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# Structural Factors Affecting the Selectivities in the Palladium (II) Catalyzed Cyclization of N-Alkenyl-2-Alkynamides

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***Abstract***: Palladium catalyzed cyclization of N-alkenyl 2-alkynamides occurred smoothly in the presence of $CuCl_2$ and LiCl affording α-chloroalkylidene-γ-butyrolactams and α-chloroalkylidene-δ-valerolactams stereoselectively. The regioselectivity of the intramolecular C-C double bond insertion was influenced by the substituent group on the substrate. When an alkyl group was introduced into the 1'-position of the alkenyl, an unusual 1,2-induction occurred. For the 3-substituted 2-alkynamides, only *cis*-β,γ-substituted γ-butyrolactams were resulted. Copyright © 1996 Elsevier Science Ltd

## INTRODUCTION

Natural products containing the α-methylene-γ-butyrolactam skeleton show some important biological activities, such as cytotoxicity,[1] antitumor,[2] antiinflammation,[3] etc. Their low toxicity as compared with the corresponding α-methylene-γ-butyrolactones makes them potentially appropriate for cancer treatment.[4] Due to their potential uses , many chemists have studied the construction of such a α-methylene-γ-butyrolactam unit.[5]

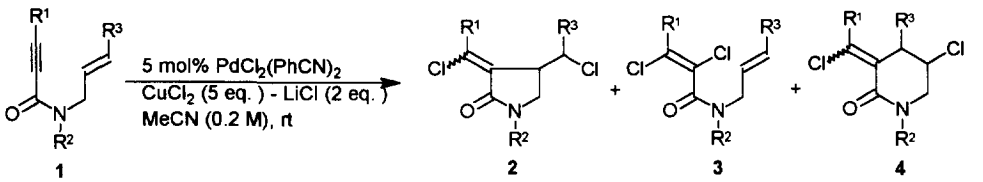
Transition metal catalyzed reactions, especially those that construct cyclic structures from easily available acyclic precursors, have received much attention due to the template action of the transition metals.[6] Recently, we found that palladium(II) catalyzed cyclization of allylic 2-alkynoates showed very high selectivities.[7] In this paper, we wish to report on selectivities in the Pd(II) catalyzed cyclization of N-alkenyl 2-alkynamides.

## RESULTS AND DISCUSSION

**Regioselectivity in the Cyclization of N-Alkenyl 2-Alkynamides.** The reaction of N-allyl propynamide (**1a**) in the presence of $CuCl_2$ (5 eq.) and LiCl (2 eq.) at room temperature with $PdCl_2(PhCN)_2$ as catalyst afforded two products: α-(*E*)-chloromethylene-β-chloromethyl-γ-butyrolactam (**2a**) and N-allyl 2,3-dichloro-*E*-propenamide (**3a**) in 67% and 22 % yields , respectively. The *E*-configuration of the exocyclic C-C double bond of **2a** is similar to the result of the cyclization of allyl propynoate.[7] We were unable to obtain correct analytical data for **3a**, which might be formed by direct reaction of **1a** with $CuCl_2$, [8] The structure of

**3a** was determined by comparing its $^1$H NMR with its known analogue, N-methyl 2, 3-dichloro-2(*E*)-propenamide.[9] Cyclization of other N-alkenyl propynamides gave similar results (entries 2, 3; Table 1).

**Table 1.** Regioselectivity in the Cyclization of N-Alkenyl 2-Alkynamides



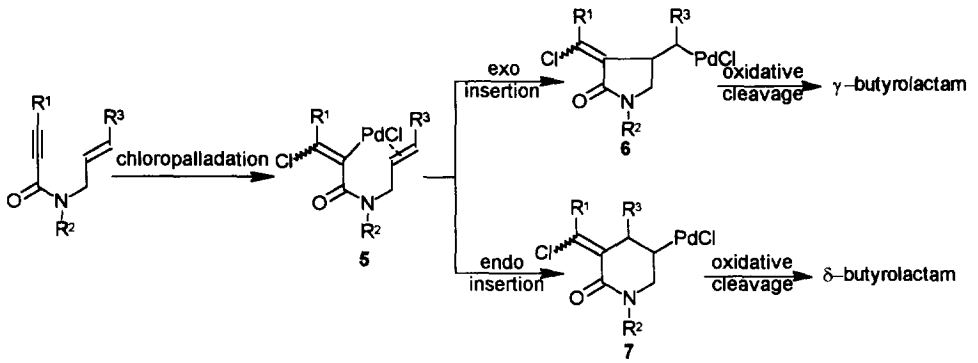

**1** **2** **3** **4**

| Entry | 1 | | | | Time | Yield (%) | | |
|---|---|---|---|---|---|---|---|---|
| | No. | $R^1$ | $R^2$ | $R^3$ | (h) | **2** ($Z$ : $E^a$) | **3** ($Z$ : $E^a$) | **4** ($Z$ : $E^a$) |
| 1 | **1a** | H | H | H | 24 | 67 ( 4 : 96) | 22 ( 4 : 96) | - |
| 2 | **1b** | H | H | Me | 20 | 57 ( 9 : 91) | 15 ( 4 : 96) | - |
| 3 | **1c** | H | H | Ph | 14 | 63 ( 9 : 91) | 35 (11 : 89) | - |
| 4 | **1d** | Me | H | H | 12 | 57 (92 : 2) | - | 43 (93 : 7) |
| 5 | **1e** | Ph | H | H | 12 | 88 (50 : 50) | - | - |
| 6[b] | **1h** | Ph | H | H | 12 | 88 (80 : 20) | - | - |
| 7 | **1f** | Ph | H | Me | 24 | 89 (63 : 37) | - | - |
| 8 | **1g** | Me | Bn | H | 6 | 85 (99 : 1) | - | - |
| 9 | **1h** | Bu | Me | H | 8 | 87 (99 : 1) | - | - |
| 10 | **1i** | Bu | Bn | H | 10 | 86 (99 : 1) | - | - |
| 11 | **1j** | Bu | Ts | H | 40 | 36 (90 : 10) | - | 56 (50 : 50) |

[a] Referring to exo cyclic double bond, ratios were determined by 300 MHz $^1$H NMR.

