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SYNTHESIS AND CHARACTERIZATION OF SOME NOVEL 1,3-THIAZINE DERIVATIVES DERIVED FROM COUMARIN

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ABSTRACT

Coumarins (2H-1-benzopyran-2-ones) are important oxygen containing fused heterocycles used in drugs and dyes. They are the family of lactones containing benzopyrone skeletal framework that have Susceptibility for isolation from plant as well as total synthesis in the laboratory. 1,3-Thiazines are six membered heterocyclic rings with N-C-S linkage which have promising pharmacological activities which have attract the attention of scientists. The present study was designed to synthesis a new Thiazine derivatives from Chalcones which are derived from Coumarin. Compound**(1)** (7-hdroxy-4-methyl coumarin) was fused with actamide to gives 1-acetyl-7-hydroxy-4-methyl quinolin-2(1H)-one **(2)**.The reaction of (2) with various benzeldehyde in presence of alcoholic NaOH leads to production a new series from Chalcones **(3-6)**. Refluxing of Chalcones with thiourea in presence of alcoholic KOH gives a new derivatives from 1,3 Thiazine **(7-10)**.These new derivatives were characterized using various physical techniques like: FT- IR ,^{1}H-NMR ,GC-Mass and C.H.N.S spectra.

KEYWORDS: Coumarin, 1,3 Thiazine, Chalcon, Methylqiunolin

INTRODUCTION

Thaizine is a six member heterocyclic which contains in its structure two hetero atoms: a sulfer atom and a nitrogen atom placed at position 1,3 from heterocyclic ring [1].Thiazens are very beneficial units in the domains of medicinal and pharmaceutical chemistry and have been mentioned to display a diversity of biological activities such as antifungal, antiviral antibacterial, anticonvulsant and analgesic activity[2]. Cephalosporin which are widely used β-lactam antibiotics have an active core which composed from 1,3 thiazine[3] .The reaction of thiourea with α,β-unsaturated ketones results in 1, 3 thiazines [4-5] . Chalcones and their analogues having α, β- unsaturated carbonyl system are very multilateral substrates for the development of various reactions and physiologically active compounds[6]. In the present study, various 1,3 thiazines derivatives have been synthesized from Chalcones by using thiourea in ethanolic KOH.

MATERIALS AND METHODS

Initial Chemical Compounds was obtaind from BDH, Merck and Fluka companies. Mellting point was determind in an capillary tubes on Sturat Scientific melting point SMPLU-K and are uncorrected. Infrared spectra was recorded on Shimadzu FT-IR (8300) spectrophotometer by using KBr pellet technique. ^{1}H-NMR spectra was recorded on (Bruker DMX-500 NMR spectrophotometer) in frequency 300 MHz, using TMS as the internal standard in (DMSO-d_6). Mass spectra was recorded on Ultra Shimadzu (GCHS-QP 2010).Also Elemental Analysis(C.H.N.S) for all new compounds was recorded in Jordan-Amman.

Step 1: Preparation of 7-Hydroxy-4-Methyl Coumarin (1)

Powdered resorcinol (0.0336 moles ,3.7g) was added to (34.6 moles ,4.4 ml)of ethyl acetoacetate and stirred then it was added slowly to (15 ml) of conc. H_2SO_4 with stirring about (5-10) ^oC for 30 min.Then left in water bath for 1 hr. Then the mixture was poured into crushed ice , the precipitate obtained was filtered, dried and recrystallized from ethanol .

Step 2: Preparation of 1-Acetyl-7-Hydroxy-4-Methyl Quinolin-2(1h)-One (2)

Compound (1) (1.76g , 0.01mol) was fused with acetamide (0.59g , 0.01mol) , then added (15ml) ethanol and keep it in refrigerator for 24h , the mixture was crystallized out later, filtered ,dried and recrystallized from ethanol .

