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ARTICLE

Synthesis of Some Pyrazole Derivatives from 5-Chloro- and 5-Azido-1,3-diphenyl-1H-pyrazole-4-carbaldehydes

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Dedicated to Professor Dr. Sultan T. Abu-Orabi on the occasion of his 70th birthday

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Abstract: N-[(5-Azido-1,3-diphenyl-1*H*-pyrazole-4-yl)methylene]-N-arylamines **(4a-c)** and *N*-[(5-Substituted-1,3-diphenyl-1*H*-pyrazole-4-yl)methylene]hydrazides **(5a-e)** were prepared from 5-azido-1,3-diphenyl-1*H*-pyrazole-4-carbaldehyde **(3)** and 5-chloro-1,3-diphenyl-1*H*-pyrazole-4-carbaldehyde **(2)**, respectively. Thermolysis of **(4a-c)** and **(5d-e)** afforded 5-arylamino-1,3-diphenyl-1*H*-pyrazol-4-carbonitriles **(8a-c)** and *N*-(4-cyano-1,3-diphenyl-1*H*-pyrazol-5-yl)hydrazides **(13a,b),** respectively. N-[2-(5-Chloro-1,3-diphenyl-1*H*-pyrazol-4-yl)-4-oxo-thiazolidin-3-yl]amides **(14a,b)** and 3-acetyl-2-(5-chloro-1,3-diphenyl-1*H*-pyrazol-4-yl)-5-aryl-2,3-dihydro-1,3,4-oxadiazoles **(15a,b)** were obtained from N-[(5-chloro-1,3-diphenyl-1*H*-pyrazole-4-yl)methylene]hydrazides **(5a,b)**. 5-Azido-1,3-diphenyl-1H-pyrazol-4-carbaldehyde **(3)** gave unexpectedly 1-(1,3-diphenyl-1,6-dihydropyrrolo-2,3-*c*]pyrazol-5-yl)ethan-1-one **(17)**.

Keywords: Synthesis, Pyrazoles, Azides, Thermolysis, Rearrangements, 1,3,4-Oxadiazoles, Pyrrolo[2,3-c]pyrazole.

Introduction

Pyrazoles represent key structural motifs and occupy a significant position in heterocyclic chemistry. They are widely reported to have significant applications in many fields, such as agrochemical, biological, pharmaceutical and industrial fields[1,2,3]. They possess a wide range of bioactivities[3,4], including anti-inflammatory[5], anti-convulsant[6], anticancer[7], antifungal[8] and antimicrobial ones[9,10]. Recently, synthesis and pharmacological activities of pyrazoles were reviewed[11,12]. Research reported in this article was carried out in view of the vast area of synthesis and applications of pyrazole containing compounds. There are various synthetic approaches in synthesizing new pyrazole-derivatives. The most common synthetic approach involves the reaction of 1,3-diketones with hydrazine derivatives. Another approach concentrates on the synthesis of pyrazole derivatives from the pyrazole as the central core. In particular, our aim here is to investigate the utility of 5-chloro- and 5-azido-1,3-diphenyl-1*H*-pyrazole-4-carbaldehydes in the synthesis of some other substituted and condensed pyrazoles and to study the reactions involved.

Materials and Methods

All melting points were determined on a Koffler melting point apparatus and are uncorrected. IR spectra in KBr were recorded on a Bruker FT-IR ISS 25 spectrophotometer

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[ν_{max} in (cm^{-1})]. Nuclear Magnetic Resonance (NMR) spectra were recorded on a Bruker Avance of 300 MHz for ^1H NMR and 75 MHz for ^{13}C NMR using DMSO-d_6 as a solvent and tetramethylsilane (TMS) as an internal standard. The chemical shift (δ) values are expressed in parts per million (ppm). Legend: s = singlet, d = doublet, t = triplet and m = multiplet. Mass spectra were recorded on Shimadzu GCMS-QP 1000 EX mass spectrometer.

Synthesis

*N-[(5-Azido-1,3-diphenyl-1H-pyrazole-4-yl)-methylene]-N-arylamines **(4a-c)***

General procedure: 5-azido-1,3-diphenyl-1*H*-pyrazole-4-carbaldehyde **(3)** (0.5 g, 0.002 mol) was dissolved in ethanol (25 ml), glacial acetic acid (0.2 ml) and amine (0.002 mol) was added. The reaction mixture was kept standing at room temperature overnight. The yellow crystalline precipitate **(4a-c)** was isolated by filtration and washed with cold ethanol.

*N-[(5-Azido-1,3-diphenyl-1H-pyrazol-4-yl)-methylene]-N-phenylamine **(4a)***

Yield: 63%; mp. 79-81°C; ν_{max} (cm^{-1}) 2141 (N_3), 1623 (C=N); δ_H 8.54 (s, H, CH=N), 6.97-8.18 (m, 15H, Ar-H); δ_C 151.3 (C=N), 147.6-114.0 (Ar-C); *m/z* (ESI) = 364.

*N-[(5-Azido-1,3-diphenyl-1H-pyrazol-4-yl)-methylene]-N-(4-methylphenyl)amine **(4b)***

Yield: 72%; mp. 130-131°C; ν_{max} (cm^{-1}) 2142 (N_3), 1625 (C=N); δ_H 8.49 (s, H, CH=N), 7.89-7.01 (m, 14H, Ar-H), 2.50 (s, 3H, CH_3); δ_C 153.3 (C=N), 150.8-112.1 (Ar-C), 24.6 (CH_3); *m/z* (ESI) = 378.

*N-[(5-Azido-1,3-diphenyl-1H-pyrazol-4-yl)-methylene]-N-(4-methoxyphenyl)amine **(4c)***

Yield: 52%; mp. 92-94°C; ν_{max} (cm^{-1}) 2140 (N_3), 1621 (C=N); δ_H 8.55 (s, H, CH=N), 7.79-6.96 (m, 14H, Ar-H), 3.76 (s, 3H, CH_3); δ_C 152.7 (C=N), 150.3-110.7 (Ar-C), 55.8 (OCH_3); *m/z* (ESI) = 394.

