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Preparation and Diagnosis of Pyrimidines Derivatives by Conventional And Microwave Ways.

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Abstract: This work includes synthesis and characterization of new derivatives of pyrimidine (R. or Ar. -1, 2, 3, 4-tetrahydropyrimidin-5-yl) ethan-1-one), via the reaction of acetyl acetone with different aldehydes and guanidine hydrochloride. Using absolute ethanol as a solvent .This mixture was refluxed for (6– 20) hrs.at pH 6 we prepared .The same derivatives of pyrimidine were prepared in microwave way. This compounds were prepared characterized by melting point, FT-IR , UV-Vis and some of the with 1H-NMR and 13C-NMR spectroscopy .

Keywords : Preparation , Diagnosis , Pyrimidines , Conventional , microwave Ways.

Introduction:

Pyrimidine are well known for their anticancer (1-2), antimicrobial (3-5) and antifungal (6-7). Pyrimidines are organic aromatic hetero cycle compounds (8). The basic skeleton of a pyrimidine ring is composed of two elements, carbon and nitrogen, are also named as diazines having two nitrogen atoms at position 1 and 3.(9) see fig 1

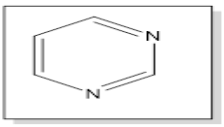


Fig 1: The basic skeleton of a pyrimidine ring

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 is the base of life. Three nucleobases (cytosine, thymine and uracil) are pyrimidine derivatives. (10) 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.(11-12), 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 backdraws associated with conventional routes i.e. larger reaction time, reduced yields and purity and slow rate of reaction .(14)

The use of microwave (MW) irradiation is the alternative heating technique in synthetic chemistry. 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 (15-17).

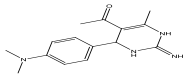
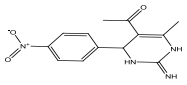
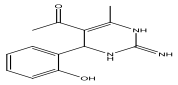
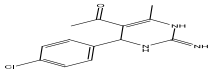
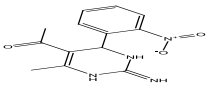
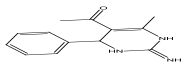
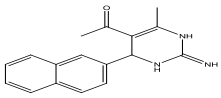
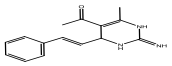
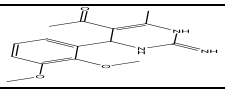
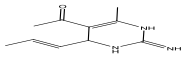
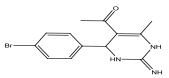
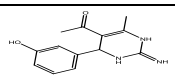
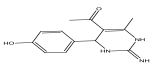
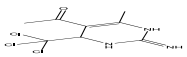
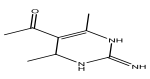
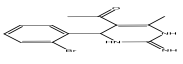
Material and methods

Acetyl acetone, Gouindin hydrochloride, Different Aldehydes (4-N,N-Dimethyl Banzaldehyde , 4-Nitro Banzaldehyde, 2-Hydroxy Banzaldehyde , 4-Chloro Banzaldehyde, O -Nitro Banzaldehyde, 1-Naphthaldehyde,2,3-Di Methoxy Banzaldehyde , But-2-enal, 4-Bromo Banzaldehyde, 3-Hydroxy Banzaldehyde , Tri Chloro Acetaldehyde, Acetaldehyde solution, 2-Bromo Banzaldehyde) ethanol absolute and HCl.

2.2 Prepare derivative pyrimidines (18)

A series of pyrimidine's derivatives were prepared from the reaction of acetylacetone (3.1 ml ,0.03 mole) with different aldehydes (0.025 mole) and guanidine hydrochloride (2.1 g 0.022 mole) in 100 ml of absolute ethanol , the pH of the mixture is 6 .This mixture was refluxed for (6-20) hrs. at (90Co) the precipitate were filtrated and recrystallized from ethanol. all phosical properties are listed in table 1.

