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

Suad J. Lafta 1                          Suzanne J. Abass 2
1= Al-Mustansyria University, 2= kerbalaa University, College of Pharmacy                      College of Science ,

ABSTRACT
The titled compound C₁ (Coumarin) was prepared through the thermal cyclization of resorcinol and ethylacetoacetate in presence of sulfuric acid. Compound C₁ (Coumarin) was treated with acetic anhydride in glacial acetic acid to obtain acetate group in the yielding compound (compound C₂). Compound C₂ was brominated to obtain compound C₃ which treated with 2-aminobenzothiazole in ethanol to obtain compound C₄. Compound C₁ was treated with POCl₃ to replace OH group by Cl atom and obtain compound C₅ which was treated with 2-aminobenzothiazole in a nucleophilic aromatic substitution to obtain compound C₆. Compound C₁ was treated with thiosemicarbazide in ethanol to obtain compound C₇ which was treated with aqueous NaOH to obtain triazole derivative (compound C₈). The later compound was treated with 2-aminobenzothiazole to obtain compound C₉. Compound C₁ was treated with 2-aminobenzothiazole in ratio 2:1 in presence of anhydrous ZnCl₂ in ethanol to obtain compound C₁₀.

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 Fourier 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$^1$ NMR spectra were recorded on Burker DMX-500 NMR (300-600 MHz) Spectrophotometer with using DMSO as a solvent in Jordan University.

Preparation of (C1) [12]
(7-hydroxy-4-methyl-2H-chromen-2-one)
A mixture of resorcinol (0.05mol, 5.5g), ethylacetoacetate (0.05mol, 6.05g) and H$_2$SO$_4$ (50mL, 75%) was heated on water bath 100°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 (C2) [13]
(4-methyl-2-oxo-2H-chromen-7-yl acetate)
Compound (C1) (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°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 (C3) [14]
(4-methyl-2-oxo-2H-chromen-7-yl bromoacetate)
Compound (C2) (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°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 (C4) [15]
(4-methyl-2-oxo-2H-chromen-7-yl (1,3-benzothiazol-2-ylamino)acetate)
Compound C3 (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 (C5) [16]
(7-chloro-4-methyl-2H-chromen-2-one)
POCl$_3$ (0.01mol, 1.52g) was added to compound (C1) (0.01mol, 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 (C₆) [17]
(7-(1,3-benzothiazol-2-ylamino)-4-methyl-2H-chromen-2-one)
A mixture of compound (C₅) (0.002mol, 0.38g) and 2-aminobenzothiazole (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 (C₇) [18]
(1-(7-hydroxy-4-methyl-2-oxoquinolin-1(2H)-yl)thiourea)
Solution of compound (C₆) (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 (C₈) [19]
(5-methyl-2-sulfanyl[1,2,4]triazolo[1,5-a]quinolin-8-ol)
Compound (C₇) (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 (C₉) [20]
(2-(1,3-benzothiazol-2-ylamino)-5-methyl[1,2,4]triazolo[1,5-a]quinolin-8-ol)
A mixture of compound (C₈) (0.005mol, 1.2g) and 2-aminobenzothiazole (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 table 1.

Synthesis of (C₁₀) [21]
7,7'-(benzod[d]thiazol-2-ylazanyldiyl)bis(4-methyl-2H-chromen-2-one)
A mixture of compound (C₁) (0.004mol, 0.7g) and 2-aminobenzothiazole (0.002mol, 0.3g) in absolute ethanol was refluxed in presence of anhydrous ZnCl₂ (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 C₁ was achieved by Pechmann Duisberge reaction of ethylacetoacetate with equimolar amount of resorcinol in presence of sulfuric acid. This reaction produces β-hydroxyester which converts to corresponding coumarin. The structure of compound (C₁) is confirmed by its physical properties and spectral data. FTIR spectrum (Fig.1) shows the appearance of (O-H) stretching frequency at 3502 cm⁻¹ and (C=O) stretching frequency at 1670 cm⁻¹ [22].

Compound C₂ was prepared through acylation of compound C₁ 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 C₁ while two (C=O) stretching frequencies appear at 1763 and 1695 cm⁻¹.

Bromination of compound C₂ 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\(^{-1}\). It also show the appearance of two stretching frequencies of two kind of (C=O) groups at 1730 cm\(^{-1}\) and at 1716 cm\(^{-1}\) beside the appearance of (C-O) stretching frequency at 1140 cm\(^{-1}\) and at 1188 cm\(^{-1}\).

Compound C\(_4\) was prepared through the substitution of 2-amino- benzothiazole instead of the brome atom in the compound C\(_3\) through S\(_{N2}\) 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\(^{-1}\) and (C=N) stretching frequency at 1635 cm\(^{-1}\). \(^1\)H NMR (Fig.4) spectrum shows the peaks at : 2.2 ppm (3H, CH\(_3\)), 4.1 ppm (1H, NH), 4.2 ppm (2H, NH-CH\(_2\)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\(_3\) 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\(^{-1}\).

Compound C\(_6\) was prepared through the nucleophilic aromatic substitution of 2-aminobenzothiazole 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\(^{-1}\) beside the appearance of (C=O) stretching frequency at 1708 cm\(^{-1}\) and (C=N) stretching frequency at 1635 cm\(^{-1}\).

