SYNTHESIS OF A NOVEL IMINOPYRIMIDOOXAZINE AND THEIR DERIVATIVES

B. Sirsat Shivraj,[a]* G. Jadhav Anilkumar,[a] S. Jadhav Madhav[a] and S. Kale Prashant[a]

Keywords: Claisen-Schmidt condensation, Michael addition reaction, 2-(bis (methylthio) methylene)malononitrle, urea.

We have synthesized 2-(4-chlorophenyl)-8-(methylthio)-6-imino-4-phenyl-2,6,9,9*a*-tetrahydropyrimido[2,1-*b*][1,3]oxazine-7-carbonitrile (**3**) by the reaction of 6-(4-chlorophenyl)-4-phenyl-6H[1,3]oxazin-2-amine (**2**) with 2-(bis (methylthio)methylene)malononitrile in the presence of catalytic amount of potassium carbonate in DMF under reflux condition. The aminooxazine was prepared by the reaction of chalcone (**1**) with urea in the presence of ethanol and sodium hydroxide under reflux condition. The synthesized compounds were characterized by spectral methods. The compound (**3**) possesses replaceable methylthio (-SCH_3) group at 8 position. The compound (**3**) react with various nucleophiles like substituted aromatic amines, aromatic phenols, hetarylamines and active methylene compounds to give 2-(4-chlorophenyl)-8-(substituted)-6-imino-4-phenyl-2,6,9,9*a*-tetrahydropyrimido[2,1-*b*][1,3]oxazine-7-carbonitriles in good yields.

* Corresponding Authors
E-Mail: sbs.igm@gmail.com
[a] P. G. Research Centre, Department of Chemistry, Yeshwant Mahavidyalaya, Nanded 431602, India

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-, 1,3- or 1,4-oxazines,[2] depending upon the relative position of these two atoms and the carbon-carbon double bond. The presence of oxygen, nitrogen heteroatoms in various relative positions along with a carbon-carbon double bonds in their structural moieties[3] have enhanced the important medicinal activities.

1,3-Oxazines attract more attention as they constitute an important class of both natural and non-natural products. Heterocycles containing the oxazine nucleus are found to possess a wide range of valuable biological properties like analgesic, anti-inflammatory, anti-leukemic, antimalarial,[4-6] antipyretic, anticonvulsant and antimicrobial activities.[7-11]

The synthesis of novel oxazine derivatives remains a main focus of research in the field of medicinal chemistry. Oxazine derivatives have been reported to possess antifungal,[12] antibacterial,[13] cytotoxic,[14] antiviral[15] and analgesic activity.[16] The structures of the various synthesized compounds have been assigned on the basis of IR, ^{1}H NMR, ^{13}C NMR and mass spectral data. In the view of this observation and extension of earlier work, we have synthesized 2-(4-chlorophenyl)-6-imino-8-(methylthio)-4-phenyl-2,6,9,9*a*-tetrahydropyrimido[2,1-*b*][1,3]oxazine-7-carbonitrile by using 6-(4-chlorophenyl)-4-phenyl-6*H*[1,3]oxazin-2-amine[17-18] and 2-bis(methylthio)-methylene)malononitrile. The aminooxazine was prepared by the reaction of chalcone[19-20] with urea in the presence of ethanol and sodium hydroxide under reflux conditions.

EXPERIMENTAL

Melting points were determined in open capillary tubes and are uncorrected. The silica gel F_{254} plates were used for thin layer chromatography (TLC), the spots were examined under UV light and then developed with iodine vapour. Column chromatography was performed with silica gel (BDH 100-200 mesh). Solvents were purified according to standard procedures. IR spectra were obtained, with KBr pellets, on a Perkin-Elmer RX1 FT-IR spectrophotometer. ^{1}H NMR, were recorded with a 400 MHz Varian Gemini 200 instrument and reported as δ in ppm with TMS as internal standard.

