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Solvent-free synthesis, antimicrobial and insect antifeedant potentials of some 4(4-chloro-1-naphthyl)-5,6-dihydro-6-(substituted phenyl)-4*H*-1,3-oxazine-2-amines

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ABSTRACT

More than 85% yields of thirteen 4-(4-chloro-1-naphthyl)-5,6-dihydro-6-(substituted phenyl)-4*H*-1,3-oxazine-2-amines weer synthesised by SiO_2-H_3PO_4 catalyzed solvent-free cyclization of substituted styryl4-chloro-1-naphthyl ketones and urea under microwave irradiation. The synthesized oxazine amines have been characterized by analytical and spectroscopic techniques. The antimicrobial activities of these 4-(4-chloro-1-naphthyl)-5,6-dihydro-6-(substituted phenyl)-4*H*-1,3-oxazine-2-amines have been appraised by means of Bauer-Kirby technique. The insect antifeedant activities of these oxazine-2-amines were assessed by Dethler's technique using 4th instar larvae *Achoea janata* L.

***Keywords*:** 4-(4-chloro-1-naphthyl)-5,6-dihydro-6-(substituted phenyl)-4*H*-1,3-oxazine-2-amines, SiO_2-H_3PO_4, solvent-free synthesis, antimicrobial potentials, insect antifeedant activity

1. INTRODUCTION

The six membered heterocyclic compounds containing one oxygen and one nitrogen atom [1], having important bio-active properties are known as oxazine or unsaturated oxazine derivatives. These molecules exist many isomeric structures such as 1, 2 or 1, 3 or 1, 4 oxazines

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[2] depending upon the inter relative position of these tow atoms and the carbon-carbon double bond. The presence of oxygen, nitrogen heteroatoms corresponding inter relative positions along with a carbon-carbon double bonds in their structural moieties [3] were enhanced the important medicinal activities. The imperative medicinal therapeutic activities of these saturated and unsaturated oxazines are anti-bacterial, anti-fungal [3-5], anti-plasmodial [6], anti-cancer [7], anti-depressants [8], cytotoxicity [9], anti-osteoplastic [10], anti- tumour [11], anti-oxidant [12], anti-tuberculosis [13], anti-neoplastic [14], antagonists [15], anti-inflammatory [16], anti-infectants [17], IKB kinase beta [18] and PTP-1B inhibition [19].

These oxazine derivatives were useful for refining the super resolve Microscope [20], synthesis of eosinophils [21], identification, separation and determination of neutrophils [22]. Countless saturated and unsaturated oxazine derivatives were used as a dyes [23]. Now-a-days scientists, organic chemists are attentive for solvent-free synthesis [3, 24-27]. Several solvent assisted and solvent-free synthetic approaches were available for synthesis of saturated and unsaturated oxazine derivatives [24, 28-30].

Hetero Diels-Alder reaction [3], ring closure [31], Betti base induced condensation [27], Mannich type condensation-cyclization [4] and cyclization of enones were used for synthesis of saturated and unsaturated oxazine derivatives. Verma et. al. [25] have synthesised some numbers of benzoxazine/oxazine merged isoquinolines and naphthyridines through solvent-free method. Elarfi and Al-difar et al., [5] partake synthesised some numbers of saturated and unsaturated 1, 3-oxazine derivatives through solvent-aided method from aryl enones and urea. More than 75% product yields of dihydro-2*H*-benzo- and naphtho-1,3-oxazine derivatives were synthesised and reported by Mathew et al. [4] by means of eco-friendly process. The competent synthesis of countless 1,3-oxazine-4-thiones stood reported through N-methyl imidazole endorsed solvent-free process.

Sapkal et al., partake the investigation of the role of ammonium acetate for solvent-free process of 1,3-disubstituted-2,3-dihydro-*1H*-naphthyl oxazines [27]. Indoors the above interpretation, there is not any evidence existing in the literature for the solvent-free process, investigation of antimicrobial and insect antifeedant activities of 4-chloro-1-naphthyl based oxazine-2-amine derivatives. Hence and consequently, the author partaken exertion to synthesize some 4-chloro-1-naphthyl based oxazine-2-amine derivatives, deliberated antimicrobial and insect antifeedant activities.

2. EXPERIMENTAL

2. 1. General

All chemicals utilized in this investigation were bought from Sigma-Aldrich and Merck Chemical companies. Mettler FP51 melting point kit was utilized for measuring the melting point of all synthesized oxazine-2-amines with open glass capillaries then remain uncorrected. The AVATAR-300 Fourier transform spectrophotometer was utilized for measuring the infrared spectral frequencies (KBr, 4000-400 cm^{-1}) of all oxazines in KBr discs. The Bruker AV400 sequence category NMR spectrometer was utilized for measuring the chemical shifts (δ, ppm) through the NMR spectra of all oxazines, functioning at 400 MHz for ^{1}H and 100 MHz for ^{13}C spectra in $CDCl_3$ solvent by means of TMS as internal standard. The mass fragments (m/z) of all obtained oxazines were fined their mass spectra and are documented on SHIMADZU mass spectrometer by means of chemical ionization system.

