Controlling Factors on the Stereochemistry of Pd(II)-Catalyzed Cyclization of 1'-Alkyl-4'-chloro-2'-alkenyl 2-Alkynoates

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β,γ-Disubstituted α-(*Z*)-(chloromethylene)-γ-butyrolactone derivatives have been prepared highly diastereoselectively via a Pd(II)-catalyzed cyclization of 1'-alkyl-4'-chloro-2'-alkenyl 2-alkynoates. Rationales for the stereochemical results of this reaction are proposed.

Introduction

The α-methylene-γ-butyrolactone ring is an integral building block of many natural products, especially the sesquiterpene lactones, which exhibit many interesting biological activities, such as cytotoxicity, antitumority, etc. The widespread biological activities have presented a considerable challenge to organic chemists over the years.[1] Recently, we have reported a new method involving a Pd(II)-catalyzed cyclization of 4'-halo-2'-alkenyl 2-alkynoates to synthesize α-methylene-γ-butyrolactone derivatives.[2] In this reaction, the butyrolactone ring is assembled by carbon–carbon bond formation, which is quite different from the other methods reported.[1] On the other hand, the stereoselective process has played a central role in the synthesis of compounds possessing medicinal or theoretical significance. In principle, transiton-metal templetes should provide a propitious environment for transformations of this variety. Thus, we wonder if a substituent is introduced into the 1'-position of the 2'-alkenyl group, which kind of stereoinduction would occur on the relative configuration of the carbon atom at the β-position of the lactone ring. In this paper, we report the stereochemistry of this reaction.

Results and Discussion

Synthesis of the Starting Material. The starting materials 1'-alkyl-4'-chloro-2'(*Z*)- or -(*E*)-alkenyl 2-alkynoates **4** were synthesized according to Scheme I in order to study the 1,2-stereoinduction[3] of the above-mentioned cyclization reaction.

1-Substituted 2-yne-1,4-diols **1** were synthesized according to the method of alkynylation of aldehydes.[4] The (*Z*)- and (*E*)-2-ene-1,4-diols **2** were obtained highly stereoselectively by catalytic hydrogenation[5] or reduction with $LiAlH_4$,[6] respectively. The selective chlorination of the primary hydroxy group of **2** could be realized by controlling the reaction temperature at −20 °C. Better results could be obtained for the esterification of 2-propynoic acid when diethyl ether was used as the solvent, while for the synthesis of substituted 2-alkynoates the reaction should be carried out in CH_2Cl_2.

Cyclization of 1'-Alkyl-4'-chloro-2'-alkenyl 2-Propynoates. We began our research with 1'-methyl-4'-chloro-2'(*E*)-butenyl 2-propynoate ((*E*)-**4a**) under the catalysis of 5 mol % of $Pd(OAc)_2$ in HOAc. The reaction did afford a pair of diastereomers: *trans*(referred to the β,γ-substituents)-γ-methyl-β-vinyl-α-(*Z*)-(chloromethylene)-γ-butyrolactone (**5a**) and its corresponding cis isomer **6a** with an isolated ratio of ca. 70:30. But, occasionally, it was found that (*Z*)-**4a** afforded **5a**(*trans*) highly stereoselectively (**5a**:**6a** > 96:4) (Table I, entry 3). The exocyclic C=C bonds in cyclization products **5** and **6** were believed to be in the *Z* configuration as compared their chemical shifts of the vinylic protons of the exocyclic C=C bond with their analogues.[2] The relative configurations referred to the β,γ-substituents were determined by ^1H 2D NOESY spectra, in which the two hydrogen atoms at the β,γ-positions of **6a**(*cis*) showed a stronger NOE correlation signal than that of **5a**(*trans*). The stereochemical results were also supported by comparing their ^1H NMR spectral data with those of similar compounds.[7]

These results imply that the configuration of allylic C=C bond in **4** plays an important role in the stereochemistry of the present reaction. Oppolzer et al. have also reported similar behaviors in the intramolecular ene reaction[8] and Pd-catalyzed allylation reaction of C=C bonds.[9] A similar observation was also reported in Pd-catalyzed cyclization of hydroxy epoxides by Hirma et al.[10] According to our previous reports,[2] stereoselective trans halopalladation affords a vinylpalladium intermediate through intramolecular insertion of a C=C bond into the C–Pd bond followed by dehalopalladation to afford the product **5** or **6**. Thus, we speculated that the stability of the transition states for the insertion reaction might be responsible for the unique stereochemical behavior as shown in Scheme II.

In a seven-membered metallocyclic transition state shown in Scheme II, in order to insert the C=C bond into the C–Pd bond, these two bonds should be as close as possible and in a position favoring the intramolecular insertion reaction. Scheme II clearly shows that in the transition states of the reaction of (*E*)-**4a,b** the energy difference between **7** and **7'** is not very large, while in that of (*Z*)-**4a,b** **8** is obviously more favorable than **8'** due to the steric hindrance present in **8'**. Thus, (*Z*)-**4a,b** afforded

(1) Hoffmann, H. N. M.; Rode, J. *Angew. Chem., Int. Ed. Engl.* **1985**, *24*, 94.
(2) (a) Ma, S.; Lu, X. *J. Chem. Soc., Chem. Commun.* **1990**, 733. (b) Ma, S.; Lu, X. *J. Org. Chem.* **1991**, *56*, 5120.
(3) Lund, E. C.; Livinghouse, T. *J. Org. Chem.* **1989**, *54*, 4487.
(4) Brandsma, L. *Preparative Acetylenic Chemistry*, 2nd ed.; Elsevier: Amsterdam, 1988; p 79.
(5) Brown, C. A.; Ahuja, V. K. *J. Chem. Soc., Chem. Commun.* **1973**, 533.
(6) Cowie, J. S.; Landor, P. D.; Landor, S. R. *J. Chem. Soc., Perkin Trans. 1*, **1973**, 720.
(7) Saimoto, H. Kishio, K.; Yamamoto, H.; Shinoda, M.; Hiyama, T.; Nozaki, H. *Bull. Chem. Soc. Jpn.* **1983**, *50*, 3093. Okuda, Y.; Nakatsukasa, S.; Oshima, K.; Nozaki, H. *Chem. Lett.* **1985**, 481.
(8) Oppolzer, W. *Pure Appl. Chem.* **1981**, *53*, 1181.
(9) Oppolzer, W.; Gaudin, J.-M.; Bedoya-Zutita, M.; Hueso-Rodriguz, J.; Raynham, T. M.; Robyr, C. *Tetrahedron Lett.* **1988**, *29*, 4709.
(10) Suzuki, T.; Sato, O.; Hirma, M. *Tetrahedron Lett.* **1990**, *31*, 4747.

