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Research Article

Synthesis of some 2-azitidinones (β-lactams) as antibiotic mimics and screening of their antimicrobial activity

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ABSTRACT

2-Azetidinones (β-lactams) possess broad and potent bioactivity owing to the presence of lactam rings. As evidence has shown, it is one of the most critical biological frameworks. Some new 2-azetidinones have been synthesized from corresponding Schiff bases using different amines and aldehydes. All compounds (Schiff bases and β- lactams) were synthesized for comparison research using conventional and microwave techniques. The microwave approach has been found to reduce reaction time and boost yield drastically. Analysis combining elemental (C, H, and N) and spectroscopic approaches (NMR, IR, and UV) have been applied to ensure the Schiff bases constitution and corresponding β-lactams constitution. The newly synthesized compound's antibacterial action was estimated opposite to one gram-positive and one gram-negative bacteria. One compound (A-03) among synthesized 2-azitidinones was shown significant activity against the gram-positive bacteria. The other synthesized compounds had no substantial activity on either of the microorganisms.

Introduction

Recently, organic chemists have emphasized finding simple, innovative, non-hazardous ways to synthesize compounds. Growing environmental awareness necessitates the creation of efficient, economical methods where fewer risky consequences are undesirable. Carbon-nitrogen double bond is crucial to the synthesis of organic compounds. This can be done by generating Schiff bases (imines) by reacting aldehydes with amines in an acidic atmosphere. Due to their remarkable biological activity, Schiff bases have gained much attention throughout the organic synthesis field (Abdulla and Fuhr, 1975). It is known that azetidinones, a kind of antibiotic with a *β*-lactam structure, have intriguing biological features. Numerous 3-chloro monocyclic *β*-lactams have potent antimicrobial (Calderon and Sabundayo, 2007), antibacterial (Doherty et al., 1994), antiphlogistic (Durckheimer et al., 1985), antiepileptic (Feigelson et al., 1993), and anti-tubercular (Georg et al., 1992) results. They positively impact the central nervous system and operate as enzyme inhibitors (Vander et al., 1991; Palomo et al., 1999; Singh, 2003). They are azetidinones' carbonyl derivatives with a carbonyl group at position 2. These can, as an alternative, be termed β-lactams or 2-azetidinone (Hossain et al., 2009).

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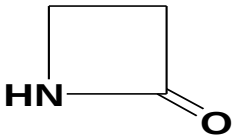


2-Azetidinone, the simplest β-lactam

Utilizing the related strain energy, azetidin-2-one, a four-membered cyclic lactam (*β*-lactam) framework, was identified as an advantageous component for synthesizing numerous chemical substances. One of the most fundamental and adaptable processes for producing a wide range of structurally different 2-azetidinone derivatives is the Staudinger reaction (ketene-imine cycloaddition reaction) (Khalafallah et al., 1995; Nantasenamat et al., 2009). Additionally, the enolate-imine condensation and cyclization reactions can be used to synthesize azetidin-2-ones. Additionally, it produces several *β*-lactam antibiotics (Parikh et al., 2000; Waksman, 1947).

Material and Methods

Physical Measurements

John's electrothermal melting point equipment. IR spectra were captured on a KBr disc using a NICOLET iS10 IR spectrophotometer. The Department of Pharmaceutical Sciences at Tokushima University in Japan recorded ^{1}H-NMR spectra using a 400 MHz AVANCE Bruker NMR spectrometer with $CDCl_3$ (solvent) and TMS (internal standard). The units of change (Chemical) are measured in parts per million (ppm). The device Elementar (Model No.Vario El Cube) carried out the elemental analysis for carbon, hydrogen, and nitrogen. By the Shimadzu UV-1800 UV spectrophotometer, ultraviolet spectrum data were collected. The pure identification of the compounds was verified using TLC and silica gel-G. An iodine chamber produced the spots, and an ultraviolet lamp was used to see them.

