Available online www.jocpr.com

Journal of Chemical and Pharmaceutical Research, 2017, 9(2):170-175

Research Article

ISSN : 0975-7384
CODEN(USA) : JCPRC5

Novel One-Pot Synthesis and Antimicrobial Activity of 2-amino-4H-1,3-Oxazines and 2-Amino-4H-1,3-Thiazines

Esam A Ishak[1*], Tamer El Malah[1], Oussama Dehbi[1], Afroz Bakht[2] and Yassine Riadi[2]

[1]Departement of Chemistry, College of Science & Arts, Aljouf University, Al Qurayat, Al Jouf, Saudi Arabia.
[2]Department of Pharmaceutical Chemistry, College of Pharmacy, Prince Sattam Bin Abdulaziz University, Alkharj, Saudi Arabia

---

ABSTRACT

An efficient synthesis of 1,3-oxazine and 1,3-thiazine derivatives has been demonstrated through a one-pot multicomponent condensation reaction (MCR). Urea and thiourea have been used as reagent and catalyst system for this reaction. The method produced good to excellent product yields. The synthesized compounds were evaluated for their antibacterial and antifungal activities in vitro against four bacteria and two fungi.

Keywords: Aldehydes; Bromovinyl; 1,3-Oxazines; 1,3-Thiazines; Antimicrobial

---

INTRODUCTION

Multicomponent reactions (MCRs) are transformations that incorporate of more than three reactants to build new. They have been used to form heterocyclic structures and they have been combined with subsequent transformations to yield complex structures which are easily accessible via classical synthetic reactions. This method offers many advantages and is becoming an important tool in the synthetic chemists arsenal. Oxazines and thiazines skeletons have been found in a few biologically compounds,[1] and vulcanization accelerators.[2] Since many of these compounds exhibit biological activities such as anti-inflammatory,[3] antibacterial,[4] antipyretic,[5] antihypertensive[6] and antifungal,[7] these derivatives have become an integral part of pharmacologically important heterocyclic compounds. These compounds are also important intermediates in organic synthesis.[8] A variety of methods can be found in the literature for the synthesis of oxazines and thiazines using different catalysts.[9]

EXPERIMENTAL SECTION

Instrumentation and Materials: 1H NMR and 13C NMR were recorded on a Bruker Avance DPX250 pectrometer (500 MHz 1H, 125 MHz 13C) using tetramethylsilane as the internal standard, multiplicities were determined by the DEPT 135 equivalence, chemical shifts were reported in parts par million (ppm, δ units). Coupling constants were reported in units of hertz (Hz) if applicable. Thin layer chromatography (TLC) was carried out on Merck silica gel 60F254 precoated plates. Visualization was made with ultraviolet light.

General procedures

A solution of benzaldehyde 1(1 mmol), (2-bromovinyl)benzene 2 (1 mmol) and urea 3 (3 mmol) in water (3 mL) was taken in a 20 mL vial and subjected to MW irradiation at (120 °C, 250W) until the reaction was completed (TLC). The reaction mixture was then cooled, and the residue was filtrated washed with acetone. The solid product was recrystallized from EtOH to give pure product.

4,6-Diphenyl-4H-1,3-oxazin-2-amine (4a)
Pal yellow crystals (0.22 g, 89%), mp = 219-221 °C. ^{1}H NMR (500 MHz, DMSO-d_6): δ 9.45 (s, 2H, NH_2), 7.76 (m, J=2 Hz, 4 Hz, 2H, H_{Ar}), 7.52 (m, J=2 Hz, 4 Hz, 8H, H_{Ar}), 6.62 (d, J=4 Hz, 1H, CH), 5.58 (d, J=4 Hz, 1H, CH). ^{13}C NMR (125 MHz, DMSO-d_6): δ 160.4, 148.6, 142.7, 138.4, 132.1, 129.9, 129.6 , 128.8, 127.9(4 x CH), 125.2 (2 x CH), 102.3, 51.9. Calcd.($C_{16}H_{14}N_2O$): C, 76.78; H, 10.46; N, 5.64; O, 6.39.Found: C, 76.79; H, 10.45; N, 5.62; O, 6.40