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Scheme I

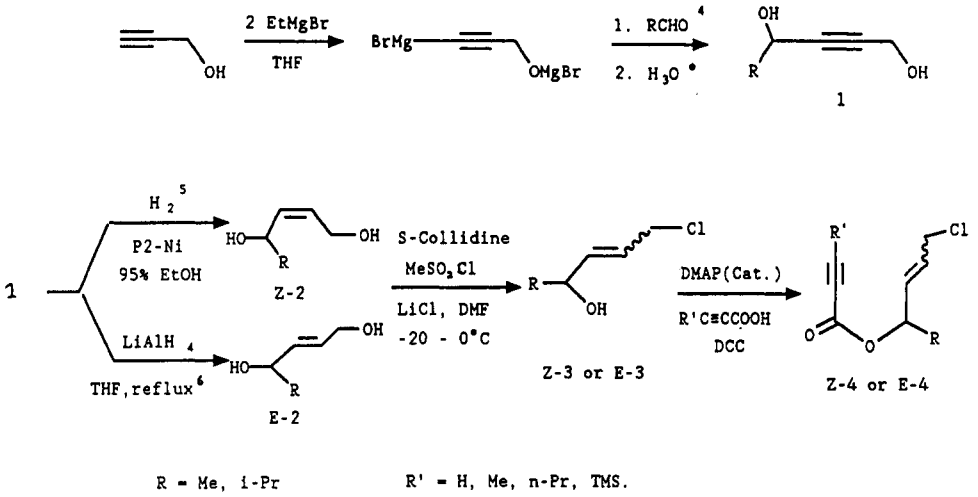
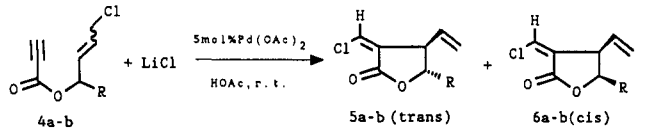


Table I. Cyclization of 2-Propynoates



entry	4 R	4 C=C	LiCl (mol%)	time (h)	total yield of 5 and 6 (%)	5/6[a]
1	Me	(*E*)-**4a**	25	1.5	94	71 (**5a**):29 (**6a**)
2	Me	(*E*)-**4a**	50	1.5	94	70 (**5a**):30 (**6a**)
3	Me	(*Z*)-**4a**	50	1.5	94	>96 (**5a**):4 (**6a**)
4	i-Pr	(*E*)-**4b**	25	2	95	>92 (**5b**):8 (**6b**)
5	i-Pr	(*E*)-**4b**	50	2	95	>92 (**5b**):8 (**6b**)
6	i-Pr	(*Z*)-**4b**	50	2	90	>98 (**5b**):2 (**6b**)

[a] Determined by 200-MHz ^{1}H NMR spectra.

the trans product **5a** highly diastereoselectively via the transition state 8.

From the transition states 7 and 7′ we can imagine readily that when R becomes bulkier steric hindrance in 7′ might also become serious. This was exactly confirmed by the fact that while R was isopropyl, both (*Z*)- and (*E*)-**4b** afforded the trans product **5b** highly diastereoselectively. Such kind of 1,2-stereoinduction was also reported in $CuCl_2$-catalyzed radical cyclization reactions[11] and Pd-catalyzed cyclization reactions.[12]

Cyclization of 1′-Alkyl-4′-chloro-2′-alkenyl 2-Alkynoates. When we extended this reaction to the substituted 2-alkynoates, the exocyclic C=C bond in products **5c-f** and **6c-f** was also believed to be in the *Z* configuration as compared the chemical shifts of methyl protons (for compounds **5c**, **5d**, **6c**, and **6d**) or methylene protons (for compounds**5e** and **6e**) adjacent to the exocyclic C=C bond with their analogues.[2,13] The stereoselectivity depends largely on the amount of LiCl added, a result similar to our previous reports.[2] With 3-(trimethylsilyl)-2-propynoate ((*Z*)- and (*E*)-**4f**), even using of 10 equiv of LiCl, the *Z*/*E* ratio is 1:1.

Interestingly, as to the stereochemistry of the β,γ-substituents in products, 1′-methyl-4′-chloro-2′(*Z*)-butenyl 2-butynoate ((*Z*)-**4c**) afforded **6c**(*cis*) as the major product with a small amount of the trans product **5c** while (*E*)-**4c** afforded **6c**(*cis*) as the sole product (Table II, entries 1 and 2). When the bulkier isopropyl group was used, both (*Z*)- and (*E*)-**4d** afforded **6d**(*cis*) as the sole product (Table II, entries 3 and 4). Similar results were obtained for 1′-methyl-4′-chloro-2′-butenyl 2-hexynoates ((*Z*)- and (*E*)-**4e**) (Table II, entries 5–7) and 3-(trimethylsilyl)-2-propynoates ((*Z*)- and (*E*)-**4f**) (Table II, entries 8 and 9). This result was in contrast to the nonsubstituted propynoates. Thus, the substitutents at the 3-position of **4** might play an important role in this unique stereochemical behavior. In all products in Table II, ^{1}H 2D NOESY spectra showed a strong NOE correlation signal between H^a–H^c and H^b–H^d and no NOE correlation signal was observed between H^b–H^c and H^a–H^d (Figure 1). These results strongly supported that the major cyclization products **6** for 3-substituted 2-alkynoates are cis referred to β,γ-substituents.[14]

As revealed by molecular models, in similar cyclic 7-membered transition states as described in Scheme II or in other representation as in the chairlike conformation 9′ (Scheme III), the substituent group R′ and the chloromethyl group might make the transition states (similar to 7[7′], 8[8′], and 9′) more crowded when the exocyclic C=C double bond is in the *Z* configuration. Thus, with 3-substituted 2-alkynoates, a cyclic 7-membered transition state **9**, which places more of the substituents in favorable pseudoequatorial position, might provide a rationale for the observed diastereoselectivity (Scheme III).[15,16]

From transition state **9**, it is obvious that when R is isopropyl (Table II, entries 3 and 4), R should show a more favorable tendency to be in pseudoequatorial position;[16] thus, both cyclization of (*Z*)- and (*E*)-**4d** occurred to form **6d**(*cis*) as the sole product.

Experimental Section

Selective Chlorination of 2(*Z*)- or 2(*E*)-ene-1,4-diols. Typical Procedure. Synthesis of 1-Chloro-2(*Z*)-penten-4-ol. To a solution of 2(*Z*)-pentene-1,4-diols (2.0 g, 19.6 mmol),

(11) Nagashima, H.; Seki, K.; Ozaki, N.; Wakamatsu, H.; Itoh, K.; Tomo, Y.; Tsuji, J. *J. Org. Chem.* **1990**, *55*, 985.

