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Synthesis and Characterization of some Pyrazoline derivatives from Chalcones containing azo and ether groups

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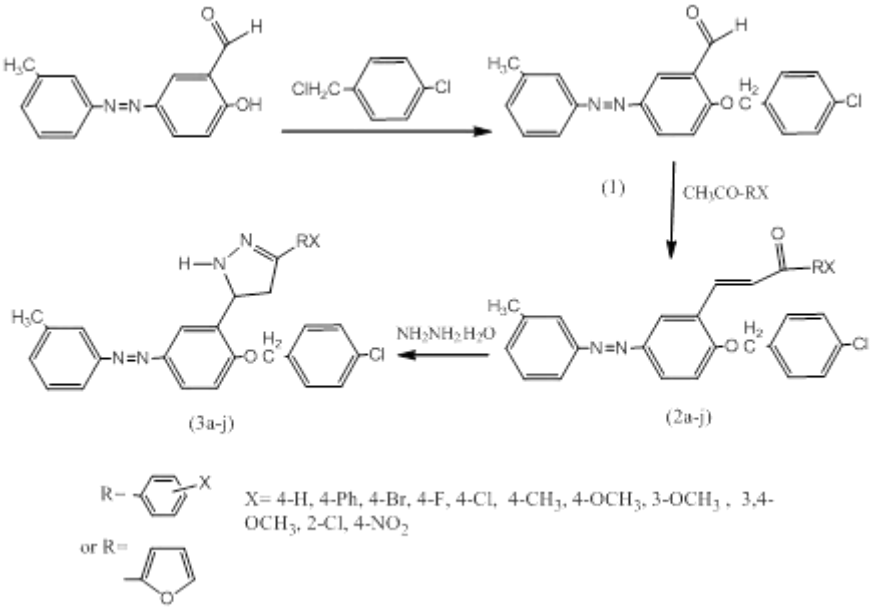
Abstract

A number of 3-(substituted)-5-(2((4-chlorobenzyl)oxy)-5-(m-tolyldizenyl) pheny l) pyrazoline (3a-j) have been synthesized by benzyloxation of hydroxyl group to give the substrate 2-((4-chlorobenzyl)oxy)-5-(m-tolyldizenyl) benzaldehyde (1). The compound (1) has been treated with different substituted acetophenone to give a new series of chalcone derivatives 1-(substituted)-3-(2-((4-chlorobenzyl)oxy)-5-(m-tolyldiazenyl) phenyl) prop-2-en-1-one (2a-j). The chalcone derivatives have been treated with hydrazine hydrate according to Michael addition reaction to afford a series of new pyrazoline derivatives. The characterization of the newly synthesized compounds elucidated by FT-IR, ^{1}H-NMR, ^{13}C-NMR, ^{13}C-DEPT and elemental analyses.

Keywords: Chalcones, Pyrazoline, Heterocycles

Introduction

Pyrazolines are one of nitrogen containing five membered heterocyclic compounds which are widespread in nature[1], which own the biological effectiveness[2] against malarias[3], fungi[4], inflammation[5] and antimicrobial [6]. Pyrazoline has been prepared using azo compound containing an aldehyde acarbonyl group[7] which interacted with a series of substituted acetophenone to give α-β unsaturated carbonyl compounds called chalcones. Chalcones have been prepared by the Claisen-Schmit condensation reaction[8], which is classified within the Aldol condensation, where the aromatic aldehydes which do not contain alpha hydrogen interact with the aromatic ketones containing alpha hydrogen presence of a strong base medium. 1,4-Michael addition[9] to chalcone interfers rations with 1,2 Claise-addition[10], depending on the nucleophile force, chalcone structural as well as temperature. Through the above addition reactions many important heterocyclic compounds which have the biological effectiveness such as pyrimidines[11], thiazines[12], oxazines[13], isoxazoles[14] and pyrazolines have been prepared.[15].



Scheme (1)

Experimental

Melting points were measured using SMP40 supplied by stuart company. Elemental analysis was measured using EuroEA 3000 in the central service laboratory in iraq. IR spectra were recorded on a shimidzu, FT-IR spectroscopy Mod IR Affinity-1 CE, using KBr disc.The ^{1}H-NMR, ^{13}C-NMR and ^{13}C-DEPT spectra were recorded on a Bruker(400MHz) with TMS as internal reference.