6-Phenyl-4-(p-tolyl)-4H-1,3-oxazin-2-amine (4b)
Pal yellow crystals (0.22 g, 84%), mp = 176-178 °C. ^{1}H NMR (500 MHz, DMSO-d_6): δ 9.43 (s, 2H, NH_2), 7.72 (m, J=2 Hz, 4 Hz, 2H, H_{Ar}), 7.46 (m, 3H, H_{Ar}), 7.28 (d, J=4 Hz, 2H, H_{Ar}), 7.16 (d, J=4 Hz, 2H, H_{Ar}), 6.60 (d, J=4 Hz, 1H, CH), 5.56 (d, J=4 Hz, 1H, CH), 2.43 (s, 3H, CH_3). ^{13}C NMR (125 MHz, DMSO-d_6): δ 160.9, 148.5, 141.8, 138.8, 132.5, 131.2, 130.7, 129.3 , 127.6 (4 x CH), 125.2 (2 x CH), 101.9, 51.1, 22.4 . Calcd.($C_{17}H_{16}N_2O$): C, 77.25; H, 6.10; N, 10.60; O, 6.05. Found C, 77.26; H, 6.11; N, 10.60; O, 6.04.

4-(o-Methoxyphenyl)-6-phenyl-4H-1,3-oxazin-2-amine (4c)
Pal yellow crystals (0.20 g, 72%), mp = 186-188 °C. ^{1}H NMR (500 MHz, DMSO-d_6): δ 9.42 (s, 2H, NH_2), 7.72 (m, J=2 Hz, 4 Hz, 2H, H_{Ar}), 7.43 (m, J=2 Hz, 4 Hz, 5H, H_{Ar}), 7.22 (d, J=4 Hz, 1H, H_{Ar}), 7.09 (d, J=4 Hz, 1H, H_{Ar}), 6.61 (d, J=4 Hz, 1H, CH), 5.54 (d, J=4 Hz, 1H, CH), 3.87 (s, 3H, OCH_3); ^{13}C NMR (125 MHz, DMSO-d_6): δ 160.6, 149.7, 142.9, 132.4, 131.2 , 130.0 , 129.7 , 127.7, 127.2, 125.2, 119.2, 111.2, 101.6, 51.0, 49.9. Calcd.($C_{17}H_{16}N_2O_2$): C, 72.84; H, 5.75; N, 9.99; O, 11.41.Found: C, 72.85; H, 5.74; N, 10.00; O, 11.40

4-(m-Nitrophenyl)-6-phenyl-4H-1,3-oxazin-2-amine (4d)
Pal brown crystals (0.25 g, 85 %), mp = 176-178 °C. ^{1}H NMR (500 MHz, DMSO-d_6): δ 9.41 (s, 2H, NH_2), 8.21 (m, J=2 Hz, 4 Hz, 2H, H_{Ar}), 7.99 (m, J=2 Hz, 4 Hz, 2H, H_{Ar}), 7.72 (m, 2H, H_{Ar}), 7.44 (m, 3H, H_{Ar}), 6.42 (d, J = 4 Hz, 1H, CH), 5.55 (d, J = 4 Hz, 1H, CH); ^{13}C NMR (125 MHz, DMSO-d_6): δ 160.3, 149.6, 144.0, 142.9, 133.4 , 132.2 , 131.6, 130.2 , 129.8 , 125.5 , 123.6, 121.6, 101.9, 51.2 MS: m/z (%) 295 (M+, 100), Calcd.($C_{16}H_{13}N_3O_3$): C, 65.08; H, 4.44; N, 14.23; O, 16.25 C, 65,10; H, 4.46; N,14.25; O,16,26.

