Tropical Journal of Pharmaceutical Research April 2016; 15 (4): 821-826
ISSN: 1596-5996 (print); 1596-9827 (electronic)

Available online at http://www.tjpr.org
http://dx.doi.org/10.4314/tjpr.v15i4.22

Original Research Article

Synthesis and antibacterial profile of novel azomethine derivatives of β-phenylacrolein moiety

Sridevi Chigurupati[1]*, Neeraj Kumar Fuloria[1], Shivkanya Fuloria[1], Sundram Karupiah[1], Ravichandran Veerasamy[1], Appala Raju Nemala[2], Lim Jun Yi[1], Ang xiang Ilan[1] and Syed Adnan Ali Shah[3]

[1]AIMST University, Faculty of Pharmacy, Semeling, 08100 Bedong, Kedah, Malaysia, [2]Department of Pharmaceutical chemistry, Sultan–Ul–Uloom College of Pharmacy, Road No. 3, Banjara hills, Hyderabad, India, [3]Universiti Teknologi MARA (UiTM), Faculty of Pharmacy, Puncak Alam Campus, Selangor D.E, Malaysia

For correspondence:* ***Email:* *sridevi.phd@gmail.com;* ***Tel:*** *+6-014-9449846*

Received: 16 December 2015 *Revised accepted: 24 March 2016*

Abstract

Purpose: *To develop some novel molecules effective against antibiotic-resistant bacterial infections.*
Methods: *A series of azomethines (**SB-1** to **SB-6**) were synthesized from β-phenyl acrolein moiety. The structures of the synthesized compounds were confirmed on the basis of their UV ultra-violet (UV) spectroscopy (λ_{max}: 200 - 400 nm), Fourier transform infra-red (FTIR, vibrational frequency: 500-4000 cm^{-1}), ^{1}H nuclear magnetic resonance (NMR, chemical shift: 0 - 10 ppm), ^{13}C NMR (chemical shift: 0 - 200 ppm), mass spectrometry (m/z values: 0 - 500) and carbon hydrogen nitrogen (CHN) elemental analysis. The new compounds were screened for antibacterial activity by test-tube dilution and disc diffusion methods using gentamicin as reference standard.*
Results: *The structures of azomethine were in full agreement with their spectral data. Among all the synthesized compounds, compounds **SB-5** and **SB-6** exhibited the highest minimum inhibitory concentration (MIC) of 62.5 µg/mL. At MIC of 250 µg/mL, all compounds **SB-1** to **SB-6** displayed significant antibacterial activity, compared to gentamycin ($p < 0.05$). **SB-5** and **SB-6** were active against S. aureus, P. aeruginosa and K. pneumoniae; **SB-3** was active against B. subtilis and S. aureus. **SB-4** was active against P. aeruginosa and S. aureus while **SB-1** and **SB-2** were active against S. aureus.*
Conclusion: *The synthesized compounds possess antibacterial activities compared to those of gentamycin.*

Keywords: *Acrolein, Imines, Azomethine, Antibacterial, Gentamycin, Minimum inhibitory concentration*

Tropical Journal of Pharmaceutical Research is indexed by Science Citation Index (SciSearch), Scopus, International Pharmaceutical Abstract, Chemical Abstracts, Embase, Index Copernicus, EBSCO, African Index Medicus, JournalSeek, Journal Citation Reports/Science Edition, Directory of Open Access Journals (DOAJ), African Journal Online, Bioline International, Open-J-Gate and Pharmacy Abstracts

INTRODUCTION

Antimicrobial drugs occupy a unique niche in the history of medicine. The increased incidence of severe opportunistic bacterial infections in immunological deficient patients together with the development of resistance among pathogenic Gram-positive and Gram-negative bacteria have revealed great need to search for new compounds that are effective against antibiotic-resistant bacteria. Literature highlights the potentials of β-phenyl acrolein as an antimicrobial [1], anticancer [2] and flavoring agent for chewing gums [3]. Many investigators have observed the importance of azomethines for their antibacterial [4,5] antifungal [6], anti-proliferative [7,8] and antipyretic properties. It is evident that azomethines with aryl substituents are more stable and readily synthesized, whereas those containing alkyl substituents are

relatively unstable. Azomethines of aliphatic aldehydes are usually unstable and readily polymerizable, while those with aromatic aldehydes having effective conjugation are more stable [9].