Synthesis of 2-((4-chlorobenzyl)oxy)-5-(m-tolyldizenyl) benzaldehyde (1)

An anhydrous K_2CO_3 (3.7g; 0.026mol) was added to a solution of 2-hydroxy-5-(m-tolyldiazenyl) benzaldehyde[16] (4.8g; 0.02mol) in (35ml) absolute

ethanol. The mixture was stirred at room temperature for 5min, then added to a solution of 4-chlorobenzylchloride (3.2g; 0.02mol) in (10ml) absolute ethanol. The final mixture was refluxed for three hours, then was added to cold distill water to give an orange-brownish precipitate, which was filtered off, then recrystallized from absolute ethanol, to give an orange-brownish precipitate.**(1)** 5.34g; 73%; IR (cm-1) str; 1678(C=O), 1577(N=N), 1255-1159(C-O-C).

Synthesis of 1-(substituted)-3-(2-((4-chlorobenzyl) oxy) -5- (m-tolyldiazenyl) phenyl) prop-2-en-1-one (2a-j)

An ethanolic NaOH (10ml; 4%) was added to a solution of **(1)** (1.1g; 0.003mol) in (30ml) absolute ethanol. The mixture was stirred at room temperature for 5min., and then substituted acetophenone or acetylfuran (0.003mol) was added to the mixture. The final mixture was refluxed for one hour to give the orange precipitate, which was filtered off, washed with cold absolute ethanol and dried under vacuum and then recrystallized from toluene.

Synthesis of 3-(substituted)-5-(2 ((4-chlorobenzyl) oxy) -5- (m-tolyldizenyl)phenyl) pyrazoline (3a-j)

Sodium hydroxide (0.04g; 0.001mol) was added to a suspension of **(2a-j)** (0.001mol) in (30ml) absolute ethanol. The mixture was stirred at room temperature for 5min., then hydrazine hydrate (1.5ml; 98%) was added to the mixture. The final mixture was refluxed for 7 hours to give the yellow precipitate, which was filtered off, washed with cold absolute ethanol and dried under vacuum and then recrystallized from chloroform, to give the yellow precipitates.

Results and Discussion

The 2-hydroxy-5-(m-tolyldiazenyl)benzaldehyde was treated with 4-chlorobenzylchloride in anhydrous K_2CO_3 to afforde compound **(1),** which was converted to chalcones **(2a-j)** by the treatment with substituted acetophenone or acetylfuran. The chalcones **(2a-j)** were converted to pyrazolines by the treatment with hydrazinhydrate in ethanol in basic medium, as shown in Scheme (1). The formation of the compound **(1)**, chalcones **(2a-j)** and pyrazolines **(3a-j)** were confirmed on the basis of their spectral data IR, ^{1}H-NMR, ^{13}C-NMR and ^{13}C-DEPT-135.

The IR spectrum of compound **(1)** Table (2), shows strong band at 1678 cm^{-1} attributed to (C=O), band at 1255 cm^{-1} (C-O-C), strong band at 1577 cm^{-1} (N=N)[7,17]. The ^{1}H-NMR spectrum of compound **(1)** Table (3), shows a singlet at δ 2.44 ppm attributed to three protons of CH_3 group, the two protons of the (-OCH_2-) group appear as a singlet at δ 5.22 ppm, the phenyl protons appear as unresolved multiplets within the δ (7.12-8.34)ppm range, where the integration value confirms the presence of 11 protons, the one proton of (COH) group appear as a singlet at δ 10.55 ppm[18]. The ^{13}C-NMR spectrum Table (4), shows signal at δ 21.47 ppm attributed to carbon of CH_3 group, the carbon (-OCH_2-) group appear at δ 70.28 ppm, the carbon of (COH) group appear at δ 189.08 ppm, the carbons of the aromatic rings appear within the δ (162.26-113.42)ppm range[21]. Also the presence of (-OCH_2-) carbon was confirmed by ^{13}C-DEPT technique through ^{13}C-DEPT spectrum of compound **(1)** Table (4) which showed signal at δ -70.27 ppm attributed to carbon of (-OCH_2-) group, The rest of the carbon atoms appeared as a signals at the expected values of δ in the ^{13}C-NMR spectrum.

