

# Microwave Assisted Synthesis, Characterizations and Antibacterial Activity of Some of Thiazole Schiff Base and Azetidinone Derivatives

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## Abstract

A series of substitution thiazole Schiff base (SB1-SB12) were synthesis by reaction substitution phenyl 2-amino thiazole with 4-N,N-dimethyl benzaldehyde Azetidinone (AZ1-AZ12) were also synthesised by reaction substitution thiazole Schiff base with acetyl chloride. The synthesis compounds have been characterized by M.P., TLC, CHN, UV, FT-IR, <sup>1</sup>HNMR, <sup>13</sup>CNMR and MS. The biological screening data of the synthesized compounds were also studied.

**Keywords:** Microwave, Thiazole, Schiff base, Azetidinone, Anti-bacterial

## Introduction

Microwave dielectric heating uses the ability of some liquids and solids to transform electromagnetic radiation into heat to drive chemical reactions. The entry of microwave ovens possible to carry out many transformations with greater efficiency and ease of workup<sup>(1-3)</sup>, the use of microwave has becomes very attractive in the field of medical sciences<sup>(4)</sup>.

The chemistry of Schiff base plays a vital role in the progress of chemistry science<sup>(5, 6)</sup>, synthesis of Schiff base through classical condensation of aldehydes (or ketone) and imines were pursued<sup>(7, 8)</sup> Schiff base are characterized by the N=CH- (imine) group which is important in elucidating the mechanism of transformation in biological systems. Due to great flexibility and diverse structural aspects, wide range of Schiff bases have been synthesized and their complexation behaviour was studied<sup>(5)</sup>. Furthermore, Schiff base are reported to show a variety of interesting biological activities, including antibacterial<sup>(9)</sup>, antifungal<sup>(10)</sup>, anticancer<sup>(11, 12)</sup>, and herbicidal activities<sup>(13)</sup>.

2-Azetidinone compounds are characterized by the ring system (amide)<sup>(14)</sup>. These compounds are shown to possess make biological activities<sup>(15-19)</sup>. 2-Azetidinone has been synthesized by the condensation of chloroacetyl chloride with Schiff base, the compound has been characterized on the base of analytical and spectral data. It has been screened of antibacterial activity against *staphylococcus* and *E.coli*.

## Experimental Work

Melting point were determined in Buchi thermal point apparatus and were uncorrected, Elemental analysis (CHN) were recorded in EA300 Euro-Vector in University of Al-albyat in Jordon. FT-IR Spectra were recorded on Shimadzu FT-IR 8400 Fourier Transformer infrared as KBr disk in the range 40-4000cm<sup>-1</sup>. Ultraviolet spectra were recorded in spectro scan 80 in the wavelength 200-800 nm. <sup>1</sup>HNMR and <sup>13</sup>CNMR spectra were recorded on Bruker spectropin ultra shield magnets 400MHz instrument using tetramethyl silane (TMS) as an internal standard and DMSO-d<sub>6</sub> as a solvent in university of Tabriz-Iran. The compounds were synthesized by microwave type Newal microwave instrument (Turkey) NWL101, compact 20L, power1200 Watt and frequency 2450 MHz, by using turntable system with different powers between 90-300W. Thin layer chromatography were performed on pre-coated sheets with 0.25 mm layer of Silica Gel GF254 of the Merck Company.

## Synthesis of Compounds

### Synthesis Schiff Base of Thiazole Derivatives

All Schiff base were synthesis by reaction substituents phenyl amino thiazole<sup>(20,21)</sup> (1mmole) and 4-N,N-dimethyl benzaldehyde (1mmole) were mixed with each other dissolve in 20ml absolute ethanol was placed in small conical flask at room temperature, then glacial acetic acid 2-3 drop was added. The mixture was then exposed to microwave irradiation at 270Wpower for 3-5min. Complete of the reaction was tested by thin layer chromatography by using eluent (chloroform: methanol) ratio (3:7) respectively. The reaction mixture was then cold at room temperature. The yellow coloured Schiff base was obtained, which was recrystallized from ethanol and dried under pressure. Other Schiff bases were synthesized in similar way; the products were obtained in 79-95%. Physical properties of thiazole Schiff bases compounds as shown in Tables 1 which include reaction substituent amino thiazole with N,N dimethyl benzaldehyde.

## Synthesis Compounds

### **SB1=H:** 4-(N,N-dimethylamino) benzylidene-4-phenyl-2-amino thiazole

CHN analysis that formula  $C_{18}H_{17}N_3S$  calculated C, 70.333 H, 5.576 N, 13.476 S, 10.431 ; Found C, 70.132 H, 5.192 N, 13.287 S, 10.177, Ultraviolet spectra  $\lambda_{max}$  210, 242 and 328nm. FT-IR spectra  $\nu_{max}$  3113, 2924, 1621, 1603, 1314, 1072 $cm^{-1}$ .  $^1H$ NMR spectra  $\delta_{ppm}$ , (7.25, 11H) and (3.4, 6H).  $^{13}C$ NMR spectra  $\delta_{ppm}$  120, 128, 121, 130, 133, 111, 170, 163, 117, 119, 113, 163, and 55.

### **SB2=4-OH** 4-(N,N-dimethylamino) benzylidene-4-(4-hydroxyphenyl)-2-amino thiazole

CHN analysis that formula  $C_{18}H_{17}N_3OS$  calculated C, 66.853 H, 5.304 N, 12.993 S, 9.912 ; Found C, 66.209 H, 5.116 N, 12.734 S, 9.881. Ultraviolet spectra  $\lambda_{max}$  210, 242 and 338nm. FT-IR spectra  $\nu_{max}$  3224, 3100, 1647, 1598, 1359, 1274, 1170 $cm^{-1}$ .  $^1H$ NMR spectra  $\delta_{ppm}$  (6.85, 10H), (11.54, 1H) and (3.35, 6H).  $^{13}C$ NMR spectra  $\delta_{ppm}$  163, 121, 33, 129, 135, 118, 169, 163, 139, 129, 120, 153 and 61.