(12) Semmelhack, M. F. Zhang, N. *J. Org. Chem.* **1989**, *54*, 4483. McCormick, M.; Monahan, R., III; Soria, J.; Goldsmith, D.; Liotta, D. *J. Org. Chem.* **1989**, *54*, 4485. Yoo, S.-E.; Lee, S.-H.; Yi, K.-Y.; Jeong, N. *Tetrahedron Lett.* **1990**, *31*, 6877. Oppolzer, W.; Keller, T. H.; Kuo, D. L.; Pachinger, W. *Tetrahedron Lett.* **1990**, *31*, 1265.

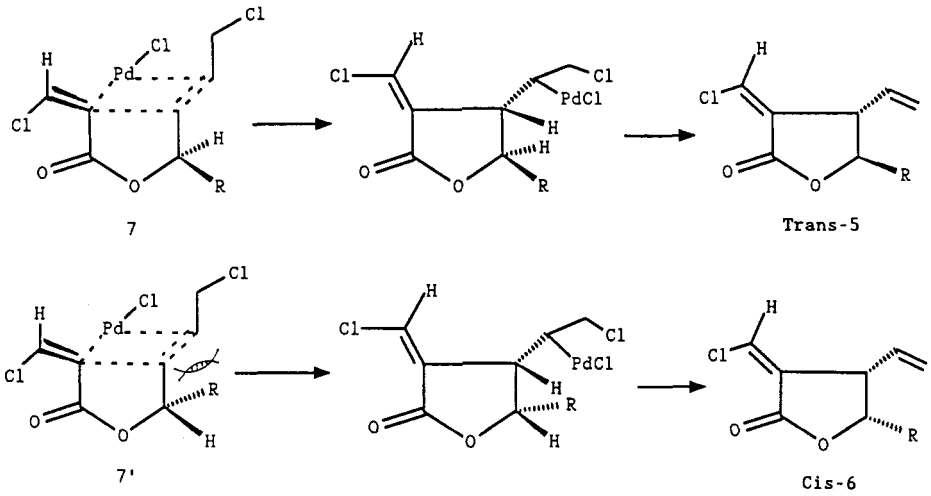
(13) In the case of **5e** and **6e**, both *Z* and *E* isomers (referred to the exocyclic C=C bond) were isolated.

(14) In the cases that both **5** and **6** were isolated, the stereochemistry was assigned by comparing their ^{1}H NMR spectra data with the similar analogues.[7]

(15) Abelman, M. W.; Overman, L. E. *J. Am. Chem. Soc.* **1988**, *110*, 2328.

(16) Gagne, M. R.; Stern, C. L.; Marks, T. J. *J. Am. Chem. Soc.* **1992**, *114*, 275.

Scheme II. Transition States for the Reaction of (*E*)-4a,b



Transition States for the Reaction of (*Z*)-4a,b

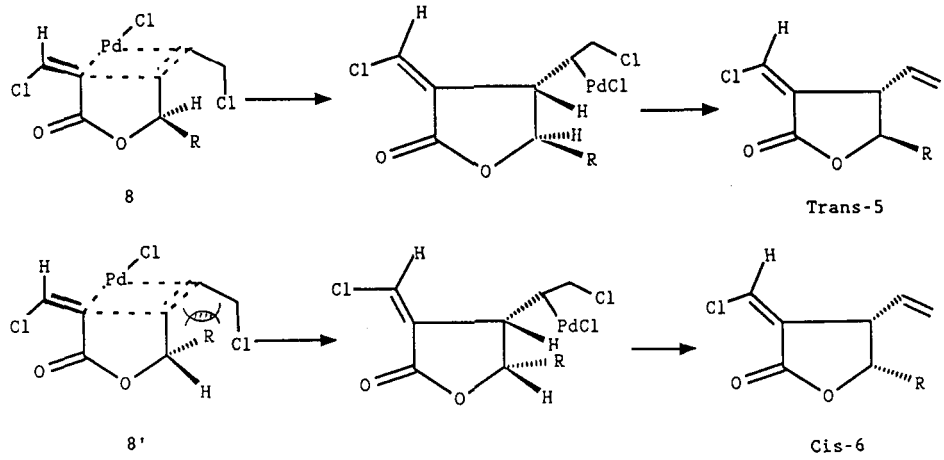
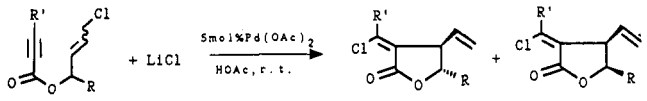


Table II. Cyclization of 2-Alkynoates



entry	4 R′	4 R	4 C=C	LiCl (equiv)	time (h)	total yield of 5 and 6[a] (%)	5:6[b]
1	Me	Me	(*E*)-4c	4	2	97 (100:0)	0 (**5c**):100 (**6c**)
2	Me	Me	(*Z*)-4c	4	2	72 (100:0)	10 (**5c**):90 (**6c**)
3	Me	i-Pr	(*E*)-4d	4	3	95 (100:0)	0 (**5d**):100 (**6d**)
4	Me	i-Pr	(*Z*)-4d	4	3	75 (100:0)	0 (**5d**):100 (**6d**)
5	n-Pr	Me	(*E*)-4e	5	3	74 (73:27)	0 (**5e**):100 (**6e**)
6	n-Pr	Me	(*E*)-4e	7.5	3	95 (84:16)	0 (**5e**):100 (**6e**)
7	n-Pr	Me	(*Z*)-4e	7.5	3	95 (84:16)	10 (**5e**):90 (**6e**)
8	TMS	Me	(*E*)-4f	10	3.5	50 (50:50)	0 (**5f**):100 (**6f**)
9	TMS	Me	(*Z*)-4f	10	3.5	50 (50:50)	0 (**5f**):100 (**6f**)

[a] The numbers in the parentheses are the ratio of *Z*:*E* isomers referred to the exocyclic C=C bond, which were determined by isolation. [b] Determined by 200-MHz or 300-MHz ^{1}H NMR spectra.

LiCl (anhyd, 1.25 g, 29.4 mmol), and *s*-collidine (3.56 g, 29.4 mmol) in DMF (anhyd, 10 mL) was added dropwise and slowly a solution of CH_3SO_2Cl (2.24 g, 19.6 mmol) in DMF (anhyd, 5 mL) at −20 °C with mechanistic stirring for ca. 1 h. After the reaction was allowed to occur at 0 °C for 4 h, ice–water (15 mL) was added, and then the mixture was extracted with ethyl acetate (4 × 10 mL). After drying ($MgSO_4$) and removal of the solvent, the crude product was submitted to chromatography on silica gel (eluent: petroleum ether:ethyl acetate = 10:1) to afford 1-chloro-2(Z)-penten-4-ol. Yield: 0.79 g (33%). The product was used without further purification. Only its ^{1}H NMR spectral data were recorded: ^{1}H NMR (60 MHz/CCl_4) δ 5.60–5.30 (m, 2H), 4.60–4.30 (m, 1H), 3.95 (d, J = 6.0 Hz, 2H), 2.50 (br, 1H), 1.05 (m, 3H).

