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Palladium Catalyzed Cyclization-Carbonylation of Allylic 2-Alkynoates: Facile Synthesis of α-Alkylidene-γ-butyrolactone β-Acetic Acid Derivatives

Jianguo Ji and Xiyan Lu*

Shanghai Institute of Organic Chemistry, Chinese Academy of Sciences

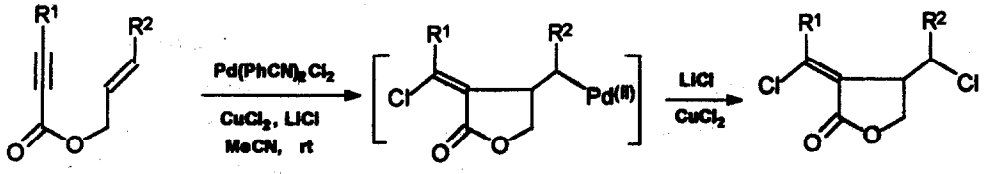
354 Fenglin Lu, Shanghai 200032, China

Abstract: α-(Z)- and (E)- Chloroalkylidene-γ-butyrolactone β-acetic acid derivatives were prepared from easily available acyclic allylic 2-alkynoates using $Pd_2(dba)_3$ $CHCl_3$ as catalyst under 1 atm of CO in the presence of $CuCl_2$ and LiCl in high stereoselectivity.

INTRODUCTION

α-Methylene-γ-butyrolactones exhibit many interesting biological activities such as cytotoxicity, antitumority, etc.[1] Many methods have been developed for the synthesis of such compounds due to their possible clinical applications.[2] However, few examples have shown practical uses because of the high toxicity.[1,2] Thus, synthesis of new α-methylene-γ-butyrolactone derivatives for screening and development of facile methods to prepare such derivatives from easily available precursors are still challenging.

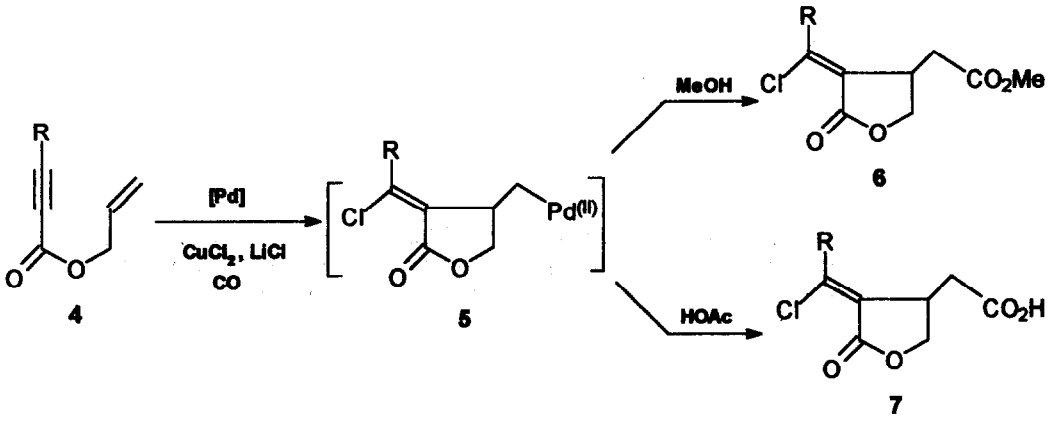
We have developed a new synthetic route to α-methylene-γ-butyrolactones (3) from allylic 2-alkynoates (1) (equation 1).[3] Based on this strategy we can develop a general method to synthesize a series of α-methylene-γ-butyrolactone derivatives if the C-Pd bond of the cyclic intermediate 2 is quenched by other methods instead of oxidative cleavage with $CuCl_2$ and LiCl.[3]



1 2 3 (1)

Recently, transition metal catalyzed carbonylation has received continuous attention because it provides an alternative method to quench the carbon-metal bond[4] and to incorporate carbon monoxide in a wide variety of chemical functions under mild conditions. Thus we wondered whether the carbonylation would occur and the products **6** and **7** would be formed (Scheme I) if we conducted our reactions under the atmosphere of carbon monoxide. In this paper, we report the results of the carbonylation of allylic 2-alkynoates (**4**) catalyzed by palladium in the presence of $CuCl_2$ under the atmosphere of carbon monoxide.

