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Synthesis of Diaznylpyrazol Derivatives

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Abstract

In our present study 4-methylaniline (1) has been reacted with acetyl acetone(2) in presence of sodium nitrite and sodium acetate yielded 3-(2-(p-tolyl) hydrazono) pentane-2,4-dione (3) which react with hydrazine hydrate to give 3,5-dimethyl-4-(p-tolyldiazenyl)-1H-pyrazole (4) and react with 2-chloro-N(substituted phenyl) acetamide(5a-5g) to give (6a-6g). All the synthesized compounds were characterized on the basis of melting point, TLC and NMR spectra.

Keywords: 4-substituted aniline; sodium nitrite; sodium acetate; hydrazine hydrate; phenyl hydrazine; 2-chloro-N (substituted phenyl) acetamide; 2-chloro-N(substituted phenyl) acetamide.

1. Introduction

The condensation of symmetrical or unsymmetrical 1,3-diketones with hydrazine or aryl hydrazines in the presence of catalyst generally produced a mixture of two regioisomers where the reactions of 1,3-diketones compounds (8) with aryl hydrazines afforded pyrazole derivatives (9) and (10) [1]. Alkynes react with diazo compounds (12) to afford pyrazoles via [3+2]-cycloaddition for the preparation of 3,5-disubstituted pyrazoles(13) [2] . Another strategy for the synthesis of pyrazoles is the cyclo condensation of an appropriate hydrazine with a carbonyl compound having two electrophilic carbons at the 1 and 3 locations. Importantly, hydrazines behave like a bidentate nucleophile and react with these α,β-unsaturated aldehydes or ketones(14) [3].

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Pyrazoles were also synthesized by the reaction between N-tosyl-N-propargylhydrazine(17) and aryliodides(18) or vinyltriflates in the presence of palladium catalyst [4]. 2-Chloro-N-Alkyl or Arylacetamide was synthesized from Chloroacetylchloride with various amines. The prepared compounds were screened for their anti-inflammatory activity by carrageenan induced paw odema method in rats [5-9].

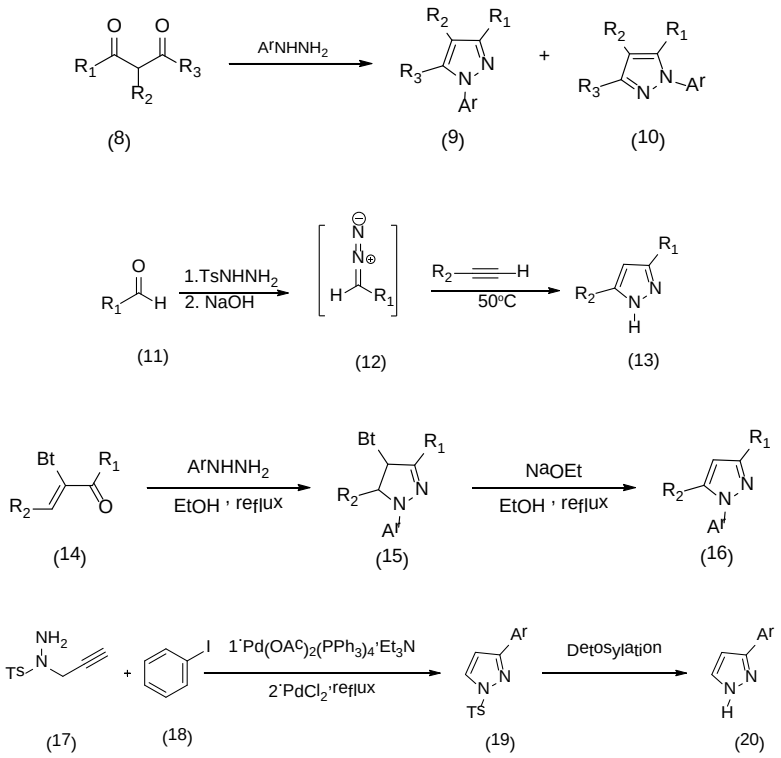


Figure 3

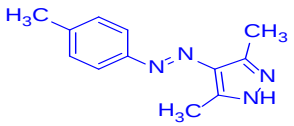
2. Materials and Methods

All chemicals were purchased from Sigma-Aldrich (St. Louis, Mo, USA). All melting points (mps) were determined by SMP3 stuart scientific melting point apparatus (stuart, Staffordshire, UK) and are uncorrected. All the reactions were monitored by thin-layer chromatography (TLC) using silica gel 60 F254 TLC plates (Merck KGaA, Darmstadt, Germany). Spectroscopic data were recorded with the following instruments: NMR, H1-NMR all the accurate analyzes of NMR were conducted in Micro-Analytical Unit at Research Center of the Faculty of Science, University of Alexandria, Proton magnetic resonance spectra were measured in (CDCl3) solution, on Bruker 500 MHz with chemical shift (δ) expressed in ppm down field from tetramethylsilane as an internal stander (δ MS=0). The multiplicity of the signal is as follow: s (Singlet), d (Doublet), t(Triplet), q(Quartet), m(Multiplet). C13-NMR were measured on Bruker 400MHz with internal reference TMS δ=0, were measured by DEPT spectroscopy (Brucker Company, Elk GroveVillage, USA).

