An Expeditious One-Pot Synthesis of Substituted Phenylazetidin-2-ones in the Presence of Zeolite

Ramakanth Pagadala,[a] Jyotsna S. Meshram,[a]* Himani N. Chopde,[a] Venkateshwarlu Jetti,[a] and V. Udayini[b]

[a]Department of Chemistry, Rashtrasant Tukadoji Maharaj Nagpur University, Nagpur 440 033, Maharashtra, India
[b]Department of Botany, Osmania University, Hyderabad 500 007, Andhra Pradesh, India
*E-mail: drjsmeshram@rediffmail.com

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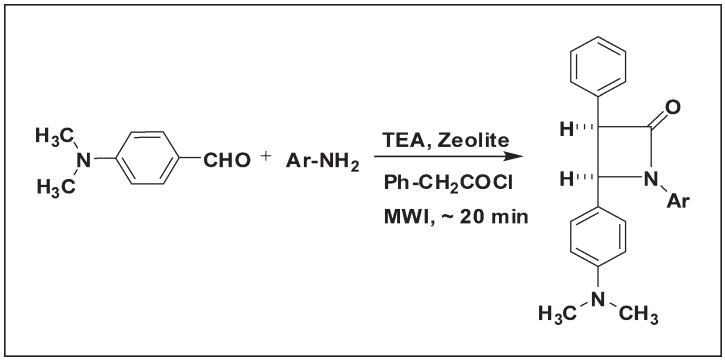

In this study, one-pot rapid and efficient series of phenylazetidin-2-ones were synthesized from N,N-dimethylaminobenzaldehyde, different substituted aromatic amines and phenylacetyl chloride in the presence of zeolite catalyst under microwave irradiation. We also reported schiff bases (1a–j) by classical and conventional microwave technique. The titled compounds are evaluated for their antimicrobial properties. The activities are due to C=O, C—N, linkages in 2-azetidinones. All the compounds have shown comparable antibacterial activities.

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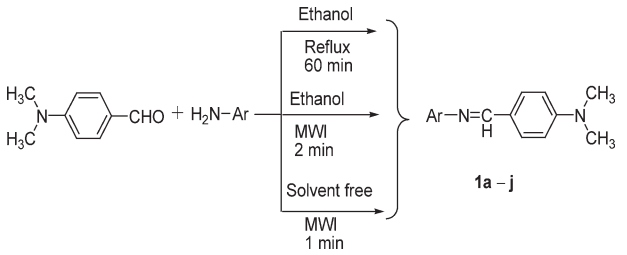
INTRODUCTION

Microwave (MW) irradiation, an unconventional energy source, has been used for a variety of applications including inorganic and organic synthesis [1], wherein chemical reactions are accelerated because of selective absorption of MW energy by polar molecules, nonpolar molecules being inert to the MW dielectric loss. The MW irradiation is used for carrying out chemical transformations, which are pollution free and eco-friendly [2]. MW reactions under solvent-free conditions are attractive in offering reduced pollution, low cost, and offer high yields together with simplicity in processing and handling [3]. MWs to organic synthesis we have developed an environmentally benign method for synthesizing N,N-dimethyl-4-((arylimino)methyl)aniline, **1a–j** (Scheme 1) is obtained good yields as compared with the synthesis by conventional method.

The interest in β-lactam compounds goes back to the 1940s, when the antibiotic properties of the first semisynthetic penicillins were discovered [4]. In recent years, their medicinal interest has been developed to other biological activities [5]. 2-azetidinone (β-lactam) nucleus is the central building blocks of β-lactam antibiotics, functionalization of the 2-azetidinone framework is essential for the development of new β-lactam antibiotics [6]. Therefore, introduction and transformation of functional groups on the ring of 2-azetidinones is one of the most important motifs in β-lactam chemistry [7].

The discovery of monocyclic β-lactam antibiotics [8], named and classified as monobactams, and the introduction of drugs such as aztreonam and carumonam (Fig. 1). One of the most powerful methods for the preparation of these compounds is the [2 + 2] cycloaddition reaction of ketenes to imines (Staudinger reaction). The Staudinger reaction in which an imine and an acid chloride react in the presence of a base, comprises a very reliable and robust method for the preparation of 2-azetidinone derivatives, although many synthetic methods have been developed [9–11]. This reaction has been well investigated experimentally and theoretically during the past decades [12,13]. Hence with these observation, we examine the feasibility and efficiency of an approach to one-pot synthesis of N,N-dimethylamino group coupled with azetidinone. Since 2-azetidinones of *p*-dimethylamine are not available, to our delight we synthesized these derivatives and resulting analogues are tested for their antibacterial activity.

Scheme 1. Synthesis of Schiff base by MW as well as classical method.



RESULTS AND DISCUSSION

The MW promoted condensation reaction of N,N-dimethylaminobenzaldehyde and aromatic amine displayed the convenient practicing way for forming an N,N-dimethyl-4-((arylimino)methyl)aniline (**1a–j**) (Scheme 1). Hence, it is clear from the yield comparison plot (Fig. 2) of classical and MW with and without solvent synthesis of the schiff base have been found to be easier, convenient and eco-friendly and yield of all the products are more than good as compared with the classical method (Table 1).

