Synthesis and Characterization of Some New Bis-(Dihydropyrimidinones-5-Carboxamide) by Using Ultrasonic Irradiation

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Received: April 19, 2018 Accepted: May 28, 2018 Online Published: June 1, 2018

doi: 10.23918/eajse.v3i3p132

Abstract: This investigation involves synthesis of two new series of bis-dihydropyrimidinone-5-carboxamides (4 a-k) and (5 a-k) from reaction of 6-methyl-2-oxo-4-phenyl-1,2,3,4-tetra-hydropyrimidine-5-carbonyl chloride and its derivatives (3 a, b) with different diamines using ultrasonic irradiation. Compounds (3a, b) were synthesized from chlorination of 6-methyl-2-oxo-4-phenyl-1,2,3,4-tetrahydropyrimidine-5-carboxylic acid and its derivatives (2a,b) which were prepared from hydrolysis of ethyl-6-methyl-2-oxo-4-phenyl-1,2,3,4-tetrahydropyrimi-dine-5-carbo-xylate and its derivatives (1a, b) which was synthesized by one-pot Biginelli condensation. The synthesized products were characterized by physico-chemical methods such as elemental analysis (CHNS-O), FT-IR, ^{1}H-NMR and ^{13}C-NMR. The prepared compounds were showed biological activity against two types of bacterial Escherichia coli Gram-negative bacteria (G -ve) and Staphylococcus aureas Gram-positive bacteria (G +ve).

Keywords: Dihydropyrimidinone, Biginelli Condensation, Ultrasonic, Hydrolysis, Catalytic Reaction

1. Introduction

Dihydropyrimidinones and their derivatives have attracted increasing interest, which are the core unit in several biological active marine alkaloids (Snidar & Shi, 1993; Patil et al., 1995; Kashman et al., 1989) among them the most potent are the erambine (Snider & Shi, 1993) and batzelladine alkaloids (Patil et al., 1995). These compounds have emerged as important target molecules due to their therapeutic and pharmacological properties (Kappe, 2000) such as antiviral (Hurst and Hull, 2000), antitumor (Hattori et al., 1961; Tawfik et al., 2009), antimitotic (Mayer et al., 1999), anticarcinogenic (Rovnyak et al., 1995), and antibacterial (Dong et al., 2007).

Organic compounds containing dihydropyrimidinones as a core unit show excellent calcium channel modulation (Singh et al., 2009) due to their therapeutic application. Different strategies have been employed for the synthesis of dihydropyrimidinones and several protocols have been reported (Salehi et al., 2003; Narsaiah et al., 2004). However, some of the methods employed have drawback

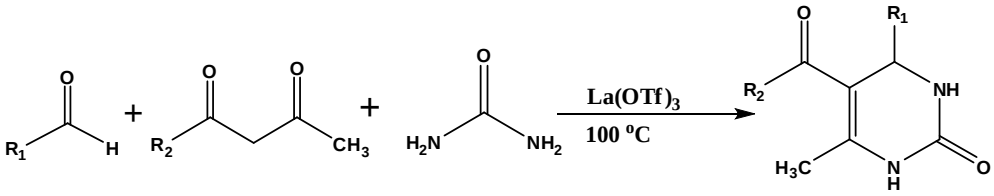
attention of researchers to the use of strongly acidic conditions (Hu et al.,1998), the use of the protic acids (Lu & Ma, 2000) and prolonged reaction times for the preparation.

Several methods for the preparation of dihydropyrimidinone have previously been developed to improve and modify this reaction by microwave (Stadler & Kappe, 2001), infrared radiation (Osnaya et al., 2003), and ultrasound irradiation (Zhidovinova et al., 2003) and by using Lewis acids (Carlos et al., 2007; Chitra & Pandiarajan, 2009; Zhu et al., 2006; Chen et al., 2007).

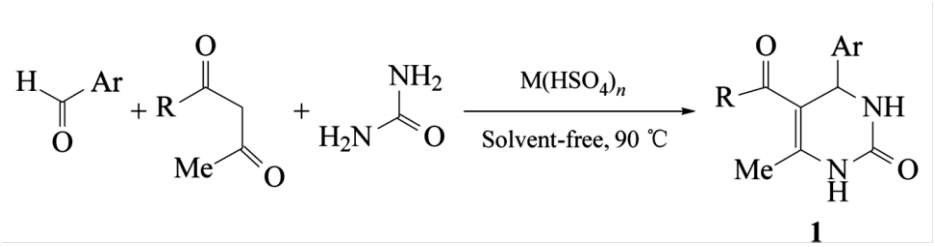
In the present work two new series of bis-dihydropyrimidi-none-5-carboxamides (4 a-k) and (5 a-k) were prepared by using ultrasonic technique. To the best of our knowledge of the open literature, these compounds have not been reported.

