An Efficient Synthesis of Phenanthroindolizidine Core via Hetero Diels-Alder Reaction of In Situ Generated \(\alpha\)-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 \(\alpha\)-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 sulfide, alkynyl propargyl selenide, \(\alpha\)-allenylthioketene, \(\alpha\)-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 phenanthroquinolizidine alkaloids, such as antofine (2), tylocrebrine (3), putative hypotesstatines (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 \(\alpha\)-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 \(\alpha\)-allenylchalcogenoketenes B, hetero Diels-Alder reaction with cyclic imines, and intramolecular biaryl coupling, and 3 different synthetic strategies for the construction of phenanthroindolizidine ring would be proposed as shown in Scheme 1.

The synthetic strategy I involves the formation of 2,3-diaryl-4-methylene-cyclobutene-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 \(\alpha\)-allenylchalcogenoketenes B with cyclic imines E,\(^{46-48}\) and both synthetic strategies II and III involve hetero Diels-Alder reaction of *in situ* generated \(\alpha\)-allenylchalcogenoketenes B with cyclic imines E forming...
indolizidine core. In strategy II, the subsequent intramolecular oxidative biaryl coupling of synthetic intermediates \( G \), structurally related to some unfused quinolizidine alkaloids as septicines, 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 \( I \).

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, such as \( \text{FeCl}_3 \), \( m \)CPBA-\( \text{FeCl}_3 \), and \( \text{MnO}_2 \), resulted in the formation of complex mixtures. Therefore, we must abandon synthetic route 1 by regarding these unsuccessful results.

On the other hand, alkynyl propargyl chalcogenides \( 14c-d \) (\( X = \text{S} \)) and \( 17c \) (\( X = \text{Se} \)) bearing a trimethylsilyl group at the \( R^1 \) substituent were prepared from trimethylsilylacetylene, \( \text{EtMgBr} \) or \( \text{n-BuLi} \), elemental chalcogen (\( X = \text{S, Se} \)), and a substituted propargyl.
bromide 11 or 13 in a similar manner, and the subsequent treatment of a benzene solution of 14c-d or 17c with 2-methylpyrrolidine according to Hua’s method 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 (R² = C₆H₅) was then treated with OsO₄ (cat.) and NaIO₄ 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 H₅IO₆ followed by base-induced desilylation of δ-lactam 22c by using anhydrous Na₂CO₃ 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-(CH₃)₂S, Ar₂Zn-Ni(acac)$_₂$, ArI-Pd(OAc)$_₂$-Ph₃P-Et$_3$N, 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, hydroxymethylation, and chlorination of propargyl alcohol 29 by using Ph$_3$P-CCl$_4$.

Trimethylsilylacetylene was then treated with n-butyllithium, elemental sulfur or selenium, and propargyl chloride 30 to afford the corresponding alkynyl propargyl sulfide 14e and so on, resulting 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.

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

| R¹ | X    | Propargyl halide (11-13) | Yield (%) |
|----|------|-------------------------|-----------|
| (CH₃)$_3$Si | S   | C₆H₅Br                  | 69 (14c)  | 87 (19c) |
| (CH₃)$_3$Si | S   | 3,4-(MeO)$_2$C₆H₃Cl     | 46 (14d)  | 47 (19d) |
| (CH₃)$_3$Si | Se  | C₆H₅Br                  | 71 (17c)  | 42 (20c) |

*Isolated yields based on trimethylsilylacetylene.

Scheme 2. Conversion of δ-thiolactam 19c into 5,8-dioxoindolizidine 23c [Procedures: (a) OsO₄, NaIO₄, H₂O, aq. dioxane; (b) H₂O, NaOH, aq. dioxane; (c) K₂CO₃, CH₃OH].