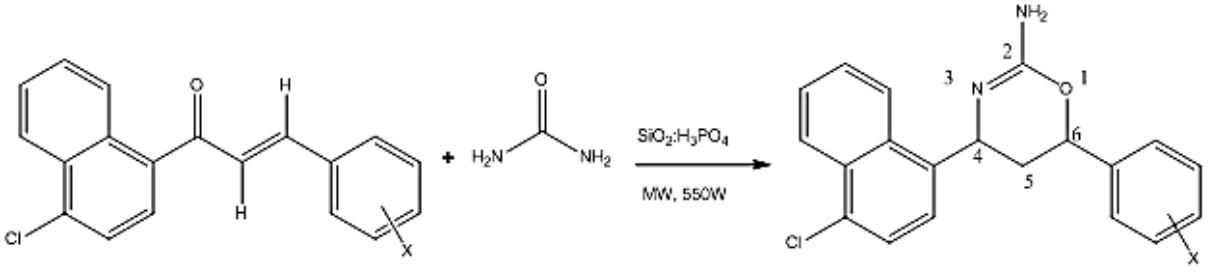
2. 2. Preparation of SiO_2-H_3PO_4 catalyst

The SiO_2-H_3PO_4 catalyst compound was prepared rendering towards the literature process [30].

2. 3. Synthesis of 4-(aryl)-5,6-dihydro-6-(substituted phenyl)-4H-1,3-oxazine-2-amines

An appropriate equi-molar quantity of 4-chloro-1-naphthyl chalcones (2 mmol), urea (2 mmol) and 0.2 g of SiO_2-H_3PO_4 were subjected to microwave irradiation for 2-4 minutes at 650W (**Scheme 1)** (Samsung, Microwave Oven, 100-700 W). Afterwards, end of the reaction, dichloromethane (20 mL) was added, followed by simple filtration for separation of 4-(aryl)-5,6-dihydro-6-(substitutedphenyl)-4*H*-1,3-oxazine-2-amines.

Concentration of dichloromethane extract gave the crude. It is further purified by re-crystallization using ethanol. The prepared 4-aryl-5,6-dihydro-6-(substituted phenyl)-4*H*-1,3-oxazine-2-amines remained analysed through analytical and spectral techniques.



Entry	1	2	3	4	5	6	7	8	9	10	11	12	13
X	H	2-NH_2	3-NH_2	3-Br	3-Cl	4-Cl	4-$N(CH_3)_2$	4-OH	4-OCH_3	4-CH_3	2-NO_2	3-NO_2	4-NO_2

Scheme 1. Synthesis of 4-aryl-5,6-dihydro-6-(substituted phenyl)-4*H*-1,3-oxazine-2-amines by SiO_2:H_3PO_4 catalysed cyclization of aryl chalcones and urea under microwave irradiation.

3. RESULTS AND DISCUSSION

The author attempted to synthesize 4-(aryl)-5,6-dihydro-6-(substituted phenyl)-4*H*-1,3-oxazine-2-amines through cyclization of 4-chloro-1-naphthyl chalcones hold electron with-drawing as well as electron contributing assembles as substituents, urea and in the existence of acidic catalyst SiO_2-H_3PO_4 through microwave irradiation. Hence the author interestingly to extend the synthesis of 4-(aryl)-5,6-dihydro-6-(substituted phenyl)-4*H*-1,3-oxazine-2-amines through the cyclization process of 2 mmole of 4-chloro-1-naphthyl chalcones, 2 mmole of urea under microwave irradiation in the existence of 0.5g of SiO_2-H_3PO_4 catalyst at 550W for 4-6 minutes (Samsung Grill, GW73BD Microwave oven, 230V A/c, 50Hz, 2450Hz, 100-750W (IEC-705), **(Scheme 1**). During the progression of this reaction SiO_2-H_3PO_4 catalyses cyclization between 4-chloro-1-naphthyl chalcones and urea tracked through rearrangement provided the 4-(aryl)-5,6-dihydro-6-(substituted phenyl)-4*H*-1,3-oxazine-2-amines.

The obtained yield of the 4-(aryl)-5,6-dihydro-6-(substituted phenyl)-4*H*-1,3-oxazine-2-amines in this solvent-free cyclization process is more than 80%. The chalcone containing

electron contributing assembly (OCH_3) provides higher yield than electron-withdrawing (halogens, NO_2) substituents. Moreover, the author have inspected this cyclization process with equimolar quantities of the styryl 4-chloro-1naphthyl ketone (**entry 1)** and urea under the same condition as above. In this cyclization process the obtained yield was 90%. The effect of catalyst on this reaction was investigated through varying the catalyst quantity from 0.1 g to 0.4 g. As the catalyst quantity is increased from 0.1 g to 0.4 g, the obtained percentage of yield of product was increased from 84 to 90%. Afterwards, increase in the catalyst quantity beyond 0.4 g, there is no significant increase in the percentage of the product. The consequence of catalyst loading is shown in **Fig. 1.** The optimal quantity of catalyst loading in this cyclization was found to be 0.4 g. The cyclization process results, analytical data and the mass fragments (m/z) presented in **Table 1.**