2. Literature Review

Various substituted 3,4-dihydropyrimidn-2-one were synthesized in one-pot reaction of aldehydes, β-ketoesters and urea using KBr in THF without any side reactions (Baruah et al., 2002), and under solvent-free conditions using lanthanide triflate as catalyst (Ma et al., 2000) (Scheme 1).



Metal hydrogen sulphate M $(HSO_4)_4$ [$Ca(HSO_4)_2$ and $Zn(HSO_4)_2$] were used to catalyze one-pot three-component condensation reactions of aldehydes , 1,3-dicarbonyl compounds and urea at 90 ^{0}C under solvent-free conditions and high yields (Khodabakhsh et al., 2007) (Scheme 2).



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Ar: C_6H_5, 4-Cl-C_6H_4, R: OC_2H_5 , CH_3

3. Experimental

Melting points were measured using Gallinkamp electrothermal 9100 melting point apparatus and are uncorrected. IR spectra were obtained on a Thermo-Mattson IR-300 spectropohotometer using KBr disk for solid materials, ^{1}H NMR and ^{13}C NMR spectra were recorded on the Bruker ultra shield 300 MHz in DMSO. Elemental analysis was obtained using Eurovector EA300A instrument, the sonication was an UltraMet Sonic Cleaner Buehler Ltd. (220/240V, 50/60Hz). TLC was carried on using precoated DC-plastic foli silica gel 60F.

Preparation of ethyl 6-methyl-2-oxo-4-phenyl-1,2,3,4-tetrahydropyri-midine-5-carboxylate and its derivatives (1a,b) under classical method and ultrasonic waves by using different catalysts :

Using HCl as catalyst:

To a mixture of benzaldehyde or 4-nitro benzaldehyde (0.01mol), urea (0.01mol, 0.6g) and ethyl acetoacetate (0.01mol, 1.26ml) in 10ml ethanol, (1-2drops) of conc. HCl was added as a catalyst.

In classical method:

The mixture was refluxed for 7-8 hours, the reaction was monitored by TLC. After cooling the precipitate was filtered and washed with water then recrystallized from ethanol to get the pure product.

Compound (1a): The yield is 45%, (m.p 202-203ºC), R_f = 0.75 [Chloroform: Ethyl acetate (3:1)], reaction time (9h).

Compound (1b): The yield is 42%, (m.p 207-208ºC), R_f = 0.38 [Chloroform: Ethyl acetate (3:1)], reaction time (10h).

In ultrasonic waves (Zhidovinova et al., 2003):

The mixture was sonicated in ultrasonic bath reactor at room temperature for (5-10) min. (Sonication was continued until the benzaldehyde disappeared, as indicated by TLC). After completion of the reaction, the crude product, which precipitated on standing, was filtered and washed with water then recrystallized from ethanol to get the pure product.

Compound (1a): The yield is 95%, reaction time (5 min.); Anal. Calcd for $C_{14}H_{16}N_2O_3$: C, 64.54; H, 6.15; N, 10.75.

Found: C, 64.1; H, 6.29; N, 10.4

Compound (1b): The yield is 91%, reaction time (10 min.).

The above procedures were followed to four other catalysts [LiBr (0.09 g, NH_4Cl (0.25 g), I_2 (3 g) and $LaCl_3$ (1.85 g)] the obtained results are shown in Table 1.

Preparation of 6-methyl-2-oxo-4-phenyl-1,2,3,4-tetrahydro-pyrimidine-5-carboxylic acid and its derivatives (2a,b) (Mehta et al. 1971):

A stirring mixture of compound (1a) or (1b) (0.005 mol) and sodium hydroxide (5% solution, 10ml) was refluxed for 7-7.5 hours. After cooling, the solution was acidified with hydrochloric acid and the precipitate was filtered then recrystallized from ethanol or [ethyl acetate: n-hexane (1:1)].

Compound (2a): The yield is 80 %,(m.p 221-223ºC), reaction time (7h), recrystallized from ethanol.

Compound (2b): The yield is 78 %,(m.p 227-229 ºC), reaction time (7.5h), recrystallized from [ethyl acetate: n-hexane (1:1)].