[b] 10 equivalents of LiCl were used.

When the reaction was extended to N-allyl 3-substituted 2-alkynamides, the reaction afforded very different results which are summarized in Table 1: i) the exocyclic C-C double bond was in the *Z* form, that is to say, *trans*-chloropalladation of these C-C triple bond favored. ii) No direct chlorination product of C-C triple bond of the internal alkyne was found. These two differences between 3-substituted 2-alkynamides and 3-unsubstituted propynamide were also found in the cyclization of the corresponding 2-alkynoates. iii) The third and most important difference was the regioselectivity in the intramolecular C-C double bond insertion into the C-Pd bond of the vinylpalladium intermediate formed by chloropalladation of the C-C triple bond. When N-allyl 2-butynamide (**1d**) was used (entry 4), besides the normal 5-membered product **2d** formed by exo insertion of the C-C double bond into the C-Pd bond, an unexpected endo insertion product **4d** was also obtained in reasonable yield (Table 1). A possible reaction mechanism is shown in Scheme I.



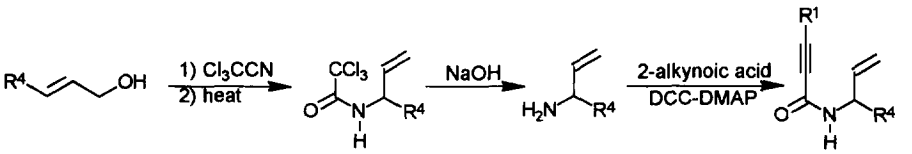

**Scheme I**

In our previous work, cyclization of allylic 2-alkynoates usually afforded 5-membered lactones as the sole products in the absense of steric hindrance due to a 2'-substituent on the C-C double bond such as 2'-methyl propenyl 2-propynoate.[7] The difference in regioselectivities between the cyclization of acyclic allylic 2-alkynoates and N-alkenyl 2-alkynamides indicated different roles for the nitrogen atom in the amide and the corresponding oxygen atom in the esters.

To study the effect of the nitrogen on the intramolecular insertion of the C-C double bond into the C-Pd bond, a series of $R^2$ groups with different electronic properties were introduced to replace the hydrogen atom on the nitrogen atom of the amide. Cyclization of N-allyl 2-heptynamide (**1d**, $R^2$ = H, entry 4 in Table 1) afforded two cyclic products **2d** and **4d** with a ratio of 57 : 43. When an electron donating group, such as Me or Bn , was introduced, the cyclization afforded only five membered lactam product. While for the substrate with an electron withdrawing group, such as $R^3 = SO_2C_6H_4CH_3$ (**1j**, entry 11, Table 1), the cyclization gave more six-membered lactam and afforded **2j** and **4j** with a ratio of 39 : 61. These results indicated that the tosyl group on the nitrogen atom strongly affects the regioselectivity of the C-C double bond insertion into C-Pd bond which would give the six-membered ring through endo insertion way. It is still early to say whether this result is due to the electron withdrawing effect of the tosyl group or its bulkiness.

**1,2-Induction in the Cyclization of 2-Alkynamides of Secondary Allylic Amines.** To study the 1, 2-induction in this cyclization, 1'-substituted N-allylic 2-alkynamides were prepared according to Scheme II:

1-Substituted allylic amines (**8**) were prepared through the literature method.[10] Direct amination of the corresponding 2-alkynoates failed to give the desired 2-alkynamide. Finally, 2-alkynamides (**9**) were prepared by the DMAP catalyzed reaction between 2-alkynoic acids and secondary allylic amines (**8**) in the presence of DCC.[11]

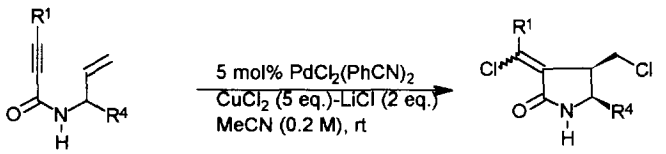



**8** **9**

**Scheme II**

The results of the $PdCl_2(PhCN)_2$ catalyzed cyclization reaction between **9**, $CuCl_2$ and LiCl are summarized in Table II. These reactions proceeded smoothly under mild conditions in high yield and afforded α-(*Z*)-chloroalkylidene-β, γ-(*cis*)-substituted-γ-butyrolactams as the sole cyclic products. The stereochemistry of the cyclic products **10** was determined by $^1H$ NMR and 2D NOESY spectra. Similar 1, 2-stereochemistry was found in the cyclization of the corresponding 2-alkynoates and can be rationalized by steric / conformational effects in the transition state for C-C double bond insertion into the carbon-palladium bond.[7b]

**Table 2.** 1,2-Induction of the Pd(II) catalyzed cyclization of 2-Alkynamides of secondary allylic amines




**9** **10**

| Entry | **9** | $R^1$ | $R^4$ | Time (h) | **10** | Isolated yield (*Z* : *E*)[a] |
|---|---|---|---|---|---|---|
| 1 | **9a** | n-Bu | Me | 9 | **10a** | 71 (> 97 : 3) |
| 3 | **9b** | Me | Ph | 9 | **10b** | 80 (> 97 : 3) |

[a] Referring to exo cyclic double bond, ratios were determined by 300 MHz $^1H$ NMR spectra.