MW assisted synthesis of phenylazetidin-2-ones (**2a–j**) are represented in (Scheme 2). Reactions were carried out simply by mixing N,N-dimethylaminobenzaldehyde with different substituted aromatic amines by using zeolite as a acid catalyst. To this reaction mixture was added TEA and a solution of phenylacetyl chloride in DMF under MW irradiation. This support allows easy separation of the solid catalyst and product by simple filtration, and in optimal conditions the supported catalyst can be reused for multiple times. This study describes a successful approach for the synthesis of substituted phenylazetidin-2-ones using a laboratory MW reactor.

The same reaction under thermal conditions (**2a–j**) is summarized in Scheme 3 affords lower yields (Table 2). MW irradiation has been found to be easier, convenient, eco-friendly and the reaction time has been drastically reduced as compared to conventional method.

All the compounds synthesized were adequately characterized by their IR, ^{1}H-NMR, ^{13}C–NMR, and Mass spectra.

Antibacterial activities of all the compounds were tested against Gram positive bacteria (*Bacillus subtilis and Staphylococcus aureus*) and Gram negative bacteria

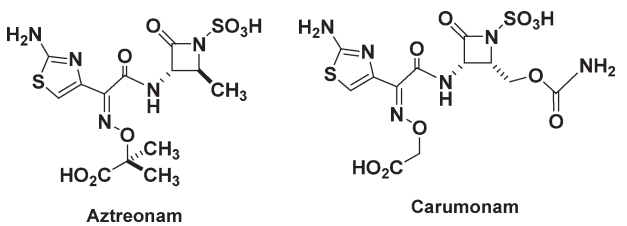


Figure 1. Clinically used monobactams.

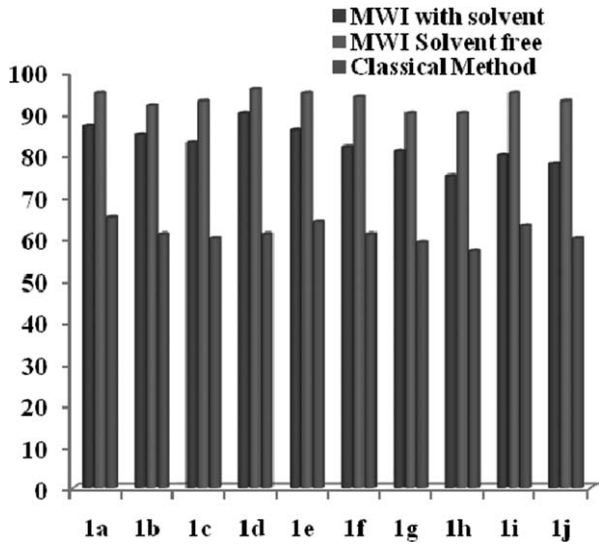


Figure 2. Graphical representation of yield comparison between classical and MW irradiation (**1a–j**).

(*E. coli* and *Klebsiella pneumoniae*) by measuring the zone of inhibition on agar plates [14]. The compounds possess moderate to good activity against all strains in comparison with standard drug (Table 3).

EXPERIMENTAL

General. All the chemicals and solvents were obtained from Merck (AR grade; Maharashtra, India) and were used without further purification. Melting points were taken in an open capillary tube. The MW assisted synthesis of Schiff base compounds were carried out in a CEM – 908010, bench mate model, 300W laboratory MW reactor. IR spectra were recorded on a Shimadzu Dr-8031 instrument. ^{1}H-NMR and ^{13}C-NMR spectra of the synthesized compounds were recorded on a Bruker-Avance (300 MHz), Varian-Gemini (200 MHz) spectrophotometer using $CDCl_3$ solvent and TMS as the internal standard. EI-MS spectra were determined on a LCQ ion trap mass spectrometer (Thermo Fisher, San Jose, CA), equipped with an EI source.

Synthesis of Schiff base (1a–1j). ***MW method without solvent.*** A quantity 0.008 mol N,N-dimethylaminobenzaldehyde and 0.008 mol aromatic amine were thoroughly mixed in a glass tube which was loosely closed. The reaction mixture was irradiated for 1 min with 100W microwaves at 110°C in MW oven in the temperature control mode. The completion of the reaction was monitored by TLC. The crude product was recrystallized with methanol.

MW method with solvent. A mixture of (0.008 mol) N,N-dimethylaminobenzaldehyde, (0.008 mol) aromatic amine, and ethanol were taken in a glass tube was monitored by TLC. The reaction mixture was allowed to attain room temperature. The crude product was recrystallized with methanol.

Classical Method. A quantity of 0.008 mol of N,N-dimethylaminobenzaldehyde, 0.008 mol of aromatic amine, and 20 mL of ethanol was refluxed for 60 min. The reaction was

Table 1

Time and yield comparison between classical and MW irradiation (**1a–j**).

