

## SYNTHESIS AND CHARACTERIZATION OF SOME NEW MONO AND BIS CYCLIC AZETIDIN-2-ONES

ABDULRHMAN YUSER KHALIFA & MAHMOOD SHAKIR MAGTOOF

Department of Chemistry, Science College Thiqr University, Thiqr, Nashyria, Iraq

### ABSTRACT

This study is concerned with the synthesis and characterization the 3-methoxy/3,3-dithio dipropyl mono and bicyclic azetid-2-ones **3 (a-d)**. These compounds **3 (a,b)** were prepared by reacting methoxyacetyl chloride with the appropriate imines **2(a,b)** in the presence of triethylamine in dry dichloromethane under nitrogen atmosphere at  $-10^{\circ}\text{C}$  and the compounds **3 (c,d)** were prepared by reacting 3,3'-dithio dipropanoic acid with the appropriate Schiff's base **2 (c,d)** in the presence of triethylamine with phosphorusoxychloride in dry dichloromethane under nitrogen atmosphere at  $-10^{\circ}\text{C}$ . The active acid chloride reacts with triethylamine to generate corresponding ketene in situ which further reacts with Schiff's base to furnish corresponding 3-methoxy/3,3-dithio dipropyl mono and bicyclic azetid-2-ones **3 (a-d)**.

**KEYWORDS:** Characterization, Heterocyclic Compounds

### INTRODUCTION

The first synthesis of a  $\beta$ -lactam was accomplished in 1907, when Staudinger discovered that ketenes and imines could undergo [2+2] cycloadditions to yield the  $\beta$ -lactam ring<sup>1</sup> (**Figure 1**).  $\beta$ -lactam, commonly known as 2-Azetidinones, are wellknown heterocyclic compounds among the organic and medicinal chemists.<sup>2</sup>

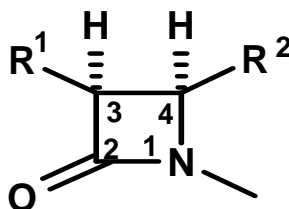


Figure 1

$\beta$ -lactam antibiotics have occupied a central role in the fight against pathogenic bacteria and the subsequent rise in quality of life for the world population as a whole.<sup>3</sup> However, the extensive use of common  $\beta$ -lactam antibiotics such as penicillins and cephalosporins (**Figure 2**) in medicine has resulted in an increasing number of resistant strains of bacteria through mutation and  $\beta$ -lactam gene transfer.<sup>4</sup> The medicinal application of  $\beta$ -lactam as cholesterol absorption inhibitor has been reported.<sup>5</sup>

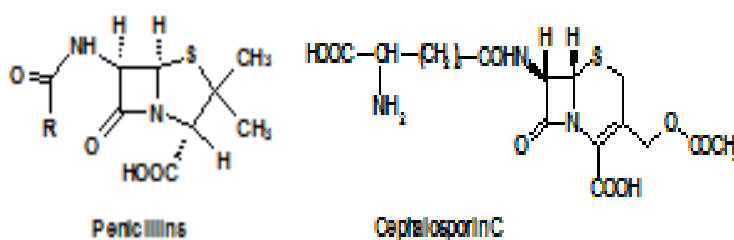


Figure 2

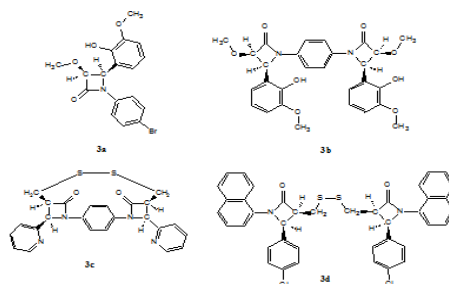
The  $\beta$ -Lactam nucleus is the key to the biological activity of a large class of compounds characterized by the presence of this four-membered ring and differentiated by side chains, unsaturations, heteroatoms, and, in many cases, by the presence of five- or six-membered rings. The successful application of  $\beta$ -lactam antibiotics in the treatment of infectious diseases has been well documented for many years<sup>6</sup>. The potential use of some  $\beta$ -lactams as therapeutic agents for lowering plasma cholesterol levels<sup>7,8</sup>, as inhibitors of enzymes such as thrombin<sup>9</sup>, HLE (human leukocyte elastase)<sup>10</sup> and the protease, responsible for capsid assembly and viral maturation of HCMV (human cytomegalovirus)<sup>11</sup> has been documented as well. The  $\beta$ -lactam structure is also the essential scaffold of several antagonists directed to the vasopressin V1 receptor<sup>12</sup> and 2-azetidinones have been reported to show apoptosis inducing properties against human solid tumor cell lines<sup>13</sup>. Due to the large pharmacological potential and use of the  $\beta$ -lactam systems, intensive research has generated numerous methods for synthesizing this skeleton.

In addition to its use in the synthesis of variety of  $\beta$ -lactam antibiotics, the  $\beta$ -lactam skeleton has been recognized as a useful building block by exploiting its strain energy associated with four member ring<sup>14</sup>. Efforts have been made in exploring such new aspects of  $\beta$ -lactam chemistry using pure  $\beta$ -lactams as versatile intermediates for organic syntheses<sup>15</sup>. Ojima et al.<sup>16</sup>, have shown the utility of bis- $\beta$ -lactams for the synthesis of peptides. The synthesis of bis- $\beta$ -lactams, in general, has been reported by a step-wise construction of  $\beta$ -lactam rings<sup>17</sup>. In continuation of our work on the synthesis of  $\beta$ -lactams (Monobactams)<sup>18</sup> and bis- $\beta$ -lactams<sup>19</sup> we were interested in building bis- $\beta$ -lactams from bisimines using the Staudinger cycloaddition reaction employing newer reagents. Infections caused by antibiotic-resistant bacteria pose a constant challenge both to physicians and researchers. Growing resistance among infectious gram-positive and gram-negative pathogens has forced the scientific community not only to develop new and innovative antibiotics to combat these advancing strains, but new ways of understanding and observing the mechanisms by which these drugs act.

