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An Efficient Synthesis of Phenanthroindolizidine Core *via* Hetero Diels-Alder Reaction of In Situ Generated α-Allenylchalcogenoketenes With Cyclic Imines

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Abstract

Synthesis of phenanthroindolizidine core was efficiently achieved through a pathway involving hetero Diels-Alder reaction of α-allenylchalcogenoketenes, generated *in situ* by thermal [3,3] sigmatropic rearrangement of alkynyl propargyl sulfides or selenides, with cyclic imines and the subsequent iodine-assisted photochemical cyclization.

Keywords

alkynyl propargyl sufide, alkynyl propargyl selenide, α-allenylthioketene, α-allenylselenoketene, hetero Diels-Alder reaction, indolizidine, phenanthroindolizidine

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Tylophorine (**1**) was first isolated as a constituent of *Tylophora asthmatica* in 1935, and since then, a variety of phenanthro-indolizidine and phenanthroqunolizidine alkaloids, such as antofine (**2**), tylocrebrine (**3**), putative hypoestestatines (**4**), and cryptopleurine (**5**) as shown in Scheme 6, were found from the natural sources, such as *Onychopetalum amazonicum*, *Guatteria dielsiana*, and *Cleistopholis patens*.[1-15] Especially, it is widely recognized that these compounds possess a variety of biologically important activities, and therefore, a lot of research works have been endeavored for the synthesis of tylophorine (**1**) and the related derivatives within this several decades.[16-39] However, these previous procedures commonly required the long-step procedure and the synthetic efficiency was not enough, and especially selective construction of polysubstituted fused-indolizidine core still remains the problem in the synthetic research work on these compounds.

In the course of our research work on the synthesis of chalcogen-containing heteroaromatic compounds by using the reactivity of chalcogenocarbonyl functionalities, we have previously reported a conversion of alkynyl propargyl chalcogenides into quinolizidine and indolizidine rings *via* α-allenylchalcogenoketenes by using a sequential [3,3] sigmatropic rearrangement and the subsequent hetero Diels-Alder reaction with cyclic imines.[40-45] These successful results urged us to the new synthesis of polysubstituted fused-indolizidine skeletons, *ie*, phenanthroindolizine alkaloid cores. It is expected that these target compounds **I** would be accessible through a combination of *in situ* generation of α-allenylchalcogenoketenes **B**, hetero Diels-Alder reaction with cyclic imines, and intramolecular biaryl coupling, and 3 different synthetic strategies for the construction of phenathroindolizidine ring would be proposed as shown in Scheme 1.

The synthetic strategy I involves the formation of 2,3-diaryl-4-methylenecyclobutene-1-chalcogenones **C** and the subsequent intramolecular oxidative biaryl coupling to form phenanthrocyclobutenone derivatives **D** prior to the hetero Diels-Alder reaction of *in situ* generated α-allenylchalcogenolketenes **B** with cyclic imines **E**,[46-48] and both synthetic strategies II and III involve hetero Diels-Alder reaction of *in situ* generated α-allenylchalco-genoketenes **B** with cyclic imines **E** forming

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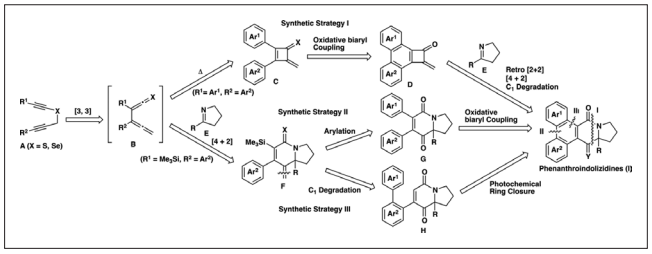
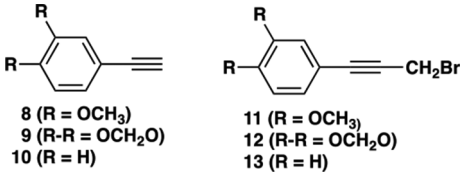


Scheme 1. Synthetic strategies for phenanthrolindolizidine alkaloid skeleton **I** *via* hetero Diels-Alder reaction of *in situ* generated α-allenylchalcogenoketene intermediates **B**.

indolizidine core. In strategy II, the subsequent intramolecular oxidative biaryl coupling of synthetic intermediates **G**,[49-55] structurally related to some unfused quinolizidine alkaloids as septicines,[56-59] is required, and synthetic strategy III requires the hetero Diels-Alder reaction of alkynyl propargyl chalcogenides **A** bearing a functionalized biphenyl moiety at the R^2 substituent in advance in order to achieve the subsequent photochemical ring closure to form phenanthroindolizidine core **I**.[60-62] Especially, we have previously reported the formation of 2,3-disubstituted 4-methylenecyclo-butene-1-chalcogenones through thermal [3,3] sigmatropic rearrangement of alkynyl propargyl chalcogenides **A**, and compounds **A** are expected to behave as novel intermediates of ketenes bearing a conjugation system at the α-position through retro [2 + 2]-type cycloreversion. It is worth noting that trimethylsilyl group at the R^1 substituent is expected to enhance the nucleophilicity of the α-allenyl part of α-allenylchalcogenoketenes **B** toward imines in addition to the role of stabilization of chalcogenoketenes by introducing a silyl group.[40-45] In this paper, we report a novel and efficient construction of phenathroindolizidine core by the combination of hetero Diels-Alder strategy of α-allenylchalcogeno-ketenes with cyclic imines and a photochemical ring closure.

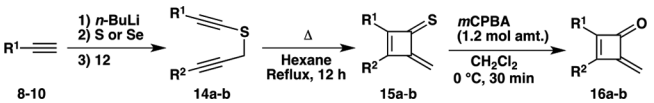
At first, 3,4-dimethoxybenzaldehyde (**7**) and piperonal were converted into terminal acetylenes **8** and **9** by using Corey-Fuchs reaction,[63,64] and **9** was converted into propargyl bromides **12** by using a 2-step procedure: (i) EtMgBr or *n*-butyllithium, paraformaldehyde; (ii) Ph_3P-CCl_4 or Ph_3P-CBr_4.[65,66] Compound **8** or phenylacetylene (**10**) was then treated with elemental sulfur and **12** to form alkynyl propargyl sulfides **14a-b** bearing 2 aryl moieties at the R^1 and R^2 positions according to our previous reports.[40-45] On the other hand, a similar treatment of **9** with **12** only gave a complex mixture.



Subsequently, alkynyl propargyl sulfides **14a-b** were converted into 4-methylene-2-cyclobutene-1-thiones **15a-b** in high yields by heating in hexane and the subsequent S-O exchanging was carried out by treating with *m*-chloroperbenzoic acid (*m*CPBA) to afford the corresponding 4-methylene-2-cyclobuten-1-ones **16a-b** as shown in Table 1. However, all attempts for intramolecular oxidative biaryl coupling of compounds **16a-b** by using a variety of oxidizing agents,[67-72] such as $FeCl_3$, *m*CPBA-$FeCl_3$, and MnO_2, resulted in the formation of complex mixtures. Therefore, we must abandon synthetic route **I** by regarding these unsuccessful results.

On the other hand, alkynyl propargyl chalcogenides **14c-d** (X = S) and **17c** (X = Se) bearing a trimethylsilyl group at the R^1 position of the alkynyl terminal were prepared from trimethylsilylacetylene, EtMgBr or *n*-butyllithium, elemental chalcogen (X = S, Se), and a substituted propargyl

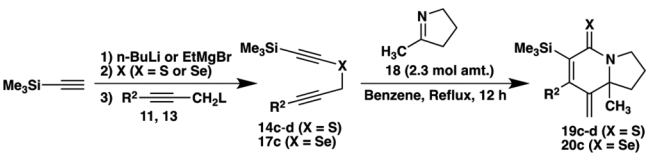
Table 1. Preparation of Alkynyl Propargyl Sulfides **14a-b**, 2,3-Diaryl-4-methylene-2-cyclobutene-1-thiones **15a-b**, and 2,3-Diaryl-4-methylene-2-cyclobuten-1-ones **16a-b**.



		Yield (%)		
R^1	R^2	**14**[a]	**15**	**16**
C_6H_5	MDP	68 (**14a**)	80 (**15a**)	40 (**16a**)
3,4-$(CH_3O)_2C_6H_3$	MDP	76 (**14b**)	84 (**15b**)	54 (**16b**)
MDP	MDP	Complex mixture		-

MDP, 3,4-(methylenedioxy)phenyl group.
[a]Isolated yields based on **7** to **9**.