4-(p-Fluorophenyl)-6-phenyl-4H-1,3-oxazin-2-amine (4e)
Pal yellow crystals (0.23 g, 86 %), mp. = 168-170 °C. ^{1}H NMR (500 MHz, DMSO-d_6): δ 9.42 (s, 2H, NH_2), 7.72 (m, J=2 Hz, 4 Hz, 2H, H_{Ar}), 7.48 (m, J=2 Hz, 4 Hz, 5H, H_{Ar}), 7.23 (m, 2H, H_{Ar}), 6.62 (d, J = 4 Hz, 1H, CH), 5.55 (d, J = 4 Hz, 1H, CH); ^{13}C NMR (125 MHz, DMSO-d_6): δ 161.6, 154.4, 142.1, 136.9 , 131.0, 130.6 , 130.0 , 129.6, 125.0, 116.4, 101.8, 51.0 . Calcd.($C_{16}H_{13}FN_2O$): C, 71.63; H, 4.88; N, 7.08; O, 5.96. Found: C, 71.63; H, 4.88; N, 7.08; O, 5.96.

4-Phenyl-6-(p-tolyl)-4H-1,3-oxazin-2-amine (4f)
Pal yellow crystals (0.22 g, 86 %), mp. = 172-174 °C. ^{1}H NMR (500 MHz, DMSO-d_6): δ 9.40 (s, 2H, NH_2), 7.63 (d, J = 4 Hz, 2H, H_{Ar}), 7.46 (m, J=2 Hz, 4 Hz, 5H, H_{Ar}), 7.26 (d, J = 4 Hz, 2H, H_{Ar}), 6.61 (d, J = 4 Hz, 1H, CH), 5.51 (d, J = 4 Hz, 1H, CH), 2.42 (s, 3H, CH_3); ^{13}C NMR (125 MHz, DMSO-d_6): δ 161.1, 142.6, 141.4, 140.2 , 130.1 , 129.4 , 128.8 , 127.8, 127.2 , 125.1 , 101.7 , 51.4 , 22.7. Calcd.($C_{17}H_{16}FN_2O$): C, 77.25; H, 6.10; N, 10.60; O, 6.05. Found: C, 77.26; H, 6.11; N, 10.58; O, 6.07.

4,6-Di(p-tolyl)-4H-1,3-oxazin-2-amine (4g)
Pal yellow crystals (0.22 g, 82 %), mp. = 163-164 °C. ^{1}H NMR (500 MHz, DMSO-d_6): δ 9.42 (s, 2H, NH_2), 7.67 (d, J = 4 Hz, 2H, H_{Ar}), 7.38 (m, J=2 Hz, 4 Hz, 6H, , H_{Ar}), 6.62 (d, J = 4 Hz, 1H, CH), 5.52 (d, J = 4 Hz, 1H, CH), 2.44 (s, 3H, CH_3), 2.42 (s, 3H, CH_3); ^{13}C NMR (125 MHz, DMSO-d_6): δ 161.0, 142.5, 140.4, 139.6, 138.6, 130.4 , 129.6 , 127.4, 127.1 , 125.2 , 101.6, 51.2, 22.6, 22.3. Calcd.($C_{18}H_{18}N_2O$): C, 77.67; H, 6.52; N, 10.06; O, 5.75 Found: C, 77.66; H, 6.54; N, 10.07; O, 5.75.

4-(p-Chlorophenyl)-6-(p-tolyl)-4H-1,3-oxazin-2-amine (4h)
Pal yellow crystals (0.28 g, 92 %), mp. = 164-166 °C. ^{1}H NMR (500 MHz, DMSO-d_6): δ 9.41 (s, 2H, NH_2), 7.68 (d, J = 4 Hz, 2H, H_{Ar}), 7.42 (m, J=2 Hz, 4 Hz, 6H, H_{Ar}), 6.66 (d, J = 4 Hz, 1H, CH), 5.49 (d, J = 4 Hz, 1H, CH), 2.42 (s, 3H, CH_3); ^{13}C NMR (125 MHz, DMSO-d_6): δ 161.6, 142.8 , 141.1 , 140.2, 138.4, 130.2 , 129.1 , 127.3 , 126.8 , 124.9 , 101.1 , 51.1, 22.2. Calcd.($C_{17}H_{15}ClN_2O$): C, 68.34; H, 5.06; N, 9.38; O, 5.36; Cl, 11.87 Found: C, 68.34; H, 5.06; N, 9.38; O, 5.36; Cl, 11.88.