The monolactam class of penicillin drugs belongs to the  $\beta$ -lactamase inhibitory class of antibiotics as a subset of the  $\beta$ -lactam class of general antibiotics<sup>20</sup>. These antibiotics operate around the key chemical structure of the four membered  $\beta$ -lactam ring. These drugs function by inhibiting the production of the bacterial cell wall through competitive inhibition of transpeptidase during cell wall synthesis<sup>21,22,23</sup>. This results in a weak, deformed cell wall that will not survive the regular changes in osmotic cellular pressure. These drugs have shown great success due to their lack of toxicity in humans. Unfortunately, many pathogens have developed bacterial resistance to  $\beta$ -lactam antibiotics through the production of a  $\beta$ -lactamase enzyme that hydrolyzes the  $\beta$ -lactam unit before it is able to reach the target, rendering the antibiotic inactive.

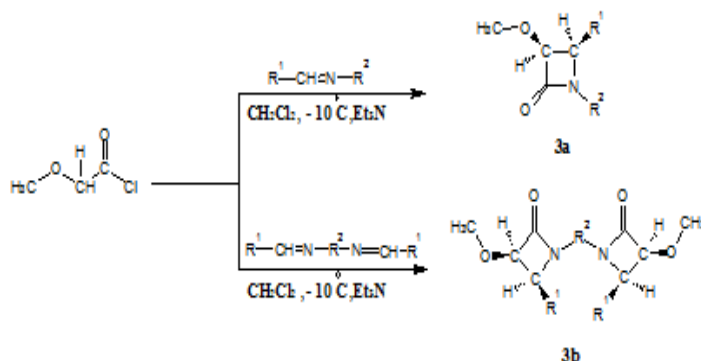
## RESULTS AND DISCUSSIONS

Taking a lead from earlier studies,<sup>24</sup> it was considered to utilize ketene-imine cyclization in the presence of triethylamine furnishing C<sub>3</sub>-C<sub>4</sub> bond formation of  $\beta$ -lactam as key steps for the synthesis of 3-methoxy/3,3-dithio dipropyl mono and bicyclic azetidin-2-ones **3 (a-d)** ( **Figure 3** )



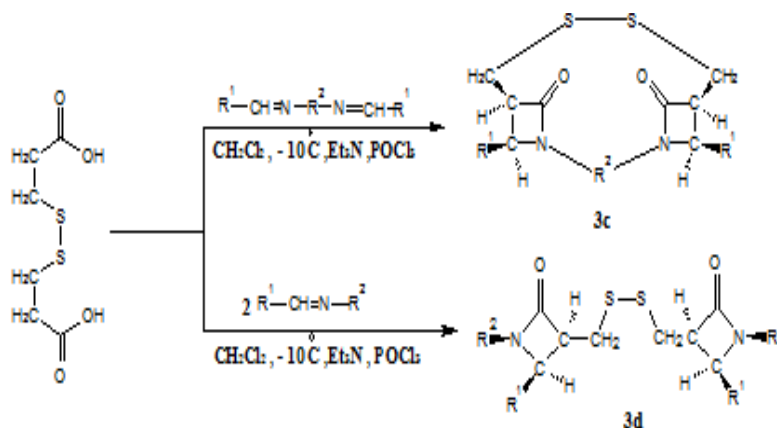
**Figure 3**

So, the key step for the synthesis of 3-methoxy dipropyl mono and bicyclic azetidin-2-ones **3 (a,b)** involve the treatment of imines **2 (a,b)** with methoxyacetyl chloride in the presence of triethylamine with dichloromethane as solvent under dry system( $N_2$  atmosphere) as shown in **Scheme 1**.



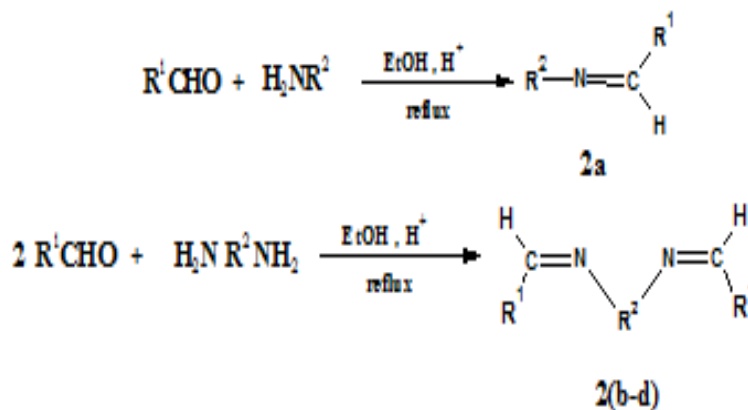
Scheme 1

The synthesis of 3,3-dithio dipropyl mono and bicyclic azetidin-2-ones **3 (c,d)** involve the treatment of imines **2 (c,d)** with 3,3'-dithio dipropanoic acid in the presence of triethylamine and phosphorus oxy-chloride with dichloromethane as solvent under dry system( $N_2$  atmosphere) as shown in **Scheme 2**.



