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Seleno-β-lactams: synthesis of monocyclic and spirocyclic selenoazetidin-2-ones

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Abstract—An efficient protocol for the synthesis of novel seleno-β-lactams using operationally simple strategies is presented. 3-Phenyl/benzylseleno-β-lactams, obtained from 2-phenyl/benzylselenoethanoic acids, are transformed to *cis*-3-chloro-3-phenyl/benzylseleno-β-lactams, which undergo reaction with various active aliphatic and aromatic substrates catalyzed by Lewis acid to produce *cis*-3-alkoxy-3-phenyl/benzylseleno-β-lactams and *C*-3 monosubstituted seleno-β-lactams. Halogen mediated intraselenyl cyclization of *cis*-3-(prop-2-ynyloxy)-3-benzylseleno-β-lactams affords novel spiro seleno-β-lactams.

1. Introduction

β-Lactam antibiotics still constitute one of the most widely employed class of antibacterial agents.[1] They continue to attract the attention of synthetic organic chemists as they present a variety of synthetic challenges. Besides this, they are useful as intermediates for α- and β-amino acids, alkaloids, heterocycles, taxoids and other important compounds of biological and medicinal interest.[2] In addition, recently some of the synthetic β-lactams have been reported to be biologically active as cholesterol acyl transferase inhibitors,[3] thrombin inhibitors,[4] human cytomegalovirus protease inhibitors,[5] matrix-metalloprotease inhibitors,[6] human leukocyte elastase,[7] cysteine protease[8] and apoptosis inductors.[9]

The ever-increasing bacterial resistance to β-lactam antibiotics presents a very serious concern[10] and efforts have been made to meet this challenge by exploring new β-lactam chemistry by the skeletal modification of naturally occurring β-lactam antibiotics. The sulfur atom of penicillins and cephalosporins has been replaced by selenium and its chemophysical and microbiological effects have been investigated. Selenium, which is an essential trace element, has been recognized to function as an active centre of redox enzyme[11] such as glutathione peroxidase, found to act as a micronutrient[12] supplement of vitamin E and as a modifying factor in the toxicities[13] of heavy metals. Apart from this, selenium is an integral part of factor 3, a dietary agent, which prevents liver necrosis in the rat and exudative diathesis in the chick[14] and also exhibits antifungal[15] as well as insecticidal[16] properties.

Over the past few years, selenium containing higher heterocycles such as ebselen,[10a,17] 1,3-selenazine derivatives,[18] 5-deoxy-5-selenopyranose sugars,[19] benzoselenazine-2,4-dione[20] and novel selenium analogues of the important antioxidant, α-tocopherol[21] have been reported. Further, Perrone et al.[22] have described the synthesis of the optically active selenapenam **I** along with its antibacterial activity. Recently, Schiesser and Carland[23] have extended the variety of available β-lactamase inhibitors by synthesizing selenium analogue **II** of sulbactam and novel selenapenem **III** (Fig. 1).

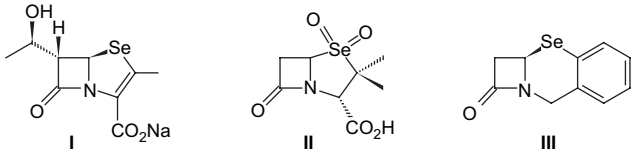

Figure 1. Biologically active seleno-β-lactams.

It was considered that substitution of the sulfur atom of azetidin-2-ones with selenium preserves its shape and electronic properties but may differ in reactivity and thus potency. Therefore, the development of convenient approaches for the synthesis of selenoazetidin-2-ones continues to be an area of active research and we wish to report here the results of our studies towards the synthesis of novel selenoazetidin-2-ones.

Keywords: Seleno-β-lactam; Selenoazetidin-2-one; Lewis acid; Nucleophile; Alkoxyseleno-β-lactam; Monosubstituted seleno-β-lactam; Spiro seleno-β-lactam.
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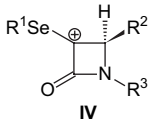
2. Results and discussion

In continuation of our earlier studies towards the synthesis of novel azetidin-2-ones and their C-3 functionalization,[24–30] we present here a convenient synthesis of novel seleno-β-lactams using efficient and operationally simple strategies. It was envisaged that *cis*-3-chloro-3-phenyl/benzylseleno-β-lactams prepared from 3-phenyl/benzylseleno-β-lactams, may provide an easy access to novel *cis*-3-alkoxy-3-phenyl/benzylseleno-β-lactams, *C*-3 monosubstituted seleno-β-lactams and spiro seleno-β-lactams employing *C*-3 carbocation equivalents[24] of type **IV**.

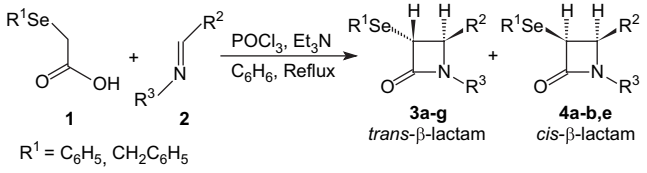


IV

2.1. 3-Phenyl/benzylselenoazetidin-2-ones

The literature reports a few effective methods for the synthesis of monocyclic 3-phenylseleno-β-lactams. These include ketene–imine cycloaddition reaction using 2-phenylselenopropanoyl chloride,[31] the direct β-lactam enolate selenation[32] and by the use of α-phenylseleno-β-amino esters as direct precursors of 3-phenylseleno-β-lactams.[33] In connection with these studies, we envisaged the synthesis of monocyclic 3-phenyl/benzylseleno-β-lactams via a direct annelation of 2-phenyl/benzylselenoethanoic acids and appropriate Schiff's bases.

Starting substrates, 2-phenyl/benzylselenoethanoic acids **1**, required for this study, were prepared from ethyl 2-phenyl/benzylselenoethanoates as reported in our recent publication.[34] 3-Phenyl/benzyl-selenoazetidin-2-ones (**3** and **4**) were synthesized by treating 2-phenyl/benzylselenoethanoic acid (**1**) and appropriate Schiff's bases **2a–e** in presence of triethylamine as the base and phosphorus oxychloride ($POCl_3$) as the condensing reagent in refluxing benzene according to the procedure reported for 3-phenyl/benzylthio-β-lactams,[27,28] in good yields (Scheme 1, Table 1).



Scheme 1. Synthesis of 3-phenyl/benzylselenoazetidin-2-ones **3a–g** and **4a,b,e**.

Initial studies were carried out by treating 2-phenylselenoethanoic acid with Schiff's base **2a** using $POCl_3$ and triethylamine in refluxing benzene. This reaction resulted in the formation of a mixture of *trans*- and *cis*-3-phenylseleno-β-lactam in the ratio of 7:1, respectively, which were separated by column chromatography. The reaction was carried out with various Schiff's bases **2b–e** and results are summarized in Table 1. This cycloaddition reaction resulted in an exclusive formation of *trans*-β-lactams **3** with Schiff's bases **2c,d** and led to the formation of a mixture of *trans*-β-lactam **3** (major product) and *cis*-β-lactam **4** (minor product) when carried out with Schiff's bases **2a,b,e**. On the other hand, 2-benzylselenoethanoic acid afforded exclusively, *trans*-β-lactam **3f,g**, when reacted with Schiff's bases **2a,c,d** under similar conditions.