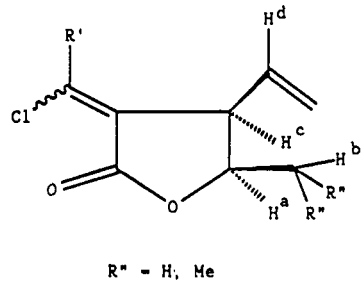


Figure 1.

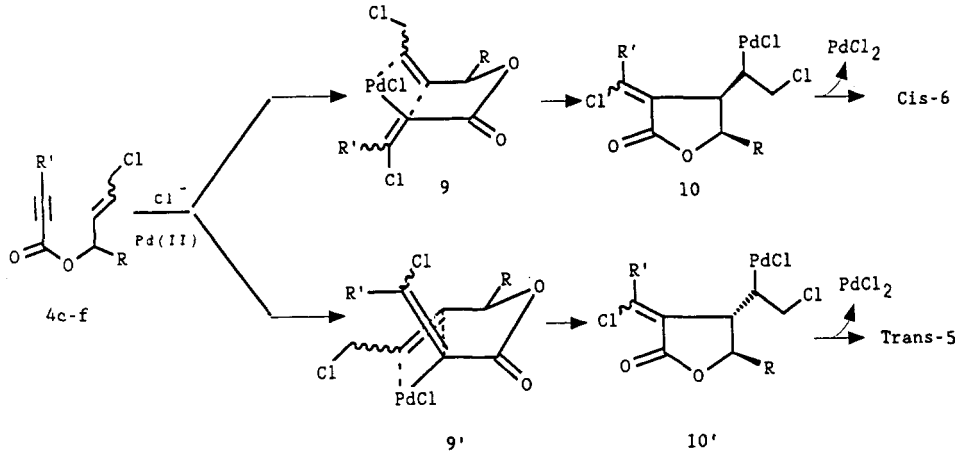
The following compounds were prepared similarly. **1-Chloro-2(E)-penten-4-ol**: yield 1.13 g (48%); ^{1}H NMR (60 MHz/CCl_4) δ 5.90–5.65 (m, 2H), 4.40–3.95 (m, 3H), 3.00 (s, 1H), 1.15 (d, J = 6.0 Hz, 3H).

1-Chloro-5-methyl-2(*Z*)-hexen-4-ol: yield 1.45 g (50%); ^{1}H NMR (60 MHz/CCl_4) δ 5.80–5.60 (m, 2H), 4.25–3.95 (m, 3H), 2.00–1.50 (m, 1H), 1.10–0.70 (m, 7H).

1-Chloro-5-methyl-2(E)-hexen-4-ol: yield 0.94 g (32%); ^{1}H NMR (60 MHz/CCl_4) δ 5.80–5.50 (m, 2H), 4.10–3.60 (m, 3H), 2.00 (br, 1H), 1.80–1.40 (m, 1H), 0.75 (m, 6H).

Synthesis of 1′-Alkyl-4′-chloro-2′-butenyl 2-Propynoates. Typical Procedure. Synthesis of 1′-Methyl-4′-chloro-2′(*Z*)-butenyl 2-Propynoate ((*Z*)-4a). To a solution of 2-propynoic acid (1.21 g, 17.3 mmol) and 5-chloro-3(*Z*)-penten-2-ol (0.52 g, 4.32 mmol) in ether (anhyd, 10 mL) was added a solution of DCC (3.56 g, 17.3 mmol) and DMAP (210 mg, 10 mol %) in ether

Scheme III



(anhyd, 10 mL) at −20 °C with stirring, and then the reaction was carried out at rt for 24 h. After filtering and removal of the solvent, the crude product was submitted to chromatography on silica gel (eluent: petroleum ether:ethyl acetate = 10:1) to afford (*Z*)-**4a**, yield 0.51 g (69%). The analytic samples were further purified by Kugelrohr distillation at the specified oven temperatures (ot): ot 84-86 °C (3 mmHg); IR (neat) 3300, 2950, 2100, 1710, 1230 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$) δ 5.92–5.40 (m, 3H, OCHCH=CH_2), 4.30 (dd, J_1 = 8.0 Hz, J_2 = 12.0 Hz, 1H, CHCl), 4.10 (dd, J_1 = 6.5 Hz, J_2 = 12.0 Hz, 1H, CHCl), 2.90 (s, 1H, H-C), 1.42 (d, J = 6.0 Hz, 3H); MS *m/e* 175 ($M^+(^{37}Cl)$ + 1, 3.66), 173 ($M+(^{35}Cl)$ + 1, 11.18), 171 (9.93), 169 (21.56), 137 (M^+ − Cl, 58.12), 105 ($M^+(^{37}Cl)$ − C_3HO_2, 49.36), 103 ($M^+(^{35}Cl)$ − C_3HO_2, 100.00). Anal. Calcd for $C_8H_9ClO_2$: C, 55.67; H, 5.26. Found: C, 55.23; H, 4.99.

Compounds (*E*)-**4a** and (*Z*)- and (*E*)-**4b** were prepared similarly.

1'-Methyl-4'-chloro-2'(*E*)-butenyl 2-propynoate ((*E*)-4a): yield 0.53 g (66%); ot 60–62 °C (1.5 mmHg); IR (neat) 3300, 2950, 2100, 1720, 1230, 970 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$) δ 6.00–5.70 (m, 2H, CH=CH), 5.46 (quintet, J = 6.0 Hz, 1H, OCH), 4.06 (d, J = 5.2 Hz, 2H, CH_2Cl), 2.90 (s, 1H, H-C), 1.40 (d, J = 6.0 Hz, 3H, CH_3); MS *m/e* 175 ($M^+(^{37}Cl)$ + 1, 0.36), 174 ($M^+(^{37}Cl)$, 0.10), 173 ($M^+(^{35}Cl)$ + 1, 1.09), 172 ($M^+(^{35}Cl)$, 0.20), 137 (M^+ − Cl, 37.89), 105 ($M^+(^{37}Cl)$ − C_3HO_2, 29.17), 103 ($M^+(^{35}Cl)$ − C_3HO_2, 88.22), 53 (100.00). Anal. Calcd for $C_8H_9ClO_2$: C, 55.67; H, 5.26. Found: C, 55.50; H, 5.82.

