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Copper-Catalyzed Facile Carbon-Carbon Bond Forming Reactions at the α-Position of α,α,γ-Trichlorinated γ-Lactams

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Abstract

Treatment of α,α,γ-trichlorinated γ-lactams with a catalytic amount of CuCl(bipyridine) complex resulted in facile activation of their carbon-chlorine bond at the α-position. Addition of the carbon moiety and the chlorine atom to olefins furnished the carbon-carbon bond forming reaction at the α-position of the carbonyl group. In certain trichlorinated γ-lactams including a carbon-carbon double bond at an appropriate position, intramolecular addition reactions took place to give bicyclic lactams. Sequential reactions consisting of the cyclization of *N*-allyl trichloroacetamides followed by the inter- or intramolecular carbon-carbon bond forming reactions at the α-position of the lactams were also achieved. Efficiency of the catalyst and reaction rate was dependent on the protecting group of the nitrogen atom of the γ-lactams; *N*-tosyl derivatives gave better results than the corresponding *N*-benzyl homologues. The molecular structure of the representative products revealed the stereochemical outcome of the reactions.

Keywords; Addition; Catalysis; Lactam; Copper

Introduction

It is known that transition metal salts or complexes easily cleave a carbon-chlorine bond of α,α,α-trichlorinated carbonyl compounds.[1)] In the presence of olefins, the carbon-chlorine bond cleavage resulted in addition of the formed carbon moiety and the chlorine atom to the carbon-carbon double bond,[2)] which offers a simple method for carbon-carbon forming reaction at the α-position of the carbonyl group.[3)] The intramolecular version of this addition reaction, the so called intramolecular Kharasch reaction, resulted in discovery of a fascinating access to trichlorinated γ-lactones,[4,5)] γ-lactams,[6,7)] cyclopentanones[8)], and other cyclic compounds. In particular, intramolecular addition reaction of a carbon-chlorine bond of *N*-allyl trichloroacetamides giving the corresponding α,α,γ–trichlorinated γ-lactams in good yields was proved to be useful for construction of various pyrrolidinone skeletons including precursors of alkaloids.[9)]

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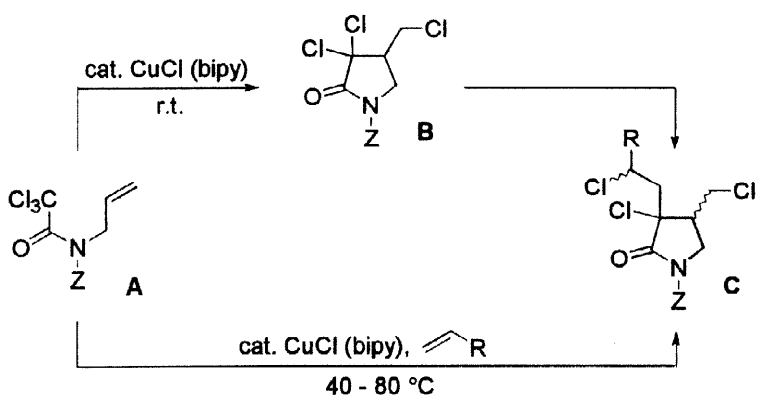
These metal-catalyzed reactions of α,α,α-trichlorinated carbonyl compounds often proceed at higher than 100 °C. Despite the great synthetic utility, heating the reaction mixture to over 100 °C is a drawback for the reactions of thermally labile starting materials and products. We have found that the cyclization of *N*-allyl trichloroacetamides can be successfully achieved with a catalytic amount of the CuCl(bipyridine) catalyst system at lower temperatures than usual and with high catalyst efficiency. For example, cyclization of *N*, *N*-diallyl trichloroacetamides with conventional catalysts [CuCl in acetonitrile or $RuCl_2(PPh_3)_3$] proceeded at 80-140 °C with moderate catalyst turnover numbers (TN < 20). In sharp contrast, the same reaction in the presence of CuCl(bipyridine) smoothly proceeded at room temperature with TN > 40. Furthermore, appropriate choice of protecting groups on the amide nitrogen is critical to affect the catalyst efficiency; the cyclization of *N*-allyl trichloroacetamides bearing electron-withdrawing groups such as Ts and Cbz on the amide nitrogen proceeded at room temperature with TN > 80.

Discovery of the powerful catalyst system gave us the idea that the copper-bipyridine catalyst system might also successfully activate α,α,γ-trichlorinated γ-lactams obtained by the above cyclization under mild conditions. Successful activation of the α-chlorine atom of the trichlorinated γ-lactams followed by the reaction of olefins could provide us a method for carbon-carbon bond forming reaction at the α-position of the γ-lactams, which would be useful for further functionalization of the trichlorinated γ-lactams. Carbonyl compounds bearing two chlorine atoms at the α-position of the carbonyl group are generally less reactive than the trichlorinated homologues. Cyclization of *N*-allyl dichloroacetamides was reported by us[6a] and Bertrand[7b] *et al.*; the reaction was much slower than that of *N*-allyl trichloroacetamide.[6a] Weinreb and his colleagues reported the transition metal catalyzed intramolecular addition reactions of α,α–dichlorocarbonyl compounds with olefins at higher than 150 °C.[8] The cyclization of *N*-tosylated *N*-allyl α,α-dichloroalkanamides was examined by Slough with $RuCl_2(PPh_3)_3$ at 100 °C,[7a] for which active catalysts proceeding at 60-100 °C were recently devised by Ghelfi's group.[10] Intermolecular addition reaction is generally slower than the intramolecular process, and to our knowledge there are not many examples of the intermolecular addition reaction of α,α-dichlorocarbonyl compounds to olefins under mild conditions.[10]

In this paper, we wish to report that the activation actually took place at temperatures around 80 °C, leading to the intermolecular reaction with α-olefins as shown in Scheme 1. Similar to the cyclization of *N*-allyl trichloroacetamides described above, the protecting group on the



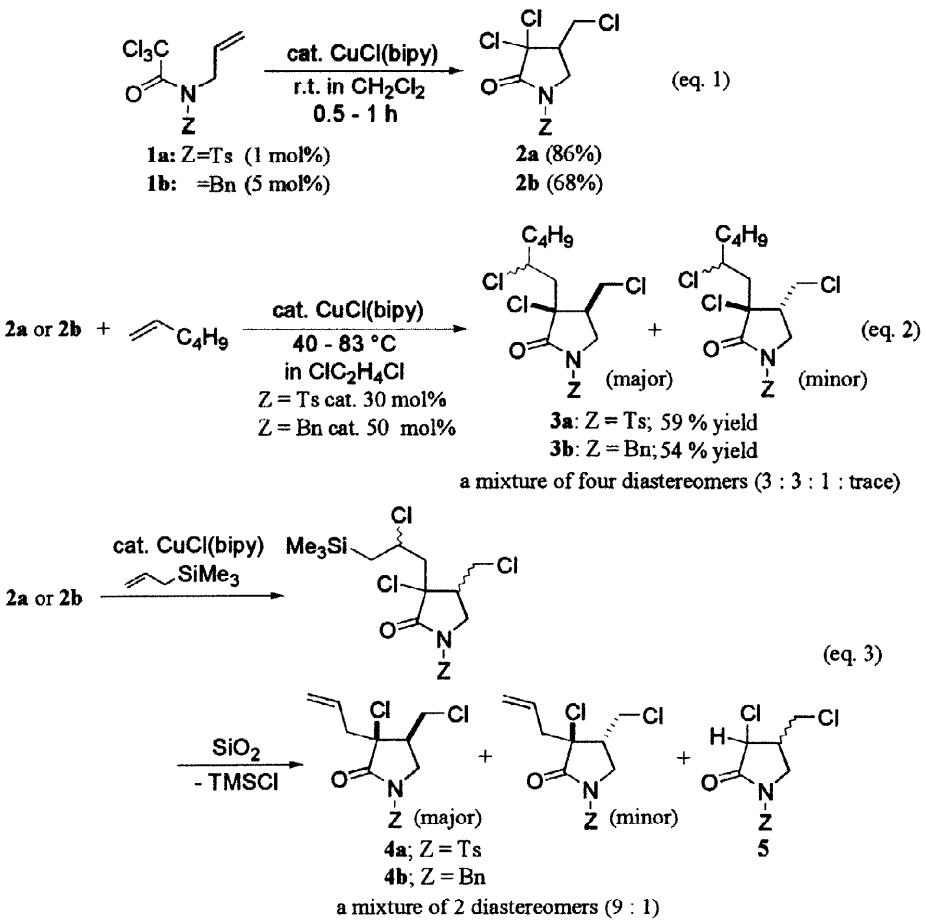
Scheme 1

nitrogen atom of α,α,γ-trichlorinated γ-lactams affected the reaction rate and the catalyst efficiency; *N*-tosyl derivatives reacted more smoothly than the *N*-benzyl analogues. Since the reaction rate of the intermolecular reaction with α-olefins is significantly lower than the cyclization of *N*-allyl trichloroacetamides, the reaction of *N*-allyl trichloroacetamides in the presence of α-olefins at 80 °C resulted in one-pot synthesis of α-functionalized lactams C. These stepwise (A —› B —› C) as well as sequential (A —› C) procedures can be applied to preparation of bicyclic lactams from acyclic *N*-allyl trichloroacetamides including two carbon-carbon double bonds at the appropriate positions. In all of the cases, the reaction produced two to three asymmetric carbons. Stereochemistry of the products were investigated in detail by spectroscopic and crystallographic analyses of the representative examples contributing to our understanding of the stereochemical outcome of the copper-catalyzed activation reactions of polyhalogenated compounds.

Results and Discussion

Reaction of α,α,γ-trichlorinated lactams with a-olefins.

As reported earlier, cyclization of *N*-tosyl or *N*-benzyl-*N*-allyltrichloroacetamide to the corresponding γ-lactam proceeded at room temperature within 1 h by catalysis of a 1 : 1



Scheme 2

Table1.
The reactions of **2a** or **2b** with allyltrimethylsilane.