## EXPERIMENTAL SECTION

Infrared spectra were obtained with a Shimadzu IR-440 instrument. Nuclear magnetic resonance spectra were recorded with a Varian EM-360L or XL-200 or Bruker AM-300 spectrometer and are reported in ppm downfield of internal tetramethylsilane (δ units). Mass spectra data were obtained on a Finnigan 4021 spectrometer. Methyl 2-alkynoates,[12] methyl 3-phenyl propynoate,[13] 2(*E*)-butenyl amine,[14] 3-phenyl-2(*E*)-propenyl amine,[15] N-benzyl allylamine,[16] 2-aminobut-3-ene,[17] 1-amino-1-phenylprop-2-ene[10] were prepared according to the reported procedure. Analytical samples were further purified by Kugelrohr distillation at the oven temperature (ot) given or recrystallization.

**Synthesis of 2-Alkynamides of Primary Allylic Amines. Typical Procedure: N-Allyl-2-propynamide (1a)**: To a solution of allylamine (1.8 mL, 24 mmol) in a solvent mixture[MeOH (2 mL) + $H_2O$ (2 mL)] was slowly added methyl propynoate (1.68 g, 20 mmol) at -20 °C to -30°C with stirring. After addition of the propynoate, the stirring was continued for 5 minutes. The solvent was evaporated and column chromatography on silica gel afforded the pure product **1a** (1.84 g, 75 %); bp. 105~107 °C (ot); IR(neat): 3300, 3100, 2120, 1650, 1280 $cm^{-1}$; $^1H$ NMR (60 MHz, $CDCl_3$) 6.60 (br, 1H), 6.20~5.50 (m, 1H), 5.45~4.95 (m, 2H), 3.90 (m, 2H), 2.80 (s, 1H); MS (m/z): 110 ($M^+$+1, 22), 81 (12), 66 (17), 56 (41), 53 (100); Anal. Calcd for $C_6H_7NO$: C, 66.04; H, 6.47; N, 12.84. Found: C, 66.11; H, 6.68; N, 13.14.

The following compounds were prepared similarly.

**N-2'-Butenyl-propynamide (1b)**: Yield: 41 %; bp. 126~127 °C/ 2 mmHg (ot); IR (neat): 3300, 3100, 2120, 1650, 1270 $cm^{-1}$; $^1H$ NMR (60 MHz, $CCl_4$): 6.95 (br, 1H), 5.70~5.40 (m, 2H), 3.73 (t, J = 6.0 Hz, 2H), 2.75 (s, 1H), 1.65 (d, J = 4.4 Hz, 3H); MS (m/z): 123 ($M^+$, 3), 122 (10), 108 (22), 95 (18), 80 (18), 70 (22), 54 (100); Anal. Calcd for $C_7H_9NO$: C, 68.27; H, 7.37; N, 11.37. Found: C, 67.89; H, 7.51; N, 11.63.

**N-3'-Phenylallyl-propynamide (1c)**: Yield: 75 %; mp. 70~72 °C ($CCl_4$); IR (Nujol) : 3300, 3150, 2120, 1650, 1620, 1310, 760, 700 $cm^{-1}$; $^1H$ NMR (200 MHz, $CDCl_3$): 7.28 (m, 5H), 6.50 (d, J = 16.0 Hz, 1H), 6.28 (br, 1H), 6.13 (dt, J= 16.0, 6.0 Hz, 1H), 4.04 (m, 2H), 2.74 (s, 1H); MS (m/z): 185 ($M^+$, 22), 184 (100), 157 (5), 142 (16), 132 (17), 130 (23), 117 (88); Anal. Calcd for $C_{12}H_{11}NO$: C, 77.81; H, 5.99; N, 7.56. Found: C, 77.62; H, 5.95; N, 7.47.

**N-Allyl-2-butynamide (1d)**: Yield: 83 %; bp. 124~126 °C / mmHg (ot); IR (neat): 3300, 2250, 1640, 1280, 975 $cm^{-1}$; $^1H$ NMR (60 MHz, $CCl_4$): 6.83 (br, 1H), 6.20~5.30 (m, 1H), 5.30~4.75 (m, 2H), 3.80 (m, 2H), 1.85 (s, 3H); MS (m/z): 123 ($M^+$, 14), 122 (68), 108 (31), 84 (4), 80 (34), 68 (100); HRMS for $C_7H_9NO$: 123.0682; found: 123.0684.

**N-Allyl-3-phenylpropynamide (1e)**: Yield: 82 %; mp. 63~65 °C ($CCl_4$); IR (Nujol): 3300, 3100, 2220, 1640, 1310, 1005, 730, 700 $cm^{-1}$; $^1H$ NMR (200 MHz, $CDCl_3$): 7.76~7.20 (m, 5H), 6.45 (br, 1H), 6.00~5.74 (m, 1H), 5.48~5.10 (m, 2H), 4.00 (t, J = 6.0 Hz, 2H); MS (m/z): 185 ($M^+$, 7), 170 (3), 157 (6), 142 (11), 130 (100).