Table 1 : Physical properties and time of reaction of compounds [A1 – A16]

Comp. No	Compound structure	Color	Yield%	M.P	Time of reaction
A1		Greenish-Brown	74	150-152	20h
A2		Brown	72	156-158	20h
A3		Light Brown	57	176-177	6h
A4		yellow	50	173-175	5h
A5		orange	35	316-318	7h
A6		yellow	80	159-161	15h
A7		Dark yellow	54	168-170	6h
A8		yellow	50	165-167	6h
A9		Light yellow	42	147-145	6h
A10		orange	88	155-157	11h
A11		Light yellow	69	140-142	20h
A12		Brown	80	78-80	11h
A13		Brown	66	110-112	11h
A14		Light yellow	48	178-180	6h
A15		yellow	48	170-172	20h
A16		yellow	55	133-135	6h

Micro Wave –Assisted Synthesis of Pyrimidine derivatives. (19)

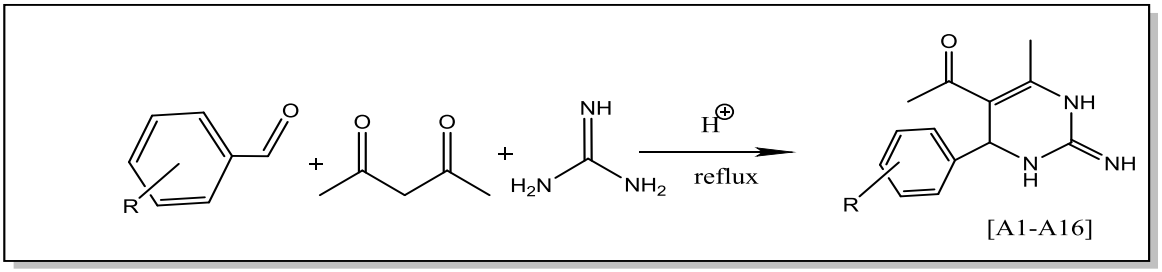
A mixture of acetylacetone (0.03 mole, 3.1 ml) with different aldehydes (0.025 mol) and guanidine hydrochloride (2.1 g ,0.022 mole) in absolute ethanol (10ml) at pH 6 was irradiated under microwave radiation for (0.39-4.00) Min. see table 2.

Table 2-a: Nomenclature, chemical formula, molecular weight and time of reaction of compounds [A1– A16]