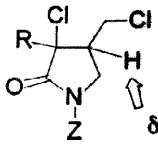
Entry	lactam	cat. (mol% to 2)	Silane (eq. To 2)	Solvent	temp. (°C)	product (yield;%)[b]	ratio of cis/trans[c]
1	**2a**	30	10	DCE[a]	83	93	**86 / 14**
2	**2a**	30	2	DCE[a]	83	85	**85 / 15**
3	**2a**	10	10	DCE[a]	83	93	**85 / 15**
4	**2a**	30	10	DCE[a]	66	78	**84 / 16**
5	**2a**	30	10	THF	66	52	**83 / 17**
6	**2a**	30	10	DCE[a]	40	22	**84 / 16**
7	**2a**	30	10	CH_2Cl_2	40	64	**86 / 14**
8	**2b**	30	10	DCE[a]	83	62	**85 / 15**
9	**2b**	50	10	DCE[a]	83	84	**90 / 10**

a. DCE = 1,2-dichloroethane. b. Isolated yields. c. Determined by ^{1}H NMR.

mixture of CuCl and bipyridine (1 – 5 mol% based on the charged acetamide). Typical examples are shown in Scheme 2, eq. 1. Attempted reactions of isolated α,α,γ-trichlorinated lactams with olefins at room temperature under the same conditions resulted in complete recovery of the starting materials. However, the reaction took place at 83 °C in 1,2-dichloroethane, leading to the carbon-carbon bond forming reaction at the α-position of the lactams. In a typical example, the reaction of *N*-tosyl lactam **2a** with 1-hexene (10 eq. to **2a**) proceeded in the presence of the CuCl/bipy catalyst system (30 mol%) in dichloroethane under reflux for 1h to give the corresponding adduct **3a** in 59% yield (Scheme 2, eq. 2). The reaction of the *N*-benzyl analogue (**2b**) was rather sluggish; higher catalyst concentration was required to obtain the corresponding product. Formation of four diastereomers derived from three asymmetric centers was confirmed by GC-mass analysis of the products. The diastereomer ratio was 3 : 3 : 1 : trace in either **3a** or **3b**. To avoid a potential problem caused by the existence of asymmetric carbons on the side chain, we carried out the reactions of **2a** or **2b** with allyltrimethylsilane. Radical addition of haloalkanes to allyl trimethylsilane is known to give adducts containing a chlorine atom at the β-position of the trimethylsilyl group, from which chlorotrimethylsilane can be easily removed to form a carbon-carbon double bond.[11] Reaction of the lactams **2a** or **2b** with allyltrimethylsilane followed by treatment of the crude product with silica gel resulted in the allylation reaction at the α-position of the lactams as shown in Scheme 2, eq. 3.

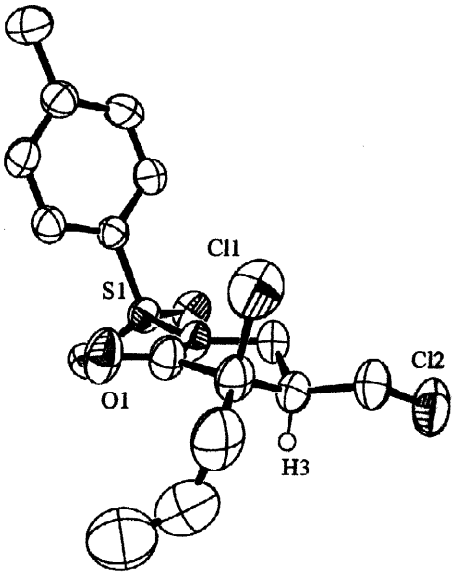
Table 1 summarizes yields and diastereomer ratios of the products seen in the reaction of **2a** or **2b** with allyltrimethylsilane. The reaction was carried out with allyltrimethylsilane (2 - 10 eq. based on **2a** or **2b**) in the presence of a 1 : 1 mixture of CuCl and bipyridine (10 – 50 mol% based on **2a** or **2b**) in refluxing 1,2-dichloroethane for 1 h. Treatment of the crude adduct with silica gel at room temperature for 1 h resulted in elimination of chlorotrimethylsilane to form the allylated lactam **4a** or **4b**. The reaction of **2a** proceeded smoothly even with a smaller amount of allyltrimethylsilane (entry 2) or the catalyst (entry 3) to give **4a** in good yield. In contrast, the reaction of **4b** was competitive with the catalyst deactivation, so that larger amounts of the catalyst were required to attain good yields of **4b**. The diastereomer ratios were determined by ^{1}H NMR spectra of the crude product, which were in a range of 85 : 15 – 90 : 10. A small amount of α- monochlorolactam **5** was also isolated as a by-product. The reaction proceeded more slowly at lower temperatures. Use of higher ratio of bipyridine to CuCl (3 : 1) led to decrease of the yield. Other solvents such as dichloromethane and THF

Table 2. Reported and observed $\delta_{\beta\text{-H}}$ values.



Z	R	Solvent	$\delta_{\beta\text{-H}}$ (ppm)	ref.
	Reported		(cis / trans)	
Ts	Me (**6a**)	C_6D_6	2.08 / 1.48	7a
Ts	^{i}Pr (**7a**)	C_6D_6	2.22 / 2.15	7a
Bn	^{n}Pr (**8b**)	$CDCl_3$	2.74 / 2.92	7c
	Observed		(major/minor)	
Ts	allyl(**4a**)	C_6D_6	2.05 / 2.11	
Ts	allyl(**4a**)	$CDCl_3$	2.82 / 2.87	
Ts	^{n}Pr (**8a**)	C_6D_6	1.98 / 2.10	this
Ts	^{n}Pr (**8a**)	$CDCl_3$	2.77 / 2.84	work
Bn	allyl(**4b**)	C_6D_6	2.29 / 2.45	
Bn	allyl(**4b**)	$CDCl_3$	2.75 / 2.90	
Bn	^{n}Pr (**8b**)	C_6D_6	2.15 / 2.43	
Bn	^{n}Pr (**8b**)	$CDCl_3$	2.71 / 2.87	

Fig. 1 The ORTEP drawing of the major isomer of **4a**.

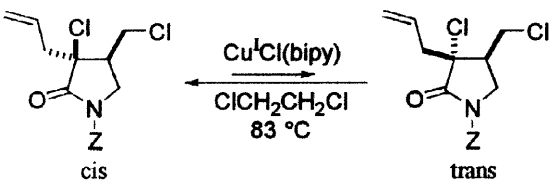


were also effective, but the by-product **5** was formed in higher yields.

Assignment of the diastereomers of **4a** and **4b** was problematic. Analogues of **4a** and **4b**, which have some alkyl groups instead of the allyl group in **4a** and **4b**, were prepared by cyclization of *N*-allyl dichloroalkamides by Slough and Ghelfi (**6a**, **7a**, and **8b** in Table 2). Slough reported that the β-H proton of the *cis*-isomer of **6a** and **7a** generally appears more downfield than that of the *trans*-isomer based on large NOE enhancement (5–10%) in the methyl (**6a**) and isopropyl (**7a**) derivatives. He claimed that this tendency would be general in the homologues of **6a** and **7a**, which could be used to assign the diastereomer of **4a**. In contrast, Ghelfi assigned the isomer showing the β-H proton appearing more downfield than the other to be *trans* in the propyl derivative **8b** based on the NOE experiments. Details of the NOE enhancement were not reported. The tendency of the chemical shift is the reverse of the Slough's assignment.

We synthesized **8a** and **8b** by catalytic hydrogenation of **4a** and **4b**, respectively, and measured ^{1}H NMR spectra of these compounds in C_6D_6 or $CDCl_3$. In all cases, ^{1}H resonance derived from the β-H proton in the major isomer appeared more upfield than that in the minor isomer as shown in Table 2. According to the assignment by Slough and Ghelfi, the major isomer of **4a** or **8a** is trans, whereas that of **4b** or **8b** is cis. This is strange to us, because electronic as well as steric circumstances around the β-hydrogen atom do not differ greatly between **4a** and **4b** or **8a** and **8b**. In order to clarify the stereochemistry, we carried out the NOE experiments of **4a**, **4b**, **8a**, and **8b**, but could not obtain satisfactory enhanced signals for unequivocal assignment of the isomers. Thus, we performed crystallographic analysis of the major isomer of **4a**. *As illustrated in Fig. 1, the molecular structure clearly showed that the stereochemistry between the chlorine atom and the β-chloromethyl moiety was cis.* ^{1}H NMR spectrum of a $CDCl_3$ solution of the crystal used for X-ray analysis showed that the solved structure is that of the major isomer of **4a**. This revealed that the assignment based on the chemical shift of ^{1}H NMR is not always effective for α-alkyl-α,γ-dichlorolactams.

An important feature of the molecular structure of **4a** is that the pyrrolidinone ring is a nearly perfect envelope with the β-carbon out of plane, and both bulky substituents, α-allyl and β-chloromethyl groups, were located at the equatorial positions. This indicates that this isomer is more thermodynamically stable than the other is. Studies on ruthenium-catalyzed cis/trans interconversion of **6a** by Slough suggest that the stereochemistry of this type of lactam may be governed by thermodynamic stability of the isomers.[7a] In fact, the cis- and trans isomer of **4a** were isolated in pure form, and each isomer was heated in the presence of a catalytic amount of CuCl and bipyridine in dichloroethane for 1 h. In both experiments, the ratio of cis- to trans isomer reached at ca. 9 : 1. Similarly, interconversion between *cis*- and *trans*-isomer of **4b** gave a ca. 9 : 1 mixture of isomers, though the rate of interconversion was slower than that of **4a**. The results are summarized in Table 3. Although Bertrand reported that interconversion between isomers of *N*-substituted α-alkoxycarbonyl-α,γ-dichloro-γ-lactams by copper-amine catalyst systems did not occur,[7b] the present results clearly showed that equilibrium between the *cis*- and *trans*-isomers of the products easily took place under the conditions of the copper-catalyzed addition reaction to α-olefins described above. In other words, the above results suggest that concomitantly occurring cis/trans interconversion during the carbon-carbon bond forming reaction at the α-position of the lactams would determine the stereochemical outcome governed by thermodynamic stability of the isomers.



Scheme 3

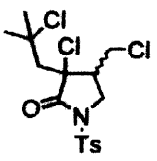
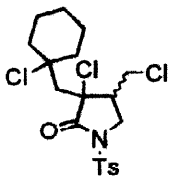
Table 3. Thermal equilibrium between two isomers of **4a** and **4b**.

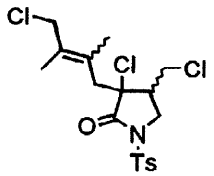
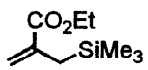
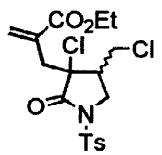
substrate	cat. (mol%)	time (h)	cis / trans
cis-**4a**	10	1	88 / 12
	10	24	89 / 12
trans-**4a**	10	1	91 / 9
	10	24	90 / 10
cis-**4b**	50	1	96 / 4
	50	24	93 / 7
trans-**4b**	50	1	38 / 62
	50	24	91 / 9

As described above, it is difficult to determine the stereochemistry of **4a**, **4b**, and their homologues by comparison in the chemical shift of β-proton between the two isomers. NOE experiments are effective only when significantly large enhancement is available. In this context, it is important that the reaction involves the cis/trans interconversion, and the stereochemistry of the product is determined by the difference in thermodynamic stability of the two isomers. In crystal structures of variously substituted α,α,γ-trichlorinated γ-lactams so far we have examined, the pyrrolidinone ring has a perfect envelope shape with the β-carbon as the most puckered center. The β-chloromethyl group was located at the equatorial position in all cases. Thus, the bulky substituent at the α-position would also be preferentially located at the equatorial position, too, in order to relieve the torsional strain of the pyrrolidinone ring. For new compounds obtained in the intermolecular addition reaction of **2a** with α–olefins, we therefore propose that the cis-isomer is the major isomer.

Other examples of the reactions of α,α,γ-trichlorinated γ-lactams with olefins are summarized in Table 4. Addition reaction of **2a** to isobutene and methylenecyclohexane

Table 4. Reaction of lactam **2a** with α-olefins.