**N-2'-Butenyl-3-phenylpropynamide (1f)**: Yield: 42 %; mp. 82~84 °C ($CCl_4$); IR (Nujol): 3300, 3050, 2220, 1640, 1630, 1310 $cm^{-1}$; $^1H$ NMR (200 MHz, $CDCl_3$): 7.56 (m, 5H), 6.53 (br, 1H), 5.76~5.57 (dq, J= 16.0, 6.0 Hz, 1H), 5.57~5.38 (m, 1H), 3.88 (t, J = 6.0 Hz, 2H), 1.68 (dd, $J_1$ = 2 Hz, $J_2$ = 6.0 Hz, 3H); MS (m/z): 199 ($M^+$, 10), 198 (25), 185 (2), 184 (55), 170 (18), 156 (22), 142 (10), 130 (100); Anal. Calcd for $C_{13}H_{13}NO$: C, 78.35; H, 6.58; N, 7.03. Found: C, 78.43; H, 6.59; N, 6.79.

**Synthesis of N-Allyl-N-benzyl-2-butynamide (1g)**: To a solution of 2-butynoic acid (0.71 g, 8.4 mmol) in $CH_2Cl_2$ (10 mL), was added dropwise a solution of DCC (2.06 g, 10 mmol) and DMAP (0.025 g, 0.2 mmol) in $CH_2Cl_2$ (10 mL) at -20°C. Benzyl allyl amine ( 1.23 g, 8.4 mmol) in $CH_2Cl_2$ (5 mL) was then added and the

mixture was stirred for 20 h at room temperature. The solid was filtered off and the filtrate was washed with 0.1 N HCl (10 mL) and dried ($MgSO_4$). After removal of the solvent, column chromatograph (silica gel; eluent: petroleum ether / ethyl acetate = 9/ 1) gave the oily product **1g** (1.52 g, 85 %); ot 143~146 °C / 10 mmHg; IR (neat): 3100, 2200, 1660, 1620, 750, 700 $cm^{-1}$; $^1H$ NMR (60 MHz, $CCl_4$) : 7.20 (m, 5H), 5.80~5.20 (m, 1H), 5.10~4.75 (m, 2H), 4.75 (s, 1H), 4.60 (s, 1H), 3.90 (d, J = 5.0 Hz, 1H), 3.73 (d, J = 6.0 Hz, 1H), 1.85 (s, 3H); MS (m/z): 214 ($M^+$+1, 18), 213 (34), 212 (25), 198 (3), 185 (3), 172 (73), 131 (31), 106 (70), 91 (61), 67 (100); Anal. Calcd for $C_{14}H_{15}NO$: C, 78.84; H, 7.09; N, 6.57. Found: C, 78.66; H, 6.90; N, 6.81.

The following compounds were prepared similarly.

**N-Allyl-N-methyl-2-butynamide (1h)**: Yield: 70%; oil; IR(neat): 3400, 2900, 2200, 16740, 1620, 1290 $cm^{-1}$; $^1H$ NMR (300 MHz, $CDCl_3$): 5.83~5.69 (m, 1H), 5.25~5.14 (m, 2H), 4.18~4.00 (m, 2H), [ 3.12 (s), 2.91 (s), 3H], 2.39~2.33 (m, 2H), 1.61~1.48 (m, 2H), 1.46~1.25 (m, 2H), 0.96~0.90 (m, 3H); MS (m/z): 179 ($M^+$, 76), 165 (17), 152 (11), 151 (61), 138 (65), 137 (91), 100 (88), 80 (100).HRMS Calcd for $C_{11}H_{17}NO$: 179.1310. Found: 179.1261.

**N-Allyl-N-benzyl 2-Heptynamide (1i)**: Yield: 81%; bp. 152~153 °C / 0.5 mmHg (ot); IR (neat): 3200, 2220, 1700, 1630, 1320 $cm^{-1}$; $^1H$ NMR (60 MHz, $CCl_4$): 7.16 (m, 5H), 6.00~5.30 (m, 1H), 5.25~4.76 (m, 2H), 4.50 (d, J = 12.0 Hz, 2H), 3.86 (dd, J= 6.0, 12.0 Hz, 2H), 2.26 (t, J = 6.0 Hz, 2H), 1.46 (m, 4H), 0.86 (t, J = 6.0 Hz, 3H); MS (m/z): 255 ($M^+$, 15), 214 (41), 213 (32), 198 (18), 146 (4), 109 (74), 91 (100); HRMS Calcd for $C_{17}H_{21}NO$: 255.1623. Found: 255.1629.

**N-1'-Methylallyl-2-heptynamide (9a)**: Yield: 63%; bp. 124~125°C / 2mmHg (ot); IR (neat): 3250, 2240, 1660, 1630, 1330 $cm^{-1}$; $^1H$ NMR (60 MHz, $CCl_4$): 7.05 (br, 1H), 6.15~5.50 (m, 1H), 5.35~4.80 (m, 2H), 4.50 (quint, J = 6.0 Hz, 1H), 2.13 (t, J = 6.0 Hz, 2H), 1.55 (m, 4H), 1.15 (d, J = 6.0 Hz, 3H), 0.86 (t, J = 6.0 Hz, 3H); MS (m/z): 180 ($M^+$+1, 39), 179 (14), 178 (15), 164 (23), 150 (21), 136 (35), 122 (28), 109 (100). Anal. Calcd for $C_{11}H_{17}NO$: C, 73.69; H, 9.56; N, 7.89. Found: C, 73.47; H, 9.26; N, 8.26.