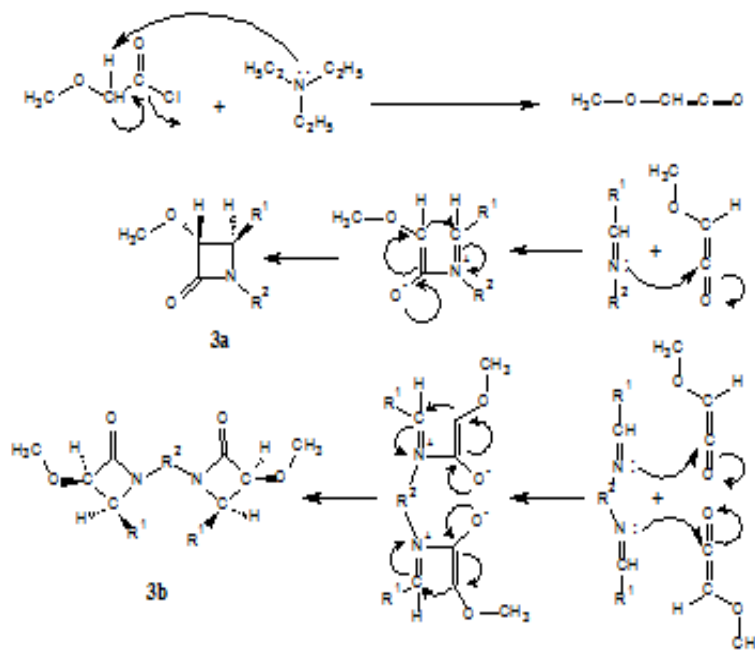
Scheme 2

The required Various Schiff's bases **2(a-d)** for the  $\beta$ -lactams formation **3(a-d)** were prepared from reacting of equimolar amounts of appropriate aromatic aldehydes and aromatic amines either in refluxing ethanol. The structures of these imines **2(a-d)** were confirmed on the basis of their spectral data IR, shown as below in (**schemes 3**) and **table (1)**.



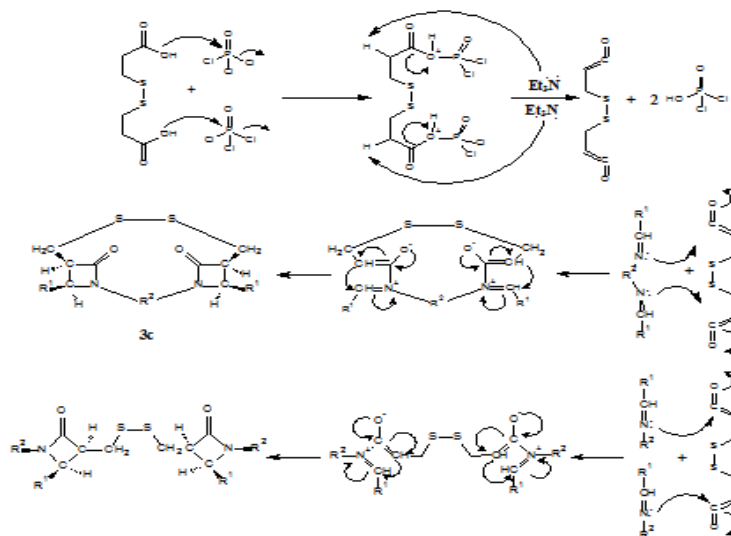
Scheme 3

Further, the 3-methoxy dipropyl mono and bicyclic azetidin-2-ones **3 (a,b)** were prepared from methoxyacetyl chloride and appropriate Schiff's bases **2(a,b)** in the presence of triethylamine. The active acid chloride was treated with triethylamine to give the corresponding ketene in situ which subsequently reacted with Schiff's base **2(a,b)** and afforded the corresponding  $\beta$ -lactam in moderate yields. The proposed mechanism for their formations was shown as below in (schemes 4) and table (1).



Scheme 4

The 3,3-dithio dipropyl mono and bicyclic azetidin-2-ones **3 (c,d)** were prepared from 3,3'-dithio dipropanoic acid and appropriate Schiff's bases **2(c,d)** in the presence of triethylamine. The active acid chloride formed from an appropriate acid with  $\text{POCl}_3$  was treated with triethylamine to give the corresponding ketene in situ which subsequently reacted with Schiff's base **2(c,d)** and afforded the corresponding  $\beta$ -lactam in moderate yields. The proposed mechanism for their formations was shown as below in (schemes 5) and table (1).



Scheme 5

Table 1: Compounds  $\beta$ -lactam and Imine

S.No	Imines	Compounds $\beta$ -lactam	R <sup>1</sup>	R <sup>2</sup>
1	2a	3a		
2	2b	3b		
3	2c	3c		
4	2d	3d		

The structures of these azetidine-2-ones were established on the basis of spectral data, Mass, <sup>1</sup>H NMR, <sup>13</sup>C NMR spectra.

The <sup>1</sup>H-NMR spectra of compound **3a** showed two doublets C<sub>3</sub>-H  $\delta$ (4.45-4.46) ppm and C<sub>4</sub>-H  $\delta$ (4.12-4.13) ppm with J= (2.5) Hz. The <sup>1</sup>H-NMR spectrum of compound **3a** showed singlet peak (equivalent protons) for two methoxy groups, one of these groups singlet at  $\delta$ (3.85) ppm for (CH<sub>3</sub>O-C<sub>3</sub>) and the other one at  $\delta$ (4.01) ppm for anisole group (CH<sub>3</sub>O-Ph) (s,3H, OCH<sub>3</sub>), and showed peak at (10.11) ppm for hydroxyl phenolic groups. Finally, <sup>1</sup>H-NMR spectra of **3a** showed aromatic protons integrated 7H at  $\delta$ (6.92 -7.98) ppm shown in **Figure (4)**.