Preparation of 6-methyl-2-oxo-4-phenyl-1,2,3,4 tetrahydro-pyrimid-ine-5-carbonyl chloride and its

derivatives (3a,b):

A mixture of compound (2a) or (2b) (0.005 mol) and thionyl chloride ($SOCl_2$) (10ml) was refluxed gently for 7-8 hours (the reaction was monitored by TLC). Excess thionyl chloride was removed under vacuum and the precipitate was collected, dried under vacuum then recrystallized from [chloroform or ethyl acetate: n-hexane (1:1) (Bose et al., 2003).

Compound (3a): The yield is 72 %, (m.p 171-173 ^oC), R_f=0.4 [Chloroform: Ethyl acetate (3:1)], reaction time (7h), recrystallized from chloroform.

Compound (3b): The yield is 70 %, (m.p 165-167 ^oC), R_f=0.4 [Chloroform: Ethyl acetate (3:1)], reaction time (8h), recrystallized from ethyl acetate: n-hexane (1:1)

General procedure for preparation of N, N'-(substituted)-bis-(6- methyl – 4 - (4-substituted phenyl)-3,4 dihydropyri-midinone-5-carboxamide) (4a-k) or (5a-k):

According to the modified procedure (Kim & Jing, 2009), to a stirring solution of compound (3a) or (3b) (0.002 mol) in toluene (20ml), a solution of different diamines (0.001mol) was added drop wise. The mixture was sonicated in a water bath of an ultrasonic cleaner, after completion of the reaction (25-45 min.), the reaction mixture was diluted with toluene and washed with hydrochloric acid (0.01M). The organic layer was washed with a solution of (%5 Na_2CO_3) then with water. The organic layer was separated, cooled and the solid desired product was filtered, dried and recrystallized from ethanol or methanol.

Compound (4a-k): recrystallized from ethanol.

Compound 4a; Anal. Calcd for $C_{38}H_{36}N_6O_4$: C, 71.2; H, 5.6; N, 13.1. Found: C, 72.3; H, 6.08; N, 13.8.

Compound 4b; Anal. Calcd for $C_{37}H_{34}N_6O_4$: C, 70.9; H, 5.4; N, 13.4. Found: C, 69.5; H, 5.6; N, 14.4.

Compound 4c; Anal. Calcd for $C_{26}H_{28}N_6O_4$: C, 63.9; H, 5.7; N, 17.2. Found: C, 64.5; H, 6.2; N, 16.8.

Compound (5a-k): recrystallized from methanol.

Compound 5b; Anal. Calcd for $C_{37}H_{32}N_8O_8$: C, 62.01; H, 4.5; N, 15.6. Found: C, 61.7; H, 5.2; N, 15.2.

Determination of antimicrobial activity:

1. The culture medium (Muller-Hinton agar) was prepared, and poured in Petri dish to a depth of 4mm.

2. Activation of the bacteria (*S-aurous* and *E-coli*) before culturing on the nutrient agar in nutrient broth which was used for dilution of bacteria and cultivation of culture incubated for (24h) in 37 ^oC.

3. Muller-Hinton agar streaked with bacteria, the pores filled by extracts, then incubated at 37 ^oC

for (24 h).

4. Reading of the zone inhibition. The larger zone of inhibition represented by more +ve but the unaffected zone represented by–ve this was interpreted by national committed for clinical laboratory.

4. Result and Discussion

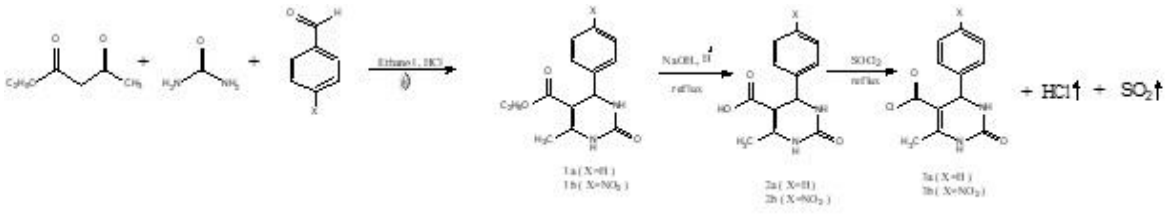
The started compounds (1 a, b) were obtained through Biginelli three components condensation of benzaldehyde or 4-nitrobenzaldehyde, ethyl acetoacetate and urea in ethanol using five different catalysts (HCl, LiBr, NH_4Cl, I_2 and $LaCl_3$) (Table 1) via both classical and ultrasonic technique (Scheme 3). In classical method the compounds (1 a,b) were produced in low yields and long reaction time while in the ultrasonic irradiation they were produced in higher yields and shorter time.The products were characterized by spectral methods (Table 3,4, and 5).