**N-1'-Phenylallyl-2-butynamide (9b)**: Yield: 85%; bp. 180~182°C/ mmHg (ot); IR (neat): 3270, 3050, 2250, 1630, 1300, 760 $cm^{-1}$; $^1H$ NMR (60 MHz, $CCl_4$): 7.13 (m, 5H), 6.50 (br, 1H), 6.30~4.86 (m, 4H), 1.73 (s, 3H); MS (m/z): 199 ($M^+$, 66), 184 (15), 156 (20), 141 (12), 117 (18), 67 (100). Anal. Calcd for $C_{13}H_{13}NO$: C, 78.36; H, 6.58; N, 7.03. Found: C, 78.11; H, 6.74; N, 7.11.

**N-Allyl-N-tosyl-2-heptynamide (1j)**: To a solution of N-tosyl-N-allyl amine (2.11 g, 10 mmol) in THF (5 mL), was added NaH (80%, 0.36 g, 12 mmol) under nitrogen. Stirring was continued for 0.5 h until no more $H_2$ evolved. The mixture was cooled to -5 °C and a solution of 2-heptynoic acid chloride (1.44 g, 10 mmol) in THF (5 mL) was added dropwise and the stirring was continued for another 2h after addition. The reaction was quenched with saturated aqueous $NH_4Cl$ (10 mL) and extracted with ethyl acetate. The combined organic layer was dried ($MgSO_4$) and concentrated. Column chromatograph gave **1m** (2.04 g, 64 %). Oil; IR

(neat): 3000, 2220, 1680, 1360; $^1$H NMR (300 MHz, $CDCl_3$): 7.89~7.85 (m, 2H), 7.32~7.27 (m, 2H), 5.96~5.85 (m, 1H), 5.37~5.26 (m, 2H), 4.63~4.61 (m, 2H), 2.43 (s, 3H), 2.33 (t, J = 6.91 Hz, 2H), 1.65~1.47 (m, 2H), 1.45~1.34 (m, 2H), 0.95~0.87 (m, 3H); MS (m/z): 319 ($M^+$, 5), 213 (56), 164 (21), 132 (28), 98 (19), 97 (87), 52 (100). HRMS Calcd $C_{10}H_{14}NO$ ($M^+$-$SO_2C_6H_4CH_3$): 164.1075. Found: 164.1014.

**Palladium Catalyzed Cyclization of 2-Alkynamides. General Procedure:** To a solution of 2-alkynamide (1 mmol) in MeCN (5 mL), was added $PdCl_2(PhCN)_2$ (20 mg, 0.05 mmol), $CuCl_2$ (680 mg, 5 mmol) and LiCl (90 mg, 2 mmol) with stirring. Stirring was continued at rt until the reaction was completed as monitored by TLC. The resulting mixture was diluted with water (5 mL) and extracted with ethyl acetate. The combined organic layer was dried ($MgSO_4$) and concentrated. The residue was purified by flash column chromatograph on silica gel to give the pure product.

**α-(*E*)-Chloromethylene-β-chloromethyl-γ-butyrolactam (2a)**: mp. 112~113°C ($CCl_4$); IR (KBr): 3150, 1690, 1630, 1320, 725 cm$^{-1}$; $^1$H NMR (200 MHz, $CDCl_3$): [6.78 (*E*-isomer), 6.14(*Z*-isomer), d, J = 2.0 Hz, 1H, Z/E = 4/96], 3.82 (m, 2H), 3.70~3.42 (m, 3H); MS (m/z): 183 ($M^+$ (2 x $^{37}$Cl), 31), 181($M^+$ ($^{35}$Cl, $^{37}$Cl), 66), 179 ($M^+$ (2 x $^{35}$Cl), 50), 154 (6), 152 (38), 150 (59), 146 (8), 144 (19), 132 (5), 130 (12), 117 (36), 115 (100), 94 (27), 89 (26), 87 (68); Anal. Calcd for $C_6H_7Cl_2NO$: C, 40.00; H, 3.88; N, 7.78. Found: C, 40.20; H, 3.73; N, 7.84.

**N-Allyl-2,3-dichloropropenamide (3a):** IR (Nujol): 3300, 1660, 1600, 1310 cm$^{-1}$; $^1$HMR (200 Mhz, $CD_3COCD_3$): [7.36 (*Z*)-isomer, 6.29 (*E*)-Isomer, s, 1H], 6.10-5.80 (m, 1H), 5.40-5.00 (m, 2H), 1.96 (m, 2H).

**α-(*E*)-Chloromethylene-β-(1''-chloroethyl)-γ-butyrolactam (2b)**: mp. 137~138°C ($CCl_4$); IR (Nujol): 3200, 1700, 1650, 1300, 730; $^1$H NMR (200 MHz, $CDCl_3$): [6.79 (*E*)-isomer, 6.14 (*Z*)-isomer, d, J = 1.8 Hz, 1H, Z/E = 9:91], 4.40 (m, 1H), 3.64~3.26 (m, 3H), 1.45 (d, J = 6.0 Hz, 3H); MS (m/z): 197($M^+$ (2 x $^{37}$Cl), 1), 195 ($M^+$ ($^{35}$Cl, $^{37}$Cl), 4), 193 ($M^+$ (2 x $^{35}$Cl), 12), 160 (18), 158 (41), 133 (17), 131 (47), 122 (24), 96 (86), 94 (88), 65 (100). Anal. Calcd for $C_7H_9Cl_2NO$: C, 43.32; H, 4.67; N, 7.22. Found: C, 43.10; H, 4.51; N, 6.91.

