



Synthesis and Characterization of Some New Pyrazoline Derivatives Containing Azo Group by One Pot Method

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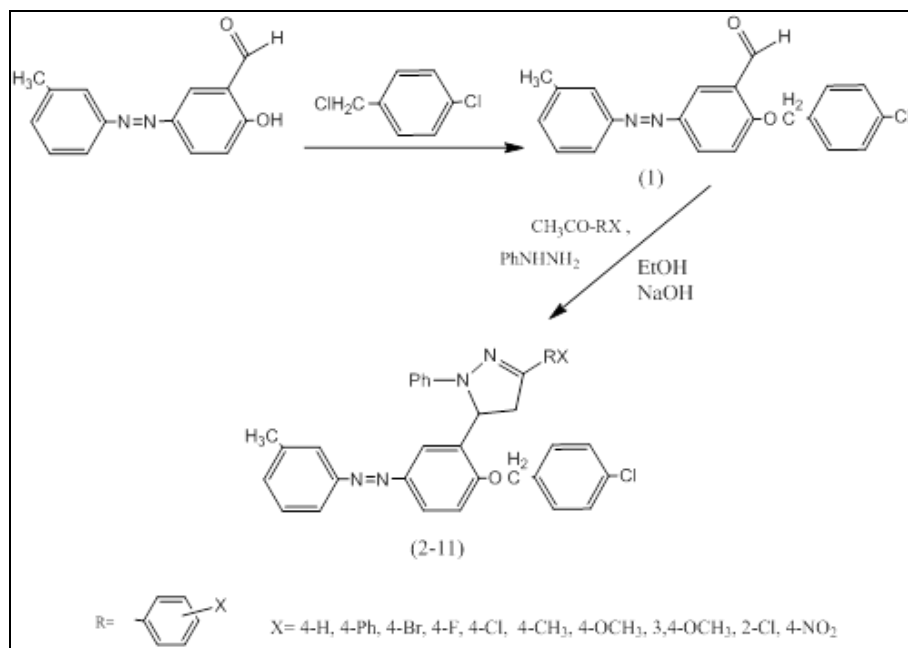
Abstract

This research includes the preparation of some of pyrazoline derivatives containing the azo group by one pot method through the treatment of the compound 2-hydroxy-5-(m-tolyldiazenyl) benzaldehyde with p-chlorobenzylchloride to give the compound(1) using the Williamson reaction. The compound (1) is treated with a series of ketones and with phenylhydrazine in the base medium to give new derivatives of pyrazoline (2-11). The synthesized compounds were characterized by elemental analyses and FT-IR, ¹H-NMR, ¹³C-NMR, ¹³C-DEPT.

Introduction

The one pot addition method was used for the preparation of pyrazoline derivatives. This method is classified within the Multi Component reaction (MCR), which interact three or more reactants at one time to produce the final compound, This method was known more than 150 years ago[1,2]. This method is preferred in organic chemistry because shorten the number of steps of preparation and avoid the length of separation and purification processes [3,4]. Pyrazolines are the heterocyclic that have high

biologic efficacy against many bacteria[5] and fungi[6]. The pyrazoline derivatives were prepared using an azo-dye containing the aldehyde carbonyl group[7] that treated with a series of acetophenone derivatives under the Claisen-Schmit condensation reaction[8-10], to give the corresponding chalcones derivatives, which treated at the same time with phenylhydrazine in a base medium via Michael's reaction[11-13] to obtain the new derivatives of pyrazoline, as shown in Scheme (1).



Scheme(1)

Experimental

The IR spectra were recorded on a Shimidzu, FT-IR spectroscopy model IR Affinity-1 using KBr disc. The $^1\text{H-NMR}$, $^{13}\text{C-NMR}$ and $^{13}\text{C-DEPT}$ spectra were recorded on Bruker (400 MHz) with TMS as internal reference and DMSO- d_6 as a solvent in university of science and technology-Jordan. The melting points were measured using SMP40 supplied by stuart company. While the elemental analysis was measured using EuroEA 3000 in the central service laboratory in iraq.

Synthesis of compound (1)

This compound (1) had been prepared by using similar method [14].

