Synthesis of selenium-containing bicyclic β-lactams *via* alkene metathesis†

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Received 9th February 2009, Accepted 26th March 2009
First published as an Advance Article on the web 28th April 2009
DOI: 10.1039/b902698c

The stereoselective insertion of allyl-seleno moieties at the *C*(4) position of azetidinones and further ring-closing metathesis afforded novel selenium-containing bicyclic β-lactams.

Introduction

The β-lactam (2-azetidinone) skeleton is the key structural element of the most widely employed class of antibacterial agents, the β-lactam antibiotics.[1] However, very few reports are available in the literature for the synthesis of selenium-containing bicyclic β-lactams due to difficulties involved in their preparation.[2] Recently, we have reported the trimethylsilylethyl (TSE)-protection[3] and iodocyclization approaches[4] for the synthesis of a variety of selenium-containing β-lactams. In continuation of the above investigations, we were interested in finding a new synthetic strategy for the preparation of novel bicyclic β-lactams. The generation of β-lactam arrays by ring-closing metathesis (RCM) has received considerable attention over the past few years (Fig. 1).[5] However, it is surprising to note that the RCM of allyl-seleno compounds has never been described thus far.[6] We describe herein, for the first time, RCM of allyl-seleno compounds in the formation of selenium-containing bicyclic β-lactams.

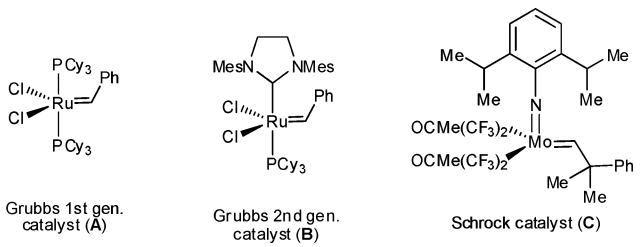
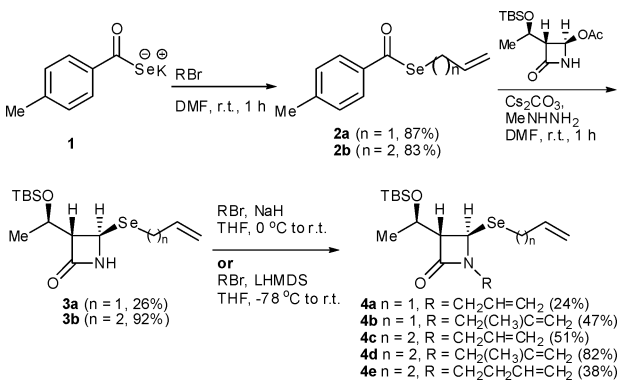


Fig. 1 Ruthenium and molybdenum carbene complexes used in ring-closing metathesis (RCM) reactions.

Results and discussion

The most difficult task in the present synthesis was the insertion of the alkene-seleno moieties at the *C*(4) position of the azetidinones. For this we considered two approaches. Recently, a novel method for seleno-glycosidation using *p*-methylselenobenzoate **1** was reported.[7] The method features the *in situ* production of glycosyl selenolate anion from the corresponding *p*-toluoylselenoglycoside resulting from the chemoselective cleavage of the C–Se bond by piperazine. The glycosyl selenolate anion can react with various electrophilic coupling partners in high yields, with complete retention of stereochemistry. Inspired by the chemistry of this method, we have designed novel selenating reagents **2a** and **2b** as depicted in Scheme 1 for the first approach. The treatment of potassium *p*-methylselenobenzoate **1**[7] with allyl bromide or 4-bromo-1-butene resulted in the formation of the novel selenating reagents **2a** or **2b**, respectively (Scheme 1). These reagents have the carbonyl carbon as the reactive site and should be susceptible to nucleophilic attack by amine, thereby producing alkeneselenolate anion. This anion is expected to react with electrophilic sites, allowing the incorporation of the alkene-seleno moiety onto the β-lactam skeleton.



Scheme 1 Synthesis of selenating reagents **2** and key intermediates **4**.

The reaction with commercially available, optically pure, 4-acetoxyazetidinone, was studied to find applications for the newly synthesized selenating reagents **2a** and **2b**. The treatment of selenating reagents **2a** or **2b** with commercially available, optically pure, 4-acetoxyazetidinone resulted in the formation of the corresponding previously unknown key intermediates **3a** or **3b** having alkene-seleno moieties at the *C*(4) position of the azetidinones with complete retention of configuration (Scheme 1). The relative configuration of **3a** or **3b** was concluded based on the coupling constant between protons C-3 and C-4 ($J_{H3\text{-}H4}$ = 2.3 Hz). This is in agreement with those of similar compounds in the literature.[3,4,8] Subsequent treatment of **3a** or **3b** with either sodium hydride in THF at 0 °C or lithium hexamethyldisilazide (LHMDS) in THF at −78 °C followed by an activated electrophile afforded the corresponding previously unknown key intermediates (**4a–4e**) in 24–82% yields (Scheme 1).

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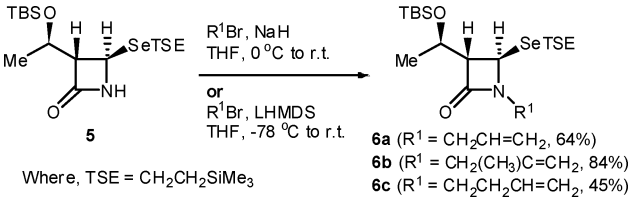
† Electronic supplementary information (ESI) available: Experimental details for the synthesis and ^{1}H and ^{13}C NMR spectra of compounds. See DOI: 10.1039/b902698c

Recently, we have shown that compound **5** is an important starting material for the synthesis of a variety of selenium-containing bicyclic β-lactams.[3] For the second approach, it was considered that the compound **5** could be an important starting material for the synthesis of the variety of key intermediates **4** *via* compounds **6**. For this the *N*-alkylation of the compound **5** was carried out with alkene bromides either with sodium hydride in THF at 0 °C or LHMDS in THF at −78 °C to afford the corresponding *N*-alkylated compounds **6a–6c** (Scheme 2).



Scheme 2

Next, deprotection of the TSE-group of **6a-6c** followed by *in situ* alkylation of the selenolate anion was tried for the synthesis of key intermediates **4** (Table 1). After screening of several reaction conditions (for details see the ESI†), we found that the treatment of **6a–6c** with 2.5 equiv. of TBAF resulted in the deprotection of the TSE-group. Furthermore, *in situ* alkylation with alkyl halide readily afforded the key intermediates **4a–4c** and **4f–4h** along with the TBS-deprotected intermediates **7b** and **7f–7h**, respectively (Table 1). The diselenide was formed as a by-product (entries 1, 4 and 5). A longer reaction time afforded the TBS-deprotected key intermediate **7** in high yields (entries 3 and 7).

The key intermediates, **4** and **7**, were next applied to ring-closing metathesis (RCM) to deliver selenium-containing bicyclic β-lactams (Table 2). Our initial attempts to bring about the cyclization of the key intermediate **4a** using 10 mol% Schrock catalyst **C** (Table 2, entry 1) or 10 mol% Grubbs 1st gen. catalyst **A** (Table 2, entry 2) in toluene were unsuccessful and only the starting material was recovered (for details see the ESI†). However, the use of 5 mol% Grubbs 2nd gen. catalyst **B** in the RCM reaction was found to be effective and a cyclized product, *i.e.* selenazepine **8a** was obtained in 36% yield (Table 2, entry 3). The loading of 10 mol% of catalyst **B** gave the best results (Table 2, entry 4).