The IR spectra of chalcones **(2a-j)** Table (2), showed the shifting of the absorption bands of (C=O) group of the two reactanting carbonyl compounds and compound **(1)** from 1678 cm^{-1} to lower wave numbers (1652-1660) cm^{-1}[20,21]; this is a strong evidence for the formation of conjugated enone of chalcones, the strong band at (1560-1616) cm^{-1} attributed to (C=C) of enone and aromatic rings. The ^{1}H-NMR spectra of chalcones **(2a-j)** Table (3), showed the singlet signals at δ (2.44-2.46)ppm attributed to three protons of CH_3 groups, the two protons of (-OCH_2-) groups appeared as the singlet signals at δ (5.20-5.22)ppm, The two protons of (-CH=CH-) groups and aromatic rings protons appeared as unresolved multiplets within the δ (7.80-8.25)ppm range. The ^{1}H-NMR spectrum of chalcone **(2e)** showed a singlet at δ 2.49 ppm attributed to three protons of (R-CH_3) groups, while the ^{1}H-NMR spectrum of chalcone **(2j)** showed a doublet at δ 6.56 ppm and a triplet at 6.57 ppm adjacent to a doublet at δ 6.57 ppm, where the integration value confirmed the presence of 3 protons attributed to three protons of furan. The ^{13}C-NMR spectra of chalcones **(2a-j)** Table (4), showed signals at δ (21.47-21.52)ppm attributed to carbons of CH_3 groups, while the carbon of the (R-CH_3) group of the **(2e)** appeared at δ 21.78 ppm, the carbons of (-OCH_2-) groups appeared at δ (70.30-70.38)ppm, the carbons of (C=O) groups appeared at δ (178.30-190.64)ppm, the carbons of the (C=C) and aromatic rings appeared within the δ (108.80-166.96)ppm range. The ^{13}C-DEPT spectra of chalcones **(2a-j)** Table (4), show signal at δ(-70.09 to -70.35)ppm attributed to carbons of (-OCH_2-) groups, The rest of the carbon atoms appeared at the expected δ in the ^{13}C-NMR spectrum.

The IR spectra of **(3a-j)** Table (2), did not show the absorption bands of (C=O) group, on the other hand they a showed strong band at 1593-1624 cm^{-1} attributed to (C=N)[22], bands at 3299-3360 cm^{-1} (NH) [23].

The ^{1}H-NMR spectrum of **(3e)** Table (3), showed the singlet at δ 2.29ppm attributed to three protons of CH_3 group, the singlet at δ 2.39ppm attributed to three protons of (R-CH_3) group, the two protons (-OCH_2-) group appeared as a singlet at δ 5.30ppm, also distinctive two signals showed a pseudo triplet at 2.78ppm and doublet of doublets at δ 3.43pmm attributed to two protons of CH_2 group in the pyrazoline, the one proton of CH group of the pyrazoline showed a pseudo triplet at δ 5.11ppm. The last three signals be exhibited an ABX system [24].

The proton of (NH) group of pyrazoline and aromatic rings protons appeared as unresolved multiplets within the δ (7.17-8.00) ppm range, where the integration value confirmed the presence of 16 protons[25]. The ^{1}H-NMR spectrum of **(3j)** Table (3), showed the singlet at δ 2.41 ppm attributed to three protons of CH_3 group, the two protons (-OCH_2-) group appeared as a singlet at δ 5.13 ppm, also distinctive two signals showed doublet of doublets at δ 2.75 ppm and doublet of doublets at δ 3.41 ppm attributed to two protons of CH_2 group in the pyrazoline, the one proton of CH group of the pyrazoline appeared as a doublet of doublets at δ 5.11 ppm. The last three signals be exhibited an ABX system. The spectrum showed a doublet at δ 6.54 ppm and δ 6.61 ppm attributed to two protons of furan ring, while the third proton of the furan ring and aromatic rings protons appeared as unresolved multiplets within the δ (7.30-7.97)ppm range, where the integration value confirmed the presence of 13 protons.

