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3-Thiolated 2-azetidinones: synthesis and in vitro antibacterial and antifungal activities

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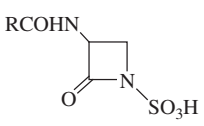
ABSTRACT

A series of 3-thiolated β-lactams were synthesized by [2+2] ketene–imine cycloaddition reaction from *S*-substituted mercaptoacetic acids and Schiff bases. Then, some of the 3-methylthio β-lactams were converted to 3-(methylsulfinyl) β-lactams and 3-(methylsulfonyl) β-lactams using *m*-CPBA under different reaction conditions. All the compounds were characterized by spectral data and elemental analyses and were evaluated for their in vitro antibacterial and antifungal activities against pathogenic strains including *Staphylococcus aureus* (Methicillin resistant strain). The preliminary screening results indicated that some of these compounds demonstrated moderate to very good antibacterial and antifungal activities.

1. Introduction

β-Lactam antibiotics are the most important antibacterial agents for human health and it began with the discovery of penicillin by Alexander Fleming in 1928.[1] During the late 1990s, a research group at Schering-Plough identified a novel compound, ezetimibe, that selectively inhibits the absorption of cholesterol and it was approved and marketed as Zetia in 2002.[2] In addition, β-lactams are an important class of heterocyclic compounds due to their wide range applications in other biological activities.[3] The side chain of Taxol and related analogues (the anti-tumor agents) is preferentially prepared by nucleophilic ring opening of suitably substituted β-lactams.[4] They have also served as precursors to several organic compounds via selective bond cleavage of the β-lactam nucleus.[5] The development of synthetic routes to monocyclic 2-azeti dinones was stimulated by the observation of antibacterial activity in monobactams **1** and norcardicins **2**.[6]

The Staudinger reaction ([2+2] ketene–imine cycloaddition reaction)[7] is regarded as one of the most fundamental and versatile methods for the synthesis of structurally diverse 2-azetidinone derivatives, although many synthetic methods have been developed to date.[8]



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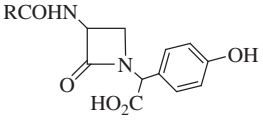

2

With the alarming trends in bacterial resistance to many β-lactam antibiotics it has become necessary to synthesize some novel β-lactams for bioassay of antibacterial activity and the need for drugs with more specific antibacterial activity.[9] Therefore, the synthesis of the new β-lactams is the subject of extensive study.

Turos and co-workers have synthesized *N*-thiolated β-lactams (β-lactam compounds have a sulfur substituent on the nitrogen center). They have reported that *N*-thiolated β-lactams have represented a broad and growing family of bioactive molecules and the thiol-substituent was effective at biological activities.[10]

Due to the adaptability, *Staphylococcus aureus* can easily develop resistance to commonly used antibiotics. This resistance involves the enzymic inactivation in resistant bacteria. Hence, there is a great need for effective antibacterial agents against *S. aureus* with new modes of action.[11]

In this paper, we report the synthesis of 3-thiolated β-lactams and evaluated these compounds for antibacterial and antifungal activities.

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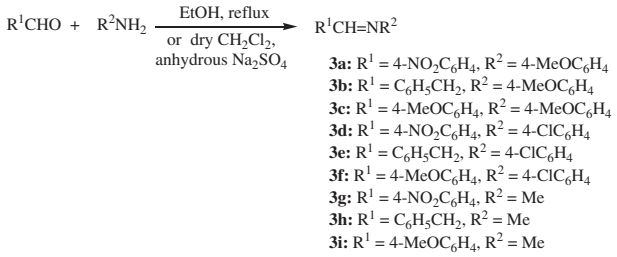
2. Results and discussion

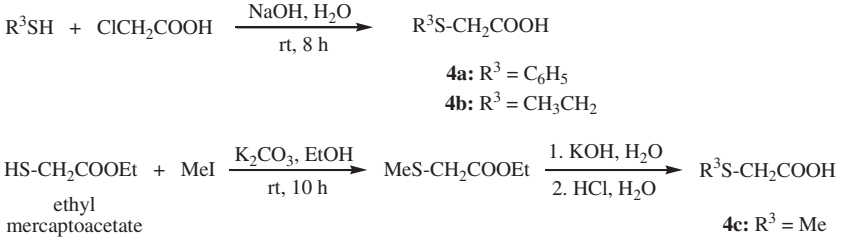
2.1. Chemistry

Firstly, we synthesized different Schiff bases **3a**–**i** from aliphatic or aromatic aldehydes and amines by condensation in ethanol at reflux or by anhydrous Na_2SO_4 in dry dichloromethane (Scheme 1).



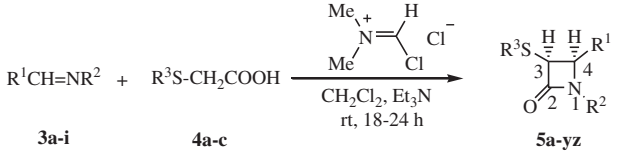
Scheme 1. Synthesis of Schiff bases **3a**–**i**.

S-Substituted mercaptoacetic acids **4a**,**b** were prepared by the alkylation of corresponding thiols and chloroacetic acid. (Methylthio)acetic acid **4c** was synthesized from ethyl mercaptoacetate because of difficult handling and availability of MeSH. The ethyl mercaptoacetate reacted with methyl iodide to give ethyl 2-(methylthio)acetate, which was hydrolyzed to (methylthio)acetic acid **4c** (Scheme 2). The IR spectra of these compounds showed the carbonyl group, hydroxyl group of COOH at 1740–1746 cm^{-1} and 2803–3336 cm^{-1} (broad peak), respectively, but SH peak was not observed.



Scheme 2. Synthesis of *S*-substituted mercaptoacetic acids **4a**–**c**.

The Staudinger reaction was chosen for synthesis of the 2-azetidinone ring. Reaction of Schiff bases **3a**–**i** and *S*-substituted mercaptoacetic acids **4a**–**c** in the presence of the Vilsmeier reagent[12] at room temperature gave the 3-thiolated β-lactams **5a**–**5yz** in good to excellent yields (Scheme 3, Table 1). The IR spectra showed the β-lactam carbonyl at 1741–1755 cm^{-1}. The indicated stereochemistry for these monocyclic β-lactams was deduced from analysis of their ^1H NMR spectra. The coupling constants of H-3 and H-4 are J=4.3–5.1 Hz for β-lactams **5a**–**5yz**, which are indicative of their cis stereochemistry. In addition, ^{13}C NMR spectroscopic data of β-lactams **5a**–**5yz** definitely showed the lactam CO signals at 160.5–165.3 ppm, whereas C-3 resonated at around 60.2–62.5 ppm and C-4 at 61.3–64.2 ppm.



Scheme 3. Synthesis of 3-thiolated β-lactams **5a**–**yz**.

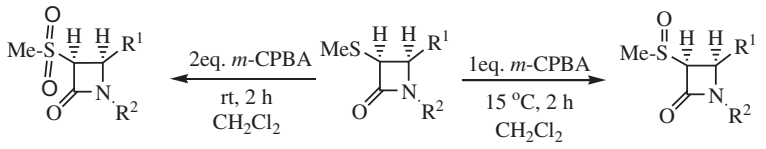
Table 1
3-Thiolated β-lactams **5a**–**yz**

Product	R^1	R^2	R^3	Isolated yield (%)
5a	$4\text{-}NO_2C_6H_4$	$4\text{-}MeOC_6H_4$	C_6H_5	91
5b	$4\text{-}NO_2C_6H_4$	$4\text{-}ClC_6H_4$	C_6H_5	84
5c	$4\text{-}NO_2C_6H_4$	Me	C_6H_5	79
5d	$C_6H_5CH_2$	$4\text{-}MeOC_6H_4$	C_6H_5	90
5e	$C_6H_5CH_2$	$4\text{-}ClC_6H_4$	C_6H_5	83
5f	$C_6H_5CH_2$	Me	C_6H_5	75
5g	$4\text{-}MeOC_6H_4$	$4\text{-}MeOC_6H_4$	C_6H_5	94
5h	$4\text{-}MeOC_6H_4$	$4\text{-}ClC_6H_4$	C_6H_5	90
5i	$4\text{-}MeOC_6H_4$	Me	C_6H_5	81
5j	$4\text{-}NO_2C_6H_4$	$4\text{-}MeOC_6H_4$	CH_3CH_2	88
5k	$4\text{-}NO_2C_6H_4$	$4\text{-}ClC_6H_4$	CH_3CH_2	86
5l	$4\text{-}NO_2C_6H_4$	Me	CH_3CH_2	73
5m	$C_6H_5CH_2$	$4\text{-}MeOC_6H_4$	CH_3CH_2	86
5n	$C_6H_5CH_2$	$4\text{-}ClC_6H_4$	CH_3CH_2	80
5o	$C_6H_5CH_2$	Me	CH_3CH_2	71
5p	$4\text{-}MeOC_6H_4$	$4\text{-}MeOC_6H_4$	CH_3CH_2	92
5q	$4\text{-}MeOC_6H_4$	$4\text{-}ClC_6H_4$	CH_3CH_2	82
5r	$4\text{-}MeOC_6H_4$	Me	CH_3CH_2	70
5s	$4\text{-}NO_2C_6H_4$	$4\text{-}MeOC_6H_4$	CH_3	93
5t	$4\text{-}NO_2C_6H_4$	$4\text{-}ClC_6H_4$	CH_3	90
5u	$4\text{-}NO_2C_6H_4$	Me	CH_3	74
5v	$C_6H_5CH_2$	$4\text{-}MeOC_6H_4$	CH_3	85
5w	$C_6H_5CH_2$	$4\text{-}ClC_6H_4$	CH_3	84
5x	$C_6H_5CH_2$	Me	CH_3	68
5y	$4\text{-}MeOC_6H_4$	$4\text{-}MeOC_6H_4$	CH_3	93
5z	$4\text{-}MeOC_6H_4$	$4\text{-}ClC_6H_4$	CH_3	90
5yz	$4\text{-}MeOC_6H_4$	Me	CH_3	72

Next *cis* 3-methylthio β-lactams **5v**–**yz** were converted to *cis* 3-(methylsulfinyl) β-lactams **6a**–**f** at −15 °C and *cis* 3-(methylsulfonyl) β-lactams **7a**–**f** at room temperature using *m*-CPBA (Scheme 4). Previously *trans* 3-sulfonyl β-lactams were prepared by several methods.[13] The synthesized compounds were characterized by IR, ^1H NMR, ^{13}C NMR, and elemental analysis. The IR spectra showed the S=O absorption (strong peak) at 1078–1089 cm^{-1} and O=S=O absorption (strong peak) at 1151–1161 cm^{-1} and 1307–1322 cm^{-1} for 3-(methylsulfinyl) β-lactams **6a**–**f** and 3-(methylsulfonyl) β-lactams **7a**–**f**, respectively. 3-(Methylsulfinyl) β-lactams **6a**–**f** were obtained as a diastereomeric mixture. The diastereomeric ratio is may be dominated by the steric hindrance of the starting 3-methylthio β-lactams **5v**–**yz**.