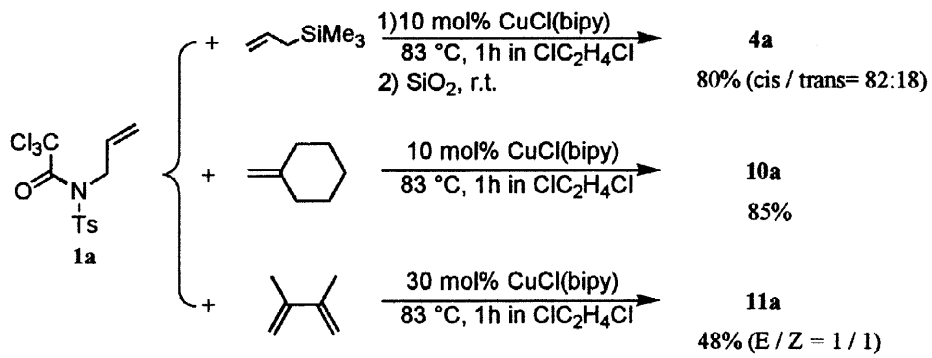
olefin	cat./mol%	product	yield /%
	10	 **9a**	52
	10	 **10a**	100

olefin	cat./mol%	product	yield /%
	10	 **11a**	86
	30	 **12a**	87

afforded the corresponding adducts **9a** and **10a** as almost a single diastereomer. Addition reaction of **2a** to 1,3-butadiene gave the 1,4-adduct **11a** as a 1:1 mixture of *E/Z* isomer. The reaction of **4a** with an allylsilane bearing ethoxycarbonyl group gave **12a** as a single diastereomer after elimination of chlorotrimethylsilane promoted by silica gel. Based on the above mentioned proposal, we assume the stereochemistry of the products to be cis.

Sequential reactions.

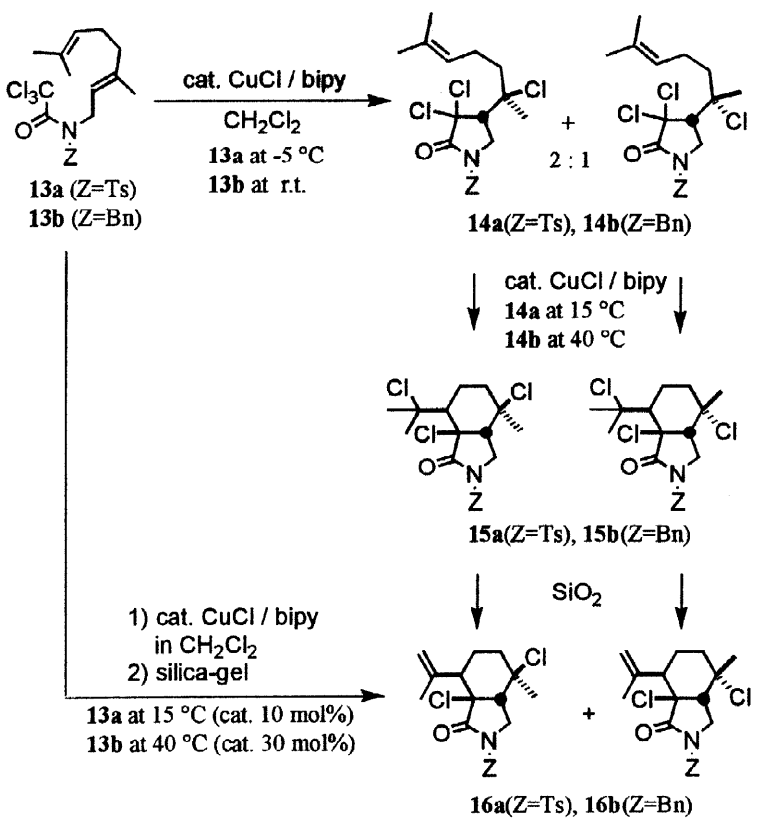
As reported earlier, the cyclization of *N*-protected *N*-allyl trichloroacetamides with copper-bipyridine catalyst system took place at ambient temperature. In contrast, the copper-bipyridine complex-catalyzed reactions of the resulting α,α,γ-lactams with olefins were apparently slower than the cyclization, occurring at 40-80 °C. These results suggest that sequential reaction involving cyclization of *N*-allyl trichloroacetamides and α-alkylation reaction could result in one-pot preparation of α-alkyl-α,γ-dichlorinated lactams from *N*-allyl trichloroacetamides. In fact, the reaction of **1a** with allyltrimethylsilane in refluxing 1,2-dichloroethane in the presence of 10 mol% CuCl/bipyridine afforded the α-allylated γ-lactam **4a** in 80% yield (*cis* : *trans* = 82 : 18). Similarly, the reaction of **1a** with methylenecyclohexane gave the corresponding α-functionalized γ-lactam **10a** in 85% yield.



Scheme 4

The reaction of **1a** with 2,3-dimethylbutadiene was sluggish, and a mixture of products containing a significant amount of **2a** was formed in the presence of 10 mol% of the catalyst. With 30 mol% of the catalyst, **11a** was isolated in 48 % yield. Intractable products were obtained as by-products.

Application of this sequential reaction to synthesis of bicyclic lactams was also possible. *N*-Tosyl-*N*-geranyl trichloroacetamide (**13a**) was treated with 10 mol% of CuCl(bipyridine) at 15 °C for 1 h to afford the corresponding bicyclic lactam **15a**. One chlorine atom of **15a** was labile and facilely eliminated to form **16a** in 83% yield from **13a**. It was proved by isolation of the intermediate **14a** that the reaction is sequential, namely that the cyclization of **13a** was followed by intramolecular carbon-carbon bond forming reaction at the α-position of the lactam. Although the lactam **16a** contains four asymmetric carbons, only two diastereomers were detected in a ratio of 2 : 1 in ^{1}H NMR. The monocyclic intermediate **14a** was also a 2 : 1 mixture of diastereomers derived from the asymmetric carbon at the γ-position of the carbonyl group. The same diastereomer ratio was obtained from either *E*- or *Z*-isomer of trichloroacetamides **13a**, showing that the monocyclization was not stereoselective. Two diastereomers of the monocyclic lactam **14a** were separated and independently subjected to catalytic cyclization at 15 °C followed by dehydrochlorination with silica gel. Each diastereomer of **14a** was stereoselectively cyclized to the corresponding isomer of **16a** via **15a**. This indicates that the diastereomers of **16a** also derived from the asymmetric carbon at the γ-position of the carbonyl group. Similar results were obtained in the double cyclization of *N*-benzyl homologue **13b** as shown in Scheme 5. Application of somewhat higher temperature (40 °C) and higher catalyst concentration (30 mol%) was required for smooth cyclization of **13b**. The stereochemistry of this bicyclic lactam **16b** was determined by crystallography.



Scheme 5

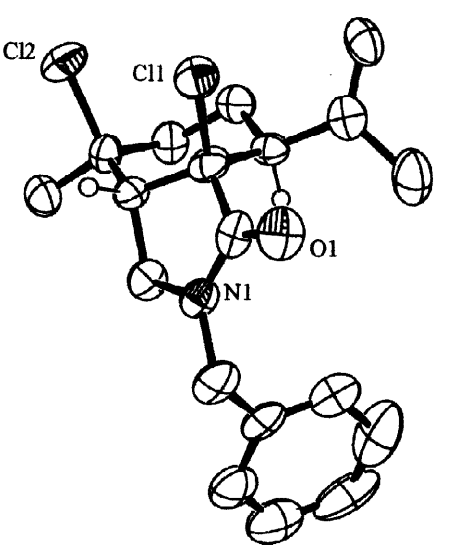
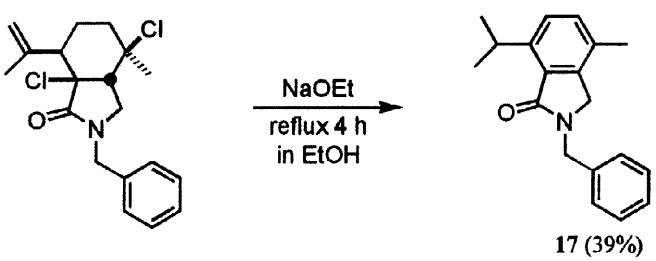


Fig. 2. The ORTEP drawing of the major isomer of **16b**.

The ORTEP drawing is illustrated in Fig.2. Conformation of the cyclohexane ring in **16b** is the chair, and the chlorine and hydrogen atoms at the junction of five- and six membered rings are cis-orientation. Both chlorine atoms occupy the axial orientation, whereas the isopropenyl group occupies the equatorial position. Since heating a solution of **16b** in the presence of the CuCl/bipyridine catalyst system at 80 °C did not result in isomerization, this isomer may be thermodynamically more stable than the isomer of which the hydrogen and chlorine atoms at the ring junction are trans-orientation. Spectroscopic similarity between **16a** and **16b** suggests that the structure of **16a** would be similar to that of **16b**.

Conclusion

A series of work on the catalytic activation of α,α,γ-trichlorinated γ-lactams has provided a simple way to introduce alkyl groups at the α–position of the lactam by the inter- and intramolecular addition reaction to olefins. Facile addition reaction below the refluxing temperature of dichloroethane was accomplished using the CuCl/bipyridine catalyst. By taking advantage of the significant rate difference between the inter- and intramolecular addition reactions, the sequential reaction consisting of cyclization of *N*-allyl trichloroacetamides followed by the addition reaction to α-olefins gave the corresponding disubstituted γ-lactams effectively. Intermolecular version of this sequential reaction resulted in double cyclization of *N*-geranyl trichloroacetamides to afford bicyclic lactams. Stereochemistry of the cyclization was determined by crystallography of two of the products, **4a** and **16b**. The former structure suggests that preferential formation of the cis-isomers would be general in the intermolecular addition reactions. These results not only offer a unique way to access substituted pyrrolidinone derivatives by catalytic methods, but also contribute to understanding the stereochemistry of substituted pyrrolidinone derivatives. Further investigation of the utilization of the CuCl/bipyridine catalyst system[12] and application of the copper-catalyzed preparation of substituted pyrrolidinone derivatives in organic synthesis are under way. As one example of this application, synthesis of an isoindolidinone derivative **17** is shown below.



17 (39%)

Scheme 6

Experimental section

General

All manipulations were performed under an argon atmosphere unless otherwise noted. Cuprous chloride (CuCl) was prepared from $CuCl_2$ hydrate,[13] and stored under a dry argon atmosphere. Purification of 2,2'-bipyridine was made by sublimation. Solvents were

distilled under an inert gas atmosphere over P_2O_5 (CH_2Cl_2 and dichloroethane) or sodium-benzophenone (THF). Other solvents and reagents were distilled before use. Column chromatography was performed on a silica gel 60 (Merck, 70-230 or 230-400 mesh). Thin layer chromatography was carried out with a silica Gel 60 F_{254} (Merck).

Melting points were recorded on a JANACO MP apparatus and are uncorrected. IR spectra were taken with JASCO A-102 or FT/IR-550 spectrometers. ^1H and ^{13}C NMR spectra were recorded with JEOL LA 600 (^1H NMR: 600 MHz) and LA 400 (400 MHz for ^1H NMR and 100 MHz for ^{13}C NMR) instruments. Chemical shifts are reported in parts per million downfield (δ) from the internal tetramethylsilane unless otherwise stated. Mass spectra were recorded with a JEOL-JMS-70 spectrometer operating at ionization energy of 70 eV. GC-mass spectra were recorded with Fining MAT GCQ apparatus. Elemental analysis was performed at the center of microanalysis of Faculty of Science, Kyushu University.