### **SB3=4-Br** 4-(N,N-dimethylamino) benzylidene-4-(4-bromophenyl)-2-amino thiazole

CHN analysis that formula  $C_{18}H_{16}N_3BrS$  calculated C, 55.936 H, 4.171 N, 10.885 S, 8.304 ; Found C, 55.865 H, 4.018 N, 10.802 S, 8.141. Ultraviolet spectra  $\lambda_{max}$  210, 242 and 338nm. FT-IR spectra  $\nu_{max}$  2923, 1643, 1450, 1299, 1002 921 $cm^{-1}$ .  $^1H$ NMR spectra  $\delta_{ppm}$  (7.32, 10H), and (3.35, 6H).  $^{13}C$ NMR spectra  $\delta_{ppm}$ , 113, 141, 121, 140, 150, 107, 170, 163, 119, 120, 111, 163 and 53.

### **SB4=4-Cl** 4-(N,N-dimethylamino) benzylidene-4-(4-chlorophenyl)-2-amino thiazole

CHN analysis that formula  $C_{18}H_{16}N_3ClS$  calculated C, 63.243 H, 4.722 N, 12.256 S, 9.382 ; Found C, 63.100 H, 4.556 N, 12.102 S, 9.208. Ultraviolet spectra  $\lambda_{max}$  210, 246 and 344nm. FT-IR spectra  $\nu_{max}$  2960, 1595, 1523, 1224, 1054, 792 $cm^{-1}$ .  $^1H$ NMR spectra  $\delta_{ppm}$  (7.33, 10H), and (3.33, 6H).  $^{13}C$ NMR spectra  $\delta_{ppm}$  129, 127, 129, 129, 136, 118, 170, 163, 121, 121, 119, 163 and 53.

### **SB5=3-NO<sub>2</sub>** 4-(N,N-dimethylamino)benzylidene-4-(3-nitrophenyl)-2-amino thiazole

CHN analysis that formula  $C_{18}H_{16}N_3O_2S$  calculated C, 61.352 H, 4.581 N, 15.906 S, 9.101 ; Found C, 61.243 H, 4.445 N, 12.102 S, 9.208. Ultraviolet spectra  $\lambda_{max}$  210, 232 and 338nm. FT-IR spectra  $\nu_{max}$  2972, 1623, 1514, 1261, 1110 $cm^{-1}$ .  $^1H$ NMR spectra  $\delta_{ppm}$  (7.30, 10H), and (3.03, 6H).  $^{13}C$ NMR spectra  $\delta_{ppm}$ , 120, 134, 129, 133, 132, 119, 135, 91, 170, 163, 121, 127, 120, 163 and 52.

### **SB6=4-NO<sub>2</sub>** 4-(N,N-dimethylamino)benzylidene-4-(4-nitrophenyl)-2-amino thiazole

CHN analysis that formula  $C_{18}H_{16}N_3O_2S$  calculated C, 61.352 H, 4.581 N, 15.906 S, 9.101; Found C, 61.344 H, 4.243 N, 15.673 S, 8.899. Ultraviolet spectra  $\lambda_{max}$  210, 250 and 340nm. FT-IR spectra  $\nu_{max}$  3055, 2923, 1629, 1596, 1323, 1234,  $cm^{-1}$ .  $^1H$ NMR spectra  $\delta_{ppm}$  (7.41, 10H), and (3.35, 6H).  $^{13}C$ NMR spectra  $\delta_{ppm}$  129, 119, 121, 125, 136, 92, 170, 163, 121, 121, 118, 163 and 61.

### **SB7=4OCH<sub>3</sub>** 4-(N,N-dimethylamino)benzylidene-4-(4-methoxyphenyl)-2-aminothiazole

CHN analysis that formula  $C_{19}H_{19}N_3OS$  calculated C, 67.632 H, 5.684 N, 12.455 S, 9.503 ; Found C, 67.568 H, 5.235 N, 12.400 S, 9.314. Ultraviolet spectra  $\lambda_{max}$  220, 242 and 388nm. FT-IR spectra  $\nu_{max}$  2964, 1618, 1577, 1319, 1217, 1024 $cm^{-1}$ .  $^1H$ NMR spectra  $\delta_{ppm}$  (7.29, 10H), (3.35, 6H) and (3.8, 3H)  $^{13}C$ NMR spectra  $\delta_{ppm}$  163, 121, 135, 122, 150, 119, 170, 163, 130, 135, 120, 155 53 and 92.

### **SB8=4-CH<sub>3</sub>** 4-(N,N-dimethylamino)benzylidene-4-(4-methylphenyl)-2-amino thiazole

CHN analysis that formula  $C_{19}H_{19}N_3S$  calculated C, 70.993 H, 5.965 N, 13.072 S, 9.981 ; Found C, 70.943 H, 5.878 N, 12.914 S, 9.791. Ultraviolet spectra  $\lambda_{max}$  224, 242 and 388nm. FT-IR spectra  $\nu_{max}$  2914, 1608, 1510, 1303, 1010 $cm^{-1}$ .  $^1H$ NMR spectra  $\delta_{ppm}$  (6.85, 10H), (3.33, 6H) and (2.3, 3H).  $^{13}C$ NMR spectra  $\delta_{ppm}$  153, 130, 121, 135, 153, 119, 170, 163, 122, 128, 120, 168, 61 and 14.

### **SB9=4-F** 4-(N,N-dimethylamino) benzylidene-4-(4-fluorophenyl)-2-amino thiazole

CHN analysis that formula  $C_{18}H_{16}N_3FS$  calculated C, 66.443 H, 4.966 N, 12.913 S, 9.850; Found C, 66.342 H, 4.662 N, 12.808 S, 9.661. Ultraviolet spectra  $\lambda_{max}$  225, 238 and 375nm. FT-IR spectra  $\nu_{max}$  2927, 1633, 1575, 1269, 1112, 962  $cm^{-1}$ .  $^1H$ NMR spectra  $\delta_{ppm}$  (7.09, 10H), and (3.34, 6H) .  $^{13}C$ NMR spectra  $\delta_{ppm}$  163, 120, 137, 134, 147, 118, 170, 163, 121, 121, 120, 147 and 61.