4-(m-Nitrophenyl)-6-(p-tolyl)-4H-1,3-oxazin-2-amine (4i)
Pal yellow crystals (0.27 g, 88 %), mp. = 184-186 °C. ^{1}H NMR (500 MHz, DMSO-d_6): δ 9.41 (s, 2H, NH_2), 8.42 (s, 1H, H_{Ar}), 8.11 (m, 1H, H_{Ar}), 7.86 (d, J = 4 Hz, 1H, H_{Ar}), 7.44 (m, 1H, H_{Ar}), 7.34 (d, J = 4 Hz, 2H, H_{Ar}), 7.21 (d, J = 4 Hz, 2H, H_{Ar}), 6.32 (d, J = 4 Hz, 1H, CH), 5.52 (d, J = 4 Hz, 1H, CH), 2.44 (s, 3H, CH_3); ^{13}C NMR

(125 MHz, DMSO-d_6): δ 161.3, 147.8 , 144.8 , 143.1 , 140.8 , 133.9, 130.9, 130.2 , 126.9 , 125.2 , 123.7 , 122.2, 101.2, 51.3 , 22.4 . Calcd.($C_{17}H_{15}N_3O_3$): C, 66.01; H, 4.89; N, 13.58; O, 15.52Found: C, 66.11; H, 4.90; N, 13.60; O, 15.3.

4,6-Diphenyl-4H-1,3-thiazin-2-amine (4j)
Pal yellow crystals (0.20 g, 76 %), mp. = 178-180 °C. ^{1}H NMR (500 MHz, DMSO-d_6): δ 9.82 (s, 2H, NH_2), 7.42 (m, 7H, H_{Ar}), 7.38 (m, 2H, H_{Ar}), 7.18 (d, J = 4 Hz, 1H, H_{Ar}), 6.62 (d, J = 2 Hz, 1H, CH), 6.22 (d, J = 2 Hz, 1H, CH); ^{13}C NMR (125 MHz, DMSO-d_6): δ 169.4, 141.2, 134.8, 132.8 , 129.2, 128.6, 128.4, 127.8 , 127.6 , 127.0 , 124.9, 69.4 . Calcd.($C_{16}H_{14}N_{22}S$): C, 72.15; H, 5.30; N, 10.52; S, 12.05 Found: C, 72.16; H, 5.33; N, 10.51; S, 12.07.

6-Phenyl-4-(p-tolyl)-4H-1,3-thiazin-2-amine (4k)
Pal yellow crystals (0.20 g, 72 %), mp. = 180-182 °C. ^{1}H NMR (500 MHz, DMSO-d_6): δ 9.86 (s, 2H, NH_2), 7.41 (d, J = 8 Hz, 1H, H_{Ar}), 7.34 (d, J = 8 Hz, 1H, H_{Ar}), 7.22 (m, 7H, H_{Ar}), 6.71 (d, J = 2 Hz, 1H, CH), 6.24 (d, J = 2 Hz, 1H, CH), 2.42 (s, 3H, CH_3); ^{13}C NMR (125 MHz, DMSO-d_6): δ 169.8, 140.1, 137.2 , 134.3 , 133.1, 130.6, 129.1 , 128.2 , 127.8 , 127.1, 125.2 , 69.8, 22.2 (CH_3).Calcd.($C_{17}H_{16}N_2S$): C, 72.82; H, 5.75; N, 9.99; S, 11.44 Found: C, 72.83; H, 5.74; N, 10.01; S, 11.45.