		MW with solvent (solvent free)		Classical method	
Compound	Ar	Reaction time (min)	Yield (%)[a]	Reaction time (min)	Yield (%)[a]
1a	C_6H_5	2 (1)	87 (95)	60	65
1b	*m*-ClC_6H_4	2 (1)	85 (92)	60	61
1c	*p*-ClC_6H_4	2 (1)	83 (93)	60	60
1d	*p*-MeC_6H_4	2 (1)	90 (96)	60	61
1e	*o*-$CO_2HC_6H_4$	2 (1)	86 (95)	60	64
1f	*p*-OHC_6H_4	2 (1)	82 (94)	60	61
1g	*p*-$OCH_3C_6H_4$	2 (1)	81 (90)	60	59
1h	*m*-OHC_6H_4	2 (1)	75 (90)	60	57
1i	*o*-ClC_6H_4	2 (1)	80 (95)	60	63
1j	*p*-$NO_2C_6H_4$	2 (1)	78 (93)	60	60

[a] Isolated yields.

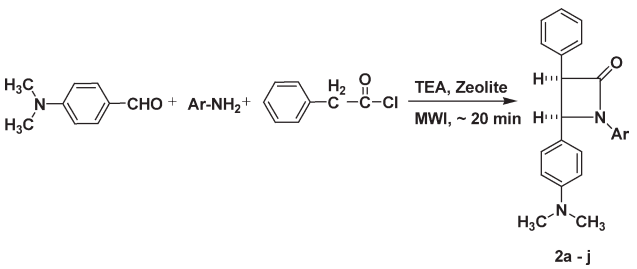
monitored by TLC. After completion of the reaction, the reaction mixture was set on one side to cool. The air that separates may be induced to crystallize by rubbing with glass rod. Collect the solid deposit by filtration and the crude product was recrystallized from methanol.

N,N-Dimethyl-4-((phenylimino)methyl)aniline (1a). IR (KBr, cm^{-1}): 1620.2 (—C=N—); ^{1}H-NMR (300 MHz, $CDCl_3$) δ (ppm) = 3.08 {s, 6H, $N(CH_3)_2$}; 6.81 (d, 2H, *J* = 8.7 Hz, Ar—H), 6.91 (d, 2H, *J* = 8.7 Hz, Ar—H), 7.1(td, 1H, *J* = 7.8 Hz, Ar—H), 7.59 (d, 2H, *J* = 8.8 Hz, Ar—H), 8.38 (s, 1H, -CH=N-); ^{13}C-NMR: δ 40.42 {$N(CH_3)_2$}, 111.9, 120.25, 124.40, 126.96, 130.13, 134.23, 153.43, 154.78 for aromatic carbons, 161.12 (—CH=N—); Mass spectra, m/z = 224 (100%).

4-((3-Chlorophenylimino)methyl)-N,N-dimethylaniline (1b). IR (KBr, cm^{-1}): 1610.8 (—C=N—); ^{1}H-NMR (300 MHz, $CDCl_3$) δ (ppm) = 3.09 {s, 6H, $N(CH_3)_2$}; 6.81–7.93 (m, 8H, Ar—H), 8.40 (s, 1H, —CH=N—); ^{13}C-NMR: δ 40.37 {$N(CH_3)_2$}, 118.9, 120.25, 121.80, 125.26, 127.8, 130.1, 132.2, 135.43, 153.52, 157.1 for aromatic carbons, 161 (—CH=N—); Mass spectra, m/z = 258 (100%).

4-((4-Chlorophenylimino)methyl)-N,N-dimethylaniline (1c). IR (KBr, cm^{-1}): 1615.7 (—C=N—); ^{1}H-NMR (300 MHz, $CDCl_3$) δ (ppm) = 3.05 {s, 6H, $N(CH_3)_2$}; 6.74 (d, 2H, *J* = 8.8 Hz, Ar—H), 6.91 (d, 2H, *J* = 8.7 Hz, Ar—H), 7.39 (d, 2H, *J* = 8.7 Hz, Ar—H), 7.43 (d, 2H, *J* = 8.7 Hz, Ar—H), 8.32 (s, 1H, —CH=N—); ^{13}C-NMR: δ 40.45 {$N(CH_3)_2$}, 111.90, 118.20, 122.40, 125.36, 130.56, 142.08, 152.73, 155.32 for aromatic carbons, 160.16 (—CH=N—); Mass spectra, m/z = 258 (100%).

Scheme 2. MW assisted synthesis of substituted phenylazetidinones (**2a-j**).



N,N-Dimethyl-4-((p-tolylimino)methyl)aniline (1d). IR (KBr, cm^{-1}): 1612.8 (—C=N—); ^{1}H-NMR (300 MHz, $CDCl_3$) δ (ppm) = 2.42 [s, 3H (—CH_3)]; 3.05 {s, 6H, $N(CH_3)_2$}; 6.73 (d, 2H, *J* = 8.8 Hz, Ar—H), 6.89 (d, 2H, *J* = 8.7 Hz, Ar—H), 7.35(d, 2H, *J* = 8.7 Hz, Ar—H), 7.41 (d, 2H, *J* = 8.7 Hz, Ar—H), 8.37 (s, 1H, —CH=N—); ^{13}C-NMR: δ 25.2 (Ar—CH_3), 40.54 {$N(CH_3)_2$}, 111.98, 119.25, 121.60, 126.96, 131.6, 138.2, 150.14, 153.12 for aromatic carbons, 159.13 (—CH=N—); Mass spectra, m/z = 238 (100%).