Step 3: Preparation of Chalcones (3-6)

(22g , 0.5mol) from NaOH were dissolved and stirred in(200ml) water and (122.5ml) absolute methanol and keep it in a path of crushed ice. (2.17g ,0.01mol) from compound [12] and (0.01mol) from a various aromatic aldehydes was added with stirred and keep the solution at about 25^oC until the mixture was thick ,then stirrer was removed and the mixture was placed in refrigerator for 24 hour .The resulting crystals filtered, washed with water until the washing water becomes neutral to litmus, dried and recrystallized from ethanol.

Step 4: Preparation of 2-Imino-3, 6-Dihydro-2h-1, 3-Thiazin-4-Yl)-7-Hydroxy-4-Methylquinolin-2(1h)-One Derivatives (7-10)

A mixture of (0.01 mol) from chalcone derivatives(3-6) and (0.76g , 0.01mol) thiourea were dissolved in ethanol abs. (25ml) ,(1.12g ,0.02 mol) from ethanolic KOH was added to this mixture and refluxed for 3h ,cooled , acidified with diluted HCl (1:1).The precipitate was filtered ,dried and recrystalized from ethanol.

RESULTS AND DISCUSSIONS

Treatment of ethyl acetoacetate with phenols in cooled medium in presence of sulfuric acid lead to production coumarin. New Thiazine derivatives was prepared which following the reactions sequence depicted in scheme(1). The structure of compounds (1-5) were confirmed by physical properties and spectral data which are listed in table (1).

The FT-IR spectrum of compound (1) shows the (C=O) stretching frequency near (1678)cm^{-1}. The frequency of the (C=C) group appears at about (1597) cm^{-1}, and absorption band at (3155)cm^{-1} due to the stretching vibration of the hydroxyl group.

Fusing process of compound (1) with acetamide lead to obtain quinolin derivative (2).The structures of the synthesized compound (2) has been characterized and confirmed by FT-IR spectrum besides the ^{1}H.NMR spectrum table (2). The FT-IR spectrum of (2), fig.(1) shows absorption band of (C=O) of quinoline ring at (1797) cm^{-1} while the (C=O) of acetyl accure at (1678) cm^{-1} . The spectrum also shows absorption bands for (C=C) at (1597) cm^{-1} and (OH) at (3159) cm^{-1}.

^{1}H.NMR spectrum of (2) ,fig(4) shows (δppm) : 2.5(s,3H,CH_3 quinolin) ;3.4(s,3H,CH_3acetyl) ; 4.5(s,1H,CH) ; (7.2-8.3)(m,3H,Ar-H) ; 9.5(s,1H,OH).

Treatment of compound(2) with a various aromatic aldehydes in presence of alcoholic NaOH produced chalcone dervatives (3-6). The structures of the synthesized compounds (3-6) has been characterized and confirmed by FT-IR spectrum besides the ^{1}H.NMR spectrum for some of them table (2). For example ;The FT-IR spectrum of compound (4) in

figure (2) shows the appearance of the (CH=CH) absorption band at(1589) cm^{-1}, (C-H) aromatic at (3062) cm^{-1}. Other bands were also absorbed in FT-IR spectra of these compound which are listed in table (1).

Compound (5) has been characterized by the mass spectrum.The mass spectrum of compound(5) shows the molecular ion peak at m/z=351 which is very close from the molecular formula $C_{19}H_{14}N_2O_5$, m/z=350.

^{1}H.NMR spectrum of (6) shows (δppm) : 3.3(s,9H,CH_3); 6.2(s,1H,CH quinolin); 6.6-7.5 (d×d,2H, CH=CH); 7.9(m,3H,Ar-H). Refluxing of compounds (3-6) with thiourea lead to closure ring and production compounds (7-10). The structure of the synthesized compounds (7-10) has been characterized and confirmed by FT-IR spectrum besides the ^{1}H.NMR spectrum for some of them table (2). for example ,The FT-IR spectrum of compound(9) in figure(3) shows the absorption bands at :(1616) cm^{-1} for (C=N), (3178) and (3275) cm^{-1} for (NH) and at (3390) cm^{-1} for (OH) group. Other bands were also absorbed in FT-IR spectra of these compounds are listed in table (1).