Scheme 3. Preparation of alkynyl propargyl chalcogenides (14e, 17e) via Suzuki coupling of 25 and 26 [Procedures: (a) Br₂, AcOH; (b) n-BuLi (1.2 mol amt.), (ii) B(OCH₃)$_2$, (1.2 mol amt.), (iii) NaH, HCl; (c) Pd(OAc)$_₂$ (10 mol%), Ph₃P (20 mol%), Et₃N (excess), DMF; (d) CBr₄ (2.0 mol amt.), Ph₃P (2.0 mol amt.), CH₂Cl₂; (e) n-BuLi (2.0 mol amt.), THF; (f) (CH₂O)$_n$ (1.0 mol amt.), Ph₃P (1.1 mol amt.), CCl₄ (excess); and (g) trimethylsilylacetylene (2.0 mol amt.), n-BuLi (2.1 mol amt.), elemental sulfur or selenium (2.0 mol amt.)].
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-dioxoindolizidine 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 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 $^1$H 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-allenylichalcogenoketenes 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...
column chromatography on silica gel to obtain alkynyl propargyl sulfide 14.

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

**14a** \( (X = \text{S}, \ R^1 = \text{C}_6\text{H}_3, \ R^2 = 3,4-(\text{methyleneoxy})\text{phenyl}) \):

Yellow oil.

IR (neat): 2898, 2166, 1501, 1487, 1250, 1226, 1039, 756 cm\(^{-1}\).

\( ^1\text{H} \) NMR (CDCl\(_3\)) \( \delta \): 3.83 (2H, s), 3.70 (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).

\( ^{13}\text{C} \) NMR (CDCl\(_3\)) \( \delta \): 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 \( \times 2 \)), 131.7 (d), 147.4 (s), 148.1 (s).

HRMS Calcd for C\(_{18}\)H\(_{12}\)O\(_2\)S: \( \text{m/z} 292.0558 \). Found: \( \text{m/z} 292.0558 \).

**14b** \( (X = \text{S}, \ R^1 = 3,4-(\text{CH}_3\text{O})_2\text{C}_6\text{H}_3, \ R^2 = 3,4-(\text{methylene-}

\text{dioxy})\text{phenyl}) \):

Reddish oil.

IR (neat): 2905, 2155, 1595, 1506, 1448, 1327, 1238, 1135, 1033, 812, 616 cm\(^{-1}\).

\( ^1\text{H} \) NMR (CDCl\(_3\)) \( \delta \): 3.81 (2H, s), 3.70 (2H, 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).

\( ^{13}\text{C} \) NMR (CDCl\(_3\)) \( \delta \): 26.6 (t), 59.1 (s), 108.4 (s), 110.8 (d), 114.4 (d), 114.7 (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\(_2\)S: \( \text{m/z} 352.0769 \). Found: \( \text{m/z} 352.0770 \).

**14c** \( (X = \text{S}, \ R^1 = \text{(CH}_3\text{)}_3\text{Si}, \ R^2 = \text{C}_6\text{H}_3) \):

Yellow oil.

IR (neat): 2960, 2095, 1491, 1250, 833 cm\(^{-1}\).

\( ^1\text{H} \) NMR (CDCl\(_3\)) \( \delta \): 0.17 (9H, s), 3.77 (2H, s), 7.30-7.31 (3H, m), 7.43-7.46 (2H, m).

\( ^{13}\text{C} \) NMR (CDCl\(_3\)) \( \delta \): 25.9 (t), 59.8 (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\(_{16}\)H\(_{18}\)SSi: C, 68.79; H, 6.60%. Found: C, 68.54; H, 6.48%.

**14d** \( (X = \text{S}, \ R^1 = \text{(CH}_3\text{)}_3\text{Si}, \ R^2 = 3,4-(\text{CH}_3\text{O})_2\text{C}_6\text{H}_3) \):

Yellow oil.

IR (neat): 2960, 2092, 1514, 1248 cm\(^{-1}\).

\( ^1\text{H} \) NMR (CDCl\(_3\)) \( \delta \): 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).

\( ^{13}\text{C} \) NMR (CDCl\(_3\)) \( \delta \): -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\(_{18}\)SSi: C, 68.79; H, 6.60%. Found: C, 68.54; H, 6.48%.

**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\(_2\)SO\(_4\) powder. The organic solvent was removed \textit{in vacuo}, and the residual crude products were subjected to 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. \(^1\text{H} \) 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 \(^1\text{H} \) NMR spectra are given in \( \delta \) relative to internal tetramethylsilane (TMS). \(^{13}\text{C} \) NMR spectra were recorded on a Bruker DRX-400P (100 MHz) or a Bruker AVANCE III 500 (126 MHz) spectrometer. \(^{13}\text{C} \) 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.

