Med Chem Res (2012) 21:844–852
DOI 10.1007/s00044-011-9592-6

MEDICINAL CHEMISTRY RESEARCH

ORIGINAL RESEARCH

Comparative study of conventional and microwave-assisted synthesis of some Schiff bases and their potential as antimicrobial agents

Vikas Pandey · Viney Chawla · Shailendra K. Saraf

Received: 29 July 2010 / Accepted: 1 February 2011 / Published online: 17 February 2011

Abstract A series of Schiff bases (compounds **1**–**10**) were synthesized by condensing heterocyclic/aromatic aldehydes with heterocyclic/aromatic amines through both, conventional method and microwave-assisted synthesis. The compounds were confirmed by means of IR spectroscopy, Mass spectrometry, ^{1}H NMR and elemental analyses. The compounds were assayed for antibacterial activity against selected strains of Gram positive, Gram negative bacteria and some fungi by zone inhibition method. Minimum inhibitory concentration (MIC) was also determined for each compound. Reaction times were drastically reduced by microwave-assisted synthesis. MIC was as low as 50 μg/ml exhibited by compounds **2** (against *Escherichia coli*, *Aspergillus niger* and *Penicillium chrysogenum*) and **10** (against *Bacillus subtilis*). The study presents a series of potential antimicrobial agents through efficient and simple reactions and mild reaction conditions, thereby offering a green chemistry approach.

Keywords Schiff base · Antibacterial · Antifungal · Microwave-assisted synthesis · Green chemistry

Introduction

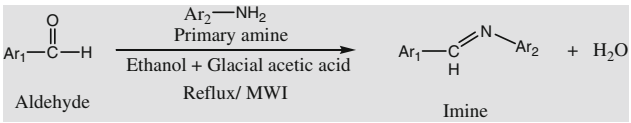
Compounds with the structure of $Ar_1C{=}NAr_2$ are known as Schiff bases, which are usually synthesized from the condensation of primary amines and active carbonyl groups. Many Schiff bases have been reported to possess antibacterial (Sridhar *et al*., 2001; Mladenova *et al*., 2002; Pannerselvam *et al*., 2005; Walsh *et al*., 1996; Bharti *et al*., 2010; Tenorio *et al*., 2005), antifungal (Walsh *et al*., 1996; Bharti *et al*., 2010; Tenorio *et al*., 2005) and antitumor activities (Liu *et al*., 1992; Hodnett and Dunn, 1970). Researchers have consistently studied the synthesis, characterization and structure–activity relationship of Schiff bases (Curini *et al*., 2002; Yadav *et al*., 2004; Byrnes *et al*., 1990; Kamel *et al*., 2010). It is well known that microwave (MW) irradiation can accelerate a great number of chemical processes and, in particular, the reaction time and energy input are supposed to be mostly reduced in the reactions that are run for a long time at high temperatures under conventional conditions (Loupy, 2002). The most successful applications of microwave irradiation are found to be related to the use of solvents and solvent-free systems, in which microwaves interact directly with reagents. Therefore, it can more efficiently accelerate chemical reactions (Burczyk *et al*., 2005). In classical organic synthesis of Schiff bases, the common problems are removal of solvents from the reaction mixture, liquid extraction especially in the case of aprotic dipolar solvents with high boiling point and product isolation through liquid–liquid extraction. The absence of solvent reduces the risk of hazardous explosions when the reaction takes place in a closed vessel or a microwave oven (Yang *et al*., 2002). Local overheating, which can lead to product, substrate and reagent degradation is avoided in microwave-assisted synthesis (Lidstorm *et al*., 2001). The solvent-free organic synthesis mediated by microwave irradiation offers several advantages such as higher atom economy, environmental friendship and reduced hazard potential. This approach has been used in past for synthesis of imines and enamines (Varma *et al*., 1997) and sulfonylimines (Vass *et al*., 1999). Thus, it was decided to utilize microwave irradiation for the synthesis of Schiff bases in

V. Pandey · V. Chawla · S. K. Saraf (✉)
Faculty of Pharmacy, Northern India Engineering College, Dr. Akhilesh Das Nagar, Sector-2, Faizabad Road, Lucknow 227105, U.P., India
e-mail: dirpharmniec@gmail.com