In the present research work, a new series of azomethine derivatives of β-phenyl acrolein was synthesized (**SB-1** to **SB-6**) and screened for antibacterial activity against Gram-positive (*Bacillus subtilis* and *Staphylococcus aureus*) and Gram-negative (*Klebsiella pneumonia* and *Pseudomonas aeruginosa*) bacteria in order to generate potent and safer antibacterial agents.

EXPERIMENTAL

Materials

All the solvents and chemicals used were of analytical grade and obtained from Sigma-Aldrich and Merck Pvt Ltd, India and were used without further purification.

General procedure for synthesis of azomethine derivatives of β-phenyl acrolein

Equimolar concentration of β-phenyl acrolein (0.01 M) and substituted aromatic amines (0.01 M) were dissolved in 50 mL of anhydrous ethanol separately. Solution of substituted aromatic amine was then added drop-wise into β-phenyl acrolein solution in a conical flask. The mixture was made up to 150 mL with 95 % anhydrous ethanol, and 2 to 3 drops of triethylamine (basic catalyst) was added [10].The mixture was then stirred using magnetic stirrer at 60 to 70 °C for 6 h over a water bath. The reaction was monitored by TLC. The sample mixture was evaporated under pressure at 65 °C using rotatory evaporator [11,12]. The solid obtained on concentration of filtrate was recrystallized from aqueous ethanol to yield the pure compounds **SB-1** to **SB-6** (physical data are given in Table 1). The melting points of the compounds were determined on a Thoshniwal electric melting point apparatus and the values were uncorrected. The reaction was mentioned by TLC on Silica gel-GF 254 (Merck) coated plates. Spots of TLC were identified in iodine chamber.

Determination of minimum inhibitory concentration (MIC)

Test tube dilution method was used to determine minimum inhibitory concentration. One mL of sterilized media (Nutrient agar) was poured into sterile test tubes. One mL of 2000 µg/mL test solution was transferred in one tube and serially diluted to give concentrations of 1000, 500, 250 and 125 µg/mL. To all the test tubes, 0.1 mL of suspension of bacteria in saline was added and the tubes were incubated at 37 °C for 24 h. The growth in the tubes was observed visually for turbidity. MIC was determined with the lowest concentration of the sample that retarded the development of turbidity [13].

Table 1: Physical data for azomethine derivatives of β-phenyl acrolein, SB-1 to SB-6

Compound	Molecular formula	Crystal colour	Rf value
SB-1	$C_{15}H_{13}N$	Yellow	0.43
SB-2	$C_{16}H_{13}NO$	White	0.50
SB-3	$C_{15}H_{13}NO$	White	0.56
SB-4	$C_{16}H_{15}NO$	Yellow	0.62
SB-5	$C_{17}H_{15}NO_3$	Brown	0.54
SB-6	$C_{16}H_{13}NO_2$	Yellow	0.58

Disc-diffusion method

The disc diffusion method [14,15] was used to determine the antibacterial activity of azomethine using a 6-mm disc were prepared from Whatman's filter paper no.1. Azomethine solutions of varying concentrations ranging from 125, 250 and 500 µg/mL were prepared. Nutrient agar was prepared, sterilized and used as the growth medium for the culture of microorganisms; 20 mL of the sterilized medium was poured into each sterilized petri dish, covered and allowed to solidify. Thereafter, the 16-h old broth cultures of the specified microorganisms were used for disc diffusion studies [13].The sample, control and standard treated discs were air-dried at room temperature, to remove any residual solvent which might interfere with the determination, sterilized and inoculated. These plates were initially placed at low temperature for 1 h to allow the maximum diffusion of compounds from the test disc into the agar plate and later incubated at 37 °C for 24 h in case bacteria [16], after which the zone of inhibition will be easily observed.

Statistical analysis

Each experimental value is expressed as the mean ± standard error mean (n = 3). Statistical analysis was performed using GraphPad Prism 5.0 and data analyzed using one-way analysis of variance (ANOVA) for comparison between groups followed by Dunnett's multiple comparison test at a significant level of $p < 0.05$.

RESULTS

Chemistry

UV-Visible, IR, NMR and mass spectral data

supported the structures of all newly synthesized compounds. The spectral data for the newly synthesized compounds are as follows.

