-2 with an IC_{50} values ranging from 16.50 - 26.73 µM [79].



Scheme 58. Synthesis of bis-*N*-acetyl and bis-*N*-phenyl pyrazoline derivatives.

Dofe *et al.,* reported the synthesis of pyrazoline derivatives from 5-[(4-ethyl-2-methoxyphenoxy)methyl]-5*H*-tetrazole react with substituted benzaldehyde in the presence of ethanol and sodium hydroxide (Scheme **60**). The synthesized compounds were evaluated for their anticancer activity against MCF-7, A549, HePG2. 5-((4-(4,5-Dihydro-5-phenyl-1*H*-pyrazol-3-yl)-2-methoxyphenoxy)methyl)-1*H*-tetrazole (**243a**) and 5-((4-(4,5-dihydro-5-phenylisoxazol-3-yl)-2-methoxyphenoxy) methyl)-1H-tetrazole (**243b**) was found to be more potent activity against HepG-2 cell lines with IC_{50} value of 0.96 and 0.85 µM respectively [80].

Nawaz *et al.,* reported the synthesis of pyrazoline derivatives from 1-[4-(benzyloxy)phenyl]ethanone react with phenylhydrazine in the presence of absolute ethanol and glacial acetic acid (Scheme **61**). The synthesized compounds were evaluated for their anticancer activity against A549, HCT-116, MCF-7, SiHa, EGFR cell lines. 3′-[4-(Benzyloxy) Phenyl]-1′-phenyl-5-(pyridin-4-yl)-3,4-dihydro-1′H,2H-[3,4′-bipyrazole]-2-carboxamide (**249**) showed significant activity against the human non-small-cell lung tumor cell line A549 cancer cell lines with an IC_{50} value of 3.65 ± 0.54 µM [81].

Prada *et al.,* reported the synthesis of pyrazoline derivatives from (2*E*)-3-{3-[(7-chloroquinolin-4-yl)amino]-phenyl}-1-phenylprop-2-en-1-one derivative in the presence of hydrazine hydrate and ethanol (Scheme **62**). The synthesized compounds were screened for their anticancer activity against A549, CCRF-CEM, HCT-15, SNB-19, MCF-7 cancer cell lines. 5–(3–((7–Chloroquinolin–4–yl) amino)phenyl)–3–(4–methoxyphenyl)–4,5–dihydro–1H– pyrazole–1–carbaldehyde (**252**) showed potent activity against 60 different cancer cell lines with the most important GI_{50} values ranging from 0.28 to 11.7 µM (0.13 to 6.05 µg/mL) and LC_{50} values ranging from 2.6 to > 100 µM (1.2 to > 51.7 µg/mL) [82].

Song *et al.,* reported the the synthesis of pyrazoline derivatives 3-(1*H*-indol-3-yl)-2,3,3a,4-tetrahydrothiochromeno[4,3-c] pyrazole (Scheme **63**). The synthesized compounds were evaluated for their anticancer activity against MCF-7, Hela, MGC-803, Bel-7404, and L929 cancer cell lines. 3–(4–Chlorophenyl)–5–(3–((7–chloroquinolin–4–yl) amino)phenyl)–4,5–dihydro–1H– pyrazole–1–carbaldehyde (**259a**) and 6,8-dichloro-3-(1H-indol-3-yl)-2-phenyl-2,3,3a,4-tetrahydrothiochromeno[4,3-c]pyrazole (**259b**) showed potent activity, with IC_{50} values of 15.43 and 20.54 µM towards MGC-803 respectively [83] .

Pyrih *et al.,* reported the synthesis of pyrazoline derivatives, 5-[3,5-di(het)aryl-4,5-dihydro-1H-pyrazoline-1-yl)methylene]−4-arylamino-1,3- thiazoline-2-one (Scheme **64**). The synthesized compounds were screened for their anticancer activity against SR, UO-31, EKVX, K-562, UACC-62 cell lines. (Z)−4-[(5-(4-Fluorophenyl)−3-(4-methoxyphenyl)−4,5-dihydro1H-pyrazol-1-yl)methylene]−2-oxo-1,3-thiazolin-4-yl)phenylamino acetate (**262**) was found to be more potent anticancer agent [84].

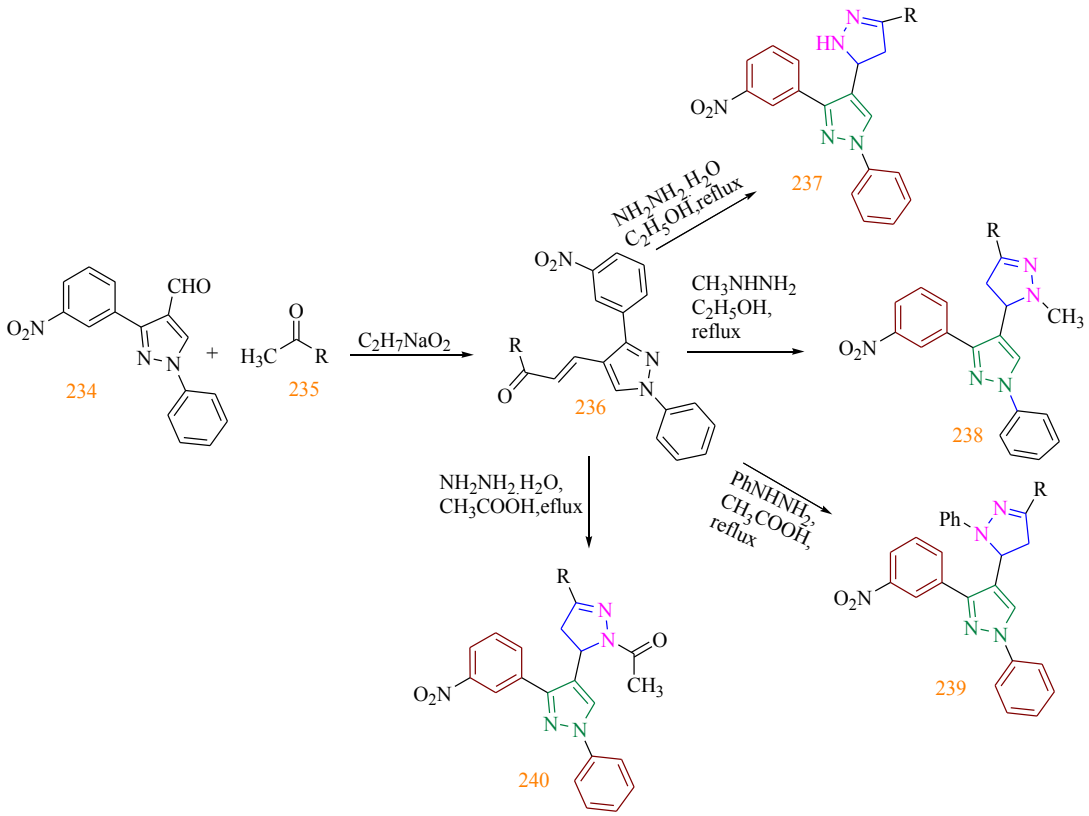
Kocyight *et al.,* reported the synthesis of pyrazoline derivatives, (3aR,4S,7R,7aS)-2-[4-[1-acetyl-5-(aryl/heteroaryl)-4,5-dihydro-1*H*-pyrazol-3-yl]phenyl]-3a,4,7,7a-tetrahydro-1*H*-4,7-methanoisoindole-1,3(2*H*)-diones (Scheme **65**). The synthesized compounds were screened for their anticancer inhibition effect on human carbonic anhydride-1, human carbonic anhydride-2, and acetylcholinesterase. (3aR,4S,7R,7aS)-2-[4-[1-Acetyl-5-(o-tolyl)-4,5-dihydro-1*H*-pyrazol-3-yl]phenyl]-3a,4,7,7a-tetrahydro-1*H*-4,7- methanoisoindole-1,3(2*H*)-dione (**264**) showed inhibition effect on HCA I, HCA II, and AChE enzymes [85].

Kucukoglu *et al.,* reported the synthesis of pyrazoline derivatives from 1-(4-methoxyphenyl)ethanone react with substituted benzaldehyde derivatives in the presence of ethanol and sodium hydroxide (Scheme **66**). The synthesized compounds were evaluated for their anticancer activity against HCA-1 and HCA-2 isoenzymes and A9-22(A), HSC-2, HSC-3, HSC-4, and regular cell lines (HGF(C), HPLF, HPC) human leukemic line (Ca9-22(A), HSC-2, HSC-3, HSC-4) cell lines. 4-(3-(4-Methoxyphenyl)-5-(3,4,5-trimethoxyphenyl)-4,5-dihydro-1H-pyrazol-1-yl) benzenesulfonamide (**268**) showed highest TS (tumor selectivity) value [86].

Kharbanda *et al.,* reported the synthesis of pyrazoline derivatives from substituted 1-(furan-2-yl)ethanone react with substituted acetaldehyde in the presence of ethanol and sodium hydroxide (Scheme **67**). The synthesized compounds were evaluated for their anti-tumor activity against UACC-62, SNB-75, HCT-IS, SR cell lines. The compounds substituted with R=N,N-dimethylphenyl, R_1=phenyl, R_2=O, R_3= chromen-2-one-3-yl (273)showed more potent activity against cancer cell lines [87].