1'-Isopropyl-4'-chloro-2'(*Z*)-butenyl 2-propynoate ((*Z*)-4b): yield 0.72 g (69%); ot 108–110 °C (2 mmHg); IR (neat) 3300, 2950, 2100, 1710, 1230 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$) δ 6.00–5.80 (m, 1H, CH=), 5.54 (t, J = 8.0 Hz, CH=), 5.34 (dd, J_1 = 6.0 Hz, J_2 = 8.8 Hz, 1H, OCH), 4.30 (dd, J_1 = 8.4 Hz, J_2 = 12.0 Hz, 1H, CHCl), 4.14 ((dd, J_1 = 12.0 Hz, J_2 = 6.0 Hz, 1H, CHCl), 2.90 (s, 1H, HC), 2.04–1.82 (m, 1H, OCCH), 1.00 (d, J = 6.80 Hz, 3H, CH_3), 0.94 (d, J = 6.80 Hz, 3H, CH_3); MS *m/e* 165 (M^+ − Cl, 23.99), 133 ($M^+(^{37}Cl)$ − C_3HO_2, 4.53), 131 ($M^+(^{35}Cl$ − C_3HO_2, 14.30), 95 (100.00), 53 (90.69). Anal. Calcd for $C_{10}H_{13}ClO_2$: C, 59.86; H, 6.53. Found: C, 59.83; H, 6.25.

1'-Isopropyl-4'-chloro-2'(*E*)-butenyl 2-propynoate ((*E*)-4b): yield 0.70 g (64%); ot 108–110 °C (2.5 mmHg); IR (neat) 3300, 2950, 2100, 1720, 1230, 970 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$) δ 6.02–5.82 (m, 1H, CH=), 5.74 (dd, J_1 = 6.5 Hz, J_2 = 16.0 Hz, 1H, CH=), 5.16 (t, J = 6.0 Hz, OCH), 4.07 (d, J = 4.8 Hz, 2H, CH_2Cl), 2.90 (s, 1H, H-C), 2.10–1.84 (m, 1H, OCCH), 0.94 (d, J = 6.0 Hz, CH_3), 0.93 (d, J = 6.0 Hz, 3H, CH_3); MS *m/e* 165 (M^+ − Cl, 12.71), 133 ($M^+(^{37}Cl)$ − C_3HO_2, 1.91), 131 ($M^+(^{35}Cl)$ − C_3HO_2, 7.62), 95 (46.69), 53 (100.00). Anal. HRMS Calcd for $C_{10}H_{13}O_2(M^+ - Cl)$: 165.0916. Found: 165.0910.

Synthesis of 1'-Methyl-4'-chloro-2'-butenyl 2-Alkynoates. Typical Procedure. Synthesis of 1'-Methyl-4'-chloro-2'(*Z*)-butenyl 2-butynoate ((*Z*)-4c). To a solution of 2-butynoic acid (3.40 g, 40.0 mmol) and 5-chloro-3(*Z*)-penten-2-ol (1.20 g, 10.0 mmol) in CH_2Cl_2 (anhyd, 30 mL) was added a solution of DCC (3.1 g, 15 mmol) and DMAP (122 mg, 1 mmol) in CH_2Cl_2 (anhyd, 20 mL) at 0 °C with stirring. After the addition, the mixture was stirred at rt for 24 h. After filtering and removal of the sovent, the crude product was submitted to chromatography on silica gel (eluent: petroleum ether:ethyl acetate = 25:1) to afford (*Z*)-**4c**, yield 1.44 g (77.5%). The analytic samples were further purified by Kugelrohr distillation at the specified oven temperatures (ot): ot 106–107 °C (5 mmHg); IR (neat) 2950, 2100, 1710, 1450, 1250 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$) δ 5.84–5.46 (m, 3H), 4.33–4.17 (m, 1H), 4.17–4.00 (m, 1H), 1.98 (s, 3H), 1.36 (d, J = 6.0 Hz, 3H); MS *m/e* 189 ($M^+(^{37}Cl)$ + 1, 5.76), 187 ($M^+(^{35}Cl)$ + 1), 21.39), 171 (2.74), 169 (10.85), 151 (M^+ − Cl, 96.5), 105 (33.86), 103 (53.50), 85 ($C_4H_5O_2^+$, 100.00). Anal. Calcd for $C_9H_{11}ClO_2$: C, 57.92; H, 5.94. Found: C, 57.98; H, 5.82.

Compounds (*E*)-**4c**, (*Z*)- and (*E*)-**4d-f** were prepared similarly.

1'-Methyl-4'-chloro-2'(*E*)-butenyl 2-butynoate ((*E*)-4c): yield 1.37 g (73.5%); ot 105–106 °C (5 mmHg); IR (neat) 2980, 2220, 1710, 1440, 1250, 970 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$) δ 5.82 (m, 2H), 5.41 (quintet, J = 6.0 Hz, 1H), 4.03 (d, J = 6.0 Hz, 2H), 1.98 (s, 3H), 1.35 (d, J = 6.0 Hz, 3H); MS *m/e* 189 ($M^+(^{37}Cl)$ + 1, 5.0), 187 ($M^+(^{35}Cl)$ + 1, 11.59), 171 (1.95), 169 (6.07), 151 (M^+ − Cl, 43.17), 133 (3.21), 105 (12.60), 85 (33.39), 67 (100.00). Anal. Calcd for $C_9H_{11}ClO_2$: C, 57.92; H, 5.94. Found: C, 57.54; H, 5.89.

1'-Isopropyl-4'-chloro-2'(*Z*)-butenyl 2-butynoate ((*Z*)-4d): yield 1.50 g (70%); ot 110–111 °C (5 mmHg); IR (neat) 2960, 2220, 1750, 1470, 1250, 1060 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$) δ 5.92–5.74 (m, 1H), 5.47 (t, J = 10.0 Hz, 1H), 5.24 (dd, J_1 = 7.2 Hz, J_2 = 8.4 Hz, 1H), 4.28 (dd, J_1 = 8.4 Hz, J_2 = 10.0 Hz, 1H), 4.08 (dd, J_1 = 7.2 Hz, J_2 = 10.0 Hz, 1H), 1.97 (s, 3H), 1.95 (m, 1H), 0.96 (d, J = 6.0 Hz, 3H), 0.92 (d, J = 6.0 Hz, 3H); MS *m/e* 217 ($M^+(^{37}Cl)$ + 1, 0.11), 215 ($M^+(^{35}Cl)$ + 1, 0.29), 199 (2.39), 197 (6.13), 179 (M^+ − Cl, 24.41), 172 ($M^+(^{37}Cl)$ − CO_2, 0.12), 170 ($M^+(^{35}Cl)$ − CO_2, 0.11), 133 (4.56), 131 (12.69), 96 (100.00). Anal. Calcd for $C_{11}H_{15}ClO_2$: C, 61.54; H, 7.04. Found: C, 61.50; H, 7.14.

