

SYNTHESIS OF NEW SCHIFF'S BASES 4-CHLORO COUMARIN DERIVATIVES

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ABSTRACT

This work included synthesis of several new Schiff bases by condensation of 4-Chloro-3-formylcoumarin[1] and appropriate aromatic amine (Aniline, p-Toluidine, p-Aminoacetophenone, p-Aminobenzoate, p-Aminophenol, m-Aminophenol, m-Toluidine and m-Aminoacetophenone) to obtain Schiff bases[2-9] and with Hydrazidecoumarin Derivatives (3-hydrazidecoumarin[10] 5-Bromo-3-hydrazidecoumarin [11]) to obtain Schiff bases[12,13] The new compounds were characterized by using of Melting point and FT-IR spectroscopy, and some of them by ¹H-NMR spectrum.

KEYWORDS: Schiff bases, 4-Hydroxycoumarin.

INTRODUCTION

Coumarin (2H-chromen-2-one) and its derivatives are some of the most important O-heterocycles and are extensively found in various bioactive natural and synthetic products[1] They are effective pharmacophores, widely used for the design and synthesis of novel bioactive compounds.^[2] Accordingly, different biological activities such as anticoagulation and cardiovascular activities (warfarin).^[3] and antimicrobial activities (novobiocin and clorobiocin),^[4] have been reported. antioxidant anti-inflammatory,^[5] antibacterial – antifungal, anti-HIV, anticoagulant, antitumor, antimicrobial,^[6,7] Analgesic, anti-pyretic.^[8]

There are many different methods for obtaining coumarin and its derivatives. Among the most popular it is worth to mention Perkin reaction.^[9,10] Pechmann condensation,^[11] Knoevenagel condensation,^[12] Reformatsky reaction and Wittig reaction.^[13]

EXPERIMENTAL**Synthesis of 4-Chloro-3-formylcoumarin[1]^[14]**

A mixture of 4-Hydroxycoumarin (1.4g, 7.93 mmol) in dry DMF (40 ml) was added dropwise to a Vilsmeier Haack adduct prepared from POCl₃ (3.7 mL, 40.3 mmol) and dry DMF (8 ml, 0.1 mol) at room temperature. The reaction mixture was then stirred for 1h at room temperature and heated with stirring for 2h at 60 °C. After the reaction completed, the mixture was poured onto crushed ice (100 g) under vigorous stirring. The pale yellow solid was collected by filtration and washed with water. The physical properties of this compound are listed in Table (1).

Synthesis of Schiff's bases compounds [2-9]