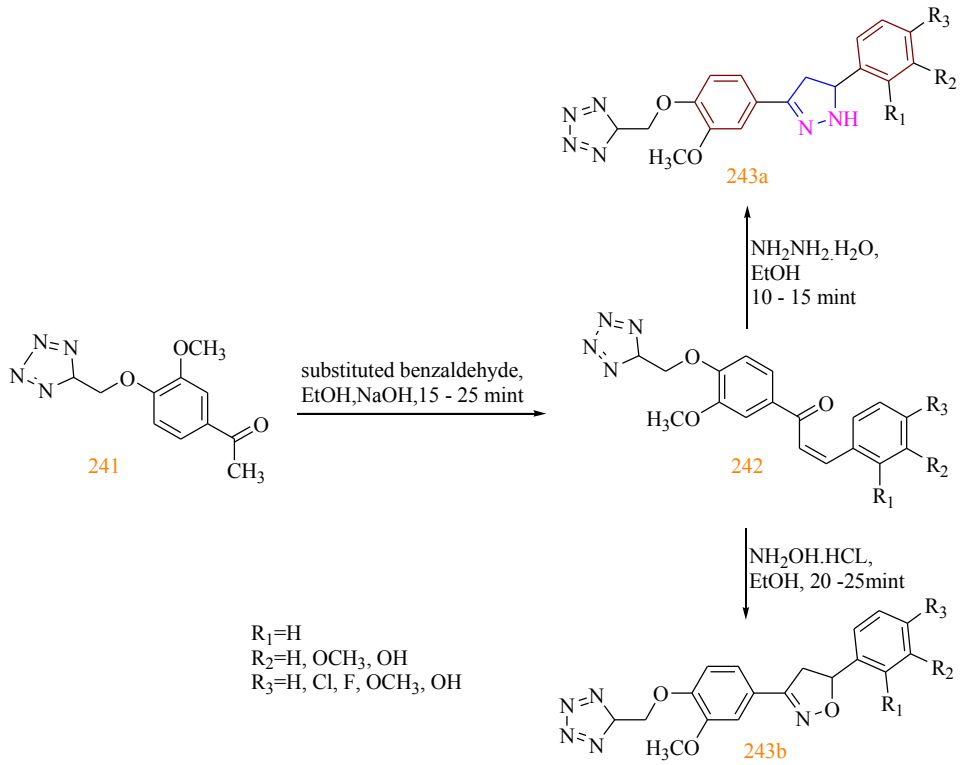
Lee *et al.,* reported the synthesis of pyrazoline derivatives from 1-(1-hydroxynaphthalen-2-yl)ethanone react and substituted 1-(naphthalen-2-yl)ethanone derivatives presence ethanolic potassium hydroxide (Scheme **68**). The synthesized compounds were evaluated for their anticancer activity against the HT-116 cell line and Apoptosis. 3-(Naphthalen-2-yl)-*N*,5-diphenyl-pyrazoline-1-carbothioamide (**278a**) was found to be more potent anticancer agent [88].

Akhtar *et al.,* reported the synthesis of pyrazoline derivatives from substituted acetophenone reacted with phenyl hydrazine in the presence of methanol and sulphuric acid (Scheme **69**). The synthesized compounds were evaluated

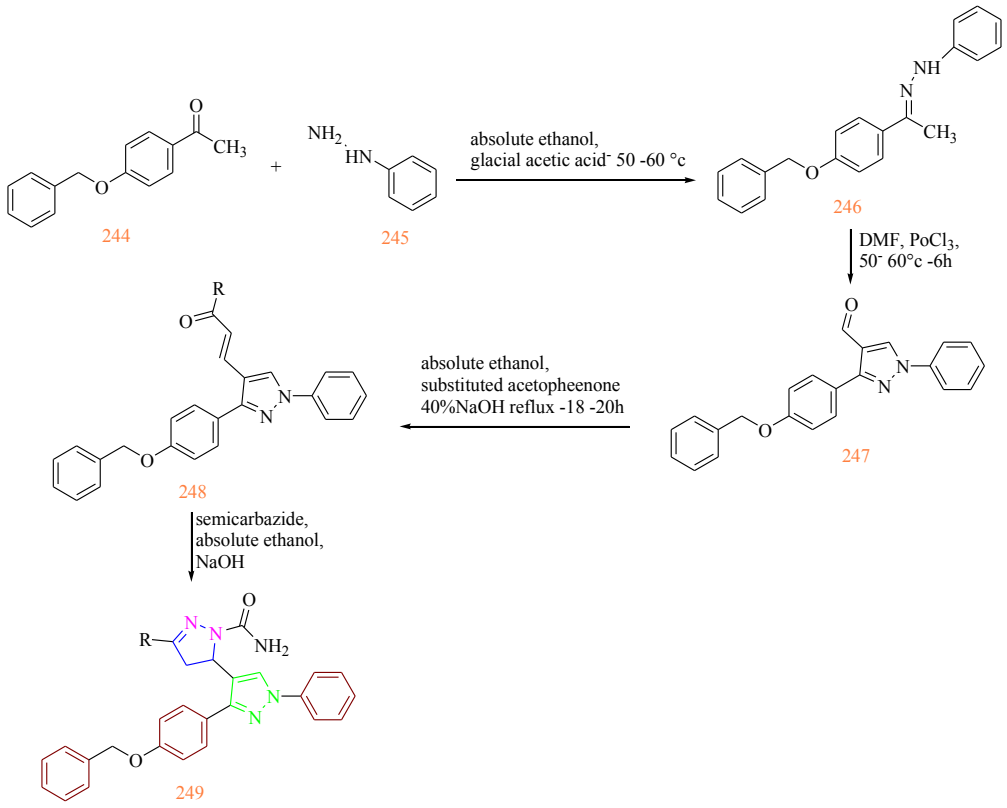


R= 2-pyridinyl, 2-pyrrolyl, 2-furanyl

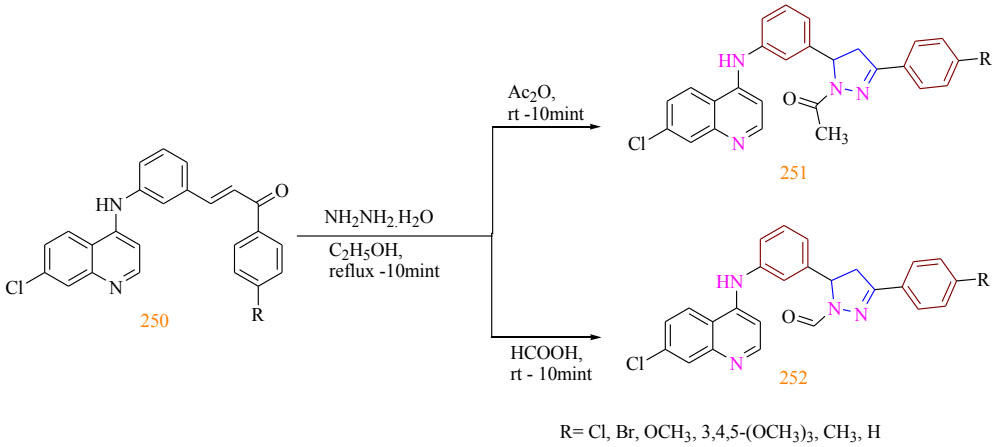
Scheme 59. Synthesis of pyrazole and pyrazoline derivative.



Scheme 60. Synthesis of tetrazole-based pyrazoline and isoxazoline derivatives.



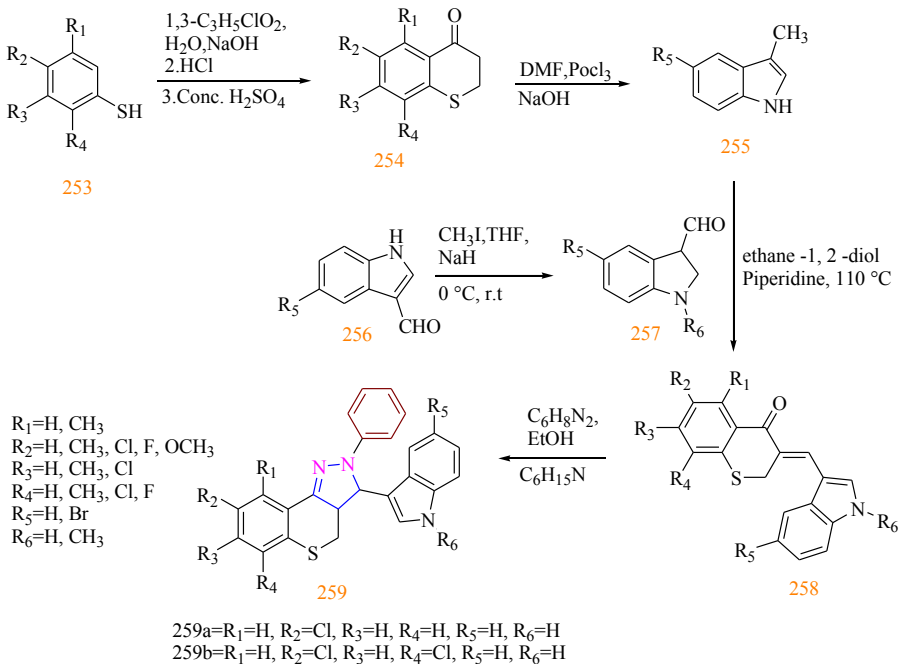
Scheme 61. Synthesis of carboxamide and pyrazoline derivatives.



Scheme 62. Synthesis of *N*-substituted-2-pyrazoline derivatives.

