Transition Metal Catalyzed Radical Cyclization: New Preparative Route to γ-Lactams from Allylic Alcohols via the [3.3]-Sigmatropic Rearrangement of Allylic Trichloroacetimidates and the Subsequent Ruthenium-Catalyzed Cyclization of *N*-Allyltrichloroacetamides

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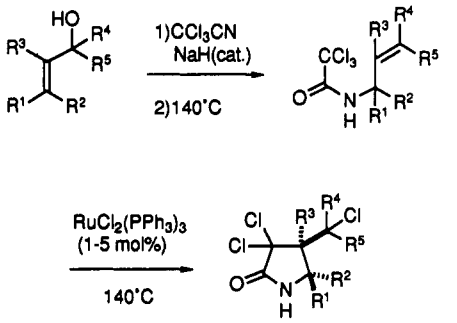
A sequence of reactions including [3.3]-sigmatropic rearrangement of allyl trichloroacetimidates (Overman rearrangement) followed by ruthenium-catalyzed cyclization of *N*-allyltrichloroacetamides provided a novel method for preparing trichlorinated γ-lactams from allylic alcohols. No δ-lactam was formed as a byproduct. The cyclization of secondary *N*-allyltrichloroacetamides proceeded with good diastereoselectivity. Two types of tandem cyclizations to form bicyclic lactams took place in the cyclization of *N*-allyltrichloroacetamides from geraniol and linalool.

Introduction

Free-radical cyclizations have become an important synthetic method for constructing five- or six-membered ring skeletons.[1] The radical cyclizations of several polyhalogenated precursors catalyzed by transition-metal salts or complexes were developed in our laboratory,[2,3a-c] by Tseng and co-workers,[4] and by Weinreb's group,[5] providing simple routes to γ-lactones,[2] γ-lactams,[3,4] and substituted cyclopentanes.[5] In our previous papers, we described the ruthenium-catalyzed cyclization of *N*-allyltrichloroacetamides.[4a,6] Since *N*-allyltrichloroacetamides are easily available from allylic alcohols by a [3.3]-sigmatropic rearrangement as reported by Overman,[7] the ruthenium-catalyzed cyclization provided us a convenient entry to γ-lactam derivatives from allylic alcohols as shown in Scheme I.

In this paper, we described detailed studies of this two-step process. The Overman rearrangement proceeds with complete 1,3-transposition in the conversion of the hydroxy group to the amide group, and the subsequent ruthenium-catalyzed cyclization of *N*-allyltrichloroacetamides provides γ-lactams selectively despite the potential for formation of δ-lactams. Furthermore, the cyclization of trichloroacetamides of secondary allylic amines proceeds with high diastereoselectivity to give either cis-fused bicyclic lactams or β,γ-trans-disubstituted monocyclic lactams. Two types of tandem radical cyalization to form bicyclic lactams from acyclic precursors are reported.

Scheme I



Results and Discussion

Cyclization of *N*-Allyltrichloroacetamides. Trichloroacetamides **1–10** were prepared in 40–90% yields from the corresponding allylic alcohols.[7,8] These trichloroacetamides are alternatively synthesized by trichloroacetylation of allylic amines; however, substituted allylic amines are less easily available than allylic alcohols. Cyclization of the *N*-allyltrichloroacetamides was accomplished by $RuCl_2(PPh_3)_3$ catalysis in aromatic solvents at 140 °C for 1–3 h. In order to avoid intermolecular addition to give diamides or polyamides, it is recommended that the reactions be carried out in relatively dilute solutions (0.05–0.2 M trichloroacetamides). Catalyst concentration (1–5 mol %) is also important: considerable amounts of *N*-allyldichloroacetamides were formed as byproducts with lower than 1 mol % of the catalyst. Although cyclization of allyltrichloroacetates to trichlorinated γ-lactones is catalyzed by cuprous salts in acetonitrile,[2] CuCl was not an efficient catalyst for the cyclization of *N*-allyltrichloroacetamides (up to 3 turnovers).

In Table I are summarized the results of ruthenium-catalyzed cyclization of various *N*-allyltrichloroacetamides obtained by the Overman rearrangement. The desired trichlorinated γ-lactams were formed in 60–80% yields without formation of the corresponding δ-lactams. Two regioisomeric *N*-allyltrichloroacetamides, **2** and **3**, which were prepared from 3-methyl-2-buten-1-ol and 2-methyl-3-buten-2-ol, respectively, afforded the regioisomeric lac-

(1) For reviews, see: Giese, B. *Radicals in Organic Synthesis: Formation of Carbon–Carbon Bonds*; Pergamon: New York, 1986. Stork, G. *Bull. Chem. Soc. Jpn.* **1989**, *28*, 723. Curran, D. P. *Synthesis* **1988**, 417, 489.

(2) Nagashima, H.; Seki, K.; Ozaki, N.; Wakamatsu, H.; Itoh, K.; Tomo, Y.; Tsuji, J. *J. Org. Chem.* **1990**, *55*, 985. Nagashima, H.; Wakamatsu, H.; Itoh, K.; Tomo, Y.; Tsuji, J. *Tetrahedron Lett.* **1983**, *24*, 2395.

(3) (a) Nagashima, H.; Wakamatsu, H.; Itoh, K. *J. Chem. Soc., Chem. Commun.* **1984**, 652. (b) Nagashima, H.; Ara, K.; Wakamatsu, H.; Itoh, K. *Ibid.* **1985**, 518. (c) Nagashima, H.; Ozaki, N.; Seki, K.; Ishii, M.; Itoh, K. *J. Org. Chem.* **1989**, *54*, 4497.

(4) Tseng, C. K.; Teach, E. G.; Simmons, R. W. *Synth. Commun.* **1984**, *14*, 1027.

(5) Hayes, T. K.; Villani, R.; Weinreb, S. M. *J. Am. Chem. Soc.* **1988**, *110*, 5533. Lee, G. M.; Parvez, M.; Weinreb, S. M. *Tetrahedron* **1988**, *44*, 4671. Phelps, J. C.; Bergbreiter, D. E.; Lee, G. M.; Villani, R.; Weinreb, S. M. *Tetrahedron Lett.* **1989**, *30*, 3915. Lee, G. M.; Weinreb, S. M. *J. Org. Chem.* **1990**, *55*, 1281.

(6) Recently, several authors reported the synthesis of γ-lactams by tin-mediated radical cyclization of α-haloamides: Hirai, Y.; Hagiwara, A.; Terada, T.; Yamazaki, T. *Chem. Lett.* **1987**, 2417. Jolly, R. S.; Livinghouse, T. *J. Am. Chem. Soc.* **1988**, *110*, 7536. Clough, J. M.; Pattenden, G.; Write, P. G. *Tetrahedron Lett.* **1989**, *30*, 7469. Stork, G.; Mah, P. *Heterocycles* **1989**, *28*, 723. Barth, F.; O-Yang, C. *Tetrahedron Lett.* **1990**, *31*, 1121. Ishibashi, H.; So, S. T.; Okouchi, K.; Sato, T.; Nakamura, N.; Nakatani, H.; Ikeda, M. *J. Org. Chem.* **1991**, *56*, 95. Curran, D. P.; Tamine, J. *J. Org. Chem.* **1991**, *56*, 2746.

(7) Overman, L. E. *J. Am. Chem. Soc.* **1976**, *98*, 2901.

(8) Vyas, D. M.; Chiang, Y.; Doyle, T. W. *J. Org. Chem.* **1984**, *49*, 2037.

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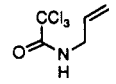
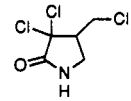
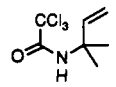
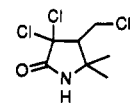
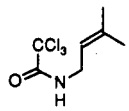
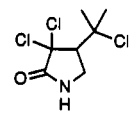
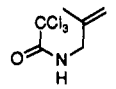
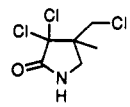
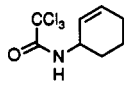
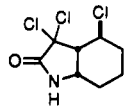
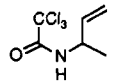
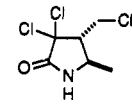
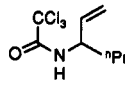
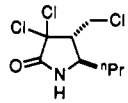
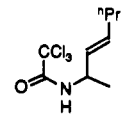
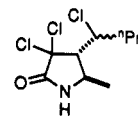
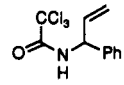
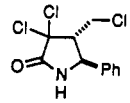
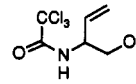
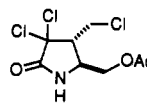
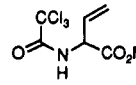
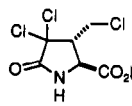
Table I. Ruthenium-Catalyzed Cyclization of *N*-Allyltrichlororacetamides

entry	substrates	cat. (%)	time (h)	solvent[a]	product	yield, % [diastereomer ratio]
1	 1	5 1	2 1	B X	 14	68 72
2	 2	1	2	X	 15	77
3	 3	1	2	X	 16	71
4	 4	5	3	B	 17	43
5	 5	5	3	B	 18	71
6	 6	5	2	B	 19	64 [16:84][b]
7	 7	5	2	B	 20	83 [11:89][b]
8	 8	1 5	1 2	X B	 21	84 [15:29:56][c] 79
9	 9	5	1	B	 22	60 [0:100][b]
10	 10'	5	2	B	 23'	85 [15:85][b]
11	 11'	5	1	B	 24'	89 [15:85][b]

