An Efficient Synthesis and Biological Testing of Novel 3-Chloro-4-aryl-1-(4-(phenyldiazenyl)phenyl)azetidin-2-ones

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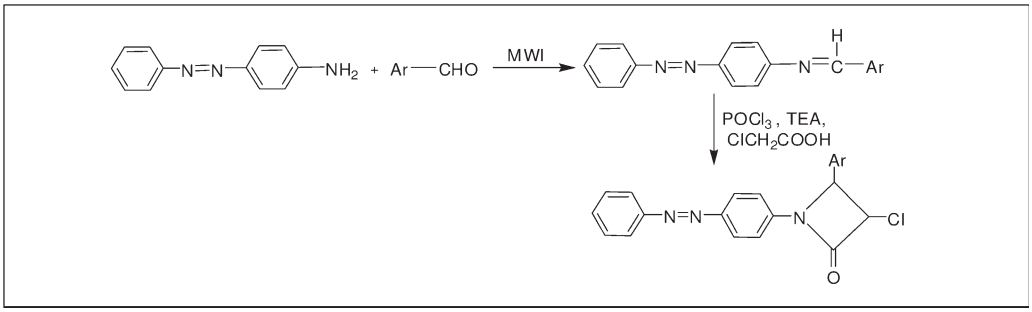

N-Benzylidene-4-(phenyldiazenyl)aniline (**Ia–Ij**) has been prepared from *p*-aminoazobenzene with different aromatic aldehydes under microwave irradiation, which on further treatment with chloro acetic acid and $POCl_3$ in the presence of triethyl amine gave the title compounds. The structure of the compounds has been confirmed by spectroscopic techniques (IR and ^1H NMR) and elemental analysis. These azetidinones analogues were screened for their antimicrobial activities against strains of different microorganisms. Some of the compounds displayed the promising antibacterial activities against some bacterial strains.

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INTRODUCTION

The β-lactam skeleton is the key structural element of the most widely used family of antimicrobial agents to date, the β-lactam antibiotics, which includes as representative structural classes (Fig. 1) the Penams 1, Cephems 2, Penems 3, Monobactams 4, Carbapenems 5, and Trinems 6, among others [1]. The first member of this class of compounds was synthesized by Staudinger in 1907 [2]. An interesting group of β-lactams are the monocyclic β-lactams, which are molecules that do not contain another ring fused to the β-lactam. The development of several synthetic 2-azetidinone was due to the growing resistant of bacteria toward the β-lactam antibiotics and need for medicines with a more specific antibacterial activities [3,4]. A large number of monocyclic β-lactams reported to have some other types of biological activity such as antifungal, antitubercular, antitumor, anti-inflamatory, anticonvulsant, cholesterol absorption inhibition, and enzyme inhibition activity [5–10].

Because of such versatile applications, these moieties always attracted the interest of synthetic and medicinal organic chemists [11–14]. A large number of chemical methods for the production of β-lactams have been developed, and the topic has been amply documented and reviewed several times [15]. The hydroxamate cyclization [16], the metalloester enolate-imine condensation [17], the chromium carbene-imine reaction [18], the isocyanate-alkene cycloaddition [19], and the ketene-imine cycloaddition [20] are the approaches most often used for the construction of the azetidin-2-one ring. In particular, the most common method for the synthesis of 2-azetidinone is the Staudinger Ketene-imine cycloaddition, which involves the reaction of imine (Schiff Base) with acid chloride in the presence of tertiary base [21]. This reaction, however, depends on many factors including temperature and reaction time, which often needs to be optimized [22,23].

Hence, to further assess the pharmacological activities of these class of molecules, it was thought worthwhile to synthesize some new derivatives of β-lactam heterocycles by incorporating the *p*-aminoazobenzene and 2-azetidinone moieties in a single framework. We herein report a novel, convenient, and highly efficient method for the preparation of 3-chloro-4-(aryl)-1-(4-(phenyldiazenyl)phenyl)azetidin-2-one **IIa–IIj** in good yields involving two steps. It involves the formation of different Schiff's bases **Ia–Ij** of *p*-aminoazobenzene and aromatic aldehydes followed by the cycloaddition reaction