N-(3-phenylallylidene)benzamine **(SB-1):** Yield: 70 %; mp: 98-100 °C; Anal. Calcd. for $C_{15}H_{13}N$: C, 86.92; H, 6.32; N, 6.76 %. Found C, 86.89; H, 6.28; N, 6.66 %; IR (KBr, cm^{-1}): 3085 (=C-H stretching of aromatic ring), 3039 (=C-H stretching of alkenyl group), 1600 (-C=N stretching azomethine group), 1540-1600 (C=C- stretching of aromatic ring), 1320 (C-N, stretching of azomethine group); ^{1}H-NMR (500.1 MHz, $CDCl_3$-*d, δ*/ppm): 5.76 (1H, *t,J* = 9.5 Hz, H-2'), 6.52 (1H, *d,J* = 12 Hz, H-3'), 7.23 - 7.60 (10H, *m*, phenyl), 8.24 (1H, *d,J* = 7.8 Hz, H-1'); ^{13}C-NMR (100 MHz, $CDCl_3$, δ / ppm): 120.2 ($C_{2'}$), 123.4 (C_3& C_5), 126.3 ($C_{5'}$& $C_{9'}$), 127.5 (C_1), 128.4 ($C_{7'}$), 129.2 ($C_{6'}$& $C_{8'}$), 131.1 (C_2& C_6), 135.8 ($C_{4'}$), 139.2 ($C_{3'}$), 150.4 (C_4), 164.3 ($C_{1'}$); MS (*m/z,* (relative abundance, %)): 207 (M^+, 18.9), 107, 102, 77, 53, 51, 130 (BP, 100); UV-Vis (MeOH) (λ_{max}/nm): 353.

4-(3-Phenylallylideneamino)benzaldehyde **(SB-2)**: Yield: 79 %; mp: 130-134 °C; Anal. Calcd. for $C_{16}H_{13}NO$: C, 81.68; H, 5.57; N, 5.95 %. Found C, 81.56; H, 5.48; N, 5.87 %; IR (KBr, cm^{-1}): 3050 (=C-H stretching of aromatic ring), 3038 (=C-H stretching of alkenyl group), 2720, 2820 (C-H stretching of aldehyde group), 1725 (C=O Stretching of aldehyde group), 1658 (-C=N stretching azomethine group), 1540-1620 (C=C- stretching of aromatic ring), 1320 (C-N, stretching of azomethine group); ^{1}H-NMR (500.1 MHz, $CDCl_3$-*d, δ*/ppm): 5.81 (1H, t, *J* = 9.5 Hz, H-2'), 6.63 (1H, d, *J* = 12 Hz, H-3'), 7.5 - 7.9 (10H, *m,* phenyl), 8.32 (1H, d, *J* = 7.8 Hz, H-1'), 9.94 (s, 1H, aldehyde); ^{13}C-NMR (100 MHz, $CDCl_3$, δ / ppm): 120.5 ($C_{2'}$), 123.8 (C_3& C_5), 126.2 ($C_{5'}$& $C_{9'}$), 128.3 ($C_{7'}$), 129.4 ($C_{6'}$& $C_{8'}$), 131.8 (C_2& C_6), 135.4 ($C_{4'}$), 136.3 (C_1), 139.6 ($C_{3'}$), 155.2 (C_4), 164.6 ($C_{1'}$), 192.4 (-CHO); MS (*m/z*, (relative abundance, %)): 235 (M^+, 20.4), 158, 105, 102, 77, 53, 51 (BP, 100); UV-Vis (MeOH) (λ_{max}/nm): 307.

4-(3-Phenylallylideneamino)phenol **(SB-3)**: Yield: 80 %; mp: 120-130 °C; Anal. Calcd. for $C_{15}H_{13}NO$: C, 80.69; H, 5.87; N, 6.27 %. Found C, 80.56; H, 5.78; N, 5.82 %; IR (KBr, cm^{-1}): 3640 (Broad, O-H Str), 3055 (=C-H stretching of aromatic ring), 3038 (=C-H stretching of alkenyl group), 1668 (-C=N stretching azomethine group), 1540-1600 (C=C- stretching of aromatic ring), 1320 (C-N, stretching of azomethine group); ^{1}H-NMR (500.1 MHz, $CDCl_3$-*d, δ*/ppm): 5.4 (1H, *s*, -OH, D_2O exchangeable), 5.72 (1H, *t*, *J* = 9.5 Hz, H-2'), 6.59 (1H, *d,J* = 12 Hz, H-3'), 7.4 - 7.8 (10H, *m,* phenyl), 8.29 (1H, *d,J* = 7.8 Hz, H-1'); ^{13}C NMR (100 MHz, $CDCl_3$, δ / ppm): 118.4 (C_2& C_6), 120.3 ($C_{2'}$), 123.9 (C_3& C_5), 126.5 ($C_{5'}$& $C_{9'}$), 128.4 ($C_{7'}$), 129.2 ($C_{6'}$& $C_{8'}$), 135.8 ($C_{4'}$), 139.2 ($C_{3'}$), 141.6 (C_4), 157.2 (C_1), 164.3 ($C_{1'}$); MS (*m/z,* (relative abundance, %)): 223 (M^+, 18.5), 146, 130, 102, 93, 77, 53, 51 (BP, 100); UV-Vis (MeOH) (λ_{max}/nm): 302.

