Radical Cyclization in Heterocycle Synthesis 15.[1] Relationship between a Radical Species and Radical Acceptors of Three Different Types of Double Bond in Radical Addition–Cyclization

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Relationship between a radical species and radical acceptors of three different types of double bond in radical addition–cyclization was systematically investigated. Substrates carrying α,β-unsaturated amide, isolated olefin, and oxime ether moieties underwent radical addition–cyclization to give differently substituted lactams depending upon the radicals used. The sulfanyl radical addition–cyclization of the substrate proceeded smoothly to give the 5-membered lactam having an alkoxyamino group as a result of preferable addition of an intermediary α-carbonyl radical to the oxime ether. On the other hand, the triethylborane-mediated radical addition-cyclization gave the lactam bearing an iodomethyl group as a result of addition to an intermediary α-carbonyl radical to isolated olefin. The different regioselectivity was explained by the stability of the intermediary radical and the interaction between SOMO and HOMO.

Key words triethylborane; thiophenol; radical cyclization; amide; oxime ether

Free radical reactions are one of the most straightforward ways for carbon–carbon bond formation in organic synthesis.[2—10] In particular, radical-mediated cyclization has been developed as a potential method for preparing various types of cyclic compounds *via* intramolecular carbon–carbon bond-forming processes. We have recently developed a new efficient carbon–carbon bond-forming reaction based on sulfanyl,[11—19] stannyl[20—32] and alkyl[33—38] radical addition-cyclization (Chart 1). These radical reactions proceed *via* formation of a carbon-centered radical species **A** generated by the addition of a radical ($Z\cdot$) to a multiple bond (C=A) in substrate **1** and subsequent intramolecular addition of the resulting carbon-centered radical **A** to a multiple bond (C=B).[39—41]

The cyclized products **2** are highly functionalized compounds and thus are regarded as a useful key intermediate for further target molecules. The synthetic potentiality was demonstrated by the synthesis of anantine,[14] oxo-parabenzlactone,[15] α-kainic acid,[16] cispentacin,[19] and the A-ring fragment of 1α,25-dihydroxyvitamin D_3,[17] balanol,[22] deoxynojirimycin,[29] martinelline[26] and other functionalized lactones,[36] lactams,[36] and sultams.[37] During the course of our previous investigations, we employed an isolated double bond, α,β-unsaturated amide, oxime ether, hydrazone, nitrone, and the related imino groups as a radical acceptor and sulfur, carbon, tin, and silicon radical as a radical in the first step (**1**→**A**) of the addition reaction, respectively.

However, it is not clarified what atom of the radical is the most suitable for the first step (**1**→**A**) in radical addition-cyclization and which double bond the newly formed radical **A** attacks in the second step (**A**→**2**). Therefore, we undertook a systematic study on radical addition–cyclization of substrates having three different radical acceptors such as acrylamide, isolated olefin, and oxime ether using sulfanyl and carbon radicals as the first-step radical (Chart 2).

We report here for the first time that both sulfanyl and carbon radicals attack first the α,β-unsaturated amide but the resulting radical exhibits different behavior. Treatment of **3** with either a sulfanyl radical or a carbon radical gave the lactam **4** or **5** as a respective major product. Additionally, a calculation study and rational explanation based on the result are also described.

Results and Discussion

Preparation and Radical Addition–Cyclization of Acrylamides Having Either an Oxime Ether or an Isolated Olefin Prior to our investigation of radical addition–cyclization of substrate **3**, we first examined the radical addition–cyclization of *N*-benzylacrylamides **9** (Chart 4) and **12** (Charts 5, 6) which carry two different types of double bond such as the oxime ether and olefin.

The requisite substrate **9** was prepared from benzylamine according to the reported procedure[19,36] as follows. The alkylation of benzylamine with α-chloroacetaldoxime ether **7**,[42] prepared from chloroacetaldehyde **6** and *O*-methylhydroxylamine hydrochloride, gave the amide **8** which was acylated with acryloyl chloride to give the oxime ether **9** in 97%

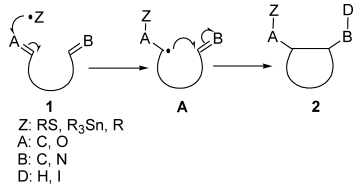

Chart 1

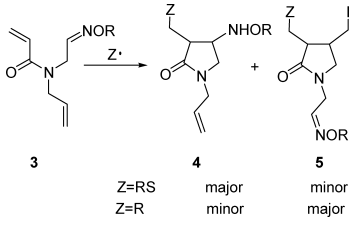

Chart 2

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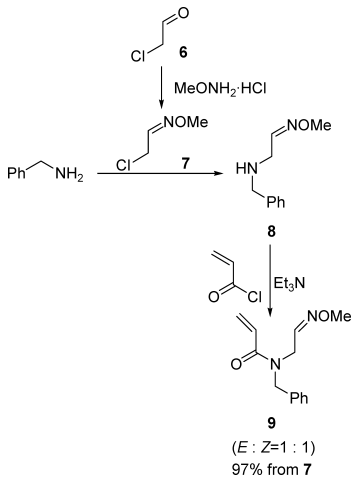


Chart 3

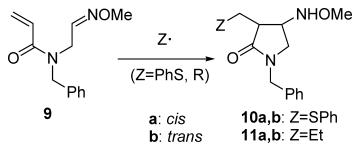


Chart 4

Table 1. Radical Addition–Cyclization of Oxime Ether **9**

Entry	Conditions	Solvent	T (°C)	Product	Z	Yield (%)	*cis* : *trans*
1	PhSH (1 eq) AIBN (0.5 eq)	benzene	80	**10**	PhS	68	37 : 63
2	Et_3B (7.5 eq)	toluene	rt	**11**	Et	57	29 : 71
3	Et_3B (7.5 eq)	toluene	−20	**11**	Et	42	15 : 85

yield as an *E*/*Z* mixture in a 1 : 1 ratio (Chart 3).

The *E*/*Z* geometrical ratios of the aldoxime ether group in **9** thus prepared were deduced by ^{1}H-NMR spectroscopy. In general, the signal due to the imino hydrogen of the *E*-aldoxime ether is shifted downfield by the influence of the alkoxy group of the aldoxime ether moiety. In the case of **9**, a signal due to the imino hydrogen of the *E*-isomer (δ: 7.37) was shifted downfield with respect to that of the *Z*-isomer (δ: 6.63).

We started to investigate radical reaction of the oxime ether **9** using either a sulfanyl radical or an alkyl radical (Chart 4, Table 1).

The sulfanyl radical addition–cyclization of **9** was examined under the same conditions used for the radical reaction[19] of *N*-tosyl allylamines with the oxime ether. A solution containing thiophenol (1 eq) and AIBN (0.5 eq) in benzene was added dropwise by a syringe pump over 2 h to a solution of the oxime ether **9** in boiling benzene with stirring under nitrogen. The solution was then refluxed for further 2 h to give a mixture of *cis*- and *trans*-amino lactams **10a** and **10b** having a phenylsulfanylmethyl group (*cis* : *trans* = 37 : 63) in moderate yield (entry 1). Next, according to our previous work,[36] we examined the alkyl radical addition–cyclization of **9** under the slightly modified conditions at room temperature. Treatment of **9** with 1 M Et_3B (7.5 eq) in toluene

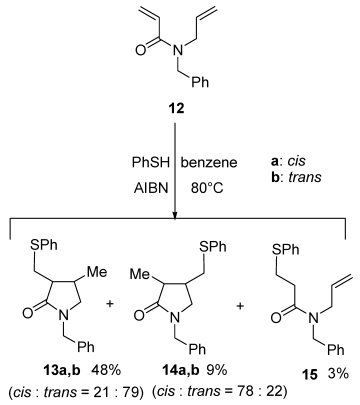


Chart 5

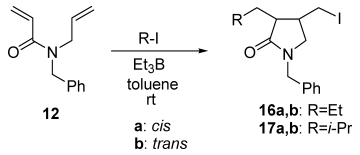


Chart 6

Table 2. Radical Addition–Cyclization of Alkene **12**

Entry	Conditions	Product	R	Yield (%)	*cis* : *trans*
1	Et_3B (1 eq) Et-I (7 eq)	**16**	Et	40	20 : 80
2	Et_3B (1 eq) *i*-Pr-I (7 eq)	**17**	*i*-Pr	58	22 : 78

at room temperature gave a mixture of *cis*- and *trans*-amino lactams **11a** and **11b** having an *n*-propyl group in favor of a *trans*-product (entry 2). The degree of stereoselectivity was shown to be dependent on the reaction temperature; thus, changing the temperature to −20 °C in toluene led to an increase in stereoselectivity to 15 : 85 (entry 3). Therefore, the acrylamide **9** underwent smooth radical addition–cyclization to afford products **10** and **11**.

We next examined the radical addition–cyclization of alkene **12** under the same conditions employed above. The alkene **12** was prepared by the reported procedure.[43] The sulfanyl radical addition–cyclization of **12** gave the lactam **13** having a 3-phenylsulfanylmethyl group as a major product, in addition to the cyclized product **14** having a 4-phenylsulfanylmethyl group and an adduct **15** (Chart 5). This result is almost the same as that of the sulfanyl radical addition–cyclization of *N*,*N*-diallylacrylamide reported previously.[11]

We then examined alkyl radical addition–cyclization of **12** with triethylborane in the presence of alkyl iodide (Chart 6, Table 2). When the radical reaction was attempted in the absence of alkyl iodide, only a complex mixture was obtained. Treatment of **12** with Et_3B in the presence of EtI gave a mixture of *cis*-**16a** and *trans*-**16b** in 40% yield as a result of radical addition–cyclization-trap reaction (entry 1). The increased yield was observed in the radical reaction of **12** in the presence of isopropyl iodide (entry 2).

