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BIO ACTIVE SYNTHESIS OF 5-(Є-3, 4-DIMETHOXYBENZYLIDENE)-3-PHENYL-2-(Є-STYRYL)-3, 5-DIHYDRO-4H-IMIDAZOL-4-ONE

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ABSTRACT

In view of potent antimicrobial activities enhanced by 5-((E)-3, 4-dimethoxybenzylidene)-3-phenyl-2-((E)-styryl)-3, 5-dihydro-4H-imidazol-4-one (7a-f) were synthesized by the cyclo condensation of 4-((E)-3, 4-dimethoxybenzylidene)-2-((E)-styryl) oxazol-5(4H)-one (1) and various substituted aryl amines. The compound (5) can be obtained from with 3, 4-dimethoxy benzaldehyde and acetic anhydride in the presence of sodium acetate and added catalyst. The compound (3) can be prepared from cinnamoyl chloride with glycine which is also obtained by the cinnamic acid with thionyl chloride. The structures of all the newly derivatives were evaluated by using advanced spectroscopic data such as IR, ^{1}H NMR, ^{13}C NMR and LCMS and also determination of the structure by elemental analysis. All the synthesized derivatives were screened for *in vitro* activities against a panel of Gram (+ve) and Gram-(-ve) bacteria and the yeast-like pathogenic fungal Candida albicans.

KEYWORDS

Cinnamoylglycine, Oxazolone, Imidazolones, Substituted aromatic amines and Antimicrobial activity.

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INTRODUCTON

Heterocycles represent an important core in many isolated natural products. Imidazolones are five-membered heterocyclic rings containing two non-adjacent nitrogen and a carbonyl group. There are two isomers of imidazolones, depending on the placement of the carbonyl imidazol-2-ones and imidazol-4-ones. The most important role play in the medicinally and synthetic organic chemistry. Imidazol-4-ones are an important heterocycles that was utilized for a broad range of applications, including medicinal chemistry and also they are associated with a vital range of therapeutic

activities[1-7] such as anti-microbial activity[8-14], Now days most of research workers have been recognized 5-imidazolone as having anticancer activity[15-18] anti-inflammatory[19-20], anticonvulsant[21,22] anti-diabetics[23,24] antidepresent hypertensive[25], antiparkinsonian[26], photo physical behavior[27], fluorescent protein chromosphere's[28] despite being found in a vast assortment of fields, there has never been a review on the preparative methods of imidazol-4-ones.

In view of these points and in continuation of our work on Imidazol-4-ones, it was thought worthwhile to study some new Imidazol-4-ones having imidazolinone moiety with an aim to get promising biological activating molecules. Thus a new series of imidazolones derivatives, were synthesized and tested for their antioxidant and antimicrobial activities.

MATERIAL AND METHODS

All the reagents chemical, reagents and solvents were procured from Fine chemicals. The melting points of newly synthesized derivatives were recorded on Agarwal 535 melting point apparatus and are uncorrected. All the reactions of desired products were monitored by thin layer chromatography performed on percolated silica gel 60F254 plates (Fine chemicals) and they were visualized with UV light in iodine chamber. IR spectra were recorded using an Avatar-330 FT-IR spectrophotometer using KBr pellets. ^{1}H NMR spectra of these compounds were recorded on BRUKER 400 MHz spectrometers and ^{13}C NMR was recorded on BRUKER 100 MHz using $CDCl_3$ tetra methyl saline as internal standard. Elemental analyses were carried out in Perkin Elmer 240 CHN elemental analyzer.

General procedure of 5-((E)-3, 4-dimethoxybenzylidene)-3-phenyl-2-((E)-styryl)-3, 5-dihydro-4H-imidazol-4-one

General producer of cinnamoyl chloride

Take clean and dry 25mL four necks RBF. 25mL methylene dichloride taken in a RBF and cinnamic acid (1mmol) is dissolved in solvent. The thionyl chloride added drop wise with help of dropping funnel in a RBF in 5-10^{o}C. The total arrangement fitted on the magnetic stirrer. The reaction is continued in 2 hrs. at reflux. After completion of the reaction time, the mixture cooled under tap water and evaporated the unreacted thionyl chloride and proceeded to the further reaction.

Colorless liquid, Yield-95%, IR (KBr cm-1): 3121, 3072, 1813, 1601, 1565, 1523, 852, 839.

