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RESEARCH PAPER

Synthesis and preliminary pharmacological profile of some new 3,5-dihydro-4H-imidazol-4-one and *α,β*-dehydroamino acid derivatives

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A B S T R A C T:

A new series of 3,5-dihydro-4H-imidazol-4-one derivatives incorporating thiazole moiety have been readily prepared through the nucleophilic acyl substitution reactions of 5(4H)-oxazolones derivatives (**2A-2J**) with 4-(benzo[d]thiazol-2-yl) aniline (**3**) using a simple synthetic strategy under mild condition. Furthermore, the ring opening reaction of same components were examined to afford a new series of *α,β*-dehydroamino acid derivatives (**4A-4J**) in good yield. The preliminary pharmacological profile of all newly synthesized compounds were evaluated in vitro for their antibacterial and antifungal activities using micro broth dilution assay method, and it was revealed that most of the synthesized derivatives were exhibiting promising pharmacological activities against both strains. The structures of the newly synthesized 3,5- dihydro-4H-imidazol-4-one (**5A-5J**)) and α,β-dehydroamino acid derivatives (4A-4J) were expounded and elucidated on the bases of their FT-IR, 1H- and 13C –NMR spectral data.

KEY WORDS: Imidazol-4-one, α,β-dehydroamino acid, thiazole, acyl substitution, antibacterial, antifungal.
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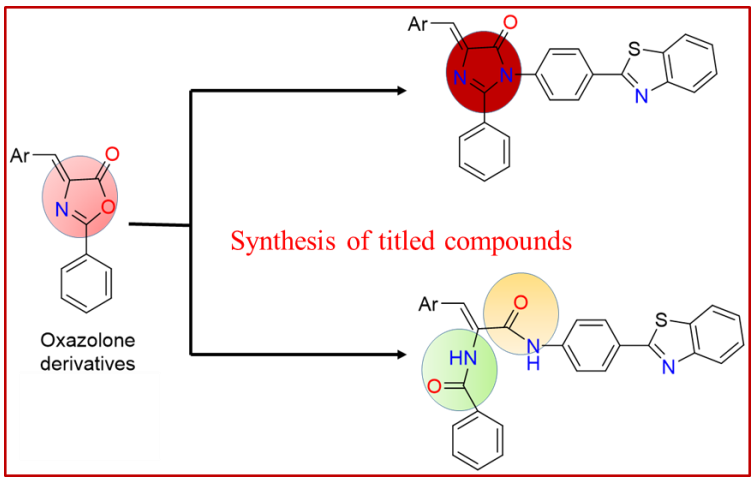

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Spreading of microorganisms with antibiotic resistance has seriously impacted the effectiveness of numerous common antibacterial agents while the advent of antifungal infections in immune-compromised population has also pointedly increased over the recent decades (Yaqub, Hannan et al. 2013), Thus, design and synthesis of new antifungal and antibacterial agents with numerous mechanisms of action are desirable for the effective control of these clinically significant infections(Salih, Ameen et al. 2020). The recent survey of new small-molecule therapeutics revealed that the majority of their results from an analogue-based method and that their market value represents two-thirds of all drug sales. Heterocyclic compounds have assumed a prominent role in the last two decades, due to their excellent pharmacological properties in the field of medicinal chemistry (Behbehani and Ibrahim 2012, Ziwar, MUSHEER et al. 2016, Hassan and Sciences 2019), and among the five-membered heterocyclic compounds that include nitrogen, 3,5-dihydro-4H-imidazol-4-one Figure (1) have highlighted attention of researchers and considered as introduction to the most common host heterocyclic systems of different substituents at positions 1,2 and 4 produces a series of molded compounds with tremendous and diverse range of biological activities . They have been long used as anti-inflammatory (Kumar, Aghara et al. 2020, Metwally and Mohamed 2020, Sanad and Mekky 2020), anti-cancer (Kamal, Ramakrishna et al. 2010, El-Hady and Abubshait 2015), anti-hypertensive (Abdellatif and Fadaly 2017)anti-consultant (Song, Qu et al. 2020, Desai, Wadekar et al. 2021), anti-fungal (Desai, Wadekar et al. 2021), anti-bacterial (Khan, Mughal et al. 2010, Satyanarayana and Sivakumar 2011), anti-epileptic agents (Mishra and Ganguly 2012) and cardiovascular (Mukaddam-Daher 2012). Small organic molecules have endlessly played an important role in the finding of new biologically active agents for treating various kinds of infections.(Chawla, Sahoo et al. 2010, Panneer, Selvam et al. 2011) Non-protein genic *α,β*-dehydroamino acids are an important class of small organic molecules with a large application spectrum in medicinal chemistry (Monteiro and Suárez 2012). The main structural feature in *α,β*-dehydroamino acid is carbon–carbon double bond which is placed between the carbon atom α of the main chain and the carbon atom β of the side chain of the α-amino acid, and they found in peptides with antifungal, antiviral, antitumor, anti-inflammatory or immunosuppressive activities(Somekh and Shanzer 1983, Monteiro and Suárez 2012) In light of these interesting biological activities and having a wide scope to discovery new and potentially drug like molecules, we have attempted to synthesize a new series of 3,5-dihydro-4H-imidazol-4-one and *α,β*-dehydroamino acid derivatives with evaluation of their pharmacological profiles.

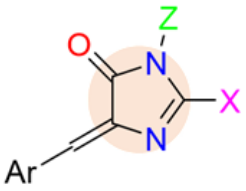


Figure 1.General structural of 1,3- imidazolones

2.Experimental (Materials and Methods)

Melting points were measured with an electro thermal melting point apparatus type (capillary method). IR spectra were recorded with FT-IR (Shimadzu) spectrophotometer with KBr pellets (at chemistry Department, college of Education Salahaddin University/Erbil). Bruker Spectrometer (400 MHz) was use to recorded ^{1}H-NMR, ^{13}C-NMR and ^{13}C-DEPT 135 NMR spectra with DMSO and $CHCl_3$ as a solvent, chemical shifts are shown in ppm. All chemical reagents in the analytical grade were used and had been purchased from commercial sources (Sigma Aldrich, Scharlau, Fluka).

2.1Preparation of Starting materials

2.1.1Preparation of Hippuric acid (1)

The solution of glycine (10.5 g ,0.14mol) in 50 mL of (10%) of sodium hydroxide in a 500 mL round bottom flask was cooled to (0-5^{o}C) in an ice bath then of benzoyl chloride (13.93 g ,0.12 mol) was added in six portions with vigorous shaking after each addition until the precipitate formed, the

resulted was cooled to (0-5^{o}C) and acidified with concentrated hydrochloric acid. pale-yellow solid product was air dried and purified based on the process outlined by (Samad and Hawaiz 2019) to obtain hippuric acid yield 89% percent and m.p 177–179 °C .

2.1.2Preparation of 4-arylidene--2-phenyl-5(4H)-Oxazolones (2)

4-arylidene-2-phenyl-5(4H)-Oxazolones (**2A-2J**) were prepared using the method previously outlined by Hamad (2016) a mixture of hippuric acid (5.37g, 0.03 mol) and different substituted benzaldehydes (0.03 mol) in acetic anhydride (30 mL) in the presence of anhydrous sodium acetate (1 g ,0.012 mol) placed in a water bath (90-100 ^{0}C) for about 2 hours. After completion of the reaction and the precipitate (**2A-2J**) were filtered, washed three times with hot water, air dried and crystallized from absolute ethanol. The physical constants and Infrared spectral data of the 4-arylidene-2-phynyl-5(4H)-Oxazolones (**2A-2J**) are shown in **Table 1**.