Table 2. Preparation of δ-Chalcogenolactams (**19c-d**, **20c**) *via* Hetero Diels-Alder Strategy Starting from Alkynyl Propargyl Chalcogenides (**14c-d**, **17c**) and 2-Methylpyrroline (**18**).



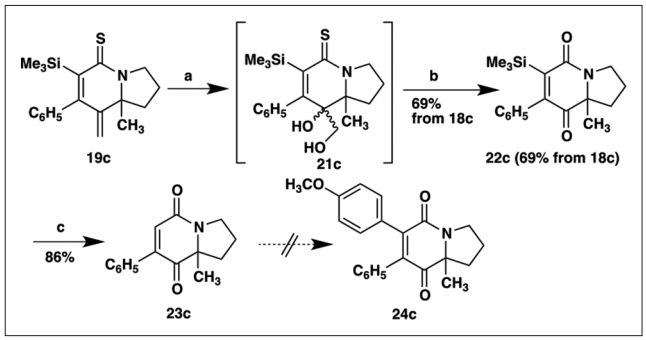
		Propargyl halide (**11-13**)			Yield (%)	
R^1	X	R^2	L		**14**, **17**[a]	**19**, **20**
$(CH_3)_3Si$	S	C_6H_5	Br	**13**	69 (**14c**)	87 (**19c**)
$(CH_3)_3Si$	S	3,4-$(MeO)_2C_6H_3$	Cl	**11**	46 (**14d**)	47 (**19d**)
$(CH_3)_3Si$	Se	C_6H_5	Br	**13**	71 (**17c**)	42 (**20c**)

[a]Isolated yields based on trimethylsilylacetylene.

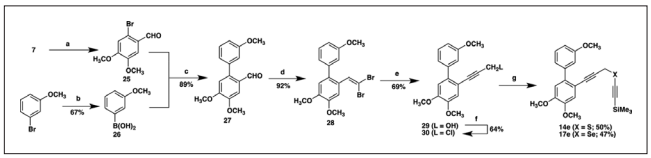
bromide **11** or **13** in a similar manner, and the subsequent treatment of a benzene solution of **14c-d** or **17c** with 2-methylpyrroline (**18**), prepared from 2-methylpyrrolidone according to Hua's method,[73,74] at refluxing temperature afforded the corresponding [4 + 2] cycloadducts **19c-d** or **20c**, respectively, in moderate to high yields. All the results for the preparation of δ-chalcogenolactams (**19c-d**, **20c**) are summarized in Table 2.

Model compound **19c** ($R^2 = C_6H_5$) was then treated with OsO_4 (cat.) and $NaIO_4$ by using a general manner, and subsequently, the resulting crude mixture of 1,2-diols **21c** was converted into 5,8-dioxoindolizidine **23c** by 2-step procedure involving oxidative glycol cleavage using H_5IO_6 followed by base-induced desilylation of δ-lactam **22c** by using anhydrous Na_2CO_3 powder as shown in Scheme 2. However, all attempts for the introduction of *p*-methoxyphenyl group to the C-2 position of **23c**, involving the use of ArMgBr-CuBr-$(CH_3)_2S$, Ar_2Zn-Ni(acac)$_2$, ArI-Pd(OAc)$_2$-Ph_3P-Et_3N, and so on, resulted in the recovery of substrate **23c** at all, and, therefore, we abandoned the synthetic route **1I** which requires the subsequent intramolecular oxidative biaryl coupling of two aryl groups of compound **24** in this case.

In order to realize the synthesis *via* route **III**, preparation of propargyl halides bearing a functionalized biphenyl moiety at the acetylenic terminal was necessary prior to the construction of indolizidine skeleton by using hetero Diels-Alder reaction with cyclic imines. Therefore, we chose *m*-bromoanisole and 2-bromo-4,5-dimethoxybenzaldehyde (**25**) as starting materials, and these compounds were efficiently converted into propargyl chloride **30** bearing a functionalized biphenyl moiety in several steps involving Suzuki coupling, Corey-Fuchs reaction,[63,64] hydroxymethylation, and chlorination of propargyl alcohol **29** by using Ph_3P-CCl_4.[65,66] Trimethylsilylacetylene was then treated with *n*-butyllithium, elemental sulfur or selenium, and propargyl chloride **30** to afford the corresponding alkynyl propargyl sulfide **14e**

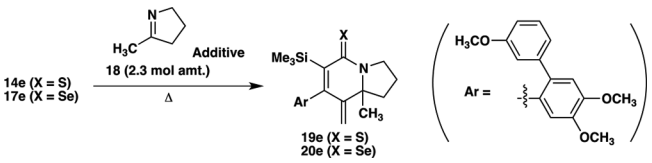


Scheme 2. Conversion of δ-thiolactam **19c** into 5,8-dioxoindolizidine **23c** [Procedures: (a) OsO_4 (2.0 mol%), $NaIO_4$ (2.0 mol amt.), aq. dioxane; (b) H_5IO_6 (2.0 mol amt.), aq. dioxane; and (c) K_2CO_3 (2.0 mol amt.), CH_3OH].



Scheme 3. Preparation of alkynyl propargyl chalcogenides (**14e**, **17e**) *via* Suzuki coupling of **25** and **26** [Procedures: (a) Br_2, AcOH; (b) (i) *n*-BuLi (1,2 mol amt.), (ii) $B(OCH_3)_3$ (1.2 mol amt.), (iii) aq. HCl; (c) Pd(OAc)$_4$ (10 mol%), Ph_3P (20 mol%), Et_3N (excess), DMF; (d) CBr_4 (2.0 mol amt.), Ph_3P (2.0 mol amt.), CH_2Cl_2; (e) (i) *n*-BuLi (2.0 mol amt.), THF, (ii) $(CH_2O)_n$ (1.0 mol amt.); (f) Ph_3P (1.1 mol amt.), CCl_4 (excess); and (g) trimethylsilylacetylene (2.0 mol amt.), *n*-BuLi (2.1 mol amt.), elemental sulfur or selenium (2.0 mol amt.)].

Table 3. Preparation of δ-Chalcogenolactams (**19e**, **20e**) from Alkynyl Propargyl Chalcogenides (**14e**, **17e**) and 2-Methylpyrroline (**18**).



Substrate		Additive		Condition		Yield of **19e**, **20e**
14e, **17e**[a]	X	(mol%)	Solvent	Temp (°C)	Time (h)	(%)
14e	S	-	Benzene	Reflux	12	9 (**19e**)
14e	S	$Yb(OTf)_3$ (10)	$ClCH_2CH_2Cl$	Reflux	12	47 (**19e**)
17e	Se	-	Benzene	Reflux	20	50 (**20e**)

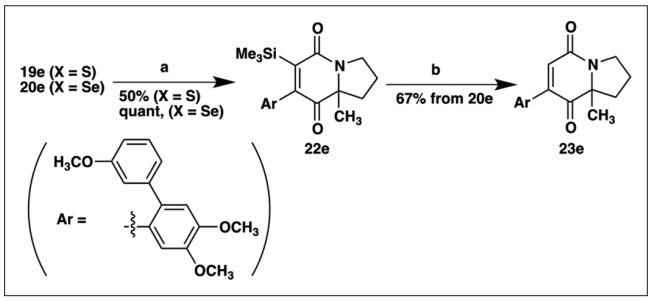
[a]Ar = 2-(3-methoxyphenyl)-4,5-dimethoxyphenyl.

and alkynyl propargyl selenide **17e**, respectively, in moderate yields as shown in Scheme 3.

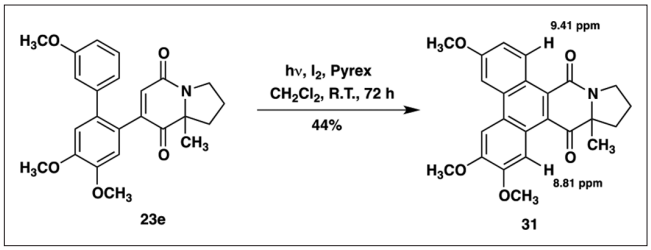
When a benzene solution of sulfide **14e** was treated with 2-methylpyrroline (**18**, 2.3 mol amt.) at refluxing temperature for 12 hours, the desired δ-thiolactam **19e** was obtained only in low yield. On the other hand, the yield of **19e** was raised up to 47% by heating **14e** and **18** in a similar manner in the presence of $Yb(OTf)_3$ (10 mol%). Furthermore, reaction of alkynyl propargyl selenide **17e** with **18** in a similar manner even in the absence of $Yb(OTf)_3$ also afforded the corresponding δ-selenolactam **20e** in 50% yield. These results were summarized in Table 3. Subsequent conversion of **19e** and **20e** into 5,8-dioxoindolizidine **23e** was carried out by the 2-step procedure mentioned above in the model reactions as summarized in Scheme 4.