Table 1: Percentage of yield obtained of prepared compounds (1a, b) from both ultrasonic and classical methods

Compounds	**Catalysts**	**Solvents**	**Classical Method**		**Ultrasonic wave Method**	
			Yield, %	Yield, %	Yield, %	Yield, %
1a	HCl	Ethanol	45	9	95	5
1b			42	10	91	10
1a	LiBr	Acetonitrile	68	4.5	85	20
1b			65	5	84	25
1a	NH_4Cl	Ethanol	70	4.5	88	25
1b			67	5	85	30
1a	I_2	Toluene	60	5	80	20
1b			56	5.5	75	30
1a	$LaCl_3$	Ethanol	82	6	90	25
1b			80	6.5	87	30

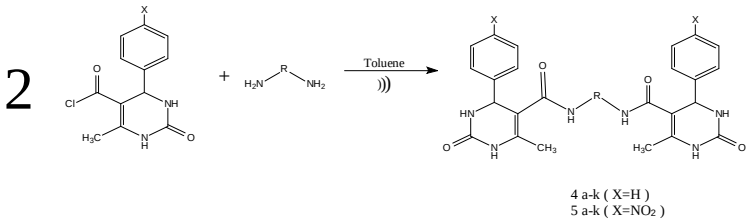
Preparation of (2a and 2b) was produced in high yields by hydrolysis of compounds (1a and 1b) respectively with sodium hydroxide by refluxing. After cooling, the solution was acidified with hydrochloric acid (Scheme 3). The spectral methods IR, ^{1}H-NMR and ^{13}C-NMR were utilized for structured determination of compound (2a and 2b) (Tables 3, 4, and 5).

The reaction of compounds (2a and 2b) with thionyl chloride yielded acid chlorides (3a and 3b) by gently refluxing. Excess thionyl chloride was removed under vacuum and the solid products were recrystallized from dry [chloroform or ethyl acetate: n-hexane (1:1)] to give pure compounds (3a) and (3b) respectively. Structures of the compounds (3a and 3b) were elucidated by using spectral methods IR, ^{1}H-NMR and ^{13}C-NMR (Tables 3, 4, and 5).



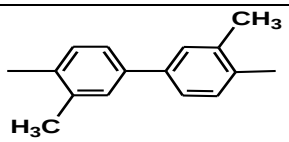
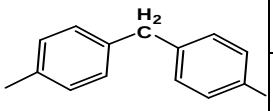
(Scheme 3)

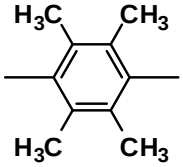
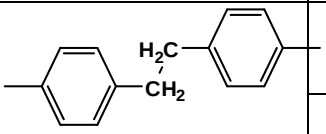
The sonication of compounds 6-methyl-4-(4-substituted phenyl)-3,4-dihydro-pyrimidin-2(1H)-one-5-carbonyl chloride (3a,b) with different diamines in ultrasonic bath yield N,N`-substituted-bis-(6-methyl-4-(4-substituted phenyl)-3,4-dihydro pyrimidin-2(1H)-one-5-carboxamide (4a-k and 5a-k) (Table 2) (Scheme 4).

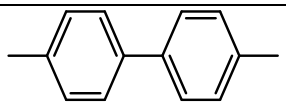
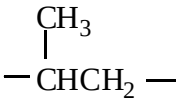
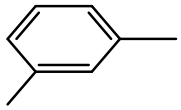


(Scheme 4)

Table 2: Some physical properties for prepared compounds (4a-k and 5a-k)

Compounds	R	Molecular formula	Reaction time(min.)	Yield%	m.p.(°C)	R_f (Chloroform:Ethylacetate 3:1)
4a		$C_{38}H_{36}N_6O_4$	40	75	182-184	0.40
5a		$C_{38}H_{34}N_8O_8$	40	72	191-193	0.39
4b		$C_{37}H_{34}N_6O_4$	35	76	189-190	0.47
5b		$C_{37}H_{32}N_8O_8$	40	75	218-220	0.55
4c	$-CH_2CH_2-$	$C_{26}H_{28}N_6O_4$	25	84	159-160	0.49
5c		$C_{26}H_{26}N_8O_8$	30	80	183-184	0.45
4d		$C_{30}H_{28}N_6O_4$	35	79	176-177	0.51
5d		$C_{30}H_{26}N_8O_8$	35	76	189-191	0.32