^{1}HNMR (400MHz, CDCl3) ppm: 7.924(s, 1H, CH=CH), 7.529-7.295 (m, 5H, Ar-H), 5.846(s, 1H, CH=CH-CO-); ^{13}CNMR (100MHz, $CDCl_3$) ppm: 191.72, 144.64, 131.09, 128.84, 128.14, 127.66 and 118.21. LCMS (m/z):168.18(M+2); Molecular formulae: C_9H_7ClO; Elemental analysis: Calculated: C- 64.86, H-4.24, Obtained: C- 64.79, H- 4.23.

General producer of Cinnamoylglycine (3)

25mL of 10% NaOH taken in clean and dry 100mL conical flask and 1mmol of glycine dissolved in flask. Cinnamoyl chloride added drop wise in above solution and shaken vigorously .The above solution is neutralized Con HCl. The crude was taken in a ethyl acetate and washed with water twice. The organic layer separated and distilled off under vacuum distillation and finally obtained desired product.

Colorless liquid, Yield-95%, IR (KBr cm-1): 3545, 3378, 3114, 3056, 2537, 1601, 1574, 1516, 1236, 846; ^{1}HNMR (400MHz, $CDCl_3$) ppm: 11.078(s, 1H, acid), 8.156(s, 1H, N-H), 7.597-7.346 (m, 5H, Aromatic), 7.108(s, 1H, =CH), 6.236(s, 1H, =CH), 3.405(s, 3H, CH3); ^{13}CNMR (100MHz, $CDCl_3$) ppm: 170.46, 166.78, 138.24, 129.32, 128.66, 128.33, 127.44, 122.91, 40.36; LCMS(m/z): 204.66 (M-H); Molecular formulae: $C_{11}H_{11}NO_3$; Elemental analysis: Calculated: C-64.38, H- 5.40, N-6.83; Obtained: C-64.30, H- 5.39, N-6.89.

4-((E)-3, 4-dimethoxybenzylidene)-2-((E)-styryl) oxazol-5(4H)-one (5)

A reaction mixture of substituted aromatic aldehydes 1 (1mmol), Cinnamoylglycine (1mmol), sodium acetate (3mmol), Acetic anhydride (5mmol %) in (5mL) was refluxed for 5-10 min and after adding 0.1mmol of zinc oxide as a catalyst. During the reaction, the progress of the reaction mixture was checked by TLC (as mobile system 3:7-Ethylacetae: n-hexane) analysis. After completion of the reaction, the system was cooled to room

temperature and the reaction mixtures poured into ethyl acetate and neutralized with a solution of sodium bi carbonate, washed with distilled water (4mL) and separate the organic layer. The organic layer distilled off under vacuum distillation. All the products were isolated pure just by recrystallization from hot ethanol, if necessary. Spectral data for some compounds are as follows:

General producer of 5-((E)-3, 4-dimethoxybenzylidene)-3-phenyl-2-((E)-styryl)-3, 5-dihydro-4H-imidazol-4-one

A reaction mixture of 4-((E)-3, 4-dimethoxybenzylidene)-2-((E)-styryl) oxazol-5(4H)-one 1(1mmol), substituted aryl amine (1 mmol), pyridine (3mmol), DMF (5mmol%) in (5mL) was introduced in 25mL four neck RBF and fitted on the magnetic stirrer and also was refluxed for 10-15 min. During the reaction, the progress of the reaction mixture was monitored by TLC (as mobile system 5:5- Ethylacetae: n-hexane) analysis. After completion of the reaction, the system was cooled to RT and the reaction mixtures poured into ethyl acetate and neutralized with a solution of sodium hydrogen carbonate, washed with distilled water (4mL), and separate the organic layer. The organic layer distilled off under vacuum distillation. All the products were isolated pure just by recrystallization from hot ethanol, if necessary.

Spectral data for some compounds are as follows.

15-((E)-3, 4-dimethoxybenzylidene)-3-phenyl-2-((E)-styryl)-3, 5-dihydro-4H-imidazol-4-one (7a)

Yeild-88%, paleornge solid, M.P- 158-160^{o}C, Rf: 0.50 (4: 6-EtOAc: n-hexane); IR (KBr,cm-1); 3125, 3068, 1652, 1596, 1546, 1512, 1352, 1281, 746; ^{1}HNMR (400MHz, $CDCl_3$): 8.112 (s, 1H, =CH); 7.584-7.390 (m, 10H, Ar-H), 7.355 (s, 1H, =CH), 7.412 (s, 1H, Ar-H), 7.244 (d, J=8.0Hz, 1H, Ar-H), 6.554 (s, 1H, =CH), 7.118 (d, J=7.2Hz, 1H, Ar-H) 3.741(s, 3H, -OCH3), 3.592 (s, 3H,-OCH_3), ^{13}CNMR (400MHz, $CDCl_3$): 166.58, 150.55, 147.08, 145.21, 137.35, 132.75, 130.02, 129.66, 128.91, 128.56, 128.12, 127.44, 127.88, 126.17, 115.65, 114.65, 113.48, 110.68, 109.56, 55.32, 54.15. Molecular formulae: $C_{26}H_{22}N_2O_3$: LCMS (m/z): 411.29 (M+H); Elemental analysis: Calculated: C- 76.08, H-5.40, N-6.82; Obtained: C-76.01, H- 5.38, N- 6.896.