Synthesis of 2-(4-chlorophenyl)-6-imino-8-(methylthio)-4-phenyl-2,6,9,9*a*-tetrahydropyrimido [2,1-*b*] [1,3]oxazine-7-carbonitrile (3)

Step 1: A 50 % solution of KOH is added to a solution of acetophenone (0.01 mol) and 4-chlorobenzaldehyde (0.01 mol) in 95 % ethanol, under energetic stirring at room temperature. The reaction is left overnight under stirring then diluted with water and acidified. The precipitate is separated by filtration, dried under vacuum and crystallized from ethanol to yield the chalcone, i.e., 3-(4-chlorophenyl)-1-phenylprop-2-en-1-one (**1**).

Step II: A mixture of chalcone (**1**) (2.42 g, 0.01mol) and urea (0.60 g 0.01 mol) was dissolved in ethanolic potassium hydroxide solution (10 mL). It was heated for 4 h, then it was poured into cold ice water to yield 6-(4-chlorophenyl)-4-phenyl-6*H*-1, 3-oxazin-2-amine (**2**).

Step III**:** A mixture of (**2**) and 2-(bis (methylthio)methylene) malononitrile in DMF was refluxed for 6 h, in the presence of catalytic amount of potassium carbonate (10 mg). The reaction was monitored by TLC. After completion, the reaction, mixture was set to cool to room temperature, washed with water and extracted with ethyl acetate.

The extract was concentrated and the residue was subjected to column chromatography (silicagel, n-hexane-ethyl acetate 8:2) to obtain pure solid compound (**3**). The structure of compound (**3**) was confirmed by IR, ^{1}H NMR, ^{13}C NMR and MS analytical data (Scheme 1).

IR (KBr): 3350, 2240, 1650,760 cm^{-1}. ^{1}H NMR (DMSO-d_6, 400 MHz) δ = 2.32 (s, 3H, SCH_3), 5.89 (s, 1H, N-H), 8.32 (s, 1H, =NH), 5.36 (s,1H =CH, 5.62(s, 1H, CH), 4.48(s, 1H, CH), 7.10 (s, 5H, Ar-H), 7.28 (dd, 2H, Ar-H), 7.36 (dd, 2H, Ar-H). S (ESI-MS): *m/z* ($M^{+)}$ 408 (M+2) 410. Mol. Formula: $C_{21}H_{17}ClN_4O_3S$, Mol. Wt: 408 and 410.

Synthesis of derivatives

General procedure

A mixture of (**3**) (1 mmol) and various substituted aromatic amines, aromatic phenols, hetarylamines or active methylene compounds (1 mmol) in DMF (10 mL) and in the presence of anhydrous potassium carbonate (10 mg) was reflux for 4 to 6 h. The reaction mixture was cooled to room temperature and then poured into ice cold water. The separated solid product was filtered, washed with water and recrystallized using ethanol.

2-(4-Chlorophenyl)-6-imino-8-phenoxy-4-phenyl-2,6,9,9*a*-tetrahydro pyrimido[2,1-*b*][1,3]oxazine-7-carbonitrile (3a)

IR (KBr) :3350,2240, 650,760 cm^{-1}. ^{1}H NMR (DMSO-d_6, 400 MHz) δ = 7.27 (s, 5H, Ar-H), 5.78 (s, 1H, N-H), 8.36 (s, 1H, =NH), 5.32 (s, 1H, =CH), 5.54 (s, 1H, CH), 4.42 (s, 1H, CH), 7.14 (s, 5H, Ar-H), 7.26 (dd, 2H, Ar-H), 7.38 (dd, 2H, Ar-H). MS (ESI-MS): *m/z* ($M^{+)}$ 454, (M+2) 456. $C_{26}H_{19}ClN_4O_2$. MW: 454 and 456.

8-(4-Bromophenoxy)-2-(4-chlorophenyl)-6-imino-4-phenyl-2,6,9,9*a*-tetrahydropyrimido[2,1-*b*][1,3]oxazine-7-carbonitrile (3b)

IR (KBr): 3350, 2240, 1650, 760, 650 cm^{-1}. ^{1}H NMR (DMSO-d_6, 400 MHz) δ = 5.81 (s, 1H, N-H), 8.36 (s, 1H, =NH). 5.50 (s, 1H, =CH), 5.51 (s, 1H, CH), 4.40 (s, 1H, CH), 7.24 (s, 5H, Ar-H), 7.26 (dd, 2H, Ar-H), 7.40 (dd, 2H, Ar-H), 6.72(dd, 2H, Ar-H), 7.34 (dd 2H, Ar-H). MS (ESI-MS): *m/z* ($M^{+)}$ 532, (M+2) 534. $C_{26}H_{18}BrClN_4O_2$. Mw: 532 and 534.