*N-[(5-Substituted-1,3-diphenyl-1H-pyrazole-4-yl)methylene]hydrazides **(5a-e)***

General procedure: 5-Chloro-1,3-diaryl-1*H*-pyrazole-4-carbaldehyde (**2**) or 5-azido-1,3-diphen-yl-1*H*-pyrazole-4-carbaldehyde (**3**) (1.30 g, 0.005 mol) was dissolved in ethanol (15 ml), glacial acetic acid (0.2 ml) and the acid hydrazide (0.005mol) were added and the reaction mixture was kept standing at room temperature for 2h. The yellow crystalline precipitate **(5a-e)** was isolated by filtration and washed with ethanol. The chloropyrrazole hydrazides **(5a-c)** were crystallized from ethanol, while the azido compounds (**5d,e)** were used without further purification.

*N-[(5-Chloro-1,3-diphenyl-1H-pyrazol-4-yl)-methylene]benzohydrazide **(5a)***

Yield: 70%; mp. 229-230°C; ν_{max} (cm^{-1}) 1645 (C=O); δ_H 11.83 (s, H, NH), 8.60 (s, 1H, CH=N), 7.52 -7.94 (m, 15H, Ar-H); δ_C 163.2 (C=O), 151.7 (C=N), 140.3-112.8 (Ar-C); *m/z* (ESI) = 402 [M+2].

*N-[(5-Chloro-1,3-diphenyl-1H-pyrazol-4-yl)-methylene]isonicotinohydrazide **(5b)***

Yield: 70%; mp. 232-233°C; ν_{max} (cm^{-1}), 1652 (C=O); δ_H 12.02 (s, H, NH), 8.80 (s, H, CH=N), 8.50-7.50 (m, 14H, Ar-H); δ_C 161.6 (C=O), 151.9 (C=N), 150.8-112.5 (Ar-C); *m/z* (ESI) = 403 [M+2].

*N-[(5-Chloro-1,3-diphenyl-1H-pyrazol-4-yl)-methylene]-2-cyanoacetohydrazide **(5c)***

Yield: 77%; mp. 234-236°C; ν_{max} (cm^{-1}), 2261 (CN), 1692 (C=O); δ_H 11.70 (s, H, NH), 8.10 (s, H, CH=N), 7.70-7.51 (m, 10H, Ar-H), 3.95 (CH_2); δ_C 164.8 (C=O), 151.5 (C=N), 116.3 (CN) 140.1-112.2 (Ar-C), 24.58(CH_2); *m/z* (ESI) = 365 [M+2].

*N-[(5-Azido-1,3-diphenyl-1H-pyrazol-4-yl)-methylene]benzohydrazide **(5d)***

Yield: 50%; mp. 118-120°C; ν_{max} (cm^{-1}) 2138 (N_3), 1644 (C=O); δ_H 11.85 (s, H, NH), 8.65 (s, H, CH=N), 7.95-7.40 (m, 15H, Ar-H); δ_C 164.8 (C=O), 152.9 (C=N), 151.7-107.5 (Ar-C); *m/z* (ESI) = 407.

*N-[(5-Azido-1,3-diphenyl-1H-pyrazol-4-yl)-methylene]isonicotinohydrazide **(5e)***

Yield: 50%; mp. 120-123°C; ν_{max} (cm^{-1}) 2140 (N_3), 1650 (C=O); δ_H 12.40 (s, H, NH), 8.77 (s, H, CH=N), 8.60-7.38 (m, 14H, Ar-H); δ_C 165.3 (C=O), 152.4 (C=N), 151.4-106.8 (Ar-C); *m/z* (ESI) = 408.

*5-Arylamino-1,3-diphenyl-1H-pyrazol-4-carbonitriles **(8a-c)***

General procedure: A solution of (5-azido-1,3-diphenyl-1*H*-pyrazol-4-ylmethylene)-N-arylamine **(4a-c)** (0.0017 mol) in ethyl acetate (15ml) was refluxed for 4h. The solution was concentrated and cooled. The

yellow solid separated was collected by filtration, dried in air and crystallized from pet-ether (bp. 60-80)/ethyl acetate 3:1.

1,3-diphenyl-5-(phenylamino)-1H-pyrazole-4-carbonitrile ***(8a)***

Yield: 81%, mp. 126-128°C; ν_{max} (cm^{-1}) 3330 (NH), 2217 (CN); δ_H 8.99 (s, 1H, NH), 8.00-6.90 (m, 15H, Ar-H); δ_C 151.8-82.4 (Ar-C), 114.6 (CN); *m/z* (ESI) = 336.

5-[(4-Methylphenyl)amino]-1,3-di-phenyl-1H-pyrazole-4-carbonitrile ***(8b)***

Yield: 90%, mp. 122-123°C; ν_{max} (cm^{-1}) 3305 (NH), 2222 (CN); δ_H 8.88 (s, H, NH), 8.01-6.93 (m, 14H, Ar-H), 2.20 (CH_3); δ_C 151.8-81.4 (Ar-C), 114.6 (CN), 20.8 (CH_3); *m/z* (ESI) = 350.

5-[(4-Methoxyphenyl)amino]-1,3-di-phenyl-1H-pyrazole-4-carbonitrile ***(8c)***

Yield: 71%, mp. 149-150°C; ν_{max} (cm^{-1}) 3442 (NH), 2223 (CN); δ_H 8.76 (s, H, NH), 7.94-6.86 (m,14H, Ar-H), 3.72 (OCH_3); δ_C 155.5-78.9 (Ar-C), 114.8 (CN), 55.7 (OCH_3); *m/z* (ESI) = 366.