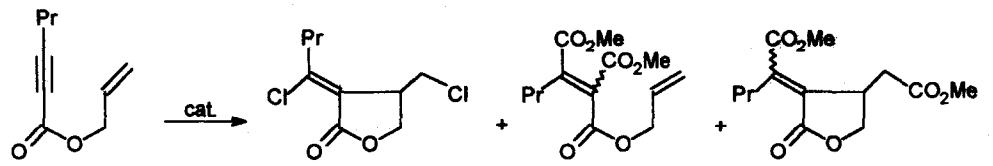
Scheme I



RESULTS AND DISCUSSION

Carbonylation of allylic 2-alkynoates in CH_3OH. Tamaru et al.[5] reported that α-methylene-γ-butyrolactones could be obtained via palladium(II)-catalyzed carbonylation of 3-butyn-1-ols. However, under similar conditions, the reaction of allylic 2-hexynoate (**4a**) with carbon monoxide afforded a complicated mixture under the catalysis of 0.05 equivalent of $PdCl_2$ in the presence of 5 equivalents of propylene oxide, 0.4 equivalent of ethyl orthoformate, 3 equivalents of $CuCl_2$ and 4 equivalents of LiCl in CH_3OH. Considering that the oxidative cleavage of carbon-palladium bond in **2** yielding **3** might take place in the presence of large amounts of free chloride ion, we tried the reaction again in the absence of LiCl. Actually, instead of **3a**, we obtained not only the acyclic dicarbonylation product **8a**, but also the cyclic dicarbonylation product **9a** (Table 1, entry 1) Some Lewis acids, I_2 and molecular sieve have been used as promoters for palladium catalyzed carbonylation of alkynes in literatures.[6] However, in our case, I_2 was found to have no promoting effect while molecular sieve 4-Å (MS-4Å) and $SnCl_2$ did promote the dicarbonylation, both of them inhibited the cyclization (Table 1, entries 2 and 3). These results implied that the palladium catalyzed carbonylation in CH_3OH can not afford the cyclization products **6**. Alper reported that the carbonylation of alkynes was quite sensitive to the solvents.[7] In our cases, the solvent effects were also important. When the reaction was tried in the mixed solvents of CH_3CN and CH_3OH (4 : 1) for a very long time (60 h), it yielded not only **8a**

Table 1. Palladium Catalyzed Dicarbonylation of Allylic 2-Hexynoate (4a).[a]



4a **3a** **8a** **9a**

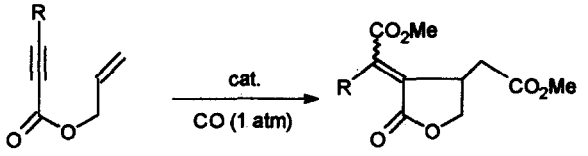
entry	solvent	additive	reaction time (h)	yield (%)[b] 3a[c]	8a[c]	9a[c]
1	CH_3OH		8	0	70	11
2	CH_3OH	MS-4Å	4	0	78	0
3	CH_3OH	$SnCl_2$	6	0	81	0
4	CH_3CN/CH_3OH(4 : 1)		60	10	20	25
5	CH_2Cl_2/CH_3OH(4 : 1)		12	0	0	73

a: A mixture of **4a** (152 mg, 1 mmol), $PdCl_2$ (9 mg, 0.05 mmol), $CuCl_2$ (405 mg, 3 mmol), propylene oxide (290 mg, 5 mmol), triethyl orthoformate (60 mg, 0.4 mmol) and the solvent (10 mL) was stirred under an atmosphere of carbon monoxide at rt. b: Isolated yield. c: The products were identified by ^1H NMR, IR, mass spectral data and microanalysis.

and **9a**, but also **3a** (Table 1, entry 4). So the solvent system of CH_3CN/CH_3OH is not suitable for the carbonylation reaction of **4a**, as might be due to the coordination of CH_3CN to palladium to compete with both **4a** and carbon monoxide.[7] While in the mixed solvent of CH_2Cl_2/CH_3OH (4 : 1), the reaction of **4a** yielded only the cyclic dicarbonylation product **9a**, which is consistent with Tamaru's report[5] on the dicarbonylation cyclization reactions of 3-butyn-1-ols. The results of preparation of **9** were summarized in Table 2. Although most of the configurations of the exocyclic carbon-carbon double bond in α-alkylidene-γ-butyrolactones have been determined by comparing the chemical shifts of allylic protons of the alkylidene groups,[3, 8] we were not able to determine the stereochemistry of the exocyclic double bond in **9** by this method. Dreiding et al. reported that methinic proton cis to the carbonyl group in methyl 3,3-diisopropyl propenoate exhibited lower field signal than the one trans to the carbonyl group by greater than 1.5 ppm.[9] In our case, H_β in the major isomer of **9** was found to be in a lower field than that of the minor isomer by ~1.3 ppm, indicating that C_β was cis to the α-(1'-methoxycarbonyl) group in the major isomer of **9**. Thus, the configuration of the exocyclic C=C double bond in the major isomer of **9** was assigned as E-form by comparing the chemical shifts of H_β.

The most plausible reaction path for the dicarbonylation of **4** is outlined in Scheme II, which is characterized by the first formation of methoxycarbonylpalladiumchloride (**10**),[4] followed by insertion of carbon-carbon triple bond to form the intermediate **11** instead of chloropalladation as in our previous results.[3] The intermediate **11** might undergo either the second methoxycarbonylation to give acyclic dicarbonylation product **8**, or the intramolecular insertion of carbon-carbon double bond followed by methoxycarbonylation to form the cyclic product **9**, depending upon various factors, such as solvents, additives, etc.