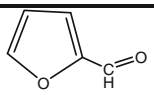
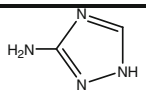
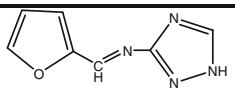
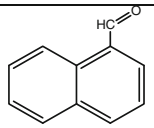
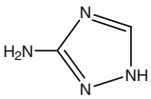
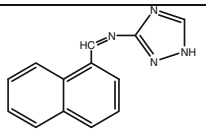
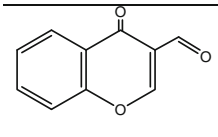
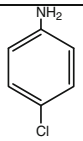
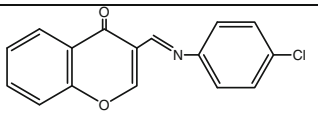
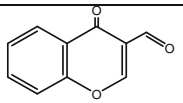
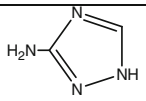
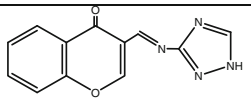
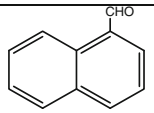
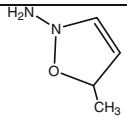
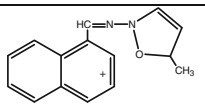
order to check whether such non-classical method of chemical activation might influence yield, selectivity and time of reaction in comparison to a conventional thermal treatment under strictly similar sets of conditions. This study reports the synthesis of some Schiff bases with heterocyclic/aromatic rings and their antimicrobial properties.

Chemistry

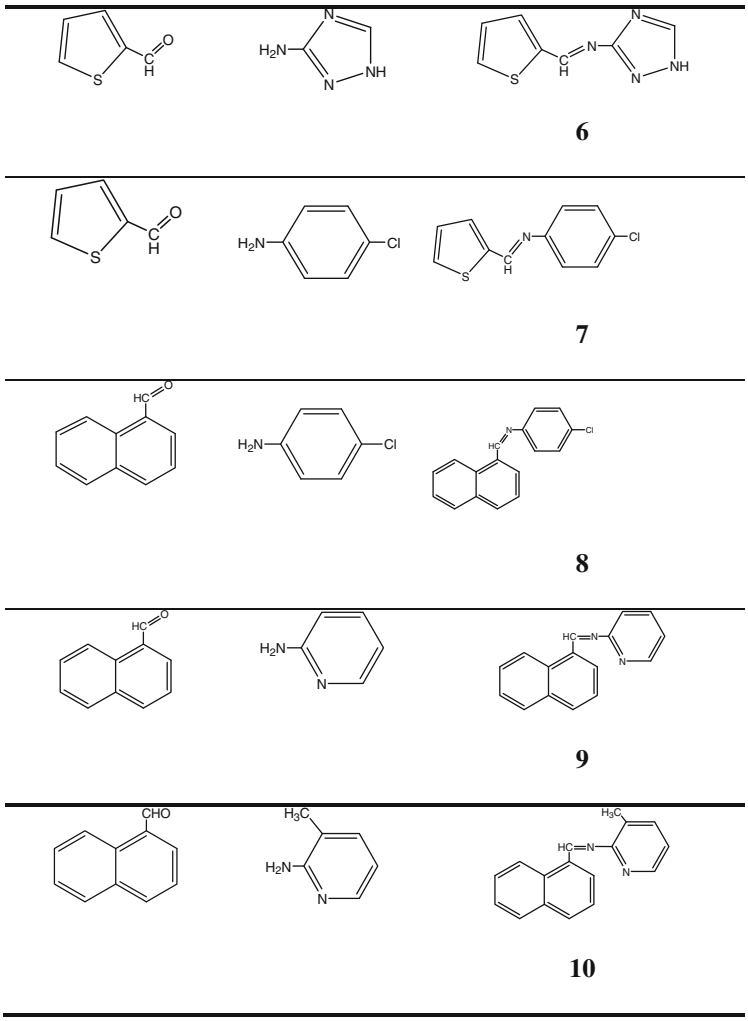
Schiff base formation is another variation on the theme of nucleophilic addition to the carbonyl group. In this case, the nucleophile is an amine. In the first part of the mechanism, the amine reacts with the aldehyde or ketone to give an unstable addition compound called carbinolamine. The carbinolamine loses water by acid or base catalyzed pathways. Since the carbinolamine is an alcohol, it undergoes acid catalyzed dehydration (Clayden *et al.*, 2001). In this study, a series of Schiff bases (compounds **1–10**) were synthesized by condensing heterocyclic/aromatic aldehyde with heterocyclic/aromatic amine in presence of glacial acetic acid, both by conventional method and microwave method (Scheme 1).