Synthesis of 5-(2-((4-chlorobenzyl)oxy)-5-(m-tolyldiazenyl)phenyl)-3-(substituted)-1-phenyl-4,5-dihydro-1H-pyrazole

The acetophenone derivatives (0.003 mol) was added to a solution of compound (1) (0.003 mol) in (35ml)

absolute ethanol then added the NaOH (0.001 mol; 0.4 g) this mixture was stirred and added the phenylhydrazine (1.5 ml) to the mixture and refluxed for (5-7) hour to give yellow precipitate, which was filtered off, washed with cold absolute ethanol and dried under vacuum and then recrystallized from chloroform, to give yellow precipitates.

Results and Discussion

The 2-hydroxy-5-(m-tolyldiazenyl)benzaldehyde was treated with 4-chlorobenzylchloride in anhydrous K_2CO_3 to afforded compound (1), which was treatment with substituted acetophenone and phenylhydrazine in ethanol in basic medium by the one pot method to give new pyrazoline derivatives, as shown in Scheme (1). The formations of the pyrazolines (2-11) were confirmed on the basis of their spectral data IR, $^1\text{H-NMR}$, $^{13}\text{C-NMR}$ and $^{13}\text{C-DEPT-135}$.

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

Comp.	Ar	X	Molecular formula	Color	M.P (°C)	Yield %	Time / hrs	Elemental Analysis (%) Found (calc.)		
								C	H	N
2	Ph	H	$\text{C}_{35}\text{H}_{29}\text{ClN}_4\text{O}$	Orange yellowish	189	73	5	75.49 (75.46)	5.76 (5.25)	10.12 (10.06)
3	Ph	4-F	$\text{C}_{35}\text{H}_{28}\text{ClFN}_4\text{O}$	Shine yellow	174	70	7	73.49 (73.10)	5.13 (4.91)	9.73 (9.74)
4	Ph	2-Cl	$\text{C}_{35}\text{H}_{28}\text{Cl}_2\text{N}_4\text{O}$	Shine yellow	180	55	6	-	-	-
5	Ph	4-Cl	$\text{C}_{35}\text{H}_{28}\text{Cl}_2\text{N}_4\text{O}$	Shine yellow	186	62	6	-	-	-
6	Ph	4- CH_3	$\text{C}_{36}\text{H}_{31}\text{ClN}_4\text{O}$	Pale yellow	191	69	7	75.98 (75.71)	5.61 (5.47)	10.01 (9.81)
7	Ph	4- NO_2	$\text{C}_{35}\text{H}_{28}\text{ClN}_5\text{O}_3$	Orange yellowish	280	66	7	-	-	-
8	Ph	4-Br	$\text{C}_{35}\text{H}_{28}\text{BrClN}_4\text{O}$	Shine yellow	144	81	5	-	-	-
9	Ph	4-Ph	$\text{C}_{41}\text{H}_{33}\text{ClN}_4\text{O}$	Pale yellow	233	53	6.5	77.85 (77.77)	5.48 (5.25)	8.89 (8.85)
10	Ph	4- OCH_3	$\text{C}_{35}\text{H}_{28}\text{ClN}_4\text{O}_2$	Pale yellow	128	71	7	-	-	-
11	Ph	3,4-di OCH_3	$\text{C}_{37}\text{H}_{33}\text{ClN}_4\text{O}_3$	Orange yellowish	201	74	6.5	70.48 (70.51)	5.78 (5.33)	10.65 (10.96)

The IR spectra of (2-11) Table (2), did not show the absorption bands of (C=O) group, on the other hand they showed strong band at (1593-1600) cm^{-1} attributed to (C=N) [15], strong bands at (1450-1468) cm^{-1} attributed to (C=C) [16,17].

