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SYNTHESIS AND CHERACTERIZATION OF SOME NEW (3-ACETYL-2*H*-CHROMEN-2-ONE) DERIVATIVES

تحضير وتشخيص بعض المشتقات الجديدة ل(3-اسيتيل-2*H* –كرومين-2-كيتون)

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ABSTRACT

Compound S_1 which is the starting compound was prepared by the reaction between salicylaldehyde and ethyl acetoacetate in the presence of piperidine. In order to prepare compound S_2, compound $S_1$was refluxed with 2-aminothiazole that dissolved in ethanol in presence of glacial acetic acid. S_3 was prepared through addition of bromine that dissolved in chloroform to compound S_1. S_4 was prepared by heating compound S_3 with thiourea in the presence of sodium acetate. S_5 was prepared by refluxing of compound S_4 with ethyl acetoacetate, while S_4 on refluxing with succinic anhydride give S_6. S_6 when refluxed with *o*-phenylenediamine give compound S_7. All the synthesized compounds were characterized through their physical properties and diagnosed by using FTIR and ^{1}H NMR spectrophotometric techniques.

الخلاصــة

تم تحضير المركب S_1 الذي هو المركب الابتدائي والأساسي لتحضير بقية المركبات من خلال التفاعل بين السلسلديهايد و اثيل اسيتواسيتيت بوجود البيريدين ومن اجل تحضير المركب S_2 تم تصعيد المركب S_1 مع المركب 2-امينوثايازول المذاب في الايثانول بوجود حامض الخليك الثلجي، اما المركب S_3 فقد تم تحضيره بإضافة البروم المذاب في الكلوروفورم الى المركب S_1 . تم تحضير المركبS_4 من خلال تسخين المركب S_3 مع الثايويوريا بوجود خلات الصوديوم. المركب S_5 عندما تم تصعيده مع الاثيل اسيتواسيتيت تم الحصول على المركب S_6. اما المركب S_7 فتم الحصول عليه بتصعيد المركب S_6 مع الاورثو ثنائي الامين باستخدام الايثانول كمذيب. جميع المركبات المحضرة تم تميزها من خلال صفاتها الفيزياوية والكيميائية وتشخيصها باستعمال التقنيات الطيفية المتمثلة بتقنية الاشعة تحت الحمراء وتقنية الرنين النووي المغناطيسي للبروتون.

INTRODUCTION

Coumarins are large family of heterocyclic compounds that occupy an important position in natural and synthetic organic chemistry. Synthesis of coumarins and their derivatives has attracted a large attention from organic and medicinal chemists for many years as a large number of natural products contain this heterocyclic nucleus[1]. There are many methods for synthesis of coumarins[2,3,4], Knoevenagel reaction is the one that have been adopted in this research. On the other hand the nitrogen and sulfur heterocyclic system families are very interesting compounds due to their physicochemical properties especially in the matter of design new drugs [5]. This study aim to combine the coumarinic system with the nitrogen and sulfur heterocyclic system in the hope of getting more potent pharmacological compounds.

EXPERIMANTAL

Materials:

All chemical materials were purchased from BDH, Scharlau and Himedia and were used without further purification.

Instruments:

Melting points were measured on a Gallan Kamp MFB-600 Melting point apparatus and were uncorrected. FTIR spectra were recorded as potassium bromide (KBr) disk on FTIR-8400S Fourer Transform Infrared Spectrophotometer "SHIMADZU". ^{1}H NMR spectra were recorded on Burker DMX- 500 NMR (300-600 MHz) Spectrophotometer with using DMSO as a solvent in Jordan University.

Preparation of compound S_1 [7]
(3-acetyl-2*H*-chromen-2-one)

Salicylaldehyde (3.05g ,0.025mol) and ethyl acetoacetate (3.25g ,0.025 mol) was mixed, stirred and cooled .To this mixture 10 mL of piperidine was added with shaking .The mixture was kept in refregerator for 2 hrs , after that a yellow solid was obtained, then was recrystallized from ethanol. The physical properties were listed in table 1.

