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SYNTHESIS AND CHARACTERIZATION OF NEW COUMARIN DERIVATIVES FROM PYRAZOLE DERIVATIVES

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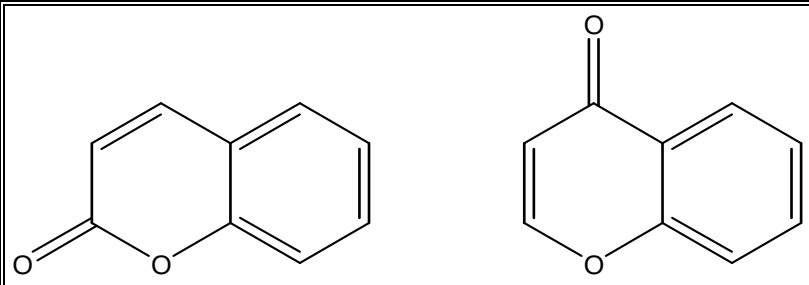
ABSTRACT

New derivatives of coumarin were synthesized by the reaction of pyrazole or pyrazol-5-one derivatives with Salicylaldehyde and 4-Bromosalicylaldehyde in presence of few drops piperidine then cyclized to form coumarin derivatives. The new compounds were characterized by some spectroscopic methods (FT-IR spectroscopy,^{1}H-NMR spectral,^{13}CNMR spectroscopy and Mass spectra)

KEYWORDS: Synthesis and Characterization of New Coumarin Derivatives from Pyrazole Derivatives

INTRODUCTION

Coumarins owe their class name to 'Coumarou', the vernacular name of the tonka bean (Dipteryx odorata Willd., Fabaceae), from which coumarin itself was isolated in 1820 [1].Coumarin is classified as a member of the benzopyrone family of compounds, all of which consist of a benzene ring joined to a pyrone ring [2]. The benzopyrones can be subdivided into the benzo- α –pyrones to which the coumarins belong and the benzo- γ-pyrones, of which the flavonoids are principal members



α-Benzopyrone γ-Benzopyrone

2H-1-benzopyran- 2-one were extensively studied and numerous application in various fields of science were found, but they are still interesting subject of research. The majority of the systems have high bioactivity, which makesthem used by the pharmacological industry [3]. Coumarins exhibitantioxidative [4], anti-cancer [5] and anti-inflammatory properties [6].They are also used as food [7] and cosmetic [8] additives,

Pyrazoles are chemical compounds of synthetic origin that have a five-membered heterocycle with two nitrogen atoms and three adjacent carbons. Pyrazole and its derivatives are an important class of compounds and attracted

widespread attention due to their pharmacological properties, being reported to have a large spectrum of biological effects, especially analgesic, anti-inflammatory properties[9], antiviral [10], antimicrobial[11], anticonvulsant [12],antitumor [13], fungicidal activities[14] and antihistaminic[15].

Experimental

The melting points were determined in open capillary tubes on a Gallen Kamp melting point apparatus and are uncorrected.The FT.IR Spectra of prepared derivatives were taken on Shimadzu-2N, FTIR-8400S,^{1}H-NMR Spectra of some prepared derivatives were recorded on a Varian-Mercury 300MHZ Spectrometer, d6-DMSO was use as a solvent in^{1}H-NMR Spectra.

Synyhesis of cyanoacetic Acid hydrazide [A_1][16].

Hydrazine hydrate (3.4mL. 0.069mole) was added as dropwise to (0.069mole) of ethyl cyanoacetate dissolved in ethanol with constant stirring in ice bath for 1hr. The white product formed was filtered and recrystallized from ethanol.

Synthesis of 1-cyanoacetyl-3,5-dimethylpyrazole[A_2-A_4].

