# SYNTHESIS AND CHARACTERIZATION OF SOME (7-HYDROXY-4-METHYL-2*H*-CHROMEN-2-ONE) DERIVATIVES

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#### الخلاصة

تم تحضير المركب الأساسي (الكيومارين) C<sub>1</sub> من الغلق الحلقي الحراري لمركب الريسور سينول مع أثيل أسيتو أسيتيت بوجود حامض الكبريتيك ثم استخدم هذا المركب لتحضير المشتقات المطلوبة و كما يلي : أو لاً : عند معاملة المركب C<sub>1</sub> مع حامض الخليك اللامائي بوجود حامض الخليك الثلجي تكون المشتق C<sub>2</sub> الذي يحتوي على مجموعة خلات و عند إضافة البروم لهذا المشتق تكون المركب C<sub>3</sub> الذي عند تفاعله مع المركب 2- أمينوبنز وثاياز ول في الأيثانول أعطى المركب C<sub>4</sub> مع حامض الخليك اللامائي بوجود حامض الخليك الثلجي تكون المشتق C<sub>2</sub> الذي يحتوي على مجموعة خلات و عند إضافة البروم لهذا المشتق تكون المركب C<sub>3</sub> الذي عند تفاعله مع المركب 2- أمينوبنز وثاياز ول في الأيثانول أعطى المركب 2- أمينوبنز وثاياز ول في تأنيأ : عند معاملة المركب C<sub>1</sub> مع POCI بحيث استبدلت مجموعة ال OH بذرة ID في المشتق C<sub>3</sub> الذي عند تفاعله مع المركب 2- أمينوبنز وثاياز ول في ثانيأ : عند معاملة المركب C<sub>1</sub> مع POCI بحيث استبدلت مجموعة ال OH بذرة ID في المشتق C<sub>3</sub> الذي عند تفاعله مع المركب 2- أمينوبنز وثاياز ول في ثانيأ : عند معاملة المركب C<sub>1</sub> مع POCI من خلال التعويض النبوكليوفيلي الأروماتي على الكيومارين . تانياً : عند معاملة المركب C<sub>1</sub> مع POCI من خلال التعويض النبوكليوفيلي الأروماتي على الكيومارين . المركب 2- أمينوبنز وثاياز ول أعطى المركب C<sub>6</sub> من خلال التعويض النبوكليوفيلي الأروماتي على الكيومارين . تالثاً : عند معاملة المركب C<sub>1</sub> مع المركب C<sub>6</sub> من خلال التعويض النبوكليوفيلي الأروماتي على الذي عومل مع محلول مائي للمركب 2- أمينوبنز وثاياز ول أعطى المركب C<sub>1</sub> مع المركب 2- أمينوبنز وثاياز ول تكون المشتق C<sub>1</sub> الذي للمائي في للمركب 2- أمينوبنز وثاياز ول تكون المشتق C<sub>1</sub> الذي لي مع المركب 2- أمينوبنز وثاياز ول مع معامل مع محلول مائي للمركب 2- أمينوبنز وثاياز ول المركب C<sub>1</sub> مع المركب 2- أمين الخلي مع معلول مائي للمركب 3- أولانا المركب 1- مع المركب 2- أمينوبنز وثاياز ول تكون المشتق C<sub>1</sub> للمركب 3- أولانا للمركب 3- أمينوبنز وثاياز ول المركب 3- أولام مع معالول مائي للمائي في المركب 3- أمينوبنز وثاياز ول المرك 3- أمينوبنز وثاياز ول مع معامل 3</sub> المرك 3- أولام مع محلول مائي المرك 3- أولام ملك 3- أولام ملك 3- أولام 3- أولام 3- أولام 3</sub> المرك 3- أولام 3- أولام

#### ABSTRUCT

The titled compound  $C_1$  (Coumarin) was prepared through the thermal cyclization of resorcinol and ethylacetoacetate in presence of sulfuric acid. Compound  $C_1$  (Coumarin) was treated with acetic anhydride in glacial acetic acid to obtain acetate group in the yielding compound (compound  $C_2$ ). Compound  $C_2$  was brominated to obtain compound  $C_3$  which treated with 2-aminobenzothiazole in ethanol to obtain compound  $C_4$ .Compound  $C_1$  was treated with POCl<sub>3</sub> to replace OH group by Cl atom and obtain compound  $C_5$  which was treated with 2-aminobenzothiazole in a nucleophilic aromatic substitution to obtain compound  $C_6$ . Compound  $C_1$  was treated with thiosemicarbazide in ethanol to obtain compound  $C_7$  which was treated with aqueous NaOH to obtain triazole derivative (compound  $C_8$ ). The later compound was treated with 2-aminobenzothiazole to obtain compound  $C_9$ . Compound  $C_1$  was treated with 2-aminobenzothiazole in ratio 2:1 in presence of anhydrous ZnCl<sub>2</sub> in ethanol to obtain compound  $C_{10}$ .