1'-Isopropyl-4'-chloro-2'(*E*)-butenyl 2-butynoate ((*E*)-4d): yield 1.87 g (87%); ot 130–131 °C (5 mmHg); IR (neat) 2960, 2100, 1710, 1470, 1250, 1060, 970 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$) δ 5.98–5.62 (m, 2H), 5.08 (t, J = 6.0 Hz, 1H), 4.04 (d, J = 6.0 Hz, 2H), 2.00 (s, 3H), 1.95 (m, 1H), 0.95 (d, J = 4.0 Hz, 3H), 0.92 (d, J = 4.0 Hz, 3H); MS *m/e* 217 ($M^+(^{37}Cl)$ + 1, 0.02), 179 (M^+ − Cl, 7.30), 133 (0.97), 131 (2.91), 95 (24.67), 67 (100.00). Anal. Calcd for $C_{11}H_{15}ClO_2$: C, 61.54; H, 7.04. Found: C, 61.46; H, 7.23.

1'-Methyl-4'-chloro-2'(*Z*)-butenyl 2-hexynoate ((*Z*)-4e): yield 1.50 g (70%); ot 130–131 °C (2 mmHg); IR (neat) 2980, 2220, 1710, 1450, 1250, 1170, 1140 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$) δ 5.81–5.48 (m, 3H), 4.28 (dd, J_1 = 8.0 Hz, J_2 = 12.0 Hz, 1H), 4.08 (dd, J_1 = 7.0 Hz, J_2 = 12.0 Hz, 1H), 2.28 (t, J = 6.0 Hz, 2H), 1.60 (sextet, J = 8.0 Hz, 2H), 1.36 (d, J = 6.0 Hz, 3H), 1.00 (t, J = 8.0 Hz, 3H); MS *m/e* 217 ($M^+(^{37}Cl)$ + 1, 2.20), 215 ($M^+(^{35}Cl)$ + 1, 5.26), 179 (M^+ − Cl, 43.99), 173 ($M^+(^{37}Cl)$ − Pr, 0.22), 171 ($M^+(^{35}Cl)$ − Pr, 0.61), 105 (7.23), 96 (100.00). Anal. Calcd for $C_{11}H_{15}ClO_2$: C, 61.54; H, 7.04. Found: C, 61.57; H, 6.82.

1'-Methyl-4'-chloro-2'(*E*)-butenyl 2-hexynoate ((*E*)-4e): yield 1.39 g (65%); ot 115–116 °C (2 mmHg); IR (neat) 2960,

2220, 1710, 1450, 1250, 970 cm^{-1}; ^{1}H NMR (200 MHz, $CDCl_3$) δ 5.90–5.78 (m, 2H), 5.40 (quintet, J = 6.0 Hz, 1H), 4.04 (d, J = 6.0 Hz, 2H), 2.30 (t, J = 6.0 Hz, 2H), 1.60 (sextet, J = 8.0 Hz, 2H), 1.36 (d, J = 6.0 Hz, 3H), 1.00 (t, J = 8.0 Hz, 3H); MS m/e 180 (M^+ – Cl, 2.67), 179 (22.80), 105 (4.82), 103 (9.17), 95 (100.00). Anal. Calcd for $C_{11}H_{15}ClO_2$: C, 61.54; H, 7.04. Found: C, 61.67; H, 6.74.

1′-Methyl-4′-chloro-2′(*E*)-butenyl 3-(trimethylsilyl)-2-propynoate ((*E*)-4f): yield 1.84 g (75%); oil; IR (neat) 2950, 2150, 1710, 1280, 1230, 970 cm^{-1}; ^{1}H NMR (200 MHz, $CDCl_3$) δ 6.00–5.84 (m, 2H), 5.44 (quintet, J = 6.0 Hz, 1H), 4.05 (d, J = 6.0 Hz, 2H), 1.38 (d, J = 6.0 Hz, 3H), 0.24 (s, 9H); MS m/e 247 ($M^+(^{37}Cl)$ + 1, 1.25), 245 ($M^+(^{35}Cl)$ + 1, 3.31), 209 (M^+ – Cl, 56.06), 201 ($M^+(^{37}Cl)$ – 3 × CH_3, 0.84), 199 ($M^+(^{35}Cl)$ – 3 × CH_3, 5.38), 137 (4.93), 135 (4.88), 125 (100.00). Anal. Calcd for $C_{11}H_{17}ClO_2Si$: C, 53.94; H, 7.00. Found: C, 54.26; H, 7.12.

1′-Methyl-4′-chloro-2′-(*Z*)-butenyl 3-(trimethylsilyl)-2-propynoate ((*Z*)-4f): yield 1.71 g (70%); oil; IR (neat) 2980, 2190, 1715, 1260, 850 cm^{-1}; ^{1}H NMR (200 MHz, $CDCl_3$) δ 5.84–5.50 (m, 3H), 4.27 (dd, J_1 = 8.0 Hz, J_2 = 12.0 Hz, 1H), 4.09 (dd, J_1 = 8.0 Hz, J_2 = 12.0 Hz, 1H), 1.39 (d, J = 6.0 Hz, 3H), 0.24 (s, 9H); MS m/e 247 ($M^+(^{37}Cl)$ + 1, 0.63), 245 ($M^+(^{35}Cl)$ + 1, 1.70), 209 (M^+ – Cl, 45.60), 125 (100.00). Anal. Calcd for $C_{11}H_{17}ClO_2Si$: C, 53.96; H, 7.00. Found: C, 53.67; H, 7.02.

Cyclization of 1′-Methyl-4′-chloro-2′-butenyl 2-Alkynoates. Typical Procedure. Synthesis of γ-Methyl-β-vinyl-α-(*Z*)-(chloromethylene)-γ-butyrolactone (5a(*trans*) and 6a(*cis*)). To a solution of (*E*)-**4a** (85 mg, 0.50 mmol) in HOAc (2.5 mL) and LiCl (5.5 mg, 0.13 mmol) was added $Pd(OAc)_2$ (5 mg, 0.025 mmol) with stirring at rt. The reaction was carried out at rt for 1.5 h (monitored by TLC on silica gel). After the reaction was complete, ethyl acetate (10 mL) was added. Then water (5 mL) was added, and the mixture was carefully neutralized with solid Na_2CO_3 in portions. The organic layer was separated, and the aqueous layer was extracted with ethyl acetate (3 × 10 mL). The combined organic layer was dried ($MgSO_4$). After removal of the solvent, the crude product was submitted to preparative TLC on silica gel (eluent: petroleum ether:ethyl acetate = 10:1) to yield **5a** and **6a**. The analytic samples were further purified by Kugelrohr distillation at the specified oven temperatures (ot).

