

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

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## ARTICLE INFO

Received: 03 / 08 /2016

Accepted: 05 / 01 /2017

Available online: 28/10/2017

DOI: 10.37652/juaps.2016.132439

### Keywords:

Preparation ,  
Diagnosis ,  
Pyrimidines,  
Conventional ,  
microwave Ways.

## 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 <sup>1</sup>H-NMR and <sup>13</sup>C-NMR spectroscopy.

## 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

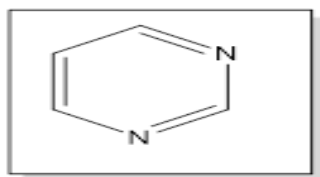


Fig 1: The basic skeleton of a pyrimidine ring

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-

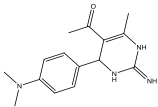
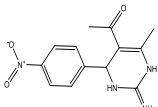
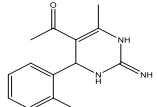
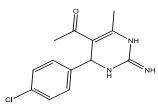
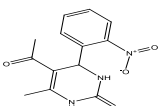
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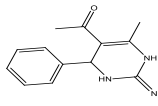
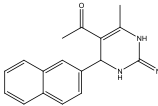
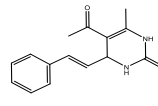
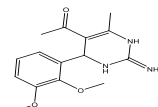
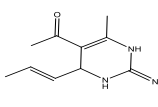
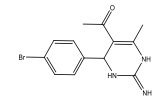
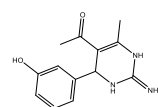
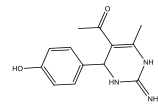
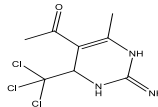
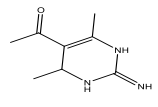
enal, 4-Bromo Benzaldehyde, 3-Hydroxy Benzaldehyde , Tri Chloro Acetaldehyde, Acetaldehyde solution, 2-Bromo Benzaldehyde ) ethanol absolute and HCl.

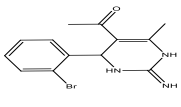
### 2.2 Prepare derivative pyrimidines (18)

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
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### 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]

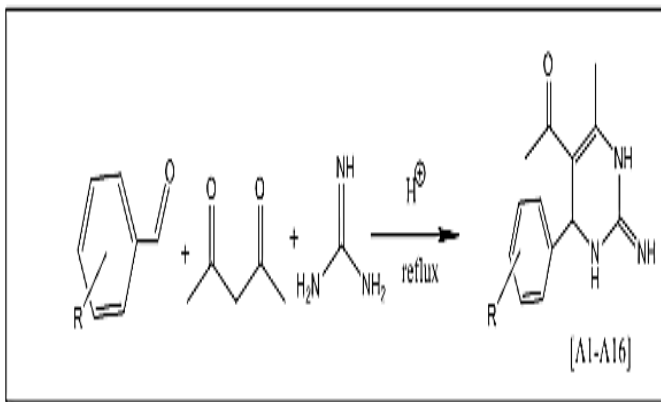
Com. No.	Name of compounds	Chemical formula	M. wt.	Time of reaction (Min.)
A1	1-(4-(4-(dimethylamino)phenyl)-2-imino-6-methyl-1,2,3,4-tetrahydropyrimidin-5-yl)ethanone	C <sub>15</sub> H <sub>20</sub> N <sub>4</sub> O	272.35	2:00
A2	1-(2-imino-6-methyl-4-(4-nitrophenyl)-1,2,3,4-tetrahydropyrimidin-5-yl)ethanone	C <sub>13</sub> H <sub>14</sub> N <sub>4</sub> O <sub>3</sub>	274.28	3:00
A3	1-(4-(2-hydroxyphenyl)-2-imino-6-methyl-1,2,3,4-tetrahydropyrimidin-5-yl)ethanone	C <sub>13</sub> H <sub>14</sub> N <sub>3</sub> O <sub>2</sub>	245.28	0:41
A4	1-(4-(4-chlorophenyl)-2-imino-6-methyl-1,2,3,4-tetrahydropyrimidin-5-yl)ethanone	C <sub>13</sub> H <sub>14</sub> ClN <sub>3</sub> O	263.72	3:00
A5	1-(2-imino-6-methyl-4-(2-nitrophenyl)-1,2,3,4-tetrahydropyrimidin-5-yl)ethanone	C <sub>13</sub> H <sub>14</sub> N <sub>4</sub> O <sub>3</sub>	274.28	0:39