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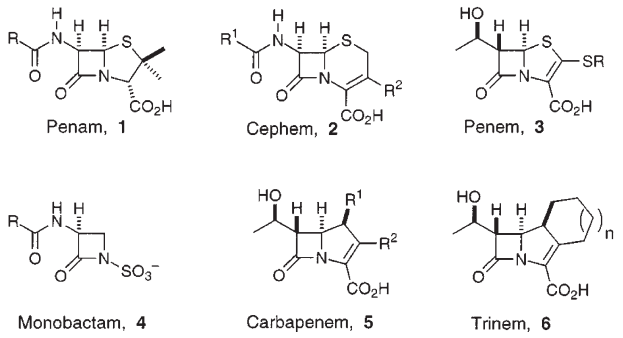

Figure 1. Some representative structural classes of β-lactam antibiotics.

of **Ia–Ij** with ketene, which is generated *in situ* from chloroacetic acid in presence of trimethylamine and $POCl_3$ (Scheme 1). The Schiff bases were also prepared by using microwave method [24].

However, the synthesis of Schiff bases **Ia–Ij** under the classical reaction was plagued by a number of serious disadvantages such as low yield of the product as given in Table 1. Therefore, to overcome the drawbacks of the classical method, modern version of this reaction by microwave superheating in solvent and solvent free condition has been adopted. All the synthesized compounds were characterized on the basis of different spectral analysis techniques such as IR and ^{1}H NMR and elemental analysis techniques. Also in the present communication, we report the antibacterial activities of the titled compounds (**IIa–IIj**) against nine different bacterial strains.

RESULTS AND DISCUSSION

As evident from data presented in Table 1, we were able to obtain *N*-arylbenzylidene-4-(phenyldiazenyl)aniline **Ia–Ij** in good yields by using neat conditions under microwave irradiation in presence of solvent and also in solvent free conditions when compared to that of conventional reflux reactions in ethanol. The comparison of isolated yields and reaction time of the three conditions used showed microwave-assisted solvent-free reactions as the most efficient synthetic method in terms of energy and time consumption. All the compounds synthesized were adequately characterized by their elemental analysis and spectral techniques such as IR, ^{1}H NMR, and mass spectra.

Antibacterial activity. Antibacterial activities of all the compounds were studied against nine different bacterial strains (*E. coli* (mixed), *B. subtilis*, Pseudomonas sp., *S. aureus*, *P.vulageris*, Salmonella sp., *E. coli*(+ve strai,), Rhodococci, *B. stearothermophilus*) by measuring the zone of inhibition on agar plates. The compounds possess moderate to good activity against all strains in comparison with standard drug (Table 2). It can be observed from these results that compounds **IIa–IIj** have shown positive bacterial activity against different bacterial species, which are also known as human pathogenic bacteria. It was also observed that within the synthesized compound extracts, highest zone of inhibition recorded in 3-chloro-4-(furan-2-yl)-1-(4-(phenyl diazenyl) phenyl)azetidin-2-one **(IIe)** extract against the *P. vulageris* 22 mm, which is more than standard, *i.e.*, 17 mm zone of inhibition.

Scheme 1. Synthesis of Schiff base with different synthetic path and 3-chloro-4-aryl-1-(4-(phenyldiazenyl)phenyl)azetidin-2-one.