Preparation of compound (S_2) [8]
(3-[(1*Z*)-*N*-(4,5-dihydro-1,3-thiazol-2-yl)ethanimidoyl]-2*H*-chromen-2-one)

Compound S_1 (0.22g, 0.001mol) was dissolved in 40mL of warm ethanol contains 5 drops of acetic acid, and 2-aminothiazole (0.1g, 0.001mol) was added. The resulting mixture was refluxed for 10 hrs. After cooling, the formed solid was filtered off, dried and recrystallized from ethanol. The physical properties were listed in table 1.

Preparation of compound (S_3) [8]
(2-oxo-2*H*-chromene-3-carbonyl bromide)

To a solution of compound S_1 (2.19g ,0.01mol) in 100 mL of ethanol ,bromine (1.6g ,0.01mol) in 25mL chloroform was added with shaking. The mixture was warmed to decompose, then it was heated for 15 minutes. The mixture was cooled and filtered to get a solid precipitate which on washing with diethyl ether gave the desired product which was recrystallized from acetic acid to give colorless needles. The physical properties were listed in table 1.

Preparation of compound S_4
(3-(2-amino-4,5-dihydro-1,3-thiazol-4-yl)-2*H*-chromen-2-one)

A suspension of compound S_3 (1.49g, 0.005mol) and thiourea (0.38g, 0.005mol) in 50 mL ethanol was heated to give a clear solution that gave deposited crystals on further heating. The crystals were filtered, washed with ethanol and then boiled with water containing sodium acetate yielding the target compound. The product was recrystallized from ethanol. The physical properties were listed in table 1.

Preparation of compound S_5 [9]
(7-methyl-3-(2-oxo-2*H*-chromen-3-yl)-2,3-dihydro-5*H*-[1,3] thiazolo[3,2-*a*]pyrimidin-5-one)

A mixture of compound S_4 (0.24g, 0.001mol) and ethylacetoacetate (0.65g, 0.005mol) was refluxed for 3hrs. After cooling, the formed solid was filtered off, dried and recrystallized from ethanol. The physical properties were listed in table 1.

Preparation of compound S_6 [10]
(4-oxo-4-{[4-(2-oxo-2*H*-chromen-3-yl)-4,5-dihydro-1,3-thiazol-2-yl]amino}butanoic acid)

A mixture of compound S_4 (0.24g, 0.001mol) and succinic anhydride (0.15g, 0.001mol) in glacial acetic acid was refluxed for 3hrs and then was cooled. The formed solid was filtered off, dried and recrystallized from dioxane. The physical properties were listed in table 1.

Preparation of compound S_7 [11]
(3-(1*H*-benzimidazol-2-yl)-*N*-[4-(2-oxo-2*H*-chromen-3-yl)-4,5-dihydro -1,3-thiazol-2-yl]propanamide)