The final ring closure of 5,8-dioindolizidine **23e** was efficiently achieved by using photochemical reactions by UV irradiation in dichloromethane in the presence of catalytic amount of I_2 to afford 9,14-dioxophenanthroindolizidine **31** in 44% yield[75-83] as shown in Scheme 5. Especially, the pentacyclic structure of **31** was supported by the characteristic low-field shift of 2 aromatic protons in the ^1H NMR spectrum of **31** in comparison with those of **23e**, *ie*, 8.81 ppm (1H, s) assignable to the C-1 proton located near to the carbonyl group at the C-14 position and 9.41 ppm (1H, dd, J = 9.4 Hz) assignable to the C-8 proton located near to the lactam carbonyl group in the spectrum of **31**, along with the disappearance of 2 proton signals of **23e**. It is worth noting that the same photoirradiation of **23e** in methanol, in place of dichloromethane as the solvent, also gave **31** in 42% yield, and we cannot find any solvent effects for the photochemical cyclization reaction. However, all attempts for the further reduction of **31** using $LiAlH_4$, Red-Al, or BH_3•THF resulted in the formation of complex mixture containing a small amount of uncharacterized products having a hydroxyl group along with the recovery of substrate **31**, and the further attempts would be required for the selective reduction of lactam carbonyl functionality of **31**.

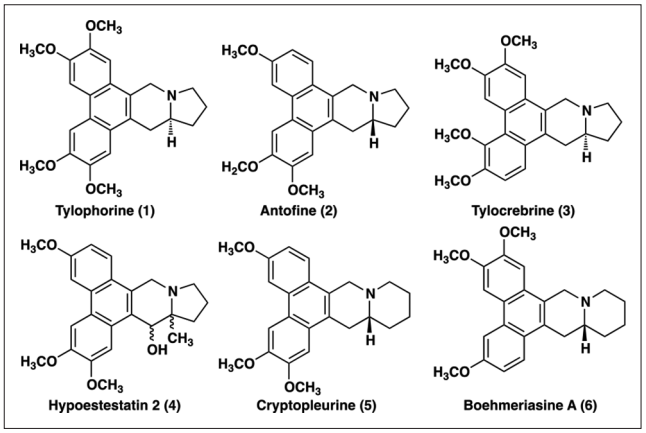
In conclusion, we found a new synthetic method of phenanthroindolizidine core *via* hetero Diels-Alder reaction of *in situ* generated α-allenylchalcogenoketenes with cyclic imines and the subsequent photochemical ring closure. Our hetero Diels-Alder methodology for the regioselective access to functionalized and fused indolizidine cores are highly flexible concerning the substitution patterns, and further applications of our new synthetic protocol to the synthesis of



Scheme 4. Conversion of δ-chalcogenolactams (**19e**, **20e**) into 5,8-dioxoindolizidine **23e** [Procedures: (a) (i) OsO_4 (2 mol%), $NaIO_4$ (4.0 mol amt.), aq. dioxane, (ii) H_5IO_6 (2.0 mol amt.), aq. dioxane; (b) anhydrous K_2CO_3 (2.0 mol amt.), CH_3OH, reflux].



Scheme 5. Synthesis of 9,14-dioxophenanthroindolizidine **31** by photocyclization of 5,8-dioxoindolizidine **23e**



Scheme 6. Phenanthroindorizidine and phenanthroquinolizidine alkaloids.

various phenanthroindolizidine derivatives having a variety of biological activities are expected in our laboratory.

Experimental

Instruments

The melting points were determined with a Barnstead International MEL-TEMP. ^{1}H NMR spectra were recorded on a Bruker DRX-400P (400 MHz) spectrometer or a Bruker AVANCE III 500 (500 MHz) spectrometer, and the chemical shifts of the ^{1}H NMR spectra are given in δ relative to internal tetramethylsilane (TMS). ^{13}C NMR spectra were recorded on a Bruker DRX-400P (100 MHz) or a Bruker AVANCE III 500 (126 MHz) spectrometer. ^{77}Se NMR spectra were recorded on a Bruker DRX-400P (76 MHz) spectrometer. Mass spectra were recorded on a JEOL JMS-700T mass spectrometer with electron-impact ionization at 20 or 70 eV using a direct inlet system. High-resolution mass spectra (HRMS) were also recorded on a JEOL JMS-700T spectrometer. IR spectra were recorded for thin film (neat) or KBr disks on a JASCO FT/IR-7300 spectrometer. Elemental analyses were performed using a Yanagimoto CHN corder MT-5.

A General Procedure for Preparation of Alkynyl Propargyl Chalcogenides (14, 17)

A THF solution of trimethylsilylacetylene was treated with *n*-butyllithium (1.1 mol amt.) at 0°C for 15 minutes, then with elemental sulfur (1.1 mol amt.) at 0°C for 15 minutes, and then with propargyl bromide (1.0 mol amt.) at room temperature for 1 hour. The reaction was quenched by the addition of water, and the reaction mixture was extracted with benzene. The organic layer was washed twice with water and was dried over anhydrous Na_2SO_4 powder. The organic solvent was removed *in vacuo*, and the residual crude products were subjected to column chromatography on silica gel to obtain alkynyl propargyl sulfide **14**.

Physical and Spectral Data for Alkynyl Propargyl Sulfides 14 and Selenides 17

14a (X = S, $R^1 = C_6H_5$, R^2 = 3,4-(methylenedioxy)phenyl):
Yellow oil.
IR (neat): 2898, 2166, 1501, 1487, 1250, 1226, 1039, 756 cm^{-1}.
^{1}H NMR ($CDCl_3$) δ: 3.83 (2H, s), 5.97 (2H, s), 6.74 (1H, d, J = 1.6 Hz), 6.89 (1H, d, J = 8.0 Hz), 6.97 (1H, dd, J = 8.0, 1.6 Hz), 7.29-7.31 (3H, m), 7.42-7.44 (2H, m).
^{13}C NMR ($CDCl_3$) δ: 25.9 (t), 78.2 (s), 81.9 (s), 85.0 (s), 95.8 (s), 101.4 (t), 108.4 (d), 111.8 (d), 115.9 (s), 123.2 (s), 126.6 (d), 128.4 (d × 2), 131.7 (d), 147.4 (s), 148.1 (s).
HRMS Calcd for $C_{18}H_{12}O_2S$: *m/z* 292.0558. Found: *m/z* 292.0558.

14b (X = S, R^1 = 3,4-$(CH_3O)_2C_6H_3$, R^2 = 3,4-(methylenedioxy)phenyl):
Reddish oil.
IR (neat): 2905, 2155, 1595, 1506, 1448, 1327, 1238, 1135, 1033, 812, 616 cm^{-1}.
^{1}H NMR ($CDCl_3$) δ: 3.81 (2H, s), 3.83 (3H, s), 3.88 (3H, s), 5.95 (2H, s), 6.72 (1H, d, J = 8.4 Hz), 6.78 (1H, d, J = 8.4 Hz), 6.88 (1H, d, J = 1.6 Hz), 6.95-6.98 (2H, m), 7.06 (1H, dd, J = 8.4, 1.6 Hz).
^{13}C NMR ($CDCl_3$) δ: 25.9 (t), 55.8 (q), 55.9 (q), 76.3 (s), 82.0 (s), 85.0 (s), 95.8 (s), 101.3 (t), 108.4 (d), 110.9 (d), 111.8 (d), 114.7 (d), 115.3 (s), 116.9 (s), 125.5 (d), 126.5 (d), 147.4 (s), 148.0 (s), 148.5 (s), 149.8 (s).
HRMS Calcd for $C_{20}H_{16}O_4S$: *m/z* 352.0769. Found: *m/z* 352.0770.