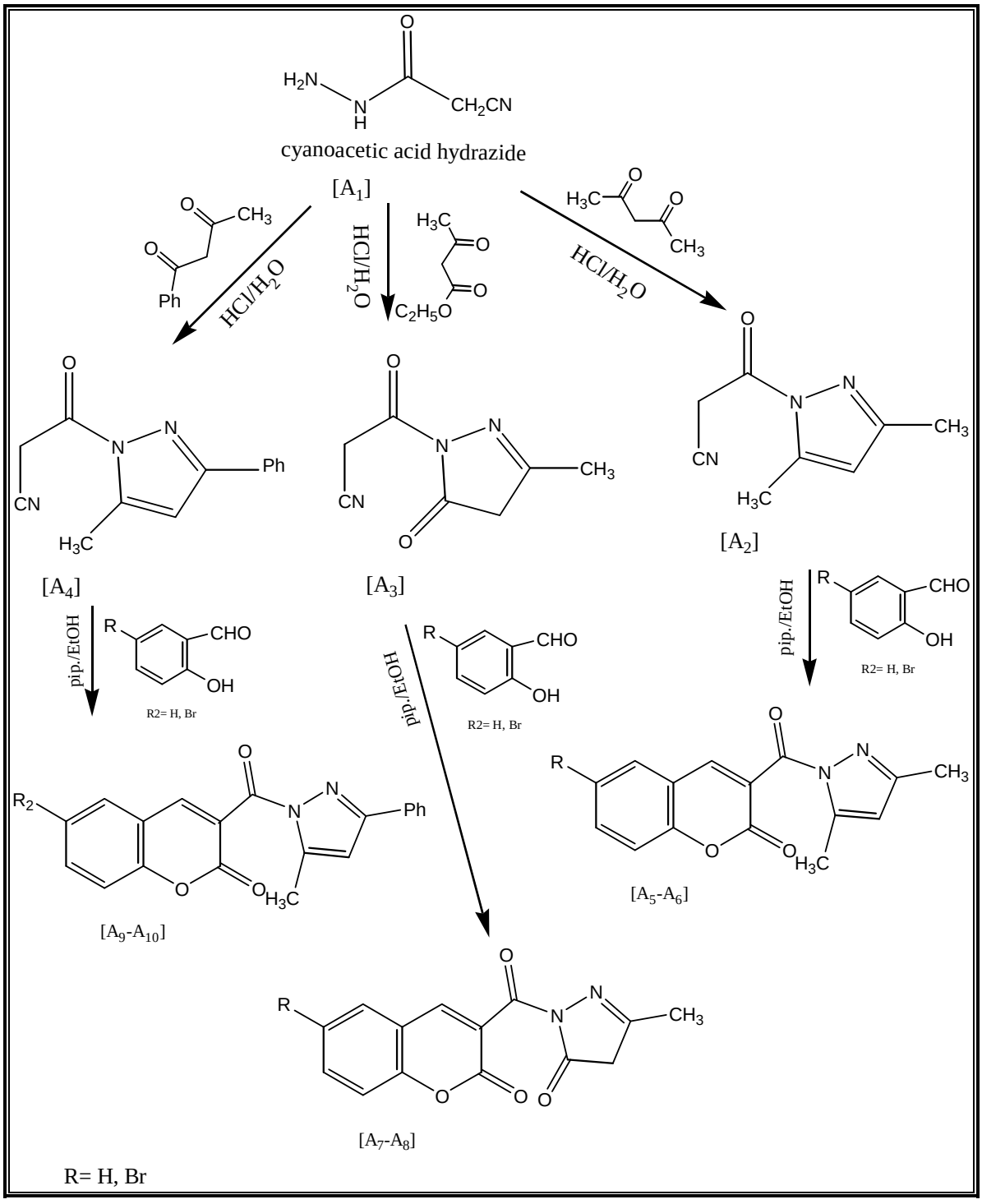
A mixture of compound [A_1] (1.5g. 0.01mol) and (0.01mol) of acetyl acetone or ethyl acetoacetate or phenyl acetyl acetone in absolute ethanol (25 ml.) was refluxed for 4 hrs. The reaction mixture was cooled to give the products.

Synthesis of 3-(acetyl-3,5-dimethyl pyrazole) coumarin[A_5-A_{10}][17].

To a solution of appropriate pyrazole [A_2-A_4] (0.01 mol) in ethanol (20 ml) containing piperidine (1.00 ml.), Salicylaldehyde (1.22g.,0.01 mol) or 5-bromo Salicylaldehyde (2.02g.,0.01 mol) was added. The reaction mixture was refluxed for 6h., then poured onto ice-water containing few drops of hydrochloric acid. The solid formed was filtrated and recrystallized from ethanol.