2.1 Synthesis of products

2.1.1 Synthesis of 3,5-dimethyl-4-(p-tolyldiazenyl)-1H-pyrazole(4)

4-methylaniline(1) (0.01 mole) was dissolved in a mixture of concentrated HCl (8 mL) with water (6 mL) then cooled to 0 ^{o}C on ice bath. A cold aqueous solution of sodium nitrite (0.02 mole) was added. The cold diazonium salt solution was filtered into a cooled solution of acetyl acetone(2) in presence of sodium nitrite (0.01 mole) and sodium acetate (0.05 mole) in ethanol (20 mL). the solution was stirred for 2 hours. Resulting solid was filtered, dried and purified by recrystallization using ethanol to afford compound(3) [10]. A mixture of 3-(2-(p-tolyl)hydrazono)pentane-2,4-dione (3) (0.01 mole) and hydrazine hydrate (0.1mole) in glacial acetic acid (15 mL) is refluxed for 4-5 hours. The resulting mixture was concentrated and allowed to cool. The resulting solid was filtered, washed, dried & recrystallized from ethanol to afford compound (4).



Yield:65%
mp: 129-130^{0}C

(4)

2.1.2 Synthesis of 2-Chloro-N-phenylacetamide derivatives (5a-5g)

In 250 ml round-bottomed flask aniline derivatives (0.1 mole) in 120 ml of ethanol were stirred for 2-3hours then chloroacetyl chloride (0.1 mole) was added drop wise to the above mixture then stirred for 1-2 hours. The stirred mixture was then refluxed for 2-2.5 hours and poured into ice cold water. The solid obtained was filtered and recrystallized from ethanol. The percentage yield of the products was 82-85%. Table (1) shows the melting points for the prepared compounds (5a-5g).

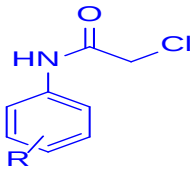


Table 1: The melting points for the prepared compounds (5a-5g)

Compound	R	M.P. (°C)
5a	H	138
5b	p-Cl	175
5c	o-Cl	79
5d	m-OCH_3	94
5e	p-$COOCH_3$	141-142
5f	p-$COOC_2H_5$	117
5g	p-$COOC_3H_7$	109

2-Chloro-N-phenylacetamide (5a)

H^1-NMR:δ =4.18 (2H, s, CH_2); 8.25 (H, s, exchangeable, NH); 7.15 &7.17&7.18(H ,t, H-Ar); 7.34&7.35& .37(2H,t,H-Ar); 7.53& 7.55(2H,d,H-Ar).

C^{13} NMR: δ**:** 42.97(1C), 120.24(2C), 125.37(1C), 129.24(2C), 136.74(1C), 163.92(1C).

DEPT: δ**:** 42.98(1C), 120.24(2C), 125.37(1C), 129.24(2C).

2-Chloro-N-(4-chlorophenyl) acetamide (5b)

H^1 NMR: δ: 4.21(2H, s, CH_2); 9.57(H, s, exchangeable, NH); 7.31& 7.33 (2H, d, H-Ar); 7.66& 7.68(2H,d,H-Ar).

C^{13} NMR: δ**:** 43.20(1C), 121.19(2C), 128.46(2C), 128.78(1C), 164.65(1C), 164.72(1C).

DEPT: δ**:** 43.24(1C), 121.08(2C), 128. 78(2C).

2-Chloro-N-(2-chlorophenyl)acetamide (5c)

H^1 NMR:δ:4.23(2H,s,CH_2); 8.92(H,s exchangeable, NH); 7.08&&7.09& 7.09& 7.11(1H,t,H-Ar); 7.27& 7.28& 7.29& 7.31& 7.31(1H,t,H-Ar); 7.39 &7.39& 7.40& 7.40(1H,d,H-Ar); 8.35& 8.35& 8.36 &8.37(1H,d,H-Ar).

C^{13} NMR: δ**:** 43.22(1C), 121.34(1C), 123.55(1C), 125.60(1C), 127.89(1C), 129.30(1C), 133.74(1C), 163.98(1C).

DEPT: δ**:** 43.22(1C), 121.34(1C), 125.59(1C), 127.89(1C), 129.30(1C).