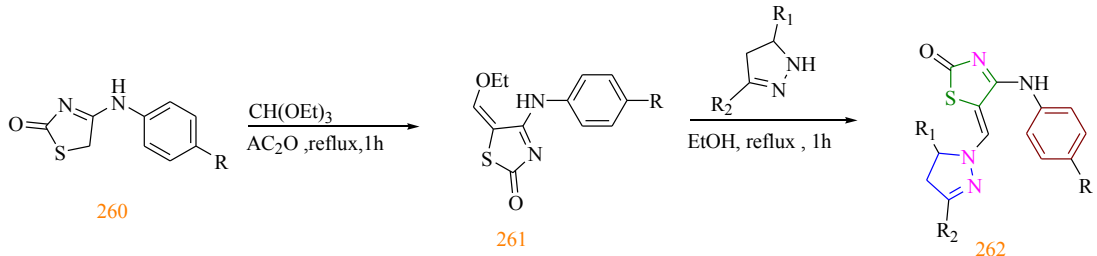
for their anticancer activity against breast cancer cell lines, HacaT, human alveolar basal epithelial cell, SiHa, COLO205, liver cancer cell lines. 5-[3-(4-Methoxyphenyl)-1-phenyl-1H-pyrazol-4-yl]-3-phenyl-4,5- dihydropyrazole-1-carboxamide (**284**) showed significant activity against A549, SiHa, COLO205 and HepG2 cell lines with an IC_{50} value of 4.94,4.54,4.86, and 2.09 µM, respectively [89].

Alkamaly *et al.,* reported the synthesis of pyrazoline derivatives from substituted acetophenone react with a substituted aldehyde in the presence of ethanol and sodium hydroxide with phenylhydrazine (Scheme **70**). The synthesized compounds were screened for their anticancer activity against kinase inhibition EGFR, HER2, FGFR2, VEGFR2, PC-3, liver, triple-negative breast cancer cell lines. 3-{4-[(4-Fluorobenzyl)oxy]phenyl}-5-(4-fluorophenyl)-4,5- dihydro-1H-pyrazole-1-carbothioamide (**291**) and 5-(4-chlorophenyl)-3-{4-[(4-fluorobenzyl)oxy]phenyl}-4,5- dihydro-1H-pyrazole (**288**) showed potent activity against PC-3, HepG-2, MDA-MB-231 with an IC_{50} value of 2.66 ± 0.15, 4.06 ± 0.21, 1.3 ± 0.05µM and 3.71 ± 0.15, 6.03 ± 0.45, 4.38 ± 0.23 respectively [90].



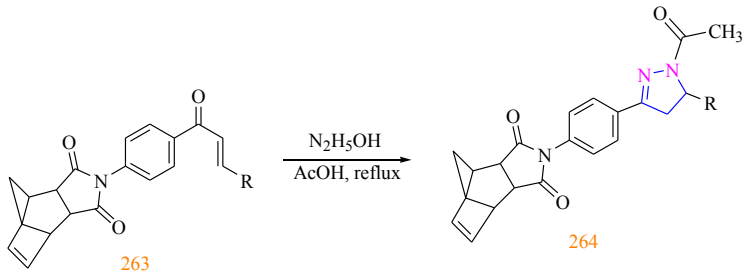
259a=R_1=H, R_2=Cl, R_3=H, R_4=H, R_5=H, R_6=H
259b=R_1=H, R_2=Cl, R_3=H, R_4=Cl, R_5=H, R_6=H

Scheme 63. Synthesis of pyrazoline derivatives.



R=OH, F, Cl, AcO
R_1= 4-F-C_6H_4,Thien -2-yl, 2,4-F_2-C_6H_3, 2,4-F_2-C_6H_4
R_2= 4-OMe-C_6H_4, 4-OMe-C_6H_4, 4-OMe-C_6H_4 ,4-OMe-C_6H_4 , 4-Cl-C_6H_4 , 4-Cl-C_6H_4, 4-Cl-C_6H_4, 4-F-C_6H_4,4-F-C_6H_4

Scheme 64. Synthesis of thiazolidinones and pyrazoline derivatives.

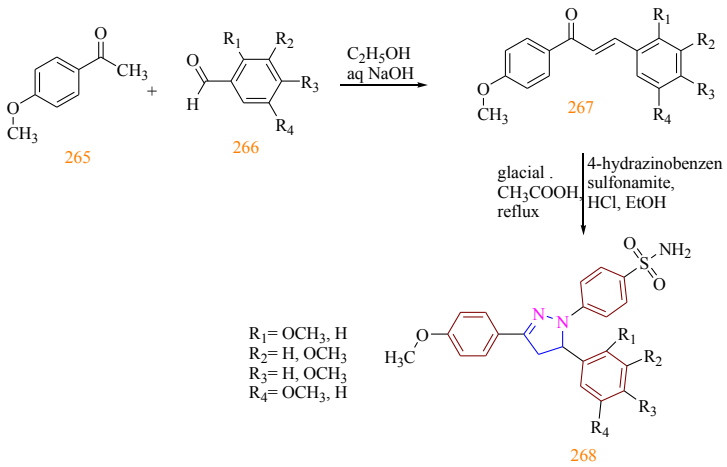


R= 3-CH_3OPh, 4-CH_3OPh, 2-CH_3Ph, 3-CH_3Ph, 4-CH_3Ph, 2-ClPh, 3-ClPh, 4-ClPh, 2-BrPh, 3-BrPh, 4-BrPh, 2-furyl, 2-thienyl, 4-pyridyl.

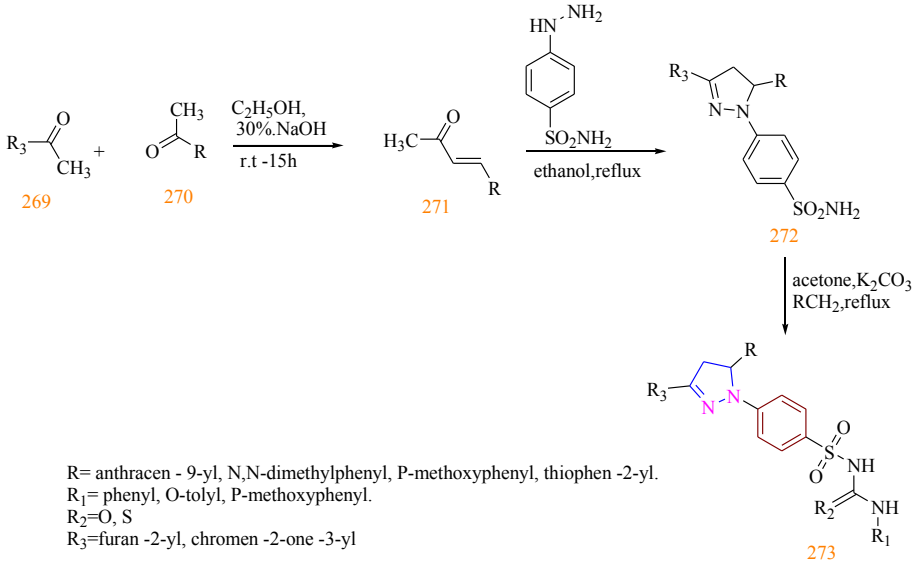
Scheme 65. Synthesis of trisubstituted pyrazoline derivatives.

Wahyuningsih *et al.,* reported the synthesis of pyrazoline derivatives from substituted acetophenone react with 3,4-dimethoxy benzaldehyde in the presence of sodium hydroxide to form chalcone derivatives (Scheme **71**). The synthesized compounds were evaluated for their anticancer activity against MCF-7, T47D, HeLa cell lines. 1-(3-(4-Chlorophenyl)-5-(3,4-dimethoxyphenyl)- 4,5-dihydro-1H-pyrazol-1-yl) ethan-1-one (**296**) showed a potent active site of the EGFR receptor *via* hydrogen bonding with MET769 [91].

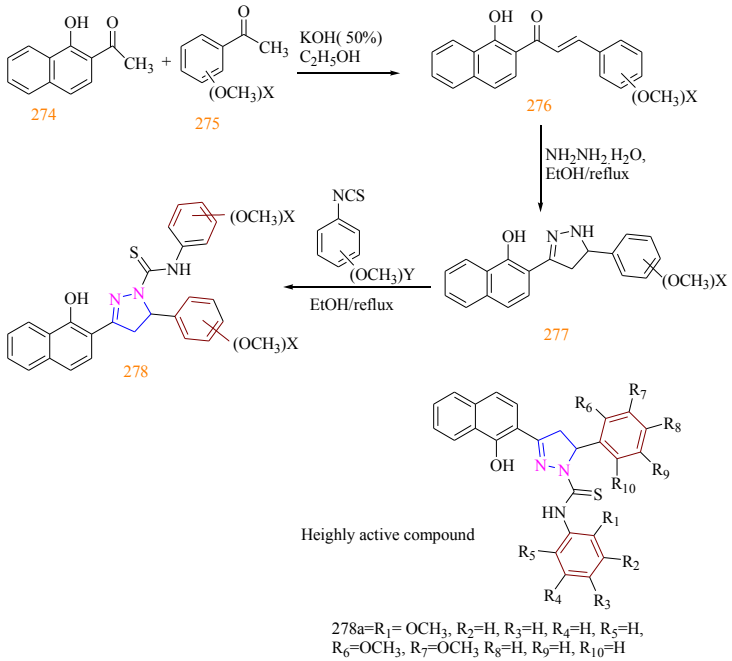
Rathore *et al.,* reported the synthesis of pyrazoline substituted benzene sulfonylureas were obtained by refluxing different pyrazolines (Scheme **72**). The synthesized compounds were evaluated for their anticancer activity against CCRF-CEM, A549/ATCC, COLO-205, SNB-19, MDA-MB-435, and MCF-7 cell lines. *N*-(Butylamino-hydroxy-methyl)-4-[3-(2,5-dimethyl-phenyl)-5-(3,4,5-trimethoxyph-enyl)-4,5-dihydro-pyrazol-1-yl]-benzenesulfonamid (**299**) showed potent activity against in 8 different cell lines with GI_{50} less than 2 µM [92].