General Procedures for α-Alkylation Reactions of α,α,γ-trichlorinated-γ-lactams

In a typical example, the lactam **2a** (71 mg, 0.199 mmol) and CuCl (2.0 mg, 0.020 mmol, 10 mol%) were measured into a 10 mL flask, and the atmosphere was replaced by argon. Then, carefully degassed dichloroethane (2 mL) and methylenecyclohexane (240 μL, 192 mg, 2.00 mmol) were added. The mixture was allowed to warm at 83 °C. Then 0.2 M dichloroethane solution of 2,2'-bipyridine (100 μL, 0.020 mmol) was added. The resulting initially brown solution was heated at this temperature for 1 h. Color of the solution quickly faded, and the green insoluble materials were precipitated. The resulting mixture was cooled to room temperature, and transferred to a head of a short pad of silica gel. Elution with Et_2O (100 mL) gave a colorless solution, which was then concentrated *in vacuo*. The residue was purified with a silica gel column by using a 1 : 4 mixture of Et_2O-hexane as the eluent to afford the desired product (91 mg, 100%).

α-Allylation Reactions of α,α,γ-trichlorinated-γ-lactams

In a typical example, the lactam **2a** (71 mg, 0.199 mmol) and CuCl (2.0 mg, 0.020 mmol, 10 mol%) were measured into a 10 mL flask, and the atmosphere was replaced by argon. Then, carefully degassed dichloroethane (2 mL) and allyltrimethylsilane (320 μL, 230 mg, 2.01 mmol) were added. The mixture was allowed to warm at 83 °C. Then 0.2 M dichloroethane solution of 2,2'-bipyridine (100 μL, 0.020 mmol) was added and heated at this temperature for 1 h. The resulting mixture was cooled to room temperature, and transferred to a head of a short pad of silica-gel. Elution with Et_2O (100 mL) gave a colorless solution, which was then concentrated *in vacuo*. In order to accelerate the elimination of chlorotrimethylsilane, a dichloromethane solution of the residue was stirred with silica-gel for 2-6 h at room temperature. Silica-gel was filtered off and rinsed with Et_2O. Solvents were evaporated *in vacuo* and the residue was purified with a silica gel column by using a 1 : 4 mixture of Et_2O-hexane as the eluent to afford the desired product.

***cis*-4a**: colorless solid; mp. 103.5-104.5 °C (CH_2Cl_2/Hex.); TLC R_f 0.41 (50% Et_2O/Hex.); IR (CH_2Cl_2) 1749 (C=O), 1373, 1273, 1174, 1119 cm^{-1}; MS: *m/z* 363 [M^++2], 361 [M^+]; Anal. calcd for $C_{15}H_{17}NO_3Cl_2S$: C, 49.73; H, 4.73; N, 3.87. found: C, 49.82; H, 4.76; N, 3.83.

***trans*-4a**: colorless oil; TLC R_f 0.31 (50% Et_2O/Hex); IR (CH_2Cl_2) 1749 (C=O), 1371, 1273,

1174, 1120 cm^{-1}; MS: *m/z* 363 [M^++2], 361 [M^+]; HRMS calcd for $C_{15}H_{17}NO_3Cl_2S$ 361.0306, found 361.0308.

***cis*-4b**: colorless oil; TLC R_f0.49 (50% Et_2O/Hex); IR (CH_2Cl_2) 1714 cm^{-1} (C=O); MS: *m/z* 299 [M^++2], 297 [M^+]; Anal. calcd for $C_{15}H_{17}NOCl_2$: C, 60.41; H, 5.75; N, 4.70. found: C, 60.37; H, 5.85; N, 4.59.

***trans*-4b**: colorless oil; TLC R_f0.44 (50% Et_2O/Hex); IR (CH_2Cl_2) 1709 cm^{-1} (C=O); MS: *m/z* 299 [M^++2], 297 [M^+]; HRMS calcd for $C_{15}H_{17}NO_2Cl_2$ 297.0687, found 297.0684.

***cis*-8a**: colorless solid; mp. 134-136 °C; TLC R_f 0.41 (50% Et_2O/Hex.); IR (CH_2Cl_2) 1751 (C=O), 1371, 1174, 1119 cm^{-1}; FAB-MS: *m/z* 366 [MH^++2], 364 [MH^+]; HRMS calcd for $C_{15}H_{19}NO_3Cl_2S$+H 364.0541, found 364.0541.

***trans*-8a**: colorless oil; TLC R_f0.31 (50% Et_2O/Hex.); IR (CH_2Cl_2) 1749 (C=O), 1371, 1174, 1120 cm^{-1}; FAB-MS: *m/z* 366 [MH^++2], 364 [MH^+]; HRMS calcd for $C_{15}H_{19}NO_3Cl_2S$+H 364.0541, found 364.0535.

3a: Three isomers were isolated in pure form: *isomer A:* colorless oil; TLC R_f0.63 (50% Et_2O/Hex); ^1H NMR ($CDCl_3$) 7.90, 7.36 (d, *J*= 8 Hz, 2Hx2, Ts), 4.31 (dd, *J*= 10, 7 Hz, 1H, NCH_2), 3.87 (dd, *J*= 11, 4 Hz, 1H, CH_2Cl), 3.66-3.58 (m, 1H, CH_2CHCl), 3.62 (dd, *J*= 11, 10 Hz, 1H, CH_2Cl), 3.48 (t, *J*= 10 Hz, 1H, NCH_2), 3.31 (ddt, *J*= 7, 4, 10 Hz, 1H, β-H), 2.68 (dd, *J*= 16, 2 Hz, 1H, α-CH_2), 2.45 (s, 3H, Me of Ts), 2.37 (dd, *J*= 16, 9 Hz, 1H, α-CH_2), 1.77-1.69, 1.52-1.22 (m, 2+4H, -C_3H_6-), 0.89 (t, *J*= 7 Hz, 3H, Me); ^{13}C NMR ($CDCl_3$) 167.86, 145.93, 133.62, 129.86, 128.04, 71.44, 58.21, 47.88, 44.06, 42.68, 40.92, 39.32, 27.89, 21.98, 21.73, 13.80; IR (CH_2Cl_2) 1747 (C=O) cm^{-1}; FAB-MS: *m/z* 444 [MH^++4], 442 [MH^++2], 440 [MH^+]; HRMS calcd for $C_{18}H_{24}NO_3Cl_3S$+H 440.0621, found 440.0622: *isomer B:* colorless oil; TLC R_f0.53 (50% Et_2O/Hex); ^1H NMR ($CDCl_3$) 7.91, 7.34 (d, *J*= 8 Hz, 2Hx2, Ts), 4.22 (dd, *J*= 10, 8 Hz, 1H, NCH_2), 4.03 (ddt, *J*= 10, 3, 7 Hz, 1H, CH_2CHCl), 3.95 (dd, *J*= 11, 6 Hz, 1H, CH_2Cl), 3.62 (dd, *J*= 11, 8 Hz, 1H, CH_2Cl), 3.47 (dd, *J*= 10, 9 Hz, 1H, NCH_2), 3.06 (ddt, *J*= 9, 6, 8 Hz, 1H, β-H), 2.61 (dd, *J*= 16, 10 Hz, 1H, α-CH_2), 2.50 (dd, *J*= 16, 3 Hz, 1H, α-CH_2), 2.44 (s, 3H, Me of Ts), 1.76-1.68, 1.51-1.21 (m, 2+4H, -C_3H_6-), 0.89 (t, *J*= 7 Hz, 3H, Me); ^{13}C NMR ($CDCl_3$) 168.23, 145.77, 133.81, 129.73, 128.22, 70.93, 57.86, 47.41, 44.50, 42.10, 41.80, 38.61, 28.13, 22.00, 21.72, 13.80; IR (CH_2Cl_2) 1751 (C=O) cm^{-1}; FAB-MS: *m/z* 444 [MH^++4], 442 [MH^++2], 440 [MH^+]; HRMS calcd for $C_{18}H_{24}NO_3Cl_3S$+H 440.0621, found 440.0622: *isomer C (minor):* colorless oil; TLC R_f0.56 (50% Et_2O/Hex); ^1H NMR ($CDCl_3$) 7.92, 7.35 (d, *J*= 8 Hz, 2Hx2, Ts), 4.34 (ddt, *J*= 10, 3, 7 Hz, 1H, CH_2CHCl), 4.11 (d, *J*= 3 Hz, 2H, NCH_2), 3.89 (dd, *J*= 11, 3 Hz, 1H, CH_2Cl), 3.45 (dd, *J*= 11, 8 Hz, 1H, CH_2Cl), 3.16 (dq, *J*= 8, 3 Hz, 1H, β-H), 2.55 (dd, *J*= 16, 3 Hz, 1H, α-CH_2), 2.45 (s, 3H, Me of Ts), 2.01 (dd, *J*= 16, 10 Hz, 1H, α-CH_2), 1.82-1.75, 1.55-1.18 (m, 2+4H, -C_3H_6-), 0.90 (t, *J*= 7 Hz, 3H, Me); ^{13}C NMR ($CDCl_3$) 167.98, 145.78, 133.95, 129.75, 128.22, 71.01, 59.27, 47.57, 46.16, 43.08, 38.69, 38.52, 28.30, 22.04, 21.75, 13.84; IR (CH_2Cl_2) 1747 (C=O) cm^{-1}; FAB-MS: *m/z* 444 [MH^++4], 442 [MH^++2], 440 [MH^+]; HRMS calcd for $C_{18}H_{24}NO_3Cl_3S$+H 440.0621, found 440.0618.

3b: Two isomers were isolated in pure form: *isomer A:* colorless oil; TLC R_f 0.62 (50% Et_2O/Hex); ^1H NMR ($CDCl_3$) 7.39-7.21 (m, 5H, Ph), 4.70, 4.36 (d, *J*= 15 Hz, 1Hx2, CH_2Ph), 3.87 (dd, *J*= 11, 4 Hz, 1H, CH_2Cl), 3.81-3.73 (m, 1H, CHCl), 3.67 (dd, *J*= 11, 10 Hz, 1H, CH_2Cl), 3.44 (dd, *J*= 10, 7 Hz, 1H, NCH_2), 3.34-3.26 (m, 1H, β-H), 3.10 (dd, *J*= 10, 9 Hz, 1H, NCH_2), 2.85 (dd, *J*= 16, 2 Hz, 1H, α-CH_2), 2.47 (dd, *J*= 16, 9 Hz, 1H, α-CH_2), 1.88-1.76, 1.60-

1.25 (m, 2+4H, -C_3H_6-), 0.92 (t, *J*= 7 Hz, 3H, Me); ^{13}C NMR ($CDCl_3$) 170.00, 135.25, 128.96, 128.12, 128.05, 71.46, 59.05, 47.73, 47.28, 44.92, 43.27, 42.07, 39.53, 28.08, 22.12, 13.92; IR (CH_2Cl_2) 1714 cm^{-1} (C=O); MS: *m/z* 377 [M$^+$+2], 375 [M$^+$]; HRMS calcd for $C_{18}H_{24}NOCl_3$: 375.0926, found 375.0909; *isomer B:* colorless oil; TLC R_f 0.51 (50% Et_2O/Hex); ^{1}H NMR ($CDCl_3$) 7.38-7.21 (m, 5H, Ph), 4.54, 4.49 (d, *J*= 15 Hz, 1Hx2, CH_2Ph), 4.22-4.15 (m, 1H, CHCl), 4.01 (dd, *J*= 11, 5 Hz, 1H, CH_2Cl), 3.61 (dd, *J*= 11, 9 Hz, 1H, CH_2Cl), 3.44 (dd, *J*= 9, 6 Hz, 1H, NCH_2), 3.13-2.97 (m, 1+1H, β-H and NCH_2), 2.70 (dd, *J*= 16, 2 Hz, 1H, α-CH_2), 2.58 (dd, *J*= 16, 10 Hz, 1H, α-CH_2), 1.90-1.78, 1.60-1.25 (m, 2+4H, -C_3H_6-), 0.92 (t, *J*= 7 Hz, 3H, Me); ^{13}C NMR ($CDCl_3$) 170.59, 135.28, 128.85, 128.08, 127.95, 71.11, 58.44, 47.86, 47.17, 46.12, 44.33, 43.24, 39.14, 28.18, 22.06, 13.86; IR (CH_2Cl_2) 1714 cm^{-1} (C=O); MS: *m/z* 377 [M$^+$+2], 375 [M$^+$]; HRMS calcd for $C_{18}H_{24}NOCl_3$: 375.0926, found 375.0958.