2-Chloro-N-(3-methoxyphenyl)acetamide(5d)

H^1 NMR: δ:3.80(3H,s,OCH_3); 4.17(2H,s,CH_2) 8.23(H,s exchangeable, NH); 6.71&6.72(1H,d,H-Ar); 7.01&7.03(1H,d,H-Ar);7.24(1H,s,H-Ar);7.25 7.26 7.27(1H,s,H-Ar).

C^{13} NMR: δ**:** 42.99(1C), 55.45(1C), 105.95(1C), 111.10(1C), 112.32(1C), 129.93(1C), 137.94(1C), 160.30(1C), 163.90(1C).

DEPT: δ**:** 43.00(1C), 55.46(2C), 105.95(1C), 111.10(1C), 112.31(1C), 129.94(1C).

Methyl 4-(2-chloroacetamido)benzoate (5e)

H^1 NMR: δ:3.90(3H,s,OCH_3); 4.19(2H,s,CH_2) 8.40(H,s exchangeable, NH); 7.63& 7.65(2H,d,H-Ar); 8.02& 8.04(2H,d,H-Ar) .

C^{13} NMR: δ**:** 42.96(1C), 52.23(1C), 119.26(2C), 126.68(1C), 130.98(2C), 140.86(1C), 164.11(1C), 166.52(1C)

DEPT: δ: 42.97(1C), 52.24(1C), 119.25(2C), 130.99(2C).

Ethyl 4-(2-chloroacetamido)benzoate (5f)

H^1 NMR: δ:1.36& 1.38& 1.39(3H,t,OCH_2CH_3); 4.19(2H,s,CH_2); 4.35& 3.45& 3.46& 3.47(2H,q,CH_2); 8.41(H,s exchangeable, NH); 7.63& 7.64 (2H,d,H-Ar); 8.02& 8.04(2H,d,H-Ar).

C^{13} NMR: δ**:** 14.42(1C), 42.97(1C), 61.12(1C), 119.22(2C), 127.05(1C), 130.92(2C), 140.76(1C), 164.11(1C), 166.04(1C) .

DEPT: δ**:** 14.43(1C), 42.98(1C), 61.12(1C), 119.22(2C), 130.93(2C).

Propyl 4-(2-chloroacetamido)benzoate (5g)

H^1 NMR: δ:1.00& 1.01& 1.03(3H,t,$OCH_2CH_2CH_3$); 1.76& 1.77& 1.78& 1.80 &1.81 (2H,m,CH2) 4.19(2H,s, CH_2); 4.24&&4.26& 4.27(2H,t, OCH_2CH_2 CH_3) 8.40(H,s exchangeable, NH); 7.63& 7.65(2H,d,H-Ar); 8.02& 8.04(2H,d,H-Ar).

C^{13} NMR: δ**:** 10.6(1C), 22.18(1C), 42.97(1C), 66.69(1C), 119.24(2C), 127.06(1C), 130.92(2C), 140.76(1C), 164.09(1C),166.10(1C).

DEPT: δ**:** 10.61(1C), 22.19(1C); 42.98(1C); 66.12(1C), 119.24(2C), 130.93(2C).

2.1.2.Synthesis of N-(4-substitutedphenyl)-2-(3,5-dimethyl-4-(p-tolyldiazenyl)-1H-pyrazol-1-yl)acetamide(6a-6g)

In 100 ml round-bottomed flask a mixture of 2-chloro-N-Alkyl/Arylacetamide derivatives (5a-5g) (0.02mole) in DMF was mixed with another mixture of 4-((4-methylphenyl)-diazenyl)-3,5-dimethyl-1H-pyrazole(4) (0.02mole) in DMF.

Anhydrous Potassium Carbonate (0.02mole) was added to above reaction mixture then heated on water bath overnight.

The desired product was isolated as precipitate after pouring the reaction mixture in an ice-cold water for 30 minute.

Precipitate was filtered, washed with cold water then dried. Product was recrystallized using 95% methanol. Table(2) indicates the % yield and melting points for the compounds (6a-6g).

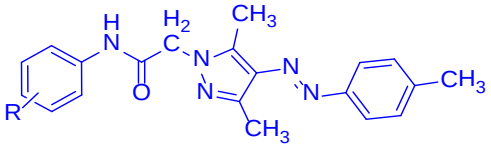


Table 1: The % yield and lting points for the compounds (6a-6g)

Compound	R	M.P. (°C)	Yiel
6a	H	219	98
6b	p-Cl	221	91
6c	o-Cl	189-190	98
6d	m-OCH_3	180-181	94
6e	p-$COOCH_3$	220-221	88
6f	p-$COOC_2H_5$	201	92
6g	p-$COOC_3H_7$	202-203	98

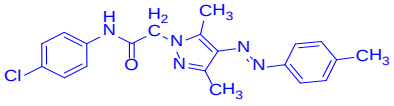
2-(3,5-dimethyl-4-(p-tolyldiazenyl)-1H-pyrazol-1-yl)-N-phenylacetamide(6a)

H^1-NMR : δ = 2.41 (3H, s, CH_3), 2.57(3H, s, CH_3), 2.63(3H, s, CH_3), 4.90 (2H, s, CH_2) 7.08& 7.10 &7.11(2H, t, H-Ar), 7.25& 7.27& 7.30(1H, t, H-Ar), 7.26 &7.29 (1H, d, H-Ar), 7.46& 7.48 (2H, d, H-Ar), 7.96,7.71(2H, d, H-Ar) 8.62 (1H, s, exchangeable, NH).