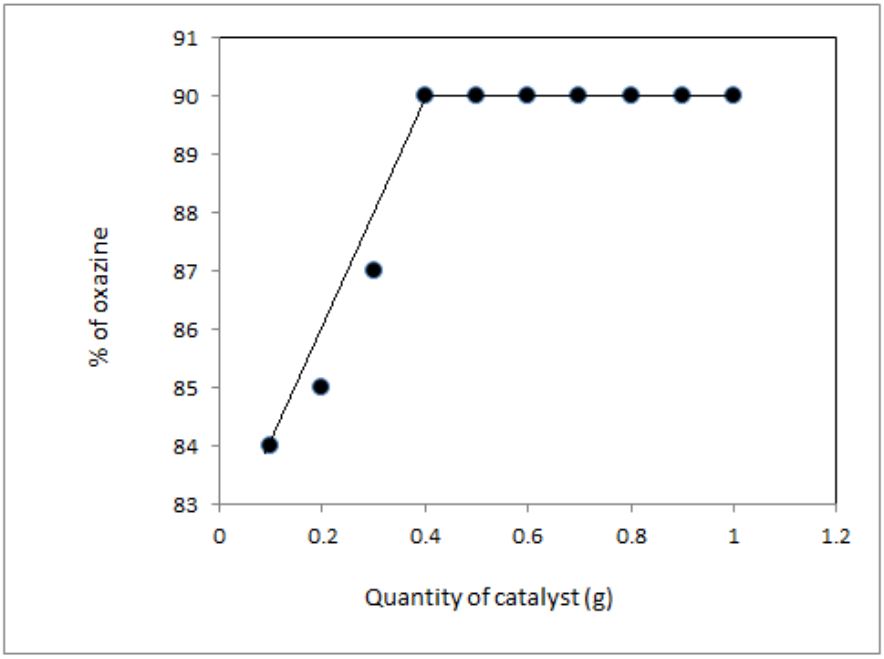


Figure 1. Effect of catalyst loading.

Table 1. Analytical, physical constants, yield and mass fragment of 4-(4-chloro-1-naphthyl)-5,6-dihydro-6(substituted phenyl)-4*H*-1,3-oxazine-2-amines

Entry	X	M.F.	M.W.	Time (m)	Yield (%)	m.p. (°C)	Mass (m/z)
1	H	$C_{20}H_7ClN_2O$	336	2.5	90	119-120	336[M^+], 338[M^{2+}], 312, 251, 175, 153, 118, 100, 99, 84, 77, 58,43, 44, 16
2	2-NH_2	$C_{20}H_{18}ClN_3O$	351	2	87	115-116	351[M^+], 353[M^{2+}], 335, 320, 259, 244, 175, 153, 127, 99, 92, 91, 84, 77, 58, 43, 44, 35, 32, 16

3	3-NH_2	$C_{20}H_{18}ClN_3O$	351	2	89	124-125	351[M^+], 353[M^{2+}], 335, 320, 259, 245, 174, 153, 127, 99, 91, 84, 77, 58, 43, 44, 35, 32, 16
4	3-Br	$C_{20}H_{16}BrClN_2O$	416	3	85	123-124	416[M^+], 418[M^{2+}], 420 [M^{4+}], 397, 379, 364, 335, 286, 259, 253, 210, 161, 154, 127, 91, 84, 79, 43, 42, 35, 16
5	3-Cl	$C_{20}H_{16}Cl_2N_2O$	370	3.5	84	105-106	370[M^+], 372[M^{2+}], 374 [M^{4+}], 335, 304, 259, 244, 232, 209, 202, 161, 111, 91, 77, 43, 42, 35, 28, 16
6	4-Cl	$C_{20}H_{16}Cl_2N_2O$	370	3.5	86	116-117	370[M^+], 372[M^{2+}], 374[M^{4+}], 335, 304, 259, 244, 232, 209, 202, 161, 111, 91, 77, 43, 42, 35, 28, 16
7	4-$N(CH_3)_2$	$C_{22}H_{22}ClN_3O$	380	3	88	105-106	380[M^+], 382[M^{2+}], 364, 363, 349, 344, 335, 259, 218, 202, 161, 120, 99, 91, 77, 58, 44, 35, 30, 16, 15,
8	4-OH	$C_{20}H_{17}ClN_2O$	352	3	86	122-123	352[M^+], 354[M^{2+}], 335, 336,317, 294, 259, 202, 191, 161, 150, 93, 91, 77, 58, 35, 17, 16
9	4-OCH_3	$C_{21}H_{19}ClN_2O_2$	366	3.5	91	116-117	366[M^+], 368[M^{2+}], 351, 350, 335, 331, 259, 205, 161, 107, 4-91, 77, 35, 16, 15
10	4-CH_3	$C_{21}H_{19}ClN_2O$	350	3	90	109-110	350[M^+], 352[M^{2+}], 335, 334, 315,259, 189, 161, 91, 77, 35, 16, 15,
11	2-NO_2	$C_{20}H_{19}ClN_3O_2$	381	4	85	135-136	381[M^+], 383[M^{2+}], 365, 346, 335, 323, 301, 289, 259, 244, 225, 220, 202, 179, 175, 161, 127, 122, 91, 84, 77, 58,45, 46, 43, 42, 35, 16
12	3-NO_2	$C_{20}H_{19}ClN_3O_2$	381	4	85	112-113	381[M^+], 383[M^{2+}], 365, 346, 335, 323, 244, 225, 220, 175, 161, 127, 122, 91, 77, 46,43, 42, 35, 16
13	4-NO_2	$C_{20}H_{19}ClN_3O_2$	381	4	85	123-124	381[M^+], 383[M^{2+}], 365, 346, 323, 301, 289, 259, 244, 225, 220, 202, 179, 161, 127, 122, 84, 77, 45, 43, 35, 16

The reusability of this catalyst was inspected in the solvent-free cyclization process of styryl 4-chloro-1-naphthyl ketone, and urea (**entry 1)** was presented in **Table 2**.

Table 2. Reusability of SiO_2-H_3PO_4 catalyst on solvent-free cyclization of styryl 4-chloro-1-naphthyl ketone (2 mmol) with urea (2 mmol) under microwave irradiation (**entry 1**).