N-(4-Cyano-1,3-diphenyl-1H-pyrazol-5-yl)-hydrazide derivatives ***(13a,b)***

General procedure: A solution of 5-azido-1,3-diphenyl-1H-pyrazol-4-yl)methylenehydrazides **(5d,e)** (0.0015 mol) in toluene (15 ml) was refluxed for 2h. The solution was concentrated and cooled and the yellow solid separated was collected by filtration, dried in air and crystallized from pet-ether (bp. 60-80)/ ethyl acetate 3:1.

N-(4-Cyano-1,3-diphenyl-1H-pyrazol-5-yl)-benzohydrazide ***(13a)***

Yield: 93%, mp. 163-165°C; ν_{max} (cm^{-1}) 3222 (NH), 3200 (NH), 2220 (CN), 1654 (C=O); δ_H 12.22 (s, 1H, CONH), 8.23 (s,1H, NH) 7.89-736 (m, 15H, Ar-H); δ_C 164.8 (C=O), 152.4-119.8 (Ar-C), 113.7 (CN); *m/z* (ESI) = 379.

N-(4-Cyano-1,3-diphenyl-1H-pyrazol-5-yl)iso-nicotinohydrazide ***(13b)***

Yield: 77%, mp. 122-123°C; ν_{max} (cm^{-1}) 3385 (NH), 3292 (NH), 2201 (CN) and 1656 (C=O); δ_H 11.83 (s, 1H, CONH), 8.79 (s, 1H, NH), 8.67-6.99 (m, 14H, Ar-H), 6.99 (s, 1H, NH); δ_C 160.9 (C=O), 150.9-97.8 (Ar-C), 114.5 (CN); *m/z* (ESI) = 380.

N-[2-(5-Chloro-1,3-diphenyl-1H-pyrazol-4-yl)-4-oxo-thiazolidin-3-yl]amides ***(14a,b)***

General procedure: A mixture of N-[(5-chloro-1,3-diphenyl-1*H*-pyrazole-4-yl)methyl-ene]hydrazide **(5a,b)** (0.015 mol) and thioglycolic acid (0.015 mol) in *N,N*-dimethylformamide (DMF) (50 ml), containing a pinch of anhydrous $ZnCl_2$, was refluxed for 6 h. The reaction mixture was cooled, poured onto crushed ice and the yellow solid thus formed was filtered off, washed with water and crystallized from ethanol.

N-[2-(5-Chloro-1,3-diphenyl-1H-pyrazol-4-yl)-4-oxo-1,3-thiazolidin-3-yl]benzamide ***(14a)***

Yield: 82%, mp. 130-133°C; ν_{max} (cm^{-1}) 3436 (NH), 1698 (br.) (2C=O); δ_H (1H, NH), 8.78-7.41 (m, 15H, Ar-H), 5.51 (s, 1H, CH), 3.46 (d, 1H, CH), 3.37 (d, 1H, CH); δ_C 170.7 (C=O), 170.2 (C=O), 152.2-115.1 (Ar-C), 44.1 (CH), 34.7 (CH_2); *m/z* (ESI) = 474.

N-[2-(5-Chloro-1,3-diphenyl-1H-pyrazol-4-yl)-4-oxo-thiazolidin-3-yl]isonicotinamide ***(14b)***

Yield: 82%, mp. 199-201°C; ν_{max} (cm^{-1}) 3400 (NH), 1697 (br.) (2C=O); δ_H (s, 1H, NH) 7.78-7.47 (m, 14H, Ar-H,), 5.51 (s, 1H, CH), 3.49 (d, 1H, CH), 3.38 (d, 1H, CH); δ_C 170.1 (C=O), 161.3 (C=O), 151.2-112.0 (Ar-C), 58.8 (CH), 37.2 (CH_2); *m/z* (ESI) = 475.

3-Acetyl-2-(5-chloro-1,3-diphenyl-1H-pyrazol-4-yl)-5-aryl-2,3-dihydro-1,3,4-oxadiazoles ***(15a,b)***

General procedure: A mixture of N-[(5-chloro-1,3-diphenyl-1*H*-pyrazole-4-yl)methyl-ene]hydrazide **(5a,b)** (0.00145 mol) and excess acetic anhydride (10 ml) was refluxed for 2h. The reaction mixture was then cooled and poured onto crushed ice. The yellow precipitate obtained was filtered, washed with water, dried in air and crystallized from ethanol.

3-Acetyl-2-(5-chloro-1,3-diphenyl-1H-pyrazol-4-yl)-5-phenyl-2,3-di-hydro-1,3,4-oxadiazole ***(15a)***

Yield: 75%, mp. 132-135°C; ν_{max} (cm^{-1}), 1663 (C=O); δ_H 7.25 ppm (s, 1H, oxadiazole-H), 8.74-7.22 (m, 14H, Ar-H), 2.21 (CH_3); δ_C 167.7 (C=O), 153.5 (C=N), 153.3-113.5 (Ar-C), 87.1 (CH), 21.7 (CH_3); *m/z* (ESI) = 442.

*4-[4-Acetyl-5-(5-chloro-1,3-diphenyl-1H-pyrazol-4-yl)-4,5-dihydro-1,3,4-oxadiazol-2-yl]pyridine **(15b)***

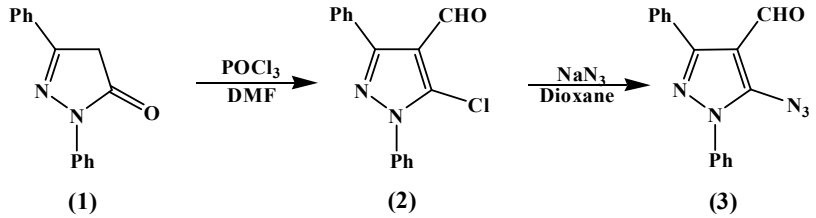
Yield: 80%, mp. 132-135°C; ν_{max} (cm^{-1}) 1663, (C=O); δ_H 7.26 ppm (s, 1H, oxadiazole-H), 7.26-7.83 (m, 14H, Ar-H), 3.4 (CH), 2.22 (CH_3); δ_C 166.8 (C=O), 154.4 (C=N), 151.4-113.1 (Ar-C), 85.8 (CH), 21.2 (CH_3); *m/z* (ESI) = 443.