C^{13}-NMR: δ = 9.97 (1C), 13.77 (1C), 21.51 (1C), 52.55 (1C), 120.16 (2C), 122.05(2C), 124.95 (1C), 129.09 (2C), 129.74 (2C), 135.27 (2C), 137.18 (1C), 140.69 (2C), 151.41 (1C), 164.8 (1C) .

DEPT: δ = 9.98(1C), 13.72(1C), 21.53(1C), 52.51(1C), 120.15(2C), 122.07(2C), 124.93(1C), 129.08(2C), 129.75(2C).

N-(4-chlorophenyl)-2-(3,5-dimethyl-4-(p-tolyldiazenyl)-1H-pyrazol-1-yl)acetamide(6b)



H^1-NMR : δ = 2.42 (3H, s, CH_3), 2.59 (3H, s, CH_3), 2.65 (3H, s, CH_3), 5.01 (2H, s, CH_2), 7.21& 7.22 (2H, d, H-Ar),7.26& 7.28 (2H, d, H-Ar),7.45& 7.47(2H, d, H-Ar), 7.70& 7.71(2H, d, H-Ar), 9.21(1H exchangeable, NH).

C^{13}-NMR: δ = 9.97 (1C), 13.96 (1C), 21.51 (1C), 52.46 (1C), 121.34 (2C), 122.03 (2C), 129.11 (2C), 129.75 (2C), 129.91 (1C), 135.34 (1C), 135.78 (1C), 140.63 (2C). 144.32 (1C), 151.43 (1C), 164.38 (1C).

DEPT: δ = 9.98(1C), 13.59(1C), 21.55(1C), 52.32(1C), 121.28(2C), 122.12(2C), 129.07(2C), 129.78(2C).

N-(2-chlorophenyl)-2-(3,5-dimethyl-4-(p-tolyldiazenyl)-1H-pyrazol-1-yl)acetamide(6c)

H[1]-NMR : δ = 2.41 (3H, s, CH_3), 2.57(3H, s, CH_3), 2.63(3H, s, CH_3), 4.89 (2H, s, CH_2), 7.04& 7.05(1H, t, H-Ar), 7.25& 7.27 (2H, d, H-Ar), 7.31 &7.33 (1H, d, H-Ar), 7.70& 7.71 (2H, d, H-Ar), 8.35& 8.37(2H, d, H-Ar), 8.92 (1H, s, NH).

C[13]-NMR: δ = 9.97 (1C), 14.02 (1C), 21.51 (1C), 52.72 (1C), 121.57 (1C), 122.01(2C), 125.29 (1C), 127.73 (1C), 129.28 (1C), 129.72 (2C), 134.22 (1C), 135.59 (1C), 140.06 (1C), 140.42 (1C), 144.79(1C), 151.48(1C), 164.99(1C) .

DEPT: δ = 9.96(1C), 14.05(1C), 21.52(1C), 52.72(1C), 122.00(1C), 125.28(2C), 127.74(1C), 129.28(2C), 129.72(2C).

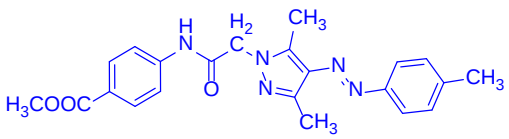
2-(3,5-dimethyl-4-(p-tolyldiazenyl)-1H-pyrazol-1-yl)-N-(3-methoxyphenyl)acetamide(6d)

H[1]-NMR : δ = 2.41 (3H, s, CH_3), 2.57(3H, s, CH_3), 2.64(3H, s, CH_3), 3.763(3H, s,OCH_3), 4.91 (2H, s, CH_2), 6.64& 6.65 (1H, d, H-Ar), 6.93& 6.95 (1H, d, H-Ar), 7.15 &7.17& 7.19 (1H, t, H-Ar), 7.23(1H, s, H-Ar), 7.25& 7.26 (2H, d, H-Ar), 7.69& 7.71(2H, d, H-Ar), 8.68 (1H, s, NH).

C[13]-NMR: δ = 9.97 (1C), 13.81 (1C), 21.53 (1C), 52.57 (1C), 55.39(1C), 105.83 (1C), 110.75(2C), 112.32 (1C), 122.05 (2C), 129.75 (2C), 135.27 (1C), 138.34(1C), 140.65 (2C), 143.95 (1C), 151.41 (1C), 160.16(1C) 164.36(1C).