9a: colorless solid; mp. 180-181 °C (CH_2Cl_2/Hex); IR (CH_2Cl_2) 1749 cm^{-1} (C=O); FAB-MS *m/z* 416 [MH$^+$+4], 414 [MH$^+$+2], 412 [MH$^+$]; Anal. calcd for $C_{16}H_{20}NO_3Cl_3S$: C, 46.56; H, 4.88; N, 3.39. found: C, 46.52; H, 4.89; N, 3.36.

10a: colorless solid; mp. 151-153 °C (Et_2O/Hex.); IR (CH_2Cl_2) 1749 cm^{-1} (C=O); FAB-MS *m/z* 456 [MH$^+$+4], 454 [MH$^+$+2], 452 [MH$^+$]; Anal. calcd for $C_{19}H_{24}NO_3Cl_3S$: C, 50.40; H, 5.04; N, 3.09. found: C, 50.23; H, 5.30; N, 3.04.

11a (1:1 mixture of *E/Z* isomers): colorless solid; mp.102–104 °C (CH_2Cl_2/Hex); IR (CH_2Cl_2) 1747 (C=O) cm^{-1}; FAB-MS *m/z* 442 [MH$^+$+4], 440 [MH$^+$+2], 438 [MH$^+$]; Anal. calcd for $C_{18}H_{22}NO_3Cl_3S$: C, 49.26; H, 5.05; N, 3.19. found: C, 49.25; H, 5.04; N, 3.28.

12a: colorless solid; mp.126–128 °C (Et_2O); IR (CH_2Cl_2) 1747 (C=O), 1708 (CO_2Et) cm^{-1}; MS *m/z* 435 [M$^+$+2], 433 [M$^+$]; Anal. calcd for $C_{18}H_{21}NO_5Cl_2S$: C, 49.78; H, 4.87; N, 3.22. found: C, 49.59; H, 4.85; N, 3.19.

General procedures for the sequential reaction

In a typical example, the amide **1a** (71 mg, 0.199 mmol) and CuCl (2.0 mg, 0.020 mmol, 10 mol%) were measured into a 10 mL flask, and the atmosphere was replaced by argon. Then, degassed dichloroethane (2 mL) and methylenecyclohexane (240 μL, 192 mg, 2.00 mmol) were added and the mixture was allowed to warm at 83 °C. A 0.2 M dichloroethane solution of 2,2'-bipyridine (100 μL, 0.020 mmol) was added and heated at this temperature for 1 h. The resulting mixture was cooled to room temperature, and transferred to a head of a short pad of silica-gel. Elution with Et_2O (100 mL) gave a colorless solution, which was then concentrated *in vacuo*. The residue was purified with a silica gel column by using a 1 : 4 mixture of Et_2O-hexane as the eluent to afford the desired product (77 mg, 85%).

The intramolecular process -stepwise-

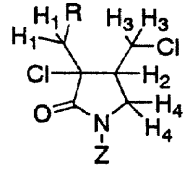
In a typical example, *N*-benzyl-*N*-geranyltrichloroacetamide **13b** (50 mg, 0.13 mmol) and CuCl (3.8 mg, 0.039 mmol, 30 mol%) were measured into a 10 mL flask, and the atmosphere was replaced by argon. Then, carefully degassed dichloromethane (0.6 mL) was added, and the mixture was allowed to keep at 15 °C. Then 2,2'-bipyridine (12.1 mg, 0.039 mmol) in 0.5 mL of dichloromethane was added, and the mixture was stirred at this temperature for 1 h. The resulting mixture was transferred to a head of a short pad of silica-gel. The elution with Et_2O was concentrated *in vacuo* to afford a 2:1 mixture of the monocyclic-γ-lactam **14b** (49 mg, 98%).

Table 5. ^{1}H Resonances of the compounds obtained by addition to α-olefins.[a,b]

Compounds	H1 (α-CH_2)	H2 (β-H)	H3 (CH_2Cl)	H4 (NCH_2)	Z	Others
cis-**4a** in $CDCl_3$	2.82[d] (dd, J=7,14, 1H) 2.77[d] (dd, J=8,14, 1H)	2.82 (dddd, J=5,7,9,10, 1H)	3.78 (dd, J=5,11, 1H) 3.57 (dd, J=9,11, 1H)	4.21 (dd, J=7,10, 1H) 3.43 (dd, J=10,10, 1H)	7.91 (d, J=8, 2H) 7.36 (d, J=8, 2H) 2.45 (s, 3H)	5.67 (dddd, J=7,8,10,17, 1H, olefin) 5.23[d] (d, J=10, 1H, olefin) 5.23[d] (d, J=17, 1H, olefin)
cis-**4a** in C_6D_6	2.43[d] (d, J=7, 2H)	2.09-2.00 (m, 1H)	3.16 (dd, J=5,11, 1H) 2.91 (dd, J=9,11, 1H)	3.92 (dd, J=7,10, 1H) 3.07 (t, J=10, 1H)	7.96 (d, J=8, 2H) 6.69 (d, J=8, 2H) 1.75 (s, 3H)	5.36 (ddt, J=7,7,10,17, 1H, olefin) 4.81[d] (d, J=17, 1H, olefin) 4.79[d] (d, J=10, 1H, olefin)
trans-**4a** in $CDCl_3$	2.76[d] (dd, J=6,16, 1H) 2.48[d] (dd, J=8,16, 1H)	2.89-2.85 (m, 1H)	3.70 (dd, J=4, 11, 1H) 3.41 (dd, J=9, 11, 1H)	4.10 (dd, J=6,11, 1H) 3.92 (dd, J=3,11, 1H)	7.92 (d, J=8, 2H) 7.35 (d, J=8, 2H) 2.44 (s, 3H)	5.79 (dddd, J=6,8,10,17, 1H, olefin) 5.20[d] (d, J=10, 1H, olefin) 5.18[d] (d, J=17, 1H, olefin)
trans-**4a** in C_6D_6	2.47[d] (dd, J=6,16, 1H) 1.98[d] (dd, J=7,16, 1H)	2.15-2.08 (m, 1H)	2.89 (dd, J=4, 11, 1H) 2.62 (dd, J=9, 11, 1H)	3.73 (dd, J=6, 10, 1H) 3.67 (dd, J=4, 10, 1H)	8.00 (d, J=8, 2H) 6.69 (d, J=8, 2H) 1.76 (s, 3H)	5.47 (dddd, J=6,7,10,17, 1H, olefin) 4.79[d] (d, J=10, 1H, olefin) 4.69[d] (d, J=17, 1H, olefin)
cis-**4b** in $CDCl_3$	2.92[d] (dd, J=7,14, 1H) 2.86[d] (dd, J=8,14, 1H)	2.75 (dddd, J=5,7,9,10, 1H)	3.79 (dd, J=5,11, 1H) 3.58 (dd, J=10,11, 1H)	3.35 (dd, J=7,10, 1H) 3.03 (dd, J=9,10, 1H)	7.36–7.18 (m,5H) 4.59 (d, J=15, 1H) 4.39 (d, J=15, 1H)	5.78 (dddd, J=7,8,10,17, 1H, olefin) 5.25[d] (d, J=17, 1H, olefin) 5.23[d] (d, J=10, 1H, olefin)
cis-**4b** in C_6D_6	2.86[d] (dd, J=7,14, 1H) 2.74[d] (dd, J=8,14, 1H)	2.29 (ddt, J=5,7,9,9, 1H)	3.37 (dd, J=5,11, 1H) 3.09 (dd, J=9,11, 1H)	2.76 (dd, J=7,10, 1H) 2.55 (dd, J=9,10, 1H)	7.09–6.91 (m,5H) 4.35 (d, J=15, 1H) 3.93 (d, J=15, 1H)	5.68 (dddd, J=7,8,10,17, 1H, olefin) 4.98[d] (d, J=17, 1H, olefin) 4.93[d] (d, J=10, 1H, olefin)
trans-**4b** in $CDCl_3$	2.93-2.87 (m, 1H) 2.58[d] (dd, J=8,16, 1H)	2.93-2.87 (m, 1H)	3.77 (dd, J=4,11, 1H) 3.41 (dd,J=10,11, 1H)	3.55 (dd, J=7,10, 1H) 3.15 (dd, J=4,10, 1H)	7.38–7.24 (m, 5H) 4.59 (d, J=15, 1H) 4.45 (d, J=15, 1H)	5.95 (dddd, J=6,8,10,17, 1H, olefin) 5.26[d] (d, J=17, 1H, olefin) 5.24[d] (d, J=10, 1H, olefin)
trans-**4b** in C_6D_6	2.77[d] (dd, J=6,16, 1H) 2.26[d] (dd, J=8,16, 1H)	2.45 (ddt, J=4,4,6,10, 1H)	3.16 (dd, J=4,11, 1H) 2.75 (dd, J=10,11, 1H)	3.02 (dd, J=6,10, 1H) 2.64 (dd, J=4,10, 1H)	7.09–7.00 (m,5H) 4.19 (d, J=15, 1H) 4.09 (d, J=15, 1H)	5.80 (dddd, J=6,8,10,17, 1H, olefin) 4.93[d] (d, J=10, 1H, olefin) 4.89[d] (d, J=17, 1H, olefin)
cis-**8a** in $CDCl_3$	2.09-1.95 (m, 2H)	2.77 (dddd, J=5,7,9,10, 1H)	3.76 (dd, J=5,11, 1H) 3.60 (dd, J=9,11, 1H)	4.22 (dd, J=7,10, 1H) 3.43 (dd, J=10,10, 1H)	7.91 (d, J=8, 2H) 7.36 (d, J=8, 2H) 2.45 (s, 3H)	1.54-1.42 (m, 1H, Pr) 1.34-1.20 (m, 1H, Pr) 0.93 (t, J=7, 3H, Pr)
cis-**8a** in C_6D_6	1.71 (ddd, J=5,12,14, 1H) 1.61 (ddd, J=5,12,14, 1H)	2.00-1.95 (m, 1H)	3.09 (dd, J=6,11, 1H) 2.97 (dd, J=9,11, 1H)	3.95 (dd, J=7,10, 1H) 3.10 (t, J=10, 1H)	7.97 (d, J=8, 2H) 6.71 (d, J=8, 2H) 1.76 (s, 3H)	1.07-0.98 (m, 1H, Pr) 0.91-0.83 (m, 1H, Pr) 0.58 (t, J=7, 3H, Pr)
trans-**8a** in $CDCl_3$	1.97-1.87 (m, 1H) 1.68-1.51 (m, 1H)	2.84 (ddt, J=4,4,6,10, 1H)	3.63 (dd, J=4,11, 1H) 3.31 (dd, J=10,11, 1H)	4.09 (dd, J=6,11, 1H) 3.94 (dd, J=4,11, 1H)	7.93 (d, J=8.2, 2H) 7.36 (d, J=8.2, 2H) 2.45 (s, 3H)	1.68-1.51 (m, 1H, Pr) 1.43-1.30 (m, 1H, Pr) 0.93 (t, J=7, 3H, Pr)
trans-**8a** in C_6D_6	1.59 (ddd, J=4,12,15, 1H) 1.03 (ddd, J=4,12,15, 1H)	2.10 (ddt, J=4,4,6,10, 1H)	2.78 (dd, J=4,11, 1H) 2.51 (dd, J=10,11, 1H)	3.74 (dd, J=6,10, 1H) 3.67 (dd, J=4,10, 1H)	8.00 (d, J=8.2, 2H) 6.69 (d, J=8.2, 2H) 1.76 (s, 3H)	1.39-1.28 (m, 1H, Pr) 0.99-0.89 (m, 1H, Pr) 0.51 (t, J=7, 3H, Pr)