2-(4-Chlorophenyl)-6-imino-8-(4-nitrophenoxy)-4-phenyl-2,6,9,9*a*-tetrahydropyrimido[2,1-*b*][1,3]oxazine-7-carbonitrile (3c)

IR (KBr): 3350, 2260, 1650, 760, 1510 cm^{-1}. ^{1}H NMR (DMSO-d_6, 400 MHz) δ = 5.77 (s, 1H N-H), 8.39 (s, 1H =NH), 5.55 (s, 1H, =CH), 5.44 (s, 1H, CH), 4.32 (s, 1H, CH), 7.30 (s, 5H, Ar-H), 7.36 (dd, 2H, Ar-H), 7.27 (dd, 2H, Ar-H), 7.16 (dd, 2H, Ar-H), 8.03 (dd, 2H, Ar-H). MS (ESI-MS): *m/z* (M^+) 499 (M+2) 501. $C_{26}H_{18}ClN_5O_4$. . Mw: 499 and 501.

2-(4-Chlorophenyl)-6-imino-4-phenyl-8-(phenylamino)-2,6,9,9*a*-tetrahydro pyrimido[2,1-*b*][1,3]oxazine-7-carbonitrile (4a)

IR (KBr): 3350, 2240, 1650, 760, 3250 cm^{-1}. ^{1}H NMR (DMSO-d_6, 400 MHz) δ = 5.76 (s, 1H, N-H), 8.42 (s, 1H, =NH), 6.34 (s, 1H, N-H), 5.53 (s, 1H, =CH), 4.51 (s, 1H, CH), 5.68 (s, 1H, CH), 7.25 (s, 5H, Ar-H), 7.28 (dd, 2H, Ar-H), 7.42 (dd, 2H, Ar-H), 7.04 (s, 5H, Ar-H). Mass (ESI-MS): *m/z* (M^+) 453, (M+2) 455. $C_{26}H_{20}ClN_5O$. Mw: 453 and 455.

8-((4-Bromophenyl) amino)-2-(4-chlorophenyl)-6-imino-4-phenyl-2,6,9,9*a*-tetrahydropyrimido [2,1-*b*]*[1,3]*oxazine-7-carbonitrile (4b)

IR (KBr): 3350, 2240, 1650, 3250, 640, 760 cm^{-1}. ^{1}H NMR (DMSO-*d*6, 400 MHz) δ = 5.74 (s, 1H, N-H), 8.35 (s, 1H, =NH), 6.27 (s, 1H, N-H), 5.48 (s, 1H, =CH), 4.42 (s, 1H, CH), 5.72 (s, 1H, CH), 7.32 (s, 5H, Ar-H), 7.34 (dd, 2H, Ar-H), 7.45 (dd, 2H, Ar-H), 6.48 (dd, 2H, Ar-H), 7.22 (dd, 2H, Ar-H). Mass (ESI-MS): *m/z* ($M^{+)}$ 531 (M+2) 533. $C_{26}H_{19}BrClN_5O$. Mw: 531 and 533 .

2-(4-Chlorophenyl)-6-imino-8-((4-nitrophenyl) amino)-4-phenyl-2, 6, 9,9*a*-tetrahydropyrimido[2,1-*b*][1,3]oxazine-7-carbonitrile (4c)

IR (KBr): 3350, 2240, 1650, 3250, 1480, 760 cm^{-1}. ^{1}H NMR (DMSO-d_6, 400 MHz) δ = 5.71 (s, 1H, N-H), 8.46 (s, 1H, =NH), 6.20 (s 1H, N-H), 5.44 (s, 1H, =CH), 4.49(s, 1H, CH), 5.78 (s, 1H, CH), 7.24 (s, 5H, Ar-H), 7.30 (dd, 2H, Ar-H), 7.40 (dd, 2H, Ar-H), 6.54 (dd, 2H, Ar-H), 7.92 (dd, 2H, Ar-H). MS (ESI-MS): *m/z* ($M^{+)}$ 498 (M+2) 500. $C_{26}H_{19}ClN_6O_3$. Mw: 498 and 500.