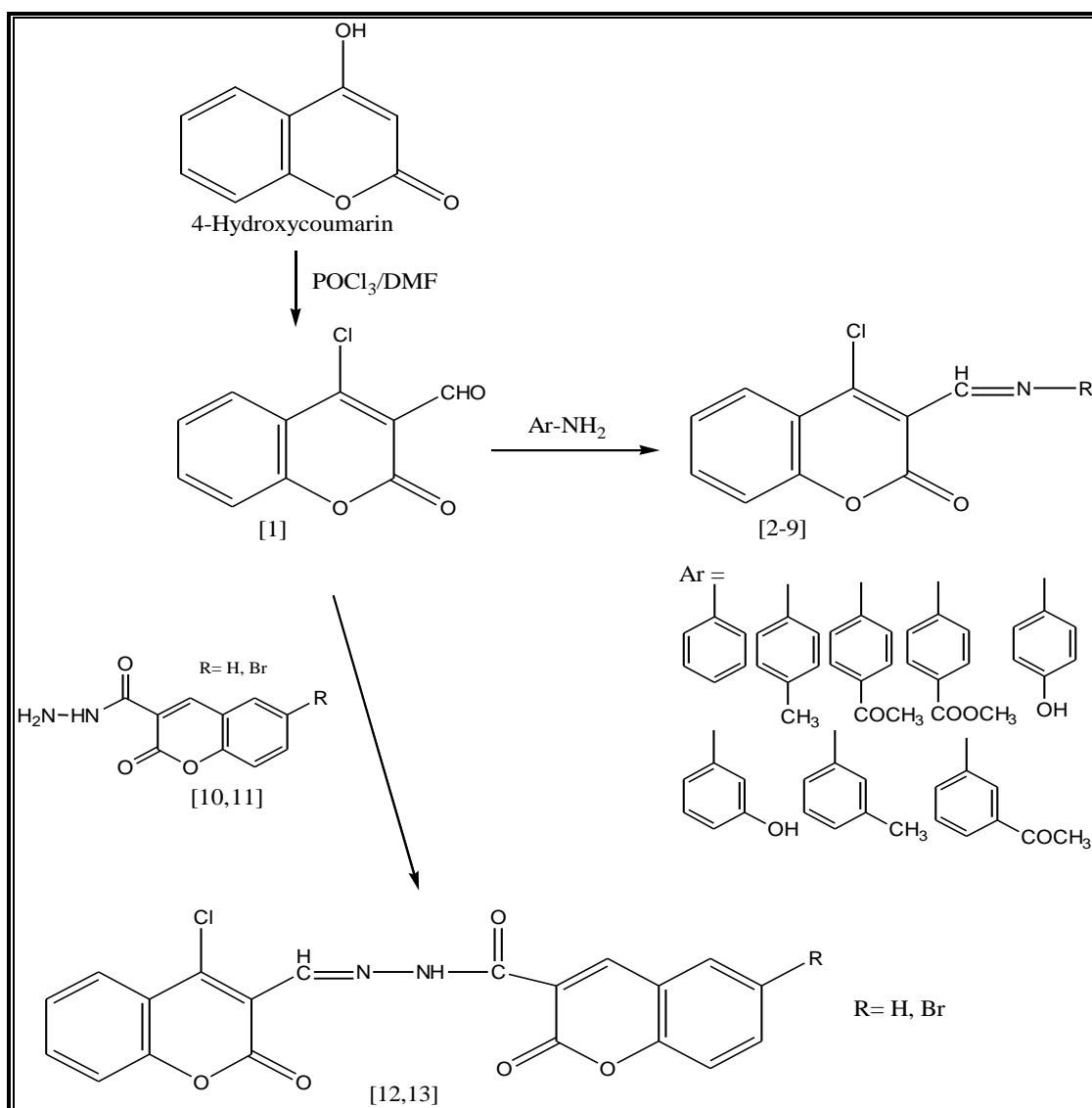
A mixture of (0.20gm, 0.001mole) of compound^[1] in (10ml) of absolute ethanol, and appropriate aromatic amine (Aniline, p-Toluidine, p-Aminoacetophenone, p-Amino benzoate, p-Aminophenol, m-Aminophenol, m-Toluidine and m-Aminoaceto phenone) (0.001mole) was refluxed for 4-6 hours in the presence of (3-4)drops of glacial acetic acid. After cooling the product, a solid formed, was filtered, dried and purified by recrystallized from ethanol. The physical properties of these compounds are listed in Table (1).

Synthesis of Hydrazoneyl coumarin derivatives [10,11]^[15]

To a solution of cyanoacetic acid hydrazide (1g, 0.01 mol) in ethanol (25 ml.) containing piperidine (1.00 ml.), and Salicylaldehyde (1.22g, 0.01 mol) or 5-Bromosalicylaldehyde (2g, 0.01 mol) was added. The reaction mixture was heated under reflux for 6h. The solid products formed upon pouring onto ice-water mixture containing few drops of hydrochloric acid was collected by filtration and crystallized from ethanol. The physical properties of these compounds are listed in Table (1).

Synthesis of 4-Chloro-3-coumarin[12,13]

A mixture of (2.08 g, 0.01mole) of compound [1] and (2.04 gm, 0.01mole) of compound[10] or (2.84 g, 0.01mole) of compound[11] in (30ml) of absolute ethanol was refluxed for 6 hours in the presence of few drops of glacial acetic acid. After cooling the product, a pale yellow solid formed, was filtered, dried and purified by recrystallized from ethanol. The physical properties of compounds[12,13] are listed in Table (1).



Scheme (1)