DEPT: δ = 9.98(1C), 13.74(1C), 21.53(1C), 52.54(1C), 55.39(1C) 105.78(1C), 110.75(2C), 112.30(1C), 122.07(2C), 129.75(2C).

methyl4-(2-(3,5-dimethyl-4-(p-tolyldiazenyl)-1H-pyrazol-1-yl)acetamido)benzoate(6e)

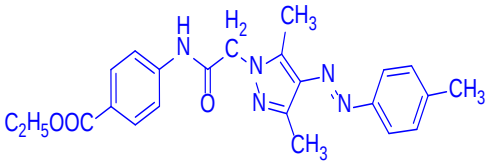


H[1]-NMR : δ = 2.41 (3H, s, CH_3), 2.61(3H, s, CH_3), 2.65(3H, s, CH_3), 3.85(3H, s,OCH_3), 5.09 (2H, s, CH_2), 7.26& 7.28 (2H, d, H-Ar), 7.58& 7.60 (2H, d, H-Ar), 7.69 &7.71 (2H, d, H-Ar), 7.91& 7.92(2H, d, H-Ar), 9.55 (1H, s, NH).

C^{13}-NMR: δ = 9.97 (1C), 13.64 (1C), 21.53 (1C), 52.13(1C), 52.40(1C), 119.19 (2C), 122.10(2C), 126.17 (1C), 129.77 (2C), 130.82 (2C), 135.17 (1C), 140.90(2C), 141.39 (1C), 143.74 (1C), 151.33 (1C), 164.42(1C), 166.53(1C) .

DEPT: δ = 9.98(1C), 13.75(1C), 21.54(1C), 52.14(1C), 52.42(1C) 119.20(2C), 122.09(2C), 129.76(2C), 130.83(2C).

Ethyl 4-(2-(3,5-dimethyl-4-(p-tolyldiazenyl)-1H-pyrazol-1-yl)acetamido)benzoate(6f)

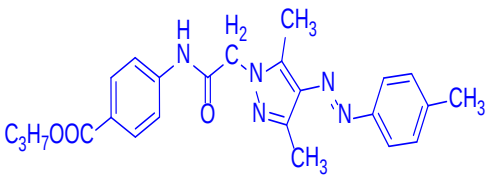


H^1-NMR : δ = 1.35 &1.36 & 1.38(3H, t, CH_3), 2.41 (3H, s, CH_3), 2.57(3H, s, CH_3), 2.64(3H, s, CH_3), 4.31& 4.32 & 4.34 & 4.35(2H, q,OCH_2), 4.91 (2H, s, CH_2), 7.25& 7.27 (2H, d, H-Ar), 7.55& 7.56 (2H, d, H-Ar), 7.69 &7.71 (2H, d, H-Ar), 7.95& 7.97(2H, d, H-Ar), 9.04 (1H, s, NH).

C^{13}-NMR: δ = 9.97 (1C), 13.64 (1C), 14.42(1C), 21.53 (1C), 52.46(1C), 61.00(1C), 119.17 (2C), 122.07(2C), 126.55 (1C), 129.75 (2C), 130.78 (2C), 135.27 (1C), 140.72(2C), 141.28 (1C), 144.02 (1C), 151.39(1C), 164.65(1C), 166.08(1C) .

DEPT: δ = 9.98(1C), 13.86(1C), 21.53(1C), 52.47(1C), 61.00(1C) 119.17(2C), 122.06(2C), 129.75(2C), 130.79(2C).

Propyl 4-(2-(3,5-dimethyl-4-(p-tolyldiazenyl)-1H-pyrazol-1-yl)acetamido)benzoate(6g)



H^1-NMR : δ = 0.99 &1.00 & 1.01(3H, t, CH_3), 1.74& 1.75& 1.77& 1.78 (2H, m, CH_2), 2.41(3H, s, CH_3), 2.57(3H, s, CH_3), 2.64(3H, s, CH3), 4.22& 4.23 & 4.25 (2H, t,OCH_2), 4.91 (2H, s, CH_2), 7.25& 7.26& (2H, d, H-Ar), 7.55& 7.57 (2H, d, H-Ar), 7.69 &7.71 (2H, d, H-Ar), 7.96& 7.98(2H, d, H-Ar), 9.01 (1H, s, NH).

C^{13}-NMR: δ = 9.97 (1C), 10.60(1C), 13.88 (1C), 21.51(1C), 22.18 (1C), 52.49(1C), 66.59(1C), 119.21 (2C), 122.05(2C), 126.61 (1C), 129.74 (2C), 130.80 (2C), 135.33 (1C), 140.63(2C), 141.24 (1C), 144.02 (1C), 151.41(1C), 164.65(1C), 166.08(1C) .