Table 1. Significant IR peaks and some physical properties of Synthesized Oxazolone-5-one compound (**2A-2J**)

NO	Nu R1	R2	Molecular Formula of Oxazolone	M.Wt	% Yield	M.P °C	C=O.str. cm^{-1}	C=N.str. cm^{-1}	Reference M.P °C	Reference
2A	-H	-F	$C_{16}H_{10}FNO_2$	266	71	176-178	1795.73	1660.71	179-180	(Jat, Mishra et al. 2012)
2B	-H	$-CH_3$	$C_{17}H_{13}NO_2$	263	65	132-134	1793.80	1653.0	144-146	(Hamad, Briem et al. 2016)
2C	$-OCH_3$	$-OCH_3$	$C_{18}H_{15}NO_4$	309	59	166-168	1789.94	1647		
2D	-Cl	-H	$C_{16}H_{10}ClNO_2$	283.5	70	140-142	1793.80	1654	152-153	(Jat, Mishra et al. 2012)
2E	-H	$-OCH_3$	$C_{17}H_{13}NO_3$	279	74	152-154	1789.94	1653	153-154	(Jat, Mishra et al. 2012)
2F	-H	$-NO_2$	$C_{16}H_{10}N_2O_2$	294	84	227-228	1797.66	1654.92	227-228	(Jat, Mishra et al. 2012)
2G	-H	$N(CH_3)_2$	$C_{18}H_{16}N_2O_2$	292	73	206-208	1764	1662	211-212	(Hamad, Briem et al. 2016)
2H	-H	-Cl	$C_{16}H_{10}ClNO_2$	283.5	71	184-186	1797.66	1654.92	189-190	(Jat, Mishra et al. 2012)
2I	C_6H_5-CH=CH-		$C_{18}H_{13}NO_2$	275	85	123-125	1786.08	1637.56	129-131	(Hamad, Briem et al. 2016)
2J	Pyridine-3-yl-		$C_{15}H_{10}N_2O_2$	250	60	152-154	1797.66	1654.92		

2.1.3General procedure for synthesis of *α,β*-dehydroamino acid derivatives (4A-4J)

Modified method (Ayoob, Hussein et al. 2021) was used for syntheses of (N-(1-(Arylidine)-3-((4-(6-methylbenzo[d]thiazol-2-yl) phenyl) amino)-3-oxoprop-1-en-2-yl) *α,β*-dehydroamino acid) (**4A-4J**), 4-arylidene-2-phenyl-5(4H)-Oxazolones (**2A-2J**) (0.001 mol) with glacial acetic acid 15 mL in round bottom flask were heated (90-100 ^{0}C) and stirred until clear solution was appeared, then treated with 4-(benzo[d]thiazol-2-yl) aniline (3) (0.002 mol, 0.48 g /10 ml glacial acetic acid) solution. the mixture was refluxed for 1 hr. The resultant solid was filtered off and then washed with hot ethanol, air dried and recrystallized from $CHCl_3$.

2.1.4Synthesis of 5-(arylidine)-3-(4-(6-methylbenzo[d]thiazol-2-yl) phenyl)-2-phenyl-3,5-dihydro-4H-imidazol-4-one (5A-5J) (Hamad, Briem et al. 2016)

4-arylidene--2-phenyl-5(4H)-Oxazolones (**2A-2J**) (0.001 mol) was treated with excess amount of 4-(benzo[d]thiazol-2-yl) aniline (**3**) (0.48 g ,0.002 mol) in 15 mL glacial acetic acid, the mixture refluxed for 10 hours. The product substance that had solidified was removed by filtration, then rinsed with cold distillate water then with absolute ethanol, air dried and purified by recrystallization from ethanol to give compounds (**5A-5J**)

2.2Biological evaluation

Micro broth dilution assay method (Kant, Kumar et al. 2016, Ziwar, MUSHEER et al. 2016) was followed to evaluate the preliminary pharmacological profiles of new 3,5-dihydro-4H-imidazol-4-one (**5A-5J**) and α,β-dehydroamino acid derivatives (**4A-4J**) against *E. coli* and *S. aureus* as anti-bacterial and *Candida albicans* as anti-fungal.. Four different concentrations 200, 400, 600, and 800 µg/mL were prepared from each synthesized compound. The imodazolone (**5A-5J**) compounds were dissolved in dimethyl sulfoxide and α, β-dehydroamino acid (**4A-4J**) compounds dissolved in tetrahydrofuran, and those solvents were considered as negative control. ciprofloxacin and fluconazole as two commercial medications with the same range of concentrations, were employed as a standard.

3.Result and discussion

5(4H)-oxazolones **2(A-J)** were synthesized by the action of aromatic aldehydes(**A**) with benzamido-acetic acid (**B**) anhydrous sodium acetate and acetic anhydride through the Erlenmeyer-Polchl reaction. Synthesized 5(4H)-oxazolones (**2A-J**) were reacted with 4-(benzo[d]thiazol-2-yl) aniline (**3**) in glacial acetic acid, which formed the α, β-dehydroamino acid derivatives (**4A-J**) derivatives by ring-opening reaction applying nucleophilic acyl substitution methods. Oxazolone derivatives were treated with the same 4-(benzo[d]thiazol-2-yl) aniline (**3**) aromatic amine, since with the increasing reflux duration the ring transformation of oxazolones into 3,5-dihydro-4H-imidazol-4-one derivatives incorporating a thiazole has been successful yielded different sets of 3,5-dihydro-4H-imidazol-4-one derivatives (**5A-J**). The synthetic pathway is depicted in (**Scheme 1**)

The IR spectra were recorded to monitor the carbonyl shifting from compound (**2**) to (**5**), physical properties and structural elucidation of some synthesized compounds (**2A-J**) in **Table 1**, compounds (**4A-4J**) in Table **2,** while compounds (**5A-5J**) in **Table 3** are shown.

The IR spectrum data of compound (**4B**) in **Table 2** and **Figure 4** confirms the formation of the *α,β*-dehydroamino acid system by showing the absorption bands at 3277cm^{-1} due to N-H stretching of the amide group, The infrared spectrum also displayed a characteristic band at 1672.28 cm^{-1} resulting from the carbonyl group of the amide moiety. On the other hand, the ^{1}H-NMR spectrum has supported the infrared finding by showing two singlet signals at (10.15, and 10.51) ppm for two different protons of N-H$_a$ and N-H$_b$ respectively, as shown in **Figure 6**. The ^{1}HNMR spectrum has also been verified the projected structure by observing two characteristic singlet signals at (2.30, 2.45) ppm for 3H of the methyl group on the phenyl ring and aromatic amine. Isolated proton of the vinyl proton is present in propylene which was appeared at 7.17 ppm as singlet signal. In addition, the (16) aromatic protons of the benzene ring resonated in the (7.20-8.06) ppm region.

In ^{13}C NMR of synthesized compound (**4B**), the carbonyl carbon (C_9) appeared at 165.93 ppm and the second carbonyl (C_{21}) performed to signal at 164.18 δ ppm shown in **figure 6**. Signals at 21.07 and 20.95 δ ppm appeared at DEPT-135, confirming the presence of (Ar-CH_3) in para

position of the phenyl ring and (CH_3) of aromatic amine respectively, Additionally, the range of aromatic carbons was validated at 115.49-160.73 ppm.

The carbonyl functional group was present in the compound (**5B**) conferred with the IR spectrum with value at 1720.50 cm^{-1} a peak is located at 1639. 49 cm^{-1} and provided evidence for -C=N group of the imidazolone ring in **Figure 7**. The ^{1}H-NMR of synthesized compound (**5B**) showed in **Figure 8**, the aromatic protons were confirmed at 7.27-8.21 ppm, a Vinyl proton (C_7) is present (H-C=C-) at 7.26 ppm. Two singlet Signals appeared at (2.42, 2.50) for 3H of both methyl groups confirmed the presence of CH_3 substituted on phenyl ring and aromatic amine respectively. In DEPT-135 spectrum two methyl group confirmed at (20.59 ,20.78) ppm. The carbon atom of a carbonyl group of imidazolone ring was found at 169.18 ppm. Vinyl carbon chemical shift was appeared at 129.17 δ ppm. The signal found at 154 δ ppm confirmed the presence of (-C=N-) group **Figure 9**. As seen from above in the ^{1}H-NMR spectra of compounds (**2,4** and **5B**), the peaks of N-H groups did not appear in oxazolone (**2B**) and 3,5-dihydro-4H-imidazol-4-one (**5B**), while the peaks appeared in the spectrum of α, β-dehydroamino acid (**4B**) as mention before.