2.2. Biological activities

All the synthesized compounds were screened for their antibacterial activity against three gram-positive bacteria *S. aureus* ATCC 29737, *S. aureus* (Methicillin resistant strain) ATCC 33591, *Bacillus subtilis* ATCC 6633, two gram-negative bacteria *Escherichia coli* ATCC 25922 and *Pseudomonas aeruginosa* ATCC 25619. They



7a-f **5v-yz** **6a-f**

7a: $R^1 = C_6H_5CH_2$, $R^2 = 4\text{-}MeOC_6H_4$
7b: $R^1 = C_6H_5CH_2$, $R^2 = 4\text{-}ClC_6H_4$
7c: $R^1 = C_6H_5CH_2$, $R^2 = Me$
7d: $R^1 = 4\text{-}MeOC_6H_4$, $R^2 = 4\text{-}MeOC_6H_4$
7e: $R^1 = 4\text{-}MeOC_6H_4$, $R^2 = 4\text{-}ClC_6H_4$
7f: $R^1 = 4\text{-}MeOC_6H_4$, $R^2 = Me$

6a: $R^1 = C_6H_5CH_2$, $R^2 = 4\text{-}MeOC_6H_4$
6b: $R^1 = C_6H_5CH_2$, $R^2 = 4\text{-}ClC_6H_4$
6c: $R^1 = C_6H_5CH_2$, $R^2 = Me$
6d: $R^1 = 4\text{-}MeOC_6H_4$, $R^2 = 4\text{-}MeOC_6H_4$
6e: $R^1 = 4\text{-}MeOC_6H_4$, $R^2 = 4\text{-}ClC_6H_4$
6f: $R^1 = 4\text{-}MeOC_6H_4$, $R^2 = Me$

Scheme 4. Synthesis of 3-(methylsulfinyl) β-lactams **6a**–**f** and 3-(methylsulfonyl) β-lactams **7a**–**f**.

were also evaluated for their in vitro antifungal activity against *Candida albicans* ATCC 10231, *Aspergillus niger* ATCC 1004, and *Trichophyton mentagrophytes* (natural isolates) using the reported method.[14] The minimum inhibitory concentrations (MICs) were defined as the lowest concentrations of the compounds that prevented visible growth. It was determined that the solvent had no antibacterial antifungal activities against any of the test microorganisms. Standard antibacterial ciprofloxacin and penicillin G and antifungal ciclopiroxolamine were also tested under the similar conditions for comparison.

Firstly 3-thiolated β-lactams **5a**–**5yz** were tested for antibacterial and antifungal activities (Table 2). The best result for antibacterial and antifungal activities was found when R^3 was methyl (3-methylthio β-lactams **5s**–**yz**). Of course in the case of

Table 2
Antimicrobial activity of the synthesized compounds (MIC, μg/mL)

Comp	Bacterial strains					Fungal strains		
	S. aureus	*S. aureus* (MRSA)	*B. subtilis*	*E. coli*	*P. aeruginosa*	*C. albicans*	*A. niger*	*T. mentagrophytes*
5a	50	50	25	100	100	100	100	100
5b	100	100	50	100	100	50	50	50
5c	100	50	100	100	100	100	100	100
5d	25	50	25	100	50	50	50	100
5e	50	50	25	100	100	25	50	50
5f	100	100	50	100	50	50	100	100
5g	25	25	25	50	100	50	50	100
5h	25	25	25	100	100	25	25	50
5i	50	25	25	100	100	50	100	100
5j	25	25	25	50	100	50	100	100
5k	25	25	50	50	100	25	12.5	50
5l	25	12.5	100	50	100	50	100	100
5m	12.5	12.5	25	50	50	25	25	100
5n	12.5	12.5	25	100	100	12.5	12.5	50
5o	25	25	50	100	100	12.5	25	100
5p	6.25	12.5	6.25	50	50	6.25	25	50
5q	6.25	6.25	12.5	50	100	6.25	12.5	50
5r	25	25	25	50	100	25	25	100
5s	6.25	12.5	6.25	25	50	25	12.5	50
5t	6.25	6.25	6.25	50	50	6.25	6.25	50
5u	25	12.5	12.5	100	100	50	25	100
5v	6.25	6.25	6.25	25	25	12.5	12.5	25
5w	12.5	12.5	6.25	25	50	6.25	6.25	25
5x	12.5	12.5	12.5	50	50	12.5	25	50
5y	3.125	3.125	3.125	6.25	12.5	6.25	3.125	50
5z	3.125	3.125	6.25	6.25	25	3.125	6.25	12.5
5yz	12.5	12.5	12.5	25	50	12.5	12.5	100
6a	25	12.5	25	50	50	50	50	100
6b	50	50	25	100	50	12.5	25	100
6c	50	50	50	100	100	50	100	100
6d	12.5	25	12.5	50	100	12.5	25	100
6e	12.5	25	25	50	100	12.5	12.5	50
6f	50	25	25	100	100	50	50	100
7a	100	100	50	100	100	6.25	6.25	25
7b	100	100	100	100	100	6.25	3.125	12.5
7c	100	100	100	100	100	12.5	12.5	25
7d	50	50	25	100	100	3.125	3.125	12.5
7e	50	50	50	100	100	3.125	3.125	6.25
7f	100	50	100	100	100	6.25	6.25	25
Ciprofloxacin	6.25	6.25	3.125	3.125	6.25	—	—	—
Penicillin G	3.125	100	3.125	25	12.5			
Ciclopiroxolamine	—	—	—	—	—	6.25	3.125	6.25

3-methylthio β-lactams **5s**–**u** (R^1=4-$NO_2C_6H_4$) decrease of antimicrobial activities was seen. Then 3-methylthio β-lactams **5s**–**yz** were selected for conversion to corresponding 3-(methylsulfinyl) β-lactams, 3-(methylsulfonyl) β-lactams and the other compounds having weak antimicrobial activities not converted. Antimicrobial activities of 3-methylsulfinyl **6a**–**f** and 3-methylsulfonyl β-lactams **7a**–**f** were also investigated. The results of the antimicrobial activities were summarized in Table 2.

From the antimicrobial studies (Table 2) we concluded that (i) 3-methylthio β-lactams **5s**–**yz** showed higher activity than 3-ethylthio β-lactams **5j**–**r** and 3-phenylthio β-lactams **5a**–**i**. It seems that these compounds could serve as alkylating agents toward cellular nucleophiles, as depicted hypothetically in Ref. 10e because attack on the carbon of the alkyl- or arylthio moiety could be deterred by placement of bulkier groups on the sulfur center. (ii) The R^1=4-methoxyphenyl group showed higher activity than R^1=benzyl and 4-nitrophenyl group. The existence of the methoxy group on the molecules enhances the various biological activities.[15] (iii) A methyl group at position N1 decreases activity. (iv) For antibacterial activity 3-methylthio β-lactams **5s**–**yz** showed higher activity than 3-methylsulfinyl β-lactams **6a**–**f**, and 3-methylsulfonyl β-lactams **7a**–**f** and 4-methoxyphenyl group at position N1 increase activity. This suggests that the availability of an electron pair on sulfur may be needed for antibacterial activity. (v) For antifungal activity, 3-methylsulfonyl β-lactams **7a**–**f** showed higher activity than 3-methylthio β-lactams **5s**–**yz**, and 3-methylsulfinyl β-lactams **6a**–**f** and 4-chlorophenyl group at position N1 increase activity. It can be concluded that the presence of a chlorine atom and sulfonyl group in the azetidinone moiety enhanced the antifungal activity of the compounds. (vi) 3-Thiolated β-lactams have the same activity against β-lactamase-producing *S. aureus* MRSA, in contrast to penicillin G whose inhibitory activity is markedly diminished for MRSA. Among the synthesized compound **5y** showed the best antibacterial activity and compound **7e** showed the best antifungal activity, which they were comparable or higher than with standards.

3. Conclusion

In conclusion, we report the successful synthesis of new 3-thiolated β-lactams. Then selected 3-methylthio β-lactams were transformed to corresponding 3-(methylsulfinyl) and 3-meth ylsulfonyl β-lactams. All the title compounds have been investigated for their antimicrobial activities. Some of the synthesized compounds showed significant antibacterial and antifungal activities. 3-Methylthio β-lactams showed the most antibacterial activity and 3-methylsulfonyl β-lactams showed the most antifungal activity. The 3-methylthio β-lactams **5y** and **5z** displayed marked antibacterial activity against *S. aureus* MRSA.