Based on the above-mentioned and our related results,[11,19,36] we propose a plausible reaction pathway that is

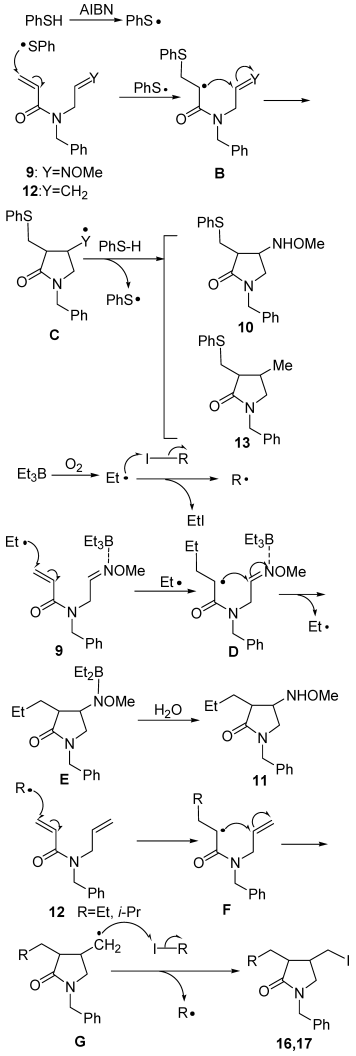


Chart 7

shown in Chart 7. At first, a sulfanyl radical is formed from thiophenol and AIBN. The addition of the sulfanyl radical takes place to the acrylamide moiety of **9** and **12** to form the carbonyl-stabilized radical **B** which then attacks intramolecularly the oxime ether and isolated olefin to give the final products **10** and **13**. As reported previously,[33—38] triethylborane acts as not only a radical initiator but also a Lewis acid and a radical terminator. The first step is generation of an ethyl radical by the reaction of Et_3B with oxygen. When alkyl iodide is present, the ethyl radical formed can abstract an iodine atom from alkyl iodide to produce an alkyl radical. This iodine atom-transfer is fast and efficient when the alkyl radical is more stable than the ethyl radical.

In the case of oxime ether **9**, the alkyl radical adds to the α,β-unsaturated carbonyl moiety to form the carbonyl-stabilized radical **D** as an intermediate which is then intramolecularly trapped with triethylborane-activated oxime ether to give the complex **E** releasing an ethyl radical. The alkylated product **11** was obtained as a result of the hydrolysis of **E**. Similarly, **12** undergoes alkyl radical addition–cyclization to form primary radical **G** which is trapped with alkyl iodide to afford iodinated products **16** and **17** *via* the route involving iodine atom-transfer reaction from alkyl iodide.

As mentioned above, it is important to note that both acrylamides **9** and **12** form the α-carbonyl-stabilized radical by the addition of sulfanyl or alkyl radicals to the acrylamide moiety and then the resulting radical reacts with alkene or oxime ether to afford the cyclized products **10**, **11**, **13**, **16**, and **17**.

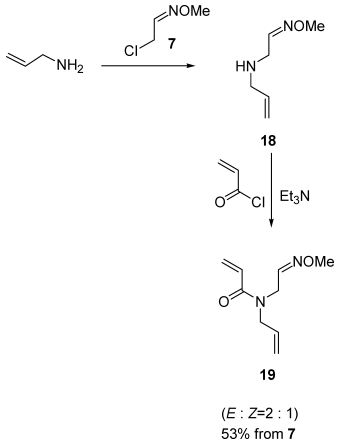


Chart 8

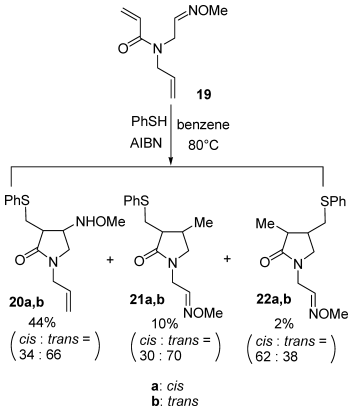


Chart 9

Preparation and Radical addition–cyclization of Substrate Having Three Different Types of Radical Acceptors Based on the above-mentioned result, the amide **19** having three different types of radical acceptors such as acrylamide, isolated olefin, and oxime ether was chosen as a substrate for radical addition–cyclization. According to the procedure given for the preparation of **9**, the alkylation of allylamine with **7** followed by acylation of the resulting oxime ether **18** with acryloyl chloride gave the substrate **19** as an *E*/*Z* mixture in a 2 : 1 ratio (Chart 8).

We next investigated the radical reaction of the oxime ether **19** under the same reaction conditions employed for **9** and **12**. (Charts 9, 10, Table 3). The sulfanyl radical addition–cyclization of **19** proceeded smoothly to give the lactam **20** having a 4-methoxyamino group in 44% yield along with a small amount of 4-methyl- and 3-methylpyrrolidinones **21** and **22** (Chart 9).

On the other hand, the ethyl radical addition–cyclization of **19** in the presence of ethyl iodide gave a 1 : 1 mixture of **23** and **26** in 44% combined yield (Chart 10, entry 1 in Table 3). The isopropyl radical addition–cyclization of **19** gave a 1 : 2 mixture of **24** and **27** in 73% yield (entry 2). Similarly, *t*-butyl radical reaction of **19** proceeded smoothly to give a

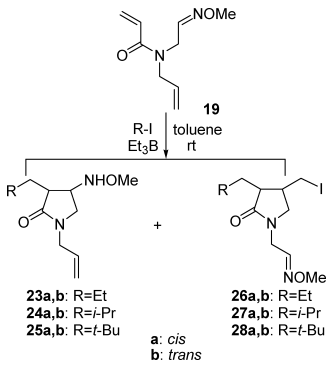


Chart 10

Table 3. Radical Addition–Cyclization of Oxime Ether **19**

Entry	Conditions	Product	R	Yield (%)		*cis* : *trans*	
				23—**25**	**26**—**28**	**23**—**25**	**26**—**28**
1	Et_3B (1 eq) Et-I (7 eq)	**23**, **26**	Et	21	23	48 : 52	22 : 78
2	Et_3B (1 eq) *i*-Pr-I (7 eq)	**24**, **27**	*i*-Pr	23	50	20 : 80	29 : 71
3	Et_3B (1 eq) *t*-Bu-I (7 eq)	**25**, **28**	*t*-Bu	22	43	26 : 74	18 : 82

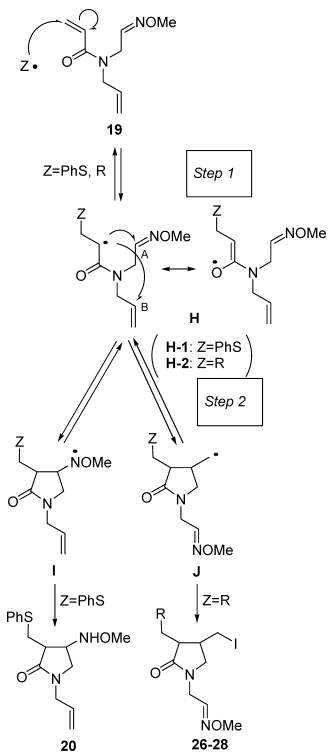


Chart 11

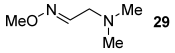
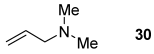
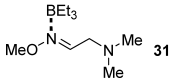
mixture of **25** and **28** in favor of **28** (entry 3).

The sulfanyl and alkyl radical addition–cyclizations of **19** can be summarized as follows (Chart 11).

The radical reaction of **19** mainly consists of two steps. The first step is addition of either a sulfanyl or an alkyl radical to the double bond (step 1) and the second is intramolecular addition of the resulting α-carbonyl radical to the double bond (step 2).

Though there are three types of double bond in compound **19**, both the sulfanyl and alkyl radicals selectively added to olefin of the α,β-unsaturated amide part to form the carbonyl-stabilized radical **H** which can possibly cyclize at either the B position in the olefin or the A position in the oxime ether. In the case of a sulfanyl radical addition–cyclization, **H-1** (Z=PhS) would attack preferably the oxime ether to give the cyclized amine **20** as a major product. On the other hand, the alkylated radical **H-2** (Z=alkyl) would react preferably with the isolated olefin and then the resulting radical is trapped with alkyl iodide to give 4-(iodomethyl)-pyrrolidinones **26**—**28** as a result of 5-*exo*-*trig* cyclization.

Table 4. Calculated HOMO Levels in **29**, **30**, and **31**

Entry	Compounds	HOMO (eV)
1	 **29**	−9.807
2	 **30**	−9.976
3	 **31**	−11.078

The radical **H** would attack the multiple bond which has higher energy level of HOMO because α-carbonyl radical **H** is typical electrophilic radical.

In order to confirm which double bond carrying higher HOMO level reacts with the electrophilic radical, we next calculated the energy levels of HOMO in oxime ether **29**, isolated olefin **30**, and triethylborane-oxime ether complex **31** which correspond to a partial structure of radicals **H-1** and **H-2** (Table 4). All calculations were carried out with a semiempirical MOPAC method utilizing a PM5 Hamiltonian.

The energy level of HOMO in the oxime ether part **29** is higher than that in the olefin part **30**. Therefore, the radical **H-1** reacts with the oxime ether to give the cyclic amine **20** as a major product. On the other hand, in the radical reaction using triethylborane, the oxime ether is known to coordinate with triethylborane that acts as a Lewis acid. Therefore, the HOMO level of olefin **30** is higher than that of coordinated oxime ether **31**. Therefore, the radical **H-2** reacts preferentially with the isolated olefin to afford the cyclized and finally, iodine-trapped product **26**—**28**.

Another explanation is also possible. There would be equilibration between three radicals, α-carbonyl radical **H**, aminyl radical **I**, and methylene radical **J**. The sulfanyl radical addition cyclization proceeded at 80 °C (thermodynamic conditions) to form preferably stable aminyl radical **I** which led to the formation of **20**. On the other hand, the alkyl radical addition cyclization could occur at room temperature (kinetic conditions) to form the products **26**—**28** *via* unstable methylene radical **J**.

Conclusion

We have found that radical cyclization using thiophenol and triethylborane shows different regioselectivity. The sulfanyl radical addition–cyclization of the substrate carrying three different types of double bond gave the pyrrolidinone-having an alkoxyamino group and an alkyl group at the 3- and 4-position, respectively, as a result of cyclization to

the oxime ether while the alkyl radical addition–cyclization gave the pyrrolidinone having two alkyl groups as a result of cyclization to the isolated olefin.

Experimental

General Melting points are uncorrected. ^{1}H- and ^{13}C-NMR spectra were recorded at 200, 300, or 500 MHz and at 75 or 125 MHz, respectively. IR spectra were recorded using FTIR apparatus. Mass spectra were obtained by EI method. Flash column chromatography (FCC) was performed using E. Merck Kieselgel 60 (230—400 mesh). Medium-pressure column chromatography (MCC) was performed using Lobar größe B (E. Merck 310-25, Lichroprep Si60). Preparative TLC (PTLC) was performed on pre-coated Silica gel 60F-254 plates (0.5 mm thick, Merck).