Table 1. 3-Phenyl/benzylselenoazetidin-2-ones **3a–g** and **4a,b,e**

Entry	R^1	R^2	R^3	Product of type (% yield)[a]	
				3 (*trans*-β-Lactam)	**4** (*cis*-β-Lactam)
1	C_6H_5	C_6H_5	4-(MeO)C_6H_4	**3a** (75)	**4a** (11)
2	C_6H_5	4-(MeO)C_6H_4	4-(MeO)C_6H_4	**3b** (78)	**4b** (06)
3	C_6H_5	C(Me)=CHC_6H_5	4-(MeO)C_6H_4	**3c** (81)	—
4	C_6H_5	C_6H_5	$CH_2C_6H_5$	**3d** (84)	—
5	C_6H_5	C_6H_5	4-(Cl)C_6H_4	**3e** (69)	**4e** (18)
6	$CH_2C_6H_5$	C_6H_5	4-(MeO)C_6H_4	**3f** (74)	—
7	$CH_2C_6H_5$	C_6H_5	$CH_2C_6H_5$	**3g** (71)	—

[a] Yields quoted are for the isolated products.

The structures of these selenoazetidin-2-ones **3a–g** and **4a,b,e** were established on the basis of their spectral data (IR, ^{1}H NMR, ^{13}C NMR, ^{77}Se NMR and MS). The spatial juxtaposition of C3–H and C4–H was assigned trans in product **3** and cis in product **4** on the basis of coupling constant values [(*J* 1.5–2.4 Hz, C3–H and C4–H) and (*J* 5.7–6.0 Hz, C3–H and C4–H)],[28] respectively, in ^{1}H NMR spectra. The stereochemistry at C-3 of *trans*-β-lactams **3a–g** was established through single crystal X-ray crystallographic studies of **3a**[35] (Fig. 2).

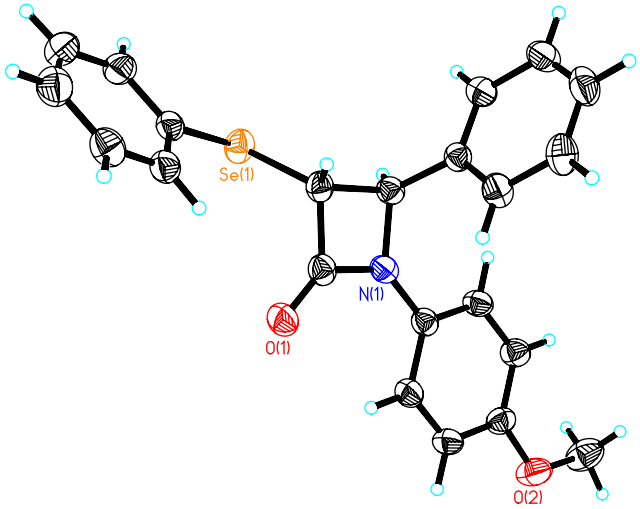


Figure 2. ORTEP diagram for compound **3a**.

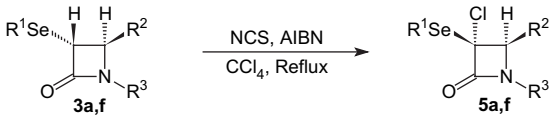
The formation of *trans*- and *cis*-3-phenyl/benzylseleno-β-lactam in this case can be rationalized on the basis of the similar mechanism as discussed for the formation of *trans*- and *cis*-3-alkoxy-3-phenyl/benzylthio-β-lactam in our recent publication.[28]

2.2. *cis*-3-Chloro-3-phenyl/benzylselenoazetidin-2-ones

The synthetic potential of *C*-3 β-lactam carbocation **IV** has been demonstrated well in our earlier publications related to the C-3 functionalization of β-lactams.[24–30] Thus, it was envisaged that *cis*-3-chloro-3-phenyl/benzylseleno-β-lactams (**5a,f**) could serve as appropriate β-lactam carbocation

equivalents for the synthesis of *cis*-3-alkoxy-3-phenyl/benzylseleno-β-lactams (**6**), *C*-3 monosubstituted seleno-β-lactams (**7**,**10**) and disubstituted β-lactams (**8**,**9**).

The β-lactam carbocation equivalents **5a**,**f** were prepared by highly stereoselective chlorination of their corresponding azetidin-2-ones **3a**,**f** using *N*-chlorosuccinimide (NCS) with catalytic amount of AIBN in carbon tetrachloride according to the reported procedure[27] (Scheme 2, Table 2). The yield of 3-chloro-3-benzylseleno-β-lactam **5f** was found to be much lower than the corresponding 3-chloro-3-phenylseleno-β-lactam **5a**. In case of **5f** no formation of product from possible chlorination at the benzylic carbon was observed by ^{1}H NMR spectroscopy. The TLC analysis did show the formation of highly polar product(s), which upon purification by chromatography yielded a complex mixture, unidentifiable by spectroscopic techniques. Keeping in mind the poor performance of this reaction, benzoylperoxide as a radical initiator as well as the sulfuryl chloride (SO_2Cl_2) as a chlorinating reagent was also tried. It was observed that AIBN is useful as a catalyst and was necessary to produce the clean 3-chloro-3-benzylseleno-β-lactam **5f**.



Scheme 2. Synthesis of *cis*-3-chloro-3-phenyl/benzylselenoazetidin-2-ones **5a**,**f**.

Table 2. *cis*-3-Chloro-3-phenyl/benzylselenoazetidin-2-ones **5a**,**f**

Entry	R^1	R^2	R^3	Product **5** (% yield)[a]
1	C_6H_5	C_6H_5	4-(MeO)C_6H_4	**5a** (72)
2	$CH_2C_6H_5$	C_6H_5	4-(MeO)C_6H_4	**5f** (24)

[a] Yields quoted are for the isolated products.

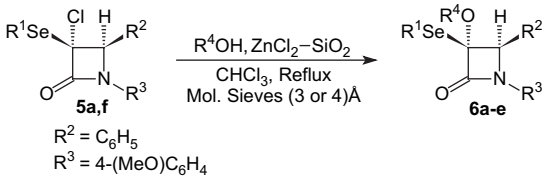
The structures of these selenoazetidin-2-ones **5a**,**f** were confirmed from IR, ^{1}H NMR, ^{13}C NMR, ^{77}Se NMR and MS spectroscopic analyses. The assignment of α-stereochemistry to chlorine atom at C-3 was made on the basis of correlation of ^{1}H and ^{13}C NMR data of these β-lactams (**5a**,**f**) with that of 3α-chloro-3-phenylthioazetidin-2-ones, whose stereochemistry has already been established by X-ray crystallographic studies.[26]

2.3. *cis*-3-Alkoxy-3-phenyl/benzylselenoazetidin-2-ones

Recently, we have reported the facile stereoselective synthesis of *cis*-3-alkoxy-3-phenyl/benzylthio-β-lactams[28] and the results of this study encouraged us to examine the applicability of this approach for the synthesis of selenium analogues. Moreover, the discoveries of 2-isocephem,[36] 2-oxa-isocephem,[36] 7-methoxycephalosporins,[37] PS-5,[38] possessing an alkoxy group at C-3 position of azetidin-2-ones and a class of novel 3-methoxy-β-lactams exhibiting antitumor activity[9] have renewed the interest in the synthesis of 3-alkoxy-3-phenyl/benzylseleno-β-lactams.

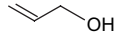
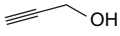
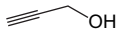
To the best of our knowledge, no such monocyclic *cis*-3-alkoxy-3-phenyl/benzylseleno-β-lactams have been reported so far. However, Fujita et al.[39] have described the synthesis of selenapenams having methylseleno on the ring juncture carbon atom with methoxy group at C-3 position and Turos et al.[40] have reported the synthesis of 3-methoxy-1-phenylseleno-β-lactam by the reaction of 3-methoxy-β-lactam with *n*-BuLi and methyl phenylselenosulfonate.

Thus, *cis*-3-alkoxy-3-phenyl/benzylseleno-β-lactams **6a–e** were synthesized successfully by treating **5a**,**f** with various alcohols in silica gel mediated by Lewis acid such as $ZnCl_2$ in refluxing chloroform according to the procedure reported for the synthesis of *cis*-3-alkoxy-3-phenyl/benzylthio-β-lactams in our earlier publication[28] in good yields (Scheme 3, Table 3).