4-(p-Chlorophenyl)-6-Phenyl-4H-1,3-thiazin-2-amine (4i)
Pal yellow crystals (0.23 g, 77%), mp. = 170-172 °C. ^{1}H NMR (500 MHz, DMSO-d_6): δ 9.88 (s, 2H, NH_2), 7.42 (m, 4H, H_{Ar}), 7.32 (m, 2H, H_{Ar}), 7.26 (m, 3H, H_{Ar}), 6.72 (d, J = 2 Hz, 1H, CH), 6.22 (d, J = 2 Hz, 1H, CH); ^{13}C NMR (125 MHz, DMSO-d_6): δ 169.8 , 140.2 , 134.8 , 133.8, 132.4, 129.8, 129.4 , 129.1, 128.2, 127.7 , 125.4, 69.7 . Calcd.($C_{16}H_{13}ClN_2S$): C, 63.89; H, 4.36; N, 11.97; S, 10.66 Found: C, 63.90; H, 4.35; N, 11.98; S, 10.67

4-(p-Nitrophenyl)-6-Phenyl-4H-1,3-thiazin-2-amine (4m)
Pal brown crystals (0.20 g, 66%), mp. = 160-162 °C. ^{1}H NMR (500 MHz, DMSO-d_6): δ 9.84 (s, 2H, NH_2), 8.32 (m, 2H, H_{Ar}), 7.82 (m, 2H, H_{Ar}), 7.45 (m, 5H, H_{Ar}), 6.72 (d, J = 2 Hz, 1H, CH), 6.26 (d, J = 2 Hz, 1H, CH); ^{13}C NMR (125 MHz, DMSO-d_6): δ 170.1, 140.1, 134.9, 134.2 , 132.2 , 129.9 , 129.6, 129.4, 127.9 , 127.4 , 125.3 , 69.5 . Calcd.($C_{16}H_{13}N_3O_2S$): C, 61.72; H, 4.21; N, 13.50; O, 10.28; S, 10.30 Found: C, 61.73; H, 4.22; N, 13.51; O, 10.27; S, 10.32

4-(p-Fluorophenyl)-6-Phenyl-4H-1,3-thiazin-2-amine (4n)
Pal yellow crystals (0.18 g, 64 %), mp. = 188-190 °C. ^{1}H NMR (500 MHz, DMSO-d_6): δ 9.81 (s, 2H, NH_2), 7.56 (m, 2H, H_{Ar}), 7.46 (m, 2H, H_{Ar}), 7.26 (m, 5H, H_{Ar}), 6.74 (d, J = 2 Hz, 1H, CH), 6.24 (d, J = 2 Hz, 1H, CH); ^{13}C NMR (125 MHz, DMSO-d_6): δ 169.8 , 138.1, 135.0, 133.9 , 131.9 , 130.2 , 129.4 , 129.2 , 127.6 , 127.2 , 125.4 , 69.6 . Calcd.($C_{16}H_{13}FN_2S$): C, 67.58; H, 4.61; N, 9.85; S, 11.28 Found): C, 67.59; H, 4.62; N, 9.86; S, 11.29

Antimicrobial activity
The synthesized compounds (4a-4n) were screened for their in vitro antimicrobial activity by using cup plate method [11-15]. Antibacterial activity was screened against two gram positive bacteria *Micrococcus roseus*, *Bacillus subtilis* and two gram negative bacteria, *Escherichia coli*, *Pseudomonas aeruginosa* by measuring the zone of inhibition on agar plates at concentrations 100µg/mL. Antifungal activity was screened against and *Penicillium italicum* by measuring the zone of inhibition on agar plates at concentrations 100µ g/mL and reported in Table 3. Nutrient agar was employed as culture medium and DMSO was used as solvent control for antimicrobial activity. Streptomycin and fluconazole were used as standard for antibacterial and antifungal activities respectively.

RESULT AND DISCUSSION

The use of urea as a catalyst has been reported only in the synthesis of the 4-aryl-3,4-dihydropyrimidin-2(1H)-one (DHP).[10] This approach demonstrated contrary to the commonly accepted mechanism, that an additional urea molecule is directly involved in the reaction and catalyzes the reaction. In general, all the methods of the synthesis of these compounds require elevated temperature non recyclable catalyst and a multi-step. Therefore, development of simple, robust and safer methodologies for the synthesis of these heterocyclic compounds is necessary for obtaining these products under conditions tolerated by sensitive functional groups from both synthetic and environmental points of view. As part of an ongoing program of research, we had to develop a rapid and efficient one-pot synthesis of aldehydes **1**, bromovinyl **2** and urea or thiourea **3** and affording a series of 1,3-oxazines and 1,3-thiazines (Figure 1).

