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Synthesis and characterization of novel *trans*-**3**-benzyl/(diphenyl) methyl/naphthyl seleno substituted monocyclic β-lactams: X-ray structure of *trans*-1-(4′-methoxyphenyl)-3-(diphenyl)methylseleno-4-(4′-methoxyphenyl) azetidin-2-one

S.S. Bari*, Aman Bhalla*, Yogesh Nagpal, S.K. Mehta, K.K. Bhasin

Department of Chemistry and Centre of Advanced Studies in Chemistry, Panjab University, Chandigarh 160 014, India

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ABSTRACT

Several novel *trans*-3-benzyl/(diphenyl)methyl/naphthylseleno substituted monocyclic β-lactams (**5**–**7**) have been synthesized in high yields. The reaction scheme inolves [2 + 2] cycloaddition (Staudinger) reaction between suitably substituted imines **4**(**a**–**h**) and ketenes (**B**) accessed from 2-benzyl/(diphenyl) methyl/naphthylselenoethanoic acids (**1**–**3**) using $POCl_3$ and triethylamine in refluxing toluene. Characterization of these newly synthesized seleno substituted β-lactams has been performed by various spectroscopic techniques viz. NMR (^1H, ^{13}C and ^{77}Se), FTIR, mass spectrometry and elemental analysis. The molecular structure of *trans*-1-(4′-methoxyphenyl)-3-(diphenyl)methylseleno-4-(4′-methoxyphenyl)azetidin-2-one (**6b**) has also been established with the help of single crystal X-ray analysis.

1. Introduction

Over recent years, there has been a surge of attention towards the synthesis of compounds containing selenium in view of their inimitable biological properties such as Glutathione peroxidase mimic [1], thioredoxin reductase inhibition [2], antioxidant activity [3], antitumor [4], antimicrobial [5], antiviral [6] and antihypertensive properties [7]. Additional impetus for research efforts in this field has been provided by the recent discovery of novel selenadiazole derivative, which caused induced time- and dose-dependent apoptotic cell death in MCF-7 human breast carcinoma cells [8].

β-Lactams have acquired a prominent place in class of heterocyclic compounds due to their significant biological applications [9] as well as synthons for the synthesis of amino acids, alkaloids and taxoids [10]. Numerous articles reported in literature reveal that the nature of the groups linked to N-1, C-3 and C-4 of the β-lactam influences biological activity and efficacy [9]. Therefore, worldwide efforts have been directed towards the structural modification of β-lactams in order to enhance their spectrum of biological activity, potency, and specificity.

Pioneering research contributions in synthesis of bicyclic seleno-β-lactams such as selenapenems and selenacephames have been made by Perrone et al. [11], Thomas et al. [12], Fujita et al. [13], Hakimelahi et al. [14] and Gallagher et al. [15,16]. In addition, Ohshiro et al. [17], Liebscher et al. [18], Torchiarolo et al. [19] and Turos et al. [20] have developed different strategies for the synthesis of monocyclic seleno-β-lactams. Recently, the revolutionary and magical development reported by Schiesser et al. [21,22] in incorporation of selenium in penam and cephalosporin nuclei provides some novel compounds of potential biological significance. Very recently, Koketsu et al. [23,24] have reported 2-(trimethylsilyl)ethyl (TSE)-protection approach for the synthesis of bicyclic seleno-β-lactams, which further involves intramolecular cycloaddition reaction of selenium with alkynes and allenes. Thus, most recent trend in the β-lactam research has emerged, is the substitution of sulfur group with selenium and synthesis of this heterocycle with variety of substitutents at C-3, C-4 as well as N-1.

We have demonstrated the synthesis of novel β-lactams and their C-3 functionalization in our previous publications [9,25–33]. In these investigations, we synthesized novel 2-phenyl/benzylselenoethanoic acids, 3-phenyl/benzylseleno substituted β-lactams and spiroseleno β-lactams by substituting the sulfur with selenium atom

* Corresponding authors. Tel.: +91 172 253 4405; fax: +91 172 254 5074.
E-mail addresses: ssbari@pu.ac.in (S.S. Bari), aman_bhalla20@yahoo.co.in (A. Bhalla).

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[29,30]. Recently, we have reported successful attempts towards the synthesis and characterization of novel 2-pyridyl/naphthyl/(diphenyl)methylselenoethanoic acids [9]. In continuation to this, herein, we wish to report the synthesis and structural characterization of novel and structurally diverse *trans*-3-benzyl/(diphenyl)methyl/naphthylseleno substituted β-lactams. To the best of our knowledge, the synthesis of *trans*-3-(diphenyl)methyl/naphthylseleno-β-lactams have not been reported in literature so far.

2. Results and discussion

2.1. Synthesis of trans-3-benzyl/(diphenyl)methyl/naphthylseleno substituted β-lactams (5–7)

The use of benzylselenide moiety in the synthesis of benzoselenazine-2-4-dione and selenocarbohydrates through nucleophilic ring closure has been listed in literature [34,35]. In our earlier publication, we have employed intraselenyl cyclization of *cis*-3-(prop-2-ynyloxy)-3-benzylseleno-β-lactams to afford novel spiroseleno-β-lactam [30]. It was envisaged to extend this scope to synthesize a variety of novel bicyclic seleno-β-lactams via intraselenyl cyclization. Therefore, present studies have been directed towards the synthesis of suitable substrates such as 3-benzylseleno-β-lactams in excellent yields (Scheme 1).