### **SB10=2-F** 4-(N,N-dimethylamino) benzylidene-4-(2-fluorophenyl)-2-amino thiazole

CHN analysis that formula  $C_{18}H_{16}N_3FS$  calculated C, 66.443 H, 4.966 N, 12.913 S, 9.850; Found C, 66.223 H, 4.419 N, 12.791 S, 9.734. Ultraviolet spectra  $\lambda_{max}$  220, 244 and 380nm. FT-IR spectra  $\nu_{max}$  3077, 2929, 1587, 1483, 1311, 1226, 941 $cm^{-1}$ .  $^1H$ NMR spectra  $\delta_{ppm}$  (7.23, 10H), and (3.35, 6H).  $^{13}C$ NMR spectra  $\delta_{ppm}$ , 129, 121, 123, 135, 129, 124, 135, 120, 170, 163, 127, 129, 118, 129 and 52.

### **SB11=2OCH<sub>3</sub>** 4-(N,N-dimethylamino)benzylidene-4-(4-methoxyphenyl)-2-amino thiazole

CHN analysis that formula  $C_{19}H_{19}N_3OS$  calculated C, 67.632 H, 5.684 N, 12.455 S, 9.503; Found C, 67.220 H, 5.311 N, 12.354 S, 9.202 . Ultraviolet spectra  $\lambda_{max}$  223, 236 and 377nm. FT-IR spectra  $\nu_{max}$ , 3096, 2961, 1596, 1533, 1280, 1141, 1088 $cm^{-1}$ .  $^1H$ NMR spectra  $\delta_{ppm}$  (7.09, 10H), (3.34, 6H) and (4.00, 3H).  $^{13}C$ NMR spectra  $\delta_{ppm}$  127, 110, 164, 113, 142, 115, 145, 107, 183, 170, 114, 125, 113, 151, 56 and 92

### **SB12=2-OH** 4-(N,N-dimethylamino)benzylidene-4-(2-hydroxyphenyl)-2-amino thiazole

CHN analysis that formula  $C_{18}H_{17}N_3OS$  calculated C, 66.853 H, 5.304 N, 12.993 S, 9.912; Found C,

66.320 H, 5.239 N, 12.666, S, 9,792. Ultraviolet spectra  $\lambda_{max}$  212, 245 and 380nm. FT-IR spectra  $\nu_{max}$  3170, 2977, 1622, 1581, 1375, 1265, 1193 $cm^{-1}$ .  $^1H$ NMR spectra  $\delta$ ppm (7.33, 10H), (3.33, 6H) and (9.15, 1H).  $^{13}C$ NMR spectra  $\delta$ ppm 130, 119, 158, 170, 148, 124, 158, 114, 182, 170, 124, 128, 119, 113, and 55.

**Table 1: Some physical data of thiazole Schiff bases compounds resulting from reaction substituents amino thiazole with *N,N*-dimethyl benzaldehyde**

| Symbol of Schiff base | Colour      | Melting Point ( $^{\circ}C$ ) | Yield (%) | $R_f$ |
|-----------------------|-------------|-------------------------------|-----------|-------|
| SB1                   | yellow      | 185-187                       | 94        | 0.79  |
| SB2                   | yellow      | 197-199                       | 87        | 0.86  |
| SB3                   | Pale yellow | 168-170                       | 95        | 0.73  |
| SB4                   | yellow      | 212-214                       | 88        | 0.69  |
| SB5                   | yellow dark | 255-257                       | 89        | 0.64  |
| SB6                   | yellow      | 151-153                       | 91        | 0.78  |
| SB7                   | yellow      | 196-198                       | 90        | 0.76  |
| SB8                   | yellow      | 159-161                       | 89        | 0.70  |
| SB9                   | yellow      | 223-225                       | 79        | 0.65  |
| SB10                  | yellow      | 200-202                       | 82        | 0.72  |
| SB11                  | orange      | 213-214                       | 84        | 0.81  |
| SB12                  | yellow      | 164-168                       | 91        | 0.72  |

### Synthesis Azetidin-2-one ( $\beta$ -Lactams)

#### 1- Preparation Chloro Acetyl Chloride:-

This reaction was carry out in the hood, chloro acetyl chloride was preparation from reaction chloro acetic acid (1mole) with phosphorous penta chloride (1mole), the components of reaction were mixed warmly by glass rode until the solid component converted to liquid solution, The resulting liquid was purified by simple distillation in the boiling point 106 $^{\circ}C$  (literature<sup>(22)</sup> 105 $^{\circ}C$ ).

#### 2- Synthesis Azetidin-2-one (General Procedure)

All azetidinone were synthesized by reaction of a mixture phenyl amino thiazole Schiff base (0.01mole) in 20ml dioxane. Chloro acetyl chloride (0.015mole) and triethylamine (0.02mole) was placed in a small conical flask copped with funnel inside a microwave oven and irradiated at 270W power for 3-4min., after completion of the reaction (monitored by thin layer chromatography TLC by using eluent (hexane: ethyl acetate) ratio (3:7) respectively, it was then diluted with ice cold water. The solid product forms was washed in THF, filtered, dried and recrystallized from absolute ethanol, as a yellow solid, Other compounds were synthesized in similar way, the products were obtained in 85-95%. Physical properties of azetidinone compounds as shown in Tables 2 which include reaction substituent amino thiazole Schiff bases of *N,N* dimethylbenzaldehyde.