[a] B, benzene; X, xylene. [b] Ratio of cis to trans. [c] Diastereomer ratio. Estimated cis/trans ratio determined after reductive dechlorination was 12:88.

tams **15** and **16**, respectively (entries 2 and 3). Thus the structure of the γ-lactams is determined by that of the allylic alcohol precursors. Cyclization of *N*-methallyltrichloroacetamide (**4**) gave γ-lactam **17** in 43% yields, generating a quaternary carbon in the process. Formation of the corresponding δ-lactam had been anticipated from our finding that the copper-catalyzed cyclization of methallyltrichloroacetates gave a mixture of the corresponding γ- and δ-lactones.[2] However, the main side reaction was intermolecular addition to form oligomeric products.[9]

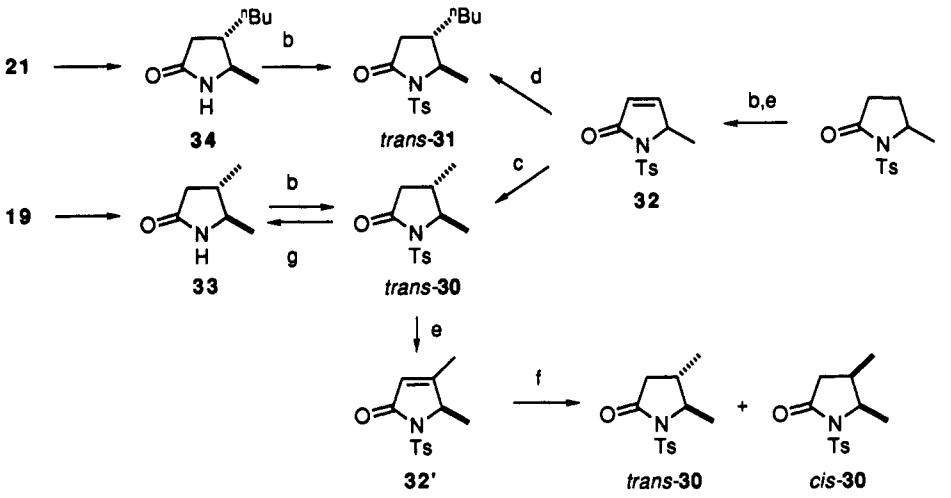
There have been few reports on the stereoselective preparation of γ-lactams having two alkyl substituents at the β- and γ-positions.[10] The ruthenium-catalyzed cyclization of *N*-allyltrichloroacetamides shown in entries 5–11 proceeds with good diastereoselectivity. *N*-(2-Cyclohexenyl)trichloroacetamide (**5**) was cyclized to a single stereoisomer of bicyclic lactam **18**. NMR analysis of **18** suggests that the angular protons are cis from a coupling constant (J = 6.8 Hz) and a 43% NOE. It is difficult to determine the stereochemistry between protons at β- and γ-positions from the coupling constant (J = 4.1 Hz); however, a 4% NOE indicates the trans configuration.

In contrast, cyclization of acyclic *N*-allyltrichloroacetamides resulted in the selective formation of β,γ-trans-

(9) One of the oligomeric products was misassigned as the δ-lactam in our preliminary account.[4a]

(10) Nagashima, H.; Ozaki, N.; Washiyama, M.; Itoh, K. *Tetrahedron Lett.* **1985**, *26*, 657.

Scheme II[a]



[a] (a) Bu_3SnH; (b) NaH, TsCl; (c) MeMgI/CuI(cat.); (d) BuMgI/CuI(cat.); (e) LDA; PhSeBr; $NaIO_4$; (f) H_2/PtO_2(cat.); (g) sodium naphthalenide.

disubstituted monocyclic lactams. In a typical example, *N*-(1-buten-3-yl)trichloroacetamide (**6**) underwent ruthenium-catalyzed cyclization at 140 °C to form lactam **19**. Only a minor amount of the cis isomer was detected in the ^1H NMR of crude **19** (cis/trans = 16:84).[11] Similarly, trans selectivity was observed in the cyclization of **7** and **9** (cis/trans = 11:89 and 0:100, respectively). In the cyclization of **8**, the product **21** was a mixture of four possible diastereomers derived from three asymmetric carbon centers. The NMR spectrum of crude **21** revealed the presence of three major diastereomers in a ratio of 15:29:56. Reductive dechlorination of this diastereomer mixture (vide infra) revealed that the stereochemistry of the major isomer between the β- and γ-substituents was trans (cis/trans ratio; 12:88). Thus the cyclization of acyclic precursors generally proceeds with good stereoselectivity to form the trans isomer. These stereochemical features are consistent with those observed in the cyclization of allyl trichloroacetates.[2] Preparation of substituted pyroglutamic acid derivatives was achieved as shown in entries 10 and 11; neither the unprotected vinylglycinol **10** nor the vinylglycine **11** was successfully cyclized to the desired lactam. However, their ester analogues **10'** and **11'** provided the corresponding trans-γ-lactams **23'** and **24'** in high yields and in cis/trans ratios of 15:85.

The stereochemistry of the monocyclic γ-lactams was determimed by preparing authentic samples by unequivocal routes in two representative cases (Scheme II). Thus N-tosylated α,β-unsaturated lactam **32** was subjected to copper-catalyzed conjugate addition of MeMgI to form the trans isomer of N-tosylated lactam **30**.[10] Hydrogenation of the N-tosylated α,β-unsaturated lactam **32'** gave **30** as a 1:1 mixture of cis and trans isomers. From these two reactions, cis and trans isomers of **30** can be unequivocally assigned. The *trans*-**30** was detosylated by sodium naphthalenide to give trans-lactam **33**. On the other hand, reductive dechlorination of trichlorinated lactam **19** provided **33** as essentially one diastereomer, of which N-tosylation gave **30** also as essentially one diastereomer. Comparison of spectral data of **30** or **33** derived from **19** with those of *trans*-**30** or *trans*-**33** obtained by the conjugate addition showed that the major isomer of lactam **19** was the trans isomer. Similarly, the copper-catalyzed conjugate addition of BuMgI to **32** gave *trans*-**31** with the same spectral features as **31** prepared from **21** by reductive dechlorination and subsequent N-tosylation. All the authentic samples we prepared (**30**, **31**, **33**, and **34**) showed similar ^1H NMR patterns in which the γ-methine signal appears at higher fields in the trans isomer than in the cis isomer, whereas the β-methine signal occurs at lower fields in the trans isomer than in the cis isomer. This effect determined the stereochemistry of the major isomers of **20**, **22**, **23'**, and **24'**.[12]

Double Cyclization. Double cyclization occurred in the reactions of *N*-linalyl- and *N*-geranyltrichloroacetamides **12** and **13**, affording bicyclic lactams from acyclic *N*-allyltrichloroacetamides. Cyclization of **12** gave a mixture of the monocyclic lactam **25** (3%) and bicyclic lactams **26** (23%) and **27** (42%). Similarly, that of **13** provided bicyclic lactam **29** as a mixture of two diastereomers [TLC, R_f 0.59 (**29a**) and 0.27 (**29b**); hexane/ethyl acetate, 1/2; yield, 22% and 42%, respectively].

These two reactions are similar in forming a bicyclic structure consisting of a γ-lactam and a cyclohexane ring. However, they differ in the position of carbon–carbon bond formation. The former reaction does not proceed through **25** as the intermediate, being analogous to the tandem free-radical cyclization of acyclic radicals with two carbon–carbon double or triple bonds to form bicyclic skeletons.[13,14] In fact, isolated **25** was subjected to the ruthenium-catalyzed cyclization to afford a new compound (54%) tentatively assigned as **25'** from its spectral data. Bicyclic lactams **26** and **27** were not obtained. The ruthenium-catalyzed cyclization of **12** at temperatures lower than 140 °C also suggests the tandem radical cyclization pathway, in which the product ratios of **25**, **26**, and **27** were

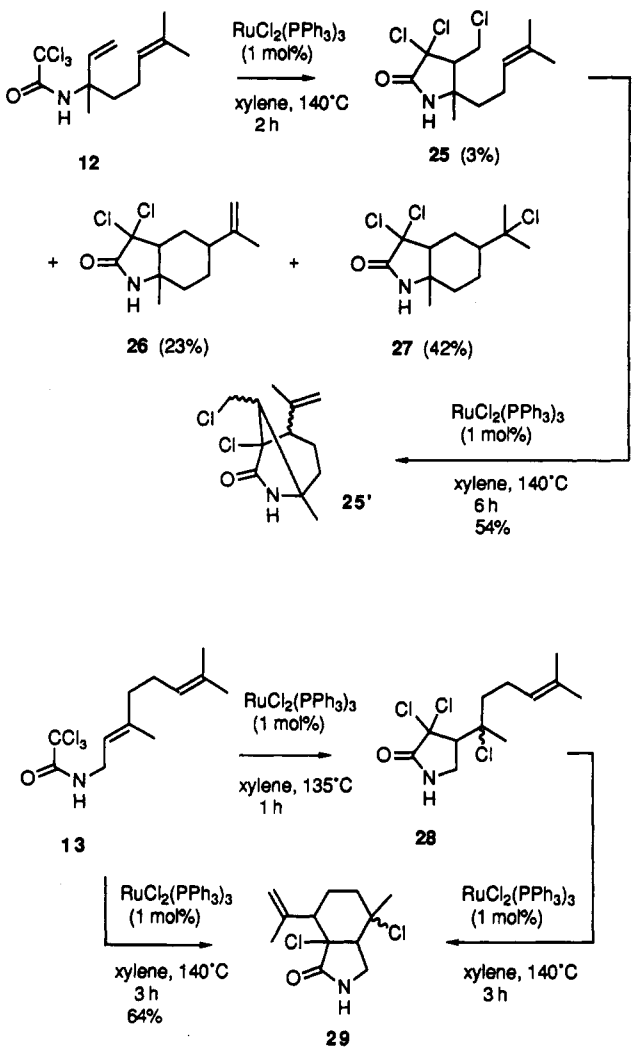
(11) The trans-selective formation of **19** and **21** was briefly mentioned in ref 4c. Since the chromatographic purification of the diastereomeric mixture of these compounds resulted in conversion of the cis isomer to the trans isomer, we reported the cis/trans ratio as 0/100. However, careful spectroscopic studies on the crude materials revealed the formation of the corresponding cis isomer in the ratios described in the text.