4. Experimental section

4.1. Chemical reagents

All required chemicals were purchased from Merck, Fluka, and Acros chemical companies. The melting points were determined on a Buchi 535 apparatus and are uncorrected. IR spectra were measured on a galaxy series FT-IR 5000 spectrometer. NMR spectra were recorded on a Bruker spectrophotometer (^{1}H NMR 300 MHz, ^{13}C NMR 75 MHz) using tetramethylsilane as an internal standard and coupling constants were given in cycles per second (Hz). Elemental analyses were run on a Vario EL III elemental analyzer. Thin-layer chromatography was carried out on silica gel 254 analytical sheets obtained from Fluka. Column chromatography was performed on silica gel 60 (Merck, 70–230 mesh).

4.2. Synthesis of Schiff bases 3a–i

*4.2.1. Typical procedure and synthesis of (4-nitrobenzylidene)-(4-methoxyphenyl)amine **3a**.* A mixture of 4-methoxyaniline (1.23 g, 10.0 mmol) and 4-nitrobenzaldehyde (1.51 g, 10.0 mmol) was heated to reflux in ethanol (20 mL) for 3 h. After cooling the solution, the precipitate was filtered and washed with ethanol to give pure Schiff base **3a** as a yellow solid (95%). Mp 125–127 °C; IR (KBr, cm^{-1}): 1618 (C=N). The data for Schiff bases previously have been reported in the literature.[8a,12a,16]

*4.2.2. Synthesis of N-methyl Schiff bases **3g**–**i**.* To a stirred solution of methylamine hydrochloride (0.67 g, 10.0 mmol) in dry CH_2Cl_2 (40 mL) were successively added triethylamine (2.1 mL, 15.0 mmol), corresponding aldehydes (10.0 mmol), and a large excess of anhydrous sodium sulfate. The resulting mixture was stirred for 18 h at room temperature. Then the organic phase was washed with H_2O (25 mL) and dried over anhydrous sodium sulfate. After removal of the solvent *N*-methyl Schiff bases were obtained as a liquid, which was used for the next step without any further purification. IR (crude) (KBr, cm^{-1}): 1626–1629 (C=N).

4.3. General procedure for the preparation of *S*-substituted mercaptoacetic acids 4a,b

To a stirred solution of corresponding thiols (5.0 mmol) and chloroacetic acid (0.47 g, 5.0 mmol) in water (10 mL) was slowly added sodium hydroxide (0.40 g, 10.0 mmol) at room temperature. The solution was stirred for 8 h and then acidified with dilute hydrochloric acid (2 N) to pH=7. Then the mixture was extracted with EtOAc (3×10 mL) and dried over anhydrous sodium sulfate. After filtration and evaporation of the solvent under reduced pressure, the products were obtained.

*4.3.1. (Phenylthio)acetic acid (**4a**).* Mp 62–64 °C (lit. 62.5–63.5 °C);[17] IR (KBr, cm^{-1}): 1746 (COOH), 2803–3299 (OH).

*4.3.2. (Ethylthio)acetic acid (**4b**).* Light yellow liquid; IR (KBr, cm^{-1}): 1740 (COOH), 2831–3336 (OH).[18]

4.4. Synthesis of (methylthio)acetic acid 4c

Ethyl mercaptoacetate (0.96 g, 0.87 mL, 8.0 mmol) was dissolved in anhydrous ethanol (25 mL) and K_2CO_3 (1.38 g, 10.0 mmol) was added. Then methyl iodide (1.28 g, 0.56 mL, 9.0 mmol) was added to the mixture and stirred at room temperature for 10 h. Reaction mixture was filtered, and the filtrate was dried in vacuo. KOH 3 M (30 mL, 5.0 g, 90.0 mmol) was added to residue. The mixture is allowed to stand at room temperature for 16 h. Then the solution of potassium salt is cooled to 0 °C, and acidified with dilute hydrochloric acid (2 N) to pH=7. Then the mixture was extracted with EtOAc (3×15 mL) and dried over Na_2SO_4. After filtration and evaporation of the solvent under reduced pressure, the (methylthio)acetic acid **4c** was obtained as a colorless liquid; IR (KBr, cm^{-1}): 1744 (COOH), 2828–3311 (OH).[19]

4.5. General procedure for the synthesis of β-lactams 5a–5yz using the Vilsmeier reagent

The Vilsmeier reagent (chloromethylenedimethylammonium chloride) was prepared according to reported procedure.[12a,b] The Vilsmeier reagent (1.5 mmol) was added to a solution of the *S*-substituted mercaptoacetic acids **4a**–**c** (1.5 mmol), corresponding Schiff bases **3a**–**i** (1.0 mmol), and triethylamine (0.51 g, 0.70 mL, 5.0 mmol) in dry CH_2Cl_2 (15 mL) at room temperature and the mixture was stirred overnight (18–24 h). Then the solution was

washed successively with 10% HCl (20 mL), saturated $NaHCO_3$ (20 mL), and brine (20 mL). The organic layer was dried (Na_2SO_4), filtered, and the solvent was removed under reduced pressure to give the crude products.

*4.5.1. 1-(4-Methoxyphenyl)-4-(4-nitrophenyl)-3-(phenylthio)azetidin-2-one (**5a**).* It was purified by crystallization from ethyl acetate. White solid (0.37 g, 91%). Mp: 144–146 °C. R_f=0.39 (7:3 hexane/EtOAc); IR (KBr, cm^{-1}): 1343, 1515 (NO_2), 1749 (CO, β-lactam). ^1H NMR ($CDCl_3$) δ 3.71 (OMe, s, 3H), 4.41 (H-4, d, 1H, J=4.5), 4.84 (H-3, d, 1H, J=4.5), 6.81–7.94 (ArH, m, 13H). ^{13}C NMR ($CDCl_3$) δ 55.8 (OMe), 60.2 (C-3), 62.6 (C-4), 113.8, 121.7, 126.5, 129.0, 129.4, 131.5, 136.3, 136.9, 138.2, 141.9, 145.6, 154.4 (aromatic carbons), 163.7 (CO, β-lactam). Anal. Calcd for $C_{22}H_{18}N_2O_4S$: C, 65.01; H, 4.46; N, 6.89; O, 15.75; S, 7.89. Found: C, 64.93; H, 4.53; N, 6.81.

*4.5.2. 1-(4-Chlorophenyl)-4-(4-nitrophenyl)-3-(phenylthio)azetidin-2-one (**5b**).* It was purified by crystallization from ethyl acetate. White solid (0.34 g, 84%). Mp: 123–125 °C. R_f=0.41 (7:3 hexane/EtOAc); IR (KBr, cm^{-1}): 1349, 1519 (NO_2), 1742 (CO, β-lactam). ^1H NMR ($CDCl_3$) δ 4.30 (H-4, d, 1H, J=4.3), 4.86 (H-3, d, 1H, J=4.3), 6.96–8.04 (ArH, m, 13H). ^{13}C NMR ($CDCl_3$) δ 61.1 (C-3), 63.0 (C-4), 118.3, 123.0, 125.2, 128.9, 130.7, 133.5, 134.1, 137.2, 137.6, 140.4, 142.9, 150.6 (aromatic carbons), 161.9 (CO, β-lactam). Anal. Calcd for $C_{21}H_{15}ClN_2O_3S$: C, 61.39; H, 3.68; Cl, 8.63; N, 6.82; O, 11.68; S, 7.80. Found: C, 61.46; H, 3.80; N, 6.90.

*4.5.3. 1-Methyl-4-(4-nitrophenyl)-3-(phenylthio)azetidin-2-one (**5c**).* It was purified by crystallization from ethyl acetate. White solid (0.25 g, 79%). Mp: 71–73 °C. R_f=0.36 (7:3 hexane/EtOAc); IR (KBr, cm^{-1}): 1343, 1516 (NO_2), 1751 (CO, β-lactam). ^1H NMR ($CDCl_3$) δ 2.92 (Me, s, 3H), 4.28 (H-4, d, 1H, J=4.8), 4.73 (H-3, d, 1H, J=4.8), 6.62–7.89 (ArH, m, 9H). ^{13}C NMR ($CDCl_3$) δ 29.7 (Me), 62.5 (C-3), 63.8 (C-4), 117.2, 120.0, 122.8, 123.2, 127.5, 133.5, 140.3, 147.7 (aromatic carbons), 160.5 (CO, β-lactam). Anal. Calcd for $C_{16}H_{14}N_2O_3S$: C, 61.13; H, 4.49; N, 8.91; O, 15.27; S, 10.20. Found: C, 61.23; H, 4.58; N, 8.84.

*4.5.4. 4-Benzyl-1-(4-methoxyphenyl)-3-(phenylthio)azetidin-2-one (**5d**).* It was purified by crystallization from ethyl acetate. White solid (0.34 g, 90%). Mp: 135–137 °C. R_f=0.44 (7:3 hexane/EtOAc); IR (KBr, cm^{-1}): 1746 (CO, β-lactam). ^1H NMR ($CDCl_3$) δ 2.47 (CH_2–benzyl, dd, 1H, J=5.8, 14.5), 2.94 (CH_2–benzyl, dd, 1H, J=5.8, 14.5), 3.66 (OMe, s, 3H), 4.09 (H-4, m, 1H), 4.68 (H-3, d, 1H, J=5.0), 6.81–8.11 (ArH, m, 14H). ^{13}C NMR ($CDCl_3$) δ 37.4 (CH_2), 56.7 (OMe), 61.1 (C-3), 61.9 (C-4), 115.1, 123.2, 127.1, 127.6, 128.6, 128.8, 129.2, 129.7, 130.0, 131.4, 135.2, 140.7, 154.4 (aromatic carbons), 162.3 (CO, β-lactam). Anal. Calcd for $C_{23}H_{21}NO_2S$: C, 73.57; H, 5.64; N, 3.73; O, 8.52; S, 8.54. Found: C, 73.49; H, 5.79; N, 3.65.