#### **INTRODUCTION**

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. The plant extracts containing coumarin-related heterocycles, which were employed as herbal remedies in early days, have now been extensively studied for their biological activities. These investigations have revealed their potentials as versatile biodynamic agents [1].

Coumarins can be classically synthesized by the Perkin [2,3], Pechmann [4,5] or Knoevenagel reactions [6,7,8]. Recently, the Wittig [9], the Kostanecki – Robinson [10] and Reformatsky reactions [11] were also conveniently applied to the synthesis of this type of heterocycles. However, it is important to note that all the methods reported have some disadvantages, since they lack generality and efficiency, making the development of new reliable high yielding methods for the synthesis of coumarins an important subject.

## **MATERIALS and METHODS** Materials :

All materials were from BDH , FLUKA and REDLE –DE HAEN . All other solvents were analar grade .

#### **Instrumentations :**

Melting points were measured on a Gallan Kamp MFB-600 Melting point apparatus in Al-Mustansyria university –Iraq and were uncorrected .

FTIR spectra were recorded as potassium bromide (KBr) disk on FTIR -8400S Fourer Transform Infrared Spectrophotometer "SHIMADZU" in Al-Mustansyria university-Iraq.

UV-Visible spectra were recorded on CARY 100 Conc UV-Visible Spectrophotometer "VARIAN" in Al-Mustansyria university-Iraq.

H<sup>1</sup> NMR spectra were recorded on Burker DMX- 500 NMR (300-600 MHz)Spectrophotometer with using DMSO as a solvent in Jordan University.

#### **Preparation of** $(C_1)$ [12]

#### (7-hydroxy-4-methyl-2H-chromen-2-one)

A mixture of resorcinol (0.05mol, 5.5g), ethylacetoacetate (0.05mol, 6.05g) and  $H_2SO_4$  (50mL,75%) was heated on water bath 100<sup>0</sup>C for 0.5h. The resulting mixture was cooled, poured onto crushed ice, then filtered off. The crude product was washed with distilled water, dried and recrystallized from ethanol. The physical properties are listed in table 1.

## Synthesis of (C<sub>2</sub>) [13] (4-methyl-2-oxo-2*H*-chromen-7-yl acetate)

Compound (C<sub>1</sub>) (0.005mol, 0.88g) was dissolved in a mixture of acetic anhydride (1.5mL) and glacial acetic acid (1mL). The mixture was heated on water bath  $100^{\circ}$ C for 2h., with occasional stirring. The reaction mixture was poured onto crushed ice. The precipitated solid was filtered off, washed with distilled water, dried and recrystallized from ethanol. The physical properties are listed in table 1.

#### Synthesis of (C<sub>3</sub>) [14] (4-methyl-2-oxo-2*H*-chromen-7-yl bromoacetate)

Compound(C<sub>2</sub>)(0.01mol, 1g) was dissolved in (15mL) of absolute ethanol, to this solution bromine (0.01mol,16mL) in glacial acetic acid (10mL) was added drop wise with constant stirring. The reaction mixture was stirred at  $40^{0}$ C for 4h. and then cooled and poured onto crushed ice. The precipitated solid was washed with distilled water, dried and recrystallized from ethanol. The physical properties are listed in table 1.

## Synthesis of (C<sub>4</sub>) [15] (4-methyl-2-oxo-2*H*-chromen-7-yl (1,3-benzothiazol-2-ylamino)acetate)

Compound  $C_3$  (0.001mol,0.29g) and 2-aminobenzothiazole(0.001mol, 0.15g) were dissolved in acetone (20mL). The reaction mixture was refluxed for 2h., then it was cooled, filtered off, dried and recrystallized from ethanol. The physical properties are listed in table 1.