Recent reports have shown that (diphenyl)methylseleno substituted compounds cause inhibition of azoxymethane-induced aberrant crypt foci in rat through down regulation of COX-2 and modulation of glutathione-*S*-transferase and lipid peroxidation [36]. Besides this, (diphenyl)methylseleno moiety has found to be involved in chemoprotection and enhancement of cancer chemotherapeutic efficacy of cyclophosphamide [37]. These attractive features along with the structural resemblance with benzyl, (diphenyl)methyl moieties impelled us to synthesize novel 3-(diphenyl)methylseleno substituted β-lactams (Scheme 1). Moreover, we wished to speculate the use of *cis*-3-(prop-2-ynyloxy)-3-(diphenyl)methylseleno-β-lactams via intraselenyl cyclization to furnish spiroseleno-β-lactams in excellent yields as compared to its benzyl counterpart.

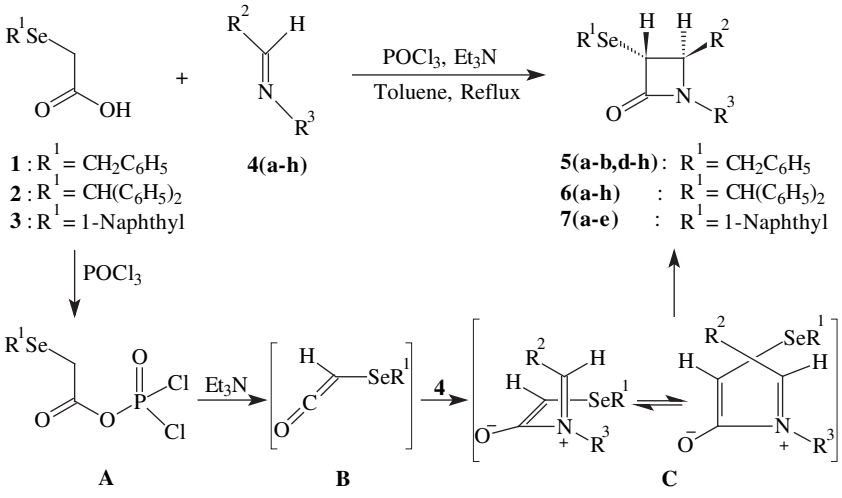
In our previous studies [25,30,31], we have introduced naphthyl moiety at C-3 of β-lactams via Lewis acid mediated functionalizations using naphthylether as the nucleophile. Enthused by the variety of applications of naphthyl moiety [9] and the results of above studies, successful attempts have been made towards the synthesis of novel *trans*-3-naphthylseleno-β-lactams via Staudinger cycloaddition of 2-naphthylselenoethanoic acid and Schiff's bases (Scheme 1).

Initial preparative endeavour began with the synthesis of 2-benzyl/(diphenyl)methyl/naphthylselenoethanoic acids (**1**–**3**) from ethyl 2-benzyl/(diphenyl)methyl/naphthylselenoethanoates using our earlier reported procedure [9,29]. The synthesis of novel *trans*-3-benzyl/(diphenyl)methyl/naphthylseleno substituted β-lactams (**5**–**7**) was performed through Staudinger cycloaddition reaction between the Schiff's bases **4**(**a**–**h**) and ketene (**B**), generated from 2-benzyl/(diphenyl)methyl/naphthylselenoethanoic acids (**1**–**3**) respectively (Scheme 1).

Initially, the reaction was performed at reflux temperature by adding dropwise a solution of phosphorus oxychloride ($POCl_3$) in dry toluene to a suspension of 2-benzylselenoethanoic acid **1**, Schiff's base **4b**, triethylamine and toluene with constant stirring. Progress of the reaction was monitored by thin-layer chromatography (TLC). This reaction resulted in the exclusive formation of *trans*-3-benzylseleno-β-lactam **5b** in excellent yield (Scheme 1 and Table 1, entry 2) and was purified by column chromatography on silica gel using ethyl acetate–hexane (8:92) as the eluent.

To obtain the molecular diversity within β-lactams **5**–**7**, a variety of different representatives of this class of compounds were prepared by altering the R^1, R^2 and R^3 substituents i.e. R^1 = $CH_2C_6H_5$, $CH(C_6H_5)_2$, 1-Naphthyl, R^2 = C_6H_5, $C_6H_4(OCH_3)(4)$, $C_6H_4(Cl)(4)$, $CH{=}CHC_6H_5$, R^3 = C_6H_5, $C_6H_4(OCH_3)(4)$, $C_6H_4(CH_3)(4)$, $C_6H_4(Cl)(4)$ (Scheme 1 and Table 1, entries 1,3–19). The *trans*-3-benzyl/(diphenyl)methyl/naphthylseleno substituted β-lactams (**5**–**7**) are air and moisture stable. These are soluble in haloalkanes and many other polar solvents such as acetone, dimethylformamide (DMF) and ethyl acetate. *trans*-3-Benzyl/(diphenyl)methylseleno substituted β-lactams (**5a**–**h, 6a**–**e,g**) were obtained as stable crystalline solids and **6f,g** as semisolid products. However, *trans*-3-naphthylseleno-β-lactams **7**(**a**–**e**) exist as highly viscous yellowish-brown oils.