The $^1\text{H-NMR}$ spectrum of (5) Table (3) Figure (1,2), showed the singlet at $\delta(2.36)$ ppm attributed to three protons of CH_3 group, the two protons of ($-\text{OCH}_2-$) group appeared as a singlet at $\delta(5.36)$ ppm, the one proton of (CH_a) group of the pyrazoline showed a doublet of doublets at $\delta(3.16)$ ppm with coupling constant ($^2J_{\text{Ha-Hb}}=17.77\text{Hz}$), ($^3J_{\text{Ha-Hx}}=6.54\text{Hz}$), and the one proton of (CH_b) group of the pyrazoline showed a pseudo triplet at $\delta(3.94)$ ppm with coupling constant ($^2J_{\text{Hb-Ha}}=17.77\text{Hz}$), ($^3J_{\text{Hb-Hx}}=12.61\text{Hz}$), also distinctive signal showed a doublet of doublets at (5.72) ppm with coupling constant ($^3J_{\text{Hx-Ha}}=6.54\text{Hz}$), ($^3J_{\text{Hx-Hb}}=12.61\text{Hz}$) attributed to proton of (CH_x) group in the pyrazoline. The last three signals be exhibited an ABX system [22-24]. There was also a multiple signal within the range of $\delta(6.72-7.86)$ ppm where the integration value confirms the presence of 20 protons attributed to the protons of the aromatic rings.

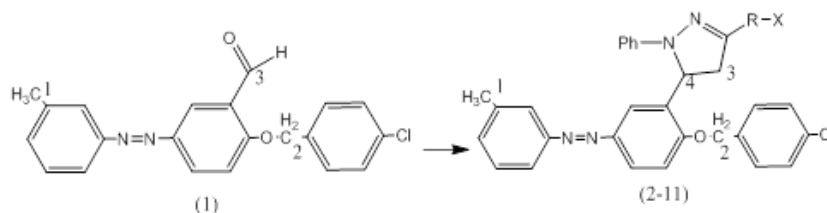
$^1\text{H-NMR}$ spectrum of (8) table(3) figure (3,4), showed a singlet at $\delta(2.33)$ ppm attributed to three protons of (CH_3) group, the two protons of ($-\text{OCH}_2-$) group appeared as a singlet at $\delta(5.33)$ ppm, the one proton of (CH_a) group of the pyrazoline showed a doublet of doublets at $\delta(3.13)$ ppm with coupling constant ($^2J_{\text{Ha-Hb}}=17.10\text{Hz}$), ($^3J_{\text{Ha-Hx}}=5.26\text{Hz}$), and the one proton of (CH_b) group of the pyrazoline showed a

doublet of doublets at $\delta(3.90)$ ppm with coupling constant ($^2J_{\text{Hb-Ha}}=17.10\text{Hz}$), ($^3J_{\text{Hb-Hx}}=12.66\text{Hz}$), also distinctive signal showed a doublet of doublets at $\delta(5.69)$ ppm with coupling constant ($^3J_{\text{Hx-Ha}}=5.26\text{Hz}$), ($^3J_{\text{Hx-Hb}}=12.66\text{Hz}$) attributed to proton of (CH_x) group in the pyrazoline. The last three signals be exhibited an ABX system [22-24]. There was also a multiple signal within the range of $\delta(6.71-7.83)$ ppm where the integration value confirms the presence of 20 protons attributed to the protons of the aromatic rings.

$^{13}\text{C-NMR}$ spectra of (5, 8) table (4) figure (5,7), showed signals at $\delta(21.26)$ ppm, attributed to carbons of (CH_3) groups, while the carbons ($-\text{OCH}_2-$) groups appeared at $\delta(71.15)$ ppm, the carbons of CH_2 groups of pyrazoline appeared at $\delta(37.59)$ ppm, $\delta(37.97)$ ppm respectively, the carbons of CH groups of pyrazoline appeared at $\delta(61.31)$ ppm, $\delta(60.81)$ ppm respectively. The carbons of the aromatic rings of (5) appeared within the $\delta(108.18-158.04)$ ppm range, while the carbons of the aromatic rings and furan ring of (8) appeared within the $\delta(115.98-158.04)$ ppm range [21]. The $^{13}\text{C-DEPT}$ spectra of (5, 8) table (4) figure (6,8), showed a signals at $\delta(-71.00,-71.10)$ ppm respectively attributed to carbons of ($-\text{OCH}_2-$) groups, the spectra showed signal at $\delta(-37.42,-37.90)$ ppm respectively attributed to ($-\text{CH}_2-$) groups of pyrazoline, the residual of the carbon atoms appeared at the expected values of δ in the $^{13}\text{C-NMR}$ spectra [25].