## Synthesis of (C<sub>5</sub>) [16] (7-chloro-4-methyl-2*H*-chromen-2-one)

 $POCl_3$  (0.01mol,1.52g) was added to compound (C<sub>1</sub>) (0.01 mol,1.76g) and the reaction mixture was refluxed for 0.5h., set aside, then poured onto crushed ice, filtered off, washed well with distilled water, dried and recrystallized from benzene. The physical properties are listed in table 1.

#### Synthesis of (C<sub>6</sub>) [17] (7-(1,3-benzothiazol-2-ylamino)-4-methyl-2*H*-chromen-2-one)

A mixture of compound (C<sub>5</sub>) (0.002mol, 0.38g) and 2-aminobenzo- thiazole (0.002mol, 0.3g) was dissolved in ethyl acetate (10mL) and then it was refluxed in presence of (1mL) triethyl amine for 6h. After cooling, the precipitated solid was filtered off and washed with ethyl acetate and distilled water. The purity of the synthesized compound was checked by TLC. The physical properties are listed in table 1.

#### Synthesis of (C<sub>7</sub>) [18]

#### (1-(7-hydroxy-4-methyl-2-oxoquinolin-1(2*H*)-yl)thiourea)

Solution of compound ( $C_6$ ) (0.02mol, 3.5g) and thiosemicarbazide (0.02mol, 1.84g) in DMF was refluxed for 8h. After cooling, the precipitated solid was filtered off and washed with cold ethanol. The physical properties are listed in table 1.

#### Synthesis of (C<sub>8</sub>) [19]

#### (5-methyl-2-sulfanyl[1,2,4]triazolo[1,5-a]quinolin-8-ol)

Compound (C<sub>7</sub>) (0.005mol, 1.23g) was added drop wise to(15mL) of 2M NaOH solution. The reaction mixture was refluxed for 24 h. It was allowed to cool and filtered. The filtrate was acidified with 2M HCl. The precipitated solid was filtered off, washed with distilled water, dried and recrystallized from 70% ethanol. The physical properties are listed in table 1.

#### Synthesis of (C<sub>9</sub>) [20]

### (2-(1,3-benzothiazol-2-ylamino)-5-methyl[1,2,4]triazolo[1,5-*a*]quinolin-8-ol)

A mixture of compound ( $C_8$ ) (0.005mol,1.2g) and 2-aminobenzo- thiazole (0.005mol, 0.7g) in absolute ethanol was refluxed for 8h. It was concentrated and then cooled, the precipitated solid was filtered off, dried and recrystallized from ethanol. The physical properties are listed in table1.

## Synthesis of (C<sub>10</sub>) [21] 7,7'-(benzo[d]thiazol-2-ylazanediyl)bis(4-methyl-2*H*-chromen-2-one)

A mixture of compound (C<sub>1</sub>) (0.004mol, 0.7g) and 2-aminobenzo- thiazole (0.002mol, 0.3g) in absolute ethanol was refluxed in presence of anhydrous  $ZnCl_2$  (0.5g) for 6h. On cooling a solid mass was separated out which was filtered off, washed with acidified distilled water to remove inorganic materials, then it was dried and recrystallized from ethanol. The physical properties are listed in table 1.

### **RESULTS AND DISCUTION**

The synthesis of compound  $C_1$  was achieved by Pechmann Duisberge reaction of ethylacetoacetate with equimolar amount of resorcinol in presence of sulfuric acid. This reaction produces  $\beta$ -hydroxyester which converts to corresponding coumarin. The structure of compound( $C_1$ ) is confirmed by its physical properties and spectral data. FTIR spectrum (Fig.1) shows the appearance of (O-H) stretching frequency at 3502 cm<sup>1</sup> and (C=O) stretching frequency at 1670 cm<sup>-1</sup>[22].

Compound  $C_2$  was prepared through acylation of compound  $C_1$  by acetic anhydride . The structure of this compound is confirmed by its physical properties and spectral data. FTIR spectrum shows the disappearance of (O-H) stretching frequency that belongs to compound  $C_1$  while two (C=O) stretching frequencies appear at 1763 and 1695 cm<sup>-1</sup>.

