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SYNTHESIS AND CHARACTERIZATION OF SOME PYRIMIDINE DERIVATIVES (R. OR AR. -1, 2, 3, 4-TETRAHYDROPYRIMIDINE-5-CARBOXYLATE)

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ABSTRACT

This study includes synthesis and characterization of new derivatives of pyrimidine (R. OR Ar. -1, 2, 3, 4-tetrahydropyrimiden-5-carboxlate), via of the reaction from Acetoacetic acid ethyl ester with different aldehydes and gouindihydrochlorid. From ethanol absolute as a solvent this mixture was refluxed for (4 – 6) hrs. (The PH of the mixture is 6). The end of the reaction was checked by (T.L.C.), the prepared compounds were characterized by melting point, FT-IR, UV-Vis and 1H- NMR spectra.

KEYWORDS: Pyrimidines, Ethyl Acetoacetate, Gouindihydrochlorid, Different of Aldehydes

1. INTRODUCTION

Pyrimidines and their derivatives are well researched due to their anti-inflammatory, analgesic, antimicrobial, antiviral, and interferon inducing activities [(1-3)]. Pyrimidines and derivatives of organic compounds were used their anticancer, anti-inflammatory,[(4)] anticonvulsant [(5)], anti nociceptive[(6)] anti-bacterial, viruses[(7)] , hypoglycemic[(8)] . Pyrimidines are aromatic hetero cycle compounds[(9)] The basic skeleton of a pyrimidine ring is composed of two elements, nitrogen and carbon and nitrogen , are also named as diazines having two nitrogen atoms at position 1 and 3.[(10)]

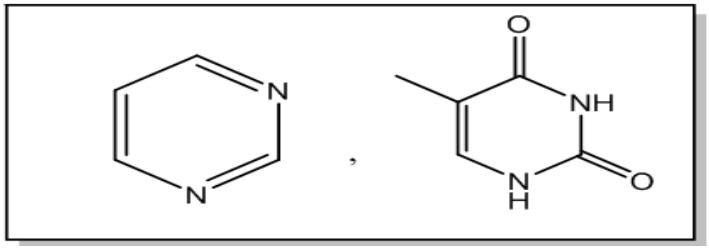


Figure 1

The significant position of pyrimidine and its derivatives in organic chemistry is primarily related to their bio activity. Above of all, they constitute nucleic acids which are the base of life. Three nucleobases (cytosine, thymine and uracil) are pyrimidine derivatives. [(11)] The biodynamic property of pyrimidine ring structure has urged the medicinal chemists to synthesize such pyrimidine derivatives which can stimulate pharmacophores and be utilized for various pharmacological applications.

The core structure of pyrimidine helps them by offering certain reaction sites that can be used to reach further with different moieties. [(12)]The present research work was designed to synthesize derivatives of pyrimidine compounds adopting conventional synthesis reported in literature and technique that is microwave assisted synthesis. [(13)] Micro wave –

assisted synthesis is acknowledged a major breakthrough in synthetic chemistry in recent years. This technique has overcome the certain back draws associated with conventional routes i.e. larger reaction time, reduced yields and purity and slow rate of reaction. The use of microwave (mw) irradiation is the alternative heating technique in synthetic chemistry. [14-15]Microwave synthesis provides more opportunities to organic chemists to expand their synthetic avenues by applying micro wave irradiation to a variety of organic reactions with improved results [16-17].

2. MATERIAL AND METHODS

2.1 Conventional Synthesis of Pyrimidine Derivatives [18]

A series of pyrimidinens derivatives were prepared of the reaction from Acetoacetic acid ethyl ester (3.8 ml, 0.03mole) with different aldehydes (0.025 moles) and gouindihydrochlorid (2.1 gm., 0.022 moles) in 100 ml from ethanol absolute as a solvent, this mixture was refluxed for (4 – 6) hrs. (The PH of the mixture is 6). The end of the reaction was checked by (T.L.C.) The sludge filtration and recrystallized from ethanol and deposited. Allphosical properties are listed in table (2-3).