### Synthesis Compounds

#### **AZ1** 3-chloro-4-[(4-dimethylamino)phenyl]-1-[4-(4-phenylthiazol-2-amino)yl]- azetidin-2-one

CHN analysis that formula  $C_{20}H_{18}ClN_3OS$  calculated C, 62.573 H, 4.733 N, 10.595 S, 8.350 ; Found C, 62.240 H, 4.588 N, 10.798 S, 8.221, Ultraviolet spectra  $\lambda_{max}$  210, 270 and 320nm. FT-IR spectra  $\nu_{max}$  3056, 1679, 1612, 1581, 1392, 1070 $cm^{-1}$ .  $^1H$ NMR spectra  $\delta$ ppm, (7.00, 9H), (1.17, 6H), (4.08, 1H) and (5.05, 1H).  $^{13}C$ NMR spectra  $\delta$ ppm 135, 127, 110, 146, 156, 96, 156, 173, 57, 74, 116, 128, 106, 148 and 30.

#### **AZ2** 3-chloro-4-[(4-dimethylamino)phenyl]-1-[4-(4-hydroxyphenyl thiazol-2-amino)yl]- azetidin-2-one

CHN analysis that formula  $C_{20}H_{18}ClN_3O_2S$  calculated C, 60.075 H, 4.542 N, 10.511 S, 8.022 ; Found C, 59.884 H, 4.399 N, 10.204 S, 7.899. Ultraviolet spectra  $\lambda_{max}$  210, 270 and 305nm. FT-IR spectra  $\nu_{max}$  3467, 3055, 2999, 1666, 1627, 1596, 1070 $cm^{-1}$ .  $^1H$ NMR spectra  $\delta$ ppm (7.0, 9H), (10.5, 1H), (1.1, 6H), (4.51, 1H) and (5.54, 1H).  $^{13}C$ NMR spectra  $\delta$ ppm 152, 129, 114, 142, 120, 104, 170, 176, 60, 74, 138, 130, 108, 146 and 50

#### **AZ3** 3-chloro-4-[(4-dimethylamino)phenyl]-1-[4-(4-bromophenyl thiazol-2-amino)yl]- azetidin-2-one

CHN analysis that formula  $C_{20}H_{17}ClBrN_3OS$  calculated C, 51.911 H, 3.702 N, 9.088 S, 6.932 ; Found C, 42.334 H, 51.722 N, 8.896 S, 6.577. Ultraviolet spectra  $\lambda_{max}$  210, 260 and 295nm. FT-IR spectra  $\nu_{max}$  3095, 2921, 1666, 1585, 1537, 1367, 1072, 781 $cm^{-1}$ .  $^1H$ NMR spectra  $\delta$ ppm (7.01, 9H), (1.20, 6H), (4.01, 1H) and (5.56, 1H).  $^{13}C$ NMR spectra  $\delta$ ppm 117, 123, 112, 135, 146, 103, 158, 167, 56, 66, 128, 125, 110, 142 and 50.

#### **AZ4** 3-chloro-4-[(4-dimethylamino)phenyl]-1-[4-(4-chlorophenylthiazol-2-amino)yl]- azetidin-2-one

CHN analysis that formula  $C_{20}H_{17}N_3OCIBrS$  calculated C, 57.420 H, 4.103 N, 10.044 S, 7.662 ;

Found C, 57.238 H, 4.056 N, 10.211 S, 7.498. Ultraviolet spectra  $\lambda_{\max}$  210, 268 and 290nm. FT-IR spectra  $\nu_{\max}$  3107, 1691, 1604, 1523, 1346, 1105, 854 $\text{cm}^{-1}$ .  $^1\text{H}$ NMR spectra  $\delta$ ppm (6.67, 9H), (1.29, 6H), (3.99, 1H) and (5.09, 1H).  $^{13}\text{C}$ NMR spectra  $\delta$ ppm 114, 120, 105, 136, 155, 107, 160, 170, 52, 60, 127, 123, 103, 150 and 27.

**SB5 3-chloro-4-[(4-dimethylamino)phenyl]-1-[4-(3-nitrophenylthiazol-2-amino)yl]- azetid-2-one**

CHN analysis that formula  $\text{C}_{20}\text{H}_{17}\text{ClN}_4\text{O}_3\text{S}$  calculated C, 56.012 H, 4.006 N, 13.066 S, 7.483 ; Found C, 55.855 H, 3.864 N, 12.882 S, 7.316. Ultraviolet spectra  $\lambda_{\max}$  210, 268 and 290nm. FT-IR spectra  $\nu_{\max}$  3062, 2943, 1685, 1602, 1479, 1330, 1224 $\text{cm}^{-1}$ .  $^1\text{H}$ NMR spectra  $\delta$ ppm (7.00, 9H), (1.18, 6H), (4.40, 1H) and (5.51, 1H).  $^{13}\text{C}$ NMR spectra  $\delta$ ppm 116, 148, 131, 135, 136, 100, 160, 89, 172, 180, 64, 70, 110, 118, 91, 142 and 63.

**AZ6 3-chloro-4-[(4-dimethylamino)phenyl]-1-[4-(4-nitrophenylthiazol-2-amino)yl]- azetid-2-one**

CHN analysis that formula  $\text{C}_{20}\text{H}_{17}\text{ClN}_4\text{O}_3\text{S}$  calculated C, 56.012 H, 4.006 N, 13.066 S, 7.483; Found C, 55.861 H, 3.838 N, 12.802 S, 7.325. Ultraviolet spectra  $\lambda_{\max}$  220, 280 and 300nm. FT-IR spectra  $\nu_{\max}$  3033, 2921, 1679, 1606, 1479, 1357, 1180 $\text{cm}^{-1}$ .  $^1\text{H}$ NMR spectra  $\delta$ ppm (7.30, 9H), (1.19, 6H), (4.10, 1H) and (5.10, 1H).  $^{13}\text{C}$ NMR spectra  $\delta$ ppm 112, 109, 108, 135, 155, 79, 169, 170, 56, 62, 122, 119, 90, 154 and 30.