Scheme 3. Synthesis of *cis*-3-alkoxy-3-phenyl/benzylselenoazetidin-2-ones **6a–e**.

Table 3. *cis*-3-Alkoxy-3-phenyl/benzylselenoazetidin-2-ones **6a–e**

Entry	**5**	R^4OH (Nucleophiles)	R^1	Product **6** (% yield)[a]
1	**5a**	MeOH	C_6H_5	**6a** (85)
2	**5a**	EtOH	C_6H_5	**6b** (74)
3	**5a**		C_6H_5	**6c** (76)
4	**5a**		C_6H_5	**6d** (61)
5	**5f**		$CH_2C_6H_5$	**6e** (38)

[a] Yields quoted are for the isolated products.

The structures of these selenoazetidin-2-ones **6a–e** were established on the basis of their spectral data (IR, ^{1}H NMR, ^{13}C NMR, DEPT-135 ^{13}C NMR and MS). The stereochemistry at C-3 of **6a–e** was established through single crystal X-ray crystallographic studies of **6a** (Fig. 3).[41]

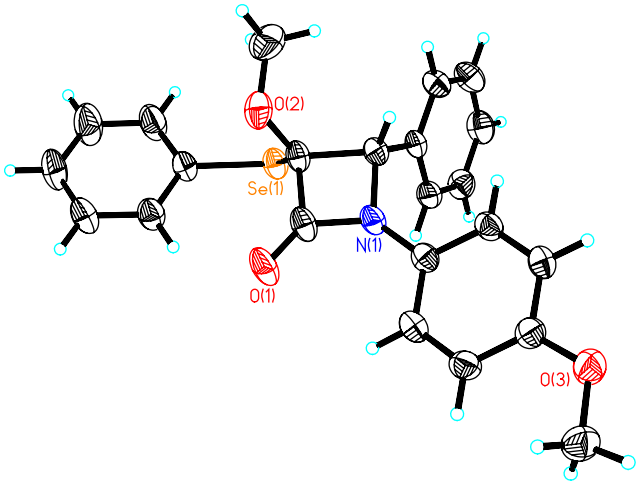


Figure 3. ORTEP diagram for compound **6a**.

2.4. *C*-3 Substituted selenoazetidin-2-ones

The synthesis of monocyclic β-lactams, bearing a varied array of appendages at C-3 and C-4 continues to be an area of active research. Turos et al.,[40] have reported the introduction of suitable electrophiles in the α-position of monocyclic seleno-β-lactams using *N*-benzyl-α-phenylselenyl-β-glycine, *t*-BuLi and alkyl halides. We envisaged further functionalization of *cis*-3-chloro-3-phenyl/benzylseleno-β-lactams employing Lewis acid catalyzed substitution reactions with different active aromatic and aliphatic substrates to afford a variety of *C*-3 substituted seleno-β-lactams.

Initial studies were carried out by reacting *cis*-3-chloro-3-phenylseleno-β-lactam **5a** with allyltrimethylsilane as the active aliphatic substrate in the presence of 1 equiv of $SnCl_4$ in dichloromethane at 0 °C. This reaction resulted in the formation of *trans*-3-chloro-3-phenylseleno-β-lactam (**10a**). However, when the reaction was performed with 3 equiv of $TiCl_4$, only monosubstituted product **7a** was formed in excellent yield. This reaction using 3 equiv of $SnCl_4$ gave only the same product, i.e., **10a**. To probe further into the underlying features, governing the C-3 functionalization of seleno-β-lactams, the reaction was studied with different active aromatic substrates. Most of the activated aromatic substrates on reaction with **5a** in the presence of $SnCl_4$ or $TiCl_4$ at 0 °C produced mainly 3,3-disubstituted azetidin-2-ones **8c**–**e**, along with the varying amount of 3,3-bis(arylseleno)azetidin-2-ones **9a** and *trans*-3-chloroselenoazetidin-2-one **10a**. However, when 2′-methoxynaphthyl ether was used, the reaction surprisingly produced exclusively monosubstituted product **7b** (Table 4, entry 3) (Scheme 4).

The structures of *C*-3 substituted selenoazetidin-2-ones were confirmed from IR, ^{1}H NMR, ^{13}C NMR, ^{77}Se NMR and MS spectroscopic analyses. The stereochemistry at C-3 of the monosubstituted allylseleno-β-lactam **7a** was confirmed through its single crystal X-ray crystallographic studies (Fig. 4).[42]

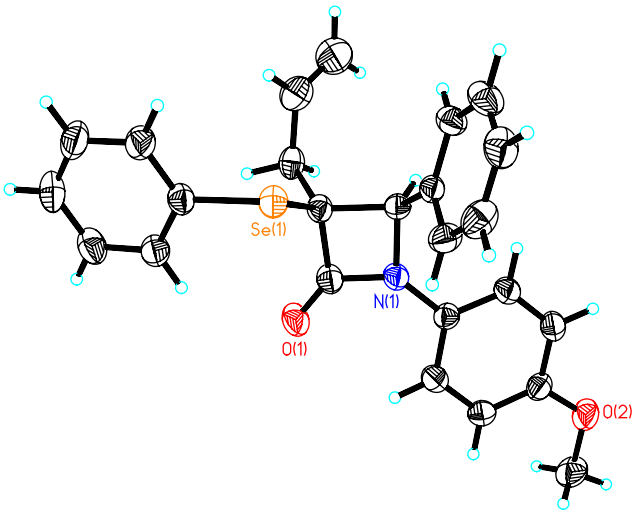
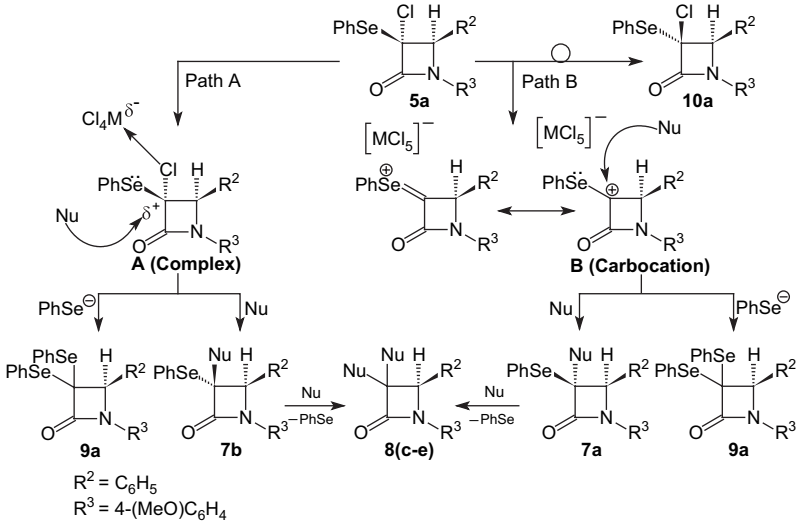


Figure 4. ORTEP diagram for compound **7a**.