Table 2: Dicarbonylation of Allylic 2-Alkynoates.[a]

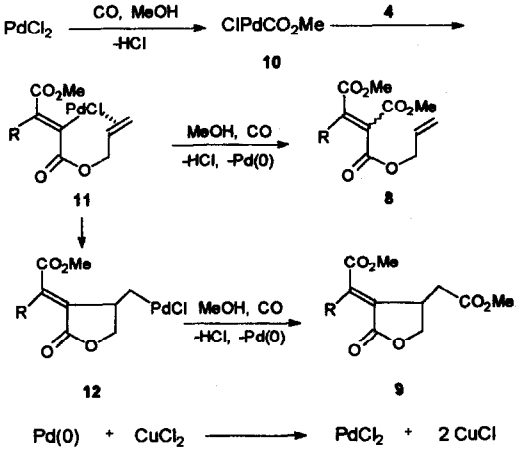


4 **9**

entry	4	R	reaction time (h)	9[b]	isolated yield (%) (Z : E)[c]	
1	**4a**	C_3H_7	15	**9a**	78	(19 : 81)
2	**4b**	C_4H_9	15	**9b**	80	(22 : 78)
3	**4c**	C_8H_{17}	35	**9c**	62	(30 : 70)

a: A mixture of **4** (1 mmol), $PdCl_2$ (9 mg, 0.05 mmol), $CuCl_2$ (405 mg, 3 mmol), propylene oxide (290 mg, 5 mmol), $HC(OC_2H_5)_3$ (60 mg, 0.4 mmol), CH_2Cl_2 (8 mL) and CH_3OH (2 mL) was stirred under CO (1atm). b: The products were confirmed by ^1H NMR, IR, mass spectral data and microanalysis. c: The ratio of Z/E (referring to the exocyclic C=C double bond in **9**) was determined by ^1H NMR spectra.

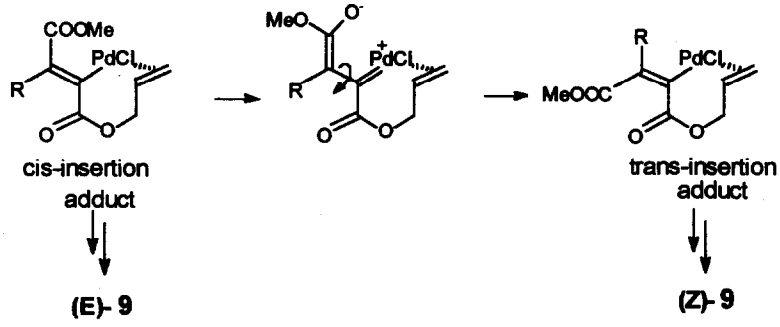
Scheme II: Plausible reaction path for the dimethoxycarbonylaton of allylic 2-alkynoates(4).



The configurations of the exocyclic C=C double bonds in **9** depend on the stereochemistry of the insertion of the carbon-carbon triple bonds of **4** into the palladium-methoxycarbonyl bond of **10**. In general, transition metal hydride and transition metal alkyls react with carbon-carbon triple bonds to give cis vinyl adducts.[10] However, results with trans insertion of alkynes into transition metal-alkyl bonds have been reported.[11] Alper reported that the palladium catalyzed carbonylation of alkynes in $HCOOH/H_2O$ yielded not only the cis products maleic acid derivatives, but also the trans products fumaric derivatives.[7a] In spite of the abundance of examples, there are few detailed mechanistic studies and little is known about the mechanism of trans insertions.[7a] Stone[12] and Schwartz[13] proposed a dipolar mechanism of cis-trans isomerization of the vinyl metal complex initially formed by a cis insertion. In our case, the major isomer (E)-**9** might result from cis- adducts of alkyne and **10**, while trans-adducts were proposed to come from the the cis-trans isomerization via a dipolar mechanism (Scheme III).

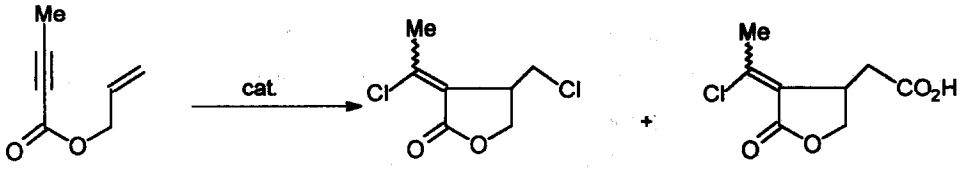
Carboxylation of allylic 2-alkynoates (4) in HOAc. Noticing the fact that the alkoxycarbonylation of allylic 2-alkynoates in the present reaction system was sensitive to the solvents, we then studied the carboxylation of **4** in HOAc. We first tried the carboxylation of **4d** under 1 atm of carbon monoxide in the presence of 3 equivalents of $CuCl_2$ using various palladium complexes as catalysts, such as $PdCl_2(PhCN)_2$,

Scheme III



$PdCl_2$, $Pd_2(dba)_3 \cdot CHCl_3$, $PdCl_2(Ph_3P)_2$ and $Pd(OAc)_2$. We found that the reaction could proceed well to give α-(E)-chloroalkylidene-γ-butyrolactone β-acetic acid (**7d**) only under the catalysis of $Pd_2(dba)_3 \cdot CHCl_3$ and MS-4Å (Table 3, entry 1). Table 3 shows the results of the effect of LiCl on the reaction. Increasing the amounts of LiCl could increase the Z/E ratio of **7d** (Table 3, entries 2 and 3). When 4 equivalents of LiCl was added, the reaction yielded mainly (Z)-**7d** (entry 4). When 6 or more equivalents of LiCl were added, almost only (Z)-**7d** was obtained(entries 5 and 6). However, increasing the amounts of LiCl also decreased the yield of