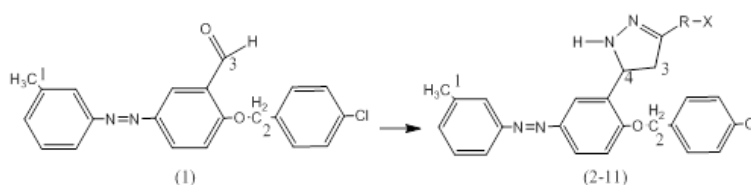
Table(2) IR stretching vibration bands (cm^{-1}) of the prepared compounds

Comp. No.	Ar	X	IR $\nu(\text{stretching}) \text{cm}^{-1}$ in KBr				
			$\nu(\text{C=N})$	$\nu(\text{C}=\text{C})_{\text{Ar}}$	$\nu(\text{C-H})_{\text{alph}}$	$\nu(\text{=CH})_{\text{arom.}}$	$\nu(\text{C-N})$ $\nu(\text{N-N})$
2	Ph	H	1596	1496	2916	3053	1134 1091
3	Ph	4-F	1598	1496	2860	3033	1132 1091
4	Ph	2-Cl	1593	1450	2928 2866	3082	1132 1091
5	Ph	4-Cl	1598	1494	2920 2858	3041	1134 1091
6	Ph	4- CH_3	1596	1496	2920	3035	1131 1091
7	Ph	4- NO_2	1597	1494	2931	3039	1120 1089
8	Ph	4-Br	1596	1496	2962	3058 3039	1132 1093
9	Ph	4-Ph	1596	1496	2923	3056	1130 1091
10	Ph	4- OCH_3	1600	1498	2940 2871	3062	1134 1091
11	Ph	3,4-di OCH_3	1596	1496	2933	3058	1132 1091

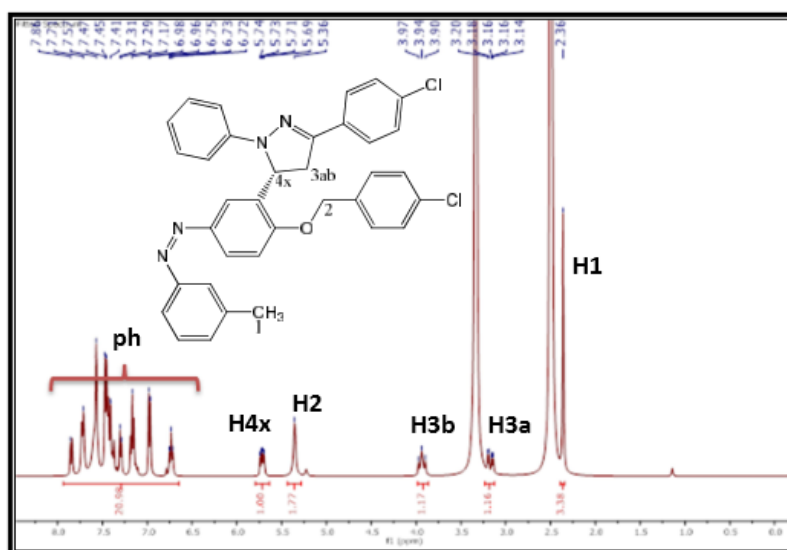
**Table(3) ¹H NMR chemical shifts for the prepared compounds**

Comp.	R-X		H-NMR ppm (mlicity,Intens.)				
	R	X	H1	H2	H3	H4	H Ph
5	Ph	4-Cl	2.36(s,3H)	5.36 (s,2H)	3.16(dd,1H), 2JHa-Hb(17.77), 3JHa-Hx(6.54); 3.94(*,1H) 2JHb-Ha(17.77), 3JHb-Hx(12.61)	5.72(dd,1H) 3JHx-Ha(6.54), 3JHx-Hb(12.61)	6.72-7.86 (m,20H)
8	Ph	4-Br	2.33(s,3H)	5.33 (s,2H)	3.13(dd,1H) 2JHa-Hb(17.10), 3JHa-Hx(5.26); 3.90(dd,1H), 2JHb-Ha(17.10), 3JHb-Hx(12.66)	5.69(dd,1H), 3JHx-Hb(12.66), 3JHx-Ha(5.26)	6.71-3.83 (m,20H)