Since it was found that the allyl-seleno moiety was compatible with Grubbs 2nd gen. catalyst **B**, reaction of the other key intermediates **4b–4h** or **7b** and **7f** was carried out under similar reaction conditions and the results are shown in Table 2. The treatment of **4b** or **4f** with 10 mol% of catalyst **B** afforded the corresponding methyl-substituted selenazepines **8b** or **8c** in high yields (Table 2, entries 5 and 6). The hydroxy group in **7b** or **7f** was also well tolerated under these reaction conditions giving **8d** or **8e** in high yields (Table 2, entries 7 and 8). Attempting to prepare a highly functionalized selenazepine **8f** was unsuccessful and only the starting material was recovered (Table 2, entry 9). The RCM of **4c**, **4h** and **4d** afforded the corresponding eight-membered selenium heterocycles *i.e.* 1,3-selenazocine **8g–8i** (Table 2, entries 10, 11 and 12). Furthermore **4e** afforded nine-membered selenium heterocycle *i.e.* 1,3-selenazonine **8j** (Table 2, entry 13). The synthesis of higher-membered selenium heterocycles has been found to be very difficult. To the best of our knowledge, there are only four reports on the preparation of seven-membered selenium-containing heterocycles, that is, 1,3-selenazepines.[3,4,9] Whereas, the eight- or nine-membered selenium heterocycles such as 1,3-selenazocine or 1,3-selenazonine, respectively, have never been described in the literature thus far. The present RCM approach allows the synthesis of previously inaccessible selenium-containing heterocycles.

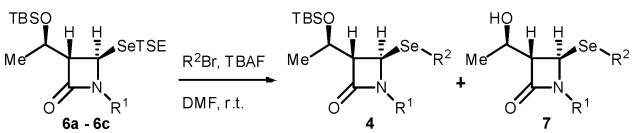
Conclusions

In conclusion, we have developed a pivotal approach to a variety of selenium-containing β-lactams, featuring selenating reagents (**2a** and **2b**) and ring-closing metathesis reactions. Further expansion of the current strategies is in progress.

Experimental

All reactions were performed in round-bottom flasks fitted with balloons filled with argon, unless otherwise specified. Transfer

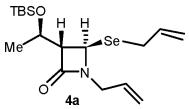
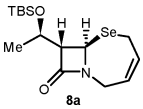
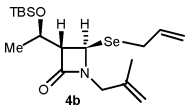
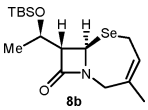
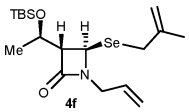
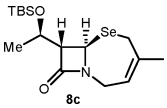
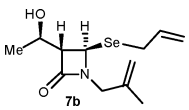
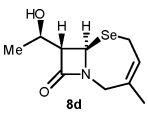
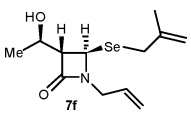
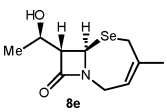
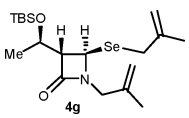
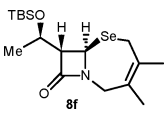
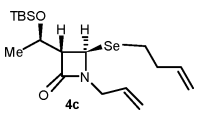
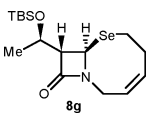
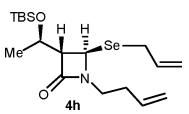
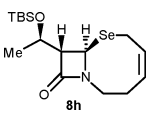
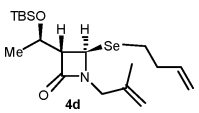
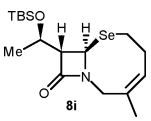
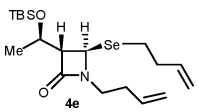
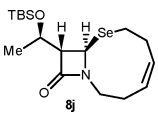
Table 1 Synthesis of key intermediates **4** and **7**



Entry	Starting	R^1	R^2	Time	Yield (%)[a] 4	7
1	**6a**	$CH_2CH=CH_2$	$CH_2CH=CH_2$	15 min	71 (**4a**)[b]	trace (**7a**)
2	**6b**	$CH_2(CH_3)C=CH_2$	$CH_2CH=CH_2$	15 min	66 (**4b**)	17 (**7b**)
3	**6b**	$CH_2(CH_3)C=CH_2$	$CH_2CH=CH_2$	45 min	3 (**4b**)	87 (**7b**)
4	**6a**	$CH_2CH=CH_2$	$CH_2CH_2CH=CH_2$	18 h	10 (**4c**)[b]	— (**7c**)
5	**6b**	$CH_2(CH_3)C=CH_2$	$CH_2CH_2CH=CH_2$	18 h	trace (**4d**)[b]	trace (**7d**)
6	**6a**	$CH_2CH=CH_2$	$CH_2(CH_3)C=CH_2$	15 min	78 (**4f**)	14 (**7f**)
7	**6a**	$CH_2CH=CH_2$	$CH_2(CH_3)C=CH_2$	45 min	27 (**4f**)	66 (**7f**)
8	**6b**	$CH_2(CH_3)C=CH_2$	$CH_2(CH_3)C=CH_2$	1 h	58 (**4g**)	35 (**7g**)
9	**6c**	$CH_2CH_2CH=CH_2$	$CH_2CH=CH_2$	1 h	76 (**4h**)	16 (**7h**)

[a] Isolated yields. [b] Corresponding diselenide was obtained as a by-product.

Table 2 Ring-closing metathesis of **4** and **7**[a]

Entry	Starting	Catalyst (10 mol%)	Time	Product	Yield of 8 (%)[b]
1	 **4a**	C	2 days	 **8a**	0[c]
2		A	4 days		trace[c]
3		B (5 mol%)	2 days		36[d]
4		B	2 h		78
5	 **4b**	B	2 h	 **8b**	92
6	 **4f**	B	2 h	 **8c**	75
7	 **7b**	B	2 h	 **8d**	82
8	 **7f**	B	2 h	 **8e**	74
9	 **4g**	B	2 days	 **8f**	0[c]
10	 **4c**	B	4 h	 **8g**	68
11	 **4h**	B	2 h	 **8h**	74
12	 **4d**	B	4 h	 **8i**	91
13	 **4e**	B	2 h	 **8j**	74

[a] All reactions were carried out on *ca.* 0.05 mmol scale in toluene at reflux. [b] Isolated yields. [c] Starting material was recovered quantitatively. [d] Starting material was recovered in 56% yield.

of air- and moisture-sensitive liquids was performed *via* cannula under a positive pressure of argon. TLC analysis was performed on Merck TLC (silica gel $60F_{254}$ on glass plate). Evaporation and condensation were carried out *in vacuo*. The compounds **1**[1] and **5**[2] were prepared according to the literature. Silica gel 60 N (spherical, neutral) manufactured by Kanto Chemical Co. Inc. was used for flash column chromatography. DMF and toluene were deoxygenated prior to use. Tetramethylammonium fluoride and methyl hydrazine were purchased from Tokyo Chemical Industry Ltd. Grubbs 1st gen. catalyst, Grubbs 2nd gen. catalyst, LHMDS (1.0 M THF solution) and 3-bromo-2-methyl-propene were purchased from Aldrich Chemical Company. Schrock's catalyst was purchased from Strem Chemicals. 4-Bromo-1-butene was purchased from Alfa Aesar Company. (3*R*,4*R*)-4-Acetoxy-3-[(*R*)-(tert-butyldimethylsilyloxy)ethyl]-2-azetidinone, allyl bromide and caesium carbonate were purchased from Wako Pure Chemical Industries Ltd. NaH was purchased from Nacalai Tesque Inc.

Melting points were measured by a Yanagimoto micromelting point apparatus (uncorrected). Optical rotation was recorded by Union PM-201 Automatic Digital Polarimeter (Horiba) at 28 °C. IR spectra were measured on a JASCO FT/IR-410 Fourier transform infrared spectrometer. The ^{1}H NMR, ^{13}C NMR spectra or ^{77}Se NMR spectra were measured on JEOL:JNM ECX-400P, JEOL:JNM ECA-500, JEOL:JNM ECA-600 spectrometers in $CDCl_3$. Chemical shifts of protons are reported in δ values referred to TMS as an internal standard. The ^{77}Se chemical shifts were expressed in δ values deshielded with respect to neat Me_2Se. $^{1}J(^{77}Se\text{-}^{1}H)$ values are observed as ^{77}Se satellites of the ^{1}H NMR spectra. MS and HRMS were measured on a JEOL JMS-700.