***N*-[2-(Methoxyimino)ethyl]-*N*-(2-phenylmethyl)-2-propenamide (9)** To benzylamine **1** (3.2 g, 30 mmol) was added chloroacetaldehyde *O*-methyloxime **7**[42] (1.0 g, 10 mmol, prepared from **6**, at 0 °C under a nitrogen atmosphere. After being stirred at room temperature for 24 h, the reaction mixture was diluted with saturated aqueous $NaHCO_3$ and with CH_2Cl_2 and then washed with water. The organic phase was dried over $MgSO_4$ and concentrated under reduced pressure to give the crude benzylamine **8** as a yellow oil. After being characterized by NMR spectrum, **8** was immediately subjected to the following reaction. To a solution of **8** (1.78 g, 10 mmol) in CH_2Cl_2 (72 ml) were added Et_3N (1.81 ml, 13.0 mmol) and a solution of acryloyl chloride (1.05 ml, 13 mmol) in CH_2Cl_2 (17 ml) at 0 °C under a nitrogen atmosphere. After being stirred at room temperature for 24 h, reaction mixture was diluted with water and extracted with $CHCl_3$. The organic phase was washed with water, dried with $MgSO_4$, and concentrated under reduced pressure. The residue was purified by FCC (hexane/AcOEt 1 : 1) to afford **9** (2.23 g, 97%) as a pale yellow oil and a 1 : 1 mixture of *E* and *Z*-isomers; IR ($CHCl_3$) cm^{-1}: 1649. ^{1}H-NMR (300 MHz, $CDCl_3$) δ: 7.39—7.17 (5H, m), 7.39—7.17 (1/2H, m), 6.69—6.42 (1/2H, m), 6.69—6.42 (2H, m), 5.80—5.70 (1H, m), 4.69 (2/6H, br s), 4.68 (2/6H, br s), 4.62 (4/6H, br s), 4.60 (4/6H, br s), 4.27 (4/6H, br d, J=4 Hz), 4.18 (2/6H, br d, J=4 Hz), 4.14 (4/6H, br d, J=6 Hz), 4.00 (2/6H, br d, J=6 Hz), 3.87 (1/2H, s), 3.84 (2/2H, s), 3.83 (1/2H, s), 3.81 (2/2H, s). ^{13}C-NMR (75 MHz, $CDCl_3$) δ: 166.8, 147.7, 147.5, 145.1, 144.6, 136.5, 136.2, 129.4, 129.3, 128.8, 128.6, 128.5, 128.3, 127.8, 127.7, 127.1, 126.9, 126.4, 62.1, 61.8, 61.5, 57.3, 52.1, 50.5, 50.1, 49.2, 45.8, 44.6, 43.7, 43.0, 42.4. HR-MS (EI) *m/z*: 232.1210 (Calcd for $C_{13}H_{16}N_2O_2$ (M^+): 232.1212). The presence of rotamers precluded a comprehensive assignment of all proton and carbon resonances.

Sulfanyl Radical Addition–Cyclization of Oxime Ether 9 To a boiling solution of the oxime ether **9** (90 mg, 0.39 mmol) in benzene (2 ml) under a nitrogen atmosphere was added a solution of thiophenol (0.04 ml, 0.39 mmol) and AIBN (33 mg, 0.2 mmol) in benzene (4 ml) by a syringe pump (5 ml/h) over 50 min. After the reaction mixture was heated at reflux for a further 2 h, the solvent was evaporated under reduced pressure. Purification of the residue by MCC (hexane/AcOEt 1 : 1) afforded *cis*-**10a** (33 mg, 25%) and *trans*-**10b** (57 mg, 43%).

***cis*-4-(Methoxyamino)-1-(phenylmethyl)-3-[(phenylsulfanyl)methyl]-2-pyrrolidinone (10a)** A pale yellow oil. IR ($CHCl_3$) cm^{-1}: 3692, 1682. ^{1}H-NMR (500 MHz, $CDCl_3$) δ: 7.42—7.18 (10H, m), 5.92 (1H, br s), 4.61 (1H, d, J=14.5 Hz), 4.31 (1H, d, J=14.5 Hz), 3.74 (1H, br t, J=6.5 Hz), 3.62 (1H, dd, J=13.5, 4 Hz), 3.31 (3H, s), 3.32 (1H, dd, J=11, 6 Hz), 3.27 (1H, dd, J=11, 1 Hz), 3.00 (1H, dd, J=13.5, 11.5 Hz), 2.76 (1H, br ddd, J=11.5, 6.5, 4 Hz). NOE was observed between NH (δ: 5.92) and C$\underline{H}_2$SPh (δ: 3.62) in NOESY spectroscopy. ^{13}C-NMR (125 MHz, $CDCl_3$) δ: 172.7, 136.1, 134.8, 129.7, 129.1, 128.6, 128.3, 127.6, 126.6, 62.5, 54.5, 49.1, 46.6, 44.0, 28.9. HR-MS (EI) *m/z*: 342.1401 (Calcd for $C_{19}H_{22}N_2O_2S$ (M^+) 342.1402).

***trans*-4-(Methoxyamino)-1-(phenylmethyl)-3-[(phenylsulfanyl)methyl]-2-pyrrolidinone (10b)** A pale yellow oil. IR ($CHCl_3$) cm^{-1}: 3692, 1682. ^{1}H-NMR (500 MHz, $CDCl_3$) δ: 7.42—7.18 (10H, m), 5.82 (1H, br s), 4.45 (2H, s), 3.71 (1H, br q, J=6 Hz), 3.60 (1H, dd, J=13.5, 3.5 Hz), 3.43 (3H, s), 3.39 (1H, dd, J=10, 7.5 Hz), 3.14 (1H, dd, J=10, 5.5 Hz), 2.97 (1H, dd, J=13.5, 10 Hz), 2.68 (1H, br ddd, J=10, 6, 3.5 Hz). NOE was observed between NH (δ: 5.82) and 3-H (δ: 2.68), 4-H (δ: 3.71) and CH_2SPh (δ: 2.97) in NOESY spectroscopy. ^{13}C-NMR (125 MHz, $CDCl_3$) δ: 172.6, 135.9, 134.9, 129.6, 129.1, 128.7, 128.3, 127.7, 126.6, 62.5, 53.4, 49.3, 46.6, 44.7, 34.5. HR-MS (EI) *m/z*: 342.1400 (Calcd for $C_{19}H_{22}N_2O_2S$ (M^+) 342.1402).

Ethyl Radical Addition–Cyclization of Oxime Ether 9 To a solution of the oxime ether **9** (50 mg, 0.22 mmol) in toluene (15 ml) under a nitrogen atmosphere was added Et_3B (1.0 M in hexane, 0.54 ml, 0.54 mmol) at the temperature shown in Table 1. After being stirred at the same temperature for 15 min, Et_3B (1.0 M in hexane, 0.54 ml, 0.54 mmol) was added 3 times every 15 min. After being stirred at the same temperature for 0.5 h, the reaction mixture was diluted with water and extracted with $CHCl_3$. The organic phase was washed with water, dried with $MgSO_4$, and concentrated under reduced pressure. The residue was purified by MCC (hexane/AcOEt 2 : 1) to afford *cis*-**11a** and *trans*-**11b** as shown in Table 1.

***cis*-4-(Methoxyamino)-1-(phenylmethyl)-3-propyl-2-pyrrolidinone (11a)** A pale yellow oil. IR ($CHCl_3$) cm^{-1}: 3430, 1678. ^{1}H-NMR (500 MHz, $CDCl_3$) δ: 7.34—7.24 (5H, m), 5.45 (1H, br s), 4.56 (1H, d, J=14.5 Hz), 4.38 (1H, d, J=14.5 Hz), 3.71—3.67 (1H, m), 3.36 (3H, s), 3.26 (1H, dd, J=10, 4 Hz), 3.24 (1H, dd, J=10, 2 Hz), 2.51 (1H, ddd, J=10, 7, 6 Hz), 1.84—1.76 (1H, m), 1.54—1.46 (2H, m), 1.46—1.38 (1H, m), 0.98 (3H, t, J=7 Hz). ^{13}C-NMR (125 MHz, $CDCl_3$) δ: 174.7, 136.5, 128.6, 128.2, 127.5, 62.2, 55.5, 49.1, 46.5, 44.7, 26.2, 21.2, 14.1. HR-MS (SI-MS) *m/z*: 262.1681 (Calcd for $C_{15}H_{22}N_2O_2$ (M^+) 262.1680).

***trans*-4-(Methoxyamino)-1-(phenylmethyl)-3-propyl-2-pyrrolidinone (11b)** A pale yellow oil. IR ($CHCl_3$) cm^{-1}: 3400, 1676. ^{1}H-NMR (500 MHz, $CDCl_3$) δ: 7.35—7.21 (5H, m), 5.46 (1H, br s), 4.48 (1H, d, J=15 Hz), 4.43 (1H, d, J=15 Hz), 3.50—3.46 (1H, m), 3.47 (3H, s), 3.35 (1H, dd, J=10, 7 Hz), 3.12 (1H, dd, J=10, 4 Hz), 2.31 (1H, dt, J=8, 5 Hz), 1.82—1.74 (1H, m), 1.55—1.40 (3H, m), 0.96 (3H, t, J=7 Hz). NOE was observed between NH (δ: 5.46) and 3-H (δ: 2.31) in NOESY spectroscopy. ^{13}C-NMR (125 MHz, $CDCl_3$) δ: 175.0, 136.3, 128.7, 128.1, 127.5, 62.4, 58.8, 49.4, 46.4, 45.6, 32.1, 20.3, 14.0. HR-MS (EI) *m/z*: 262.1679 (Calcd for $C_{15}H_{22}N_2O_2$ (M^+) 262.1680).