Run	**1**	**2**	**3**	**4**	**5**
Yield	90	90	89.5	89.5	89

From the Table 2, first two cyclization provides 90% product. The third, fourth and fifth cyclization process provide the respective 89.5%, 89.5% and 93% yields of oxazines. There was no on accountable loss in its effect of catalytic activity observed up to fifth cyclization process. The influence of solvents on the yield was also inspected with methanol, ethanol, dichloromethane and tetrahydrofuran through the solvent-free cyclization as well as conventional heating process of styryl 4-chloro-1-naphhtyl ketone and urea in the existing of catalyst (**entry 1**). Likewise, the influence of microwave irradiation was inspected on optimal quantity of the catalyst in the cyclization process. The influence of solvents on the yield of oxazine derivative (**entry 1**) was presented in **Table 3.**

Table 3. The effect of solvents in conventional heating and without solvent in microwave irradiation on yield of oxazine amine (**entry 1**).

Solvents												**Microwave irradiation**		
MeOH			**EtOH**			**DCM**			**THF**					
SA	**PA**	**SPA**	**SA**	**PA**	**SPA**	**SA**	**PA**	**SPA**	**SA**	**PA**	**SPA**	**SA**	**PA**	**SPA**
51	42	71	50	43	72	64	43	70	65	54	82	73	61	90
MeOH = Methanol; EtOH = Ethanol; DCM = Dichloromethane; THF = Tetrahydrofuran; SA = Silica; PA = Phosphoric acid; SPA = SiO_2-H_3PO_4														

From the table maximum yield of oxazine found from the cyclization of styryl 4-chloro-1-naphthyl ketone and urea in the existing of SiO_2-H_3PO_4 catalyst through microwave irradiation technique.

The spectroscopic information data of all obtained 4-(4-chloro-1-naphthyl)-5,6-dihydro-6(substitutedphenyl)-4*H*-1,3-oxazine-2-amines are conceised below.

4-(4-Chloro-1-naphthyl)-5,6-dihydro-6-phenyl-4*H*-1,3-oxazine-2-amine (1): FTIR(KBr): 3534(NH_2), 1598(C=N), 1234(C-O-C) cm^{-1}. ^1H NMR ($CDCl_3$-d_6, TMS) δ: 2.345(s, 1H, NH_2), 2.625(dd, 1H, H_4), 2.425(dd, 1H, H_5), 2.214(dd, 1H, $H_{5'}$), 4.275(dd, 1H, H_6), 6.545-7.345(m,

11H, Ar-H) ppm. ^{13}C NMR ($CDCl_3$-d_6, TMS) δ: 165.33(C_2), 52.56 (C_4), 47.33 (C_5), 65.90 (C_6), 125.36-142.25(Ar-C).

4-(4-Chloro-1-naphthyl)-5,6-dihydro-6-(3-aminoyphenyl)-4*H*-1,3-oxazine-2-amine (2): FTIR(KBr): 3564(NH_2), 1612(C=N), 1245(C-O-C) cm^{-1}. ^{1}H NMR ($CDCl_3$-d_6, TMS) δ: 2.295 (s, 1H, NH_2), 2.598 (dd, 1H, H_4), 2.465 (dd, 1H, H_5), 2.201 (dd, 1H, $H_{5'}$), 4.351 (dd, 1H, H_6), 6.289-7.258 (m, 10H, Ar-H) ppm. ^{13}C NMR ($CDCl_3$-d_6, TMS) δ: 164.82 (C_2), 51.36 (C_4), 47.98 (C_5), 66.25 (C_6), 126.25-139.38 (Ar-C).

4-(4-Chloro-1-naphthyl)-5,6-dihydro-6-(4-aminophenyl)-4*H*-1,3-oxazine-2-amine (3): FTIR(KBr): 3556(NH_2), 1602(C=N), 1212(C-O-C) cm^{-1}. ^{1}H NMR ($CDCl_3$-d_6, TMS) δ: 2.295 (s, 1H, NH_2), 2.523 (dd, 1H, H_4), 2.412(dd, 1H, H_5), 2.232 (dd, 1H, $H_{5'}$), 4.387(dd, 1H, H_6), 6.286-7.265 (m, 10H, Ar-H) ppm. ^{13}C NMR ($CDCl_3$-d_6, TMS) δ: 164.84 (C_2), 51.32 (C_4), 47.93(C_5), 66.54 (C_6), 126.11-139.32 (Ar-C).

4-(4-Chloro-1-naphthyl)-5,6-dihydro-6-(3-bromophenyl)-4*H*-1,3-oxazine-2-amine (4): FTIR(KBr): 3552(NH_2), 1627(C=N), 1211(C-O-C) cm^{-1}. ^{1}H NMR ($CDCl_3$-d_6, TMS) δ: 2.211 (s, 1H, NH_2), 2.384 (dd, 1H, H_4), 2.42dd, 1H, H_5), 2.216 (dd, 1H, $H_{5'}$), 4.326(dd, 1H, H_6), 6.215-7.249 (m, 10H, Ar-H) ppm. ^{13}C NMR ($CDCl_3$-d_6, TMS) δ: 164.04 (C_2), 51.31 (C_4), 47.63(C_5), 66.87 (C_6), 124.21-139.48 (Ar-C).