2-(4-Chlorophenyl)-6-imino-4-phenyl-8-(pyrrolidin-1-yl)-2,6,9,9*a*-tetrahydropyrimido[2,1-*b*][1,3]oxazine-7-carbonitrile (5a)

IR (KBr): 3350, 2240, 1650, 760 cm^{-1}. ^{1}H NMR (DMSO-d_6, 400 MHz) δ = 5.77 (s, 1H, N-H), 8.42 (s, 1H, =NH), 5.54 (s, 1H, =CH) 4.52 (s, 1H, CH), 5.68 (s, 1H, CH), 7.23 (s, 5H, Ar-H), 7.34 (dd, 2H, Ar-H), 7.40 (dd, 2H, Ar-H), 2.54 (t, 4H), 1.62 (m, 4H). MS (ESI-MS): *m/z* ($M^{+)}$ 431 (M+2) 433. $C_{24}H_{22}ClN_5O$. Mw: 431 and 433.

2-(4-Chlorophenyl)-6-imino-4-phenyl-8-(piperidin-1-yl)-2,6,9,9*a*-tetrahydropyrimido[2,1-*b*][1,3]oxazine-7-carbonitrile (5b)

IR (KBr): 3350, 2240, 1650, 760 cm^{-1}. ^{1}H NMR (DMSO-d_6, 400 MHz) δ = 5.88 (s, 1H, N-H), 8.49 (s, 1H, =NH), 5.46 (s, 1H, =CH) 4.62 (s, 1H, CH), 5.62 (s, 1H, CH), 7.25 (s, 5H, Ar-H), 7.30 (dd, 2H, Ar-H), 7.36 (dd, 2H, Ar-H), 3.08 (t, 4H), 1.50 (m, 6H). MS (ESI-MS): *m/z* ($M^{+)}$ 445 (M+2) 447. $C_{25}H_{24}ClN_5O$. Mw: 445 and 447.

2-(2-(4-Chlorophenyl)-7-cyano-6-imino-4-phenyl-2,6,9,9*a*-tetrahydropyrimido[2,1-*b*][1,3]oxazin-8-yl)malononitrle (6a)

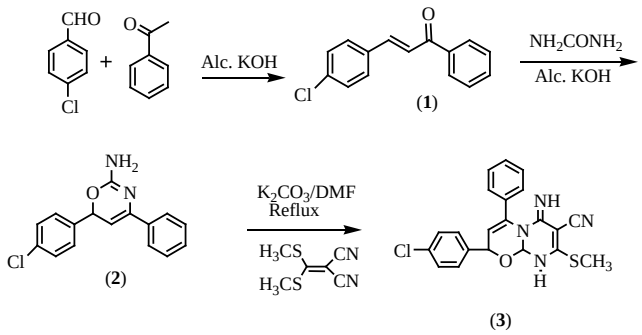
IR (KBr, cm^{-1}): 3350, 2240, 1650, 2950, 760 cm^{-1}. ^1H NMR (DMSO-d_6, 400 MHz) δ =5.82 (s, 1H, N-H), 8.46 (s, 1H, =NH), 5.41 (s, 1H, =CH) 4.52 (s, 1H, CH), 5.70 (s, 1H, CH), 7.21 (s, 5H, Ar-H), 7.28 (dd, 2H, Ar-H), 7.38 (dd, 2H, Ar- H), 4.12 (s, 1H, act-CH). MS (ESI-MS): *m/z* ($M^{+)}$ 426 (M+2) 428. $C_{23}H_{15}ClN_6O$. Mw: 426 and 428.