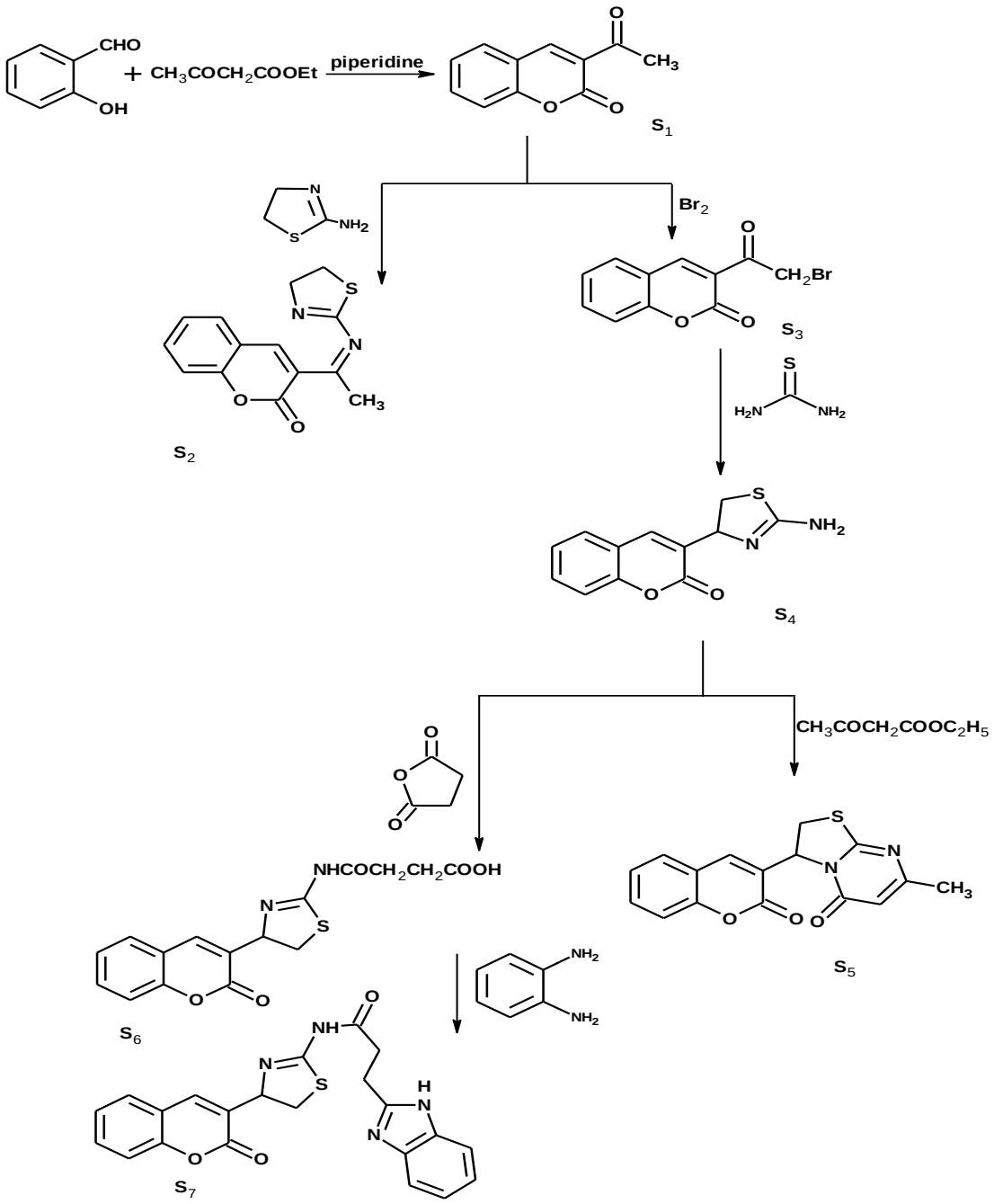
Compound S_5 (1.7g, 0.005mol) and *o*-phenylenediamine (0.54g, 0.005mol) were dissolved in absolute ethanol and was refluxed for 12hrs. The resulting mixture was cooled and poured onto 30mL of ice cold water containing 1mL of conc. HCl. The precipitate which was allowed to settle down, was filtered off, dried and recrystallized from ethanol. The physical properties are listed in table 1.

Table 1: The physical properties for the synthesized compounds

Comp. No.	Color	m.p^{0}C	Yield%	Mol. Formula
S_1	yellow	123-125	85	$C_{11}H_8O_3$
S_2	Greenish yellow	152-154	93	$C_{18}H_{12}N_2SO_2$
S_3	pale yellow	163-165	55	$C_{11}H_8O_3Br$
S_4	Yellow	220-222	56	$C_{12}H_8N_2SO_2$
S_5	Brown	190-192	78	$C_{15}H_{10}N_2O_4$
S_6	Pale yellow	210-212	53	$C_{16}H_{12}N_2SO_5$
S_7	dark yellow	240-243	69	$C_{22}H_{16}N_4SO_3$

RESULTS AND DISCUTION

All the synthesized compounds were characterized through their physical properties and diagnosed by using FTIR and ^{1}H NMR spectrophotometric techniques.