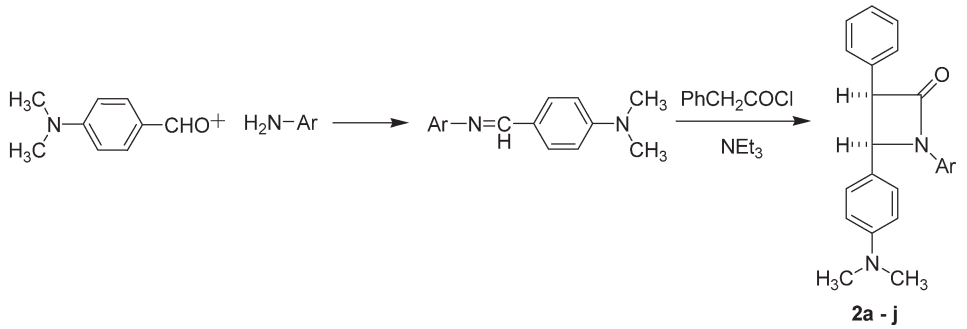
2-(4-(Dimethylamino)benzylideneamino)benzoicacid (1e). IR (KBr, cm^{-1}): 1626.1 (—C=N—); ^{1}H-NMR (300 MHz, $CDCl_3$) δ (ppm) = 3.08 {s, 6H, $N(CH_3)_2$}; 6.79–8.3 (m, 8H, Ar—H), 8.40 (s, 1H, —CH=N—); 12.52 (s, 1H, —COOH); ^{13}C-NMR: δ 40.60 {$N(CH_3)_2$}, 111.93, 115.80, 123.63, 125.21, 126.42, 127.96, 128.21, 134.23, 151.98, 152.05, for aromatic carbons, 159.92 (—CH=N—); 168.06 (—COOH); Mass spectra, m/z = 268 (100%).

4-(4-(Dimethylamino)benzylideneamino)phenol (1f). IR (KBr, cm^{-1}): 1618.5 (—C=N—); ^{1}H-NMR (300 MHz, $CDCl_3$) δ (ppm) = 3.07 {s, 6H, $N(CH_3)_2$}; 6.84 (d, 2H, *J* = 8.8 Hz, Ar—H), 6.89 (d, 2H, *J* = 8.7 Hz, Ar—H), 7.19 (d, 2H, *J* = 8.7 Hz, Ar—H), 7.71 (d, 2H, *J* = 8.7 Hz, Ar—H), 8.37 (s, 1H, —CH=N—); 9.32 (s, 1H, —OH); ^{13}C-NMR: δ 40.57 {$N(CH_3)_2$}, 111.98, 119.25, 121.40, 124.96, 130.59, 135.08, 151.54, 153.42 for aromatic carbons, 159.06 (—CH=N—); Mass spectra, m/z = 240 (100%).

4-((4-Methoxyphenylimino)methyl)-N,N-dimethylanline (1g). IR (KBr, cm^{-1}): 1610.8 (—C=N—); ^{1}H-NMR (300 MHz, $CDCl_3$) δ (ppm) = 3.05 {s, 6H, $N(CH_3)_2$}; 3.91 (s, 3H, —OCH_3); 6.83 (d, 2H, *J* = 8.8 Hz, Ar—H), 6.91 (d, 2H, *J* = 8.7 Hz, Ar—H), 7.21 (d, 2H, *J* = 8.7 Hz, Ar—H), 7.69 (d, 2H, *J* = 8.7 Hz, Ar—H), 8.36 (s, 1H, —CH=N—); ^{13}C-NMR: δ 40.49 {$N(CH_3)_2$}, 56.38 (—OCH_3), 111.96, 118.05, 121.82, 125.34, 130.02, 139.94, 152.87, 156.85 for aromatic carbons, 159.66 (—CH=N—); Mass spectra, m/z = 254 (100%).

3-(4-(Dimethylamino)benzylideneamino)phenol (1h). IR (KBr, cm^{-1}): 1611.3 (—C=N—); ^{1}H-NMR (300 MHz, $CDCl_3$) δ (ppm) = 3.08 {s, 6H, $N(CH_3)_2$}; 6.73–7.89 (m, 8H, Ar—H), 8.38 (s, 1H, —CH=N—); 9.25 (s, 1H, —OH); ^{13}C-NMR: δ 40.48 {$N(CH_3)_2$}, 109.10, 111.95, 115.25, 115.70, 123.93, 126.46, 132.24, 149.54, 153.76 for aromatic carbons, 160.12 (—CH=N—); Mass spectra, m/z = 240 (100%).

Scheme 3. Synthesis of 4-[4-(dimethylamino)phenyl]-1-substitutedaryl-3-phenylazetidin-2-ones (**2a–j**) under thermal condition.



4-((2-Chlorophenylimino)methyl)-N,N-dimethylaniline (1i). IR (KBr, cm^{-1}): 1610.5 (—C=N—); ^{1}H-NMR (300 MHz, $CDCl_3$) δ (ppm) = 3.05 {s, 6H, $N(CH_3)_2$}; 6.72–7.84 (m, 8H, Ar—H), 8.24 (s, 1H, —CH=N—); ^{13}C-NMR: δ 40.57 {$N(CH_3)_2$}, 111.97, 120.79, 124.55, 125.83, 127.94, 128.32, 130.19, 131.20, 150.89, 153.23 for aromatic carbons, 161.98 (—CH=N—); Mass spectra, m/z = 258 (100%).