^{1}H.NMR spectrum of (7) ,fig(5) shows (δppm): 3(s,3H,CH_3 quinolin) ; 3.3(s,6H,2(N-CH_3)) ;6.7(s,1H,CH quinolin) ;7(b.s,2H,2NH) ;7.7(s,1H,CH thiazine ring) ;8.4-10(m,7H,Ar-H) ;12.3(b.s,1H,OH).

Also Elemental Analysis(C.H.N.S) for all new compounds are listed in table (3).

Table 1: Physical Properties and Spectral Data of the Prepared Compounds

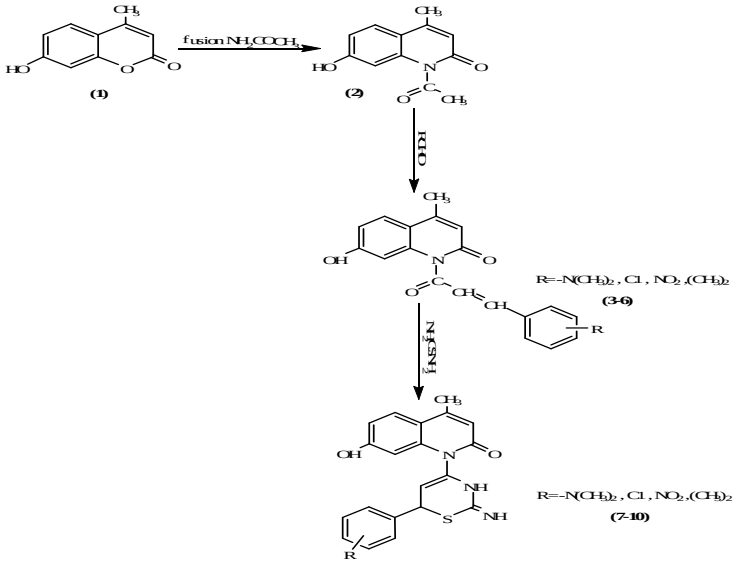
Comd. No.	Formul	M. P.°C	Yield %	Color	Infrared data cm^{-1}
1	$[C_{10}H_8O_3]$	173-175	89	White	1678(C=O) , 3155(O-H) , 3012(C-H) ar. , (2808-2939) (C-H) al. , 1597(C=C) , 1068(C-O)
2	$[C_{12}H_{11}NO_3]$	172-174	79	Yellow	1678(C=O) acetyl , 1797(C=O) quinolin , 1597(C=C) , 3016(C-H) ar. 2808(C-H)al. 3159(O-H) , 1068 (C-O)
3	$[C_{21}H_{20}N_2O_3]$	71-73	69	Light Yellow	1662(C=O) , 1597(C=C) , 2908(C-H)ar. , (2769-2819)(C-H) al. , 3410(O-H) , 1165(C-O)
4	$[C_{19}H_{14}ClNO_3]$	68-70	71	Yellow	1670 and 1616(C=O) , 1585(C=C) , 3062(C-H) ar. , (2866-2924)(C-H) al. , 729.9(C-Cl) , 1099(C-O)
5	$[C_{19}H_{14}N_2O_5]$	186-188	64	Light Brown	1627 and 1651(C=O) , 1600(C=C) , (3082-3109)(C-H) ar. , 3394(O-H) , (2854-2927)(C-H) al. , 1111(C-O) , 1346 and 1535(NO_2)
6	$[C_{21}H_{21}NO_3]$	58-60	70	White	1662(C=O) , 1597(C=C) , 3047(C-H)ar. , (22819-2908)(C-H)al. , 1161(C=O)
7	$[C_{22}H_{22}N_4O_2S]$	158-160	78	Light Yellow	1635(C=N) , (3150 and 3214)(2N-H) , 3400(O-H) , 2790(C-H) al. , 1165(C-O) , 1585(C=C) ,1670(C=O)
8	$[C_{20}H_{16}ClN_3O_2S]$	157-159	82	Light Yellow	1608(C=N) , (3167 and 3278)(2NH) , 3383(O-H) , 2688(C-H) al. , 729(C-Cl) , 1083(C-O) , 1697(C=O)
9	$[C_{20}H_{16}N_4O_4S]$	289-290	73	Dark Beige	1616(C=N) , (3178 and 3275)(2NH) , 3390(O-H) , (2897-2978)(C-H) al. , (1134 and 1415)(NO_2) , 1002(C-O) , 1678(C=O)
10	$[C_{22}H_{23}N_3O_2S]$	140-142	68	Yellow	1616(C=N) , (3174 and 3278)(2NH) , 3379(O-H) , 2908(C-H) al. , 1083(C-O) , 1546(C=C)