Synthesis and characterization S_1

The synthesis of this compound was achieved by the reaction between salicylaldehyde and ethyl acetoacetate in the precence of piperidine .This compound is confirmed by FT-IR spectrum which shows appearance of a strong band at 1741 cm^{-1} for the stretching frequency of carbonyl of the lactone ring [12] and another band appears at 1680 cm^{-1} for the ketone which is conjugated with (C=C) group.

Synthesis and characterization of S_2

This compound was prepared as a Schiff's base which is the result from the reaction between the ketonic group of the coumarin molecule (compound **S_1**) with 2-amino thiazoline. Compound **S_2** is confirmed by the FT-IR spectrum which shows band at 1608 cm^{-1} for (C=N) group and disappearance of the stretching band of the ketonic carbonyl group, while the stretching frequency of the (C-S) group of the thiazoline ring appeared at 1113 cm^{-1}.

Synthesis and characterization of S_3

This compound is synthesized by the bromination of compound **S_1**. FT-IR spectrum shows the appearance of a stretching frequency of (C-Br) group at 875 cm^{-1} beside two carbonyl group stretching frequency at 1734 cm^{-1} and at 1687 cm^{-1}.

Synthesis and characterization of S_4

Compound S_4 was prepared through the reaction between compound **S_3** and thiourea. This compound was confirmed by its spectral data. FT-IR spectrum shows the appearance of double band at 3315 cm^{-1} and 3383 cm^{-1} belong to (NH_2) group and a stretching frequency at 1095 cm^{-1} for (C-S) group beside the carbonyl group stretching frequency at 1747 cm^{-1}. It also show a single band at 1643 cm^{-1} for (C=N) group. ^{1} HNMR spectrum shows peaks at: 2.4 ppm for (H, CH of thiazoline ring), 3.2 ppm for (2H, CH_2 of thiazole ring), 7.4-7.9 ppm for (4H, CH of aromatic ring + CH olefinic of coumarin ring), 9.8 ppm for (2H, NH_2).

Synthesis and characterization of S_5

The reaction between compound **S_4** and ethyl acetoacetate produce compound **S_5** which is confirmed by FT-IR spectrum that shows the appearance of a strong band at 1722 cm^{-1} for the carbonyl group of the coumarin molecule and another band at1637 cm^{-1} for the carbonyl group of the pyrimidinone ring .It also shows the a stretching frequency at 2995 cm^{-1} for the aliphatic (C-H) bond. ^{1} HNMR spectrum shows peaks at: 2.35ppm for (3H, CH_3), 3.34ppm for (H, CH of thiazoline ring), 3.99ppm for (2H, CH_2 of thiazol ring), 6.45ppm for (H, CH of pyrimidine ring) and 6.99-7.95 ppm for (5H, CH of coumarin rings).

Synthesis and characterization of S_6

This compound was prepared from the reaction of compound **S_4** with succinic anhydride. FT-IR of this compound shows a brood band at 3257 cm^{-1} for (O-H) group and another band at 3180 cm^{-1} for (N-H) group beside three bands at 1722 cm^{-1}, 1714 cm^{-1} and 1649 cm^{-1}, the first for stretching carbonyl group of the coumarin molecule, the second for the stretching carbonyl group of the carboxylic group and the third for the stretching carbonyl group of the amide group.

Synthesis and characterization of S_7

Compound **S_6** on reaction with *o*-phenelendiamine produces compound **S_7**. FT-IR spectrum shows the appearance of two stretching frequencies at 3240 cm^{-1} and at 3233 cm^{-1} for two (N-H) groups and two bands at 1739 cm^{-1} and 1645 cm^{-1} the first for the carbonyl group of the coumarin molecule and the second for the carbonyl of the amide group. ^{1}H NMR spectrum shows peaks at: 2.35 ppm for (2H, CH_2 of aliphatic CH_2-C=O), 2.77 ppm for (2H, CH_2 aliphatic), 2.44 ppm for (H, CH of thiazoline ring), 3.83 ppm for (2H, CH_2 of thiazoline ring), 7.1-7.9 ppm for (8H, CH of aromatic ring + CH olefinic of coumarin ring), 11.5 ppm for (H, NH of imidazole ring) and 12.5 ppm for (H, NH of amide moiety).