*: pseudo

**Table(4) ¹³C NMR and DEPT NMR chemical shifts (ppm) for the prepared compounds**

Compound	R-X		¹³ C-NMR ppm					Ph
	R	X	C1	C2	C2-Dept	C3	C3-Dept	
5	4-Cl	21.26	71.15	-68.82	37.59	-37.42	61.31	108.18-158.04
8	4-Br	21.26	71.15	-71.00	37.97	-37.90	60.81	115.98-158.04

**Figure (1) ¹H-NMR spectrum of compound (5)**

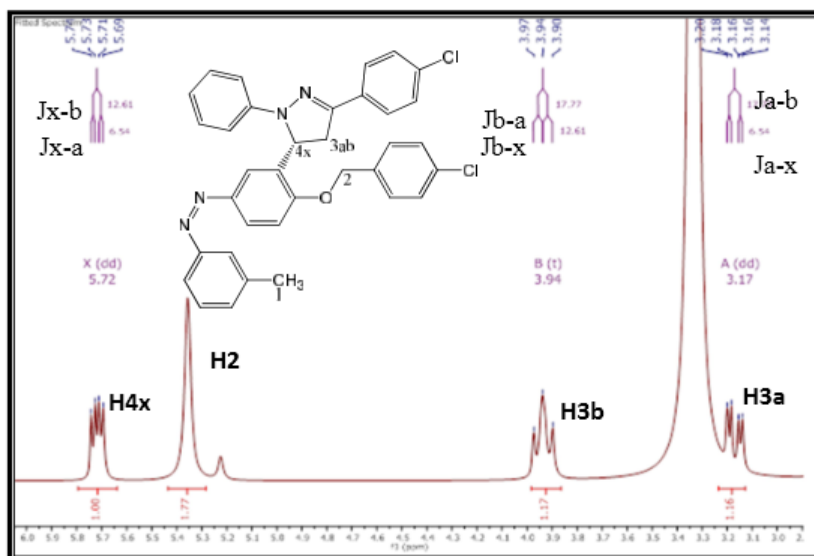


Figure (2) coupling constant for ¹H-NMR spectrum of compound (5)

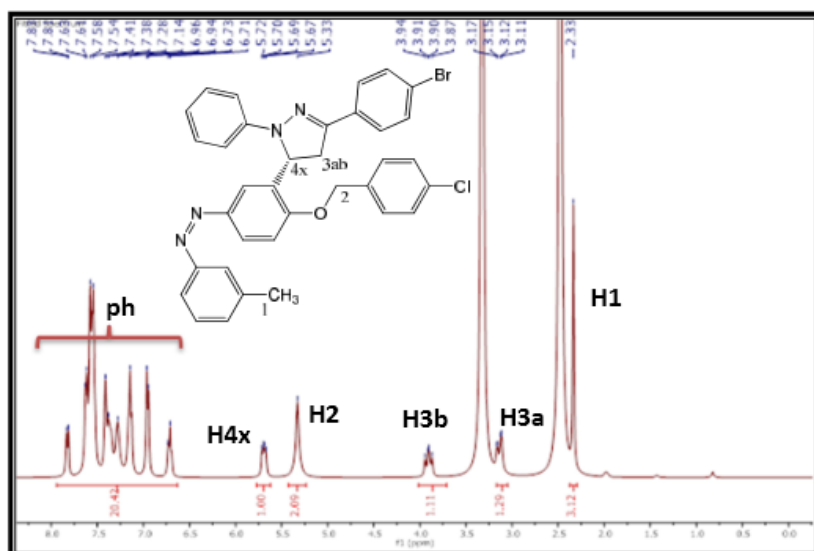


Figure (3) ¹H-NMR spectrum of compound (8)