4-(4-Chloro-1-naphthyl)-5,6-dihydro-6-(3-chlorophenyl)-4*H*-1,3-oxazine-2-amine (5): FTIR(KBr): 3548(NH_2), 1604(C=N), 1236(C-O-C) cm^{-1}. ^{1}H NMR ($CDCl_3$-d_6, TMS) δ: 2.205 (s, 1H, NH_2), 2.298 (dd, 1H, H_4), 2.416(dd, 1H, H_5), 2.232 (dd, 1H, $H_{5'}$), 4.316(dd, 1H, H_6), 6.225-7.276 (m, 10H, Ar-H) ppm. ^{13}C NMR ($CDCl_3$-d_6, TMS) δ: 164.18 (C_2), 51.34(C_4), 47.67(C_5), 66.28 (C_6), 126.32-139. 24 (Ar-C).

4-(4-Chloro-1-naphthyl)-5,6-dihydro-6-(4-chlorophenyl)-4*H*-1,3-oxazine-2-amine (6): FTIR(KBr): 3552(NH_2), 1621(C=N), 1224(C-O-C) cm^{-1}. ^{1}H NMR ($CDCl_3$-d_6, TMS) δ: 2.119 (s, 1H, NH_2), 2.312 (dd, 1H, H_4), 2.392(dd, 1H, H_5), 2.241(dd, 1H, $H_{5'}$), 4.363(dd, 1H, H_6), 6.232-7.276 (m, 10H, Ar-H) ppm. ^{13}C NMR ($CDCl_3$-d_6, TMS) δ: 164.43 (C_2), 51.26 (C_4), 47.58(C_5), 66.39 (C_6), 126.46-139. 62(Ar-C).

(4-Chloro-1-naphthyl)-5,6-dihydro-6-(4-dimethylaminophenyl)-4*H*-1,3-oxazine-2-amine (7): FTIR(KBr): 3535(NH_2), 1611(C=N), 1212(C-O-C) cm^{-1}. ^{1}H NMR ($CDCl_3$-d_6, TMS) δ: 2.223 (s, 1H, NH_2), 2.324 (dd, 1H, H_4), 2.431(dd, 1H, H_5), 2.237(dd, 1H, $H_{5'}$), 4.316(dd, 1H, H_6), 3.634(s, 6H, $N(CH_3)_2$), 26.278-7.298 (m, 10H, Ar-H) ppm. ^{13}C NMR ($CDCl_3$-d_6, TMS) δ: 164.26 (C_2), 51.22 (C_4), 47.53(C_5), 66.41(C_6), 44.87 ($N(CH_3)_2$), 126.67-139.23(Ar-C).

4-(4-Chloro-1-naphthyl)-5,6-dihydro-6-(4-hydroxyphenyl)-4*H*-1,3-oxazine-2-amine (8): FTIR(KBr): 3546(NH_2), 1601(C=N), 1243(C-O-C) cm^{-1}. ^{1}H NMR ($CDCl_3$-d_6, TMS) δ: 2.212 (s, 1H, NH_2), 2.345 (dd, 1H, H_4), 2.461(dd, 1H, H_5), 2.224(dd, 1H, $H_{5'}$), 4.365(dd, 1H, H_6), 6.234-7.236 (m, 10H, Ar-H) ppm. ^{13}C NMR ($CDCl_3$-d_6, TMS) δ: 164.34 (C_2), 51.76 (C_4), 47.54 (C_5), 66.89 (C_6), 44.19 ($N(CH_3)_2$), 126.34-139.80(Ar-C).

4-(4-Chloro-1-naphthyl)-5,6-dihydro-6-(4-methoxyphenyl)-4*H*-1,3-oxazine-2-amine (9): FTIR(KBr): 3540(NH_2), 1611(C=N), 1223(C-O-C) cm^{-1}. ^1H NMR ($CDCl_3$-d_6, TMS) δ: 2.210 (s, 1H, NH_2), 2.319 (dd, 1H, H_4), 2.446(dd, 1H, H_5), 2.223(dd, 1H, $H_{5'}$), 4.356(dd, 1H, H_6), 4.262 (s, 3H, OCH_3), 6.254-7.237 (m, 10H, Ar-H) ppm. ^{13}C NMR ($CDCl_3$-d_6, TMS) δ: 164.29 (C_2), 51.28 (C_4), 47.55(C_5), 66.68 (C_6), 126.32-139.59(Ar-C).

4-(4-Chloro-1-naphthyl)-5,6-dihydro-6-(4-methylphenyl)-4*H*-1,3-oxazine-2-amine (10): FTIR(KBr): 3534(NH_2), 1610(C=N), 1231(C-O-C) cm^{-1}. ^1H NMR ($CDCl_3$-d_6, TMS) δ: 2.212 (s, 1H, NH_2), 2.329 (dd, 1H, H_4), 2.437(dd, 1H, H_5), 2.224(dd, 1H, $H_{5'}$), 4.357(dd, 1H, H_6), 2.786 (s, 3H, CH_3), 6.234-7.229 (m, 10H, Ar-H) ppm. ^{13}C NMR ($CDCl_3$-d_6, TMS) δ: 164.25 (C_2), 51.36 (C_4), 47.80(C_5), 66.29 (C_6), 114.98-145.09(Ar-C).

4-(4-Chloro-1-naphthyl)-5,6-dihydro-6-(2-nitrophenyl)-4*H*-1,3-oxazine-2-amine (11): FTIR(KBr): 3555(NH_2), 1620(C=N), 1245(C-O-C) cm^{-1}. ^1H NMR ($CDCl_3$-d_6, TMS) δ: 2.216 (s, 1H, NH_2), 2.333 (dd, 1H, H_4), 2.443(dd, 1H, H_5), 2.224(dd, 1H, $H_{5'}$), 4.346(dd, 1H, H_6), 6.214-7.256 (m, 10H, Ar-H) ppm. ^{13}C NMR ($CDCl_3$-d_6, TMS) δ: 164.11 (C_2), 51.29 (C_4), 47.36(C_5), 66.23 (C_6), 114.23-145.25(Ar-C).

