Synthesis of New Pyrazolines Derivatives from Coumarine Compounds

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الخلاصة

يتضمن البحث تحضير سلسله من الجالكونات وتكثيفها مع هيدرازيدات الكومارين المحضرة قي وسط حامضي لينتج البايرازوليينات الجديدة . تم أثبات الصيغ التركيبية باستخدام الطرق الفيزياويه والطيفية المتاحة.

Abstract

The present work includes preparation of series of chalcones and condensation of these chalcones with a series of prepared coumarin hydrazides in acidic medium to afford the new pyrazolines. Physical and available spectral were used to confirm structures

Introduction

Pyrazoline are well known nitrogen-containing heterocyclic compounds and several procedures have been developed for synthesis[1-3]. Numerous pyrazoline have been found to pocess important bioactivities likes videlicet central nervous system[4], antibacterial[3, 5], antifungal[6], antimicrobial[7] and antimycotic[8] activities. Various methods are used for preparation of 2-pyrazolines.

Treatment of α, β- unsaturated aldehyd and ketones with hydrazines seems to be the most popular procedure for this purpose. This reaction has been condensed under various conditions [9-11]. In this paper hydrazides were used hydrazine or to afford the new 1- substituted 2-pyrazolines, by condensation with chalcones.

Some chalcones were prepared by condensation of acetophenone or substituted acetophenone with benzaldehyde or substituted benzaldehyde in ethanolic NaOH solution [13,14], on the other hand 4-Methyl-7-coumarinloxy methyl hydrazide and coumarine-3-carboxylic acid

hydrazide has been prepared by refluxing the4-Methyl-7-ethoxy carbonyl methyl coumarine and ethyl coumarine-3-carboxylate with hydrazine hydrate [15].

As mentioned 2-pyrazolines posse's valuable bioactivities which stimulated the preparation of their numerous derivatives. In insertion of cumarine compound into pyrazoline molecules may gave beneficial to increase their bioactivities. Taking this expectation into condensation, we report have the preparation of new coumarine derivatives of 2-pyrazoline.

Experimental

1- Melting point was determined by Electro thermal IA 9000.
2- Infra red spectrophotometer Model Tanser 27 Bruker Co. Germany

4-Methyl-7- hydroxy coumarine (1).
This compound was prepared as mentioned in the literature [16] yield 98% m.p.183Cº (litt.m.p.185Cº).
4-Methyl-7-O-(ethoxy carbonyl methyl) coumarin (2).
This compound was prepared as mentioned in the literature [17] yield 92%, m.p. 100-105Cº (litt.102Cº).
Ethyl coumarin-3-carbxylate (3).
This compound was prepared as mentioned in the literature [18] yield 77%, m.p.92-93Cº (litt.94Cº).
4-Methyl-7-coumarinloxy methyl hydrazide (4) and coumarin-3-carboxylic acid hydrazide (5).

Method 1[17]:

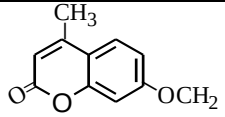
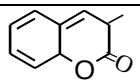
A mixture of the appropriate ester (2,3) (0.0125 mole) and hydrazine hydrate (0.0625 mole, 3ml) 99% in absolute ethanol (100 ml) was refluxed for 10 hours, then the solvent evaporated under reduced pressure, the residue was washed with water, dried and recrystallized from ethanol. Table (1).

Method 2:

A mixture of the ester (2, 3) (0.05 mole) and hydrazine hydrate (99%) was refluxed for (45 min.). the product crystallized out on cooling, wash with water and recrystallized from ethanol. Table (1).

Table (1): some physical properties and spectral data of hydrazide

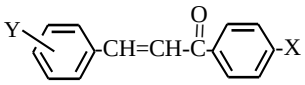
G-C(=O)NHNH$_2$

Cpd.No.	G	m.p.cº	Colour	Yield (%)	IR(KBr)ν cm^{-1}	
					N-H	C=O
4		203-205	White	93	3500	1680
5		99- 101	yellow	85	3550	1660

Preparation of chalcones (General procedures)[13] (6-12).

In a round bottom flask provided with a mechanical stirrer and immersed in an ice-bath, a mixture of (0.75gm, 0.0183 mole) of sodium hydroxide pellets, (10ml) of water and (15 ml) of ethanol was stirred. A (0.0143 mol) of freshly distilled acetophenone was poured on the stirred mixture followed by adding a purified substituted benzaldehyde (0.0143 mole). The temperature of the mixture kept at (20-25)Cº with vigorous stirring for (1-3) hrs until the mixture became thick (i.e. the stirring was no longer effective). The mixture was then kept in a refrigerator overnight. The product was filtrate, was neutral to litmus then washed with (20 ml) ice-cold ethanol. The crude chalcone after drying in air was recrystallized from ethanol .Some physical properties and spectral data were illustrated in table (2, 4).