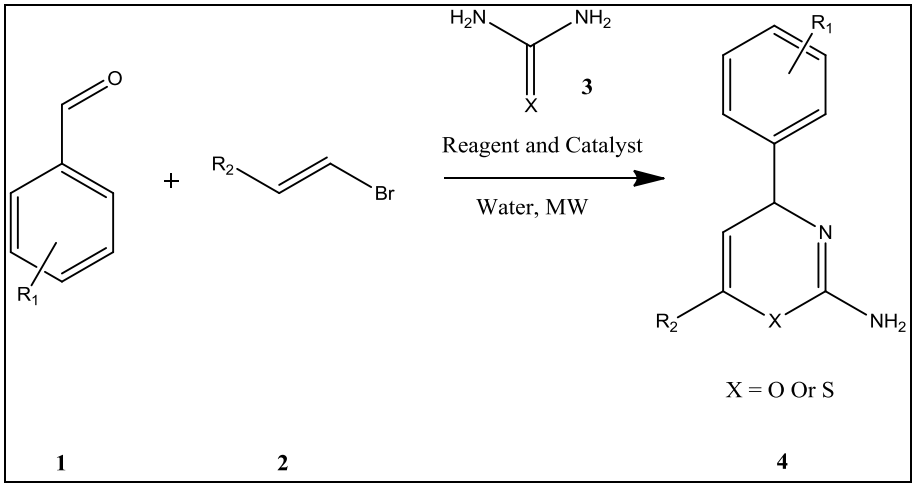

Figure 1: Synthesis of 2-amino-1,3-oxazines or 2-amino-1,3-thiazines from 2-bromovinyl

The first part of the study was aimed to optimize the reaction conditions. To do this, in the first instance, we explain the effect of various ratios of urea and temperature on the reaction as well as the product yield. In this regard, as depicted from Table 1, reactions were carried out using different ratios of urea at room and at higher temperatures. We observed that reaction of an equimolar quantity of aldehyde with bromovinyl and 3 equivalent of urea with the use of water as a solvent medium at 120 °C improved yields as well decreased in total reaction time to afford required 1,3-oxazine in sequential one-pot reaction (Table 1).

Table1: Optimization of reaction conditions.[a]

Entry	Urea ratio (eq.)	Temperature (°C)	Times (h)	Yield[b](%)
1	1	RT	4	NR
2	1	120	0.5	25
3	2	120	0.5	48
4	3	60	2	68
5	3	120	0.5	89
6	4	120	0.5	89

[a] Reaction conditions: aldehyde (1 mmol), (2-bromovinyl)benzene (1 mmol) and solvent water (5mL); [b] Isolated yields. RT: room temperature. NR: No reaction.

As the matter of fact, we observed that rise in temperature directs the reaction to the achievement in shorter periods of time. Whereas, under the similar set of conditions, the addition of 3 eq. of urea leads to 89% higher product yield in 30 min. Unfortunately, further inflating concentration to 4 eq. of urea led to the downfall in reaction yield. Through these experiments, a temperature of 120 ºC along with 3 eq. of urea or thiourea were the optimal conditions to complete the reaction in an efficient way. Based on the optimal conditions and the above reaction results, a scope of the reaction was then investigated with various aldehydes 1, bromovinyls 2 and urea or thiourea 3 under the established protocol. All reactions proceeded smoothly to give the corresponding 2-amino-4H- 1,3-oxazines or 1,3-thiazines (4a-n) in moderate to good yields (Table 2). All the products were characterized by ^{1}H NMR, ^{13}C NMR and compared the available data.[9d]

Table 2: Synthesis of 2-amino-1,3-oxazines or 2-amino-1,3-thiazines from 2-bromovinyl.[a]