Table 3. Effect of LiCl on the Cyclization-Carboxylation of Allylic 2-Butynoate (4d).[a]

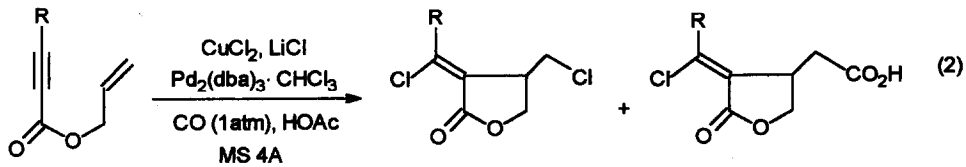


4d **3d** **7d**

entry	LiCl (mmol)	reaction time (h)	Isolated yield (%) 3d[b]	7d[b] (Z : E)[c]
1	0	40	0	77 (< 3 : 97)
2	1	35	4	70 (20 : 80)
3	2	35	8	70 (33 : 67)
4	4	25	15	66 (90 : 10)
5	6	20	20	64 (>97 : 3)
6	10	15	59	10 (>97 : 3)

a: Reaction conditions: A mixture of **4d** (124 mg, 1 mmol), $Pd_2(dba)_3 \cdot CHCl_3$ (51 mg, 0.05 mmol), $CuCl_2$ (405 mg, 3 mmol), MS-4Å (100 mg) and HOAc (10 mL) was stirred at rt. under 1 atm of CO; b: The products were confirmed by ^1H NMR, IR, mass spectral data and microanalysis; c: The Z:E ratio referred to the exocyclic carbon-carbon double bond in **7d.**

7d and increased the yield of dichlorosubstituted lactone **3d**, although the reaction time was shortened (Table 3, entries 2-6).



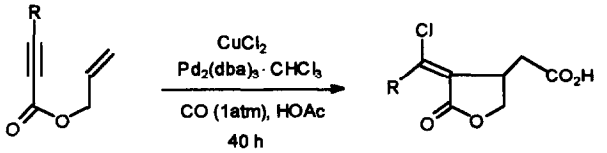
(2)

4 (Z)-3 (%) (Z)-7 (%)

a: R = n-C_3H_7	18	58
b: R = n-C_4H_9	19	61
d: R = CH_3	20	64
e: R = n-C_7H_{15}	21	59
f: R = Ph	16	56

When the reactions of allylic 2-alkynoates (**4**) were carried out in the presence of 1 atm of carbon monoxide, 3 equivalents of $CuCl_2$ and 6 equivalents of LiCl under the catalysis of $Pd_2(dba)_3 \cdot CHCl_3$ and MS-4Å in HOAc, (Z)-7 and (Z)-3 were obtained (equation 2) in the ratio of 3 to 1 [(Z)-7/(Z)-3]. Under

similar conditions, when the reactions of **4** were run in the absence of LiCl, only (E)-**7** were obtained (equation 3). All products were confirmed by ^{1}H NMR, IR and mass spectral data. The configuration of the exocyclic carbon-carbon double bond in the products **3** and **7** were determined by comparing the chemical shifts of allylic protons in R group, in which E-form products exhibited lower field signals for allylic protons than Z-form products in ^{1}H NMR spectra because of the deshielding effect of the carbonyl group in lactones.[3, 8] Thus, by controlling the amounts of added LiCl, we could synthesize both α-(Z)- and α-(E)-chloroalkylidene-γ-butyrolactone β-acetic acid (**7**) in high stereoselectivity.



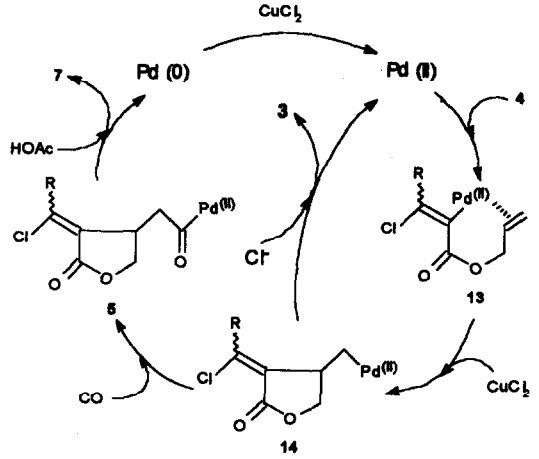
4 (E)-**7** (%) (3)

a: R = n-C_3H_7	69
b: R = n-C_4H_9	72
d: R = CH_3	77
e: R = n-C_7H_{15}	70
f: R = Ph	71

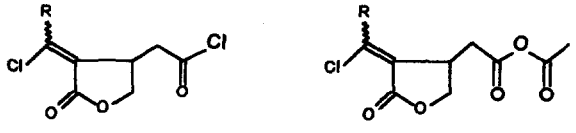
The plausible reaction path is assumed in Scheme IV. Vinylpalladium intermediate **13** was first formed by chloropalladation of carbon-carbon triple bond in the presence of $CuCl_2$,[3] Then an intramolecular insertion of allylic carbon-carbon double bond into the carbon-palladium bond in **13** would predominate to form the cyclic intermediate **14** over the insertion of carbon monoxide. Finally, in the presence of HOAc, α-chloroalkylidene-γ-butyrolactone β-acetic acid (**7**) would be formed via the intermediate **5** formed by the insertion of carbon monoxide into the carbon-palladium bond in **14**. If there exists enough free chloride ion in the reaction system, the oxidative cleavage of the carbon-palladium bond might compete with the insertion of CO in **14**, which afforded dichlorosubstituted lactones **3**.[3, 8]