Table 2: The FT-IR spectra data for the synthesized compounds

Comp No.	Characteristic bands of FT-IR (cm^{-1} , KBr disc)			
	ν (N-H) cm^{-1}	ν (C=O) cm^{-1}	ν (C-H) cm^{-1}	ν (others) cm^{-1}
S_1	----------	1741,1680	ar.=3032 al.=2931	ν (C-O)= 1207 ν (C=C) =1610,1558
S_2	----------	1734	ar.=3086 al. =2978	ν (C-S) =1113 ν (C=N)=1608,1612
S_3	--------	1734,1687	ar.=3026 al. =2958	ν (C-O) =1074 ν (C-Br) =875
S_4	3383,3315	1747	ar.=3002	ν (C-S) =1095 ν (C=N) =1643
S_5	----------	1722,1637	ar. =3086 al. =2995	ν (C=N) =1604 ν (C-S) =1160 ν (C-N) =1187
S_6	3144	1722,1714,1649	ar. =3051 al. =2982	ν (C-S) =1141 ν (C-O)=1185 ν (O-H)=3180
S_7	3240,3233	1739,1645	ar =3059 al=2929	ν (C=N)=1600 ν (C-S) =1140 ν (C-S) =1199

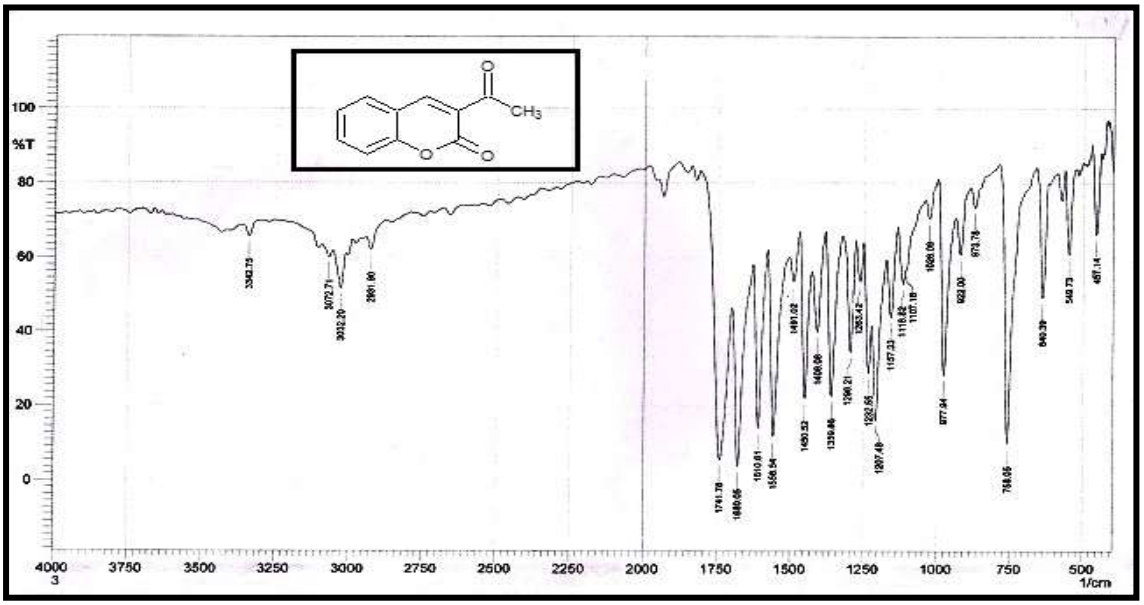


Figure 1: FTIR Spectrum for compound S_1

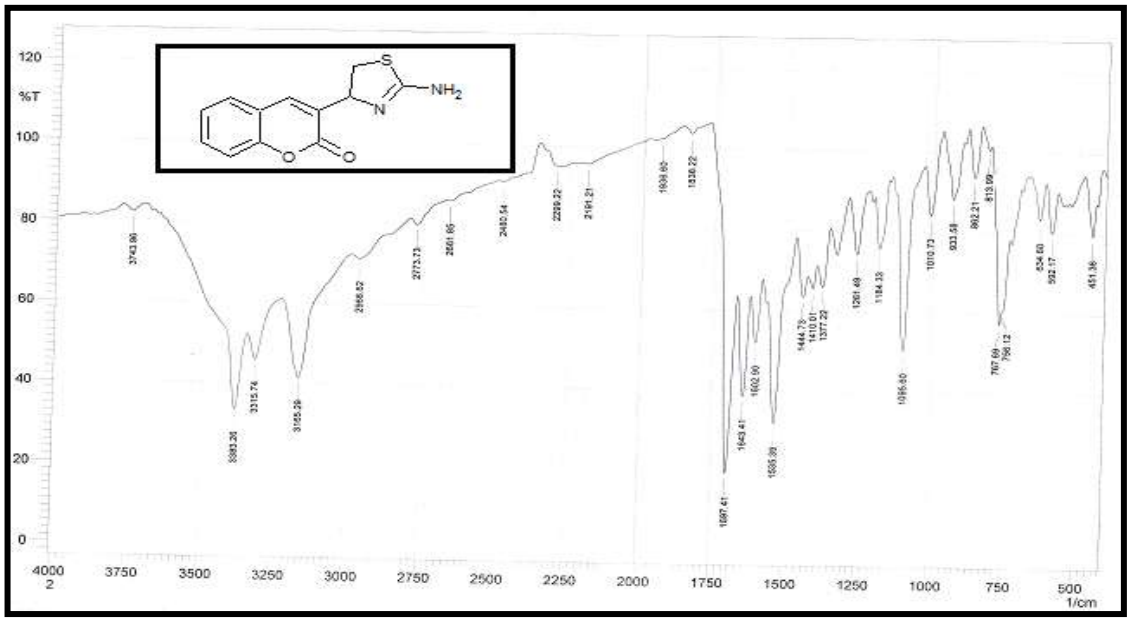


Figure 1: FTIR Spectrum for compound S_4

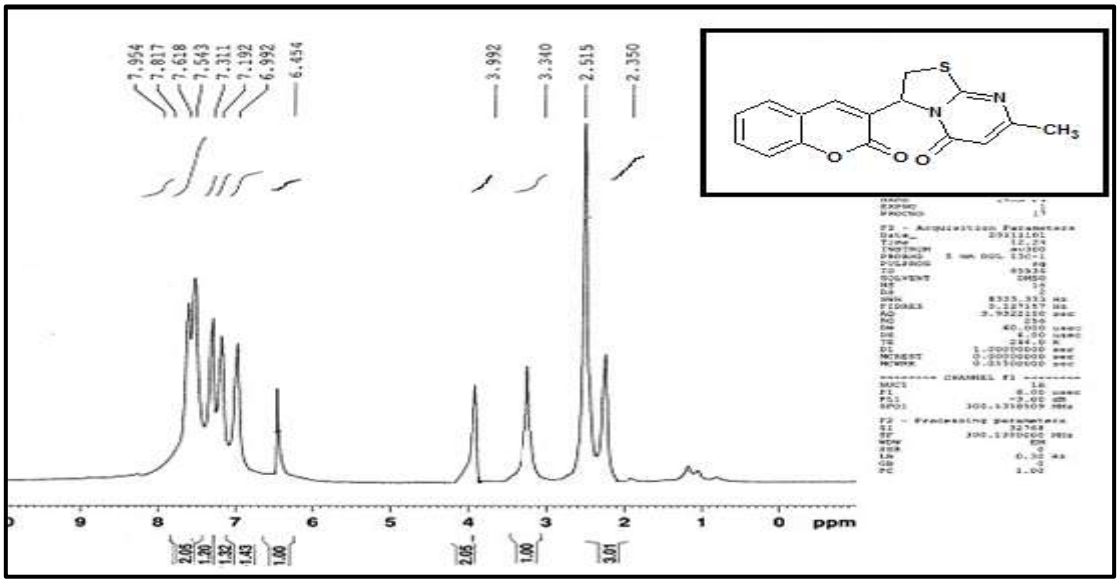


Figure 3: [1] HNMR Spectrum for compound S_5

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