The ^{13}C-NMR spectra of **(3e, 3j)** Table (4), showed signals at δ 20.45 ppm, 20.62 ppm attributed to carbons of CH_3 groups respectively, the carbons (-OCH_2-) groups appeared at δ 68.68 ppm, 68.82 ppm respectively, the carbons of CH_2 groups of pyrazoline appeared at δ 38.61 ppm, 38.90 ppm respectively, the carbons of CH groups of pyrazoline appeared at δ 57.36 ppm, 57.26 ppm respectively. The carbons of the aromatic rings of **(3e)** appeared within the δ (112.22-157.66)ppm range, while the carbons of the aromatic rings and furan ring of **(3j)** appeared within the δ (108.80-157.76)ppm range. The ^{13}C-DEPT spectra of chalcones **(3e, 3j)** Table (4), showed a signals at δ -68.69 ppm, -68.82 ppm respectively attributed to carbons of (-OCH_2-) groups, the spectra showed signal at δ -39.65 ppm, -39.31 ppm respectively attributed to carbons of (-CH_2-) groups of pyrazoline, the rest of the carbon atoms appeared at the expected values of δ in the ^{13}C-NMR spectra.

Table (1) Color, Yield (%), M.P. and Elemental Analysis for the prepared compounds

compounds	R-X		Color	M.P (C°)	Yield %	Element analysis (%) Found(calc.)		
	R	X				C	H	N
1	-	-	Orange brownish	101	73	69.56(69.14)	4.88(4.70)	8.05(7.68)
2a	Ph	H	Pale orange	155	91	74.08(74.59)	5.21(4.96)	6.04(6.00)
2b	Ph	4-F	Pale orange	196	78	71.70(71.82)	4.65(4.57)	5.76(5.78)
2c	Ph	2-Cl	dark orange	125	84			
2d	Ph	4-Cl	Pale orange	177	70			
2e	Ph	4-CH3	dark orange	172	82	75.33(74.91)	5.88(5.24)	5.71(5.82)
2f	Ph	4-NO2	Orange	224	55	68.23(68.04)	4.73(4.33)	8.32(8.21)
2g	Ph	4-Br	Pale orange	119	65			
2h	Ph	4-Ph	Pale orange	136	71	77.67(77.41)	5.33(5.01)	5.91(5.89)
2i	Ph	4-OCH3	Pale orange	166	73			
2j	Ph	Fur	Orange	127	56			
3a	Ph	H	Shining yellow	122	79	72.87(72.42)	5.53(5.24)	11.89(11.65)
3b	Ph	4-F	Pale yellow	222	70			
3c	Ph	2-Cl	Dark yellow	161	72			
3d	Ph	4-Cl	Dark yellow	148	77			
3e	Ph	4-CH3	Shining yellow	133	82			
3f	Ph	4-NO2	Orange yellowsh	180	55			
3g	Ph	4-Br	Shining yellow	212	68			
3h	Ph	4-Ph	Pale yellow	170	65			
3i	Ph	4-OCH3	Pale yellow	145	71			
3j	Ph	Fur	Orange yellowsh	196	64			

Table (2) Selected IR Stretching Vibration Bands (cm^{-1}) of the Prepared Compounds

R	X	2a-j		3a-j	
		C=O	C=C	N-H	C=N
Ph	H	1654	1600,1593	3355	1598
Ph	4-F	1653	1600,1583	3325	1600
Ph	2-Cl	1653	1598,1585	3356	1604
Ph	4-Cl	1652	1600,1562	3360	1593
Ph	4-CH3	1653	1608,1595	3360	1598
Ph	4-NO2	1660	1598,1591	3452	1624
	4-Br	1652	1598,1583	3360	1604
Ph	4-Ph	1654	1616,1602	3340	1622
Ph	4-OCH3	1653	1604,1589	3353	1600
Ph	Fur	1652	1596,1560	3299	1596

