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Stereoselective synthesis and Lewis acid mediated functionalization of novel 3-methylthio-β-lactams

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ABSTRACT

A proficient etiquette for the stereoselective synthesis of novel 3-methylthio-β-lactams and their Lewis acid mediated functionalization is described. Treatment of 2-methylthioethanoic acid and appropriate imines in the Staudinger reaction leads to the stereocontrolled synthesis of novel *trans*-3-methylthio-β-lactams in excellent yields. *cis*-3-Chloro-3-methylthio-β-lactams, obtained from stereoselective chlorination of *trans*-3-methylthio-β-lactams using *N*-chlorosuccinimide (NCS) and AIBN, were subjected to Lewis acid ($TiCl_4$ or $SnCl_4$) mediated functionalization using various active aromatic, heterocyclic and aliphatic compounds (nucleophiles). This reaction provides an easy access to novel, stereoselective *cis*-3-monosubstituted-3-methylthio-β-lactams, which further undergo smooth desulfurization with Raney-nickel to afford C-3 *cis*- and *trans*-monosubstituted-β-lactams. The cis or trans configuration of the hydrogen/chloro/nucleophile substituent at C-3 was assigned with respect to C4–H.

1. Introduction

The effectiveness of β-lactam heterocycle in various important areas, such as in medicine, biology and chemistry has been clearly demonstrated.[1,2] The azetidin-2-one nucleus is the central building block of β-lactam antibiotics, so functionalization of the azetidin-2-one framework is pivotal for the development of new β-lactam antibiotics.[3] Recently, C-3 alkylaryl substituted monocyclic β-lactams have been shown to be potential inhibitors of cholesterol acyl transferase **I**[4] and prostate specific antigen **II**[5] (Fig. 1).

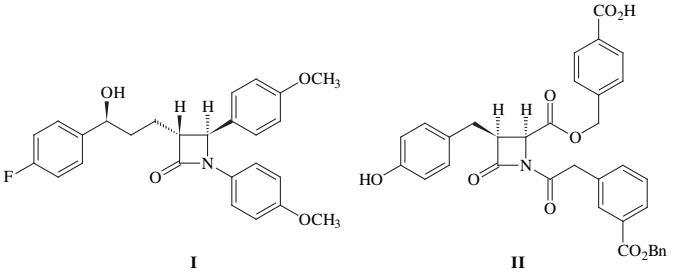
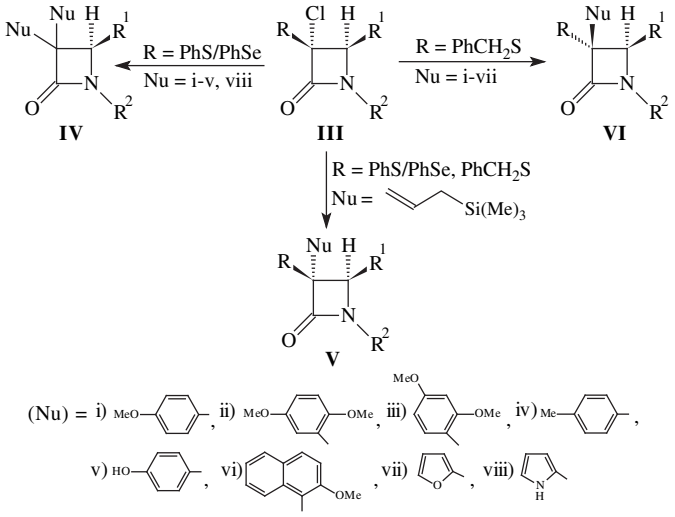


Figure 1. Biologically active C-3 alkylaryl substituted monocyclic β-lactams.

Our previous studies have revealed[2,6–14] that *cis*-3-chloro-3-phenyl/benzylthio/seleno-β-lactams served as β-lactam carbocation equivalents in the presence of a Lewis acid ($TiCl_4$ or $SnCl_4$) and reacted with a number of active aromatic, heterocyclic and aliphatic compounds (nucleophiles) to afford variety of C-3 monosubstituted as well as disubstituted β-lactams (Scheme 1). The *cis*-3-chloro-3-



Scheme 1. Lewis acid mediated functionalization of *cis*-3-chloro-3-phenyl/benzylthio/seleno-β-lactams.

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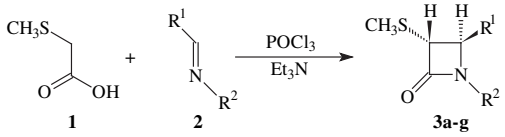
phenylthio/seleno-β-lactams **III** on treatment with a number of active aromatic and heterocyclic compounds (nucleophiles) in the presence of a Lewis acid ($TiCl_4$ or $SnCl_4$) preferentially afforded C-3 disubstituted β-lactams **IV**.[2,6,9] However, the reaction of *cis*-3-chloro-3-phenyl/benzylthio/seleno-β-lactams **III** with trimethylallylsilane as the reactive aliphatic nucleophile furnished *cis*-3-allyl substituted β-lactams **V**.[2,9] Whereas, the presence of benzylthio ($PhCH_2S$–) group at C-3 position led to the exclusive formation of *trans*-3-monosubstited-3-benzylthio-β-lactams **VI** from *cis*-3-chloro-3-benzylthio-β-lactams **III**.[9] These studies indicate that the presence of different groups at various positions of the β-lactam ring effect the Lewis acid mediated functionalization and give variety of 3-monosubstituted-3-alkyl/aryl-thio/seleno-β-lactams **V** and **VI** and disubstituted-β-lactams **IV**.

To gain deeper insight into the unique reactivity of β-lactam carbocation equivalents and to further explore the effect of alkylthio group on reactivity, stereospecifity and regioselectivity in Lewis acid mediated functionalization, we undertook the synthesis of novel 3-methylthio-β-lactams and their Lewis acid mediated functionalization. In addition, the appropriately substituted 3-methylthio-β-lactams are potential synthons for bicyclic as well as spirocyclic-β-lactams.

2. Results and discussion

Recently, Jiaxi et al.[15] have reported the stereoselective and stereospecific synthesis of variety of 3-phenoxy/phenylthio-β-lactams and 3-phenyl/methyl-β-lactams. However, in literature, there is no report yet listed so far for the synthesis of 3-methylthio-β-lactams. We began our study by looking into the reaction of appropriate Schiff's bases **2a**–**g** and the ketene in situ generated from the 2-methylthioethanoic acid (**1**). According to the earlier reported procedure,[9] **1** was reacted with **2a** in the presence of triethylamine and phosphorous oxychloride ($POCl_3$) in dichloromethane to access novel *trans*-3-methylthio-β-lactams (**3a**) via Staudinger cycloaddition reaction (Scheme 2).



Scheme 2. Synthesis of *trans*-3-methylthio-β-lactams **3a**–**g**.

Although, the formation of **3a** took place at 0 °C in dichloromethane, but the reaction resulted **3a** in very low yield, i.e., 19% (Table 1, entry 1). However, the yield of the product (**3a**) was enhanced to 45% (Table 1, entry 2) when this reaction was carried out in refluxing dichloromethane. As observed, higher temperature conditions enhanced the yield of the product. The reaction when performed using benzene and toluene as the solvents afforded the product **3a** in 51% and 90%, respectively, at the refluxing temperature (Table 1, entries 3 and 4). The reaction conditions were optimized by varying the solvent and reaction temperature. As indicated in Table 1, entry 4, toluene was observed to be the best solvent.

Table 1
Synthesis of **3a** in different solvent and temperature conditions

Entry	Solvent	Temperature (°C)	Yield[a] (%)
1	Dichloromethane	0	19
2	Dichloromethane	40 (reflux)	45
3	Benzene	80 (reflux)	51
4	Toluene	110 (reflux)	90

[a] Yields quoted are for the isolated product **3a**.

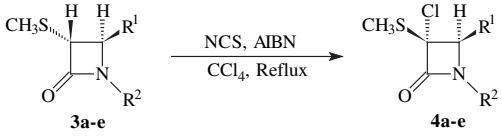
Using these optimum reaction conditions, a variety of *trans*-3-methylthio-β-lactams **3b**–**g** were prepared in good yields (Scheme 2) and results are listed in Table 2. The structures of these *trans*-3-methylthio-β-lactams **3a**–**g** were established on the basis of elemental analysis and spectroscopic techniques viz., FTIR and NMR (^1H, ^{13}C). The cycloaddition reaction of **1** and **2** resulted in the exclusive formation of *trans*-β-lactam **3** (*J* 2.1–2.4 Hz, C3–H and C4–H) and which can be rationalized on the basis of the similar mechanism as discussed for the *cis*-3-alkoxy-3-phenyl/benzylthio-β-lactams in our recent publication.[10]

Table 2
trans-3-Methylthio-β-lactams **3a**–**g**

Entry	3	R^1	R^2	Yield[a] (%)
1	**a**	C_6H_5	4-(MeO)C_6H_4	90
2	**b**	C_6H_5	C_6H_5	76
3	**c**	4-(MeO)C_6H_4	$CH_2C_6H_5$	74
4	**d**	4-(MeO)C_6H_4	4-(MeO)C_6H_4	80
5	**e**	C_6H_5	4-(Me)C_6H_4	72
6	**f**	4-(Cl)C_6H_4	4-(MeO)C_6H_4	70
7	**g**	C_6H_5	$CH_2C_6H_5$	75

[a] Yields quoted are for the isolated products.

Our earlier studies[2,6–14] established the use of *cis*-3-chloro-3-phenyl/benzylthio/seleno-β-lactams as the suitable C-3 carbocations for Lewis acid mediated functionalizations. So, it was envisaged to synthesize *cis*-3-chloro-3-methylthio-β-lactams following the procedure reported in the cited references. Quite interestingly, the stereoselective chlorination of 3-methylthio-β-lactam (**3**) with sulfuryl chloride (SO_2Cl_2) furnished a complex mixture, which was unidentifiable by spectroscopic techniques. The synthesis of *cis*-3-chloro-3-methylthio-β-lactams **4a**–**e** in good yields was successfully achieved by treatment of **3a**–**e** with *N*-chlorosuccinimide (NCS) and catalytic amount of AIBN in refluxing carbon tetrachloride (Scheme 3, Table 3). The structures of **4a**–**e** were confirmed from FTIR, ^1H NMR and ^{13}C NMR spectroscopic analysis. The stereochemistry was assigned cis with respect to C4–H on the basis of correlation of ^1H and ^{13}C NMR data of **4a**–**e** with that of *cis*-3-chloro-3-phenyl/benzylthio-β-lactams, whose stereochemistry has already been established by X-ray crystallographic analysis.[8,9]



Scheme 3. Synthesis of *cis*-3-chloro-3-methylthio-β-lactams **4a**–**e**.