(12) A similar tendency on the chemical shifts of ^1H NMR was also observed in the cis and trans isomers of β,γ-disubstituted lactones.[3]

(13) Typical examples of double cyclization: Stork, G.; Mook, R. *J. Am. Chem. Soc.* **1983**, *105*, 3721. Curran, D. P.; Kuo, S. C. *J. Am. Chem. Soc.* **1986**, *108*, 1106. Beckwith, A. L. J.; Roberts, D. H.; Schiesser, A.; Wallner, A. *Tetrahedron Lett.* **1985**, *26*, 3349. Winkler, J. D.; Srider, V. *J. Am. Chem. Soc.* **1986**, *108*, 1708. Kano, S.; Yuasa, Y.; Yokomatsu, T.; Asami, K.; Shibuya, S. *Chem. Pharm. Bull.* **1988**, *36*, 2934.

(14) For earlier work on tandem radical cyclization to form polycyclic terpenoids: Julia, M. *Acc. Chem. Res.* **1971**, *4*, 386. Breslow, R.; Groves, J. T.; Olin, S. S. *Tetrahedron Lett.* **1966**, 4717. Breslow, R.; Olin, S. S.; Groves, J. T. *Ibid.* **1968**, 1837.

Scheme III



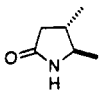
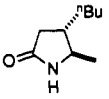
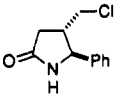
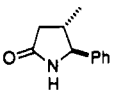
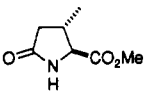
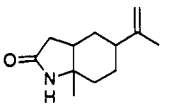
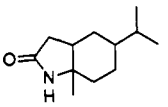
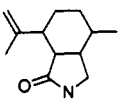
independent of the reaction temperature.

In contrast, the reaction of **13** is interpreted as two independent reactions occurring stepwise. The initial reaction is the ruthenium-catalyzed monocyclization of **13** to form **28**. The second reaction from **28** to **29** proceeds via ruthenium-catalyzed addition of a carbon–chlorine bond at the α-position of **28** to the olefinic bond. Isolation of **28** was accomplished as follows: cyclization of **21** at 135 °C for 1 h gave **28** in 22% yield as a 1:1 mixture of two diastereomers [TLC, R_f 0.46 (**28a**) and 0.33 (**28b**) by elution with hexane/ethyl acetate 1/1]. Each diastereomer independently underwent the second cyclization catalyzed by $RuCl_2(PPh_3)_3$ to give bicyclic lactam **29**; **29a** was selectively formed from **28b** in 76% yield, whereas **29b** was formed from **28a** in 65% yield. The reactions from **25** to **25'** and **28** to **29** are similar to the carbocyclization reported by Weinreb and co-workers, in which transition-metal complexes catalyzed the cyclization of 2,2-dichloro-7-octenoates to cyclohexanecarboxylic acid derivatives.[5]

Mechanism. A mechanism for the cyclization of *N*-allyltrichloroacetamides is shown in Scheme IV.[2,15] The envelope-shaped transition states[16] resemble those proposed for free-radical cyclizations and for cyclization of allyl trichloroacetates.[3] The preference for exo cyclization over endo cyclization is implied by states A and B, respectively. State C leads to formation of the cis-fused bycyclic system in the cyclization of *N*-(2-cyclohexenyl)-trichloroacetamide. State D explains the high trans selectivity in the cyclization of *N*-allyltrichloroacetamides from acyclic secondary allylic amines.

The double cyclization of *N*-linalyl- and *N*-geranyltrichloroacetamides is also initiated by chlorine atom abstraction by Ru(II) (Scheme V). In the case of **12**, the carbon radical formed first adds to the allylic olefin to form the new carbon radical E, which then adds to another olefinic bond to form the six-membered ring a new carbon radical F. This tandem radical cyclization is terminated either by chlorine atom abstraction from F by Cl–Ru(III) or formation of an olefinic bond. In contrast, the initial

Table II. Reductive Dechlorination of Trichlorinated Lactams[a]

entry	substrates	time (h)	product	yield (%)
1	**19**	1	 **33**	74
2	**21**	4	 **34**	88
3[b]	**22**	3.5	 **35**	76
4	**22**	2	 **36**	88
5	**24'**	4	 **37**	70
6	**26**	2	 **38**	95
7	**27**	4	 **39**	93
8	**29a**	4	 **40**	65[c]
9	**29b**	4	**40**	53[c]

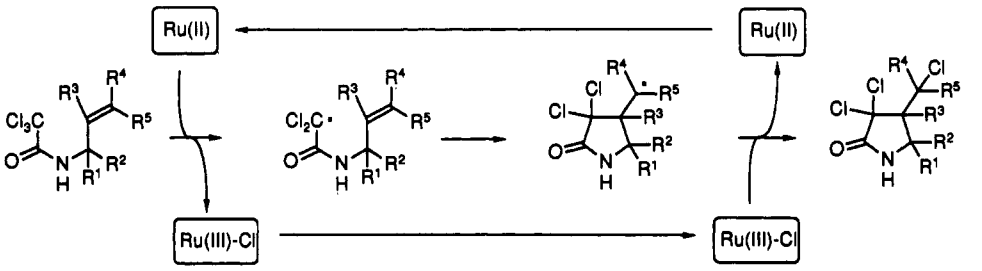
[a] The reaction was carried out with 3 equiv of tributylstannane in toluene under reflux. [b] The reaction was done with 2 equiv of tributylstannane in benzene at 50 °C. [c] The yield after recrystallization from ethyl acetate and hexane.

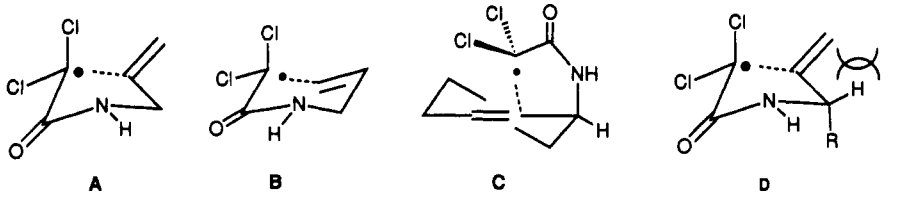
(15) For a proposed mechanism and related studies on the transition metal catalyzed addition reactions of polyhalogenated alkanes to olefins: Asscher, M.; Vofsi, D. *J. Chem. Soc.* **1961**, 2261; **1963**, 1887, 3921. Minisci, F. *Acc. Chem. Res.* **1975**, *8*, 165. Matsumoto, H.; Nakano, T.; Nagai, Y. *Tetrahedron Lett.* **1973**, 5147. Kochi, J. K. *Organometallic Mechanisms and Catalysis*; Academic Press: New York, 1978. Davis, R.; Groves, I. F. *J. Chem. Soc., Dalton Trans.* **1982**, 2281. Davis, R.; Durrant, J. L. A.; Rowland, C. C. *J. Organomet. Chem.* **1986**, *316*, 147.

(16) Beckwith, A. L.; Schiesser, C. H. *Tetrahedron* **1985**, *41*, 3925. Spellmeyer, D. C.; Houk, K. N. *J. Org. Chem.* **1987**, *52*, 959.

(17) Sharpless, K. B.; Laher, R. F.; Teranishi, A. Y. *J. Am. Chem. Soc.* **1973**, *95*, 6137.