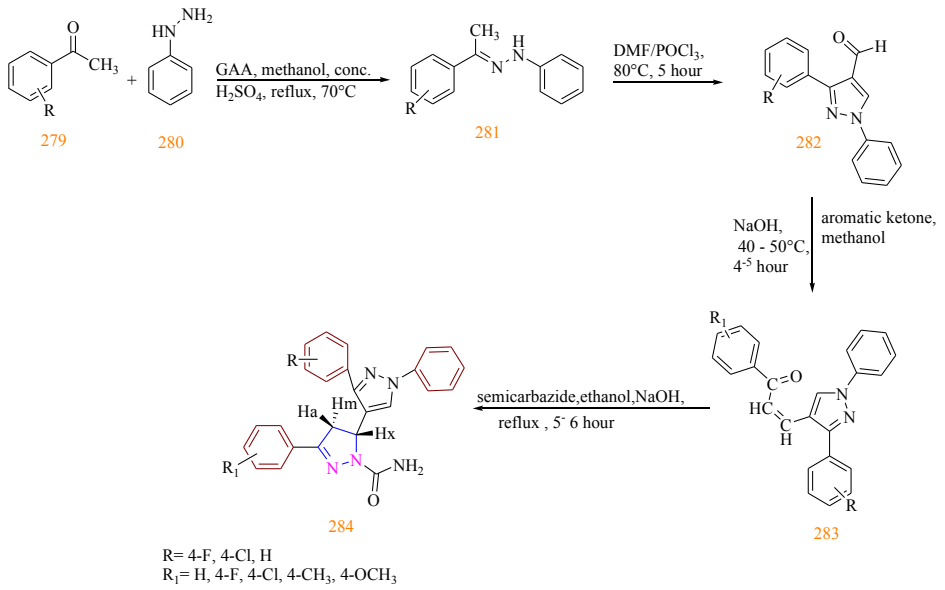
Scheme 66. Synthesis of polymethoxylated -pyrazoline benzene sulfonamide derivatives.



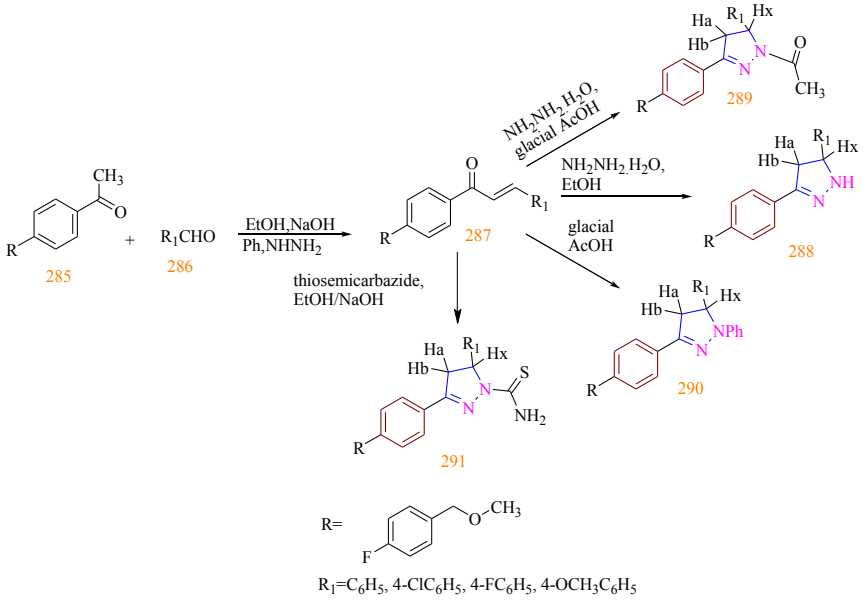
Scheme 67. Synthesis of benzene sulfonylurea containing one pyrazoline derivatives.



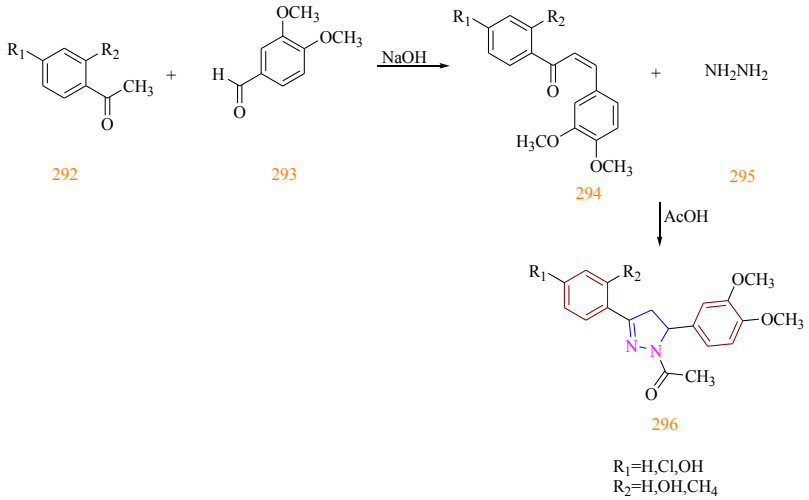
Scheme 68. Synthesis of 3-(naphthalen2-yl)-*N*,5-diphenyl-pyrazoline-1-carbothioamide.



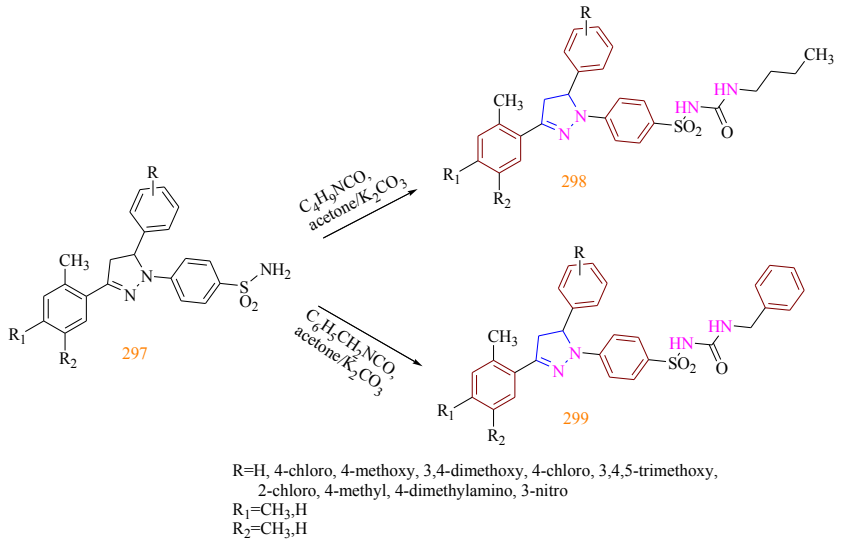
Scheme 69. Synthesis of 15 novel pyrazole-pyrazoline derivatives.



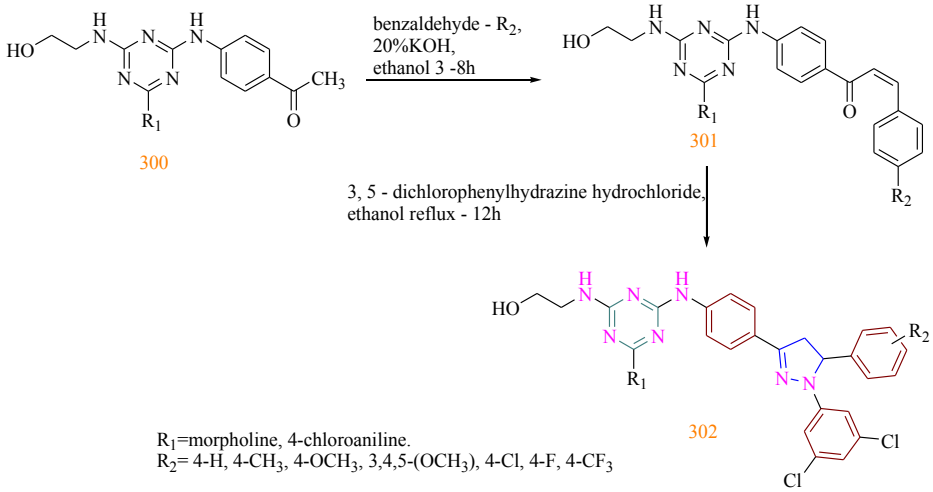
Scheme 70. Synthesis of pyrazoline derivatives.



Scheme 71. Synthesis of chalcone and *N*-acetyl pyrazoline derivatives.



Scheme 72. Synthesis of pyrazoline substituted benzenesulfonylurea derivatives.



Scheme 73. Synthesis of *N*-(3,4-dichlorophenyl) pyrazoline derivative.

