Ultrasound-Assisted Synthesis of Some New N-(Substituted Carboxylic Acid-2-yl)-6-Methyl-4-Substituted Phenyl-3, 4-Dihydropyrimidine-2(1*H*)-One Carboxamides

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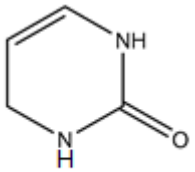
Abstract: In this work, the starting material 6-methyl-4- substituted phenyl-3,4-dihydropyrimidine-2-(1H)-one-5-carboxylic acid ethyl ester (3a,b) have been prepared from the condensation of benzaldehyde (or anisaldehyde), urea and ethyl acetoacetate, in presence of an acid in ethanol under sonication, then hydrolysed to the corresponding acids (4a,b) which were chlorinated with $SOCl_2$ to produce 6-methyl-4-substituted phenyl-3, 4-dihydropyrimidine-2-(1H)-one-carbonyl chloride (5a,b). The compounds (5a,b) then subjected to react with different amino acids in the presence of $LaCl_3.7H_2O$ as a catalyst using a green method (ultrasound assisted technique) to give a new series of N-(Substituted carboxylic acid-2-yl)-6-methyl-4-substituted phenyl-3,4- dihydropyrimidine-2-(1H)-one-5-carboxamide (6a-e and 7a-h). The structures of the synthesized compounds were characterized by using FT-IR, ^{1}H-NMR, ^{13}C-NMR and elemental analysis.

Keywords: Dihydropyrimidinone, Biginelli Reaction, $Lacl_3.7H_2O$, Amino Acids, Ultrasonic Technique, Green Chemistry

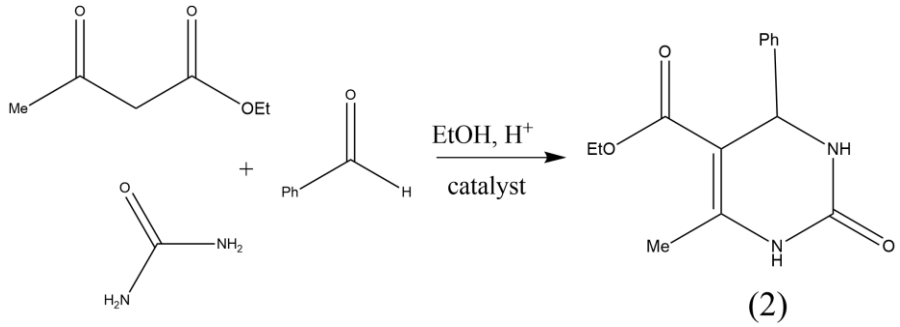
1. Introduction

Dihydropyrimidinone (1) and their derivatives are classified as heterocyclic compounds and containing pyrimidine ring system of remarkable pharmacological efficiency (Kappe, 2000), which exhibit wide range of biological and pharmacological activities such as calcium channel blockers (Steele *et al*, 1998) (e.g., nifedipine) are used in the treatment of cardiovascular disorders including hypertension (Dondoni *et al*, 2001; Eynde *et al*, 2001), cardiac arrhythmias or angina pectoris (Dondoni *et al*, 2001), for the treatment of benign prostatic hyperplasia (BPH) (Dondoni *et al*, 2002), antiviral, antitumor (Yarapathi *et al*, 2004), anti-inflammatory (El-Badaoui *et al*, 2005) , antibacterial actions, mitotic kinesin inhibitor (Sabitha *et al*,2005) antihypertensive agents (Hassani *et al*, 2006), B virus replication inhibitors (Azizian *et al*,2006) α-1a–receptor antagonists (Lin *et al*, 2007) and neuropeptide Y(NPY) antagonists (Maradur & Gokavi, 2008). Several biologically active marine alkaloids were also found to contain the dihydropyrimidinone-5-carboxylate core. Most notable among them are batezelladine alkaloids (Ismaili *et al*, 2008) which have been found to be potent HIV gp-120-CD4 inhibitors (Fustero *et al*, 2009).



(1)

Dihydropyrimidinones (2) have been synthesized in different techniques such as, solvent-free synthesis (Jain *et al*, 2008), metal-catalysed condensation synthesis (Kumar *et al*, 2001), microwave-assisted synthesis (Pathak *et al*, 2006) and ultrasound-assisted synthesis (Ramazani *et al*, 2015) (scheme 1).



(2)

Scheme (1)

2. Experimental

The melting points were determined on a Gallen Kamp electrothermal apparatus by open capillary method and are uncorrected. IR spectra were recorded on a Thermo-Mattson- 300 Spectrophotometer and Bio-Rad Merlin, as KBr disc. ^{1}H and ^{13}C-NMR spectra were measured using a Bruker ultra shield 300 MHz with internal reference TMS (AL-Bait University/Jordon. The sonicator was ultramet sonic cleaner Buehler Ltd. (220/240V, 50/60 Hz).