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\(^{-1}\) and two bands of (NH\(_2\)) stretching frequency at 3267-3180 cm\(^{-1}\). (C=O) stretching frequency decreases from 1708 cm\(^{-1}\) in compound C\(_6\) to 1645 cm\(^{-1}\) 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.
HNMR spectrum (Fig.5) shows the peaks at: 2.2 ppm (3H, CH₃), 5.1 ppm (OH & NH), 6.43 ppm (1H, C-H olefinic), 7.4-7.8 ppm (3H, Ar-H), 8.6 ppm (2H, NH₂).

Compound C₇ on reaction with aqueous NaOH produces triazole derivative (compound C₈). 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⁻¹ and (S-H) stretching frequency at 2364 cm⁻¹. It also shows the disappearance of (C=O) frequency that belongs to compound C₇.

Compound C₉ was prepared through the reaction between compound C₈ and 2-aminobenzothiazole and this occurs by the nucleophilic attack of amine group of 2-aminobenzothiazole on the carbon atom that hold the sulfur atom in compound C₈ through the Tetrahedral mechanism then H₂S 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⁻¹ and (O-H) stretching frequency at 3338 cm⁻¹.

Compound C₁₀ was prepared through the condensation of 2-aminobenzothiazole with compound C₁ at ratio of 1:2 in presence of anhydrous ZnCl₂. 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\(^{-1}\) and the other at 1737 cm\(^{-1}\), 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).

<table>
<thead>
<tr>
<th>Comp. No.</th>
<th>Color</th>
<th>m.p (^{1})C</th>
<th>Yield %</th>
<th>Molecular Formula</th>
</tr>
</thead>
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<tr>
<td>C(_1)</td>
<td>pale yellow</td>
<td>185-187</td>
<td>81</td>
<td>(\text{C}<em>{10}\text{H}</em>{8}\text{O}_{3})</td>
</tr>
<tr>
<td>C(_2)</td>
<td>White</td>
<td>141-142</td>
<td>75</td>
<td>(\text{C}<em>{12}\text{H}</em>{10}\text{O}_{4})</td>
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<td>C(_3)</td>
<td>Off white</td>
<td>95-97</td>
<td>51</td>
<td>(\text{C}<em>{12}\text{H}</em>{9}\text{O}_{4}\text{Br})</td>
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<tr>
<td>C(_4)</td>
<td>yellow</td>
<td>190-192</td>
<td>85</td>
<td>(\text{C}<em>{10}\text{H}</em>{14}\text{N}<em>{2}\text{SO}</em>{4})</td>
</tr>
<tr>
<td>C(_5)</td>
<td>brown</td>
<td>217-220</td>
<td>85</td>
<td>(\text{C}<em>{10}\text{H}</em>{7}\text{O}_{2}\text{Cl})</td>
</tr>
<tr>
<td>C(_6)</td>
<td>Light green</td>
<td>200-203</td>
<td>55</td>
<td>(\text{C}<em>{17}\text{H}</em>{12}\text{N}<em>{2}\text{SO}</em>{2})</td>
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<tr>
<td>C(_7)</td>
<td>White</td>
<td>162-165</td>
<td>60</td>
<td>(\text{C}<em>{11}\text{H}</em>{10}\text{N}<em>{2}\text{SO}</em>{2})</td>
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<tr>
<td>C(_8)</td>
<td>Pale yellow</td>
<td>198-200</td>
<td>43</td>
<td>(\text{C}<em>{11}\text{H}</em>{9}\text{N}_{3}\text{SO})</td>
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<td>C(_9)</td>
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<td>245-248</td>
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<tr>
<td>C(_{10})</td>
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<td>285-287</td>
<td>40</td>
<td>(\text{C}<em>{27}\text{H}</em>{18}\text{N}<em>{2}\text{SO}</em>{4})</td>
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## Table 2: Spectral data for compounds C₁⁻C₁₀

<table>
<thead>
<tr>
<th>Comp. No.</th>
<th>UV (EtOH)</th>
<th>Characteristic bands of FT-IR (cm⁻¹) KBr disk</th>
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<tr>
<td></td>
<td>λ max (nm) (10⁻⁴M)</td>
<td>v (N-H)</td>
<td>v (C=O)</td>
<td>v (C-H)</td>
<td>v (others)</td>
</tr>
<tr>
<td>C₁</td>
<td>323</td>
<td>205</td>
<td>1670</td>
<td>Ar. =3005</td>
<td>Al.=2953</td>
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<tr>
<td>C₂</td>
<td>350</td>
<td>313</td>
<td>315</td>
<td>255</td>
<td>206</td>
</tr>
<tr>
<td>C₃</td>
<td>336</td>
<td>213</td>
<td>1730,1716</td>
<td>Ar. =3097</td>
<td>Al.=2825</td>
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<tr>
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<td>3265</td>
<td>1722</td>
<td>Ar. =3078</td>
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<tr>
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<td>1708</td>
<td>Ar. =3072</td>
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<tr>
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<td>241</td>
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<td>205</td>
<td>3360</td>
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<td>371</td>
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</table>
Fig. (1) FTIR Spectrum for compound C₁

Fig. (2) FTIR Spectrum for compound C₇
Fig. (3) FTIR Spectrum for compound C_{10}

Fig. (4) H$^1$NMR Spectrum for compound C_{4}
Fig. (5) $^1$H NMR Spectrum for compound C$_7$

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


19) Khoosro Zamani, Khalil Faghihi and Reza Sangi M., "Synthesis of some new substituted 1,2,4-tiazole and 1,3,4-thiadiazole and ather derivatives", Turkish J. Chem., 2003 ;27: 119-125.