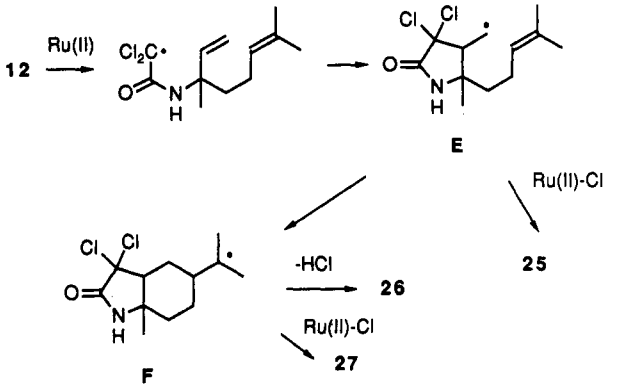
Scheme IV

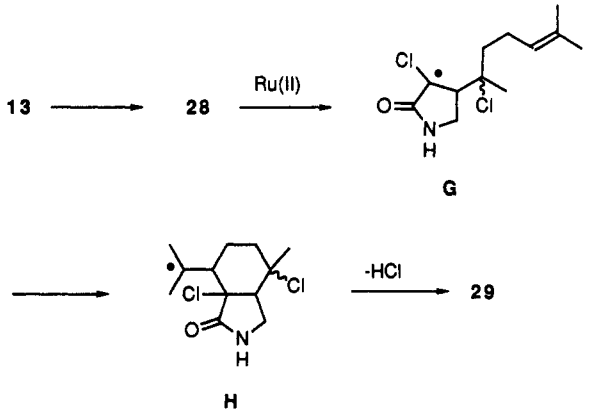




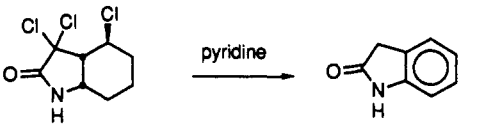
A B C D

Scheme V





Scheme VI



product of the cyclization of **13** is monocyclic lactam **28**, from which the α-chlorine atom is abstracted by Ru(II) to form the intermediate G. The radical G undergoes facile addition to the olefinic bond to form the new carbon radical H, which subsequently forms the olefinic bond.

Reductive Dechlorination and Dehydrochlorination of Trichlorinated γ-Lactams. The chlorine atoms of the trichlorinated lactams were attractive functional groups for further transformation. Treatment of the lactams with 3 equiv of Bu_3SnH in refluxing toluene resulted in complete replacement of the chlorine atoms by hydrogen atoms. Representative results are summarized in Table II. Interestingly, reduction with 2 equiv of Bu_3SnH at 50 °C resulted in selective replacement of two α-chlorine atoms to give the corresponding γ-monochloro lactam. Reductive dechlorination of two diastereomers of bicyclic lactam **29** (isomer I and isomer II) afforded **40** as a mixture of diastereomers. From either isomer of **29**, two isomers of **40** (**40a** and **40b**) were obtained in similar ratios (24:76 and 31:69, respectively). Dehydrochlorination of bicyclic lactam **18** with refluxing pyridine gave 2-indolidinone (Scheme VI).

Experimental Section

General. All manipulations were carried out under an inert atmosphere. All solvents were distilled from standard drying reagents before use. IR data are reported in cm^{-1}. NMR spectra were measured in $CDCl_3$ and are reported in δ values from tetramethylsilane. The coupling constants (*J*) are reported in hertz. Elemental analyses were done at the Analytical Center of Kyoto University. All solid samples were purified by recrystallization from a mixture of hexane and ethyl acetate.

Preparation of *N*-Allyltrichloroacetamides. *N*-Allyltrichloroacetamide (**1**) was prepared by trichloroacetylation with CCl_3COCl in the presence of Et_3N and can alternatively be prepared by the Overman rearrangement.[7] Other *N*-allyltrichloroacetamides **2–9** and **13** were prepared according to procedures reported by Overman.[7] Spectral data for new compounds **2–4** and **6** are listed below.

2: 48% yield from 3-methyl-2-buten-1-ol; white solid (mp 49.5–50.0 °C); ^1H NMR (90 MHz) 1.54 (Me), 5.14–6.02 (olefin), 6.59 (NH); IR (CH_2Cl_2) 1720. Anal. Calcd for $C_7H_{10}NCl_3$: C, 36.47; H, 4.37; N, 6.08. Found: C, 36.61; H, 4.42; N, 6.04.

3: 60% yield from 2-methyl-3-buten-2-ol; white solid (mp 40.5–41 °C); ^1H NMR (90 MHz) 1.72 and 1.76 (Me), 3.90 (t, J = 5.7, 2 H, CH_2NH), 5.24 (t, J = 5.7, 1 H, olefin), 6.48 (NH); IR (CH_2Cl_2) 1710. Anal. Calcd for $C_7H_{10}NOCl_3$: C, 36.47; H, 4.37; N, 6.08. Found: C, 36.34; H, 4.39; N, 6.08.

4: 37% yield from methallyl alcohol; white solid (mp 56–57 °C); ^1H NMR (90 MHz) 1.80 (Me), 3.94 (d, J = 6.0, CH_2NH), 4.80–5.00 (olefin), 6.96 (NH); IR ($CHCl_3$) 1710. Anal. Calcd for $C_6H_8NOCl_3$: C, 33.29; H, 3.72; N, 6.47. Found: C, 33.53; H, 3.59; N, 6.45.

6: 88% yield from 2-buten-1-ol; white solid (mp 42 °C); ^1H NMR (270 MHz) 1.35 (d, J = 6.8, 3 H, Me), 4.54 (quint, J = 6.8, 1 H, CHNH), 5.20–5.95 (olefin), 6.48–6.65 (NH); ^{13}C NMR (67.8 MHz) 19.2, 48.9, 91.8, 114.8, 137.3, 160.5; IR (Nujol) 1700. Anal.

Cacld for $C_6H_8NOCl_3$: C, 33.29; H, 3.72; N, 6.47. Found: C, 33.21; H, 3.72; N, 6.47.

Preparation of Amino Alcohol Derivatives 10, 10′, 11, and 11′. Slight modification was made to the procedure for synthesizing **10** reported by Vyas.[8] Thermal rearrangement was carried out in mesitylene instead of *tert*-butylbenzene. The crude amide alcohol was stirred in 1 N HCl at 0 °C before the chromatographic purification in order to remove the concomitantly formed trichloroacetimidate of **10** upon hydrolysis.[8] Acetylation of **10** (230 mg, 1 mmol) with acetic anhydride (0.2 mL, 2 mmol) and pyridine (0.16 mL, 2 mmol) in ether at room temperature overnight gave **10′** in 79% yield. Esterification of **11**[8] (580 mg, 2.4 mmol) was carried out by heating in anhydrous methanol (10 mL) in the presence of sulfuric acid (0.1 mL) for 3 h to give **11′** in 52% yield.

10′: pale yellow oil; ^{1}H NMR (270 MHz) 2.09 (Ac), 4.20 (dd, J = 6.3, 11.9, 1 H, C*H*OAc), 4.32 (dd, J = 6.9, 11.7, 1 H, C*H*OAc), 4.72 (m, 1 H, C*H*NH), 5.32–5.82 (olefin), 7.13 (NH); IR (CH_2Cl_2) 1720, 1740. Anal. Calcd for $C_8H_{10}NO_3Cl_3$: C, 35.00; H, 3.67; N, 5.10. Found: C, 35.45; H, 3.74; N, 4.84.

11′: yellow oil; ^{1}H NMR (270 MHz) 3.84 (Me), 5.06–5.12 (m, 1 H, C*H*NH), 5.32–5.98 (olefin), 7.37 (NH); IR (CH_2Cl_2) 1720, 1750. Anal. Calcd for $C_7H_8NO_3Cl_3$: C, 32.27; H, 3.10; N, 5.38. Found: C, 32.36; H, 3.12; N, 5.02.

General Procedure for the Ruthenium-Catalyzed Cyclization of *N*-Allyltrichloroacetamides. A mixture of *N*-allyltrichloroacetamide (4.9 mmol), $RuCl_2(PPh_3)_3$ (47 mg, 0.05 mmol, 1 mol % to 1), and xylene (40 mL) was heated under reflux for 1 h. After removal of the solvent in vacuo, the mixture was purified on a silica gel column eluting with hexane and ether to give the desired lactam. Alternatively, the reaction can be carried out in a pressure bottle using benzene as the solvent.

14: white solid (mp 100–101 °C); ^{1}H NMR (270 MHz) 3.12–3.23 (m, 1 H, CCl_2CH), 3.28 (dd, J = 7.8, 9.8, 1 H, NHC*H*), 3.70 (dd, J = 5.9, 7.8, 1 H, NHC*H*), 3.76 (dd, J = 9.3, 12.2, 1 H, ClCH), 4.00 (dd, J = 4.4, 12.2, 1 H, ClCH), 7.40 (NH); ^{13}C NMR (22.5 MHz) 40.8 (t, ClC or NC), 43.6 (t, ClC or NC), 53.7 (d, CCl_2CH), 83.1 (s, CCl_2), 169.3 (s, CO); IR (CH_2Cl_2) 1740. Anal. Calcd for $C_5H_6NOCl_3$: C, 29.66; H, 2.99; N, 6.92. Found: C, 29.76; H, 2.98; N, 7.17.

15: white solid (mp 156.5–157.5 °C); ^{1}H NMR (90 MHz) 1.40 and 1.53 (s, 3 H each, Me), 3.00 (dd, J = 6.3, 9.0, 1 H, Cl_2CCH), 3.82 (dd, J = 9.0, 11.6, 1 H, ClCH), 4.00 (dd, J = 6.3, 11.6, 1 H, ClCH), 7.94 (NH); IR (CH_2Cl_2) 1740. Anal. Calcd for $C_7H_{10}NOCl_3$: C, 36.47; H, 4.37; N, 6.08. Found: C, 36.37; H, 4.33; N, 6.09.

16: white solid (mp 159.0–159.5 °C); ^{1}H NMR (270 MHz) 1.91 and 1.94 (s, 3 H each, Me), 3.26, 3.82 (t, J = 8.1, 1 H, each, C*H*NH), 7.58 (NH); IR (CH_2Cl_2) 1750. Anal. Calcd for $C_7H_{10}NOCl_3$: C, 36.47; H, 4.37; N, 6.08. Found: C, 36.37; H, 4.33; N, 6.09.