Bromination of compound  $C_2$  produces bromoester derivative which is important compound in the synthesis of various heterocyclic compounds. The structure of this compound is confirmed by its physical properties and spectral data. FTIR spectrum shows the appearance of (C-Br) stretching

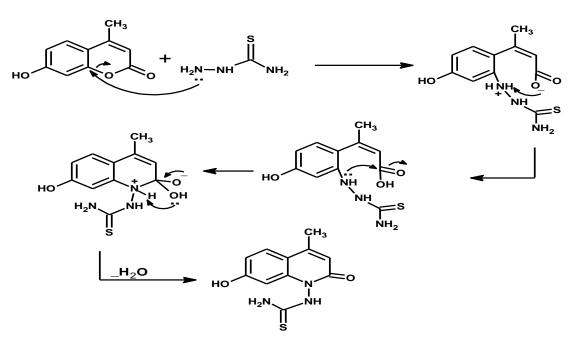
frequency at 752 cm<sup>-1</sup>. It also show the appearance of two stretching frequencies of two kind of (C=O) groups at 1730 cm<sup>-1</sup> and at 1716 cm<sup>-1</sup> beside the appearance of (C-O) stretching frequency at 1140 cm<sup>-1</sup> and at 1188 cm<sup>-1</sup>.

Compound C<sub>4</sub> was prepared through the substitution of 2-amino- benzothiazole instead of the brome atom in the compound C<sub>3</sub> through S<sub>N</sub>2 mechanism. The structure of this compound is confirmed by its physical properties and spectral data. FTIR spectrum shows the appearance of (N-H) stretching frequency that belongs to 2-aminobenzothiazole at 3265 cm<sup>-1</sup> and (C=N) stretching frequency at 1635 cm<sup>-1</sup>. <sup>1</sup> H NMR (Fig.4) spectrum shows the peaks at : 2.2 ppm (3H, CH<sub>3</sub>), 4.1 ppm (1H, NH), 4.2 ppm (2H, NH-CH<sub>2</sub>COO), 6.34 ppm (1H, olefinic H), 7.1-7.9 ppm (8H, Ar-H).

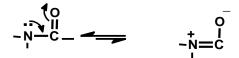
Compound  $C_5$  was prepared through the reaction of compound  $C_1$  with POCl<sub>3</sub> without any other solvent .The structure of this compound is confirmed by its physical properties and spectral data. FTIR spectrum shows the disappearance of (O-H) stretching frequency that belongs to compound  $C_4$  and the appearance of (C-Cl) stretching frequency at 1044 cm<sup>-1</sup>.

Compound  $C_6$  was prepared through the nucleophilic aromatic substitution of 2aminobenzothiazole on the aromatic ring of compound  $C_5$ . The structure of this compound is confirmed by its physical properties and spectral data. FTIR spectrum shows the appearance of (N-H) stretching frequency at 3304 cm<sup>-1</sup> beside the appearance of (C=O) stretching frequency at 1708 cm<sup>-1</sup> and (C=N) stretching frequency at 1635 cm<sup>-1</sup>.

Compound  $C_7$  was prepared through the condensation between compound  $C_1$  and thiosemicarbazide as it is illustrated in the mechanism bellow .



The structure of this compound is confirmed by its physical properties and spectral data. FTIR spectrum (Fig. 2) shows the appearance of (O-H) stretching frequency at 3369 cm<sup>-1</sup> and two bands of (NH<sub>2</sub>) stretching frequency at 3267-3180 cm<sup>-1</sup>. (C=O) stretching frequency decreases from 1708 cm<sup>-1</sup> in compound C<sub>6</sub> to 1645 cm<sup>-1</sup> in this compound and this is because of the bonded nitrogen atom which causes resonance in this specific area in the molecule that decreases the force constant of the carbonyl group.

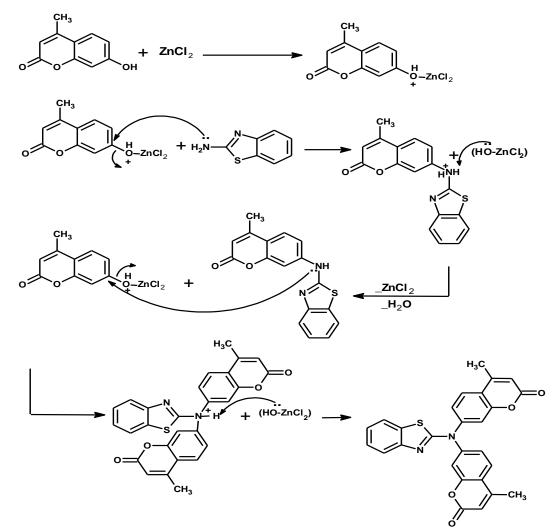


 $^1$  HNMR spectrum ( Fig.5) shows the peaks at : 2.2 ppm (3H ,CH<sub>3</sub>), 5.1ppm (OH& NH), 6.43 ppm (1H, C-H olefinic) 7.4-7.8 ppm (3H , Ar-H), 8.6 ppm (2H , NH<sub>2</sub> ) .