*4.5.5. 4-Benzyl-1-(4-chlorophenyl)-3-(phenylthio)azetidin-2-one (**5e**).* It was purified by crystallization from ethyl acetate. White solid (0.32 g, 83%). Mp: 126–128 °C. R_f=0.44 (7:3 hexane/EtOAc); IR (KBr, cm^{-1}): 1743 (CO, β-lactam). ^1H NMR ($CDCl_3$) δ 2.39 (CH_2–benzyl, dd, 1H, J=5.5, 14.8), 2.90 (CH_2–benzyl, dd, 1H, J=5.5, 14.8), 4.17 (H-4, m, 1H), 4.66 (H-3, d, 1H, J=4.8), 6.77–7.73 (ArH, m, 14H). ^{13}C NMR ($CDCl_3$) δ 33.7 (CH_2), 60.8 (C-3), 62.0 (C-4), 113.7, 118.8, 127.3, 128.5, 128.8, 129.7, 130.4, 130.9, 133.1, 136.7, 143.2, 146.5 (aromatic carbons), 161.5 (CO, β-lactam). Anal. Calcd for $C_{22}H_{18}ClNOS$: C, 69.55; H, 4.78; Cl, 9.33; N, 3.69; O, 4.21; S, 8.44. Found: C, 69.47; H, 4.86; N, 3.66.

*4.5.6. 4-Benzyl-1-methyl-3-(phenylthio)azetidin-2-one (**5f**).* It was purified by crystallization from ethyl acetate. White solid (0.21 g, 75%). Mp: 60–62 °C. R_f=0.43 (7:3 hexane/EtOAc); IR (KBr, cm^{-1}): 1749 (CO, β-lactam). ^1H NMR ($CDCl_3$) δ 2.27 (CH_2–benzyl, dd, 1H, J=5.6, 14.7), 2.84 (CH_2–benzyl, dd, 1H, J=5.6, 14.7), 2.96 (Me, s, 3H), 4.22 (H-4, m, 1H), 4.64 (H-3, d, 1H, J=5.1), 6.96–7.24 (ArH, m, 10H). ^{13}C NMR ($CDCl_3$) δ 28.3 (Me), 32.1 (CH_2), 61.3 (C-3), 63.7 (C-4), 117.2, 126.9, 127.7, 129.0, 131.5, 137.4, 139.2, 144.5, (aromatic carbons), 162.2 (CO, β-lactam). Anal. Calcd for $C_{17}H_{17}NOS$: C, 72.05; H, 6.05; N, 4.94; O, 5.65; S, 11.31. Found: C, 72.14; H, 6.18; N, 5.01.

*4.5.7. 1,4-Bis(4-methoxyphenyl)-3-(phenylthio)azetidin-2-one (**5g**).* It was purified by crystallization from ethyl acetate. White solid (0.37 g, 94%). Mp: 141–143 °C. R_f=0.41 (7:3 hexane/EtOAc); IR (KBr, cm^{-1}): 1751 (CO, β-lactam). ^1H NMR ($CDCl_3$) δ 3.69, 3.76 (2OMe, 2s, 6H), 4.53 (H-4, d, 1H, J=4.9), 5.01 (H-3, d, 1H, J=4.9), 6.73–7.90 (ArH, m, 13H). ^{13}C NMR ($CDCl_3$) δ 56.1, 57.5 (OMe), 61.9 (C-3), 64.2 (C-4), 111.6, 122.9, 125.1, 125.3, 129.4, 130.1, 133.8, 134.5, 140.6, 143.1, 147.3, 157.2 (aromatic carbons), 164.4 (CO, β-lactam). Anal. Calcd for $C_{23}H_{21}NO_3S$: C, 70.56; H, 5.41; N, 3.58; O, 12.26; S, 8.19. Found: C, 70.48; H, 5.49; N, 3.51.

*4.5.8. 1-(4-Chlorophenyl)-4-(4-methoxyphenyl)-3-(phenylthio)azetidin-2-one (**5h**).* It was purified by crystallization from ethyl acetate. White solid (0.36 g, 90%). Mp: 129–131 °C. R_f=0.42 (7:3 hexane/EtOAc); IR (KBr, cm^{-1}): 1747 (CO, β-lactam). ^1H NMR ($CDCl_3$) δ 3.63 (OMe, s, 3H), 4.29 (H-4, d, 1H, J=4.5), 4.71 (H-3, d, 1H, J=4.5), 6.69–7.78 (ArH, m, 13H). ^{13}C NMR ($CDCl_3$) δ 55.3 (OMe), 61.2 (C-3), 62.8 (C-4), 116.2, 120.5, 121.6, 122.2, 125.8, 126.5, 132.4, 138.9, 141.3, 142.1, 146.0, 158.5 (aromatic carbons), 163.1 (CO, β-lactam). Anal. Calcd for $C_{22}H_{18}ClNO_2S$: C, 66.74; H, 4.58; Cl, 8.95; N, 3.54; O, 8.08; S, 8.10. Found: C, 66.85; H, 4.72; N, 3.61.

*4.5.9. 4-(4-Methoxyphenyl)-1-methyl-3-(phenylthio)azetidin-2-one (**5i**).* It was purified by crystallization from ethyl acetate. White solid (0.24 g, 81%). Mp: 63–65 °C. R_f=0.41 (7:3 hexane/EtOAc); IR (KBr, cm^{-1}): 1750 (CO, β-lactam). ^1H NMR ($CDCl_3$) δ 2.98 (Me, s, 3H), 3.55 (OMe, s, 3H), 4.21 (H-4, d, 1H, J=4.4), 4.83 (H-3, d, 1H, J=4.4), 6.75–7.63 (ArH, m, 9H). ^{13}C NMR ($CDCl_3$) δ 30.3 (Me), 56.6 (OMe), 60.8 (C-3), 62.5 (C-4), 119.0, 122.1, 122.4, 123.4, 123.9, 136.1, 142.4, 149.6 (aromatic carbons), 161.0 (CO, β-lactam). Anal. Calcd for $C_{17}H_{17}NO_2S$: C, 68.20; H, 5.72; N, 4.68; O, 10.69; S, 10.71. Found: C, 68.11; H, 5.84; N, 4.74.

*4.5.10. 3-(Ethylthio)-1-(4-methoxyphenyl)-4-(4-nitrophenyl)azetidin-2-one (**5j**).* It was purified by crystallization from ethyl acetate. White solid (0.32 g, 88%). Mp: 79–81 °C. R_f=0.38 (7:3 hexane/EtOAc); IR (KBr, cm^{-1}): 1347, 1528 (NO_2), 1741 (CO, β-lactam). ^1H NMR ($CDCl_3$) δ 1.27 (Me, t, 3H, J=6.7), 2.71 (SCH_2, q, 2H, J=6.7), 3.65 (OMe, s, 3H), 4.38 (H-4, d, 1H, J=4.8), 4.91 (H-3, d, 1H, J=4.8), 6.78–8.11 (ArH, m, 8H). ^{13}C NMR ($CDCl_3$) δ 14.1 (Me), 29.6 (SCH_2), 56.3 (OMe), 60.4 (C-3), 61.8 (C-4), 115.2, 122.7, 124.0, 125.3, 130.6, 135.2, 144.9, 156.8 (aromatic carbons), 162.4 (CO, β-lactam). Anal. Calcd for $C_{18}H_{18}N_2O_4S$: C, 60.32; H, 5.06; N, 7.82; O, 17.86; S, 8.95. Found: C, 60.44; H, 5.15; N, 7.90.

*4.5.11. 1-(4-Chlorophenyl)-3-(ethylthio)-4-(4-nitrophenyl)azetidin-2-one (**5k**).* It was purified by crystallization from ethyl acetate. White solid (0.31 g, 86%). Mp: 76–78 °C. R_f=0.39 (7:3 hexane/EtOAc); IR (KBr, cm^{-1}): 1341, 1532 (NO_2), 1745 (CO, β-lactam). ^1H NMR ($CDCl_3$) δ 1.23 (Me, t, 3H, J=6.9), 2.75 (SCH_2, q, 2H, J=6.9), 4.28 (H-4, d, 1H, J=5.1), 4.77 (H-3, d, 1H, J=5.1), 6.78–8.11 (ArH, m, 8H). ^{13}C NMR ($CDCl_3$) δ 15.3 (Me), 30.3 (SCH_2), 61.4 (C-3), 63.1 (C-4), 111.5, 119.7, 122.1, 122.7, 131.5, 133.6, 145.4, 150.4 (aromatic carbons), 162.9 (CO, β-lactam). Anal. Calcd for $C_{17}H_{15}ClN_2O_3S$: C, 56.27; H, 4.17; Cl, 9.77; N, 7.72; O, 13.23; S, 8.84. Found: C, 56.39; H, 4.25; N, 7.77.

*4.5.12. 3-(Ethylthio)-1-methyl-4-(4-nitrophenyl)azetidin-2-one (**5l**).* It was purified by column chromatography on silica gel

(hexane/EtOAc 8:2). Colorless oil (0.19 g, 73%). R_f=0.41 (7:3 hexane/EtOAc); IR (KBr, cm^{-1}): 1347, 1539 (NO_2), 1752 (CO, β-lactam). ^1H NMR ($CDCl_3$) δ 1.28 (Me, t, 3H, J=7.0), 2.82 (SCH_2, q, 2H, J=7.0), 2.96 (*N*–Me, s, 3H), 4.41 (H-4, d, 1H, J=4.4), 4.86 (H-3, d, 1H, J=4.4), 7.26–8.01 (ArH, m, 4H). ^{13}C NMR ($CDCl_3$) δ 14.7 (Me), 28.2 (SCH_2), 28.9 (*N*–Me), 60.6 (C-3), 62.7 (C-4), 120.5, 128.3, 146.7, 148.2 (aromatic carbons), 161.7 (CO, β-lactam). Anal. Calcd for $C_{12}H_{14}N_2O_3S$: C, 54.12; H, 5.30; N, 10.52; O, 18.02; S, 12.04. Found: C, 54.06; H, 5.38; N, 10.47.