14c (X = S, $R^1 = (CH_3)_3Si$, $R^2 = C_6H_5$)
Yellow oil.
IR (neat): 2960, 2095, 1491, 1250, 833 cm^{-1}.
^{1}H NMR ($CDCl_3$) δ: 0.18 (9H, s), 3.77 (2H, s), 7.30-7.31 (3H, m), 7.43-7.46 (2H, m).
^{13}C NMR ($CDCl_3$) δ: 0.20 (q), 25.5 (t), 83.2 (s), 85.0 (s), 93.0 (s), 103.5 (s), 122.5 (s), 128.1 (d), 128.4 (d), 131.7 (d).
MS (*m/z*): 244 (M^+; bp), 230 (M^+-CH_3; 96%).
Calcd for $C_{14}H_{16}SSi$: C, 68.79; H, 6.60%. Found: C, 68.54; H, 6.48%.

14d (X = S, $R^1 = (CH_3)_3Si$, R^2 = 3,4-$(CH_3O)_2C_6H_3$):
Yellow oil.
IR (neat): 2960, 2092, 1514, 1248 cm^{-1}.
^{1}H NMR ($CDCl_3$) δ: 0.17 (9H, s), 3.77 (2H, s), 3.87 (6H, s), 6.79 (1H, d, J = 8.3 Hz), 6.94 (1H, s), 7.05 (1H, dd, J = 8.3, 1.8 Hz).
^{13}C NMR ($CDCl_3$) δ: −0.20 (q), 25.6 (t), 55.7 (q × 2), 81.6 (s), 85.0 (s), 91.3 (s), 103.4 (s), 110.8 (d), 114.4 (d), 114.7 (s), 125.0 (d), 148.4 (s), 149.5 (s).
MS (*m/z*): 304 (M^+; 3%), 175 (M^+-TMSCCS; bp).
Calcd for $C_{16}H_{20}O_2SSi$: C, 63.11; H, 6.62%. Found: C, 62.94; H, 6.51%.

17c (X = Se, $R^1 = (CH_3)_3Si$, $R^2 = C_6H_5$):

Pale yellow oil.

IR (neat): 2960, 2088, 1491, 1250, 860, 844, 758 cm^{-1}.

^1H NMR ($CDCl_3$) δ: 0.18 (9H, s), 3.78 (2H, s), 7.25-7.31 (3H, m), 7.42-7.44 (2H, m).

^{13}C NMR ($CDCl_3$) δ: −0.10 (q), 15.4 (t), 84.4 (s), 85.3 (s), 110.5 (s), 122.7 (s), 128.2 (d), 128.4 (d), 131.8 (d).

^{77}Se NMR ($CDCl_3$) δ: 260.0.

MS (*m/z*): 292 (M^+; bp, ^{80}Se), 277 (M^+-CH_3; 74%, ^{80}Se), 195 ($C_6H_5CCCH_2Se$; 60%).

Calcd for $C_{14}H_{16}SeSi$: C, 57.72, H, 5.54%. Found: C, 57.80, H, 5.59%

A General Procedure for the Synthesis of 2,3-Disubstituted 4-Methylene-2-cyclobutene-1-thiones 15

A hexane solution of alkynyl propargyl sulfide **14** was heated at refluxing temperature for 12 hours. The reaction mixture was then subjected to evaporation *in vacuo*, and the crude products were purified by column chromatography on silica gel to obtain 2,3-disubstituted 4-methyl-2-cyclobutene-1-thione **15**.

Physical and Spectral Data for 4-Methylene-2-cyclobutene-1-thiones 15

15a (X = S, $R^1 = C_6H_5$, R^2 = 3,4-(methylenedioxy)phenyl):

Red oil.

IR (neat): 2899, 1610, 1478, 1244, 1099, 1037, 756 cm^{-1}.

^1H NMR ($CDCl_3$) δ: 5.06 (1H, s), 5.40 (1H, s), 6.08 (2H, s), 6.74 (1H, d, *J* = 8.0 Hz), 6.89 (1H, d, *J* = 1.6 Hz), 6.95 (1H, d, *J* = 8.0 Hz), 7.32 (1H, s), 7.38-7.46 (3H, m), 7.49 (1H, d, *J* = 8.0 Hz), 7.90 (1H, d, *J* = 8.0 Hz).

^{13}C NMR ($CDCl_3$) δ: 94.6 (t), 102.0 (t), 107.8 (d), 109.2 (d), 124.6 (d), 124.8 (s), 128.1 (d), 128.6 (d), 129.7 (s), 129.8 (d), 148.4 (s), 151.2 (s), 153.9 (s), 157.7 (s), 171.4 (s), 225.8 (s).

HRMS Calcd for $C_{18}H_{12}O_2S$: *m/z* 292.0558. Found: *m/z* 292.0561.

15b (X = S, R^1 = 3,4-$(CH_3O)_2C_6H_3$, R^2 = 3,4-(methylenedioxy)phenyl):

Red powder.

MP: 160.5°C-161.7°C

IR (KBr) 2929, 1590, 1510, 1445, 1368, 1267, 1031, 851 cm^{-1}.

^1H NMR ($CDCl_3$) δ: 3.86 (3H, s), 3.93 (3H, s), 4.99 (1H, d, *J* = 1.6 Hz), 5.34 (1H, d, *J* = 1.6 Hz), 6.09 (2H, s), 6.92 (1H, d, *J* = 8.4 Hz), 6.96 (1H, d, *J* = 8.4 Hz), 7.37 (1H, d, *J* = 1.6 Hz), 7.51 (1H, dd, *J* = 8.4, 1.6 Hz), 7.57-7.60 (2H, m).

^{13}C NMR ($CDCl_3$) δ: 54.9 (q × 2), 92.3 (t), 101.0 (t), 106.7 (d), 108.1 (d), 110.0 (d × 2), 120.5 (d), 121.5 (s), 123.3 (d), 124.0 (s), 147.3 (s), 147.7 (s), 149.4 (s), 149.9 (s), 153.0 (s), 156.2 (s), 169.0 (s), 225.2 (s).

HRMS Calcd for $C_{20}H_{16}O_4S$: *m/z* 352.0769. Found: *m/z* 352.0781.

A General Procedure for the Synthesis of 2,3-Disubstituted 4-Methylene-2-cyclobuten-1-ones 16

A dichloromethane solution of 4-methylene-2-cyclobutene-1-thione **15** was treated with *m*CPBA (1.2 mol amt.) at 0°C for 30 minutes. The reaction was quenched by the addition of saturated aqueous Na_2SO_3 solution, and the reaction mixture was extracted with dichloromethane. The organic layer was washed with water and was dried over anhydrous Na_2SO_4 powder. The organic solvent was removed *in vacuo*, and the residual crude products were subjected to column chromatography on silica gel to obtain 4-methylene-2-cyclobuten-1-one **16** as yellow oil.

Physical and Spectral Data for 4-Methylene-2-cyclobuten-1-ones 16

16a ($R^1 = C_6H_5$, R^2 = 3,4-(methylenedioxy)phenyl):

Yellow oil.

IR (neat): 2908, 1748, 1548, 1484, 1441, 1351, 1243, 1031, 699 cm^{-1}.

^1H NMR ($CDCl_3$) δ: 5.01 (1H, s), 5.26 (1H, s), 6.07 (2H, s), 6.94 (1H, d, *J* = 8.0 Hz), 7.26 (1H, d, *J* = 1.6 Hz), 7.36-7.42 (4H, m), 7.80 (2H, dd, *J* = 8.0, 1.6 Hz).

^{13}C NMR ($CDCl_3$) δ: 95.6 (t), 101.9 (t), 107.8 (d), 109.0 (d), 123.7 (d), 125.0 (s), 127.6 (d), 128.8 (d), 129.4 (s), 129.8 (d), 148.2 (s), 150.5 (s), 154.4 (s), 156.9 (s), 171.6 (s), 188.3 (s).

HRMS Calcd for $C_{18}H_{12}O_2S$: *m/z* 276.0786. Found: *m/z* 276.0780.

16b (R^1 = 3,4-$(CH_3O)_2C_6H_3$, R^2 = 3,4-(methylenedioxy)phenyl):

Yellow oil.

IR (neat): 2910, 1757, 1595, 1512, 1445, 1359, 1256, 1032 cm^{-1}.

^1H NMR ($CDCl_3$) δ: 3.86 (3H, s), 3.92 (3H, s), 4.94 (1H, d, *J* = 1.6 Hz), 5.20 (1H, d, *J* = 1.6 Hz), 6.08 (2H, s), 6.88 (1H, d, *J* = 8.4 Hz), 6.95 (1H, d, *J* = 8.4 Hz), 7.30 (1H, s), 7.37-7.41 (2H, m), 7.48 (1H, dd, *J* = 8.4, 1.6 Hz).