Ethyl 2-(2-(4-chlorophenyl)-7-cyano-6-imino-4-phenyl-2,6,9,9*a*-tetrahydropyrimido[2,1-*b*][1,3]oxazin-8-yl)-2-cyanoacetate (6b)

IR (KBr, cm^{-1}): 3350, 2240, 1650, 1950, 1710, 760 cm^{-1}. ^1H NMR (DMSO-d_6, 400 MHz) δ = 5.79 (s, 1H, NH), 8.46 (s, 1H, =NH), 5.52 (s, 1H, =CH), 4.39 (s, 1H, CH), 5.59 (s, 1H, CH), 7.23 (s, 5H, Ar-H), 7.30 (dd, 2H, Ar-H), 7.41 (dd, 2H, Ar-H), 3.96 (s, 1H, act-CH), 4.16 (q, 2H), 1.21 (t, 3H). Mass (ESI-MS): *m/z* ($M^{+)}$ 473 (M+2) 475. $C_{25}H_{20}ClN_5O_3$. Mw: 473 and 475.

RESULT AND DISCUSSION

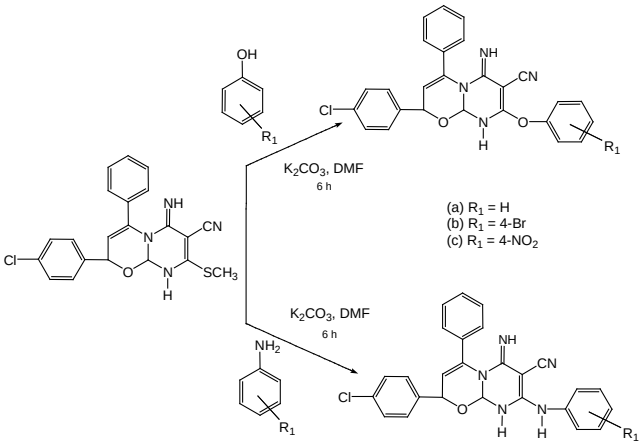
Synthesis of 2-(4-chlorophenyl)-6-imino-8-(methylthio)-4-phenyl-2,6,9,9*a*-tetrahydropyrimido[2,1-*b*][1,3]oxazine-7-carbonitrile (**3**) as starting material has been performed with refluxing 6-(4-chlorophenyl)-4-phenyl-6H[1,3]oxazin-2-amine and 2-(bis(methylthio)methylene)malononitrile in DMF in presence of K_2CO_3.



Scheme 1. Synthesis of 2-(4-chlorophenyl)-6-imino-8-(methylthio)-4-phenyl-2,6,9,9*a*-tetrahydropyrimido[2,1-*b*][1,3]oxazine-7-carbonitrile (**3**).

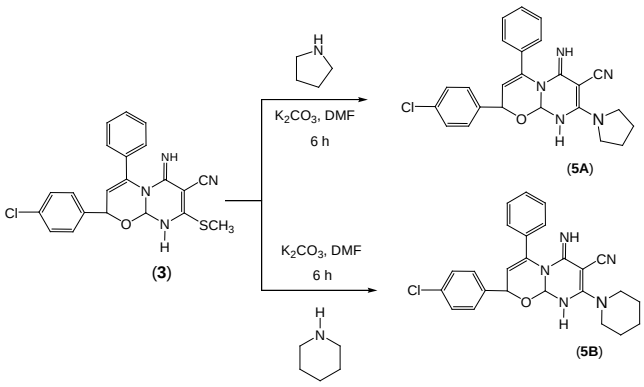
A 50 % solution of KOH is reacted with a solution of equimolar amount of acetophenone and 4-chlorobenzaldehyde in 95 % ethanol with stirring at room temperature. The chalcone, i.e., 3-(4-chlorophenyl)-1-phenylprop-2-en-1-one (**1**) was reacted with 1 equiv. of urea dissolved in ethanolic potassium hydroxide solution with 4 h heating to yield 6-(4-chlorophenyl)-4-phenyl-6*H*-1, 3-oxazin-2-amine (**2**). A mixture of (**2**) and 2-(bis (methylthio)methylene)malononitrile in DMF was refluxed for 6 h, in the presence of catalytic amount of potassium carbonate to yield the target compound (Scheme 1).

The synthesized compound acts as electrophilic species, reacting with various substituted aromatic amines and phenols to give 2-(4-chlorophenyl)-6-imino-8-(substituted)-4-phenyl-2,6,9,9*a*-tetrahydropyrimido[2,1-*b*][1,3]oxazine-7-carbonitrile derivatives in good yields (Schemes 2).