The <sup>1</sup>H-NMR spectra of compound **3b** showed four distinct doublets C<sub>3</sub>-H  $\delta$ (6.61-6.64) ppm and C<sub>4</sub>-H  $\delta$ (6.48-6.52) ppm with J = (8.75) Hz. The <sup>1</sup>H-NMR spectrum of compound **3b** showed singlet peak (equivalent protons) for four methoxy groups, two of these groups singlet at  $\delta$ (3.82) ppm for (CH<sub>3</sub>O-C<sub>3</sub>) and the other two at  $\delta$ (4.03) ppm for anisole group (CH<sub>3</sub>O-Ph) (s,3H, OCH<sub>3</sub>), and showed peak at (9.92) ppm for hydroxyl phenolic groups. Finally, <sup>1</sup>H-NMR spectra of **3b** showed aromatic protons integrated 10H at  $\delta$ (6.92 - 7.98) ppm shown in **Figure (5)**.

The <sup>1</sup>H-NMR spectra of compound **3c** showed four distinct doublets C<sub>3</sub>-H  $\delta$ (4.093-4.121) ppm and C<sub>4</sub>-H  $\delta$ (4.036-4.064) ppm with J = (7) Hz. The <sup>1</sup>H-NMR spectrum of compound **3c** showed doublet peak at 3.04 ppm for four hydrogen (d-4H-CH<sub>2</sub>-), Finally, <sup>1</sup>H-NMR spectra of **3c** showed aromatic protons integrated 14H at  $\delta$ (7.34-8.93) ppm shown in **Figure (6)**.

The <sup>1</sup>H-NMR spectra of compound **3d** showed four distinct doublets C<sub>3</sub>-H  $\delta$ (4.094-4.122) ppm and C<sub>4</sub>-H  $\delta$ (4.016-4.044) ppm with J = (7) Hz. The <sup>1</sup>H-NMR spectrum of compound **3c** showed doublet peak at 3.14 ppm for four hydrogen (d-4H-CH<sub>2</sub>-), Finally, <sup>1</sup>H-NMR spectra of **3c** showed aromatic protons integrated 22H at  $\delta$ (7.03-8.74) ppm shown in **Figure (7)**.

The <sup>13</sup>C NMR spectra of the **3a,3b,3c and 3d** of the azetidine -2-ones. The resonance as between  $\delta$ 163.9-171.2 ppm were assigned to the carbonyl<sup>82,83,84</sup> groups. The resonance compound **3a** at  $\delta$  168.74 ppm assigned to the carbonyl carbon atom, whereas the singlet at  $\delta$  150.88, 148.36, 138.31, 132.76, 131.88, 124.31, 122.12, 119.64, 116.16, 115.63 ppm were belonged to the aromatic carbons. C<sub>4</sub>-H and C<sub>3</sub>-H were appeared at  $\delta$  72.12 and 59.11 ppm respectively, where as the resonance at  $\delta$  56.51 and 56.32 ppm were assigned to the methoxy carbon atom of anisole and C<sub>3</sub>-OMe shown in **Figure (8)**.

The <sup>13</sup>C NMR spectra of the **3b** showed two peaks, appeared at 59.13 ppm for (C<sub>3</sub>-H) and another one at  $\delta$  72.19 for carbon (C<sub>4</sub>-H) (equivalent carbon). And the singlet at  $\delta$  56.33 ppm for two methoxy groups (equivalent carbon), also the <sup>13</sup>C NMR spectra of **3b** showed singlet at  $\delta$  59.03 ppm for two methoxy groups of anisole (equivalent carbon), also the <sup>13</sup>C NMR spectra of **3b** showed singlet peak at  $\delta$  168.58 ppm for two carbonyl groups (equivalent carbon).

Finally the  $^{13}\text{C}$  NMR spectrum of the **3b** showed aromatic carbon at  $\delta$  150.96, 143.42, 138.05, 124.27, 122.16, 120.95, 119.59, 114.60 ppm shown in **Figure (9)**.

The  $^{13}\text{C}$  NMR spectra of the **3c** showed two peaks, appeared at 79.96 ppm for ( $\text{C}_3\text{-H}$ ) and another one at  $\delta$  60.62 for carbon ( $\text{C}_4\text{-H}$ ) (equivalent carbon). also the  $^{13}\text{C}$  NMR spectra of **3c** showed singlet peak at  $\delta$  39.6 ppm for two methylene carbon atom (equivalent carbon), also the  $^{13}\text{C}$  NMR spectra of **3c** showed singlet peak at  $\delta$  173.1 ppm for two carbonyl groups (equivalent carbon). Finally the  $^{13}\text{C}$  NMR spectrum of the **3c** showed aromatic carbon at  $\delta$  150.98, 142.09, 138.19, 127.65, 126.5, 120.07, 119.15 ppm shown in **Figure (10)**.

The  $^{13}\text{C}$  NMR spectra of the **3d** showed two peaks, appeared at 65.1 ppm for ( $\text{C}_3\text{-H}$ ) and another one at  $\delta$  60.66 for carbon ( $\text{C}_4\text{-H}$ ) (equivalent carbon). also the  $^{13}\text{C}$  NMR spectra of **3d** showed singlet peak at  $\delta$  39.2 ppm for two methylene carbon atom (equivalent carbon), also the  $^{13}\text{C}$  NMR spectra of **3d** showed singlet peak at  $\delta$  170.36 ppm for two carbonyl groups (equivalent carbon). Finally the  $^{13}\text{C}$  NMR spectrum of the **3d** showed aromatic carbon at  $\delta$  139.72, 134.16, 133.94, 131.64, 129.83, 129.04, 128, 71, 128.55, 126.9, 126.47, 126.01, 125.87, 123.17, 122.2 ppm shown in **Figures (11)**.