Alper[7] reported that the dicarbonylation reactions of alkynes could take place under the catalysis of $PdCl_2$ and $CuCl_2$ in the presence of CO and O_2. However, we were not able to observe the acyclic dicarbonylation products in the present reaction system. The results might be attributed to the electron-deficient carbon-carbon triple bond and the excess amount of $CuCl_2$ in our cases which made the chloropalladation of carbon-carbon triple bonds occur predominantly in acetic acid.[3,14] The stereochemistry of halopalladation of carbon-carbon triple bonds has been reported [14-16] to be quite sensitive to the solvents and the amount of LiCl. Trans halopalladation of carbon-carbon triple bond occurs in polar solvents with large amount of LiX; otherwise, cis halopalladation takes place predominantly. In our case, the results that Z/E ratio of cyclic products increased with the amount of LiCl are consistent with this rule and our previous reports.[3]

Scheme IV



Tsuji[17] reported that the carbonylation of alkenes gave acyl chloride under the catalysis of $PdCl_2$. Fujiwara[18] reported that the $Pd(OAc)_2$ catalyzed carbonylation of benzene in HOAc afforded benzoic acid via a mechanism involving the formation of the acetic-benzoic anhydride followed by acidolysis. Thus in our cases, α-chloroalkylidene-γ-butyrolactone β-acetic acid (7) might be formed via acyl chloride **15** and / or anhydride **16** followed by acidolysis in the presence of HOAc.



EXPERIMENTAL SECTION

Infrared spectra were obtained with a Shimadzu IR-440 instrument. Nuclear magnetic resonance spectra were recorded with a Varian EM-360L or Varian XL-200 spectrometer and were reported in ppm downfield of internal tetramethylsilane (δ units). Mass spectral data were taken on a Finnigan 4021 spectrometer. The starting materials allylic 2-alkynoates **4** were synthesized according to the reported procedure.[3a]

General Procedure for Palladium Catalyzed Dicarbonylation of Allylic 2-Hexynoate (4a) in CH_3OH. In an atmosphere of CO, the solvents (10 mL, see Table 1), propylene oxide (290 mg, 5 mmol), ethyl orthoformate (60 mg, 0.4 mmol) and allylic 2-hexynoate (**4a**) (152mg, 1mmol) were introduced successively into the flask containing $PdCl_2$ (9 mg, 0.05 mmol) and anhydrous $CuCl_2$ (405 mg, 3 mmol) via syringes. The mixture was stirred at room temperature for the period of time indicated in Table 1. After evaporation of the

solvents under reduced pressure, ether (80 mL) was added to the flask and the mixture was then filtered through a celite pad. The filter cake was washed with ether (3 x 10 mL). The combined filtrates were washed with saturated brine. After being dried ($MgSO_4$) and removal of ether, the yellow residue was subjected to column chromatography on silica gel (eluent: petroleum ether : ethyl acetate = 10 : 1) for purification. The results are shown in Table 1 and Table 2. The spectral and analytical data of the products are as follows:

Allyl 2,3-Dimethoxycarbonyl-2-hexenoate (8a): IR (neat) 3050, 1740, 1720, 1630, 1460, 1240, 1020, 970 cm^{-1}; ^1H NMR (60 MHz/CCl_4) δ 6.2-5.6(m, 1H), 5.4-5.1(m, 2H), 4.6(d, J=5.0Hz, 2H), 3.7(s, 3H), 3.6(s, 3H), 2.8(t, J=8.0Hz, 2H), 1.3(m, 2H), 1.0(t, J=7.0Hz, 3H) ppm; MS m/e 271(M^++1), 243, 211, 185, 152, 125, 109, 93. Anal. Calc. for $C_{13}H_{18}O_6$: C. 57.77; H. 6.71. Found: C. 58.25; H. 7.17.

α-(1'-Methoxycarbonylbutylidene)-β-methoxycarbonyl-γ-butyrolactone (9a): IR (neat) 1770, 1720, 1440, 1200, 980, 750 cm^{-1}; ^1H NMR (200 MHz/$CDCl_3$) δ 4.36(dd, J=10.0, 6.0Hz, 1H), 4.24(d, J=10.0Hz, 1H), 3.90{m, 0.81H[H_β of (E)-**9a**]}, 3.80(s, 3H), 3.72(s, 3H), 3.04-2.82(m, 2H), 2.60{m, 0.19H[H_β of (Z)-**9a**]}, 2.54(m, 2H), 1.50(m, 2H), 0.98(t, J=7.0Hz, 3H) ppm; MS m/e 271(M^++1), 255, 239, 211, 197, 183, 178, 165, 149, 119. Anal. Calc. for $C_{13}H_{18}O_6$: C. 57.77; H. 6.71. Found: C. 57.92; H. 6.50.