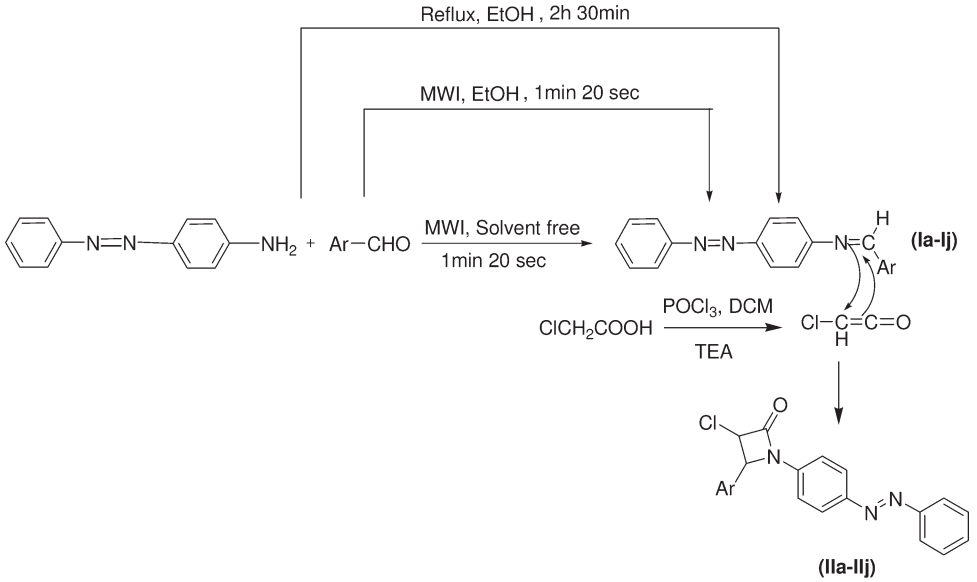

Table 1

Time and yield comparison between classical and MW irradiation.

Compound	Ar	Reaction time (min/sec)			Yield (%)[a]		
		MWI, Solvent Free	MWI, EtOH	Classical, EtOH	MWI, Solvent Free	MWI, EtOH	Classical, EtOH
Ia	C_6H_5	1 min 20 sec	1 min 20 sec	150 min	92	90	85
Ib	2-OHC_6H_4	1 min 20 sec	1 min 20 sec	150 min	90	85	80
Ic	2-$NO_2C_6H_4$	1 min 20 sec	1 min 20 sec	150 min	87	82	75
Id	3-$NO_2C_6H_4$	1 min 20 sec	1 min 20 sec	150 min	95	92	85
Ie	C_4H_3O	1 min 20 sec	1 min 20 sec	150 min	90	85	70
If	4-OHC_6H_4	1 min 20 sec	1 min 20 sec	150 min	85	80	65
Ig	4-$N(CH_3)_2C_6H_4$	1 min 20 sec	1 min 20 sec	150 min	92	87	80
Ih	2-ClC_6H_4	1 min 20 sec	1 min 20 sec	150 min	95	88	75
Ii	3-BrC_6H_4	1 min 20 sec	1 min 20 sec	150 min	97	95	85
Ij	4-ClC_6H_4	1 min 20 sec	1 min 20 sec	150 min	88	80	60

[a] Isolated yields.

EXPERIMENTAL

General. All the chemicals and solvents were obtained from E-Merck, India (AR grade) and were used without further purification. Melting points were taken in an open capillary tube. The microwave assisted synthesis of Schiff base compounds were carried out in a CEM–908010, bench mate model, 300 watts laboratory microwave reactor. IR spectra were recorded on a Shimadzu Dr-8031 instrument. Elemental analyses were carried out using a Perkin-Elmer, CHN elemental analyzer model 2400. ^{1}H NMR spectra of the synthesized compounds were recorded on a Bruker-Avance (300 MHz) and Varian-Gemini (200 MHz) spectrophotometer using $CDCl_3$ solvent and TMS as an the internal standard. EI-MS spectra were determined on a LCQ ion trap mass spectrometer (Thermo Fisher, San Jose, CA, USA), equipped with an EI source.

Synthesis of Schiff base (Ia–Ij). ***Microwave method without solvent.*** Equimolar amount of *p*-aminoazo benzene (0.001 mol) and aromatic aldehyde (0.001 mol) were thoroughly mixed in a glass tube, which was loosely closed. The reaction mixture was irradiated for 1min 20 sec with 100 W 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.

Microwave method with solvent. Equimolar amount of *p*-aminoazobenzene (0.001 mol) and aromatic aldehyde (0.001 mol) and ethanol were taken in a glass tube which was loosely closed and irradiated in MW oven for 1min 20 sec. The completion of the reaction was monitored by TLC. The reaction mixture was allowed to attain room temperature. The solvent was removed, and the crude product was recrystallized with methanol.

Classical method. Equimolar amount of *p*-aminoazobenzene (0.001 mol), aromatic aldehyde (0.001 mol), and 10 mL of ethanol was refluxed for 2 hr 30 min. The reaction was monitored by TLC. After completion of the reaction, the reaction mixture was set on one side to cool. Then, the reaction mixture was poured in ice cold water and the solid precipitate was separated out. The precipitate was filtered and collected crude product was recrystallized using methanol.

Table 2

Biological activities of compounds chloro-4-(aryl)-1-(4-(phenyldiazenyl) phenyl)azetidin-2-one (**IIa–IIj**).