17: white solid (mp 120–122 °C); ^{1}H NMR (270 MHz) 1.47 (s, 3 H, Me), 3.24 and 3.56 (d, J = 10.3, 1 H each, C*H*NH), 3.69 and 3.81 (d, J = 10.8, 1 H each, CHCl), 3.81 (d, J = 11.2, 1 H, CHCl), 7.50 (NH); IR (Nujol) 1745. Anal. Calcd for $C_6H_8NOCl_3$: C, 33.29; H, 3.72; N, 6.47. Found: C, 33.36; H, 3.72; N, 6.01.

18: white solid (mp 142–143.5 °C); ^{1}H NMR (270 MHz) 1.62–1.83, 1.89–2.02, 2.29–2.45 (m, 6 H, CH_2), 3.34 (dd, J = 3.4, 6.8, 1 H, CCl_2CH), 3.99 (br q, J = 6.8, 1 H, NHC*H*), 4.62 (q, J = 4.1, ClCH), 6.55 (NH); IR (CH_2Cl_2) 1740. Anal. Calcd for $C_8H_{10}NOCl_3$: C, 39.62; H, 4.16; N, 5.78. Found: C, 39.81; H, 4.13; N, 5.77.

19: white solid (mp 121–122 °C); ^{1}H NMR (270 MHz) (trans isomer) 1.49 (d, J = 6.3, 3 H, Me), 2.75 (tq, J = 5.4, 7.8, 1 H, CCl_2CH), 3.63 (dq, J = 6.3, 7.8, 1 H, NHC*H*), 3.77 (dd, J = 7.8, 11.7, 1 H, CHCl), 4.02 (dd, J = 5.4, 11.7, CHCl), 7.69 (NH); ^{13}C NMR (67.8 MHz) 19.8 (q, Me), 39.8 (t, ClC), 52.0 (d, CCl_2C), 60.1 (d, NC), 83.9 (s, Cl_2C), 167.5 (s, C=O); (cis isomer) 1.38 (d, J = 6.8, 3 H, Me), 3.29 (ddd, J = 4.0, 6.8, 10.8, 1 H, CCl_2CH), 3.81 (dd, J = 10.8, 11.8, 1 H, ClCH), 4.02 (dd, J = 4.0, 11.8, 1 H, ClCH), 3.95–4.05 (m, 1 H, NHC*H*), 6.88–7.05 (NH); IR (neat) 1740. Anal. Calcd for $C_6H_8NOCl_3$: C, 33.29; H, 3.72; N, 6.47. Found: C, 33.38; H, 3.65; N, 6.53.

20: white solid (mp 131 °C); ^{1}H NMR (90 MHz) 1.03 (br t, J = 7.5, 3 H, Me), 1.20–1.70, 1.80–2.00 (m, 4 H, CH_2), 2.84 (br q, J = 7.3, 1 H, *trans*-Cl_2CCH), 3.32 (ddd, J = 4.5, 7.4, 10.1, *cis*-CCl_2CH), 3.50 (m, 1 H, C*H*NH), 3.72 (dd, J = 7.3, 12.9, 1 H, ClCH), 4.02 (dd, J = 6.3, 12.9, 1 H, ClCH), 7.94 (NH); IR (Nujol) 1725. Anal. Calcd for $C_9H_{14}NOCl_3$: C, 39.29; H, 4.95; N, 5.73. Found: C, 39.51; H, 5.48; N, 5.12.

21: a mixture of three diastereomers in a ratio of 15 (isomer A):29 isomer B):56 (isomer C) on the ^{1}H NMR spectrum: yellow oil; TLC (hexane/ethyl acetate, 1/1): R_f 0.71 (A and C), 0.58 (B); ^{1}H NMR (270 MHz) (isomer A) 1.00 (Me), 1.45 (d, J = 6.6, 3 H, NHCH*Me*), 1.60–2.45 (CH_2), 3.20 (dd, J = 7.1, 10.7, 1 H, β-CH), 3.98 (dt, J = 1.7, 7.1, 1 H, NHC*H*), 4.28 (dt, J = 2.7, 10.7, CClCH), 7.11 (NH); (isomer B) 0.98 (Me), 1.47 (d, J = 6.4, 3 H, NHCH*Me*), 1.38–1.96 (CH_2), 2.94 (t, J = 5.9, 1 H, β-CH), 3.82 (dq, J = 5.9, 6.4, 1 H, NHC*H*), 4.42 (m, 1 H, CClCH), 7.50 (NH); (isomer C) 1.01 (Me), 1.55 (d, J = 6.4, 3 H, NHCH*Me*), 1.60–2.45 (CH_2), 2.70 (t, J = 7.3, 1 H, β-CH), 3.81 (quint, J = 6.4, 1 H, NHC*H*), 4.41 (dt, J = 3.4, 9.3, CClCH), 6.80 (NH); IR (CH_2Cl_2) 1745. Anal. Calcd for $C_9H_{14}NOCl_3$: C, 41.80; H, 5.46; N, 5.42. Found: C, 41.85; H, 5.48; N, 5.12.

22: white solid (mp 165–166 °C); ^{1}H NMR (270 MHz) (only the trans isomer was observed) 3.05 (ddd, J = 5.6, 7.4, 8.3, 1 H, Cl_2CCH), 3.70 (dd, J = 5.6, 12.0, 1 H, ClCH), 4.02 (dd, J = 7.4, 12.0, 1 H, ClCH), 4.40 (d, J = 8.3, 1 H, ClCH), 6.30 (NH), 7.40 (Ph); IR (CH_2Cl_2) 1750. Anal. Calcd for $C_{11}H_{10}NOCl_3$: C, 47.42; H, 3.62; N, 5.03. Found: C, 47.10; H, 3.62; N, 4.96.

23′: white solid (mp 99–100 °C); ^{1}H NMR (270 MHz) 2.15 (s, 3 H, Ac), 2.98 (ddd, J = 4.5, 4.5, 8.3, 1 H, CCl_2CH), 3.44 (dd, J = 4.5, 7.5, 11.3, *cis*-CCl_2CH), 3.79–3.87 (m, 2 H, C*H*OAc, C*H*N), 4.04 (dd, J = 4.5, 11.7, 1 H, CHCl), 4.17 (dd, J = 4.5, 11.7, 1 H, CHCl), 4.22–4.44 (m, 2 H, *cis*-$ClCH_2$), 4.61 (dd, J = 3.0, 11.8, 1 H, C*H*OAc), 7.61 (NH); IR (CH_2Cl_2) 1745. Anal. Calcd for $C_8H_{10}NOCl_3$: C, 35.00; H, 3.67; N, 5.10. Found: C, 35.01; H, 3.72; N, 4.70.

24′: yellow oil; ^{1}H NMR (270 MHz) 3.37 (q, J = 6.8, 1 H, *trans*-CCl_2CH), 3.49 (q, J = 7.8, *cis*-CCl_2CH), 3.88 (s, 3 H, Me), 3.93 (dd, J = 6.8, 11.3, 1 H, ClCH), 4.08 (dd, J = 6.8, 11.3, 1 H, ClCH), 4.13 (d, J = 6.8, 1 H, NHC*H*), 4.49 (d, J = 7.8, *cis*-NHC*H*), 6.87 (NH); IR (CH_2Cl_2) 1755. Anal. Calcd for $C_7H_8NO_3Cl_3$: C, 32.27; H, 3.10; N, 5.38. Found: C, 32.01; H, 3.09; N, 5.07.

Stereochemistry of Disubstituted Lactams 19 and 21. (A) Reductive Dechlorination of 19 and 21. Trichlorinated lactam **19** (600 mg, 2.8 mmol) was treated with Bu_3SnH (2.7 mL, 10 mmol) and AIBN (5 mg) at 140 °C for 8 h. After removal of tin products on a short silica gel column eluting by hexane and ether, distillation of the crude dechlorinated lactam (120 °C (4 mmHg)) afforded **33** in 85% yield (200 mg) as essentially a single stereoisomer. By a similar procedure, **34** was prepared from **21** in 44% yield (trans/cis = 92:8).

33: colorless oil (bp 120 °C (4 mmHg)); ^{1}H NMR (270 MHz) (trans isomer) 1.13 (d, J = 6.8, 3 H, β-Me), 1.22 (d, J = 6.8, 3 H, γ-Me), 1.95–2.62 (α- and β-CH), 3.39 (quint, J = 6.8, 1 H, NHC*H*), 5.60–5.86 (NH); (cis isomer) 1.02 (d, J = 6.8, 3 H, β-Me), 1.10 (d, J = 6.8, 3 H, γ-Me), 2.08–2.62 (α- and β-CH), 3.76 (quint, J = 6.8, 1 H, NCH), 5.60–5.80 (NH); IR (neat) 1680. Anal. Calcd for $C_6H_{11}NO$: C, 63.09; H, 9.80; N, 12.38. Found: C, 62.54; H, 9.67; N, 12.05.

34: colorless oil; ^{1}H NMR (270 MHz) (trans isomer) 0.98 (CH_2Me), 1.26 (d, J = 6.3, 3 H, NCH*Me*), 1.15–1.60 (CH_2), 1.8–2.49 (α- and β-CH), 3.36 (quint, J = 6.3, 1 H, NCH), 7.16 (NH); (cis isomer) 0.98 (CH_2Me), 1.06 (d, J = 6.4, 3 H, NCH*Me*), 1.15–1.60 (CH_2), 2.03–2.50 (α- and β-CH), 3.72 (quint, J = 6.4, NCH), 6.37 (NH); ^{13}C NMR (67.8 MHz) (trans isomer) 177.5, 55.8, 42.9, 37.2, 33.1, 29.6, 22.4, 20.8, 13.6; (cis isomer) 177.8, 52.2, 38.1, 35.2, 29.8, 28.9, 22.4, 16.0, 13.6; IR (neat) 1690; HRMS calcd for $C_9H_{17}NO$ 155.1311, found 155.1309.