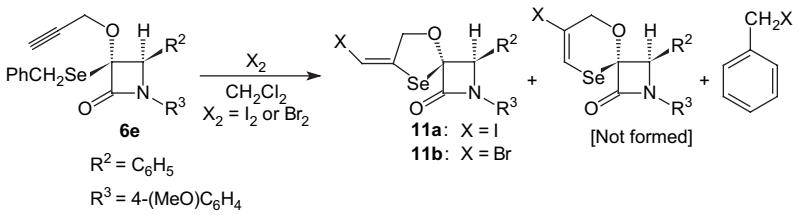
Table 4. Reaction of **5a** with various active aliphatic and aromatic substrates

Entry	Substrate (Nu)	Lewis acid	Products of type (% yield)[a]			
			7	**8**	**9**	**10**
1	CH_2=$CHCH_2SiMe_3$	$SnCl_4$	—	—	—	**10a** (82)
2	CH_2=$CHCH_2SiMe_3$	$TiCl_4$	**7a** (86)	—	—	—
3	2-(MeO)$C_{10}H_6$	$TiCl_4$ or $SnCl_4$	**7b** (42)	—	—	—
4	C_6H_5OMe	$TiCl_4$ or $SnCl_4$	—	**8c** (45)	**9a** (16)	**10a** (08)
5	1,4-$(MeO)_2C_6H_4$	$TiCl_4$ or $SnCl_4$	—	**8d** (44)	**9a** (20)	**10a** (05)
6	1,3-$(MeO)_2C_6H_4$	$TiCl_4$ or $SnCl_4$	—	**8e** (35)	**9a** (15)	**10a** (07)

[a] Yields quoted are for the isolated products.



Scheme 4. Synthesis of *C*-3 substituted selenoazetidin-2-ones.



Scheme 5. Synthesis of spiro selenoazetidin-2-ones.

The spatial juxtaposition of the C4–H and the new substituent at C-3 in case of **7b** was assigned trans on the basis of correlation of ^{1}H and ^{13}C NMR data of **7b** with that of *cis*-3-(2′-methoxynaphthyl)-3-phenylthioazetidin-2-one, whose stereochemistry has been established by X-ray crystallographic studies.[27] These nucleophilic substitution reactions are believed to proceed via a similar plausible mechanism as reported for nucleophilic substitution reaction of phenylthio- and benzylthio-β-lactam.[27,29]

The structure of the product **10a** was established from spectroscopic studies. The ^{1}H NMR spectral analysis of the compound **10a** showed the C4–H proton resonating upfield at δ 5.10 ppm as compared to substrate **5a**, which exhibits a C4–H proton resonance at δ 5.35 ppm. There were also small changes in the positions of the remaining proton resonances in the spectrum, compared to the resonances of substrate **5a**. The ^{13}C NMR spectrum also showed a similar upward shift in resonance of both the C-3 and C-4 carbons appearing at δ 69.82 and 69.27 ppm, respectively, in comparison to substrate **5a** (δ 71.38 and 71.10 ppm). The IR spectrum confirmed the presence of β-lactam carbonyl (1701 cm^{-1}) in it. The compound **10a** with an R_f very close to **5a** melts at 146–147 °C as compared to **5a** at 154–156 °C. All the spectroscopic information given above is consistent with an epimerization at C-3[26] of seleno-β-lactam, resulting in isomerization of **5a**.

2.5. Spiro selenoazetidin-2-ones

The ever-increasing applications of azetidin-2-ones have triggered a renewed interest in the spiro-β-lactams, as they behave as β-turn mimetics[43] and β-turn nucleators,[44] they are also precursors of α,α-disubstituted β-amino acids,[45] good inhibitors of both poliovirus and human rhinovirus *C*3-proteinase[46] and exhibit cholesterol absorption inhibiting activity.[47]

Our recent studies directed towards the synthesis of spiro-β-lactams[30] prompted us to examine the synthesis of spiro seleno-β-lactams. Moreover, quite a few strategies for the synthesis of bicyclic seleno-β-lactams, such as, selenapenems have been described in literature[22,23,39,48] and no reports on the synthesis of spiro seleno-β-lactams have appeared so far. Thus, it was proposed to study the synthesis of spiro seleno-β-lactams by halogen mediated intraselenyl cyclization of a *cis*-3-(prop-2-ynyloxy)-3-benzylseleno-β-lactams.

Initially, **6e** was exposed to 1 equiv of iodine in dry dichloromethane at room temperature according to the procedure reported earlier.[30] The reaction resulted in the exclusive formation of a five-membered ring, affording spiro seleno-β-lactam 2-(4′-methoxyphenyl)-3-phenyl-5-oxa-7-iodomethylene-8-seleno-2-azaspiro[3.4]octan-1-one **11a** in quantitative yield (Scheme 5). Furthermore, when this reaction was performed with bromine as the halogenating reagent, similar products were obtained but with lower yields (Table 5).

Table 5. Spiro selenoazetidin-2-ones **11a**,**b**

Entry	Substrate **6**	X_2	Product **11**	Yield[a] (%)
1	**6e**	I_2	**11a**	85
2	**6e**	Br_2	**11b**	61

[a] Yields quoted are for the isolated products.

The structures of spiro selenoazetidin-2-ones **11a**,**b** were established by spectroscopic means such as IR, ^{1}H NMR, ^{13}C NMR, DEPT-135 ^{13}C NMR and MS. However, the exclusive formation of the five-membered ring cycloadducts and stereochemistry at the *C*-3 spiro junction were assigned on the basis of correlation of ^{1}H and ^{13}C NMR data of these β-lactams **11a**,**b** with that of spiro thioazetidin-2-ones, whose stereochemistry has already been established by X-ray crystallographic studies.[30] The exclusive formation of five-membered ring spiro seleno-β-lactams via a 5-*exo* closure process, instead of 6-*endo* closure may be attributed to the kinetic preference and can be rationalized on the basis of similar mechanism as depicted for spiro thioazetidin-2-ones.[30]

3. Conclusion

In conclusion, a successful attempt has been made to synthesize novel 3-phenyl/benzylseleno-β-lactams from their corresponding selenoethanoic acids and appropriate Schiff's bases using $POCl_3$ and Et_3N in refluxing benzene. In addition, we have shown that *cis*-3-chloro-3-phenyl/benzylseleno-β-lactams provide an easy access to *cis*-3-alkoxy-3-phenyl/benzylseleno-β-lactams, *C*-3 monosubstituted seleno-β-lactams and disubstituted β-lactams. Moreover, a new class of spiro seleno-β-lactams has been accessed through halogen mediated intraselenyl cyclization reactions.

4. Experimental

4.1. General

^{1}H, ^{13}C and ^{77}Se NMR spectra were recorded at 300, 75 and 57 MHz, respectively, in $CDCl_3$ solution using JEOL 300 MHz NMR spectrometers. Chemical shifts are given in parts per million relative to tetramethylsilane as an

internal standard (δ=0 ppm) for ^{1}H NMR, $CDCl_3$ (δ=77.0 ppm) for ^{13}C NMR and $SeMe_2$ (δ=0 ppm) for ^{77}Se spectra. IR spectra were taken on an FTIR spectrophotometer and are reported in cm^{-1}. MS (EI) spectra were recorded on Shimadzu GCMS-QT 5000. The elemental analysis (C, H, N) was carried out using a PERKIN–ELMER 2400 elemental analyzer. Column chromatography was performed using Merck Silica Gel (100–200 mesh). Thin-layer chromatography (TLC) was performed using Merck Silica Gel G. For visualization, TLC plates were stained with iodine vapours. Melting points are uncorrected. All commercially available compounds/reagents were used without further purification. Dichloromethane, chloroform and carbon tetrachloride distilled over P_2O_5 were redistilled over CaH_2 before use. Crystallographic data (excluding structural factors) of compounds **3a**,[35] **6a**[41] and **7a**[42] in CIF format have been deposited at 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]. All other relevant information regarding the data and supplementary publication CCDC number is presented in respective references.

4.2. General procedure for the synthesis of *trans*- and *cis*-3-phenyl/benzylseleno-β-lactams (3a–g and 4a,b,e)

Compounds **3a**–**g** and **4a**,**b**,**e** were prepared by the procedure as described for the synthesis of *trans*-3-phenyl/benzylthio-β-lactams[27] in the cited reference, starting from 2-phenyl/benzylselenoethanoic acids.