Table (2-3): Physical Properties of Compounds [B1 – B16]

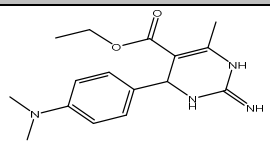
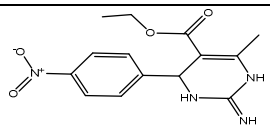
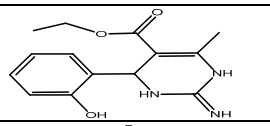
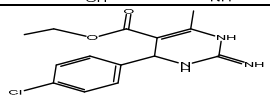
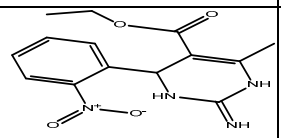
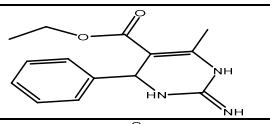
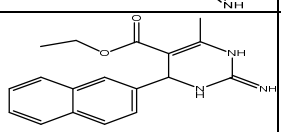
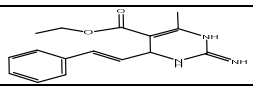
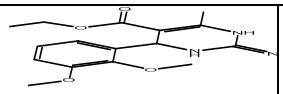
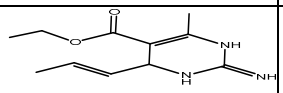
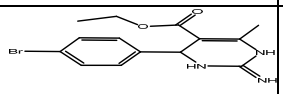
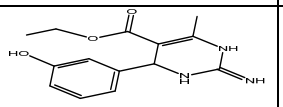
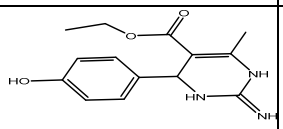
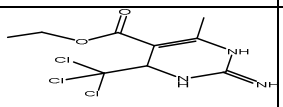
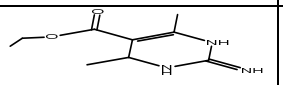
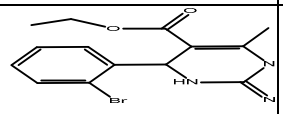
Comp. No	The Structure Of Compound	Color	Yield %	M.P	Time of Reaction	Aldehydes Weight (g)or(ml)
B1		Brown-greenish	70	178-180	6h	3.05 g
B2		Dark yellow	62	135-137	5h	3.78 g
B3		Light Brown	80	166-168	4h	3.05 g
B4		Light yellow	55	188-190	4h	3.5 g
B5		yellow	57	More than 3000	5h	3.78 g
B6		white	75	180-182	5h	2.5 ml
B7		Brown	64	178-180	5h	3.6 ml
B8		Light yellow	75	150-152	6h	3.1 ml

Table (2-3): Contd.,						
B9		Brown	53	160-162	6h	3.19 g
B10		Light yellow	76	155-157	5h	2.07 ml
B11		Light yellow	70	oily	5h	4.63 g
B12		Light yellow	80	oily	4h	3.05 g
B13		Light yellow	60	110-112	6h	3.05 g
B14		white	48	176-178	4h	2.62ml
B15		white	95	155-157	4h	1.4 ml
B16		Light yellow	80	172-174	5h	2.92 ml

2.2 Micro Wave –Assisted Synthesis of Pyrimidine Derivatives. (R, Or, Ar -1, 2, 3, 4-Tetrahydropyrimidine-5-Carboxylate)[19]

A mixture of ethyl acetoacetate (0.03mole, 3.8 ml), with different aldehydes (0.025 mol), with gouindihydrochlorid (0.022 mole, 2.1 gm.) in ethanol absolute (10ml) the PH of the mixture is (6). Then reaction mixture was irradiated under microwave radiation for (2-4) seconds, shown table [2.4].

Table (2.4): Physical Properties of Compounds [B1 – B16]

Comp. No	Name Compound	Chemical formula	Time of Reaction Min.	M .Wt. g/Mol
B1	Ethyl 4- (4-(dimethylamino) phenyl)-2 imino-6-methyl-1,2,3,4-tetrahy dropyrimidine -5-carboxylate	$C_{16}H_{22}N_4O_2$	0:09	302,38
B2	Ethyl 2-imino-6-methyl-4-(4-nitrophenyl)-1,2,3,4-tetrahydropyrimidine-5-carboxylate	$C_{14}H_{16}N_4O_5$	0:38	304,31
B3	Ethyl 4-(2-hydroxyphenyl) – 2 – imino – 6 – methyl - 1, 2, 3, 4 – tetrahydropyrimidine -5 - carboxylate	$C_{14}H_{17}N_3O_3$	0:14	275.31
B4	Ethyl 4-(4-chlorophenyl)-2-imino-6-methyl-1,2,3,4-tetrahydropyrimidine-5-carboxylate	$C_{14}H_{16}ClN_3O_2$	0:23	293.75
B5	Ethyl 2-imino-6-methyl-4-(2-nitrophenyl)-1,2,3,4-tetrahydropyrimidine-5-carboxylate	$C_{14}H_{16}N_4O_5$	0:05	304.31