Scheme 1 Synthetic route to title compounds. *MWI* microwave irradiation, Ar_1 different heterocyclic/aromatic ring, Ar_2 different heterocyclic/aromatic ring

Aldehyde	Primary amine	Schiff base
		 **1**
		 **2**
		 **3**
		 **4**
		 **5**

Scheme 1 continued



Antimicrobial investigation

Antimicrobial studies of the compounds were performed by cup-plate method as well as by tube assay method against bacterial strains *Staphylococcus aureus* (MTCC no. 1430), *Bacillus subtilis* (MTCC no. 441), *Bacillus pumilus* (MTCC no. 1456), *Micrococcus luteus* (MTCC no. 1538), *Pseudomonas aeruginosa* (MTCC no. 424), *Pseudomonas fluorescens* (MTCC no. 2421), *Escherichia coli* (MTCC no. 1573) and fungal strains *Aspergillus niger* (MTCC no. 2546), *Penicillium chrysogenum* (MTCC no. 161).

Results and discussion

Different Schiff bases have been successfully synthesized both by conventional and microwave method. Microwave method offered a less time consuming approach with milder reaction conditions, increased yield and drastically reduced reaction times (Table 1). The ways in which different Schiff base compounds react with bacteria and fungi vary due to the difference in their structures. Structural analysis of these compounds may provide some explanation for the structure–activity relationships. Such an analysis might be helpful in the design of better inhibitors. The biological activity of a particular substance depends on a complex sum of individual properties including compound structure, affinity for the target site and survival in the medium of application, survival within the biological system, transport properties and state of the target organism (Kosower and Miyadera, 1972). In this study, the focus was on the structure–activity relationship.

Amongst all tested compounds, compound **10** was found to be most active against gram positive bacteria whereas compounds **1**–**7** exhibited moderate to good activity. In case of gram negative bacteria, compound **2** was highly active whereas compounds **1**, **3**–**7** and **10** exhibited moderate to good activity. Compound **2** was found to be most active against all fungal strains whereas compounds **1**, **3**–**7** and **10** exhibited moderate to good activity. Minimum inhibitory

Table 1 Comparative reaction time and yield of conventional and microwave-assisted synthesis

Comp. no.	Molecular formula	Reaction time		Yield (%)	
		CM	MAS	CM	MAS
1	$C_7H_6N_4O$	20–21 h	4 min	35	79
2	$C_{13}H_{10}N_4$	10–11 h	3 min	32	80
3	$C_{16}H_{10}ClNO_2$	16–17 h	5 min	48	78
4	$C_{12}H_8N_4O_2$	13–14 h	5 min	43	81
5	$C_{15}H_{12}N_2O$	20–21 h	6 min	29	73
6	$C_7H_6N_4S$	10–11 h	5 min	52	80
7	$C_{11}H_8ClNS$	9–10 h	5 min	57	80
8	$C_{17}H_{12}ClN$	6–7 h	5 min	23	69
9	$C_{16}H_{12}N_2$	12–13 h	4 min	40	70
10	$C_{17}H_{14}N_2$	7–8 h	3 min	34	84

Comp. compound, *CM* conventional method, *MAS* microwave assisted synthesis

concentration was as low as 50 μg/ml exhibited by compounds **2** (against *Escherichia coli*, *Aspergillus niger*, *Penicillium chrysogenum*) and **10** (against *Bacillus subtilis*).

The antimicrobial activity of the compounds was found to vary with structure. The order of activity indicated that the activity of compounds against microbial strains was mainly due to the naphthalen-1-yl group. The results also implied that heterocyclic structures were helpful in the activity of compounds. Compounds containing chromen-4-one, furan-2-yl and thiophene-2-yl groups were responsible for moderate to good antimicrobial activity. Compounds **2** and **10** were found to be most active. This observation indicated that heterocyclic ring containing N atom and methyl group played an important role in antimicrobial activity of compounds. Pyridine-2-yl ring with methyl group at 3-C position in Schiff base was found to be most active against gram positive bacteria whereas 5-membered heterocyclic aromatic ring containing nitrogen at 1, 2 and 4 position was active against fungal strains. Aromatic ring containing chlorine atom at *para* position with heterocyclic structure like chromen-4-one, furan-2-yl and thiophene-2-yl showed moderate to good antibacterial and antifungal activity. Also, the activity of the compounds was found to be concentration dependent.

Conclusion

A series of Schiff bases have been prepared both by conventional method and microwave-assisted synthesis. All compounds exhibited good antimicrobial activity with two compounds **2** and **10** showing excellent potential. There was a marked decrease in the reaction time, under mild conditions through microwave synthesis wherein it presented a green approach towards syntheses of the Schiff bases.