4-(4-Chloro-1-naphthyl)-5,6-dihydro-6-(2-nitrophenyl)-4*H*-1,3-oxazine-2-amine (12): FTIR(KBr): 3550(NH_2), 1625(C=N), 1230(C-O-C) cm^{-1}. ^1H NMR ($CDCl_3$-d_6, TMS) δ: 2.213 (s, 1H, NH_2), 2.336 (dd, 1H, H_4), 2.456(dd, 1H, H_5), 2.236(dd, 1H, $H_{5'}$), 4.359(dd, 1H, H_6), 6.512-7.290 (m, 10H, Ar-H) ppm. ^{13}C NMR ($CDCl_3$-d_6, TMS) δ: 164.69 (C_2), 51.35 (C_4), 47.42(C_5), 66.36 (C_6), 124.90-145.69(Ar-C).

4-(4-Chloro-1-naphthyl)-5,6-dihydro-6-(2-nitrophenyl)-4*H*-1,3-oxazine-2-amine (13): FTIR(KBr): 3545(NH_2), 1627(C=N), 1235(C-O-C) cm^{-1}. ^1H NMR ($CDCl_3$-d_6, TMS) δ: 2.212 (s, 1H, NH_2), 2.361(dd, 1H, H_4), 2.447(dd, 1H, H_5), 2.225(dd, 1H, $H_{5'}$), 4.319(dd, 1H, H_6), 6.577-7.289 (m, 10H, Ar-H) ppm. ^{13}C NMR ($CDCl_3$-d_6, TMS) δ: 164.70(C_2), 51.38 (C_4), 47.48(C_5), 66.85 (C_6), 124.58-145.90(Ar-C).

3. 1. Antimicrobial activities

3. 1. 1. Antibacterial sensitivity assay

Antibacterial potential assay of all 4-(4-chloro-1-naphthyl)-5,6-dihydro-6-(substituted phenyl)-4*H*-1,3-oxazine-2-amines were evaluated using Kirby-Bauer [32] disc diffusion technique. In every Petri plates around 0.5 mL of the test bacterial sample was spread uniform homogeneously over the solidified Mueller Hinton agar through sterile glass diffuser. Afterwards, 5 mm diameter of Whatmann No.1 filter paper rounds were impregnated with the solution of the compound and placed on the medium through sterile forceps. Then the plates remained incubated for 24 h at 37 ºC by keeping the plates upside downcast to avoid the gathering of water droplets over the medium. After 24 h, the plates were visually inspected and the diameter of the zone of inhibition were measured. Triplicate results were documented through repeating the same technique [33-36].

The antibacterial potential of all prepared 4-(4-chloro-1-naphthyl)-5,6-dihydro-6-(substituted phenyl)-4*H*-1,3-oxazine-2-amines have been assessed against two gram positive microbes namely, *Staphylococcus aureus*, *Enterococcus faecalis* and four gram negative strains

namely *Escherichia coli*, *Klebsiella species*, *Psuedomonas* and *Proteus vulgaris.* The disc diffusion process was applied through the Kirby-Bauer [32] technique, at a concentration of 250 μg/mL with Ampicillin and Streptomycin used as the standard drugs. The measured antibacterial potentials of all 4-(4-chloro-1-naphthyl)-5,6-dihydro-6-(substituted phenyl)-4*H*-1,3-oxazine-2-amines were existing in **Table 4.** The oxazine-2-amines **4-6** exhibited maximum zone of inhibition counter to *Escherichia coli*, with greater than 20 mm compared to the oxazines **1-3, 7-13** are moderately active in 13-19 mm of zone of inhibition. The oxazine-2-amine derivatives **2, 3** and **6** were found to be effective against *S. aureus* within 20-24 mm of zone of inhibition. Compound **4** was moderately active within 13-19 mm of zone of inhibition.

The oxazines **1**, **5, 7-10** were active within 8-12 mm of zone of inhibition. The oxazine derivatives **4-6** were more active against *Pseudomonas* a displayed greater than 20 mm zone of inhibition and the other derivatives **2-3, 11** and **12** were showed the zone of inhibitions between 12-19 mm. The oxazines **1, 7-10** and **13** displayed active within 8-12 mm of zone of inhibition. The oxazine-2-amines **3** and **4** were effective within 20-24 mm of zone of inhibition against *Klebsiella*. The compounds **5** and **6** were with 12-12 mm zone of inhibition while the other oxazine showed a moderate activity. The compounds **1, 7-10**, **11** and **13** were active when it is screened *Klebsiella* strains within 8-12 mm of zone of inhibition. The oxazine derivative **6** was active against *P. vulgaris* greater than 20mm of zone of inhibition. The other compounds are less effective. The oxazines **4** and **6** showed activities against *E-faecalis* when they are screened with 20-24 mm zone of inhibition.

Table 4. Antibacterial potentials of 4-(4-chloro-1-naphthyl)-5,6-dihydro-6(substituted phenyl)-4*H*-1,3-oxazine-2-amines.