α-(1'-Methoxycarbonylpentylidene)-β-methoxycarbonyl-γ-butyrolactone (9b): IR (neat) 1770, 1730, 1630, 1220, 1140, 790 680cm^{-1} ; ^1H NMR (200 MHz/$CDCl_3$) δ 4.36(dd, J=10.0, 6.0Hz, 1H), 4.16(d, J=10.0Hz, 1H), 3.88{m, 0.78H[H_β of (E)-**9b**]}, 3.78(s, 3H), 3.70(s, 3H), 2.98-2.78(m, 2H), 2.60{m, 0.22H[H_β of (Z)-**9b**]},2.50(m, 2H), 1.70(m, 2H), 1.40(m, 2H), 0.98(t, J=6.0Hz, 3H) ppm; MS m/e 284(M^+) 252, 210, 187, 151, 107. Anal. Calc. for $C_{14}H_{20}O_6$: C. 59.14; H. 7.09. Found: C: 59.46; H. 6.72.

α-(1'-Methoxycarbonylnonylidene)-β-methoxycarbonyl-γ-butyrolactone (9c): IR (neat) 1770, 1730, 1650, 1420, 1210, 890, 780 cm^{-1} ; ^1H NMR (200 MHz/$CDCl_3$) δ 4.40(dd, J=10.0, 6.0 Hz, 1H), 4.20(dd, J=10.0, 1.0Hz, 1H), 3.90{m, 0.70H[H_β of (E)-**9c**]}, 3.84(s, 3H), 3.72(s, 3H), 2.94(m, 2H), 2.70{m, 0.30H[H_β of (Z)-**9c**]},2.60(m, 2H), 1.30(m, 12H), 0.90(t, J=6.0Hz, 3H) ppm ; MS m/e 341(M^++1), 309, 267, 223, 210, 177, 151, 119. Anal. Calc. for $C_{18}H_{28}O_6$: C. 63.51; H. 8.29. Found: C.63.32; H. 7.85.

Palladium Catalyzed Carbonylation of Allylic 2-Alkynoates (4) in HOAc: Typical procedure: In an atmosphere of CO, HOAc (10 mL) and **4a** (152 mg, 1 mmol) were added into a flask containing $Pd_2(dba)_3$·$CHCl_3$ (51 mg, 0.05 mmol), $CuCl_2$ (405 mg, 3 mmol), LiCl (255 mg, 6 mmol) and MS-4Å (100 mg) via syringe and the mixture was stirred at room temperature with monitoring by TLC on silica gel. After the reaction was completed, ether (100 mL) was added and the brown mixture was washed with water (2 x 10 mL) and saturated brine (3 x 10 mL) to give a colorless solution. After being dried over $MgSO_4$ and removal of ether, the residue was subjected to purification by preparative TLC on silica gel (eluent: petroleum ether: acetone = 1 : 2). **3a** (40 mg, y. 18%) and **7a** (135 mg, y. 58%) were finally obtained.

The results are shown in equations 2 and 3. The spectral data of compounds (Z)-(**3a, 3b, 3d and 3e**) were reported in ref. 3a.

α-(Z)-(1'-Chlorobenzylidene)-β-chloromethyl-γ-butyrolactone [(Z)-3f]: mp 144-147°C; IR (nujol) 3080, 1760, 1640, 1600, 1580, 1500, 1480, 1240, 920, 770, 730, 700, 630, 570 cm^{-1} ; ^1H NMR(200 MHz/$CDCl_3$) δ 7.44(m, 5H), 4.48(m, J=2.0Hz, 2H), 3.92(m, 1H), 3.80(m, 2H) ppm; MS m/e (%) 260[M^+(^{37}Cl), 2.12], 258[M^+(^{37}Cl, ^{35}Cl), 12.84], 256[M^+($2^{35}Cl$), 20.03], 209, 207, 183, 181, 179, 115. Anal. Calc. for $C_{12}H_{10}Cl_2O_2$: C. 56.06; H. 3.92. Found: C. 56.32; H. 3.85.

α-(Z)-(1'-Chlorobutylidene)-γ-butyrolactone β-Acetic Acid [(Z)-7a]: mp 138-140°C; ; IR (nujol) 3000-2500, 1750, 1700, 1640, 1470, 1380, 1220, 920 720, 680 cm^{-1} ; ^1H NMR(200 MHz/CD_3COCD_3) δ 4.40(dd, J=10.0, 6.0Hz, 1H), 4.20(dd, J=10.0, 2.0Hz, 1H), 3.70(m, 1H), 2.64(m, 4H), 1.70(m, 2H), 1.0(t, J=6.0Hz, 3H) ppm; MS m/e (%) 234[M^+(^{37}Cl), 13.48], 232[M^+(^{35}Cl), 38.60], 197, 175, 173, 151, 137, 109. Anal. Calc. for $C_{10}H_{13}ClO_4$: C. 51.62; H. 5.63. Found: C. 51.36; H. 5.93.