The antibacterial and anti-fungal profile results described in **tables. 4-6**. Absorbance or Optical density (OD) for each compound and antibiotics with difference concentrations against *Staphylococus aureus as G+Ve*, *E.Coli as G-Ve*, and *fungal Candida albicans*. showed that some of the synthesized compounds under examination displayed substantial activity. According to the results, the tested compounds (**4A** and **5B**) displayed more potent activity than the reference Ciprofloxacin against Escherichia coli. Compounds (**4I & 5H**) showed more potency against *Staphylococcus aureus* than the reference Ciprofloxacin. Compounds (**4B** and **4E**) with all compounds (**5**) except **5C** were more active than reference *Fluconazole against* and *Candida albicans.* Compounds (**4** and **5**) are more active against Candida albicans than Staphylococcus aureus and Escherichia coli. Compounds 1,3-imidazolinones exhibited higher activity against all types of bacteria compared to the *α,β*-dehydroamino acids due to the ring strain. The current study discusses the significance of imidazole ring characteristics responsible for the anti-bacterial activities and may serve as a lead molecule for further modification to create novel entities with clinically advantageous properties.

Table 2. Important IR peaks and some physical properties of synthesized *α,β*-dehydroamino acid derivatives (**4A-4J**).

	NO	Nu R1	Nu R2	Molecular Formula	M.Wt	Yield %	M.P °C	C=O Str. cm^{-1}	N-H Str. cm^{-1}
	A	-H	-F	$C_{30}H_{22}FSN_3O_2$	507	82	245-247	1685.79	3317
	B	-H	$-CH_3$	$C_{31}H_{25}SN_3O_2$	503	83	274-276	1672.28	3277
	C	$-OCH_3$	$-OCH_3$	$C_{32}H_{28}SN_3O_4$	550	81	222-224	1649.14	3275
	D	-Cl	-H	$C_{30}H_{22}ClSN_3O_2$	517.5	83	242-244	1651.07	3257
	E	-H	$-OCH_3$	$C_{31}H_{25}SN_3O_3$	519	81	256-258	1685.79	3338
4	F	-H	$-NO_2$	$C_{30}H_{22}SN_4O_4$	534	85	272-274	1654.92	3300
	G	-H	$-N(CH_3)_2$	$C_{32}H_{28}SN_4O_2$	532	75	225-227	1681.93	3325
	H	-H	-Cl	$C_{30}H_{22}ClSN_3O_2$	523.5	84	243-245	1685.79	3277
	I	C_6H_5-CH=CH-		$C_{32}H_{25}SN_3O_2$	515	84	264-266	1681.93	3263
	J	Pyridine-3-yl-		$C_{29}H_{22}SN_4O_2$	490	73	220-222	1651.07	3240

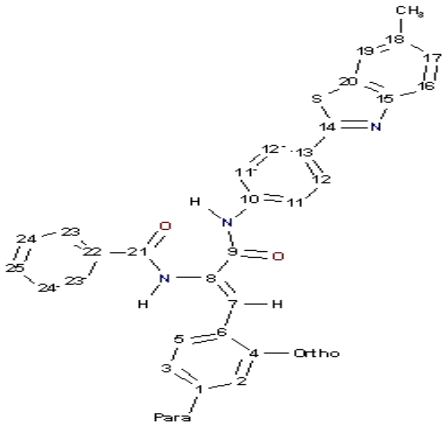
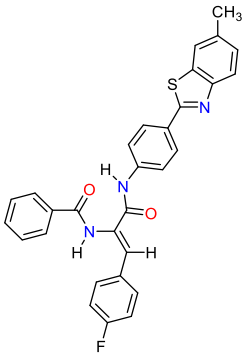
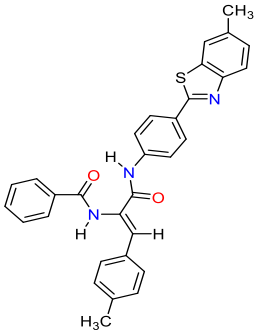
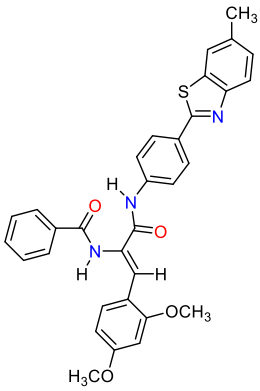


Figure 2. Carbon atoms numbering of synthesized α,β-dehydroamino acids (**4A-4E**) for ^{1}H-NMR and ^{13}C-NMR spectra.

^{1}H- and ^{13}C-NMR chemical shift assignment in ppm of the α, β-dehydroamino acid compounds (4A-4J)

	**N-(1-(4-fluorophenyl)-3-((4-(6-methylbenzo[d]thiazol-2-yl) phenyl)amino)-3-oxoprop-1-en-2-yl)benzamide (4A):-** $C_{30}H_{22}FSN_3O_2$; **^{1}H-NMR** (δ, ppm) (400MHz D6-DMSO): 2.45 (S,3H,CH_3), (7.18-8.06) ppm (m, 17H, Ar-H, C-Vinylic), 10.19 (S,1H,N-H_a), 10.54 (S, 1H,N-H_b); **^{13}C-NMR**(δ, ppm): 166.6:C_{14} of C=N, 165.91:C_9 C=O, 164.72:C_{21} C=O benzyl, 160.73:C_1 C-F, 151.81:C_{15}, 142.09:C_{10}, 135.03:C_{20}, 134.45:C_{18}, 133.28:C_{22}, 131.93:C_{25}, 130.76:C_8 C=C vinyl, 130.70:C_6, 128.45:C_{12},C_{12}-, 128.05:C_{24},C_{24}-, 127.95:C_4,C_5, 127.83:C_{13}, 127.67:C_{23},C_{23}-, 127.29:C_{17}, 122.17:C_{16}, 121.8:C_{19}, 120.13:C_{11},C_{11}-, 115.71:C_2,C_3, 115.49:C_7 Vinyl, 21.07: CH_3-C_{18}.

	**N-(3-((4-(6-methylbenzo[d]thiazol-2-yl)phenyl)amino)-3-oxo-1-(p-tolyl)prop-1-en-2-yl)benzamide (4B):** $C_{31}H_{25}SN_3O_2$; **^{1}H-NMR** (δ, ppm): 2.45 (S, 3H,CH_3), 2.30 (S, 3H,*p*-CH_3), (7.18-8.06)ppm (m, 17H, Ar-H, C-Vinylic), 10.15 (S,1H,N-H_a), 10.51 (S, 1H,N-H_b); **^{13}C-NMR** (δ, ppm): 165.99:C_{14} C=N, 165.93:C_9 C=O, 164.81:C_{21} C=O benzyl, 151.81:C_{15}, 142.15:C_{10}, 138.53:C_1 C-CH_3, 135.02:C_{20}, 134.45:C_{18}, 133.41:C_{22}, 131.85:C_{25}, 131.35:C_6, 130.08:C_8 C=C vinyl, 129.59:C_2,C_3, 129.02:C_{24},C_{24}-, 128.77:C_{16}, 128.43:C_{23},C_{23}-, 128.04:C_{17}, 127.93:C_{12},C_{12}-, 127.78:C_{13}, 127.65:C_4,C_5, 122.16:C_{19}, 121.81:C_7 Vinyl, 120.15:C_{11},C_{11}-, 21.07: CH_3-C_{18}, 20.95: *P*-CH_3.
	**N-(1-(2,4-dimethoxyphenyl)-3-((4-(6-methylbenzo[d]thiazol-2-yl)phenyl)amino)-3-oxoprop-1-en-2-yl)benzamide (4C):** $C_{32}H_{28}SN_3O_4$;**^{1}H-NMR** (δ, ppm): 2.45 (S, 3H,CH_3), 3.84 (S, 3H, *p*-O-CH_3), 3.91 (S, 3H, *O*-O-CH_3), (6.6-8.16) ppm (m, 16H, Ar-H, C-Vinylic), 10.07 (S,1H,N-H_a), 10.46 (S, 1H,N-H_b); **^{13}C-NMR**(δ ppm): 165.91:C_{14} C=N, 164.87:C_9 C=O, 161.32:C_{21} C=O benzyl, 158.61:C_1, 151.76:C_{15}, 142.15:C_{10}, 134.97:C_{20}, 134.40:C_4, 133.47:C_{18}, 131.71:C_{25}, 129.76:C_5, 128.63:C_8 C=C vinyl, 128.33:C_{12},C_{12}-, 128.00:C_{24},C_{24}-,127.88:C_{17}, 127.63:C_{13}, 127.58:C_{23},C_{23}-, 123.29:C_7 Vinyl, 122.11:C_{16}, 121.19:C_{19}, 120.11:C_{11},C_{11}-, 115.20:C_6, 105.38:C_3, 98.20:C_2, 55.70: *O*-O-CH_3, 55.34: *P*-O-CH_3, 21.04: CH_3-C_{18}.