General preparation of *Se*-alkene *p*-methylselenobenzoate (2)

To a solution of potassium *p*-methylselenobenzoate **1** (12.65 mmol) in degassed DMF (50 mL) was added alkyl bromide (18.97 mmol) under an argon atmosphere, and the mixture was stirred for 1 h (TLC; $CHCl_3$:*n*-hexane = 1:5). The reaction mixture was filtered through celite and washed with $CHCl_3$. The combined filtrate and washings were extracted with $CHCl_3$ and washed with water and brine. The organic layer was dried over Na_2SO_4 and concentrated. The resulted residue was purified by column chromatography on silica gel ($CHCl_3$:*n*-hexane = 1:15 → 1:10 → 1:5) to give **2**.

The isolated yield and the spectral data for **2a** and **2b** are as follows:

***Se*-Allyl 4-methylbenzoselenoate (2a).** Yield: 87%; IR (neat): 2921, 1682, 1661, 1604, 1203, 1172, 887 cm^{-1}; ^{1}H NMR ($CDCl_3$): δ 2.39 (s, 3H), 3.71 (d, J = 8.0 Hz, $^{2}J(^{77}Se\text{-}^{1}H)$ = 14.0 Hz, 2H), 5.05 (d, J = 9.2 Hz, 1H), 5.26 (dd, J = 1.1, 17.2 Hz, 1H), 5.92–6.02 (m, 1H), 7.23 (d, J = 8.0 Hz, 2H), 7.78 (d, J = 8.0 Hz, 2H); ^{13}C NMR ($CDCl_3$): δ 21.7, 27.7, 117.3, 127.3, 129.4, 134.6, 136.4, 144.6, 193.7; ^{77}Se NMR ($CDCl_3$): δ 553.3; HRMS (EI): m/z = 240.0053 calcd. for $C_{11}H_{12}OSe$, found 240.0042.

***Se*-3-Butenyl 4-methylbenzoselenoate (2b).** Yield: 83%; IR (neat): 2924, 1681, 1661, 1604, 1406, 1202, 1172, 886 cm^{-1}; ^{1}H NMR ($CDCl_3$): δ 2.38 (s, 3H), 2.48–2.54 (m, 2H), 3.13 (t, J = 6.9 Hz, $^{2}J(^{77}Se\text{-}^{1}H)$ = 26.3 Hz, 2H), 5.05 (dd, J = 1.7, 10.3 Hz, 1H), 5.10 (dd, J = 1.7, 17.2 Hz, 1H), 5.80–5.90 (m, 1H), 7.22 (d, J = 8.0 Hz, 2H), 7.79 (d, J = 8.0 Hz, 2H); ^{13}C NMR ($CDCl_3$): δ 21.6, 24.4, 34.5, 116.0, 127.2, 129.3, 136.5, 137.2, 144.4, 194.0; ^{77}Se NMR ($CDCl_3$): δ 521.1; HRMS (EI): m/z = 254.0210 calcd. for $C_{12}H_{14}OSe$, found 254.0197.

Typical procedure for the preparation of 4-alkylseleno-2-azetidinone (3). To stirred solution of selenium reagent **2** (3.83 mmol) and Cs_2CO_3 (3.83 mmol) in dry DMF (5 mL) at r.t. was added methyl hydrazine (3.83 mmol) under an argon atmosphere. After stirring at this temperature for 10 minutes, (3*R*,4*R*)-4-acetoxy-3-[(*R*)-(*tert*-butyldimethylsilyloxy)ethyl]-2-azetidinone (3.48 mmol) was added and stirring continued for an additional 30 min. The reaction mixture was extracted with dichloromethane and washed with water. The combined organic extracts were dried (Na_2SO_4) and concentrated *in vacuo* to afford a residue that was further subjected to flash chromatography (SiO_2: hexane/diethyl ether = 5/1) to afford compound **3**.

The isolated yields and the spectral data for **3a–3b** are as follows

(3*S*,4*R*)-4-Allylseleno-3-[(*R*)-*tert*-butyldimethylsilyloxyethyl]-2-azetidinone (3a). Yield: 26%; Mp. 58–59 °C; IR (neat): 2955, 1766, 1723, 1654, 1637, 1374, 1250, 958, 835 cm^{-1}; ^{1}H NMR ($CDCl_3$): δ 0.07 (s, 3H), 0.08 (s, 3H), 0.87 (s, 9H), 1.23 (d, J = 6.3 Hz, 3H), 3.24 (s, 1H), 3.28–3.40 (m, 2H), 4.22–4.28 (m, 1H), 4.97 (d, J = 2.3 Hz, $^{2}J(^{77}Se\text{-}^{1}H)$ = 18.9 Hz, 1H), 5.04 (d, J = 9.7 Hz, 1H), 5.14 (dd, J = 1.1, 17.2 Hz, 1H), 5.92–6.00 (m, 1H), 6.18 (brs, 1H); ^{13}C NMR ($CDCl_3$): δ −5.12, −4.33, 17.9, 22.2, 25.7, 26.4, 46.8, 64.7, 67.0, 116.9, 135.4, 167.2; ^{77}Se NMR ($CDCl_3$): δ 310.5; HRMS: m/z = 292.0272 calcd. for $C_{10}H_{18}NO_2SeSi$, found 292.0231.

(3*S*,4*R*)-4-(3-Buteneseleno)-3-[(*R*)-*tert*-butyldimethylsilyloxyethyl]-2-azetidinone (3b). Yield 92%; Mp. 70–71 °C; IR (neat): 2952, 1761, 1672, 1567, 1386, 1257, 1095, 832 cm^{-1}; ^{1}H NMR ($CDCl_3$): δ 0.07 (s, 3H), 0.08 (s, 3H), 0.88 (s, 9H), 1.24 (d, J = 6.3 Hz, 3H), 2.41–2.53 (m, 2H), 2.75 (t, J = 7.4 Hz, 2H), 3.21 (s, 1H), 4.23–4.28 (m, 1H), 4.99 (d, J = 1.7 Hz, $^{2}J(^{77}Se\text{-}^{1}H)$ = 26.9 Hz, 1H), 5.05–5.13 (m, 2H), 5.77–5.87 (m, 1H), 5.92 (brs, 1H); ^{13}C NMR ($CDCl_3$): δ −5.07, −4.31, 17.9, 22.1, 22.2, 25.7, 34.8, 46.4, 64.8, 67.4, 116.4, 136.9, 167.0; ^{77}Se NMR ($CDCl_3$): δ 277.3; HRMS: m/z = 306.0429 calcd. for $C_{11}H_{20}NO_2SeSi$, found 306.0420.

General procedure for the *N*-alkylation reaction of 3

Method A. To a suspension of NaH (60% in mineral oil, 2.07 mmol) in 5 mL of THF at 0 °C was added compound **3** (1.38 mmol) in 15 mL THF over 15 minutes. The mixture was stirred at 0 °C for an additional 15 min, then alkyl bromide (2.07 mmol) was added dropwise. The reaction mixture was stirred at r.t. for 1 hour to 3 days and then taken up in 10 mL of ammonium chloride solution. The organic layer was washed with 10 mL of a saturated solution of sodium bicarbonate. The aqueous layer was extracted 3 times with 20 mL of diethyl ether each time. The combined organic layers were dried (Na_2SO_4) and concentrated. The residue was purified by column chromatography (SiO_2: hexane/diethyl ether = 15/1) to afford compound **4**.