4.2.1. *trans*-1-(4′-Methoxyphenyl)-3-phenylseleno-4-phenylazetidin-2-one (3a). Yellowish-white blocks (0.740 g, 75%); mp 126–127 °C. [Found: C, 64.66; H, 4.63; N, 3.39. $C_{22}H_{19}NO_2Se$ requires: C, 64.71; H, 4.69; N, 3.43%.] R_f (10% EtOAc/hexane) 0.52; IR (cm^{-1}, KBr): 1734 (C=O); δ_H (300 MHz, $CDCl_3$) 7.65–6.65 (14H, m, Ph), 4.68 (1H, d, *J* 2.4 Hz, C3–*H*), 4.21 (1H, d, *J* 2.4 Hz, C4–*H*), 3.69 (3H, s, OCH_3); δ_C (75 MHz, $CDCl_3$) 162.6, 156.1, 137.1, 135.3, 131.0, 129.2, 128.7, 128.4, 126.8, 125.9, 118.3, 114.3, 62.9, 55.1, 53.3; δ_{Se} (57 MHz, $CDCl_3$) 353.2.

4.2.2. *trans*-1-(4′-Methoxyphenyl)-3-phenylseleno-4-(4′-methoxyphenyl)azetidin-2-one (3b). Yellow oil (0.710 g, 78%). [Found: C, 62.91; H, 4.74; N, 3.11. $C_{23}H_{21}NO_3Se$ requires: C, 63.02; H, 4.83; N, 3.19%.] R_f (10% EtOAc/hexane) 0.48; IR (cm^{-1}, $CHCl_3$): 1747 (C=O); δ_H (300 MHz, $CDCl_3$) 7.56–6.68 (13H, m, Ph), 4.58 (1H, d, *J* 1.8 Hz, C3–*H*), 4.13 (1H, d, *J* 1.8 Hz, C4–*H*), 3.69 (3H, s, OCH_3), 3.61 (3H, s, OCH_3); δ_C (75 MHz, $CDCl_3$) 163.1, 159.9, 156.0, 135.1, 130.9, 129.2, 128.6, 128.4, 127.3, 126.7, 118.3, 114.5, 114.2, 62.8, 55.1, 55.0, 53.3; δ_{Se} (57 MHz, $CDCl_3$) 341.7.

4.2.3. *trans*-1-(4′-Methoxyphenyl)-3-phenylseleno-4-(1′-methyl-2′-phenylvinyl)azetidin-2-one (3c). Yellowish-white solid (0.720 g, 81%); mp 99–100 °C. [Found: C, 66.89; H, 5.08; N, 3.04. $C_{25}H_{23}NO_2Se$ requires: C, 66.96; H, 5.17; N, 3.12%.] R_f (10% EtOAc/hexane) 0.47; IR (cm^{-1}, KBr): 1746 (C=O), 1668 (C=C); δ_H (300 MHz, $CDCl_3$) 7.56–6.57 (15H, m, Ph and –(CH_3)C=C*H*Ph), 4.50 (1H, d, *J* 1.8 Hz, C3–*H*), 4.11 (1H, d, *J* 1.8 Hz, C4–*H*), 3.61 (3H, s, OCH_3), 2.25 (3H, s, CH_3); δ_C (75 MHz, $CDCl_3$) 162.8, 156.1, 138.4, 135.2, 134.0, 131.0, 129.8, 129.2, 128.4, 126.8, 125.9, 118.3, 114.2, 62.9, 55.1, 53.4, 21.3; δ_{Se} (57 MHz, $CDCl_3$) 334.8.

4.2.4. *trans*-1-Benzyl-3-phenylseleno-4-phenylazetidin-2-one (3d). Yellowish-white solid (0.840 g, 84%); mp 134–135 °C. [Found: C, 67.26; H, 4.82; N, 3.53. $C_{22}H_{19}NOSe$ requires: C, 67.35; H, 4.88; N, 3.57%.] R_f (10% EtOAc/hexane) 0.54; IR (cm^{-1}, KBr): 1762 (C=O); δ_H (300 MHz, $CDCl_3$) 7.58–6.57 (15H, m, Ph), 4.67 (1H, d, *J* 1.5 Hz, C3–*H*), 4.07 (2H, s, CH_2Ph), 3.57 (1H, d, *J* 1.5 Hz, C4–*H*); δ_C (75 MHz, $CDCl_3$) 165.9, 136.5, 136.3, 134.6, 129.3, 129.1, 128.8, 128.7, 128.6, 128.1, 127.4, 126.5, 125.7, 62.1, 53.5, 44.6; δ_{Se} (57 MHz, $CDCl_3$) 327.5.

4.2.5. *trans*-1-(4′-Chlorophenyl)-3-phenylseleno-4-phenylazetidin-2-one (3e). Yellow oil (0.560 g, 69%). [Found: C, 61.06; H, 3.88; N, 3.33. $C_{21}H_{16}ClNOSe$ requires: C, 61.11; H, 3.91; N, 3.39%.] R_f (10% EtOAc/hexane) 0.53; IR (cm^{-1}, $CHCl_3$): 1752 (C=O); δ_H (300 MHz, $CDCl_3$) 7.59–6.99 (14H, m, Ph), 4.64 (1H, d, *J* 2.1 Hz, C3–*H*), 4.18 (1H, d, *J* 2.1 Hz, C4–*H*); δ_C (75 MHz, $CDCl_3$) 163.3, 136.5, 135.9, 135.6, 131.6, 129.3, 129.2, 129.0, 128.8, 125.9, 118.1, 63.0, 53.4; δ_{Se} (57 MHz, $CDCl_3$) 347.2.

4.2.6. *trans*-1-(4′-Methoxyphenyl)-3-benzylseleno-4-phenylazetidin-2-one (3f). Yellowish-white solid (0.740 g, 74%); mp 116–117 °C. [Found: C, 65.41; H, 4.92; N, 3.22. $C_{23}H_{21}NO_2Se$ requires: C, 65.40; H, 5.01; N, 3.32%.] R_f (10% EtOAc/hexane) 0.49; IR (cm^{-1}, KBr): 1753 (C=O); δ_H (300 MHz, $CDCl_3$) 7.31–6.72 (14H, m, Ph), 4.51 (1H, d, *J* 1.8 Hz, C3–*H*), 4.03 (2H, s, CH_2Se), 4.00 (1H, d, *J* 1.8 Hz, C4–*H*), 3.74 (3H, s, OCH_3); δ_C (75 MHz, $CDCl_3$) 163.0, 156.2, 138.3, 137.2, 131.1, 129.2, 128.7, 128.6, 127.0, 125.9, 117.4, 114.3, 65.5, 55.2, 50.2, 27.3; δ_{Se} (57 MHz, $CDCl_3$) 340.4.

4.2.7. *trans*-1-Benzyl-3-benzylseleno-4-phenylazetidin-2-one (3g). Yellow oil (0.737 g, 71%). [Found: C, 67.93; H, 5.16; N, 3.40. $C_{23}H_{21}NOSe$ requires: C, 67.98; H, 5.21; N, 3.45%.] R_f (10% EtOAc/hexane) 0.51; IR (cm^{-1}, $CHCl_3$): 1758 (C=O); δ_H (300 MHz, $CDCl_3$) 7.24–7.02 (15H, m, Ph), 4.74 (1H, d, *J* 14.7 Hz, CH_aH_bPh), 4.09 (1H, d, *J* 2.1 Hz, C3–*H*), 3.96 (1H, d, *J* 11.4 Hz, CH_aH_bSe), 3.84 (1H, d, *J* 2.1 Hz, C4–*H*), 3.71 (1H, d, *J* 11.4 Hz, CH_aH_bSe), 3.70 (1H, d, *J* 14.7 Hz, CH_aH_bPh); δ_C (75 MHz, $CDCl_3$) 166.5, 138.0, 136.8, 135.2, 129.0 (2), 128.7, 128.6, 127.8, 126.9, 126.5, 62.9, 49.7, 44.9, 26.8; δ_{Se} (57 MHz, $CDCl_3$) 352.3.