cis-**8b** in $CDCl_3$	2.20-2.06 (m, 2H)	2.71 (dddd, J=5,7,9,10, 1H)	3.79 (dd, J=5,11, 1H) 3.63 (dd, J=10,11, 1H)	3.38 (dd, J=7,10, 1H) 3.05 (dd, J=9,10, 1H)	7.40–7.20 (m, 5H) 4.59, 4.42 (d, J= 15, 1Hx2)	1.61-1.47 (m, 1H, Pr) 1.44-1.30 (m, 1H, Pr) 1.00 (t, J=7, 3H, Pr)
cis-**8b** in C_6D_6	2.05 (ddd, J=5,12,14, 1H) 1.93 (ddd, J=5,12,14, 1H)	2.19-2.12 (m, 1H)	3.32 (dd, J=5,11, 1H) 3.16 (dd, J=9,11, 1H)	2.81 (dd, J=7,10, 1H) 2.59 (dd, J=9,10, 1H)	7.11–7.01 (m, 5H) 4.32 (d, J= 15, 1H) 4.01 (d, J= 15, 1H)	1.30-1.21 (m, 1H, Pr) 1.19-1.10 (m, 1H, Pr) 0.74 (t, J=7, 3H, Pr)
trans-**8b** in $CDCl_3$	2.04 (ddd,J=4,12,15,1H) 1.64 (ddd,J=4,12,15,1H)	2.87 (ddt, J=4,4,6,11,1H)	3.67 (dd, J=4,11, 1H) 3.32 (t, J=11, 1H)	3.54 (dd, J=6,10, 1H) 3.14 (dd, J=4,10, 1H)	7.37–7.23 (m, 5H) 4.58, 4.44 (d, J= 15, 1Hx2)	1.82-1.72 (m, 1H, Pr) 1.53-1.43 (m, 1H, Pr) 0.99 (t, J=7, 3H, Pr)
trans-**8b** in C_6D_6	1.87 (ddd,J=4,12,15,1H) 1.28 (ddd,J=4,12,15,1H)	2.43 (ddt, J=4,4,6,11, 1H)	3.04 (dd, J=4,10, 1H) 3.04 (dd, J=6,10, 1H)	2.64 (t, J=11, 1H) 2.64 (dd, J=4, 11, 1H)	7.09–7.01 (m, 5H), 4.17, 4.11 (d, J=15, 1Hx2)	1.73-1.62 (m, 1H, Pr) 1.26-1.18 (m, 1H, Pr) 0.70 (t, J=7, 3H, Pr)
9a in $CDCl_3$	2.75 (d, J= 16, 1H) 2.48 (d, J= 16, 1H)	3.54-3.46 (m, 1H)	4.00-3.95 (m, 1H) 3.65-3.59 (m, 1H)	4.40-4.34 (m, 1H) 3.54-3.46 (m, 1H)	7.91 (d, J=8, 2H) 7.35 (d, J=8, 2H) 2.44 (s, 3H)	1.64 (s, 3H, Me) 1.35 (s, 3H, Me)
10a in $CDCl_3$	2.75 (d, J=16, 1H) 2.48 (d, J=16, 1H)	3.54-3.47 (m, 1H)	4.02 (dd, J=3,11, 1H) 3.63 (t, J= 11, 1H)	4.38-4.32 (m, 1H) 3.54-3.47 (m, 1H)	7.91 (d, J=8, 2H), 7.35 (d, J=8, 2H) 2.44 (s, 3H)	1.95–1.40, 1.16-1.10 (m, 9+1H, *cyclo*-C_6H_{10})
11a (*E*/*Z*=1/1) in $CDCl_3$	2.98-2.85 (m, 2H)	2.73-2.66 (m, 1H) *2.68-2.62 (m, 1H)*	3.75 (dd, J=4,11, 1H) *3.71 (dd, J=4,11, 1H)* 3.56 (t, J=11, 1H) *3.54 (t, J=11, 1H)*	4.31-4.26 (m, 1H) 3.49-3.40 (m, 1H)	7.91 (d, J=8, 2H) 7.35 (d, J=8, 2H) 2.44 (s, 3H)	4.19, 4.02 (d, J= 11, 1Hx2, CH_2Cl) *4.08, 4.01 (d, J= 11, 1Hx2, CH_2Cl)* 1.85, 1.69 (s, 3H, Me) *1.79, 1.62 (s, 3H, Me)*
12a in $CDCl_3$	3.11-3.06 (m, 2H)	2.62 (m, 1H)	3.92 (dd, J=4,11, 1H) 3.54 (t, J=11, 1H)	4.29-4.20 (m, 1H) 3.42 (t, J=10, 1H)	7.90 (d, J=8, 2H) 7.36 (d, J=8, 2H) 2.45 (s, 3H)	6.39, 5.88 (d, J=1, 1H, $=CH_2$) 4.29-4.20 (m, 2H, OCH_2CH_3) 1.33 (t, J= 7, 3H, OCH_2CH_3)

a. Chemical shifts (δ-values from TMS; ppm) are listed.
b. Coupling constants (*J*) are recorded in Hz.
c. Numbering of the protons is as follows:



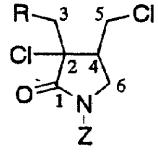
d. The long range couplings were also seen.

Table 6. ^{13}C Resonances of the compounds obtained by addition to α-olefins.[a]

Compounds	C1 (C=O)	C2	C3	C4	C5	C6	Z	others
cis-**4a** in $CDCl_3$	168.03	71.09	40.94	42.86	41.22	47.74	145.86, 133.78, 129.84, 128.10, 21.75	130.33, 121.83 ($CH=CH_2$)
trans-**4a** in $CDCl_3$	168.07	70.09	37.78	46.49	41.26	47.44	145.80, 134.01, 129.77, 128.16, 21.70	129.98, 120.84 ($CH=CH_2$)
cis-**8a** in C_6D_6	168.17	72.86	38.75	43.03	41.44	47.70	145.28, 134.91, 129.72, 128.53, 21.15	18.27, 13.89 ($CH_2CH_2CH_3$)
trans-**8a** in C_6D_6	168.03	71.94	34.90	46.73	41.21	47.39	145.19, 135.23, 129.68, 128.59, 21.12	17.23, 13.72 ($CH_2CH_2CH_3$)
cis-**4b** in $CDCl_3$	170.25	71.08	42.05	43.27	42.49	47.75	135.31, 128.85, 127.99 127.91, 47.04	131.54, 120.88 ($CH=CH_2$)
trans-**4b** in $CDCl_3$	170.17	70.56	38.70	47.90	41.96	47.26	135.29, 128.87, 128.27, 128.01, 47.33	131.34, 120.08 ($CH=CH_2$)
cis-**8b** in $CDCl_3$	170.76	72.40	39.75	43.75	42.78	47.78	135.48, 128.90, 128.06, 127.94, 47.07	18.52, 14.12 ($CH_2CH_2CH_3$)
trans-**8b** in $CDCl_3$	170.52	72.03	35.81	48.08	42.11	47.16	135.43, 128.88, 128.18, 127.97, 47.26	17.64, 14.08 ($CH_2CH_2CH_3$)
9a in $CDCl_3$	168.25	71.64	48.67	41.88	41.69	48.01	145.86, 133.67, 129.78, 128.15, 21.73	67.17, 36.07, 30.48 ($CClMe_2$)
10a in $CDCl_3$	168.38	71.72 (72.81)	49.36	42.26	41.87	48.02	145.78, 133.58, 129.71, 128.07, 21.69	72.81 (71.72), 42.12, 37.14, 24.60, 21.53, 21.29 ($-C_5H_{10}-$)
11a (*E*/*Z* = 1/1) in $CDCl_3$	168.42 168.34	71.54 71.53	41.01 40.35	43.37 42.88	41.91 41.86	48.07, 48.01	145.87, 133.59, 133.58, 129.79, 128.12, 128.11, 21.70	132.52, 132.39, 129.31, 128.27 (C=C) 45.82, 45.74 (CH_2Cl), 19.84, 19.08, 17.94, 17.73 (Me)
12a in $CDCl_3$	167.81	71.69	36.47	42.77	41.72	48.08	145.83, 133.71 (or133.17) 129.80, 128.07, 21.72	166.63, 61.72, 14.09 (CO_2Et) 133.17 (or133.71), 133.12 ($C=CH_2$)

a. Chemical shifts (δ-values from TMS; ppm) are listed.

b. Numbering of the carbons is as follows:



To a solution of the lactam **14b** (27 mg, 0.067 mmol) and CuCl (2.1 mg, 0.021 mmol, 30 mol%) in dichloromethane (0.7 mL) was added 2,2'-bipyridine (3.3 mg, 0.019 mmol) in 0.5 mL of dichloromethane at 40 °C and the resulting mixture was stirred at this temperature for 1h. The mixture was passed through a silica-gel column (elution with Et_2O), and the combined eluents were concentrated. The resulting crude product **15b** was then treated with silica-gel in CH_2Cl_2 at room temperature, filtered, and concentrated *in vacuo*. The residue was purified with a silica gel column by using a 1 : 2 mixture of Et_2O-hexane as the eluent to afford 9 mg (31%, minor isomer) and 17 mg (63%, major isomer) of the bicyclic lactam **16b**.

The cyclization of *N*-tosyl derivative **13a** gave the monocyclic lactam **14a** (65%) at -5 °C using 10 mol% of catalyst. A small amount of the bicyclic lactam **15a** (27%) was also obtained.