Table (2.4): Contd.,				
B6	Ethyl 2-imino-6-methyl-4-phenyl-1,2,3,4-tetrahydropyrimidine-5-carboxylate	$C_{14}H_{17}N_3O_2$	0:06	259.31
B7	Ethyl 2-imino-6-methyl-4-(naphthalen-2-yl)-1,2,3,4-tetrahydropyrimidine-5-carboxylate	$C_{18}H_{19}N_3O_2$	0:15	309.37
B8	Ethyl (e)-2-imino-6-methyl-4-styryl-1,2,3,4-tetrahydropyrimidine-5-carboxylate	$C_{16}H_{19}N_3O_2$	1:00	285.35
B9	Ethyl 4-(2,3-dimethoxyphenyl)-2-imino-6-methyl-1,2,3,4-tetrahydropyrimidine-5-carboxylate	$C_{16}H_{21}N_3O_4$	1:31	319.36
B10	Ethyl (e)-2-imino-6-methyl-4-(prop-1-en-1-yl)-1,2,3,4-tetrahydropyrimidine-5-carboxylate	$C_{11}H_{17}N_3O_2$	0:08	223.28
B11	Ethyl 4-(4-bromophenyl)-2-imino-6-methyl-1,2,3,4-tetrahydropyrimidine-5-carboxylate	$C_{14}H_{16}BrN_3O_2$	0:41	338.21
B12	Ethyl4-(3-hydroxyphenyl)-2-imino-6-methyl-1,2,3,4- tetrahydropyrimidine-5-carboxylate	$C_{14}H_{17}N_3O_3$	0:54	275.31
B13	Ethyl 4-(4-hydroxyphenyl)-2-imino-6-methyl-1,2,3,4-tetrahydropyrimidine-5-carboxylate	$C_{14}H_{17}N_3O_3$	0:30	275.31
B14	Ethyl 2-imino-6-methyl-4-(trichloromethyl)-1,2,3,4-tetrahydropyrimidine-5-carboxylate	$C_9H_{12}Cl_3N_3O_2$	0:32	300.56
B15	Ethyl 2-imino-4,6-dimethyl-1,2,3,4-tetrahydropyrimidine-5-carboxylate	$C_9H_{15}N_3O_2$	0:23	197.24
B16	Ethyl 4-(2-bromophenyl)-2-imino-6-methyl-1,2,3,4-tetrahydropyrimidine-5-carboxylate	$C_{14}H_{16}BrN_3O_2$	0:40	338.21

3. RESULTS AND DISCUSSIONS

For the synthesis of the targeted many pyrimidines compounds by the Biginelli reaction .The chemical reaction of pyrimidinens derivatives were prepared from the reaction from (ethyl acetoacetate,) aldehyde derivatives and gouindihydrochlorid.