4.2.8. *cis*-1-(4′-Methoxyphenyl)-3-phenylseleno-4-phenylazetidin-2-one (4a). White solid (0.110 g, 11%); mp 139–140 °C. [Found: C, 64.63; H, 4.60; N, 3.34. $C_{22}H_{19}NO_2Se$ requires: C, 64.71; H, 4.69; N, 3.43%.] R_f (10% EtOAc/hexane) 0.50; IR (cm^{-1}, KBr): 1727 (C=O); δ_H (300 MHz, $CDCl_3$) 7.55–6.76 (14H, m, Ph), 5.31 (1H, d, *J* 5.7 Hz, C3–*H*), 4.93 (1H, d, *J* 5.7 Hz, C4–*H*), 3.77 (3H, s, OCH_3); δ_C (75 MHz, $CDCl_3$) 164.1, 156.2, 134.9, 134.1, 131.1, 129.1, 128.9, 128.6, 127.6, 127.2, 118.4, 114.4, 59.1, 55.2, 52.3; δ_{Se} (57 MHz, $CDCl_3$) 388.9.

4.2.9. *cis*-1-(4′-Methoxyphenyl)-3-phenylseleno-4-(4′-methoxyphenyl)azetidin-2-one (4b). Yellow oil (0.050 g,

6%). [Found: C, 62.95; H, 4.76; N, 3.09. $C_{23}H_{21}NO_3Se$ requires: C, 63.02; H, 4.83; N, 3.19%.] R_f (10% EtOAc/hexane) 0.47; IR (cm^{-1}, $CHCl_3$): 1746 (C=O); δ_H (300 MHz, $CDCl_3$) 7.71–6.87 (13H, m, Ph), 5.20 (1H, d, *J* 6.0 Hz, C3–*H*), 4.12 (1H, d, *J* 6.0 Hz, C4–*H*), 3.80 (3H, s, OCH_3), 3.69 (3H, s, OCH_3); δ_C (75 MHz, $CDCl_3$) 165.0, 160.2, 156.3, 134.9, 131.8, 129.1, 128.9, 128.5, 127.6, 126.9, 118.4, 114.7, 114.4, 64.1, 55.4, 55.1, 53.8; δ_{Se} (57 MHz, $CDCl_3$) 374.1.

4.2.10. *cis*-1-(4′-Chlorophenyl)-3-phenylseleno-4-phenylazetidin-2-one (4e). Yellow oil (0.150 g, 18%). [Found: C, 61.02; H, 3.83; N, 3.30. $C_{21}H_{16}ClNOSe$ requires: C, 61.11; H, 3.91; N, 3.39%.] R_f (10% EtOAc/hexane) 0.52; IR (cm^{-1}, $CHCl_3$): 1745 (C=O); δ_H (300 MHz, $CDCl_3$) 7.99–7.05 (14H, m, Ph), 5.24 (1H, d, *J* 5.7 Hz, C3–*H*), 4.85 (1H, d, *J* 5.7 Hz, C4–*H*); δ_C (75 MHz, $CDCl_3$) 163.6, 136.6, 136.1, 135.9, 131.7, 129.4, 129.2, 128.9, 128.6, 126.3, 118.3, 63.7, 53.8; δ_{Se} (57 MHz, $CDCl_3$) 368.1.

4.3. General procedure for the synthesis of *cis*-3-chloro-3-phenyl/benzylseleno-β-lactams (5a,f)

Compounds **5a**,**f** were prepared by the procedure as described for the synthesis of *trans*-3-chloro-3-benzylthio-β-lactams[27] in the cited reference.

4.3.1. *cis*-1-(4′-Methoxyphenyl)-3-chloro-3-phenylseleno-4-phenylazetidin-2-one (5a). White solid (0.240 g, 72%); mp 154–156 °C. [Found: C, 59.64; H, 4.03; N, 3.09. $C_{22}H_{18}ClNO_2Se$ requires: C, 59.67; H, 4.10; N, 3.16%.] R_f (10% EtOAc/hexane) 0.54; IR (cm^{-1}, KBr): 1752 (C=O); δ_H (300 MHz, $CDCl_3$) 7.75–6.75 (14H, m, Ph), 5.35 (1H, s, C4–*H*), 3.74 (3H, s, OCH_3); δ_C (75 MHz, $CDCl_3$) 161.0, 156.7, 136.9, 132.6, 130.1, 129.7, 129.2, 128.8, 128.6, 127.8, 125.7, 119.0, 114.5, 71.3, 71.1, 55.2; δ_{Se} (57 MHz, $CDCl_3$) 498.1; *m*/*z* (EIMS) 443 [M (^{35}Cl, ^{80}Se)]$^+$(18%), 445 [M (^{37}Cl, ^{80}Se)]$^+$(6%), 211 [PhCH=NPh–OCH_3(4)]$^+$ (100%).

4.3.2. *cis*-1-(4′-Methoxyphenyl)-3-chloro-3-benzylseleno-4-phenylazetidin-2-one (5f). White solid (0.080 g, 24%); mp 123–124 °C. [Found: C, 60.42; H, 4.38; N, 3.01. $C_{23}H_{20}ClNO_2Se$ requires: C, 60.47; H, 4.41; N, 3.07%.] R_f (10% EtOAc/hexane) 0.51; IR (cm^{-1}, KBr): 1750 (C=O); δ_H (300 MHz, $CDCl_3$) 7.23–6.68 (14H, m, Ph), 5.24 (1H, s, C4–*H*), 4.39 (1H, d, *J* 10.5 Hz, CH_aH_bSe), 4.07 (1H, d, *J* 10.5 Hz, CH_aH_bSe), 3.65 (3H, s, OCH_3); δ_C (75 MHz, $CDCl_3$) 161.0, 156.7, 136.4, 133.5, 132.4, 130.2, 130.0, 129.5, 128.5, 127.5, 119.0, 114.4, 80.4, 71.2, 55.1, 29.7; δ_{Se} (57 MHz, $CDCl_3$) 505.6.

4.4. General procedure for the synthesis of *cis*-3-alkoxy-3-phenyl/benzylseleno-β-lactams (6a–e)

Compounds **6a–e** were prepared by the procedure as described for the synthesis of *cis*-3-alkoxy-3-phenyl/benzylthio-β-lactams[28] in the cited reference.

4.4.1. *cis*-1-(4′-Methoxyphenyl)-3-methoxy-3-phenylseleno-4-phenylazetidin-2-one (6a). Yellowish-white blocks (0.042 g, 85%); mp 139–140 °C. [Found: C, 62.96; H, 4.79; N, 3.11. $C_{23}H_{21}NO_3Se$ requires: C, 63.02; H, 4.83; N, 3.19%.] R_f (10% EtOAc/hexane) 0.51; IR (cm^{-1}, KBr): 1752 (C=O); δ_H (300 MHz, $CDCl_3$) 7.36–6.67 (14H, m, Ph), 5.02 (1H, s, C4–*H*), 3.69 (3H, s, OCH_3), 3.62 (3H, s, OCH_3); δ_C (75 MHz, $CDCl_3$) 162.2, 156.4, 135.1, 133.5, 130.5, 128.9, 128.6, 128.3, 127.9, 127.8, 126.3, 118.9, 114.4, 98.4, 68.0, 55.2, 54.4; δ_{Se} (57 MHz, $CDCl_3$) 376.2.