Table 2: Chemical Shifts ^{1}H.NMR Spectra

Comd. NO.	1H.NMR (DMSO-d6) δppm
2	2.5(s,3H,CH_3quinolin) ; 3.4(s,3H,CH_3acetyl) ; 4.5(s,1H,CH) ; (7.2-8.3)(m,3H,Ar-H) ; 9.5(s,1H,OH).
6	3.3(s,9H,CH_3); 6.2(s,1H,CH quinolin) ; 6.6-7.5 (d×d,2H, CH=CH) ; 7.9(m,3H,Ar-H).
7	3(s,3H,CH_3 quinolin) ; 3.3(s,6H,2(N-CH_3)) ;6.7(s,1H,CH quinolin) ; 7(b.s,2H,2NH) ;7.7(s,1H,CH thiazine ring) ;8.4-10(m,7H,Ar-H) ;12.3(b.s,1H,OH).

Table 3: The Elemental Analysis of New Synthesized Compounds

Comd. NO.	Chemical Formula	Elemental Analysis			
		C%	H%	N%	S%
2	$[C_{12}H_{11}NO_3]$	**Calc.** 66.30	5.06	6.45	-
		Found 66.22	5.13	6.31	-
3	$[C_{21}H_{20}N_2O_3]$	**Calc.** 72.33	5.74	8.03	-
		Found 72.25	5.66	7.97	-
4	$[C_{19}H_{14}ClNO_3]$	**Calc.** 56.52	4.12	4.12	-
		Found 56.48	4.35	4.05	-
5	$[C_{19}H_{14}N_2O_5]$	**Calc.** 65.08	3.99	7.99	-
		Found 65.01	3.89	7.91	-
6	$[C_{21}H_{21}NO_3]$	**Calc.** 75.13	6.26	4.17	-
		Found 75.06	6.19	4.10	-
7	$[C_{22}H_{22}N_4O_2S]$	**Calc.** 65.00	5.41	13.78	7.87
		Found 64.97	5.36	13.66	7.65
8	$[C_{20}H_{16}ClN_3O_2S]$	**Calc.** 60.37	4.02	10.56	8.06
		Found 60.12	3.79	10.20	7.73
9	$[C_{20}H_{16}N_4O_4S]$	**Calc.** 58.76	3.91	13.71	7.83
		Found 58.20	3.45	13.48	7.70
10	$[C_{22}H_{23}N_3O_2S]$	**Calc.** 67.09	5.84	10.67	8.13
		Found 67.01	5.77	10.60	8.05