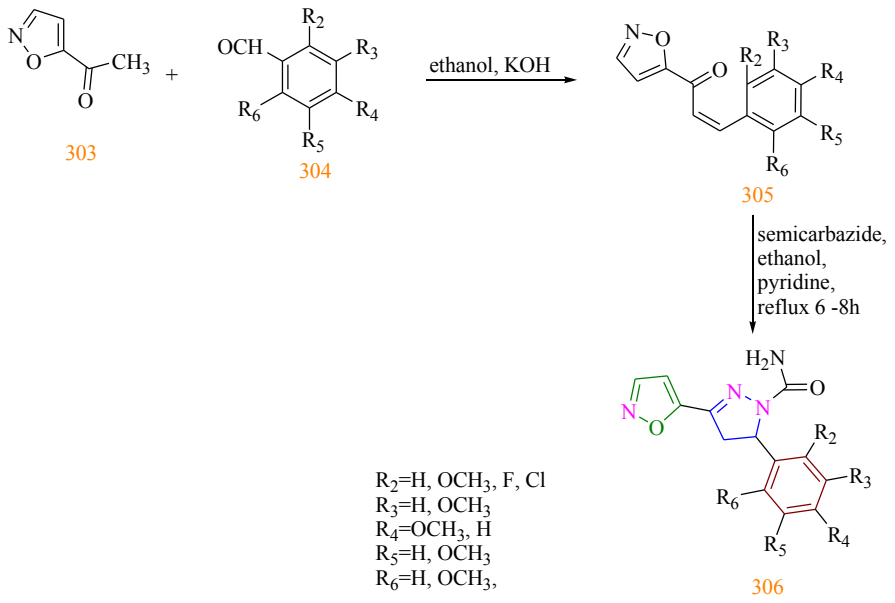
Moreno *et al.,* reported the synthesis of pyrazoline derivatives, 2-((4-((4-(1- (3,5-dichlorophenyl)-5-(aryl)-4,5-dihydro-1H-pyrazol-3-yl)phenyl)amino)-6-morpholino-1,3,5-triazin-2-yl)amino)ethanol (Scheme **73**).The synthesized compounds were screened for their anticancer activity against HL-60(TB), EKVX, KM12, SF-268, UACC-257, OVCAR-8, RXF-393, DU-145, MDA-MB-468 cell lines. (*E*)-1-(4-((4-((2-Hydroxyethyl)amino)-6-morpholino-1,3,5-triazin-2-yl)amino)phenyl)-3-(3,4,5-trimethoxyphenyl)prop-2-en-1-one (**302**) showed significant activity, with outstanding GI_{50} values ranging from 0.422 to 14.9 µM and LC_{50} values ranging from 5.08 mM to >100 µM [93].

Shaik *et al.,* reported the synthesis of pyrazoline derivatives from 1-(isoxazole-5- yl)ethanone condensed was substituted benzaldehyde in the presence of ethanolic potassium hydroxide (Scheme **74**). The synthesized compounds were evaluated for their anticancer activity against the DU-145 (Prostate cancel) cell line. The synthesized compound substituted with R_2=F, R_3, R_4=OCH_3, R_5, R_6=H (**306**) showed more potent activity against DU-145 (Prostate cancel)cell line [94].

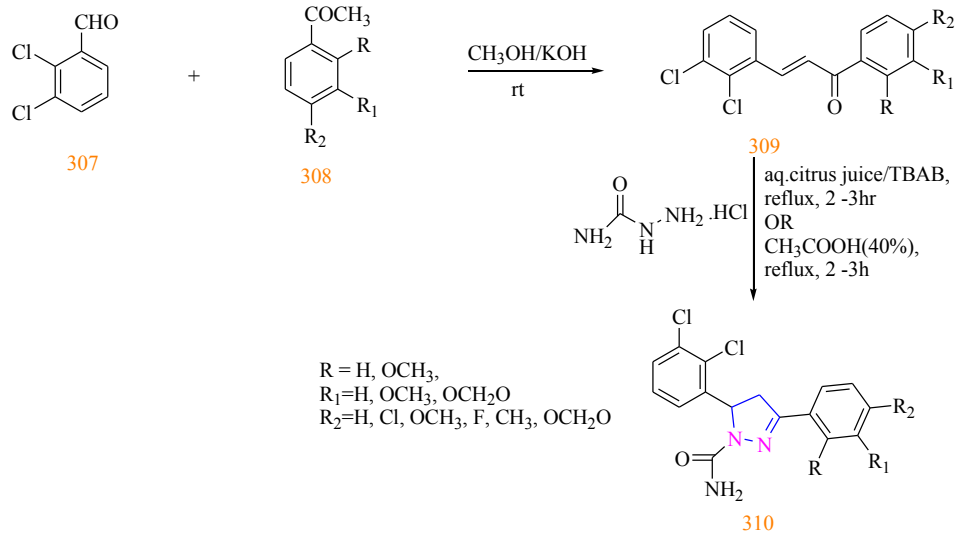
Kumar *et al.,* reported the synthesis of pyrazoline derivatives, 5-(2,3-dichlorophenyl)-4,5-dihydro-1H-pyrazole-1-carbothioamides (Scheme **75**). The synthesized compounds were evaluated for their anticancer against the MCF-7 Cell line. 5-(2,3-Dichlorophenyl)-3-(4-chlorophenyl)-4,5-dihydro-1H-pyrazole-1-carbothioamide (**310**) was found to be more potent activity against MCF-7 cancer cell line [95].

Ozdemir *et al.,* reported the synthesis of pyrazoline derivatives from 2-acetylthiophen react with substituted benzaldehyde in the presence of sodium hydroxide in ethanol (Scheme **76**). The synthesized compounds were evaluated for their anticancer activity against A549, C6 cell lines. The synthesized compounds substituted with R= CH_3 (**314**) showed more potent activity [96].

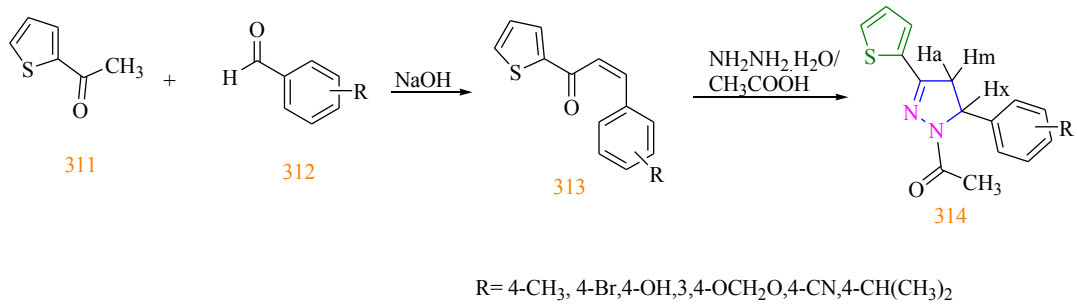
Zhang *et al.,* reported the synthesis of pyrazoline derivatives, 1-methyl-1*H*-indole–pyrazoline (Scheme **77**). The synthesized compounds were screened for their anticancer activity against HeLa, MCF-7, A549, HepG2 cell lines. 5-(5-Bromo-1-methyl-1*H*-indol-3-yl)-3-(3,4,5-trimethoxyphenyl)-4,5-dihydro-1H-pyrazole-1-carboxamide (**319**) showed potent inducer of apoptosis in HeLa cell line [97].



Scheme 74. Synthesis of isoxazolyl chalcones and pyrazoline derivatives.

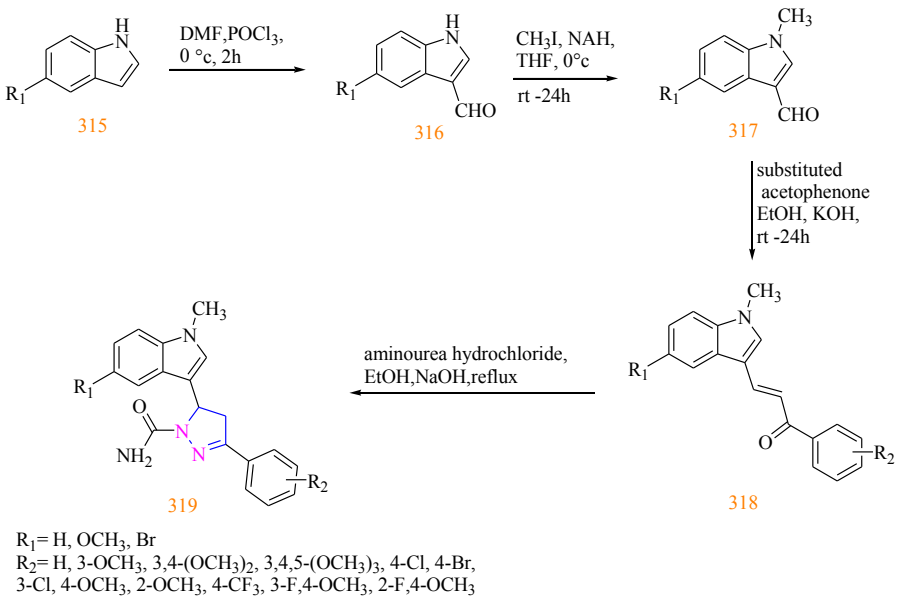


Scheme 75. Synthesis of pyrazole carbothioamides derivative.

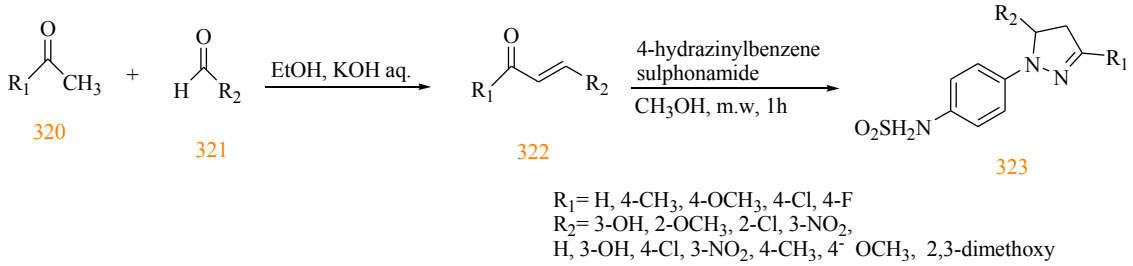


Scheme 76. Synthesis of 1-(2-thienyl)-3-aryl-2-propen-1-ones and pyrazoline derivatives.