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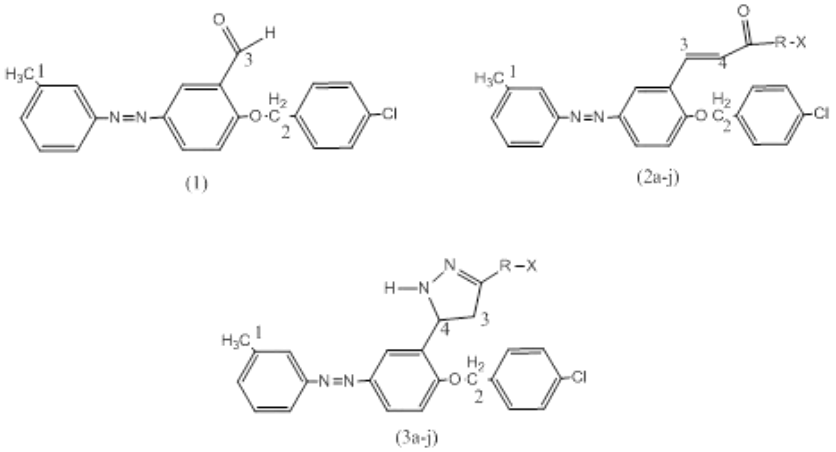

Figure (1) shows the positions of the hydrogen atoms in the prepared compounds

Table (3) ^{1}H NMR Chemical Shifts for the Prepared Compounds

Comp.	R-X		H-NMR ppm (mltiplicity,Intens.)					
	R	X	H1	H2	H3	H4	H Ph	HR
1			2.44(s,3 H)	5.22(s,2 H)	10.55(s,1H)		7.12-8.43(m,11H)	
2a	Ph	H	2.46(s,3 H)	5.21(s,2 H)	with Ph	with Ph	7.09-8.25(m,18H)	with Ph
2b	Ph	4-F	2.46(s,3 H)	5.21(s,2 H)	with Ph	with Ph	7.10-8.23(m,17H)	with Ph
2e	Ph	4-CH3	2.45(s,3 H)	5.21(s,2 H)	with Ph	with Ph	7.09-8.24(m,17H)	2.49(s,3H)
2g	Ph	4-Br	2.45(s,3 H)	5.21(s,2 H)	with Ph	with Ph	7.10-8.23(m,17H)	with Ph
2h	Ph	4-Ph	2.46(s,3 H)	5.20(s,2 H)	with Ph	with Ph	7.09-8.25(m,22H)	with Ph
2j	Ph	Fur	2.46(s,3 H)	5.22(s,2 H)	with Ph	with Ph	7.08-8.25(m,13H)	6.56(d,1H),6.57(t,1H),6.57(d,1H)
3e	Ph	4-CH3	2.29(s,3 H)	5.30(s,2 H)	2.78(t*,1H), 3.43(dd,1H)	5.11(t*,1 H)	7.17-8.00(m,16H) Ph & NH	2.39(s,3H)
3j	Ph	Fur	2.41(s,3 H)	5.13(s,2 H)	2.75(dd,1H), 3.41(dd,1H)	5.11(dd,1 H)	7.30-7.97(m,13H) Ph & NH	6.54(d,1H),6.61(d,1H),with Ph

*: pseudo

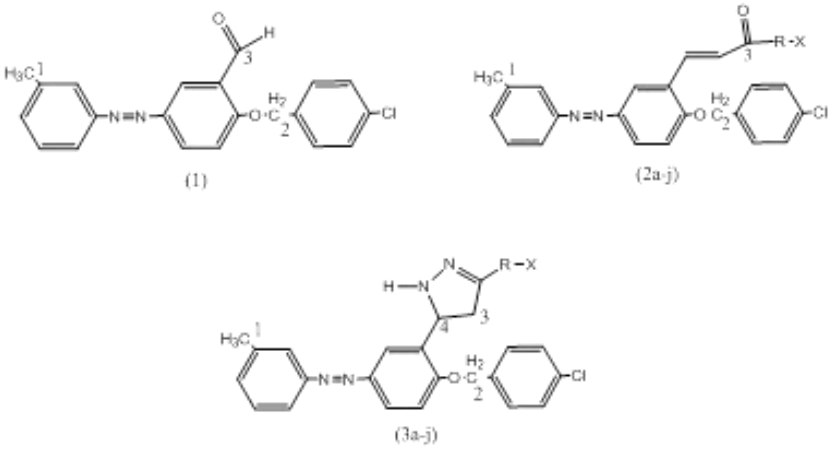

Figure (2) shows the positions of the carbon atoms in the prepared compounds

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Table (4) ^{13}C NMR and DEPT NMR Chemical Shifts (ppm) for the prepared compounds