A6	1-(2-imino-6-methyl-4-phenyl-1,2,3,4-tetrahydropyrimidin-5-yl)ethanone	C <sub>13</sub> H <sub>15</sub> N <sub>3</sub> O	229.28	0:51
A7	1-(2-imino-6-methyl-4-(2-nitrophenyl)-1,2,3,4-tetrahydropyrimidin-5-yl)ethanone	C <sub>22</sub> H <sub>27</sub> O	453.49	0:49
A8	1-(2-imino-6-methyl-4-styryl-1,2,3,4-tetrahydropyrimidin-5-yl)ethanone	C <sub>15</sub> H <sub>17</sub> N <sub>3</sub> O	255.31	0:54
A9	1-(4-(2,3-dimethoxyphenyl)-2-imino-6-methyl-1,2,3,4-tetrahydropyrimidin-5-yl)ethanone	C <sub>15</sub> H <sub>17</sub> N <sub>3</sub> O	289.33	1:26
A10	1-(4-(2,3-dimethoxyphenyl)-2-imino-6-methyl-1,2,3,4-tetrahydropyrimidin-5-yl)ethanone	C <sub>15</sub> H <sub>19</sub> N <sub>3</sub> O <sub>3</sub>	372.46	4:00
A11	1-(4-(4-bromophenyl)-2-imino-6-methyl-1,2,3,4-tetrahydropyrimidin-5-yl)ethanone	C <sub>13</sub> H <sub>14</sub> N <sub>3</sub> OBr	308.17	0:50
A12	1-(4-(3-hydroxyphenyl)-2-imino-6-methyl-1,2,3,4-tetrahydropyrimidin-5-yl)ethanone	C <sub>13</sub> H <sub>14</sub> N <sub>3</sub> O <sub>2</sub>	245.28	0:48
A13	1-(4-(4-chlorophenyl)-2-imino-6-methyl-1,2,3,4-tetrahydropyrimidin-5-yl)ethanone	C <sub>13</sub> H <sub>14</sub> N <sub>3</sub> O <sub>2</sub>	245.28	0:46
A14	1-(2-imino-6-methyl-4-(trichloromethyl)-1,2,3,4-tetrahydropyrimidin-5-yl)ethanone	C <sub>8</sub> H <sub>10</sub> N <sub>3</sub> OCl <sub>3</sub>	270.54	3:00
A15	1-(2-imino-4,6-dimethyl-1,2,3,4-tetrahydropyrimidin-5-yl)ethanone	C <sub>8</sub> H <sub>13</sub> N <sub>3</sub> O	167.21	1:40