Table (2): Some physical properties and spectral data of chlcones (6-12)

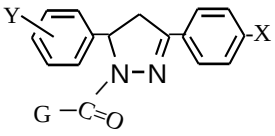


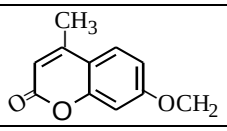
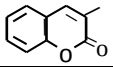
Cpd. No.	X	Y	Colure	m.p. Cº	Yield (%)	Name of chalcone
6	Br	4-NO_2	Yellow	135-138	51	1-(ρ-bromophenyl) 3-(ρ-Nitro phenyl)2-propene-1-one
7	Br	4-H(CH_3)	Brown	68-70	55	1- (ρ-bromophenyl)-3 ρ-(N,N-Dimethyl amino phenyl)-2-propene-1-one
8	Br	2-CL	White	76-78	51	1-(ρ-bromophenyl)-3-(o-Chlorophenyl)-2-propene-1-one
9	CH_3O	2-CL	Yellow	91-93	78	1-(ρ-methoxyphenyl)-3-(ρ-Bromophenyl)-2-propene-1-one
10	CH_3O	4-NO_2	Yellow	158-160	48	1-(ρ-methoxyphenyl)-3-(ρ-Nitro phenyl)-2-propene-1-one
11	CH_3O	4-N(CH_3)$_2$	Yellow	121-123	77	1-(ρ-methoxyphenyl)-3-(ρ-N,N-Dimethylamino) -2-propene-1-one
12	CH_3O	4-CH_3O	Yellow	100-102	77	1-(ρ-methoxyphenyl)-3-(ρ-methoxphenyl)-2-propene-1-one

Preparation of derivatives of 2- pyrazolines (12-26) [3].

A mixture of chalcone derivatives (6-12) (0.01mole), hydrazide (4 or 5, 0.03 mole) and glacial acetic acid (60 ml) were heated under reflux for 6 hr then the mixture poured onto crushed ice. The precipitate was separated by filtration, washed with water/ ethanol to obtain 2-pyrazolines (13-26). Some physical properties and spectral data were illustrated in tables (3, 5).

Table (3): Some physical properties 1- substituted -2- pyrazoline



Cpd. No.	X	Y	G	m.p. C°	Colour	Yield (%)
13	Br	4-NO_2		264-267	Brown	89
14	Br	4-$N(CH_3)_2$	=	270-273	Brown	91
15	Br	2-CL	=	287-290	White	96
16	OCH_3	2-CL	=	281-284	White	98
17	OCH_3	4-NO_2	=	285-287	White	93
18	OCH_3	4-$N(CH_3)_2$	=	138-140	Brown	88
19	OCH_3	4-OCH_3	=	290-292	White	96
20	Br	4-NO_2		204-206	Brown	96
21	Br	4-$N(CH_3)_2$	=	206-208	Brown	77
22	Br	2-CL	=	204-206	Yellow	94
23	OCH_3	2-CL	=	188-190	Yellow	87
24	OCH_3	4-NO_2	=	208-209	Yellow	95
25	OCH_3	4-$N(CH_3)_2$	=	209-210	Brown	64
26	OCH_3	4-OCH_3	=	190-192	Yellow	99

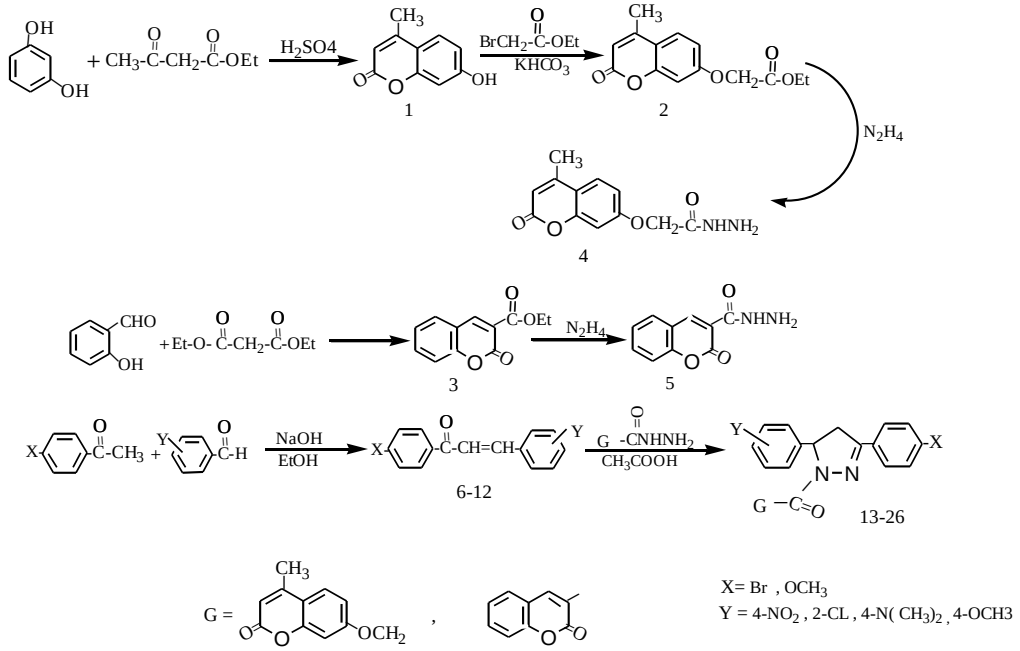
Results and Discussion

The parent compound (1) was allowed to react with ethyl bromo acetate in the presence of anhydrous potassium bicarbonate to give compound No. (2), while the reaction of salicyladehyde with diethyl malonate give the ester (3).