Experimental protocols

Chemistry

Commercially available reagent grade chemicals were used as received. The synthesized compounds were subjected to physicochemical and spectral characterization. All reactions were monitored on thin layer chromatography using precoated aluminium silica G plates (20 × 20 cm) using ethyl acetate and n-hexane (60:40). The spots were developed in both UV chamber (long and short wavelength) and iodine chamber. Melting range was determined by Open Capillary Method and is uncorrected. IR, Mass and NMR spectra confirmed all the compounds. IR spectra were recorded as thin films (KBr) on Shimadzu 8400S and Perkin Elmer Spectrum RX1 FTIR spectrophotometers. Characteristic peaks observed were of N–H str, C=N str, C–N str etc. Mass spectra were recorded on JEOL-AccuTOF JMS-T100LC spectrometer and NMR spectra were recorded on Bruker DRX-300 spectrometer and Elemental analysis was performed on Elemental Vario EL III analyzer.

General method of synthesis of compounds **1**–**10**

Equimolar quantities of aldehyde and primary amine were dissolved in 20 ml of methanol, in the presence of few drops of glacial acetic acid, and reaction mixture was subjected to reflux for variable times between 7 and 21 h (in microwave-assisted synthesis the reaction mixture was subjected to microwave irradiation at 160 W intermittently at 30 s intervals for 3–6 min). The progress of reaction was monitored by TLC. The reaction mixture was then allowed to stand overnight and excess of solvent was removed under reduced pressure. The residue left behind was purified by recrystallization from methanol to obtain compounds **1**–**10**. The quantities of reactants used in synthesis are summarized in Table 2.

*Furan-2-ylmethylene-(1H-[1,2,4]triazol-3-yl)-amine (**1**)*

Brown powder, yield 35% (CM); 79% (MAS), melting range (in °C): 178–182, R_f 0.62 (ethylacetate: n-hexane 60:40), IR (KBr, cm^{-1}): 720 (aromatic C–H_{bend}); 1427 (aromatic C=C_{str}); 1643 (imine HC=N); 3415 (amine N–H); 1047 (5-membered C–O_{str}); 1217 (asymmetric C–O_{str}), Mass (m/z): 163 $[M + H]^+$, ^{1}H NMR (δ ppm): 6.959–7.547 (m, 3H, furan); 7.264 (s, 1H, CH); 7.224 (s, 1H, CH 1,2,4-triazole); 12.305 (d, 1H, NH). Anal. Calcd. for $C_7H_6N_4O$:

Table 2 Quantity of reactants used in synthesis

Compound no.	Quantity of reactants	
	Aldehyde	Amine
1	0.03 mol furan-2-carbaldehyde (2.5 ml)	0.03 mol 3-amino-1,2,4-triazole (2.5 g)
2	0.024 mol naphthalene-1-carbaldehyde (3.26 g)	0.024 mol 3-amino-1,2,4-triazole (2.0 g)
3	0.006 mol 3-formylchromone (1.0 g)	0.006 mol *p*-chloroaniline (0.762 g)
4	0.006 mol each of 3-formylchromone (1.0 g)	0.006 mol 3-amino-1,2,4-triazole (0.5 g)
5	0.012 mol naphthalene-1-carbaldehyde (1.8 ml)	0.012 mol 2-amino-5-methylisoxazole (1.2 g)
6	0.012 mol thiophene-2-carbaldehyde (1.1 ml)	0.012 mol 3-amino-1,2,4-triazole (1 g)
7	0.012 mol thiophene-2-carbaldehyde (1.1 ml)	0.012 mol *p*-chloroaniline (1.5 g)
8	0.024 mol naphthalene-1-carbaldehyde (3.2 ml)	0.024 mol *p*-chloroaniline (3.0 g)
9	0.03 mol naphthalene-1-carbaldehyde (4.0 ml)	3-aminopyridine (2.82 g)
10	0.012 mol naphthalene-1-carbaldehyde (1.8 ml)	0.012 mol 2-amino-3-methylpyridine (1.2 ml)

C, 51.85; H, 3.73; N, 34.55. Found: C, 50.88; H, 3.94; N, 33.84.

*Naphthalen-1-ylmethylene-(1H-[1,2,4]triazol-3-yl)-amine (**2**)*

Cream powder, yield: 32% (CM), 80% (MAS), melting range (in °C): 160–165, R_f: 0.76 (ethylacetate: n-hexane 60:40), IR (KBr, cm^{-1}): 763 (aromatic C–H_{bend}), 1479 (aromatic C=C_{str}), 1608 (imine HC=N), 3415 (amine N–H), Mass (m/z): 223 $[M + H]^+$, ^1H NMR (δ ppm): 7.591–7.927 (m, 7H, aromatic); 7.954 (s, 1H, CH); 7.264 (s, 1H, CH 1,2,4-triazole); 10.410 (d, 1H, NH). Anal. Calcd. for $C_{13}H_{10}N_4$: C, 70.26; H, 4.54; N, 25.21. Found: C, 64.53; H, 4.44; N, 26.87.