2.1 Preparation of 6-Methyl-4-Phenyl-3,4-Dihydro Pyrimidine-2(1H)-One-5-Carboxylic Acid Ethyl Ester (3a,B): (Memarian & Abdoli-Senejani, 2008)

A mixture of benzaldehyde or anisaldehyde (0.01mol), urea (0.01mol) and ethyl acetoacetate (0.01mol) in ethanol (10ml), was acidified with conc. HCl. The mixture was sonicated in ultrasonic bath reactor at room temperature for (5-10) min. (sonication was continued until the benzaldehyde or anisaldehyde disappeared, as indicated by TLC). After completion of the reaction, the crude product, which precipitated on cooling, was filtered and washed with water and recrytallized from ethanol to get the pure products.

3a: Yield is 90%, (m.p. 199-201^{o}C), R_f = 0.75 (Chloroform: Ethyl acetate 3:1), reaction time (5 min).

3b: Yield is 80%, (m.p.198-200 ^{o}C), R_f = 0.58 (Chloroform:Ethyl acetate 3:1), reaction time (10 min).

2.2 Preparation of 6-Methyl -4-Phenyl-3,4-Dihydro Pyrimidine-2(1H)-One-5-Acetic Acid (4a,B): (Bose *et al*, 2003)

A stirring mixture of compounds (3a, b) (0.005 mol) and sodium hydroxide (0.08 mol., 10ml) was refluxed for 7 hours. After cooling, the solution was acidified with hydrochloric acid and the precipitate was filtered and recrytallized from ethanol.

4a: Yield is 75 %, (m.p. 221-223 ^{o}C), reaction time (7 h).

4b: Yield is 77%, (m.p. 223-225 ^{o}C), reaction time (7 h).

2.3 Preparation of 6-Methyl-4-Phenyl-3,4-Dihydro Pyrimidine-2(1H)-One-5-Carbonylchloride (5a,B): (George *et al*, 1971)

A mixture of compound (4a, b) (0.005 mol) and thionyl chloride (10ml) was refluxed gently for 7-7.5 hours (the reaction monitored by TLC). Excess thionyl chloride was removed under vacuum and the precipitate was collected and recrytallized from chloroform.

5a: Yield is 60% (m.p 171-173ºC), R_f= 0.81 (Chloroform: Ethyl acetate 3:1), reaction time (7 h)

5b: Yield is 62%, (m.p. 125-126 ^{o}C), $R_{f=}$ 0.69 (Chloroform: Ethyl acetate 3:1), reaction time (7.5 h).

2.4. General Procedure for Preparation of N-(Substituted Carboxylic Acid-2-Yl)-6-Methyl- -4-Phenyl- 3, 4-Dihydropyrimidine-2(1H)-One-5-Carboxamide (6a-J and 7a-H)

According to the modified procedure[24] to a stirring solution of compound (5a,b) (0.005 mol) in 10 ml of ethanol, a solution of different amino acids (0.005mol) in 10ml water was added drop wise in the presence of $LaCl_3.7H_2O$ (0.3g) as a catalyst. The mixture was sonicated in a water bath for 32-40 min. at (40-60)ºC, then the solution was cooled, the desired solid product was filtered, washed and dried then recrytallized from methanol.

2.5 Determination of Antimicrobial Activity

1- The medium of culture was Muller-Hinton that will be prepared by using of nutrient agar and sterilized by autoclave and poured in Petri dish to a depth of 4mm.
2- Activation of the bacteria (*S-aureas* and *E-coli*) before culturing on the nutrient agar in nutrient broth which was used for dilution of bacteria and cultivation of culture isolate for (24h) in 37 C^0
3- Incubation: the inoculated disks were incubated for 24 h at 37 C^0