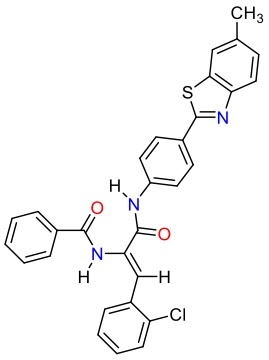
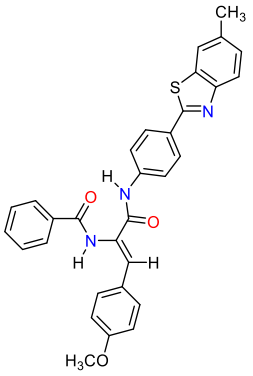
	**N-(1-(2-Chlorophenyl)-3-((4-(6-methylbenzo[d]thiazol-2-yl)phenyl) amino)-3-oxoprop-1-en-2-yl)benzamide (4D):** $C_{32}H_{28}SN_3O_4$; **^{1}H-NMR** (δ, ppm): 2.52 (S, 3H,CH_3), (7.43-7.79)ppm (m, 17H, Ar-H, C-Vinylic), 10.34 (S,1H,N-H_a), 10.72 (S, 1H,N-H_b); **^{13}C-NMR**(δ, ppm): 166.70:C_{14} C=N, 165.82:C_9 C=O, 164.14:C_{21} (C=O benzyl), 151.75:C_{15}, 141.82:C_{10}, 135.10:C_{20}, 134.42:C_{18}, 133.22:C_4 C-Cl, 133.12:C_{22}, 133.07:C_6, 132.51:C_8 of C=C vinyl, 131.92:C_2, 130.09: C_1, 129.83:C_5, 129.57:C_3, 128.34:C_{12},$C_{12\text{-}}$, 128.02:C_{17}, 127.93:C_{24},$C_{24\text{-}}$, 127.65:C_{23},$C_{23\text{-}}$, 127.21:C_{13}, 123.38:C_7 Vinyl, 122.14:C_{16}, 121.79:C_{19}, 120.20:C_{11},$C_{11\text{-}}$, 21.04: $\underline{CH_3}$-C_{18}.
	**N-(1-(4-methoxyphenyl)-3-((4-(6-methylbenzo[d]thiazol-2-yl)phenyl)amino)-3-oxoprop-1-en-2-yl)benzamide (4E):** $C_{31}H_{25}SN_3O_3$; **^{1}H-NMR** (δ, ppm): 2.45 (S, 3H,CH_3), 3.77 (S, 3H,*p*-OCH_3), (6.97-8.07) ppm (m, 17H, Ar-H, C-Vinylic), 10.11 (S,1H, N-H_a), 10.44 (S, 1H,N-H_b); **^{13}C-NMR** (δ, ppm): 165.97:C_{14} C=N, 165.93:C_9 C=O, 164.89:C_{21} C=O benzyl, 159.71:C_1 $\underline{C}$-OCH_3 151.81:C_{15}, 142.20:C_{10}, 135.01:C_{20}, 134.44:C_{18}, 133.46:C_{22}, 131.81:C_{25}, 131.34:C_4,C_5, 128.95:C_{16}, 128.64:C_8 C=C vinyl, 128.42:C_{24},$C_{24\text{-}}$, 128.03:C_{17}, 127.93:C_{23},$C_{23\text{-}}$, 127.71:C_{13}, 127.63:C_{12},$C_{12\text{-}}$, 126.56:C_6, 122.15:C_{19}, 121.81:C_7Vinyl, 120.14:C_{11},C_{11}, 114.09:C_2,C_3, 55.23:*p*-$O\underline{CH_3}$, 21.07: $\underline{CH_3}$-C_{18}.

Table 3. Significant IR peaks and some physical properties for the synthesized 3,5-dihydro-4H-imidazol-4-one Compound (5A-5E).

NO	Nu R_1	Nu R_2	Molecular Formula	M.Wt	Yield%	M.P °C	C=O str. cm^{-1}	C=N str. cm^{-1}
A	-H	-F	$C_{30}H_{20}FSN_3O$	489	77	282-284	1716.65	1641.42
B	-H	$-CH_3$	$C_{31}H_{23}SN_3O$	485	80	275-277	1720.50	1639.49
C	$-OCH_3$	$-OCH_3$	$C_{32}H_{25}SN_3O_3$	531	85	285-287	1714.72	1635.64
D	-Cl	H	$C_{30}H_{20}ClSN_3O$	505.5	86	250-252	1718.58	1635.64

	E	-H	-OCH_3	$C_{31}H_{23}SN_3O_2$	501	87	285-287	1720.50	1643.35
5	F	-H	-NO_2	$C_{30}H_{20}SN_4O_3$	516	87	288-290	1722.43	1637.56
	G	-H	-$N(CH_3)_2$	$C_{32}H_{26}SN_4O$	514	76	286-288	1699.29	1655.00
	H	-H	-Cl	$C_{30}H_{20}ClSN_3O$	505.5	80	278-280	1722.43	1639.49
	I	C_6H_5-CH=CH-		$C_{32}H_{23}SN_3O$	497	82	258-260	1730.15	1629.95
	J	Pyridine-3-yl-		$C_{29}H_{20}SN_4O$	472	72	266-268	1730.15	1647.21

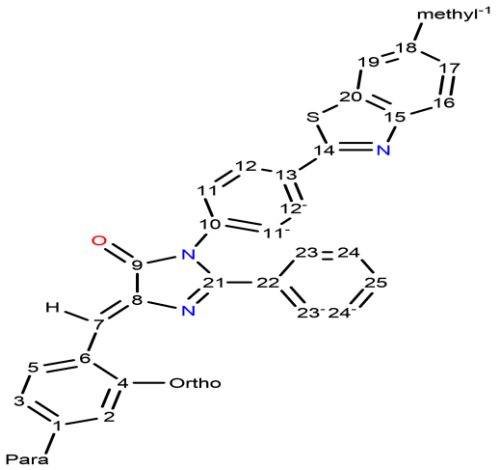
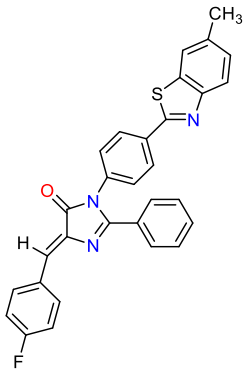
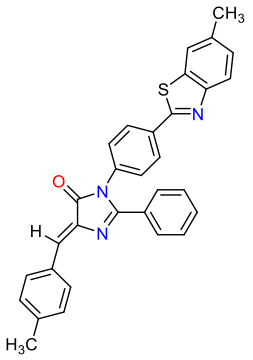
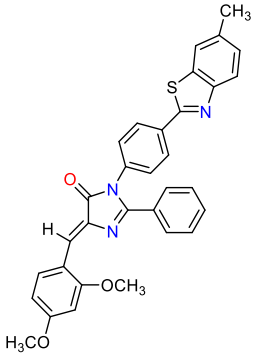


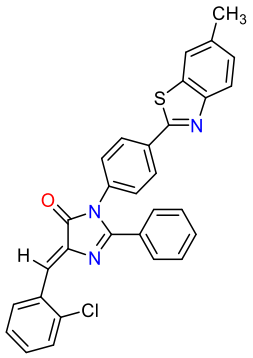
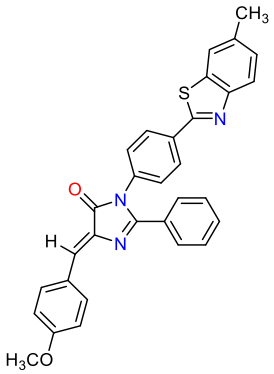
Figure 3. Carbon atoms numbering of the synthesized 3,5-dihydro-4H-imidazol-4-one (5A-5E) for 1H-NMR and 13C-NMR spectra