*1-(1,3-diphenyl-1,6-dihydropyrrolo[2,3-c]-pyrazol-5-yl)ethan-1-one **(17)***

A mixture of 5-azido-1,3-di phenyl-1H-pyrazol-4-carbaldehyde **(3)** (1.00 g, 0.003 mol) and acetone (0.003 mol) was added to 4% ethanolic potassium hydroxide solution (50ml) and the resulting mixture was stirred at (0-5°C) for 2h. The white precipitate that formed was isolated by filtration, washed with cold ethanol, dried in air and crystallized from ethanol. Yield: 71%, mp. 125-128°C; IR (cm^{-1}) 3427 (NH), 1643, (C=O); δ_H 8.50-7.26 (m, 10H, Ar-H, 1H, pyrrole-H and NH), 2.65 (s, 3H, CH_3); δ_C 159.4 (C=O), 151.5-113.2 (Ar-C), 25.1 (CH_3); *m/z* (ESI) = 301.

Results and Discussion

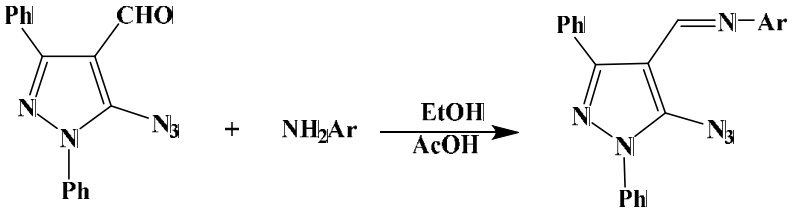
1,3-diphenyl-1,4-dihydropyrazole-5-one (**1**) has been synthesized by treating a mixture of ethyl benzoylacetate and phenylhydrazine following a reported procedure[13]. Upon Vilsmeier-Haack formylation reaction (DMF-$POCl_3$), pyrazolone **(1)** yielded pyrazole-4-carbaldehydes (**2)** as reported in the literature[14,15] (scheme 1). Treating 5-chloro-1,3-diphenyl-1*H*-pyrazole-4-carbalde-hyde (**2**) with sodium azide in DMSO gave 5-azido-1,3-diphenyl-1*H*-pyrazole-4-carbaldehyde **(3)**[16]. These bifunctional compounds **(2)** and **(3)** would be useful in the synthesis of other pyrazole derivatives.



(1) (2) (3)

Scheme 1. Synthesis of 2 and 3.

Synthesis of 5-azidopyrazole-4-methylene-arylamines **(4a-c)** was carried out successfully, using well-established procedures for making azomethines by condensing 5-azido-1,3-diphenyl-1*H*-pyrazole-4-carbaldehyde **(3)** with some aromatic amines (scheme 2).



(3) (4a-c)

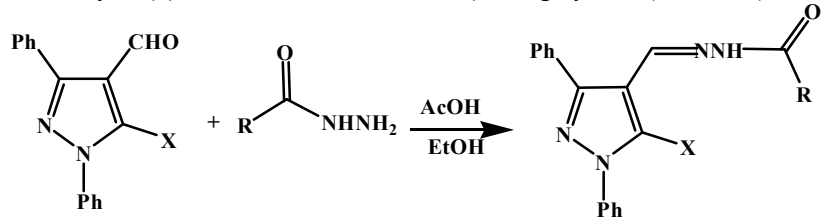
a: Ar = Ph; b: Ar = 4-$CH_3C_6H_4$; c: Ar = 4-$OCH_3C_6H_4$

Scheme 2. Synthesis of 5-azidopyrazole-4-methylenearylamines (4a-c).

The spectral data of the synthesized compounds **(4a-c)** are in agreement with their proposed structures. The IR spectra showed absorption bands at *v* 2140-2142 cm^{-1} and *v* 1621-1625 cm^{-1} corresponding to N_3 and C=N groups, respectively. The ^1H NMR spectra showed the azomethine protons as singlets at δ 8.55-8.5 and the aromatic protons as multiplets at δ 8.00-6.50 ppm. Methyl and methoxy protons appeared as singlets at δ 2.50 ppm for **(4b)** and at δ 3.70 ppm for **(4c)**. The ^{13}C NMR spectra showed signals at δ 153.30-151.29

ppm representing the azomethine carbons. The signals at δ 24.6 ppm and δ 55.8 ppm were assigned to the methyl carbon in **(4b)** and to the methoxy carbon in **(4c),** respectively.

Condensing 5-chloro-1,3-diphenyl-1*H*-pyraazole-4-carbaldehyde **(2)** and 5-azido-1,3-diphenyl-1*H*-pyrazole-4-carbaldehyde **(3)** with acid hydrazides in ethanol, in the presence glacial acetic acid as catalyst, resulted in the formation of *N*-[(5-substituted-1,3-diphenyl-1*H*-pyrazole-4-yl)-methylene]hydrazides **(5a-e)** in high yields (scheme 3).