N,N-Dimethyl-4-((4-nitrophenylimino)methyl)aniline (1j). IR (KBr, cm^{-1}): 1621.4 (—C=N—); ^{1}H-NMR (300 MHz, $CDCl_3$) δ (ppm) = 3.06 {s, 6H, $N(CH_3)_2$}; 6.73 (d, 2H, J = 8.8 Hz, Ar—H), 6.90 (d, 2H, J = 8.7 Hz, Ar—H), 7.27 (d, 2H, J = 8.7 Hz, Ar—H), 7.81 (d, 2H, J = 8.7 Hz, Ar—H), 8.28 (s, 1H, —CH=N—); ^{13}C-NMR: δ 40.60 {$N(CH_3)_2$}, 111.89, 116.42, 122.43, 124.78, 130.80, 141.02, 150.54, 154.12 for aromatic carbons, 159.28 (—CH=N—); Mass spectra, m/z = 269 (100%).

Synthesis of azetidinones (2a–2j) by MW method. N,N-dimethylaminobenzaldehyde (0.008 mol), 0.008 mol aromatic amine, and zeolite (montmorillonite K-10; 0.2 g) were stirred with glass rod in DMF (2 mL). To this solution added triethylamine (0.024 mol) and a solution of phenylacetyl chloride (0.008 mol) in DMF (3 mL). The reaction mixture was irradiated for ~20 min with 100W microwaves at 110°C in MW oven in the temperature control mode. The completion of the reaction was monitored by TLC. After the irradiation was over, the reaction mixture was cooled and added into water. After filtering the zeolite particles, the obtained solid product was separated and purified from ethyl acetate and *n*-hexane.

Synthesis of azetidinones (2a–2j) by classical method. A solution of phenylacetyl chloride (0.01 mol) in dry dichloromethane was added dropwise to a well-stirred solution of appropriate Schiff base (0.01 mol) and triethylamine (0.02 mol) in anhydrous dichloromethane (50 mL). After the addition had been completed, the solution was stirred for 14 h. The completion of the reaction was monitored by TLC. The reaction mixture was washed with water and dried over sodium sulfate. The products that were obtained after removing the solvent were purified from ethyl acetate and *n*-hexane.

4-(4-(Dimethylamino)phenyl)-1,3-diphenylazetidin-2-one (2a). IR (KBr, cm^{-1}): 1756 (C=O β-lactam), 1365 (C—N); ^{1}H-NMR (300 MHz, $CDCl_3$) δ (ppm) = 3.05 (s, 6H, $N(CH_3)_2$), 4.3 (d, 1H, J = 5.4 Hz, —N—CH), 5.1 (d, 1H, J = 5.4, —CH—C=O), 6.5–7.5 (m, 14H, Ar—H); ^{13}C-NMR: δ 40.39 {$N(CH_3)_2$}, 165.8 (cyclic, =C=O), 64.0 (=CH—N=), 51.6 (=CH—Ar), 112.8–152.3 (Ar—C); Mass spectra, m/z = 342 (100%).

1-(3-Chlorophenyl)-4-(4-(dimethylamino)phenyl)-3-phenylazetidin-2-one (2b). IR (KBr, cm^{-1}): 1745 (C=O β-lactam), 1385 (C—N); ^{1}H-NMR (300 MHz, $CDCl_3$) δ (ppm) = 3.06 (s, 6H, $N(CH_3)_2$), 4.3 (d, 1H, J = 5.4 Hz, —N—CH), 5.2 (d, 1H, J = 5.4 Hz, —CH—C=O), 6.6—7.6 (m, 13H, Ar—H); ^{13}C-NMR: δ 40.5 {$N(CH_3)_2$}, 161.9 (cyclic, =C=O), 66.0 (=CH—N=), 51.4 (=CH—Ar), 111.4–153.0 (Ar—C); Mass spectra, m/z = 376 (100%).

1-(4-Chlorophenyl)-4-(4-(dimethylamino)phenyl)-3-phenylazetidin-2-one (2c). IR (KBr, cm^{-1}): 1758 (C=O β-lactam), 1364 (C—N); ^{1}H-NMR (300 MHz, $CDCl_3$) δ (ppm) = 3.05 (s,

Table 2

Time and yield comparison of azetidinones between classical and MW irradiation (**2a–j**).

		MW method		Classical method	
Compound	Ar	Reaction time (min)	Yield (%)[a]	Reaction time (h)	Yield (%)[a]
2a	C_6H_5	21	90	14	66
2b	*m*-ClC_6H_4	24	89	14	64
2c	*p*-ClC_6H_4	23	86	14	69
2d	*p*-MeC_6H_4	18	89	14	70
2e	*o*-$CO_2HC_6H_4$	19	90	16	72
2f	*p*-OHC_6H_4	24	85	17	61
2g	*p*-$OCH_3C_6H_4$	21	89	16	67
2h	*m*-OHC_6H_4	20	84	15	74
2i	*o*-ClC_6H_4	20	85	14	70
2j	*p*-$NO_2C_6H_4$	22	87	16	72

[a] Isolated yields.