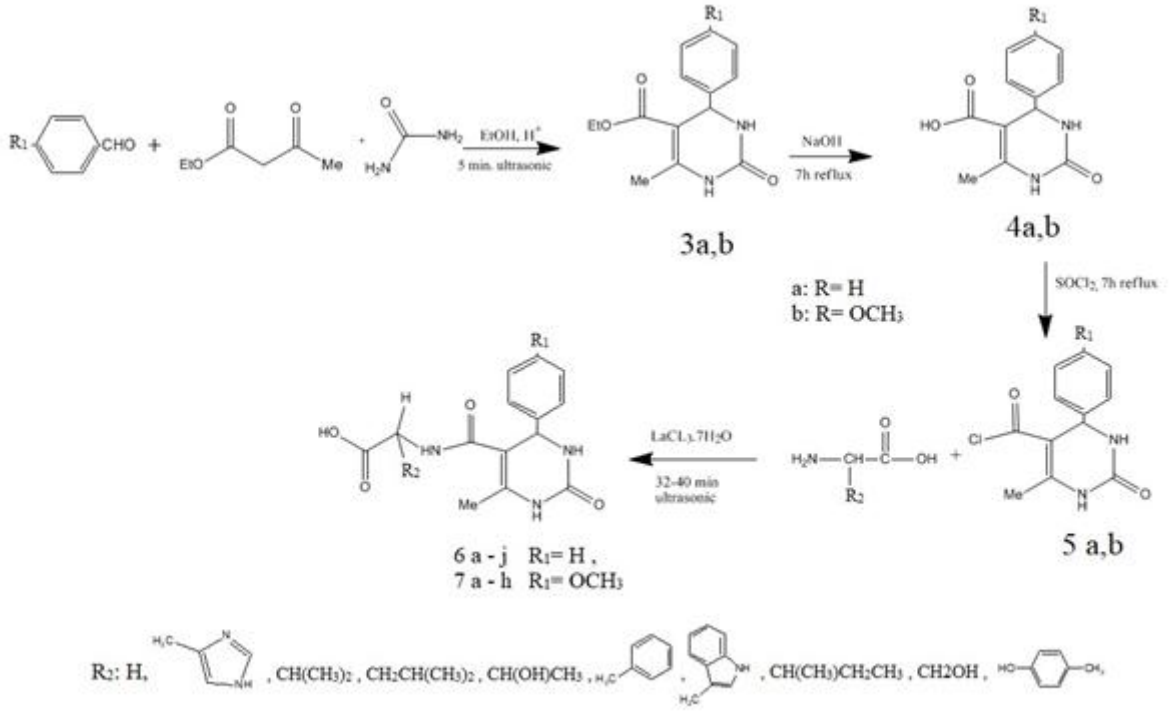
The larger zone of inhibition is represented by more +ve but the unaffected zone is represented by– ve and this was interpreted by national committed for clinical laboratory.

3. Results and Discussion

3.1 Synthesis of 6-Methyl-4-Substituted Phenyl-3,4-Dihydroprymidine-2(1H)-One-5-Carboxylic Acid Ethyl Ester (3a,B)

Many methods have been reported for synthesis of Biginelli compounds among these, the synthesis has been achieved by the condensation of an aromatic aldehyde, 1,3-dicarbonyl compound and urea in the presence of amount of a solvent and a catalyst. In this work, 6-methyl -4-substituted phenyl-3,4-dihydro pyrimidine-2(1H)-one 5-carboxylic acid ethyl esters were synthesized from one-pot cyclocondensation of benzaldehyde or anisaldehyde, ethyl acetoacetate and urea in appropriate amount of ethanol (used as an energy transfer media) and conc. HCl was used as a catalyst under sonication for (5-10) min. at room temperature in an ultrasonic bath (Scheme 1). The reaction was monitored by TLC, after the reaction was completed the desired product was cooled and filtered. It was found that it is a very fast reaction and gives high yield with good purity of final product by using ultrasound. The ultrasound effect on the Biginelli reaction was found to reduce the reaction time and accelerates the reaction [114, 115.]

The structure of the products has been confirmed by IR, ^{1}H-NMR, ^{13}C-NMR and elemental analysis. In the IR spectrum, fig.(1) for compounds (3a) the appearance of a band at 3242 cm^{-1} attributed to N-H stretching vibration119, two strong bands at 1705 and 1648 cm-1 for C=O stretching vibration of ester and cyclic amide respectively.



Scheme (2)

The ^{1}H-NMR spectra of the compounds (3a, b) in fig. (2) and in Table (3) show a singlet peak at (9.10-9.12) ppm for one protons of N1–H in the heterocyclic rings, a singlet at 7.6 ppm due to one proton of N_3-H, 7.2-7.4 ppm which is attributed to five protons of aromatic ring (3a), a singlet peak at (5.16-5.0) ppm correspond to one proton for –CH group, this proton is deshielding due to attached to Sp^2 carbon atoms in two sides and it is attached to N_3–H on the other side, a singlet at 2.2 ppm for three protons of CH_3 group, quartet peak at 4.ppm for two protons of –O$\underline{CH_2}CH_3$ and a triplet at 1.2ppm for three protons of –$OCH_2\underline{CH_3}$. While the spectrum of 3b shows a singlet peak at 3.7 ppm for three protons of methoxy group attached to phenyl group on para position and doublet-doublet signals at (6.88 – 6.85 ppm) and (7.16-7.13 ppm) for four protons of symmetrical para substituted phenyl ring. From the ^{13}C-NMR spectrum of the compounds (3a,b), in fig.(3) and Table (4) the chemical shift values of carbon atoms, a signal appear at 152 ppm attributed to the carbonyl carbon atoms(C_2) of cyclic amide, a signal at C_4 (53-54) ppm corresponding to the deshielded of the –CH group by the attached nitrogen, C_5 at 100 ppm and C_6 at 148 ppm for carbon-carbon double bonds (C_5=C_6), C_7, 18 ppm for methyl carbon atoms, and C_8 appear at 165.8 ppm for the carbonyl carbon atoms, C_{10} appear a singlet peak at 59.5 ppm corresponding to the deshielded methylene group by the attached oxygen of carboxylate group and C_{11} a singlet at 14.2δ for methyl carbon atom. A signal at 55δ for $C_{4"}$ of methoxy group leads to downfield due to higher electronegativity of oxygen.