**Scheme 6.** Phenanthroindolizidine and phenanthroquinolizidine alkaloids.
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, R1 = C6H5, R2 = 3,4-(methylenedioxy)phenyl):
Red oil.
IR (neat): 2989, 1610, 1478, 1244, 1099, 1037, 756 cm⁻¹.
1H NMR (CDCl3) 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).
13C NMR (CDCl3) 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 C18H12O2S: m/z 292.0558. Found: m/z 292.0561.

15b (X = S, R1 = 3,4-(CH3O)2C6H5, R2 = 3,4-(methylenedioxy)phenyl):
Red powder.
MP: 160.5°C-161.7°C
IR (KBr) 2929, 1757, 1595, 1445, 1368, 1267, 1031, 851 cm⁻¹.
1H NMR (CDCl3) 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).
13C NMR (CDCl3) 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 C20H16O2S: 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-cyclobuten-1-thione 15 was treated with mCPBA (1.2 mol amt.) at 0°C for 30 minutes. The reaction was quenched by the addition of saturated aqueous Na2SO3 solution, and the reaction mixture was extracted with dichloromethane. The organic layer was washed with water and was dried over anhydrous Na2SO4 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 (R1 = C6H5, R2 = 3,4-(methylenedioxy)phenyl):
Yellow oil.
IR (neat): 2908, 1748, 1548, 1484, 1441, 1351, 1243, 1031, 699 cm⁻¹.
1H NMR (CDCl3) 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).
13C NMR (CDCl3) 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 C18H12O2S: m/z 276.0786. Found: m/z 276.0780.

16b (R1 = 3,4-(CH3O)2C6H5, R2 = 3,4-(methylenedioxy)phenyl):
Yellow oil.
IR (neat): 2910, 1757, 1595, 1512, 1445, 1359, 1256, 1032 cm⁻¹.
1H NMR (CDCl3) 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).
13C NMR (CDCl3) 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 C20H16O2S: 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, R¹ = (CH₃)₃Si, R² = C₆H₅): Yellow needles.

MP: 155.0°C-156.5°C

IR (KBr): 2971, 2359, 1623, 1246 cm⁻¹.

1H NMR (CDCl₃) 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).

13C NMR (CDCl₃) 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 (CH₃)₂Si; 19%

Calcd for C₁₉H₂₅NO₂SSi: C, 60.94; H, 6.73; N, 3.74%.

Found: C, 64.95; H, 7.56; N, 4.33%.

**20c** (X = Se, R¹ = (CH₃)₃Si, R² = C₆H₅): Yellow needles.

MP: 131.5°C-132.6°C

IR (KBr): 2971, 2359, 1623, 1246 cm⁻¹.

1H NMR (CDCl₃) 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), 7.05-7.16 (1H, m), 7.28-7.38 (4H, m).

13C NMR (CDCl₃) δ: −0.21 (9H, s), 1.47 (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).

MS (m/z): 387 (M⁺; 2%), 327 (M⁺−CH₃; bp), 73 ((CH₃)₂Si; 30%)

Calcd for C₂₁H₂₃NO₂SeSi: C, 69.67; H, 7.69; N, 4.28%.

Found: C, 69.45; H, 7.56; N, 4.33%.

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

An aqueous dioxane solution (dioxane:H₂O = 4:1) of δ-thiolactam 19c (300 mg, 0.92 mmol) was treated with NaIO₄ (790 mg, 4.0 mol amt.) at 0°C and then the reaction mixture was treated with an aqueous OsO₄ 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 Na₂SO₃ solution and was dried over anhydrous Na₂SO₄ powder. The organic solvent was removed in vacuo to obtain the crude mixture of 21 as brown oil. An aqueous dioxane solution (dioxane:H₂O = 1:1) of the crude mixture of 21 was then treated with H₂O (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 Na₂SO₄ solution and was dried over anhydrous Na₂SO₄ 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** (R¹ = (CH₃)₃Si, R² = C₆H₅): Yellow needles.

MP: 118.6°C-119.4°C

IR (neat): 2997, 1694, 1655, 1597, 1433, 1112, 704 cm⁻¹.