Representative procedure for the Synthesis of Schiff Bases (2a-h)

A small amount of glacial acetic acid (a few drops) was added to 30 ml of ethanol to dissolve the 4-methylaniline (0.01 mol). The same reaction mixture added 0.01 mol of the suitable aromatic aldehyde, such as 4-hydroxybenzaldehyde. The mixture for the reaction was then refluxed for 2-4 hours. TLC was used to track the reaction's development at a solvent ratio of 1:4 EtOAc to cyclohexane. It was cooled and neutralized with 5% $NaHCO_3$ (aq. solution) once the reaction was finished. The reaction mixture was then placed onto crushed ice and refrigerated for the following day. A solid compound was filtered, water washed, and vacuum desiccators were used to dry it. The desired compounds (2a-h) were then obtained by recrystallizing the end products with ethyl acetate from the resultant products. Most of the reaction was likewise conducted in a microwave-irradiated environment. Although the other parameters, such as reaction time, solvent quantity, etc., were much better, the yields were comparable (Tables 1 and 2).

The characterization of all Schiff bases was done using spectral methods, which are as follows.

4-Methyl-N-[(4-hydroxyphenyl)methyl-idene] aniline(2a)

Yield: 97% (light brown solid)

Melting point: 250°C

^{1}H- **NMR (ppm)($CDCl_3$): δ** 2.25 (s, 3H, CH_3), 8.32 (s, 1H, -CH=N), 6.79 (d, 2H, J_o = 7.5 Hz, H-2′), 7.02 (d, 2H, J_o = 7.5 Hz, H-3′), 7.10 (d, 2H, J_o = 8.0 Hz, H-3″), 7.66 (d, 2H, J_o = 8.0 Hz, H-2″), 8.68 (s, 1H, Ar-OH).

IR, υ_{max}, KBr (cm^{-1}): ν 3454 (O-H str.), 3025 (Ar. C-H str.), 2916, 2858 (Ali. C-H str.), 1609 (m, C=N str.), 1576, 1509 (m, C=C Ar.), 1286, 1163(s, C-N str.), 839, 818 (substituted phenyl ring).

UV, λ_{max}: 280 nm, 320 nm

Elemental Analysis, $C_{14}H_{13}NO$: Theoretical: C, 79.62; H, 6.16; N, 6.63; Experimental Found: C, 79.52; H, 6.13; N, 6.54.

4-Methyl-N-[(4-dimethylaminophenyl)methyl-dene]aniline(2b)

Yield: 90% (yellow solid)

Melting point:134°C

IR, υ_{max}, KBr ($cm^{-1)}$: 3049 (Ar. C-H str.), 2907, 2853 (Ali. C-H str.), 1614 (m, C=N str.), 1588, 1553,

1532, 1503 (m, C=C str. Ar.), 1314, 1234, 1174 (C-N str.), 884, 821 (substituted phenyl ring).

UV, λ_{max}: 350 nm

Elemental Analysis, $C_{16}H_{18}N_2$: Theoretical:C, 80.67; H, 7.56; N, 11.76; Experimental Found: C, 80.17; H, 7.53; N, 11.66.

4-Methyl-N-[(4-nitrophenyl)methylidene]aniline (2c)

Yield: 92% (pale yellow solid)

Melting point:139°C

IR, υ_{max}, KBr (cm^{-1}): 3099 (Ar. C-H str.), 2951, 2855 (Ali. C-H str.), 1624, 1598 (m, C=N str.), 1584, 1338 (NO_2), 1513, 1504 (s, C=C ring str.), 1189, 1107 (C-N str.), 854, 821 (substituted phenyl ring).

λ_{max}: 294nm, 354 nm

Elemental Analysis, $C_{14}H_{12}N_2O_2$: Theoretical:C, 70.00; H, 5.00; N, 11.67; Experimental Found: C, 69.98; H, 5.03; N, 11.56.

4-Methoxy-N-[(4-hydroxyphenyl)methyldene]aniline (2d)

Yield: 87% (greenish-yellow)

Melting point: 242°C.

^{1}H-NMR ($CDCl_3$) δ_H (ppm):3.78 (s, 3H, OCH_3), 8.39 (s,1H, -CH=N), 6.84 (d, 2H, J_o =7.7Hz, H-2′), 6.91(d, 2H, J_o=7.7Hz, H-3′), 7.16(d, 2H, J_o=8.4Hz, H-3″),7.71(d,2H, J_o=8.4Hz, H-2″),8.79(s,1H, Ar-OH).