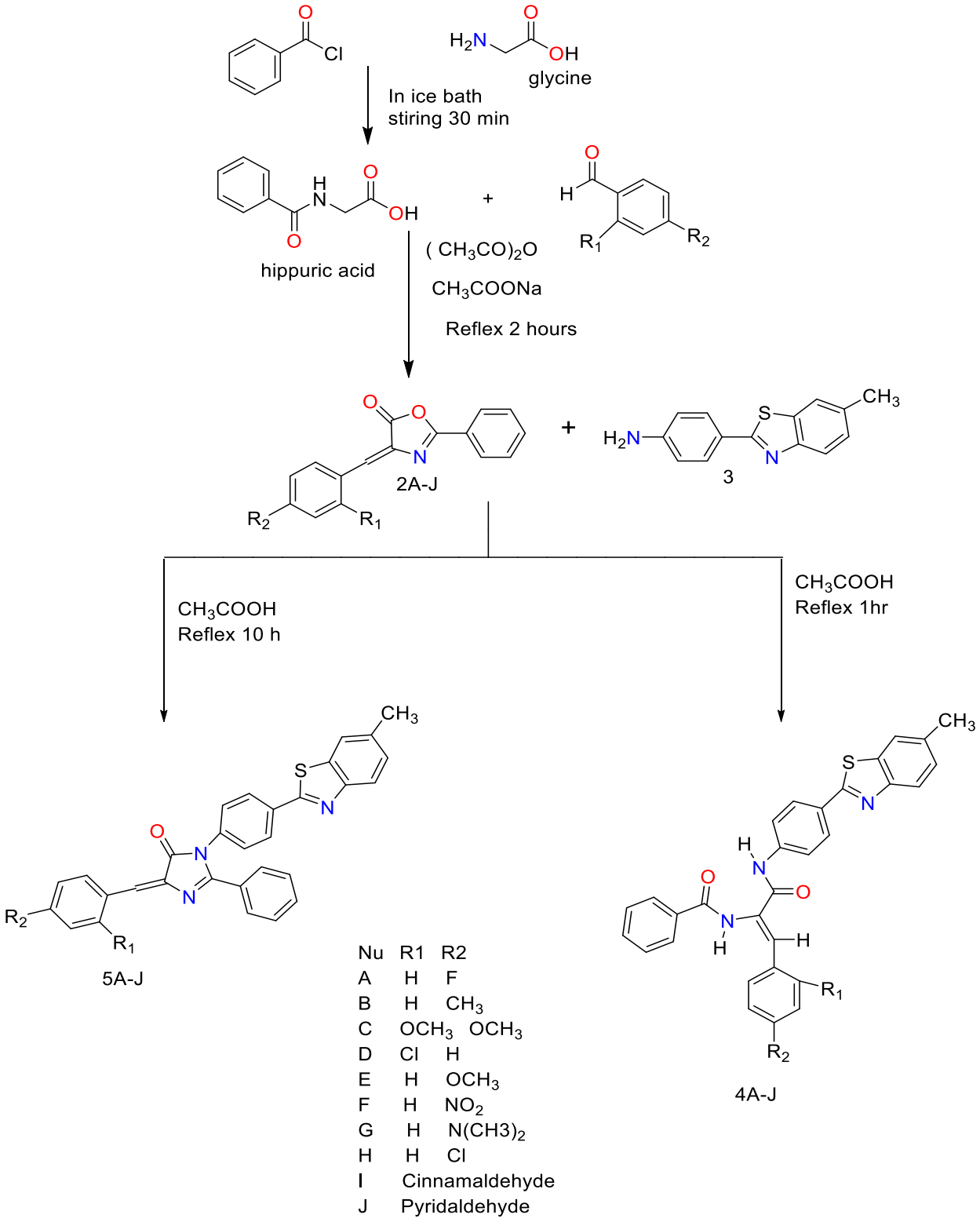
^{1}H- and ^{13}C-NMR chemical shift assignment in ppm of the 3,5-dihydro-4H-imidazol-4-one compounds (**5A-5J***)*



5-(4-fluorobenzylidene)-3-(4-(6-methylbenzo[d]thiazol-2-yl)phenyl)-2-phenyl-3,5-dihydro-4H-imidazol-4-one (5A): $C_{30}H_{20}FSN_3O$; **^{1}H-NMR** (δ, ppm) (400 MHz $CHCl_3$): 2.51 (S, 3H,CH_3-C_{18}), (7.16-8.33) ppm (m, 17H, Ar-H, C-Vinylic); **^{13}C-NMR** (δ, ppm): 169.10:C_9 (C=O Imidazolone), 164.53:C_1 C-F, 164.23:C_{21}, 164.01:C_{14} C=N, 151.19:C_{15}, 135.44:C_{10}, 134.76:C_{20}, 134.34:C_{22}, 133.85:C_4,C_5, 133.76:C_{18}, 132.49:C_6, 130.62:C_{25}, 129.56:C_8 C=C vinyl, 128.20:C_{11},C_{11}-, 127.55:C_{12},C_{12}-, 127.42:C_{13}, 127.32:C_{24},C_{24}-, 127.16:C_{17}, 126.55:C_{23},C_{23}-, 121.84:C_{16}, 120.43:C_{19}, 115.18:C_2,C_3, 114.60:C_7 Vinyl 20.06: CH_3-C_{18}.

	**3-(4-(6-methylbenzo[d]thiazol-2-yl)phenyl)-5-(4-methylbenzylidene)-2-phenyl-3,5-dihydro-4H-imidazol-4-one (5B):** $C_{31}H_{23}SN_3O$; **^{1}H-NMR** (δ, ppm) (400 MHz $CHCl_3$): 2.51 (S, 3H,CH_3-C_{18}), 2.42 (S, 3H,CH_3-C_1), (7.26-8.21) ppm (m, 17H, Ar-H, C-Vinylic); **^{13}C-NMR**(δ, ppm): 169.18:C_9 of (C=O Imidazolone), 164.62:C_{14} C=N, 158.10:C_{21}, 151.10:C_{15}, 140.45:C_{10}, 136.58: C_1 C-CH_3, 135.62:C_{20}, 134.70:C_{22}, 134.30:C_6, 132.32:C_{18}, 131.75:C_{11},C_{11}-, 130.52:C_8 C=C vinyl, 130.41:C_{25}, 129.17:C_7 Vinyl, 128.64:C_{12},C_{12}-, 128.18:C_2,C_3, 127.68:C_{13}, 127.49:C_4,C_5, 127.29:C_{23},C_{23}-, 127.14:C_{17}, 126.56:C_{24},C_{24}-, 121.80:C_{16}, 120.41:C_{19}, 20.78 *P*-CH_3, 20.59: CH_3-C_{18}.
	**5-(2,4-dimethoxybenzylidene)-3-(4-(6-methylbenzo[d]thiazol-2-yl)phenyl)-2-phenyl-3,5-dihydro-4H-imidazol-4-one (5C):** $C_{31}H_{23}SN_3O$; **^{1}H-NMR** (δ, ppm) (400 MHz $CHCl_3$): 2.50 (S, 3H, CH_3-$C_{18}CH_3$), 3.89 (S, 3H,*O*-OCH_3), 3.90 (S,3H,*P*-OCH_3), (7.26-8.21) ppm (m, 16H, Ar-H, C-Vinylic); **^{13}C-NMR**(δ, ppm): 169.41:C_9 (C=O Imidazolone), 164.75:C_{14} C=N, 162.6:C_1 C-OCH_3, 160.20:C_{21}, 157.01:C_{15}, 151.22:C_4 C-OCH_3, 135.93:C_{10}, 134.78:C_{20}, 134.65:C_{22}, 134.34:C_{18}, 133.96:C_{25}, 132.16:C_8, 130.03:C_{11},C_{11}-, 128.08:C_{12},C_{12}-, 127.42:C_{24},C_{24}-, 127.22:C_{23},C_{23}-, 127.09:C_{17}, 126.60:C_{13}, 123.24:C_{16}, 121.81:C_{19}, 120.41:C_7 Vinyl, 115.74:C_6, 105.13C_3, 96.66:C_2, 54.64 of *O*- OCH_3, 54.51 *P*-OCH_3, 20.58: CH_3-C_{18}.