Table 3

Antimicrobial activities of synthesized compounds.

	Zone of inhibition (mm)			
	Gram positive		Gram negative	
Compound	*Staphylococcus*	*Bacillus*	*Klebsiella*	*E. coli*
2a	+ +	−	−	+
2b	+ +	+	−	+ +
2c	+	+ +	+ +	+
2d	−	−	+	+
2e	+ +	+ + +	+ +	+
2f	+	+	+ +	−
2g	+ +	+	−	+ + +
2h	−	+	+ +	+
2i	+ +	+	+ + +	+ +
2j	+ + +	+ +	+	+ + +
Ampicillin	+ + +	+ + +	+ + +	+ + +

Key to symbols: Inactive = − (inhibition zone <6 mm); Slightly active = + (inhibition zone 6−9 mm); Moderately active = + + (inhibition zone 9−12 mm); Highly active = + + + (inhibition zone >12 mm).

6H, $N(CH_3)_2$), 4.3 (d, 1H, J = 5.4 Hz, —N—CH), 5.1 (d, 1H, J = 5.4 Hz, —CH—C=O), 6.5–7.5 (m, 13H, Ar—H); ^{13}C-NMR: δ 40.48 {$N(CH_3)_2$}, 162.5 (cyclic, =C=O), 66.4 (=CH—N=), 52.2 (=CH—Ar), 111.5–153.0 (Ar—C); Mass spectra, m/z = 376 (100%).

4-(4-(Dimethylamino)phenyl)-3-phenyl-1-p-tolylazetidin -2-one (2d). IR (KBr, cm^{-1}): 1765 (C=O β-lactam), 1386 (C—N); ^{1}H-NMR (300 MHz, $CDCl_3$) δ (ppm) = 2.3 (s, 3H, —CH_3), 3.07 (s, 6H, $N(CH_3)_2$), 4.3 (d, 1H, J = 5.4 Hz, —N—CH), 5.3 (d, 1H, J = 5.4 Hz, —CH—C=O), 6.6–7.4 (m, 13H, Ar—H), ^{13}C-NMR: δ 25.2 (Ar—CH_3), 40.52 {$N(CH_3)_2$}, 160.6 (cyclic, =C=O), 67.1 (=CH—N=), 50.8 (=CH—Ar), 111.4–153.0 (Ar—C); Mass spectra, m/z = 356 (100%).

2-(2-(4-(Dimethylamino)phenyl)-4-oxo-3-phenylazetidin-1-yl)-benzoicacid (2e). IR (KBr, cm^{-1}): 1768 (C=O β-lactam), 1365 (C—N); ^{1}H-NMR (300 MHz, $CDCl_3$) δ (ppm) = 3.06 (s, 6H, $N(CH_3)_2$), 4.4 (d, 1H, J = 5.4 Hz, —N—CH), 5.2 (d, 1H, J = 5.4 Hz, —CH—C=O), 6.7–8.2 (m, 13H, Ar—H), 12.5 (s, 1H, —COOH); ^{13}C-NMR: δ 40.47 {$N(CH_3)_2$}, 161.3 (cyclic, =C=O), 66.5 (=CH—N=), 51.8 (=CH—Ar), 110.8–153.0 (Ar—C), 168.2 (—COOH); Mass spectra, m/z = 386 (100%).

4-(4-(Dimethylamino)phenyl)-1-(4-hydroxyphenyl)-3-phenyl-azetidin-2-one (2f). IR (KBr, cm^{-1}): 1752 (C=O β-lactam), 1365 (C—N); ^{1}H-NMR (300 MHz, $CDCl_3$) δ (ppm) = 3.06 (s, 6H, $N(CH_3)_2$), 4.3 (d, 1H, J = 5.4 Hz, —N—CH), 5.1 (d, 1H, J = 5.4 Hz, —CH—C=O), 6.6–7.5 (m, 13H, Ar—H), 9.4 (s, 1H, —OH); ^{13}C-NMR: δ 40.51 {$N(CH_3)_2$}, 160.4 (cyclic, =C=O), 66.5 (=CH—N=), 51.8 (=CH—Ar), 110.8–152.4 (Ar—C); Mass spectra, m/z = 358 (100%).

4-(4-(Dimethylamino)phenyl)-1-(4-methoxyphenyl)-3-phenyl-azetidin-2-one (2g). IR (KBr, cm^{-1}): 1765 (C=O β-lactam), 1388 (C—N); ^{1}H-NMR (300 MHz, $CDCl_3$) δ (ppm) = 3.07 (s, 6H, $N(CH_3)_2$), 3.8 (s, 3H, —OCH_3), 4.2 (d, 1H, J = 5.4 Hz, —N—CH), 5.1 (d, 1H, J = 5.3 Hz, CH—C=O), 6.5–7.4 (m, 13H, Ar—H); ^{13}C-NMR: δ 41.3 {$N(CH_3)_2$}, 56.3 (—OCH_3), 160.5 (cyclic, =C=O), 65.8 (=CH—N=), 52.5 (=CH—Ar), 110.5–153.0 (Ar—C); Mass spectra, m/z = 372 (100%).