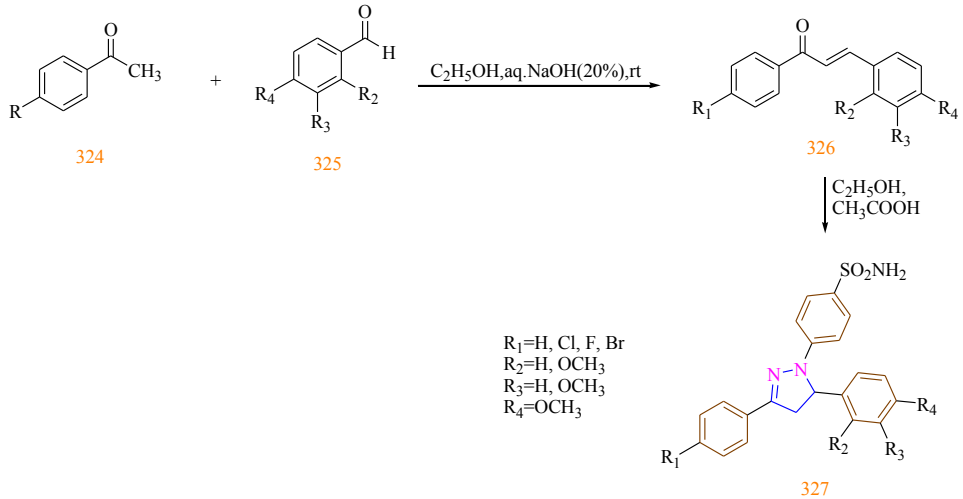
Thach *et al.,* reported pyrazoline derivatives, dihydro-1*H*-pyrazol1-ylbenzene sulfonamides (Scheme **78**). The synthesized compounds were screened for their anticancer activity against Hep-2C, A549, Vero cell lines. 4-(3-(2,3-Dimethoxyphenyl)-5-(4-methoxyphenyl)-4,5-dihydro-1H-pyrazol-1-yl)benzenesulfonamide (**323**) showed potent activity against Hep-2C, and A549 cell lines with an IC_{50} value of 17.23 ± 2.38, 19.82 ± 1.75 µM respectively [98].



Scheme 77. Synthesis of 1-methyl-1*H*-indole–pyrazoline derivatives.



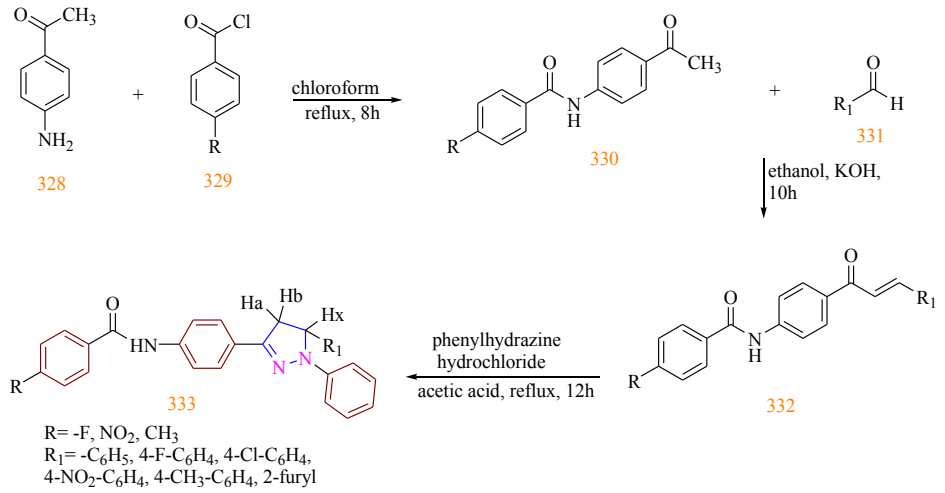
Scheme 78. Synthesis of 1,3,5-substituted pyrazoline sulphonamides.



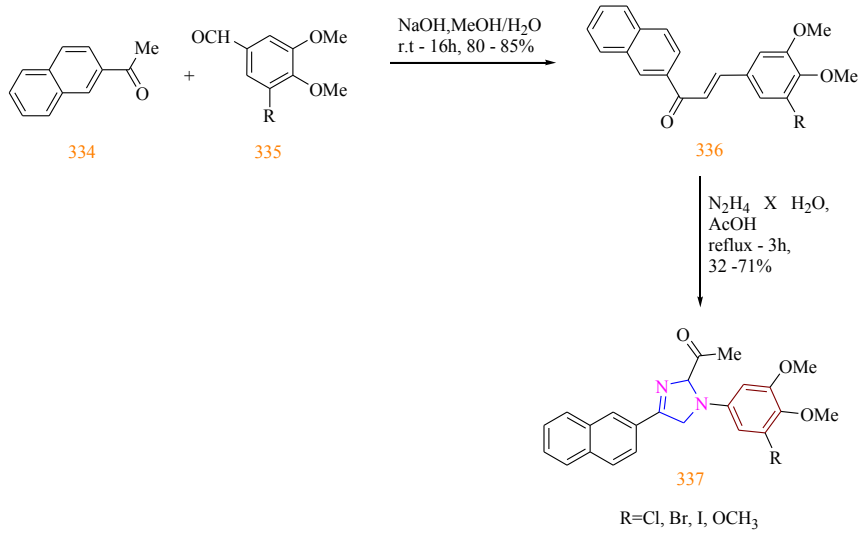
Scheme 79. Synthesis of sulfonamide and pyrazoline derivatives.

Ozgun. *et al.* syntheiszed pyrazoline derivatives, 4-(3-substituted phenyl-5-polymethoxyphenyl-4,5-dihydro-1*H*-pyrazol-1-yl)benzene sulphonamides (Scheme **79**). The synthesized compounds were evaluated for their anticancer activity against HCA-1 and HCA-2, AchE (Acetylcholinesterase), Non-cancer cell lines (Ga9-22,HSC-2,HSC-3,HSC-4) and oral squamous cell lines (Ga9-22,HSC-2,HSC-3,HSC-4) (HGF,HPLF,HPC). 4-(3-(4-Bromophenyl)-5-(2,4-dimethoxyphenyl)-4,5-dihydro-1H-pyrazol-1-yl)benzene sulphonamide (**327**) showed potent activity against 60 cancer cell lines [99].

Tok *et al.,* synthesized *N*-(4-(1-Phenyl-5-aryl-4,5-dihydro-1H-pyrazol-3-yl) phenyl)-4- substituted benzamide (Scheme **80**) and evaluated for their anticancer activity against HeLa, MCF-7, MKN-45, and NIH-3T3 cell lines. 4-Fluoro-*N*-(4-(5-(furan-2-yl)-1-phenyl-4,5-dihydro-1H-pyrazol-3- yl) phenyl) benzamide (**333**) showed potent activity against HeLa, MCF-7, MKN-45 cancer cell lines with an



Scheme 80. Synthesis of pyrazoline derivatives.



Scheme 81. Synthesis of dimethoxyphenyl and pyrazoline derivatives.

IC_{50} value of 17.96±3.34, 0.69±0.13, and 0.88±0.16 μM respectively [100].

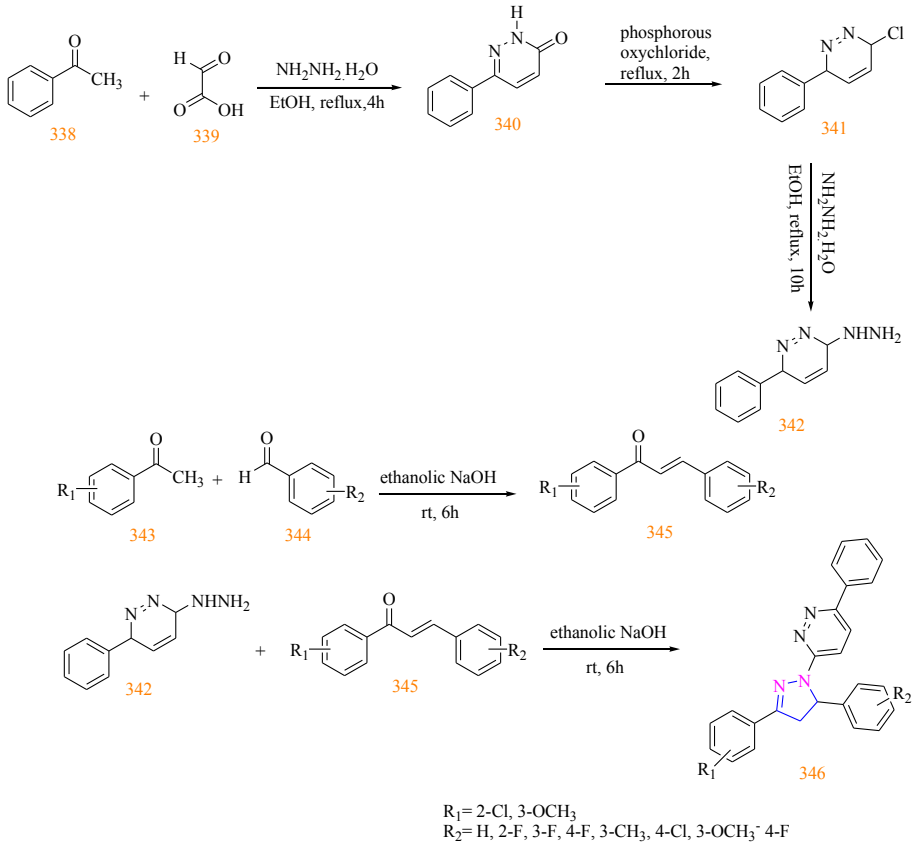
Schmitt *et al.,* synthesized 3-(3-halo-4,5-dimethoxyphenyl)-1-(2-napthyl) prop-2-en-1-one (Scheme **81**) and evaluated their anticancer activity against colorectal cancer, colon cancer, cello Saurus, breast cancer, and BCRP, P-GP cell lines. The compounds substituted with OCH_3 (**337**) were found to be more potent activity against the MCF-7 cancer cell line [101].