1H NMR (CDCl₃) δ: 0.08 (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⁺−CH₃; bp).

Calcd for C₁₉H₂₃NO₂SSi: 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 K₂CO₃ 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** (R¹ = H, R² = C₆H₅): Yellow oil.

IR (neat): 2997, 1694, 1655, 1597, 1433, 1112, 704 cm⁻¹.

1H NMR (CDCl₃) 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-butyl lithium (1.2 mol amt.) at −78°C for 30 minutes, and the reaction mixture was treated with B(OCH3)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 Na2SO4 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 colorless needles (822 mg, quantitative yield). Subsequently, a Na2SO4 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** (CDCl₃): 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).

**¹³C NMR** (CDCl₃): 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⁺; 2%), 268 (M⁺-OCH₃; 2%).

Calcd for C₁₆H₁₆Br₂O₃: C, 47.69; H, 3.77%. 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, 20 mol amt.) and carbon tetrabromide (6.918 g, 20 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 NaHCO₃ solution to the reaction mixture. The reaction mixture was extracted with chloroform, and the organic layer was dried over anhydrous Na₂SO₄ 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, 1446, 1254, 1137, 1051, 1030, 872, 753 cm⁻¹

**¹H NMR** (CDCl₃): 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).

**¹³C NMR** (CDCl₃): 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%, ²ⁱBr), 428 (M⁺; 3%, ²¹Br+²⁹Br), 426 (M⁺; 2%, ²⁹Br), 320 (M⁺-C₆H₄OCH₃; 3%), 268 (M⁺-Br₂; 39%).

Calcd for C₁₇H₁₄Br₂O₃: C, 47.69; H, 3.77%. Found: C, 47.61; H, 3.72%.

Conversion of Biphenyl Aldehyde 27 Into Propargyl Alcohol 29

A THF solution of 1,1-dibromoalkene 28 (3.719 g, 8.69 mmol) was treated with n-butyl lithium (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 Na₂SO₄ 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, 1496, 1255, 1152, 1028, 999, 755 cm⁻¹

**¹H NMR** (CDCl₃): 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).

**¹³C NMR** (CDCl₃): 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⁺-OCH₃; 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 CCl₄ 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.

- **Physical:** MP: 80.5°C-81.2°C
- **IR** (neat): 2937, 1602, 1516, 778 cm⁻¹
- **1H NMR** (CDCl₃): δ: 3.78 (3H, s), 3.89 (6H, s), 4.25 (2H, d, J = 8.3 Hz), 7.02 (1H, s), 7.07-7.13 (1H, m), 7.32 (1H, t, J = 8.3 Hz).
- **13C NMR** (CDCl₃): 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), 141.4 (s), 147.7 (s), 149.3 (s), 159.1 (s). MS (m/z): 458 (M+; 8%), 281 (M+-C₆H₃SSi; 70%), 73 ((CH₃)₃Si; bp), 49 (CH₂Cl₂; 3%; 35Cl). Calcd for C₁₈H₁₂ClO₃: 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 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, R¹ = (CH₃)₃Si, R² = 2-(3-methoxyphenyl)-4,5-dimethoxyphenyl):

Yellow oil.

- **IR** (neat): 2961, 2093, 1562, 1250, 880, 845 cm⁻¹
- **1H NMR** (CDCl₃): 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).
- **13C NMR** (CDCl₃): δ: -0.22 (q), 25.8 (t), 55.1 (q), 55.7 (q), 55.8 (q), 84.2 (s), 93.2 (s), 103.2 (s), 111.9 (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+-CH₃Si; 7%), 281 (M⁺-C₆H₃SSi; 87%), 73 ((CH₃)₃Si; bp).

Calcd for C₂₃H₂₆O₄Si: C, 67.28; H, 6.38%. Found: C, 67.11; H, 6.21%.

17e (X = Se, R¹ = (CH₃)₃Si, R² = 2-(3-methoxyphenyl)-4,5-dimethoxyphenyl):

Orange oil.