^{13}C NMR ($CDCl_3$) δ: 55.9 (q), 94.4 (t), 101.9 (t), 107.8 (d), 108.8 (d), 110.2 (d), 111.1 (d), 121.2 (d), 122.2 (d), 123.4 (d), 125.2 (s), 148.2 (s), 148.9 (s), 150.2 (s), 150.5 (s), 154.1 (s), 156.9 (s), 169.8 (s), 188.6 (s).

HRMS Calcd for $C_{20}H_{16}O_5$: *m/z* 336.0998. Found: *m/z* 336.0994.

A Typical Procedure for the Synthesis of δ-Chalcogenolactams (19, 20)

A benzene solution of alkynyl propargyl sulfide **14** was treated with 2-methylpyrroline **18** (1.5 mol amt.) at refluxing

temperature for 14 hours. The reaction mixture was then subjected to evaporation *in vacuo*, and the crude products were purified by column chromatography on silica gel to obtain δ-thiolactam **19** as yellow needles.

Physical and Spectral Data for δ-Chalcogenolactams (19, 20)

19c (X = S, $R^1 = (CH_3)_3Si$, $R^2 = C_6H_5$):

Yellow needles.

MP: 155.0°C-156.5°C

IR (KBr): 2971, 2359, 1623, 1246 cm^{-1}.

^1H NMR ($CDCl_3$) δ: −0.26 (9H, s), 1.48 (3H, s), 2.09-2.30 (4H, m), 3.81 (1H, br. dt, *J* = 14.1, 9.3 Hz), 4.07 (1H, br. dt, *J* = 14.1, 2.2 Hz), 4.88 (1H, s), 5.26 (1H, s), 7.14-7.17 (1H, m), 7.28–7.38 (4H, m).

^{13}C NMR ($CDCl_3$) δ: 2.29 (q), 21.4 (t), 26.2 (q), 38.2 (t), 52.3 (t), 65.3 (s), 118.8 (dd), 127.7 (d), 127.9 (d), 128.5 (d), 130.0 (d), 139.7 (s), 140.9 (s), 147.7 (s), 151.5 (s), 190.4 (s).

MS (*m/z*): 327 (M^+−1; 4%), 296 (M^+-S; bp), 73 ($(CH_3)_3Si$; 30%).

Calcd for $C_{19}H_{25}NSSi$: C, 69.67; H, 7.69; N, 4.28%. Found: C, 69.45; H, 7.56; N, 4.33%.

19d (X = S, $R^1 = (CH_3)_3Si$, $R^2 = 3,4\text{-}(CH_3O)_2C_6H_3$):

Yellow needles.

MP: 131.5°C-132.6°C

IR (KBr): 3097, 2971, 1602, 1454, 1266, 1246 cm^{-1}.

^1H NMR ($CDCl_3$) δ = −0.21 (9H, s), 1.47 (3H, s), 2.12-2.27 (4H, m), 3.76 (3H, s), 3.83 (3H, s), 3.80-–4.10 (2H, m), 4.96 (1H, s), 5.26 (1H, s), 6.76-6.83 (3H, m).

^{13}C NMR ($CDCl_3$) δ: 2.11 (q), 2.13 (q), 21.1 (t), 25.7 (q), 37.8 (t), 37.9 (t), 51.8 (t), 51.9 (t), 65.0 (s), 109.9 (d), 110.7 (d), 112.7 (d), 114.4 (d), 118.3 (s), 139.7 (s), 140.1 (s), 146.9 (s), 151.1 (s), 190.1 (s).

MS (*m/z*): 387 (M^+; 2%), 327 (M^+-CH_3; bp), 73 ($(CH_3)_3Si$; 3%).

Calcd for $C_{21}H_{29}NO_2SSi$: C, 65.07; H, 7.54; N, 3.61%. Found: C, 64.92; H, 7.44; N, 3.57%.

20c (X = Se, $R^1 = (CH_3)_3Si$, $R^2 = C_6H_5$):

Red needles.

MP: 142.9°C-133.1°C

IR (KBr): 3074, 2970, 1635, 1519, 1488, 1241, 1176, 861 cm^{-1}.

^1H NMR ($CDCl_3$) δ: 0.08 (9H, s), 1.48 (3H, s), 2.15-2.36 (4H, m), 3.72-3.80 (1H, m), 4.06-4.12 (1H, m), 5.00 (1H, s), 5.34 (1H, s), 7.16-7.18 (1H, m), 7.32-7.39 (4H, m).

^{13}C NMR ($CDCl_3$) δ: 2.68 (q), 21.4 (t), 25.2 (q), 38.1 (t), 55.9 (t), 65.8 (s), 119.2 (d), 127.7 (d), 128.1 (d), 128.6 (d), 130.1 (d), 131.0 (d), 139.7 (s), 144.0 (s), 145.2 (s), 151.5 (s), 192.2 (s).

^{77}Se NMR ($CDCl_3$) δ: 671.5 (s).

MS (*m/z*): 375 (M^+; 18%), 360 (M^+-CH_3; bp), 83 (C_5H_9N; 95%).

Calcd for $C_{19}H_{25}NSeSi$: C, 60.94; H, 6.73; N, 3.74%. Found: C, 61.21; H, 6.48; N, 3.51%.

Conversion of δ-Thiolactam 19c Into δ-Lactam 22c

An aqueous dioxane solution (dioxane:H_2O = 4:1) of δ-thiolactam **19c** (300 mg, 0.92 mmol) was treated with $NaIO_4$ (790 mg, 4.0 mol amt.) at 0°C and then the reaction mixture was treated with an aqueous OsO_4 solution (*c* = 1 mg/1 mL) (4.7 mL, 2.0 mol%) at room temperature for 20 hours. Then, the reaction mixture was extracted with diethyl ether. The organic layer was washed with an aqueous $Na_2S_2O_3$ solution and was dried over anhydrous Na_2SO_4 powder. The organic solvent was removed *in vacuo* to obtain the crude mixture of **21** as brown oil. An aqueous dioxane solution (dioxane:H_2O = 1:1) of the crude mixture of **21** was then treated with H_5IO_6 (419 mg, 2.0 mol amt.) at room temperature for 2 hours, and the reaction mixture was extracted with diethyl ether. The organic layer was washed with an aqueous $Na_2S_2O_3$ solution and was dried over anhydrous Na_2SO_4 powder. The organic solvent was removed *in vacuo*, and the residual crude products were subjected to column chromatography on silica gel to obtain the corresponding δ-lactam **22c** (198 mg, 69% yield) as yellow needles.

Physical and Spectral Data for δ-Lactam 22c

22c ($R^1 = (CH_3)_3Si$, $R^2 = C_6H_5$):

Yellow needles.

MP: 118.6°C-119.4°C

IR (neat): 2974, 1713, 1441, 1243 cm^{-1}.

^1H NMR ($CDCl_3$) δ: −0.03 (9H, s), 1.35 (3H, s), 1.95-2.20 (4H, m), 3.60-3.70 (1H, m), 3.74-3.81 (1H, m), 7.05-7.20 (2H, m), 7.35-7.40 (3H, m).

MS (*m/z*): 314 (M^++1; 54%), 298 (M^+-CH_3; bp).

Calcd for $C_{18}H_{23}NO_2Si$: C, 68.97; H, 7.40; N, 4.47%. Found: C, 68.72; H, 7.34; N, 4.56%.

Desilylation of δ-Lactam 22c

A methanol solution of δ-lactam **22c** (144 mg, 0.46 mmol) was treated with anhydrous K_2CO_3 powder (121 mg, 2.0 mol amt.) at refluxing temperature for 5 hours. The reaction mixture was then cooled to room temperature, and the solvent was removed by evaporation. The residual crude products were subjected to chromatography on silica gel to obtain 5,8-dioxoindolizidine **23** (95 mg, 86% yield) as yellow oil.

Physical and Spectral Data for 5,8-Dioxoindolizidine 23c

23c (R^1 = H, $R^2 = C_6H_5$):

Yellow oil.

IR (neat): 2997, 1694, 1655, 1597, 1433, 1112, 704 cm^{-1}.