Ahmed *et al.,* reported the synthesis of pyrazoline derivatives from acetophenone reacted with oxoacetic acid in the presence of hydrazine hydrate and ethanol (Scheme **82**). The synthesized compounds were evaluated for their anticancer activity against Leukemia, Non-small-cell Lung cancer, Colon cancer, CNS cancer Melanoma, Ovarian Cancer, Renal Cancer, Prostate cancer, Breast cancer cell lines. 3-(5-(4-Fluoro-3-methoxyphenyl)-4,5-dihydro-3-(3-methoxyphenyl)- pyrazol-1-yl)-6-phenylpyridazine (**346**) showed excellent activity against UO-31 renal cancer cell line [102].

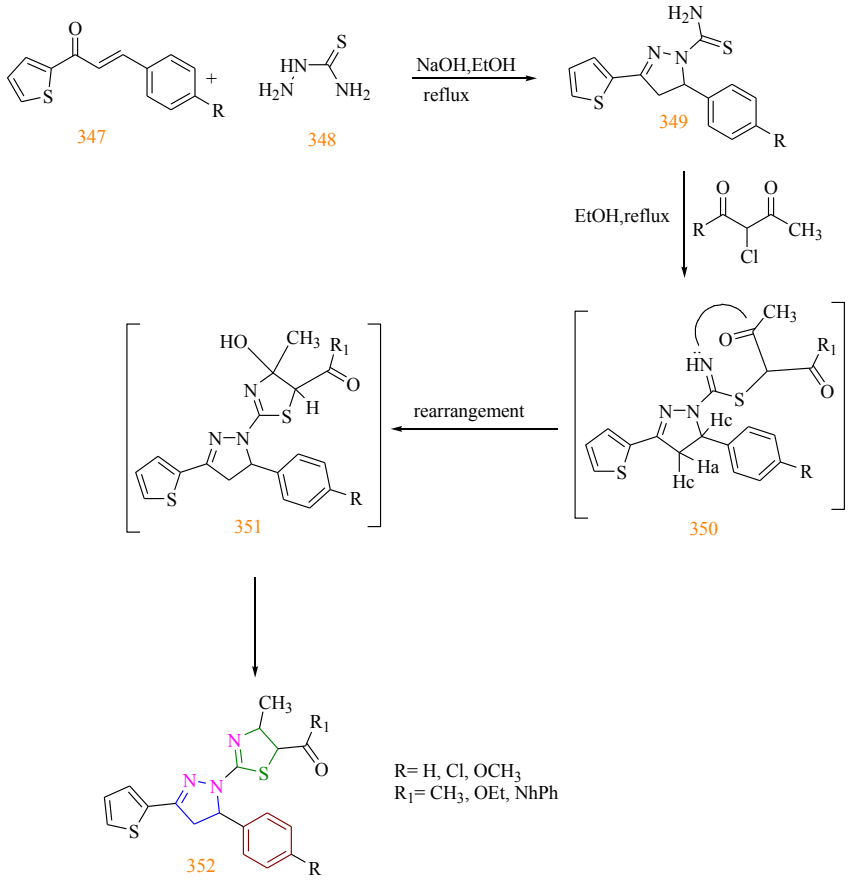
Elwa *et al.,* reported the synthesis of pyrazoline derivatives from 3-(2-thienyl)-5-aryl-1-thiocarbamoyl-2 pyrazoline reacts and 3-(2-thienyl)-5-aryl-1-thiocarbamoyl-2 pyrazoline to yield thiazolyl pyrazoline (Scheme **83**). The synthesized compounds were evaluated for their anticancer activity against BHK, CACO2, HCT-116, MCF-7, HEPG2 cell lines. Ethyl-4-methyl-2-(5-phenyl-3-(thiophen-2-yl)-4,5- dihydropyrazol-1-yl) thiazole-5-carboxylate (**352**) was found to be more potent against HCT-116 cancer cell line [103].

Lopez *et al.,* reported the synthesis of pyrazoline derivatives from a new pregnenolone fused with benzaldehyde (Scheme **84**). The synthesized compounds were evaluated for their anticancer activity against HeLa, MCF-7, A2780, A431 cell lines. (50R)-17b-(1-Acetyl-5-phenyl-3-pyrazolinyl) androst-5-en-3b-ol (**355**) showed significant activity against MCF-7 cancer cell line [104].

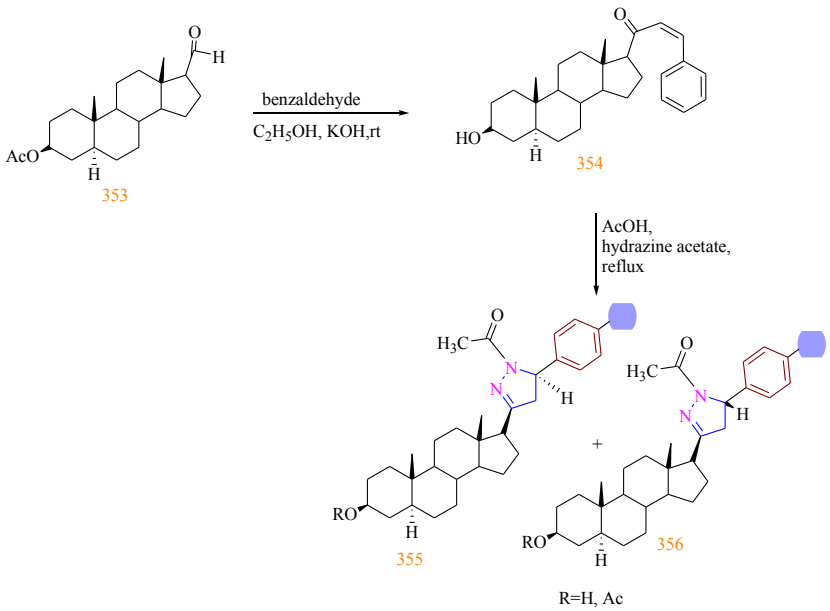
Sharma *et al.,* reported the synthesis of pyrazoline derivatives from substituted acetophenone react with 4-hydroxy-3-methoxybenzaldehyde in the presence of acetic acid and sulphuric acid (Scheme **85**). The synthesized compounds were tested for their anticancer activity against CAKI-I, PC-3, and HeLa cell lines. The compounds substituted with R=H(361) showed potent activity against HeLa and PC-3 cancer cell lines [105].



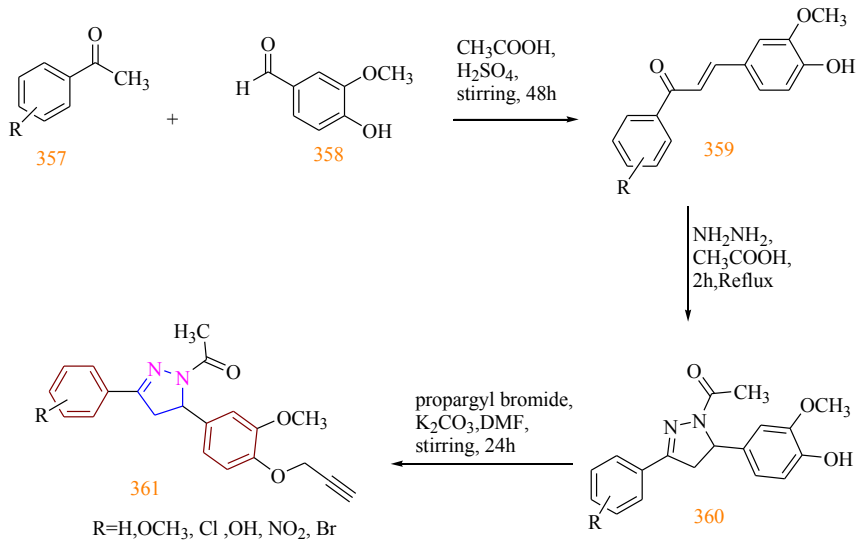
Scheme 82. Synthesis of 4-thiazolidinones, isatin, and pyrazoline derivatives.



Scheme 83. Synthesis of thiophene, thiazole, and pyrazoline derivatives.



Scheme 84. Steroidal benzylidene, pregnenolone, benzaldehyde, and p-substituted benzaldehyde.



Scheme 85. Synthesis of isatin and 3,5-diaryl *N*-acetyl-pyrazolines derivatives.