*3-[(4-chloro-phenylimino)-methyl]-chromen-4-one (**3**)*

Yellow amorphous, yield: 48% (CM), 78% (MAS), melting range (in °C): 120–124, R_f: 0.81 (ethylacetate: n-hexane 60:40), IR (KBr, cm^{-1}): 670 (aromatic C–H_{bend}), 1470 (aromatic C=C_{str}), 1650 (imine HC=N), 1013 (C–Cl_{str}), 1067 (5-membered C–O_{str}), 1216 (asymmetric C–O_{str}), Mass (m/z): 284$[M + H]^+$, ^1H NMR (δ ppm): 7.077–7.466 (m, 8H, aromatic); 5.788 (d, 1H, pyran); 7.349 (s, 1H, CH); 10.410 (d, 1H, NH). Anal. Calcd. for $C_{16}H_{10}ClNO_2$: C, 64.74; H, 5.55; N, 4.94. Found: C, 64.68; H, 5.14; N, 4.10.

*3-[(1H-[1,2,4]triazol-3-ylimino)-methyl]-chromen-4-one (**4**)*

Yellow powder, yield: 43% (CM), 81% (MAS), melting range (in °C): 105–110, R_f: 0.61 (ethylacetate: n-hexane 60:40), IR (KBr, cm^{-1}): 754 (aromatic C–H_{bend}), 1483 (aromatic C=C_{str}), 1610 (imine HC=N), 3442 (amine N–H), 1110 (5-membered C–O_{str}), 1283 (asymmetric C–O_{str}), Mass (m/z): 241 $[M + H]^+$, ^1H NMR (δ ppm): 7.157–7.541 (m, 4H, aromatic); 6.993 (d, 1H, pyran); 7.520 (s, 1H, CH); 7.265 (s, 1H, CH 1,2,4-triazole); 11.447 (d, 1H, NH). Anal. Calcd. for $C_{12}H_8N_4O_2$: C, 60.00; H, 3.30; N, 16.32. Found: C, 60.99; H, 3.30; N, 17.75.

*(5-methyl-5H-isoxazol-2-yl)-naphthalen-1-ylmethylene-amine (**5**)*

White powder, yield: 29% (CM), 73% (MAS), melting range (in °C): 59–63, R_f: 0.80 (ethylacetate: n-hexane 60:40), IR (KBr, cm^{-1}): 763(aromatic C–H_{bend}), 1431 (aromatic C=C_{str}), 1516 (imine HC=N), 1088 (5-membered C–O_{str}), Mass (m/z): 237 $[M + H]^+$, ^1H NMR (δ ppm): 7.564–7.637 (m, 7H, aromatic); 7.265 (s, 1H, CH); 6.157–6.189 (m, 2H, isoxazole); 2.391 (d, 3H, CH_3). Anal. Calcd. for $C_{15}H_{12}N_2O$: C, 64.25; H, 5.12; N, 11.86. Found: C, 67.00; H, 6.11; N, 16.23.

*Thiophen-2-ylmethylene-(1H-[1,2,4]triazol-3-yl)-amine (**6**)*

Dark brown powder, yield: 52% (CM), 80% (MAS), melting range (in °C): 100–105, R_f: 0.66 (ethylacetate: n-hexane 60:40), IR (KBr, cm^{-1}): 709 (aromatic C–H_{bend}), 1407 (aromatic C=C_{str}), 1604 (imine HC=N), 3122 (amine N–H), Mass (m/z): 179 $[M + H]^+$, ^1H NMR (δ ppm): 7.076–7.215 (m, 3H, thiophene); 7.265 (s, 1H, CH 1,2,4-triazole); 9.412 (d, 1H, NH). Anal. Calcd. for $C_7H_6N_4S$: C, 43.09; H, 3.39; N, 34.44. Found: C, 42.89; H, 3.61; N, 35.23.

*(4-chloro-phenyl)-thiophen-2-ylmethylene-amine (**7**)*

Dark brown flakes, yield: 57% (CM), 80% (MAS), melting range (in °C): 56–60, R_f: 0.50 (ethylacetate: n-hexane 60:40), IR (KBr, cm^{-1}): 713 (aromatic C–H_{bend}), 1481

(aromatic C=C_{str}), 1614 (imine HC=N), 1008 (C–Cl_{str}), Mass (m/z): 222 $[M + H]^+$, ^1H NMR (δ ppm): 6.775–6.833 (m, 3H, thiophene); 7.139 (s, 1H, CH); 7.166–7.355 (m, 4H, aromatic). Anal. Calcd. for $C_{11}H_8ClNS$: C, 59.37; H, 3.64; N, 6.32. Found: C, 59.37; H, 3.69; N, 6.20.