Table 1: The Physical Properties of Compounds

Comp. No	M.P ° C	Color	Yield %	Rec. Solvent	Molecular Formula
A_2	117-119	white	92	ethanol	$C_8H_9N_3O$
A_3	95-97	white	88	ethanol	$C_7H_6N_3O_2$
A_4	107-109	white	90	ethanol	$C_{13}H_{11}N_3O$
A_5	122-125	Yellow	30	ethanol	$C_{15}H_{13}N_2O_3$
A_6	96-98	Dark yellow	28	ethanol	$C_{15}H_{12}N_2O_3Br$
A_7	221-223	yellow	42	ethanol	$C_{14}H_{10}N_2O_4$
A_8	186-188 d	yellow	40	ethanol	$C_{14}H_9N_2O_4Br$
A_9	192-194	yellow	68	ethanol	$C_{20}H_{14}N_2O_3$
A_{10}	154-157	yellow	55	ethanol	$C_{20}H_{13}N_2O_3Br$



Scheme 1

RESULTS AND DISCUSSION

The new derivatives pyrazole were synthesized by condensation of cyanoacetic acid with 1,3-diketones using absolute ethanol as a solvent at refluxed to 4 hrs. All pyrazole derivatives [A_2], [A_3] and [A_4] were obtained with good yield from 70 to 90 %. Indicated by disappearance of NH_2 and NH stretching band at (3346.61-3184) cm^{-1} and appearance (1653.05-1668.48) cm^{-1} due to N=C stretching vibration respectively [A_2], [A_3] and [A_4], The characteristic bands of compounds [A_2-A_4] are shown in table (2).

Synthesis of the 3-substituted coumarins derivatives [A_5-A_{10}] were achieved by The Knoevenagel reaction[17] of compound [A_2-A_4] with salicylaldehyde or 5-bromo salicylaldehyde using piperidine as a catalyst.

The FTIR spectrum of compound [A_5] shows bands at the frequency of(1734.06 cm-^{1}) due to the carbonyl Lactone groups appears, also shows the appearance of absorption band at (1716.70) cm-^{1} due to (C=O) ofamid moiety, and the disappearance of absorption band at (2264.51) cm^{-1} for CN group.

The characteristic bands of compound [A_5] are shown in table (2).The FTIR spectrum of compound [A_6] shows bands at the frequency of(1716.70 cm-^{1}) due to the carbonyl Lactone groups appears, also shows the appearance of absorption band at (1683.91) cm-^{1} due to (C=O) of amid moiety, and the disappearance of absorption band at (2264.51) cm^{-1} for CN group. The Characteristic bands of compound [A_6] are shown in table (2). The ^{1}H-NMR spectrum of compound [A_6] in DMSO-d_6 as a solvent was showed the following data : 3.4 ppm(s, 3H, 2CH_3 of pyrazole ring), 4.2 ppm (s,2H, -CH_2- of Pyrazole ring), 6.6 ppm(s,1H, C=C-H of lactone ring), 6.83-8.5 ppm (m,3H, CH aromatic protons)

The FTIR spectrum of compound [A_7] shows bands at the frequency of(1718.63 cm-^{1})due to the carbonyl lactone groups appears, also shows the appearance of absorption band at (1641.48) cm-^{1} due to (C=O) of amid moiety, and the disappearance of absorption band at (2258.72) cm^{-1} for CN group. The characteristic bands of compound [A_7] are shown in table (2).

The ^{1}H-NMR spectrum of compound [A_7] in DMSO-d_6 as a solvent was showed the following data : 3.3 ppm (s, 3H, CH_3 of Pyrazole ring), 5.7 ppm (s,2H, -CH_2- of pyrazole ring), 6.8 ppm(s,1H, C=C-H of lactone ring), 7.3-7.8 ppm (m,4H, CH aromatic protons). In addition mass spectrum of compound [A_7] gives the following data values (M/Z): 272, 257, 245, 202, 199, 171, 155, 136, 120, 81, 57, and 46.