25-((E)-3, 4-dimethoxybenzylidene)-3-(4-methoxyphenyl)-2-((E)-styryl)-3, 5-dihydro-4H-imidazol-4-one (7b)

Yeild-94%, pale red solid, M.P-189=191^{o}C, Rf: 0.40 (4:6-EtOAc: n-hexane); IR (KBr, cm-1); 3221, 3128, 1632, 1592, 1564, 1536, 1355, 1299, 1079, 748, 689. ^{1}HNMR (400MHz, $CDCl_3$): 8.052 (s, 1H, =CH); 7.567-7.382 (m, 5H, Ar-H), 7.361 (s, 1H, =CH), 7.315-7.292 (m, 2H, aromatic), 7.225 (s, 1H, Ar-H), 7.172-7.058 (m, 3H, Ar-H), 6.394 (s, 1H, =CH), 3.653(s, 3H, -OCH_3), 3.589(s, 3H, -OCH_3), 3.587 (s, 3H,-OCH3); ^{13}CNMR (400MHz, $CDCl_3$): 166.08, 123.35, 150.12, 147.38, 145.77, 136.16, 133.57, 130.29, 129.45, 128.92, 128.65, 128.24, 127.94, 127.35, 1263.56, 119.65, 115.75, 114.32, 112.68, 110.56, 55.32, 54.15. Molecular formulae: $C_{27}H_{24}N_2O_4$: LCMS (m/z): 439.58 (M+2); Elemental analysis: Calculated: C-73.62, H-5.49, N-6.36; Obtained: C-73.55, H- 5.47, N- 6.36.

35-((E)-3, 4-dimethoxybenzylidene)-2-((E)-styryl)-3-(p-tolyl)-3, 5-dihydro-4H-imidazol-4-one (7c)

Yeild-92%, palered solid, M.P- 167-169^{o}C, Rf: 0.49 (3: 7-EtOAc: n-hexane); IR (KBr, cm-1); 3226, 3137, 3064, 1633, 1592, 1556, 1356, 1278, 1084, 749, 692; ^{1}HNMR (400MHz, $CDCl_3$): 8.045 (s, 1H, =CH); 7.566-7.385 (m, 5H, Ar-H), 7.352 (s, 1H, =CH), 7.322 (d, J=5.4Hz, 1H, aromatic), 7.284 (d, J=8.8Hz, 1H, aromatic), 7.276 (d, J=8.0Hz, 1H, aromatic), 7.221 (s, 1H, Ar-H), 7.148 (d, J=7.6Hz, 1H, aromatic), 6.416 (s, 1H, =CH), 3.664 (s, 3H, -OCH_3), 3.586 (s, 3H, -OCH_3) 1.645 (s, 3H, -CH_3); ^{13}CNMR (400MHz, $CDCl_3$): Molecular formulae: $C_{27}H_{24}N_2O_3$: LCMS (m/z): 425.58 (M+2); Elemental analysis: Calculated: C-76.40, H-5.70, N-6.60; Obtained: C-76.32, H- 5.68, N- 6.69.

5-((E)-3, 4-dimethoxybenzylidene)-3-(4-fluorophenyl)-2-((E)-styryl)-3, 5-dihydro-4H-imidazol-4-one (7d)

Yeild-90%, yellow solid, M.P-204-206^{o}C, Rf: 0.422 (3: 7-EtOAc: n-hexane); IR (KBr, cm-1); 3262, 3104, 3046, 1665, 1629, 15914, 1564, 1539, 1489, 1294, 755, 702; ^{1}HNMR (400MHz, $CDCl_3$): 8.105 (s, 1H, =CH); 7.612-7.342 (m, 9H, Ar-H), 7.312 (s,

1H, =CH), 7.296 (d, J=8.8Hz, 1H, aromatic), 7.225 (s, 1H, Ar-H), 7.139 (d, J=6.8Hz, 1H, aromatic), 6.423 (s, 1H=CH), 3.686 (s, 3H, -OCH_3), 3.583 (s, 3H, -OCH_3); ^{13}CNMR (400MHz, $CDCl_3$): Molecular formulae: $C_{26}H_{21}FN_2O_3$: LCMS(m/z): 430.33 (M+2); Elemental analysis: Calculated: C- 72.89, H-4.94, N-6.54; Obtained: C-72.81, H- 4.93, N- 6.63.