Bacterial strain	Zone of inhibition in mm along without well diameter (5 mm)										
	Chemical compounds										
	IIa	**IIb**	**IIc**	**IId**	**IIe**	**IIf**	**IIg**	**IIh**	**IIi**	**IIj**	Standard Nystatin
E. coil (mixed)	20	16	6	12	–	7	14	9	13	16	17
B. subtilis	3	5	2	–	3	2	8	6	9	2	6
Pseudomonas sp.	13	3	15	6	10	6	5	10	13	9	12
S. aureus	–	–	4	7	5	10	8	4	8	6	9
P. vulageris	15	11	9	13	22	16	8	14	10	5	17
Salmonella sp.	9	15	13	20	17	10	8	16	14	15	19.1
E. coil(+ve strain)	–	–	6	4	9	10	13	7	–	2	11
Rhodococci	–	–	–	4	2	5	3	3	2	1	6
B. stearothermopelus	5	2	4	6	2	5	3	4	10	6	7.2

"–" represent "not active."

N-Benzylidene-4-(phenyldiazenyl)aniline (Ia). m. p.: 150°C, IR (KBr): 1410 cm^{-1} (N=N), 1620.2 (—C=N—); ^1H NMR: δ = 6.80 (d, *J* = 8.4 Hz, 2H, Ar-CH); 7.20 (s, 1H, Ar-CH); 7.50–7.70 (m, 7H, Ar-CH); 7.80 (d, *J* = 8.7 Hz, 2H, Ar-CH); 8.00 (d, *J* = 8.2 Hz, 2H, Ar-CH); 8.60 (s, 1H, N=CH); Anal. Calcd. For $C_{19}H_{15}N_3$: C, 79.98; H, 5.30; N, 14.73; Found: C, 79.50; H, 5.00; N, 14.50; Mass spectra, m/z = 285 (100%).

2-((4-(Phenyldiazenyl)phenylimino)methyl)phenol (Ib). m. p.: 165°C, IR (KBr): 1430 cm^{-1} (N=N), 1600 (—C=N—); ^1H NMR: δ = 6.70 (d, *J* = 8.8 Hz, 2H, Ar-CH); 7.0–7.60 (m, 9H, Ar-CH); 7.90 (d, J = 8.9 Hz, 2H, Ar-CH); 8.35 (s, 1H, —N=CH); 11.20 (s, 1H, Ar-OH); Anal. Calcd. For $C_{19}H_{15}ON_3$: C, 75.73; H, 5.02; N, 13.94; Found: C, 75.50; H, 5.00; N, 13.60; Mass spectra, m/z = 301 (100%).

N-(2-Nitrobenzylidene)-4-(phenyldiazenyl)aniline (Ic). m. p.: 160°C, IR (KBr): 1420 cm^{-1} (N=N), 1610 (—C=N—); ^1H NMR: δ = 6.50 (d, *J* = 8.1 Hz, 2H, Ar-CH); 7.20 (s, 1H, Ar-CH); 7.50–7.70 (m, 5H, Ar-CH); 7.80–8.00 (t, *J* = 7.9 Hz, 3H, Ar-CH); 8.20 (d, *J* = 8.8 Hz, 2H, Ar-CH); 8.64 (s, 1H, —N=CH); Anal. Calcd. For $C_{19}H_{14}N_4O_2$: C, 69.68; H, 4.27; N, 16.96; Found: C, 69.40; H, 4.10; N, 16.60; Mass spectra, m/z = 330.11 (100%).

N-(3-Nitrobenzylidene)-4-(phenyldiazenyl)aniline (Id). m. p.: 175°C, IR (KBr): 1430 cm^{-1} (N=N), 1650 (—C=N—); ^1H NMR: δ = 6.80 (d, *J* = 8.7 Hz,2H, Ar-CH); 7.20–8.30 (m, 10H, Ar-CH); 8.50 (s, 1H, Ar-CH); 8.60 (s, 1H, —N=CH); Anal. Calcd. For $C_{19}H_{14}N_4O_2$: C, 69.68; H, 4.27; N, 16.96; Found: C, 69.20; H, 4.00; N, 16.20 ; Mass spectra, m/z = 330 (100%).