***trans*-γ-Methyl-β-vinyl-α-(*Z*)-(chloromethylene)-γ-butyrolactone (5a)**: ot 168–170 °C (8 mmHg); IR (neat) 2950, 1755, 1610, 1200 cm^{-1}; ^{1}H NMR (200 MHz, $CDCl_3$) δ 6.50 (d, J = 2.60 Hz, 1H, CHCl=), 5.80–5.60 (m, 1H, CH=), 5.44–5.24 (m, 2H, CH_2=), 4.28 (m, 1H, OCH), 3.28 (dt, J_1 = 2.60 Hz, J_2 = 8.0 Hz, 1H, OC-CH), 1.44 (d, J = 6.2 Hz, 3H, CH_3); MS m/e 175 ($M^+(^{37}$-Cl) + 1, 54.95), 173 ($M^+(^{35}Cl)$ + 1, 100.00), 157 ($M^+(^{37}Cl)$ – OH, 4.75), 155 ($M^+(^{35}Cl)$ – OH), 11.88), 131 (2.26), 130 ($M^+(^{37}Cl)$ – CO_2, 8.09), 129 (8.13), 128 ($M^+(^{35}Cl)$ – CO_2, 24.54), 102 (M^+)^{37}Cl) – CO_2 – $CHCH_3$, 9.78), 100 ($M^+(^{35}Cl)$ – CO_2 – $CHCH_3$, 28.43), 93 (M^+ – Cl – CO_2, 89.96), 65 (77.09). Anal. Calcd for $C_8H_9ClO_2$: C, 55.67; H, 5.26. Found: C, 55.39; H, 5.09.

***cis*-γ-Methyl-β-vinyl-α-(*Z*)-(chloromethylene)-γ-butyrolactone (6a)**: ot 110–112 °C (5 mmHg); IR (neat) 2950, 1760, 1630, 1190 cm^{-1}; ^{1}H NMR (200 MHz, $CDCl_3$) δ 6.52 (d, J = 2.60 Hz, 1H, CHCl=), 5.90–5.60 (m, 1H, CH=), 5.44–5.20 (m, 2H, CH_2=), 4.75 (m, 1H, OCH), 3.80 (dt, J_1 = 2.60 Hz, J_2 = 8.0 Hz, 1H, OC-CH), 1.28 (d, J = 6.2 Hz, 3H, CH_3); MS m/e 175 ($M^+(^{37}$-Cl) + 1, 2.09), 173 ($M^+(^{35}Cl)$ + 1, 6.25), 144 ($M^+(^{37}Cl)$ – O – CH_2, 2.34), 142 ($M^+(^{35}Cl)$ – O – CH_2, 8.44), 130 ($M^+(^{37}Cl)$ – CO_2, 27.41), 128 ($M^+(^{35}Cl)$ – CO_2, 69.50), 107 (M^+ – Cl – O – CH_2, 10.65), 102 ($M^+(^{37}Cl)$ – CO_2 – $CHCH_3$, 17.52), 100 ($M^+(^{35}Cl)$ – CO_2 – $CHCH_3$, 39.05), 93 (M^+ – Cl – CO_2, 95.53), 65 (100.00); HRMS calcd for $C_8H_9ClO_2$ 174.0261 (^{37}Cl), 172.0291 (^{35}Cl); found 174.0263 (^{37}Cl), 172.0286 (^{35}Cl).

The following compounds were prepared similarly. **γ-Isopropyl-β-vinyl-α-(*Z*)-(chloromethylene)-γ-butyrolactone (5b + 6b)**: ot 150–152 °C (9 mmHg). IR (neat) 2950, 1760, 1620, 1185 cm^{-1}, ^{1}H NMR (200 MHz, $CDCl_3$) δ [6.56 (**6b**), 6.52 (**5b**) (d, J = 2.50 Hz, 1H, CHCl=)], 5.90–5.60 (m, 1H, CH=), 5.38–5.18 (m, 2H, CH_2=), [4.08 (**6b**), 4.00 (**5b**) (m, 1H, OCH)], [3.76 (**6b**), 3.48 (**5b**) (dt, J_1 = 2.50 Hz, J_2 = 8.0 Hz, 1H, OC-CH)], 1.95 (m, 1H, CH), 1.01 (d, J = 6.0 Hz, 3H, CH_3), 1.00 (d, J = 6.0 Hz, 3H, CH_3); MS m/e 203 ($M^+(^{37}Cl)$ + 1, 0.04), 201 ($M^+(^{35}Cl)$ + 1, 0.32), 175 ($M^+(^{37}Cl)$ – CH=CH_2, 33.07), 173 ($M^+(^{35}Cl)$ – CH=CH_2, 100.00), 157 (M^+)^{37}Cl) – 1 – CO_2, 5.09), 155 ($M^+(^{35}Cl)$ – 1 – CO_2, 10.48), 130 ($M^+(^{37}Cl)$ – 1 – CO_2 – CH=CH_2, 10.65), 128 ($M^+(^{35}Cl)$ – 1 – CO_2 – CH=CH_2, 32.35), 102 ($M^+(^{37}Cl)$ – CO_2 – $CHCH(CH_3)_2$, 9.48), 100 ($M^+(^{35}Cl)$ – CO_2 – $CHCH(CH_3)_2$, 28.12). HRMS calcd for $C_7H_8ClO_2$ (M^+ – C_3H_7 159.0026 (^{37}Cl), 157.0056 (^{35}Cl), found 159.0013 (^{37}Cl), 157.0061 (^{35}Cl). Anal. Calcd for $C_{10}H_{13}ClO_2$: C, 59.86; H, 6.53. Found: C, 59.41; H, 5.76.

***cis*-γ-Methyl-β-vinyl-α-(*Z*)-(chloroethylene)-γ-butyrolactone (6c)**: mp 54–55 °C; IR (neat) 2950, 1750, 1660, 1380, 1210, 1120 cm^{-1}; ^{1}H NMR (200 MHZ, $CDCl_3$) for **5c** + **6c** δ 5.71 (dt, J_1 = 10.0 Hz, J_2 = 16.0 Hz, 1H), 5.30 (d, J = 10.0 Hz, 1H), [4.59, 4.28 (quintet, J = 6.0 Hz), 1H], 3.66 (m, 1H), 2.25 (s, 3H), [1.39, 1.33 (d, J = 6.0 Hz), 3H]; MS m/e 189 ($M^+(^{37}Cl)$ + 1, 53.64), 187 ($M^+(^{35}Cl)$ + 1, 100.00), 171 (1.27), 169 (3.73), 151 (M^+ – Cl, 4.63), 144 ($M^+(^{37}Cl)$ – CO_2, 13.16), 142 ($M^+(^{35}Cl)$ – CO_2, 31.98). Anal. Calcd for $C_9H_{11}ClO_2$: C, 57.92; H, 5.94. Found: C, 58.03; H, 5.90.