Sulfanyl Radical Addition–Cyclization of Alkene 12 To a boiling solution of the alkene **12**[11,43] (100 mg, 0.5 mmol) in benzene (5 ml) under a nitrogen atmosphere was added a solution of thiophenol (0.05 ml, 0.5 mmol) and AIBN (41 mg, 0.25 mmol) in benzene (10 ml) by a syringe pump (5 ml/h) over 2 h. After the reaction mixture was heated at reflux for a further 2 h, the solvent was evaporated under reduced pressure. Purification of the residue by MPCC (hexane/AcOEt 2 : 1) afforded *cis*-**13a** (16 mg, 10%), *trans*-**13b** (59 mg, 38%), *cis*-**14a** (11 mg, 7%), *trans*-**14b** (3 mg, 2%), and **15** (5 mg, 3%).

***cis*-4-Methyl-1-(phenylmethyl)-3-[(phenylsulfanyl)methyl]-2-pyrrolidinone (13a)** A pale yellow oil. IR ($CHCl_3$) cm^{-1}: 1678. ^{1}H-NMR (500 MHz, $CDCl_3$) δ: 7.40—7.17 (10H, m), 4.51 (1H, d, J=14.5 Hz), 4.37 (1H, d, J=14.5 Hz), 3.58 (1H, dd, J=13, 3.5 Hz), 3.33 (1H, dd, J=9.5, 6 Hz), 2.87 (1H, dd, J=13, 11.5 Hz), 2.79 (1H, dd, J=9.5, 1.5 Hz), 2.76 (1H, ddd, J=11.5, 7.5, 3.5 Hz), 2.61—2.52 (1H, m), 0.99 (3H, d, J=7.5 Hz). NOE was observed between 4-Me (δ: 0.99) and C$\underline{H}_2$SPh (δ: 2.87) in NOESY spectroscopy. ^{13}C-NMR (125 MHz, $CDCl_3$) δ: 173.7, 136.3, 135.7, 129.3, 129.0, 128.6, 128.2, 127.6, 126.2, 52.3, 46.8, 45.4, 30.0, 29.1, 14.5. HR-MS (EI) *m/z*: 311.1362 (Calcd for $C_{19}H_{21}NOS$ (M^+) 311.1344).

***trans*-4-Methyl-1-(phenylmethyl)-3-[(phenylsulfanyl)methyl]-2-pyrrolidinone (13b)** A pale yellow oil. IR ($CHCl_3$) cm^{-1}: 1679. ^{1}H-NMR (500 MHz, $CDCl_3$) δ: 7.41—7.16 (10H, m), 4.47 (1H, d, J=14.5 Hz), 4.41 (1H, d, J=14.5 Hz), 3.55 (1H, dd, J=13, 3.5 Hz), 3.30 (1H, dd, J=9.5, 8 Hz), 3.04 (1H, dd, J=13, 8 Hz), 2.75 (1H, dd, J=9.5, 7 Hz), 2.38 (1H, td, J=8, 3.5 Hz), 2.35—2.29 (1H, m), 1.12 (3H, d, J=6.5 Hz). NOE was observed between 4-Me (δ: 1.12) and 3-H (δ: 2.38), 4-H (δ: 2.35—2.29) and C$\underline{H}_2$SPh (δ: 3.55, 3.04) in NOESY spectroscopy. ^{13}C-NMR (125 MHz, $CDCl_3$) δ: 174.2, 136.3, 136.1, 129.2, 128.9, 128.6, 128.0, 127.5, 126.1, 52.1, 49.2, 46.6, 34.7, 32.5, 19.1. HR-MS (EI) *m/z*: 311.1336 (Calcd for $C_{19}H_{21}NOS$ (M^+) 311.1344).

***cis*-3-Methyl-1-(phenylmethyl)-4-[(phenylsulfanyl)methyl]-2-pyrrolidinone (14a)** A pale yellow oil. IR ($CHCl_3$) cm^{-1}: 1678. ^{1}H-NMR (500 MHz, $CDCl_3$) δ: 7.34—7.19 (10H, m), 4.45 (1H, d, J=14.5 Hz), 4.42 (1H, d, J=14.5 Hz), 3.30 (1H, dd, J=10, 7 Hz), 3.10 (1H, dd, J=10, 6 Hz), 3.06 (1H, dd, J=12.5, 5.5 Hz), 2.69 (1H, dd, J=12.5, 10 Hz), 2.70—2.63 (1H, m), 2.58—2.51 (1H, m), 1.18 (3H, d, J=7.5 Hz). NOE was observed between 3-Me (δ: 1.18) and C$\underline{H}_2$SPh (δ: 3.06, 2.69) in NOESY spectroscopy. ^{13}C-NMR (125 MHz, $CDCl_3$) δ: 176.5, 136.4, 135.4, 129.9, 129.1, 128.7, 128.1, 127.6, 126.6, 49.5, 46.6, 40.0, 35.4, 33.7, 10.7. HR-MS (EI) *m/z*: 311.1349 (Calcd for $C_{19}H_{21}NOS$ (M^+) 311.1344).

***trans*-3-Methyl-1-(phenylmethyl)-4-[(phenylsulfanyl)methyl]-2-pyrrolidinone (14b)** A pale yellow oil. IR ($CHCl_3$) cm^{-1}: 1678. ^{1}H-NMR (500 MHz, $CDCl_3$) δ: 7.34—7.18 (10H, m), 4.43 (2H, s), 3.35 (1H, dd, J=10, 8 Hz), 3.19 (1H, dd, J=13, 5 Hz), 2.97 (1H, dd, J=10, 7.5 Hz), 2.85 (1H, dd, J=13, 9 Hz), 2.34—2.28 (1H, m), 2.18—2.10 (1H, m), 1.25 (3H, d, J=7 Hz). NOE was observed between 3-Me (δ: 1.25) and 4-H (δ: 2.18—2.10), and 3-H (δ: 2.34—2.28) and C$\underline{H}_2$SPh (δ: 3.19, 2.85) in NOESY spectroscopy. ^{13}C-NMR (125 MHz, $CDCl_3$) δ: 176.0, 136.4, 135.5, 129.6, 129.1,

128.7, 128.1, 127.6, 126.5, 50.0, 46.7, 42.8, 40.2, 37.4, 15.3. HR-MS (EI) *m/z*: 311.1359 (Calcd for $C_{19}H_{21}NOS$ (M^+) 311.1344).

***N*-Phenylmethyl-3-(phenylsulfanyl)-*N*-propenylpropanamide (15)** A pale yellow oil. IR ($CHCl_3$) cm^{-1}: 1638. ^{1}H-NMR 200 MHz, $CDCl_3$) δ: 7.40—7.05 (10H, m), 5.85—5.45 (1H, m), 5.20—5.03 (2H, m), 4.59 (8/7H, s), 4.43 (6/7H, s), 4.02 (6/7H, br d, J=6 Hz), 3.74 (8/7H, br d, J=5 Hz), 3.28 (2H, br t, J=7 Hz), 2.68 (2H, br t, J=7 Hz). ^{13}C-NMR (75 MHz, $CDCl_3$) δ: 171.2, 171.1, 137.2, 136.3, 135.8, 132.7, 132.1, 129.1, 129.0, 128.8, 128.7, 128.4, 128.1, 127.4, 127.3, 126.1, 126.0, 125.9, 117.5, 116.7, 49.8, 48.8, 48.3, 48.1, 32.9, 32.7, 29.02, 28.98. HR-MS (EI) *m/z*: 311.1347 (Calcd for $C_{19}H_{21}NOS$ (M^+) 311.1344). The presence of rotamers precluded a comprehensive assignment of all proton and carbon resonances.

Ethyl Radical Addition–Cyclization of Alkene 12 To a solution of the alkene **12** (50 mg, 0.25 mmol) in toluene (1 ml) under a nitrogen atmosphere was added EtI (0.14 ml, 1.75 mmol) and Et_3B (1.0 M in hexane, 0.25 ml, 0.25 mmol) at room temperature. After being stirred at the same temperature for 3 h, the reaction mixture was diluted with water and extracted with $CHCl_3$. The organic phase was washed with water, dried with $MgSO_4$, and concentrated under reduced pressure. The residue was purified by PTLC (hexane/AcOEt 1 : 1) to afford *cis*-**16a** (8 mg, 8%) and *trans*-**16b** (29 mg, 32%).

***cis*-4-Iodomethyl-1-(phenylmethyl)-3-propyl-2-pyrrolidinone (16a)** A pale yellow oil. IR ($CHCl_3$) cm^{-1}: 1638. ^{1}H-NMR (500 MHz, $CDCl_3$) δ: 7.36—7.20 (5H, m), 4.47 (1H, d, J=15 Hz), 4.44 (1H, d, J=15 Hz), 3.34 (1H, dd, J=10, 7 Hz), 3.26 (1H, dd, J=10, 5 Hz), 3.08 (1H, dd, J=10, 4.5 Hz), 2.97 (1H, br t, J=10 Hz), 2.77—2.70 (1H, m), 2.50 (1H, br td, J=8, 6 Hz), 1.73—1.65 (1H, m), 1.60—1.40 (3H, m), 0.97 (3H, t, J=7 Hz). NOE was observed between 3-CH_2 (δ: 1.73—1.65, 1.60—1.40) and 4-CH_2 (δ: 2.97, 3.26) in NOESY spectroscopy. ^{13}C-NMR (125 MHz, $CDCl_3$) δ: 175.0, 136.4, 128.8, 128.2, 127.7, 51.4, 46.6, 46.2, 39.2, 27.4, 20.8, 14.1, 5.1. HR-MS (EI) *m/z*: 357.0589 (Calcd for $C_{15}H_{20}INO$ (M^+) 357.0589).

***trans*-4-Iodomethyl-1-(phenylmethyl)-3-propyl-2-pyrrolidinone (16b)** A pale yellow oil. IR ($CHCl_3$) cm^{-1}: 1677. ^{1}H-NMR (500 MHz, $CDCl_3$) δ: 7.36—7.20 (5H, m), 4.51 (1H, d, J=14.5 Hz), 4.39 (1H, d, J=14.5 Hz), 3.34 (1H, dd, J=10, 8 Hz), 3.32 (1H, dd, J=10, 4.5 Hz), 3.12 (1H, dd, J=10, 8.5 Hz), 2.91 (1H, dd, J=10, 6 Hz), 2.31—2.22 (2H, m), 1.84—1.76 (1H, m), 1.60—1.40 (3H, m), 0.97 (3H, t, J=7 Hz). ^{13}C-NMR (125 MHz, $CDCl_3$) δ: 175.4, 136.2, 128.7, 128.1, 127.7, 51.9, 48.9, 46.6, 39.9, 32.5, 20.1, 14.1, 9.8. HR-MS (EI) *m/z*: 357.0591 (Calcd for $C_{15}H_{20}INO$ (M^+) 357.0589).