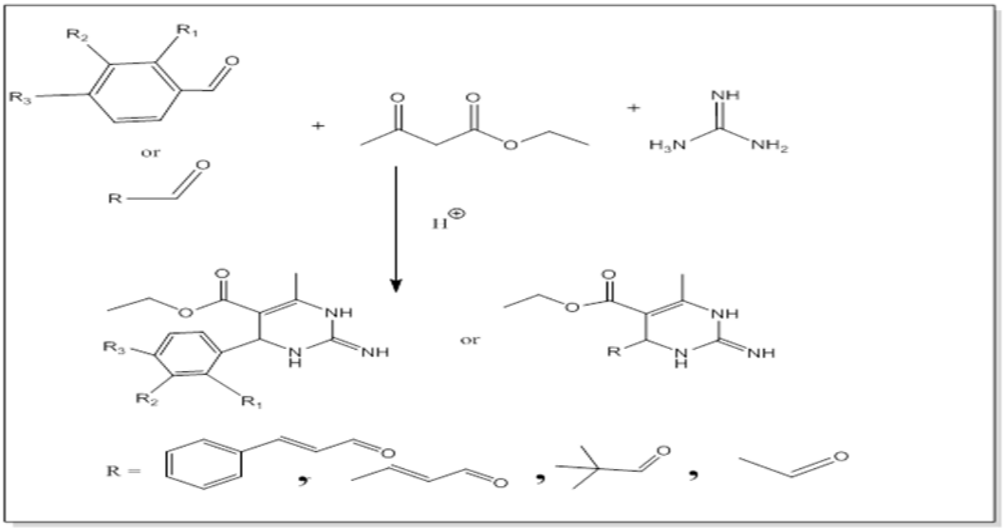


Figure 2

R1	H	NO_2	OCH_3	H	H	OH	H	H	H	H	Cl	Br
R2	H	H	OCH_3	H	OH	H	H	H	NO_2	H	H	H
R3	$N(CH_3)_2$	H	H	H	H	H	NO_2	Cl	H	OH	H	H

Compound [B1] prepared from the reaction from ethylacetoacetate, 4-(dimethylamino) benzaldehyde and

gouindihydrochlorid in the presence of HCl and ethanol absolute

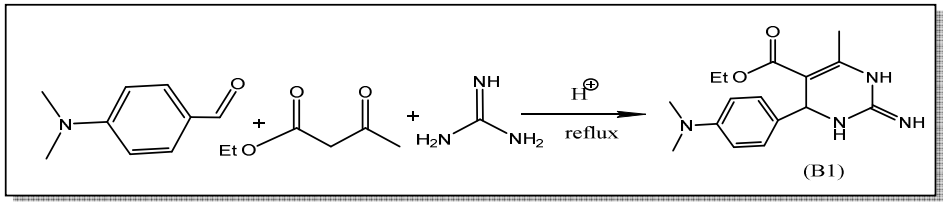


Figure 3

Eq (3-2): Preparation B1

The mechanism involves nucleophilic attack of amino group in gouindinhydrochlorid on carbonyl group in benzaldehyde followed by elimination of water molecule. As shown in the following scheme:

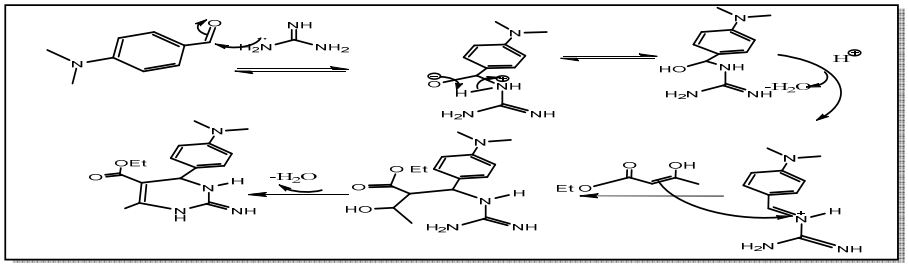


Figure 4

Schem (3-2): The Mechanism Preparation B1

The physical properties of compound are Brown - greenish his color, 74%, M.P (138-140) Co this reaction refuxed for 5 hrs at (100Co), in this methods were prepared [B2-B16] shown table (2-2).

The structure of compound was confirmed by FT-IR, and U.V spectrum. The FT-IR spectrum of compound [B1] (Figure 3-12), table [3-2] shows disappearing of stretching vibration of (NH) group of amine at(3336) cm-1 and increasing frequency of (C=O) to(1650) cm-1 ,also spectrum shows anther bands, (3050) cm-1 for aromatic (C-H) , band at(1550,1450,1406) cm-1 due to aromatic (C=C), bands at (1600) cm-1 for stretching vibration of (N=C)group , bands at(1350) cm-1 for stretching vibration of (CH3C=O)group and bands at (1168-1539) cm-1 for stretching vibration of (C-N)group. Figure (3-14).

Table (3-2): FT-IR Spectral Data of Compound (B1_B16)

Comp. Code	vs N-H Amine	vs C-H Aromatic	vs C-H Aliphatic	vs C=O	vs C=N	vs C=C Ar.	CH-C=O	Others
B1	3336.8	3080	2900	1705	1650	1550,1450,1406	1350	C-N…. 1178.5, 1555
B2	3429	3047	2887	1676	1602	1504,1446,1400	1371	N-O 1388,1371
B3	3385	3066	2900	1670	1645	1539,,1508,1406	1350	OH…3396
B4	3396	3040	2987	1720	1662	1537,1490,1400	1382	C-Cl..773
B5	3400	3082	2981	1700	1670	1520,1458,1400	1325	NO…1550
B6	3385	3101	2887	1650	1639	1535,1489,1423	1390	C-N..1111
B7	3398	3050	2850	1687	1625	1573,1510,1444	1340	C-N..1114
B8	3406	3010	2993	1700	1650	1537,1449,1450	1421	C-N..1124
B9	3406	3018	2999	1700	1685	1587,1514,1469	1350	C-0 1273,11244