**The Mass Spectral** data of the prepared derivatives are gathered in the **Figures (12), (13) and (14)**, The mass spectra of compound **3a,3b** and **3d** showed the molecular ion peak corresponding to the particular compound [ $\text{M}^+$ ],  $m/z=377, 520, 705$ . The fragmentation of **3a,3b** and **3d** lead to ketene, isocyanates and imine. The fragmentation of **3(a,b,d)** leading to the ketene  $m/z = 72, 72, 174$  and the corresponding isocyanates  $m/z = 197, 160, 1469$  also the fragmentation of this compound **3a,3b** and **3d** showed the imine peaks  $m/z = 305, 376, 265.5$ . The fragmentation mechanism of compounds **3(a,b,d)** is shown below<sup>25,26</sup>.

## The Experimental

All solvents were distilled / dried prior to use, when this seemed necessary by standard methods. All solvent extracts were dried over anhydrous sodium sulphate unless other wise specified.  $^{13}\text{C}$  NMR;  $^1\text{H}$ NMR Spectroscopy were recorded using Bruker DRX system AL 250 (250 MHz). in the Department of Chemistry, University of Kashan, Iran.. **Mass spectrum** were recorded at 70 eV using agalint technologes Spectrum 5973 in the Department of Chemistry, University of Kashan, Iran.. **IR spectra** were recorded, using shimadzu FT-IR affinity spectrophotometer and Bruker in the Department of Chemistry, College of Science, Thi-Qar University, Iraq, as KBr disks. Only principal absorption bands of interest are reported and expressed in  $\text{cm}^{-1}$ .

- **Preparatio of Schiff base 2(a-d)**<sup>27</sup>
- **{[(4-bromophenyl)imino]methyl}-6-methoxyphenol (2a).**

A mixture of an appropriate 4-bromoaniline (**0.01 mole**) and an o-vanillin (**0.01 mole**) in **25 ml** of absolute ethanol and one drop of glacial acetic acid was heated at (70-80°C) for 30 min. The progress of the reaction was checked by TLC. After completion the solvent was evaporated then recrystallized from a suitable solvent.

### ***N, N'*-bis [(2-Hydroxy-3-Methoxyphenyl) Methylidene] Benzene 1,4-Diamine (2b)**

A mixture of an appropriate p-phenylenediamin (**0.01 mole**) and an o-vanillin (**0.02 mole**) in **25 ml** of absolute ethanol and one drop of glacial acetic acid was heated at (70-80°C) for 30 min. The progress of the reaction was checked by TLC. After completion the solvent was evaporated then recrystallized from a suitable solvent.

***N,N'*-bis (Pyridin-2-Ylmethylidene) Benzene-1,4-Diamine (2c)**

A mixture of an appropriate p-phenylenediamin (**0.01 mole**) and an 2-pyridinecarboxaldehyde (**0.02 mole**) in **25 ml** of absolute ethanol and one drop of glacial acetic acid was heated at (70-80°C) for 30 min. The progress of the reaction was checked by TLC. After completion the solvent was evaporated then recrystallized from a suitable solvent.

***N*-[(4-Chlorophenyl) Methylidene] Naphthalen-1-amine (2d)**

A mixture of an appropriate 1-aminonaphthalene (**0.01 mole**) and an 4-chlorobenzaldehyde (**0.01 mole**) in **25 ml** of absolute ethanol and one drop of glacial acetic acid was heated at (70-80°C) for

(5-6) h. The progress of the reaction was checked by TLC. After completion the solvent was evaporated then recrystallized from a suitable solvent.

**Preparation of  $\beta$ -lactam<sup>28,29</sup>****1-(4-Bromophenyl)-4-(2-Hydroxy-3-Methoxyphenyl)-3-Methoxy Azetidin-2-One. (3a)**

To a suspension of 2-[(4-bromophenyl)imino]methyl-6-methoxyphenol **2a** (1.0 g, 3.26 mmole) and triethylamine (0.99 g, 3 mmole, 1.37 mL) in 40 mL of dry dichloro methane, was added dropwise, under nitrogen atmosphere at 0°C, a solution of methoxyacetyl chloride (0.35 g, 3.26 mmole, 0.29 mL), in 20 mL of dry dichloromethane with stirring at 0°C. The reactants were stirred overnight at room temperature. There after, the contents were washed successively with 1N HCL (20 mL), water (2×20 mL), 5% NaHCO<sub>3</sub> (20 mL) and brine (20 mL). The organic layer was dried Na<sub>2</sub>SO<sub>4</sub>. The solvent was evaporated under vacuum to give a crude product which was purified on a silica gel column using 3:7 ethyl acetate/ hexane as eluent. furnished pure  $\beta$ -lactam **3a**. Yield: 70%, m.p.: 133-135, <sup>1</sup>H-NMR (DMSO-*d*<sub>6</sub>): 4.12 (d, 1H, C<sub>3</sub>-H), 4.45 (d, 1H, C<sub>4</sub>-H), 3.85 (s, 3H, CH<sub>3</sub>-O-C<sub>3</sub>), 4.01 (s, 3H, CH<sub>3</sub>-O-Ar), 10.11 (s, 1H, OH), 6.92 -7.98 (7H, Ar-H), <sup>13</sup>C NMR (DMSO-*d*<sub>6</sub>): 72.12 (C<sub>4</sub>-H), 59.11 (C<sub>3</sub>-H), 168.74 (C=O), 56.51 (CH<sub>3</sub>-O-Ar), 56.32 (CH<sub>3</sub>-O-C<sub>3</sub>), 150.88, 148.36, 138.31, 132.76, 131.88, 124.31, 122.12, 119.64, 116.16, 115.63 (Ar-C). Mass: 377 m/s