Table (1): The physical properties of compounds

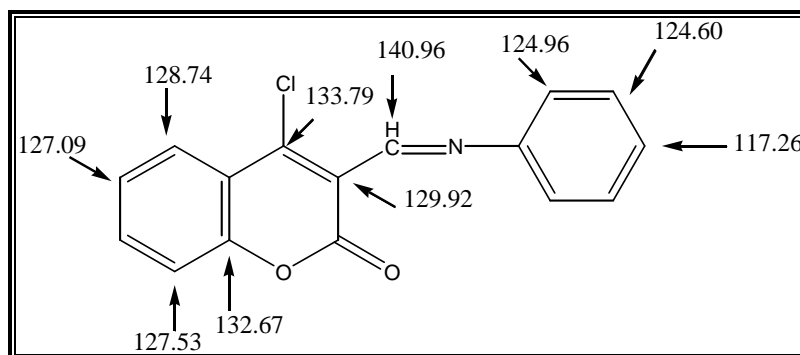
Comp. No	M.P ° C	color	Yield %	Rec. solvent	Molecular formula
[1]	121-124	Yellow	75	Ethanol/Water 1:1	$\text{C}_{10}\text{H}_5\text{O}_3\text{Cl}$
[2]	222-224	Milky	90	Ethanol	$\text{C}_{16}\text{H}_{10}\text{NO}_2\text{Cl}$
[3]	234-235	Milky	91	Ethanol	$\text{C}_{17}\text{H}_{12}\text{NO}_2\text{Cl}$
[4]	297-300 d	Yellow	93	Ethanol	$\text{C}_{18}\text{H}_{12}\text{NO}_3\text{Cl}$
[5]	252-254	Pale yellow	92	Ethanol	$\text{C}_{18}\text{H}_{12}\text{NO}_4\text{Cl}$
[6]	301-303	Yellow	84	Ethanol	$\text{C}_{16}\text{H}_{10}\text{NO}_3\text{Cl}$
[7]	340-343 d	Yellow	87	Ethanol	$\text{C}_{16}\text{H}_{10}\text{NO}_3\text{Cl}$
[8]	Up 350	Dark orange	82	Ethanol	$\text{C}_{17}\text{H}_{12}\text{NO}_2\text{Cl}$
[9]	236-238	Yellow	95	Ethanol	$\text{C}_{18}\text{H}_{12}\text{NO}_3\text{Cl}$
[10]	194-196	yellow	79	Ethanol	$\text{C}_{10}\text{H}_8\text{N}_2\text{O}_3$
[11]	181-183	Orange	73	Ethanol	$\text{C}_{10}\text{H}_7\text{N}_2\text{O}_3\text{Br}$
[12]	282-284	Yellow	75	Ethanol	$\text{C}_{20}\text{H}_{11}\text{N}_2\text{O}_5\text{Cl}$
[13]	332-335	Milky	85	Ethanol:Dioxane	$\text{C}_{20}\text{H}_{10}\text{N}_2\text{O}_5\text{ClBr}$

RESULTS AND DISCUSSION

The new ten Schiff's bases compounds [2-9] and [12,13] were synthesized by the reaction of compound [1] with different aromatic amine and 3-hydrazonylcoumarin in presence of glacial acetic acid as catalytic, show in scheme (1). The physical properties of compounds [2-9] and [12,13] are listed in Table (1), the % Yield percentage of the prepared Schiff bases were in the range {73-95} % and were identified by FT-IR and some of them by ^1H NMR and ^{13}C NMR spectroscopy. FT-IR spectra of Schiff bases (2-9) and [12,13] showed clear absorption bands at $(1608.69)\text{ cm}^{-1}$ which is assigned to $\text{C}=\text{N}$, the disappearance of absorption band at $(1701.27)\text{ cm}^{-1}$ for $(\text{C}=\text{O})$ of aldehyde and another bands. The characteristic bands of compounds [2-9] are shown in table (2) and compounds [12,13] are shown in Table (4)

The ^1H NMR spectrum of compound [2] showed the following data: (DMSO): 7.49-8.68 ppm(m, 9H, C=C-H), and 8.70 ppm (s, 1H, N=C-H).

The ^{13}C -NMR spectrum of compound [2] showed signal at 117.26, 124.60, 124.96, 127.09, 127.53, 128.74, 129.92, 132.67, 133.79, 140.96 ppm.



The ^1H NMR spectrum of compound [3] showed the following data: (DMSO): 7.48-8.68 ppm(m, 8H, C=C-H), 2.68 (s, 3H, CH_3 of aromatic ring) and 8.70 ppm (s, 1H, N=C-H).

The ^{13}C -NMR spectrum of compound [3] showed signal at 21.11, 117.22, 119.34, 124.45, 124.92, 128.23, 128.50, 132.42, 136.12, 139.97 ppm.

The ^1H NMR spectrum of [4] in DMSO-d_6 as a solvent was showed the following data: 2.96 (s, 3H, $\text{O}=\text{C}-\text{CH}_3$), 7.35-8.96 (m, 8H, Ar-H), and The ^{13}C -NMR spectrum of compound [4] showed signal at 26.71, 117.18, 119.14, 124.41, 125.56, 129.96, 133, 135, 142, 152, 171, 192, 198.