Method B. Lithium bis(trimethylsilyl)amide (0.66 mmol, 1.0 M solution in THF) was added dropwise to a stirred solution of compound **3** (0.55 mmol) in THF (10 mL) at −78 °C under an argon atmosphere. The resultant solution was stirred at −78 °C for 10 minutes. Alkyl bromide (2.76 mmol) was added over 5 minutes and the resulting mixture allowed to warm to ambient temperature overnight. The resulting mixture was quenched with 10% HCl and extracted with diethyl ether. The combined organic extracts were dried (Na_2SO_4) and concentrated *in vacuo* to afford a residue that was further subjected to flash chromatography (SiO_2: hexane/diethyl ether = 15/1) to afford the title compound **4** as clear oil

The isolated yields and the spectral data for **4a–e** are as follows:

(3*S*,4*R*)-1-Allyl-4-(allylseleno)-3-[(*R*)-1-*tert*-butyldimethylsilyloxyethyl]-2-azetidinone (4a). Method A; Yield: 24%; IR (neat): 2928, 1763, 1633, 1388, 1251, 1065, 836 cm^{-1}; ^{1}H NMR ($CDCl_3$): δ 0.06 (s, 3H), 0.08 (s, 3H), 0.87 (s, 9H), 1.22 (d, J = 6.2 Hz, 3H), 3.20–3.30 (m, 3H), 3.50 (dd, J = 7.5, 15.8 Hz, 1H), 4.08 (dd, J = 4.8, 15.8 Hz, 1H), 4.24–4.30 (m, 1H), 4.92 (d, J = 2.1 Hz,

$^2J(^{77}Se\text{-}^1H)$ = 19.9 Hz, 1H), 5.04 (d, J = 9.7 Hz, 1H), 5.10 (dd, J = 1.4, 17.2 Hz, 1H), 5.21 (dd, J = 1.4, 10.3 Hz, 1H), 5.29 (dd, J = 1.4, 17.2 Hz, 1H), 5.74–5.82 (m, 1H), 5.86–5.93 (m, 1H); ^{13}C NMR ($CDCl_3$): δ –4.80, –4.61, 17.9, 22.3, 25.8, 42.7, 51.8, 64.7, 65.7, 117.2, 118.6, 131.8, 134.6, 166.2; ^{77}Se NMR ($CDCl_3$): δ 235.6; HRMS: m/z = 332.0585 calcd. for $C_{13}H_{22}NO_2SeSi$, found 332.0587.

(3*S*,4*R*)-4-(Allylseleno)-3-[(*R*)-1-*tert*-butyldimethylsilyloxyethyl]-1-(2-methylallyl)-2-azetidinone (4b). Method A; Yield: 47%; IR ($CHCl_3$): 2955, 1758, 1633, 1462, 1387, 1254, 836 cm^{-1}; ^1H NMR ($CDCl_3$): δ 0.06 (s, 3H), 0.09 (s, 3H), 0.88 (s, 9H), 1.24 (d, J = 6.3 Hz, 3H), 1.76 (s, 3H), 3.19–3.30 (m, 3H), 3.45 (d, J = 16.0 Hz, 1H), 3.97 (d, J = 15.5 Hz, 1H), 4.22–4.31 (m, 1H), 4.88 (d, J = 1.7 Hz, 1H), 4.92 (s, 1H), 4.96 (s, 1H), 5.03 (d, J = 9.7 Hz, 1H), 5.08 (d, J = 16.7 Hz, 1H), 5.84–5.93 (m, 1H); ^{13}C NMR ($CDCl_3$): δ –4.81, –4.49, 18.0, 20.6, 22.3, 25.8, 26.0, 46.0, 52.4, 65.0, 65.8, 113.4, 117.2, 134.6, 139.6, 166.5; ^{77}Se NMR ($CDCl_3$): δ 233.7; HRMS: m/z = 346.0742 calcd. for $C_{14}H_{24}NO_2SeSi$, found 346.0760.

(3*S*,4*R*)-1-Allyl-4-(3-butenylseleno)-3-[(*R*)-1-*tert*-butyldimethylsilyloxyethyl]-2-azetidinone (4c). Method A; Yield: 51%; IR (neat): 2955, 1762, 1643, 1387, 1252, 1063, 836 cm^{-1}; ^1H NMR ($CDCl_3$): δ 0.07 (s, 3H), 0.09 (s, 3H), 0.88 (s, 9H), 1.24 (d, J = 6.4 Hz, 3H), 2.38–2.50 (m, 2H), 2.58–2.71 (m, 2H), 3.19 (s, 1H), 3.49 (dd, J = 7.3, 15.6 Hz, 1H), 4.09 (dd, J = 4.6, 15.6 Hz, 1H), 4.23–4.31 (m, 1H), 4.91 (d, J = 2.3 Hz, $^2J(^{77}Se\text{-}^1H)$ = 27.0 Hz, 1H), 5.02–5.12 (m, 2H), 5.20 (d, J = 10.1 Hz, 1H), 5.28 (d, J = 17.0 Hz, 1H), 5.71–5.86 (m, 2H); ^{13}C NMR ($CDCl_3$): δ –4.81, –4.60, 18.0, 21.6, 22.3, 25.8, 34.7, 42.7, 51.5, 64.7, 65.9, 116.2, 118.6, 131.6, 136.8, 166.2; ^{77}Se NMR ($CDCl_3$): δ 213.0; HRMS: m/z = 346.0742 calcd. for $C_{14}H_{24}NO_2SeSi$, found 346.0724.

(3*S*,4*R*)-4-(3-Butenylseleno)-3-[(*R*)-1-*tert*-butyldimethylsilyloxyethyl]-1-(2-methylallyl)-2-azetidinone (4d). Method A; Yield: 82%; IR (neat): 2955, 1762, 1657, 1641, 1471, 1387, 1254, 1054, 836 cm^{-1}; ^1H NMR ($CDCl_3$): δ 0.06 (s, 3H), 0.09 (s, 3H), 0.88 (s, 9H), 1.25 (d, J = 6.3 Hz, 3H), 1.75 (s, 3H), 2.40–2.47 (m, 2H), 2.59–2.69 (m, 2H), 3.21 (t, J = 2.3 Hz,1H), 3.41 (d, J = 16.0 Hz, 1H), 3.99 (d, J = 16.0 Hz, 1H), 4.25–4.31 (m, 1H), 4.87 (d, J = 2.3 Hz, 1H), 4.91 (s, 1H), 4.95 (s, 1H), 5.03–5.12 (m, 2H), 5.75–5.85 (m, 1H); ^{13}C NMR ($CDCl_3$): δ –4.82, –4.54, 18.0, 20.5, 21.9, 22.3, 25.8, 34.6, 45.9, 52.2, 65.1, 66.0, 113.3, 116.2, 136.8, 139.3, 166.3; ^{77}Se NMR ($CDCl_3$): δ 211.8; HRMS: m/z = 360.0898 calcd. for $C_{15}H_{26}NO_2SeSi$, found 360.0887.

(3*S*,4*R*)-1-(3-Butenyl)-4-(3-butenylseleno)-3-[(*R*)-1-*tert*-butyldimethylsilyloxyethyl]-2-azetidinone (4e). Method B; Yield: 38%; IR (neat): 2954, 1759, 1641, 1393, 1253, 1059, 836 cm^{-1}; ^1H NMR ($CDCl_3$): δ 0.07 (s, 3H), 0.08 (s, 3H), 0.88 (s, 9H), 1.24 (d, J = 6.3 Hz, 3H), 2.30–2.49 (m, 4H), 2.59–2.70 (m, 2H), 2.97–3.04 (m, 1H), 3.17 (t, J = 1.8 Hz, 1H), 3.41–3.48 (m, 1H), 4.19–4.25 (m, 1H), 4.86 (d, J = 1.7 Hz, $^2J(^{77}Se\text{-}^1H)$ = 30.9 Hz, 1H), 5.03–5.15 (m, 4H), 5.76–5.85 (m, 2H); ^{13}C NMR ($CDCl_3$): δ –4.82, –4.52, 17.9, 21.0, 22.4, 25.7, 32.2, 34.6, 39.7, 52.0, 65.1, 65.9, 116.3, 117.0, 134.9, 136.8, 166.3; ^{77}Se NMR ($CDCl_3$): δ 212.1; HRMS: m/z = 360.0898 calcd. for $C_{15}H_{26}NO_2SeSi$, found 360.0890

General procedure for the *N*-alkylation reaction of 5

Method A. To a suspension of NaH (60% in mineral oil, 1.84 mmol) in 5 mL of THF at 0 °C was added (3*S*,4*R*)-3-[(*R*)-*tert*-butyldimethylsilyloxyethyl]-4-[2-(trimethylsilyl)ethylseleno]-2-azetidinone **5** (1.22 mmol) in 15 mL THF over 15 minutes. The mixture was stirred at 0 °C for an additional 15 min, then alkyl bromide (1.84 mmol) was added dropwise. The reaction mixture was stirred at r.t. for 1 hour to 3 days and then taken up in 10 mL of ammonium chloride solution. The organic layer was washed with 10 mL of a saturated solution of sodium bicarbonate. The aqueous layer was extracted 3 times with 20 mL of diethyl ether each time. The combined organic layers were dried (Na_2SO_4) and concentrated. The residue was purified by column chromatography (SiO_2: hexane/diethyl ether = 15/1) to afford compound **6**.