3-(4-chlorophenyl)-5-((E)-3, 4-dimethoxybenzylidene)-2-((E)-styryl)-3, 5-dihydro-4H-imidazol-4-one (7e)

Yeild-91%, yellow solid, M.P- 210-212^{o}C, Rf: 0.492 (3: 7-EtOAc: n-hexane); IR (KBr, cm-1); 3221, 3126, 3064, 1664, 1627, 1592, 1566, 1542, 1488, 1291, 756, 696; ^{1}HNMR (400MHz, $CDCl_3$): 8.094 (s,1H,=CH); 7.734-7.616 (m, 4H, Ar-H), 7.535-7.385 (m, 9H, Ar-H), 7.368 (s, 1H, =CH), 7.318 (d, J=7.6Hz, 1H, aromatic), 7.229 (s, 1H, Ar-H), 7.147 (d, J=8.8Hz, 1H, aromatic); 6.472 (s, 1H, =CH), 3.672 (s, 3H, -OCH_3), 3.605 (s, 3H, -OCH_3); ^{13}CNMR (400MHz, $CDCl_3$): 168.74, 150.66, 147.92, 148.35, 136.63, 134.54, 131.78, 130.44, 129.68, 129.08, 128.95, 128.62, 128.37, 128.02, 127.64, 126.94, 115.54, 114.34, 112.53, 110.66, 55.37. Molecular formulae: $C_{26}H_{21}ClN_2O_3$: LCMS (m/z): 445.29 (M+2); Elemental analysis: Calculated: C- 70.19, H-4.76, N-6.30; Obtained: C-70.19, H- 4.75, N- 6.22.

4-(4-((E)-3, 4-dimethoxybenzylidene)-5-oxo-2-((E)-styryl)-4, 5-dihydro-1H-imidazol-1-yl) benzonitrile (7f)

Yeild-89%, orangered solid, M.P-194-196^{o}C, Rf: 0.474 (3:7-EtOAc: n-hexane); IR (KBr, cm-1); 3224, 3136, 3072, 2215, 1672, 1628, 1594, 1578, 1432, 1284, 751, 692; ^{1}HNMR (400MHz, $CDCl_3$): 8.045 (s, 1H, =CH); 7.864 (d, J=7.2Hz, 2H, aromatic), 7.648 (d, J=8.0Hz, 2H, aromatic); 7.526-7.324 (m, 5H, Aromatic); 7.294 (d, J=6.8Hz, 1H, aromatic 7.252(s, 1H, =CH), 7.225 (s, 1H, =CH), 7.114 (d, J=7.6Hz, 1H, aromatic), 3.653 (s, 3H, -OCH3), 3.594 (s, 3H, -OCH3); ^{13}CNMR (400MHz, $CDCl_3$): 170.25, 150.49, 147.74, 138.06, 136.24, 133.37, 131.24, 130.47, 130.02, 129.46, 128.94, 128.45, 128.13, 128.13, 127.65, 127.41, 126.65, 121.56, 119.74, 115.74, 114.03, 112.66, 111.53, 55.74. Molecular formulae: $C_{27}H_{21}N_3O_3$: LCMS (m/z): 436.38 (M+H); Elemental analysis: Calculated: C- 74.47, H-4.86, N-9.65; Obtained: C-74.40, H- 4.85, N- 9.73.

5-((E)-3, 4-dimethoxybenzylidene)-3-(4-nitrophenyl)-2-((E)-styryl)-3, 5-dihydro-4H-imidazol-4-one (7g)

Yeild-87%, orange yellow solid, M.P- 203-205^{o}C, Rf: 0.452 (4: 6-EtOAc: n-hexane); IR (KBr, cm-1); 3202, 3119, 3042, 1658, 1624, 1482, 1292, 751^{1}HNMR (400MHz, $CDCl_3$): 8.245 - 8.143 (m, 2H, Aromatic); 8.013 (s, 1H, =CH); 7.782-7.648 (m, 2H, Aromatic); 7.492-7.314 (m, 5H, Aromatic), 7.296 (s, 1H, =CH) , 7.274 (d, J=7.6Hz, 1H, aromatic), 7.205(s, 1H, aromatic), 7.136 (d, J=8.0Hz, 1H, aromatic), 6.427 (d, J=8.0Hz, 1H, =CH), 3.653 (s, 3H, -OCH3), 3.594 (s, 3H, -OCH3); ^{13}CNMR (400MHz, $CDCl_3$): 170.71, 150.62, 147.04, 146.36, 136.45, 134.15, 130.05, 129.22, 128.41, 128.16, 127.36, 115.69, 113.65, 110.62, 109.84, 55.32. Molecular formulae: $C_{26}H_{21}N_3O_5$: LCMS (m/z): 457.09 (M+H); Elemental analysis: Calculated: C- 68.54, H-4.64, N-9.23; Obtained: C-68.45, H- 4.63, N- 9.31.