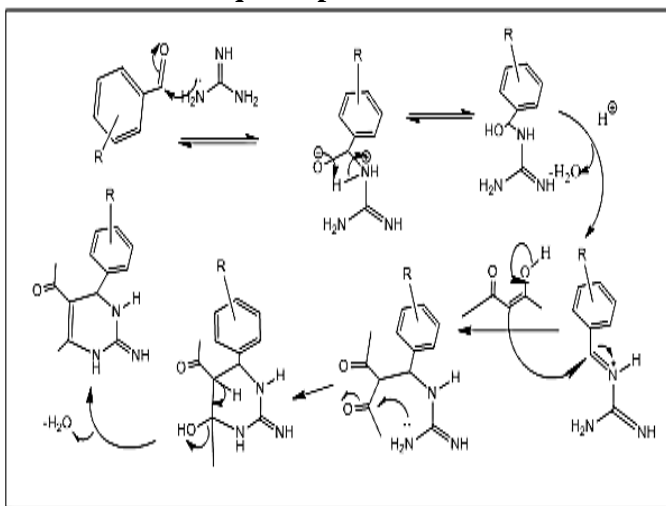
A16	1-(4-(2-bromophenyl)-2-imino-6-methyl-1,2,3,4-tetrahydropyrimidin-5-yl)ethanone	C <sub>13</sub> H <sub>14</sub> N <sub>3</sub> OBr	308.17	2:00
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### Result and Discussion :

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	Ns N-H Amine	vs C-H Aromatic	vs C-H Aliphatic	vs C=O	vs C=N	vs C=C Arom.	CH <sub>3</sub> C=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 <sub>2</sub> ....1388,1371

11A	10A	9A	8A	7A	6A	5A	4A	3A
3346	3327	3392	3396	3392	3387	3325	3398	3385
3150	-----	3012	3010	3010	3101	3010	3035	3010
2894	2997	2978	2953	2880	2889	2980	2850	2887
1725	1701	1675	1658	1663	1650	1665	1662	1668
1700	1603	1629	1635	1639	1639	1639	1641	1645
1550,1543,1398	-----	1500,1450,1425	1577,1450,1417	1537,1450,1404	1535,1489,1423	1533,1458,1404	1535,1425,1400	1541,1508,1404
1325	1350	1338	1350	1380	1360	1385	1300	1340
C-Br...768	-----	C-O 1244,1271	-----	-----	-----	NO <sub>2</sub> ...1533	C-Cl...852	OH...3397

16A	15A	14A	13A	12A
3396	3379	3400	3420	3396
3151	-----	-----	3047	3030
2953	2879	2904	2968	2985
1732	1624	1650	1676	1668
1651	1625	1612	1602	1620
1560,1521,1448	-----	-----	1446,1400,1388	1581,1494,1458
1350	1364	1355	1371	1359
C-Br...779	----	C-Cl 555,731,844	C-OH...3429	C-OH--3425

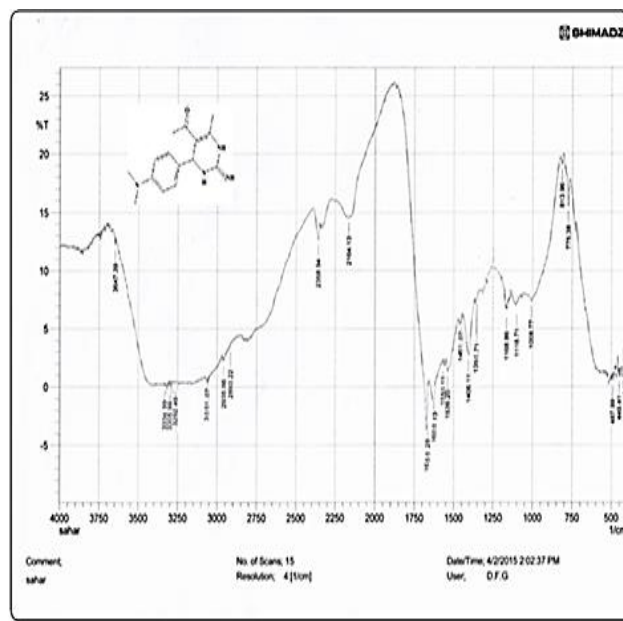


Fig 2: FT-IR spectrum for compound (A1)