Table (3-2): Contd.,								
B10	3396	-----	2974	1665	1640	1533,1456,1400	1363	C-N..199
B11	3360	3045	2960	1676	1668	1575,1550,1396	1350	C-Br…788
B12	3383	3049	2900	1662	1622	1581,1492,1406	1361	C-OH—3410
B13	3370	3050	2950	1718	1675	1583 ,1564,1447	1377	C-OH..3425
B14	3398	----	2900	1650	1643	1550,1404,1400	1350	C-Cl.. 819,773 , 516 ,
B15	3350	-----	2890	1680	1653	1533,1404	1300	C-N ..1111
B16	3358	3100	2883	1660	1643	1537,1471,1433	1309	C-Br…779 C-N..1118

In compound [B14] C-Cl note three bounds (819, 773, and 516) because found Neighboring group, disappearing of stretching vibration of (NH) group of amine at (3350-3400) cm-1 because found deferent Neighboring group.

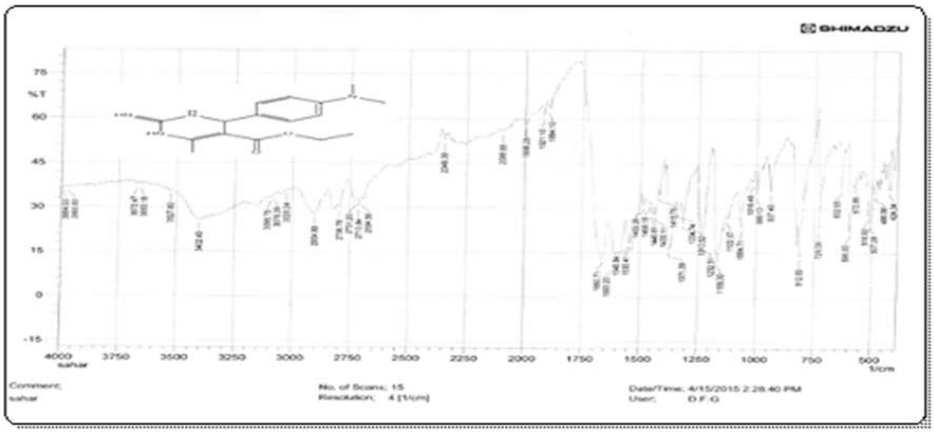


Figure (3-14): FT-IR Spectrum for Compound (B1)