Isopropyl Radical Addition–Cyclization of Alkene 12 To a solution of the alkene **12** (50 mg, 0.25 mmol) in toluene (1 ml) under a nitrogen atmosphere was added *i*-PrI (0.175 ml, 1.75 mmol) and Et_3B (1.0 M in hexane, 0.25 ml, 0.25 mmol) at room temperature. After being stirred at the same temperature for 1 h, the reaction mixture was diluted with water and extracted with $CHCl_3$. The organic phase was washed with water, dried with $MgSO_4$, and concentrated under reduced pressure. The residue was purified by PTLC (hexane/AcOEt 3 : 1) to afford *cis*-**17a** (12 mg, 13%) and *trans*-**17b** (44 mg, 45%).

***cis*-4-Iodomethyl-1-(phenylmethyl)-3-(2-methyl-propyl)-2-pyrrolidinone (17a)** A pale yellow oil. IR ($CHCl_3$) cm^{-1}: 1677. ^{1}H-NMR (500 MHz, $CDCl_3$) δ: 7.36—7.21 (5H, m), 4.48 (1H, d, J=15 Hz), 4.43 (1H, d, J=15 Hz), 3.34 (1H, dd, J=10, 6 Hz), 3.25 (1H, dd, J=10, 4.5 Hz), 3.10 (1H, dd, J=10, 3.5 Hz), 2.95 (1H, br t, J=10 Hz), 2.74—2.67 (1H, m), 2.57 (1H, br dt, J=9, 6.5 Hz), 1.85—1.77 (1H, m), 1.62—1.55 (1H, m), 1.32 (1H, ddd, J=14, 9, 6 Hz), 0.99 (3H, d, J=6.5 Hz), 0.94 (3H, d, J=6.5 Hz). NOE was observed between 3-CH_2 (δ: 1.32) and 4-CH_2 (δ: 3.25, 2.95) in NOESY spectroscopy. ^{13}C-NMR (125 MHz, $CDCl_3$) δ: 175.0, 136.4, 128.8, 128.15, 128.12, 127.7, 51.2, 46.7, 44.3, 39.3, 33.8, 25.7, 22.8, 22.3, 5.5. HR-MS (EI) *m/z*: 371.0748 (Calcd for $C_{16}H_{22}INO$ (M^+) 371.0745).

***trans*-4-Iodomethyl-1-(phenylmethyl)-3-(2-methylpropyl)-2-pyrrolidinone (17b)** A pale yellow oil. IR ($CHCl_3$) cm^{-1}: 1678. ^{1}H-NMR (500 MHz, $CDCl_3$) δ: 7.36—7.20 (5H, m), 4.49 (1H, d, J=15 Hz), 4.40 (1H, d, J=15 Hz), 3.35 (1H, dd, J=10, 8 Hz), 3.32 (1H, dd, J=10, 4 Hz), 3.13 (1H, dd, J=10, 9 Hz), 2.92 (1H, dd, J=10, 6 Hz,), 2.31—2.26 (1H, m), 2.25—2.17 (1H, m), 1.90—1.80 (1H, m), 1.74 (1H, ddd, J=14, 8, 5 Hz), 1.33 (1H, ddd, J=14, 8, 6 Hz), 0.96 (6H, d, J=6.5 Hz). NOE was observed between 4-H (δ: 2.25—2.17) and 3-CH_2 (δ: 1.13), 3-H (δ: 2.31—2.26) and 4-CH_2 (δ: 3.32, 3.13) in NOESY spectroscopy. ^{13}C-NMR (125 MHz, $CDCl_3$) δ: 175.8, 136.2, 128.7, 128.14, 128.11, 127.6, 51.7, 46.9, 46.6, 40.7, 40.2, 25.7, 23.1, 22.1, 9.8. HR-MS (EI) *m/z*: 371.0742 (Calcd for $C_{16}H_{22}INO$ (M^+) 371.0745).

***N*-[2-(Methoxyimino)ethyl]-*N*-propenyl-2-propenamide (19)** To allylamine (7.95 g, 139.5 mmol) was added chloroacetaldehyde *O*-methyloxime **7** (5.0 g, 46.5 mmol) at 0 °C under a nitrogen atmosphere. After being stirred at room temperature for 24 h, the reaction mixture was diluted with CH_2Cl_2 and washed with water. The organic phase was dried over $MgSO_4$ and concentrated under reduced pressure to give the crude allylamine **18** as a yellow oil. After being characterized by NMR spectrum, **18** was immediately subjected to the following reaction. To a solution of **18** (5.24 g, 41 mmol) in CH_2Cl_2 (70 ml) were added Et_3N (11.5 ml, 83 mmol) and a solution of acryloyl chloride (4.0 ml, 45 mmol) in CH_2Cl_2 (30 ml) at 0 °C under a nitrogen atmosphere. After being stirred at room temperature for 2 h, the reaction mixture was diluted with water and extracted with $CHCl_3$. The organic phase was washed with water, dried with $MgSO_4$, and concentrated under reduced pressure. The residue was purified by FCC (hexane/AcOEt 1 : 1) to afford **19** (4.5 g, 53%) as a yellow oil and a 2 : 1 mixture of *E* and *Z*-isomers; IR ($CHCl_3$) cm^{-1}: 1651, 1615. ^{1}H-NMR (300 MHz, $CDCl_3$) δ: 7.36 (2/3H, t, J=6 Hz), 6.68 (1/3H, t, J=4 Hz), 6.60—6.34 (2H, m), 5.88—5.68 (2H, m), 5.30—5.14 (2H, m), 4.26 (6/12H, br d, J=4 Hz), 4.21 (2/12H, br d, J=4 Hz), 4.14 (12/12H, br d, J=6 Hz), 4.08 (4/12H, br d, J=6 Hz), 4.05 (4/12H, br d, J=5 Hz), 3.98 (12/12H, br d, J=5 Hz), 4.02—3.95 (2/3H, m), 3.92 (1/3H, s), 3.89 (2/3H, s), 3.84 (6/3H, s): ^{13}C-NMR (75 MHz, $CDCl_3$) δ: 165.9, 147.6, 144.8, 144.4, 132.2, 132.1, 132.0, 128.1, 127.0, 126.8, 126.6, 117.4, 116.7, 116.4, 61.3, 61.0, 50.5, 48.9, 48.1, 45.3, 44.1, 41.9; HR-MS (EI) *m/z*: 182.1054 (Calcd for $C_9H_{14}N_2O_2$ (M^+) 182.1055). The presence of rotamers precluded a comprehensive assignment of all proton and carbon resonances.

Sulfanyl Radical Addition–Cyclization of Oxime Ether 19 To a boiling solution of **19** (273 mg, 1.5 mmol) in benzene (24 ml) under a nitrogen atmosphere was added a solution of thiophenol (0.15 ml, 1.5 mmol) and AIBN (123 mg, 0.75 mmol) in benzene (30 ml) by a syringe pump (5 ml/h) over 6 h. After the reaction mixture was heated at reflux for a further 2 h, the solvent was evaporated under reduced pressure. Purification of the residue by MCC (hexane/AcOEt 2 : 1) afforded *cis*-**20a** (66 mg, 15%), *trans*-**20b** (127 mg, 29%), *cis*-**21a** (13 mg, 3%), *trans*-**21b** (31 mg, 7%), *cis*-**22a** (5.7 mg, 1.3%), and *trans*-**22b** (3.1 mg, 0.7%).

***cis*-4-(Methoxyamino)-3-[(phenylsulfanyl)methyl]-1-propenyl-2-pyrrolidinone (20a)** A pale yellow oil. IR ($CHCl_3$) cm^{-1}: 3470, 1682. ^{1}H-NMR (500 MHz, $CDCl_3$) δ: 7.42—7.19 (5H, m), 5.94 (1H, br s), 5.76—5.67 (1H, m), 5.26—5.18 (2H, m), 4.01 (1H, br dd, J=15, 6 Hz), 3.82—3.76 (2H, m), 3.58 (1H, dd, J=13.5, 4 Hz), 3.50 (3H, s), 3.39 (2H, br d, J=3.5 Hz), 2.97 (1H, dd, J=13.5, 12 Hz), 2.74 (1H, br ddd, J=12, 7, 4 Hz). NOE was observed between NH (δ: 5.94) and C$\underline{H}_2$SPh (δ: 2.97) in NOESY spectroscopy. ^{13}C-NMR (125 MHz, $CDCl_3$) δ: 172.5, 134.9, 132.1, 129.6, 129.1, 126.6, 118.2, 62.6, 54.6, 49.3, 45.2, 44.1, 28.9. HR-MS (EI) *m/z*: 292.1255 (Calcd for $C_{15}H_{20}N_2O_2S$ (M^+) 292.1245).

***trans*-4-(Methoxyamino)-3-[(phenylsulfanyl)methyl]-1-propenyl-2-pyrrolidinone (20b)** A pale yellow oil. IR ($CHCl_3$) cm^{-1}: 3450, 1682. ^{1}H-NMR (500 MHz, $CDCl_3$) δ: 7.41—7.18 (5H, m), 5.84 (1H, br s), 5.74—5.65 (1H, m), 5.24—5.18 (2H, m), 3.92—3.83 (2H, m), 3.77 (1H, br ddd, J=7.5, 6, 5.5 Hz), 3.56 (1H, dd, J=14, 4 Hz), 3.53 (3H, s), 3.50 (1H, dd, J=10, 7.5 Hz), 3.26 (1H, dd, J=10, 5.5 Hz), 2.99 (1H, dd, J=14, 10 Hz), 2.70 (1H, br ddd, J=10, 6, 4 Hz). NOE was observed between 4-H (δ: 3.77) and C$\underline{H}_2$SPh (δ: 2.99) in NOESY spectroscopy. ^{13}C-NMR (125 MHz, $CDCl_3$) δ: 172.4, 131.8, 129.6, 129.1, 129.0, 126.6, 118.3, 62.5, 58.9, 49.3, 45.3, 44.6, 34.4; HR-MS (EI) *m/z*: 292.1245 (Calcd for $C_{15}H_{20}N_2O_2S$ (M^+) 292.1245).