	R-X		13C-NMR ppm						
Compound	R	X	C1	C2	C2-Dept	C3	C3-Dept	C4	Ph
1			21.47	70.28	-70.27	189.08			113.42-162.26
2a	Ph	H	21.48	70.33	-70.11	190.64			112.74-159.72
2b	Ph	4-F	21.48	70.37	-70.35	188.91			112.74-166.96
2e	Ph	4-CH_3	21.4921.78	70.31	-70.30	190.18			112.70-159.70
2g	Ph	4-Br	21.47	70.38	-70.18	189.54			112.76-159.76
2h	Ph	4-Ph	21.52	70.34	-70.15	190.05			112.68-159.80
2j	Ph	Fur	21.48	70.3	-70.09	178.3			112.54-159.73
3e	Ph	4-CH_3	20.45 21.45	68.68	-68.69	38.61	-38.65	57.36	112.22-157.66
3j	Ph	Fur	20.62	68.82	-68.82	38.9	-39.31	57.26	108.80-157.76

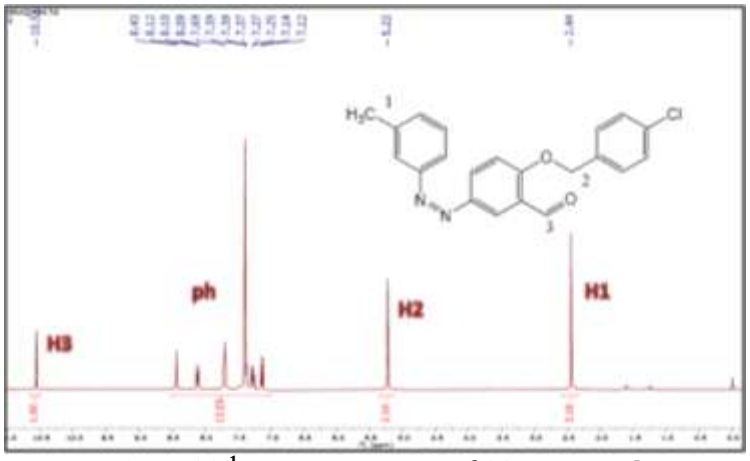

Figure (3) ^{1}H-NMR Spectrum of (1) compound

Figure (4) ^{13}C-NMR Spectrum of (1) compound

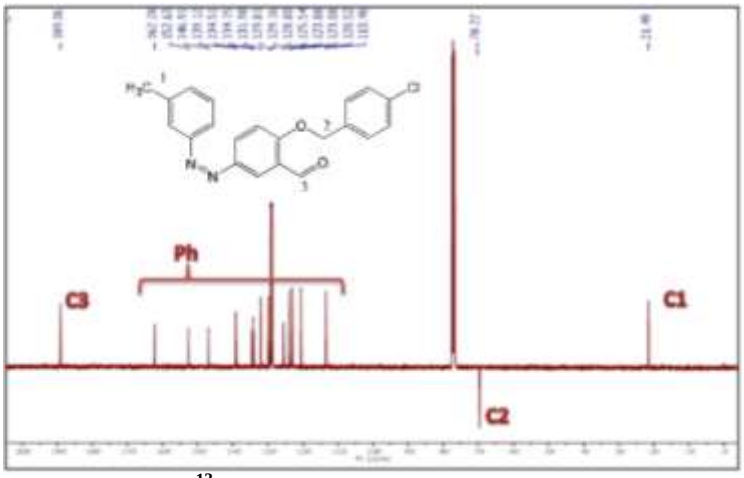

Figure (5) ^{13}C-DEPT-135 Spectrum of (1) compound

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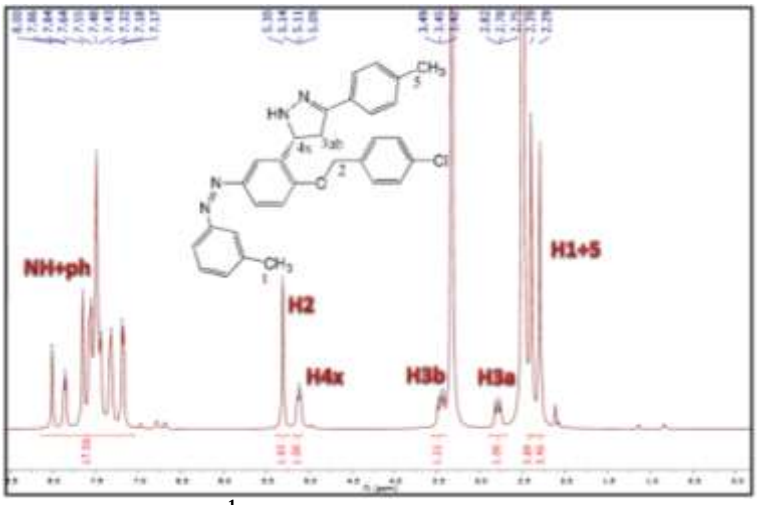