N-(Furan-2-ylmethylene)-4-(phenyldiazenyl)aniline (Ie). m. p.: 180°C, IR (KBr): 1460 cm^{-1} (N=N), 1630 (—C=N—); ^1H NMR: δ = 6.50 (s, 1H, Ar-CH); 6.85 (d, *J* = 8.8 Hz, 2H, Ar-CH); 6.90 (s, 1H, Ar-CH); 7.20 (s, 1H, Ar-CH), 7.50 (s, 1H, —N=CH); 7.55–7.65 (m, 4H, Ar-CH); 7.70 (s, 1H, Ar-CH); 8.00 (d, *J* = 8.6 Hz, 2H, Ar-CH); Anal. Calcd. For $C_{17}H_{13}ON_3$: C, 74.17; H, 4.76; N, 15.26; Found: C, 74.00; H, 4.50; N, 15.00; Mass spectra, m/z = 275 (100%).

4-((4-(Phenyldiazenyl)phenylimino)methyl)phenol (If). m. p.: 155°C, IR (KBr): 1450 cm^{-1} (N=N), 1640 (—C=N—); ^1H NMR: δ = 6.85 (m, 4H, Ar-CH); 7.20 (s, 1H, Ar-CH); 7.55–7.60 (m, 4H, Ar-CH); 7.75–7.80 (d, *J* = 8.4 Hz, 2H, Ar-CH), 8.00 (d, *J* = 8.7 Hz, 2H, Ar-CH); 8.50 (s, 1H, —N=CH); 9.40 (s, 1H, Ar-OH); Anal. Calcd. For $C_{19}H_{15}N_3O$: C, 75.73; H, 5.02; N, 13.94; Found: C, 75.00; H, 4.90; N, 13.40; Mass spectra, m/z = 301.20 (100%).

N,N-dimethyl-4-((4-phenyldiazenyl)phenylimino) methyl)aniline (Ig). m. p.: 180°C, IR (KBr): 1400 cm^{-1} (N=N), 1620 (—C=N—); ^1H NMR: δ = 3.00 (s, 6H, —N(CH3)2); 6.80–6.85 (m, 4H, Ar-CH); 7.20 (s, 1H, Ar-CH); 7.50 (d, *J* = 8.6 Hz, 2H, Ar-CH); 7.60–7.68 (m, 4H, Ar-CH), 7.90 (d, *J* = 8.7 Hz, 2H, Ar-CH); 8.55 (s, 1H, —N=CH); Anal. Calcd. For $C_{21}H_{20}N_4$: C, 76.80; H, 6.14; N, 17.06; Found: C, 76.40; H, 6.00; N, 17.00; Mass spectra, m/z = 328 (100%).

N-(2-Chlorobenzylidene)-4-(phenyldiazenyl)aniline (Ih). m. p.: 195°C, IR (KBr): 1420 cm^{-1} (N=N), 1630 (—C=N—); ^1H NMR: δ = 6.80–7.50 (m, 4H, Ar-CH); 7.20–7.60(m, 7H, Ar-CH); 8.00 (d, *J* = 8.5 Hz, 2H, Ar-CH); 8.30(s, 1H, —N=CH); Anal. Calcd.For $C_{19}H_{14}N_3Cl$: C, 71.36; H, 4.41; N, 13.14; Found: C, 71.00; H, 4.20; N, 13.00; Mass spectra, m/z = 319 (100%).

N-(3-Bromobenzylidene)-4-(phenyldiazenyl)aniline (Ii). m. p.: 170°C, IR (KBr): 1440 cm^{-1} (N=N), 1650 (—C=N—); ^1H NMR: δ = 6.60–7.30 (t, *J* = 7.2 Hz, 3H, Ar-CH); 7.41 (s, 1H, Ar-CH); 7.25–7.80(m, 7H, Ar-CH); 8.20 (d, *J* = 8.8 Hz, 2H, Ar-CH); 8.70(s, 1H, —N=CH); Anal. Calcd.For $C_{19}H_{14}N_3Br$: C, 62.65; H, 3.87; N, 11.54; Found: C, 62.50; H, 3.60; N, 11.30; Mass spectra, m/z = 363.50 (100%).