The double cyclization

In a typical example, *N*-benzyl-*N*-geranyltrichloroacetamide **13b** (25 mg, 0.064 mmol) and CuCl (1.9 mg, 0.019 mmol, 30 mol%) were measured into a 10 mL flask, and the atmosphere was replaced by argon. Then, carefully degassed dichloromethane (0.8 mL) and the mixture was allowed to warm at 40 °C. Then 2,2'-bipyridine (3.0 mg, 0.019 mmol) in 0.3 mL of dichloromethane was added and stirred at this temperature for 1 h. The resulting mixture was transferred to a head of a short pad of silica-gel. Elution with Et_2O (100 mL) was concentrated *in vacuo*. The resulting crude product was then treated with silica-gel in CH_2Cl_2 at room temperature, filtered, and concentrated *in vacuo*. The residue was purified with a silica gel column by using a 1 : 2 mixture of Et_2O-hexane as the eluent to afford 7 mg (31%, minor isomer) and 14 mg (62%, major isomer) of the bicyclic lactam **16b**. As for the *N*-tosyl derivative, silica-gel mediated dehydrochlorination of **15a** was carried out at 40 °C.

13a: *E-form:* pale yellow oil; TLC R_f 0.78 (50% Et_2O/Hex); ^1H NMR ($CDCl_3$) 7.92, 7.32 (d, J= 8 Hz, 2Hx2, Ts), 5.22 (t, J= 6 Hz, 1H, =CH), 5.07 (t, J= 7 Hz, 1H, =CH), 4.91 (d, J= 6 Hz, 2H, NCH_2), 2.45 (s, 3H, Me of Ts), 2.13-2.05 (m, 4H, C_2H_4), 1.78, 1.67, 1.60 (s, 3Hx3, Me); ^{13}C NMR ($CDCl_3$) 159.24, 145.41, 140.25, 135.08, 131.96, 129.53, 129.31, 123.60, 119.23, 92.25, 47.75, 39.44, 26.13, 25.70, 21.72, 17.71, 16.61; IR (CH_2Cl_2) 1708 (C=O), 1366, 1259, 1172, 1086 cm^{-1}; *Z-form:* pale yellow oil; TLC R_f 0.75 (50% Et_2O/Hex); ^1H NMR ($CDCl_3$) 7.92, 7.32 (d, J= 8 Hz, 2Hx2, Ts), 5.20 (t, J= 6 Hz, 1H, =CH), 5.15 (t, J= 7 Hz, 1H, =CH), 4.89 (d, J= 6 Hz, 2H, NCH_2), 2.45 (s, 3H, Me of Ts), 2.23-2.20, 2.18-2.13 (m, 2Hx2, C_2H_4), 1.78, 1.71, 1.63 (s, 3Hx3, Me); ^{13}C NMR ($CDCl_3$) 159.23, 145.40, 140.44, 135.07, 132.42, 129.59, 129.28, 123.63, 120.17, 92.24, 47.56 , 32.31, 26.13, 25.81, 23.36, 21.72, 17.72; IR (CH_2Cl_2) 1710 (C=O), 1366, 1259, 1173, 1087 cm^{-1}.

14a: Since separation of concomitantly formed **15a** was difficult to achieve, the compounds were not isolated in pure form; *major isomer*: colorless oil; TLC R_f0.62 (50% Et_2O/Hex); ^1H NMR ($CDCl_3$) 7.95, 7.38 (d, J= 8 Hz, 2Hx2, Ts), 5.10 (t, J= 7 Hz, 1H, =CH), 4.22 (dd, J= 10, 7 Hz, 1H, NCH_2), 3.93 (t, J= 10 Hz, 1H, NCH_2), 3.13 (dd, J= 10, 7 Hz, 1H, β-H), 2.47 (s, 3H, Me of Ts), 2.38-2.13, 2.08-1.90 (m, 2Hx2, C_2H_4), 1.86, 1.70, 1.64 (s, 3Hx3, Me); ^{13}C NMR ($CDCl_3$) 163.25, 146.31, 133.42, 133.22, 130.01, 128.33, 122.22, 81.93, 72.03, 56.69, 45.95, 44.32, 27.10, 25.65, 23.14, 21.78, 17.76; *minor isomer*: colorless oil; TLC R_f0.58 (50% Et_2O/Hex); ^1H NMR ($CDCl_3$) 7.95, 7.38 (d, J= 8 Hz, 2Hx2, Ts), 5.10 (t, J= 7 Hz; 1H, =CH), 4.21 (dd, J= 10, 7 Hz, 1H, NCH_2), 3.96 (t, J= 10 Hz, 1H, NCH_2), 3.13 (dd, J= 10, 7 Hz, 1H, β-H), 2.47 (s, 3H, Me of Ts), 2.37-1.97 (m, 1+2+1H, C_2H_4), 1.79, 1.70, 1.63 (s, 3Hx3, Me); ^{13}C NMR

($CDCl_3$) 163.30, 146.32, 133.39, 133.06, 130.02, 128.36, 122.51, 81.82, 71.61, 58.30, 45.62, 40.82, 29.56, 25.67, 23.31, 21.79, 17.72; IR (CH_2Cl_2) 1763 (C=O), 1377, 1273, 1176, 1130 cm^{-1}.

15a: *major isomer*: colorless solid; mp. 153-156 °C; TLC R_f0.46 (50% Et_2O/Hex); ^1H NMR ($CDCl_3$) 7.95, 7.38 (d, *J*= 8 Hz, 2Hx2, Ts), 3.84 (dd, *J*= 10, 8 Hz, 1H, NCH_2), 3.59 (t, *J*= 10 Hz, 1H, NCH_2), 2.80 (dd, *J*= 10, 8 Hz, 1H, *fused*-CH), 2.46 (s, 3H, Me of Ts), 2.30-2.16 (m, 4H, CH + 3H of C_2H_4), 1.96-1.89 (m, 1H, C_2H_4), 1.71, 1.60, 1.57 (s, 3Hx3, Me); ^{13}C NMR ($CDCl_3$) 168.49, 146.08, 134.21, 129.99, 128.34, 76.08, 70.56, 65.61, 55.53, 51.08, 45.43, 38.23, 33.40, 30.71, 29.27, 21.73, 21.46; IR (CH_2Cl_2) 1755 (C=O), 1373, 1271, 1174 cm^{-1}; FAB-MS: *m/z* 456 [MH^++4], 454 [MH^++2], 452 [MH^+]; HRMS calcd for $C_{19}H_{24}NO_3Cl_3S$+H 452.0621, found 452.0621; *minor isomer*: colorless solid; mp. 158-161 °C; TLC R_f0.61 (50% Et_2O/Hex); ^1H NMR ($CDCl_3$) 7.97, 7.38 (d, *J*= 8 Hz, 2Hx2, Ts), 4.05 (dd, *J*= 11, 8 Hz, 1H, NCH_2), 3.86 (t, *J*= 11 Hz, 1H, NCH_2), 2.65 (dd, *J*= 11, 8 Hz, 1H, *fused*-CH), 2.46 (s, 3H, Me of Ts), 2.37-2.33 (m, 1H, CH), 2.32-2.26, 2.26-2.21, 1.90-1.80 (m, 1+2+1H, C_2H_4), 1.87, 1.67, 1.60 (s, 3Hx3, Me); ^{13}C NMR ($CDCl_3$) 169.02, 145.92, 134.37, 129.96, 128.39, 74.85, 72.28, 67.94, 55.45, 50.35, 46.60, 38.72, 33.46, 31.86, 29.81, 23.37, 21.75; IR (CH_2Cl_2) 1753 (C=O), 1373, 1271, 1174 cm^{-1}; FAB-MS *m/z* 456 [MH^++4], 454 [MH^++2], 452 [MH^+]; HRMS calcd for $C_{19}H_{24}NO_3Cl_3S$+H 452.0621, found 452.0628.

16a: *major isomer*: colorless solid; mp. 178.5-180.5 °C; ^1H NMR ($CDCl_3$) 7.96, 7.36 (d, *J*= 8 Hz, 2Hx2, Ts), 4.92, 4.39 (s, 1Hx2, $=CH_2$), 3.97 (dd, *J*= 10, 8 Hz, 1H, NCH_2), 3.56 (t, *J*= 10 Hz, 1H, NCH_2), 3.00 (dd, *J*= 10, 8 Hz, 1H, *fused*-CH), 2.45 (s, 3H, Me of Ts), 2.28-2.14 (m, 3H, CH + 2H of C_2H_4), 1.89-1.84, 1.58-1.54 (m, 1Hx2, C_2H_4), 1.68, 1.62 (s, 3Hx2, Me); ^{13}C NMR ($CDCl_3$) 168.27, 145.91, 141.61, 134.31, 129.83, 128.43, 116.99, 70.56, 65.64, 53.06, 46.32, 45.68, 38.11, 23.02, 30.66, 22.00, 21.71; IR (CH_2Cl_2) 1759 (C=O), 1370, 1261, 1175 cm^{-1}; MS: *m/z* 417 [M^++2], 415 [M^+]; HRMS calcd for $C_{19}H_{23}NO_3Cl_2S$ 415.0776, found 415.0775; *minor isomer*: colorless solid; mp. 174.5-176 °C; ^1H NMR ($CDCl_3$) 7.97, 7.36 (d, *J*= 8 Hz, 2Hx2, Ts), 4.93, 4.42 (s, 1Hx2, $=CH_2$), 4.14 (dd, *J*= 11, 8 Hz, 1H, NCH_2), 3.83 (t, *J*= 11 Hz, 1H, NCH_2), 2.82 (dd, *J*= 11, 8 Hz, 1H, *fused*-CH), 2.45 (s, 3H, Me of Ts), 2.39 (dd, *J*= 12, 3 Hz, 1H, CH), 2.18-2.15, 1.90-1.83, 1.68-1.60 (m, 2+1+1H, C_2H_4), 1.89, 1.65 (s, 3Hx2, Me); ^{13}C NMR ($CDCl_3$) 167.95, 145.75, 141.28, 134.51, 129.80, 128.44, 116.99, 72.26, 68.08, 53.11, 46.87, 45.91, 38.60, 24.79, 32.18, 22.25, 21.71; IR (CH_2Cl_2) 1752 (C=O), 1371, 1175, 1119 cm^{-1}; MS: *m/z* 417 [M^++2], 415 [M^+]; HRMS calcd for $C_{19}H_{23}NO_3Cl_2S$ 415.0776, found 415.0783.

13b: pale yellow oil; TLC R_f0.58 (15% Et_2O/Hex); ^1H NMR ($CDCl_3$) 7.4-7.1 (m, 5H, Ph), 5.16, 5.07 (br, 1Hx2, =CHx2), 4.91, 4.63, 4.22, 3.98 (br, total 4H, CH_2Ph, NCH_2), 2.08 (br, 4H, C_2H_4), 1.69, 1.62, 1.56, 1.51 (br, total 9H, Mex3); ^{13}C NMR ($CDCl_3$) 160.25, 140.64, 135.59, 131.28, 128.23, 127.19, 126.79, 123.25, 118.35, 117.03, 93.01, 51.31, 49.41, 46.21, 44.95, 38.99, 25.66, 25.23, 17.22, 15.78; IR (CH_2Cl_2) 1677 (C=O) cm^{-1}; FAB-MS *m/z* 392 [MH^++4], 390 [MH^++2], 388 [MH^+]; HRMS calcd for $C_{19}H_{24}NOCl_3$+H 388.1002, found 388.0996.