These studies have revealed some interesting features of the chlorination of 3-phenyl/benzyl/methylthio-β-lactams. Sulfuryl chloride (SO_2Cl_2) was found to be the suitable chlorinating agent for the β-lactams possessing 3-arylthio moiety as visualized in the case of 3-phenylthio-β-lactams.[6,9] However, for efficient synthesis of *cis*-3-chloro-3-benzyl/methylthio-β-lactams *N*-chlorosuccinimide

Table 3
cis-3-Chloro-3-methylthio-β-lactams **4a**–**e**

Entry	4	R^1	R^2	Yield[a] (%)
1	**a**	C_6H_5	4-(MeO)C_6H_4	56
2	**b**	C_6H_5	C_6H_5	53
3	**c**	4-(MeO)C_6H_4	$CH_2C_6H_5$	55
4	**d**	4-(MeO)C_6H_4	4-(MeO)C_6H_4	52
5	**e**	C_6H_5	4-(Me)C_6H_4	50

[a] Yields quoted are for the isolated products.

(NCS) is the most appropriate chlorinating agent for 3-alkyl and 3-alkylaryl substituted β-lactams.

As the $PhCH_2S$-substituted *cis*-3-chloro-β-lactams **III** were stereoselectively converted into corresponding *trans*-3-monosubstituted-3-benzylthio-β-lactams **VI** (Scheme 1), CH_3S-substituted 3-chloro-β-lactams **4** were selected as an appropriate model to investigate the Lewis acid mediated functionalization with a number of active aromatic, heterocyclic and aliphatic compounds (nucleophiles). We considered two main questions: (a) Whether the presence of methylthio group at C-3 position affords 3-monosubstituted-3-methylthio-β-lactams or disubstituted β-lactams and (b) If, monosubstituted then, will this group have any influence on the stereoselective generation of *cis*- or *trans*-3-monosubstituted 3-methylthio-β-lactams.

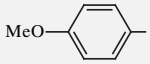
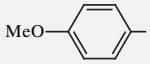
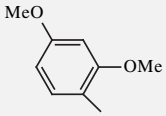
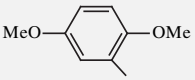
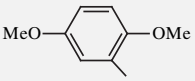
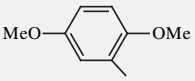
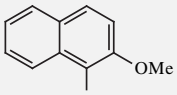
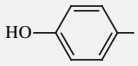
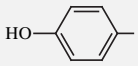
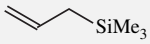
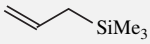
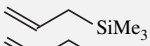
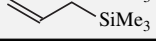
Initially, the *cis*-3-chloro-3-methylthio-β-lactam (**4a**) was exposed to 1 equiv of $SnCl_4$ using anisole as an active substrate in dichloromethane under nitrogen atmosphere at 0 to −5 °C. This reaction resulted in the exclusive formation of one isomer of 3-monosubstituted-3-methylthio-β-lactam, **5h** in good yield (Scheme 4). Whereas, treatment of **4b** with 1,4-dimethoxybenzene under similar condition furnished a mixture of two isomers of 3-monosubstituted-3-methylthio-β-lactams **5l** and **6l** in the ratio of 9:1, respectively, as was evident from ^1H NMR spectroscopy (Table 4, entry 5). These isomeric 3-monosubstituted-3-methylthio-β-lactams **5l** and **6l**, with similar R_f value were inseparable through column chromatography, however, the major isomer **5l** was isolated in pure form through recrystallization of the mixture of two isomers from dichloromethane/hexanes and was identified as *cis*-2′,4′-dimethoxyphenyl-3-methylthio-β-lactam whereas, the other isomer **6l** remained as liquid product and was identified as *trans*-2′,4′-dimethoxyphenyl-3-methylthio-β-lactam.

In order to examine the versatility of this reaction, CH_3S-substituted 3-chloro-β-lactams **4a–e** were subjected to Lewis acid mediated functionalization with a number of active aromatic, heterocyclic and aliphatic compounds (nucleophiles) and the results are summarized in Table 4. The heterocyclic compound furan on treatment with **4a** under similar conditions afforded *cis*-3-furanyl-3-methylthio-β-lactam as the major product, whereas *trans*-3-furanyl product was obtained in the case of 3-benzylthio-β-lactam.[9] However, pyrrole and aliphatic compounds allyltrimethylsilane gave the similar results (Table 4, entries 12–17) as described earlier for 3-benzylthio-β-lactams.[9] 3,3-Disbustituted-β-lactams **7** and **8** were also accompanied with major products in very low yields. Similar results were obtained using $TiCl_4$ as the Lewis acid.

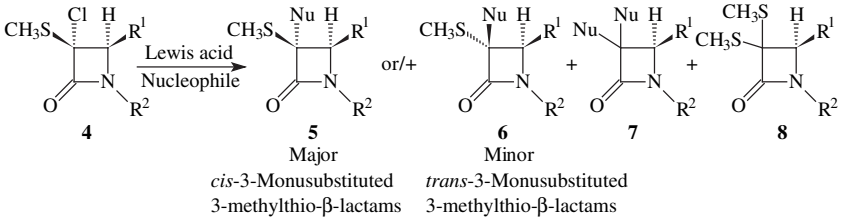
The structures of these β-lactams (**5–8**) were established by spectroscopic means such as FTIR, ^1H NMR and ^{13}C NMR and elemental analysis. The stereochemical assignment of the new substituent at C-3 of **5h–x** with respect to C4–H was confirmed cis through single crystal X-ray structure analysis[16,17] of **5l** and **5m** because the torsion angles C16–C2–C1–H1 and C16–C2–C1–C4 in **5l** are −11.5(3) and 119.7(3)° and C18–C3–C1–H1 and C18–C3–C1–C4 in **5m** are −1.3(2) and −134.6(2)°, respectively (Fig. 2).

This study reveals that 3-methylthio moiety preferably allow monosubstitutions at C-3 position of 3-methylthio-β-lactams with cis configuration of the incoming nucleophile to the C4–H. Thus, on the basis of stability and steric effects, $PhCH_2S$-substituted 3-chloro-β-lactams following *Path A* (S_N2 mechanism) provide *trans*-3-monosubstituted-3-benzylthio-β-lactams whereas, CH_3S-substituted

Table 4
Reaction of **4** with various active aromatic, heterocyclic and aliphatic compounds (nucleophiles) using $SnCl_4$ or $TiCl_4$ as the Lewis acid

Entry	4	Compound (Nu)	Products of type (% yield)[a]			
			5	6	7	8
1	**4a**		**5h** (61)	—	**7h** (07)	**8a** (04)
2	**4c**		**5i** (63)	—	**7i** (09)	**8c** (12)
3	**4a**		**5j** (42)	—	**7j** (20)	**8a** (11)
4	**4a**		**5k** (57)	**6k** (07)	**7k** (04)	**8a** (06)
5	**4b**		**5l** (51)	**6l** (06)	**7l** (06)	**8b** (05)
6	**4c**		**5m** (63)	—	**7m** (04)	**8c** (06)
7	**4b**		**5n** (47)	—	—	**8b** (03)
8	**4a**		**5o** (51)	—	**7o** (12)	**8a** (07)
9	**4b**		**5p** (49)	**6p** (06)	**7p** (20)	**8b** (09)
10	**4a**		**5q** (63)	**6q** (08)	—	—
11	**4c**		**5r** (72)	**6r** (09)	—	—
12	**4a**		—	—	**7s** (80)	**8a** (14)
13	**4c**		—	—	**7t** (60)	**8c** (21)
14	**4a**		**5u** (75)	—	—	—
15	**4b**		**5v** (77)	—	—	—
16	**4d**		**5w** (72)	—	—	—
17	**4e**		**5x** (70)	—	—	—

[a] Yields quoted are for the isolated products.



Scheme 4. Reaction of **4** with various active aromatic, heterocyclic and aliphatic compounds (nucleophiles) using $SnCl_4$ or $TiCl_4$ as the Lewis acid.

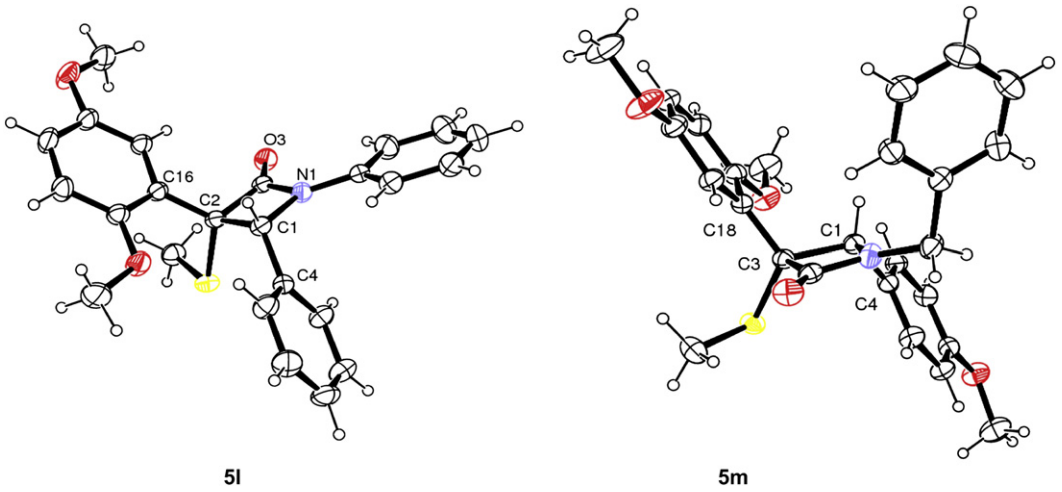
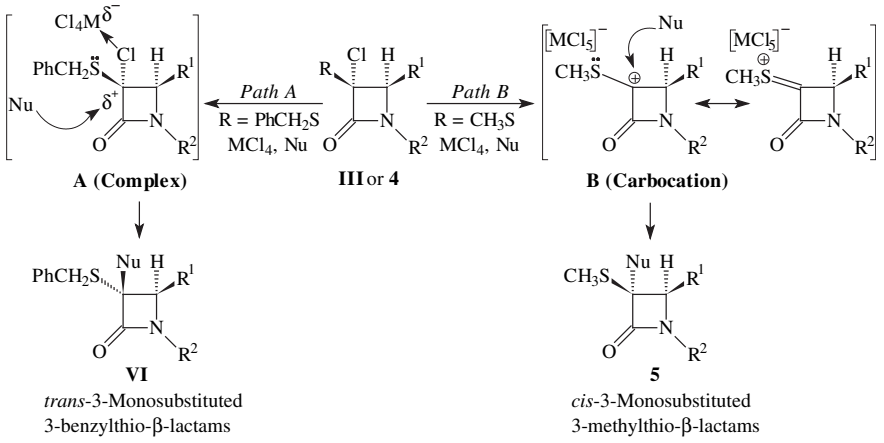


Figure 2. Partially labeled ORTEP diagrams for compounds **5l** and **5m**.