4-Methoxy-N-(3-phenylallylidene)benzamine **(SB-4)**: Yield: 87 %; mp: 140-143 °C; Anal. Calcd. for $C_{16}H_{15}NO$: C, 80.98; H, 6.37; N, 5.90 %. Found C, 80.96; H, 6.33; N, 4.89 %; 80.59; IR (KBr, cm^{-1}): 3052 (=C-H stretching of aromatic ring), 3037 (=C-H stretching of alkenyl group), 2934, 2876 (C-H, Str), 1658 (-C=N stretching azomethine group), 1540-1620 (C=C- stretching of aromatic ring), 1320 (C-N, stretching of azomethine group), 1255 (C-O-C, Str); ^{1}H-NMR (500.1 MHz, $CDCl_3$-*d, δ*/ppm): 3.73 (3H, *s*, CH_3), 5.74 (1H, *t*, *J* = 9.5 Hz, H-2'), 6.56 (1H, *d*, *J* = 12 Hz, H-3'), 7.3 - 7.75 (10H, *m*, phenyl), 8.36 (1H, *d*, *J* = 7.8 Hz, H-1'); ^{13}C-NMR (100 MHz, $CDCl_3$, δ / ppm): 56.3 (-CH_3), 116.2 (C_3& C_5), 120.4 ($C_{2'}$), 123.7 (C_3& C_5), 126.2 ($C_{5'}$& $C_{9'}$), 126.9 ($C_{7'}$), 128.1 ($C_{6'}$& $C_{8'}$), 135.8 ($C_{4'}$), 139.3 ($C_{3'}$), 141.2 (C_4), 160.4 (C_1), 164.3; MS (m/z, (relative abundance, %)): 237 (M^+, 19.0), 160, 130, 107, 102, 77, 53, 51 (BP, 100); UV-Vis (MeOH) (λ_{max}/nm): 306.

4-Methoxy-2-(3-phenylallylideneamino)benzoic acid **(SB-5):** Yield: 80 %; mp: 150-154 °C; Anal. Calcd. for $C_{17}H_{15}NO_3$: C, 72.58; H, 5.37; N, 4.98 %. Found C, 72.52; H, 5.39; N, 4.92 %; IR (KBr, cm^{-1}): 3400-2500 (OH Str of COOH), 3057 (=C-H stretching of aromatic ring), 3038 (=C-H stretching of alkenyl group), 2500-2900 (O-H of COOH, Str), 1720 (C=O of COOH Str), 1658 (-C=N stretching azomethine group), 1540-1620 (C=C- stretching of aromatic ring), 1280 (C-O stretching of COOH group), 1323 (C-N, stretching of azomethine group), 1250 (C-O-C stretching of ether group); ^{1}H-NMR (500.1 MHz, $CDCl_3$-*d, δ*/ppm): 3.74 (3H, *s,* OCH_3), 5.76 (1H, *t,J* = 9.5 Hz, H-2'), 6.8 (1H, *d,J* = 12 Hz, H-3'), 7.64 - 7.92 (10H, *m,* phenyl), 8.38 (1H, *d,J* = 7.8 Hz, H-1'), 11.00 (1H, *s,* COOH); ^{13}C-NMR (100 MHz, $CDCl_3$, δ / ppm): 56.8 (-CH_3), 108.4 (C_5), 109.1 (C_3), 112.6 (C_1), 119.8 ($C_{2'}$), 126.1 ($C_{5'}$& $C_{9'}$), 127.2 ($C_{7'}$), 128.6 ($C_{6'}$& $C_{8'}$), 132.4 (C_2), 135.7 ($C_{4'}$), 138.3 ($C_{3'}$), 150.5 (C_4), 163.2 ($C_{1'}$), 167.8 (C_6) , 169.6 (-COOH); MS (*m/z,* (relative abundance, %)): 281 (M^+, 20.7), 204, 151, 130, 102, 77, 53, 51 (BP, 100); UV-Vis (MeOH) (λ_{max}/nm): 338.