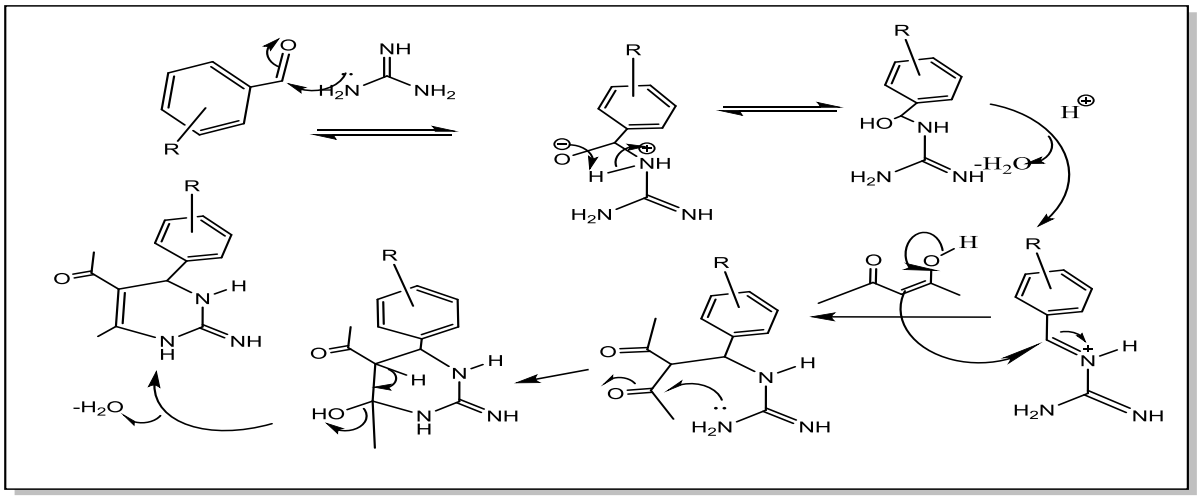
Com. No.	Name of compuonds	Chemical formula	M. wt.	Time of reaction (Min.)
A1	1-(4-(4-(dimethylamino)phenyl)-2-imino-6-methyl-1,2,3,4-tetrahydropyrimidin-5-yl)ethanone	$C_{15}H_{20}N_4O$	272.35	2:00
A2	1-(2-imino-6-methyl-4-(4-nitrophenyl)-1,2,3,4-tetrahydropyrimidin-5-yl)ethanone	$C_{13}H_{14}N_4O_3$	274.28	3:00
A3	1-(4-(2-hydroxyphenyl)-2-imino-6-methyl-1,2,3,4-tetrahydropyrimidin-5-yl)ethanon	$C_{13}H_{14}N_3O_2$	245.28	0:41
A4	1-(4-(4-chlorophenyl)-2-imino-6-methyl-1,2,3,4-tetrahydropyrimidin-5-yl)ethanone	$C_{13}H_{14}ClN_3O$	263.72	3:00
A5	1-(2-imino-6-methyl-4-(2-nitrophenyl)-1,2,3,4-tetrahydropyrimidin-5-yl)ethanone	$C_{13}H_{14}N_4O_3$	274.28	0:39
A6	1-(2-imino-6-methyl-4-phenyl-1,2,3,4-tetrahydropyrimidin-5-yl)ethanone	$C_{13}H_{15}N_3O$	229.28	0:51
A7	1-(2-imino-6-methyl-4-(2-nitrophenyl)-1,2,3,4-tetrahydropyrimidin-5-yl)ethanone	$C_{22}H_{27}O$	453.49	0:49
A8	1-(2-imino-6-methyl-4-styryl-1,2,3,4-tetrahydropyrimidin-5-yl)ethanone	$C_{15}H_{17}N_3O$	255.31	0:54
A9	1-(4-(2,3-dimethoxyphenyl)-2-imino-6-methyl-1,2,3,4-tetrahydropyrimidin-5-yl)ethanone	$C_{15}H_{17}N_3O$	289.33	1:26
A10	1-(4-(2,3-dimethoxyphenyl)-2-imino-6-methyl-1,2,3,4-tetrahydropyrimidin-5-yl)ethanone	$C_{15}H_{19}N_3O_3$	372.46	4:00
A11	1-(4-(4-bromophenyl)-2-imino-6-methyl-1,2,3,4-tetrahydropyrimidin-5-yl)ethanone	$C_{13}H_{14}N_3OBr$	308.17	0:50
A12	1-(4-(3-hydroxyphenyl)-2-imino-6-methyl-1,2,3,4-tetrahydropyrimidin-5-yl)ethanone	$C_{13}H_{14}N_3O_2$	245.28	0:48
A13	1-(4-(4-chlorophenyl)-2-imino-6-methyl-1,2,3,4-tetrahydropyrimidin-5-yl)ethanone	$C_{13}H_{14}N_3O_2$	245.28	0:46
A14	1-(2-imino-6-methyl-4-(trichloromethyl)-1,2,3,4-tetrahydropyrimidin-5-yl)ethanone	$C_8H_{10}N_3O\ Cl_3$	270.54	3:00
A15	1-(2-imino-4,6-dimethyl-1,2,3,4-tetrahydropyrimidin-5-yl)ethanone	$C_8H_{13}N_3O$	167.21	1:40
A16	1-(4-(2-bromophenyl)-2-imino-6-methyl-1,2,3,4-tetrahydropyrimidin-5-yl)ethanone	$C_{13}H_{14}N_3OBr$	308.17	2:00

Result and Discussion :

For the synthesis of the targeted different pyrimidine compounds by The Biginelli reaction which were prepared from the reaction of acetylacetone, guanidine hydrochloride and different aldehyde in the presence of HCl and absolute ethanol. As shown Eq. 1 , The mechanism involves nucleophilic attack of amino group in gouindin hydrochlorid on carbonyl group in benzaldehyde followed by elimination of water molecule. as shown in the following scheme 1



Eq 1 Preparation A1



Schem 1 The mechanism Preparation [A1-A16]

The physical properties of compound [A1] is Greenish- Brown it's color, 74% and it's M.P (150-152) Co this reaction refluxed for 20 hrs. at (90Co) ,compounds [A2-A16] were prepared in the same method.