Entry	R_1	R_2	X	Yield(%)
1	H	C	O	89
2	p-CH_3	C_6H_5	O	84
3	o-CH_3O	C_6H_5	O	72
4	m-NO_2	C_6H_5	O	85
5	p-F	C_6H_5	O	86
6	H	p-$CH_3C_6H_5$	O	86
7	p-CH_3	p-$CH_3C_6H_5$	O	82
8	p-Cl	p-$CH_3C_6H_5$	O	92
9	m-NO_2	p-$CH_3C_6H_5$	O	88
10	H	C_6H_5	S	76
11	p-CH_3	C_6H_5	S	72
12	p-Cl	C_6H_5	S	77
13	p-NO_2	C_6H_5	S	66
14	p-F	C_6H_5	S	64

[a] Reaction conditions: aldehyde (1 mmol), (2-bromovinyl)benzene (1 mmol) urea or thiourea (3 eq.) and solvent water (5mL); [b] Isolated yields

The presence of electron-with- drawing groups and electron-releasing groups on the aromatic rings of aromatic aldehydes or 2-bromovinyls, did not exhibit significant effects on yields and all products are obtained with excellent to moderate yields.

Antimicrobial screening

The Antibacterial and Antifungal activities of the compounds have also been evaluated. The antibacterial activity was compared with the known antibiotic streptomycin . The Compounds 3, 5, 8, 12, 14 exhibited good activity against bacteria Micrococcus roseus, Bacillus subtilis , Escherichia coli and Pseudomonas aeruginosa. Compound 1 is almost inactive against all the four organisms. The remaining compounds show moderated to poor activity against the tested bacteria strains. The antifungal activity was compared with the known antibiotic fluconazole the compound 14e showed excellent activity against Aspergillus niger and Penicillium italicum. Also compounds 5, 8, 12,14 showed good activity against Aspergillus flavus and moderated activities of Penicillium italicum. Compounds 1,6,9,10 are almost inactive against Aspergillus flavus and Penicillium italicum. While the remaining compounds were found to be weekly activity against the tested fungus.

Table 3: Antimicrobial activity of synthesized compounds

Comp. (100µg/ml)	Antimicrobial				Antifungal	
	Gram-negative bacteria		Gram-positive bacteria			
	E. coli	*P. Aeruginosa*	*Micrococcus roseus*	*B. subtilis*	*Aspergillus flavus*	*Penicillium Italicum*
1	N	N	N	N	N	N
2	+	+	+	+	+	+
3	++	++	+++	+++	+	++
4	N	N	N	N	+	+
5	++	++	+++	+++	+++	++
6	++	+	+	+	N	N
7	++	++	++	+	+	+
8	++	++	+++	+++	+++	++
9	N	N	+	+	N	N
10	+	+	+	+	N	N
11	++	++	+	+	+++	++
12	++	++	++	++	+++	++
13	N	N	N	N	+	++
14	++	++	+++	+++	+++	++
Standard	++++	++++	++++	++++	++++	++++

N = No effect; + : Less active (0.1-0.5 Cm) ; ++ : Moderately active (0.6-l.4 Cm); +++ : Highly active (1.5-3.0 Cm); ++++ : Very Highly active (over 3.0 Cm)

CONCLUSION

In summary, an efficient method for the one-pot multicomponent synthesis of 2-amino-4H-1,3-oxazines and 2-amino-4H-1,3-thiazines has been demonstrated using arylaldehydes, 2-bromovinyls and urea or thiourea in water under micro-wave irradiation condition. The method utilizes the very mild, efficient, friendly conditions and urea or thiourea as an effective catalyst system. Compared to the other known methods available in the literature, this method being gentle also grants the opportunity for the synthesis of a wide range of 2-amino-4H-1,3-oxazine and 2-amino-4H- 1,3-thiazine derivatives. The synthesized compounds were evaluated for their antibacterial and antifungal activities in vitro against four bacteria and two fungi.