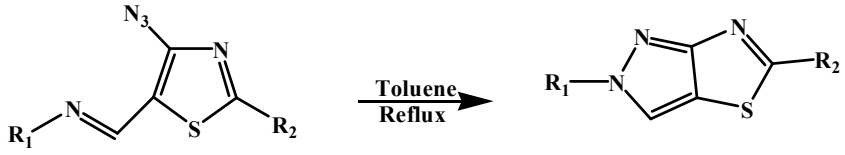
(2),(3) **(5a-e)**

a: R = Ph, X = Cl; b: R = 4-Pyridyl, X = Cl
c: R = CH_2CN, X = Cl; d: R = Ph, X = N_3
e: R = 4-Pyridyl, X = N_3

Scheme 3. Synthesis of *N*-[(5-substituted-1,3-diphenyl-1*H*-pyrazole-4-yl)-methylene]hydrazides (5a-e).

The spectral data of the synthesized 5-substituted pyrazole-4-methylene hydrazides **(5a-e)** agree with the proposed structures. The IR spectra showed absorption bands at *v* 1692-1645 cm^{-1} and *v* 1625-1621 cm^{-1} corresponding to C=O and C=N groups, respectively. The spectrum of compound **(5c)** revealed the presence of CN absorption at 2262 cm^{-1}, while compounds **(5d,e)** showed bands at *v* 2138 and *v* 2140 cm^{-1} corresponding to N_3 absorptions, respectively. The ^1H NMR spectra of the synthesized hydrazides **(5a-e)** showed D_2O-exchangable NH signals at δ 12.39-11.70 ppm. The azomethine protons appeared as singlets at δ 8.80-8.60 ppm, while the aromatic protons appeared as multiplets at δ 8.75-7.38 ppm. The spectrum of **(5c)** showed the methylene group protons as singlets at 3.95 ppm. The ^{13}C NMR spectra of the hydrazides **(5a-e)** gave signals at δ 165.3-161.2 ppm which were assigned to carbonyl groups, while the signals at δ 152.0-151.3 ppm were assigned to the azomethine carbons. The signal at δ 114.2 ppm was assigned to cyano group and the peak at δ 24.5 ppm was assigned to methylene carbon **(5c).**

Previously, we reported that thermolysis of (4-azidothiazol-5-ylmethylene)-*p*-tolylamine derivatives **(6a,b)** afforded 2-*p*-tolyl-2*H*–pyrazolo[3,4-*d*]thiazoles **(7a,b)**[17] (scheme 4).



(6a,b) **(7a,b)**

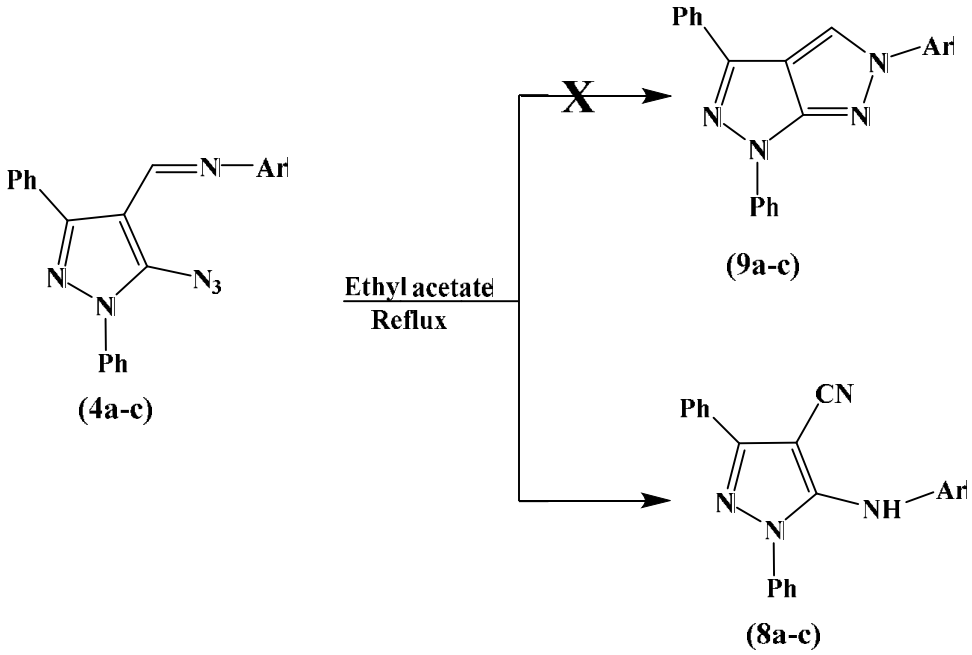
a: R_1 = *p*-tolyl, R_2 = H; b:R_1 = *p*-tolyl, R_2 = SCH_3

Scheme 4. Synthesis of the thiazoles (7a,b).

Hence, it was thought that performing this type of reactions on the 5-azidopyrazole-4-methylene-arylamine derivatives (**4a-c)** would give pyrazolo-pyrazole derivatives (**9a-c)**. However, heating of 5-azido-1,3-di-phenyl-1*H*-pyrazol-4-ylmethylene)-N-arylamines (**4a-c)** in ethyl acetate under reflux did not produce the expected pyrazolopyrazole derivatives (**9a-c),** but gave instead the 5-aryl- amino-1,3-diphenyl-1*H*-pyrazol-4-carbonitriles (**8a-c)** in excellent yields (Scheme 5). The presence of

NH and CN groups was clearly revealed in IR and ^{1}H NMR spectra.

The IR spectra of (**8a-c)** showed absorption bands at *v* 3400-3442 cm^{-1} corresponding to NH groups and absorption bands at *v* 2217-2223 cm^{-1} corresponding to CN groups. The ^{1}H NMR spectra showed D_2O-exchangable NH groups at δ 8.76-8.99 ppm, as well as aromatic protons multiplets at δ 6.80-8.01 ppm, methyl group protons in (**8b)** as a singlet at 2.50 ppm and methoxy group protons in (**8c)** as a singlet at 3.70 ppm. The ^{13}C NMR spectra showed signals at δ 114.82-114.65 ppm that were attributed to cyano groups. The signals at δ 20.8 and δ 55.7 ppm were attributed to the methyl and methoxy carbons in compounds **((8b)** and (**8c)**, respectively. Mass spectra gave the exact mass of these compounds as well. The observed formation of the cyanoanils (**8a-c)** can be explained in terms of ring-opening/ring-closure of the pyrazole azirine inter-mediates (**11a-c)** which are believed to occur through initially formed nitrenes (**10a-c)** (scheme 6). The intermediacy of these azirines (**11a-c)** and nitrenes (**10a-c)** was only circumstantial.