Method B. Lithium bis(trimethylsilyl)amide (1.46 mmol, 1.0 M solution in THF) was added dropwise to a stirred solution of (3*S*,4*R*)-3-[(*R*)-*tert*-butyldimethylsilyloxyethyl]-4-[2-(trimethylsilyl)ethylseleno]-2-azetidinone **5** (1.22 mmol) in THF (10 mL) at –78 °C under an argon atmosphere. The resultant solution was stirred at –78 °C for 10 minutes. Alkyl bromide (12.2 mmol) was added over 5 minutes and the resulting mixture allowed to warm to ambient temperature overnight. The resulting mixture was quenched with 10% HCl and extracted with diethyl ether. The combined organic extracts were dried (Na_2SO_4) and concentrated *in vacuo* to afford a residue that was further subjected to flash chromatography (SiO_2: hexane/diethyl ether = 15/1) to afford the title compound **6** as a clear oil.

The isolated yields and the spectral data for **6a–c** are as follows:

(3*S*,4*R*)-1-Allyl-3-[(*R*)-*tert*-butyldimethylsilyloxyethyl]-4-[2-(trimethylsilyl)ethylseleno]-2-azetidinone (6a). Method A; Yield: 64%; IR (neat): 2953, 2360, 1763, 1644, 1539, 1387, 1249, 837 cm^{-1}; ^1H NMR ($CDCl_3$): δ 0.00 (s, 9H), 0.04 (s, 3H), 0.06 (s, 3H), 0.86 (s, 9H), 0.90–1.00 (m, 2H), 1.22 (d, J = 6.3 Hz, 3H), 2.56–2.67 (m, 2H), 3.17 (t, J = 2.2 Hz, 1H), 3.48 (dd, J = 6.3, 14.8 Hz, 1H), 4.06 (dd, J = 5.2, 16.1 Hz, 1H), 4.22–4.27 (m, 1H), 4.88 (d, J = 2.3 Hz, $^2J(^{77}Se\text{-}^1H)$ = 21.8 Hz, 1H), 5.17 (dd, J = 1.1, 10.4 Hz, 1H), 5.24 (dd, J = 1.1, 17.1 Hz, 1H), 5.71–5.80 (m, 1H); ^{13}C NMR ($CDCl_3$): δ –4.82, –4.58, –1.91, 18.0, 18.2, 18.7, 22.3, 25.8, 42.7, 51.6, 64.8, 65.8, 118.5, 131.8, 166.3; ^{77}Se NMR ($CDCl_3$): δ 262.9; HRMS: m/z = 392.0980 calcd. for $C_{15}H_{30}NO_2SeSi_2$, found 392.0976.

(3*S*,4*R*)-3-[(*R*)-*tert*-Butyldimethylsilyloxyethyl]-1-(2-methylallyl)-4-[2-(trimethylsilyl)ethylseleno]-2-azetidinone (6b). Method A; Yield: 84%; IR (neat): 2954, 1764, 1658, 1472, 1386, 1249, 838 cm^{-1}; ^1H NMR ($CDCl_3$): δ 0.00 (s, 9H), 0.04 (s, 3H), 0.08 (s, 3H), 0.86 (s, 9H), 0.90–1.03 (m, 2H), 1.24 (d, J = 6.0 Hz, 3H), 1.73 (s, 3H), 2.53–2.68 (m, 2H), 3.16–3.22 (m, 1H), 3.43 (d, J = 15.5 Hz, 1H), 3.98 (d, J = 15.5 Hz, 1H), 4.22–4.30 (m, 1H), 4.85 (d, J = 1.8 Hz, 1H), 4.88 (s, 1H), 4.92 (s, 1H); ^{13}C NMR ($CDCl_3$): δ –4.82, –4.59, –2.00, 18.0, 18.5, 18.7, 20.5, 22.3, 25.8, 45.9, 52.3, 65.1, 65.7, 113.1, 139.4, 166.4; ^{77}Se NMR ($CDCl_3$): δ 262.9; HRMS: m/z = 406.1137 calcd. for $C_{16}H_{32}NO_2SeSi_2$, found 406.1127.

(3*S*,4*R*)-1-(3-Butenyl)-3-[(*R*)-*tert*-butyldimethylsilyloxyethyl]-4-[2-(trimethylsilyl)ethylseleno]-2-azetidinone (6c). Method A; Yield: 14%; Method B; Yield: 45%; IR (neat): 2953, 1758, 1643,

1472, 1393, 1249, 838 cm^{-1}; ^1H NMR ($CDCl_3$): δ 0.02 (s, 9H), 0.06 (s, 3H), 0.08 (s, 3H), 0.88 (s, 9H), 0.92–1.01 (m, 2H), 1.24 (d, J = 6.3 Hz, 3H), 2.28–2.41 (m, 2H), 2.55–2.70 (m, 2H), 2.96–3.05 (m, 1H), 3.18 (s, 1H), 3.40–3.48 (m, 1H), 4.17–4.26 (m, 1H), 4.85 (d, J = 1.7 Hz, $^2J(^{77}Se\text{-}^1H)$ = 28.1 Hz, 1H), 5.06 (dd, J = 1.1, 10.3 Hz, 1H), 5.12 (dd, J = 1.1, 17.2 Hz, 1H), 5.72–5.83 (m, 1H); ^{13}C NMR ($CDCl_3$): δ –4.83, –4.50, –1.90, 17.5, 18.0, 18.6, 22.4, 25.8, 32.2, 39.7, 52.2, 65.2, 65.8, 117.0, 135.0, 166.4; ^{77}Se NMR ($CDCl_3$): δ 262.1; HRMS: m/z = 406.1137 calcd. for $C_{16}H_{32}NO_2SeSi_2$, found 406.1134.

Typical procedure for the synthesis of 4 and 7

To a stirred solution of **6** (0.22 mmol) and alkyl bromide (2.23 mmol) in degassed dry DMF (2 mL) was added TBAF (1 M solution in THF, 0.56 mmol) at r.t. with argon bubbling into the reaction mixture. The stirring was continued for the above mentioned time and then the reaction mixture was extracted with chloroform and washed with water. The combined organic layers were dried (Na_2SO_4) and concentrated. The residue was purified by column chromatography (SiO_2: hexane/diethyl ether = 15/1) to afford compounds **4**, **7** or corresponding diselenide.

The isolated yields and the spectral data for **4**, **7** and diselenide are as follows:

Diselenide a. Table 1, Entry 1; Yield: 9%; IR (neat): 2954, 1767, 1644, 1539, 1384, 1255, 837 cm^{-1}; ^1H NMR ($CDCl_3$): δ 0.06 (s, 3H), 0.08 (s, 3H), 0.87 (s, 9H), 1.22 (d, J = 6.4 Hz, 3H), 3.29 (s, 1H), 3.45 (dd, J = 7.3, 15.5 Hz, 1H), 4.10 (dd, J = 5.0, 15.5 Hz, 1H), 4.26–4.32 (m, 1H), 5.02 (d, J = 1.9 Hz, $^2J(^{77}Se\text{-}^1H)$ = 40.8 Hz, 1H), 5.22 (d, J = 10.0 Hz, 1H), 5.30 (d, J = 16.9 Hz, 1H), 5.70–5.80 (m, 1H); ^{13}C NMR ($CDCl_3$): δ –4.83, –4.64, 18.0, 22.4, 25.8, 43.0, 53.5, 64.4, 66.8, 119.4, 131.1, 165.7; ^{77}Se NMR ($CDCl_3$): δ 320.4; HRMS: m/z = 637.1100 calcd. for $C_{24}H_{43}N_2O_4{}^{78}Se^{80}SeSi_2$, found 637.1107.