The structures of these seleno-β-lactams **5**–**7** were established on the basis of various spectroscopic techniques *viz.*, FTIR, NMR (^1H, ^{13}C, ^{77}Se), mass spectrometry (in few representative cases) and their elemental analysis. The spatial juxtaposition of the C3–H and C4–H was assigned *trans* in products **5**–**7** on the basis of coupling constant values (J = 1.5–2.4 Hz, C3–H and C4–H) respectively in ^1H NMR spectra [25,26]. The stereochemistry at C-3 of *trans*-β-lactams **5**–**7** was established through single crystal X-ray crystallographic studies of **6b** (Fig. 1). [^1H–^1H] COSY (HOMCOR-2D) and [^1H–^{13}C]



Scheme 1. Synthesis of *trans*-3-benzyl/(diphenyl)methyl/naphthylseleno substituted β-lactams (**5**–**7**).

Table 1
Synthesis of *trans*-3-benzyl/(diphenyl)methyl/naphthylseleno substituted β-lactams (**5**–**7**).

Entry	R^1	R^2	R^3	Product	Yield[a] (%)	M.p. (°C)
1	$CH_2C_6H_5$	C_6H_5	C_6H_5	**5a**	66	110–111
2	$CH_2C_6H_5$	$C_6H_4(OCH_3)(4)$	$C_6H_4(OCH_3)(4)$	**5b**	74	82–83
3	$CH_2C_6H_5$	$C_6H_4(Cl)(4)$	$C_6H_4(OCH_3)(4)$	**5d**	73	120–121
4	$CH_2C_6H_5$	$CH{=}CHC_6H_5$	$C_6H_4(CH_3)(4)$	**5f**	70	100–101
5	$CH_2C_6H_5$	$CH{=}CHC_6H_5$	$C_6H_4(Cl)$	**5g**	71	108–109
6	$CH_2C_6H_5$	$CH{=}CHC_6H_5$	$C_6H_4(OCH_3)(4)$	**5h**	74	81–82
7	$CH(C_6H_5)_2$	C_6H_5	C_6H_5	**6a**	59	110–111
8	$CH(C_6H_5)_2$	$C_6H_4(OCH_3)(4)$	$C_6H_4(OCH_3)(4)$	**6b**	60	93–94
9	$CH(C_6H_5)_2$	C_6H_5	$C_6H_4(OCH_3)(4)$	**6c**	64	89–90
10	$CH(C_6H_5)_2$	$C_6H_4(Cl)(4)$	$C_6H_4(OCH_3)(4)$	**6d**	66	121–122
11	$CH(C_6H_5)_2$	C_6H_5	$CH_2C_6H_5$	**6e**	63	137–138
12	$CH(C_6H_5)_2$	$CH{=}CHC_6H_5$	$C_6H_4(CH_3)(4)$	**6f**	69	Semisolid
13	$CH(C_6H_5)_2$	$CH{=}CHC_6H_5$	$C_6H_4(Cl)(4)$	**6g**	66	142–143
14	$CH(C_6H_5)_2$	$CH{=}CHC_6H_5$	$C_6H_4(OCH_3)(4)$	**6h**	72	Semisolid
15	1-Naphthyl	C_6H_5	C_6H_5	**7a**	53	Oil
16	1-Naphthyl	$C_6H_4(OCH_3)(4)$	$C_6H_4(OCH_3)(4)$	**7b**	62	Oil
17	1-Naphthyl	C_6H_5	$C_6H_4(OCH_3)(4)$	**7c**	60	Oil
18	1-Naphthyl	$C_6H_4(Cl)(4)$	$C_6H_4(OCH_3)(4)$	**7d**	57	Oil
19	1-Naphthyl	C_6H_5	$CH_2C_6H_5$	**7e**	51	Oil

[a] Yields quoted are for isolated products characterized by FTIR, NMR (^{1}H, ^{13}C, ^{77}Se) and EIMS.

COSY (HETCOR-2D) studies of representative compound (**6g**) confirmed the target products (Fig. 2).

All these cycloaddition reactions are found to be highly stereoselective. The presence of benzylseleno ($PhCH_2Se-$), (diphenyl) methylseleno (Ph_2CHSe-) and naphthylseleno group at C-3 position led to exclusive formation of *trans*-3-benzyl/(diphenyl)methyl/naphthyl seleno-β-lactams. However, in our earlier publication [30], the formation of mixture of *trans*- and *cis*-3-phenylseleno-β-lactams in the ratio of 7:1 were observed on presence of phenylseleno (PhSe–) moiety at C-3 position and these *trans*- and *cis*-seleno-β-lactams were further separated by column chromatography. These studies indicate that the presence of different groups in the substrate moieties effect the stereochemical outcome of the targeted seleno-β-lactams. Mechanistically, the synthesis of *trans*-3-benzyl/(diphenyl)methyl/naphthyl seleno substituted β-lactams (**5**–**7**) proceed via ketene (**B**) generated by treatment of 2-benzyl/(diphenyl)methyl/naphthylselenoethanoic acids (**1**–**3**) with phosphorus oxychloride ($POCl_3$) and triethylamine in refluxing toluene. Subsequently, nucleophilic attack of imino nitrogen of Schiff's base (**4**) on the sp hybridized carbon of ketene (**B**) furnished zwitterionic intermediate (**C**) which on direct ring closure or conrotatory electrocyclization produced exclusively the *trans* seleno-β-lactams **5**–**7** (Scheme 1).