**1, 1'-(Benzene-1, 4-Diyl) bis[4-(2-Hydroxy-3-Methoxyphenyl)-3-Methoxy Azetidin-2-one] (3b)**

To a suspension of *N,N'*-bis[(2-hydroxy-3-methoxyphenyl) methylidene]benzene-1,4-diamine **3b** (1.0g, 2.65 mmole) and triethylamine (1.61 g, 6.0 mmole, 2.23 mL) in 40 mL of dry dichloro methane was added dropwise under nitrogen atm a solution of methoxyacetyl chloride (0.57 g, 5.3 mmole, 0.48 mL) in 20 mL of dry dichloro methane with stirring. The reaction mixture was worked up as usual. The crude product was poured on a silica gel column using 4:6 ethyl acetate: hexane as eluent furnished the pure  $\beta$ -lactam **3b**. Yield: 67%, m.p.: 140-142, <sup>1</sup>H-NMR (DMSO-*d*<sub>6</sub>): 6.48 (d, 2H, C<sub>3</sub>-H), 6.61 (d, 2H, C<sub>4</sub>-H), 3.82 (s, 6H, CH<sub>3</sub>-O-C<sub>3</sub>), 4.03 (s, 6H, CH<sub>3</sub>-O-Ar), 9.92 (s, 2H, OH), 6.92 -7.98 (10H, Ar-H), <sup>13</sup>C NMR (DMSO-*d*<sub>6</sub>): 59.13 (C<sub>3</sub>-H), 72.19 (C<sub>4</sub>-H), 168.58 (C=O), 59.03 (CH<sub>3</sub>-O-Ar), 56.33 (CH<sub>3</sub>-O-C<sub>3</sub>), 150.96, 143.42, 138.05, 124.27, 122.16, 120.95, 119.59, 114.60 (Ar-C). Mass: 520 m/s

**1, 1'-(Benzene-1,4-Diyl)-3,3'-(Dithiodimethyl) Bis[4-(Pyridin-2-yl) Azetidin-2-One]. (3c)**

To a suspension of 3,3'-dithiodipropanoic acid (0.73 g, 3.49 mmole), *N,N'*-bis(pyridin-2-ylmethylidene)benzene-1,4-diamine **2c** (1.0g, 3.49 mmole) and triethylamine (2.11 g, 6.0 mmole, 2.94 mL) in 40 mL of dry dichloro methane was added dropwise under nitrogen atm a solution of POCl<sub>3</sub> (1.34 g, 2.5 mmole, 0.8 mL) in 20 mL of dry dichloro methane with stirring. The reaction mixture was worked up as usual. The crude product was poured on a silica gel column using 4:6 ethyl acetate : hexane as eluent furnished the pure  $\beta$ -lactam **3c**. Yield: 63%, m.p.: 125-127 <sup>1</sup>H-NMR (DMSO-*d*<sub>6</sub>): 4.03 (d, 2H, C<sub>3</sub>-H), 4.09 (d, 2H, C<sub>4</sub>-H), 3.04 (d, 4H, -CH<sub>2</sub>-), 7.34 -8.93 (14H, Ar-H). <sup>13</sup>C NMR (DMSO-*d*<sub>6</sub>): 79.96 (C<sub>3</sub>-H), 60.62 (C<sub>4</sub>-H), 173.1 (C=O), 39.6 (CH<sub>2</sub>), 150.98, 142.09, 138.19, 127.65, 126.5, 120.07, 119.15 (Ar-C).

### 3, 3'-(Dithiodimethyl)Bis[4-(4-Chlorophenyl)-1-(Naphthalen-1-yl) Azetidin-2-One] (3d)

To a suspension of 3,3'-dithiodipropionic acid (0.39 g, 1.88 mmole), *N*-(4-chlorophenyl) methylidene)naphthalen-1-amine **3d** (1.0g, 3.76 mmole) and triethylamine (1.14 g, 6.0 mmole, 1.58 mL) in 40 mL of dry dichloro methane was added dropwise under nitrogen atm a solution of POCl<sub>3</sub> (0.69 g, 2.5 mmole, 0.41 mL) in 20 mL of dry dichloro methane with stirring. The reaction mixture was worked up as usual. The crude product was poured on a silica gel column using 4:6 ethyl acetate : hexane as eluent furnished the pure  $\beta$ -lactam **3d**. Yield: 78%, m.p.:163-165

<sup>1</sup>H-NMR (DMSO-*d*<sub>6</sub>): 4.01 (d, 2H, C<sub>3</sub>-H), 4.09 (d, 2H, C<sub>4</sub>-H), 3.14 (d, 4H, -CH<sub>2</sub>-), 7.03-8.74 (22H, Ar-H). <sup>13</sup>C NMR (DMSO-*d*<sub>6</sub>): 65.1 (C<sub>3</sub>-H), 60.66 (C<sub>4</sub>-H), 170.36 (C=O), 39.02 (CH<sub>2</sub>), 139.72, 134.16, 133.94, 131.64, 129.83, 129.04, 128, 71, 128.55, 126.9, 126.47, 126.01, 125.87, 123.17, 122.2 (Ar-C). Mass: 705 m/s.