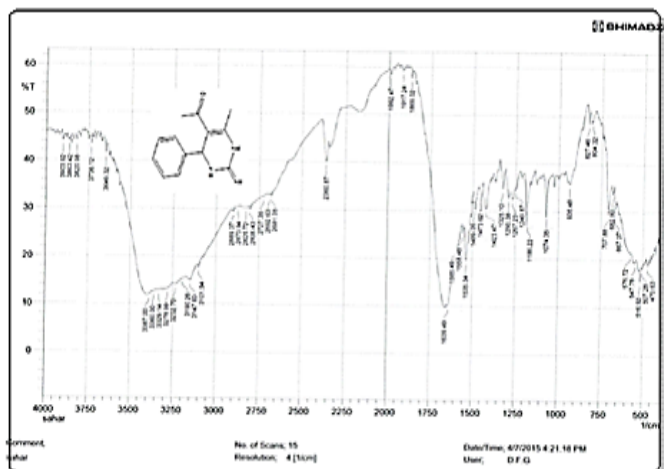


Fig 3: FT-IR spectrum for compound (A6)

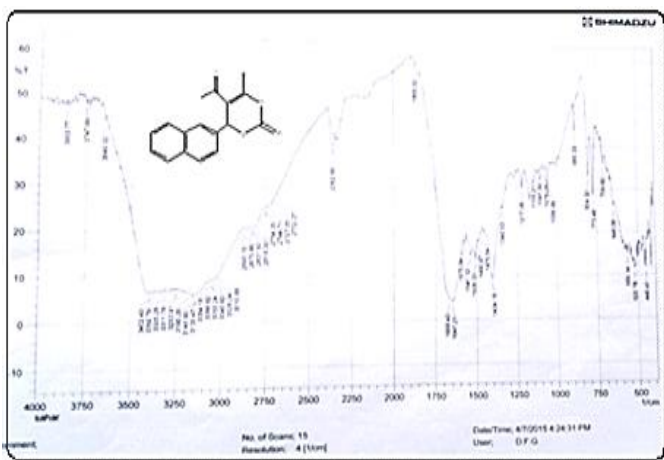


Fig (4a): FT-IR spectrum for compound [A 7] by Microwave methode

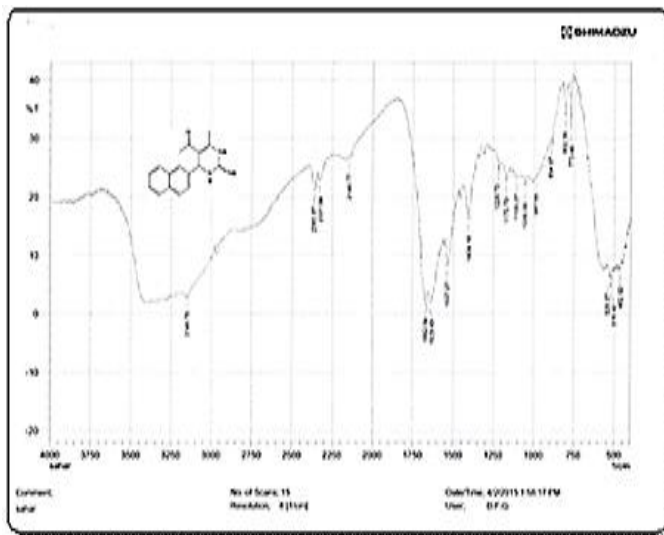


Fig (4b): FT-IR spectrum for compound [A7] Classical

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.