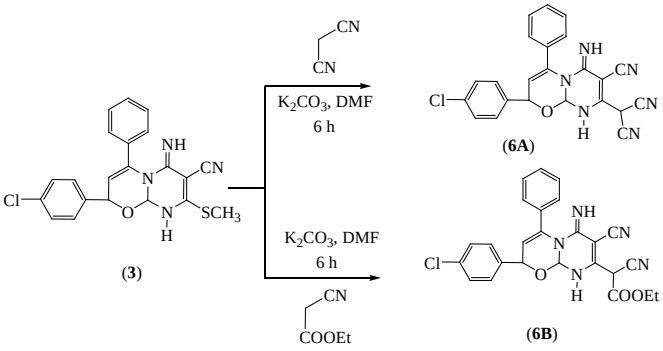


Scheme 2. Synthesis of ether and amino derivatives from compound **3.**

Analogous recations of compound **3** with hetaryl amines and active methylene compounds resulted ring-N attached substitution and ring-condensed derivatives, respectively (Scheme 3 and 4).



Scheme 3. Synthesis of heterocyclic derivatives from compound **3**.



Scheme 4. Reaction products of compound **3** with active methylene compounds

The spectroscopic parameters of the synthesized new compounds (IR, NMR and MS) are given in the experimental section.

CONCLUSION

Several new 2-(4-chlorophenyl)-8-(substituted)-6-imino-4-phenyl-2,6,9,9*a*-tetrahydropyrimido[2,1-*b*][1,3]oxazine-7-carbonitrile are synthesized by using simple and efficient chemistry and this synthesized compounds possesses methylthio group at 8-position which is a good leaving group and, therefore, acts as an electrophilic species and reacting with various nucleophiles. In compound **3,** cyano and thiomethyl groups are at adjacent position it also undergo cyclization to give polycyclic heterocyclic compound.

ACKNOWLEDGEMENTS

The authors are grateful to Dr. G.N. Shinde, Principal, Yeshwant Mahavidyalaya, Nanded, for providing laboratory facilities & Vishnu Chemicals Ltd., Hyderabad, for providing spectral data.

REFERENCES

[1]Thompson, A. M., Sutherland, H. S., Palmer, B. D., Kmentova, I., Blaser, A., Franzblau, S. G., Wan, B., Wang, Y., Ma, Z., Denny, W. A., Synthesis and structure-activity relationships of varied ether linker analogues of the antitubercular drug (6S)-2-nitro-6-{[4-(trifluoromethoxy)benzyl]oxy}-6,7-dihydro-5H-imidazo[2,1-b][1,3]oxazines. *J. Med. Chem*, **2011**, *54*, 6563-6585. https://doi.org/10.1021/jm200377r

[2]Yakovlev, I. P., Prep'yalov, A. V., Ivin, B. A. , Unsaturated 4H-1, 3-Oxazines (Review). *Chem. Heterocyclic. Compd.*, **1994**, *30(3)*, 255-271.

[3]Manjula, M., Rai, K., Gaonkar, M. L., Ravesha, S. L., Satish, K.A., Synthesis of new series of 5, 6-dihydro-4*H*-1, 2-oxazines via hetero Deils-Alder reaction and evaluation of antimicrobial activity. *Eur. J. Med. Chem*, **2009**, *44*, 280-288.

[4]Takimoto C.H., Calvo E., *Principles of oncologic pharmacotherapy in cancer Management: A multidisciplinary approach*, UBM Medica Londen, **2008**, 42-58.

[5]Kalirajan, R., Sivakumar, S.U., Jubie, S., Gowramma, B., Suresh, B., Synthesis and biological evaluation of some heterocyclic derivatives of Chalcones, *Int. J. Chem. Tech. Res*, **2009**, *1(1)***,** 27- 34.

[6]Vennerstrom, J. L., Makler, M. T., Angerhofer, C. K., Williams, J. A., Antimalarial dyes revisited: Xanthenes, azines, Oxazine and thiazines, Antimicrobial, *Agents Chemother.*, **1995**. 2671-2677. doi.org/10.1128/aac.39.12. 2671.