3-chloro-β-lactams pursuing *Path B* (S_N1 mechanism) furnish *cis*-3-monosubstituted-3-methylthio-β-lactams as depicted in Scheme 5 and reported earlier for Lewis acid mediated reaction of phenylthio- reversal of selectivity in the case of desulfurization using Raney-Ni is not surprising. It seems that due to small size of 3-methylthio group at C-3 carbon and its easy approach to the hydrogen



Scheme 5. Plausible reaction pathway for the synthesis of *cis*- and *trans*-3-monosubstituted-β-lactams.

and benzylthio-β-lactams.[2,9,11] As a consequence, the stereochemical outcome of the Lewis acid mediated functionalization of C-3 carbocation equivalents with active aromatic, heterocyclic and aliphatic compounds (nucleophiles) can be controlled stereoselectively by an appropriate choice of the PhS–, $PhCH_2S$– and CH_3S– moieties, respectively, at C-3 position of the 3-chloro-β-lactams.

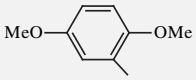
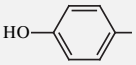
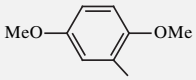
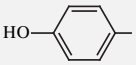
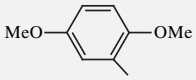
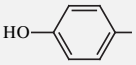
The *cis*-3-monosubstituted-3-methylthio-β-lactams **5k** and **5p** were further subjected to the Raney-nickel[18] desulfurization in different solvents such as methanol, ethanol and acetone to study the effect on the conditions such as temperature, time for completion of the reaction, stereochemistry and yield of the product. Out of these three solvents, methanol afforded the 3-monosubstituted-β-lactams **9** at room temperature with high yield, lower reaction time and results are summarized in Table 5. The Raney-nickel desulfurization of **5k** and **5p** led to the formation of *cis*-β-lactams **9k** and **9p** (J 5.7 Hz, C3–H and C4–H) as the major products and *trans*-β-lactams **10k** and **10p** (J 2.4–2.7 Hz, C3–H and C4–H) as the minor products (Scheme 6).

The 3-methylthio-β-lactams have shown a different reactivity profile for a reaction with some of the nucleophiles in the presence of Lewis acid as compared to 3-phenyl/benzylthio-β-lactams. Thus, rich catalyst surface, the reactivity of this β-lactam towards desulfurization is much more even in reduced concentration of hydrogen atom in acetone as compared to higher concentration of hydrogen in methanol and ethanol.

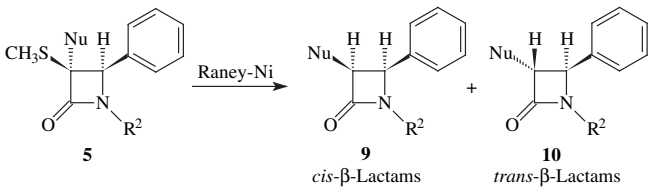
3. Conclusion

In conclusion, we have developed a highly stereoselective synthesis of novel *cis*-3-monosubstituted-3-methylthio-β-lactams from *cis*-3-chloro-3-methylthio-β-lactams using various active aromatic, heterocyclic and aliphatic compounds (nucleophiles) in the presence of Lewis acid ($TiCl_4$ or $SnCl_4$). In contrast to our earlier studies on phenyl/benzylthio-β-lactams, where the relationship between new substituent at C-3 position and C4–H hydrogen is trans, cis relationship has been established in methylthio-β-lactams. In addition, for the first time an array of novel 3-methylthio-β-lactams have been reported. Further elaboration of the *cis*-3-monosubstituted-3-methylthio-β-lactams to potential spirocyclic and bicyclic β-lactams is underway in our laboratory.

Table 5
Raney-nickel desulfurization of 3-methylthio-β-lactams (**5k** and **5p**)

Entry	5	R^2	Compound (Nu)	Solvent	Temp (°C)	Products of type (% yield)[a]	
						9	**10**
1	**5k**	4-(MeO)C_6H_4		Methanol	rt	**9k** (75)	**10k** (10)
2	**5p**	C_6H_5		Methanol	rt	**9p** (77)	**10p** (13)
3	**5k**	4-(MeO)C_6H_4		Ethanol	78–85	**9k** (68)	**10k** (12)
4	**5p**	C_6H_5		Ethanol	78–85	**9p** (65)	**10p** (15)
5	**5k**	4-(MeO)C_6H_4		Acetone	56–60	**9k** (70)	**10k** (18)
6	**5p**	C_6H_5		Acetone	56–60	**9p** (71)	**10p** (21)

[a] Yields quoted are for the isolated products.



Scheme 6. Raney-nickel desulfurization of 3-methylthio-β-lactams (**5k** and **5p**).

4. Experimental

4.1. General

^1H and ^{13}C NMR spectra were recorded at 300/400 and 75/100 MHz, respectively, in $CDCl_3$ solution using JEOL 300 and BRUCKER AVANCE II 400 MHz NMR spectrometers. Chemical shifts are given in parts per million relative to tetramethylsilane as an internal standard (δ=0 ppm) for ^1H NMR and $CDCl_3$ (δ=77.0 ppm) for ^{13}C NMR. IR spectra were taken on an FTIR spectrophotometer and are reported in cm^{-1}. The elemental analysis (C, H, N) was carried out in microanalytical section of Sophisticated Analytical Instrumentation Facility (SAIF), Panjab University, Chandigarh using a PERKIN–ELMER 2400 elemental analyzer. Column chromatography was performed using Merck Silica Gel (60–120 mesh) using ethyl acetate/hexanes (8:92) as an eluant system. Thin-layer chromatography (TLC) was performed using Merck Silica Gel G using ethyl acetate/hexanes (10:90) as an eluant system. For visualization, TLC plates were stained with iodine vapours. Melting points are uncorrected. All commercially available compounds/reagents were used without further purification. Dichloromethane, and carbon tetrachloride distilled over P_2O_5 was redistilled over CaH_2 before use. Toluene and benzene were distilled over sodium and benzophenone immediately before use. Single crystals of **5l** and **5m**, suitable for X-ray diffraction studies, were grown from dichloromethane/hexane (3:1). The intensity data were collected at 295 K on a Siemens P4 X-ray diffractometer by using θ–2θ scanning mode with graphite monochromatized Mo Kα radiation. The data were corrected for Lorentz and polarization effects but not for absorption. The structures were solved by direct methods using SIR97[19] and refined by full matrix least-square refinement techniques on F^2 using SHELXTL.[20] All non-hydrogen atoms were refined anisotropically. All hydrogen atoms were fixed geometrically with U_{iso} values of 1.2 times (for methylene and phenylene carbons) and 1.5 times (methyl carbons) the U_{iso} values of their respective carrier atoms. Details of the crystallographic data and supplementary publication CCDC numbers are provided in Refs. 16 and 17. Crystallographic data (excluding structure factors) of compounds **5l**[16] and **5m**[17] in CIF format have been deposited with the Cambridge Crystallographic Data Centre. Copies of the data can be obtained free of charge on application to CCDC, 12 Union Road, Cambridge CB2 1EZ, UK [Fax: (internet.) +44 1223/336 033: E-mail: deposit@ccdc.cam.ac.uk].

4.2. General procedure for the synthesis of *trans*-3-methylthio-β-lactams (3a–g)

Compounds **3a**–**g** and **4a**–**b**,**e** were prepared by the procedure as described for the synthesis of *trans*-3-phenyl/benzylthio-β-lactams[9] in the cited reference, starting from 2-methylthioethanoic acid.

*4.2.1. (±)-trans-1-(4′-Methoxyphenyl)-3-methylthio-4-phenylazetidin-2-one (**3a**).* Colourless solid (0.320 g, 90%); mp 115–117 °C; [Found: C, 68.53; H, 5.37; N, 4.62. $C_{17}H_{17}NO_2S$ requires: C, 68.20; H, 5.72; N, 4.68%.]; R_f (10% EtOAc/hexane) 0.54; IR (cm^{-1}, KBr): 1751 (C=O); δ_H (300 MHz, $CDCl_3$) 7.38–6.71 (9H, m, Ph), 4.74 (1H, d, *J* 2.4 Hz, C3–*H*), 3.87 (1H, d, *J* 2.4 Hz, C4–*H*), 3.70 (3H, s, OCH_3), 2.22 (3H, s, CH_3S); δ_C (75 MHz, $CDCl_3$) 162.2, 156.2, 137.0, 130.9, 129.2, 128.7, 125.8, 118.3, 114.3, 62.4, 60.2, 55.1, 12.9.

*4.2.2. (±)-trans-1-Phenyl-3-methylthio-4-phenylazetidin-2-one (**3b**).* Colourless crystalline solid (0.245 g, 76%); mp 124–125 °C; [Found: C, 71.28, H, 5.57, N, 5.12. $C_{16}H_{15}NOS$ requires: C, 71.34; H, 5.61; N, 5.20%]; R_f (10% EtOAc/hexane) 0.56; IR (cm^{-1}, KBr): 1764 (C=O); δ_H (300 MHz, $CDCl_3$) 7.33–6.93 (10H, m, Ph), 4.73 (1H, d, *J* 2.4 Hz, C3–*H*), 3.83 (1H, d, *J* 2.4 Hz, C4–*H*), 2.17 (3H, s, CH_3S); δ_C (75 MHz, $CDCl_3$) 163.1, 137.4, 136.8, 129.3, 129.2, 128.9, 125.8, 124.2, 117.2, 62.5, 60.2, 13.0.

*4.2.3. (±)-trans-1-Benzyl-3-methylthio-4-(4′-methoxyphenyl)azetidin-2-one (**3c**).* Yellow oil (0.277 g, 74%); [Found: C, 68.81; H, 6.01; N, 4.40. $C_{18}H_{19}NO_2S$ requires: C, 68.98; H, 6.11; N,

4.47%]; R_f (10% EtOAc/hexane) 0.53; IR (cm^{-1}, KBr): 1761 (C=O); δ_H (300 MHz, $CDCl_3$) 7.29–6.80 (9H, m, Ph), 4.76 (1H, d, *J* 14.7 Hz, CH_aH_bPh), 4.10 (1H, d, *J* 2.1 Hz, C3–*H*), 3.73 (1H, d, *J* 2.1 Hz, C4–*H*), 3.71 (3H, s, OCH_3), 3.60 (1H, d, *J* 15.0 Hz, CH_aH_bPh), 1.98 (3H, s, CH_3S); δ_C (75 MHz, $CDCl_3$) 165.8, 159.8, 135.0, 128.6, 128.5, 128.3, 128.2, 127.8, 127.6, 114.3, 114.2, 61.0, 59.7, 55.1, 44.4, 12.3.