N-(4-Chlorobenzylidene)-4-(phenyldiazenyl)aniline (Ij). m. p.: 190°C, IR (KBr): 1470 cm^{-1} (N=N), 1660 (—C=N—); ^1H NMR: δ = 6.80–7.45 (m, 4H, Ar-CH); 7.25–7.80(m, 7H, Ar-CH); 8.30 (d, *J* = 8.6 Hz, 2H, Ar-CH); 8.50(s, 1H, —N=CH); Anal. Calcd.For $C_{19}H_{14}N_3Cl$: C, 71.36; H, 4.41; N, 13.14; Found: C, 71.20; H, 4.30; N, 12.90; Mass spectra, m/z = 319 (100%).

General procedure for the preparation of 3-chloro-4-aryl-1-(4-(phenyldiazenyl) phenyl) azetidin-2-one (IIa-IIj). A mixture of Schiff base **Ia–Ij** (0.002 moles) and chloroacetic acid (0.002 moles) was dissolved in dichloromethane (10 mL) in stoppered conical flask, cooled, and stirred. In cold condition of the reaction mixture, triethylamine [TEA] (0.002 moles) was added in it, followed by dropwise addition of $POCl_3$ in dichloromethane (0.002 moles) with vigorous stirring. The reaction mixture was then stirred for additional 16 hr. The completion of the reaction was monitored by TLC. The reaction mixture was washed with water and dried over sodium sulphate. The products that were obtained after removing the solvent were purified from chloroform.

3-Chloro-4-phenyl-1-(4-(phenyldiazenyl)phenyl)azetidin-2-one (IIa). Yield: 80%; m. p.: 210°C; IR (KBr, cm^{-1}): 1364 (C—N); 1460 (N=N); 1760 (C=O β-lactam); ^1H NMR (300 MHz, $CDCl_3$) δ (ppm) = 5.10 (s, 1H, —N—CH), 5.40 (s, 1H, —CH—C=O), 6.80 (m, 4H, Ar-H); 7.25–7.40 (m, 6H, Ar-H); 7.60 (d, *J* = 8.4 Hz, 2H, Ar-H); 8.00 (d, *J* = 8.3 Hz, 2H, Ar-H). Anal. Calcd. for $C_{21}H_{16}N_3OCl$: C, 69.61; H, 4.41; N, 11.60; Found C, 69.50; H, 4.20; N, 11.40; Mass spectra, m/z = 361 (100%).

3-Chloro-4-(2-hydroxyphenyl)-1-(4-(phenyldiazenyl)phe-nyl) azetidin-2-one (IIb). Yield: 91%; m. p.: 220°C; IR (KBr, cm^{-1}): 2973 (OH), 1360 (C—N); 1567 (N=N); 1765 (C=O β-lactam); ^1H NMR ($CDCl_3$): δ(ppm) = 5.16 (s, 1H, —N—CH), 5.35 (s, 1H, —CH—C=O), 6.80–6.95 (m, 4H, Ar-H); 7.20 (s, 1H, Ar-H); 7.65 (t, *J* = 7.2 Hz, 3H, Ar-H); 7.90 (d, *J* = 8.1 Hz, 2H, Ar-H); 8.30 (t, *J* = 7.3 Hz, 3H, Ar-H); 9.50 (s, 1H, Ar-OH). Anal. Calcd. for $C_{21}H_{16}O_2N_3Cl$: C, 66.66; H, 4.23; N, 11.11; Found: C, 66.40; H, 4.10; N, 11.00; Mass spectra, m/z = 377 (100%).

3-Chloro-4-(2-nitrophenyl)-1-(4-(phenyldiazenyl)phenyl) azetidin-2-one (IIc). Yield: 95%; m. p.: 225°C; IR (KBr, cm^{-1}): 1340 (C—N); 1580 (N=N); 1755 (C=O β-lactam); ^1H NMR ($CDCl_3$): δ(ppm) = 5.00 (s, 1H, —N—CH), 5.30 (s, 1H, —CH—C=O), 6.90 (m, 4H, Ar-H); 7.10 (s, 1H, Ar-H); 7.40 (d, *J* = 8.1 Hz, 2H, Ar-H); 7.60 (d, *J* = 8.4 Hz, 2H, Ar-H); 7.70 (d, *J* = 8.1 Hz, 2H, Ar-H); 8.00 (t, *J* = 7.6 Hz, 3H, Ar-H); 8.30 (t, *J* = 7.4 Hz, 3H, Ar-H). Anal. Calcd. for $C_{21}H_{19}N_4O_3Cl$: C, 61.91; H, 3.68; N, 13.75; Found: C, 61.00.; H, 3.60; N, 13.60; Mass spectra, m/z = 406 (100%).