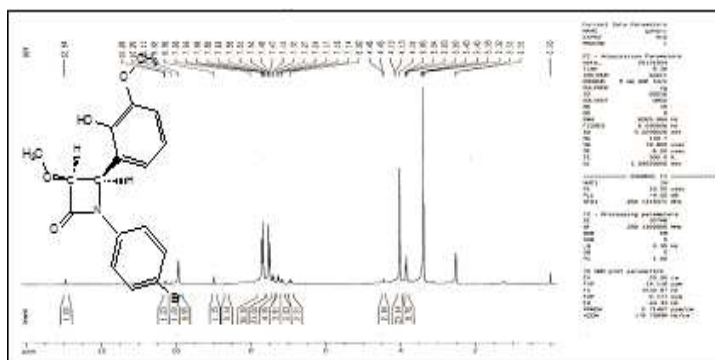


Figure 4: <sup>1</sup>H NMR Spectrum of 1-(4-Bromophenyl)-4-(2-Hydroxy-3-Methoxy-Phenyl)-3-Methoxyazetidin-2-One. **3a**

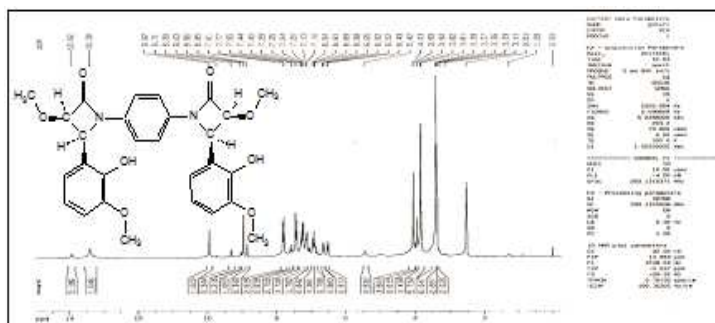


Figure 5: <sup>1</sup>H NMR Spectrum of 1,1'-(Benzene-1,4-Diyl) bis[4-(2-Hydroxy-3-Methoxy-Phenyl)-3-Methoxyazetidin-2-One]. **3b**

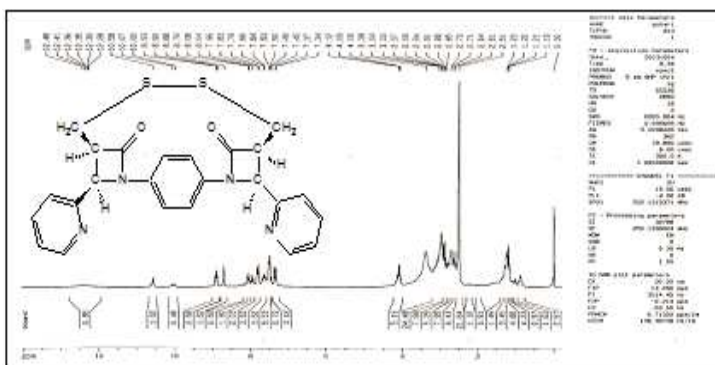


Figure 6: <sup>1</sup>H NMR Spectrum of 1,1'-(Benzene-1,4-Diyl)-3,3'-(Dithiodimethyl) Bis[4-(Pyridin-2-yl)Azetidin-2-One]. **3c**



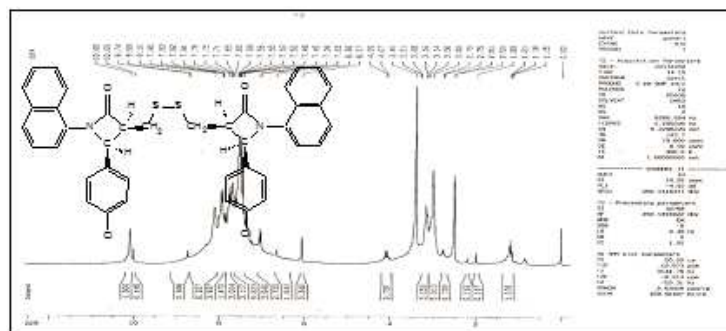


Figure 7: <sup>1</sup>H NMR Spectrum of 3,3'-(Dithiodimethyl) bis [4-(4-Chlorophenyl)-1-(Naphthalene-1-yl) Azetidin-2-One]. 3d

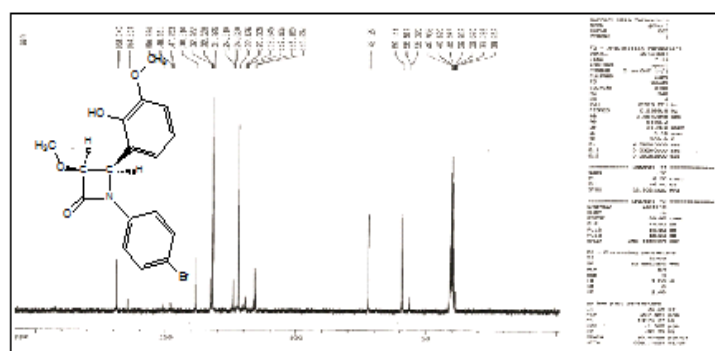


Figure 8: <sup>13</sup>C NMR Spectrum 1-(4-Bromophenyl)-4-(2-Hydroxy-3-Methoxyphenyl)-3-Methoxyazetidin-2-one. 3a

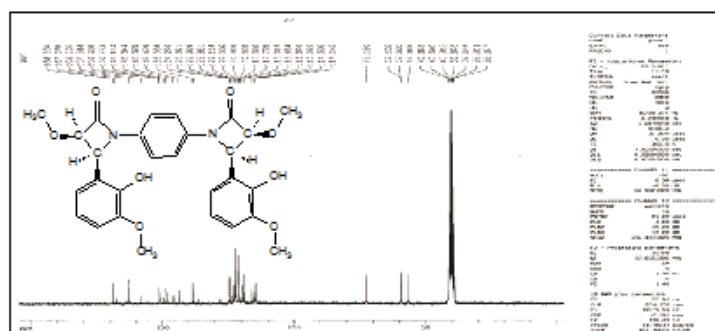


Figure 9: <sup>13</sup>C NMR spectrum 1,1'-(benzene-1,4-diyl) bis [4-(2-hydroxy-3-methoxyphenyl)-3-methoxyazetidin-2-one]. 3b