DEPT: δ = 9.98(1C), 10.60(1C), 13.83(1C), 21.53(1C), 22.17(1C), 52.47(1C), 66.58(1C) 119.20(2C), 122.07(2C), 129.75(2C), 130.79(2C).

3. Discussion

In this study 2-chloro-N-(substituted phenyl) acetamides (5a-5g) were synthesized by the method described in experimental section. Compounds (6a-6g) were prepared by reaction of 3,5-dimethyl-4-(p-tolyldiazenyl)-1H-pyrazole (4) with amide derivatives (5a-5g) as shown in Figure (1). The desired products obtained in good yield. Their formation was tested by TLC and The melting point which compared with the literature.

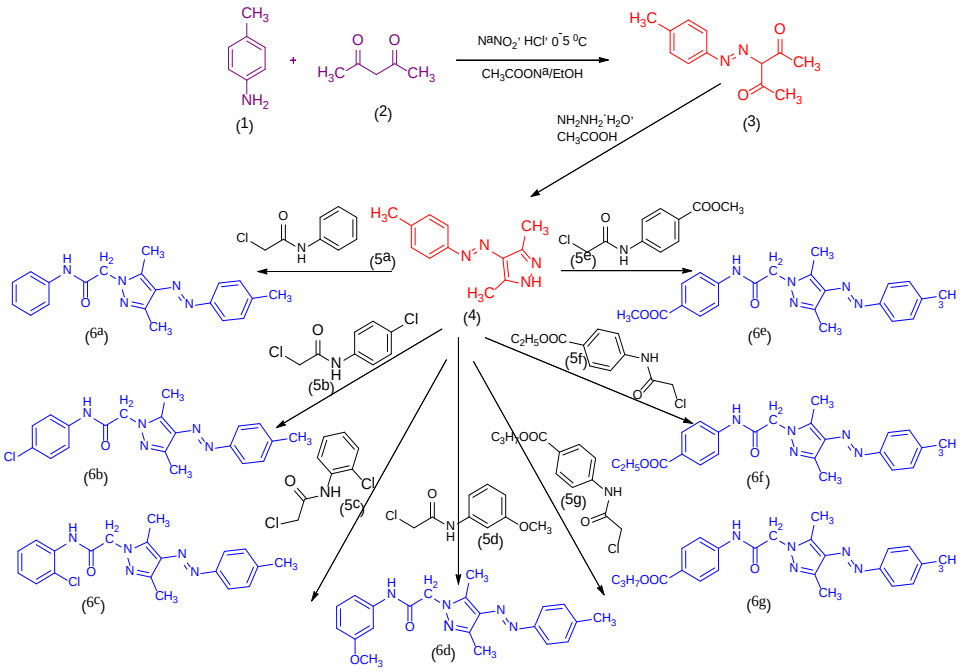


Figure 1: Reaction Figure

The Mechanism of this reaction (Figure 2) is SN2 reaction where the nucleophile (HN-) attacks the carbon atom which attached with the good leaving group, forming a C–N bond and followed by breaking the C–Cl bond.

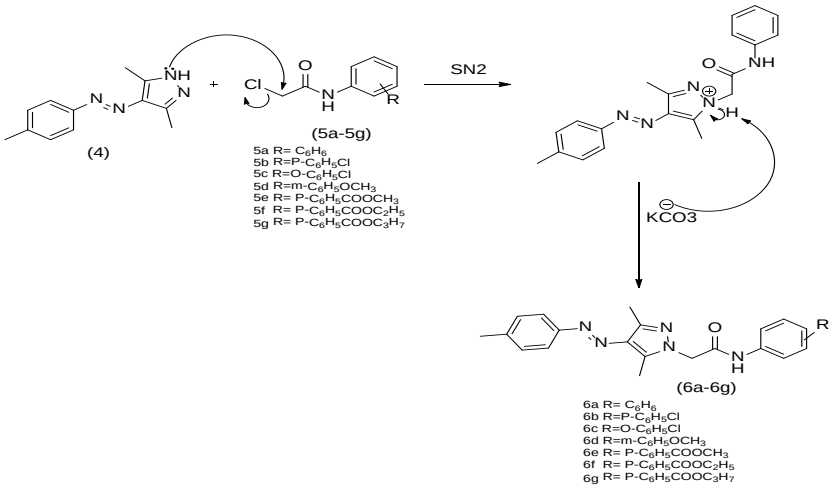


Figure 2: Mechanism of the reaction

The structure obtained was confirmed by satisfactory spectroscopic analysis ^{1}H-NMR spectra which showed ten different types of protons, the CH_2 signal was deshielded and shifted from 4.18 ppm for compound (5a) to 4.90 ppm for compound (6a) and the -NH group of amide has been disappeared. a singlet signal at 8.62 ppm belong to NH was appear using D_2O exchange.