(3*S*,4*R*)-4-(Allylseleno)-3-[(*R*)-1-hydroxyethyl]-1-(2-methylallyl)-2-azetidinone (7b). Table 1, Entry 2; Yield: 17%; Entry 3; Yield: 87%; IR (neat): 3419, 2928, 1740, 1656, 1633, 1542, 1377, 1240, 815 cm^{-1}; ^1H NMR ($CDCl_3$): δ 1.31 (d, J = 7.5 Hz, 3H), 1.75 (s, 3H), 2.04 (brs, 1H), 3.21–3.34 (m, 3H), 3.40 (d, J = 15.5 Hz, 1H), 4.03 (d, J = 15.5 Hz, 1H), 4.23–4.32 (m, 1H), 4.84 (d, J = 1.7 Hz, $^2J(^{77}Se\text{-}^1H)$ = 22.4 Hz, 1H), 4.93 (s, 1H), 4.96 (s, 1H), 5.04 (d, J = 9.7 Hz, 1H), 5.12 (d, J = 17.2 Hz, 1H), 5.84–5.95 (m, 1H); ^{13}C NMR ($CDCl_3$): δ 20.2, 21.1, 26.0, 46.1, 52.1, 64.5, 65.5, 113.7, 117.3, 134.6, 139.3, 166.5; ^{77}Se NMR ($CDCl_3$): δ 238.7; HRMS: m/z = 289.0581 calcd. for $C_{12}H_{19}NO_2Se$, found 289.0596.

Diselenide b. Table 1, Entry 5; Yield: 12%; IR (neat): 2954, 1766, 1658, 1471, 1377, 1256, 836 cm^{-1}; ^1H NMR ($CDCl_3$): δ 0.06 (s, 3H), 0.09 (s, 3H), 0.87 (s, 9H), 1.24 (d, J = 6.4 Hz, 3H), 1.76 (s, 3H), 3.32 (s, 1H), 3.39 (d, J = 16.0 Hz, 1H), 3.99 (d, J = 16.0 Hz, 1H), 4.27–4.33 (m, 1H), 4.92 (s, 1H), 4.95–5.00 (m, 2H); ^{13}C NMR ($CDCl_3$): δ –4.82, –4.47, 18.1, 20.7, 22.5, 25.8, 46.2, 54.3, 64.8, 66.9, 114.0, 138.8, 165.8; MS (EI): m/z = 667 [$M^+ - {}^t$Bu].

(3*S*,4*R*)-1-Allyl-3-[(*R*)-1-*tert*-butyldimethylsilyloxyethyl]-4-(2-methylallylseleno)-2-azetidinone (4f). Table 1, Entry 6; Yield: 78%; Entry 7; Yield: 27%; IR ($CHCl_3$): 2955, 2360, 1755, 1644, 1471, 1389, 1253, 1064, 756 cm^{-1}; ^1H NMR ($CDCl_3$): δ 0.06 (s, 3H), 0.08 (s, 3H), 0.87 (s, 9H), 1.21 (d, J = 6.3 Hz, 3H), 1.86 (s, 3H), 3.19–3.30 (m, 3H), 3.50 (dd, J = 6.8, 16.1 Hz, 1H), 4.05 (dd, J = 5.1, 16.1 Hz, 1H), 4.24–4.31 (m, 1H), 4.84 (s, 1H), 4.89 (s, 1H), 4.93 (d, J = 2.3 Hz, $^2J(^{77}Se\text{-}^1H)$ = 22.9 Hz, 1H), 5.20 (d, J = 10.3 Hz, 1H), 5.27 (d, J = 17.2 Hz, 1H), 5.73–5.82 (m, 1H); ^{13}C NMR ($CDCl_3$): δ –4.80, –4.62, 17.9, 21.1, 22.2, 25.8, 30.9, 42.8, 52.0, 64.6, 65.8, 113.9, 118.5, 131.9, 141.7, 166.3; ^{77}Se NMR ($CDCl_3$): δ 221.0; HRMS: m/z = 346.0742 calcd. for $C_{14}H_{24}NO_2SeSi$, found 346.0727.

(3*S*,4*R*)-1-Allyl-3-[(*R*)-1-hydroxyethyl]-4-(2-methylallylseleno)-2-azetidinone (7f). Table 1, Entry 6; Yield: 14%; Entry 7; Yield: 66%; IR (neat): 3419, 2969, 1740, 1644, 1589, 1427, 1375, 1244, 865 cm^{-1}; ^1H NMR ($CDCl_3$): δ 1.26 (d, J = 6.3 Hz, 3H), 1.84 (s, 3H), 2.64 (brs, 1H), 3.19–3.35 (m, 3H), 3.47 (dd, J = 6.3, 16.0 Hz, 1H), 4.05 (d, J = 4.6, 16.0 Hz, 1H), 4.19–4.26 (m, 1H), 4.82 (s, 1H), 4.85 (d, J = 2.3 Hz, 1H), 4.88 (s, 1H), 5.19 (d, J = 10.3 Hz, 1H), 5.28 (d, J = 17.2 Hz, 1H), 5.70–5.80 (m, 1H); ^{13}C NMR ($CDCl_3$): δ 20.9, 21.1, 31.0, 42.6, 52.2, 64.2, 65.6, 114.0, 118.1, 131.4, 141.7, 166.5; ^{77}Se NMR ($CDCl_3$): δ 228.5; HRMS: m/z = 289.0581 calcd. for $C_{12}H_{19}NO_2Se$, found 289.0591.

(3*S*,4*R*)-3-[(*R*)-1-*tert*-Butyldimethylsilyloxyethyl]-1-(2-methylallyl)-4-(2-methylallylseleno)-2-azetidinone (4g). Table 1, Entry 8; Yield: 58%; IR (neat): 2955, 1763, 1657, 1471, 1375, 1253, 836 cm^{-1}; ^1H NMR ($CDCl_3$): δ 0.04 (s, 3H), 0.08 (s, 3H), 0.87 (s, 9H), 1.21 (d, J = 6.3 Hz, 3H), 1.75 (s, 3H), 1.85 (s, 3H), 3.17 (d, J = 12.0 Hz, 1H), 3.21–3.30 (m, 2H), 3.42 (d, J = 16.0 Hz, 1H), 3.96 (d, J = 16.0 Hz, 1H), 4.23–4.31 (m, 1H), 4.82 (s, 1H), 4.86 (s, 1H), 4.88 (d, J = 2.3 Hz, 1H), 4.90 (s, 1H), 4.95 (s, 1H); ^{13}C NMR ($CDCl_3$): δ –4.86, –4.49, 18.0, 20.6, 21.1, 22.2, 25.8, 31.1, 46.0, 52.6, 64.9, 65.7, 113.3, 113.9, 139.6, 141.6, 166.5; ^{77}Se NMR ($CDCl_3$): δ 219.1; HRMS: m/z = 360.0898 calcd. for $C_{15}H_{26}NO_2SeSi$, found 360.0893.

(3*S*,4*R*)-3-[(*R*)-1-Hydroxyethyl]-1-(2-methylallyl)-4-(2-methylallylseleno)-2-azetidinone (7g). Table 1, Entry 8; Yield: 35%; IR (neat): 3419, 2969, 1746, 1657, 1538, 1375, 1247, 861 cm^{-1}; ^1H NMR ($CDCl_3$): δ 1.27 (d, J = 6.3 Hz, 3H), 1.72 (s, 3H), 1.84 (s, 3H), 2.14 (brs, 1H), 3.20 (d, J = 12.0 Hz, 1H), 3.27 (d, J = 12.0 Hz, 1H), 3.30–3.33 (m, 1H), 3.36 (d, J = 16.1 Hz, 1H), 4.02 (d, J = 16.1 Hz, 1H), 4.20–4.29 (m, 1H), 4.78–4.84 (m, 2H), 4.87 (s, 1H), 4.91 (s, 1H), 4.94 (s, 1H); ^{13}C NMR ($CDCl_3$): δ 20.2, 21.0, 21.1, 31.1, 46.1, 52.3, 64.4, 65.5, 113.7, 114.0, 139.3, 141.7, 166.5; ^{77}Se NMR ($CDCl_3$): δ 222.7; HRMS: m/z = 303.0738 calcd. for $C_{13}H_{21}NO_2Se$, found 303.0732.