4e	$-(CH_2)_{10}-$	$C_{34}H_{44}N_6O_4$	30	73	156-158	0.55
5e		$C_{34}H_{42}N_8O_8$	35	77	161-163	0.36
4f		$C_{34}H_{36}N_6O_4$	35	79	180-182	0.50
5f		$C_{34}H_{34}N_8O_8$	35	76	195-197	0.42
4g	$-(CH_2)_{12}-$	$C_{36}H_{48}N_6O_4$	30	69	153-155	0.47
5g		$C_{36}H_{46}N_8O_8$	35	65	177-179	0.37
4h		$C_{38}H_{36}N_6O_4$	40	70	208-209.5	0.43
5h		$C_{38}H_{34}N_8O_8$	35	69	215.5-217	0.42

4i		$C_{36}H_{32}N_6O_4$	35	72	211-213	0.46
5i		$C_{36}H_{30}N_8O_8$	35	71	217-219	0.34
4j		$C_{27}H_{30}N_6O_4$	25	76	179-180	0.39
5j		$C_{27}H_{28}N_8O_8$	35	72	186-187	0.38
4k		$C_{30}H_{28}N_6O_4$	45	59	213-215	0.41
5k		$C_{30}H_{26}N_8O_8$	45	53	227-229	0.43

For synthesis of bis-(3, 4-dihydropyrimidinone-5-carbox-amide), one equivalent of diamines and two equivalents of dihydropyrimidinones-5-carbonyl chloride was used. A variety of substituted diamines provided favorable results in this reaction. The synthesis compounds (4a-k) and (5a-k) were characterized by IR, ^{1}H-NMR and ^{13}C-NMR (Table 3, 4 and 5).

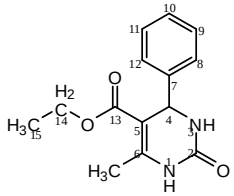
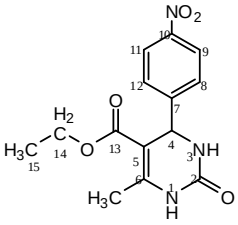
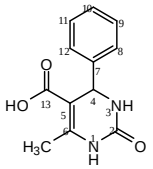
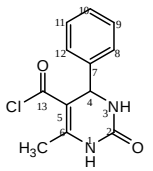
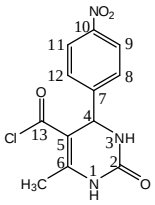
Table 3: Assignment of characteristic frequencies (cm-1) of IR data for the prepared compounds

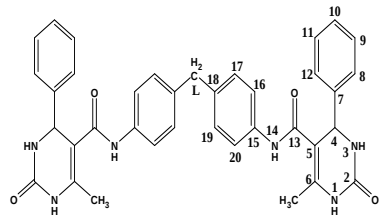
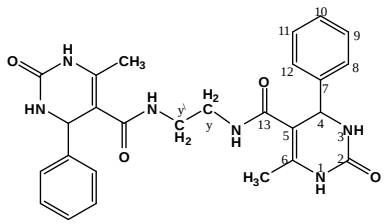
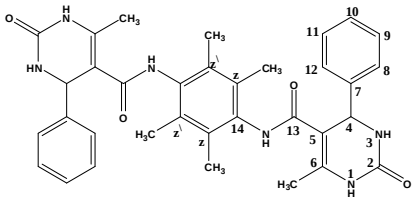
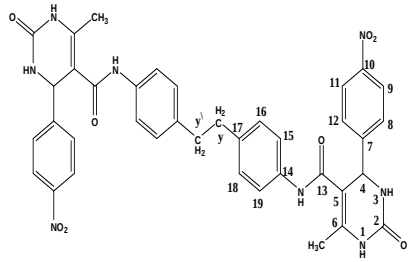
Compounds	O-H str.	N-H str. Amide	C-H str. Arom.	C-H str. Aliph.	C=O str. Ester, Carboxylic acid , Acid chloride	C=O str Amide	N-H def.	C=C str.	NO_2 str.	
									Assym.	Symm.
1a	-	3242	3116	2978	1724	1702	1648	1599	-	-
1b	-	3233	3116	2976	1729	1699	1645	1606	1520	1349
2a	2600-3500	3244	3112	2978	1720	1703	1647	1599	-	-
2b	2600-3500	3210	3060	2920	1720	1697	1647	1608	1520	1349
3a	-	3249	3107	2957	1809	1694	1646	1610	-	-
3b	-	3242	3110	2977	1807	1698	1648	1607	1520	1348
4a	-	3210	3060	2920	-	1690	1633	1618	-	-
4b	-	3234	3062	2924	-	1690	1637	1612	-	-
4c	-	3233	3101	2932	-	1691	1640	1615	-	-
4d	-	3230	3101	2977	-	1697	1641	1622	-	-
4e	-	3227	3053	2928	-	1691	1647	1605	-	-
4f	-	3238	3115	2926	-	1691	1652	1620	-	-
4g	-	3227	3064	2917	-	1691	1639	1595	-	-
4h	-	3208	3030	2915	-	1692	1638	1597	-	-
4i	-	3230	3087	2924	-	1689	1635	1613	-	-
4j	-	3230	3091	2927	-	1691	1653	1623	-	-
4k	-	3231	3086	2922	-	1688	1634	1624	-	-
5a	-	3239	3110	2926	-	1698	1637	1612	1520	1347
5b	-	3244	3119	2928	-	1690	1645	1603	1521	1348
5c	-	3232	3054	2912	-	1698	1637	1618	1520	1348
5d	-	3244	3119	2928	-	1699	1645	1622	1521	1348
5e	-	3234	3108	2928	-	1690	1637	1604	1520	1347
5f	-	3240	3109	2920	-	1697	1636	1612	1520	1347
5g	-	3244	3119	2928	-	1690	1645	1625	1521	1348
5h	-	3246	3116	2925	-	1696	1648	1607	1519	1348
5i	-	3245	3116	2927	-	1698	1645	1628	1516	1348
5j	-	3275	3116	2924	-	1691	1647	1617	1519	1348
5k	-	3237	3114	2927	-	1697	1637	1611	1518	1347