Further elaboration of 3-benzyl/(diphenyl)methylseleno substituted β-lactams (**5**–**6**) to potential bicyclic and spirocyclic seleno-β-lactams is underway in our laboratory. In addition, 3-naphthylseleno-β-lactams (**7**) would serve as the synthons for variety of monocyclic seleno-β-lactams.

2.2. X-ray crystallographic analysis

The crystal structure of *trans*-1-(4′-methoxyphenyl)-3-(diphenyl)methylseleno-4-(4′-methoxyphenyl) azetidin-2-one (**6b**) was established by X-ray crystallographic analysis (Fig. 1). It was crystallized from dichloromethane–hexane (3:1) as colorless crystalline solids suitable for single crystal X-ray diffraction. A prospective view of the molecular structure with atom numbering scheme has been given in Fig. 1. Selected bond lengths [Å], bond angles [°] and torsion angles [°] are presented in Table 2. All the relevant information about data collection and refinement parameters has been listed in Table 3.

The Se–C bond length between Se and C-3 of β-lactam **6b** [Se–C (14), 1.94 Å] lie within the range (1.90–1.95 Å), reported for several organoseleno compounds possessing Se–C bond [38,39]. However, the Se–C bond length between Se and methine carbon atom of (diphenyl)methyl is slightly longer i.e., [Se–C(1), 1.99 Å], indicating the weakening of C–Se bond as a result of another phenyl substitutient. The bond angle of C(14)–Se(1)–C(1) bond in (**6b**) is 97.07 (16) indicating the distortion of sp^3 carbon from its regular tetrahedral geometry and established the 'V' shaped geometry about C–Se–C bond. Further, the *trans* stereochemistry between C3–H and C4–H of the β-lactam **5**–**7** was evident through torsional angle between Se(1)–C(14)–C(16)–C(24), Se(1)–C(14)–C(16)–H(16), H (14)–C(14)–C(16)–H(16) and H(14)–C(14)–C(16)–C(24) which are −127.2(3), 4.08, 135.88, 4.62 respectively of compound **6b**. Additionally, torsional angle of −2.74 between O(1)–C(15)–N(1)–C(17) reveals that β-lactam ring and *p*-methoxyphenyl ring at N-1 postion are almost planar. Interestingly, a single crystal unit of β-lactam **6b** is involved in intermolecular hydrogen bonding interactions with two crystal units via different modes. In one mode, carbonyl oxygen [O(1)] of one crystal unit is showing hydrogen bonding with methine hydrogen [H(1A)] and C3–H [H (14A)] of other crystal unit. Whereas, in second mode, methoxy oxygens of same crystal unit [O(2) and O(3)] shows hydrogen bonding with phenylic hydrogen [H(29) and H(19)] of other crystal unit respectively (Fig. 1, Table 4). Although intermolecular C–H interactions are also present but they are quite weak in comparison with hydrogen bonding.