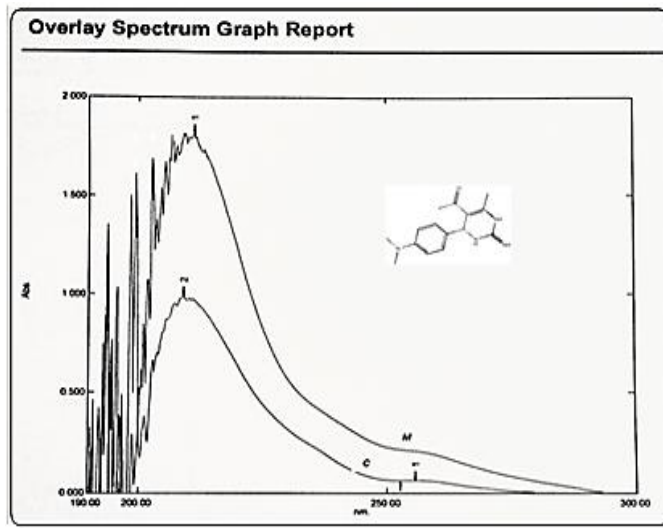


Fig 4 : U.V -Visible spectrum for compound (A1)  
 M – microwave C – classical

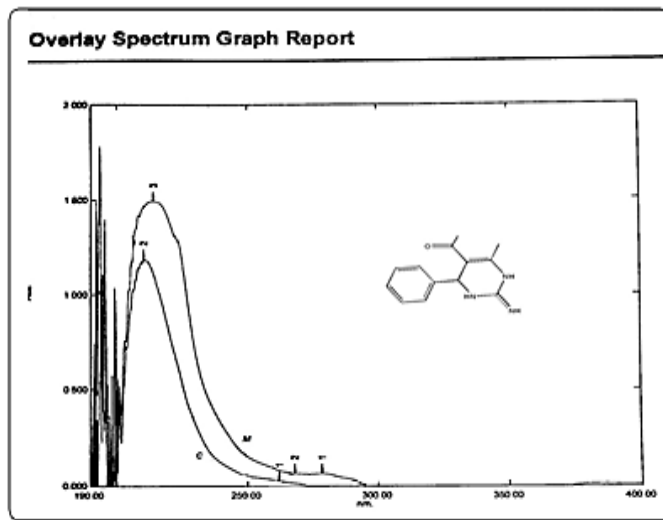


Fig 5 :U.V –Visible spectrum for compound (A6)  
 M – microwave C – classical

**<sup>13</sup>C- NMR spectrum for Compound**

The <sup>13</sup>C-NMR spectrum for the compound (A1), Fig. (6) ,shows  $\delta = 25.8$  ppm assigned to (H<sub>3</sub>C CO). Signal related to (CH<sub>3</sub>-N) was detected at  $\delta = 40.03 - 40.31$  ppm. Chemical shift at  $\delta = 111.2-124$  ppm



assigned to (C-Ar). Chemical shift at  $\delta=154.16$  ppm assigned to (C=N). Chemical shift at  $\delta=154.2$  ppm assigned to (C=C-CH). Chemical shift at  $\delta=189.9$ ppm assigned to (C=O). The solvent residual signal at  $\delta=40.3$  ppm.

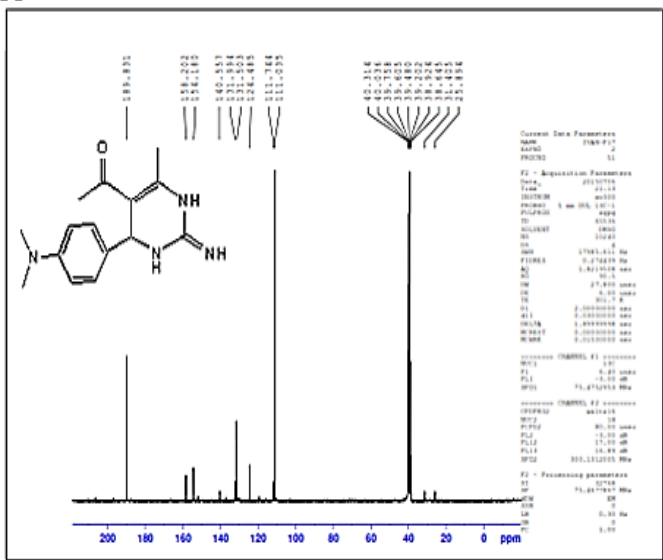
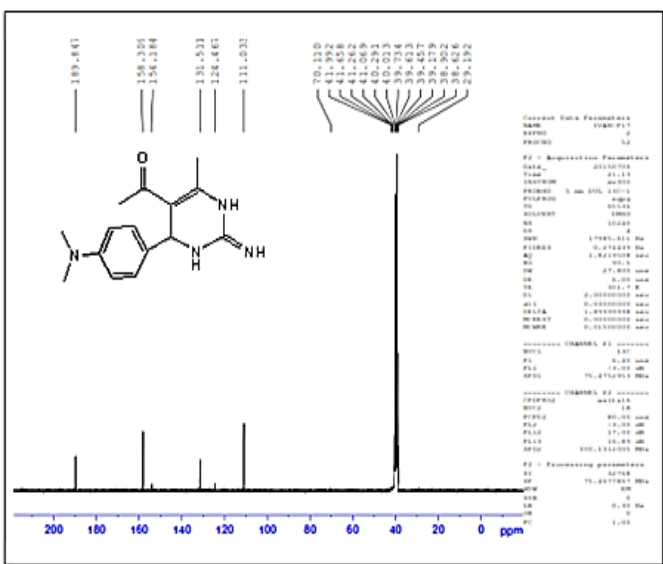