4-(3-Phenylallylideneamino)benzoic acid **(SB-6):** Yield: 86 %; mp: 130-140 °C; Anal. Calcd. for $C_{16}H_{13}NO_2$: C, 76.42; H, 5.29 N, 5.52 %. Found

Table 2: Minimum inhibitory concentration (MIC) of β-phenyl acrolein derivatives, **SB-1** to **SB-6**

Compound	Minimum inhibitory concentration (MIC, µg/mL)			
	Gram positive bacteria		***Gram negative bacteria***	
	B. subtilis	*S. aureus*	*P. aeruginosa*	*K. pneumoniae*
SB-1	250	62.5	250	250
SB-2	125	62.5	125	250
SB-3	62.5	62.5	250	250
SB-4	125	62.5	62.5	250
SB-5	125	62.5	62.5	62.5
SB-6	125	62.5	62.5	62.5

Table 3: Zone of inhibition of β-phenyl acrolein derivatives, **SB-1** to **SB-6**

Compound	Zone of inhibition (mm, 250µg/mL)			
	Gram positive bacteria		**Gram negative bacteria**	
	B. subtilis	***S. aureus***	***P. aeruginosa***	***K. pneumoniae***
SB-1	8.5±0.28	9.9±0.57*	8.6 ±0.33	7.8±0.17
SB-2	10.1±0.72	10.8±0.92*	7.3±0.33	7.3±0.67
SB-3	12.0± 0.57*	10.0±1.00*	8.3±0.33	7.3±0.33
SB-4	9.6±0.33	10.6 ±0.33*	10.3±0.33*	6.3±0.33
SB-5	10.3±0.33	11.3 ±0.33*	10.6 ± 0.33*	12.0+0.10*
SB-6	9.6±0.33	10.3 ±0.88*	11.6± 0.88*	12.3±0.57*
Gentamicin	12.3±0.33	9.3±0.57	10.0 ±0.57	12.6±0.67

**p<0.05, compared to Gentamycin (one-way ANOVA followed by Dunnett's multiple comparison test (p < 0.05.); values are mean ± SEM (n = 3)*

C, 72.51; H, 5.32N, 4.88 %; IR (KBr cm^{-1}): 3052 (=C-H stretching of aromatic ring), 3036 (=C-H stretching of alkenyl group), 2926, 2872 (C-H stretching of methyl group), 1668 (-C=N stretching azomethine group), 1540-1600 (C=C- stretching of aromatic ring), 1320 (C-N, stretching of azomethine group); ^{1}H-NMR (500.1 MHz, $CDCl_3$-*d,δ*/ppm): 5.85 (1H, *t*, *J* = 9.5 Hz, H-2'), 6.76 (1H, *d*, *J* = 12 Hz, H-3'), 7.64 - 7.92 (10H, *m,*phenyl), 8.41 (1H, *d*, *J* = 7.8 Hz, H-1'), 11.00 (1H, *s,* COOH); ^{13}C-NMR (100 MHz, CDCl3, δ / ppm): 120.4 ($C_{2'}$), 123.5 (C_3& C_5), 126.7 ($C_{5'}$& $C_{9'}$), 127.4 ($C_{7'}$), 128.4 ($C_{6'}$& $C_{8'}$), 129.2 (C_1), 131.2 (C_2& C_6), 135.9 ($C_{4'}$), 139.4 ($C_{3'}$), 155.4 (C_4), 164.8 ($C_{1'}$), 169.6 (-COOH); MS (*m/z,* (relative abundance, %)): 251 (M^+, 32.6), 174, 130, 121, 102, 77, 53, 51 (BP, 100); UV-Vis (MeOH) (λ_{max}/nm): 307.

Antibacterial activity

The newly synthesized β-phenyl acrolein derivatives were tested for their antibacterial potential against *B. subtilis* and *S. aureus*, *K. pneumoniae*, and *P. aeruginosa*, using gentamycin as standard. The results are given in Table 2 and Table 3.