ACKNOWLEDGEMENTS

The authors express their gratitude to Aljouf university - KSA for the research funds and its support of this work (project number 35/339) .

REFERENCES

[1] (a) TY Ilyuchenok; LM Frigidova; KS Shadursky; VP Lepekhin; LA Ignatova; BV Unkovsky. *Farmakol. Toksikol.* **1979**, 42, 643. (b) Z Eckstein; T Urbanski. *AdV.Heterocycl. Chem.* **1963**, 2, 311. (c) Z Eckstein; T Urbanski. *AdV.Heterocycl. Chem***. 1978**, 23, 1. (d) SM Sondhi; N Singhal; RP Verma; SK Arora; R Shukla; R Raghubir. *Monatsh. Chem.* **2000**, 131, 501.

[2] IT Gridunov; BV Unkovskii; MM Donskaya; LV Andreev; GS Korol'kova; LA Ignatova; AG Grigoryan. *U.S. Patent* 3 681 278, **1972**.

[3] (a) M Akhter; A Husain; N Akhter; MSY Khan, *Indian J Pharm Sci*, **2011**, 73, 101. (b) A Nagaraj; RC Sanjeeva. *J Iran Chem Soc* **2008**, 5, 262.

[4] (a) R Sawant; L Bhangale; J Wadekar; P Gaikwad. *Farmacia*. **2012**, 60, 32. (b) JE Mohamed; AA Hussniyia. *Sci Revs Chem Commun.* **2012**, 2, 103.
[5] (a) C Singh; HK Parwana; G Singh, *Indian J Pharm Sci*,**1995**, 57, 198.
(b) D Bonzsing; P Sohar; G Giggler; G Kovacs. E*ur J Med Chem*, **1996**, 31, 663.
[6] (a) A Moran, E Martín, C Velasco; ML Martín, RL San; E Caballero; P Puebla; M Medarde; FA San; *J Pharm Pharmacol*, **1997**, 49, 421. (b) AW Faull. Patent Application W 29 104. InChem. Abstr **1997**, 127, 234328.
[7] (a) KP Beena; T Akelesh. *Der Pharmacia Lettre*, **2013**, 5, 257. (b) VS Patel; AR Parikh. *J. Indian Chem. Soc*., **1978**, 50, 241.
[8] (a) RR Schmidt. *Synthesis* **1972**, 333. (b) JC.Jochims, R Abu-El-Halawa, MO Glocker; L Zsolnai; G.Huttner. *Synthesis* **1990**, 763. (c) C Vanier; A Wagner; C Mioskowski. *J Comb Chem* **2004**, 6, 846.
[9] (a) S Putatunda; A Chakraborty. *Chem. Heterocycl Compd*, **2015**, 51, 763. (b) SS Didwagh; PB Piste. *Int J Pharm Sci Res* **2013**, 4, 2045. (c) PK Mandal; AK Misra. *Lett Org Chem*, **2006**, 3, 848. (d) S Huang; Y Pan; Y Zhu; A Wu. *Org Lett* **2005**, 7, 17. (e) GA Mironova; VN Kuklin; EN Kirillova; BA Ivin, *Chem. Heterocycl. Compd*. **1986**, 22, 1.
[10] M Puripat; R Ramozzi; M Hatanaka; W Parasuk; V Parasuk; KJ Morokuma. *Org Chem.* **2015**, 80, 6959.
[11] M Shiradkar; RKale; B Baviskar; R Dighe. *Asian J Chem***. 2007**, 19, 449.
[12] HA Soleiman; AK Khalafallah; HMA Abdelzaher. *J Chinese Chem Soc* **2000**, 47, 1267.
[13] AL Banty. The Antimicrobial Susceptibility Test; Principle and Practice, edited by Illus Lea and Febiger, Philadelphia, USA, **1976**, 180.
[14] AA Aly; EA Ishak; T El Malah; AB Brown; WM Elayat. J *Heterocyclic Chem.*, **2015**, 52, 1758.
[15] AM Hussein; EA Ishak; FA; Abu-Shanab. *Open Access Library J*, **2015**.