	**5-(2-chlorobenzylidene)-3-(4-(6-methylbenzo[d]thiazol-2-yl) phenyl)-2-phenyl-3,5-dihydro-4H-imidazol-4-one (5D):** $C_{30}H_{20}ClSN_3O$; **^{1}H-NMR** (δ, ppm) (400 MHz $CHCl_3$): 2.54 (S, 3H, $\underline{CH_3}$-C_{18}), (7.29-9.09) ppm (m, 17H, Ar-H, C-Vinylic); **^{13}C-NMR** (δ, ppm): 169.93:C_9 (C=O Imidazolone), 165.55:C_{14} C=N, 161.25:C_{15}, 152.23:C_{21}, 139.46:C_{10}, 136.39:C_{20}, 135.80:C_{22}, 135.38:C_{18}, 133.80:C_{25}, 133.57:C_4 of C-Cl,132.13:C_6, 131.81:C_2, 131.29:C_1, 129.88:C_5, 129.31:C_{12},C_{12}-, 128.96:C_8, 128.59:C_{24},C_{24}-, 128.45:C_{13}, 128.36:C_{11},C_{11}, 128.18:C_3, 127.59:C_{23},C_{23}-, 127.10:C_{17}, 124.58:C_{16}, 122.88:C_{19}, 121.46:C_7 Vinyl, 21.62: $\underline{CH_3}$-C_{18}.
	**5-(4-methoxybenzylidene)-3-(4-(6-methylbenzo[d]thiazol-2-yl)phenyl)-2-phenyl-3,5-dihydro-4H-imidazol-4-one(5E):** $C_{31}H_{23}SN_3O_2$; **^{1}H-NMR** (δ, ppm) (400 MHz $CHCl_3$) : 2.50 (S, 3H,CH_3), 3.89 (S, 3H, -OCH_3), (6.99-8.30) ppm (m, 17H, Ar-H, C-Vinylic); **^{13}C-NMR**(δ, ppm): 169.15:C_9 (C=O Imidazolone), 164.70:C_{14} C=N, 160.77: C_1 $\underline{C}$-OCH_3, 157.78:C_{21}, 151.22:C_{15}, 135.73:C_{10}, 135.50:C_{20}, 134.70:C_{22}, 134.35:C_{18}, 133.74:C_4,C_5, 132.35:C_8 C=C, 130.26:C_{25}, 128.99:C_{11},C_{11}-, 128.12:C_{12},C_{12}-, 127.82:C_6, 127.48:C_{23},C_{23}-, 127.27:C_{24},C_{24}-, 127.12:C_{17}, 126.58:C_{16}, 126.24:C_{13}, 121.83:C_{19}, 120.41:C_7 Vinyl, 113.42:C_2,C_3, 54.42:*P*-OCH_3, 20.59: $\underline{CH_3}$-C_{18}.



Scheme 1.Synthetic way of 3,5-dihydro-4H-imidazol-4-one and *α,β*-dehydroamino acid derivatives

Table 4. Antimicrobial activity of the gram-negative bacteria *Escherichia coli* (positive control OD=1.123)
Percent of Inhibition/ Killing = ((OD of control-OD of tested)/(OD of control)) *100

	4A	**4B**	**4C**	**4D**	**4E**	**4F**	**4G**	**4H**	**4I**	**4J**	**CIPR**
200	92.9	0	0	0	98.4	82.7	0	0	98.3	73.3	88.42
400	100	48.8	0	7.9	99.5	95.9	81.4	60.8	99.55	86.46	94.6
600	100	100	95.7	96	99.8	99.0	95.7	95.2	99.8	95.8	94.6
800	100	100	95.9	95.7	100	100	95.9	95.7	100	95.72	100
	5A	5B	5C	5D	5E	5F	5G	5H	5I	5J	
200	80.5	98.5	0	0	79.5	0	0	81.3	92.0	68.6	
400	96.2	100	91.0	96.7	81.3	91.0	86.3	81.9	99.8	87.2	
600	100	100	94.1	100	99.8	96.5	87.4	100	100	98.2	
800	100	100	100	100	100	99.1	97.8	100	100	100	

Table 5. Antimicrobial activity of the gram positive *Staphylococcus Aureus* (positive control OD=1.203)

Percent of Inhibition/ Killing = ((OD of control-OD of tested)/(OD of control)) *100

	4A	**4B**	**4C**	**4D**	**4E**	**4F**	**4G**	**4H**	**4I**	**4J**	**CIPR**
200	0	89.11	0	0	0	86.5	71.8	54.2	79.6	70.6	75.0
400	91.5	96.0	5.8	16.4	89.7	92.2	85.2	70.8	100	83.7	91.6
600	100	100	96.3	96.0	100	100	85.6	100	100	95.9	95.8
800	100	100	96.2	96.1	100	100	100	100	100	96.5	100
	5A	5B	5C	5D	5E	5F	5G	5H	5I	5J	
200	0	0	0	0	89.1	0	0	86.5	77.9	0	
400	87.2	98.4	95.2	81.7	95.1	84.6	0	99.9	91.6	67.9	
600	100	100	95.3	89.1	100	100	10.88	100	94.4	90.3	
800	100	100	100	100	100	100	100	100	100	100	

Table 6. Anti-fungal activity of the fungal *Candida albicans* (positive control OD=1.029)

Percent of Inhibition/ Killing = ((OD of control-OD of tested)/(OD of control)) *100

	4A	**4B**	**4C**	**4D**	**4E**	**4F**	**4G**	**4H**	**4I**	**4J**	**FLU**
200	0	71.8	0	0	89.7	80.0	0	85.4	55.9	64.8	89.3
400	86.8	100	3.6	6.8	100	98.1	60.7	72.7	89.5	77.6	89.3
600	100	100	95.6	95.5	100	100	94.3	100	100	95.1	92.2
800	100	100	95.6	96.0	100	100	94.6	100	100	95.3	100
	5A	5B	5C	5D	5E	5F	5G	5H	5I	5J	
200	97.2	83.0	0	93.4	90.6	92.5	0	0	73.9	60.3	
400	100	100	24.1	100	100	100	95.1	86.8	91.6	91.3	
600	100	100	89.9	100	100	100	98.9	100	100	100	
800	100	100	97.7	100	100	100	100	100	100	100	

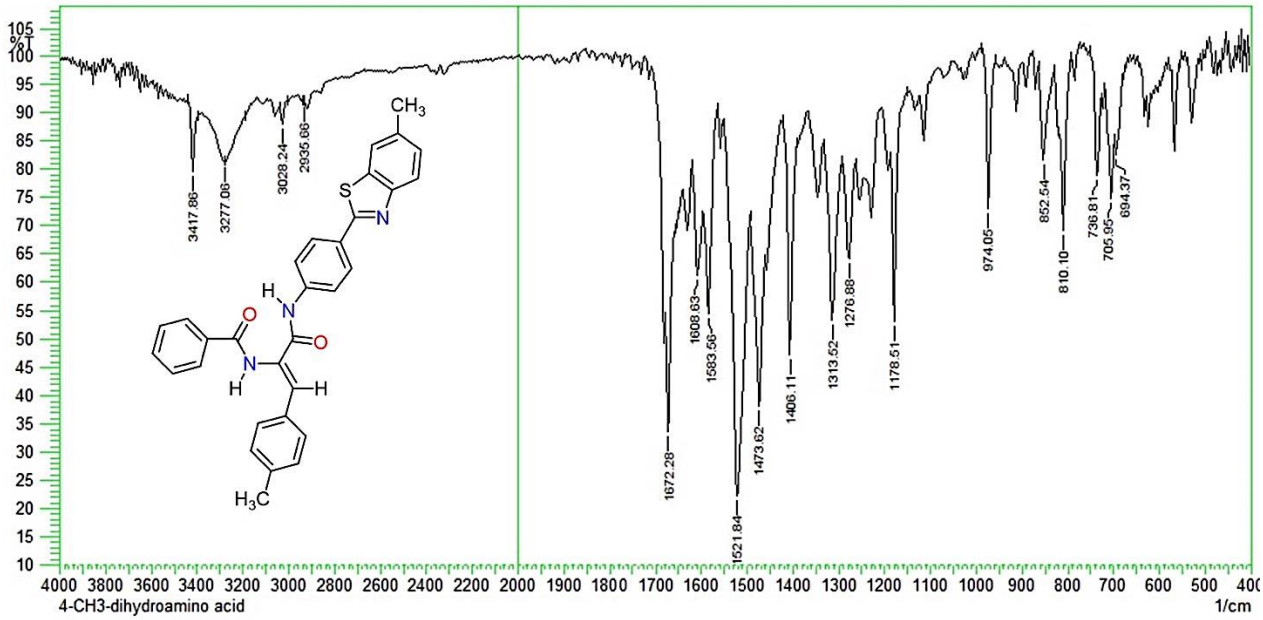


Figure 4. *(FT-IR) spectrum of compound* N-(3-((4-(6-methylbenzo[d]thiazol-2-yl)phenyl)amino)-3-oxo-1-(p-tolyl)prop-1-en-2-yl)benzamide (**4B).**