Table 4: Assignment of ^{1}H-NMR data of compounds(1a,b , 2a , 3a,b , 4b,c,f and 5h: solvent DMSO

Compounds	δppm (Multiplicity , Intensity , Assignment)
1a	9.1(s, 1H, N_1–H), 7.6(s, 1H, N_3–H), 7.34-7.2(m, 5H, Ar-H), 5.1(s, 1H, CH), 4(q, 2H, O$\underline{CH_2}CH_3$), 2.2(s, 3H, CH_3), 1.1(t, 3H, $OCH_2\underline{CH_3}$)
1b	9.1(s, 1H, N_1–H), 7.6(s, 1H, N_3–H), 7.4-7.5(d, 2H, Ar-H), 8.2-8.22(d, 2H, Ar-H), 5.2(s, 1H, CH), 4(q, 2H, O$\underline{CH_2}CH_3$), 2.2(s, 3H, CH_3), 1.1(t, 3H, $OCH_2\underline{CH_3}$)
2a	12.3(s, 1H, -OH), 9.1(s, 1H, N_1–H), 7.6(s, 1H, N_3–H), 7.3-7.0(m, 5H, Ar-H), 5.16(s, 1H, CH), 2.2(s, 3H, CH_3)
3a	9.1 (s, 1H, N_1–H), 7.7(s, 1H, N_3–H), 7.5-7.2(m, 5H, Ar-H), 5.2(s, 1H, CH), 2.25(s, 3H, CH_3)
3b	9.3 (s, 1H, N_1–H), 7.8(s, 1H, N_3–H), 7.4-7.5(d, 2H, Ar-H), 8.2-8.22(d, 2H, Ar-H), 5.2(s, 1H, C_4–H), 2.2(s, 3H, CH_3)
4b	9.8(s, 2H, 2N–H), 9.1(s, 2H, $2N_1$–H), 7.6(s, 2H, $2N_3$–H), 7.2-7.5 and 7.8-8.0(m, 18H, Ar-H), 5.1(s, 2H, $2C_4$–H), 3.9(s, 2H, CH_2), 2.2(s, 6H, $2CH_3$)
4c	8.9(s, 2H, 2N–H), 9.1(s, 2H, $2N_1$–H), 7.6(s, 2H, $2N_3$–H), 7.2-7.33(m, 10H, Ar-H), 5.1(s, 2H, $2C_4$–H), 3.2(s, 4H, $2CH_2$),2.2(s, 6H, $2CH_3$)
4f	10.07(s, 2H, 2N–H), 9.1(s, 2H, $2N_1$–H), 7.6(s, 2H, $2N_3$–H), 7.2-7.33(m, 10H, Ar-H), 5.1(s, 2H, $2C_4$–H), 2(s, 12H, $4CH_3$),2.2(s, 6H, $2CH_3$)
5h	9.6(s, 2H, 2N–H), 9.1(s, 2H, $2N_1$–H), 7.6(s, 2H, $2N_3$–H), 7.1-7.5 and 7.8-8.2 (m, 16H, Ar-H), 5.1(s, 2H, $2C_4$–H), 2.8(s, 4H, $2CH_2$),2.2(s, 6H, $2CH_3$)