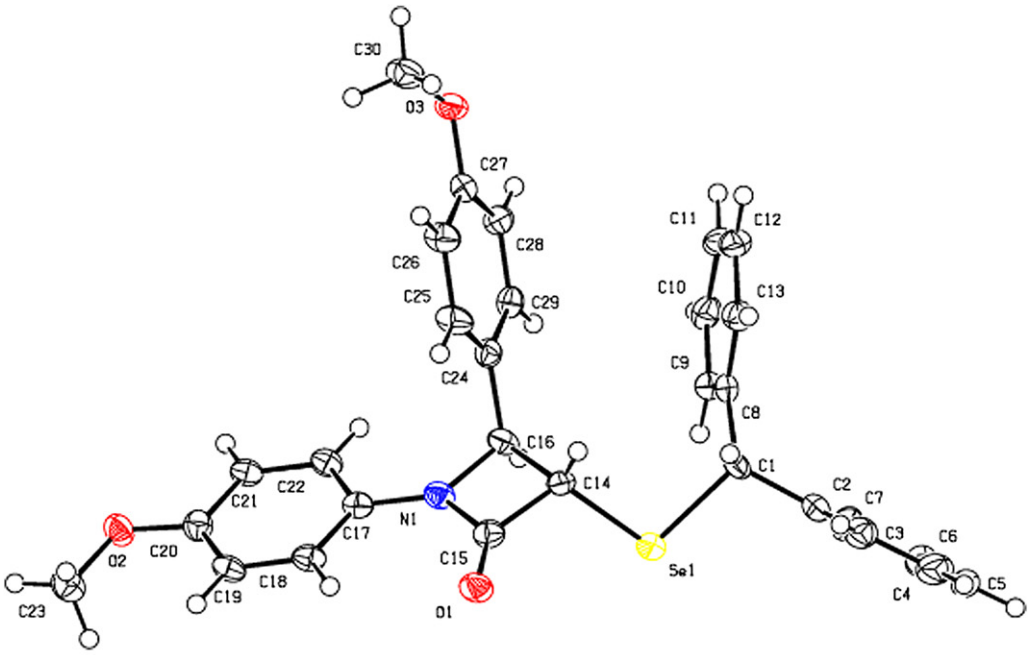
2.3. Spectroscopic studies

FTIR, NMR (^{1}H, ^{13}C, ^{77}Se) spectroscopy and mass spectrometry (only in few representative cases) supported the formulation of the *trans*-3-benzyl/(diphenyl)methyl/naphthylseleno-β-lactams (**5**–**7**). Initial indicative for the formation of seleno-β-lactams **5**–**7**, is the IR absorption band in the range 1739–1761 cm^{-1} for the C=O of β-lactam ring.

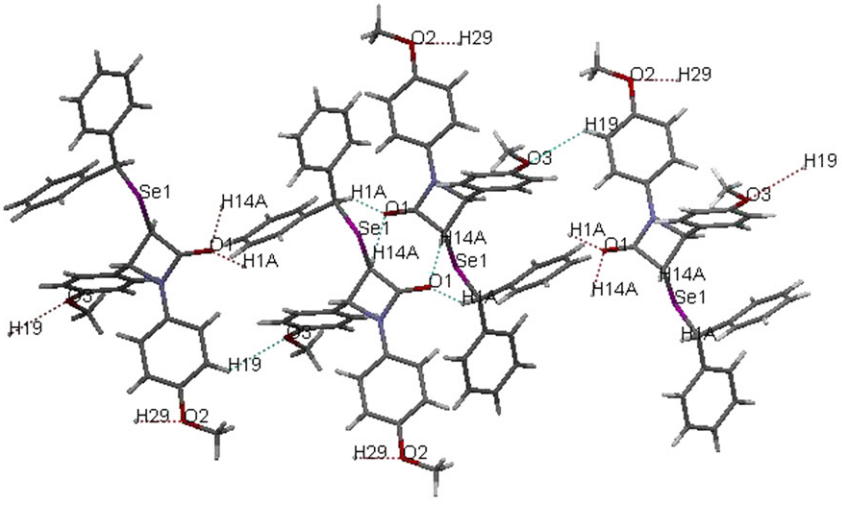
The ^{1}H, ^{13}C and ^{77}Se NMR data of *trans*-3-benzyl/(diphenyl) methyl/naphthylseleno substituted β-lactams (**5**–**7**) were obtained as expected and listed in the experimental section. The *trans* stereochemistry of products was assigned on the basis of coupling constant values (J = 1.5–2.4 Hz, C3–H and C4–H) in ^{1}H NMR spectrum which is also in good agreement with the single crystal X-ray crystallographic analysis of (**6b**). The chemical shift values for C3–H and C4–H in ^{1}H and ^{13}C NMR spectrum of compounds **5b**, **6b** and **7b** were tabulated in the Table 5 and showed significant downfield shift in C3–H and C4–H values when C-3 position of β-lactam is substituted with naphthylselenide moiety in comparison to benzyl or (diphenyl)methyl. This can be attributed to greater deshielding influence of electron withdrawing naphthyl ring over benzyl or (diphenyl)methyl.

2D Correlation spectroscopic studies such as proton–proton COSY [^{1}H–^{1}H COSY] and hetero-nuclear single quantum correlation (HSQC) were performed to explain the splitting due to allylic couplings. ^{1}H–^{1}H COSY spectrum of **6g** [Fig. 2(i)] showed the correlation between C4–H and C4–CH=(a and b; δ 4.03 and 5.84 ppm) and C4–CH=and Ph–CH=(c and d; δ 5.84 and 6.42 ppm). The HSQC spectrum of **6g** [Fig. 2(ii)] confirmed the assignment of *C*3–H (a; δ 3.90 and 48.0 ppm), *C*4–*H* (b; δ 4.03 and 61.0 ppm), $(Ph)_2CH$ (c; δ 5.74 and 47.0 ppm), C4–*C*H=(d; δ 5.78 and 116.9 ppm) and Ph–*C*H=(e; δ 6.39 and 133.5 ppm) and all aromatic CHs.

In the EIMS spectrum of *trans*-3-benzyl/(diphenyl)methylseleno substituted β-lactams, a peak corresponding to the fragment $[M+Na]^+$ with low to moderate intensity (i.e. 5.90–40.08) confirmed the formation of target products. β-Lactams **6b** and **6e** has shown a low intensity peak at *m/z* 415 corresponding to *bis*(diphenylmethyl) selenide apart from other fragmentation peaks (mentioned in



6b



6b (Hydrogen bonding interactions)

Fig. 1. ORTEP diagram of *trans*-1-(4′-methoxyphenyl)-3-(diphenyl)methylseleno-4-(4′-methoxyphenyl) azetidin-2-one (**6b**) showing atom numbering and hydrogen bonding interactions.

experimental section). In the EIMS spectra of **5d**, the base peak was observed at *m/z* 331 (100%) corresponds to $[C_{17}H_{16}NOSe]^+$, whereas, $[C_{17}H_{16}NOSe]^+$ in **5b, 6b** and **6e**, was identified at *m/z* 331 (92%), *m/z* 331 (75%) and *m/z* 331 (52%) respectively.