α-(E)-(1'-Chlorobutylidene)-γ-butyrolactone β-Acetic Acid [(E)-7a]: oil; IR (neat) 3500, 1760, 1720, 1660, 1650, 1380, 1220, 910, 790, 650 cm^{-1} ; ^1H NMR(200 MHz/CD_3COCD_3) δ 4.43(dd, J=9.0, 7.0Hz, 1H), 4.18(dd, J=9.0, 2.0Hz, 1H), 3.58(m, 1H), 3.10(m, 2H), 2.70(m, 2H), 1.60(m, 2H), 0.96(t, J=7.0Hz, 3H) ppm; MS m/e (%) 234[M^+(^{37}Cl), 12.24], 232[M^+(^{35}Cl), 34.48], 219(4.27), 217(8.42), 197, 175(32.41), 173(100.00), 151, 137, 109. Anal. Calc. for $C_{10}H_{13}ClO_4$: C. 51.62; H. 5.63. Found: C. 52.00; H. 6.05.

α-(Z)-(1'-Chloropentylidene)-γ-butyrolactone β-Acetic Acid [(Z)-7b]: mp 140-142°C; IR (nujol) 3000-2500, 1750, 1700, 1640, 1470, 1280, 1210, 920, 780, 680 cm^{-1} ; ^1H NMR(200 MHz/CD_3COCD_3) δ 4.40(dd, J=10.0, 6.0Hz, 1H), 4.18(dd, J=10.0, 2.0Hz, 1H), 3.73(m, 1H), 2.64(m, 4H), 1.70(m, 2H), 1.49(m, 2H), 0.95(t, J=6.0Hz, 3H) ppm; MS m/e (%) 249[M^+(^{37}Cl)+1, 24.46], 247[M^+(^{35}Cl)+1, 71.69], 220(16.06), 218(50.75), 189, 187, 151, 145, 112, 105. Anal. Calc. for $C_{11}H_{15}ClO_4$: C. 53.56; H. 6.13. Found: C. 53.51; H. 6.37.

α-(E)-(1'-Chloropentylidene)-γ-butyrolactone β-Acetic Acid [(E)-7b]: oil; IR (neat) 3400, 1760, 1700, 1660, 1640, 1470, 1380, 1220, 940, 830, 770, 740, 660 540 cm^{-1} ; ^1H NMR(200 MHz/CD_3COCD_3) δ 4.50(dd, J=10.0, 6.0Hz, 1H), 4.20(dd, J=10.0, 2.0Hz, 1H), 3.53(m, 1H), 3.20(m, 2H), 2.80(m, 2H), 1.60(m, 2H), 1.41(m, 2H), 0.90(t, J=7.0Hz, 3H) ppm; MS m/e (%) 248[M^+(^{37}Cl), 8.24], 246[M^+(^{35}Cl), 20.82], 219(11.83), 217(35.60), 211, 189(14.03), 187(39.35), 171, 169, 145, 112, 105. Anal. Calc. for $C_{11}H_{15}ClO_4$: C. 53.56; H. 6.13. Found: C. 53.35; H. 6.29.

α-(Z)-(1'-Chloroethylidene)-γ-butyrolactone β-Acetic Acid [(Z)-7d]: mp 159-162°C; ; IR (nujol) 3000-2500, 1750, 1700, 1650, 1470, 1380, 1220, 920 780, 680 cm^{-1} ; ^1H NMR(200 MHz/CD_3COCD_3) δ 4.40(dd, J=9.0, 6.0Hz, 1H), 4.18(dd, J=9.0, 2.0Hz, 1H), 3.72(m, 1H), 2.68(m, 2H), 2.40(s, 3H) ppm; MS m/e (%) 206[M^+(^{37}Cl), 0.8], 204[M^+(^{35}Cl), 2.50], 185, 171, 128, 115, 105, 102. Anal. Calc. for $C_8H_9ClO_4$: C.46.96; H. 4.43. Found: C. 46.75; H. 4.40.

α-(E)-(1'-Chloroethylidene)-γ-butyrolactone β-Acetic Acid [(E)-7d]: mp 90-92°C; IR (nujol) 3000-2500, 1750, 1700, 1660, 1640, 1370, 1230, 960, 810, 780, 740, 660 480 cm^{-1}; ^1H NMR(200

MHz/CD_3COCD_3) δ 4.50(dd, J=9.0, 6.0Hz, 1H), 4.22(dd, J=9.0, 2.0Hz, 1H), 3.66(m, 1H), 2.80(m, 2H), 2.64(s, 3H) ppm; MS m/e (%) 207[$M^+(^{37}Cl)$+1, 16.65], 205[$M^+(^{35}Cl)$+1, 53.44], 188(9.16), 186(26.75), 160(13.97), 158(33.97), 147(36.10), 145(100.00), 123, 117. Anal. Calc. for $C_8H_9ClO_4$: C.46.96; H. 4.43. Found: C. 46.70; H. 4.18.

α-(Z)-(1'-Chlorooctylidene)-γ-butyrolactone β-Acetic Acid [(Z)-7e]: mp 110-112°C; IR (nujol) 3000-2500, 1750, 1700, 1640, 1470, 1380, 1220, 910, 680 cm^{-1} ; ^1H NMR(200 MHz/CD_3COCD_3) δ 4.40(dd, J=10.0, 6.0Hz, 1H), 4.20(dd, J=10.0, 2.0Hz, 1H), 3.76(m, 1H), 2.60(m, 4H), 1.70-1.20(m, 10H), 0.98(t, J=7.0Hz, 3H) ppm; MS m/e (%) 289[$M^+(^{37}Cl)$-1, 1.52], 287[$M^+(^{35}Cl)$-1, 4.53], 276, 274, 261, 259, 234(22.53), 232(60.59), 197, 175, 173, 137, 109. Anal. Calc. for $C_{14}H_{21}ClO_4$: C. 58.23; H. 7.33. Found: C. 58.39; H. 7.72.