The structures of compounds were confirmed by FT-IR, 1H-NMR, 13C-NMR and U.V spectrum. The FT-IR spectrum of compound [A1] Fig.2, table 3, 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, (3051) 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. As shown fig.2

In compound [A14] C-Cl note three bounds (555,731,844) because found Neighboring group , appearing of stretching vibration of (NH) group of amine at (3303-3400) cm-1 because found deferent Neighboring group.

By measuring the FT-IR of the pyrimidine derivatives were prepared by biginelli reaction and microwave method. Shown fig (4a),(4b)

Table 3: FT-IR spectral data of compound (A1_A16)

Comp. Code	vs N-H Amine	vs C-H Aromatic	vs C-H Aliphatic	vs C=O	vs C=N	vs C=C Arom.	$CH_3C=O$	Others
1A	3336	3051	2900	1650	1600	1550,1451,1406	1350	C-N…. 1168,1118
2A	3429	3047	2887	1676	1602	1504,1446,1400	1371	NO_2….1388,1371
3A	3385	3010	2887	1668	1645	1541,1508,1404	1340	OH…3397
4A	3398	3035	2850	1662	1641	1535,1425,1400	1300	C-Cl..852
5A	3325	3010	2980	1665	1639	1533,1458,1404	1385	NO_2…1533
6A	3387	3101	2889	1650	1639	1535,1489,1423	1360	------
7A	3392	3010	2880	1663	1639	1537,1450,1404	1380	-------
8A	3396	3010	2953	1658	1635	1577,1450,1417	1350	--------
9A	3392	3012	2978	1675	1629	1500,1450,1425	1338	C-O 1244,1271
10A	3327	------	2997	1701	1603	----------	1350	-------
11A	3346	3150	2894	1725	1700	1550,1543,1398	1325	C-Br…768
12A	3396	3030	2985	1668	1620	1581,1494,1458	1359	C-OH--3425
13A	3420	3047	2968	1676	1602	1446,1400,1388	1371	C-OH..3429
14A	3400	------	2904	1650	1612	----------	1355	C-Cl. 555,731,844
15A	3379	--------	2879	1624	1625	----------	1364	----
16A	3396	3151	2953	1732	1651	1560,1521,1448	1350	C-Br…779

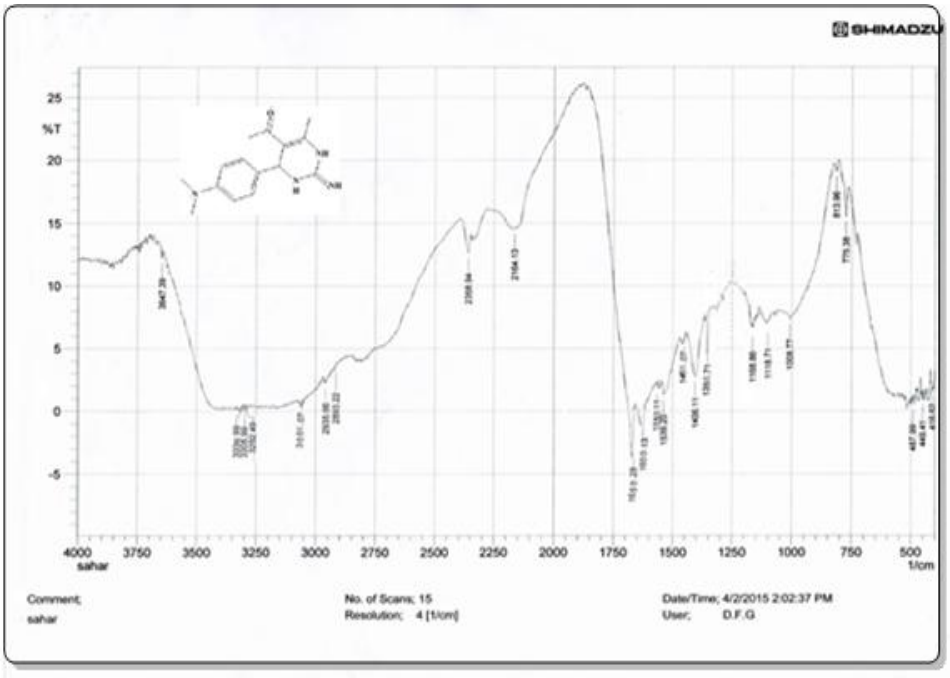


Fig 2: FT-IR spectrum for compound (A1)