4-(4-(Dimethylamino)phenyl)-1-(3-hydroxyphenyl)-3-phenyl-azetidin-2-one (2h). IR (KBr, cm^{-1}): 1734 (C=O β-lactam), 1336 (C—N); ^{1}H-NMR (300 MHz, $CDCl_3$) δ (ppm) = 3.05 (s, 6H, $N(CH_3)_2$), 4.3 (d, 1H, J = 5.4 Hz, —N—CH), 5.2 (d, 1H, J = 5.4 Hz, —CH—C=O), 6.6–7.5 (m, 13H, Ar—H), 9.3 (s, 1H, —OH); ^{13}C-NMR: δ 41.7 {$N(CH_3)_2$}, 160.8 (cyclic, =C=O), 65.8 (=CH—N=), 52.1 (=CH—Ar), 110.5–152.5 (Ar—C); Mass spectra, m/z = 358 (100%).

1-(2-Chlorophenyl)-4-(4-(dimethylamino)phenyl)-3-phenylazetidin-2-one (2i). IR (KBr, cm^{-1}): 1754 (C=O β-lactam), 1357 (C—N); ^{1}H-NMR (300 MHz, $CDCl_3$) δ (ppm) = 3.07 (s, 6H, $N(CH_3)_2$), 4.8 (d, 1H, J = 5.5 Hz, —N—CH), 5.2 (d, 1H, J = 5.4 Hz, —CH—C=O), 6.6–7.9 (m, 13H, Ar—H); ^{13}C-NMR: δ 40.47 {$N(CH_3)_2$}, 161.6 (cyclic, =C=O), 64.6 (=CH—N=), 52.9 (=CH—Ar), 110.5–153.0 (Ar—C); Mass spectra, m/z = 376 (100%).

4-(4-(Dimethylamino)phenyl)-1-(4-nitrophenyl)-3-phenylazetidin-2-one (2j). IR (KBr, cm^{-1}): 1766 (C=O β-lactam), 1364 (C—N); ^{1}H-NMR (300 MHz, $CDCl_3$) δ (ppm) = 3.06 (s, 6H, N(CH3)2), 4.4 (d, 1H, J = 5.4 Hz, —N—CH), 5.6 (d, 1H, J = 5.4 Hz, —CH—C=O), 6.6–8.1 (m, 13H, Ar—H); ^{13}C-NMR: δ 40.42 {$N(CH_3)_2$}, 164.77 (cyclic, =C=O), 62.1 (=CH—N=), 52.4 (=CH—Ar), 111.7–153.8 (Ar—C); Mass spectra, m/z = 387 (100%).

CONCLUSION

A series of differently substituted Schiff base was prepared by applying a fast, highly efficient and environmentally friendly solvent-free procedure under MW irradiation and we have reported an highly efficient MW assisted rapid synthesis of N,N-dimethylamino group coupled with azetidinone. The one-pot nature of the present procedure makes it an acceptable alternative to multi-step approaches. The procedure has several advantages including short reaction time, high yields, and simple workup. It also simplifies the laborious procedures and offers considerable advantages, such as: elimination

of solvents, the use of substances without any modification or activation, employment of reusable solid catalysts and environmentally friendly character over the existing methodologies.

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REFERENCES AND NOTES

[1] (a) Kaczmarek, K. T.; Renata, J.; Hołderna-Kedzia, E.; Radecka-Paryzek, W. Inorganica Chimica Acta, 2009, 362, 3127; (b) Dede, B.; Karipcin, F.; Cengiz, M. J Hazard Mater 2009, 163, 1148; (c) Varma, R. S. J Heterocycl Chem 1999, 35, 1565; (d) Caddick, S. Tetrahedron 1995, 51, 10403; (e) Varma, R. S. Green Chem 1999, 1, 43. (f) Loupy, A.; Petit, A.; Hamelin, J.; Texier-Boullet, F.; Jacquault, P.; Mathe, D. Synthesis 1998, 1213; (g) Galema, S. A. Chem Soc Rev 1997, 26, 233; (h) Varma, R. S. Clean Prod Processes 1999, 1, 132.

[2] (a) Kidwai, M. Chem Edu Rev 2000, 15, 34; (b) Srivastava, K. P. Res J Chem Environ 2001, 5, 77.

[3] (a) Adam, D. Nature 2003, 421, 571; (b) Ramakanth P.; Jyotsna S. M.; Himani N. C.; Nagender Reddy P. J. Heterocyclic Chem 2010, 47, 350.

[4] Palomo, C.; Aizpurua, J. M.; Ganboa, I.; Oiarbide, M. Curr Med Chem 2004, 11, 1837.