The FTIR spectrum of compound [10] shows bands at the frequency of (1691.63 cm^{-1}) due to the carbonyl groups appears, the appearance of new bands in the regions (3311.89-3269.45) cm^{-1} due to asymmetric and symmetric stretching vibration of the (NH_2) group, also shows the appearance of absorption band at (1678.13) cm^{-1} due to (C=O) of amide moiety and appearance (N-H) bending vibration band at (1504.53), and the disappearance of absorption band at (2262.58) cm^{-1} for CN group.

The characteristic bands of compound [10] are shown in Table (3). The FTIR spectrum of compound [11] shows bands at the frequency of (1735.99 cm^{-1}) due to the carbonyl groups appears, the appearance of new bands in the regions (3308.89-3200) cm^{-1} due to asymmetric and symmetric stretching vibration of the ($-\text{NHNH}_2$) group, also shows the appearance of absorption band at (1670.41) cm^{-1} due to (C=O) of amide moiety, and the disappearance of absorption band at (2262.58) cm^{-1} for CN group. The characteristic bands of compound [11] are shown in Table (3).

The FTIR spectrum of compound [12] showed appearance of new band at (1608.69) cm^{-1} which is assigned to C=N, the disappearance of absorption band at (1701.27) cm^{-1} for (C=O) of aldehyde and another bands. The characteristic bands of compounds [12] are shown in Table (4).

The FTIR spectrum of compound [13] showed appearance of new band at (1608.69) cm^{-1} which is assigned to C=N, the disappearance of absorption band at (1701.27) cm^{-1} for (C=O) of aldehyde and another bands. The characteristic bands of compound [13] are shown in Table (4).

Table (2): Spectral data of compounds in scheme (1):

Comp. No.	Characteristic bands of FT-IR spectrum (cm^{-1} , KBr)				
	$\nu\text{C=O}$ Lactone	$\nu\text{C=N}$	$\nu\text{C=C}$ ar.	$\nu\text{C-Cl}$	Others
[2]	1735.99	1618.33	1599.04, 1494.88	754.19	-
[3]	1730.21	1624.12	1612.45, 1554.68	752.26	825.56 for 1,4 subs.Ar., 2920.32 for $\nu\text{C-H}$ alph.
[4]	1730.21	1625	1602.90, 1541.18	756.12	848.71 for 1,4 subs.Ar., 1722.49 for $\nu\text{C=O}$ ket.
[5]	1737.92	1625	1606.76, 1583.61	752.26	852.56 for 1,4 subs.Ar., 1710.92 for $\nu\text{C=O}$ ester.
[6]	1749.49	1635.69	1616.40, 1560.46	759.98	848.71 for 1,4 subs.Ar., 3325.39 for $\nu\text{O-H}$.

[7]	1741.68	1622.19	1600.97, 1577.82	750.33	840.99, 692.47 for 1,3 subs.Ar. 1168.90 for ν C-O .
[8]	1726.35	1612.54	1600.97, 1566.25	750.33	898.86, 684.75 for 1,3 subs.Ar. 2951.19 for ν C-H alph.
[9]	1743.71	1630	1604.83, 1583.61	759.98	896.93, 700.18 for 1,3 subs.Ar. 1685.84 for ν C=O ket.

Table (3): Spectral data of compounds in scheme (1):

Comp. No.	Characteristic bands of FT-IR spectrum (cm^{-1} ,KBr)				
	ν C=O Lactone	ν C=C ar.	ν C-H ar.	ν C=O amide	Others
[10]	1691.63	1622.19, 1573.96	3068.85	1678.13	ν NH ₂ 3311.89-3269.45 ν NH 3163.36
[11]	1735.99	1604.83, 1581.68	2920.85	1670.32	ν NH ₂ , ν NH 3308.89-3200

Table (4): Spectral data of compounds in scheme (1)

Comp. No.	Characteristic bands of FT-IR spectrum (cm^{-1} ,KBr)					Others
	ν C=O Lactone	ν C=N	ν C=O Lactone2	ν C=C ar.	ν C-Cl	
[12]	1714.77	1608.69	1683.91	1564.32	759.98	3223.16 for -NH.
[13]	1724.42	1608.69	1697.41	1562.39	761.91	3221.23 for -NH.

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