IR, υ_{max}, KBr(cm^{-1}): 3447 (O-H str. H-bond), 3043 (Ar. C-H str.), 2922, 2853 (Ali. C H str.), 1605 (s, C=N str.), 1577, 1515, 1503 (s, C=C ring str.), 1283, 1244, 1191, 1163 (s, C-N str.), 841, 823 (substituted phenyl ring).

UV λ_{max}(log ε) (EtOAc): 283 (1.878), 329 (1.715).

Elemental Analysis, $C_{14}H_{13}NO_2$: Theoretical:C, 74.01; H, 5.73; N,6.17; Experimental Found: C, 74.11; H, 5.60; N, 6.22.

4-Methoxy-N- [(4-dimethylamino phenyl) methylidene]aniline (2e)

Yield: 82% (brown solid)

Melting point: 152°C.

^{1}H-NMR ($CDCl_3$) δ_H (ppm): 3.82 (s, 3H, OCH_3), 3.04 (s,6H, $N(CH_3)_2$), 8.34(s,1H-CH=N), 6.73 (d,2H, J_o=7.2Hz, H-2′),6.91(d, 2H, J_o=7.2Hz, H-3′), 7.19 (d, 2H, J_o=8.3Hz, H-3″), 7.75(d, 2H, J_o=8.3 Hz, H-2″).

IR, υ_{max}, KBr (cm^{-1}): 3000(Ar. C-H str.), 2953, 2883(Ali. C-H str.), 1608 (s, C=N str.), 1553, 1524, 1500 (C=C ring str.), 1254, 1298, 1286, 1239, 1177 (C-N str.), 840, 819 (substituted phenyl ring).

UV λ_{max} (log ε) (EtOAc): 355(0.717).

Elemental Analysis, $C_{16}H_{18}N_2O$: Theoretical:C, 75.59; H, 7.09; N, 11.02; Experimental Found: C, 75.60; H, 7.00; N, 11.16.

4-Methoxy-N-[(4-nitrophenyl)methyldene]aniline(2f)

Yield:*98%*

Melting point: 150°C

^{1}H-NMR ($CDCl_3$) δ_H (ppm): 3.80 (s, 3H, OCH_3), 8.58 (s, 1H, -CH=N), 6.97 (d, 2H, J_o =7.9 Hz, H-2′), 7.30 (d, 2H, J_o=7.9Hz, H-3′), 8.06 (d, 2H, J_o=8.8Hz, H-3″), 8.31 (d, 2H, J_o=8.8Hz, H-2″).

IR, υ_{max}, KBr (cm^{-1}): 3081 (Ar. C-H str.), 2957, 2837 (Ali. C-H str.), 1598 (m, C=N str.),

1514 (s, C=C ring str.), 1568(NO_2), 1245, 1191, 1168 (C-N str.), 888, 835 (substituted phenyl ring).

UV λ_{max}(log ε) (EtOAc): 257(1.497), 373(1.650).

Elemental Analysis, $C_{14}H_{12}O_3N_2$: Theoretical:C, 65.63; H, 4.69; N, 10.94; Experimental Found: C, 65.60; H, 4.66; N, 10.88.

4-Methyl-N-anthranylmethylideneaniline (2g)

Yield: 77% (yellowish orange solid),

Melting point: 108°C

IR, υ_{max}, KBr (cm^{-1}): 3046 (Ar. C-H str.), 2917, 2857 (Ali. C-H str.), 1622, 1609 (C=N str.), 1587, 1518, 1498 (C=C ring str.), 1254, 1203, 1157 (C-N str.), 845, 810 (substituted phenyl ring).

λ_{max}: 259nm

Elemental Analysis, $C_{22}H_{17}N_2$: Theoretical:C, 89.49; H, 5.76; N, 4.75; Experimental Found: C, 89.40; H, 5.58; N, 4.60.