*4.2.4. (±)-trans-1-(4′-Methoxyphenyl)-3-methylthio-4-(4′-methoxyphenyl)azetidin-2-one (**3d**).* Colourless oil (0.312 g, 80%); [Found: C, 65.52; H, 5.73; N, 4.15. $C_{18}H_{19}NO_3S$ requires: C, 65.63; H, 5.81; N, 4.25%]; R_f (10% EtOAc/hexane) 0.50; IR (cm^{-1}, CCl_4): 1768 (C=O); δ_H (300 MHz, $CDCl_3$) 7.26–6.70 (8H, m, Ph), 4.71 (1H, d, *J* 2.1 Hz, C3–*H*), 3.85 (1H, d, *J* 2.1 Hz, C4–*H*), 3.78 (3H, s, OCH_3); 3.71 (3H, s, OCH_3), 2.22 (3H, s, CH_3S); δ_C (75 MHz, $CDCl_3$) 162.4, 160.0, 159.9, 156.1, 130.8, 128.6, 127.1, 118.4, 114.6, 114.3, 62.1, 60.1, 55.1, 55.0, 12.8.

*4.2.5. (±)-trans-1-(4′-Methylphenyl)-3-methylthio-4-phenylazetidin-2-one (**3e**).* Colourless crystalline solid (0.244 g, 72%); mp 108–110 °C; [Found: C, 72.00; H, 5.98; N, 4.89. $C_{17}H_{17}NOS$ requires: C, 72.05; H, 6.05; N, 4.94%]; R_f (10% EtOAc/hexane) 0.52; IR (cm^{-1}, KBr): 1761 (C=O); δ_H (300 MHz, $CDCl_3$) 7.29–6.93 (9H, m, Ph), 4.71 (1H, d, *J* 2.4 Hz, C3–*H*), 3.81 (1H, d, *J* 2.4 Hz, C4–*H*), 2.20 (3H, s, CH_3S), 2.17 (3H, s, CH_3); δ_C (75 MHz, $CDCl_3$) 162.8, 136.9, 134.9, 133.7, 129.6, 129.3, 128.8, 125.8, 117.1, 62.3, 60.1, 21.0, 12.9.

*4.2.6. (±)-trans-1-(4′-Methoxyphenyl)-3-methylthio-4-(4′-chlorophenyl)azetidin-2-one (**3f**).* White crystalline solid (0.272 g, 70%); mp 80–82 °C; [Found: C, 61.08; H, 4.72; N, 4.12. $C_{17}H_{16}ClNO_2S$ requires: C, 61.16; H, 4.83; N, 4.20%]; R_f (10% EtOAc/hexane) 0.49; IR (cm^{-1}, KBr): 1753 (C=O); δ_H (300 MHz, $CDCl_3$) 7.30–6.69 (8H, m, Ph), 4.72 (1H, d, *J* 2.1 Hz, C3–*H*), 3.83 (1H, d, *J* 2.1 Hz, C4–*H*), 3.66 (3H, s, OCH_3), 2.16 (3H, s, CH_3S); δ_C (75 MHz, $CDCl_3$) 162.5, 156.4, 135.1, 134.7, 130.4, 129.4, 127.2, 118.4, 114.4, 61.9, 60.3, 55.4, 12.9.

*4.2.7. (±)-trans-1-Benzyl-3-methylthio-4-phenylazetidin-2-one (**3g**).* Yellow oil (0.241 g, 76%); [Found: C, 71.98; H, 6.01; N, 4.82. $C_{17}H_{17}NOS$ requires: C, 72.05; H, 6.05; N, 4.94%]; R_f (10% EtOAc/hexane) 0.51; IR (cm^{-1}, CCl_4): 1762 (C=O); δ_H (300 MHz, $CDCl_3$) 7.30–6.99 (10H, m, Ph), 4.77 (1H, d, *J* 15.0 Hz, CH_aH_bPh), 4.14 (1H, d, *J* 2.1 Hz, C3–*H*), 3.76 (1H, d, *J* 2.1 Hz, C4–*H*), 3.65 (1H, d, *J* 14.7 Hz, CH_aH_bPh), 1.97 (3H, s, CH_3S); δ_C (75 MHz, $CDCl_3$) 165.2, 157.1, 138.1, 128.6, 128.4, 128.2, 128.0, 127.63, 127.1, 118.5, 114.3, 61.3, 60.8, 45.6, 12.6.

4.3. General procedure for the synthesis of *cis*-3-chloro-3-methylthio-β-lactams (4a–e)

Compounds **4a**–**e** were prepared by the procedure as described for the synthesis of *trans*-3-chloro-3-benzylthio-β-lactams[9] in the cited reference, starting from *trans*-3-methylthio-β-lactams (**3a**–**e**).

*4.3.1. (±)-cis-1-(4′-Methoxyphenyl)-3-chloro-3-methylthio-4-phenyl azetidin-2-one (**4a**).* Colourless crystalline solid (0.125 g, 56%); mp 103–105 °C; [Found: C, 61.02; H, 4.78; N, 4.12. $C_{17}H_{16}ClNO_2S$ requires: C, 61.16; H, 4.83; N, 4.20%]; R_f (10% EtOAc/hexane) 0.55; IR (cm^{-1}, KBr): 1769 (C=O); δ_H (300 MHz, $CDCl_3$) 7.31–6.69 (9H, m, Ph), 5.29 (1H, s, C4–*H*), 3.68 (3H, s, OCH_3), 2.27 (3H, s, CH_3S); δ_C (75 MHz, $CDCl_3$) 159.6, 156.7, 131.8, 130.0, 129.5, 128.5, 128.0, 119.0, 114.5, 81.0, 71.2, 55.2, 12.7.

*4.3.2. (±)-cis-1-Phenyl-3-chloro-3-methylthio-4-phenylazetidin-2-one (**4b**).* Colourless crystalline solid (0.120 g, 53%); mp 133–135 °C; [Found: C, 63.15; H, 4.56; N, 4.64. $C_{16}H_{14}ClNOS$ requires: C, 63.25; H, 4.64; N, 4.61%]; R_f (10% EtOAc/hexane) 0.57; IR (cm^{-1}, KBr): 1753 (C=O); δ_H (300 MHz, $CDCl_3$) 7.35–7.01 (10H, m, Ph), 5.38 (1H, s, C4–*H*), 2.25 (3H, s, CH_3S); δ_C (75 MHz, $CDCl_3$) 160.6, 136.4, 131.4, 129.6, 129.2, 129.1, 128.7, 128.5, 127.8, 124.8, 117.7, 80.7, 71.1, 12.6.

*4.3.3. (±)-cis-1-Benzyl-3-chloro-3-methylthio-4-(4′-methoxyphenyl) azetidin-2-one (**4c**).* Colourless crystalline solid (0.120 g, 55%); mp 84–86 °C; [Found: C, 62.01; H, 5.16; N, 4.06. $C_{18}H_{18}ClNO_2S$ requires: C, 62.15; H, 5.22; N, 4.03%]; R_f (10% EtOAc/hexane) 0.54; IR (cm^{-1}, KBr): 1777 (C=O); δ_H (300 MHz, $CDCl_3$) 7.29–6.82 (9H, m, Ph), 4.85 (1H, d, *J* 15.0 Hz, CH_aH_bPh), 4.68 (1H, s, C4–*H*), 3.86 (1H, d, *J* 15.0 Hz, CH_aH_bPh), 3.77 (3H, s, OCH_3), 2.15 (3H, s, CH_3S); δ_C (75 MHz, $CDCl_3$); 163.8, 160.5, 134.2, 128.9, 128.8, 128.2, 128.0, 123.4, 113.8, 82.0, 70.3, 55.2, 44.2, 12.4.

*4.3.4. (±)-cis-1-(4′-Methoxyphenyl)-3-chloro-3-methylthio-4-(4′-methoxyphenyl)-azetidin-2-one (**4d**).* Colourless crystalline solid (0.115 g, 52%); mp 78–80 °C; [Found: C, 59.32; H, 4.94; N, 3.79. $C_{18}H_{18}ClNO_3S$ requires: C, 59.42; H, 4.99; N, 3.85%]; R_f (10% EtOAc/hexane) 0.51; IR (cm^{-1}, KBr): 1761 (C=O); δ_H (300 MHz, $CDCl_3$) 7.27–6.76 (8H, m, Ph), 5.34 (1H, s, C4–*H*), 3.79 (3H, s, OCH_3), 3.73 (3H, s, OCH_3), 2.29 (3H, s, CH_3S); δ_C (75 MHz, $CDCl_3$) 180.2, 160.5, 160.2, 156.6, 129.7, 129.3, 127.1, 123.3, 119.1, 114.4, 114.1, 113.8, 81.2, 71.0, 55.4, 55.2, 12.6.

*4.3.5. (±)-cis-1-(4′-Methylphenyl)-3-chloro-3-methylthio-4-phenylazetidin-2-one (**4e**).* Colourless crystalline solid (0.110 g, 50%); mp 102–103 °C; [Found: C, 64.15; H, 5.01; N, 4.43. $C_{17}H_{16}ClNOS$ requires: C, 64.2; H, 5.07; N, 4.41%]; R_f (10% EtOAc/hexane) 0.53; IR (cm^{-1}, KBr): 1764 (C=O); δ_H (300 MHz, $CDCl_3$) 7.38–7.04 (9H, m, Ph), 5.40 (1H, s, C4–*H*), 2.31 (3H, s, CH_3S), 2.27 (3H, s, CH_3); δ_C (75 MHz, $CDCl_3$) 159.9, 134.2, 131.8, 129.7, 129.5, 128.5, 127.9, 117.7, 80.9, 71.1, 21.1, 12.7.

4.4. General procedure for the synthesis of C-3 substituted β-lactams (5–8)

Compounds **5h**–**x**, **6k**–**r**, **7h**–**7t** and **8a**–**c** were prepared by the procedure as described for the synthesis of C-3 substituted thioazetidin-2-ones[9] in the cited reference using tin tetrachloride (1.2 mmol) or titanium tetrachloride (1.2 mmol) via a syringe, under inert temperature, at 0 to −5 °C. The spectroscopic data of compounds **7h**,**j**–**l**,**s**[9] were also reported in the cited reference.

*4.4.1. (±)-cis-1-(4′-Methoxyphenyl)-3-(4′-methoxyphenyl)-3-methylthio-4-phenylazetidin-2-one (**5h**).* White semisolid (0.037 g, 61%); [Found: C, 70.90; H, 5.60; N, 3.32. $C_{24}H_{23}NO_3S$ requires: C, 71.08; H, 5.72; N, 3.45%]; R_f (10% EtOAc/hexane) 0.37; IR (cm^{-1}, CCl_4): 1750 (C=O); δ_H (300 MHz, $CDCl_3$) 7.54–6.48 (13H, m, Ph), 5.09 (1H, s, C4–*H*), 3.75 (3H, s, OCH_3), 3.65 (3H, s, OCH_3) 1.81 (3H, s, CH_3S); δ_C (75 MHz, $CDCl_3$) 165.3, 159.3, 156.2, 133.4, 130.8, 130.1, 128.7, 128.3, 128.0, 118.7, 114.1, 67.6, 66.6, 55.3, 55.1, 12.6.