Figure (6) ^{1}H-NMR Spectrum of (3e) compound

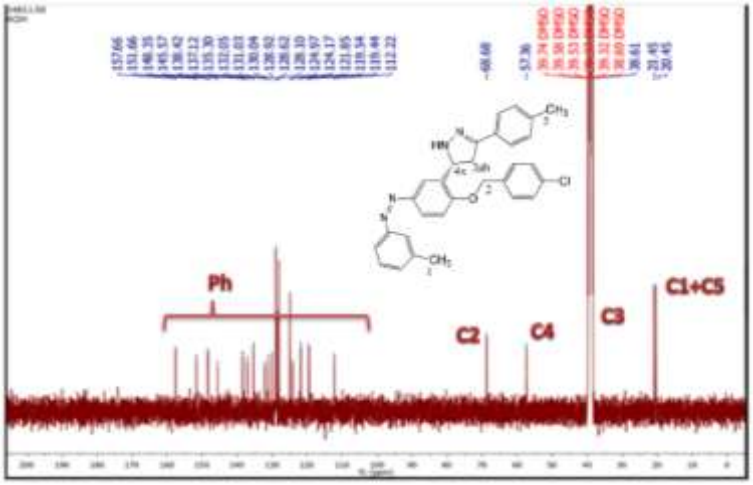

Figure (7) ^{13}C-NMR Spectrum of (3e) compound

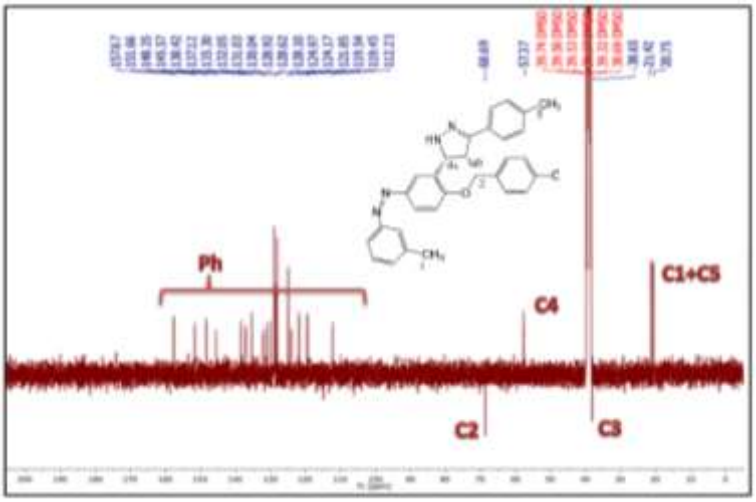

Figure (8) ^{13}C-DEPT-135 Spectrum of (3e) compound

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تحضير وتشخيص بعض مشتقات البايرازولين من الجالكونات المحتوية على الازو ومجاميع اخرى

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الملخص

يتضمن هذا البحث تحضير عدد من مشتقات البايرازولين الحاوية على مجموعة الازو والتي حضرت عن طريق معاملة المركب 2-((4-كلوروبنزايلوكسي)-5-(ميتاتولودايازينايل)بنزلدهايد مع معوضات مختلفة للاسيتوفينون للحصول على سلسلة جديدة من مشتقات الجالكونات، وهذه المشتقات عوملت مع الهايدرازين المائي بموجب تفاعل تكاثف مايكل حيث تم الحصول على سلسلة جديدة من مشتقات البارازولين، وشخصت المركبات المحضرة بواسطة FT-IR و ^{1}H-NMR و ^{13}C-NMR و ^{13}C-DEPT-135 والتحليل الدقيق للعناصر.

الكلمات المفتاحية: الجالكونات، البايرازولين، حلقات حاوية على ذرة مغايرة.