4-Methoxy-N-anthranylmethylideneaniline(2h)

Yield: 95%

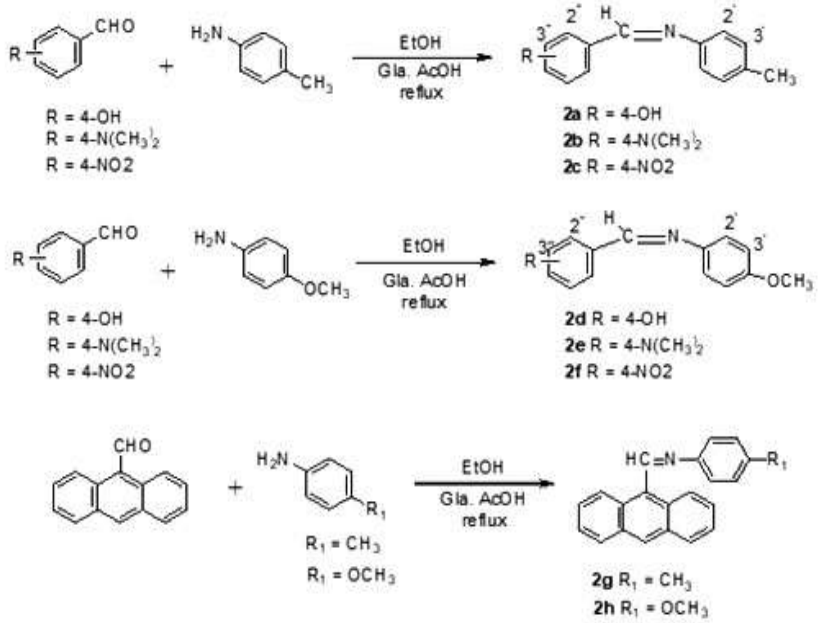
Melting point: 165°C

^{1}H-NMR ($CDCl_3$) δ_H (ppm): 3.88 (s, 3H, OCH_3), 8.53 (s, 1H, -CH=N), 7.02-8.72 (m,13H, Ar-H).

IR, υ_{max}, KBr (cm^{-1}): 3048 (Ar. C-H str.), 2991, 2830 (Ali. C-H str.),1606(m, C=N str.), 1519, 1503 (C=C ring str.), 1293,1246,1185 (C-N str.), 841, 820 (substituted phenyl ring).

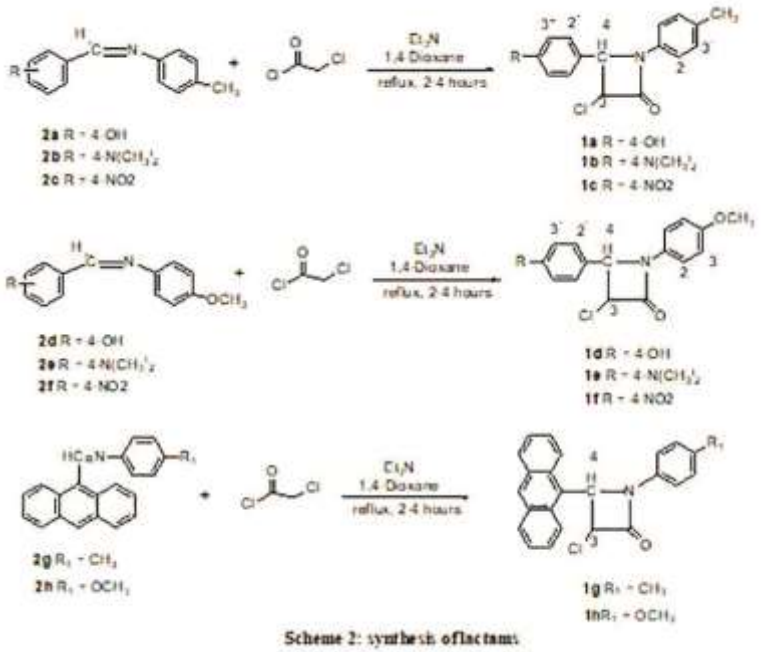
UV λ_{max}(log ε) (EtOAc): 258(1.424).

Elemental Analysis, $C_{22}H_{17}NO$: Theoretical: C, 84.89; H, 5.47; N, 4.50; Experimental Found: C, 84.80; H,5.33; N, 4.56.



Scheme 1. Synthesis of Schiff-bases.

Synthesis of 2-Azetidinones/β-lactams (1a-h)



Scheme 2: synthesis of lactams

Table 1. Comparison of conventional and microwave synthesis (2a-c, 2g).