*4.5.13. 4-Benzyl-3-(ethylthio)-1-(4-methoxyphenyl)azetidin-2-one (**5m**).* It was purified by crystallization from ethyl acetate. White solid (0.28 g, 86%). Mp: 64–66 °C. R_f=0.44 (7:3 hexane/EtOAc); IR (KBr, cm^{-1}): 1746 (CO, β-lactam). ^1H NMR ($CDCl_3$) δ 1.24 (Me, t, 3H, J=6.9), 2.41 (CH_2–benzyl, dd, 1H, J=5.8, 15.0), 2.86 (SCH_2, q, 2H, J=6.9), 2.97 (CH_2–benzyl, dd, 1H, J=5.8, 15.0), 3.71 (OMe, s, 3H), 4.17 (H-4, m, 1H), 4.83 (H-3, d, 1H, J=4.7), 6.90–7.74 (ArH, m, 9H). ^{13}C NMR ($CDCl_3$) δ 15.5 (Me), 29.3 (SCH_2), 33.8 (CH_2), 55.3 (OMe), 61.5 (C-3), 62.8 (C-4), 114.3, 121.9, 126.5, 128.3, 128.7, 130.8, 144.2, 155.7 (aromatic carbons), 161.9 (CO, β-lactam). Anal. Calcd for $C_{19}H_{21}NO_2S$: C, 69.69; H, 6.46; N, 4.28; O, 9.77; S, 9.79. Found: C, 69.75; H, 6.58; N, 4.21.

*4.5.14. 4-Benzyl-1-(4-chlorophenyl)-3-(ethylthio)azetidin-2-one (**5n**).* It was purified by crystallization from ethyl acetate. White solid (0.26 g, 80%). Mp: 71–73 °C. R_f=0.43 (7:3 hexane/EtOAc); IR (KBr, cm^{-1}): 1742 (CO, β-lactam). ^1H NMR ($CDCl_3$) δ 1.29 (Me, t, 3H, J=6.7), 2.38 (CH_2–benzyl, dd, 1H, J=5.4, 14.8), 2.81 (SCH_2, q, 2H, J=6.7), 2.94 (CH_2–benzyl, dd, 1H, J=5.4, 14.8), 4.26 (H-4, m, 1H), 4.89 (H-3, d, 1H, J=4.4), 6.97–7.69 (ArH, m, 9H). ^{13}C NMR ($CDCl_3$) δ 15.0 (Me), 28.4 (SCH_2), 32.1 (CH_2), 60.8 (C-3), 62.2 (C-4), 119.2, 122.7, 123.4, 126.1, 129.9, 130.5, 141.6, 143.3 (aromatic carbons), 160.6 (CO, β-lactam). Anal. Calcd for $C_{18}H_{18}ClNOS$: C, 65.15; H, 5.47; Cl, 10.68; N, 4.22; O, 4.82; S, 9.66. Found: C, 65.04; H, 5.58; N, 4.27.

*4.5.15. 4-Benzyl-3-(ethylthio)-1-methylazetidin-2-one (**5o**).* It was purified by column chromatography on silica gel (hexane/EtOAc 9:1). Colorless oil (0.17 g, 71%). R_f=0.47 (7:3 hexane/EtOAc); IR (KBr, cm^{-1}): 1750 (CO, β-lactam). ^1H NMR ($CDCl_3$) δ 1.22 (Me, t, 3H, J=7.0), 2.29 (CH_2–benzyl, dd, 1H, J=5.7, 14.9), 2.78 (SCH_2, q, 2H, J=7.0), 2.87 (CH_2–benzyl, dd, 1H, J=5.7, 14.9), 2.99 (*N*–Me, s, 3H), 4.36 (H-4, m, 1H), 4.88 (H-3, d, 1H, J=4.8), 7.03–7.34 (ArH, m, 5H). ^{13}C NMR ($CDCl_3$) δ 14.5 (Me), 27.7 (SCH_2), 28.5 (*N*–Me), 31.3 (CH_2), 61.7 (C-3), 63.1 (C-4), 122.2, 123.6, 128.0, 143.7, (aromatic carbons), 165.3 (CO, β-lactam). Anal. Calcd for $C_{13}H_{17}NOS$: C, 66.34; H, 7.28; N, 5.95; O, 6.80; S, 13.62. Found: C, 66.39; H, 7.41; N, 6.03.

*4.5.16. 3-(Ethylthio)-1,4-bis(4-methoxyphenyl)azetidin-2-one (**5p**).* It was purified by crystallization from ethyl acetate. White solid (0.32 g, 92%). Mp: 73–75 °C. R_f=0.42 (7:3 hexane/EtOAc); IR (KBr, cm^{-1}): 1747 (CO, β-lactam). ^1H NMR ($CDCl_3$) δ 1.29 (Me, t, 3H, J=6.9), 2.79 (SCH_2, q, 2H, J=6.9), 3.63, 3.71 (2OMe, 2s, 6H), 4.41 (H-4, d, 1H, J=4.4), 4.96 (H-3, d, 1H, J=4.4), 6.69–7.84 (ArH, m, 8H). ^{13}C NMR δ 14.9 (Me), 29.3 (SCH_2), 55.5, 56.2 (2OMe), 61.8 (C-3), 63.4 (C-4), 114.7, 123.2, 123.8, 128.1, 133.5, 137.0, 154.1, 156.6 (aromatic carbons), 163.7 (CO, β-lactam). Anal. Calcd for $C_{19}H_{21}NO_3S$: C, 66.45; H, 6.16; N, 4.08; O, 13.98; S, 9.34. Found: C, 66.37; H, 6.24; N, 4.00.

*4.5.17. 1-(4-Chlorophenyl)-3-(ethylthio)-4-(4-methoxyphenyl)azetidin-2-one (**5q**).* It was purified by crystallization from ethyl acetate. White solid (0.29 g, 82%). Mp: 81–83 °C. R_f=0.43 (7:3 hexane/EtOAc); IR (KBr, cm^{-1}): 1743 (CO, β-lactam). ^1H NMR ($CDCl_3$) δ 1.25 (Me, t, 3H, J=7.0), 2.86 (SCH_2, q, 2H, J=7.0), 3.66 (OMe, s, 3H), 4.50 (H-4, d, 1H, J=4.6), 4.96 (H-3, d, 1H, J=4.6), 6.69–7.84 (ArH, m, 8H). ^{13}C NMR ($CDCl_3$) δ 14.6 (Me), 28.7 (SCH_2), 55.9 (OMe), 60.6 (C-3), 63.1 (C-4), 117.2, 122.7, 123.3, 127.9, 128.6, 134.1, 147.5, 155.8 (aromatic carbons), 162.4 (CO, β-lactam). Anal. Calcd for $C_{18}H_{18}ClNO_2S$: C, 62.15; H, 5.22; Cl, 10.19; N, 4.03; O, 9.20; S, 9.22. Found: C, 62.21; H, 5.33; N, 4.09.

*4.5.18. 3-(Ethylthio)-4-(4-methoxyphenyl)-1-methyl azetidin-2-one (**5r**).* It was purified by column chromatography on silica gel (hexane/EtOAc 9:1). Colorless oil (0.18 g, 70%). R_f=0.46 (7:3 hexane/EtOAc); IR (KBr, cm^{-1}): 1753 (CO, β-lactam). ^1H NMR ($CDCl_3$) δ 1.28 (Me, t, 3H, J=6.7), 2.91 (SCH_2, q, 2H, J=6.7), 2.97 (*N*–Me, s, 3H), 3.69 (OMe, s, 3H), 4.46 (H-4, d, 1H, J=5.1), 4.87 (H-3, d, 1H, J=5.1), 6.75–7.49 (ArH, m, 4H). ^{13}C NMR ($CDCl_3$) δ 15.6 (Me), 28.0 (SCH_2), 29.7 (*N*–Me), 56.5 (OMe), 60.9 (C-3), 62.2 (C-4), 115.9, 124.6, 125.1, 155.3 (aromatic carbons), 161.6 (CO, β-lactam). Anal. Calcd for $C_{13}H_{17}NO_2S$: C, 62.12; H, 6.82; N, 5.57; O, 12.73; S, 12.76. Found: C, 62.03; H, 6.90; N, 5.48.

*4.5.19. 1-(4-Methoxyphenyl)-3-(methylthio)-4-(4-nitrophenyl)azetidin-2-one (**5s**).* It was purified by crystallization from ethyl acetate. White solid (0.32 g, 93%). Mp: 61–63 °C. R_f=0.40 (7:3 hexane/EtOAc); IR (KBr, cm^{-1}): 1345, 1539 (NO_2), 1743 (CO, β-lactam). ^1H NMR ($CDCl_3$) δ 2.11 (*S*–Me, s, 3H), 3.69 (OMe, s, 3H), 4.49 (H-4, d, 1H, J=4.5), 4.95 (H-3, d, 1H, J=4.5), 6.74–8.12 (ArH, m, 8H). ^{13}C NMR ($CDCl_3$) δ 16.5 (*S*–Me), 55.8 (OMe), 61.1 (C-3), 63.2 (C-4), 113.5, 121.8, 122.3, 127.1, 134.2, 134.8, 150.4, 156.3 (aromatic carbons), 163.0 (CO, β-lactam). Anal. Calcd for $C_{17}H_{16}N_2O_4S$: C, 59.29; H, 4.68; N, 8.13; O, 18.58; S, 9.31. Found: C, 59.36; H, 4.82; N, 8.05.