(B) Preparation of *N*-Tosylamides 30 and 31 from 33 and 34. The N-tosylation of **33** and **34** was carried out in the same manner as that of 5-methyl-2-pyrrolidinone (vide infra), giving the product in 40–60% yield, with the spectral data shown below.

30: white solid (mp 110 °C); ^{1}H NMR (270 MHz) (trans isomer) 1.00 (d, J = 7.3, 3 H, β-Me), 1.50 (d, J = 6.8, 3 H, γ-Me), 2.00 (dd, J = 2.8, 17.2, 1 H, β-CH), 2.43 (Ts), 2.72 (dd, J = 8.4, 17.2, 1 H, COCH), 4.03 (dq, J = 2.2, 6.6, 1 H, CHN), 7.36, 7.96 (d, J = 9.4, 2 H each, Ts); (cis isomer) 1.03 (d, J = 6.8, 3 H, β-Me), 1.30 (d, J = 6.8, 3 H, γ-Me), 2.22 (dd, 1 H, J = 12.7, 15.5, COCH), 2.34 (dd, 1 H, J = 7.8, 15.5, COCH), 2.43 (Ts), 2.38–2.51 (m, 1 H, β-CH), 4.45 (q, 1 H, J = 6.8, NCH), 7.29 and 7.95 (Ts); IR (Nujol) 1725. Anal. Calcd for $C_{13}H_{17}NO_3S$: C, 58.40; H, 6.41; N, 5.24. Found: C, 58.72; H, 6.63; N, 5.08.

31: white solid (mp 90–91 °C); ^{1}H NMR (270 MHz) (trans isomer) 0.86 (Me), 1.10–1.40 (CH_2), 1.48 (d, J = 6.4, 3 H, γ-Me), 1.80–1.93 (m, 1 H, β-CH), 2.04 (dd, J = 2.9, 17.6, 1 H, α-CH), 2.43 (s, 3 H, Ts), 2.70 (dd, J = 8.3, 17.6, 1 H, α-CH), 4.11 (dq, J = 2.0, 6.4, 1 H, NCH), 7.32 and 7.92 (Ts); (cis isomer) 0.89 (Me), 1.15–1.45 (CH_2), 1.29 (d, J = 6.4, 3 H, γ-Me), 2.10–2.45 (α- and β-CH), 2.43 (Ts), 4.49 (quint, J = 6.4, 1 H, NCH), 7.32 and 7.95 (Ts); IR (CH_2Cl_2) 1730. Anal. Calcd for $C_{16}H_{23}NO_3S$: C, 62.11; H, 7.49; N, 4.53. Found: C, 61.80; H, 7.56; N, 4.63.

(C) Preparation of Unsaturated Lactam 32. Treatment of 5-methyl-2-pyrrolidinone (426 mg, 5 mmol) with 50% NaH (576 mg) in THF, followed by addition of *p*-toluenesulfonyl chloride (950 mg, 5 mmol) at 0 °C. After the usual workup, the mixture was passed through a short silica gel column to give the tosyl compound in 60% yield (757 mg): white solid (mp 119–121 °C); ^{1}H NMR (90 MHz) 1.47 (d, J = 6.3, 3 H, Me), 1.66–2.70 (α- and β-CH), 2.43 (Ts), 4.35–4.62 (m, 1 H, NCH), 7.32, 7.95 (Ts); IR (Nujol) 1730. Anal. Calcd for $C_{12}H_{15}NO_3S$: C, 56.90; H, 5.97; N, 5.53. Found: C, 56.92; H, 5.93; N, 4.93.

Preparation of **32** from this lactam was achieved by using PhSeBr.[18] The tosyl lactam (950 mg, 3.73 mmol) was treated successively with LDA (4.1 mmol) and PhSeBr (1.05 g, 4.5 mmol) in THF at −78 °C for 30 min. The crude 1-tosyl-3-(phenylselenenyl)-5-methyl-2-pyrrolidinone was oxidized with $NaIO_4$ (960 mg, 4.5 mmol) in a mixture of methanol and water at room temperature overnight. After workup, the mixture was purified on a silica gel column by eluting with hexane/ether to give the unsaturated lactam **32** in 59% yield (554 mg).

32: white solid (mp 65–67 °C); ^{1}H NMR (270 MHz) 1.59 (d, J = 6.8, 3 H, Me), 2.43 (Ts), 4.87 (tq, J = 2.0, 6.8, 1 H, NCH), 6.00 (dd, J = 2.0, 6.1, 1 H, olefin), 7.32, 8.00 (Ts); IR (CH_2Cl_2) 1725. Anal. Calcd for $C_{12}H_{13}NO_3S$: C, 57.35; H, 5.21; N, 5.37. Found: C, 57.45; H, 5.32; N, 5.52.

(D) Preparation of Trans Isomers of 30 and 31 by Conjugate Addition of Organocopper Reagents to 32. A mixture of CH_3MgI (1 N, 0.16 mmol) in ether and CuI (1 mg) was stirred at 0 °C for 10 min. The unsaturated lactam **32** (20 mg, 0.08 mmol) in ether (0.5 mL) was added to this mixture at −20 °C. After being stirred at this temperature for 3 h, the mixture was subjected to the usual workup followed by chromatographic purification (silica gel, hexane/ether) to give *trans*-**30** in 74% yield (16 mg). Similar treatment of **32** with BuMgI and CuI afforded *trans*-**31** in 94% yield.

(E) Removal of the Tosyl Group of *trans*-30 Obtained by the Conjugate Addition To Form *trans*-33. To a solution of sodium naphthalenide prepared from naphthalene (288 mg, 2.2 mmol) and sodium (52 mg, 2.2 mmol) in dimethoxyethane (2.3 mL) was added *trans*-**33** (86 mg, 0.3 mmol) dissolved in dimethoxyethane (1 mL) at 0 °C. After being stirred for 4.5 h at room temperature, the solution was treated with water to decompose excess naphthalenide. The mixture was extracted with ether. The combined extracts were washed with brine, dried over $MgSO_4$, and concentrated. The residue was purified on a short alumina column eluting with hexane/ether to give *trans*-**33** in 76% yield (27 mg).

(F) Preparation of the Cis Isomer of 30 by Hydrogenation of Unsaturated Lactam 32′. The unsaturated lactam **32′** was prepared by dehydrogenation of **30** in the same manner as the preparation of **32**. From 458 mg of **30** (1.7 mmol) was obtained 194 mg of **32** (0.73 mmol) (43%). An acetic acid solution (1.6 mL) of **32′** (44 mg, 0.16 mmol) was stirred at room temperature under hydrogen in the presence of PtO_2 (4 mg, 0.02 mmol, 10 mol %) for 24 h. After removal of the catalyst by filtration, the solution was concentrated to give **30** in quantitative yield, in which the ratio of cis to trans was 1:1.

32′: white solid (mp 93–94 °C); ^{1}H NMR (270 MHz) 1.57 (d, J = 6.8, 3 H, γ-Me), 2.02 (s, 3 H, β-Me), 2.42 (Ts), 4.67 (q, J = 6.8, 1 H, γ-CH), 5.67 (s, 1 H, α-CH), 7.31 and 7.95 (Ts); IR (CH_2Cl_2) 1725. Anal. Calcd for $C_{13}H_{15}O_3NS$: C, 58.85; H, 5.70; N, 5.28. Found: C, 58.81; H, 5.75; N, 4.66.

Double Cyclization of *N*-Linalyltrichloroacetamide (12). A xylene (81 mL) solution of **12** (3 g, 10 mmol) and $RuCl_2(PPh_3)_3$ (97 mg, 0.1 mmol, 1 mol %) was heated at 140 °C for 2 h to give a mixture of the monocyclic lactam **25** (0.106 g, 3%) and the bicyclic lactams **26** (0.692 g, 23%) and **27** (0.862 g, 42%).

25: TLC R_f 0.50 (hexane/ether, 1:8); slightly yellow oil; ^{1}H NMR (270 MHz) 1.38, 1.62, and 1.68 (Me), 1.65–1.95, 2.00–2.20 (CH_2), 3.14 (dd, J = 5.4, 8.8, 1 H, CCl_2CH), 3.82 (dd, J = 8.8, 11.7, 1 H, ClCH), 4.03 (dd, J = 5.4, 11.7, 1 H, ClCH), 5.08 (olefin), 8.00 (NH); ^{13}C NMR (67.8 MHz) 17.6 (q) 21.5 (q), 22.2 (t), 25.6 (q), 39.1 (t), 41.1 (t, ClC), 58.0 (d, CCl_2C), 60.0 (s, NHC), 83.8 (s, Cl_2C), 122.6 (d, olefin), 132.9 (s, olefin), 167.3 (s, CO); IR (CH_2Cl_2) 1730; MS 301 (M + 4), 299 (M + 2), 297 (M), 262 (M − Me); HRMS calcd for $C_{12}H_{18}NOCl_2Cl^*$ 297.0423, found 297.0456.