On the other hand, carbon magnetic resonance spectrum showed 14 signals at 120.16 (2C), 122.05(2C), 129.09 (2C), 129.74 (2C), 135.27 (2C), 140.69 (2C), and at 164.8 (1C) for carbonyl group .DEPT spectroscopy technique established existence of CH_2 & CH_3, as well as CH groups of benzene ring.

The compound (6b) showed good solubility in chloroform. The nuclear magnetic resonance spectral data gave additional support for the composition of the compound. The observed changes are evidence of the reaction that occurred because the chemical shift of a compound is deeply depending on its electronic environment.

The ^{1}H-NMR spectrum of compound (6b) showed the appearance of a proton signal of CH_2 at about 5.01ppm that differ from CH2 signal of compound (5b) which appear at 4.21 ppm due to the effect of pyrazole ring . Furthermore, the proton signal of NH appeared at 9.21 ppm which is lower than the value in compound (6b) which detected at about 9.57 ppm because of the deshielding by withdrawing groups in para position.

Reaction of 3,5-dimethyl-4-(p-tolyldiazenyl)-1H-pyrazole (4) with 2-chloro-N-(2-chlorophenyl) acetamide (5c) gave N-(2-chlorophenyl) -2-(3,5-dimethyl-4-(p-tolyldiazenyl)-1H-pyrazol-1-yl) acetamide (6c). In this case the value of the chemical shifts for the CH_2 group and NH decreased compared to the values of CH_2 in compounds (6a) ,(6b) due to the presence of chlorine atom in the ortho position.

Reaction of 3,5-dimethyl-4-(p-tolyldiazenyl)-1H-pyrazole (4) with 2-chloro-N-(3-methoxyphenyl) acetamide (5d) afforded 2-(3,5-dimethyl-4-(p-tolyldiazenyl)-1H-pyrazol-1-yl)-N-(3-methoxyphenyl)acetamide (6d). This compound showed ten types of protons, singlet signal of OCH_3 at about 3.76 ppm, in addition there were some differences in chemical shift of CH_2 and NH group as a result of the presence of methoxy group in meta position.

Reaction of 3,5-dimethyl-4-(p-tolyldiazenyl)-1H-pyrazole (4) with methyl 4-(2-chloroacetamido) benzoate (5e) produced methyl 4-(2-(3,5-dimethyl-4-(p-tolyldiazenyl)-1H-pyrazol-1-yl) acetamido) benzoate (6e). ^{1}H-NMR spectra show eleven different types of protons the most important signals between of them signal at about3.85 ppm belongs to OCH_3 group as well as ^{13}C-NMR shows beak for $COOCH_3$ at 166.53 ppm.

Reaction of 3,5-dimethyl-4-(p-tolyldiazenyl)-1H-pyrazole (4) with ethyl4-(2-chloroacetamido) (5f) generated ethyl 4-(2-(3,5-dimethyl-4-(p-tolyldiazenyl)-1H-pyrazol-1-yl)acetamido)benzoate (6f). ^{1}H-NMR spectra show twelve different types of protons, triplet signal of OCH2CH3 at 1.35, 1.36, 1.38 ppm and quartet signal of OCH_2CH_3 at 4.31, 4.32, 4.34, 4.35 ppm. On the other hand, ^{13}C- NMR spectrums clarified a $COOCH_2CH_3$ signal at about 166.08 ppm.

Reaction of 3,5-dimethyl-4-(p-tolyldiazenyl)-1H-pyrazole (4) with propyl4-(2-chloroacetamido) benzoate (5g) resulted propyl 4-(2-(3,5-dimethyl-4-(p-tolyldiazenyl)-1H-pyrazol-1-yl)acetamido)benzoate (6g). ^{1}H- NMR

spectra show thirteen different types of protons triplet signal of $OCH_2CH_2CH_3$ at 0.99 , 1.00 , 1.01 ppm , triplet signal of OCH2CH2CH3 at 4.22 , 4.23 , 4.25 ppm ,and sextet signal of $OCH_2CH_2CH_3$ at 1.74 , 1.75 , 1.77 , 1.78 ppm. ^{13}C-NMR analysis for the compound (6g) illustrated a beak at 166.13 ppm belongs to $COOCH_2CH_2CH_3$.

There is an increasing in NH chemical shifts of compound (6e),(6f), and (6g), due to the effect of ester group which located in para position. In comparison between two chemical shift values of CH_2 group for compound (6a),(6b) found that increasing the chemical shift value from 4.9 ppm for compound (6a) to 5.9 ppm for compound (6e) due to the presence of ester group which was not noticed in the compound contained ester group with more carbon atoms (6f) and (6g)

4. Conclusion

N-(4-substitutedphenyl)-2-(3,5-dimethyl-4-(p-tolyldiazenyl)-1H-pyrazol-1-yl)acetamide(6a-6g) was successfully synthesized with high percentage yield (88-98%) using with 2-chloro-N(substituted phenyl) acetamide (5a-5g) with 3,5-dimethyl-4-(p-tolyldiazenyl)-1H-pyrazole (4) which prepared by adding hydrazine hydrate in glacial acetic acid to 3-(2-(p-tolyl) hydrazono) pentane-2,4-dione (3). The ^{1}H, ^{13}C-NMR and dept analysis proved the proposed structure for the resulting compounds.