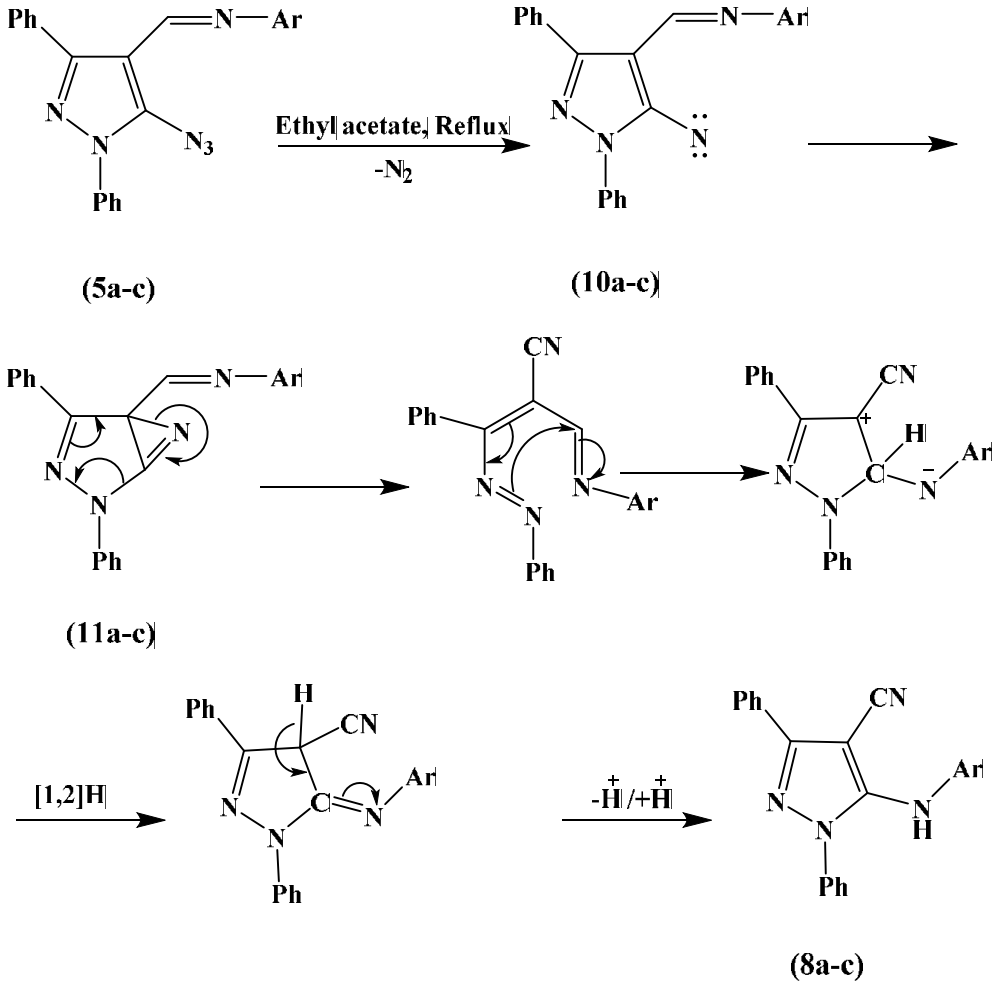
a: Ar = Ph; b: Ar = 4-CH$_3$C$_6$H$_4$;
c: Ar = 4-CH$_3$OC$_6$H$_4$

Scheme 5. Formation of 5-arylamino-1,3-diphenyl-1*H*-pyrazol-4-carbonitriles (8a-c).

Similarly, the decomposition of (5-azido-1,3-diphenyl-1*H*-pyrazol-4-yl)methylenehydr-azides **(5d,e)** in refluxing toluene did not give the pyrazolopyrazole derivatives (**12a,b)**, but afforded *N*-(4-cyano-2,5-diphenyl-2*H*-pyrazol-3-l)hydrazide derivatives (**13a,b)** in high yields (scheme 7). The spectral data of the cyanohydrazide derivatives (**13,b)** is in agreement with their proposed structures. The IR spectra of **(13a,b)** showed absorptions at *v* 3222-3385 cm^{-1}, *v* 2201-2220 cm^{-1} and *v* 1654-1656 cm^{-1} corresponding to NH, CN and C=O groups, respectively. The ^{1}H NMR spectra showed D_2O-exchangable protons representing NH groups at δ 12.30-11.83 ppm. The aromatic protons appeared as multiplets at δ 8.79-6.99 ppm. The ^{13}C NMR spectra showed signals at δ 164.82-160.91 ppm which were attributed to C=O group. The signals at δ 96.7 and 71.3 ppm were assigned to CN groups. The mass spectra gave their exact masses.