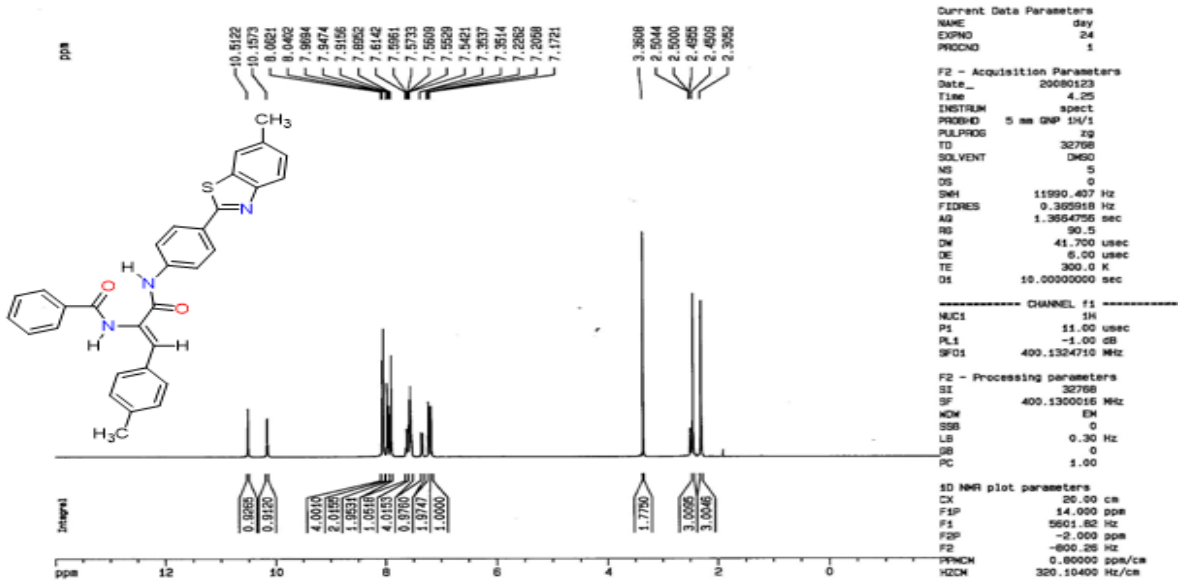


Figure 5.*[1]H-NMR spectrum of Compound N-(3-((4-(6-methylbenzo[d]thiazol-2-yl)phenyl)amino)-3-oxo-1-(p-tolyl)prop-1-en-2-yl)benzamide (**4B).***

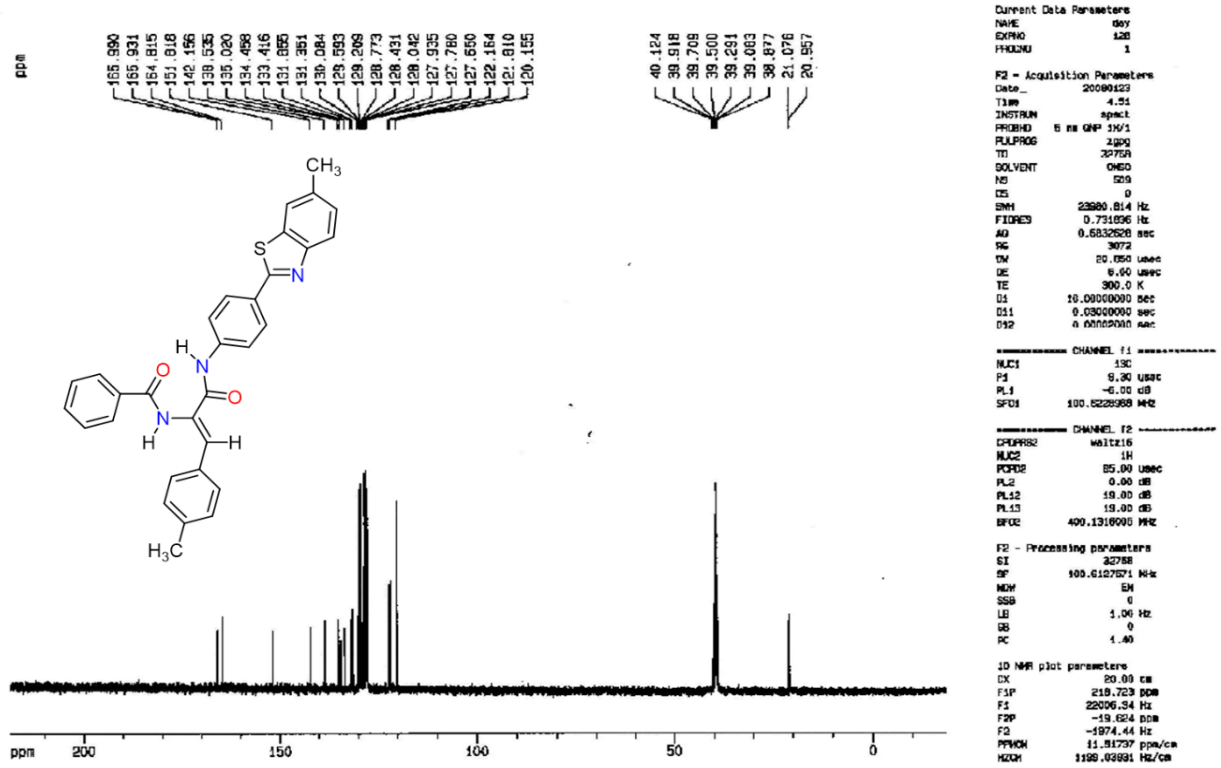


Figure 6.[13]*C-NMR spectrum of Compound N-(3-((4-(6-methylbenzo[d]thiazol-2-yl)phenyl)amino)-3-oxo-1-(p-tolyl)prop-1-en-2-yl)benzamide (**4B).***