**AZ7 3-chloro-4-[(4-dimethylamino)phenyl]-1-[4-(4-methoxyphenyl thiazol-2-amino)yl]- azetid-2-one**

CHN analysis that formula  $\text{C}_{21}\text{H}_{20}\text{ClN}_3\text{O}_2\text{S}$  calculated C, 60.941 H, 4.870 N, 10.153 S, 7.652 ; Found C, 60.729 H, 4.335 N, 9.982 S, 7.659. Ultraviolet spectra  $\lambda_{\max}$  220, 280 and 310nm. FT-IR spectra  $\nu_{\max}$  1674, 1579, 1481, 1359, 1272, 1074 $\text{cm}^{-1}$ .  $^1\text{H}$ NMR spectra  $\delta$ ppm (7.20, 9H), (1.14, 6H), (4.42, 1H), (4.04, 3H) and (5.40, 1H).  $^{13}\text{C}$ NMR spectra  $\delta$ ppm 101, 119, 100, 140, 160, 98, 167, 170, 162, 80, 132, 126, 99, 150 and 51.

**AZ8 3-chloro-4-[(4-dimethylamino)phenyl]-1-[4-(4-methylphenyl thiazol-2-amino)yl]- azetid-2-one**

CHN analysis that formula  $\text{C}_{21}\text{H}_{20}\text{ClN}_3\text{OS}$  calculated C, 63.395 H, 5.077 N, 10.562 S, 8.065 ; Found C, 63.281 H, 5.590 N, 10.344 S, 7.893. Ultraviolet spectra  $\lambda_{\max}$  210, 270 and 315nm. FT-IR spectra  $\nu_{\max}$  3076, 2962, 1672, 1512, 1481, 1371, 1108 $\text{cm}^{-1}$ .  $^1\text{H}$ NMR spectra  $\delta$ ppm (7.00, 9H), (1.14, 2H), (4.04, 1H), (1.88, 3H) and (5.00, 1H).  $^{13}\text{C}$ NMR spectra  $\delta$ ppm 105, 119, 104, 148, 160, 69, 173, 176, 48, 65, 136, 120, 99, 150, 39, and 92.

**AZ9 3-chloro-4-[(4-dimethylamino)phenyl]-1-[4-(4-fluorophenyl thiazol-2-amino)yl]- azetid-2-one**

CHN analysis that formula  $\text{C}_9\text{H}_7\text{N}_2\text{OFS}$  calculated C, 59.775 H, 4.262 N, 10.462 S, 7.982; Found C, 59.221 H, 4.192 N, 10.220 S, 7.812. Ultraviolet spectra  $\lambda_{\max}$  210, 270 and 298nm. FT-IR spectra  $\nu_{\max}$  3062, 2962, 1679, 1606, 1479, 1269, 1176 $\text{cm}^{-1}$ .  $^1\text{H}$ NMR spectra  $\delta$ ppm (6.71, 9H), (1.26, 6H), (3.77, 1H) and (4.66, 1H).  $^{13}\text{C}$ NMR spectra  $\delta$ ppm 122, 129, 118, 145, 155, 108, 162, 170, 62, 70, 135, 130, 113, 150 and 25.

**AZ10 3-chloro-4-[(4-dimethylamino)phenyl]-1-[4-(2-fluorophenyl thiazol-2-amino)yl]- azetid-2-one**

CHN analysis that formula  $\text{C}_9\text{H}_7\text{N}_2\text{OFS}$  calculated C, 59.775 H, 4.262 N, 10.462 S, 7.982; Found C, 59.335 H, 4.192 N, 10.220 S, 7.709. Ultraviolet spectra  $\lambda_{\max}$  225, 265 and 295nm. FT-IR spectra  $\nu_{\max}$  1676, 1583, 1481, 1357, 1074, 823 $\text{cm}^{-1}$ .  $^1\text{H}$ NMR spectra  $\delta$ ppm (7.01, 9H), (1.29, 6H), (3.45, 1H) and (5.09, 1H).  $^{13}\text{C}$ NMR spectra  $\delta$ ppm 116, 119, 160, 135, 121, 130, 164, 81, 165, 81, 165, 174, 56, 64, 131, 118, 88, 142 and 50.

**AZ11 3-chloro-4-[(4-dimethylamino)phenyl]-1-[4-(2-methoxyphenyl thiazol-2-amino)yl]- azetid-2-one**

CHN analysis that formula  $\text{C}_{21}\text{H}_{20}\text{ClN}_3\text{O}_2\text{S}$  calculated C, 60.941 H, 4.870 N, 10.153 S, 7.652; Found C, 66.781 H, 4.243 N, 9.840 S, 7.599 . Ultraviolet spectra  $\lambda_{\max}$  220, 275 and 296nm. FT-IR spectra  $\nu_{\max}$  3105, 1691, 1604, 1523, 1346, 1251, 1103 $\text{cm}^{-1}$ .  $^1\text{H}$ NMR spectra  $\delta$ ppm (7.00, 9H), (1.15, 6H), (4.50, 1H), (3.59, 3H) and (5.50, 1H).  $^{13}\text{C}$ NMR spectra  $\delta$ ppm 116, 118, 170, 138, 92, 91, 171, 74, 172, 178, 60, 72, 115, 116, 89, 141 and 50.