Compound no.	Conventional method		Microwave method	
	Time (hours)	% Yield	Time (minutes)	% yield
2a	4	97	2.5	96
2b	2	90	2	94
2c	2	92	1.5	87
2g	2	77	1.5	75

The representative procedure of lactam synthesis

Between 0°C and 5°C, a well-stirred combination of triethylamine (0.0066 mol) and chloroacetyl chloride (0.0067 mol) was mixed to a solution of compound 2a (0.0033 mol) in 1, 4-dioxane (16.5 ml). After 30 minutes of stirring, the reaction mixture refluxed for three hours. For a whole day, the reaction mixture remained at room temperature. The TLC was used to monitor the reaction's progress, using a solvent ratio of 3:7 (EtOAc:cyclohexane). After using a vacuum evaporator to evaporate the mixture and remove the solvent, the residue was then flooded over cold water containing ice. After filtering, the crude product was dried. The impure solid contains the precursor Schiff-base, separated by column chromatography using a solvent mixture of EtOAc:cyclohexane = 3:7. Evaporating the solvent afforded the desired compounds1a. All other lactams (1b-1h) were obtained through a similar procedure.

The above compounds were also synthesized using the microwave method. Table 2 provides a comparative analysis of yield and reaction time.

The spectral data of the synthesized lactams/ azetidinones are as follows:

3-Chloro-4(4′-hydroxyphenyl)-N(4″-methyl-phenyl)-2-azetidinone (1a)

Yield: 74% (Off-white solid).

Melting point: 184°C

IR, υ_{max}, KBr (cm^{-1}): 3432 (O-H str. H-bond), 3087 (Ar. C-H str.), 2916, 2852 (Ali. C-H str.), 1673 (m, C=O str. lactam), 1617, 1553, 1509 (C=C ring str.), 865, 820 (substituted phenyl ring), 668 (C-Cl str.).

^{1}H-NMR (ppm): 2.33 (s, 3H, CH_3), 4.27 (d, 1H, J = 4.22 Hz, H-4), 5.43 (d, 1H, J = 4.22 Hz, H-3), 7.15-7.43 (m, 8H, Ar-H), 8.18 (s, 1H, Ar-OH).

λ_{max}: 251 nm

Elemental Analysis, $C_{16}H_{14}NO_2Cl$: Theoretical:C 66.90; H, 4.88; N, 4.88; Experimental Found: C, 67.05; H, 4.92; N, 4.18.

3-Chloro-4(4′-dimethylaminophenyl)-N(4″-methylphenyl)-2-azetidinone(1b)

Yield: 58%

Melting point: 124°C

IR, υ_{max}, KBr (cm^{-1}): 3090 (Ar. C-H str.), 2954, 2863 (Ali. C-H str.), 1676 (s, C=O str. lactam), 1599, 1553, 1513 (s, C=C ring str.), 864, 818 (substituted phenyl ring), 668, 596 (C-Clstr.).

^{1}H-NMR (ppm): 2.33 (s, 3H, CH_3), 3.21 (s, 6H, -$N(CH_3)_2$), 4.27 (d, 1H, J = 4.35 Hz, H-4), 5.28 (d, 1H, J = 4.35 Hz, H-3), 6.90 (d, 2H, J_o = 7.7 Hz, H-2′), 6.97 (d, 2H, J_o = 7.7 Hz, H-3′), 7.44 (d, 2H, J_o = 8.5 Hz, H-3″), 7.80 (d, 2H, J_o = 8.5 Hz, H-2″).

λ_{max}: 329 nm

Elemental Analysis, $C_{18}H_{19}N_2OCl$: Theoretical:C 68.79; H, 6.05; N, 8.92; Experimental Found: C, 69.01; H, 5.89; N, 8.68

3-Chloro-4(4′-nitrophenyl)-N(4″-methylphenyl)-2-azetidinone (1c)

Yield: 78% (light brown)

Melting point: 188°C

IR, υ_{max}, KBr (cm^{-1}): 3093 (Ar. C-H str.), 2951, 2861 (Ali. C-H str.), 1670 (s, C=O str. lactam), 1617, 1513 (s, C=C ring str.), (1558 NO_2), 865, 815 (substituted phenyl ring), 668 (C-Clstr.).