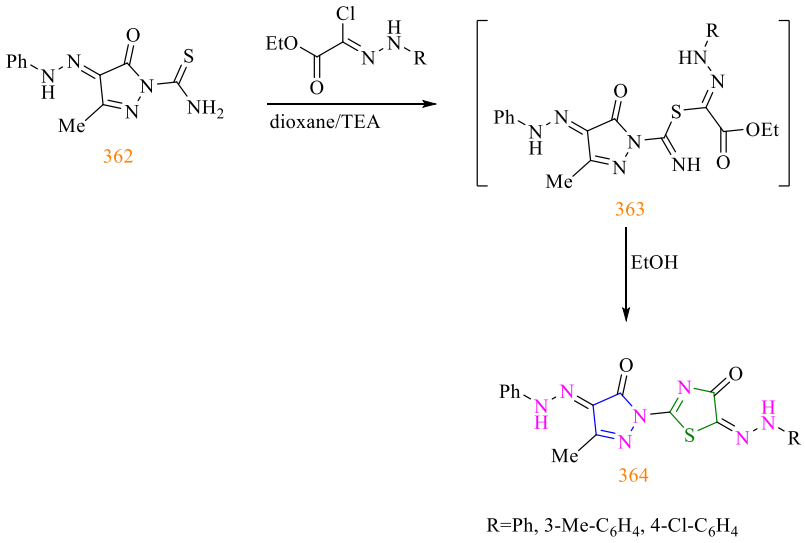
Sayed *et al.,* reported the synthesis of pyrazoline derivatives from (4*E*)-3-methyl-5-oxo-4-(2-phenylhydrazinylidene)-4,5-dihydro-1*H*-pyrazole-1-carbothioamide react with ethyl (2*Z*)-chloro(hydrazinylidene)ethanoate in the presence of dioxane (Scheme **86**). The synthesized compounds were evaluated for their anticancer activity against the HepG-2 cell line. (3-Methyl-5-oxo-4-(2-phenylhydrazono)-4,5-dihydro-1*H*-pyrazol-1-yl)-5-(2-phenylhydra-zono)thia-zol-4(5*H*)-one (**364**) showed significant activity against HepG-2 cancer cell line [106].

Lin *et al.,* reported the synthesis of pyrazoline derivatives from substituted acetophenone react with a substituted aldehyde in the presence of sodium hydroxide and ethanol (Scheme **87**). The synthesized compounds were evaluated for their anticancer against the A549(Human Lung cancer) cell line and promoted FKBP12 and inhibited mTOR. The compound substituted with R=4-Cl and R_1= OMePh (369) showed significant activity against A549 cell lines [107].

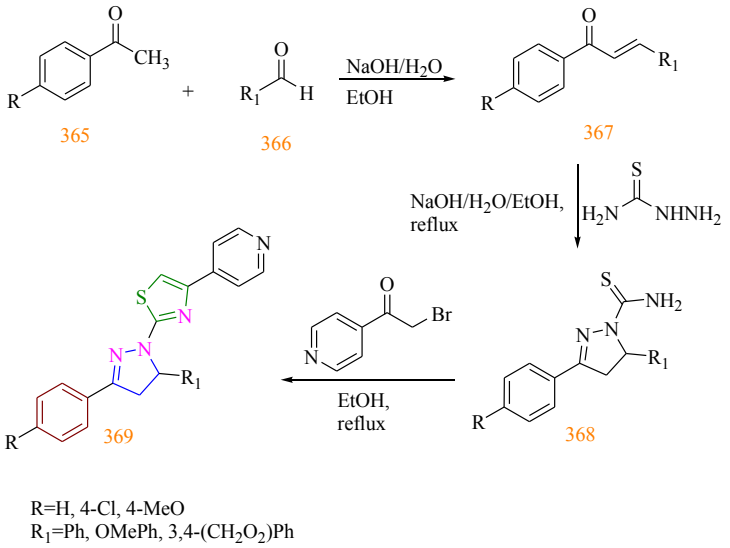
Latif *et al.,* reported the synthesis of 3-(5-aryl-4,5-dihydro-1-phenyl-1H-pyrazol-3-yl)-4-hydroxy2H-chromen-2-one derivative (Scheme **88**) and evaluated for their anticancer activity against HT29, A549, H460, HeLa, HL60, and K562 cancer cell lines, and kinase Inhibition CDK9T1, CDK7H, CDK1B, CDK2E, CDK6D3. 3-(4,5-Dihydro-5-(3,4-dimethoxyphenyl)-1-phenyl-1H-pyrazol-3-yl)-4- hydroxy-2H-chromen-2-one (**372**) showed potent activity against MCF-7 cell line with an IC_{50} value of 0.21μM [108].

Sever *et al.,* reported the synthesis of 1-(4-arylthiazol-2-yl)-3-(4-morpholino/piperidinophenyl)-5-(4-chlorophenyl)-2-pyrazolines (Scheme **89**) and screened for their anticancer activity against A549, MCF-7, and A375 cell lines. 1-(4-(4-Cyanophenyl)thiazol-2-yl)-3-(4-morpholinophenyl)-5-(4-chlorophenyl)-2-pyrazoline (**376**) showed high affinity into the ATP binding sites EGFR and HER2 kinase [109].

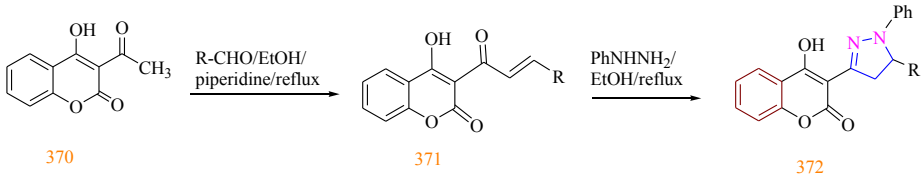
Ahmad *et al.,* reported the synthesis of pyrazoline derivatives from chalcones reacted with hydrazide in the presence



Scheme 86. Synthesis of hydrazonoyl and pyrazolones derivatives.



Scheme 87. Synthesis of fluorescent thiazole-pyrazoline derivatives.

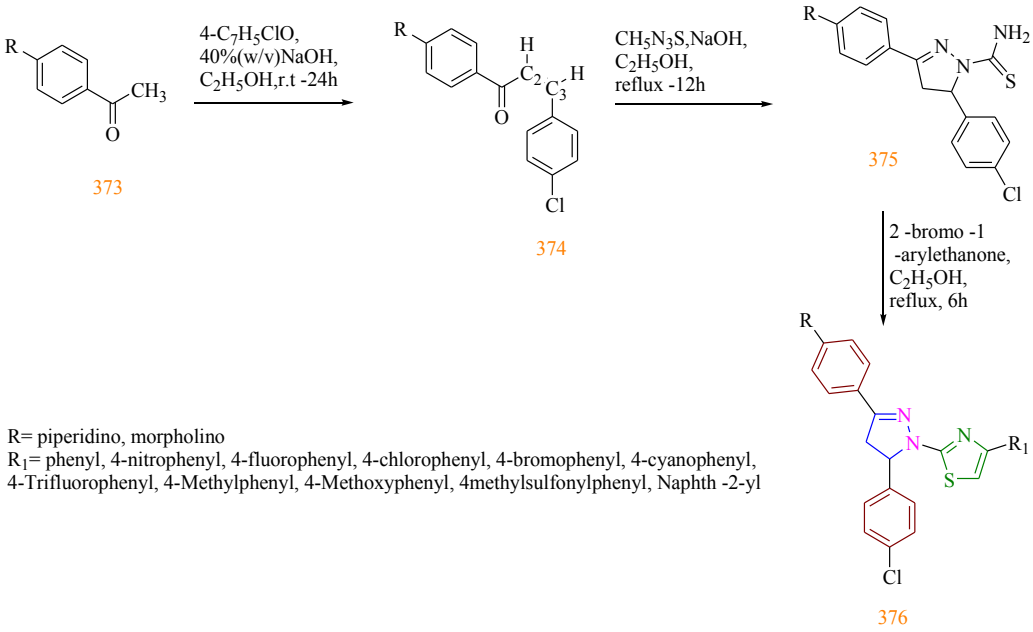


Scheme 88. Synthesis of *N*-phenyl pyrazoline derivatives.

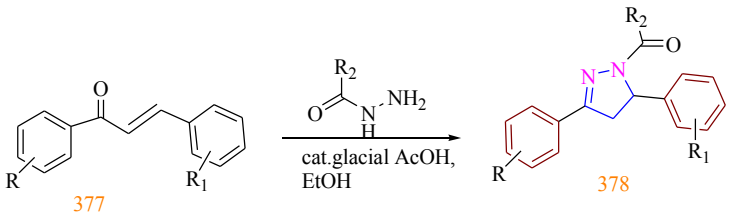
of glacial acetic acid and ethanol (Scheme **90**). The synthesized compounds were screened for their anticancer activity against HCT-15, BT-474, T47D cell lines. (3-(4-Chlorophenyl)-5-(furan-2-yl)-4,5-dihydro-1H-pyrazol-1-yl)(furan-2- yl)methanone (**378**) showed potent activity against BT474 cell lines with IC_{50} value of >50μM [110].

CONCLUSION

The heterocyclic compound pyrazolines is well-known. Pyrazoline is a five-membered heterocyclic ring with three carbon and two nitrogen atoms in close proximity. A variety of methods are used to determine to carry out their synthesis. Several Pyrazoline derivatives have been discovered to retain a significant amount of biological activity against various types of cancer, sparking interest in this field of study. The introduction, general procedure, and synthetic scheme for the synthesis of pyrazoline derivatives are described in the current review based on the review literature reported between 2000 and 2021. This review article discusses various pharmacological profiles of pyrazoline derivatives. The use of pyrazoline to treat cancer is a novel substrate that has piqued the interest of researchers.



Scheme 89. Synthesis of thiazolyl and pyrazoline derivatives.



Scheme 90. Synthesis of pyrazoline derivatives.

LIST OF ABBREVIATIONS

PBMC = Peripheral Blood Mononuclear Cells

VEGFRs = Vascular Endothelial Growth Factor Receptors

CONSENT FOR PUBLICATION

Not applicable.

FUNDING

None.

CONFLICT OF INTEREST

The authors declare no conflict of interest, financial or otherwise.

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