**AZ12 3-chloro-4-[(4-dimethylamino)phenyl]-1-[4-(2-hydroxyphenyl thiazol-2-amino)yl]- azetid-2-one**

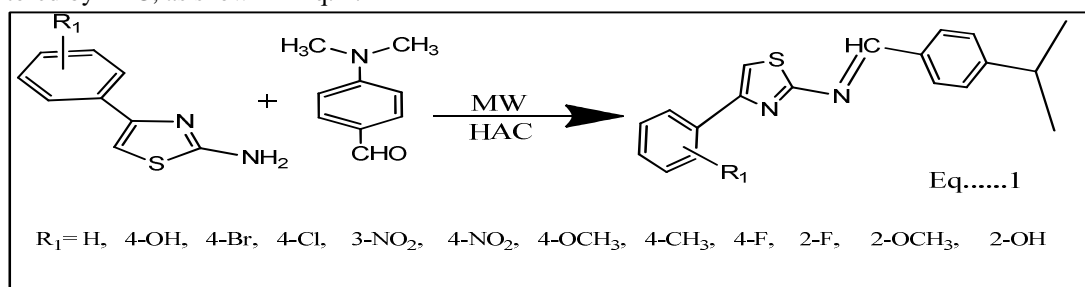
CHN analysis that formula  $\text{C}_{20}\text{H}_{18}\text{ClN}_3\text{O}_2\text{S}$  calculated C, 60.075 H, 4.542 N, 10.511 S, 8.022; Found C, 59.902 H, 4.333 N, 10.322, S, 7.864. Ultraviolet spectra  $\lambda_{\max}$  215, 265 and 310nm. FT-IR spectra  $\nu_{\max}$  3400, 3060, 2933, 1676, 1600, 1508, 1298, 1255, 1173 $\text{cm}^{-1}$ .  $^1\text{H}$ NMR spectra  $\delta$ ppm (7.00, 9H), (1.7, 6H), (10.2, 1H), (4.00, 1H) and (5.07, 1H).  $^{13}\text{C}$ NMR spectra  $\delta$ ppm 129, 141, 165, 150, 131, 93, 166, 80, 174, 181, 59, 64, 100, 131, 81, 160 and 48.

**Table 2: Some physical data of azetidinone compounds resulting from reaction *N,N*-dimethyl benzaldehyde Schiff base thiazole with chloro acetyl chloride.**

| Symbol of Azetidinone | Colour         | Melting Point (°C) | Yield (%) | R <sub>f</sub> |
|-----------------------|----------------|--------------------|-----------|----------------|
| AZ1                   | Crystal yellow | 228-230            | 89        | 0.66           |
| AZ2                   | Crystal white  | 227-229            | 87        | 0.68           |
| AZ3                   | Crystal white  | 218-220            | 85        | 0.75           |
| AZ4                   | Crystal yellow | 247-250            | 92        | 0.79           |
| AZ5                   | Crystal yellow | 244-246            | 90        | 0.71           |
| AZ6                   | Crystal yellow | 186-188            | 93        | 0.78           |
| AZ7                   | Crystal white  | 166-168            | 94        | 0.66           |
| AZ8                   | Crystal white  | 228-230            | 89        | 0.77           |
| AZ9                   | Crystal yellow | 187-189            | 88        | 0.67           |
| AZ10                  | Crystal yellow | 189-191            | 80        | 0.80           |
| AZ11                  | Crystal white  | 220-222            | 86        | 0.86           |
| AZ12                  | Crystal yellow | 177-179            | 95        | 0.82           |

### Results and discussion

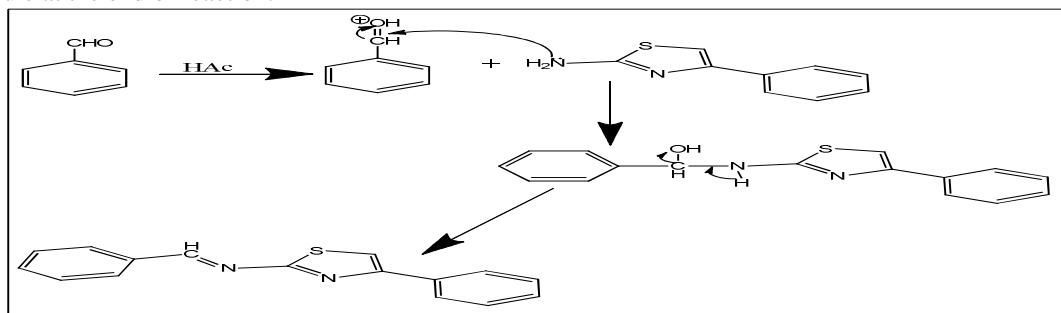
The thiazole Schiff base compounds were synthesized by the reaction of amino thiazole group with appropriate aldehydes in absolute ethanol. Glacial acetic acid was used as a catalyst for the protonation of carbonyl group in aldehyde compounds, using microwave irradiation in power 270W in different time. All the reactions were monitored by TLC, as shown in Eq. 1.



The electron withdrawing groups in the aldehyde led to decreasing the electron density at the carbon atom of carbonyl, so the electrophilic properties were enhanced, therefore increasing the positive charge of the carbon of carbonyl and making it easy to attack by the nucleophilic, whereas, the electron donating groups in the thiazole increased the nucleophilic properties which make it easy to attack aldehydes. These factors increased the yields of products.

The purification of Schiff base compounds was tested by thin layer chromatography (TLC) using different eluents. The best separation was obtained in a mixture of (chloroform: methanol) (3:7) respectively as eluent. Then, the compounds were purified by using ethanol and benzene.

The mechanism of reaction can be explained in scheme 1, which showed the nucleophilic reaction attack of amino thiazole at the carbon atom of the carbonyl group in the aldehyde with the elimination of a water molecule at the end of the reaction.

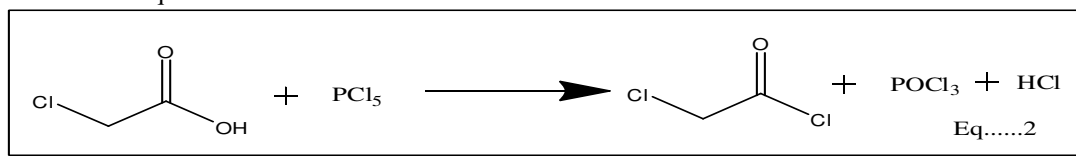


**Scheme 1**

The structures of the synthesized substituted phenyl thiazole Schiff bases were confirmed by their elemental analysis, UV, IR, NMR and MS. The C, H, and N values were situated within the range which confirmed the validity of the suggested structure of the prepared compounds.