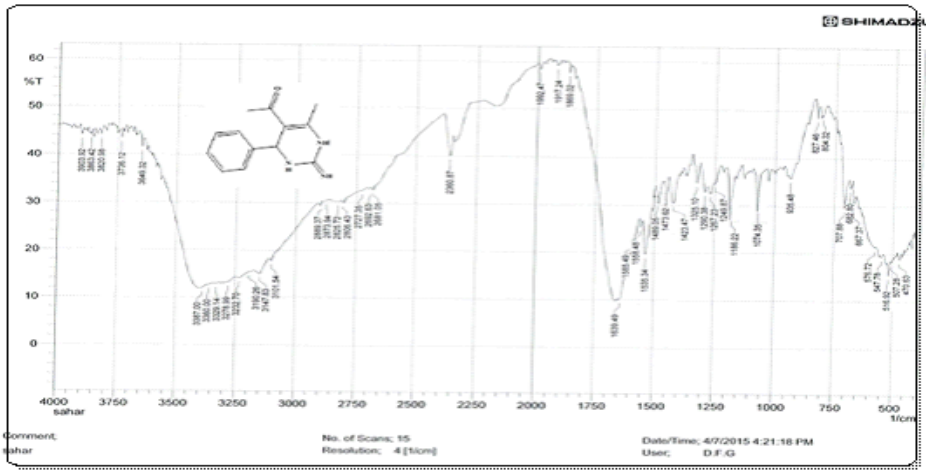


Fig 3: FT-IR spectrum for compound (A6)