***cis*-1-[2-(Methoxyimino)ethyl]-4-methyl-3-[(phenylsulfanyl)methyl]-2-pyrrolidinone (21a)** The oxime ether **21a** was obtained as a 2 : 1 inseparable mixture of *E*- and *Z*-isomers. A pale yellow oil IR ($CHCl_3$) cm^{-1}: 1684. ^{1}H-NMR (500 MHz, $CDCl_3$) δ: 7.40—7.17 (5H, m), 7.23 (2/3H, t, J=5.5 Hz), 6.57 (1/3H, t, J=4.5 Hz), 4.19 (1/3H, dd, J=17, 4.5 Hz), 4.11 (1/3H, dd, J=17, 4.5 Hz), 4.08 (2/3H, dd, J=15, 5.5 Hz), 3.94 (2/3H, dd, J=15, 5.5 Hz), 3.89 (3/3H, s), 3.84 (6/3H, s), 3.52 (1H, br dd, J=13, 3.5 Hz), 3.47 (1H, br dd, J=10, 6 Hz), 2.95 (2/3H, dd, J=10, 2 Hz), 2.94 (1/3H, dd, J=10, 2 Hz), 2.85 (1/3H, dd, J=13, 11 Hz), 2.84 (2/3H, dd, J=13, 11 Hz), 2.73 (1H, br ddd, J=11, 7, 3.5 Hz), 2.67—2.58 (1H, m), 1.07 (3H, d, J=7 Hz). NOE was observed between 4-Me (δ: 1.07) and C$\underline{H}_2$SPh (δ: 2.85, 2.84) in NOESY spectroscopy. ^{13}C-NMR (125 MHz, $CDCl_3$) δ: 173.9, 146.4, 144.6, 135.6, 129.49, 129.46, 129.4, 129.0, 126.35, 126.32, 61.8, 53.6, 52.8, 45.2, 45.1, 41.5, 38.3, 30.1, 30.0, 29.7, 29.4, 14.5. HR-MS (EI) *m/z*: 292.1250 (Calcd for $C_{15}H_{20}N_2O_2S$ (M^+) 292.1244).

***trans*-1-[2-(Methoxyimino)ethyl]-4-methyl-3-[(phenylsulfanyl)methyl]-2-pyrrolidinone (21b)** The oxime ether **21b** was obtained as a 2 : 1 inseparable mixture of *E*- and *Z*-isomers. A pale yellow oil. IR ($CHCl_3$) cm^{-1}: 1684. ^{1}H-NMR (500 MHz, $CDCl_3$) δ: 7.40—7.16 (5H, m), 7.23 (2/3H, t, J=6 Hz), 6.57 (1/3H, t, J=5 Hz), 4.16 (1/3H, dd, J=17, 5 Hz), 4.12 (1/3H,

dd, J=17, 5 Hz), 4.02 (2/3H, dd, J=17, 6 Hz), 3.98 (2/3H, dd, J=17, 6 Hz), 3.90 (3/3H, s), 3.84 (6/3H, s), 3.51 (1/3H, dd, J=13, 4 Hz), 3.50 (2/3H, dd, J=13, 4 Hz), 3.47 (1/3H, dd, J=9.5, 8 Hz), 3.45 (2/3H, dd, J=9.5, 8 Hz), 3.02 (1/3H, dd, J=13, 8 Hz), 3.01 (2/3H, dd, J=13, 8 Hz), 2.91 (1/3H, dd, J=9.5, 7 Hz), 2.91 (2/3H, dd, J=9.5, 7 Hz), 2.43—2.35 (1H, m), 2.38—2.32 (1H, m), 1.19 (3H, d, J=6.5 Hz). ^{13}C-NMR (125 MHz, $CDCl_3$) δ: 175.5, 147.4, 145.6, 136.9, 130.33, 130.32, 129.99, 129.98, 127.24, 127.21, 63.1, 62.8, 54.3, 53.6, 50.0, 49.9, 42.5, 39.3, 35.7, 35.6, 33.8, 20.3, 20.2. HR-MS (EI) m/z: 292.1251 (Calcd for $C_{15}H_{20}N_2O_2S$ (M^+) 292.1244).

***cis*-1-[2-(Methoxyimino)ethyl]-3-methyl-4-[(phenylsulfanyl)methyl]-2-pyrrolidinone (22a)** The oxime ether **22a** was obtained as a 2 : 1 inseparable mixture of *E*- and *Z*-isomers. A pale yellow oil. IR ($CHCl_3$) cm^{-1}: 1684. ^{1}H-NMR (500 MHz, $CDCl_3$) δ: 7.36—7.20 (5H, m), 7.24 (2/3H, t, J=5.5 Hz), 6.57 (1/3H, t, J=4.5 Hz), 4.15 (1/3H, dd, J=17, 4.5 Hz), 4.12 (1/3H, dd, J=17, 4.5 Hz), 4.04 (2/3H, dd, J=15.5, 5.5 Hz), 3.97 (2/3H, dd, J=15.5, 5.5 Hz), 3.90 (3/3H, s), 3.84 (6/3H, s), 3.45 (1/3H, dd, J=10, 7 Hz), 3.44 (2/3H, dd, J=10, 7 Hz), 3.30 (2/3H, dd, J=10, 6 Hz), 3.29 (1/3H, dd, J=10, 6 Hz), 3.11 (1/3H, dd, J=13, 5 Hz), 3.10 (2/3H, dd, J=13, 5 Hz), 2.78 (2/3H, dd, J=13, 9 Hz), 2.77 (1/3H, dd, J=13, 9 Hz), 2.68—2.58 (1H, m), 2.64—2.56 (1H, m), 1.17 (3H, br d, J=7 Hz). NOE was observed between 3-Me (δ: 1.17) and C$\underline{H}_2$SPh (δ: 3.11, 3.10, 2.78, 2.77) in NOESY spectroscopy. ^{13}C-NMR (125 MHz, $CDCl_3$) δ: 176.8, 176.7, 146.4, 144.5, 135.4, 135.3, 130.02, 129.96, 129.2, 129.1, 126.8, 126.7, 62.1, 61.8, 50.6, 49.9, 41.3, 39.8, 39.7, 38.2, 35.6, 35.5, 33.7, 33.6, 10.6. HR-MS (EI) m/z: 292.1255 (Calcd for $C_{15}H_{20}N_2O_2S$ (M^+) 292.1244).

***trans*-1-[2-(Methoxyimino)ethyl]-3-methyl-4-[(phenylsulfanyl)methyl]-2-pyrrolidinone (22b)** The oxime ether **22b** was obtained as a 2 : 1 inseparable mixture of *E*- and *Z*-isomers. A pale yellow oil. IR ($CHCl_3$) cm^{-1}: 1685. ^{1}H-NMR (500 MHz, $CDCl_3$) δ: 7.40—7.20 (5H, m), 7.24 (2/3H, t, J=6 Hz), 6.58 (1/3H, t, J=5 Hz), 4.17 (1/3H, dd, J=17, 5 Hz), 4.13 (1/3H, dd, J=17, 5 Hz), 4.01 (2/3H, dd, J=17, 6 Hz), 4.00 (2/3H, dd, J=17, 6 Hz), 3.89 (3/3H, s), 3.85 (6/3H, s), 3.49 (1H, br dd, J=10, 8 Hz), 3.24 (1/3H, dd, J=13, 5 Hz), 3.22 (2/3H, dd, J=13, 5 Hz), 3.13 (1/3H, dd, J=10, 8 Hz), 3.12 (2/3H, dd, J=10, 7.5 Hz), 2.90 (1H, br dd, J=13, 9 Hz), 2.32—2.24 (1H, m), 2.24—2.14 (1H, m), 1.22 (3/3H, d, J=7 Hz), 1.21 (6/3H, d, J=7 Hz). NOE was observed between 3-H (δ: 2.32—2.24) and C$\underline{H}_2$SPh (δ: 2.90) in NOESY spectroscopy. ^{13}C-NMR (125 MHz, $CDCl_3$) δ: 176.2, 146.5, 144.6, 129.8, 129.7, 129.2, 129.1, 126.6, 61.8, 51.1, 50.4, 42.5, 42.3, 41.4, 40.4, 40.3, 38.2, 37.39, 37.35, 31.9, 29.7, 22.7, 15.1, 14.1. HR-MS (EI) m/z: 292.1250 (Calcd for $C_{15}H_{20}N_2O_2S$ (M^+) 292.1244).

Ethyl Radical Addition–Cyclization of Oxime Ether 19 To a solution of the oxime ether **19** (47 mg, 0.25 mmol) in toluene (1 ml) under a nitrogen atmosphere was added EtI (0.14 ml, 1.75 mmol) and Et_3B (1.0 M in hexane, 0.25 ml, 0.25 mmol) at room temperature. After being stirred at the same temperature for 1 h, the reaction mixture was diluted with water and extracted with $CHCl_3$. The organic phase was washed with water, dried with $MgSO_4$, and concentrated under reduced pressure. The residue was purified by PTLC (hexane/AcOEt 1 : 1) to afford *cis*-**23a** (5.3 mg, 10%), *trans*-**23b** (5.8 mg, 11%), *cis*-**26a** (4.3 mg, 5%), and *trans*-**26b** (15 mg, 18%).

***cis*-4-(Methoxyamino)-1-propenyl-3-propyl-2-pyrrolidinone (23a)** A pale yellow oil. IR ($CHCl_3$) cm^{-1}: 3659, 1679. ^{1}H-NMR (500 MHz, $CDCl_3$) δ: 5.77—5.68 (1H, m), 5.60—5.40 (1H, very br), 5.26—5.17 (2H, m), 3.99 (1H, br dd, J=15, 6 Hz), 3.83 (1H, br dd, J=15, 6.5 Hz), 3.73 (1H, ddd, J=7, 4.5, 2 Hz), 3.51 (3H, s), 3.37—3.32 (2H, m), 2.48 (1H, ddd, J=10, 7, 6 Hz), 1.80—1.72 (1H, m), 1.54—1.45 (2H, m), 1.44—1.35 (1H, m), 0.97 (3H, t, J=7 Hz). ^{13}C-NMR (125 MHz, $CDCl_3$) δ: 174.5, 132.4, 117.9, 62.3, 55.5, 49.3, 45.1, 44.7, 26.2, 21.2, 14.1. HR-MS (EI) m/z: 212.1542 (Calcd for $C_{11}H_{20}N_2O_2$ (M^+) 212.1524).