Entry	*E. coli*	*S. aures*	*Pseudomonas*	*Klebsiella*	*P. vulgaris*	*E. faecalis*
1	±	±	±	±	±	±
2	±	++	+	++	±	±
3	±	++	+	++	±	±
4	++	+	++	++	+	++
5	++	±	++	+	+	+
6	++	++	++	+	++	++
7	±	±	±	±	±	±
8	±	±	±	±	±	±
9	±	±	±	±	±	±
10	±	±	±	±	±	±
11	±	+	+	+	±	±

12	±	+	+	±	+	±
13	±	+	±	+	+	±

Disc size: 6.35 mm; Duration: 24-45 h; Standard: Ampicillin (30-33 mm) and Streptomycin (20-25 mm);
Control: Methanol; ---: No activities; ±: Active (8-12 mm); +: Moderately active (13-19 mm); ++: Active (20-24 mm).

3. 1. 2. Antifungal sensitivity assay

Table 5. Antifungal potentials of 4-(4-chloro-1-naphthyl)-5,6-dihydro-6-(substituted phenyl)-4*H*-1,3-oxazine-2-amines.

Entry	**Disc diffusion technique**	**Drug dilution method (50 µg/mL)**	
	Candida albicans	*Penicillium species*	*Aspergillus niger*
1	±	±	±
2	±	±	±
3	±	±	±
4	±	±	+
5	++	++	+
6	+	++	+
7	±	±	±
8	---	---	---
9	+	---	+
10	+	+	---
11	++	++	++
12	++	++	++
13	++	++	++

Standard: Griseofulvin and Gentamycin; Duration : 72 h; Control: Methanol; Medium: Potato dextrose agar; ++: No fungal colony; +: One fungal colony; ±: Two-three fungal colonies; ---: Heavy fungal colony.

Antifungal sensitivity assay of all 4-(4-chloro-1-naphthyl)-5,6-dihydro-6-(substituted phenyl)-4*H*-1,3-oxazine-2-amines were performed using Kirby-Bauer [33] disc diffusion technique. PDA medium was prepared and sterilized as above. It was poured (ear bearing heating condition) in the Petri-plate which was already filled with 1 mL of the fungal species. The plate was rotated clockwise and counter clock-wise for uniform spreading of the species. The discs were impregnated with the test solution. The test solution was prepared by dissolving 15 mg of the chalcone in 1mL of DMSO solvent. The medium could solidify and kept for 24 h. Then the plates were visually examined and the diameter values of zone of inhibition were restrained. Triplicate results were documented through the same technique [33-36].

The inspection of antifungal activities of all 4-(4-chloro-1-naphthyl)-5,6-dihydro-6-(substituted phenyl)-4*H*-1,3-oxazine-2-amines has been completed with *Candida albicans* as the fungal strain through the disc diffusion technique and dilution method was adopted for the other two strains *Penicillium* species and *Aspergillus niger*. The drug dilution concentration is 50 μg/mL. *Griseofulvin* is the standard drug for comparison of the mm of zones of inhibition of all compounds against their stains.

The detected antifungal potential by means of mm of zone of inhibition of all 4-(4-chloro-1-naphthyl)-5,6-dihydro-6-(substituted phenyl)-oxazine-2-amines were presented in **Table 5.** The inspection of antifungal potential of all 4-(4-chloro-1-naphthyl)-5,6-dihydro-6-(substituted phenyl)-oxazine-2-amines (entries 11-23) against *C. albicans*, showed that, the four compounds **5, 11-13** were effective with 20 mm as the zone of inhibition in 250 μg/L. The oxazine-2-amines **6** and **9** were active with 13-19 mm zone of inhibition and the compound **1-4** and **7** were the least active with 8-12 mm zone of inhibitions. The oxazine derivatives **5, 6, 11-13 we**re more visible against *Penicillum* species, in the development of the fungal colony and 2-3 colonies are recorded for the compound **10**. The inhibition of oxazine-2-amines against *A. niger* was more active in two compounds **11-13**. The compounds **1, 6** and **9** were active with 13-19 mm zone of inhibitions. Presence of amino, dimethylamino, methoxy, methyl, dimethyl, chloro, bromo and nitro substituents are responsible for antimicrobial activities of 4-(4-chloro-1-naphthyl)-5,6-dihydro-6-(substituted phenyl)-oxazine-2-amines.

3. 2. Insect antifeedant activity

In General, organic substrates which are partaking carbonyl, unsaturation and halogen assemblies as substituents, they displayed the insect antifeedant activity. Therefore, the author wishes to inspect the insect antifeedant activity of these 4-(4-chloro-1-naphthyl)-5,6-dihydro-6-(substituted phenyl)-oxazine-2-amine derivatives and found to be active as insect antifeedants. This test was completed with a 4th instar larva *Achoea janata* L against castor *semilooper*, remained reared as described on the leaves of castor, *Ricinus communis* in the laboratory at the temperature range of 26 °C ±1 °C and a relative humidity of 75-85%. The leaf – disc bioassay technique [38-40] was adopted against the 4th instar larvae to assess the antifeedant activity. The 4th instar larvae were nominated for examining because the larvae at this stage feed very greedily.