Compound C<sub>7</sub> on reaction with aqueous NaOH produces triazole derivative (compound C<sub>8</sub>). The structure of this compound is confirmed by its physical properties and spectral data. FTIR spectrum shows the appearance of (C=N) stretching frequency at 1600 cm<sup>-1</sup> and (S-H) stretching frequency at 2364 cm<sup>-1</sup>. It also shows the disappearance of (C=O) frequency that belongs to compound C<sub>7</sub>.

Compound C<sub>9</sub> was prepared through the reaction between compound C<sub>8</sub> and 2aminobenzothiazole and this occurs by the nucleophilic attack of amine group of 2aminobenzothiazole on the carbon atom that hold the sulfur atom in compound C<sub>8</sub> through the Tetrahedral mechanism then H<sub>2</sub>S molecule is displaced. The structure of this compound is confirmed by its physical properties and spectral data. FTIR spectrum shows the appearance of (N-H) stretching frequency at 3215 cm<sup>-1</sup> and (O-H) stretching frequency at 3338 cm<sup>-1</sup>.

Compound  $C_{10}$  was prepared through the condensation of 2-aminobenzothiazole with compound  $C_1$  at ratio of 1:2 in presence of anhydrous  $ZnCl_2$ . The mechanism is expected to be as follows:



The structure of this compound is confirmed by its physical properties and spectral data. FTIR spectrum (Fig.3) shows the appearance of two (C=O) stretching frequencies one at 1772 cm<sup>-1</sup> and the other at 1737 cm<sup>-1</sup>, it also shows the disappearance of  $(NH_2)$  stretching frequency that belongs to 2-aminobenzothiazole.

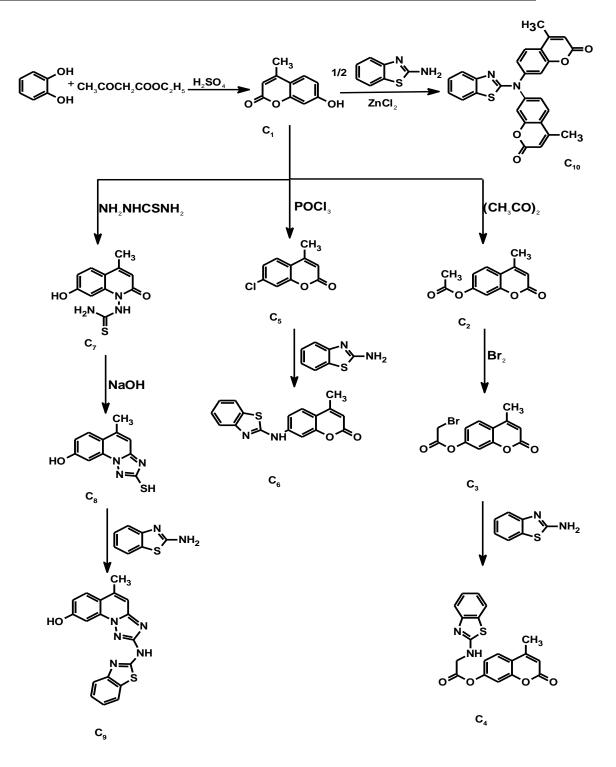
 $^1$  HNMR spectrum (Fig.6) shows the peaks at : 2.3 ppm (6H, 2CH\_3) ,6.1 (2H , olefinic H), 6.4- 8.0 ppm (10H, Ar-H) .