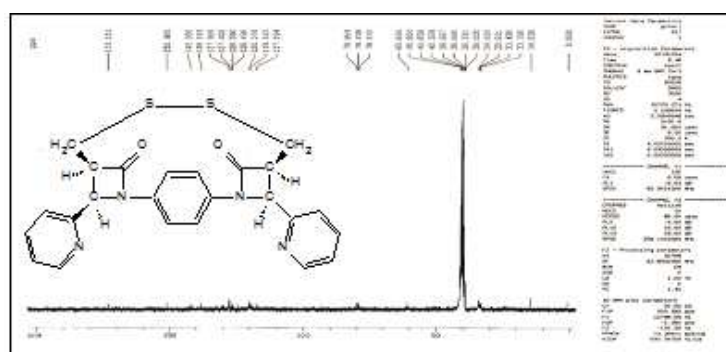
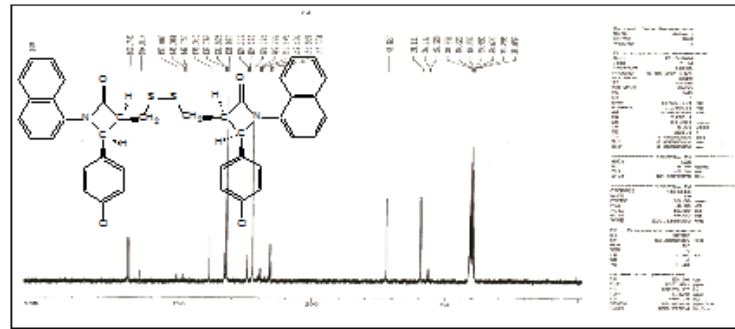
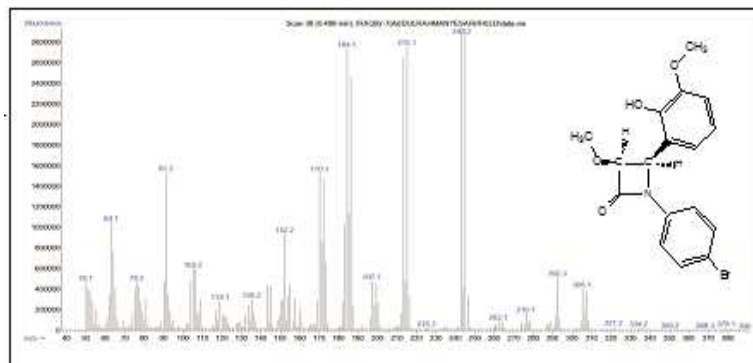


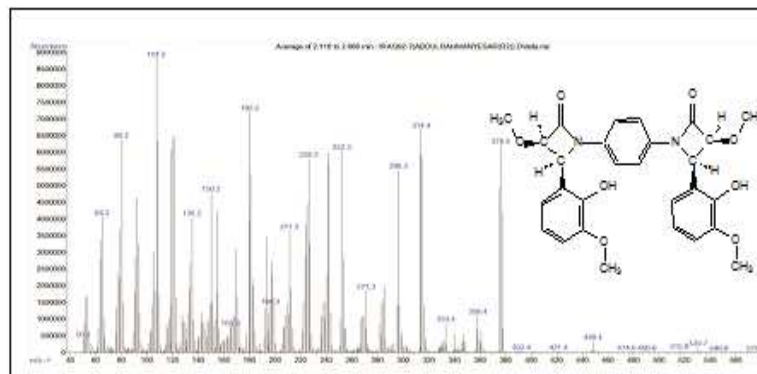
Figure 10: <sup>13</sup>C NMR Spectrum 1,1'-(Benzene-1,4-Diyl)-3,3'-(Dithiodimethyl) bis [4-(Pyridin-2-yl) Azetidin-2-one]. 3c



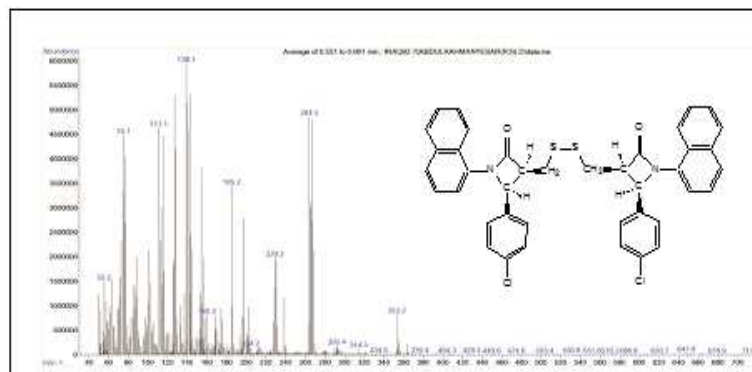
**Figure 11:** <sup>13</sup>C NMR Spectrum 3,3'-(Dithiodimethyl) bis [4-(4-Chlorophenyl)-1-(Naphthalen-1-yl) Azetidin-2-one].3d



**Figure 12:** Mass Spectrum of 1-(4-Bromophenyl)-4-(2-Hydroxy-3-Methoxy Phenyl)-3-Methoxyazetidin-2-one. 3a



**Figure 13:** Mass Spectrum of 1,1'-(Benzene-1,4-Diyl) Bis [4-(2-Hydroxy-3-Methoxyphenyl)-3-Methoxy Azetidin-2-one]. 3b

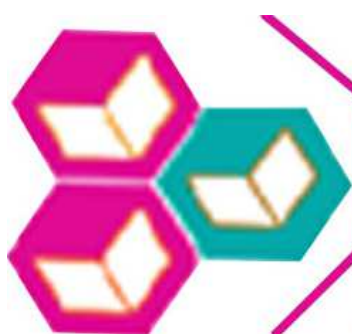


**Figure 14:** Mass Spectrum of 3,3'-(Dithiodimethyl) bis [4-(4-Chlorophenyl)-1-(Naphthalen-1-yl) Azetidin-2-one]. 3d

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