*(4-chloro-phenyl)-naphthalen-1-ylmethylene-amine (**8**)*

Yellow powder, yield: 23% (CM), 69% (MAS), melting range (in °C): 62–65, R_f: 0.78 (ethylacetate: n-hexane 60:40), IR (KBr, cm^{-1}): 775 (aromatic C–H_{bend}), 1483 (aromatic C=C_{str}), 1608 (imine HC=N), 1083 (C–Cl_{str}), Mass (m/z): 266 $[M + H]^+$, ^1H NMR (δ ppm): 1H NMR (δ ppm) 6.976–8.095 (m, 11H, aromatic); 7.411 (s, 1H, CH). Anal. Calcd. for $C_{17}H_{12}ClN$: C, 76.84; H, 4.55; N, 5.27. Found: C, 76.17; H, 5.31; N, 5.16.

*Naphthalen-1-ylmethylene-pyridin-2-yl-amine (**9**)*

Brown powder, yield: 40% (CM), 70% (MAS), melting range (in °C): 89–92, R_f: 0.72 (ethylacetate: n-hexane 60:40), IR (KBr, cm^{-1}): 771 (aromatic C–H_{bend}), 1431 (aromatic C=C_{str}), 1689 (imine HC=N), Mass (m/z): 233 $[M + H]^+$, ^1H NMR (δ ppm): 1H NMR (δ ppm) 6.640–7.905 (m, 11H, aromatic); 7.925 (s, 1H, CH). Anal. Calcd. for $C_{16}H_{12}N_2$: C, 77.86; H, 5.21; N, 12.06. Found: C, 77.78; H, 5.99; N, 12.16.

*(3-methyl-pyridin-2-yl)-naphthalen-1-ylmethylene-amine (**10**)*

Brown sticky solid, yield: 34% (CM), 84% (MAS), melting range (in °C): 136–140, R_f: 0.70 (ethylacetate: n-hexane 60:40), IR (KBr, cm^{-1}): 764 (aromatic C–H_{bend}), 1454 (aromatic C=C_{str}), 1689 (imine HC=N), Mass (m/z): 247 $[M + H]^+$, ^1H NMR (δ ppm): 7.569–8.075 (m, 10H, aromatic); 7.429 (s, 1H, CH); 2.482 (d, 3H, CH_3). Anal. Calcd. for $C_{17}H_{14}N_2$: C, 75.00; H, 5.73; N, 11.37. Found: C, 78.55; H, 5.70; N, 12.54.

Antimicrobial activity

Determination of zone of inhibition by cup plate method

A previously liquefied medium was inoculated with the requisite quantity of suspension of the microorganism. Then, the suspension was added to the medium at a temperature between 40 and 50°C and the inoculated medium was poured immediately into petri dishes with uniform thickness, by placing the dishes on a uniform level surface. The prepared dishes were stored in a manner so as to ensure that no significant growth or death of test organism occurred before the dishes were used and that surface of agar layer was dry at the time of use. The solution of antimicrobial agents 1–10 (with dilutions in the range 100 to 1500 μg/ml in DMSO) was poured into cavities (6 mm) prepared on the surface of the solid agar medium. Standard drugs used (Norfloxacin and Fluconazole) were taken in reported quantities, i.e. 100 μg/ml. A solution of DMSO (10%) was used as control. Same volume of the solution was added to each cavity. The quantities were carefully chosen to fill the holes. The plates were left for 1–4 h at room temperature, as a period of pre-incubation diffusion to minimize the effects of variation in the time between the applications of the different solutions. They were incubated for about 18 h at the temperature suitable for individual microorganism (Indian Pharmacopoeia, 1996). The diameters of the circular zones of inhibition were measured and are reported in the Table 3.

Table 3 Results of antimicrobial activity of the tested compounds

Compound no.	Conc. (μg/ml)	Diameter of zone of inhibition (mm)								
		Gram +ve bacteria				Gram −ve bacteria			Fungal strains	
		SA	*BS*	*BP*	*ML*	*PA*	*PF*	*EC*	*AN*	*PC*
1	100	–	11	11	12	10	13	10	11	11
	200	12	15	15	16	11	16	13	16	15
	500	14	16	16	18	13	18	14	18	17
	1000	15	17	17	21	15	20	15	19	18
	1500	18	22	20	22	21	23	25	23	21
2	100	12	15	13	12	17	14	17	16	17
	200	13	16	16	15	18	16	18	17	18
	500	14	18	17	18	20	19	19	18	20
	1000	16	19	18	20	22	21	23	21	21
	1500	18	21	20	23	24	23	25	22	24