3.2 Hydrolysis of Esters (3a, b)

6-Methyl-4-substituted phenyl-3,4-dihydroprymidine-2(1H)-one-5-acetic acid (4a,b) were obtained

from the hydrolysis of compounds (3a,b) by refluxing with 5% solution of sodium hydroxide for 7 hours, the mixture was cooled, filtered then washed with diluted HCl. The desired products were obtained in high yields (75 – 77 %) and good purities.

The IR spectra for compounds (4a, b), appeared a broad band at 2500-3500 cm^{-1} for O-H stretching vibration of carboxylic acids. further evidence is the appearance of strong bands at 1703 cm^{-1} and 1698 cm^{-1} which are assigned to be for C=O str. vibration of carboxylic acids and amides, respectively .The ^{1}H-NMR spectrum of the compound (4a,b) fig. (5) in Table (3) shows a singlet at 12.3ppm for one proton of –OH group of carboxylic acid and multiplet signal at 7.0-7.3 ppm for five protons of phenyl ring. The ^{13}C-NMR spectrum of the compound (4a) fig. (6) in Table (6) shows the position of the carbonyl carbon atom of carboxylic acid C_8 at 172 ppm.

3.3 Synthesis of 6-Methyl-4-Substituted Phenyl-3,4-Dihydroprymidine-2(1H)-One-5-Carbonyl Chloride (5a,B)

Reaction of 6-methyl-4-substituted phenyl-3,4-dihydroprymidine-2(1H)-one-5-acetic acid (4a, b) with excess of thionyl chloride under reflux produced 6-methyl-4-substituted phenyl-3,4-dihydroprymidine-2(1H)-one-5-carbonyl chloride (5a,b). The reaction was monitored by TLC which indicated the disappearance of starting material and conforms the formation of the product. After cooling the excess thionyl chloride was removed under vacuum and the obtained products were collected in (60-61 %).

The IR spectra of compounds (5a,b), show a band at 749-751 cm^{-1} related to C-Cl vibration frequency, the appearance of a band at 3230-3380 cm-1 attributed to N-H stretching vibration, and a sharp band at 1809 cm-1 for C=O stretching vibration frequency of acid chloride. The ^{1}H-NMR spectrum of the compound (5a,b) fig. (7) in Table (3) multiplet signals appear at (7.0-7.3) ppm for five protons of phenyl ring in compound (5a), while in compound (5b) doublet-doublet signals at (6.88-6.85) ppm and (7.16-7.13) ppm for four protons of symmetrical para substituted of phenyl ring. From the ^{13}C-NMR spectrum of compound (5a), fig. (8) in Table (4) shows three signals of phenyl ring: C_{2}`, $C_{4}$`and C_{6}` appear at 126.8 ppm, $C_{3}$`and C_{5}` 128.9 ppm and $C_{1}$` 143.9 ppm, while for compound (5b) shows four signals of phenyl ring C_{2}` and $C_{6}$` appear at 127.8 ppm, C_{3}` and $C_{5}$` at 114.3 ppm, C_{1}` appear at 136 ppm and $C_{4}$` at 159 ppm due to attachment of methoxy group which shifting the signal of C_8 of acid chloride to 167.5 ppm.

3.4 Reaction of 6-Methyl-4-Substituted Phenyl-3,4-Dihydroprymidine-2(1H)-One-5-Carbonyl Chloride (5a,B) With Different Amino Acids

A mixture of 6-methyl-4-substituted phenyl-3,4-dihydroprymidine-5-2(1H)-one-5-carbonyl chloride (in ethanol) and different amino acids (in water) in the presence of $LaCl_3.7H_2O$ was sonicated in ultrasonic bath at 40 ^{o}C. Then the mixture was cooled, the desired solid product was filtered, dried and recrystallized by methanol. The obtained 2-(6-methyl-4-substituted phenyl-3,4-dihydroprymidine-2(1H)-one-5-carboxamido) derivatives (6a-j and 7a-h) were in moderate yields (44.5-65.9 %). The IR, ^{1}H-NMR, ^{13}C-NMR spectral data and the physical data in Table (1) are indicating the disappearance of starting materials and formation of desired products.

The IR spectra of the compounds 6 and 7, in fig. (9) and Table (2) showed the shifting C=O stretching vibration of acid chloride to 1809 cm^{-1} and the appearance of C=O stretching vibration of

amide group at 1683-1705 cm^{-1}. Further evidence is the broad band at (2500-3500 cm^{-1}) which is assigned to the hydrogen bond of O–H str. vibration of carboxylic acids. The ^{1}H-NMR spectra of fig. (10), in Table (3) for compounds (6a, 6e and 7a), respectively showed a singlet peak at (12.3-12.8) ppm for one proton of hydroxyl group of carboxylic acid, singlet peak at (8.2-8.0) ppm for one proton of N-H amide. A singlet peak deshielded appear at 4.2 ppm for two protons of CH_2 group due to their α-position to carboxylic group which has (–I) effect, a singlet peak appear at (4.7) ppm for one proton of hydroxyl group. A singlet peak appear at (3.6-3.7) ppm for three protons of methoxy group attached to phenyl ring on para position and doublet-doublet signals at (6.9) ppm and (7.18) ppm for four protons of symmetrical para-substituted phenyl ring.