(3*S*,4*R*)-4-Allylseleno-1-(3-butenyl)-3-[(*R*)-1-*tert*-butyldimethylsilyloxyethyl]-2-azetidinone (4h). Table 1, Entry 9; Yield: 76%; IR (neat): 2954, 1760, 1633, 1393, 1253, 1060, 836 cm^{-1}; ^1H NMR ($CDCl_3$): δ 0.06 (s, 3H), 0.08 (s, 3H), 0.88 (s, 9H), 1.24 (d, J = 6.3 Hz, 3H), 2.31–2.37 (m, 2H), 2.95–3.04 (m, 1H), 3.21–3.29 (m, 3H), 3.37–3.46 (m, 1H), 4.19–4.27 (m, 1H), 4.87 (d, J = 2.3 Hz, $^2J(^{77}Se\text{-}^1H)$ = 30.8 Hz, 1H), 5.02–5.18 (m, 4H), 5.75–5.84 (m, 1H), 5.88–5.98 (m, 1H); ^{13}C NMR ($CDCl_3$): δ –4.84, –4.53, 17.9, 22.3, 25.3, 25.7, 32.2, 39.8, 52.4, 65.0, 65.8, 117.0, 117.1, 134.8, 136.9, 166.4; ^{77}Se NMR ($CDCl_3$): δ 238.5; HRMS: m/z = 346.0742 calcd. for $C_{14}H_{24}NO_2SeSi$, found 346.0733.

(3*S*,4*R*)-4-Allylseleno-1-(3-butenyl)-3-[(*R*)-1-hydroxyethyl]-2-azetidinone (7h). Table 1, Entry 9; Yield: 16%; IR (neat): 3419, 2968, 1737, 1634, 1402, 1241, 1043, 862 cm^{-1}; ^1H NMR ($CDCl_3$):

δ 1.32 (d, J = 6.3 Hz, 3H), 2.27–2.41 (m, 2H), 2.96–3.04 (m, 1H), 3.25–3.34 (m, 3H), 3.45–3.53 (m, 1H), 4.17–4.24 (m, 1H), 4.83 (d, J = 1.7 Hz, $^2J(^{77}Se\text{-}^1H)$ = 20.6 Hz, 1H), 5.03–5.19 (m, 4H), 5.72–5.84 (m, 1H), 5.89–5.99 (m, 1H); ^{13}C NMR ($CDCl_3$): δ 21.1, 25.5, 32.0, 39.7, 52.3, 64.9, 65.8, 117.3, 117.4, 134.8, 134.9, 166.2; ^{77}Se NMR ($CDCl_3$): δ 238.5; HRMS: m/z = 289.0581 calcd. for $C_{12}H_{19}NO_2Se$, found 289.0583.

Typical procedure for the RCM reaction

10 mol% of catalyst **B** was added to the compound **4** or **7** (0.05 mmol) in toluene (2 mL). The mixture was allowed to stir for 2–4 days under reflux prior to destruction of the catalyst by exposure to air. The mixture was evaporated and chromatographed to afford compound **8**.

The isolated yields and the spectral data for **8a–j** are as follows:

(7*R*,8*S*)-8-[(*R*)-1-*tert*-Butyldimethylsilyloxyethyl]-1-aza-6-selenabicyclo[5.2.0]non-3-en-9-one (8a). Yield: 78%; IR (neat): 2954, 1762, 1652, 1471, 1396, 1252, 836 cm^{-1}; ^1H NMR ($CDCl_3$): δ 0.06 (s, 3H), 0.08 (s, 3H), 0.86 (s, 9H), 1.22 (d, J = 6.3 Hz, 3H), 3.10 (dd, J = 8.6, 14.3 Hz, 1H), 3.26 (dd, J = 1.7, 3.4 Hz, 1H), 3.56 (dd, J = 6.3, 14.3 Hz, 1H), 3.68 (dt, J = 1.7, 17.2 Hz, 1H), 4.21–4.26 (m, 1H), 4.37 (dd, J = 5.8, 17.2 Hz, 1H), 5.10 (d, J = 1.7 Hz, $^2J(^{77}Se\text{-}^1H)$ = 30.9 Hz, 1H), 5.44–5.49 (m, 1H), 6.09–6.19 (m, 1H); ^{13}C NMR ($CDCl_3$): δ −5.14, −4.22, 16.3, 17.9, 22.5, 25.7, 40.5, 49.5, 64.8, 68.5, 125.3, 132.0, 166.2; ^{77}Se NMR ($CDCl_3$): δ 359.4; HRMS: m/z = 304.0272 calcd. for $C_{11}H_{18}NO_2SeSi$, found 304.0258.

(7*R*,8*S*)-8-[(*R*)-1-*tert*-Butyldimethylsilyloxyethyl]-3-methyl-1-aza-6-selenabicyclo[5.2.0]non-3-en-9-one (8b). Yield: 92%; IR (KBr): 2955, 1760, 1661, 1471, 1400, 1256, 1135, 838 cm^{-1}; ^1H NMR ($CDCl_3$): δ 0.06 (s, 3H), 0.07 (s, 3H), 0.86 (s, 9H), 1.20 (d, J = 6.3 Hz, 3H), 1.73 (s, 3H), 3.02 (dd, J = 9.2, 14.3 Hz, 1H), 3.23–3.26 (m, 1H), 3.54 (dd, J = 6.9, 14.3 Hz, 1H), 3.60 (d, J = 17.2 Hz, 1H), 4.20–4.29 (m, 2H), 5.08 (d, J = 1.7 Hz, $^2J(^{77}Se\text{-}^1H)$ = 29.3 Hz, 1H), 5.84 (t, J = 7.4 Hz, 1H); ^{13}C NMR ($CDCl_3$): δ −5.15, −4.25, 16.4, 17.9, 22.4, 23.1, 25.7, 44.9, 48.9, 64.7, 68.5, 126.3, 133.8, 166.3; ^{77}Se NMR ($CDCl_3$): δ 361.6; HRMS: m/z = 318.0429 calcd. for $C_{12}H_{20}NO_2SeSi$, found 318.0412.

(7*R*,8*S*)-8-[(*R*)-1-*tert*-Butyldimethylsilyloxyethyl]-4-methyl-1-aza-6-selenabicyclo[5.2.0]non-3-en-9-one (8c). Yield: 75%; Mp. 48–49 °C; IR (KBr): 2958, 1754, 1733, 1655, 1542, 1400, 1256, 1136, 839 cm^{-1}; ^1H NMR ($CDCl_3$): δ 0.05 (s, 3H), 0.06 (s, 3H), 0.86 (s, 9H), 1.20 (d, J = 6.3 Hz, 3H), 1.86 (s, 3H), 3.15–3.21 (m, 2H), 3.40 (d, J = 13.2 Hz, 1H), 3.68 (dd, J = 5.8, 16.0 Hz, 1H), 4.17–4.25 (m, 2H), 5.04 (d, J = 1.7 Hz, $^2J(^{77}Se\text{-}^1H)$ = 20.0 Hz, 1H), 5.29 (t, J = 5.8 Hz, 1H); ^{13}C NMR ($CDCl_3$): δ −5.16, −4.24, 17.8, 22.6, 22.9, 24.2, 25.6, 39.5, 49.1, 64.7, 68.2, 117.4, 142.9, 165.5; ^{77}Se NMR ($CDCl_3$): δ 335.9; HRMS: m/z = 318.0429 calcd. for $C_{12}H_{20}NO_2SeSi$, found 318.0389.