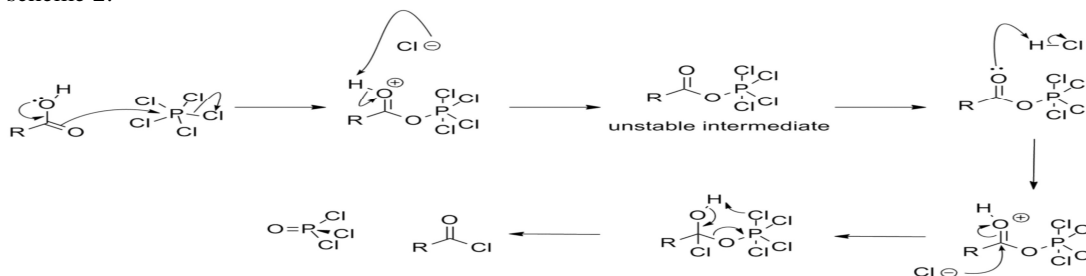
The UV spectra of all Schiff base compounds were characterized by appearance of three bands in absolute ethanol, the first band appeared within the range (210-225) nm [ $\epsilon = (580-2382) \text{ l. mole}^{-1} \cdot \text{cm}^{-1}$ ] which was attributed to the ( $\pi-\pi^*$ ) for the aromatic system. The second band appeared in the range (240-250) nm [ $\epsilon = (500-2485) \text{ l. mole}^{-1} \cdot \text{cm}^{-1}$ ] which was attributed to the ( $\pi-\pi^*$ ) for the aromatic system. The third band appeared in the range (328-388) nm [ $\epsilon = (305-2344) \text{ l. mole}^{-1} \cdot \text{cm}^{-1}$ ] which was attributed to the ( $\pi-\pi^*$ ) transition of azomethane (C=N). The IR spectra of substituent phenyl thiazole Schiff base compounds were characterized by the disappearance of the absorption band that was attributed to the (C=O) stretching which appeared at (1700-1750)  $\text{cm}^{-1}$  due to the aldehydes compounds and ( $\text{NH}_2$ ) stretching bands (3224-3430)  $\text{cm}^{-1}$  which were present in spectrum of amino phenyl thiazole, these fact confirmed the correct expected chemical structure of these compounds. The  $^1\text{HNMR}$  spectra of (SB1-SB12) substituent phenyl thiazole compounds showed multiplet signal within the region (6.7-8) ppm due to aromatic ring system. While the protons of thiazole ring and azomethane was interferences with the protons of aromatic ring in the same region. In addition, the  $^1\text{HNMR}$  spectrum of SB7, SB8 and SB11 compounds showed singlet signals at the chemical shift (2-4) ppm due to the three-proton equivalent of methoxy, methyl and six-proton equivalent of N, N-dimethyl groups. All  $^{13}\text{CNMR}$  spectra showed (12) peak, come back to SBI-SB9 expect TH5 and (16) peak for SB1, SB10-SB12.

The synthesis 2-Azetidinone method was include to convert chloroacetic acid into chloroacetyl chloride with high selectivity; this is achieved by using phosphorous penta chloride ( $\text{PCl}_5$ ) without any catalyst as shown in Eq. 2.



The compound was purified by fractional distillation in the boiling point  $105^\circ\text{C}$ .

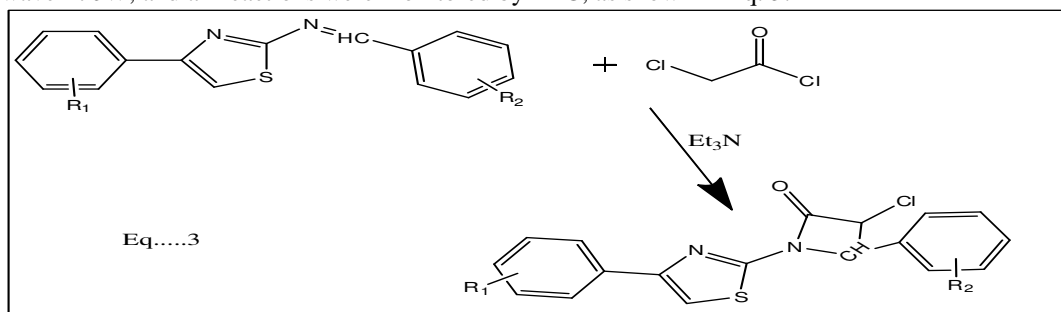
The mechanism was detailed and established, the first step is thought to be formation of an unstable intermediate, and then chlorine atom attack the carbonyl group to formation acetyl chloride as shown in the scheme 2.



Scheme 2

2-azetidinones, commonly known as  $\beta$ -lactam, are well known heterocyclic compounds among the organic and medicinal chemistry. The activity of known antibiotics such as penicillin, cephalosporin and carbapenems are attributed to the presence of 2-azetidinone ring in there structure<sup>(23)</sup>.

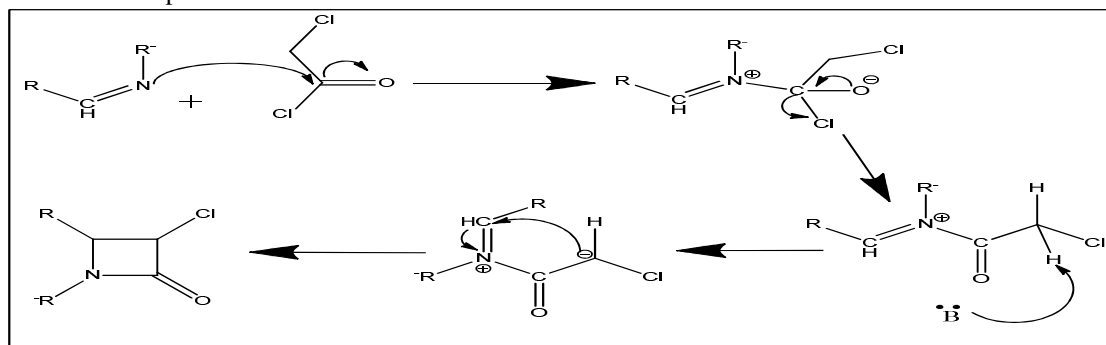
The investigated 2-azetidinone compounds in our research were synthesized by cycloaddition reaction of substituted thiazole Schiff bases with chloroacetyl chloride in dioxane by using triethylamine as catalyst in microwave 270W, and all reactions were monitored by TLC, as shown in Eq. 3.