Table 3 continued

Compound no.	Conc. (μg/ml)	Diameter of zone of inhibition (mm)								
		Gram +ve bacteria				Gram −ve bacteria			Fungal strains	
		SA	*BS*	*BP*	*ML*	*PA*	*PF*	*EC*	*AN*	*PC*
3	100	12	13	12	16	16	11	13	16	15
	200	14	15	15	19	18	12	16	18	17
	500	16	17	17	21	19	14	17	19	19
	1000	18	19	18	23	20	16	19	20	20
	1500	21	21	19	24	21	18	20	21	21
4	100	11	12	14	11	14	13	13	16	15
	200	13	16	16	15	15	15	14	18	17
	500	14	17	17	16	16	17	15	19	19
	1000	17	18	19	18	18	19	16	20	20
	1500	19	20	21	23	20	20	18	22	22
5	100	13	13	13	16	14	11	12	13	15
	200	14	16	15	18	16	13	13	18	16
	500	15	17	16	20	17	15	14	19	18
	1000	16	19	17	22	18	18	15	20	19
	1500	20	20	18	24	20	19	17	21	20
6	100	11	10	13	13	12	11	14	11	13
	200	13	11	15	16	13	13	16	13	15
	500	16	14	16	18	15	15	18	15	16
	1000	18	16	17	20	18	18	20	16	18
	1500	19	22	18	22	20	21	21	19	19
7	100	12	11	13	11	10	11	13	10	13
	200	13	12	15	15	13	13	15	11	14
	500	15	14	17	18	16	16	16	12	16
	1000	16	18	18	20	17	18	19	17	17
	1500	18	21	20	24	19	20	20	18	19
8	100	11	–	–	13	–	11	–	–	–
	200	13	–	–	16	–	12	–	–	–
	500	15	–	–	19	–	14	–	11	11
	1000	18	15	9	21	13	17	11	13	13
	1500	21	17	10	25	14	19	17	15	14
9	100	11	–	–	11	–	11	–	–	–
	200	12	–	–	12	–	13	–	–	–
	500	14	–	–	17	–	15	11	12	10
	1000	16	–	–	20	–	17	14	13	12
	1500	20	–	–	24	15	19	16	15	17
10	100	10	12	13	16	12	17	13	13	11
	200	13	13	16	18	13	20	14	16	13
	500	15	16	18	22	14	22	15	19	15
	1000	18	18	19	24	16	23	16	20	17
	1500	20	19	20	26	18	24	19	21	18
STD.	100	25	23	28	26	28	25	36	28	16
Control	DMSO	–	–	–	–	–	–	–	–	–

SA Staphylococcus aureus, *BS Bacillus subtilis*, *BP Bacillus pumilus*, *ML Micrococcus luteus*, *PA Pseudomonas aeruginos*, *PF Pseudomonas fluorescens*, *EC Escherichia coli*, *AN Aspergillus niger*, *PC Penicillium chrysogenum*, *STD*. standard (Norfloxacin for bacteria, Fluconazole for fungi)

Table 4 Minimum inhibitory concentration of synthesized compounds

Microbial strains	MIC of compounds in μg/ml									
	Comp. **1**	Comp. **2**	Comp. **3**	Comp. **4**	Comp. **5**	Comp. **6**	Comp. **7**	Comp. **8**	Comp. **9**	Comp. **10**
Staphylococcus aureus	600	400	300	400	400	300	300	400	400	400
Bacillus subtilis	300	300	300	400	300	300	400	500	500	50
Bacillus pumilus	300	300	200	400	300	200	200	500	500	200
Micrococcus luteus	300	300	200	300	200	200	400	300	400	200
Pseudomonas aeruginosa	500	200	200	300	300	200	300	500	500	300
Pseudomonas fluorescens	300	300	300	200	300	300	300	300	300	300
Escherichia coli	400	50	400	400	300	200	200	500	400	200
Aspergillus niger	500	50	200	200	300	300	400	500	500	200
Penicillium chrysogenum	500	50	200	200	200	400	300	500	500	400
Standard (Norfloxacin)	50	50	50	50	50	50	50	50	50	50

Comp. compound

Minimum inhibitory concentrations

Minimum inhibitory concentrations (MICs) are considered the 'gold standard' for determining the susceptibility of organisms to antimicrobials and are therefore used to judge the performance of all other methods of susceptibility testing (Andrews, 2001). For each test, five test tubes containing 4.5 ml of nutrient broth, previously mixed with bacterial/fungal inoculum, were taken. To each test tube, 0.5 ml of the synthesized compounds of different concentrations (50, 100, 200, 300, 400 and 500 μg/ml) were added. An inoculated broth containing no antibiotic was included as growth control and a tube of uninoculated broth was used as sterility control. These test tubes were then incubated for 24 h at suitable temperature. Then, optical density was recorded using Labotronics digital photo colorimeter at 530 nm. The point of sharp fall in the readings of optical density was considered as MIC. The observed MICs are presented in Table 4.