*4.4.2. (±)-cis-1-Benzyl-3-(4′-methoxyphenyl)-3-methylthio-4-(4′-methoxyphenyl)azetidin-2-one (**5i**).* White semisolid (0.038 g, 63%); [Found: C, 71.42; H, 5.91; N, 3.22. $C_{25}H_{25}NO_3S$ requires: C, 71.57; H, 6.01; N, 3.34%]; R_f (10% EtOAc/hexane) 0.35; IR (cm^{-1}, CCl_4): 1754 (C=O); δ_H (300 MHz, $CDCl_3$) 7.44–6.79 (13H, m, Ph), 4.85 (1H, d, 15.0 Hz, CH_aH_bPh), 4.52 (1H, s, C4–*H*), 3.84 (1H, d, *J* 15.0 Hz, CH_aH_bPh), 3.76 (3H, s, OCH_3), 3.74 (3H, s, OCH_3), 1.76 (3H, s, CH_3S); δ_C (75 MHz, $CDCl_3$) 169.0, 160.0, 159.0, 147.5, 135.2, 130.2, 129.5, 129.3, 129.2, 128.6, 128.5, 127.7, 125.1, 114.4, 113.9, 67.3, 55.9, 55.1, 44.3, 43.7, 12.3.

*4.4.3. (±)-cis-1-(4′-Methoxyphenyl)-3-(2′,4′-dimethoxyphenyl)-3-methylthio-4-phenylazetidin-2-one (**5j**).* White semisolid (0.026 g, 22%); [Found: C, 68.81; H, 5.65; N, 3.15. $C_{25}H_{25}NO_4S$ requires: C, 68.94; H, 5.79; N, 3.22%]; R_f (10% EtOAc/hexane) 0.32; IR (cm^{-1}, CCl_4): 1739 (C=O); δ_H (300 MHz, $CDCl_3$) 7.68–6.34 (12H, m, Ph),

5.12 (1H, s, C4–*H*), 3.80 (3H, s, OCH_3), 3.65 (3H, s, OCH_3), 3.60 (3H, s, OCH_3), 1.94 (3H, s, CH_3S); δ_C (75 MHz, $CDCl_3$) 165.3, 161.0, 158.1, 155.9, 134.0, 131.2, 129.9, 129.1, 128.6, 127.8, 118.6, 118.2, 114.2, 103.4, 100.0, 66.6, 64.1, 55.4, 55.2, 55.0, 12.7.

*4.4.4. (±)-cis-1-(4′-Methoxyphenyl)-3-(2′,5′-dimethoxyphenyl)-3-methylthio-4-phenylazetidin-2-one (**5k**).* White semisolid (0.037 g, 57%); [Found: C, 68.85; H, 5.71; N, 3.18. $C_{25}H_{25}NO_4S$ requires: C, 68.94; H, 5.79; N, 3.22%]; R_f (10% EtOAc/hexane) 0.34; IR (cm^{-1}, CCl_4): 1750 (C=O); δ_H (300 MHz, $CDCl_3$) 7.41–6.61 (12H, m, Ph), 5.21 (1H, s, C4–*H*), 3.76 (3H, s, OCH_3), 3.71 (3H, s, OCH_3), 3.63 (3H, s, OCH_3), 1.93 (3H, s, CH_3S); δ_C (75 MHz, $CDCl_3$) 165.0, 155.9, 153.3, 151.1, 133.8, 131.0, 129.2, 128.6, 127.7, 126.9, 118.6, 114.7, 114.2, 113.0, 66.5, 64.1, 55.8, 55.5, 55.1, 12.8.

*4.4.5. (±)-cis-1-Phenyl-3-(2′,5′-dimethoxyphenyl)-3-methylthio-4-phenylazetidin-2-one (**5l**).* Colourless crystalline solid (0.040 g, 61%); mp 135–136 °C; [Found: C, 71.01; H, 5.64; N, 3.39. $C_{24}H_{23}NO_3S$ requires: C, 71.08; H, 5.72; N, 3.45%]; R_f (10% EtOAc/hexane) 0.36; IR (cm^{-1}, KBr): 1752 (C=O); δ_H (300 MHz, $CDCl_3$) 7.49–6.78 (13H, m, Ph), 5.32 (1H, s, C4–*H*), 3.84 (3H, s, OCH_3), 3.79 (3H, s, OCH_3), 2.02 (3H, s, CH_3S); δ_C (75 MHz, $CDCl_3$) 165.7, 153.4, 151.2, 137.6, 133.8, 129.1, 128.9, 128.7, 127.8, 126.7, 123.8, 117.5, 114.8, 114.5, 113.1, 66.5, 64.3, 55.9, 55.6, 12.9.

*4.4.6. (±)-cis-1-Benzyl-3-(2′,5′-dimethoxyphenyl)-3-methylthio-4-(4′-methoxyphenyl)azetidin-2-one (**5m**).* Colourless crystalline solid (0.038 g, 64%); mp 117–119 °C; [Found: C, 69.35; H, 6.00; N, 3.05. $C_{26}H_{27}NO_4S$ requires: C, 69.46; H, 6.05; N, 3.12%]; R_f (10% EtOAc/hexane) 0.35; IR (cm^{-1}, KBr): 1745 (C=O); δ_H (300 MHz, $CDCl_3$) 7.63–6.85 (12H, m, Ph), 4.91 (1H, d, *J* 15.0 Hz, CH_aH$_b$Ph), 4.77 (1H, s, C4–*H*), 4.09 (1H, d, *J* 14.4 Hz, CH$_a$H$_b$Ph), 3.88 (3H, s, OCH_3), 3.83 (3H, s, OCH_3), 3.75 (3H, s, OCH_3), 2.00 (3H, s, CH_3S); δ_C (75 MHz, $CDCl_3$) 168.6, 159.8, 152.9, 150.9, 135.3, 130.7, 128.6, 128.3, 127.5, 126.9, 125.4, 114.7, 113.7, 113.0, 112.3, 66.0, 64.9, 55.8, 55.3, 55.2, 43.6, 12.7.

*4.4.7. (±)-cis-1-Phenyl-3-(2′-methoxynaphthyl)-3-methylthio-4-phenylazetidin-2-one (**5n**).* Yellow semisolid (0.026 g, 37%); [Found: C, 76.14; H, 5.50; N, 3.34. $C_{27}H_{23}NO_2S$ requires: C, 76.21; H, 5.45; N, 3.29%]; R_f (10% EtOAc/hexane) 0.39; IR (cm^{-1}, $CHCl_3$): 1744 (C=O); δ_H (300 MHz, $CDCl_3$) 8.23–6.61 (16H, m, Ph), 5.14 (1H, s, C4–*H*), 3.49 (3H, s, OCH_3), 2.06 (3H, s, CH_3S) (for one isomer) and 9.47–6.61 (16H, m, Ph), 5.21 (1H, s, C4–*H*), 3.96 (3H, s, OCH_3), 2.26 (3H, s, CH_3S) (for other isomer). The ^{1}H NMR spectrum showed it to be a mixture of two rotamers as evident from the appearance of two signals for C4–*H* and downfield appearance of an aromatic proton; δ_C (75 MHz, $CDCl_3$) 169.4, 157.3, 152.6, 151.8, 133.8, 129.4, 128.7, 127.6, 126.9, 126.7, 126.1, 125.8, 125.3, 125.2, 121.8, 115.5, 114.7, 67.2, 66.7, 55.6, 11.9.

*4.4.8. (±)-cis-1-(4′-Methoxyphenyl)-3-(4′-hydroxyphenyl)-3-methylthio-4-phenylazetidin-2-one (**5o**).* White solid (0.030 g, 51%); mp 167–169 °C; [Found: C, 70.41; H, 5.48; N, 3.44. $C_{23}H_{21}NO_3S$ requires: C, 70.56; H, 5.41; N, 3.58%]; *Rf* (10% EtOAc/hexane) 0.38; IR (cm^{-1}, KBr): 1740 (C=O), 3392 (OH); δ_H (300 MHz, $CDCl_3$) 7.54–6.49 (13H, m, Ph), 5.20 (1H, br s, O*H*), 5.17 (1H, s, C4–*H*), 3.72 (3H, s, OCH_3), 1.87 (3H, s, CH_3S); δ_C (75 MHz, $CDCl_3$) 165.5, 156.2, 133.2, 130.7, 128.9, 128.3, 128.0, 118.8, 115.7, 114.4, 84.6, 68.0, 66.6, 55.3, 12.5.

*4.4.9. (±)-cis-1-Phenyl-3-(4′-hydroxyphenyl)-3-methylthio-4-phenylazetidin-2-one (**5p**).* White semisolid (0.029 g, 42%); [Found: C, 73.19; H, 5.21; N, 3.82. $C_{22}H_{19}NO_2S$ requires: C, 73.10; H, 5.30; N, 3.88%]; R_f (10% EtOAc/hexane) 0.39; IR (cm^{-1}, CCl_4): 1754 (C=O), 3400 (OH); δ_H (300 MHz, $CDCl_3$) 7.44–6.43 (15H, m, Ph, O*H*), 5.13 (1H, s, C4–*H*), 1.80 (3H, s, CH_3S); δ_C (75 MHz, $CDCl_3$) 166.3, 156.1, 137.2, 133.1, 129.3, 129.1, 128.8, 128.4, 128.0, 124.2, 117.6, 115.9, 68.0, 66.7, 12.6.

*4.4.10. (±)-cis-1-(4′-Methoxyphenyl)-3-(2′-furanyl)-3-methylthio-4-phenylazetidin-2-one (**5q**).* White solid (0.034 g, 42%); mp 106–111 °C; [Found: C, 68.94; H, 5.19; N, 3.79. $C_{21}H_{19}NO_3S$ requires: C, 69.02; H, 5.24; N, 3.83%]; R_f (10% EtOAc/hexane) 0.40; IR (cm^{-1}, KBr): 1752 (C=O); δ_H (300 MHz, $CDCl_3$) 7.46 (1H, dd, *J* 0.9, 2.1 Hz C$_4H_a$H$_b$H$_c$O), 7.32–6.71 (9H, m, Ph), 6.39 (1H, dd *J* 0.6, 2.1 Hz, C$_4$H$_a$H$_b$H$_c$O), 6.34 (1H, dd, *J* 0.9, 2.1 Hz, C$_4$H$_a$H$_b$H$_c$O), 5.31 (1H, s, C4–*H*), 3.68 (3H, s, OCH_3), 1.91 (3H, s, CH_3S); δ_C 163.1, 156.3, 148.7, 143.6, 132.7, 130.7, 128.9, 128.2, 127.9, 127.8, 126.9, 118.7, 114.3, 110.4, 109.7, 64.8, 62.6, 55.4, 12.7.