*4.5.20. 1-(4-Chlorophenyl)-3-(methylthio)-4-(4-nitrophenyl)azetidin-2-one (**5t**).* It was purified by crystallization from ethyl acetate. White solid (0.31 g, 90%). Mp: 66–68 °C. R_f=0.39 (7:3 hexane/EtOAc); IR (KBr, cm^{-1}): 1347, 1533 (NO_2), 1744 (CO, β-lactam). ^1H NMR ($CDCl_3$) δ 2.09 (*S*–Me, s, 3H), 4.53 (H-4, d, 1H, J=4.8), 5.05 (H-3, d, 1H, J=4.8), 6.89–8.15 (ArH, m, 8H). ^{13}C NMR ($CDCl_3$) δ 16.1 (*S*–Me), 60.5 (C-3), 62.7 (C-4), 117.9, 122.1, 122.9, 125.3, 126.0, 140.4, 149.3, 155.7 (aromatic carbons), 162.5 (CO, β-lactam). Anal. Calcd for $C_{16}H_{13}ClN_2O_3S$: C, 55.09; H, 3.76; Cl, 10.16; N, 8.03; O, 13.76; S, 9.19. Found: C, 55.19; H, 3.84; N, 8.08.

*4.5.21. 1-Methyl-3-(methylthio)-4-(4-nitrophenyl)azetidin-2-one (**5u**).* It was purified by column chromatography on silica gel (hexane/EtOAc 8:2). Colorless oil (0.19 g, 74%). R_f=0.40 (7:3 hexane/EtOAc); IR (KBr, cm^{-1}): 1341, 1534 (NO_2), 1753 (CO, β-lactam). ^1H NMR ($CDCl_3$) δ 2.13 (*S*–Me, s, 3H), 2.96 (*N*–Me, s, 3H), 4.38 (H-4, d, 1H, J=4.3), 4.72 (H-3, d, 1H, J=4.3), 7.16–8.06 (ArH, m, 4H). ^{13}C NMR ($CDCl_3$) δ 15.3 (*S*–Me), 28.9 (*N*–Me), 61.7 (C-3), 63.4 (C-4), 122.6, 124.8, 142.7, 151.4 (aromatic carbons), 163.8 (CO, β-lactam). Anal. Calcd for $C_{11}H_{12}N_2O_3S$: C, 52.37; H, 4.79; N, 11.10; O, 19.03; S, 12.71. Found: C, 52.42; H, 4.90; N, 11.16.

*4.5.22. 4-Benzyl-1-(4-methoxyphenyl)-3-(methylthio)azetidin-2-one (**5v**).* It was purified by crystallization from ethyl acetate. White solid (0.27 g, 85%). Mp: 51–53 °C. R_f=0.42 (7:3 hexane/EtOAc); IR (KBr, cm^{-1}): 1742 (CO, β-lactam). ^1H NMR ($CDCl_3$) δ 2.07 (*S*–Me, s, 3H), 2.47 (CH_2–benzyl, dd, 1H, J=5.9, 14.6), 2.88 (CH_2–benzyl, dd, 1H, J=5.9, 14.6), 3.67 (OMe, s, 3H), 4.25 (H-4, m, 1H), 4.77 (H-3, d, 1H, J=4.9), 6.95–7.83 (ArH, m, 9H). ^{13}C NMR ($CDCl_3$) δ 15.8 (*S*–Me), 32.5 (CH_2), 56.1 (OMe), 61.3 (C-3), 63.0 (C-4), 112.8, 117.4, 127.9, 128.5, 128.9, 135.8, 146.1, 156.7 (aromatic carbons), 162.4 (CO, β-lactam). Anal. Calcd for $C_{18}H_{19}NO_2S$: C, 68.98; H, 6.11; N, 4.47; O, 10.21; S, 10.23. Found: C, 68.91; H, 6.20; N, 4.42.

*4.5.23. 4-Benzyl-1-(4-chlorophenyl)-3-(methylthio)azetidin-2-one (**5w**).* It was purified by crystallization from ethyl acetate. White solid (0.27 g, 84%). Mp: 57–59 °C. R_f=0.43 (7:3 hexane/EtOAc); IR (KBr, cm^{-1}): 1744 (CO, β-lactam). ^1H NMR ($CDCl_3$) δ 2.11 (*S*–Me, s, 3H), 2.40 (CH_2–benzyl, dd, 1H, J=5.7, 15.0), 2.82 (CH_2–benzyl, dd,

1H, *J*=5.7, 15.0), 4.18 (H-4, m, 1H), 4.69 (H-3, d, 1H, *J*=4.5), 6.84–7.55 (ArH, m, 9H). ^{13}C NMR ($CDCl_3$) δ 14.9 (*S*–Me), 33.7 (CH_2), 60.7 (C-3), 61.3 (C-4), 118.4, 120.8, 123.5, 123.7, 129.6, 131.2, 134.8, 147.5 (aromatic carbons), 160.9 (CO, β-lactam). Anal. Calcd for $C_{17}H_{16}ClNOS$: C, 64.24; H, 5.07; Cl, 11.15; N, 4.41; O, 5.03; S, 10.09. Found: C, 64.16; H, 5.18; N, 4.37.

*4.5.24. 4-Benzyl-1-methyl-3-(methylthio)azetidin-2-one (**5x**).* It was purified by column chromatography on silica gel (hexane/EtOAc 9:1). Colorless oil (0.15 g, 68%). R_f=0.45 (7:3 hexane/EtOAc); IR (KBr, cm^{-1}): 1755 (CO, β-lactam). ^{1}H NMR ($CDCl_3$) δ 2.14 (*S*–Me, s, 3H), 2.33 (CH_2–benzyl, dd, 1H, *J*=5.7, 14.5), 2.84 (CH_2–benzyl, dd, 1H, *J*=5.7, 14.5), 2.96 (*N*–Me, s, 3H), 4.28 (H-4, m, 1H), 4.84 (H-3, d, 1H, *J*=4.8), 7.03–7.49 (ArH, m, 5H). ^{13}C NMR ($CDCl_3$) δ 14.1 (*S*–Me), 29.7 (*N*–Me), 33.1 (CH_2), 61.2 (C-3), 62.9 (C-4), 121.5, 122.1, 131.7, 145.3 (aromatic carbons), 161.7 (CO, β-lactam). Anal. Calcd for $C_{12}H_{15}NOS$: C, 65.12; H, 6.83; N, 6.33; O, 7.23; S, 14.49. Found: C, 65.22; H, 6.96; N, 6.39.

*4.5.25. 1,4-Bis(4-methoxyphenyl)-3-(methylthio)azetidin-2-one (**5y**).* It was purified by crystallization from ethyl acetate. White solid (0.31 g, 93%). Mp: 59–61 °C. R_f=0.41 (7:3 hexane/EtOAc); IR (KBr, cm^{-1}): 1745 (CO, β-lactam). ^{1}H NMR ($CDCl_3$) δ 2.19 (*S*–Me, s, 3H), 3.59, 3.66 (2OMe, 2s, 6H), 4.53 (H-4, d, 1H, *J*=4.7), 5.03 (H-3, d, 1H, *J*=4.7), 6.71–7.84 (ArH, m, 8H). ^{13}C NMR ($CDCl_3$) δ 15.3 (*S*–Me), 55.9, 56.6 (2OMe), 61.8 (C-3), 63.4 (C-4), 112.4, 118.8, 123.4, 123.7, 136.9, 140.2, 152.7, 155.3 (aromatic carbons), 161.9 (CO, β-lactam). Anal. Calcd for $C_{18}H_{19}NO_3S$: C, 65.63; H, 5.81; N, 4.25; O, 14.57; S, 9.73. Found: C, 65.55; H, 5.96; N, 4.17.

*4.5.26. 1-(4-Chlorophenyl)-4-(4-methoxyphenyl)-3-(methylthio)azetidin-2-one (**5z**).* It was purified by crystallization from ethyl acetate. White solid (0.30 g, 90%). Mp: 64–66 °C. R_f=0.40 (7:3 hexane/EtOAc); IR (KBr, cm^{-1}): 1744 (CO, β-lactam). ^{1}H NMR ($CDCl_3$) δ 2.28 (*S*–Me, s, 3H), 3.64 (OMe, s, 3H), 4.59 (H-4, d, 1H, *J*=4.3), 5.09 (H-3, d, 1H, *J*=4.3), 6.60–7.59 (ArH, m, 8H). ^{13}C NMR ($CDCl_3$) δ 14.7 (*S*–Me), 56.1 (OMe), 61.3 (C-3), 62.5 (C-4), 113.3, 116.3, 122.8, 123.4, 131.7, 141.4, 146.9, 154.5 (aromatic carbons), 163.1 (CO, β-lactam). Anal. Calcd for $C_{17}H_{16}ClNO_2S$: C, 61.16; H, 4.83; Cl, 10.62; N, 4.20; O, 9.59; S, 9.61. Found: C, 61.22; H, 4.98; N, 4.27.

*4.5.27. 4-(4-Methoxyphenyl)-1-methyl-3-(methylthio)azetidin-2-one (**5yz**).* It was purified by column chromatography on silica gel (hexane/EtOAc 9:1). Colorless oil (0.17 g, 72%). R_f=0.45 (7:3 hexane/EtOAc); IR (KBr, cm^{-1}): 1752 (CO, β-lactam). ^{1}H NMR ($CDCl_3$) δ 2.20 (*S*–Me, s, 3H), 2.91 (*N*–Me, s, 3H), 3.58 (OMe, s, 3H), 4.44 (H-4, d, 1H, *J*=4.8), 4.83 (H-3, d, 1H, *J*=4.8), 6.84–7.31 (ArH, m, 4H). ^{13}C NMR ($CDCl_3$) δ 14.8 (*S*–Me), 29.7 (*N*–Me), 56.7 (OMe), 60.9 (C-3), 62.7 (C-4), 116.4, 125.3, 138.6, 152.5 (aromatic carbons), 162.9 (CO, β-lactam). Anal. Calcd for $C_{12}H_{15}NO_2S$: C, 60.73; H, 6.37; N, 5.90; O, 13.48; S, 13.51. Found: C, 60.64; H, 6.49; N, 5.86.