3. Experimental

3.1. General

Melting points were determined in an open capillary on melting point apparatus and are uncorrected. Fourier transform infrared spectra were recorded on a Perkin–Elmer 1430 (FTIR) spectrophotometer (υ_{max} in cm^{-1}). ^1H (300 MHz), ^{13}C (75 MHz) and ^{77}Se (57 MHz) NMR spectra were recorded on JEOL AL 300 (300 MHz) spectrometer. Chemical shifts are given in ppm relative to Me_4Si as an internal standard (δ = 0 ppm) for ^1H NMR, $CDCl_3$ (δ = 77.0 ppm) for ^{13}C NMR spectra and Me_2Se (δ = 0 ppm) for ^{77}Se NMR spectra. The mass spectra (EI) were obtained using QTOF mass spectrometer. The elemental analysis (C, H, N) was recorded on Flash EA 112 elemental analyzer. Column chromatography was performed using Merck Silica Gel (60–120 mesh) using ethyl acetate–hexanes (8:92) as an eluant system. Reactions were monitored by analytical thin-layer chromatography (TLC) using Merck Silica Gel G using ethyl acetate–hexanes (10:90) as an eluant system. For visualization, TLC plates were stained with iodine vapors.

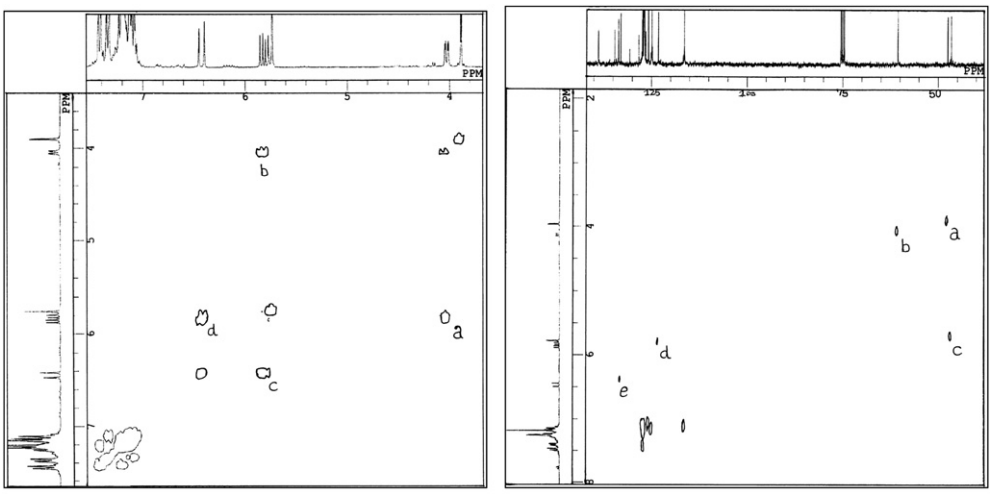


Fig. 2. (i) [^{1}H–^{1}H] COSY (HOMCOR-2D) spectrum of compound **6g**, (ii) [^{1}H–^{13}C] COSY (HETCOR-2D) spectrum of compound **6g**.

The reactions for the preparation of *trans*-3-benzyl/(diphenyl) methyl/naphthylseleno substituted β-lactams were carried out under dry and deoxygenated nitrogen atmosphere. 2-Benzyl/(diphenyl)methyl/naphthylselenoethanoic acids (**1**–**3**) were prepared using our earlier reported procedure [29]. Phosphorus oxychloride (Merck), triethylamine (Qualigen) and all other commercially available compounds/reagents/solvents were of reagent grade quality and used without any further purification. Toluene was distilled under N_2 from sodium-benzophenone immediately before use.

3.2. Crystal structure analysis

Diffraction quality, colorless single crystals of compound **6b**, undertaken for crystallographic study were grown from the slow evaporation of dichloromethane–hexane (3:1) solution of the compounds. Single crystals were mounted on glass capillaries of Bruker Smart Apex diffractometer using graphite-monochromated Mo Kα radiation at room temperature. The data integration and reduction were processed with SAINT software. The crystal structures of these compounds were solved by direct methods using SHELX-97 [40] and refined by full-matrix least-squares method. All the non-hydrogen atoms were refined anisotropically. The hydrogen atoms were included in the ideal position with fixed isotropic U values and were riding. The empirical absorption corrections for these compounds were performed using SADBAS program [41]. All other information regarding the refinement is given in Table 3 and the ORTEP representations are with atom numbering scheme (thermal ellipsoids are at 50% probability level) (Fig. 1).