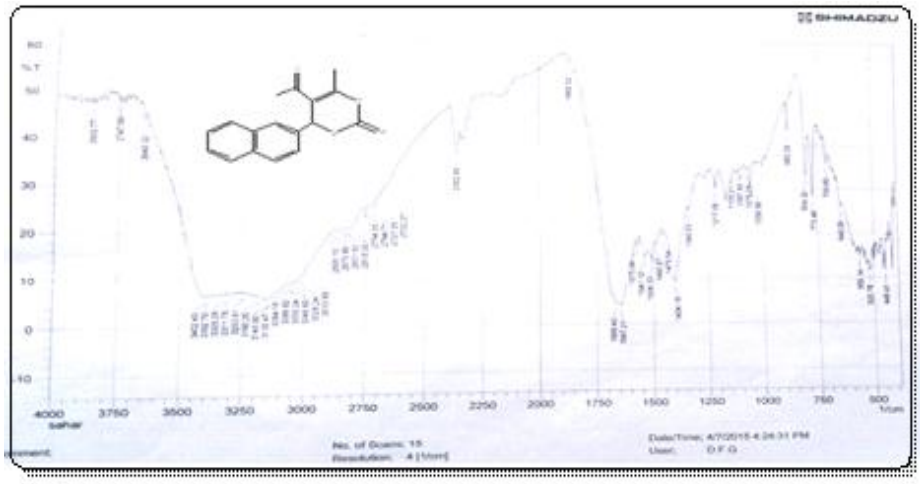


Fig (4a): FT-IR spectrum for compound [A 7] by Microwave methode

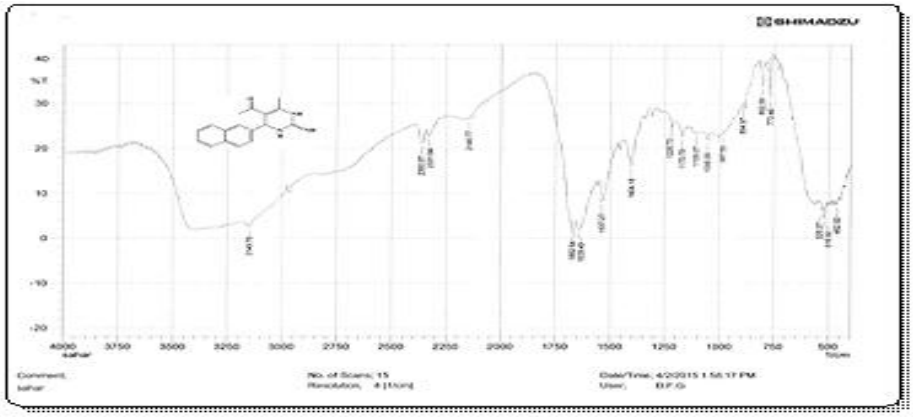


Fig (4b): FT-IR spectrum for compound [A7] Classical

In fig 4a-4b we noticed that there is matching between these peaks which mean that this method is good for the preparation but with a little differences.In the U.V visible spectra of the compounds prepared by biginelli reaction and microwave method. Shown fig 4 and 5 . We noticed that there is matching between these peaks which mean that this method is good , for the preparation but with a little differences

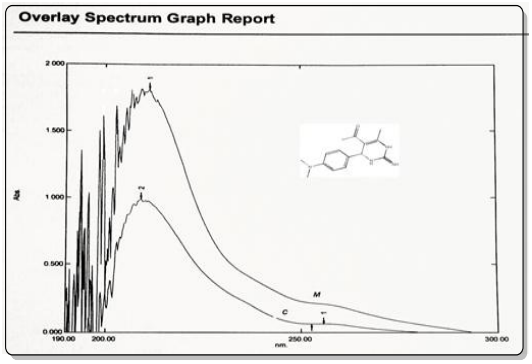


Fig 4 : U.V -Visible spectrum for compound (A1)

M – microwave C – classical

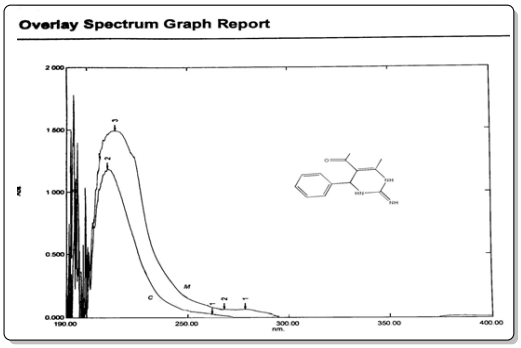
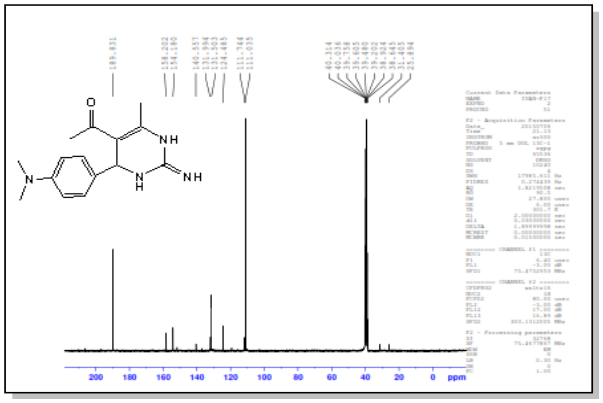


Fig 5 :U.V –Visible spectrum for compound (A6)

M – microwave C – classical

^{13}C- NMR spectrum for Compound

The 13C-NMR spectrum for the compound (A1), Fig. (6) ,shows δ= 25.8 ppm assigned to (H3C CO). Signal related to (CH3-N) was detected at δ=40.03 - 40.31 ppm ppm. Chemical shift at δ= 111.2-124 ppm assigned to (C-Ar). Chemical shift at δ=154.16 ppm assigned to (C=N). Chemical shift at δ=154.2 ppm assigned to (C=C-CH). Chemical shift at δ=189.9ppm assigned to (C=O). The solvent residual signal at δ=40.3 ppm.