Scheme 1

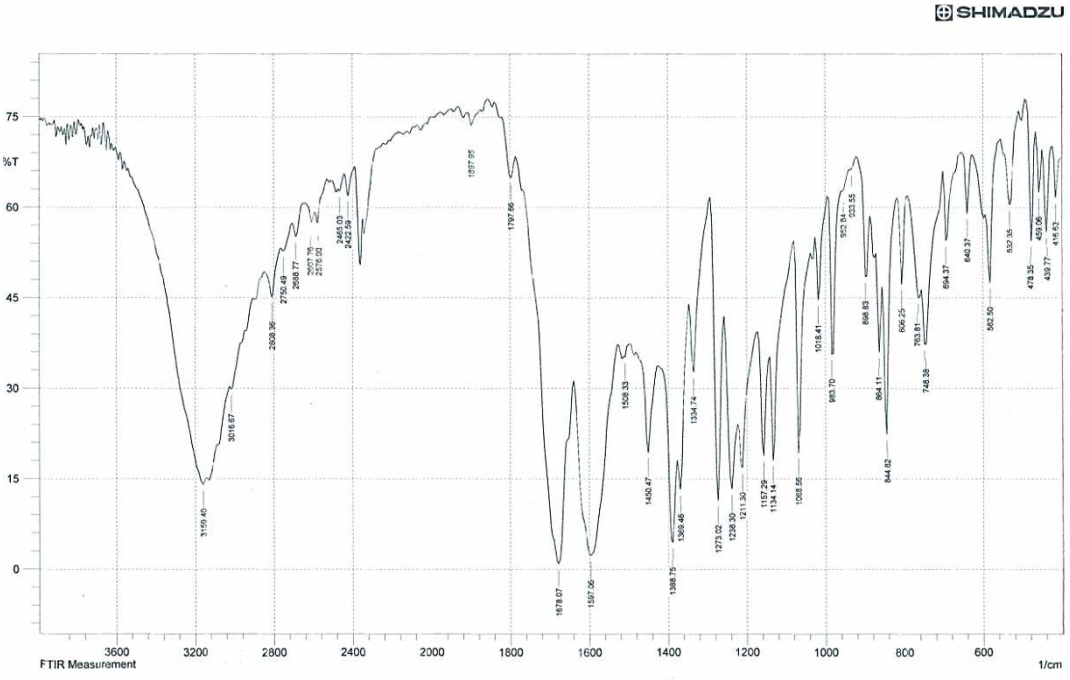


Figure 1: FT-IR Spectrum of Compound (2)