The ester (2) & (3) react with excess of hydrazine hydrate to produce 4-Methyl-7-coumarinloxy hydrazide (4) and coumarine-3-carboxylic acid hydrazide (5).

The hydrazides (4, 5) were identified by the appearance of the following bands at (3500-3550 cm^{-1}) for the N-H starching, carbonyl of hydrazide at (1160- 1680 cm^{-1}) lower than the carbonyl ester due to the presence of resonance effect [22].

The chalcone (6-12) were synthesized by condensation of substituted acetophenone with substituted benzaldehyde as shown in Scheme. (1).



Scheme (1): synthesis of pyrazoline derivatives from coumarine compounds

The structure of these compounds was substantially identified by IR spectroscopy. The IR spectra Table (4) shows significant absorption peak at (1654- 1679 cm^{-1}) and (1592- 1603 cm^{-1}) related to ν(C=O) and ν(C=C) band respectively [14]. The depression in the absorption frequencies of the (C=O) was attributed to the resonance of the conjugated system. The infra red spectrum of compound (6, 10) exhibited an additional absorption peaks at (1515- 1518 cm^{-1}) & (1343- 1344 cm^{-1}) for asymmetrical and symmetrical NO2 bond stretching, while the IR spectrum of compound (8, 9) showed absorption peak at (808-829 cm^{-1}) for C-CL. Also absorption peaks at (1252-1259 $cm^{-1}$and 1166- 1183 cm^{-1}) for asymmetrical and symmetrical CH_3O bond stretching for (9-12) compounds. Peak at (1288 cm^{-1}) for $(CH_3)_2N$ bond stretching for compounds (7,11).

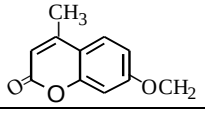
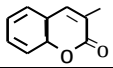
Table (4): Some IR spectral data of chalcones (6-12)

Cpd NO.	X	Y	IR(KBr)ν cm^{-1}		
			C=O	C=C	Others
6	Br	4-NO_2	1679	1597	1518 as (C-NO_2) 1343 sy (C-NO2)
7	Br	4-$N(CH_3)_2$	1659	1598	1288 (C-N)
8	Br	2-CL	1697	1597	808 (C-CL)
9	CH_3O	2-CL	1653	1598	829 (C-CL) 1259 as (C-O-C) 1183 sy (C-O-C)
10	CH_3O	4-NO_2	1654	1592	1525 as (C-NO2) 1344 sy (C-NO_2)
11	CH_3O	4-$N(CH_3)_2$	1658	1603	1288 (C-N)
12	CH_3O	4-CH_3O	1654	1598	1252 as (C-O-C) 1166 sy (C-O-C)

The condensation of chalcones (6-12) with hydrazides (4, 5) may proceed via the attack of the hydrizides at the, β- unsaturated bond of the chalcone lead to the corresponding Δ^2- pyrazoline (13-26).

The IR spectrum (table 5) shows a strong absorption band at (1723-1618) and (1669-1618 cm^{-1}) corresponds to the stretching vibration of lactone and carbonyl group respectively and bands at (1571-1619 cm^{-1}) attributed to the stretching vibration of carbon – nitrogen double bonds. Also bands at (1285- 1266 cm^{-1}) attributed to the C-N bonds. While the stretching vibration of N-H group appeared at (3241- 3449 cm^{-1}).

Table (5): IR spectral data for 1-substitutsd -2-pyrazolines (13-26)

Cpd. No.	X	Y	G	IR(KBr) νcm^{-1}					
				COO Lactones	C=O	C=N	C-C	N-C	N-H
13	Br	4-NO_2		1719	1667	1615	1511	1270	3410
14	Br	4-$N(CH_3)_2$	=	1720	1666	1616	1512	1282	3416
15	Br	2-CL	=	1719	1667	1618	1523	1272	
16	OCH_3	2-CL	=	1718	1667	1615	1510	1276	3444
17	OCH_3	4-NO_2	=	1723	1669	1619	1515	1266	
18	OCH_3	4-$N(CH_3)_2$	=	1718	1666	1615	1561	1266	3241
19	OCH_3	4-OCH_3	=	1720	1667	1618	1493	1285	3417
20	Br	4-NO_2		1701	1619	1572	1525	1271	3430
21	Br	4-$N(CH_3)_2$	=	1701	1619	1571	1524	1271	3449
22	Br	2-CL	=	1702	1618	1618	1523	1271	3442
23	OCH_3	2-CL	=	1688	1622	1572	1521	1275	3440
24	OCH_3	4-NO_2	=	1693	1619	1572	1524	1271	3453
25	OCH_3	4-$N(CH_3)_2$	=	1701	1619	1571	1524	1271	3443
26	OCH_3	4-OCH_3	=	1678	1622	1572	1526	1266	7441

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