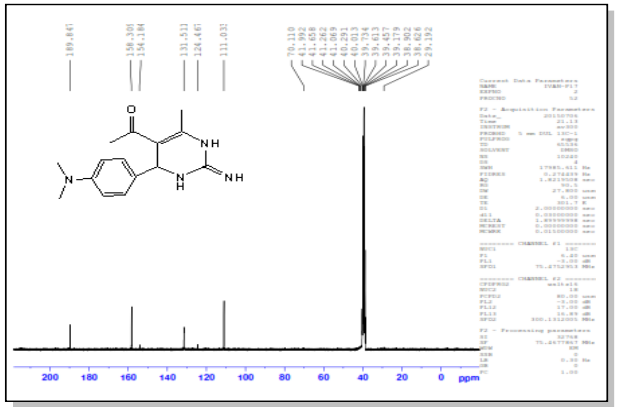


Fig.6 :^{13}C-NMR spectrum for compound (A1)
classical microwave

1H -NMR spectrum for Compouend

The 1H NMR spectrum for compound (A1), Figure (8), shows chemical shift at δ =3.038 ppm (s,3H,CH3-C=O). Signal at δ = 3.044 ppm (s, 3H,) equivalent to 3 protons has been assigned to (CH3-C=C) protons. Chemical shift at δ = 3.39 ppm (s, H,) equivalent to One protons has been assigned to (HC-NH) protons .Chemical shift at δ= 6.77-7.17 ppm assigned to aromatic para- ring substitution protons has been assigned to (d,d,4H,H-Ar) protons. Signal at δ = 7.69 ppm (s, H,) equivalent to This is due to deshielding occurred by the nitrogen atom and carbonyl group (HC-NH-C) . which decrease the electron density on the C-H moiety, and therefore appeared at higher chemical shift. The solvent residual signal at δ = 2.5 ppm is due to DMSO.

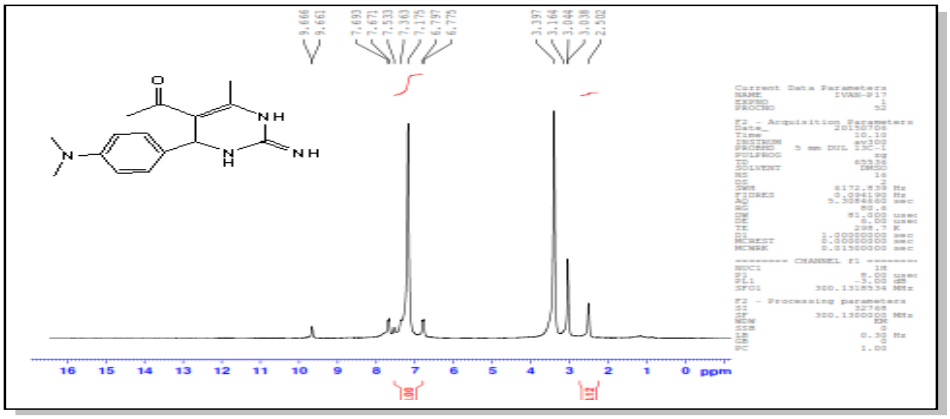


fig.(8) H1-NMR spectrum for compound (A1) microwave way

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تحضير وتشخيص مشتقات البريميدينات بواسطة الطريقة التقليدية والطريقة المايكروية

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الخلاصة

تضمن هذا البحث تحضير وتشخيص بعض مشتقات البريميدين (ألكيل.او اريل -4,3,2,1 رباعي هايدوربريمدين5-يل ايثان -1-اون) عبر تفاعل استيل اسيتون مع الديهايدات مختلفة و الكواندين هيدروكلورايد باستعمال الايثانول المطلق كمذيب من خلال تصعيد التفاعل بمده تتراوح بين (6-20) ساعة درجة الحموضة pH هو 6 وتم تحضير بريمدينات السابقة بطريقة المايكرويف ومن ثم تشخيص المركبات المحضرة من قياس درجة انصهار وأشعة تحدت الحمراء والاشعة فوق البنفسجية والبعض منها الرنين النووي المغناطيسي لنوى الهيدروجين (1H-NMR) والرنين النووي المغناطيسي لذرة الكاربون 13 (13C-NMR) .