Biological Activity

Antibacterial Activity

The antibacterial activity of the newly synthesized compounds enhanced viz; The 5-((E)-3, 4-dimethoxybenzylidene)-3-phenyl-2-((E)-styryl)-3, 5-dihydro-4H-imidazol-4-one and its derivatives have being screened *in vitro* for its potent active bacterial strains such as, *S. aureus* and *Escherichia coli*. The *in vitro* activities of the test compound were examined using agar plates containing in nutrient broth for bacteria. The test compounds were tested against each microbial species[9-12]. The antibacterial potent of the test derivatives have being compared with Streptomycin as standard drug. The antimicrobial inhibitions of the derivatives are measured as the area of zone of inhibition and summarized in Table No.1. This marked and antibacterial activity may be due to the presence of high hydrophobic content of these titled derivatives. The desired compounds contain derivatives segments are more active against bacteria strains and fungal strains. Presumptively due to the strong interaction of the later with the

agar medium, this hinders their diffusion in agar medium.

Antibacterial Activity

In vitro antifungal screening against A. Ngier and Candida albicans was used as test strain. The tested derivatives were dissolved in dimethyl sulfoxide (DMSO) and prepare to concentration of 10mg/mL. Antifungal activity of these compounds was performed by broth microdilution method. The absorbance was recorded at 530 nm in order to yield the desired transmittance of 70 to 75%. The tested fungal culture was prepared from the stock fungal culture, a 1:1000 dilution with broth (e.g. 10µL stock fungal culture: 10µL broth) was prepared. Sabouraud maltose broth was used as the growth medium and modified antimicrobial susceptibility testing is based on references drug. Finally all the wells were filled with 100µL of working fungal culture. Fluconazole were used as a reference in the antifungal test. Wells containing serial dilution of DMSO and broth were prepared as control tests. The plate was sealed and incubated at 37°C for 24 to 36 h. The minimum inhibitory concentration (MIC) values of tested derivatives were measured by reading the lowest concentration of compound in the well showing no growth.

RESULTS AND DISCUSSION

Chemistry

In the present investigation of the novel derivatives a series of 5-((E)-3, 4-dimethoxybenzylidene)-3-phenyl-2-((E)-styryl)-3, 5-dihydro-4H-imidazol-4-one (7a-f). These derivatives were synthesized from 4-((E)-3, 4-dimethoxybenzylidene)-2-((E)-styryl) oxazol-5(4H)-one and substituted aromatic amines in presence of pyridine and DMF as solvent and corresponding cinnamic acid through multi-step reactions. First step involves the reaction of cinnamoyl chloride (2) obtained from cinnamic acid with thionyl chloride in DCM and which also followed cinnamoylglycine can be synthesized from cinnamoyl chloride and glycine. Further the compounds (5) can be obtained from with substituted aromatic aldehyde and acetic anhydride in the presence of sodium acetate and added catalyst. 5-((E)-3, 4-dimethoxybenzylidene)-3-phenyl-2-((E)-styryl)-3, 5-dihydro-4H-imidazol-4-one can be synthesized by the 4-((E)-3, 4-dimethoxybenzylidene)-2-((E)-styryl) oxazol-5(4H)-one with substituted aniline (Scheme No.1).

The structures of the titled compounds were characterized by IR, 1HNMR, 13CNMR, mass spectral and elemental analyses. The IR spectrum of compound 4a showed absorption bands at 3228, 3129, 3065, 2210, 1635, 1594cm-1 which corresponds to N-H, C≡N, C=O and C=N stretching respectively. Similarly, ^{1}H NMR spectrum of the titled derivatives showed in various aromatic protons appear at δ 8.112 to 8.013ppm and olefin protons of cinnamic acid appear at δ7.368 to 6.394 and the methoxy protons showed at 3.741 to 3.583. The mass spectrum of "7e" showed molecular ion peak at m/z = 445.29 (M+2), which is in agreement with the molecular formula$C_{26}H_{21}ClN_2O_3$.