3.3. Synthesis of trans-3-benzyl/(diphenyl)methyl/naphthylseleno-β-lactams

The *trans*-3-benzyl/(diphenyl)methyl/naphthylseleno substituted β-lactams (**5**–**7**) were synthesized by the procedure as reported

Table 2
Selected bond parameters of **6b.**

Bond length (Å)[a]		Bond angle [°][a]		Torsion angle [°][a]	
Se(1)–C(14)	1.948(4)	C(14)–Se(1)–C(1)	97.07(16)	C(14)–Se(1)–C(1)–C(8)	−62.2(3)
Se(1)–C(1)	1.993(4)	C(20)–O(2)–C(23)	117.1(3)	C(14)–Se(1)–C(1)–C(2)	169.9(3)
O(1)–C(15)	1.216(4)	C(15)–N(1)–C(17)	133.5(3)	Se(1)–C(1)–C(2)–C(7)	77.8(4)
O(2)–C(20)	1.377(4)	C(15)–N(1)–C(16)	95.1(3)	Se(1)–C(1)–C(2)–C(3)	−102.0(4)
O(2)–C(23)	1.427(5)	C(8)–C(1)–C(2)	115.0(3)	Se(1)–C(1)–C(8)–C(13)	135.7(3)
O(3)–C(27)	1.367(4)	C(8)–C(1)–Se(1)	114.1(3)	Se(1)–C(1)–C(8)–C(9)	−46.8(4)
O(3)–C(30)	1.426(5)	C(2)–C(1)–Se(1)	106.3(2)	C(1)–Se(1)–C(14)–C(15)	−158.7(3)
N(1)–C(15)	1.372(5)	C(7)–C(2)–C(3)	118.1(4)	C(1)–Se(1)–C(14)–C(16)	102.9(3)
N(1)–C(17)	1.408(5)	C(7)–C(2)–C(1)	122.4(4)	C(17)–N(1)–C(15)–O(1)	−2.6(7)
N(1)–C(16)	1.489(5)	C(15)–C(14)–Se(1)	112.9(3)	C(16)–N(1)–C(15)–O(1)	−179.0(4)
C(1)–C(8)	1.509(5)	C(16)–C(14)–Se(1)	118.6(3)	C(16)–N(1)–C(15)–C(14)	2.0(3)
C(1)–C(2)	1.511(5)	O(1)–C(15)–N(1)	131.4(4)	C(16)–C(14)–C(15)–O(1)	179.2(5)
C(2)–C(7)	1.389(6)	O(1)–C(15)–C(14)	135.8(4)	Se(1)–C(14)–C(15)–O(1)	59.8(6)
C(14)–C(15)	1.515(5)	N(1)–C(15)–C(14)	92.8(3)	Se(1)–C(14)–C(15)–N(1)	−121.3(3)
C(14)–C(16)	1.578(5)	N(1)–C(16)–C(24)	115.8(3)	C(17)–N(1)–C(16)–C(24)	62.9(5)
C(16)–C(24)	1.502(5)	N(1)–C(16)–C(14)	86.0(3)	C(15)–N(1)–C(16)–C(14)	−1.9(3)
		C(24)–C(16)–C(14)	117.5(3)	C(17)–N(1)–C(16)–C(14)	−178.4(4)
		C(18)–C(17)–N(1)	120.4(3)	C(15)–C(14)–C(16)–N(1)	1.7(3)
		C(22)–C(17)–N(1)	119.8(3)	Se(1)–C(14)–C(16)–N(1)	115.7(3)
				Se(1)–C(14)–C(16)–C(24)	−127.2(3)
				C(15)–N(1)–C(17)–C(18)	7.1(6)
				C(16)–N(1)–C(17)–C(18)	−177.7(4)

[a] Estimated standard deviation in least significant figure are given in parentheses.

Table 3
Crystallographic data and measurements of compound **6b.**

	Compound **6b**
Empirical formula	$C_{30}H_{27}NO_3Se$
Formula weight (g/mol)	528.49
Temperature (K)	293(2)
Diffractometer used	Bruker Smart Apex
Radiation used, λ Mo Kα (Å)	0.71069
Crystal system/space group	Monoclinic, $P2_{1/n}$
Unit cell dimensions	
a (Å)	10.105(5)
b (Å)	10.441(5)
c (Å)	23.653(5)
α (°)	90.000(5)
β (°)	92.385(5)
γ (°)	90.000(5)
V (Å^3)	2493.4(18)
Z, calculated density (mg/m^3)	4
Absorption coefficient (mm^{-1})	1.538
F(000)	1088
Crystal size (mm^3)	0.16 × 0.12 × 0.10
θ range for data collection (°)	2.1–28.3
Index ranges	$-13 \le h \le 13$ $-13 \le k \le 13$ $-23 \le l \le 31$
Reflection collected/unique	15 934/6144
[$R_{(int)}$]	0.0515
Reflection with [$I > 2\sigma(I)$]	4327
Refinement method	Full-matrix least-square on F^2
Final *R* indices, [$I > 2\sigma(I)$]	$R_1 = 0.0492$, $wR_2 = 0.0971$
R indices [all data]	$R_1 = 0.0858$, $wR_2 = 0.1369$
Largest difference in peak and hole (e Å^{-3})	1.006 and −0.815

earlier for the preparation of 3-phenyl/benzylseleno substituted azetidin-2-ones [25] in the cited reference.