26: TLC R_f 0.39 (hexane/ether, 1:8); white solid (mp 187–189 °C); ^{1}H NMR (270 MHz) 1.44, 1.80 (Me), 1.50–2.32 (CH_2 and CH), 2.60 (dd, J = 2.4, 12.2, 1 H, Cl_2CH), 4.80 (s, 2 H, olefin), 6.95 (NH); ^{13}C NMR (67.8 MHz) 20.3 (q), 20.8 (q), 20.9 (t), 27.3 (t), 38.7 (t), 44.9 (d, allylic CH), 57.4 (s, CN), 61.3 (CCl_2CCH), 83.1 (s, Cl_2C), 110.0 (t, olefin), 147.9 (s, olefin), 169.8 (s, C=O); IR (CH_2Cl_2) 1730; MS 265 (M + 4), 263 (M + 2), 261 (M), 246 (M − Me). Anal. Calcd for $C_{12}H_{17}NOCl_2$: C, 54.97; H, 6.54; N, 5.34. Found: 54.63; H, 6.46; N, 5.39.

27: TLC R_f 0.30 (hexane/ether, 1:8); white solid (mp 163–165 °C); ^{1}H NMR (270 MHz) 1.42, 1.62, 1.67 (Me), 1.50–2.25 (CH_2 and CH), 2.53 (dd, J = 2.4, 11.7, 1 H, CCl_2CH), 7.27 (NH); ^{13}C NMR (67.8 MHz) 20.1 (q), 21.6 (t), 23.5 (t), 31.1 (q), 31.3 (q), 38.4 (t), 48.7 (d), 57.2 (s, CN), 60.7 (CCl_2CCH), 73.4 ($CClMe_2$), 82.9 (CCl_2), 169.6 (C=O); MS 297 (M), 284 (M + 2 − Me), 282 (M − Me), 264 (M + 2 − Cl), 262 (M − Cl); IR (CH_2Cl_2) 1730. Anal. Calcd for $C_{12}H_{18}NOCl_3$: C, 48.26; H, 6.07; N, 4.69. Found: C, 48.13; H, 6.10; N, 4.80.

Double Cyclization of *N*-Geranyltrichloroacetamide (13). A mixture of geranyltrichloroacetamide (**13**) (1.5 g, 5 mmol) and $RuCl_2(PPh_3)_3$ (49 mg, 0.05 mmol, 1 mol %) dissolved in xylene (40 mL) was heated at 140 °C for 2 h to give two diastereomers of the bicyclic lactams **29a** (301 mg, 22%) and **29b** (564 mg, 42%), with a recovery of **13** (214 mg, 14%). When the reaction was carried out at 130 °C for 1 h, a diastereomeric mixture of the monocyclic lactams **28a** and **28b** was obtained. Cyclization of **28a** in a similar manner afforded **29a** as a single product, whereas that of **28b** gave **29b** selectively.

28a: white solid (mp 47–48 °C); TLC R_f 0.46 (hexane/ethyl acetate, 1:1); ^{1}H NMR (270 MHz) 1.65, 1.71, and 1.92 (Me), 1.95–2.10 and 2.10–2.40 (CH_2), 3.30 (t, J = 7.8, 1 H, CCl_2CH), 3.68 (d, J = 7.8, 2 H, CH_2NH), 5.13 (olefin), 7.90 (NH); ^{13}C NMR (67.8 MHz) 17.6 (q), 23.0 (t), 25.5 (q), 26.6 (q), 41.7 (t), 43.9 (t), 59.5 (d), 72.5 (s), 82.3 (s), 122.4 (d), 132.6 (s), 169.1 (s); IR (CH_2Cl_2) 1740. Anal. Calcd for $C_{12}H_{18}NOCl_3$: C, 48.26; H, 6.07; N, 4.69. Found: C, 48.12; H, 6.02; N, 4.77.

28b: white solid (mp 113–114 °C); TLC R_f 0.33 (hexane/ethyl acetate, 1:1); ^{1}H NMR (270 MHz) 1.65, 1.71, and 1.80 (Me), 2.00–2.40 (CH_2), 3.28 (dd, J = 7.5, 9.3, 1 H, NHC*H*), 3.63 (1 H, dd, J = 7.5, 8.4, 1 H, CCl_2CH), 3.71 (dd, J = 8.4, 9.3, 1 H, NHC*H*), 5.14 (olefin), 7.35 (NH), 17.4 (q), 23.0 (t), 25.4 (q), 29.0 (q), 40.5 (t), 41.3 (t), 60.6 (d), 71.7 (s), 82.2 (s), 122.5 (d), 132.3 (s), 169.0 (s); IR (CH_2Cl_2) 1750. Anal. Calcd for $C_{12}H_{18}NOCl_3$: C, 48.26; H, 6.07; N, 4.69. Found: C, 48.22 H, 6.05; N, 4.78.

29a: white solid (mp 154–156 °C); TLC R_f 0.59 (hexane/ethyl acetate, 1:2); ^{1}H NMR (270 MHz) 1.84 and 1.94 (Me), 1.55–2.25 (CH_2), 2.50 (dd, J = 3.4, 12.2, 1 H, C*H*CMe=CH_2), 3.00 (dd, J = 8.3, 9.8, 1 H, NHC*H*), 3.42 (dd, J = 9.8, 10.3, 1 H, NHC*H*), 3.59 (ddd, J = 2.4, 8.3, 10.3, 1 H, CCl_2CH), 4.80 and 5.06 (olefin), 6.63 (NH); ^{13}C NMR (67.8 MHz) 22.6 (q), 25.2 (t), 31.9 (q), 39.1 (t), 42.9 (t), 46.6 (d), 56.8 (d), 68.5 (s), 72.1 (s), 116.0 (t, olefin), 142.1 (s, olefin), 173.6 (s, C=O); IR (CH_2Cl_2) 1730. Anal. Calcd for $C_{12}H_{17}NOCl_2$: C, 54.97; H, 6.54; N, 5.34. Found: C, 54.87; H, 6.63; N, 5.51.

29b: white solid (mp 145–147 °C); TLC R_f 0.27 (hexane/ethyl acetate, 1:2); ^{1}H NMR (270 MHz) 1.59 and 1.87 (Me), 1.50–1.65, 1.80–2.45 (CH_2 and CH), 3.08–3.20 (m, 2 H, NHCH_2), 3.41 (dd, J = 13.2, 14.7, CClCH), 4.80 and 5.06 (olefin), 6.96 (NH); ^{13}C NMR (67.8 MHz) 22.6 (q), 23.4 (t), 30.7 (q), 38.4 (t), 41.9 (t), 47.1 (d), 56.7 (d), 66.6 (s), 70.3 (s), 116.1 (t, olefin), 142.8 (s, olefin), 174.4 (s, C=O); IR (CH_2Cl_2) 1730. Anal. Calcd for $C_{12}H_{17}NOCl_2$: C, 54.97; H, 6.54; N, 5.34. Found: C, 54.64; H, 6.54; N, 5.39.

Ruthenium-Catalyzed Cyclization of 25. A mixture of **25** (130 mg, 0.435 mmol), $RuCl_2(PPh_3)_3$ (4.2 mg, 0.0044 mmol), and xylene (3.5 mL) was heated under reflux for 6 h. The resulting

(18) Neill, A. B. *J. Am. Chem. Soc.* **1953**, *75*, 1508.

mixture was concentrated, and the residue was purified on a silica gel column eluting with hexane/ethyl acetate to give **25′** (22 mg, 54%) as a white solid (mp 104–105 °C): ^{1}H NMR (270 MHz) 1.45 (s, 3 H, NH*Me*), 1.65–2.00 (CH_2), 1.79 (s, 3 H, allylic-*Me*), 2.32 (dd, J = 2.4, 7.8, 1 H, $ClCH_2CH$), 2.67 (dd, J = 6.8, 11.2, 1 H, allylic-C*H*), 3.65 (dd, J = 7.8, 12.2, 1 H, ClCH), 4.03 (dd, J = 2.4, 12.2, 1 H, ClCH), 4.88 and 4.98 (olefin), 7.35 (NH); ^{13}C NMR (67.8 MHz) 20.7 (q), 22.2 (q), 27.0 (t), 37.0 (t), 40.8 (t), 55.0 (d), 58.8 (s), 62.9 (d), 74.6 (s), 115.6 (t, olefin), 144.4 (s, olefin), 171.3 (C=O); IR (CH_2Cl_2) 1730. Anal. Calcd for $C_{12}H_{17}ONCl_2$: C, 54.97; H, 6.54; N, 5.34. Found: C, 55.07; H, 6.67; N, 5.31.

Reductive Dechlorination of the Trichlorinated Lactams. The reactions were carried out in the same manner as used in the reductive dechlorination of **19** and **21**.

36: white solid (mp 115–116 °C); ^{1}H NMR (270 MHz) 1.16 (d, J = 6.8, 3 H, Me), 2.12 (dd, J = 9.3, 16.1, 1 H, α-CH), 2.20–2.31 (m, 1 H, β-CH), 2.61 (dd, J = 7.8, 16.1, 1 H, α-CH), 4.22 (d, J = 7.3, 1 H, NHC*H*), 5.99 (NH), 7.21–7.41 (Ph); IR ($CHCl_3$) 1705. Anal. Calcd for $C_{11}H_{13}NO$: C, 75.41; H, 7.48; N, 7.99. Found: C, 75.21; H, 7.42; N, 8.02.