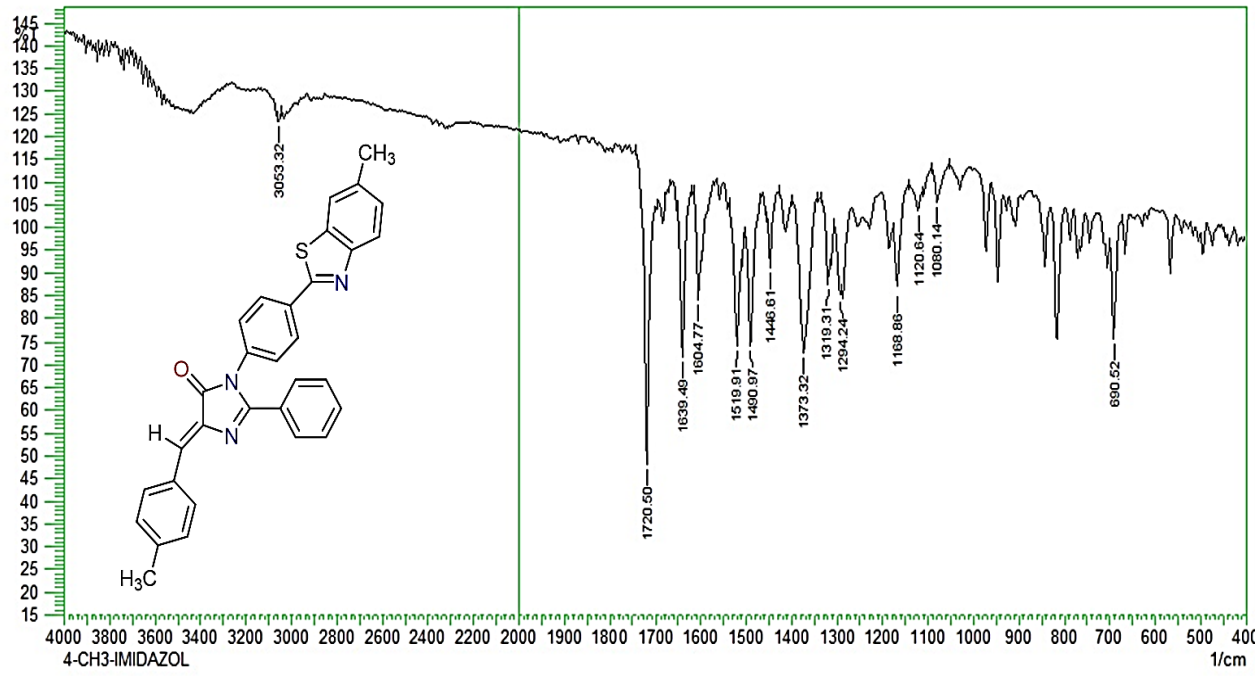


Figure 7. *FT- IR spectrum of compound 3-(4-(6-methylbenzo[d]thiazol-2-yl) phenyl)-5-(4-methylbenzylidene)-2-phenyl-3,5-dihydro-4H-imidazol-4-one (**5B).***

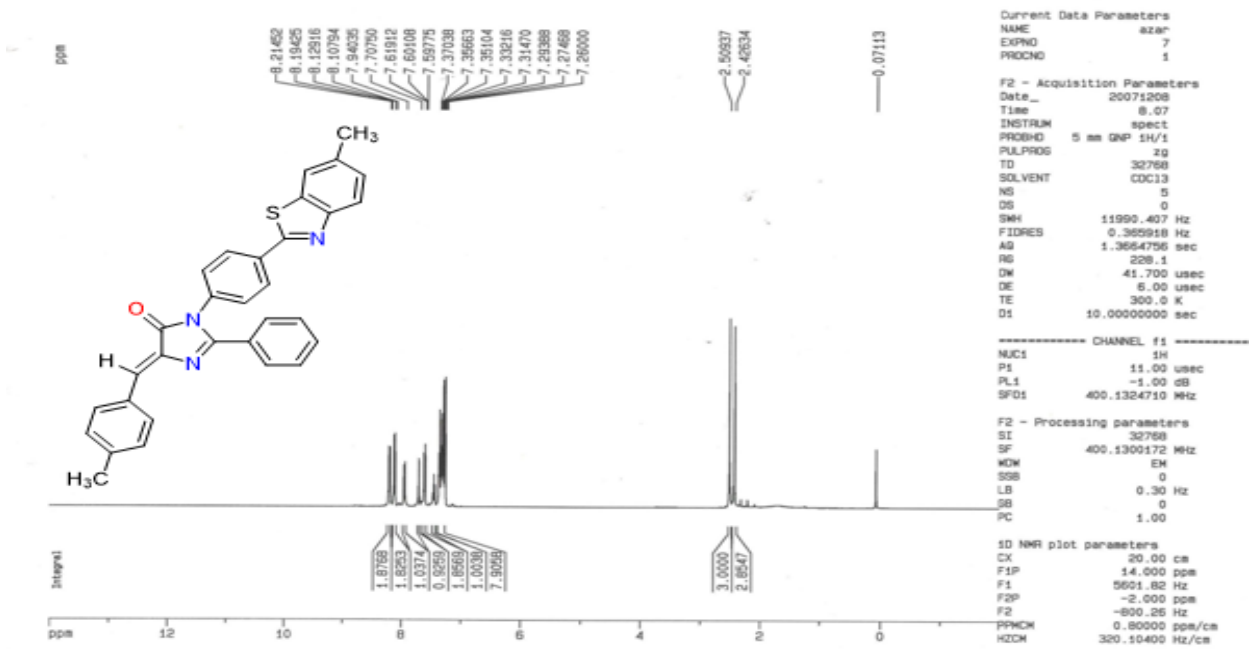


Figure 8. *[1]H-NMR spectrum of compound 3-(4-(6-methylbenzo[d]thiazol-2-yl) phenyl)-5-(4-methylbenzylidene)-2-phenyl-3,5-dihydro-4H-imidazol-4-one (**5B**).*

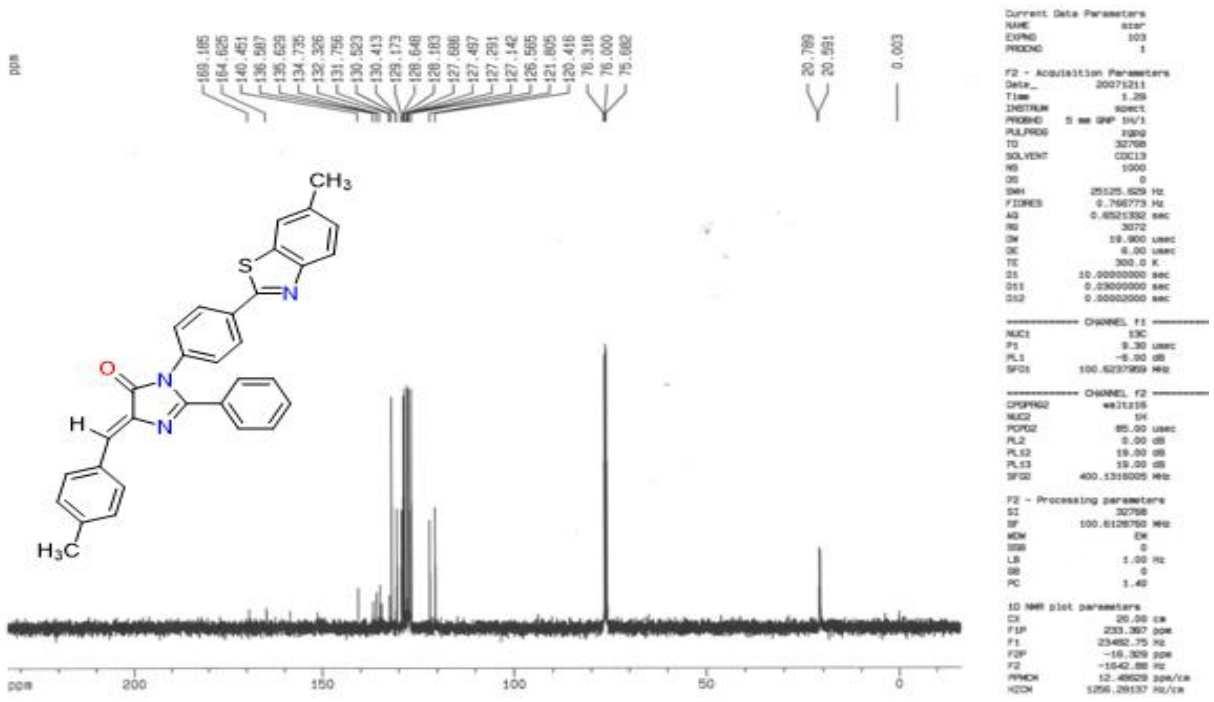


Figure 9. *[13]C-NMR spectrum of compound 3-(4-(6-methylbenzo[d]thiazol-2-yl) phenyl)-5-(4-methylbenzylidene)-2-phenyl-3,5-dihydro-4H-imidazol-4-one (**5B**).*

4. Conclusion

Some new N-substituted *α,β*-dehydroamino acid derivatives incorporating thiazole ring and 3,5-dihydro-4H-imidazol-4-one combined with thiazole moiety were prepared with the goal of achieving good anti-fungal and antibacterial activities under available laboratory condition. Some of the synthesized compounds revealed moderate to good bactericidal and bacteriostatic

effects against *Escherichia coli, Staphylococcus aureus* and *Candida albicans* but not at the same concentration, according to the study, concluded that the presence of imidazole group is important for anti-fungal and antibacterial activity and the data recorded in this study may be a helpful guide for the medicinal chemists who are studying in this area.

Conflict of interest:

There is no Conflict of interest,

Referance

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