4.4.2. *cis*-1-(4′-Methoxyphenyl)-3-ethoxy-3-phenylseleno-4-phenylazetidin-2-one (6b). Yellowish-white blocks (0.038 g, 74%); mp 128–129 °C. [Found: C, 63.66; H, 5.09; N, 3.12. $C_{24}H_{23}NO_3Se$ requires: C, 63.72; H, 5.12; N, 3.10%.] R_f (10% EtOAc/hexane) 0.52; IR (cm^{-1}, KBr): 1754 (C=O); δ_H (300 MHz, $CDCl_3$) 7.39–6.64 (14H, m, Ph), 5.03 (1H, s, C4-*H*), 4.01 (1H, m, OCH_aH_b), 3.87 (1H, m, OCH_aH_b), 3.67 (3H, s, OCH_3), 1.15 (3H, t, *J* 7.2 Hz, CH_3); δ_C (75 MHz, $CDCl_3$) 162.6, 156.4, 135.2, 133.5, 130.4, 128.9, 128.6, 128.3, 127.8, 126.5, 118.9, 114.4, 97.3, 68.0, 63.0, 55.2, 14.9; δ_{Se} (57 MHz, $CDCl_3$) 394.5.

4.4.3. *cis*-1-(4′-Methoxyphenyl)-3-(prop-2-enyloxy)-3-phenylseleno-4-phenylazetidin-2-one (6c). White solid (0.040 g, 76%); mp 116–117 °C. [Found: C, 64.60; H, 4.94; N, 2.93. $C_{25}H_{23}NO_3Se$ requires: C, 64.65; H, 4.99; N, 3.02%.] R_f (10% EtOAc/hexane) 0.53; IR (cm^{-1}, KBr): 1748 (C=O), 1583 (C=C); δ_H (300 MHz, $CDCl_3$) 7.36–6.65 (14H, m, Ph), 5.92 (1H, m, H_2C=C*H*–), 5.24 (1H, m, H_bH_aCO), 5.12 (1H, m, H_bH_aCO), 5.07 (1H, s, C4–*H*), 4.49 (1H, m, H_bH_aC=CH–), 4.37 (1H, m, H_bH_aC=CH–), 3.66 (3H, s, OCH_3); δ_C (75 MHz, $CDCl_3$) (DEPT-135) 162.4, 156.4, 135.3, 133.3, 133.0, 130.3 (+), 128.9 (+), 128.6 (+), 128.3 (+), 127.8 (+), 126.2, 119.0 (+), 117.8 (−), 114.4 (+), 97.3, 68.2 (−), 68.1 (+), 55.3 (+); δ_{Se} (57 MHz, $CDCl_3$) 388.2; *m*/*z* (EIMS) 465 [M (^{80}Se)]$^+$ (0.69%), 41 [H_2C=CH–CH_2]$^+$ (100%).

4.4.4. *cis*-1-(4′-Methoxyphenyl)-3-(prop-2-ynyloxy)-3-phenylseleno-4-phenylazetidin-2-one (6d). Yellow oil (0.031 g, 61%). [Found: C, 64.89; H, 4.55; N, 2.99. $C_{25}H_{21}NO_3Se$ requires: C, 64.94; H, 4.58; N, 3.03%.] R_f (10% EtOAc/hexane) 0.52; IR (cm^{-1}, $CHCl_3$): 1756 (C=O); δ_H (300 MHz, $CDCl_3$) 7.36–6.66 (14H, m, Ph), 5.33 (1H, s, C4–*H*), 4.68 (1H, dd, *J* 2.4, 15.6 Hz, H_bH_aCO), 4.40 (1H, dd, *J* 2.4, 15.6 Hz, H_bH_aCO), 3.67 (3H, s, OCH_3), 2.46 (1H, t, *J* 2.4 Hz, *H*C≡); δ_C (75 MHz, $CDCl_3$) (DEPT-135) 161.9, 156.3, 135.2, 133.2, 130.2 (+), 129.6, 129.0 (+), 128.8 (+), 128.3 (+), 128.1 (+), 127.9 (+), 125.7 (+), 119.0 (+), 114.4 (+), 97.6, 79.2 (+), 75.7 (+), 67.7 (+), 55.3 (+), 55.1 (−); δ_{Se} (57 MHz, $CDCl_3$) 391.3.

4.4.5. *cis*-1-(4′-Methoxyphenyl)-3-(prop-2-ynyloxy)-3-benzylseleno-4-phenylazetidin-2-one (6e). Yellow oil (0.020 g, 38%). [Found: C, 65.49; H, 4.79; N, 2.87. $C_{26}H_{23}NO_3Se$ requires: C, 65.55; H, 4.87; N, 2.94%.] R_f (10% EtOAc/hexane) 0.49; IR (cm^{-1}, $CHCl_3$): 1751 (C=O); δ_H (300 MHz, $CDCl_3$) 7.38–6.79 (14H, m, Ph), 5.44 (1H, s, C4–*H*), 4.58 (1H, dd, *J* 2.4, 15.6 Hz, H_bH_aCO), 4.39 (1H, dd, *J* 2.4, 15.6 Hz, H_bH_aCO), 4.14 (1H, d, *J* 11.4 Hz, CH_aH_bSe), 3.95 (1H, d, *J* 11.4 Hz, CH_aH_bSe), 3.75 (3H, s, OCH_3), 2.59 (1H, t, *J* 2.4 Hz, *H*C≡); δ_C (75 MHz, $CDCl_3$) (DEPT-135) 162.3, 156.4, 138.5, 133.5,

130.5, 129.2, 129.0 (+), 128.5 (+), 128.4 (+), 127.7 (+), 118.9 (+), 114.4 (+), 98.2, 79.6 (+), 75.8 (+), 65.5 (+), 55.1 (+), 54.6 (−), 29.5 (−); δ_{Se} (57 MHz, $CDCl_3$) 398.4.

4.5. General procedure for the synthesis of *C*-3 substituted seleno-β-lactams (7–10)

Compounds **7a**,**b**, **8c**–**e**, **9a** and **10a** were prepared by the procedure as described for the synthesis of *C*-3 substituted thioazetidin-2-ones[27] in the cited reference. The spectroscopic data of compounds **8c**–**e**[27] were also reported in the cited reference.

4.5.1. *trans*-1-(4′-Methoxyphenyl)-3-allyl-3-phenylseleno-4-phenylazetidin-2-one (7a). Yellowish-white blocks (0.044 g, 86%); mp 119–120 °C. [Found: C, 66.91; H, 5.14; N, 3.06. $C_{25}H_{23}NO_2Se$ requires: C, 66.96; H, 5.17; N, 3.12%.] R_f (10% EtOAc/hexane) 0.56; IR (cm^{-1}, KBr): 1752 (C═O); δ_H (300 MHz, $CDCl_3$) 7.67–6.71 (14H, m, Ph), 5.93 (1H, m, H_2C═C*H*–CH_2–), 5.22 (1H, br s, H_2C═CH–CH_2–), 5.18 (1H, m, H_2C═CH–CH_2–), 4.99 (1H, s, C4–*H*), 3.72 (3H, s, OCH_3), 2.60 (2H, d, *J* 7.3 Hz, H_2C═CH–CH_2–); δ_C (75 MHz, $CDCl_3$) 167.1, 136.9, 133.5, 131.0, 128.9, 128.6, 128.3, 127.6, 119.3, 118.5, 114.4, 63.0, 61.3, 55.3, 38.5; δ_{Se} (57 MHz, $CDCl_3$) 382.7.

4.5.2. *cis*-1-(4′-Methoxyphenyl)-3-(2′-methoxynaphthyl)-3-phenylseleno-4-phenylazetidin-2-one (7b). Colourless oil (0.025 g, 42%). [Found: C, 70.11; H, 4.73; N, 2.39. $C_{33}H_{27}NO_3Se$ requires: C, 70.20; H, 4.82; N, 2.48%.] R_f (10% EtOAc/hexane) 0.38; IR (cm^{-1}, $CHCl_3$): 1753 (C═O); δ_H (300 MHz, $CDCl_3$) 7.35–6.67 (20H, m, Ph), 5.09 (1H, s, C4–*H*), 3.68 (3H, s, OCH_3), 3.56 (3H, s, OCH_3) (for one isomer) and 7.93–6.67 (20H, m, Ph), 5.13 (1H, s, C4–*H*), 3.87 (3H, s, OCH_3), 3.72 (3H, s, OCH_3) (for other isomer). The ^1H NMR spectrum showed it to be a mixture of two rotamers as evident from the appearance of two signals for C4–*H* and a downfield appearance of an aromatic proton; δ_{Se} (57 MHz, $CDCl_3$) 369.4.