^1H NMR ($CDCl_3$) δ: 1.25 (3H, s), 1.60-1.80 (2H, m), 1.90-2.05 (2H, m), 3.35-3.50 (1H, m), 3.55-3.75 (1H, m), 7.06 (1H, s), 7.10-7.30 (5H, m).

Preparation of Biphenyl Derivative 27

A THF solution of 3-bromoanisole was treated with *n*-butyllithium (1.2 mol amt.) at −78°C for 30 minutes, and the reaction mixture was treated with $B(OCH_3)_3$ (1.2 mol amt.) at −78°C for 1 hour and then at room temperature for 2 hours. The reaction was quenched by the addition of aqueous 1 M HCl solution, and the reaction mixture was extracted with diethyl ether. The organic layer was washed with water and was dried over anhydrous Na_2SO_4 powder. The organic solvent was removed *in vacuo*, and the residual crude products were washed with hexane to obtain boronic acid **26** as colorless needles (822 mg, quantitative yield). Subsequently, a *N,N*-dimethylformamide (DMF) solution of 2-bromo-4,5-dimethoxybenzaldehyde (**25**) was treated with boronic acid **26** (1.2 mol amt.), triphenylphosphine (20 mol%), $Pd(OAc)_2$ (10 mol%), and triethylamine (excess) at 110°C for 5 hours. After removal of DMF by evaporation, the residual mixture was extracted with chloroform. The organic layer was washed twice with water and was dried over anhydrous Na_2SO_4 powder. The organic solvent was removed *in vacuo*, and the residual crude products were subjected to column chromatography on silica gel to obtain biphenyl aldehyde **27** as yellow solids.

Physical and Spectral Data for Biphenyl Aldehyde 27

Yellow prisms.

MP: 97.5°C-97.9°C

IR (KBr): 2940, 1669, 1506, 1272, 1154, 1042, 991, 757 cm^{-1}.

^1H NMR ($CDCl_3$) δ: 3.85 (3H, s), 3.95 (3H, s), 3.97 (3H, s), 6.86 (1H, s), 6.91-6.98 (3H, m), 7.30-7.38 (1H, m), 7.53 (1H, m), 9.84 (1H, s).

^{13}C NMR ($CDCl_3$) δ: 55.0 (q), 55.8 (q), 55.9 (q), 108.2 (d), 112.2 (d), 113.1 (d), 115.7 (d), 122.5 (d), 126.7 (d), 129.0 (d), 138.7 (s), 141.0 (s), 148.5 (s), 153.1 (s), 159.2 (s), 190.8 (d).

MS (*m/z*): 272 (M^+; bp), 241 (M^+-OCH_3; 20%).

Calcd for $C_{16}H_{16}O_4$: C, 70.57; H, 5.92%. Found: C, 70.67; H, 5.85%.

Conversion of Biphenyl Aldehyde 27 Into 1,1-Dibromoalkene 28

A dichloromethane solution of biphenyl aldehyde **27** (2.840 g, 10.4 mmol) was treated with triphenylphosphine (5.472 g, 2.0 mol amt.) and carbon tetrabromide (6.918 g, 2.0 mol amt.) at refluxing temperature for 10 hours. The reaction mixture was then cooled to room temperature, and the reaction was quenched by the addition of saturated aqueous $NaHCO_3$ solution to the reaction mixture. The reaction mixture was extracted with chloroform, and the organic layer was dried over anhydrous Na_2SO_4 powder. The organic solvent was removed *in vacuo*, and the residual crude products were subjected to column chromatography on silica gel to obtain 1,1-dibromoalkene **28** (4.110 g, 92% yield) as yellow needles.

Physical and Spectral Data for 1,1-Dibromoalkene 28

Yellow needles.

MP: 78.0°C-78.7°C

IR (KBr): 3018, 2936, 1606, 1566, 1488, 1464, 1254, 1137, 1051, 1030, 872, 753 cm^{-1}.

^1H NMR ($CDCl_3$) δ: 3.85 (3H, s), 3.91 (3H, s), 3.94 (3H, s), 6.86 (1H, s), 6.86 (1H, s), 6.90 (1H, br. d, J = 7.8 Hz), 6.92 (1H, br. d, J = 7.8 Hz), 7.21 (1H, s), 7.28 (1H, s), 7.33 (1H, t, J = 7.8 Hz).

^{13}C NMR ($CDCl_3$) δ: 55.2 (q), 55.9 (q), 56.0 (q), 89.1 (s), 111.8 (d), 112.4 (d), 113.1 (d), 115.0 (d), 121.9 (d), 125.7 (s), 129.2 (d), 134.2 (s), 137.0 (d), 141.3 (s), 147.7 (s), 148.9 (s), 159.2 (s).

MS (*m/z*): 430 (M^+; 2%, ^{81}Br), 428 (M^+; 3%, ^{81}Br+^{79}Br), 426 (M^+; 2%, ^{79}Br), 320 (M^+-$C_6H_4OCH_3$; 3%), 268 (M^+-Br_2; 39%).

Calcd for $C_{17}H_{16}Br_2O_3$: C, 47.69; H, 3.77%. Found: C, 47.61; H, 3.72%.

Conversion of 1,1-Dibromoalkene 28 Into Propargyl Alcohol 29

A THF solution of 1,1-dibromoalkene **28** (3.719 g, 8.69 mmol) was treated with *n*-butyllithium (11.0 mL, 2.0 mol amt.) at −78°C for 30 minutes, and subsequently, the reaction mixture was treated with paraformaldehyde (260 mg, 1.0 mol amt.) at room temperature for 15 hours and then at refluxing temperature for 1 hour. The reaction was quenched by the addition of water at room temperature. The reaction mixture was extracted with chloroform, and the organic layer was dried over anhydrous Na_2SO_4 powder. The organic solvent was removed *in vacuo*, and the residual crude products were subjected to column chromatography on silica gel to obtain propargyl alcohol **29** (1.788 g, 69% yield) as yellow oil.

Physical and Spectral Data for Propargyl Alcohol 29

Yellow oil.

IR (neat): 3504, 2920, 2225, 1516, 1496, 1255, 1219, 1152, 1028, 999, 755 cm^{-1}.

^1H NMR ($CDCl_3$) δ: 1.70 (1H, br. s), 3.86 (3H, s), 3.90 (6H, s), 4.35 (2H, d, J = 5.8 Hz), 6.87 (1H, s), 7.02 (1H, s), 7.10-7.16 (2H, m), 7.16 (1H, s), 7.32 (1H, t, J = 7.9 Hz).

^{13}C NMR ($CDCl_3$) δ: 51.5 (t), 55.2 (q), 55.8 (q), 55.9 (q), 85.2 (s), 88.5 (s), 112.2 (d), 112.5 (s), 112.7 (d), 114.8 (d), 115.3 (d), 121.5 (d), 128.9 (d), 137.0 (s), 141.6 (s), 147.7 (s), 149.3 (s), 159.0 (s).

MS (*m/z*): 298 (M^+; 37%), 281 (M^+-OH; 6%), 267 (M^+-OCH_3; 7%).

Calcd for $C_{18}H_{18}O_4$: C, 72.47; H, 6.08%. Found: C, 72.31; H, 6.20%

Conversion of Propargyl Alcohol 29 Into Propargyl Chloride 30

A CCl_4 solution (excess) of propargyl alcohol **29** (1.311 g, 4.39 mmol) was treated with triphenylphosphine (1.267 g, 1.1 mol amt.) at refluxing temperature for 14 hours and then the reaction mixture was cooled to room temperature. The reaction mixture was subjected to suction filtration through a silica gel layer, and the residual solids were washed with a 3:1 mixture of hexane and ethyl acetate. The organic solvents were removed *in vacuo*, and the residual crude products were subjected to column chromatography on silica gel to obtain propargyl chloride **30** (1.159 g, 82% yield) as yellow needles.

Physical and Spectral Data for Propargyl Chloride 30

Yellow needles.

MP: 80.5°C-81.2°C

IR (KBr): 2937, 1602, 1516, 778 cm^{-1}.

^1H NMR ($CDCl_3$) δ: 3.78 (3H, s), 3.89 (6H, s), 4.25 (2H, d, J = 0.7 Hz), 6.68 (1H, s), 6.89 (1H, d, J = 8.3 Hz), 7.02 (1H, s), 7.07-7.13 (1H, m), 7.32 (1H, t, J = 8.3 Hz).