^{1}H-NMR (ppm): 2.33 (s, 3H, CH_3), 4.26 (d, 1H, *J* = 4.33 Hz, H-4), 5.50 (d, 1H, *J* = 4.33 Hz, H-3), 7.15-7.43 (m, 8H, Ar-H).

λ_{max}: 253 nm

Elemental Analysis, $C_{16}H_{13}N_2O_3Cl$: Theoretical:C 60.76; H, 4.11; N, 8.86; Experimental Found: C, 59.45; H, 4.42; N, 8.02.

3-Chloro-4(4′-hydroxyphenyl)-N(4″-methoxy-phenyl)-2-azetidinone (1d)

Yield: 52%

Meltingpoint: 96°C

^{1}H-NMR ($CDCl_3$) δH (ppm): 3.80 (s, 3H, OCH_3), 4.31 (d, 1H, *J*=4.55Hz, H-4), 5.54 (d, 1H, *J*=4.55Hz, H-3), 6.89 (d, 2H, J_o=7.8Hz, H-2′), 6.96 (d, 2H, J_o=7.8Hz, H-3′), 7.43 (d, 2H, J_0=8.0 Hz, H-3″), 7.81 (d, 2H, J_o=8.0 Hz, H-2″), 9.86 (s, 1H, Ar-OH)

IR, υ_{max}, KBr (cm^{-1}): 3295 (O-H str. H-bond), 3066 (Ar. C-H str.), 2957, 2834 (Ali. C-H str.), 1666 (s, C=O str. lactam), 1602, 1548, 1512 (s, C=C ring str.), 832(substituted phenyl ring), 606 (C-Clstr.).

UV λ_{max}(log ε) (EtOAc):267(1.724).

Elemental Analysis, $C_{16}H_{14}NO_3Cl$: Theoretical:C 63.37; H, 4.62; N, 4.62; Experimental Found: C,62.89; H, 4.63; N, 4.41

3-chloro-4(4′-dimethylaminophenyl)-N(4″-methoxyphenyl)-2-azetidinone (1e)

Yield:72%

Meltingpoint:125°C

^{1}H-NMR ($CDCl_3$) δ_H(ppm): 3.71 (s, 3H, OCH_3), 3.04 (s, 6H, $N(CH_3)_2$), 4.08 (d, 1H, *J*=4.45Hz, H-4), 4.14 (d, 1H, *J*=4.45 Hz, H-3), 6.65-7.71 (m, 8H, Ar-H).

IR, υ_{max}, KBr (cm^{-1}): 3072 (Ar. C-H, str.), 2957, 2837 (Ali. C-H, str.), 1663 (s, C=O, str. lactam), 1602, 1550, 1511, 1465 (s, C=C ring str.), 830 (substituted phenyl ring), 685 (C- Clstr.).

UV λ_{max}(log ε) (EtOAc): 329(0.720).

Elemental Analysis, $C_{18}H_{19}N_2O_2Cl$: Theoretical: C 65.35; H,5.79; N, 8.47; Experimental Found: C, 65.34; H, 5.97; N,8.53.

3-chloro-4(4′-nitrophenyl)-N(4″-methoxy-phenyl)-2-azetidinone(1f)

Yield: 85%

Meltingpoint: 132°C

^{1}H-NMR ($CDCl_3$) δ_H (ppm): 3.80 (s, 3H, OCH_3), 4.19 (d, 1H, *J*=4.75 Hz, H-4), 5.26(d, 1H, *J*=4.75 Hz, H-3), 6.87-7.45 (m, 8H, Ar-H).

IR, υ_{max}, KBr (cm^{-1}): 3072 (Ar. C-H str.), 2958, 2831 (Ali. C-H str.), 1664 (s, C=O str. lactam), 1607, 1511, 1465 (C=C ring str.), 1549, 1347 (NO_2), 830 (substituted phenyl ring), 685 (C-Clstr.).

UV λ_{max}(log ε) (EtOAc): 253(0.876).

Elemental Analysis, $C_{16}H_{13}N_2O_4Cl$: Theoretical:C 57.75; H, 3.94; N, 8.42; Experimental Found: C, 56.97; H, 3.43; N,8.08.