***trans*-4-(Methoxyamino)-1-propenyl-3-propyl-2-pyrrolidinone (23b)** A pale yellow oil. IR ($CHCl_3$) cm^{-1}: 3692, 1677. ^{1}H-NMR (500 MHz, $CDCl_3$) δ: 5.76—5.68 (1H, m), 5.58—5.42 (1H, very br), 5.22—5.17 (2H, m), 3.89 (2H, br d, J=6 Hz), 3.54 (3H, s), 3.54—3.49 (1H, m), 3.45 (1H, dd, J=10, 7 Hz), 3.21 (1H, dd, J=10, 4 Hz), 2.30—2.26 (1H, m), 1.79—1.72 (1H, m), 1.54—1.40 (3H, m), 0.95 (3H, t, J=7 Hz). NOE was observed between 4-H (δ: 3.54—3.49) and C$\underline{H}_2$SPh (δ: 1.79—1.72) in NOESY spectroscopy. ^{13}C-NMR (125 MHz, $CDCl_3$) δ: 174.8, 132.2, 117.9, 62.4, 58.9, 49.6, 45.6, 45.0, 32.2, 20.2, 14.0; HR-MS (EI) m/z: 212.1524 (Calcd for $C_{11}H_{20}N_2O_2$ (M^+) 212.1524).

***cis*-4-Iodomethyl-1-[2-(methoxyimino)ethyl]-3-propyl-2-pyrrolidinone (26a)** The oxime ether **26a** was obtained as a 2 : 1 inseparable mixture of *E*- and *Z*-isomers. A pale yellow oil; IR ($CHCl_3$) cm^{-1}: 1685. ^{1}H-NMR (500 MHz, $CDCl_3$) δ: 7.26 (2/3H, t, J=5 Hz), 6.62 (1/3H, t, J=4.5 Hz), 4.19 (1/3H, dd, J=16, 4.5 Hz), 4.13 (1/3H, dd, J=16, 4.5 Hz), 4.11 (2/3H, dd, J=16, 5 Hz), 3.95 (2/3H, dd, J=16, 5 Hz), 3.91 (3/3H, s), 3.86 (6/3H, s), 3.51 (1/3H, dd, J=10, 6 Hz), 3.48 (2/3H, dd, J=10, 6 Hz), 3.33—3.23 (2H, m), 3.10 (2/3H, t, J=10 Hz), 3.05 (1/3H, t, J=10 Hz), 2.82—2.75 (1H, m), 2.47 (1H, br td, J=7, 6.5 Hz), 1.74—1.64 (1H, m), 1.54—1.38 (3H, m), 0.96 (3H, br t, J=7 Hz). ^{13}C-NMR (125 MHz, $CDCl_3$) δ: 175.1, 146.3, 144.4, 62.2, 61.9, 52.6, 51.8, 46.0, 45.8, 41.2, 39.3, 39.1, 38.2, 27.30, 27.28, 20.9, 20.8, 20.1, 14.1, 5.2, 4.9. HR-MS (EI) m/z: 338.0491 (Calcd for $C_{11}H_{19}IN_2O_2$ (M^+) 338.0490).

***trans*-4-Iodomethyl-1-[2-(methoxyimino)ethyl]-3-propyl-2-pyrrolidinone (26b)** The oxime ether **26b** was obtained as a 2 : 1 inseparable mixture of *E*- and *Z*-isomers. A pale yellow oil. IR ($CHCl_3$) cm^{-1}: 1683. ^{1}H-NMR (500 MHz, $CDCl_3$) δ: 7.25 (2/3H, t, J=5.5 Hz), 6.60 (1/3H, t, J=4.5 Hz), 4.18 (1/3H, dd, J=16, 4.5 Hz), 4.14 (1/3H, dd, J=16, 4.5 Hz), 4.03 (2/3H, dd, J=15, 5.5 Hz), 4.00 (2/3H, dd, J=15, 5.5 Hz), 3.91 (3/3H, s), 3.86 (6/3H, s), 3.50 (1/3H, dd, J=10, 8 Hz), 3.49 (2/3H, dd, J=10, 8 Hz), 3.38 (1/3H, dd, J=10, 4.5 Hz), 3.36 (2/3H, dd, J=10, 5 Hz), 3.19 (2/3H, dd, J=10, 8.5 Hz), 3.18 (1/3H, dd, J=10, 8.5 Hz), 3.07 (1H, br dd, J=10, 6 Hz), 2.35—2.27 (1H, m), 2.21 (1H, br td, J=7, 5 Hz), 1.80—1.76 (1H, m), 1.56—1.38 (3H, m), 0.96 (1/3H, t, J=7 Hz), 0.95 (2/3H, t, J=7 Hz). NOE was observed between 3-H (δ: 2.21) and 4-CH_2 (δ: 3.38, 3.36, 3.19, 3.18) in NOESY spectroscopy. ^{13}C-NMR (125 MHz, $CDCl_3$) δ: 175.6, 146.3, 144.4, 62.1, 61.8, 53.0, 52.2, 48.7, 48.5, 41.3, 40.0, 39.9, 38.1, 32.5, 32.4, 20.0, 14.1, 9.75, 9.70. HR-MS (EI) m/z: 338.0493 (Calcd for $C_{11}H_{19}IN_2O_2$ (M^+) 338.0490).

Isopropyl Radical Addition–Cyclization of Oxime Ether 19 To a solution of the oxime ether **19** (47 mg, 0.25 mmol) in toluene (1 ml) under a nitrogen atmosphere was added *i*-PrI (0.18 ml, 1.75 mmol) and Et_3B (1.0 M in hexane, 0.25 ml, 0.25 mmol) at room temperature. After being stirred at the same temperature for 1 h, the reaction mixture was diluted with water and extracted with $CHCl_3$. The organic phase was washed with water, dried with $MgSO_4$, and concentrated under reduced pressure. The residue was purified by PTLC (hexane/AcOEt 1 : 1) to afford *cis*-**24a** (2.6 mg, 4.6%), *trans*-**24b** (10.4 mg, 18.4%), *cis*-**27a** (12.8 mg, 14.5%), and *trans*-**27b** (31.3 mg, 35.5%).

***cis*-4-(Methoxyamino)-3-(2-methylpropyl)-1-propenyl-2-pyrrolidinone (24a)** A pale yellow oil. IR ($CHCl_3$) cm^{-1}: 3438, 1679. ^{1}H-NMR (500 MHz, $CDCl_3$) δ: 5.77—5.68 (1H, m), 5.48 (1H, br s), 5.26—5.18 (2H, m), 3.99 (1H, br dd, J=15, 6 Hz), 3.83 (1H, br dd, J=15, 6 Hz), 3.71 (1H, br ddd, J=6.5, 5, 1.5 Hz), 3.51 (3H, s), 3.36 (1H, dd, J=10, 1.5 Hz), 3.33 (1H, dd, J=10, 5 Hz), 2.58—2.53 (1H, m), 1.83—1.76 (1H, m), 1.63 (1H, br ddd, J=14, 8.5, 5 Hz), 1.33 (1H, br ddd, J=14, 10, 5.5 Hz), 0.97 (3H, d, J=6.5 Hz), 0.95 (3H, d, J=6.5 Hz). NOE was observed between NH (δ: 5.48) and 3-CH_2 (δ: 1.33) in NOESY spectroscopy. ^{13}C-NMR (125 MHz, $CDCl_3$) δ: 174.6, 132.5, 117.9, 62.3, 55.8, 49.2, 45.2, 42.8, 32.6, 26.2, 23.1, 22.0. HR-MS (EI) m/z: 226.1686 (Calcd for $C_{12}H_{22}N_2O_2$ (M^+) 226.1680).

***trans*-4-(Methoxyamino)-3-(2-methylpropyl)-1-propenyl-2-pyrrolidinone (24b)** A pale yellow oil. IR ($CHCl_3$) cm^{-1}: 3442, 1678. ^{1}H-NMR (500 MHz, $CDCl_3$) δ: 5.76—5.68 (1H, m), 5.58—5.42 (1H, very br), 5.22—5.18 (2H, m), 3.93—3.84 (2H, m), 3.54 (3H, s), 3.52—3.44 (2H, m), 3.24—3.18 (1H, m), 2.36—2.32 (1H, m), 1.88—1.79 (1H, m), 1.65 (1H, br ddd, J=14.5, 8.5, 4 Hz), 1.33 (1H, br ddd, J=14.5, 9.5, 5.5 Hz), 0.96 (3H, d, J=6.5 Hz), 0.94 (3H, d, J=6.5 Hz). ^{13}C-NMR (125 MHz, $CDCl_3$) δ: 175.2, 132.2, 117.9, 62.4, 59.4, 49.3, 45.0, 43.8, 39.3, 25.8, 23.1, 21.8. HR-MS (EI) m/z: 226.1674 (Calcd for $C_{12}H_{22}N_2O_2$ (M^+) 226.1680).

***cis*-4-Iodomethyl-1-[2-(methoxyimino)ethyl]-3-(2-methylpropyl)-2-pyrrolidinone (27a)** The oxime ether **27a** was obtained as a 2 : 1 inseparable mixture of *E*- and *Z*-isomers. A pale yellow oil. IR ($CHCl_3$) cm^{-1}: 1684. ^{1}H-NMR (500 MHz, $CDCl_3$) δ: 7.27 (2/3H, t, J=5 Hz), 6.62 (1/3H, t, J=4 Hz), 4.18—4.10 (2/3H, m), 4.12 (2/3H, dd, J=16, 5 Hz), 3.94 (2/3H, dd, J=16, 5 Hz), 3.91 (3/3H, s), 3.86 (6/3H, s), 3.51 (1/3H, dd, J=10, 7 Hz), 3.49 (2/3H, dd, J=10, 6 Hz), 3.32—3.26 (2H, m), 3.09 (2/3H, br t, J=10 Hz), 3.03 (1/3H, t, J=10 Hz), 2.80—2.72 (1H, m), 2.55 (1H, br dt, J=9, 7 Hz), 1.82—1.76 (1H, m), 1.62—1.52 (1H, m), 1.35—1.28 (1H, m), 0.98 (3H, d, J=6 Hz), 0.94 (3H, d, J=6 Hz). NOE was observed between 3-CH_2 (δ: 1.35—1.28) and 4-CH_2 (δ: 3.09, 3.03) in NOESY spectroscopy. ^{13}C-NMR (125 MHz, $CDCl_3$) δ: 175.2, 146.3, 144.4, 62.2, 61.9, 52.4, 51.5, 44.1, 43.9, 41.2, 39.4, 39.2, 38.2, 33.7, 25.73, 25.70, 22.8, 22.2, 5.5, 5.3. HR-MS (EI) m/z: 352.0646 (Calcd for $C_{12}H_{21}IN_2O_2$ (M^+) 352.0647).