^{13}C NMR ($CDCl_3$) δ = 31.3 (t), 55.1 (q), 55.8 (q), 55.9 (q), 84.8 (s), 86.2 (s), 111.8 (s), 112.2 (d), 113.1 (d), 114.4 (d), 115.4 (d), 121.4 (d), 128.9 (d), 137.6 (s), 141.3 (s), 147.7 (s), 149.6 (s), 159.0 (s). MS (*m/z*): 318 (M^+; 10%, ^{37}Cl), 316 (M^+; 23%, ^{35}Cl), 281 (M^+-Cl; 11%), 175 ($C_6H_3(OCH_3)_2CCCH_2$; bp), 51 (CH_2Cl; 3%, ^{37}Cl), 49 (CH_2Cl; 11%, ^{35}Cl).

Calcd for $C_{18}H_{17}ClO_3$: C, 68.25; H, 5.41%. Found: C, 68.10; H, 5.42%.

A Typical Procedure for Preparation of Alkynyl Propargyl Chalcogenides (14e, 17e)

A THF solution of trimethylsilylacetylene (930 mg, 2.0 mol amt.) was treated with *n*-butyllithium (7.0 mL, 2.1 mol amt.) at 0°C for 30 minutes, then with elemental selenium (748 mg, 2.0 mol amt.) at 0°C for 15 minutes, and then with propargyl chloride **30** (1.500 g, 4.74 mmol) at room temperature for 30 minutes. The reaction was quenched by the addition of water, and the reaction mixture was extracted with benzene. The organic layer was washed twice with water and was dried over anhydrous Na_2SO_4 powder. The organic solvent was removed *in vacuo*, and the residual crude products were subjected to column chromatography on silica gel to obtain alkynyl propargyl selenide **17e** (910 mg, 42% yield) as orange oil.

Physical and Spectral Data for 14e and 17e

14e (X = S, R^1 = $(CH_3)_3Si$, R^2 = 2-(3-methoxyphenyl)−4,5-dimethoxyphenyl):

Yellow oil.

IR (neat): 2961, 2093, 1602, 1516, 1252, 1029, 880, 845 cm^{-1}.

^1H NMR ($CDCl_3$) δ: 0.15 (9H, s), 3.68 (2H, s), 3.84 (3H, s), 3.89 (6H, s), 6.84-6.89 (3H, m), 7.02 (1H, s), 7.11 (1H, s), 7.29-7.34 (1H, m).

^{13}C NMR ($CDCl_3$) δ = −0.22 (q), 25.8 (t), 55.1 (q), 55.7 (q), 55.8 (q), 84.2 (s), 84.8 (s), 93.2 (s), 103.2 (s), 111.8 (s), 112.2 (d), 113.1 (d), 114.4 (d), 115.4 (d), 121.4 (d), 128.9 (d), 137.6 (s), 141.4 (s), 147.7 (s), 149.6 (s), 159.0 (s).

MS (*m/z*): 410 (M^+; 12%), 395 (M^+-CH_3; 7%), 281 (M^+-C_5H_3SSi; 87%), 73 ($(CH_3)_3Si$; bp).

Calcd for $C_{23}H_{26}O_3SSi$: C, 67.28; H, 6.38%. Found: C, 67.11; H, 6.21%.

17e (X = Se, R^1 = $(CH_3)_3Si$, R^2 = 2-(3-methoxyphenyl)−4,5-dimethoxyphenyl):

Orange oil.

IR (neat): 2958, 2087, 1712, 1602, 1516, 1250, 860 cm^{-1}.

^1H NMR ($CDCl_3$) δ: 0.14 (9H, s), 3.70 (2H, s), 3.87 (3H, s), 3.91 (6H, s), 6.85-6.87 (1H, m), 6.90 (1H, d, J = 7.9 Hz), 7.01 (1H, s), 7.10-7.11 (1H, m), 7.17 (1H, d, J = 7.9 Hz), 7.34 (1H, t, J = 7.9 Hz).

^{13}C NMR ($CDCl_3$) δ: −0.12 (q), 15.3 (t), 55.2 (q), 55.8 (q), 55.9 (q), 85.1 (s), 85.3 (s), 85.8 (s), 110.2 (s), 112.2 (d), 112.7 (d), 112.9 (d), 114.5 (d), 115.4 (d), 121.5 (d), 129.0 (d), 137.4 (s), 141.5 (s), 147.7 (s), 149.3 (s), 159.1 (s).

MS (*m/z*): 458 (M^+; 8%), 281 (M^+-C_5H_9SeSi; bp), 250 (M^+-$C_6H_{12}OSeSi$; 70%), 73 ($(CH_3)_3Si$; 19%).

Calcd for $C_{23}H_{26}O_3SeSi$: C, 60.38; H, 5.73%. Found: C, 60.23; H, 5.82%.

A Typical Procedure for the Synthesis of δ-Chalcogenolactams (19e, 20e)

A benzene solution of alkynyl propargyl selenide **17e** (328 mg, 0.72 mmol) was treated with 2-methylpyrroline **18** (2.0 mol amt.) at refluxing temperature for 20 hours. The reaction mixture was then subjected to evaporation *in vacuo*, and the crude products were purified by column chromatography on silica gel to obtain δ-selenolactam **20e** (194 mg, 50% yield) as yellow needles.

Synthesis of δ-Thiolactam 19e by Thermal Reaction of 14e in the Presence of $Yb(OTf)_3$

A dichloromethane solution of alkynyl propargyl sulfide **14e** (4.791 g, 11.7 mmol) was treated with 2-methylpyrroline (**18**, 2.910 g, 1.0 mol amt.) and $Yb(OTf)_3$ (940 mg, 10 mol%) at refluxing temperature for 12 hours. The reaction mixture was then subjected to evaporation *in vacuo*, and the crude products were purified by column chromatography on silica gel to obtain δ-thiolactam **19e** (2.708 g, 47% yield) as yellow needles.

Physical and Spectral Data for 19e and 20e

19e (X = S, R^1 = $(CH_3)_3Si$, R^2 = 2-(3-methoxyphenyl)−4,5-dimethoxyphenyl):

Yellow needles.

IR (KBr): 2958, 1711, 1602, 1516, 1253 cm^{-1}.

^1H NMR ($CDCl_3$) δ: 0.21 (9H, s), 0.78 (3H, s), 1.24-1.27 (2H, m), 1.95-2.04 (4H, m), 3.75 (3H, s), 3.88 (3H,s), 3.92 (3H, s), 4.67 (1H, s), 4.86 (1H, s), 6.74-6.79 (4H, m), 7.19-7.32 (2H, m).

^{13}C NMR ($CDCl_3$) δ: 3.33 (q), 20.7 (t), 26.7 (q), 38.5 (t), 52.5 (t), 55.1 (q), 55.9 (q × 2), 65.2 (s), 111.7 (d), 113.4 (d), 115.2 (d), 115.5 (d), 118.9 (d), 121.6 (d), 129.0 (d), 129.9 (s), 133.5 (s), 140.2 (s), 142.7 (s), 147.6 (s), 148.4 (s), 148.8 (s), 149.0 (s), 159.0 (s), 189.4 (s).

MS (*m/z*): 493 (M^+; 4%), 478 (M^+-CH_3; bp), 462 (M^+-OCH_3; 10%), 31 (CH_3O; 11%).

Calcd for $C_{28}H_{35}NO_3SSi$: C, 68.11; H, 7.15; N, 2.84%. Found: C, 67.97; H, 7.18; N, 2.81%.

20e (X = Se, R^1 = $(CH_3)_3Si$, R^2 = 2-(3-methoxyphenyl)-4,5-dimethoxyphenyl):

Red needles.

MP: 79.9°C-80.6°C

IR (KBr): 2958, 1601, 1521, 1437, 1251, 1173, 842 cm^{-1}.

^1H NMR ($CDCl_3$) δ: 0.26 (9H, s), 0.86 (3H, s), 2.02-2.04 (4H, m), 3.70-3.74 (1H, m), 3.76 (3H, s), 3.92 (3H, s), 3.94 (3H, s), 4.00-4.06 (1H, m), 4.77 (1H, s), 4.92 (1H, s), 6.77 (1H, d, *J* = 7.8 Hz), 6.81 (1H, s), 6.87-6.89 (3H, m), 7.20 (1H, t, *J* = 7.8 Hz).