Antimicrobial Activity

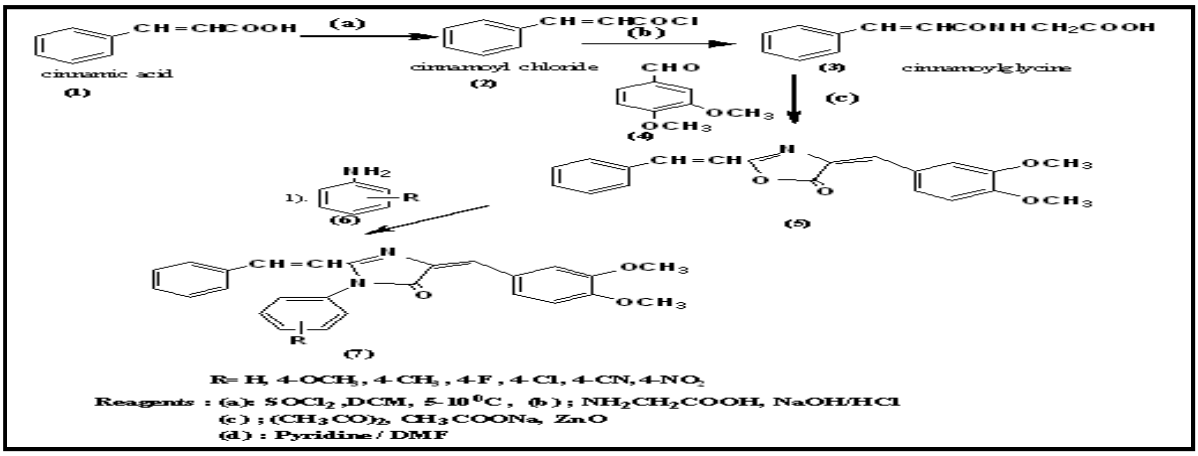
All the newly synthesized and procured derivatives were evaluated for anti-micro bacterial and antifungal activity; the results represented to shown in Table No.1.

As indicated in Table No.1 the majority of the MIC results for the tested compounds showed a potentially good effect against. The compound 7d showed the highest antimicrobial activity) and compounds "7e and 7f"exhibited an excellent activity against bacterial strains (Table-I). It reveals that the activity of derivatives 7b and 7c, which bearing electron donor groups and also the4-position of substituents in aromatic ring. It is also evident that the benzene rings substituted with electron attracting groups such as F, Cl, CN and NO_2 exhibited better activity than donor substituent such as Me, OMe in 4c or substituted phenyl ring compound such as 7d and 7e compounds Presence of F and Cl substitution in 4-position in benzene ring (compound 4f) resulted in better activity against. Mycobacterium than compound 4e which include Cl substitution in 4-position.In of 5-((E)-3, 4-dimethoxybenzylidene)-3-phenyl-2-((E)-styryl)-3, 5-dihydro-4H-imidazol-4-one, such as 7a-7f, showed better anti-mycobacterial activity. Moreover, to assess antimicrobial activity of these derivatives of antifungal activity was also

evaluated. *A.Ngier and C.albicans* are introduced as a good to excellent for antifungal activity test. Mainly, the treated compounds showed poor activity against *C.albicans*, compounds 7a-7d, which was synthesized from 5-((E)-3, 4-dimethoxybenzylidene)-3-phenyl-2-((E)-styryl)-3, 5-dihydro-4H-imidazol-4-one can be synthesized by the 4-((E)-3, 4-dimethoxybenzylidene)-2-((E)-styryl) oxazol-5(4H)-one with substituted aniline scored the highest antifungal activity.

Table No.1: Antimicrobial activity screening activity synthesized scaffold

Compound Code	*Zone of inhibition in (mm)					
	Bacteria				*Fungi*	
	S.aureus	*E.coli*	*S. typhi*	*B.substill*	*A. niger*	*C. albicans*
7a	04	06	08	06	06	08
7b	14	16	13	16	10	10
7c	14	13	15	14	08	11
7d	20	21	20	19	15	16
7e	21	20	22	20	10	08
7f	19	19	21	20	16	17
7g	21	19	20	20	17	16
Streptomycin	25	25	22	22	NA	NA
fluconazole	NA	NA	NA	NA	20	20
DMSO	---	----	---	---	---	---



Scheme No.1

CONCLUSION

In conclusion, we have been achieved a convenient protocol for the synthesis 5-((E)-3, 4-dimethoxybenzylidene)-3-phenyl-2-((E)-styryl)-3, 5-dihydro-4H-imidazol-4-one (7a-f) Incorporated moiety in excellent yield and evaluated their *in vitro* antimicrobial activity against anti-bacterial and anti-fungal strains. Our antimicrobial activity evaluated results represented that exciting was observed in compounds in comparison with standard Streptomycin and Fluclozones. The majority derivatives emerging with the most active potent and antimicrobial activity in this study will be further structurally modified towards the discovery of a compound with optimal antimicrobial activity. These results may also provide some significance guidance for the development of new class biological studies.