3-Chloro-4-anthranyl-N(4″-methylphenyl)-2-azetidinone (1g)

Yield: 80% (Grey solid)

Melting point: 185°C,

IR, υ_{max}, KBr (cm^{-1}): 3084 (Ar. C-H str.), 2955, 2857 (Ali. C-H str.), 1672 (s, C=O str. lactam), 1617, 1555, 1512 (s, C=C ring str.), 859, 816 (substituted phenyl ring), 503 (C-Clstr.).

^{1}H-NMR (ppm): 2.33 (s, 3H, CH_3), 4.25 (d, 1H, *J* = 4.65 Hz, H-4), 5.34 (d, 1H, *J* = 4.65 Hz, H-3), 7.16-7.44 (m, 13H, Ar-H).

λ_{max}: 250 nm

Elemental Analysis, $C_{24}H_{18}NOCl$: Theoretical:C 77.52; H, 4.88; N, 3.77; Experimental Found: C, 77.01; H, 5.03; N, 3.25.

3-Chloro-4-anthranyl-N(4″-methoxy-phenyl)-2-azetidinone(1h)

Yield: 65%

Meltingpoint: 135°C

^{1}H-NMR ($CDCl_3$) δ_H(ppm): 3.81 (s, 3H, OCH_3), 4.60 (d, 1H, *J*=4.65 Hz, H-4), 5.71(d, 1H, *J*=4.65 Hz, H-3), 6.88-7.45 (m, 13H, Ar-H).

IR, υ_{max}, KBr (cm^{-1}): 3072 (Ar. C-H str.), 2958, 2831(Ali. C-H str.), 1664(s, C=O str. lactam), 1600, 1547, 1511, 1466 (C=C ring str.), 831 (substituted phenyl ring), 685 (C-Clstr.).

UV, λ_{max}(log ε) (EtOAc): 251 (0.364).

Elemental Analysis, $C_{24}H_{18}NO_2Cl$: Theoretical:C 74.32; H, 4.68; N, 3.61; Experimental Found: C,73.99; H, 5.01; N, 3.23.

Antibacterial activity

Antimicrobial agents are substances that work as growth inhibitors or kill agents for microorganisms in treating disease. They can function as virus-killing vermicides, bacteria-killing bactericides, algae-killing algaecides, or fungal-killing fungicides. The antibacterial activity of newly produced compounds was assessed opposite to one gram-positive (*Staphylococcus aureus*) and one gram-negative (*Escherichia coli*) bacterium using the conventional Kirby-Bauer disk diffusion method. Table 3 describes the findings.

Table 2. Comparison of conventional and microwave synthesis (1a-c, 1g)

Compound no.	Conventional method		Microwave method	
	Time (hours)	%Yield	Time (minute)	% Yield
1a	3	74	3.5	**77**
1b	3	58	3.5	60
1c	3	78	4	80
1g	3	80	3	85

Table 3. Antimicrobial/Antibacterial activity assay of synthesized compounds by disc diffusion method.

Sl.	Compound ID	Zone of inhibition (mm) for *E. coli*			Zone of inhibition(mm) for *S. aureus*		
		256 µg/disc	128 µg/disc	64 µg/disc	256 µg/disc	128 µg/disc	64 µg/disc
1	2a	0	0	0	0	0	0
2	2b	0	0	0	0	0	0
3	2c	0	0	0	0	0	0
4	2g	0	0	0	0	0	0
5	1a	0	0	0	0	0	0
6	1b	0	0	0	0	0	0
7	1c	0	0	0	11.5	9.5	8.5
8	1g	10	0	0	0	0	0
Zone of inhibition (mm) for Reference standard							
		E. coli			*S. aureus*		
		i	ii	iii	i	ii	iii
11	Positive Control (Ciprofloxacin 5µg)	18	18	18	18.5	18	18
12	Negative control (100% Acetone)	0	0	0	0	0	0