Fig.6 :<sup>13</sup>C-NMR spectrum for compound (A1)  
classical microwave

### <sup>1</sup>H -NMR spectrum for Compound

The <sup>1</sup>H NMR spectrum for compound (A1), Figure (8), shows chemical shift at  $\delta = 3.038$  ppm (s,3H,CH<sub>3</sub>-C=O). Signal at  $\delta = 3.044$  ppm (s, 3H,) equivalent to 3 protons has been assigned to (CH<sub>3</sub>-C=C) protons. Chemical shift at  $\delta = 3.39$  ppm (s, H,) equivalent to One protons has been assigned to



(HC-NH) protons .Chemical shift at  $\delta= 6.77-7.17$  ppm assigned to aromatic para- ring substitution protons has been assigned to (d,d,4H,H-Ar) protons. Signal at  $\delta = 7.69$  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  $\delta = 2.5$  ppm is due to DMSO.

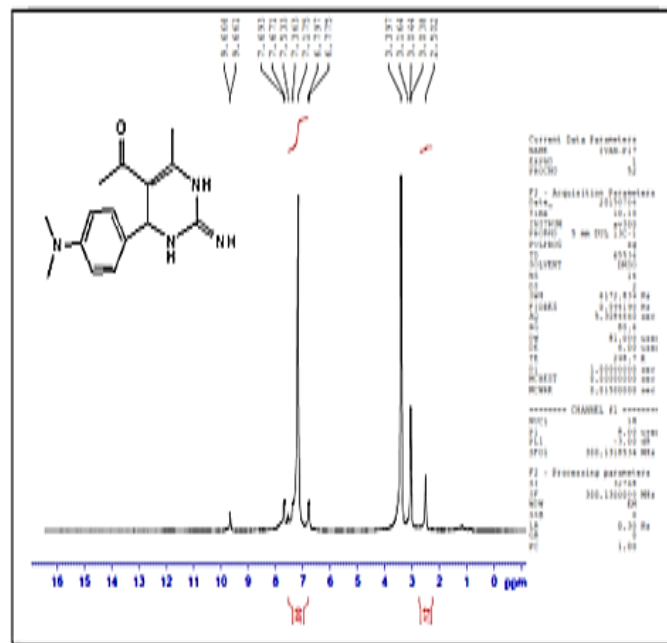


Fig.(8) H1-NMR spectrum for compound (A1)  
microwave way

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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 -1,2,3,4 رباعي هايدوربريميدين-5-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 تحدد الحمراء والاشعة فوق البنفسجية والبعض منها الرنين النووي المغناطيسي لنوى الهيدروجين (1H-NMR) والرنين النووي المغناطيسي لذرة الكربون 13C-13 (NMR) .