Table 5: The ^{13}C-NMR data for the synthesized compounds (1a,b , 2a, 3a,b , 4b,c,f and 5h): solvent DMSO

Compounds	(δ) in ppm	Assignment	(δ) in ppm	Assignment
 **1a**	14 18 54 59 99 126	C_{15} C_6-$\underline{C}H_3$ C_4 C_{14} C_5 $C_{8,12}$	127 128 145 148 152 165	C_{10} $C_{9,11}$ C_7 C_6 C_2 C_{13}
 1b	14 18 54 59 98 124	C_{15} C_6-$\underline{C}H_3$ C_4 C_{14} C_5 $C_{8,12}$	147 128 149 152.4 152 165	C_{10} $C_{9,11}$ C_7 C_6 C_2 C_{13}
 **2a**	18 54 99 126 127	C6-CH3 C4 C5 C8,12 C10	128 149 152.4 152 172	C9,11 C7 C6 C2 C13
 **3a**	18 54 99 126 127	C6-CH3 C4 C5 C8,12 C10	128 149 152.4 152 165.8	C9,11 C7 C6 C2 C13
 **3b**	18 54 99 124 128	C6-CH3 C4 C5 C8,12 C9,11	147 149 152 152.4 165.5	C10 C7 C2 C6 C13

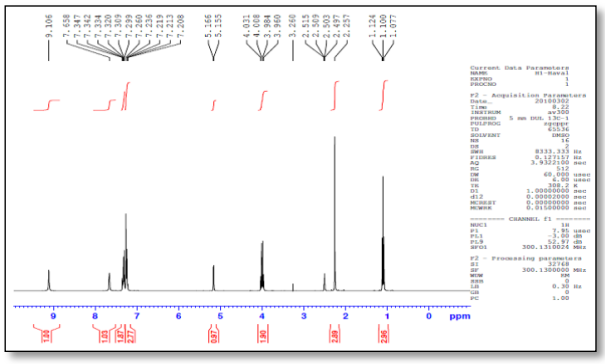
 **4b**	18 54 61 99 122 125 126 127.1	2C6-CH3 2C4 CL 2C5 2C16,20 2C10 2C8,12 2C18	127.7 128.5 130 141 146 152 162	2C9,11 2C17,19 2C15 2C7 2C6 2C2 2C13
 **4c**	18 34 54 99 126 127	2C6-CH3 Cy,y\ 2C4 2C5 2C8,12 2C10	128 141 146 152 164	2C9,11 2C7 2C6 2C2 2C13
 **4f**	14 18 54 99 123 126	2Cz,z\-CH3 2C6-CH3 2C4 2C5 2Cz,z\ 2C8,12	127 128 141 146 152 161	2C10 2C9,11 2C7 2C6 2C2 2C13
 **5h**	18 41 54 99 124 127 128 129	2C6-CH3 Cy,y\ 2C4 2C5 2C15,19 2C8,12 2C16,18 2C9,11	132 134 141.09 141.8 147 152 170	2C14 2C17 2C10 2C6 2C7 2C2 2C13

5. Conclusion

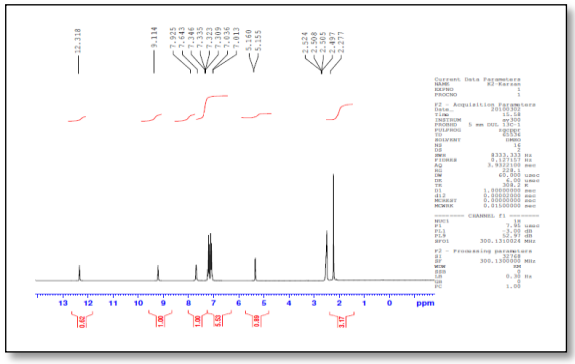
It has been noted that in this work, ultrasonic irradiation was applied successfully in the reaction of dihydropyrimidinone-5-carbonyl chloride with diamines. There was substantial enhancing effect in the yield and the rate of the reaction. On the other hand, most of the prepared compounds have

biological activity against two types of micro-organisms, S. aureus (Gr +ve) and E-coli (Gr-ve).