Table (4) shows the ^{13}C-NMR data (fig. (11)) of the compounds (6a, 6e and 7a). The chemical shift values of carbon atoms, a signal appear at (45) and (62.8) δ for carbon C_{10} atom of CH_2 and CH group respectively and C_{11} signals appear at (170-172) δ for carbonyl carbon atoms of carboxylic acids respectively. In compound (6e), fig. (30) a signal of $C_{10`}$ appear at (65) δ for carbon of CH group and $C_{11`}$ a signal at (18) δ for methyl carbon atom. While in compound (7a) $C_{4"}$ appear at (55) δ for carbon of methyl group which is lead to downfield due to higher electronegativity of oxygen.

4. Determination of Bacterial Sensitivity

Action of some prepared tetrahydropyrimidine derivatives on the two types of micro-organisms will be shown in Table (5); there are different effects of the compounds against *S. aureus* (Gr +ve) and *E-coli* (Gr-ve). The most active compound against *S. aureus* was (6c and 6i), but the others show moderate or inactive influences.

5. Conclusion

It has been noted that, ultrasonic was applied successfully to perform the 2-(6-methyl-4-substituted phenyl-3, 4-dihydro pyrimidine-5-carboxamido) derivatives. There was an enhancement in the percentage of products, and reduction of the reaction time. The pure product was produced in the presence of solvent condition. The prepared compounds, which were biologically examined against *Escherichia coli and Staphylococcus aureus*, showed moderate activity.

Table 1: some physical properties for the synthesized compounds (6a-j and 7a-h)

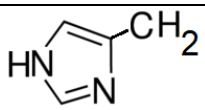
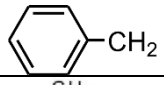
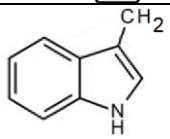
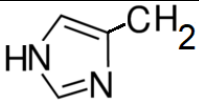
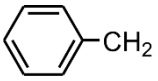
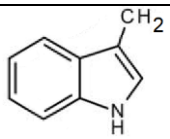
Compound	R	Molecular Formula	m.p °C	Yield (%)
6a	H	$C_{14}H_{15}N_3O_4$	158-160	61
6b		$C_{18}H_{19}N_5O_4$	124-126	65.9
6c	$CH(CH_3)_2$	$C_{17}H_{21}N_3O_4$	145-147	46
6d	$CH_2CH(CH_3)_2$	$C_{18}H_{23}N_3O_4$	149-150	44.5
6e	$CH(OH)CH_3$	$C_{16}H_{19}N_3O_5$	153-155	53
6f		$C_{21}H_{21}N_3O_4$	142-143	51.9
6g		$C_{23}H_{22}N_4O_4$	150-152	47
6h	$CH(CH_3)CH_2CH_3$	$C_{18}H_{23}N_3O_4$	150-151	54
6i	CH_2OH	$C_{15}H_{17}N_3O_5$	122-124	45.3
6j		$C_{21}H_{21}N_3O_5$	180-182	48
7a	H	$C_{15}H_{17}N_3O_5$	158-160	59
7b		$C_{19}H_{21}N_5O_5$	164-166	64
7c	$CH(CH_3)_2$	$C_{18}H_{23}N_3O_5$	171-173	50
7d	$CH_2CH(CH_3)_2$	$C_{19}H_{25}N_3O_5$	119-121	59
7e	$CH(OH)CH_3$	$C_{17}H_{21}N_3O_6$	188-190	61
7f		$C_{22}H_{23}N_3O_5$	150-152	45
7g		$C_{24}H_{24}N_4O_5$	160-162	63
7h	$CH(CH_3)CH_2CH_3$	$C_{19}H_{25}N_3O_5$	170-172	56

Table 2: Assignment of characteristic frequencies (cm-1) of IR data for the synthesized products (6a-j and 7a-h)

Compounds	O-H str.	N-H str.	C=O str. C_5	C=O str. C_2
6a	2600-3600	3239	1697	1670
6b	2500-3500	3410	1705	1633
6c	2500-3500	3372	1698	1653
6d	2500-3500	3384	1695	1640
6e	2500-3500	3384	1695	1660
6f	2400-3400	3249	1704	1662
6g	2500-3500	3400	1684	1652
6h	2500-3500	3339	1701	1636
6i	2600-3500	3400	1696	1671
6j	2500-3500	3413, 3207	1696	1620
7a	2500-3500	3192	1692	1608
7b	2500-3500	3408	1683	1630
7c	2500-3500	3384	1695	1610
7d	2500-3500	3383	1685	1609
7e	2500-3500	3384	1683	1608
7f	2500-3500	3363	1691	1608
7g	2500-3500	3376	1682	1609
7h	2400-3400	3334	1699	1635