4.5.3. 1-(4′-Methoxyphenyl)-3,3-bis(phenylseleno)-4-phenylazetidin-2-one (9a). White solid (0.010 g, 16%); mp 127–128 °C. [Found: C, 59.56; H, 3.54; N, 2.71. $C_{28}H_{23}NO_2Se_2$ requires: C, 59.69; H, 4.11; N, 2.48%.] R_f (10% EtOAc/hexane) 0.58; IR (cm^{-1}, KBr): 1744 (C═O); δ_H (300 MHz, $CDCl_3$) 7.75–6.61 (19H, m, Ph), 4.93 (1H, s, C4–*H*), 3.66 (3H, s, OCH_3); δ_C (75 MHz, $CDCl_3$) 161.7, 156.2, 137.1, 136.7, 133.8, 129.5, 129.2, 128.9, 128.7, 128.3, 127.7, 118.5, 114.2, 71.3, 66.8, 55.0; δ_{Se} (57 MHz, $CDCl_3$) 372.7; *m*/*z* (EIMS) 565 [M (^{80}Se)]$^+$ (1%), 211 [PhCH═NPh–OCH_3(4)]$^+$ (100%).

4.5.4. *trans*-1-(4′-Methoxyphenyl)-3-chloro-3-phenylseleno-4-phenylazetidin-2-one (10a). White needles (0.041 g, 82%); mp 146–147 °C. [Found: C, 59.64; H, 4.03; N, 3.09. $C_{22}H_{18}ClNO_2Se$ requires: C, 59.67; H, 4.10; N, 3.16%.] R_f (10% EtOAc/hexane) 0.55; IR (cm^{-1}, KBr): 1749 (C═O); δ_H (300 MHz, $CDCl_3$) 7.75–6.75 (14H, m, Ph), 5.35 (1H, s, C4–*H*), 3.74 (3H, s, OCH_3); δ_C (75 MHz, $CDCl_3$) 160.6, 156.7, 137.1, 136.9, 133.1, 129.9, 129.4, 129.1, 128.8, 128.6, 127.7, 126.1, 118.8, 114.4, 69.8, 69.2, 55.2; δ_{Se} (57 MHz, $CDCl_3$) 551.1.

4.6. General procedure for the synthesis of spiro seleno-β-lactams (11a,b)

Compounds **11a**,**b** were prepared by the procedure as described for the synthesis of spiro thioazetidin-2-ones[30] in the cited reference.

4.6.1. 2-(4′-Methoxyphenyl)-3-phenyl-5-oxa-7-iodomethylene-8-seleno-2-aza-spiro[3.4]octan-1-one (11a). White solid (0.045 g, 85%); mp 124–125 °C. [Found: C, 44.49; H, 3.10; N, 2.69. $C_{19}H_{16}INO_3Se$ requires: C, 44.55; H, 3.15; N, 2.73%.] R_f (10% EtOAc/hexane) 0.51; IR (cm^{-1}, KBr): 1762 (C═O); δ_H (300 MHz, $CDCl_3$) 7.31–6.68 (9H, m, Ph), 5.78 (1H, t, *J* 2.4 Hz, IC*H*═), 5.13 (1H, s, C3–*H*), 4.82 (1H, dd, *J* 2.1, 13.5 Hz, CH_aH_bO), 4.68 (1H, dd, *J* 2.4, 13.5 Hz, CH_aH_bO), 3.67 (3H, s, OCH_3); δ_C (75 MHz, $CDCl_3$) (DEPT-135) 163.2, 156.7, 141.9, 135.6, 130.3 (−), 129.4 (+), 126.2 (+), 126.0 (+), 119.0 (+), 114.5 (+), 105.9, 67.0 (+), 59.9 (+), 55.1 (+); δ_{Se} (57 MHz, $CDCl_3$) 456.3; *m*/*z* (EIMS) 513 [M (^{80}Se)]$^+$ (8%), 211 [PhCH═NPh–OCH_3(4)]$^+$ (100%).

4.6.2. 2-(4′-Methoxyphenyl)-3-phenyl-5-oxa-7-bromomethylene-8-seleno-2-aza-spiro[3.4]octan-1-one (11b). White solid (0.030 g, 61%); mp 119–120 °C. [Found: C, 49.01; H, 3.51; N, 2.89. $C_{19}H_{16}BrNO_3Se$ requires: C, 49.06; H, 3.47; N, 3.01%.] R_f (10% EtOAc/hexane) 0.50; IR (cm^{-1}, KBr): 1763 (C═O); δ_H (300 MHz, $CDCl_3$) 7.26–6.60 (9H, m, Ph), 5.79 (1H, t, *J* 2.4 Hz, BrC*H*═), 5.17 (1H, s, C3–*H*), 4.68 (1H, dd, *J* 2.4, 13.5 Hz, CH_aH_bO), 4.55 (1H, dd, *J* 2.4, 13.5 Hz, CH_aH_bO), 3.73 (3H, s, OCH_3); δ_C (75 MHz, $CDCl_3$) 163.0, 156.2, 141.4, 135.8, 130.2, 129.1, 126.0, 125.9, 118.5, 114.1, 105.4, 66.9, 59.0, 55.4; δ_{Se} (57 MHz, $CDCl_3$) 478.9.

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35. Crystal data for **3a**: monoclinic; *C*2/*c*; a=16.1252(3) Å, b=10.0420(2) Å, c=23.2974(3) Å; α=90°, β=97.301(1)°, γ=90°; V=3741.94(11) Å^3; Z=8; ρ_{Calcd}=1.450 mg/m^3; μ(Mo Kα)=2.022 mm^{-1}; full matrix least-square on F^2; R_1=0.0310, wR_2=0.0805 for 3016 reflections [$I>2\sigma(I)$]; T=293(2) K; GOF=1.017. Crystallographic data (excluding structural factors) for the structure **3a** in this paper have been deposited at the Cambridge Crystallographic Data Centre as supplementary publication number CCDC 622152.
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41. Crystal data for **6a**: monoclinic; $P2_1/c$; a=12.8817(3) Å, b=10.1371(2) Å, c=16.6546(4) Å; α=90°, β=112.060(1)°, γ=90°; V=2015.59(8) Å^3; Z=4; ρ_{Calcd}=1.445 mg/m^3; μ(Mo Kα)=1.886 mm^{-1}; full matrix least-square on F^2;

R_1=0.0387, wR_2=0.0964 for 3195 reflections [$I>2\sigma(I)$]; T=293(2) K; GOF=1.026. Crystallographic data (excluding structural factors) for the structure **6a** in this paper have been deposited at the Cambridge Crystallographic Data Centre as supplementary publication number CCDC 622153.

42. Crystal data for **7a**: monoclinic; $P2_1/n$; a=12.6539(3) Å, b=10.5318(2) Å, c=17.0804(4) Å; α=90°, β=110.2920(10)°, γ=90°; V=2135.00(8) Å^3; Z=4; ρ_{Calcd}=1.395 mg/m^3; μ(Mo Kα)=1.779 mm^{-1}; full matrix least-square on F^2; R_1=0.0331, wR_2=0.0817 for 3358 reflections [$I>2\sigma(I)$]; T=293(2) K; GOF=1.011. Crystallographic data (excluding structure factors) for the structure **7a** in this paper have been deposited at the Cambridge Crystallographic Data Centre as supplementary publication number CCDC 622154.
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