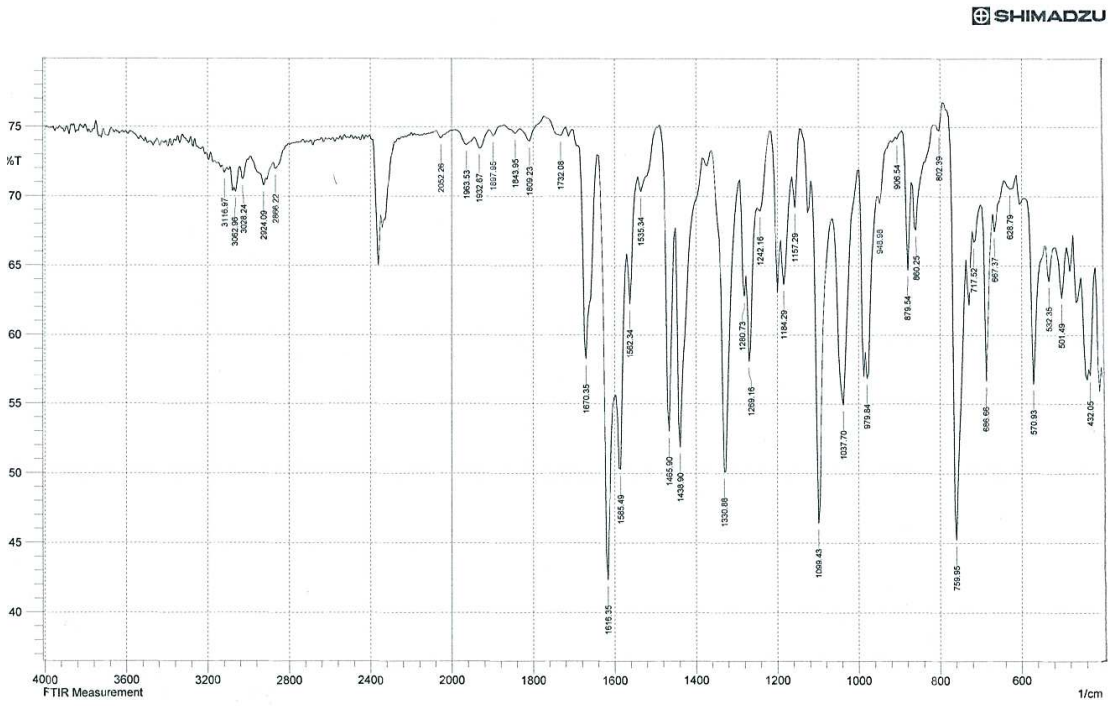


Figure 2: FT-IR Spectrum of Compound (4)

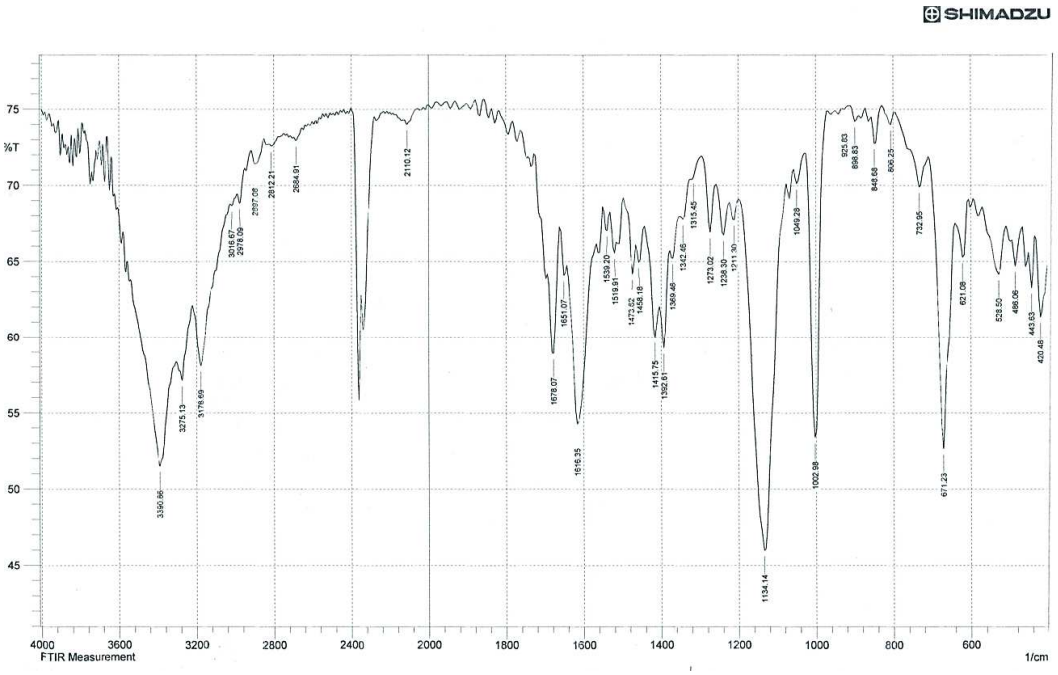


Figure 3: FT-IR Spectrum of Compound (9)