*4.4.11. (±)-cis-1-Benzyl-3-(2′-furanyl)-3-methylthio-4-(4′-methoxyphenyl)azetidin-2-one (**5r**).* White semisolid (0.039 g, 55%); [Found: C, 69.59; H, 5.51; N, 3.62. $C_{22}H_{21}NO_3S$ requires: C, 69.63; H, 5.58; N, 3.69%]; R_f (10% EtOAc/hexane) 0.38; IR (cm^{-1}, KBr): 1762 (C=O); δ_H (300 MHz, $CDCl_3$) 7.35 (1H, dd, *J* 0.9, 1.8 Hz, C$_4H_a$H$_b$H$_c$O), 7.24–6.57 (9H, m, Ph), 6.44 (1H, dd, *J* 0.9, 3.3 Hz, C$_4$H$_a$H$_b$H$_c$O), 6.27 (1H, dd, *J* 2.1, 3.3 Hz, C$_4$H$_a$H$_b$H$_c$O), 4.85 (1H, d, *J* 15.0 Hz, CH_aH$_b$Ph), 4.56 (1H, s, C4–*H*), 3.86 (1H, d, *J* 14.7 Hz, CH$_a$H$_b$Ph), 3.75 (3H, s, OCH_3), 1.85 (3H, s, CH_3S); δ_C (75 MHz, $CDCl_3$) 166.4, 160.1, 149.6, 146.6, 143.2, 135.2, 129.6, 128.9, 128.4, 127.9, 124.8, 113.7, 110.4, 109.3, 65.7, 64.4, 55.0, 44.5, 44.2, 12.6.

*4.4.12. (±)-cis-1-(4′-Methoxyphenyl)-3-allyl-3-methylthio-4-phenyl azetidin-2-one (**5u**).* White semisolid (0.038 g, 75%); [Found: C, 70.65; H, 6.15; N, 4.08. $C_{20}H_{21}NO_2S$ requires: C, 70.77; H, 6.24; N, 4.13%]; R_f (10% EtOAc/hexane) 0.57; IR (cm^{-1}, $CHCl_3$): 1745 (C=O); 1632 (C=C); δ_H (300 MHz, $CDCl_3$) 7.31–6.66 (9H, m, Ph), 5.97–5.86 (1H, m, C*H*=CH$_2$), 5.30 (1H, d, *J* 1.5 Hz, CH=CH$_a$H$_b$), 5.29–5.20 (1H, m, CH=CH$_a$H$_b$), 4.91 (1H, s, C4–*H*), 3.66 (3H, s, OCH_3), 2.79–2.74 (2H, m, CH_2CH=), 2.00 (3H, s, CH_3S); δ_C (75 MHz, $CDCl_3$) 165.6, 156.2, 133.8, 132.7, 131.0, 128.8, 128.4, 128.1, 127.7, 127.2, 126.7, 119.5, 118.5, 114.4, 64.3, 64.1, 55.2, 38.0, 11.9.

*4.4.13. (±)-cis-1-Phenyl-3-allyl-3-methylthio-4-phenylazetidin-2-one (**5v**).* White semisolid (0.037 g, 76%); [Found: C, 73.64; H, 6.09; N, 4.45. $C_{19}H_{19}NOS$ requires: C, 73.75; H, 6.19; N, 4.53%]; R_f (10% EtOAc/hexane) 0.58; IR (cm^{-1}, CCl_4): 1758 (C=O), 1656 (C=C); δ_H (300 MHz, $CDCl_3$) 7.33–6.93 (10H, m, Ph), 5.97–5.88 (1H, m, *CH*=CH$_2$), 5.30 (1H, d, *J* 1.8 Hz, CH=CH$_a$H$_b$), 5.28–5.20 (1H, m, CH=CH$_a$H$_b$), 4.94 (1H, s, C4–*H*), 2.80–2.75 (2H, m, CH_2CH=), 2.04 (3H, s, CH_3S); δ_C (75 MHz, $CDCl_3$) (DEPT-135) 166.4, 137.3, 133.4, 132.3 (+), 129.0 (+), 128.7 (+), 128.4 (+), 128.1 (+), 127.2 (+), 124.0 (+), 119.6 (−), 117.3 (+), 64.1, 63.9 (+), 37.6 (−), 11.8 (+).

*4.4.14. (±)-cis-1-(4′-Methoxyphenyl)-3-allyl-3-methylthio-(4′-methoxyphenyl)azetidin-2-one (**5w**).* Yellow oil (0.036 g, 72%); [Found: C, 68.12; H, 6.19; N, 3.71. $C_{21}H_{23}NO_3S$ requires: C, 68.27; H, 6.27; N, 3.79%]; R_f (10% EtOAc/hexane) 0.52; IR (cm^{-1}, $CHCl_3$): 1745 (C=O), 1611 (C=C); δ_H (300 MHz, $CDCl_3$) 7.18–6.69 (8H, m, Ph), 5.96–5.85 (1H, m, *CH*=CH$_2$), 5.28 (1H, d, *J* 1.8 Hz, CH=CH$_a$H$_b$), 5.22–5.18 (1H, m, CH=CH$_a$H$_b$), 4.91 (1H, s, C4–*H*), 3.70 (3H, s, OCH_3), 3.66 (3H, s, OCH_3), 2.78–2.71 (2H, m, CH_2CH=), 2.03 (3H, s, CH_3S); δ_C (75 MHz, $CDCl_3$) (DEPT-135) 166.1, 159.6, 156.0, 132.4 (+), 130.8 (+), 128.9 (+), 125.3, 119.4 (−), 118.6 (+), 114.3 (+), 113.5 (+), 64.2, 63.6 (+), 55.4 (+), 55.1 (+), 37.4 (−), 11.7 (+).

*4.4.15. (±)-cis-1-(4′-Methylphenyl)-3-allyl-3-methylthio-4-phenylazetidin-2-one (**5x**).* White semisolid (0.037 g, 74%); [Found C, 74.22; H, 6.47; N, 4.26. $C_{20}H_{21}NOS$ requires: C, 74.27; H, 6.54; N, 4.33%]; R_f (10% EtOAc/hexane) 0.54; IR (cm^{-1}, CCl_4): 1755 (C=O), 1612 (C=C); δ_H (300 MHz, $CDCl_3$) 7.31–6.97 (9H, m, Ph), 5.98–5.86 (1H, m, *CH*=CH$_2$), 5.30 (1H, d, *J* 0.9 Hz, CH=CH$_a$H$_b$), 5.28–5.19 (1H,

m, CH=CH$_a$H$_b$), 4.98 (1H, s, C4–*H*), 2.80–2.74 (2H, m, *CH*$_2$CH=), 2.15 (3H, s, C*H*$_3$S), 2.01 (3H, s, C*H*$_3$); δ_C (75 MHz, $CDCl_3$) (DEPT-135) 166.2, 134.8, 133.6, 132.3 (+), 129.5 (+), 128.4 (+), 127.9 (+), 127.5 (+), 119.6 (−), 117.2 (+), 64.1, 63.8 (+), 37.6 (−), 20.8 (+), 11.8 (+), 11.7 (+).

*4.4.16. (±)-trans-1-(4′-Methoxyphenyl)-3-(2′,5′-dimethoxyphenyl)-3-methylthio-4-phenylazetidin-2-one (**6k**).* Colourless oil (0.004 g, 7%); [Found: C, 68.82; H, 5.69; N, 3.14. $C_{25}H_{25}NO_4S$ requires: C, 68.94; H, 5.79; N, 3.22%]; R_f (10% EtOAc/hexane) 0.34; IR (cm^{-1}, CCl_4): 1747 (C=O); δ_H (300 MHz, $CDCl_3$) 7.43–6.62 (12H, m, Ph), 4.97 (1H, s, C4–*H*), 3.70 (3H, s, OC*H*$_3$), 3.67 (3H, s, OC*H*$_3$), 3.62 (3H, s, OC*H*$_3$), 2.16 (3H, s, C*H*$_3$S); δ_C (75 MHz, $CDCl_3$) 164.9, 155.6, 153.4, 151.0, 133.5, 131.4, 129.0, 128.3, 127.5, 126.7, 118.3, 114.8, 114.4, 112.9, 66.2, 64.2, 55.9, 55.5, 55.2, 12.9.

*4.4.17. (±)-trans-1-Phenyl-3-(2′,5′-dimethoxyphenyl)-3-methylthio-4-phenylazetidin-2-one (**6l**).* Yellow oil (0.004 g, 6%); [Found: C, 70.94; H, 5.61; N, 3.34. $C_{24}H_{23}NO_3S$ requires: C, 71.08; H, 5.72; N, 3.45%]; R_f (10% EtOAc/hexane) 0.36; IR (cm^{-1}, CCl_4): 1750 (C=O); δ_H (300 MHz, $CDCl_3$) 7.47–6.82 (13H, m, Ph), 5.35 (1H, s, C4–*H*), 3.87 (3H, s, OC*H*$_3$), 3.82 (3H, s, OC*H*$_3$), 2.05 (3H, s, C*H*$_3$S); δ_C (75 MHz, $CDCl_3$) 165.1, 153.9, 151.0, 137.4, 133.6, 129.0, 128.4, 128.1, 127.3, 126.2, 123.6, 117.3, 115.1, 114.7, 113.4, 66.3, 64.1, 55.7, 55.2, 12.6.

*4.4.18. (±)-trans-1-Phenyl-3-(4′-hydroxyphenyl)-3-methylthio-4-phenylazetidin-2-one (**6p**).* Yellow oil (0.003 g, 6%); [Found: C, 73.14; H, 5.15; N, 3.75. $C_{22}H_{19}NO_2S$ requires: C, 73.10; H, 5.30; N, 3.88%]; R_f (10% EtOAc/hexane) 0.39; IR (cm^{-1}, CCl_4): 1747 (C=O), 3382 (OH); δ_H (300 MHz, $CDCl_3$) 7.49–6.48 (15H, m, Ph, OH), 5.00 (1H, s, C4–*H*), 2.04 (3H, s, C*H*$_3$S); δ_C (75 MHz, $CDCl_3$) 166.4, 155.6, 137.4, 133.2, 130.1, 129.2, 128.9, 128.4, 127.4, 124.6, 117.5, 115.1, 68.1, 64.5, 13.2.