Acknowledgments The authors are thankful to the Central Drug Research Institute (CDRI), Lucknow for providing library facility and spectral data.

References

Andrews JM (2001) Determination of minimum inhibitory concentrations. J Antimicrob Chemother 48S:5–16

Bharti SK, Nath G, Tilak R, Singh SK (2010) Synthesis, anti-bacterial and anti-fungal activities of some novel Schiff bases containing 2,4-disubstituted thiazole ring. Eur J Med Chem 45:651–660

Biological assay, Indian Pharmacopoeia (1996), vol 2, Govt. of India, Delhi, pp A100-102

Burczyk A, Loupy A, Bogdal D, Petit A (2005) Improvement in the synthesis of metallophthalocyanines using microwave irradiation. Tetrahedron 61:179–188

Byrnes RW, Mohan M, Antholine WE, Xu RX, Petering DH (1990) Oxidative stress induced by a copper–thiosemicarbazone complex. Biochemistry 29:7046–7053

Clayden J, Greeves N, Warren S, Wothers P (2001) Organic chemistry, 1st edn. Oxford University Press Inc, New York, pp 1385–1387

Curini M, Epifano F, Maltese F, Marcotullio MC (2002) Novel chiral Schiff base ligands from amino acid amides and salicylaldehyde. Tetrahedron Lett 43:3821–3823

Hodnett EM, Dunn WJ (1970) Structure–antitumor activity correlation of some Schiff bases. J Med Chem 13:768–770

Kamel MM, Ali HI, Anwar MM, Mohamed NA, Soliman AMM (2010) Synthesis, antitumour activity and molecular docking study of novel sulphonamide-Schiff's bases, thiazolidinones, benzothiazones and their C-nucleoside derivatives. Eur J Med Chem 45:572–580

Kosower EM, Miyadera T (1972) Glutathione.6. Probable mechanism of action of diazene antibiotics. J Med Chem 15:307–312

Lidstorm P, Tierney J, Wathey B, Westman J (2001) Microwave assisted organic synthesis—a review. Tetrahedron 57:9225–9283

Liu MC, Lin TS, Sartorelli AC (1992) Synthesis and antitumor activity of amino derivatives of pyridine-2-carboxaldehyde thiosemicarbazone. J Med Chem 35:3672–3677

Loupy A (2002) Microwaves in organic synthesis. Wiley, Weinheim

Mladenova R, Ignatova M, Manolova N, Petrova T, Rashkov I (2002) Preparation, characterization and biological activity of Schiff base compounds derived from 8-hydoxy quinoline-2-carboxaldehyde and Jeffamines ED®. Eur Polym J 38:989–999

Pannerselvam P, Nair RR, Vijayalakshmi G, Subramanian EH, Sridhar SK (2005) Synthesis of Schiff bases of 4-(4-aminophenyl)-morpholine as potential antimicrobial agents. Eur J Med Chem 40:225–229

Sridhar SK, Saravanan M, Ramesh A (2001) Synthesis and antibacterial screening of hydrazones, Schiff and Mannich bases of hydrazone derivatives. Eur J Med Chem 36:615–625

Tenorio RP, Carvalho CS, Pessanha CS, Delima JG (2005) Synthesis of thiosemicarbazone and 4-thiazolidinone derivatives and their in vitro anti-Toxoplasma gondii activity. Bioorg Med Chem Lett 15:2575–2578

Varma RS, Dahiya R, Kumar S (1997) Clay catalyzed synthesis of imines and enamines under solvent-free conditions using microwave irradiation. Tetrahedron Lett 38:2039–2042

Vass A, Dudas J, Varma RS (1999) Solvent-free synthesis of *N*-sulfonylimines using microwave irradiation. Tetrahedron Lett 40:4951–4954

Walsh OM, Meegan MJ, Prendergast RM, Nakib TA (1996) Synthesis of 3-acetoxy-azetidin-2-ones and 3-hydoxy-azetidin-2-ones with

antifungal and antibacterial activity. Eur J Med Chem 31:989–1000

Yadav LDS, Yadav BS, Rai VK (2004) A novel salicylaldehyde based mineral supported expedient synthesis of benzoxazinone nucleosides. Tetrahedron Lett 45:5351–5353

Yang HJ, Sun WH, Li ZL, Ma Z (2002) The rapid synthesis of Schiff-base without solvent under microwave irradiation. Chin Chem Lett 13:3–6