4.6. General procedure for the synthesis of 3-(methylsulfinyl) β-lactams 6a–f

To a solution of 3-methylthio β-lactams **5v**–**yz** (0.7 mmol) in CH_2Cl_2 (20 mL) at −15 °C was added *m*-CPBA (0.12 g, 0.7 mmol). After 2 h, a saturated solution of $NaHSO_3$ (10 mL) was added, and the mixture was allowed to warm to room temperature and then extracted with EtOAc (2×15 mL). The organic layer was purified by chromatography on silica gel using EtOAc/hexane (4:6) to give pure products.

*4.6.1. 4-Benzyl-1-(4-methoxyphenyl)-3-(methylsulfinyl)azetidin-2-one (**6a**).* White solid (0.18 g, 78%) (2.5:1 mixture of diastereomers by NMR). Mp: 83–85 °C. R_f=0.48 (1:1 hexane/EtOAc); IR (KBr, cm^{-1}): 1085 (S=O), 1748 (CO, β-lactam). ^{1}H NMR ($CDCl_3$) δ 2.39 (SO–Me, s, 3H, minor stereoisomer), 2.44 (SO–Me, s, 3H, major stereoisomer), 2.52 (CH_2–benzyl, m, 2H, both stereoisomers), 2.93 (CH_2–benzyl, m, 2H, both stereoisomers), 3.59 (OMe, s, 3H, minor stereoisomer), 3.67 (OMe, s, 3H, major stereoisomer), 4.42 (H-4, m, 1H, minor stereoisomer), 4.60 (H-4, m, 1H, major stereoisomer), 5.09 (H-3, d, 1H, *J*=4.4, minor stereoisomer), 5.18 (H-3, d, 1H, *J*=4.5, major stereoisomer), 6.88–7.56 (ArH, m, 18H, both stereoisomers). ^{13}C NMR ($CDCl_3$) δ 31.7 (SO–Me), 34.3 (CH_2), 55.9 (OMe), 60.6 (C-4), 76.1 (C-3), 116.3, 119.0, 129.4, 130.5, 130.9, 138.1, 147.7, 156.0 (aromatic carbons), 163.3 (CO, β-lactam). Anal. Calcd for $C_{18}H_{19}NO_3S$: C, 65.63; H, 5.81; N, 4.25; O, 14.57; S, 9.73. Found: C, 65.75; H, 5.98; N, 4.18.

*4.6.2. 4-Benzyl-1-(4-chlorophenyl)-3-(methylsulfinyl)azetidin-2-one (**6b**).* White solid (0.19 g, 83%) (2.5:1 mixture of diastereomers by NMR). Mp: 91–93 °C. R_f=0.47 (1:1 hexane/EtOAc); IR (KBr, cm^{-1}): 1088 (S=O), 1745 (CO, β-lactam). ^{1}H NMR ($CDCl_3$) δ 2.31 (SO–Me, s, 3H, minor stereoisomer), 2.42 (SO–Me, s, 3H, major stereoisomer), 2.55 (CH_2–benzyl, m, 2H, both stereoisomers), 2.83 (CH_2–benzyl, m, 2H, both stereoisomers), 4.54 (H-4, m, 1H, minor stereoisomer), 4.68 (H-4, m, 1H, major stereoisomer), 5.08 (H-3, d, 1H, *J*=4.7, minor stereoisomer), 5.20 (H-3, d, 1H, *J*=4.6, major stereoisomer), 6.96–7.49 (ArH, m, 18H, both stereoisomers). ^{13}C NMR ($CDCl_3$) δ 32.5 (SO–Me), 36.0 (CH_2), 61.2 (C-4), 75.2 (C-3), 118.1, 120.5, 125.9, 133.1, 134.0, 137.4, 141.8, 150.7 (aromatic carbons), 161.5 (CO, β-lactam). Anal. Calcd for $C_{17}H_{16}ClNO_2S$: C, 61.16; H, 4.83; Cl, 10.62; N, 4.20; O, 9.59; S, 9.61. Found: C, 61.07; H, 4.5; N, 4.13.

*4.6.3. 4-Benzyl-1-methyl-3-(methylsulfinyl)azetidin-2-one (**6c**).* Colorless oil (0.12 g, 71%) (2.5:1 mixture of diastereomers by NMR). R_f=0.51 (1:1 hexane/EtOAc); IR (KBr, cm^{-1}): 1078 (S=O), 1751 (CO, β-lactam). ^{1}H NMR ($CDCl_3$) δ 2.33 (SO–Me, s, 3H, minor stereoisomer), 2.41 (SO–Me, s, 3H, major stereoisomer), 2.48 (CH_2–benzyl, m, 2H, both stereoisomers), 2.85 (CH_2–benzyl, m, 2H, both stereoisomers), 2.92 (*N*–Me, s, 3H, minor stereoisomer), 2.99 (*N*–Me, s, 3H, major stereoisomer), 4.59 (H-4, m, 1H, minor stereoisomer), 4.66 (H-4, m, 1H, major stereoisomer), 5.14 (H-3, d, 1H, *J*=4.3, minor stereoisomer), 5.27 (H-3, d, 1H, *J*=4.5, major stereoisomer), 7.01–7.38 (ArH, m, 10H, both stereoisomers). ^{13}C NMR ($CDCl_3$) δ 29.8 (*N*–Me), 31.1 (SO–Me), 33.6 (CH_2), 61.3 (C-4), 77.5 (C-3), 119.7, 123.8, 125.6, 143.9 (aromatic carbons), 162.7 (CO, β-lactam). Anal. Calcd for $C_{12}H_{15}NO_2S$: C, 60.73; H, 6.37; N, 5.90; O, 13.48; S, 13.51. Found: C, 60.79; H, 6.50; N, 5.83.

*4.6.4. 1,4-Bis(4-methoxyphenyl)-3-(methylsulfinyl)azetidin-2-one (**6d**).* White solid (0.18 g, 75%) (2.5:1 mixture of diastereomers by NMR). Mp: 96–98 °C. R_f=0.43 (1:1 hexane/EtOAc); IR (KBr, cm^{-1}): 1089 (S=O), 1745 (CO, β-lactam). ^{1}H NMR ($CDCl_3$) δ 2.32 (SO–Me, s, 3H, minor stereoisomer), 2.40 (SO–Me, s, 3H, major stereoisomer), 3.55, 3.61 (2OMe, 2s, 6H, minor stereoisomer), 3.64, 3.68 (2OMe, 2s, 6H, major stereoisomer), 4.47 (H-4, d, 1H, *J*=4.8, minor stereoisomer), 4.59 (H-4, d, 1H, *J*=4.7, major stereoisomer), 5.16 (H-3, d, 1H, *J*=4.8, minor stereoisomer), 5.25 (H-3, d, 1H, *J*=4.7, major stereoisomer), 6.82–7.62 (ArH, m, 16H, both stereoisomers). ^{13}C NMR ($CDCl_3$) δ 32.3 (SO–Me), 56.3, 58.0 (2OMe), 63.2 (C-4), 77.8 (C-3), 114.8, 117.3, 124.6, 131.5, 132.1, 139.4, 152.2, 155.8 (aromatic carbons), 162.6 (CO, β-lactam). Anal. Calcd for $C_{18}H_{19}NO_4S$: C, 62.59; H, 5.54; N, 4.06; O, 18.53; S, 9.28. Found: C, 62.69; H, 5.71; N, 4.13.

*4.6.5. 1-(4-Chlorophenyl)-4-(4-methoxyphenyl)-3-(methylsulfinyl) azetidin-2-one (**6e**).* White solid (0.18 g, 72%) (2.5:1 mixture of diastereomers by NMR). Mp: 99–101 °C. R_f=0.43 (1:1 hexane/EtOAc); IR (KBr, cm^{-1}): 1081 (S=O), 1748 (CO, β-lactam). ^{1}H NMR ($CDCl_3$) δ 2.37 (SO–Me, s, 3H, minor stereoisomer), 2.44 (SO–Me, s, 3H, major stereoisomer), 3.57 (OMe, s, 3H, minor stereoisomer), 3.62

(OMe, s, 3H, major stereoisomer), 4.51 (H-4, d, 1H, J=4.3, minor stereoisomer), 4.57 (H-4, d, 1H, J=4.6, major stereoisomer), 5.13 (H-3, d, 1H, J=4.3, minor stereoisomer), 5.17 (H-3, d, 1H, J=4.6, major stereoisomer), 6.79–7.93 (ArH, m, 16H, both stereoisomers). ^{13}C NMR ($CDCl_3$) δ 33.8 (SO–Me), 56.7 (OMe), 61.6 (C-4), 78.4 (C-3), 116.2, 118.0, 122.3, 132.5, 132.8, 135.7, 142.2, 156.8 (aromatic carbons), 162.1 (CO, β-lactam). Anal. Calcd for $C_{17}H_{16}ClNO_3S$: C, 58.37; H, 4.61; Cl, 10.13; N, 4.00; O, 13.72; S, 9.17. Found: C, 58.26; H, 4.70; N, 3.92.