***trans*-4-Iodomethyl-1-[2-(methoxyimino)ethyl]-3-(2-methylpropyl)-2-pyrrolidinone (27b)** The oxime ether **27b** was obtained as a 2 : 1 inseparable mixture of *E*- and *Z*-isomers. A pale yellow oil. IR ($CHCl_3$) cm^{-1}: 1685. ^{1}H-NMR (500 MHz, $CDCl_3$) δ: 7.26 (2/3H, t, J=5.5 Hz), 6.61 (1/3H, t, J=4.5 Hz), 4.17 (1/3H, dd, J=17, 4.5 Hz), 4.14 (1/3H, dd, J=17, 4.5 Hz), 4.03 (2/3H, dd, J=15, 5.5 Hz), 4.00 (2/3H, dd, J=15, 5.5 Hz), 3.91 (3/3H, s),

3.86 (6/3H, s), 3.52—3.48 (1H, m), 3.38 (1/3H, dd, J=10, 4 Hz), 3.36 (2/3H, dd, J=10, 4 Hz), 3.20 (2/3H, dd, J=10, 8 Hz), 3.19 (1/3H, dd, J=10, 8 Hz), 3.08 (1H, br dd, J=10, 6 Hz), 2.30—2.22 (2H, m), 1.90—1.80 (1H, m), 1.73—1.66 (1H, m), 1.32 (1H, br ddd, J=13.5, 8, 6 Hz), 0.95 (6H, d, J=6.5 Hz). ^{13}C-NMR (125 MHz, $CDCl_3$) δ: 175.9, 146.3, 144.4, 62.1, 61.8, 52.8, 52.0, 46.7, 46.5, 41.3, 40.8, 40.7, 40.1, 40.0, 38.1, 25.7, 23.0, 22.07, 22.05, 9.73, 9.67. HR-MS (EI) m/z: 352.0651 (Calcd for $C_{12}H_{21}IN_2O_2$ (M^+) 352.0647).

***tert*-Butyl Radical Addition–Cyclization of Oxime Ether 19** To a solution of the oxime ether **19** (47 mg, 0.25 mmol) in toluene (1 ml) under a nitrogen atmosphere was added *t*-BuI (0.22 ml, 1.75 mmol) and Et_3B (1.0 M in hexane, 0.25 ml, 0.25 mmol) at room temperature. After being stirred at the same temperature for 1 h, the reaction mixture was diluted with water and extracted with $CHCl_3$. The organic phase was washed with water, dried with $MgSO_4$, and concentrated under reduced pressure. The residue was purified by PTLC (hexane/AcOEt 1 : 1) to afford *cis*-**25a** (4.4 mg, 1.3%), *trans*-**25b** (12.4 mg, 20.7%), *cis*-**28a** (7 mg, 7.7%), and *trans*-**28b** (32 mg, 35.3%).

***cis*-4-(Methoxyamino)-3-(2,2-dimethylpropyl)-1-propenyl-2-pyrrolidinone (25a)** A pale yellow oil. IR ($CHCl_3$) cm^{-1}: 3694, 1681. ^{1}H-NMR (500 MHz, $CDCl_3$) δ: 5.78—5.69 (1H, m), 5.58—5.42 (1H, very br), 5.26—5.18 (2H, m), 4.01 (1H, br dd, J=15, 6 Hz), 3.83 (1H, br dd, J=15, 6 Hz), 3.70 (1H, dd, J=6.5, 5 Hz), 3.51 (3H, s), 3.42 (1H, br d, J=10.5 Hz), 3.33 (1H, dd, J=10.5, 5 Hz), 2.48 (1H, ddd, J=10, 6.5, 2.5 Hz), 1.81 (1H, dd, J=15, 2.5 Hz), 1.38 (1H, dd, J=15, 10 Hz), 0.98 (9H, s). ^{13}C-NMR (125 MHz, $CDCl_3$) δ: 174.8, 132.5, 118.0, 62.3, 56.7, 49.2, 45.4, 42.0, 35.9, 30.5, 29.7, 29.6. HR-MS (EI) m/z: 240.1834 (Calcd for $C_{13}H_{24}N_2O_2$ (M^+) 240.1837).

***trans*-4-(Methoxyamino)-3-(2,2-dimethylpropyl)-1-propenyl-2-pyrrolidinone (25b)** A pale yellow oil. IR ($CHCl_3$) cm^{-1}: 3424, 1678. ^{1}H-NMR (500 MHz, $CDCl_3$) δ: 5.76—5.67 (1H, m), 5.58—5.42 (1H, very br), 5.22—5.18 (2H, m), 3.94—3.83 (2H, m), 3.54 (3H, s), 3.50 (1H, br dd, J=6.5, 3 Hz), 3.45 (1H, dd, J=10, 6.5 Hz), 3.26 (1H, dd, J=10, 3 Hz), 2.25 (1H, dt, J=8.5, 3 Hz), 1.77 (1H, dd, J=14, 3 Hz), 1.29 (1H, dd, J=14, 8.5 Hz), 0.99 (9H, s). NOE was observed between 4-H (δ: 3.50) and 3-CH_2 (δ: 1.29) in NOESY spectroscopy. ^{13}C-NMR (125 MHz, $CDCl_3$) δ: 175.9, 132.2, 117.9, 62.3, 60.5, 49.3, 45.2, 43.6, 42.8, 31.1, 29.6. HR-MS (EI) m/z: 240.1840 (Calcd for $C_{13}H_{24}N_2O_2$ (M^+) 240.1837).

***cis*-4-Iodomethyl-1-[2-(methoxyimino)ethyl]-3-(2,2-dimethylpropyl)-2-pyrrolidinone (28a)** The oxime ether **28a** was obtained as a 2 : 1 inseparable mixture of *E*- and *Z*-isomers. A pale yellow oil. IR ($CHCl_3$) cm^{-1}: 1686. ^{1}H-NMR (500 MHz, $CDCl_3$) δ: 7.28 (2/3H, t, J=5 Hz), 6.65 (1/3H, t, J=4.5 Hz), 4.21 (1/3H, dd, J=17, 4.5 Hz), 4.15 (2/3H, dd, J=16, 5 Hz), 4.13 (1/3H, dd, J=17, 4.5 Hz), 3.94 (2/3H, dd, J=16, 5 Hz), 3.92 (3/3H, s), 3.87 (6/3H, s), 3.53 (1/3H, br dd, J=11, 7 Hz), 3.50 (2/3H, br dd, J=10, 7 Hz), 3.44—3.32 (2H, m), 3.03 (2/3H, br t, J=10.5 Hz), 2.95 (1/3H, br t, J=10.5 Hz), 2.80—2.72 (1H, m), 2.50—2.44 (1H, m), 1.84 (1H, dd, J=15, 3 Hz), 1.36 (1H, dd, J=15, 9 Hz), 0.97 (9H, s). NOE was observed between 3-CH_2 (δ: 1.36) and 4-CH_2 (δ: 3.03, 2.95) in NOESY spectroscopy. ^{13}C-NMR (125 MHz, $CDCl_3$) δ: 174.9, 146.3, 144.4, 62.2, 61.9, 52.3, 51.5, 43.4, 43.3, 41.4, 40.3, 39.9, 38.5, 36.9, 30.5, 29.7, 29.6, 6.6, 6.4. HR-MS (EI) m/z: 366.0801 (Calcd for $C_{13}H_{23}IN_2O_2$ (M^+) 366.0803).

***trans*-4-Iodomethyl-1-[2-(methoxyimino)ethyl]-3-(2,2-dimethylpropyl)-2-pyrrolidinone (28b)** The oxime ether **28b** was obtained as a 2 : 1 inseparable mixture of *E*- and *Z*-isomers. A pale yellow oil. IR ($CHCl_3$) cm^{-1}: 1685. ^{1}H-NMR (500 MHz, $CDCl_3$) δ: 7.26 (2/3H, t, J=5.5 Hz), 6.61 (1/3H, t, J=4.5 Hz), 4.16 (2/3H, d, J=4.5 Hz), 4.02 (4/3H, d, J=5.5 Hz), 3.91 (3/3H, s), 3.86 (6/3H, s), 3.49 (1/3H, dd, J=10, 7.5 Hz), 3.48 (2/3H, dd, J=10, 7.5 Hz), 3.42 (1/3H, dd, J=10, 4 Hz), 3.41 (2/3H, dd, J=10, 4 Hz), 3.19 (2/3H, dd, J=10, 9 Hz), 3.18 (1/3H, dd, J=10, 9 Hz), 3.13 (1H, br dd, J=10, 6 Hz), 2.30—2.20 (1H, m), 2.16—2.10 (1H, m), 1.87 (1/3H, dd, J=14, 4.5 Hz), 1.85 (2/3H, J=14, 4.5 Hz), 1.22 (2/3H, dd, J=14, 5.5 Hz), 1.21 (1/3H, J=14, 5.5 Hz), 0.97 (9H, s). NOE was observed between 3-H (δ: 2.16—2.10) and 4-CH_2 (δ: 3.42, 3.41, 3.19, 3.18), and 4-H (δ: 2.30—2.20) and 3-CH_2 (δ: 1.22—1.21) in NOESY spectroscopy. ^{13}C-NMR (125 MHz, $CDCl_3$) δ: 177.3, 177.2, 147.0, 145.1, 62.8, 62.5, 53.3, 52.5, 46.3, 46.1, 45.1, 45.0, 43.2, 43.1, 42.1, 38.9, 31.6, 30.3, 9.6. HR-MS (EI) m/z: 366.0806 (Calcd for $C_{13}H_{23}IN_2O_2$ (M^+) 366.0803).

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