*3.3.1. trans-1-(4′-methoxyphenyl)-3-benzylseleno-4-(4′-methoxyphenyl)azetidin-2-one (**5b**)*

Yield 74%; colorless crystalline solid; m.p. 82–83 °C; ^{1}H NMR: δ 7.18–6.64 (m, 13H), 4.44–4.43 (d, 1H, 2.1 Hz), 3.94 (s, 2H), 3.92–3.91 (d, 1H, 2.1 Hz), 3.70 (s, 3H), 3.66 (s, 3H); ^{13}C NMR: δ 161.3, 157.9, 154.1, 136.3, 129.1, 127.1, 126.8, 126.5, 125.1, 124.9, 116.4, 112.5, 112.2, 61.2, 53.2, 48.1, 25.3; ^{77}Se NMR: δ 337.2; IR ($CHCl_3$, ν cm^{-1}): 1749.1; MS–EI, *m/e* (R.I., assignment): 476 (38, $[M + Na]^+$), 391 (6, $[C_{22}H_{17}NOSe]^+$), 345 (35, $[C_{17}H_{16}NO_2Se]^+$), 331 (92, $[C_{17}H_{16}NOSe]^+$), 282 (8, $[C_{17}H_{16}NO_3]^+$); Anal. Calc. for $C_{24}H_{23}NO_3Se$: C, 63.72; H, 5.12; N, 3.10; Found: C, 63.64; H, 4.97; N, 2.99%.

*3.3.2. trans-1-(4′-methoxyphenyl)-3-(diphenyl)methylseleno-4-(4′-methoxyphenyl)azetidin-2-one (**6b**)*

Yield 60%; colorless crystalline solid; m.p. 93–94 °C; ^{1}H NMR: δ 7.45–6.67 (m, 18H), 5.78 (s, 1H), 4.36–4.35 (d, 1H, 2.4 Hz), 3.93–3.92 (d, 1H, 2.1 Hz), 3.75 (s, 3H), 3.71 (s, 3H); ^{13}C NMR: δ 161.3, 158.0, 154.1, 139.0, 138.8, 129.2, 127.1, 127.0, 126.9, 126.7, 126.6, 125.4, 116.5, 112.6, 112.2, 60.6, 53.3, 53.2, 50.2, 46.2; ^{77}Se NMR: δ 351.9 IR ($CHCl_3$, ν cm^{-1}): 1748.1; MS–EI, *m/e* (R.I., assignment): 552 (15, $[M + Na]^+$), 415 (7, $[C_{26}H_{22}Se]^+$), 331 (75, $[C_{17}H_{16}NOSe]^+$), 316 (5, $[C_{16}H_{13}NOSe]^+$); Anal. Calc. for $C_{30}H_{27}NO_3Se$: C, 68.18; H, 5.15; N, 2.65; Found: C, 68.11; H, 5.12; N, 2.76%.

*3.3.3. trans-1-(4′-methoxyphenyl)-3-naphthylseleno-4-(4′-methoxyphenyl)azetidin-2-one (**7b**)*

Yield 62%; yellowish-brown oil; ^{1}H NMR: δ 8.50–6.69 (m, 15H), 4.67–4.66 (d, 1H, 2.1 Hz), 4.32–4.31 (d, 1H, 2.1 Hz), 3.74 (s, 3H), 3.70 (s, 3H); ^{13}C NMR: δ 161.5, 158.1, 154.3, 133.4, 133.0, 132.2, 129.1, 127.9, 126.9, 126.8, 126.1, 125.3, 124.7, 124.6, 124.0, 116.6, 112.7, 61.2, 53.4, 53.3, 51.7; ^{77}Se NMR: δ 275.6; IR ($CHCl_3$, ν cm^{-1}): 1748.6.

Table 4
Hydrogen bonding interactions for compound **6b.**

Entry	Intermolecular Hydrogen bond	Bond Length(Å)
1	O(1)···H(1A)	2.590
2	O(1)···H(14A)	2.601
3	O(2)···H(29)	2.630
4	O(3)···H(19)	2.666

Table 5
^{1}H and ^{13}C NMR values of C3–H and C4–H of *trans*-3-benzyl/(diphenyl)methyl/naphthylseleno-β-lactams (**5**–**7**)**b.**

Seleno-β-lactams	C3–H		C4–H	
	δ ^{1}H NMR	δ ^{13}C NMR	δ ^{1}H NMR	δ ^{13}C NMR
5b	3.95–3.90	51.7	4.44–4.43	53.3
6b	3.93–3.92	50.2	4.36–4.35	53.2
7b	4.32–4.31	48.1	4.67–4.66	53.2

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Appendix A. Supplementary material

CCDC 768085 contains the supplementary crystallographic data for **6b**. This data can be obtained free of charge from the Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/data_request/cif. Spectroscopic data for compounds **5a, 5d, 5f–h, 6a, 6c–h, 7a, 7c–e**. Supplementary data associated with this article can be found, in the on-line version at doi:10.1016/j.jorganchem.2010.05.005.

Appendix A. Supplementary material

Supplementary information associated with this article could be found on-line, at doi:10.1016/j.jorganchem.2010.05.005.

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