[5] (a) O'Driscoll, M.; Greenhalgh, K.; Young, A.; Turos, E.; Dickey, S.; Lim, D. V. Bioorg Med Chem 2008, 16, 7832; (b) Bai, X.; Xu, X.; Fu, R.; Chen, J.; Chen, S. Bioorg Med Chem Lett 2007, 17, 101; (c) Turos, E.; Reddy, G. S. K.; Greenhalgh, K.; Ramaraju, P.; Abeylath, S. C.; Jang, S.; Dickey, S.; Lim, D. V. Bioorg Med Chem Lett 2007, 17, 3468; (d) Tozsera, J.; Sperka, T.; Pitlik, J.; Bagossia, P. Bioorg Med Chem Lett 2005, 15, 3086; (e) Banik, B. K.; Becker, F. F.; Banik, I. Bioorg Med Chem 2005, 13, 3611; (f) Nivsarkar, M.; Thavaselvam, D.; Prasanna, S.; Sharma, M.; Kaushik, M. P. Bioorg Med Chem Lett 2005, 15, 1371; (g) Sutton, J. C.; Bolton, S. A.; Harti, K. S.; Huang, M. H.; Jacobs, G.; Meng, W.; Zhao, G.; Bisacchi, G. S. Bioorg Med Chem Lett 2004, 14, 2233; (h) Marchand-Brynaert, J.; Dive, G.; Galleni, M.; Gerard, S. Bioorg Med Chem 2004, 12, 129; (i) Adlington, R. M.; Baldwin, J. E.; Chen, B.; Cooper, S. L.; McCoull, W.; Pritchard, G. J.; Howe, T. J.; Becker, G. W.; Hermann, R. B.; McNulty, A. M.; Neubauer, B. L. Bioorg Med Chem Lett 1997, 7, 1689.

[6] (a) Ojima, I. Adv Asym Synth 1995, 1, 95; (b) Ojima, I.; Delaloge, F. Chem Soc Rev 1997, 26, 377; (c) Manhas, M. S.; Wagle, D. R.; Chiang, J.; Bose, A. K. Heterocycles 1988, 27, 1755; (d) Alcaide, B.; Almendros, P. Chem Soc Rev 2001, 30, 226; (e) Alcaide, B.; Almendros, P. Org Prep Proced Int 2001, 33, 315; (f) Palomo, C.; Aizpurua, J. M.; Ganboa, I.; Oiarbide, M. Synlett 2001, 1813; (j) Alcaide, B.; Almendros, P. Synlett 2002, 381.

[7] Alcaide, B.; Almendros, P.; Aragoncillo, C. Chem Rev 2007, 107, 4437.

[8] (a) Imada, A.; Kitano, K.; Kintaka, K.; Muroi, M.; Asai, M. Nature 1981, 289, 590; (b) Sykes, R. B.; Cimarusti, C. M.; Bonner, D. P.; Bush, K.; Floyd, D. M.; Georgopadakou, N. H.; Koster, W. H.; Liu, W. C.; Parker, W. L.; Principe, P. A.; Rathnum. M. L.; Slusarchick, W. A.; Trejo W. H.; Wells, T. S. Nature 1981, 291, 489.

[9] Palomo, C.; Aizpurua, J. M.; Inaki, G.; Oiarbide, M. Eur J Org Chem 1999, 3223.

[10] Cossio, F. P.; Ugalde, J. M.; Lopez, X.; Lecea, B.; Palomo, C. J Am Chem Soc 1993, 115, 995.

[11] (a) Van der Steen, F. H.; Van Koten, G. Tetrahedron 1991, 47, 7503; (b) Singh, G. S. Tetrahedron 2003, 59, 7631.

[12] (a) Moore, H. W.; Hernandez, L. Jr.; Chambers, R. J Am Chem Soc 1978, 100, 2245; (b) Pacansky, J.; Chang, J. S.; Brown, D. W.; Schwarz, W. J Org Chem 1982, 47, 2233; (c) Moore, H. W.; Hughes, G.; Srinivasachar, K.; Fernandez, M.; Nguyen, N. V.; Schoon, D.; Tranne, A. J Org Chem 1985, 50, 4231; (d) Brady, W. T.; Gu, Y. Q. J Org Chem 1989, 54, 2838; (e) Lynch, J. E.; Riseman, S. M.; Laswell, W. L.; Tschaen, D. M.; Volante, R.; Smith, G. B.; Shinkai, I. J Org Chem 1989, 54, 3792; (f) Hegedus, L. S.; Montgomery, J.; Narukawa, Y.; Snustad, D. C. J Am Chem Soc 1991, 113, 5784; (g) Georg, G. I.; He, P.; Kant, J.; Wu, Z. J. J Org Chem 1993, 58, 5771.

[13] (a) Sordo, J. A.; González, J.; Sordo, T. L. J Am Chem Soc 1992, 114, 6249; (b) Cossio, F. P.; Ugalde, J. M.; Lopez, X.; Lecea, B.; Palomo, C. J Am Chem Soc 1993, 115, 995; (c) Arrieta, A.; Ugalde, J. M.; Cossio, F. P. Tetrahedron Lett 1994, 35, 4465; (d) Cossio, F. P.; Arrieta, A.; Lecea, B.; Ugalde, J. M. J Am Chem Soc 1994, 116, 2085; (e) Arrieta, A.; Lecea, B.; Cossio, F. P. J Org Chem 1998, 63, 5869; (f) Arrieta, A.; Cossio, F. P.; Fernandez, I.; Gomez-Gallego, M.; Lecea, B.; Mancheno, M. J.; Sierra, M. A. J Am Chem Soc 2000, 122, 11509; (g) Venturini, A.; González, J. J Org Chem 2002, 67, 9089.

[14] Weber, A. D.; Sanders, C. S. Antimicrob Agents Chemother 1990, 34, 156.