Table 3: The ^{1}H-NMR data for some synthesized products

Compounds	δppm (Multiplicity, Intensity, Assignment)
3a	9.1 (s, 1H, N_1-H), 7.6 (s, 1H, N_3-H), 7.34-7.2 (m, 5H, Ar-H), 5.16 (s, 1H, CH), 4.0 (q, 2H, O$\underline{CH_2}CH_3$), 2.2(s, 3H, CH_3), 1.1(t, 3H, $OCH_2\underline{CH_3}$)
3b	9.1 (s, 1H, N_1-H), 7.6(s, 1H, N_3-H), 7.1-6.86(m, 4H, Ar-H), 5.0(s, 1H, CH), 4.1 (q, 2H, O$\underline{CH_2}CH_3$), 3.7(s, 3H, OCH_3), 2.3(s, 3H, CH_3), 1.2(t, 3H, $OCH_2\underline{CH_3}$)
4a	12.3 (s, 1H, OH), 9.1 (s, 1H, N_1-H), 7.9 (s, 1H, N_3-H), 7.3-7.0 (m, 5H, Ar-H), 5.16 (s, 1H, CH), 2.2 (s, 3H, CH_3)
5a	9.1 (s, 1H, N_1-H), 7.8 (s, 1H, N_3-H), 7.5-7.2 (m, 5H, Ar-H), 5.19 (s, 1H, CH), 2.25 (s, 3H, CH_3).
5b	9.3 (s, 1H, N_1-H), 7.8 (s, 1H, N_3-H), 7.2-6.9 (m, 4H, Ar-H), 5.17 (s, 1H, CH), 3.88 (s, 3H, OCH_3), 2.2 (s, 3H, CH_3)
6a	12.3 (s, 1H, OH), 9.2 (s, 1H, N_1-H), 8.1 (s, 1H, N_9-H), 7.7 (s, 1H, N_3-H), 7.5-7.1 (m, 5H, Ar-H), 5.3 (s, 1H, CH), 4.2 (s, 2H, CH_2), 2.2 (s, 3H, CH_3)
6e	12.25 (s, 1H, OH), 9.2 (s, 1H, N_1-H), 8.0 (s, 1H, N_9-H), 7.61 (s, 1H, N_3-H), 7.3-7.0 (m, 5H, Ar-H), 5.2 (s, 1H, CH), 4.7 (s, 1H, OH), 4.4 (d, 1H, CH), 4.0 (m, 1H, CH), 2.2 (s,3H, CH3), 1.2 (d, 3H, CH_3)
7a	12.8 (s, 1H, OH), 8.7 (s, 1H, N_1-H), 8.1 (s, 1H, N_9-H amide), 7.8 (s, 1H, N_3-H), 7.18-6.9 (m, 4H, Ar-H), 5.3 (s, 1H, CH), 4.3 (s, 2H, CH_2), 4.0 (s, 3H, CH_3), 2.2 (s,3H , CH_3)

Table 4: The ^{13}C-NMR data for some synthesized products

Comp.														
3a	δppm	14.5	18.2	54.4	59.6	99.8	126.8	128.5	145	148	152	165.7		
	Assign.	C_{11}	C_7	C_4	C_{10}	C_5	$C_{2',4',6'}$	$C_{3',4'}$	$C_{1'}$	C_6	C_2	C_8		
3b	δppm	14	18	53	55	59	100	114.1	127	137	148	152	158.9	165.8
	Assign.	C_{11}	C_7	C_4	$C_{4''}$	C_{10}	C_5	$C_{3',5'}$	$C_{2',6'}$	$C_{1'}$	C_6	C_2	$C_{4'}$	C_8
4a	δppm	18.1	53	107	126.5	128.5	144	151	172					
	Assign.	C_7	C_4	C_5	$C_{2',4',6'}$	$C_{3',4'}$	$C_{1'}$	C_2	C_8					
5a	δppm	14.3	53	109	126.8	128.9	143.8	151	152.2	169				
	Assign.	C_7	C_4	C_5	$C_{2',4',6'}$	$C_{3',4'}$	$C_{1'}$	C_2	C_6	C_8				
5b	δppm	17.1	51	58.8	113	114.3	127.5	136	150.8	152	159	167.5		
	Assign.	C_7	C_4	$C_{4''}$	C_5	$C_{3',5'}$	$C_{2',6'}$	$C_{1'}$	C_2	C_6	$C_{4'}$	C_8		
6a	δppm	17	45	53	106.2	126.8	128.7	144	145	152	168	170		
	Assign.	C_7	C_{10}	C_4	C_5	$C_{2',4',6'}$	$C_{3',4'}$	$C_{1'}$	C_6	C_2	C_8	C_{11}		
6e	δppm	17.2	19.4	50	61.3	66.7	108.6	126.7-128.5	143.3	146.1	150.2	168.2	174.7	
	Assign.	C_7	$C_{11'}$	C_4	C_{10}	$C_{10'}$	C_5	$C_{2',3',4',5',6'}$	$C_{1'}$	C_6	C_2	C_8	C_{11}	
7a	δppm	18	45	54	55.8	106	114.4	127.8	142	143	152	159	165	170
	Assign.	C_7	C_{10}	C_4	$C_{4''}$	C_5	$C_{3',5'}$	$C_{2',6'}$	$C_{1'}$	C_6	C_2	$C_{4'}$	C_8	C_{11}