*4.6.6. 4-(4-Methoxyphenyl)-1-methyl-3-(methylsulfinyl)azetidin-2-one (**6f**).* Colorless oil (0.13 g, 76%) (2.5:1 mixture of diastereomers by NMR). R_f=0.46 (1:1 hexane/EtOAc); IR (KBr, cm^{-1}): 1084 (S=O), 1755 (CO, β-lactam). ^{1}H NMR ($CDCl_3$) δ 2.29 (SO–Me, s, 3H, minor stereoisomer), 2.34 (SO–Me, s, 3H, major stereoisomer), 2.88 (*N*–Me, s, 3H, minor stereoisomer), 2.96 (*N*–Me, s, 3H, major stereoisomer), 3.63 (OMe, s, 3H, minor stereoisomer), 3.68 (OMe, s, 3H, major stereoisomer), 4.47 (H-4, d, 1H, J=5.0, minor stereoisomer), 4.53 (H-4, d, 1H, J=4.8, major stereoisomer), 5.08 (H-3, d, 1H, J=5.0, minor stereoisomer), 5.15 (H-3, d, 1H, J=4.8, major stereoisomer), 6.92–7.29 (ArH, m, 8H, both stereoisomers). ^{13}C NMR ($CDCl_3$) δ 29.0 (*N*–Me), 31.8 (SO–Me), 55.4 (OMe), 61.5 (C-4), 76.9 (C-3), 116.3, 121.1, 127.5, 152.9 (aromatic carbons), 161.7 (CO, β-lactam). Anal. Calcd for $C_{12}H_{15}NO_3S$: C, 56.90; H, 5.97; N, 5.53; O, 18.95; S, 12.66. Found: C, 56.97; H, 6.11; N, 5.56.

4.7. General procedure for the synthesis of 3-(methylsulfonyl) β-lactams 7a–f

To a solution of 3-methylthio β-lactams **5v–yz** (0.5 mmol) in CH_2Cl_2 (20 mL) was added *m*-CPBA (0.2 g, 1.16 mmol) at room temperature. After 3 h, a saturated solution of $NaHSO_3$ (10 mL) and $NaHCO_3$ (20 mL) was added, and the mixture was extracted with EtOAc (2×15 mL). The organic layer was purified by chromatography on silica gel using EtOAc/hexane (3:7) to give pure products.

*4.7.1. 4-Benzyl-1-(4-methoxyphenyl)-3-(methylsulfonyl)azetidin-2-one (**7a**).* White solid (0.14 g, 82%). Mp: 117–119 °C. R_f=0.40 (1:1 hexane/EtOAc); IR (KBr, cm^{-1}): 1161, 1318 (SO_2), 1753 (CO, β-lactam). ^{1}H NMR ($CDCl_3$) δ 2.40 (CH_2–benzyl, dd, 1H, J=5.7, 15.0), 2.79 (CH_2–benzyl, dd, 1H, J=5.7, 15.0), 3.08 (SO_2-Me, s, 3H), 3.56 (OMe, s, 3H), 4.19 (H-4, m, 1H), 5.52 (H-3, d, 1H, J=4.5), 6.81–7.69 (ArH, m, 9H). ^{13}C NMR ($CDCl_3$) δ 32.2 (CH_2), 34.0 (SO_2-Me), 56.7 (OMe), 60.8 (C-4), 81.2 (C-3), 117.6, 121.4, 123.5, 129.1, 129.7, 133.2, 148.6, 156.1 (aromatic carbons), 163.9 (CO, β-lactam). Anal. Calcd for $C_{18}H_{19}NO_4S$: C, 62.59; H, 5.54; N, 4.06; O, 18.53; S, 9.28. Found: C, 62.50; H, 5.67; N, 4.11.

*4.7.2. 4-Benzyl-1-(4-chlorophenyl)-3-(methylsulfonyl)azetidin-2-one (**7b**).* White solid (0.13 g, 77%). Mp: 124–126 °C. R_f=0.41 (1:1 hexane/EtOAc); IR (KBr, cm^{-1}): 1157, 1322 (SO_2), 1755 (CO, β-lactam). ^{1}H NMR ($CDCl_3$) δ 2.45 (CH_2–benzyl, dd, 1H, J=5.8, 14.5), 2.81 (CH_2–benzyl, dd, 1H, J=5.8, 14.5), 3.01 (SO_2-Me, s, 3H), 4.13 (H-4, m, 1H), 5.57 (H-3, d, 1H, J=4.3), 6.93–7.46 (ArH, m, 9H). ^{13}C NMR ($CDCl_3$) δ 31.6 (CH_2), 33.3 (SO_2-Me), 61.3 (C-4), 81.8 (C-3), 119.9, 123.7, 123.9, 128.7, 129.4, 132.8, 141.4, 148.2 (aromatic carbons), 162.9 (CO, β-lactam). Anal. Calcd for $C_{17}H_{16}ClNO_3S$: C, 58.37; H, 4.61; Cl, 10.13; N, 4.00; O, 13.72; S, 9.17. Found: C, 58.44; H, 4.74; N, 4.08.

*4.7.3. 4-Benzyl-1-methyl-3-(methylsulfonyl)azetidin-2-one (**7c**).* Colorless oil (0.10 g, 79%). R_f=0.43 (1:1 hexane/EtOAc); IR (KBr, cm^{-1}): 1155, 1308 (SO_2), 1752 (CO, β-lactam). ^{1}H NMR ($CDCl_3$) δ 2.48 (CH_2–benzyl, dd, 1H, J=5.6, 14.6), 2.88 (CH_2–benzyl, dd, 1H, J=5.6, 14.6), 2.97 (*N*–Me, s, 3H), 3.13 (SO_2-Me, s, 3H), 4.26 (H-4, m, 1H), 5.59 (H-3, d, 1H, J=4.7), 6.95–7.27 (ArH, m, 5H). ^{13}C NMR ($CDCl_3$) δ 29.4 (*N*–Me), 32.7 (CH_2), 35.1 (SO_2-Me), 60.3 (C-4), 81.4 (C-3), 120.8, 125.3, 126.1, 143.2 (aromatic carbons), 163.4 (CO, β-lactam). Anal. Calcd for $C_{12}H_{15}NO_3S$: C, 56.90; H, 5.97; N, 5.53; O, 18.95; S, 12.66. Found: C, 56.82; H, 6.07; N, 5.58.

*4.7.4. 1,4-Bis(4-methoxyphenyl)-3-(methylsulfonyl)azetidin-2-one (**7d**).* White solid (0.14 g, 80%). Mp: 111–113 °C. R_f=0.38 (1:1 hexane/EtOAc); IR (KBr, cm^{-1}): 1159, 1313 (SO_2), 1756 (CO, β-lactam). ^{1}H NMR ($CDCl_3$) δ 3.15 (SO_2-Me, s, 3H), 3.53, 3.61 (2OMe, 2s, 6H), 4.31 (H-4, d, 1H, J=4.9), 5.59 (H-3, d, 1H, J=4.9), 6.70–7.73 (ArH, m, 8H). ^{13}C NMR ($CDCl_3$) δ 32.9 (SO_2-Me), 56.0, 56.9 (2OMe), 61.8 (C-4), 83.5 (C-3), 115.1, 120.8, 121.3, 125.7, 129.9, 130.2, 146.1, 157.4 (aromatic carbons), 164.2 (CO, β-lactam). Anal. Calcd for $C_{18}H_{19}NO_5S$: C, 59.82; H, 5.30; N, 3.88; O, 22.13; S, 8.87. Found: C, 59.91; H, 5.44; N, 3.93.

*4.7.5. 1-(4-Chlorophenyl)-4-(4-methoxyphenyl)-3-(methylsulfonyl) azetidin-2-one (**7e**).* White solid (0.13 g, 74%). Mp: 123–125 °C. R_f=0.40 (1:1 hexane/EtOAc); IR (KBr, cm^{-1}): 1155, 1314 (SO_2), 1751 (CO, β-lactam). ^{1}H NMR ($CDCl_3$) δ 3.10 (SO_2-Me, s, 3H), 3.54 (OMe, s, 3H), 4.36 (H-4, d, 1H, J=4.2), 5.50 (H-3, d, 1H, J=4.2), 6.83–7.46 (ArH, m, 8H). ^{13}C NMR ($CDCl_3$) δ 33.5 (SO_2-Me), 55.7(OMe), 62.0 (C-4), 82.8 (C-3), 116.4, 119.1, 121.8, 122.6, 125.7, 133.9, 140.4, 147.2 (aromatic carbons), 163.7 (CO, β-lactam). Anal. Calcd for $C_{17}H_{16}ClNO_4S$: C, 55.81; H, 4.41; Cl, 9.69; N, 3.83; O, 17.49; S, 8.76. Found: C, 55.76; H, 4.50; N, 3.86.

*4.7.6. 4-(4-Methoxyphenyl)-1-methyl-3-(methylsulfonyl)azetidin-2-one (**7f**).* Colorless oil (0.10 g, 77%). R_f=0.45 (1:1 hexane/EtOAc); IR (KBr, cm^{-1}): 1151, 1307 (SO_2), 1754 (CO, β-lactam). ^{1}H NMR ($CDCl_3$) δ 2.90 (*N*–Me, s, 3H), 3.06 (SO_2–Me, s, 3H), 3.58 (OMe, s, 3H), 4.43 (H-4, d, 1H, J=4.7), 5.57 (H-3, d, 1H, J=4.7), 6.79–7.25 (ArH, m, 4H). ^{13}C NMR ($CDCl_3$) δ 29.5 (*N*–Me), 32.8 (SO_2-Me), 56.3 (OMe), 62.4 (C-4), 83.7 (C-3), 117.1, 118.9, 137.4, 155.0 (aromatic carbons), 162.6 (CO, β-lactam). Anal. Calcd for $C_{12}H_{15}NO_4S$: C, 53.52; H, 5.61; N, 5.20; O, 23.76; S, 11.91. Found: C, 53.64; H, 5.77; N, 5.28.

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Supplementary data

Supplementary data associated with this article can be found in the online version, at doi:10.1016/j.tet.2011.05.043. These data include MOL files and InChiKeys of the most important compounds described in this article.

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