^{13}C NMR ($CDCl_3$) δ: 3.85 (q), 20.7 (t), 26.0 (q), 38.5 (t), 55.1 (q), 55.9 (q × 2), 56.3 (t), 65.8 (s), 111.7 (d), 113.5 (d), 115.2 (d), 115.4 (d), 119.5 (s), 121.6 (d), 129.0 (d), 129.9 (s), 133.4 (s), 142.7 (s), 143.0 (s), 146.6 (s), 147.6 (s), 148.3 (s), 149.1 (s), 159.0 (s), 190.8 (s).

MS (*m/z*): 541 (M^+; 14%), 526 (M^+-CH_3; bp), 462 (M^+-Se; 9%), 388 (M^+-Se-$(CH_3)_3Si$; 7%).

Calcd for $C_{28}H_{35}NO_3SeSi$: C, 62.21; H, 6.53; N, 2.59%. Found: C, 62.02; H, 6.63; N, 2.52%

A Typical Procedure for the Conversion of δ-Chalcogenolactams (19e, 20e) Into δ-Lactam 22e

An aqueous dioxane solution (dioxane:H_2O = 4:1) of δ-selenolactam **20e** (100 mg, 0.18 mmol) was treated with $NaIO_4$ (158 mg, 4.0 mol amt.) at 0°C and then the reaction mixture was treated with an aqueous OsO_4 solution (*c* = 1 mg/1 mL) (0.9 mL, 2.0 mol%) at room temperature for 21 hours. Then, the reaction mixture was extracted with diethyl ether. The organic layer was washed with an aqueous $Na_2S_2O_3$ solution and was dried over anhydrous Na_2SO_4 powder. The organic solvent was removed *in vacuo* to obtain the crude mixture of **21** as brown oil. An aqueous dioxane solution (dioxane:H_2O = 1:1) of the crude mixture of **21** was then treated with H_5IO_6 (84 mg, 2.0 mol amt.) at room temperature for 4 hours, and the reaction mixture was extracted with diethyl ether. The organic layer was washed with an aqueous $Na_2S_2O_3$ solution and was dried over anhydrous Na_2SO_4 powder. The organic solvent was removed *in vacuo*, and the residual crude products were subjected to column chromatography on silica gel to obtain δ-lactam **22e** (89 mg, quantitative yield) as yellow needles.

Physical and Spectral Data for δ-Lactam 22e

22e (R^1 = $(CH_3)_3Si$, R^2 = 2-(3-methoxyphenyl)-4,5-dimethoxyphenyl):

Yellow needles.

MP: 74.6°C-75.6°C

IR (KBr): 2977, 1689, 1629, 1604, 1512, 1420, 1251, 1049 cm^{-1}.

^1H NMR ($CDCl_3$) δ: 0.17 (3H, s), 0.78 (9H, s), 1.90-1.92 (4H, m), 3.55-3.60 (1H, m), 3.67-3.73 (1H, m), 3.77 (3H, s), 3.89 (3H, s), 3.92 (3H, s), 6.64 (1H, s), 6.79 (1H, s), 6.79 (1H, d, *J* = 8.4 Hz), 6.86 (1H, d, *J* = 7.2 Hz), 6.87 (1H, s), 7.23 (1H, t, *J* = 8.4, 7.2 Hz).

^{13}C NMR ($CDCl_3$) δ: 0.58 (q), 20.3 (dd), 25.8 (q), 34.6 (t), 55.0 (q), 55.8 (q), 55.9 (q), 68.3 (s), 112.1 (d), 113.0 (d), 114.5 (d), 115.2 (d), 121.6 (d), 126.0 (s), 129.1 (d), 133.8 (s), 142.3 (s), 147.7 (s), 149.3 (s), 151.4 (s), 152.6 (s), 159.0 (s), 163.9 (s), 198.3 (s).

MS (*m/z*): 478 (M^+−1; 50%), 464 (M^+-CH_3; bp), 448 (M^+-OCH_3; 6%), 406 (M^+-$(CH_3)_3Si$; 36%), 73 ($(CH_3)_3Si$; 10%).

Calcd for $C_{27}H_{33}NO_5Si$: C, 67.61; H, 6.93; N, 2.92%. Found: C, 67.25; H, 7.05; N, 3.01%.

Desilylation of δ-Lactam 22e

A methanol solution of δ-lactam **22e** (701 mg, 1.46 mmol) was treated with anhydrous K_2CO_3 powder (391 mg, 2.0 mol amt.) at refluxing temperature for 13 hours. The reaction mixture was then cooled to room temperature, and the solvent was removed by evaporation. The residual crude products were subjected to chromatography on silica gel to obtain 5,8-dioxoindolizidine **23e** (399 mg, 67% yield) as yellow needles.

Physical and Spectral Data for 5,8-Dioxoindolizidine 23e

23e (R^1 = H, R^2 = 2-(3-methoxyphenyl)-4,5-dimethoxyphenyl):

Yellow needles.

MP: 75.3°C-76.7°C

IR (KBr): 2976, 1704, 1651, 1516, 1455, 1254, 1161, 1047 cm^{-1}.

^1H NMR ($CDCl_3$) δ: 0.97 (3H, s), 1.92-1.97 (4H, m), 3.56-3.62 (1H, m), 3.74-3.78 (1H, m), 3.79 (3H, s), 3.90 (3H, s), 3.91 (3H, s), 6.75 (1H, s), 6.78-6.79 (1H, m), 6.83 (2H, d, *J* = 7.5 Hz), 6.86 (1H, s), 6.88 (1H, s), 7.23 (1H, t, *J* = 7.5 Hz).

^{13}C NMR ($CDCl_3$) δ: 20.1 (t), 25.6 (q), 34.2 (t), 44.9 (t), 55.2 (q), 55.9 (q), 56.0 (q), 62.6 (s), 112.1 (d), 113.1 (d), 113.4 (d), 115.5 (d), 121.9 (d), 123.7 (s), 129.3 (d), 134.7 (s),

142.4 (s), 145.6 (s), 148.2 (s), 149.6 (s), 159.2 (s), 160.3 (s), 197.6 (s).

MS (*m/z*): 406 (M^+-1; bp), 391 (M^+-CH_3-1; 35%).

Calcd for $C_{24}H_{25}NO_5$: C, 70.74; H, 6.18; N, 3.44%. Found: C, 70.59; H, 6.02; N, 6.21%.

Synthesis of 9,14-Dioxophenanthroindolizidine 31 by Iodine-Assisted Photochemical Cyclization of 5,8-Dioxoindolizidine 23e

A dichloromethane or a methanol solution of 5,8-dioxoindolizidine **23e** (354 mg, 0.836 mmol) and iodine (10 mg) in a Pyrex test tube was subjected to photoirradiation using a high-pressure Hg lamp at room temperature for 72 hours. The reaction mixture was then subjected to evaporation *in vacuo*, and the crude products were purified by column chromatography on silica gel to obtain 9,14-dioxophenanthroindolizidine **31** (155 mg, 44% yield) as pale yellow needles.

Physical and Spectral Data for 9,14-Dioxophenanthroindolizidine 31

Pale yellow needles.

MP: 218.7°C-219.4°C

IR (KBr): 3119, 2980, 1646, 1614, 1520, 1425, 1260, 1112, 1051 cm^{-1}.

^1H NMR ($CDCl_3$) δ: 1.47 (3H, s), 2.12-2.18 (3H, m), 2.47-2.50 (1H, m), 3.88-3.92 (2H, m), 4.05 (3H, s), 4.09 (3H, s), 4.14 (3H, s), 7.03 (1H, dd, $J = 9.4$, 2.6 Hz), 7.86 (1H, d, $J = 2.6$ Hz), 7.89 (1H, s), 8.81 (1H, s), 9.41 (1H, d, $J = 9.4$ Hz).

^{13}C NMR ($CDCl_3$) δ: 21.3 (t), 26.2 (q), 34.6 (dd), 46.6 (t), 55.4 (q), 55.7 (q), 55.8 (q), 68.9 (s), 102.8 (d), 103.8 (d), 106.9 (d), 116.0 (d), 122.1 (s), 122.4 (s), 123.2 (s), 126.0 (s), 131.1 (s), 131.9 (d), 134.9 (s), 150.2 (s), 160.2 (s), 161.9 (s), 201.6 (s).

MS (*m/z*): 406 (M^++1; bp), 391 (M^+-CH_3 + 1; 35%).

Calcd for $C_{24}H_{23}NO_5$: C, 71.10; H, 5.72; N, 3.45%. Found: C, 71.21; H, 5.85; N, 3.49%.

Declaration of Conflicting Interests

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