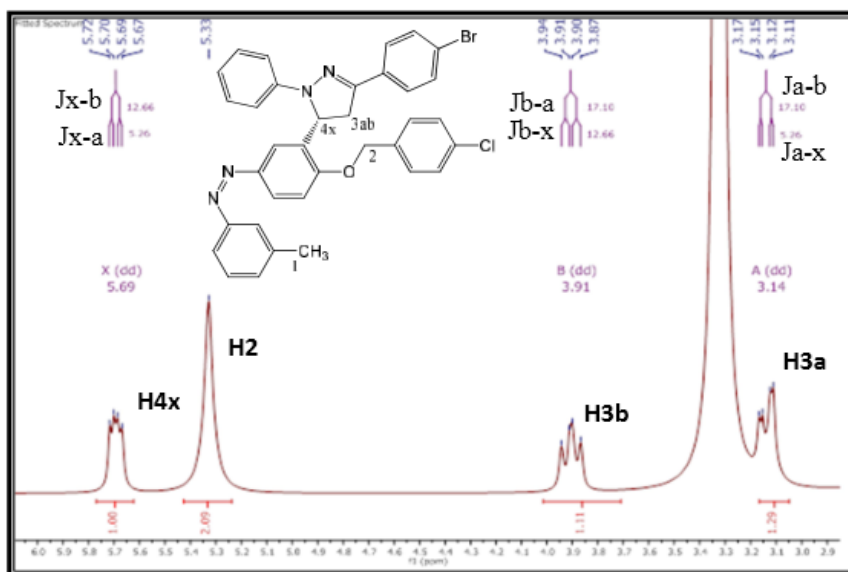


Figure (4) coupling constant for ¹H-NMR spectrum of compound (8)

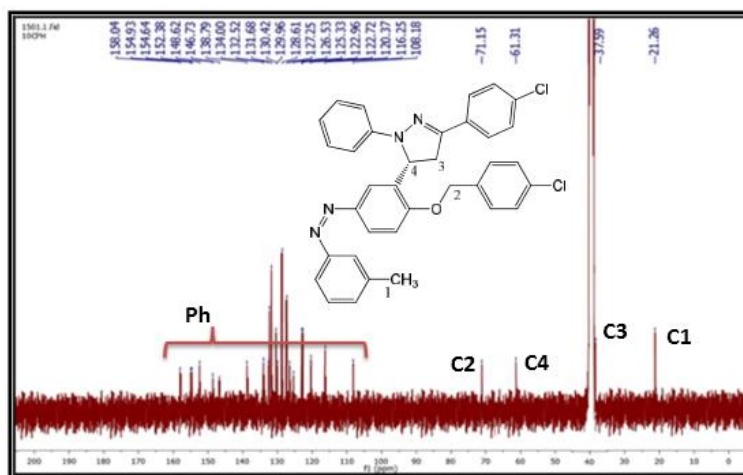


Figure (5) ¹³C-NMR spectrum of compound (5)

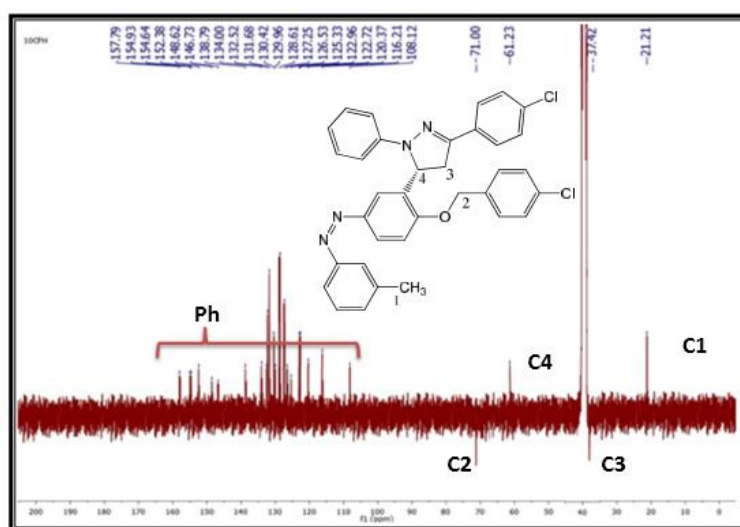


Figure (6) ¹³C-DEPT-135 spectrum of compound (5)