14b: *major isomer*: colorless oil; TLC R_f0.41 (50% Et_2O/Hex); ^1H NMR ($CDCl_3$) 7.40-7.24 (m, 5H, Ph), 5.09 (t, *J*= 7 Hz, 1H, =CH), 4.61, 4.51 (d, *J*= 15 Hz, 1Hx2, CH_2Ph), 3.52 (t, *J*= 10 Hz, 1H, NCH_2), 3.42 (dd, *J*= 10, 7 Hz, 1H, NCH_2), 3.20 (dd, *J*= 10, 7 Hz, 1H, β-H), 2.38-2.26, 2.23-2.15, 2.05-1.94 (m, 1+1+2H, C_2H_4), 1.86, 1.68, 1.61 (s, 3Hx3, Me); ^{13}C NMR ($CDCl_3$) 166.17, 134.59, 132.96, 129.06, 128.26, 128.17, 122.51, 82.75, 73.08, 57.93, 47.84, 45.59, 44.09, 26.81, 25.69, 23.18, 17.74; IR (CH_2Cl_2) 1728 (C=O), 1435, 1257, 1136 cm^{-1}; FAB-MS *m/z* 392 [MH^++4], 390 [MH^++2], 388 [MH^+]; HRMS calcd for $C_{19}H_{24}NOCl_3$+H 388.1002,

found 388.1003; *minor isomer*: colorless oil; TLC R_f0.31 (50% Et_2O/Hex); ^1H NMR ($CDCl_3$) 7.40-7.21 (m, 5H, Ph), 5.10 (t, J= 7 Hz, 1H, =CH), 4.61, 4.52 (d, J= 15 Hz, 1Hx2, CH_2Ph), 3.57 (t, J= 10 Hz, 1H, NCH_2), 3.40 (dd, J= 10, 8 Hz, 1H, NCH_2), 3.19 (dd, J= 10, 8 Hz, 1H, β-H), 2.33-2.15, 2.08-1.98 (m, 3+1H, C_2H_4), 1.77, 1.69, 1.62 (s, 3Hx3, Me); ^{13}C NMR ($CDCl_3$) 166.21, 134.59, 132.83, 129.07, 128.27, 128.19, 122.78, 82.63, 72.53, 59.48, 47.86, 45.25, 40.43, 29.38, 25.70, 23.38, 17.71; IR (CH_2Cl_2) 1728 (C=O), 1437, 1255, 1136 cm^{-1}; FAB-MS *m/z* 392 [MH^++4], 390 [MH^++2], 388 [MH^+]; HRMS calcd for $C_{19}H_{24}NOCl_3$+H 388.1002, found 388.1009.

15b: Because of facile dehydrochlorination from **15b**, the products were not isolated in pure form; *major isomer*: colorless oil; TLC R_f0.21 (30% Et_2O/Hex); ^1H NMR ($CDCl_3$) 7.42-7.15 (m, 5H, Ph), 4.56, 4.42 (d, J= 15 Hz, 1Hx2, CH_2Ph), 3.10 (dd, J= 10, 9 Hz, 1H, NCH_2), 3.04 (dd, J= 10, 9 Hz, 1H, NCH_2), 2.88 (t, J= 10 Hz, 1H, *fused*-CH), 2.35-2.07 (m, 4H, CH+3H of C_2H_4), 1.89, 1.79 (s, 3Hx2, Me), 1.85-1.73 (m, 1H, C_2H_4), 1.48 (s, 3H, Me); ^{13}C NMR ($CDCl_3$) 171.65, 135.28, 129.08, 128.17, 128.11, 77.95, 70.93, 66.77, 57.79, 51.96, 47.77, 45.72, 38.59, 34.30, 30.89, 29.39, 21.84; IR (CH_2Cl_2) 1730 (C=O), 1605 cm^{-1}; MS *m/z* 316 [M-HCl-Cl]; *minor isomer*: colorless oil; TLC R_f0.39 (30% Et_2O/Hex); ^1H NMR ($CDCl_3$) 7.40-7.15 (m, 5H, Ph), 4.56, 4.41 (d, J= 15 Hz, 1Hx2, CH_2Ph), 3.38-3.28 (m, 2H, NCH_2), 2.71 (t, J= 9 Hz, 1H, *fused*-CH), 2.35-2.19 (m, 2H, CH+1H of C_2H_4), 2.19-2.10, 1.91-1.76 (m, 2+1H, C_2H_4), 1.85, 1.83, 1.72 (s, 3Hx3, Me); ^{13}C NMR ($CDCl_3$) 171.05, 135.40, 128.98, 128.21, 128.05, 76.41, 72.87, 69.00, 57.60, 51.16, 47.85, 46.91, 39.06 , 34.13, 32.06, 29.83, 23.68; IR (CH_2Cl_2) 1714 (C=O) cm^{-1}; MS *m/z* 351 [M-HCl].

16b: *major isomer*; colorless solid; mp.144.5–146 °C (Et_2O/Hex); TLC R_f0.10 (30% Et_2O/Hex); ^1H NMR ($CDCl_3$) 7.39-7.24 (m, 5H, Ph), 5.07, 4.79 (s, 1Hx2, $=CH_2$), 4.76, 4.28 (d, J= 15 Hz, 1Hx2, CH_2Ph), 3.21 (dd, J= 9, 8 Hz, 1H, NCH_2), 3.06 (dd, J= 10, 8 Hz, 1H, *fused*-CH), 2.98 (dd, J= 10, 9 Hz, 1H, NCH_2), 2.36-2.28 (m, 1H, C_2H_4), 2.21 (dd, J= 12.3, 2.7 Hz, 1H, CH), 2.14-2.08 (m, 1H, C_2H_4), 1.89 (s, 3H, Me), 1.78-1.73, 1.54-1.49 (m, 1Hx2, C_2H_4), 1.52 (s, 3H, Me); ^{13}C NMR ($CDCl_3$) 170.75, 143.12, 135.46, 128.93, 128.28, 128.05, 116.33 , 70.85, 66.82, 54.96, 47.37, 47.12, 45.92, 38.53, 30.79, 23.72, 22.94; IR (CH_2Cl_2) 1714 (C=O) cm^{-1}; MS *m/z* 353 [M^++2], 351 [M^+]; Anal. calcd for $C_{19}H_{23}NOCl_2$: C, 64.78; H, 6.58; N, 3.98. found: C, 64.56; H, 6.64; N, 4.11: *minor isomer*; colorless solid; TLC R_f0.29 (30% Et_2O/Hex); ^1H NMR ($CDCl_3$) 7.39-7.26 (m, 5H, Ph), 5.06, 4.74 (s, 1Hx2, $=CH_2$), 4.71, 4.34 (d, J= 15 Hz, 1Hx2, CH_2Ph), 3.40 (dd, J= 10, 8 Hz, 1H, NCH_2), 3.26 (dd, J= 10, 9 Hz, 1H, NCH_2), 2.88 (dd, J= 9, 8 Hz, 1H, *fused*-CH), 2.37 (dd, J= 12, 3 Hz, 1H, CH), 2.15-2.05 (m, 2H, C_2H_4), 1.91, 1.84 (s, 3Hx2, Me), 1.95-1.87, 1.62-1.57 (m, 1Hx2, C_2H_4); ^{13}C NMR ($CDCl_3$) 170.38, 142.73, 135.62, 128.92, 128.42, 128.01, 116.32, 72.84, 69.31, 55.02, 47.50, 47.21, 46.71, 39.11, 32.45, 25.50, 23.13; IR (CH_2Cl_2) 1713 (C=O) cm^{-1}; MS *m/z* 353 [M^++2], 351 [M^+]; HRMS calcd for $C_{19}H_{23}NOCl_2$ 351.1157, found 351.1151.

Dehydrochlorination of ***16b***.

The bicyclic lactam **16b** (26 mg, 0.074 mmol) was treated with an ethanolic solution of NaOEt (0.16 mmol). After heating the mixture at 80 °C for 4 h, the reaction was quenched with 1N HCl (5 mL), and the mixture was extracted with ether (3 times). The organic extract was washed with brine, dried over $MgSO_4$, filtered, and concentrated. Silica gel chromatography (Et_2O/Hex) of the residue afforded the dehydrochlorinated product **17** (7.8 mg, 39%).

17: colorless solid; mp. 112-114 °C (Hex); TLC R_f 0.45 (30% Et_2O/Hex); ^1H NMR ($CDCl_3$) 7.40-7.20 (m, 5H, Ph), 4.79 (s, 2H, CH_2Ph), 4.41 (sep, J= 9 Hz, 1H, CH of Pr^i), 4.10 (s, 2H, NCH_2), 2.22 (s, 3H, Me), 1.27 (d, J= 9 Hz, 6H, Me of Pr^i); ^{13}C NMR ($CDCl_3$) 169.39, 146.65, 140.54, 137.36, 132.21, 129.37, 128.76, 128.19, 127.86, 127.57, 124.99, 48.02, 46.29, 26.34 , 23.62, 17.10; IR (KBr) 1666 (C=O) cm^{-1}; MS *m/z* 279 [M^+]; Anal. calcd for $C_{19}H_{21}NO$: C, 81.68; H, 7.58; N, 5.01. found: C, 81.77; H, 7.64; N, 5.03.

X-ray Data Collection and Reduction

Single crystals of **4a** were grown from a mixture of pentane and dichloromethane, whereas those of **16b** were done from a mixture of hexane and dichloromethane; both crystals were colorless prisms. X-ray crystallography measurement was performed on an Enraf-Nonius FR590 computer-controlled κ axis diffractometer with graphite monochromated Cu Kα radiation (λ = 1.54184 Å). The data were collected at 23±2 °C using ω-2θ technique to a maximum 2θ value of 67.96 and 67.71 deg, respectively. The structure was solved by direct method (SIR92) and was refined using full-matrix least squares (SHELEXL93) based on F^2 of all independent reflections measured. All H atoms were located at ideal positions and were included in refinement, but restricted to riding on the atom to which they are bonded. Isotopic thermal factors of H atoms were held to 1.2 times or 1.5 times (for methyl groups) U_{eq} of the riding atoms. The crystallographic data are listed in Table 7.

Table 7. Crystallographic data of **4a** and **16b**.

	4a	**16b**
Formula	$C_{15}H_{17}Cl_2NO_3S$	$C_{38}H_{48}Cl_4N_2O_2$
Formula weight	362.26	706.58
Crystal Size (mm)	0.06 x 0.15 x 0.30	0.09 x 0.12 x 0.12
Crystal System	Monoclinic	monoclinic
Space Group	$P2_1/n$ (#14)	$P2_1$ (#4)
a / Å	13.851 (5)	15.498 (5)
b / Å	8.090 (5)	11.745 (5)
c / Å	16.035 (5)	9.907 (5)
β (deg)	106.851 (5)	100.456 (5)
V / Å^3	1719.6 (13)	1773.4(3)
Z	4	2
Dcalc / g cm^{-3}	1.399	1.323
μ / mm^{-1}	4.628	3.311
No. of Reflections	3141	3391
No. of Obsd. refl. [$I > 2\sigma(I)$]	1865	2064
Refined Parameters	200	415
Refinement	F^2 (SHELEXL93)	F^2 (SHELEXL93)
$R[F^2 > 2\sigma(F^2)]$	0.0591	0.0367
$\omega R(F^2)$	0.1367	0.0920
GOF	1.06	1.08

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