The FTIR spectrum of compound [A_8] shows bands at the frequency of(1734.06 cm-^{1})due to the carbonyl lactone groups appears, also shows the appearance of absorption band at (1681.98) cm-^{1} due to (C=O) of amide moiety, and the disappearance of absorption band at (2258.72) cm^{-1} for CN group. The characteristic bands of compound [A_8] are shown in table (2). The ^{1}H-NMR spectrum of compound [A_8] in DMSO-d_6 as a solvent was showed the following data : 3.4 ppm(s, 3H, CH_3 of pyrazole ring), 4.49 ppm (s,2H, -CH_2- of pyrazole ring), 6.8 ppm(s,1H, C=C-H of lactone ring), 7.4-8.6 ppm (m,3H, CH aromatic protons). The ^{13}C-NMR spectrum of compound [A_8]shows the following bands of carbon: 11.68, 14.49, 30.89, 60.11, 118.45, 126.37, 133.68, 138.18, 153.48, 167.21, 174.95, and 175.39. In addation mass spectrum of compound [A_8] gives the following data values (M/Z): 346, 298, 296, 268, 240, 200, 187, 155, 135, 122, 81, 64, and 42.

The FTIR spectrum of compound [A_9] shows bands at the frequency of(1712.85 cm-^{1})due to the carbonyl lactone groups appears, also shows the appearance of absorption band at (1680.05) cm-^{1} due to (C=O) of amide moiety, and the disappearance of absorption band at (2260.65) cm^{-1} for CN group. The characteristic bands of compound [A_9] are shown in table (2). The ^{1}H-NMR spectrum of compound [A_9] in DMSO-d_6 as a solvent was showed the following data : 3.4 ppm(s, 3H, CH_3 of pyrazole ring), 4.3 ppm (s,1H, C=C-H of pyrazole ring), 6.2 ppm(s,1H, C=C-H of lactone ring), 6.3-8.2 ppm (m,9H, CH aromatic protons).

The ^{13}C-NMR spectrum of compound [A_9]shows the following band of carbon: 13.82, 61.38, 70.99, 116.53, 118.28, 118.38, 120.31, 120.47, 124.89, 127.02, 128.13, 128.22, 128.38, 128.57, 128.78, 129.51, 130.69, 131.75, 132.04,

136.19, 146.39, 153.03, 159.78, 162.20, and 174.76. In addition mass the spectrum of compound [A_9] gives the following data values (M/Z): 330, 307, 291, 248, 240, 199, 189, 172, 171, 144, 120, 116, 81, 64, and 42.

The FTIR spectrum of compound [A_{10}] shows bands at the frequency of(1728.28 cm^{-1})due to the carbonyl lactone groups appears, also shows the appearance of absorption band at (1678.13) cm^{-1} due to (C=O) of amid moiety, and the disappearance of absorption band at (2260.65) cm^{-1} for CN group. The characteristic bands of compound [A_{10}] are shown in table (2). The ^{1}H-NMR spectrum of compound [A_{10}] in DMSO-d_6 as a solvent was showed the following data : 3.8 ppm(s, 3H, CH_3 of pyrazole ring), 4.3 ppm (s,1H, C=C-H of pyrazole ring), 6.1 ppm(s,1H, C=C-H of lactone ring), 7.2-8.25 ppm (m,8H, CH aromatic protone). In addition mass spectrum of compound [A_{10}] gives the following data values (M/Z), : 408, 382, 358, 335, 305, 282, 251, 225, 198, 155, 144, 112, 79, 61, and 46.

Table 2: Spectral Data of Compounds in Scheme (1)

Comp. No.	Characteristic Bands of FT-IR Spectrum (cm^{-1},KBr)					
	υC=O	υC=O Lactone	υC=C ar.	υC=N	υC≡N	Others
A_2	1730.21	-	-	1653.05	2264.51	-
A_3	1722.49	-	-	1668.48	2258.72	C=O 1701.27
A_4	1730.21	-	-	1660.77	2260.65	-
A_5	1716.70	1734.06	1575.89-1541.18	1616.40	-	-
A_6	1683.91	1732.13	1587.47-1535.39	1626.05	-	-
A_7	1641.48	1718.63	1696.76-1573.97	1641.48	-	C=O 1695.49
A_8	1681.98	1734.06	1604.83-1595.18	1649.19	-	C=O 1708.99
A_9	1680.05	1712.85	1600.97-1566.25	1635.69	-	-
A_{10}	1 678.13	1728.28	1635.69-1593.25	1678.13	-	-

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