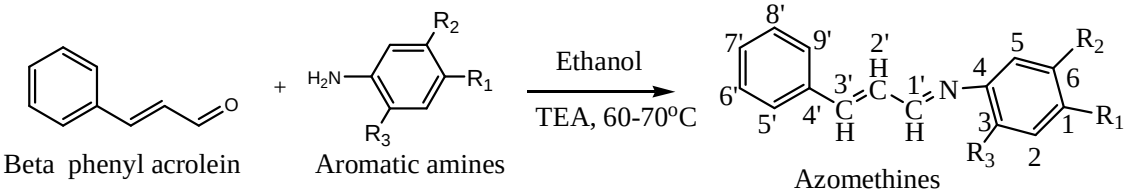
DISCUSSION

Equimolar concentration of β-phenyl acrolein and substituted aromatic amines in the presence of basic catalyst, triethylamine resulted in formation of azomethine derivatives of β-phenyl acrolein moiety shown in Figure 1.

The λ_{max} for the newly synthesized azomethines was found to be in range from 300-440 nm. The IR stretch at around 1650-1680 cm^{-1} showed the C=N bond formation. The formation of azomethines was identified by the presence of triplet between 5.7 to 5.8 ppm, in proton NMR spectra. All other aliphatic and aromatic protons were observed within the expected regions. The novel compounds were further confirmed by their characteristic mass fragment spectra. The mass fragment pattern of compound **SB-4** given in Figure 2, displayed parent ion peak at 237, base peak at 51, and different fragment peaks at 160, 130, 107, 102, 77, and 53.

Similarly, all the new compounds were characterized. This part confirmed the synthesis of a series of six new azomethines derivatives of β-phenyl acrolein.

The antibacterial potential of newly synthesized molecules was estimated by tube dilution and disc diffusion method; using Gram positive bacteria (*Bacillus subtilis* and *Staphylococcus aureus*) and Gram negative bacteria (*Klebsiella pneumoniae* and *Pseudomonas aeruginosa*). Tube dilution method depends upon the inhibition of growth of a microbial culture in a uniform solution of antibiotic in a fluid medium that is favorable to its rapid growth in the absence of the antibiotic [17]. In this method minimum inhibitory



Where,

R1 = -H,	R2 = -H,	R3 = -H,	for SB-1
R2 = -CHO,	R2 = -H,	R3 = -H,	for SB-2
R1 = -OH,	R2 = -H,	R3 = -H,	for SB-3
R1 = -OCH_3,	R2 = -H,	R3 = -H,	for SB-4
R1 = -H,	R2 = -OCH_3,	R3 = -COOH,	for SB-5
R1 = -COOH,	R2 = -H,	R3 = -H,	for SB-6

Figure 1: Scheme for synthesis of azomethine derivatives of β-phenyl acrolein moiety