Comp .No.	Color	m.p <sup>0</sup> C	Yield %	Molecular Formula
$C_1$	pale yellow	185-187	81	$C_{10}H_8O_3$
		Lit: 185		
C <sub>2</sub>	White	141-142	75	$C_{12}H_{10}O_4$
C <sub>3</sub>	Off white	95-97	51	$C_{12}H_9O_4Br$
$C_4$	yellow	190-192	85	$C_{19}H_{14}N_2SO_4$
C <sub>5</sub>	brown	217-220	85	$C_{10}H_7O_2Cl$
C <sub>6</sub>	Light green	200-203	55	$C_{17}H_{12}N_2SO_2$
C <sub>7</sub>	White	162-165	60	$C_{11}H_{10}N_3SO_2$
C <sub>8</sub>	Pale yellow	198-200	43	$C_{11}H_9N_3SO$
C <sub>9</sub>	Dark yellow	245-248	60	$C_{18}H_{13}N_5SO$
C <sub>10</sub>	Grey	285-287	40	$C_{27}H_{18}N_2SO_4$

Table 1: physical properties for compounds  $C_1$ - $C_{10}$ 

	UV (EtOH) Characteristic bands of FT-IR( cm <sup>-1</sup> KBr disk )					
Comp.	$\lambda \max(nm)$	v (N-H)	v (C=O)	v (C-H)	v (others)	
No.	$(10^{-4}M)$					
C <sub>1</sub>	323		1670	Ar. =3005	v (C-O) =1147	
	205			Al.=2953	v (O-H)=3502	
C <sub>2</sub>	350		1763,1695	Ar. =3057	v (C-O)	
	313			Al.=2989	=1147 ,1190	
	255					
	206					
C <sub>3</sub>	336		1730,1716	Ar. =3097	v (C-Br) =752	
	213			Al.=2825	v (C-O)	
					=1140,1188	
$C_4$	300	3265	1722	Ar. =3078	ν(C=N)=1635 ν	
	219			Al.=2729	(C-N) =1390	
					v (C-S) =1166	
C <sub>5</sub>	317		1707	Ar. =3080	v (C-Cl) =1044 v	
	204			Al.=2983	(C-O) = 1159	
C <sub>6</sub>	262	3304	1708	Ar. =3072	v (C=N)= 1635	
	222			Al.=2987	v (C-O) =1124 v	
					(C-N) =1282	
C <sub>7</sub>	351	3267-	1645	Ar. =3043	v (O-H) =3369	
	334	3180		Al.=2974	v (C=S) =1317	
	241					
	205					
C <sub>8</sub>	321	3360		Ar. =3068	v (C=N) =1600	
	341			Al.=2974	v (S-H) = 2364	
	205				v (C-N) =1273 v	
					(C-S) =1166	
C <sub>9</sub>	323	3215		Ar. =3049	v (C=N) =1602	
	371			Al.=2941	v (O-H) = 3338	
	219				v (C-N) =1292 v	
	207				(C-S) =1166	
C <sub>10</sub>	350		1772,1737	Ar. =3095	v (C=N) =1626 v	
	335			Al.=2962	(C-N) = 1273	
	260				v (C-O)=1058 v	
	205				(C-S) =1145	