Table 5: The sensitivity of some prepared derivatives against E-coli and S. aureus bacteria

Compounds	S. aureus	E. coli
3a	-	-
3b	-	+
4a	-	-
4b	-	+
5a	-	-
5b	-	+
6a	+	-
6b	+	-
6c	++	-
6d	+	-
6e	+	-
6f	+	-
6g	+	-
6h	+	-
6i	++	-
6j	+	-
7a	+	+
7b	-	+
7c	-	+
7d	-	+
7e	-	+
7f	-	+
7g	-	+
7h	-	+

Key to the symbols: Highly active ++++ (inhibitition zone >24mm); Active +++ (inhibition zone 20-24mm); Moderately active ++ (inhibition zone 16-20 mm); Slightly active + (inhibition zone 12-16 mm). Inactive – (inhibition zone < 12).

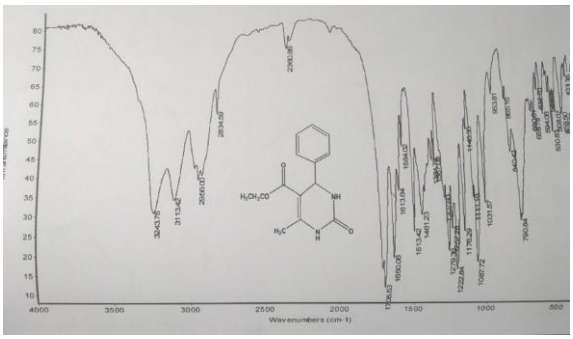


Fig.(1) IR Spectrum of compound 3a

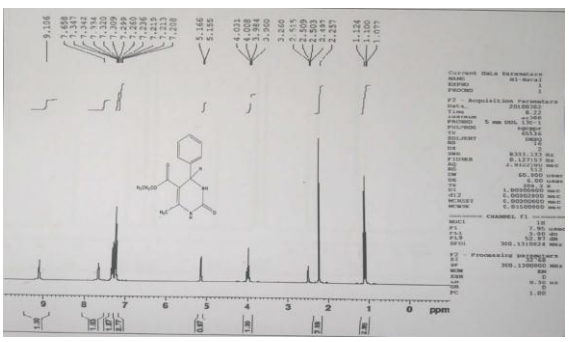


Fig. (2) ^{1}H-NMR Spectrum of compound 3a

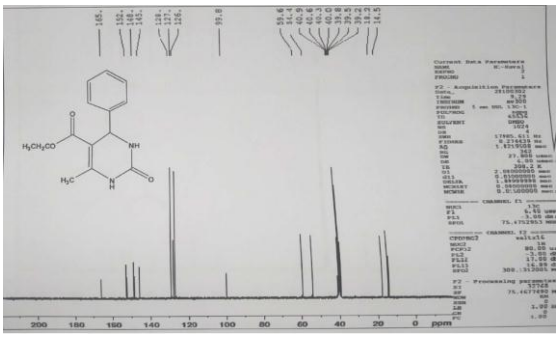


Fig. (3) ^{13}C-NMR Spectrum of compound 3a