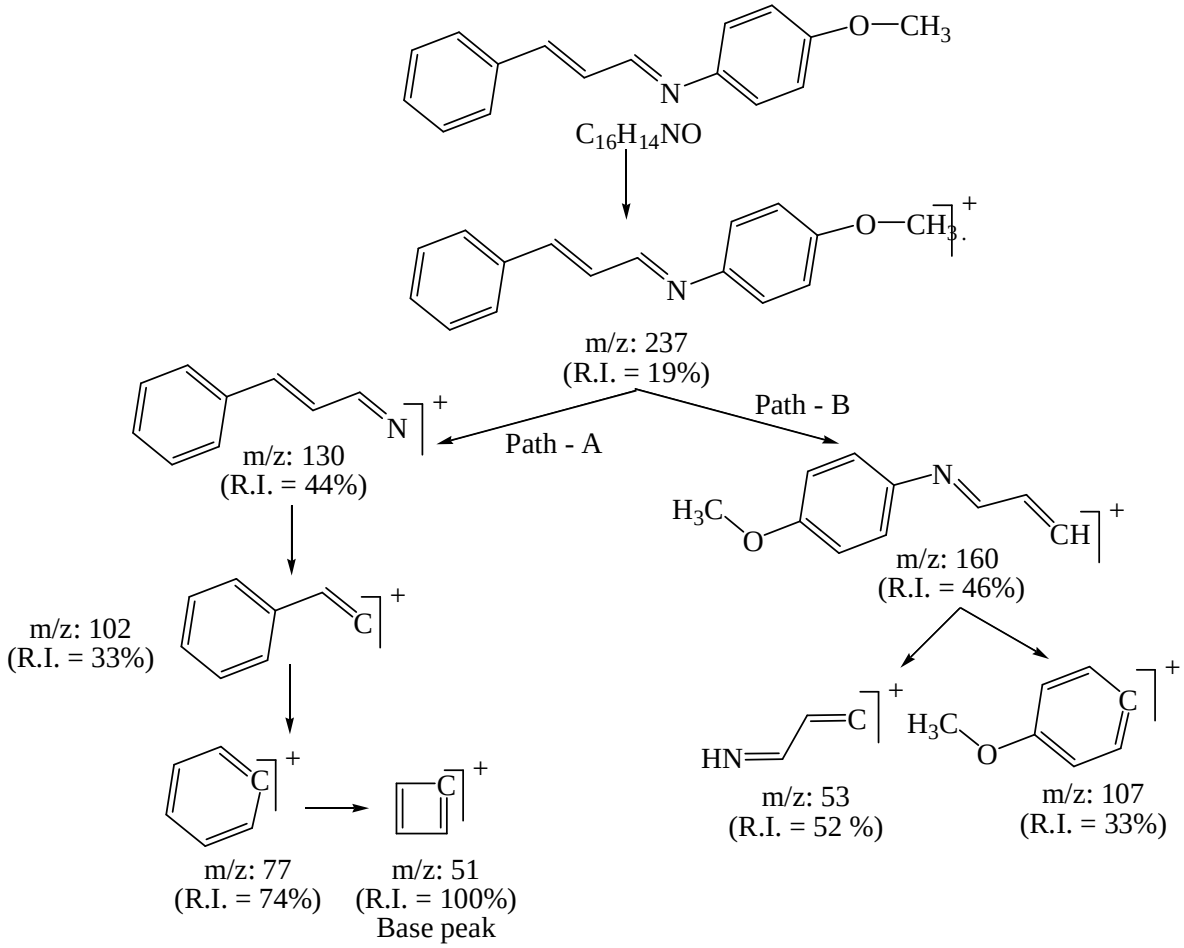


Figure 2: Mass fragmentation pattern of SB-4

concentration of the test compounds was determined. Gentamycin was used as a standard drug [18].

As per the minimum inhibitory concentration study results given in Table 2 and Table 3, among all synthesized compounds, **SB-5** and **SB-6** displayed highest MIC value of 62.5 µg/ml. The zone of inhibition experiment, revealed that at MIC of 250 µg/ml, all compounds **SB-1** to **SB-6** showed significant antibacterial activity ($p < 0.05$). **SB-5** and **SB-6** were active against *S. aureus*, *P. aeruginosa* and *K. pneumoniae*; **SB-3** was active against *B. subtilis* and *S. aureus*, **SB-4** was active against *P. aeruginosa* and *S. aureus*. **SB-1** and **SB-2** were active against *S. aureus*. The antimicrobial results proved that all

synthesized azomethines of β-phenyl acrolein moiety possess significant antibiotic potential.

CONCLUSION

β-Phenyl acrolein derivatives have been successfully synthesized and appear to be a novel and important class of antibacterial agents against Gram-positive and Gram-negative bacteria including *S. aureus*, *P. aeruginosa*, and *K. pneumonia*. The synthetic route and antibacterial potential of the compounds may be useful in guiding future efforts to synthesize new compounds with improved antibacterial activity.

ACKNOWLEDGEMENT

The authors are thankful to AIMST University, Malaysia, for providing funds via a grant, and also for the facilities to carry out the research. The authors are also thankful to UiTM, Malaysia for providing technical support in generating the analytical data.

CONFLICT OF INTEREST

No conflict of interest associated with this work.

AUTHORS' CONTRIBUTION

We declare that this work was done by the author(s) named in this article and all liabilities pertaining to claims relating to the content of this article will be borne by them. Sridevi Chigurupati, Neeraj kumar Fuloria and Ravichandran Veerasamy carried out the synthetic work, Syed adnan ali Shah, Shivkanya Fuloria and Sundram Karupia performed the analytical work while Appala raju Nemala, Lim jun Yi and Ang xiang Ilan carried carried out the antibacterial activities. All authors approved the manuscript for publication.