**N-3'Methylallyl-2,3-dichloropropenamide (3b)**: IR (Nujol): 3300, 1660, 1600,1310 cm$^{-1}$; 1H NMR (200 Mhz, $CD_3COCD_3$): [7.36 (*Z*)-isomer, 6.44 (*E*)-isomer, s, 1H), 5.80-5.40 (m, 2H), 3.94 (m, 2H), 1.65 (d, J=8.0 Hz, 3H).

**α-(*E*)-Chloromethylene-β-(1''-chlorobenzyl)-γ-butyrolactam (2c)**: mp. 170°C (dec.); IR (Nujol): 3300, 1680, 1640, 1320, 760, 700 cm$^{-1}$; $^1$H NMR (200 MHz, $CDCl_3$): 7.38 (m, 5H), [6.74 (*E*)-isomer, 6.14 (*Z*)-isomer, br, 1H, Z/E = 9/91), 6.30 (br, 1H), 4.88 (d, J = 8.8 Hz, 1H), 3.62 (m, 1H), 3.36 (dd, $J_1$ = 7.5 Hz, $J_2$ = 10.0 Hz,1H), 3.07 (dd, J = 2.0, 10.0 Hz, 1H); MS (m/z): 260 ($M^+$ (2 x $^{37}$Cl) +1, 0.05), 258($M^+$ ($^{35}$Cl, $^{37}$Cl)+1, 0.5), 256 ($M^+$ (2 x $^{35}$Cl)+1, 0.6), 222 (0.7), 220 (1), 184 (17), 128 (13), 125 (100). Anal. Calcd for $C_{12}H_{11}Cl_2NO$: C, 56.47; H, 4.35; N, 5.49. Found: C, 56.57; H, 4.25; N, 5.20.

**N-3'-Phenylallyl 2,3-dichloropropenamide (3c)**: IR (Nujol): 3300, 1660, 1600, 1310,,740, 700 cm$^{-1}$; $^1$H NMR (200 MHz, $CDCl_3$): 7.50~7.20 (m, 5H), [7.34 (*Z*)-isomer, 6.74 (*E*)-isomer, s, 1H), 6.62 (d, J = 16.0

Hz, 1H), 6.48 (br, 1H), 6.23 (dt, $J_1$= 16.0, 6.0 Hz, 1H), 4.17 (dt, J = 6.0, 2.0 Hz, 2H); MS (m/z): 259 ($M^+$ (2 x $^{37}Cl$), 2), 257 ($M^+$ ($^{35}Cl$, $^{37}Cl$), 9), 255 ($M^+$ (2 x $^{35}Cl$), 13), 222 (53), 220 (100).

**α-(Z)-(1'-Chloroethylidene)-β-chloromethyl-γ-butyrolactam (2d)**: mp. 120-122°C ($CCl_4$); IR (Nujol): 3220, 1700, 1650, 1300, 700 $cm^{-1}$; $^1H$ NMR (200 MHz, $CDCl_3$): 3.83~3.46 (m, 5H), [2.62 (*E*-isomer), 2.34 (*Z*-isomer), s, 3H, Z/E = 98/2]; MS (m/z): 198 ($M^+$ (2 x $^{37}Cl$) +1, 10), 196 ($M^+$ ($^{35}Cl$, $^{37}Cl$)+1, 58), 194 ($M^+$ (2x $^{35}Cl$)+1, 100), 160 (9), 158 (32), 146 (28), 144 (76), 131 (12), 129 (37), 108 (22). Anal. Calcd for $C_7H_9Cl_2NO$: C, 43.32; H, 4.67; N, 7.22. Found: C, 43.17; H, 4.63; N, 7.10.

**α-(Z)-(1'-Chloroethylidene)-γ-chloro-δ-valerolactam (4d)**: mp. 130-132°C ($CCl_4$); IR (Nujol): 3200, 1710, 1290, 640, 720 $cm^{-1}$; $^1H$ NMR (200 MHz, $CDCl_3$): 4.66 (m, 1H), 3.75 (dd, J= 3.6, 13.4 Hz, 1H), 3.45 (dd, J= 4.0, 13.40 Hz, 1H), 3.15 (dd, J = 6.0, 17.6 Hz, 1H), 2.95 (dd, J = 6.0, 18.0 Hz, 1H), [2.44 (*E*)-isomer, 2.22 (*Z*)-isomer, s, 3H]; MS (m/z): 198 ($M^+$ (2 x $^{37}Cl$) +1, 5), 196 ($M^+$ ($^{35}Cl$, $^{37}Cl$)+1, 26), 194 ($M^+$ (2 x $^{35}Cl$)+1, 39), 160 (33), 158 (100), 131 (20), 129 (59). Anal. Calcd for $C_7H_9Cl_2NO$: C, 43.32; H, 4.67; N, 7.22. Found: C, 43.35; H, 4.69; N, 7.11.