3-Chloro-4-(3-nitrophenyl)-1-(4-(phenyldiazenyl)phenyl) azetidin-2-one (IId). Yield: 90%; m. p.: 205°C; IR (KBr, cm^{-1}): 1330 (C—N); 1590 (N=N); 1740 (C=O β-lactam); ^1H NMR ($CDCl_3$): δ (ppm) = 5.10 (s, 1H, —N—CH), 5.40 (s, 1H, —CH—C=O), 6.70 (d, *J* = 8.5 Hz, 2H, Ar-H); 7.20 (s, 1H, Ar-H); 7.60–7.68 (m, 4H, Ar-H); 8.00–8.08 (t, *J* = 7.1 Hz, 3H, Ar-H); 8.18 (s, 1H, Ar-H); 8.20 (d, *J* = 8.4 Hz, 2H, Ar-

H). Anal. Calcd. for $C_{21}H_{15}N_4O_3Cl$: C, 61.91; H, 3.68; N, 13.75; Found: C, 61.20; H, 3.40; N, 13.50; Mass spectra, m/z = 405.9 (100%).

3-chloro-4-(furan-2-yl)-1-(4-(phenyldiazenyl)phenyl)az-etidin-2-one (IIe). Yield: 85%; m.p.: 225°C; IR (KBr, cm^{-1}): 1310 (C—N); 1560 (N=N); 1710 (C=O β-lactam); ^1H NMR ($CDCl_3$): δ(ppm) = 5.35 (s, 1H, —N—CH), 5.45 (s, 1H, —CH—C=O), 6.40–6.45 (t, *J* = 7.4 Hz, 3H, Ar-H); 6.80 (s, 1H, Ar-H); 7.10 (d, *J* = 8.1 Hz, 2H, Ar-H); 7.60 (d, *J* = 8.3 Hz, 2H, Ar-H); 7.70 (d, *J* = 8.2 Hz, 2H, Ar-H); 8.10 (d, *J* = 8.3 Hz, 2H, Ar-H). Anal. Calcd. for $C_{19}H_{14}O_2N_3Cl$: C, 64.77; H, 3.97; N, 11.93; Found: C, 64.60; H, 3.80; N, 11.80; Mass spectra, m/z = 351 (100%).

3-chloro-4-(4-hydroxyphenyl)-1-(4-(phenyldiazenyl) phenyl) azetidin-2-one (IIf) Yield: 75%; m. p.: 230°C; IR (KBr, cm^{-1}): 1345 (C—N); 1600 (N=N); 1755 (C=O β-lactam); ^1H NMR ($CDCl_3$): δ(ppm) = 5.00 (s, 1H, —N—CH), 5.40 (s, 1H, —CH—C=O), 6.70–6.80 (m, 4H, Ar-H); 7.00 (d, *J* = 8.4 Hz, 2H, Ar-H); 7.50 (d, *J* = 8.6 Hz, 2H, Ar-H); 7.90 (t, *J* = 7.6 Hz, 3H, Ar-H); 8.20 (d, *J* = 8.4 Hz, 2H, Ar-H); 9.30 (s, 1H, Ar-OH). Anal. Calcd. for $C_{21}H_{16}N_3O_2Cl$: C, 66.66; H, 4.23; N, 11.11; Found : C, 66.30; H, 4.20; N, 11.10 ; Mass spectra, m/z = 377 (100%).

3-chloro-4-(4-(dimethylamino)phenyl)-1-(4-(phenyldiaz-enyl) phenyl)azetidin-2-one (IIg). Yield: 95%; m. p.: 220°C; IR (KBr, cm^{-1}): 1335 (C—N); 1620 (N=N); 1765 (C=O β-lactam); ^1H NMR ($CDCl_3$): δ(ppm) = 2.90 (s, 6H, $N(CH_3)_2$) 5.15 (s, 1H, —N—CH), 5.30 (s, 1H, —CH—C=O), 6.70 (d, *J* = 8.3 Hz, 2H, Ar-H); 6.80 (d, *J* = 8.2 Hz, 2H, Ar-H); 7.10 (d, *J* = 8.2 Hz, 2H, Ar-H); 7.20 (s, 1H, Ar-H); 7.55 (d, *J* = 8.5 Hz, 2H, Ar-H); 8.00 (d, *J* = 8.4 Hz, 2H, Ar-H); 8.40 (d, *J* = 8.2 Hz, 2H, Ar-H); Anal. Calcd. for $C_{23}H_{21}ON_4Cl$: C, 68.14; H, 5.18; N, 13.82; Found: C, 68.10; H, 5.10; N, 13.60; Mass spectra, m/z = 404 (100%).