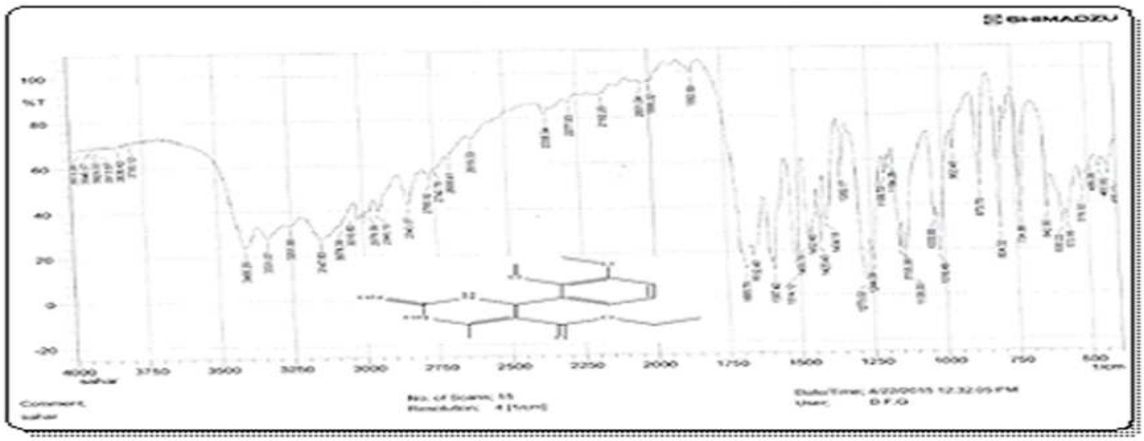
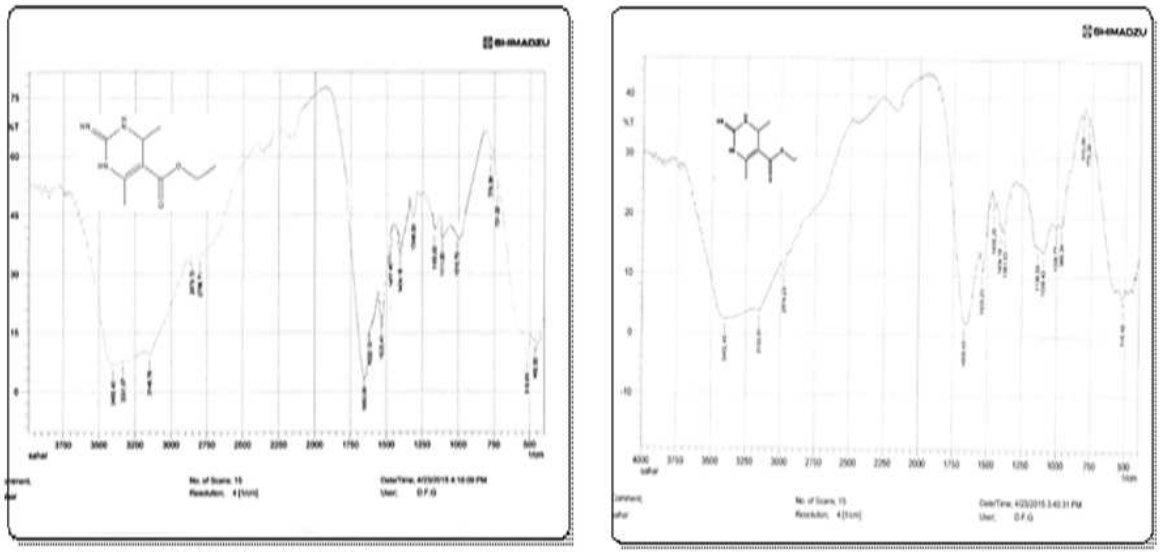


Figure (3-16): FT-IR Spectrum for Compound (B9)

By measuring the FT-IR of the pyrimidine derivatives were prepared by biginelli reaction and microwave method. Shown figure (3-19)



a- Classical (B15) **b-Microwave (B15)**

Figure (3-19): FT-IR Spectrum for Compound Classical and Microwave (B15)

CONCLUSIONS

We can noticed that there is matching between these peaks which mean that this method is good, for the preparation but with a little differences.

By measuring the U.V visible of the compounds is prepared by biginelli reaction and microwave method. Shown figure (3-22)

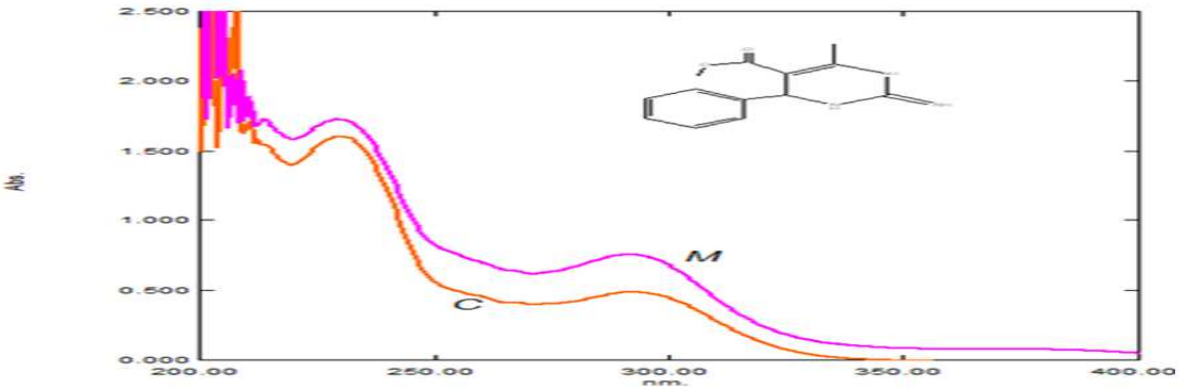


Figure (3- 22): U.V Visible Spectrum for Compound (B6)

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