**α-(*Z*)-(1'-Chloro-1'-phenylmethylene)-β-chloromethyl-γ-butyrolactam (2e)**: mp. 168~170 ($CCl_4$); IR (Nujol): 3200, 3000, 1720, 1650, 1310, 730 $cm^{-1}$; $^1H$ NMR (200 MHz, $CDCl_3$): [7.37 (*E*)-isomer, 7.28 (*Z*)-isomer, m, 5H], 6.75 (br, 1H), 3.80~3.00 (m, 5H); MS (m/z): 259 ($M^+$ (2 x $^{37}Cl$), 5), 257 ($M^+$ ($^{35}Cl$, $^{37}Cl$), 24), 255 ($M^+$ (2 x $^{35}Cl$), 43), 254 (100), 208 (7), 206 (26), 170 (23), 141 (11). Anal. Calcd for $C_{12}H_{11}Cl_2NO$: C, 56.47; H, 4.35; N, 5.49. Found: C, 56.32; H, 4.20; 5.35.

**α-(*Z*)-(1'-Chloro-1'-phenylmethylene)-β-(1''-chloroethyl)-γ-butyrolactam ((*Z*)-2f))**: mp. 174~176°C ($CCl_4$); IR (Nujol): 3200, 3100, 1700, 1650, 1630, 1300, 760, 700 $cm^{-1}$; $^1H$ NMR (200 MHz, $CDCl_3$): 7.45 (m, 5H), 6.28 (br, 1H), 3.76 (m, 2H), 3.50 (d, J = 4.4 Hz, 2H), 1.33 (d, J = 6.8 Hz, 3H); MS (m/z): 274 ($M^+$ (2 x $^{37}Cl$) +1, 3), 272 ($M^+$ ($^{35}Cl$, $^{37}Cl$)+1, 19), 270 ($M^+$ (2 x $^{35}Cl$)+1, 34), 236 (1), 234 (4), 208 (27), 206 (100). Anal. Calcd for $C_{13}H_{13}Cl_2NO$: C, 57.98; H, 4.87; N, 5.20. Found: C, 57.79; H, 4.67; N, 5.01.

**α-(*E*)-(1'-Chloro-1'-phenylmethylene)-β-(1''-chloroethyl)-γ-butyrolactam ((*E*)-2f))**: IR (Nujol): 3210, 3100, 1700, 1640, 1330, 730 $cm^{-1}$; $^1H$ NMR (200 MHz, $CDCl_3$): 7.44 (m, 5H), 6.44 (br, 1H), 3.75 (m, 1H)), 3.50 (m, 3H), 1.20 (d, J = 6.8 Hz, 3H); MS (m/z): 273 ($M^+$ (2 x $^{37}Cl$) , 2), 271 ($M^+$ ($^{35}Cl$, $^{37}Cl$), 12), 269 ($M^+$ (2 x $^{35}Cl$), 19), 234 (1), 208 (29), 206 (100), 170 (39).

**α-(*Z*)-(1'-Chloroethylene)-β-chloromethyl-N-benzyl-γ-butyrolactam (2g)**: IR (Nujol): 2980, 1700, 1640, 1310, 730 $cm^{-1}$; $^1H$ NMR (300 MHz, $CDCl_3$): 7.35~7.10 (m, 5H), 4.50 (s, 2H), 3.60~3.10 (m, 5H), 2.30 (s, 3H); MS (m/z): 287 ($M^+$ (2 x $^{37}Cl$) , 6), 285 ($M^+$ ($^{35}Cl$, $^{37}Cl$), 27), 283 ($M^+$ (2 x $^{35}Cl$, 47), 250 (9), 248 (37), 236 (14), 234 (38), 91 (100). HRMS Calcd for $C_{14}H_{15}Cl_2NO$: 283.0532 (2 x $^{35}Cl$); 285.0503 ($^{35}Cl$, $^{37}Cl$). Found: 283.0563 (2 x $^{35}Cl$); 285.0515 ($^{35}Cl$, $^{37}Cl$).

**α-(*Z*)-(1'-Chloropentylene)-β-chloromethyl-N-methyl-γ-butyrolactam (2h)**: IR (Nujol): 3400; 2900, 1680, 1640, 1300, 730 $cm^{-1}$; $^1H$ NMR (300 MHz, $CDCl_3$): 3.60~3.28 (m, 5H), 2.93 (s, 3H), 2.45 (t, J = 7.0

Hz, 2H), 1.80~1.55 (m, 2H), 1.48~1.20 (m, 2H), 0.95 (t, J = 8.0 Hz, 3H); MS (m/z): ): 253 ($M^+$ (2 x $^{37}Cl$) , 4), 251 ($M^+$ ($^{35}Cl$, $^{37}Cl$), 28), 249 ($M^+$ (2 x $^{35}Cl$, 44), 224 (3), 222 (20), 220 (32), 216 (17), 214 (57), 202 (31), 200 (100). HRMS Calcd for $C_{11}H_{17}Cl_2NO$: 249.0688 (2 x $^{35}Cl$).. Found: 249.0713.

**α-(*Z*)-(1'-Chloropenylene)-β-chloromethyl-N-benzyl-γ-butyrolactam (2i)**: IR (Nujol): 3300, 2900, 1690, 1640, 1290, 760 $cm^{-1}$; $^1H$ NMR (300 MHz, $CDCl_3$): 73.7~7.25 (m, 5H), 4.60~4.46 (m, 2H), 3.49 (dd, J = 1.98, 9.26 Hz, 1H), 3.38~3.22 (m, 2H), 2.44 (dt, J= 1.41, 8.44 Hz, 2H), 1.75~1.59 (m, 2H), 1.42~1.34 (m, 2H), 0.95 (t, J = 7.26 Hz, 3H); MS (m/z): 329 ($M^+$ (2 x $^{37}Cl$) , 6), 327 ($M^+$ ($^{35}Cl$, $^{37}Cl$), 14), 325 ($M^+$ (2 x $^{35}Cl$,39), 292 (5), 290 (15), 278 (14), 276 (65), 90 (100). HRMS Calcd for $C_{17}H_{21}Cl_2NO$: 325.1000 (2 x $^{35}Cl$), 327.0971 ($^{35}Cl$, $^{37}Cl$). Found: 325.1011 (2 x $^{35}Cl$), 327.1056 ($^{35}Cl$, $^{37}Cl$).