37: white solid (mp 44–45 °C); ^{1}H NMR (270 MHz) trans:cis = 86:14; trans isomer 1.30 (d, J = 6.3, 3 H, Me), 2.03–2.68 (α- and β-CH), 3.78 (s, 3 H, CO_2Me), 3.84 (d, J = 5.4, 1 H, NHC*H*), 6.68 (NH); cis isomer 1.04 (d, J = 6.8, 3 H, Me), 2.11–2.92 (a- and β-CH), 3.78 (s, 3 H, CO_2Me), 4.28 (d, J = 7.8, 1 H, NHC*H*), 6.68 (NH); IR (CH_2Cl_2) 1710, 1740. Anal. Calcd for C, 53.49; H, 7.05; N, 8.91. Found: C, 53.31; H, 7.04 N, 8.80.

38: white solid (mp 101–102 °C); ^{1}H NMR (270 MHz) 1.15 (s, 3 H, NCMe), 1.30–1.95 and 2.00–2.25 (CH_2 and CH), 1.74 (s, 3 H, Me), 4.73 (olefin), 6.16 (NH); ^{13}C NMR (67.8 MHz) 18.7 (q), 20.6 (q), 27.2 (t), 28.5 (t), 34.6 (t), 36.7 (t), 46.0 (d), 58.3 (d), 76.5 (s), 109.0 (t), 148.6 (s), 177.9 (s); IR (CH_2Cl_2) 1695, 1710. Anal. Calcd for $C_{12}H_{19}NO$: C, 74.57; H, 9.91; N, 7.25. Found: C, 74.32; H, 9.94; N, 7.24.

39: white solid (mp 84–85 °C); ^{1}H NMR (270 MHz) 0.89 and 0.92 (d, J = 6.8, 3 H each, Me), 1.10 (NCMe), 1.02–2.20 (CH_2, CH), 6.10 (NH); ^{13}C NMR (67.8 MHz) 18.7 (q), 19.6 (q), 19.9 (q), 25.7 (t), 26.6 (t), 32.6 (d), 34.8 (t), 36.8 (t), 44.1 (d), 46.1 (d), 58.7 (s), 178.2 (s); IR (CH_2Cl_2) 1695, 1710. Anal. Calcd for $C_{12}H_{21}NO$: C, 73.80; H, 10.84; N, 7.17. Found: C, 73.73; H, 10.90; N, 7.09.

40a: TLC R_f 0.28 (hexane/ethyl acetate, 1:1); white solid (mp 129–130 °C); ^{1}H NMR (270 MHz) 0.85–1.15, 1.22–1.45, 1.65–1.85 (CH_2, CH), 0.94 (d, J = 6.4, 3 H, CH*Me*), 1.79 (s, 3 H, allylic-*Me*), 2.02–2.23 (m, 1 H, β-CH), 2.61 (d, J = 6.8, 1 H, α-CH), 2.80 (br s, 1 H, allylic-C*H*), 3.09 (d, J = 9.8, 1 H, NHC*H*), 3.38 (dd, J = 5.4, 9.8, 1 H, NHC*H*), 4.74 and 4.91 (olefin), 6.37 (NH); ^{13}C NMR (67.8 MHz) 20.5 (q), 22.2 (q), 24.7 (t), 26.9 (t), 32.3 (d), 37.6 (d), 41.0 (d), and 43.9 (d), 44.6 (t), 110.3 (t), 147.2 (s), 178.3 (s); IR (CH_2Cl_2) 1700. Anal. Calcd for $C_{12}H_{19}NO$: C, 74.57; H, 9.91; N, 7.25. Found: C, 74.76; H, 10.00; N, 7.20.

40b: TLC R_f 0.23 (hexane/ethyl acetate, 1:1); white solid (mp 109–110 °C); ^{1}H NMR (270 MHz) 0.91 (d, J = 7.3, 3 H, CH*Me*), 1.10–1.40, 1.55–1.73, 1.73–1.88 (CH_2, CH), 1.78 (s, 3 H, allylic-*Me*), 2.06 (dt, J = 3.4, 11.7, allylic-CH), 2.25 (dd, J = 6.8, 11.7, COCH), 2.25–2.65 (m, 1 H, COCHC*H*), 3.11–3.29 (m, 2 H, NHC*H*$_2$), 4.78 and 4.83 (olefin), 6.49 (NH); ^{13}C NMR (67.8 MHz) 18.2 (q), 19.0 (q), 29.3 (t), 30.2 (d), 31.0 (t), 40.3 (t), 41.0 (d), 44.2 (d), 44.6 (d), 113.2 (t), 146.7 (s), 179.5 (s); IR (CH_2Cl_2) 1700. Anal. Calcd for $C_{12}H_{19}NO$: C, 74.57; H, 9.91; N, 7.25. Found: C, 73.94; H, 9.99; N, 7.25.

Reductive Dechlorination of Two Chlorine Atoms from 32. A mixture of **32** (40 mg, 0.144 mmol), Bu_3SnH (80 mg, 0.274 mmol), AIBN (2.63 mg), and benzene (1.5 mL) was heated at 50 °C for 3.5 h. KF (80 mg, 1.4 mmol) was added, and the mixture was stirred at room temperature overnight. After filtration, the filtrate was concentrated. The residue was purified on a silica gel column by eluting with hexane and ether to afford **36** in 76% yield.

36: white solid (mp 120–122 °C); ^{1}H NMR (270 MHz) 2.44–2.71 (α- and β-CH), 3.61 and 3.65 (dd, J = 5.1, 11.3, 1 H each, CH_2Cl), 6.28 (NH), 7.22–7.45 (m, 5 H, Ph); IR ($CHCl_3$) 1700. Anal. Calcd for $C_{11}H_{12}NOCl$: C, 63.01; H, 5.77; N, 6.68. Found: C, 63.34; H, 5.77; N, 6.72.

Dehydrochlorination of 18 To Form Oxindole. A mixture of **18** (100 mg, 0.4 mmol) and pyridine (4 mL) was heated under reflux for 3 h. The mixture was poured into cold HCl and extracted with ether. The combined extracts were washed with $NaHCO_3$ and brine and then dried over $MgSO_4$ and concentrated. Purification of the residue on a silica gel column (hexane/ether) afforded oxindole (33 mg, 60%) mp 125–127 °C (lit.[18] mp 127 °C).

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Registry No. **1**, 39089-56-0; **2**, 91989-80-9; **3**, 91989-81-0; **4**, 91989-82-1; (±)-**5**, 138816-11-2; (±)-**6**, 138816-12-3; (±)-**7**, 138834-52-3; (±)-**8**, 138816-13-4; (±)-**9**, 136755-26-5; *dl*-**10**, 89619-77-2; *dl*-**10′**, 138816-41-8; *dl*-**11**, 89619-80-7; *dl*-**11′**, 138816-42-9; (±)-**12**, 138816-14-5; **13**, 59874-96-3; (±)-**14**, 138816-15-6; (±)-**15**, 138816-16-7; (±)-**16**, 138816-17-8; (±)-**17**, 138816-18-9; (±)-**18**, 138816-19-0; (±)-*trans*-**19**, 138816-20-3; (±)-*cis*-**19**, 138816-43-0; (±)-*trans*-**20**, 138816-21-4; (±)-*cis*-**20**, 138816-44-1; (±)-**21** (isomer A), 138816-45-2; (±)-**21** (isomer B), 138816-46-3; (±)-**21** (isomer C), 138816-22-5; (±)-**21** (isomer D), 138816-58-7; (±)-**22**, 138816-24-7; (±)-*trans*-**23′**, 138816-24-7; (±)-*cis*-**23′**, 138816-47-4; (±)-*trans*-**24′**, 138816-25-8; (±)-*cis*-**24′**, 138816-48-5; **25**, 138816-26-9; **25′**, 138816-57-6; **26**, 138816-27-0; **27**, 138816-28-1; (±)-**28a**, 138816-29-2; (±)-**28b**, 138816-56-5; **29**, 138816-30-5; (±)-*trans*-**30**, 138816-31-6; (±)-*cis*-**30**, 138816-51-0; (±)-*trans*-**31**, 138816-32-7; (±)-*cis*-**31**, 138816-52-1; (±)-**32**, 138816-33-8; (±)-**32** 3,4-dihydro, 138816-53-2; (±)-**32′**, 138816-55-4; (±)-*trans*-**33**, 138816-34-9; (±)-*cis*-**33**, 138816-49-6; (±)-*trans*-**34**, 138816-35-0; (±)-*cis*-**34**, 138816-50-9; (±)-**35**, 138816-36-1; (±)-**36**, 138816-37-2; *dl*-*trans*-**37**, 76251-46-2; *dl*-*cis*-**37**, 76251-51-9; **38**, 138816-38-3; **39**, 138816-39-4; **40**, 138816-40-7; $RuCl_2(PPh_3)_3$, 15529-49-4; oxindole, 59-48-3; 3-methyl-2-buten-1-ol, 556-82-1; 2-methyl-3-buten-2-ol, 115-18-4; methallyl alcohol, 513-42-8; 2-buten-1-ol, 6117-91-5; 5-methyl-2-pyrrolidinone, 108-27-0; 1-tosyl-3-(phenylselenyl)-5-methyl-2-pyrrolidine, 138816-54-3.

Supplementary Material Available: Spectral data of compounds and ^{1}H and ^{13}C NMR spectra of **25** and **34** (10 pages). Ordering information is given on any current masthead page.