3-chloro-4-(2-chlorophenyl)-1-(4-(phenyldiazenyl) phenyl)-azetidin-2-one (IIh). Yield: 80%; m. p.: 240°C; IR (KBr, cm^{-1}): 1355 (C—N); 1660 (N=N); 1770 (C=O β-lactam); ^1H NMR ($CDCl_3$): δ(ppm) = 4.90 (s, 1H, —N—CH), 5.20 (s, 1H, —CH—C=O), 6.60 (d, *J* = 8.4 Hz, 2H, Ar-H); 7.20–7.30 (m, 4H, Ar-H); 7.60–7.75 (t, *J* = 7.5 Hz, 3H, Ar-H); 7.80 (d, *J* = 8.1 Hz, 2H, Ar-H); 8.20 (d, *J* = 8.3 Hz, 2H, Ar-H); Anal. Calcd. for $C_{21}H_{15}ON_3Cl_2$: C, 63.63; H, 3.78, N, 10.60; Found: C, 63.50; H, 3.60; N, 10.50; Mass spectra, m/z = 395 (100%).

4-(3-bromophenyl)-3-chloro-1-(4-(phenyldiazenyl) phenyl)-azetidin-2-one (IIi). Yield: 87%; m. p.: 245°C; IR (KBr, cm^{-1}): 1365 (C—N); 1630 (N=N); 1740 (C=O β-lactam); ^1H NMR ($CDCl_3$): δ(ppm) = 5.10 (s, 1H, —N—CH), 5.30 (s, 1H, —CH—C=O), 6.70 (d, *J* = 8.3 Hz, 2H, Ar-H); 7.20–7.30 (t, *J* = 7.6 Hz, 3H, Ar-H); 7.40–7.45 (d, *J* = 8.6 Hz, 2H, Ar-H); 7.60 (d, *J* = 8.4 Hz, 2H, Ar-H); 7.90 (d, *J* = 8.4 Hz, 2H, Ar-H); 8.40 (d, *J* = 8.5 Hz, 2H, Ar-H); Anal. Calcd. for $C_{21}H_{15}ON_3BrCl$: C, 57.14; H, 3.40; N, 9.52; Found: C, 57.10; H, 3.30; N, 9.40; Mass spectra, m/z = 439 (100%).

3-chloro-4-(4-chlorophenyl)-1-(4-(phenyldiazenyl) phenyl)-azetidin-2-one (IIj). Yield: 90%; m. p.: 250°C; IR (KBr, cm^{-1}): 1370 (C—N); 1650 (N=N); 1720 (C=O β-lactam); ^1H NMR ($CDCl_3$): δ(ppm) = 5.00 (s, 1H, —N—CH), 5.40 (s, 1H, —CH—C=O), 6.90 (d, *J* = 8.4 Hz, 2H, Ar-H); 7.20 (s, 1H, Ar-H); 7.40–7.50 (m, 4H, Ar-H); 7.60 (d, *J* = 8.2 Hz, 2H, Ar-H); 7.80 (d, *J* = 8.1 Hz, 2H, Ar-H); 8.50 (d, *J* = 8.3 Hz, 2H, Ar-H); Anal. Calcd. for $C_{21}H_{15}N_3OCl_2$: C, 63.63; H, 3.78; N, 10.60; Found: C, 63.40; H, 3.50; N, 10.30; Mass spectra, m/z = 395 (100%).

CONCLUSIONS

A new method for the synthesis of Schiff base **Ia–Ij** using microwave irradiation offers significant improvements over existing procedures. Also, this simple and reproducible technique affords the products with short reaction times, excellent yields, and without formation of undesirable side products. From data of antimicrobial activity, it could be observed that compounds of the series **IIa–IIj** showing good comparable activity against standard drugs.

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