(7*R*,8*S*)-8-[(*R*)-1-Hydroxyethyl]-3-methyl-1-aza-6-selenabicyclo[5.2.0]non-3-en-9-one (8d). Yield: 82%; Mp. 97–98 °C; IR (KBr): 3365, 2969, 1747, 1715, 1663, 1445, 1376, 1121, 835 cm^{-1}; ^1H NMR ($CDCl_3$): δ 1.31 (d, J = 6.3 Hz, 3H), 1.74 (s, 3H), 1.94 (brs, 1H), 3.04 (dd, J = 8.6, 14.4 Hz, 1H), 3.33 (dd, J = 1.7, 5.1 Hz, 1H), 3.54 (dd, J = 5.1, 13.7 Hz, 1H), 3.67 (d, J = 17.2 Hz, 1H), 4.20–4.31 (m, 2H), 5.10 (d, J = 1.8 Hz, $^2J(^{77}Se\text{-}^1H)$ = 30.9 Hz, 1H), 5.84 (t, J = 7.9 Hz, 1H); ^{13}C NMR ($CDCl_3$): δ 16.2, 21.4, 23.0, 45.1, 49.2, 64.6, 68.0, 126.1, 134.0, 166.2; ^{77}Se NMR ($CDCl_3$): δ 367.4; HRMS: m/z = 261.0268 calcd. for $C_{10}H_{15}NO_2Se$, found 261.0225.

(7*R*,8*S*)-8-[(*R*)-1-Hydroxyethyl]-4-methyl-1-aza-6-selenabicyclo[5.2.0]non-3-en-9-one (8e). Yield: 74%; Mp. 110–111 °C; IR (KBr): 3365, 2927, 1737, 1676, 1655, 1399, 1289, 1152, 840 cm^{-1}; ^1H NMR ($CDCl_3$): δ 1.30 (d, J = 6.3 Hz, 3H), 1.70 (brs, 1H), 1.86 (s, 3H), 3.19–3.26 (m, 2H), 3.40 (d, J = 13.2 Hz, 1H), 3.75 (dd, J = 5.2, 16.0 Hz, 1H), 4.19–4.26 (m, 2H), 5.06 (d, J = 1.7 Hz, $^2J(^{77}Se\text{-}^1H)$ = 18.3 Hz, 1H), 5.31 (t, J = 5.2 Hz, 1H); ^{13}C NMR ($CDCl_3$): δ 21.5, 22.8, 24.2, 39.7, 49.1, 64.6, 67.7, 117.5, 142.9, 165.4; ^{77}Se NMR ($CDCl_3$): δ 341.0; HRMS: m/z = 261.0268 calcd. for $C_{10}H_{15}NO_2Se$, found 261.0223.

(8*R*,9*S*)-9-[(*R*)-1-*tert*-Butyldimethylsilyloxyethyl]-1-aza-7-selenabicyclo[6.2.0]dec-3-en-10-one (8g). Yield: 68%; IR ($CHCl_3$): 2953, 1758, 1692, 1566, 1486, 1255, 836 cm^{-1}; ^1H NMR ($CDCl_3$): δ 0.06 (s, 6H), 0.86 (s, 9H), 1.21 (d, J = 6.4 Hz, 3H), 2.66–2.78 (m, 3H), 2.82–2.97 (m, 2H), 3.67 (dd, J = 10.0, 13.2 Hz, 1H), 3.94 (dd, J = 6.9, 13.2 Hz, 1H), 4.21–4.28 (m, 1H), 5.00 (d, J = 2.3 Hz, $^2J(^{77}Se\text{-}^1H)$ = 23.0 Hz, 1H), 5.53–5.61 (m, 1H), 5.90–5.99 (m, 1H); ^{13}C NMR ($CDCl_3$): δ −5.19, −4.30, 17.9, 22.1, 23.6, 25.7, 30.7, 35.7, 50.3, 62.6, 64.5, 122.6, 135.0, 164.8; HRMS: m/z = 318.0429 calcd. for $C_{12}H_{20}NO_2SeSi$, found 318.0405.

(8*R*,9*S*)-9-[(*R*)-1-*tert*-Butyldimethylsilyloxyethyl]-1-aza-7-selenabicyclo[6.2.0]dec-4-en-10-one (8h). Yield: 74%; IR ($CHCl_3$): 2952, 1760, 1690, 1598, 1461, 1375, 1256, 1057, 836 cm^{-1}; ^1H NMR ($CDCl_3$): δ 0.05 (s, 3H), 0.07 (s, 3H), 0.87 (s, 9H), 1.19 (d, J = 6.3 Hz, 3H), 2.26–2.34 (m, 1H), 2.45–2.54 (m, 1H), 3.01 (t, J = 12.0 Hz, 1H), 3.13–3.18 (m, 1H), 3.25 (dd, J = 8.1, 12.0 Hz, 1H), 3.64 (dd, J = 9.7, 12.0 Hz, 1H), 3.82–3.88 (m, 1H), 4.21–4.27 (m, 1H), 5.10 (d, J = 2.3 Hz, 1H), 5.66–5.74 (m, 1H), 5.92–5.99 (m, 1H); ^{13}C NMR ($CDCl_3$): δ −4.94, −4.36, 17.8, 18.7, 22.4, 25.2, 25.7, 42.9, 49.4, 64.7, 64.8, 128.6, 130.2, 168.2; HRMS: m/z = 318.0429 calcd. for $C_{12}H_{20}NO_2SeSi$, found 318.0403.

(8*R*,9*S*)-9-[(*R*)-1-*tert*-Butyldimethylsilyloxyethyl]-3-methyl-1-aza-7-selenabicyclo[6.2.0]dec-3-en-10-one (8i). Yield: 91%; IR ($CHCl_3$): 2954, 1758, 1670, 1461, 1377, 1255, 1064, 836 cm^{-1}; ^1H NMR ($CDCl_3$): δ 0.07 (s, 3H), 0.08 (s, 3H), 0.88 (s, 9H), 1.21 (d, J = 6.3 Hz, 3H), 1.77 (s, 3H), 2.58–2.86 (m, 4H), 2.94–2.97 (m, 1H), 3.75–3.82 (m, 2H), 4.23–4.29 (m, 1H), 4.93 (d, J = 2.3 Hz, 1H), 5.60 (t, J = 9.2 Hz, 1H); ^{13}C NMR ($CDCl_3$): δ −4.77, −4.67, 18.0, 22.1, 22.8, 24.6, 25.8, 31.6, 40.6, 50.4, 62.9, 64.7, 128.9, 130.8, 165.2; ^{77}Se NMR ($CDCl_3$): δ 299.4; HRMS: m/z = 332.0585 calcd. for $C_{13}H_{22}NO_2SeSi$, found 332.0543.

(9*R*,10*S*)-10-[(*R*)-1-*tert*-Butyldimethylsilyloxyethyl]-1-aza-8-selenabicyclo[7.2.0]undec-4-en-11-one (8j). Yield: 74%; Mp. 77–78 °C; IR ($CHCl_3$): 2952, 1749, 1652, 1564, 1463, 1393, 1249, 1059, 833 cm^{-1}; ^1H NMR ($CDCl_3$): δ 0.05 (s, 3H), 0.06 (s, 3H), 0.86 (s, 9H), 1.22 (d, J = 6.3 Hz, 3H), 2.46–2.56 (m, 3H), 2.60–2.73 (m, 2H), 2.76–2.82 (m, 1H), 3.03 (dt, J = 5.7, 14.3 Hz, 1H), 3.19 (t, J = 2.3 Hz, 1H), 3.62–3.69 (m, 1H), 4.22–4.29 (m, 1H), 4.99 (d, J = 1.7 Hz, 1H), 5.58–5.69 (m, 2H); ^{13}C NMR ($CDCl_3$): δ −5.13, −4.26, 17.9, 21.9, 22.2, 25.0, 25.7, 29.1, 40.6, 51.1, 64.6, 64.7, 129.4, 130.4, 167.3; HRMS: m/z = 332.0585 calcd. for $C_{13}H_{22}NO_2SeSi$, found 332.0551.

Acknowledgements

This work was supported by a Grant-in-Aid for Science Research from the Ministry of Education, Culture, Sports, Science, and Technology of Japan (No. 20590005) for which we are grateful.

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