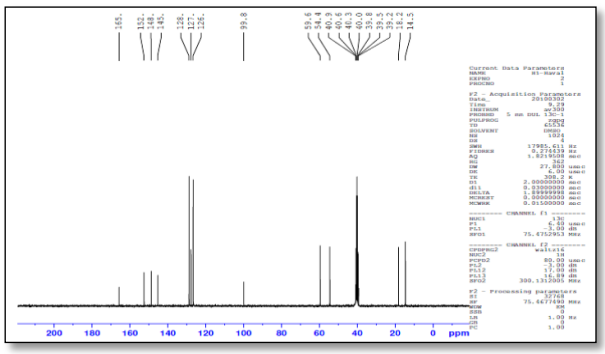
Appendices



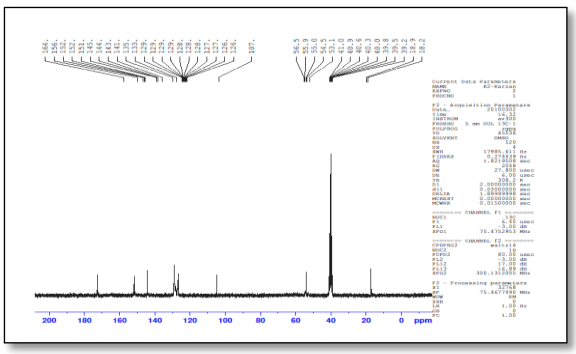
^{1}H-NMR spectrum of compound (1a)



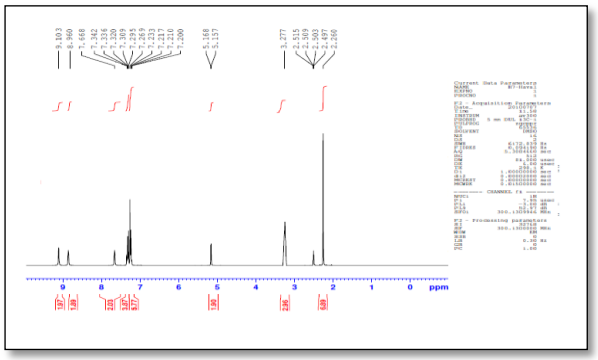
^{1}H-NMR spectrum of compound (2a)



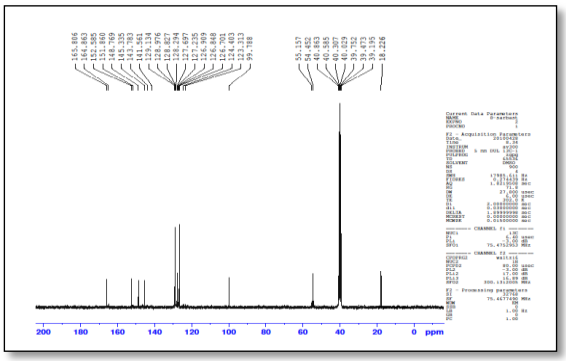
^{13}C-NMR spectrum of compound (1a)



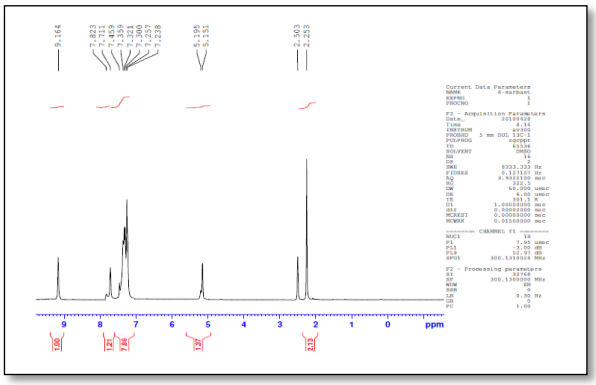
^{13}C-NMR spectrum of compound (2a)



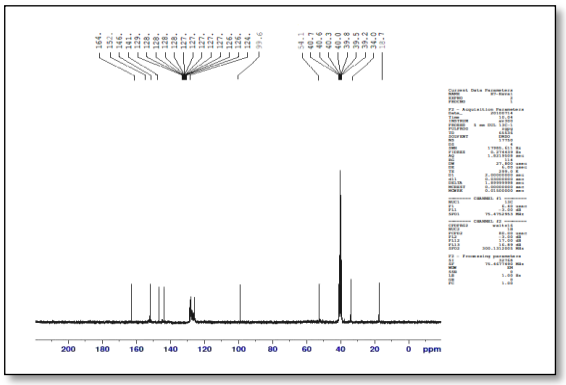
^{1}H-NMR spectrum of compound (3a)



^{13}C-NMR spectrum of compound (3a)



^{1}H-NMR spectrum of compound (4c)



^{13}C-NMR spectrum of compound (4c)

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