[7]Singh C., Parwana H. K., Singh G., Synthesis of 3,6-diaryl-2h,3h,4h,5h,6h- [1, 3]- Oxazine-2-Thiones as potential anticonvulsants, *Indian J. Pharm. Sci.*, **1995**, *57*,198-202

[8]Latif N., Mishriky N., Assad F. M., Carbonyl and Thiocarbonyl compounds, XIX. Intramolecular cyclization of (2-nitroethenyl)aryl N-arylcarbamates: Synthesis of newer series of 3,4-dihydro-2H[1,3]oxazin-2-ones and their antimicrobial activities, *Aust. J. Chem.*, **1982**, *35*, 1037-1043**.** doi.org/10.1071/ch9821037.

[9]Cassady, J. M., Chan, K. K., J. M., Floss, H. G., Leistner, E., Recent developments in the Maytansinoid antitumor agents, *Chem. Pharm. Bull.*, **2004**, *52*, 1-26. doi.org/10.1002/chin.200427222.

[10]Turgut Z., Pelit E., Koycu A., Synthesis of new 1,3-disubstituted-2,3-dihydro-1*H*-naphth[1,2-*e*][1,3]oxazines, *Molecules*, **2007**, *12*, 345-352. doi.org/10.3390/12030345.

[11]Salwa, F. M., Mohamed, M. Y., Abd El-Galil, E. A., Eman, R. K., Antimicrobial Activities of some synthesized pyridines, Oxazine and Thiazole from 3-Aryl-1-(2-naphthyl)prop-2-en-1-ones, *Sci. Pharm.*, **2008**, *76*, 279-303. doi.org/10.3797/scipharm.0804-09.

[12]Beena, K. P., Design, synthesis, characterization and evaluation of 1,3-oxazine derivatives as potent antifungal agents, *Der Pharm. Lett.*, **2013**, *5*, 257-260.

[13]Prasad, D., Rohilla, R., Roy, N., Nath, M., Synthesis and antibacterial evaluation of benzazoles tethered dihydro-[1,3]oxazines. *Indian J. Chem.*, **2012**, *51B (5)*, 739-745.

[14]Temple, C. Jr., Wheeler, G. P., Comber, R. N., Elliott, R. D., Montgomery J. A., Synthesis of potential anticancer agents. Pyrido [4, 3-b] [1, 4] oxazines and pyrido [4, 3-b] [1, 4] thiazines. *J. Med. Chem*, **1983**, *26 (11)*, 1614-1619. Doi.10.1021/jm00365a012

[15]Selvam, P., Sridharan, D., Murugesh, N., Chandra Mohan, M., Witurouw, M., Synthesis and anti-hiv activity of some novel 2, 3-disubstituted quinazolin 4(3*h*)-ones, *Int. J. Chem. Sci.*, **2008**, *6*, 1196-1201.

[16]Sindhu, T. J., Arikkatt, S. D., Vincent, G., Chandran, M., Bhat, A. R., Krishna Kumar, K., Biological activities of Oxazine and its derivatives: A Review., *Int. J. Pharm. Sci. Res.*, **2013**, *4*, 134-143.

[17]Sawant R. L., Bhangale, L., Wadekar, J., Gaikwad, P., Substituent Selection for Design and Synthesis of Antimicrobial 1,3-Oxazine, a Topliss Modified Approach, *Farmacia*, **2012**, *60***,** 3-39.

[18]Kategaonkar, A. H., Sonar, S. S., Shelke, S. K., Shingate, B. B., Shingare, M. S., Ionic liquid catalyzed multicomponent synthesis of 3,4-dihydro-3-substituted-2*H*-naphthol[2,1-*e*][1,3]oxazine derivatives, *Org. Commun.*, **2010**, *3*, 1-7.

[19]Lafta, S. J., Abd, H. J., Abdulla, A., Synthesis, characterization, antimicrobial evaluation and docking study of new chalcone derivatives containing 1,3,5-triazinane-1,3,5-triyl moiety, *Int. J. Chem. Sci.*, **2016**, 141.

[20]Prasad, Y. R., Kumar, P. P., Ravi Kumar, P., Srinivasa Rao, A., Synthesis and antimicrobial activity of some new chalcone of 2-acetylpyridine, *J. Chem.*, **2008**, ***5(1)***, 144-148. doi.org/10.1155/2008/602458.

Received: 12.01.2020
Accepted: 04.04.2020