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CONFLICT OF INTEREST

We declare that we have no conflict of Interest.

BIBLIOGRAPHY

1. Heather M. Lima and Carl J. Lovely. Synthesis of 2-imidazolones and 2-Iminoimidazoles, *Org. Lett,* 13(21), 2011, 5736-5739.
2. Dakshayini Chandrashekarachar, Chaitramallu M, Devaraju Kesagudu. Synthesis, characterization of novel furan based imidazolones and their boilogical studies, *British Journal of Pharmaceutical Research,* 11(4), 2016, 1-7.
3. Magda D, Ismail M F *et al*. Synthesis and biological evaluation of novel, imidazolone, derivatives as potential cox-2 inhibitors, *Arch Pharm Res,* 31(5), 2008, 562-568.
4. Lu T *et al*. Design and synthesis of a series of bioavailable fatty acid synthase (FASN) KR domain inhibitors for cancer therapy, *Bioorg. Med. Chem. Lett,* 28(12), 2018, 2159-2164.
5. Sanchez-Murcia P A, Bueren-Calabuig J A, Camacho-Artacho M, Cortes-Cabrera Á, Gago F. Stepwise simulation of 3, 5-dihydro-5-methylidene-4 h- imidazol-4-one (MIO) biogenesis in histidine ammonia-lyase, *Biochemistry,* 55(41), 2016, 5854-5864.
6. Finko A V, Sokolov A I, Skvortsov D A, Al-Khazraji A S H, Ofitserov E N, Beloglazkina E K. Synthesis of 4, 4′-substituted 2, 2′-[ethane-1, 2-diylbis(selanediyl)]bis(1H-imidazol-5(4H)-ones), *Russian Chemical Bulletin,* 70(3), 2021, 457-462.
7. Yao-Wu Li, Jia Liu, Xiao-Tian Zhou, Jia-Guo Lv, Ju Zhu, Can-Hui Zheng, You-Jun Zhou. Imidazolone-amide bridges and their effects on tubulin polymerization in CIS-locked vinylogous combretastatin-A4 analogues: Synthesis and biological evaluation, *Bioorganic and Medicinal Chemistry,* 19(11), 2011, 3579-3584.
8. Desai N C, Dave D, Shah M D, Vyas G D. Synthesis and antibacterial activity of some novel 4-oxo-1, 3-thiazolidines, 2-oxoazetidines and 5-oxoimidazolines, *Indian J Chem,* 39(B), 2000, 277-282.
9. Hirpara K V, Patel S P, Parikh K A, Bhimani A S, Parekh H H. Preparation, characterisation and antimicrobial activities of some novelnitriles and imidazolines, *J Sci Islam Rep Iran,* 15(2), 2004, 135-138.
10. Solankee A, Kapadiya K, Thakor I, Patel J, Lad S. Synthesis and antimicrobial activity of 1-(4'-Trifluoromethylphenyl)-2-phenyl-4-(benzylidene/substituted benzylidene/2'-furylidene /2'-thienylidene)-imidazolin-5-ones, *Asian J Chem,* 16(2), 2004, 917-920.
11. Desai C, Bhavsar A M, Baldaniya B B. Synthesis and antimicrobial activity of 5-imidazolinone derivatives, *Indian J. Pharm. Sci,* 71(1), 2009, 90-94.
12. Ashwani Kumar Dhingra, Bhawna Chopra, Rameshwar Dass, Sanjeev Kumar Mitta. Synthesis, antimicrobial and anti-inflammatory activities of some novel 5-substituted imidazolone analogs, *Chinese Chemical Letters,* 27(5), 2016, 707-710.
13. Mais Saad Hussein, Naeemah Al-Lami, Oday H. R Al-Jeilawi. Design, synthesis of imidazolone and oxazepine derivatives bearing imidazo (2, 1-b) thiazole along with its antimicrobial activity, *Chemical Methodologies,* 6(4), 2022, 319-330.
14. Khalid Mohammed Khan, Uzma Rasool Mughal, Sadia Khan, Saira Khan, Shahnaz Perveen, Iqbal Choudhary M. Synthesis and antibacterial and antifungal activity of 5-substituted imidazolones, *Letters in Drug Design and Discovery,* 6(1), 2009, 69-77.
15. Gulshan Kumar, Chinmay Das, Ayan Acharya, Subhasmita Bhal, Mayank Joshi, Chanakya Nath Kundu, Angshuman Roy Choudhury, Sankar K. Guchhait. Organo catalyzed umpolung addition for synthesis of heterocyclic-fused arylidene-imidazolones as anticancer agents, *Bioorganic and Medicinal Chemistry,* 67(1), 2022, 116835.