***cis*-γ-Isopropyl-β-vinyl-α-(*Z*)-(chloroethylene)-γ-butyrolactone (6d)**: mp 52–52.5 °C; IR (neat) 2950, 1750, 1660, 1380, 1220, 1000 cm^{-1}; ^{1}H NMR (200 MHz, $CDCl_3$) δ 5.88–5.62 (m, 1H), 5.40–5.08 (m, 2H), 3.85 (dd, J_1 = 8.0 Hz, J_2 = 10.0 Hz, 1H), 3.80–3.60 (m, 1H), 2.23 (s, 3H), 2.04–1.74 (m, 1H), 1.08 (d, J = 6.6 Hz, 3H), 0.88 (d, J = 6.66 Hz, 3H); MS m/e 217 ($M^+(^{37}Cl)$ + 1, 6.89), 216 ($M^+(^{37}Cl)$, 3.00), 215 (M^+)(^{35}Cl) + 1, 22.38), 144 (39.85), 142 (100.00). Anal. Calcd for $C_{11}H_{15}ClO_2$: C, 61.54; H, 7.04. Found: C, 61.15; H, 7.05.

***cis*-γ-Methyl-β-vinyl-α-(*Z*)-(chlorobutylene)-γ-butyrolactone ((*Z*)-6e)**: IR (neat) 2980, 1770, 1650, 1460, 1210, 1180, 1130, 930 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 5.75 (m, 1H), 5.29–5.15 (m, 2H), 4.58 (quintet, J = 6.52 Hz, 1H), 3.70 (dd, J_1 = J_2 = 6.88 Hz, 1H), 2.43 (t, J = 7.87 Hz, 2H), 1.70 (m, 2H), 1.32 (d, J = 6.53 Hz, 3H), 0.94 (t, J = 7.4 Hz, 3H); MS m/e 217 ($M^+(^{37}Cl)$ + 1, 35.83), 215 ($M^+(^{35}Cl)$ + 1, 100.00), 179 (M^+ – Cl, 2.86), 172 ($M^+(^{37}Cl)$ – CO_2, 5.34), 170 ($M^+(^{35}Cl)$ – CO_2, 17.48), 135 (M^+ – Cl – Pr, 19.60). Anal. Calcd for $C_{11}H_{15}ClO_2$: C, 61.54; H, 7.04. Found: C, 61.52, H, 6.84.

***cis*-γ-Methyl-β-vinyl-α-(*E*)-(chlorobutylene)-γ-butyrolactone ((*E*)-6e)**: IR (neat) 2950, 1760, 1660, 1460, 1260, 1240, 1220, 1050, 800 cm^{-1}; ^{1}H NMR (200 MHz, $CDCl_3$) δ 5.70–5.50 (m, 1H), 5.26–5.08 (m, 2H), 4.60 (quintet, J = 6.0 Hz, 1H), 3.74 (t, J = 6.0 Hz, 1H), 3.00 (m, 2H), 1.64 (m, 2H), 1.30 (m, 2H), 0.92 (t, J = 8.0 Hz, 3H); MS m/e 217 ($M^+(^{37}Cl)$ + 1, 34.74), 216 ($M^+(^{37}$-Cl), 18.10), 215 ($M^+(^{35}Cl)$ + 1, 100.00), 214 ($M^+(^{35}Cl)$, 21.14), 179 (M^+ – Cl, 16.17), 173 ($M^+(^{37}Cl)$ – Pr, 2.97), 172 ($M^+(^{37}Cl)$ – CO_2, 6.15), 171 ($M^+(^{35}Cl)$ – Pr, 6.31), 170 ($M^+(^{35}Cl)$ – CO_2, 18.59). Anal. Calcd for $C_{11}H_{15}ClO_2$: C, 61.54; H, 7.04. Found: C 61.55; H, 6.84.

***cis*-γ-Methyl-β-vinyl-α-(*E*)-(chloro(trimethylsilyl)methylene)-γ-butyrolactone ((*E*)-6f)**: IR (neat) 2900, 1760, 1600, 1250, 1210, 920 cm^{-1}; ^{1}H NMR (200 MHz, $CDCl_3$) δ 5.73–5.54 (m, 1H), 5.34–5.12 (m, 2H), 4.68 (quintet, J = 6.0 Hz, 1H), 3.88 (m, 1H), 1.34 (d, J = 6.0 Hz, 3H), 0.32 (s, 9H); MS m/e 231 ($M^+(^{37}Cl)$ – CH_3, 10.59), 229 (25.93), 203 ($M^+(^{37}Cl)$ + 1 – CO_2, 3.24), 201 ($M^+(^{35}Cl)$ + 1 – CO_2, 3.84), 43 (100.00). Anal. Calcd for $C_{11}H_{17}ClO_2Si$: C, 53.94; H, 7.00. Found: C, 53.83; H, 7.14.

***cis*-γ-Methyl-β-vinyl-α-(*Z*)-(chloro(trimethylsilyl)methylene)-γ-butyrolactone ((*Z*)-6f)**: IR (neat) 2920, 1760, 1620, 1600, 1460, 1260, 1200, 920 cm^{-1}; ^{1}H NMR (200 MHz, $CDCl_3$) δ 5.90–5.72 (m, 1H), 5.34 (d, J = 8.0 Hz, 1H), 5.12 (d, J = 16.0 Hz, 1H), 4.56 (quintet, J = 6.0 Hz, 1H), 3.75 (m, 1H), 1.35 (d, J = 6.0 Hz, 3H), 0.28 (s, 9H); MS m/e 247 ($M^+(^{37}Cl)$ + 1, 13.08), 245 ($M^+(^{35}Cl)$ + 1, 33.18), 231 ($M^+(^{37}Cl)$ – CH_3, 1.82), 229 ($M^+(^{35}Cl)$ – CH_3, 5.16), 202 ($M^+(^{37}Cl)$ – CO_2, 0.87), 200 ($M^+(^{35}Cl)$ – CO_2, 2.29), 74 (100.00). Anal. Calcd for $C_{11}H_{17}ClO_2Si$: C, 53.94; H, 7.00. Found: C, 53.41; H, 7.02.

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Supplementary Material Available: ^{1}H NMR spectra for compounds (*Z*)-**4a**, (*E*)-**4a**, (*E*)-**4b**, **5b** + **6b**, **6a**, and (*Z*)-**6f** and ^{1}H 2D-NOESY spectra of compounds **5a**, **5b** + **6b**, **6a**, **6c**, **6d**, (*Z*)-**6e**, and (*E*)-**6e** (13 pages). This material is contained in libraries on microfiche, immediately follows this article in the microfilm version of the journal, and can be ordered from the ACS; see any current masthead page for ordering information.