*4.4.19. (±)-trans-1-(4′-Methoxyphenyl)-3-(2′-furanyl)-3-methylthio-4-phenylazetidin-2-one (**6q**).* Yellow oil (0.004 g, 6%); [Found: C, 68.90; H, 5.15; N, 3.75. $C_{21}H_{19}NO_3S$ requires: C, 69.02; H, 5.24; N, 3.83%]; R_f (10% EtOAc/hexane) 0.40; IR (cm^{-1}, CCl_4): 1745 (C=O); δ_H (300 MHz, $CDCl_3$) 7.35–6.76 (9H, m, Ph), 6.99 (1H, dd, *J* 0.9, 1.8 Hz, C$_4$*H*$_a$H$_b$H$_c$O), 6.39 (1H, dd *J* 0.6, 2.1 Hz, C$_4$H$_a$*H*$_b$H$_c$O), 6.04 (1H, dd, *J* 1.8, 3.3 Hz, C$_4$H$_a$H$_b$*H*$_c$O), 4.99 (1H, s, C4–*H*), 3.67 (3H, s, OC*H*$_3$), 2.15 (3H, s, C*H*$_3$S); δ_C 163.9, 156.2, 148.5, 143.7, 132.4, 130.2, 128.8, 128.4, 127.9, 127.6, 127.2, 118.1, 114.0, 110.2, 109.6, 64.4, 62.4, 55.2, 13.0.

*4.4.20. (±)-trans-1-Benzyl-3-(2′-furanyl)-3-methylthio-4-(4′-methoxyphenyl)azetidin-2-one (**6r**).* Yellow oil (0.004 g, 9%); [Found: C, 69.52; H, 5.47; N, 3.58. $C_{22}H_{21}NO_3S$ requires: C, 69.63; H, 5.58; N, 3.69%]; R_f (10% EtOAc/hexane) 0.38; IR (cm^{-1}, CCl_4): 1760 (C=O); δ_H (300 MHz, $CDCl_3$) 7.28–6.62 (9H, m, Ph), 7.00 (1H, dd, *J* 0.6, 1.8 Hz, C$_4$*H*$_a$H$_b$H$_c$O), 6.36 (1H, dd, *J* 0.6, 3.3 Hz, C$_4$H$_a$*H*$_b$H$_c$O), 6.05 (1H, dd, *J* 1.8, 3.3 Hz, C$_4$H$_a$H$_b$*H*$_c$O), 4.73 (1H, d, *J* 15.0 Hz, C*H*$_a$H$_b$Ph), 4.56 (1H, s, C4–*H*), 3.79 (1H, d, *J* 14.7 Hz, CH$_a$*H*$_b$Ph), 3.67 (3H, s, OC*H*$_3$), 2.04 (3H, s, C*H*$_3$S); δ_C (75 MHz, $CDCl_3$) 166.0, 159.8, 149.4, 146.7, 143.3, 134.9, 129.8, 128.8, 128.5, 127.8, 125.6, 113.7, 111.5, 109.8, 64.2, 63.5, 54.9, 44.2, 12.9.

*4.4.21. 1-Benzyl-3,3-bis(4′-methoxyphenyl)-4-(4′-methoxyphenyl)azetidin-2-one (**7i**).* White semisolid (0.004 g, 9%); [Found: C, 77.58; H, 6.02; N, 2.95. $C_{31}H_{29}NO_4$ requires: C, 77.64; H, 6.10; N, 2.92%]; R_f (10% EtOAc/hexane) 0.30; IR (cm^{-1}, $CHCl_3$): 1740 (C=O); δ_H (300 MHz, $CDCl_3$) 7.18–6.46 (17H, m, Ph), 4.85 (1H, s, C4–*H*), 4.82 (1H, d, *J* 14.7 Hz, C*H*$_a$H$_b$Ph), 3.70 (1H, d, *J* 15.0 Hz, CH$_a$*H*$_b$Ph), 3.68 (3H, s, OC*H*$_3$), 3.67 (3H, s, OC*H*$_3$), 3.61 (3H, s, OC*H*$_3$); δ_C (75 MHz, $CDCl_3$) 168.7, 160.1, 159.5, 158.2, 133.9, 130.1, 129.7, 129.3, 129.1, 128.9, 128.4, 127.2, 126.3, 114.8, 114.6, 114.0, 113.7, 67.9, 55.9, 55.7, 55.5, 44.6.

*4.4.22. 1-Benzyl-3,3-bis(2′,5′-dimethoxyphenyl)-4-(4′-methoxyphenyl)-azetidin-2-one (**7m**).* White semisolid (0.002 g, 4%); [Found: C, 73.40; H, 6.08; N, 2.64. $C_{33}H_{33}NO_6$ requires: C, 73.45; H, 6.16; N, 2.60%]; R_f (10% EtOAc/hexane) 0.32; IR (cm^{-1}, $CHCl_3$): 1740 (C=O); δ_H (300 MHz, $CDCl_3$) 7.32–6.20 (15H, m, Ph), 5.37 (1H, s, C4–*H*), 4.57 (1H, d, *J* 14.4 Hz, PhC*H*$_a$H$_b$), 3.82 (1H, d, *J* 14.4 Hz, PhCH$_a$*H*$_b$), 3.73 (3H, s, OC*H*$_3$), 3.64 (3H, s, OC*H*$_3$), 3.48 (3H, s, OC*H*$_3$), 3.27 (3H, s, OC*H*$_3$), 2.86 (3H, s, OC*H*$_3$); δ_C (75 MHz, $CDCl_3$) 168.3, 159.2, 153.4, 153.4, 150.3, 135.1, 134.3, 130.7, 129.6, 129.4, 128.3, 128.0, 127.5, 126.9, 125.4, 114.9, 114.7, 113.6, 113.2, 112.9, 112.7, 67.6, 55.8, 55.6, 55.5, 55.4, 55.2, 45.9.

*4.4.23. 1-(4′-Methoxyphenyl)-3,3-bis(4′-hydroxyphenyl)-4-phenylazetidin-2-one (**7o**).* Yellow oil (0.007 g, 12%); [Found: C, 76.92; H, 5.27; N, 3.24. $C_{28}H_{23}NO_4$ requires: C, 76.87; H, 5.30; N, 3.20%]; R_f (10% EtOAc/hexane) 0.31; IR (cm^{-1}, $CHCl_3$): 1723 (C=O), 3375 (OH); δ_H (300 MHz, $CDCl_3$) 7.26–6.31 (19H, m, Ph, O*H*), 5.54 (1H, s, C4–*H*), 3.64 (3H, s, OC*H*$_3$); δ_C (75 MHz, $CDCl_3$) 169.7, 154.0, 132.8, 130.7, 128.8, 127.6, 126.4, 126.2, 125.9, 125.4, 116.7, 113.5, 112.6, 112.1, 69.0, 65.5, 55.3.

*4.4.24. 1-Phenyl-3,3-bis(4′-hydroxyphenyl)-4-phenylzetidin-2-one (**7p**).* Yellow oil (0.013 g, 20%); [Found: C, 79.64; H, 5.20; N, 3.50. $C_{27}H_{21}NO_3$ requires: C, 79.59; H, 5.19; N, 3.44%]; R_f (10% EtOAc/hexane) 0.33; IR (cm^{-1}, $CHCl_3$): 1729 (C=O), 3362 (OH); δ_H (300 MHz, $CDCl_3$) 7.36–6.37 (20H, m, Ph, O*H*), 5.64 (1H, s, C4–*H*); δ_C (75 MHz, $CDCl_3$) 167.9, 155.0, 154.2, 139.4, 137.4, 134.8, 129.7, 129.4, 129.0, 128.6, 128.3, 128.1, 127.5, 124.2, 117.5, 115.6, 114.7, 71.1, 67.4.

*4.4.25. 1-Benzyl-3,3-bis(3′-pyrrolyl)-4-(4′-methoxyphenyl)azetidin-2-one (**7t**).* Black semisolid (0.034 g, 60%); [Found: C, 75.50; H, 5.79; N, 10.54. $C_{25}H_{23}N_3O_2$ requires: C, 75.54; H, 5.83; N, 10.57%]; R_f (10% EtOAc/hexane) 0.31; IR (cm^{-1}, $CHCl_3$): 1746 (C=O), 3367 (NH); δ_H (300 MHz, $CDCl_3$) 8.03 (1H, br s, N*H*, D_2O exchangeable), 7.89 (1H, br s, N*H*, D_2O exchangeable), 7.25–5.69 (15H, m, Ph, 2C$_4$*H*$_3$NH), 4.82 (1H, d, *J* 15.0 Hz, C*H*$_a$H$_b$Ph), 4.75 (1H, s, C4–*H*), 3.72 (1H, d, *J* 15.0 Hz, CH$_a$*H*$_b$Ph), 3.67 (3H, s, OC*H*$_3$); δ_C (75 MHz, $CDCl_3$) 168.3, 159.6, 135.1, 128.9, 128.8, 128.6, 128.4, 127.8, 126.0, 124.9, 118.1, 118.0, 113.6, 108.8, 108.6, 108.2, 105.0, 66.8, 63.4, 55.1, 44.4.

*4.4.26. 1-(4′-Methoxyphenyl)-3,3-bis(methylthio)-4-phenylazetidin-2-one (**8a**).* White solid (0.002 g, 4%); mp 77–78 °C; [Found: C, 62.51; H, 5.48, N, 4.01. $C_{18}H_{19}NO_2S_2$ requires: C, 62.58; H, 5.54; N, 4.05%]; R_f (10% EtOAc/hexane) 0.57; IR (cm^{-1}, CCl_4): 1759 (C=O); δ_H (300 MHz, $CDCl_3$) 7.28–6.65 (9H, m, Ph), 4.96 (1H, s, C4–*H*), 3.65 (3H, s, OC*H*$_3$), 2.28 (3H, s, C*H*$_3$S), 1.81 (3H, s, C*H*$_3$S); δ_C (75 MHz, $CDCl_3$) 162.1, 156.4, 133.1, 130.7, 129.0, 128.3, 128.1, 118.7, 114.4, 70.9, 68.5, 55.2, 13.1, 12.1.

*4.4.27. 1-Phenyl-3,3-bis(methylthio)-4-phenylazetidin-2-one (**8b**).* White semisolid (0.002 g, 6%); [Found: C, 64.65; H, 5.39; N, 4.46. $C_{17}H_{17}NOS_2$ requires: C, 64.73; H, 5.43; N, 4.44%]; R_f (10% EtOAc/hexane) 0.58; IR (cm^{-1}, $CHCl_3$): 1753 (C=O); δ_H (400 MHz, $CDCl_3$): 7.35–7.09 (10H, m, Ph), 5.15 (1H, s, C4–*H*), 2.36 (3H, s, C*H*$_3$S), 1.93 (3H, s, C*H*$_3$S); δ_C (100 MHz, $CDCl_3$) 163.9, 134.4, 130.5, 130.2, 129.3, 128.7, 128.4, 118.6, 114.2, 72.4, 68.1, 13.4, 12.5.