Table 2 : Spectral data for compounds  $C_1$ - $C_{10}$ 



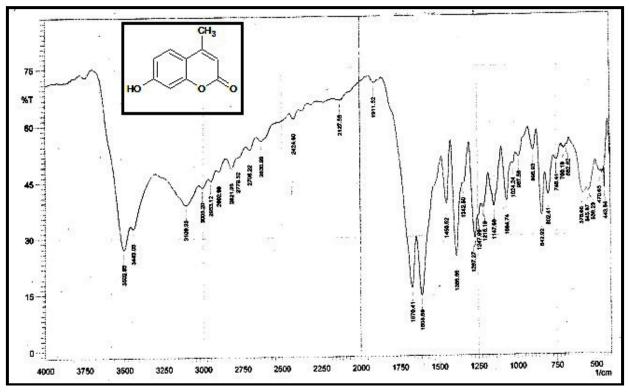


Fig. (1) FTIR Spectrum for compound C<sub>1</sub>

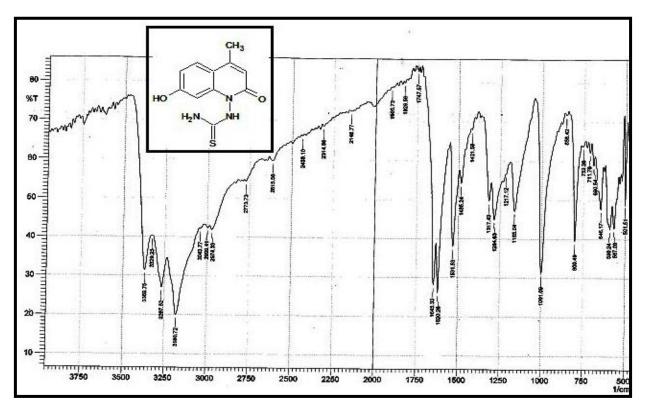


Fig. (2) FTIR Spectrum for compound C<sub>7</sub>

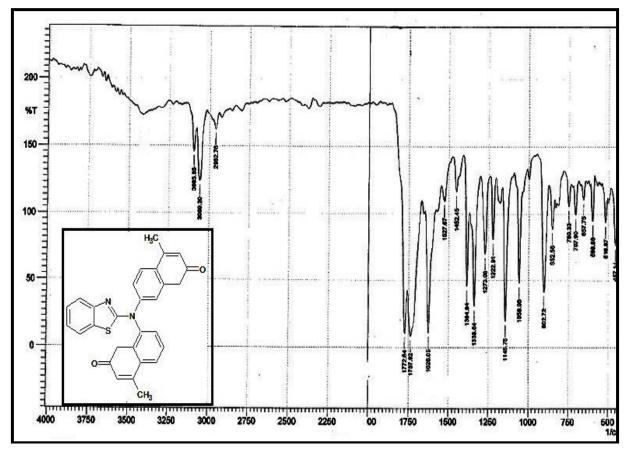


Fig. (3) FTIR Spectrum for compound  $C_{10}$ 

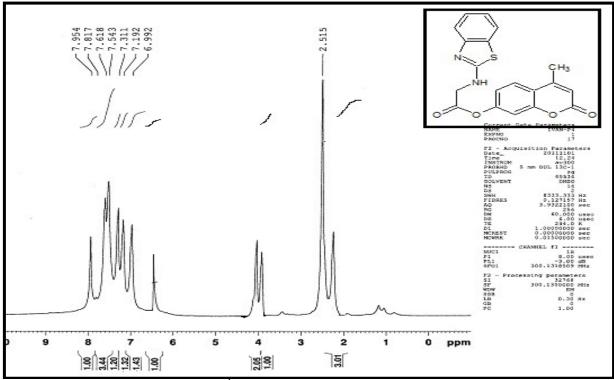


Fig.(4) H<sup>1</sup>NMR Spectrum for compound C<sub>4</sub>

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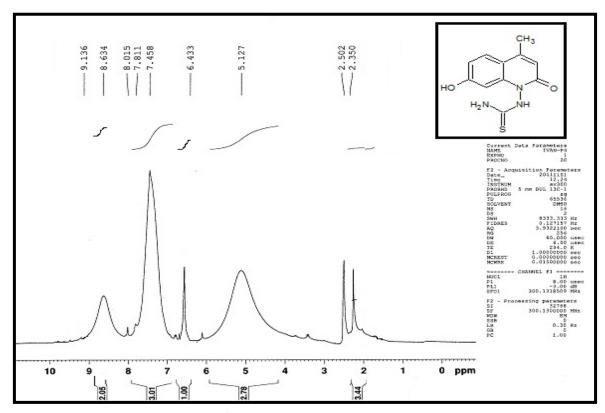


Fig. (5) H<sup>1</sup>NMR Spectrum for compound C<sub>7</sub>

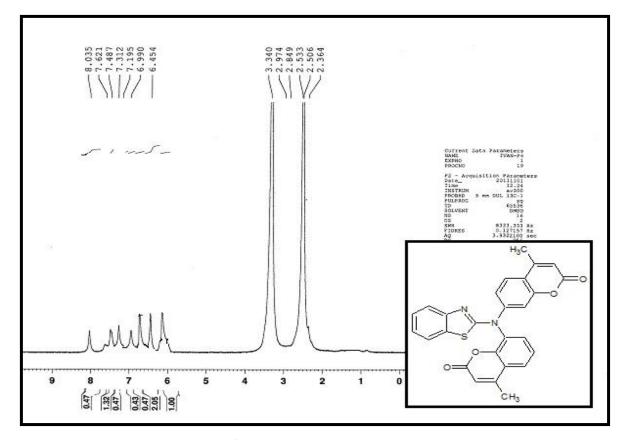


Fig. (6)  $H^1$ NMR Spectrum for compound  $C_{10}$ 

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