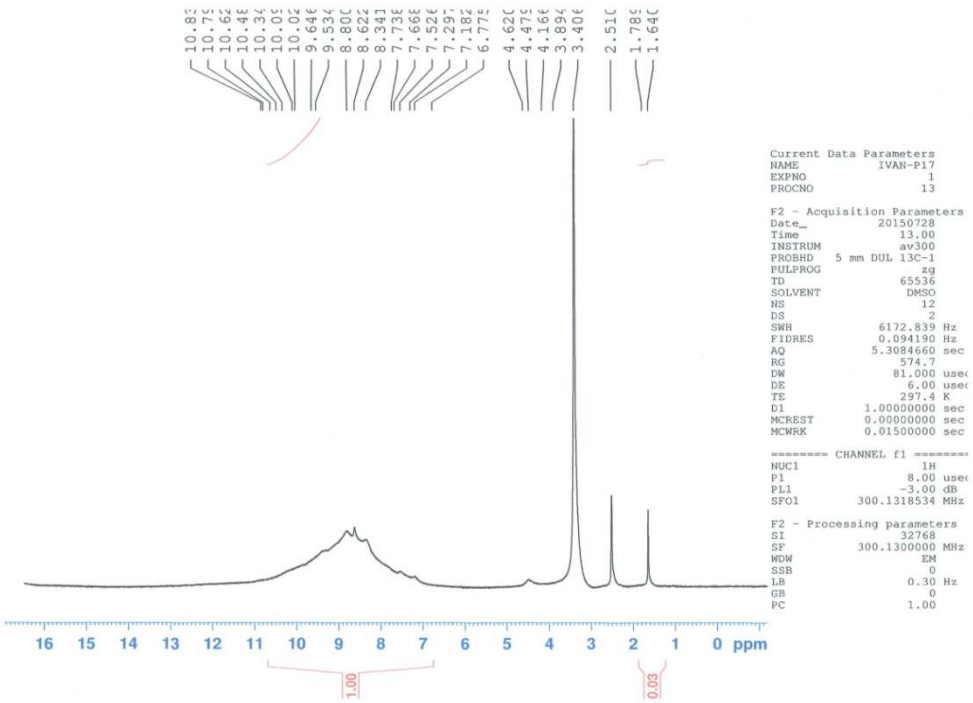


Figure 4: FT-IR Spectrum of Compound (2)

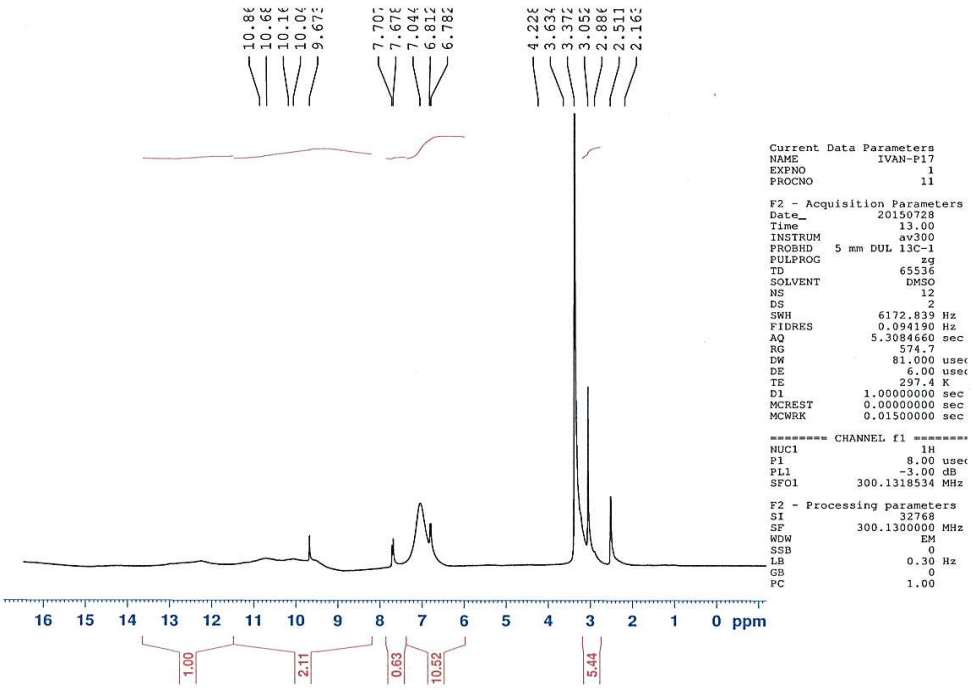


Figure 5: ^{1}H.NMR Spectrum of Compound (7)

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