3. 2. 1. Measurement of insect antifeedant activity of 4-(4-chloro-1-naphthyl)-5,6-dihydro-6-(substituted phenyl)-4*H*-1,3-oxazine-2-amines

Castor leaf diskettes of a diameter of 1.85 cm were cuts and intact with the petioles. All synthesized 4-(4-chloro-1-naphthyl)-5,6-dihydro-6-(substituted phenyl)-4*H*-1,3-oxazine-2-

amines were dissolved in acetone at a concentration of 200 ppm dipped for 5 minutes. The leaf discs remained air-dried and positioned in one litre beaker holding tiny of water in order to enable the translocation of water. Therefore, the leaf discs remain fresh throughout the completion of the experiment, the 4th instar larvae of the test insect, which had been restored on the leaf discs of all 4-(4-chloro-1-naphthyl)-5,6-dihydro-6-(substituted phenyl)-oxazine-2-amines and permitted to feeded on them for 24 h. The area of the leaf disc spent were measured by Dethler's method [37-40]. The detected antifeedant activity of 4-(4-chloro-1-naphthyl)-5,6-dihydro-6-(substituted phenyl)-oxazine-2-amines were presented in **Table 6**.

Table 6. The insect antifeedant activities of the 4-(4-chloro-1-naphthyl)-5,6-dihydro-6(substituted phenyl)-4*H*-1,3-oxazine-2-amines

Cpd.	X	4-6 pm	6-8 pm	8-10 pm	10-12 pm	12-6 am	6-8 am	8 am-12 Nn	12 Nn – 4 pm	2-4 pm	Total leaf disc consumed in 24 h
1	H	2	2	1	0.5	0.5	1	1	1	1	10
2	2-NH_2	2	2	1	0.5	1	1	1	1	0.5	11
3	3-NH_2	1	2	2	1	0	0	1	1	1	9
4	3-Br	0.5	0.25	0.5	0.25	0.5	0.5	0.5	1	1	5
5	3-Cl	0.25	0.25	0.25	0.25	0.5	0.5	0.5	1	0.5	4
6	4-Cl	0.25	0.25	0.25	0.25	0.25	0.5	0.25	1	0.5	3.5
7	4-$N(CH_3)_2$	1	1	1	1	1	1	0.5	0.5	0.5	7
8	4-OH	1	1	1	0.25	0.25	1	0.5	1	0.5	7
9	4-OCH_3	1	0.5	1	1	1	0.5	1	0.5	0.5	6
10	4-CH_3	1	1	0.5	1	0.5	0.5	0.5	0.5	0.5	6
11	2-NO_2	1	0.5	1	0.5	0.5	1	1	1	1	8
12	3-NO_2	2	1	1	0.5	0.5	1	2	1	1	9
13	4-NO_2	1	0.5	1	0.5	0.5	1	1	1	1	8
Number of leaf discs consumed by the insect (Values are mean + SE of five)											

The outcomes of the antifeedant activity of 4-(4-chloro-1-naphthyl)-5,6-dihydro-6-(substituted phenyl)-4*H*-1,3-oxazine-2-amines are presented in **Table 6** and it exposes that the compound **(6)** (3-(2,4-dichlorophenyl)bicyclo[2.2.1]hept-5-en-2-yl)(naphthalen-3-yl)

methanone was found to reflect satisfactory antifeedant activity. This test was completed with the insects which ate only two-leaf disc soaked under the solution of this compound [36-40]. Compound **5** displayed adequate antifeedant activity but smaller than **6**. Further the compound **6** was subjected to measured the antifeedant activity at different 50, 100, 150 ppm concentrations and the observation exposed that as the concentrations decreased, the activity also decreased. It is observed from the results in **Table 7** and that the **6** 4-(4-chloro-1-naphthyl)-5,6-dihydro-6-(4-chloro phenyl)-oxazine-2-amines displayed a substantial activity at 150 ppm concentration

Table 7. Antifeedant activity of compound **6** 4-(4-chloro-1-naphthyl)-5,6-dihydro-6 (substituted phenyl)-4H-1,3-oxazine-2-amines showed an appreciable antifeedant activity at 3 different concentrations

ppm	4-6 pm	6-8 pm	8-10 pm	10-12 pm	12-6 am	6-8 am	8 am-12 Nn	12 Nn-4 pm	2-4 pm	Total leaf disc consumed in 24 h
50	0	0.25	0.25	0	0	0	0	0	0.25	0.75
100	0.5	0.25	0.25	0	0	0	0	0	0	1
150	0.25	0.25	0	0	0	0	0	0	0	0.5
Number of leaf discs consumed by the insect (Values are mean + SE of five).										

4. CONCLUSIONS

More than 85% yields of thirteen 4-(4-chloro-1-naphthyl)-5,6-dihydro-6-(substituted phenyl) -oxazine-2-amines were synthesised through solvent-free cyclization of 4-chloro-1-naphthyl chalcones and urea in the existence of SiO_2-H_3PO_4 catalyst underneath microwave irradiation.

This synthetic practice suggested non-hazardous, solvent-free cyclization, easy-workup practice, shorter reaction time and better yields. These oxazine derivatives were analysed through analytical and spectroscopic technique. The antimicrobial activities of these amines have been inspected using Bauer-Kirby method. Oxazine amines holding amino, dimethylamino, methoxy, methyl, dimethyl, chloro, bromo and nitro assemblies as substituents are amswerable for antimicrobial potentials.

The insect antifeedant activities of all 4-(4-chloro-1-naphthyl)-5,6-dihydro-6-(substituted phenyl)-oxazine-2-amines were assessed through the 4^{th} instar larvae *Achoea Janata L.*by castor leaf discs bio-assay technique. The oxazine amine derivative **6** 4-(4-chloro-1-naphthyl)-5,6-dihydro-6-(4-chloro phenyl)-oxazine-2-amine displayed vitreous insect antifeedant activity.

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