REFERENCES

1. *Yossa N, Patel J, Dumitru M, Patricia M, Charles M. Antibacterial activity of Cinnamaldehyde and Sporan Against Escherichia Coli O157:H7 and Salmonella. J Food Process Preserv 2012; 38: 749-757.*
2. *Cabello CM, Bair WB 3rd, Sarah Lamore D, Stephanie, L, Alexandra Bause S, Sara A, Georg Wondrak, T. The Cinnamon-derived Michael Acceptor Cinnamic Aldehyde Impairs Melanoma Cell Proliferation, Invasiveness, and Tumor Growth. Free Radic Biol Med 2009; 46: 220-231.*
3. *Karl-Georg F, Franz-Josef H, Johannes P, Wilhelm P, Dietmar S, Kurt B, Dorothea G, Horst S. Flavors and Fragrances in Ullmann's Encyclopedia of Industrial Chemistry, Wiley-VCH, Verlag GmbH & Co. 2002; p 141.*
4. *Amin RM, Abdel-Kader NS, El-Ansary AL. Microplate assay for screening the antibacterial activity of Schiff bases derived from substituted benzopyran-4-one. SpectrochimActa. Part A 2012; 9: 517-525.*
5. *Neelakantan M, Esakkiammal M, Mariappan S, Dharmaraja J, Jeyakumar T. Synthesis, Characterization and Biocidal Activities of Some Schiff Base Metal Complexes. Indian J Pharm Sci 2010; 72: 216-222.*
6. *Fugu MB, Ndahi NP, Paul BB, Mustapha AN. Synthesis, characterization, and antimicrobial studies of some vanillin schiff base metal (II) complexes. J Chem Pharm Res 2013; 5: 22-28.*
7. *Song WJ, Cheng JP, Jiang DH, Guo L, Cai MF, Yang HB, Lin, QY. Synthesis, interaction with DNA and antiproliferative activities of two novel Cu(II) complexes with Schiff base of benzimidazole. Spectrochimica acta. Part A 2014; 121: 70-76.*
8. *Liang C, Xia J, Lei D, Li X, Yao Q, Gao J. Synthesis, in vitro and in vivo antitumor activity of symmetrical bis-Schiff base derivatives of isatin. Euro J Med Chem 2014; 74: 742-750.*
9. *Zoubi WA. Biological Activities of Schiff Bases and Their Complexes: A Review of Recent Works. Int J Org Chem 2013; 3: 73-95.*
10. *Amirnasar M, Mahmoudkhani AH, Gorji A, Dehghanpour S, Bijanzadeh HR. Cobalt(II), nickel(II), and zinc(II) complexes with bidentate N,N'-bis(phenylcinna-maldehyde)-1,2-diiminoethane Schiff base: synthesis and structures. Polyhedron 2002; 21: 2733-2742.*
11. *Juan S, Yong Y, Gui-Hua S, Zhi-Bo Y Hai-Liang Z. Synthesis, molecular modeling and structural characterization of vanillin derivatives as antimicrobial agents. J Mol Struct 2013; 1039: 214-218.*
12. *Chigurupati S. Designing new vanillin schiff bases and their antibacterial Studies. J Med Bioeng 2015; 4: 363-366.*
13. *Sridevi CH, Balaji K, Naidu A, Sudhakaran R. Antimicrobial evaluation and synthesis of some phenylpyrazolo benzothiazolo quinoxaline derivatives. J Chem 2009; 6: 866-870.*
14. *Delignette-Muller ML, Flandrois, JP. An accurate diffusion method for determining bacterial sensitivity to antibiotics. J Antimicrob Chemother 1994; 34: 73-81.*
15. *Jessy EM, Thirugnana Sambanthan A, Alex J, Sridevi CH, Srinivasan KK. Synthesis and biological evaluation of some novel quinazolones. Indian J Pharm Sci 2007; 69: 476-478.*
16. *Sridevi CH, Kannan MM, Abhinayani G, Sravya N. Designing and Biological Evaluation of new benzimidazole compounds. Chem Sci Trans 2013; 2: 922-926.*
17. *Cappucino JG.; Sherman N. Microbiology - A Laboratory Mannual,4th edn, Addison Wesley Longmann, New York, USA; 1999; p 45.*

18. *Bala S, Sharma N, Kajal A, Kamboj S. Design, Synthesis, Characterization, and Computational Studies on Benzamide Substituted Mannich Bases as Novel, Potential Antibacterial Agents. Sci World J 2014; 2014: 1-9.*