One of the most widely employed methods for synthesis of 4-thiazolidinones, which belong to an important group of heterocyclic compounds, involves the reaction of

azomethines or hydrazones with α–mercapto-acetic acid[18]. Hence, (5-azido-1,3- diphenyl-1 *H*-pyrazol-4-yl)methylenehydrazides **(5a,b)** were successfully converted into N-[2-(5-chloro-1,3-diphenyl-1*H*-pyrazol-4-yl)-4-oxo-thiazolidin-3-yl]amides **(14a-b)** in high yields (scheme 7). The IR spectra of these amides showed absorption bands at *v* 3410-3430 cm^{-1}, at *v* 1698 and at *v* 1697 cm^{-1} (br.) corresponding to NH and amidic carbonyl groups, respectively. The ^{1}H NMR spectra showed D_2O-exchangable NH singlets at δ 7.79 ppm for compound **(14a)** and δ 7.84 ppm for **(14b)**. The methine protons of the thiazolidine rings appeared as singlets at δ 5.51 ppm for **(14a)** and δ 5.52 ppm for **(14b)**, while the methylene protons appeared as two duplets; at δ 3.46 and δ 3.37 ppm for **(14a)** and at 3.49 and 3.38 ppm for **(14b)**. These splittings are probably due to long-range couplings with methine protons of each thiazolidine ring.



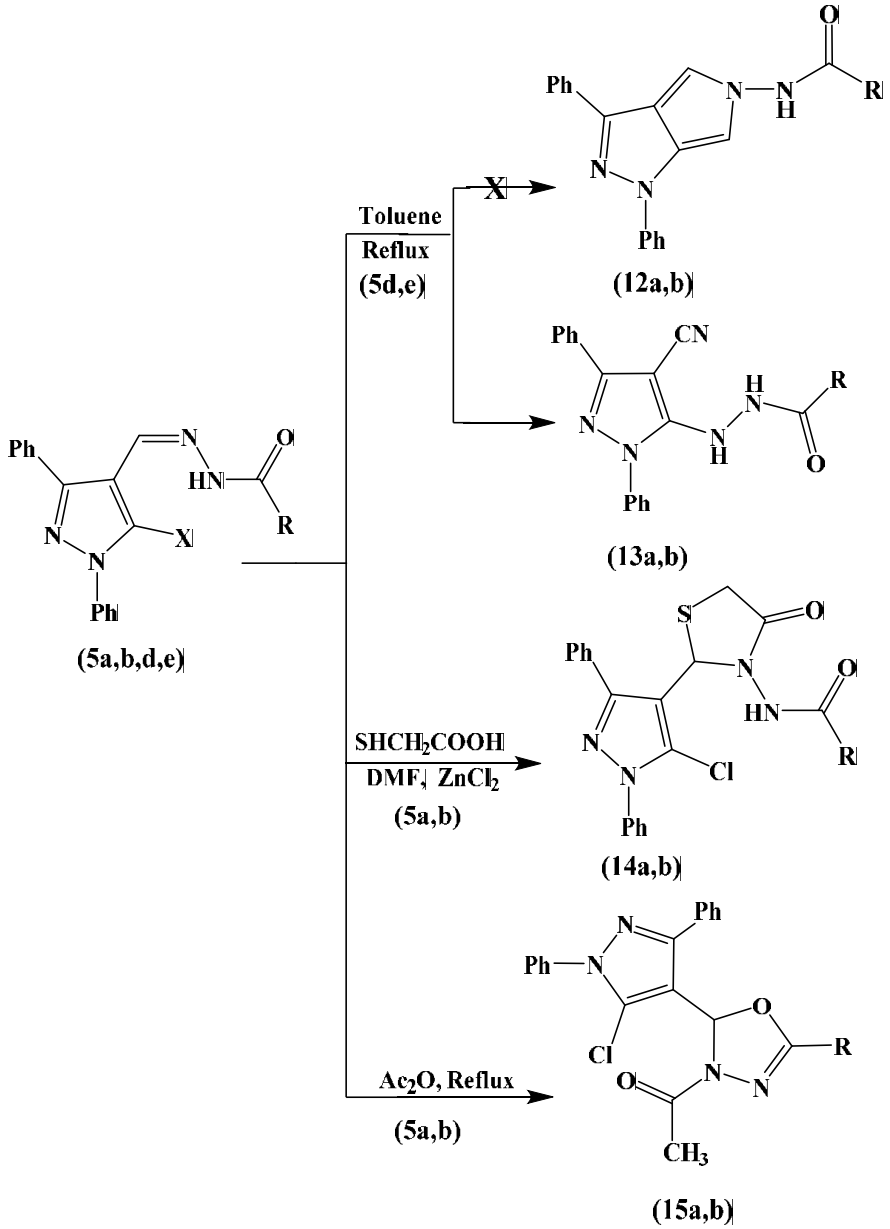
Scheme 6. Proposed mechanism for the formation of 1,3-Diphenyl-5-arylamino-1H-pyrazol-4-carbonitrile (8a-c).

The ^{13}C NMR spectra showed carbonyl group signals at δ 170.7 and δ 170.2 ppm for **(14a)** and at δ 170.1 and δ 161.3 ppm for **(14b)**. The methine protons of the thiazolidine rings of compounds **(14a,b)** appear at δ 44.1 and δ 58.8 ppm, respectively, while their methylene protons are apparent at δ 43.9 and δ 37.3 ppm. These last signals did not disappear but were reversed to opposite direction on applying DEPT technique.

Heating N-[(5-chloro-1,3-di-phenyl-1*H*-pyrazole-4-yl)methylene]hydrazides **(5a,b)** in refluxing acetic anhydride produced 3-acetyl-2-(5-chloro-1,3-di-phenyl-1*H*-pyrazol-4-yl)-5-aryl-2,3-di-hydro-1,3,4-oxadiazoles **(15a,b)** in good yields (scheme 7). The spectral data of