16. Wagdy M. Eldehna, Mohamed A. Abdelrahman, Alessio Nocentini, Silvia Bua, Sara T. Al-Rashood, Ghada S. Hassan, Alessandro Bonardi, Abdulrahman A. Almehizia, Hamad M. Alkahtani, Amal Alharbi, Paola Gratteri, Claudiu T. Supuran. Synthesis, biological evaluation and in silico studies with 4-benzylidene-2-phenyl-5(4H)-imidazolone-based benzene sulfonamides as novel selective carbonic anhydrase IX inhibitors endowed with anticancer activity, *Bioorganic Chemistry,* 90(1), 2019, 103102.
17. Ahmed Kamal, Ramakrishna G, Raju P, Viswanath A, Janaki Ramaiah M, Balakishan G, Manika Pal-Bhadra. Synthesis and anti-cancer activity of chalcone linked imidazolones, *Bioorganic and Medicinal Chemistry Letters,* 20(16), 2010, 4865-4869.
18. Ling Li, Dongling Quan, Jingxuan Chen, Jiahao Ding, Jinwu Zhao, Lin Lv, Jianjun Chen. Design, synthesis and biological evaluation of 1-substituted -2-aryl imidazoles targeting tubulin polymerization as potential anticancer agents, *European Journal of Medicinal Chemistry,* 184(10), 2019 111732.
19. Moustafa El-Araby, Abdelsattar Omar, Hassanein H. Hassanein, Abdel-Ghany H. El-Helby, Asharf A. Abdel-Rahman. Design, synthesis and *in vivo* anti-inflammatory activities of 2, 4-diaryl-5-4h-imidazolone derivatives, *Molecules,* 17(10), 2012, 12262-12275.
20. Asif Husain, Abdullah F. AlAsmari, Syed Najmul Hejaz Azmi, Nemat Ali, Moklesur Rahman Sarker, Metab Alharbi, Mohd Ishtikhar, Shah Alam Khan. Rational drug design, synthesis and *in vivo* biological activity of new indolyl-imidazolonehybrids as potential and safer non-steroidal anti-inflammatory agents, *Journal of King Saud University - Science,* 34(4), 2022, 102023.
21. Upadhyay P S, Joshi H D, Baxi A J, Parikh A R. Synthesis and pharmacological evaluation of some new imidazolinone as anticonvulsant's, *Indian J Heterocyc Chem,* 1, 1991, 71.
22. Meenakshi S, Reena K, Renu S, Dixit K S, Nath C, Barthwal J P. Synthesis, anticonvusant and enzyme inhibitory activities of somendolyl-1, 3, 4-thiadiazoles, *Indian J Chem,* 29(B), 1990, 85.
23. Matafome P, Sena C, Seica R. Methylglyoxal, obesity and diabetes, *Endocrine,* 43(3), 2013, 472-484.
24. Fishman S L, Sonmez H, Basman C, Singh V, and Poretsky L. The role of advanced glycation end-products in the development of coronary artery disease in patients with and without diabetes mellitus: A review, *Mol. Med,* 24(1), 2018, 1-12.
25. Harfenist M, Soroko E F, Mckenzie G M. 2-(Alkoxyaryl)-2-imidazolinemonoamine oxidase inhibitors with antidepressant activity, *J Med Chem,* 21(4), 1978, 405-409.
26. Naithani D K, Srivastava V K, Barthwal J P, Saxena A K, Gupta T K, Shanker K. Synthesis and antiparkinsonian activity of newerimidazolones, *Indian J Chem,* 28(B), 1989, 990.
27. Santra K, Geraskin I, Nilsen-Hamilton M, Kraus G A, Petrich J W. Characterization of the photophysical behavior of DFHBI derivatives: Fluorogenic molecules that illuminate the spinach RNA aptamer, *J. Phys. Chem. B,* 123(11), 2019, 2536-2545.
28. Gutierrez S *et al*. Highly fluorescent green fluorescent protein chromospheres analogues made by decorating the imidazolones ring, *Chem-Eur. J,* 21(51), 2015, 18758-18763.

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