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References

[1] (a) L. Knorr (1883, July). "Ein wirkung von acettessiges ter auf phenyl hydrazine", Beriche Der Deutschen Chemischen Gesellschaft [on-line], 16 (2), pp. 2597-2599. Available: http://onlinelibrary.wiley.com/doi/10.1002/cber.188301602194/abstract;jsessionid=877B9714679A4608CEC5F556DCB69FCF.f03t03

(b) L. Knorr (1884, July). "Ueber die constitution der chinizinderivate ", Beriche Der Deutschen Chemischen Gesellschaft [on-line], 17 (2), pp. 2032-2049. Available: http://onlinelibrary.wiley.com/doi/10.1002/cber.18840170298/full

(c) T. L. Jacobs. “Pyrazoles and related compounds,” in Heterocyclic Compound, vol. 5. R. C. Elderfield, Ed. New York: John Willy & Sons, 1957, pp.45.

(d) S. M. Sakya. "Knorr Pyrazole Synthesis", In Name Reactions in Heterocyclic Chemistry,. J. J. Li,. E. J.;Corey, Eds. Hoboken, New Jersey: John Willy & Sons, 2005, pp.292-300.

[2] V. K. Aggarwal, J. De Vicente, R. V. Bonnert , (2003,May). " A Novel One-Pot Method for the Preparation of Pyrazoles by 1,3-Dipolar Cycloadditions of Diazo Compounds Generated in Situ". The Journal of Organic Chemistry. 68 (13),pp. 5381-5383.

[3] S. Fustero, A. Simon-Fuentes, J. F. Sanz-Cervera, (2009, July). "Recent advances in the synthesis of pyrazoles. A Review ", Organic Preparations and Procedures International, 41 (4), pp. 253-290.

[4] S. Cacchi, G. Fabrizi, A. Carangio, (1997). "Functionalised pyrazoles through a facile one-pot procedure from N-tosyl-N-propargyl-hydrazine and aryl iodides or vinyl triflates", Synlett. 8, pp. 959-961, (1997).

[5] Vivek, K.K, International Conference on Bioencapsulation, Groningen, Netherlands, 17, 24-26, (2009).

[6] T. Amita, M. Maridula, K. Sushil, (2011,November)."Synthesis, computional study and preliminary pharmacological evaluation of 2-[4-(2-chlorobenzyl/benzoyl) substituted piperazin-1-yl]-N-phenylacetamide: potential anti psychotics". International Journal of Research in Ayurveda and Pharmacy.6 (2), pp. 1822-1824. Available: http://www.ijrap.net/admin/php/uploads/727_pdf.pdf

[7] S. Banerjee, S. Ganguly, K. K. Sen, K. Choowongkomon, S. Seetaha, (2013) "Synthesis, evaluation and binding mode analysis of some novel triazole derivatives as antimicrobials". Journal of Advanced Pharmacy Education & Research , 3, pp. 494-511.

[8] L. Yurttas, Y. Ozkay,; F. Demirci, G. Goger, S.U. Yildirim, U. Abu mohsen, O. Ozturk, Z.A. Kaplancikli, (2014). "Synthesis, anti candidal activity, and cytotoxicity of some thiazole derivatives with dithiocarbamate side chain". Turkish Journal of Chemistry 38(5), p.p. 815- 824.

[9] S.K. Mohanty, A. Khuntia, M.S. Harika, S.P. Sarangi, D.J. Susmitha, (2015, February)." Synthesis, characterization and antimicrobial activity of some oxazole and thiazole derivatives" International Journal of Pharmacy and Pharmaceutical Research, 2 (3), pp. 60-66. Available: http://ijppr.humanjournals.com/wp-content/uploads/2015/02/12.Sujit-Kumar-Mohanty-Anuradha-Khuntia-M.-Sai-Harika-Sarada-Prasad-Sarangi-D.-Jenny-Susmitha.pdf

[10] N.R Thakare, A.K. Dhawas, P.S. Ganoskar, P.D. Kale (2012) ,"Synthesis, characterization of some new 3, 5-dimethyl azopyrazoles and its derivatives". Journal of Chemical and Pharmaceutical Research, 4(6), p.p, 3329-3332. Available: http://www.jocpr.com/articles/synthesis-characterization-of-some-new-3-5dimethyl-azopyrazoles-and-its-derivatives.pdf