All these reactions are needed short time between (3-4min.) and companied increasing in the yield of products.

The purified Azetidinone compounds were tested by thin layer chromatography (TLC) using different eluents. The best separation was obtained in mixture of (hexane: ethyl acetate) (3:7) as eluent. The compounds were purified by using absolute ethanol.

The mechanism of reaction can be explained in scheme 3, synthesis of  $\beta$ -lactam by the addition (C-N) to (C=O) component to form a ring substituted acetyl chloride with electron. At least carbanion was added to imine cation in the presence of amine bases.



Scheme 3

The structures of the synthesized azetidinone were confirmed by their elemental analysis; UV, IR, NMR and MS. CHN were situated within the range, which confirmed the validity of the suggested structure of the prepared compounds. The UV spectra of all 2-azetidinone compounds were characterized by appearance of three bands in absolute ethanol, the first band appeared within the range (210-225) nm [ $\epsilon = (600-1580)$  l.mole<sup>-1</sup>. cm<sup>-1</sup>] which was attributed to the ( $\pi-\pi^*$ ) for the aromatic system. The second band appeared within the range (260-280) nm [ $\epsilon = (650-1814)$  l.mole<sup>-1</sup>. cm<sup>-1</sup>] which was attributed to the ( $\pi-\pi^*$ ) for the aromatic system. The third band appeared in the range (290-320) nm [ $\epsilon = (292-1775)$  l.mole<sup>-1</sup>. cm<sup>-1</sup>] which was attributed to the ( $\pi-\pi^*$ ) transition of amide (N-C=O). The spectra of all 2-azetidinone compounds were characterized by the appearance of the absorption band that was attributed to the (C=O) stretching of amide which appeared at (1630-1690) cm<sup>-1</sup>. The <sup>1</sup>HNMR spectra of (AZ1-AZ12) 2-azetidinone compounds showed multiplet signal within the region (6.7-8) ppm due to aromatic ring system. While the proton of thiazole ring was interference with the protons of aromatic ring in the same region. The <sup>1</sup>HNMR spectrum appears two signals in the region (3.5-5.5) ppm which was due to aliphatic protons of azetidine ring, the first was due to proton that near nitrogen atom and the other from proton that near carbonyl group. In addition, the <sup>1</sup>HNMR spectrum of AZ6, AZ7 and AZ11 compounds showed singlet signals at the chemical shift (2-4) ppm due to the three proton equivalent of methoxy, methyl and six three proton equivalent of N,N-dimethyl groups. All <sup>13</sup>CNMR spectra showed (15) peak, come back to AZI-AZ9 expect AZ5 and (19) peak for AZ1, AZ10-AZ12.

### Biological Activities

The antibacterial<sup>(24, 25)</sup> activities of the series (SB1-SB12) and (AZ1-AZ12) have been carried out against some strain of bacteria. The result (Table 3) showed that prepared compounds are toxic against the bacteria. The Schiff base and azetidinone compounds were found more active against the above microbes. The comparison of the antibacterial activity of these compounds with Streptomycin shows that these compounds have almost similar activity.

The bacterial cultures for *S. aureus*, and *E. coli* were obtained from Department of biology University of Basrah, Iraq. The bacterial cultures were incubated at 30 °C for 24 hours by inoculation into nutrient agar. Schiff bases and azetidinone were stored dry at room temperature and dissolved 20mg/ml in dimethyl sulfoxide (DMSO). Antibacterial activities of each compound were evaluated by the agar disc-diffusion method. Mueller Hinton Agar Media (15 cm<sup>3</sup>) kept at 45°C was poured in the petridishes and allowed to solidify. Poured Petri plates (9 cm) were incubated with 50 $\mu$ L of normal saline solution of above culture media (105-106 bacteria per ml). Discs injected with prepared Schiff bases and azetidinone (50 $\mu$ L) were applied on the solid agar medium by pressing tightly. The Petri plates were placed at 37°C for 24 hours. At the end of period, the inhibition zones formed on media were measured with a zone reader in millimetres.

**Table 3: inhibition zones (mm) of the synthesis thiazoles, Schiff bases and azetidinones**

| Sym.         | IZ( <i>S.aureus</i> ) mm | IZ ( <i>E.coli</i> ) mm, | Sym. | IZ( <i>S.aureus</i> ) mm | IZ ( <i>E.coli</i> ) mm |
|--------------|--------------------------|--------------------------|------|--------------------------|-------------------------|
| SB1          | 5                        | 3                        | AZ1  | 11                       | X                       |
| SB2          | 12                       | X                        | AZ2  | 16                       | 15                      |
| SB3          | 13                       | X                        | AZ3  | 14                       | 13                      |
| SB4          | 11                       | 10                       | AZ4  | 14                       | 14                      |
| SB5          | 14                       | 12                       | AZ5  | 13                       | 10                      |
| SB6          | 15                       | 13                       | AZ6  | 17                       | 16                      |
| SB7          | 19                       | 18                       | AZ7  | 9                        | 7                       |
| SB8          | 7                        | 5                        | AZ8  | 9                        | 7                       |
| SB9          | X                        | X                        | AZ9  | 18                       | 14                      |
| SB10         | 12                       | 9                        | AZ10 | 19                       | 12                      |
| SB11         | 18                       | 15                       | AZ11 | 5                        | X                       |
| SB12         | X                        | X                        | AZ12 | 5                        | X                       |
| streptomycin | 9                        | 12                       |      |                          |                         |

X=zero activity

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