- **IR** (neat): 2958, 2087, 1712, 1602, 1516, 1250, 860 cm⁻¹
- **1H NMR** (CDCl₃): 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).
- **13C NMR** (CDCl₃): 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⁺-C₆H₃SeSi; bp), 250 (M⁺-C₆H₃OSeSi; 70%), 73 ((CH₃)₃Si; 19%). Calcd for C₂₃H₂₆O₄SeSi: 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, R¹ = (CH₃)₃Si, R² = 2-(3-methoxyphenyl)-4,5-dimethoxyphenyl):
products were subjected to column chromatography on silica gel to obtain \( \delta \)-lactam 22e (89 mg, quantitative yield) as yellow needles.

**Physical and Spectral Data for \( \delta \)-Lactam 22e**

22e \( R^1 = (CH_3)_3Si, \quad R^2 = 2-(3-methoxyphenyl)-4,5-dimethoxyphenyl): Yellow needles.

MP: 74.6°C-75.6°C

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

\(^{1}H\) NMR (CDCl\(_3\)) \( \delta \): 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, \( J = 8.4 \) Hz).

\(^{13}C\) NMR (CDCl\(_3\)) \( \delta \): 133.4 (s), 140.2 (s), 142.7 (s), 147.6 (s), 148.8 (s), 148.8 (s); 198.3 (s). Red needles.

MP: 79.9°C-80.6°C

IR (KBr): 2976, 1711, 1602, 1516, 1455, 1455, 1254, 1161, 1047 cm\(^{-1}\). Red needles.

MP: 75.3°C-76.7°C

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

\(^{1}H\) NMR (CDCl\(_3\)) \( \delta \): 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, \( J = 8.4 \) Hz). Yellow needles.

**Desilylation of \( \delta \)-Lactam 22e**

A methanol solution of \( \delta \)-lactam 22e (701 mg, 1.46 mmol) was treated with anhydrous K\(_2\)CO\(_3\) powder (391 mg, 2.0 mol amt.) at 0°C for 15 minutes. The reaction mixture was then cooled to 0°C 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, \quad 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\(^{-1}\).

\(^{1}H\) NMR (CDCl\(_3\)) \( \delta \): 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\(_3\)) \( \delta \): 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), 149.0 (s), 159.0 (s), 189.4 (s).

MS (m/z): 478 (M\(^{-1}\); 50%), 464 (M\(^{-}\)CH\(_3\); bp), 448 (M\(^{-}\)OCH\(_3\); 6%), 406 (M\(^{-}\)(CH\(_3\))\(_3\)Si; 36%), 73 ((CH\(_3\))\(_3\)Si; 10%).

Calcd for C\(_{25}\)H\(_{33}\)NO\(_3\)Si: C, 67.61; H, 6.93; N, 2.92%.

Found: C, 67.25; H, 7.05; N, 3.01%.

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

An aqueous dioxane solution (dioxane:H\(_2\)O = 4:1) of \( \delta \)-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\(_2\)SO\(_4\) solution and was dried over anhydrous Na\(_2\)SO\(_4\) powder. The organic solvent was removed in vacuo to obtain the crude mixture of 21 as brown oil. An aqueous dioxane solution (dioxane:H\(_2\)O = 1:1) of the crude mixture of 21 was then treated with H\(_2\)IO\(_6\) (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\(_2\)SO\(_4\) solution and was dried over anhydrous Na\(_2\)SO\(_4\) powder. The organic solvent was removed in vacuo, and the residual crude products were subjected to column chromatography on silica gel
201.6 (s), 131.1 (s), 131.9 (d), 134.9 (s), 150.2 (s), 160.2 (s), 161.9 (s), 106.9 (d), 116.0 (d), 122.1 (s), 122.4 (s), 123.2 (s), 126.0 (s), 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⁺–CH₃; 35%). Caled for C₂₅H₂₃N₂O₅: C, 70.74; H, 6.18; N, 3.44%. Found: C, 71.21; H, 5.85; N, 3.49%.

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 (CDCl₃) 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), = 2.6 Hz), 7.89 (1H, s), 8.81 (1H, s), 9.41 (1H, d, J = 9.4 Hz), 13C NMR (CDCl₃) 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⁺–CH₃; 35%). Caled for C₂₅H₂₃N₂O₅: C, 70.74; H, 6.18; N, 3.44%. Found: C, 71.21; H, 5.85; N, 3.49%.

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