*4.4.28. 1-Benzyl-3,3-bis(methylthio)-4-(4′-methoxyphenyl)azetidin-2-one (**8c**).* White semisolid (0.002 g, 4%); [Found: C, 63.40; H, 5.75; N, 3.81. $C_{19}H_{21}NO_2S_2$ requires: C, 63.48; H, 5.89; N, 3.90%]; R_f (10% EtOAc/hexane) 0.56; IR (cm^{-1}, $CHCl_3$): 1767 (C=O); δ_H (400 MHz, $CDCl_3$) 7.52–6.92 (9H, m, Ph), 5.01 (1H, d, *J* 11.5 Hz, C*H*$_a$H$_b$Ph), 4.84 (1H, d, *J* 11.6 Hz, CH$_a$*H*$_b$Ph), 4.52 (1H, s, C4–*H*), 3.83 (3H, s, OC*H*$_3$), 2.35 (3H, s, C*H*$_3$S), 2.33 (3H, s, C*H*$_3$S); δ_C (100 MHz, $CDCl_3$) 164.7, 156.4, 135.2, 128.8, 128.6, 128.2, 128.1, 127.5, 127.4, 118.3, 114.2, 69.6, 55.1, 44.4, 13.6, 12.3.

4.5. General procedure for Raney-nickel desulfurization

Compounds **9**,**10**(**p**,**k**)[9] were prepared by the procedure as described for Raney-nickel desulfurization of monosubstituted 3-phenyl/benzylthio-β-lactams in the cited reference. The spectroscopic data of compounds **9k**[9] were also reported in the cited reference.

*4.5.1. (±)-cis-1-Phenyl-3-(4′-hydroxyphenyl)-4-phenylazetidin-2-one (**9p**).* White solid (0.020 g, 77%); mp 175–177 °C; [Found: C, 79.82; H, 5.40; N, 4.50. $C_{21}H_{17}NO_2$ requires: C, 79.98; H, 5.43; N, 4.44%]; R_f (10% EtOAc/hexane) 0.34; IR (cm^{-1}, KBr): 1740 (C═O), 3381 (OH); δ_H (400 MHz, $CDCl_3$) 7.26–6.51 (15H, m, Ph, O*H*), 5.43 (1H, d, *J* 6.0 Hz, C3–*H*), 4.93 (1H, d, *J* 6.0 Hz, C4–*H*); δ_C (100 MHz, $CDCl_3$) 166.5, 155.0, 137.7, 134.5, 130.3, 129.1, 128.3, 127.9, 127.1, 124.1, 117.3, 115.1, 60.5, 59.8.

*4.5.2. (±)-trans-1-(4′-Methoxyphenyl)-3-(2′,5′-dimethoxyphenyl)-4-phenylazetidin-2-one (**10k**).* White solid (0.002 g, 10%); mp 124–126 °C; [Found: C, 73.98; H, 5.83; N, 3.52. $C_{24}H_{23}NO_4$ requires: C, 74.02; H, 5.95; N, 3.60%]; R_f (10% EtOAc/hexane) 0.31; IR (cm^{-1}, KBr): 1745 (C═O); δ_H (300 MHz, $CDCl_3$) 7.32–6.25 (12H, m, Ph), 4.78 (1H, d, *J* 2.7 Hz, C3–*H*), 4.18 (1H, d, *J* 2.4 Hz, C4–*H*), 3.68 (3H, s, OCH_3), 3.60 (3H, s, OCH_3), 3.49 (3H, s, OCH_3); δ_C (100 MHz, $CDCl_3$) 165.3, 155.9, 153.0, 150.8, 134.8, 131.5, 128.2, 127.6, 127.1, 124.3, 122.0, 118.5, 115.9, 114.4, 113.5, 110.3, 109.9, 60.9, 59.5, 55.6, 55.2, 55.1.

*4.5.3. (±)-trans-1-Phenyl-3-(4′-hydroxyphenyl)-4-phenylazetidin-2-one (**10p**).* White solid (0.004 g, 15%); mp 179–181 °C; [Found: C, 79.86; H, 5.37; N, 4.48. $C_{21}H_{17}NO_2$ requires: C, 79.98; H, 5.43; N, 4.44%]; R_f (10% EtOAc/hexane) 0.34; IR (cm^{-1}, KBr): 1742 (C═O), 3400 (OH); δ_H (400 MHz, $CDCl_3$) 7.34–6.80 (14H, m, Ph), 4.90 (1H, d, *J* 2.5 Hz, C3–*H*), 4.20 (1H, d, *J* 2.4 Hz, C4–*H*); δ_C (100 MHz, $CDCl_3$) 166.0, 155.4, 137.2, 134.1, 130.1, 129.7, 128.4, 127.6, 126.9, 124.4, 117.0, 114.9, 60.2, 60.0.

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References and notes

1. (a) Alcaide, B.; Almendros, P. *Synlett* **2002**, 381–393; (b) Palomo, C.; Aizpurua, J. M.; Ganboa, I.; Oiarbide, M. *Synlett* **2001**, 1813–1826; (c) Alcaide, B.; Almendros, P. *Chem. Soc. Rev.* **2001**, *30*, 226–240; (d) Palomo, C.; Aizpurua, J. M.; Ganboa, I.; Oiarbide, M. *Amino Acids* **1999**, *16*, 321–343; (e) Ojima, I.; Delaloge, F. *Chem. Soc. Rev.* **1997**, *26*, 377–386; (f) Manhas, M. S.; Wagle, D. R.; Chiang, J.; Bose, A. K. *Heterocycles* **1988**, *27*, 1755–1802.
2. Bhalla, A.; Venugopalan, P.; Bhasin, K. K.; Bari, S. S. *Tetrahedron* **2007**, *63*, 3195–3204 and references therein.
3. (a) *The Organic Chemistry of β-lactams*; Georg, G. I., Ed.; VCH: New York, NY, 1993; (b) Ojima, I. *Adv. Asym. Synth.* **1995**, *1*, 95; (c) Alcaide, B.; Almendros, P. *Org. Prep. Proced. Int.* **2001**, *33*, 317–334; (d) Alcaide, B.; Almendros, P.; Aragonillo, C. *Chem. Rev.* **2007**, *107*, 4437–4492; (e) Brandi, A.; Cicchi, S.; Cordero, F. M. *Chem. Rev.* **2008**, *108*, 3988–4035; (f) Xu, J. *Arkivoc* **2009**, *ix*, 21–44.
4. (a) Burnett, D. A.; Caplen, M. A.; Davis, H. R., Jr.; Burrie, R. E.; Clader, J. W. *J. Med. Chem.* **1994**, *37*, 1733–1736; (b) Dugar, S.; Yumibe, N.; Clader, J. W.; Vizziano, M.; Huie, K.; van Heek, M.; Compton, D. S.; Davis, H. R., Jr. *Bioorg. Med. Chem. Lett.* **1996**, *6*, 1271–1274; (c) Wu, G. G. *Org. Process Res. Dev.* **2004**, *4*, 298–300.
5. Adlington, R. M.; Baldwin, J. E.; Chen, B. N.; Cooper, S. L.; McCoull, W.; Pritchard, G. J.; Howe, T. J. *Bioorg. Med. Chem. Lett.* **1997**, *7*, 1689–1694.
6. Madan, S.; Arora, R.; Venugopalan, P.; Bari, S. S. *Tetrahedron Lett.* **2000**, *41*, 5577–5581.
7. Bari, S. S.; Venugopalan, P.; Arora, R. *Tetrahedron Lett.* **2003**, *44*, 895–897.
8. Bari, S. S.; Venugopalan, P.; Arora, R.; Modi, G.; Madan, S. *Heterocycles* **2006**, *68*, 749–762.
9. Bhalla, A.; Madan, S.; Venugopalan, P.; Bari, S. S. *Tetrahedron* **2006**, *62*, 5054–5063.
10. Bhalla, A.; Venugopalan, P.; Bari, S. S. *Tetrahedron* **2006**, *62*, 8291–8302.
11. Bhalla, A.; Rathee, S.; Madan, S.; Venugopalan, P.; Bari, S. S. *Tetrahedron Lett.* **2006**, *47*, 5255–5259.
12. Bhalla, A.; Venugopalan, P.; Bari, S. S. *Eur. J. Org. Chem.* **2006**, 4943–4950.
13. Bhalla, A.; Sharma, S.; Bhasin, K. K.; Bari, S. S. *Synth. Commun.* **2007**, *37*, 783–793.
14. Bhalla, A.; Nagpal, Y.; Kumar, R.; Mehta, S. K.; Bhasin, K. K.; Bari, S. S. *J. Organomet. Chem.* **2009**, *694*, 179–189.
15. (a) Jiao, L.; Liang, Y.; Zhang, Q.; Zhang, S.; Xu, J. *Synthesis* **2006**, 659–665; (b) Jiao, L.; Liang, Y.; Xu, J. *J. Am. Chem. Soc.* **2006**, *128*, 6060–6069; (c) Jiao, L.; Liang, Y.; Zhang, Q.; Zhang, S.; Xu, J. *J. Org. Chem.* **2006**, *71*, 815–818.
16. Crystal data for **5l**: monoclinic; *P*21/*n*; *a*=14.8100(10) Å, *b*=9.0470(10) Å, *c*=16.5910(10) Å; *α*=90°, *β*=110.36°, *γ*=90 °C; *V*=2084.1(3) $Å^3$; *Z*=4; ρ_{Calcd}=1.292 mg/m^3; *μ*(Mo Kα)=0.180 mm^{-1}; full matrix least-square on F^2; *R*1=0.0565, *wR*2=0.1048 for 2166 observed reflections [$I>2\sigma(I)$] and *R*1=0.1222, *wR*2=0.1278 for all 2865 reflections; GOF=1.013. Crystallographic data (excluding structure factors) for the structure **5l** in this paper has been deposited with the Cambridge Crystallographic Data Centre as supplementary publication number CCDC 736044.
17. Crystal data for **5m**: triclinic; *P*-1; *a*=8.484(1) Å, *b*=11.103(2) Å, *c*=13.385(3) Å; *α*=84.80(2)°, *β*=78.62(2)°, *γ*=69.04(1) °C; *V*=1154.0(4) $Å^3$; Z=2; ρ_{Calcd}=1.294 mg/m^3; *μ*(Mo Kα)=0.173 mm^{-1}; full matrix least-square on F^2; *R*1=0.0517, *wR*2=0.1330 for 3176 observed reflections [$I>2\sigma(I)$] and *R*1=0.0908, *wR*2=0.1595 for all 5214 reflections; GOF=0.905. Crystallographic data (excluding structure factors) for the structure **5m** in this paper has been deposited with the Cambridge Crystallographic Data Centre as supplementary publication number CCDC 650920.
18. Ireland, R. E.; Marshall, J. A. *J. Org. Chem.* **1962**, *27*, 1615–1619.
19. Altomore, A.; Burla, M. C.; Carnalli, M.; Cascarano, G.; Giacovazzo, C.; Guagliardi, A.; Moliterni, A. G. G.; Polidori, G.; Spagna, R. *J. Appl. Crystallogr.* **1999**, *32*, 115–119.
20. Sheldrick, G. M. *SHELXTL/PC. Siemens, XSCANS, X-ray Single Crystal Analysis System, Version 5.05*; Siemens Analytical Instruments: Madison, WI, 1994.