N.B: Zone of inhibition given in mm (diameter). '0': no inhibitory activity

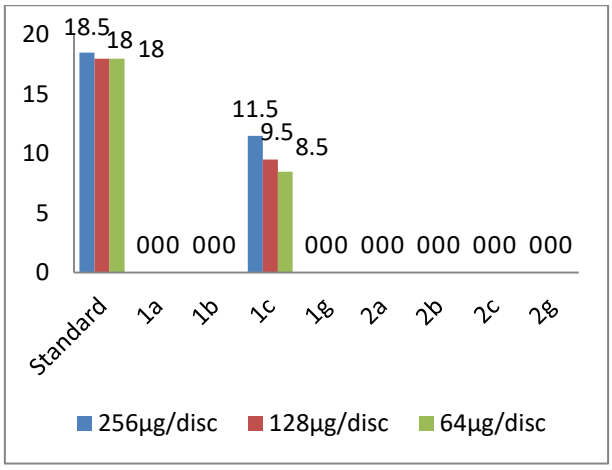


Fig. 1. Graphical representation of zone of inhibition (mm) of synthesized compounds for *S. aureus* in three different concentrations.

Results and Discussion

The special features of the spectroscopic data of the final synthesized compounds (*β*-lactams/azitidinones) can be explained from the general structure of the molecule.

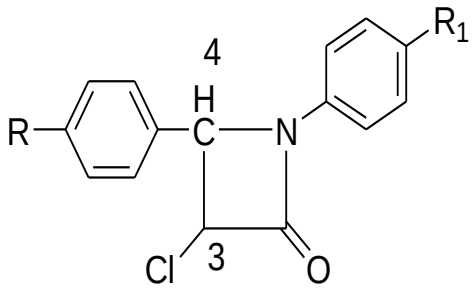


Fig. 2.General structure of synthesized *β*-lactam.

Because the lactam molecule contained an H-bonded O-H group, an unusually strong and broad absorption band was discovered at 3432 cm^{-1} in the infrared spectrum analysis. The NO_2 group's existence is the cause of the band at 1558 cm^{-1}. A doublet at δ (4.25-4.27) ppm in the ^{1}H-NMR spectra of produced azitidinone compounds corresponds to an H-4 proton with a coupling constant of *J* = (4.22-4.65) Hz because of the coupling with an adjacent H-3 proton. Pick is given by the nearby proton H-3 at δ (5.28-5.50) ppm with a *J* value (4.22-4.65) Hz. A singlet appeared at δ 2.33 ppm for $–CH_3$ protons. Aromatic protons appeared at δ (6.9-8.5) ppm as multiplets. The broad singlet was found to be at δ 8.18 ppm for phenolic –OH proton (compound (**1a**), and a singlet appeared at δ 3.21 ppm for $-N(CH_3)_2$ protons (compound (**1c**). The synthesized compounds show characteristic absorption at (251, 329, 253, 250) nm for the compounds **1a-h**, respectively, in the UV spectrum, which is responsible for a carbonyl chromophoric group. It consists of both n→π* and π→π* transitions. The spectral data of all the synthesized compounds were consistent with their structures., and the microanalyses also supported these structures

Antimicrobial Studies

In the disc diffusion method, Gram-positive and Gram-negative bacteria were used to investigate the antibacterial qualities of the produced compounds. Of all the compounds screened for bacteria, only compound 1c showed action. None of the other chemicals showed robust efficacy against any species at the specified doses. Let's look at the structural variation of compounds. They show antibacterial potency, and the compounds did not show activity at all, which gives a clear idea about the importance of the lactam rings. Compound framework variation conducts bioactivity, and framework modification of molecules commonly changes biological activity.(Vashi et al., 1995; Von Nussbaum et al., 2006) The cyclized products are the *β*-lactams, which showed marked antibacterial activity.

Conclusion

A plethora of β-lactams have been successfully synthesized as antibiotic mimics. A comparison between conventional and microwave techniques provided data on noteworthy reductions in reaction time, eco-friendly nature, and high product yield. The characterizations of newly synthesized compounds were ensured based on IR, UV, and ^{1}H-NMR evidence and were consistent with the desired structure.

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Conflict of interest declaration

The authors declared that there is no conflict of interest.

Author's Contributions

Professor Md. Mamun Hossain and Sumaiya Khan contributed to the idea, supervision, data analysis, and manuscript writing. Kamrunnahar Happy, Sumaiya Khan, Umme Aiman Liza, and Afsana Mimi performed laboratory experiments, data analysis, and literature review and made the table and graphs. M. Rafikul Islam contributed to the Microbial assay of the synthesized compounds.

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