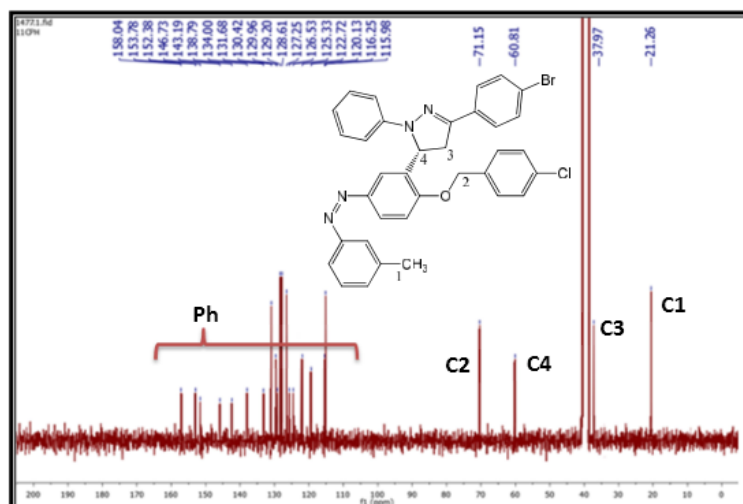


Figure (7) ¹³C-NMR spectrum of compound (8)

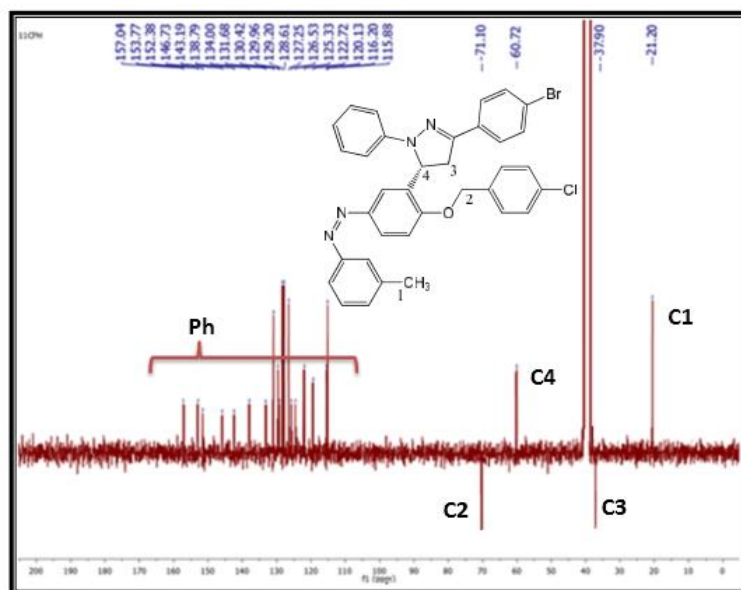


Figure (8) ^{13}C -DEPT-135 spectrum of compound (8)

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تحضير وتشخيص بعض مشتقات البايرازولين الجديدة المحتوية على مجموعة الازو بطريقة الاضافة الواحدة

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الملخص

يتضمن هذا البحث تحضير بعض مشتقات البايرازولين الحاوية على مجموعة الازو بطريقة الاضافة الواحدة (One Pot) من خلال مفاعلة المركب 2-hydroxy-5-(m-tolyldiazenyl)benzaldehyde مع p-chlorobenzylchloride ليعطي المركب (1) وفق تفاعل وليامسن. وبمفاعلة المركب (1) مع سلسلة من الكيتونات والفنيل هيدرازين في وسط قاعدي ليعطي مشتقات جديدة للبايرازولين (2-11). وشخصت المركبات المحضرة بواسطة FT-IR و¹H-NMR و¹³C-NMR و¹³C-DEPT-135 والتحليل الدقيق للعناصر.

الكلمات المفتاحية: الاضافة الواحدة، بايرازولين، حلقات غير متجانسة