**α-(*Z*)-(1'-Chloropenylene)-β-chloromethyl-N-tosyl-γ-butyrolactam (2j)**: IR (Nujol): 2900, 2850, 1720, 1630, 1580, 1460, 1380, 1360 $cm^{-1}$; $^1H$ NMR (300 MHz, $CDCl_3$): 7.97 (d, J = 8.29 Hz, 2H), 7.34 (d, J = 8.22 Hz, 2H), 4.04 (d, J = 10.4 Hz, 1H), 3.82 (dd, J = 10.4, 5.5 Hz, 1H), 3.50~3.30 (m, 3H), 2.44~2.42 (m, 5H), 1.70~1.50 (m, 2H), 1.40~1.25 (m, 2H), 0.93 (t, J = 7.30, 3H); MS (m/z): 394 ($M^+$ (2 x $^{37}Cl$) +1, 2), 392 ($M^+$ ($^{35}Cl$, $^{37}Cl$)+1, 6), 390 ($M^+$ (2 x $^{35}Cl$)+1, 19), 363 (4), 361 (11), 356 (14), 354 (3), 340 (41), 198 (13), 155 (59), 76 (23); HRMS Calcd for $C_{17}H_{21}Cl_2NO_3S$: 389.0619 (2 x $^{35}Cl$). Found: 389.0600.

**α-(*Z*)-(1'-Chloropenylene)-γ-chloro-N-tosyl-δ-valerolactam (4j):** IR (Nujol): 2900, 2850, 1730, 1650, 1600, 1370, 1140 $cm^{-1}$; $^1H$ NMR (300 MHz, $CDCl_3$): 7.94 (d, J = 7.63 Hz, 2H), 7.34 (d, J = 7.55 Hz, 2H), 4.03~3.40 (m, 5H), 3.12~3.07 (m, 1H), 2.95~2.93 (m, 1H), 2.44 (br, 3H), 1.55~1.51 (m, 2H), 1.33~1.26 (m, 2H), 0.87 (t, J = 6.80 Hz, 3H); MS (m/z): 393 ($M^+$ (2 x $^{37}Cl$), 3), 391 ($M^+$ ($^{35}Cl$, $^{37}Cl$), 12), 389 ($M^+$ (2 x $^{35}Cl$), 15), 362 (14), 360 (19), 342 (26), 340 (62), 327 (3), 325 (5), 292 (2), 290 (6), 278 (45), 276 (14), 200 (6), 198 (17), 157 (8), 155 (67), 91 (100); HRMS Calcd for $C_{17}H_{21}Cl_2NO_3S$: 389.0619 (2 x $^{35}Cl$). Found: 389.0592.

**α-(*Z*)-(1'-Chloropentylene)-*cis*-β-chloromethyl-γ-methyl-γ-butyrolactam (10a)**: IR (Nujol): 3200, 1680, 1310, 730 $cm^{-1}$; $^1H$ NMR (200 MHz, $CDCl_3$): 7.63 (br, 1H), 3.95 (dq, J= 6.0, 6.80 Hz, 1H), 3.83 (dd, J= 12.0, 8.0 Hz, 1H), 3.50 (dd, J = 12.0, 6.0 Hz, 1H), 3.37 (dt, J = 6.0, 6.80 Hz, 1H), 2.50 (m, 2H), 1.70 (m, 2H), 1.40 (d, J = 6.0 Hz, 3H), 1.25 (m, 2H), 0.97 (t, J = 6.0 Hz, 3H); MS (m/z): 254 ($M^+$ (2 x $^{37}Cl$) +1, 7), 252 ($M^+$ ($^{35}Cl$, $^{37}Cl$)+1, 51), 250 ($M^+$ (2 x $^{35}Cl$)+1, 51), 216 (14), 214 (31), 202 (13), 200 (41), 173 (28), 171 (100). HRMS Calcd for $C_{11}H_{17}Cl_2NO$: 249.0687 (2 x $^{35}Cl$), 251.0658 ($^{35}Cl$, $^{37}Cl$). Found: 249.0680, 251.0694.

**α-(*Z*)-(1'-Chloroethylene)-*cis*-β-chloromethyl-γ-phenyl-γ-butyrolactam (10b)**: IR (Nujol): 3300, 1700, 1650, 1280, 730 $cm^{-1}$; $^1H$ NMR (200 MHz, $CDCl_3$): 7.50~7.20 (m, 5H), 6.73 (br, 1H), 4.98 (d, J = 6.0 Hz, 1H), 3.60 (m, 1H), 3.18 (m, 2H), 2.35 (s, 3H); MS (m/z): 273 ($M^+$ (2 x $^{37}Cl$), 1), 271 ($M^+$ ($^{35}Cl$, $^{37}Cl$), 6), 269 ($M^+$ (2 x $^{35}Cl$), 8), 236 (18), 234 (51), 198 (3, 131 (31), 129 (100). Anal. Calcd for $C_{13}H_{13}Cl_2NO$: C, 57.98; H, 4.87; N, 5.20. Found: C, 58.12; H, 5.12; N, 5.16.

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