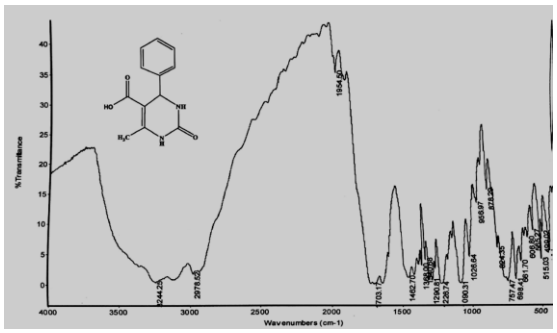


Fig. (4) IR Spectrum of compound 4a

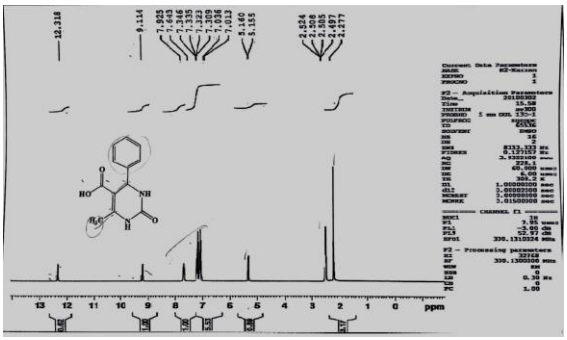


Fig. (5) ^{1}H-NMR Spectrum of compound 4a

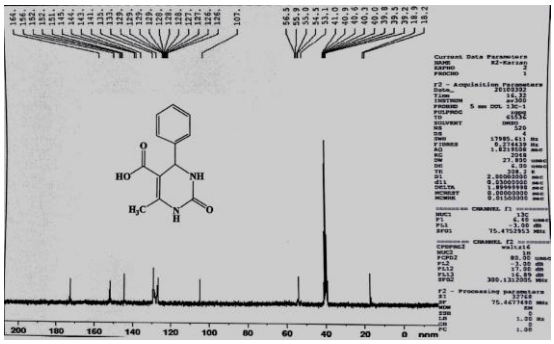


Fig. (6) ^{13}C-NMR Spectrum of compound 4a

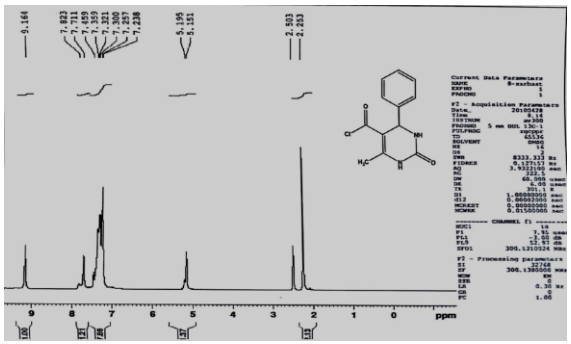


Fig. (7) ^{1}H-NMR Spectrum of compound 5a

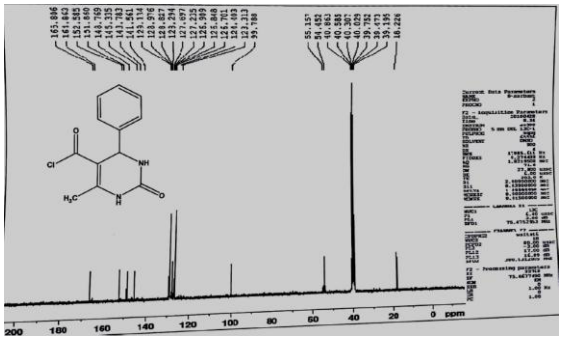


Fig. (8) ^{13}C-NMR Spectrum of compound 5a

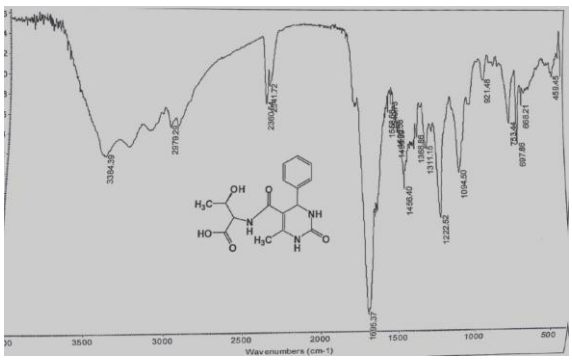


Fig. (9) IR Spectrum of compound 6a

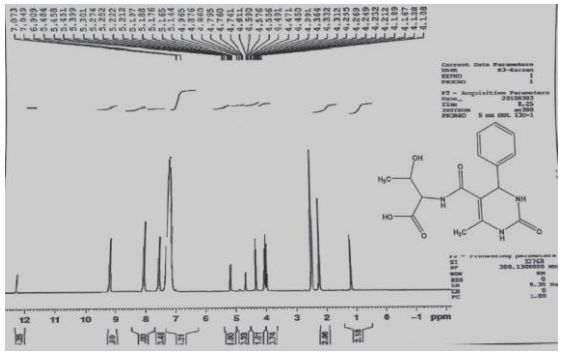


Fig. (10) ^{1}H-NMR Spectrum of compound 6a

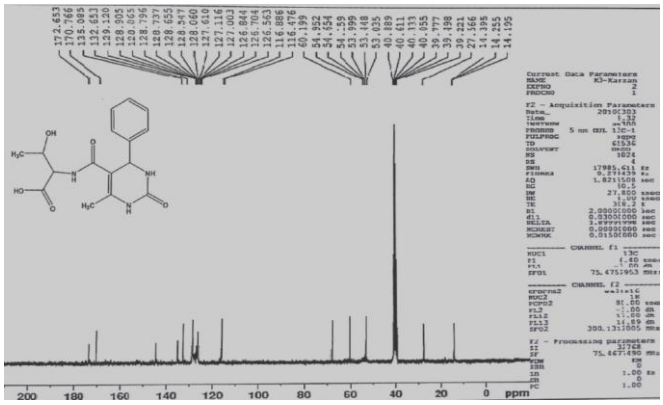


Fig. (11) ^{13}C-NMR Spectrum of compound 6a

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