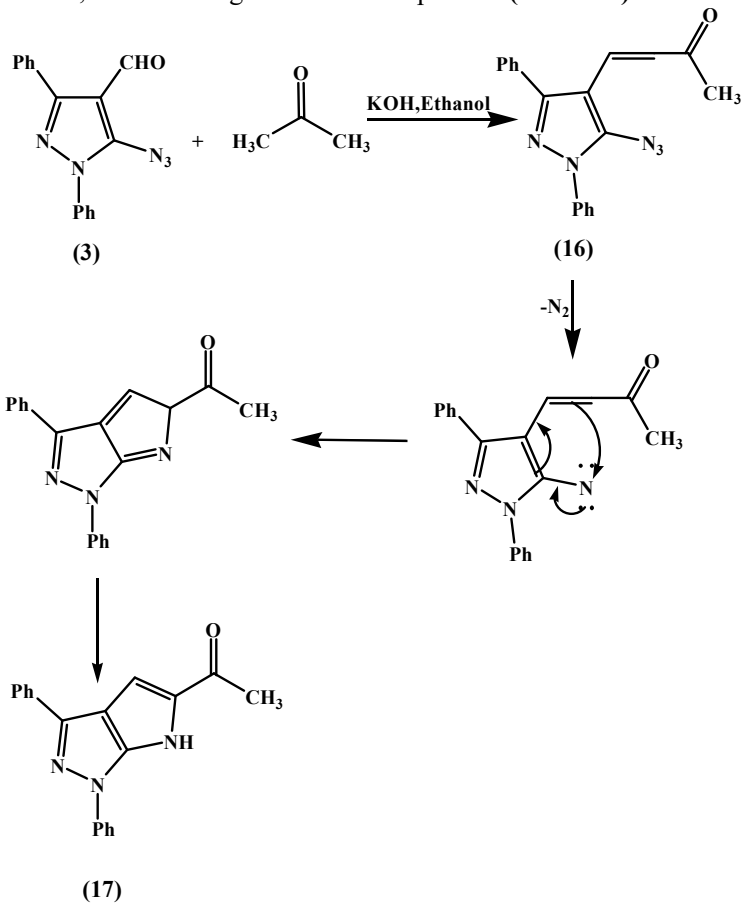
(15a,b) is in accordance with the proposed structure. IR spectra showed absorption bands at ν 1663 cm^{1} corresponding to C=O groups. The ^{1}H NMR spectra showed multiplets at δ 7.83-7.26 ppm corresponding to aromatic protons and to oxadiazole CH protons. The methyl group protons appeared as singlets at δ 2.22 ppm **(15a)** and δ 2.21 ppm **(15b)**. The ^{13}C NMR spectra gave signals at δ 167.7 ppm and δ 166.8 ppm corresponding to the C=O groups. The signals at δ 87.1 **(15a)** and δ 85.8 **(15b)** ppm were assigned to the oxadiazole C-2, while the methyl group protons appeared at δ 21.6 ppm **(15a)** and δ 21.1 **(15b)**.

Claisen–Schmidt condensation of 5-azido-1,3-diphenyl-1*H*-pyrazol-4-carbaldehyde **(3)** with acetone in 4% ethanolic potassium hydroxide solution was originally carried out with the aim to produce the 5-azidopyrazole chalcone derivative **(16)**. However, this reaction gave 1-(1,3-diphenyl-1,6-dihydro-pyrrolo[2,3-c]pyrazol-5-yl)ethan-1-one **(17)** in a moderate yield. The IR spectrum of this condensed pyrrolopyrazole compound **(17)**



Scheme 7. Some reactions of (5-substituted-1,3-diphenyl-1H-pyrazol-4-yl)methylenehydrazides (5a,b,d,e).

lacked the absorption band corresponding to N_3 group and showed strong absorption bands at ν 3426 cm^{-1} and at ν 1643 cm^{-1} corresponding to NH and C=O groups, respectively. The ^1H NMR spectrum showed a multiplet at δ 8.50-7.28 ppm attributed to one NH and aromatic protons and CH_3 protons appeared as singlet at δ 2.65 ppm. The ^{13}C NMR spectrum showed signals at δ 159.4 ppm corresponding to C=O group. The signals at δ 151.5-113.2 ppm were assigned to 2Ph and pyrrolopyrazole carbons, while the signal at δ 25.1 ppm was assigned to the methyl group. Mass spectra gave the correct molecular mass. The absence of exocyclic CH=CH group in the product, as revealed by ^{1}HNMR spectrum, gave a strong evidence of the formation of the pyrrolopyrazole **(17)** (scheme 8). We believe that the desired chalcone **(16)** was actually formed first, then proceeded to produce the pyrrolopyrazole derivative **(17)** *via* the formation of a nitrene that underwent intramolecular cyclization giving the end product **(**scheme 8**)**.



Scheme 8. Formation of 1-(1,3-diphenyl-1,6-dihydropyrrolo[2,3-c]pyrazol-5-yl)ethan-1-one (17).

Conclusions

1. N-[(5-Azido-1,3-diphenyl-1*H*-pyrazole-4-yl)-methylene]-N-arylamines **(4a-c)** and *N*-[(5-substituted-1,3-diphenyl-1*H*-pyrazole-4-yl)-methylene]hydrazides **(5a-e)** were successfully synthesized and thermolyzed to afford 5-aryl-amino-1,3-diphenyl-1*H*-pyrazol-4-carbonitriles (**8a-c)** and *N*-(4-cyano-1,3-diphenyl-1*H*-pyrazol-5-yl) hydrazides (**13a,b)**, respectively.

2. N-[2-(5-Chloro-1,3-diphenyl-1*H*-pyrazol-4-yl)-4-oxo-thiazolidin-3-yl]amides (**14a,b)** and 3-acetyl-2- (5-chloro-1,3-diphenyl-1*H*-pyrazol-4-yl)-5-substituted-2,3-dihydro-1,3,4-oxadiazoles (**15a,b)** were prepared from *N*-[(5-chloro-1,3-diphenyl-1*H*-yrazole-4-yl)methylene]hydrazides **(5a-e)**.

3. 1-(1,3-Diphenyl-1,6-dihydropyrrolo-[2,3-*c*]-pyrazol-5-yl)ethan-1-one (**17)** was unexpectedly obtained and a mechanism of its formation was proposed.

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