α-(E)-(1'-Chlorooctylidene)-γ-butyrolactone β-Acetic Acid [(E)-7e]: oil; IR (neat) 3400, 1750, 1710, 1660, 1470, 1380, 1260, 820, 720, 660 cm^{-1} ; ^1H NMR(90 MHz/CD_3COCD_3) δ 4.45(dd, J=9.0, 7.0Hz, 1H), 4.15(dd, J=9.0, 2.0Hz, 1H), 3.60(m, 1H), 3.10(m, 2H), 2.75(d, J=4.0Hz, 2H), 1.60-1.20(m, 10H), 0.90(t, J=6.0Hz, 3H) ppm; MS m/e (%) 290[$M^+(^{37}Cl)$, 5.30], 288[$M^+(^{35}Cl)$, 17.24], 219(19.56), 217(61.23), 175, 173, 157, 137, 123, 109. Anal. Calc. for $C_{14}H_{21}ClO_4$: C. 58.23; H. 7.33. Found: C. 58.24; H. 7.64.

α-(Z)-(1'-Chlorobenzylidene)-γ-butyrolactone β-Acetic Acid [(Z)-7f]: mp 166-168°C; IR (nujol) 3000-2500, 1750, 1710, 1640, 1600, 1470, 1220, 910, 790, 720, 690 cm^{-1} ; ^1H NMR(200 MHz/CD_3COCD_3) δ 7.42(m, 5H), 4.58(dd, J=9.0, 7.0Hz, 1H), 4.24(dd, J=9.0, 2.0Hz, 1H), 3.84(m, 1H), 2.96(m, 2H) ppm; MS m/e (%) 269[$M^+(^{37}Cl)$+1, 19.30], 267[$M^+(^{35}Cl)$+1, 100.00], 222, 220, 185, 171, 128, 115, 105. Anal. Calc. for $C_{13}H_{11}ClO_4$: C. 58.55; H. 4.16. Found: C. 58.49; H. 3.91.

α-(E)-(1'-Chlorobenzylidene)-γ-butyrolactone β-Acetic Acid [(E)-7f]: mp 121-123°C; IR (nujol) 3000-2500, 1750, 1710, 1640, 1600, 1470, 1290, 910, 790, 760, 700 cm^{-1} ; ^1H NMR(200 MHz/CD_3COCD_3) δ 7.56(m, 5H), 4.52(d, J=9.0Hz, 1H), 4.14(dd, J=9.0, 4.0Hz, 1H), 3.84(m, 1H), 2.30(m, 2H) ppm; MS m/e (%) 268[$M^+(^{37}Cl)$, 7.35], 266[$M^+(^{35}Cl)$, 19.67], 222(31.66), 220(100.00), 185, 171, 145, 128, 115, 105. Anal. Calc. for $C_{13}H_{11}ClO_4$: C. 58.55; H. 4.16. Found: C. 58.32; H. 4.30.

REFERENCES

1. (a) Oliver, E. J.; Fisher, H. D. in *Progress in the Chemistry of Organic Natural Products*; Herz, W. ; Grisebach, H.; Kirby, G. W. Eds.; Springer-Verlag: New York. **1979**; Vol. *38*, pp. 47.; (b) Tang, W.; Eisenbrand, G. *Chinese Drugs of Plant Origin*; Springer-Verlag: Berlin. **1992**.
2. (a) Petranani, N.; Ferraz, H. M. C.; Silva, G. V. *Synthesis*, **1986**, 157.; (b) Hoffman, H. M. R.; Rabe, A. J. *Angew. Chem. Int. Ed. Engl.* **1985**, *24*, 94.; (c) Boyd, G. V. in *The Chemistry of Acid Derivatives: Supplement B*; Patai, S. Ed.; John Wiley & Sons, Inc.: New York. **1992**; vol. *2*, part 1, pp. 547.

3. (a) Ma, S.; Lu, X. *J. Org. Chem.* **1993**, *58*, 1245.; (b) Lu, X.; Zhu, G. *Synlett*, **1993**, 68
4. (a) Thompson, D. J. in *Comprehensive Organic Synthesis*; Trost, B. M.; Fleming, I. Eds.; Pergamon Press: Oxford. **1991**; vol. *3*, pp. 1015.; (b) Colquhoun, H. M.; Thompson, D. J.; Twigg, M. V. *Carbonylation*; Plenum Press: New York. **1991**.
5. Tamaru, Y.; Hojo, M.; Yoshida, Z. *J. Org. Chem.* **1991**, *56*, 1099.
6. (a) Wender, J. Pino, P. *Organic Synthesis via Metal Carbonyl*; John Wiley & Sons, Inc.: New York. **1977**; vol. *2*.; (b) Mori, K.; Mizoroki, T.; Ozaki, A.; *Chem. Lett.* **1975**, 39.; (c) Kiji, J.; Konishi, H.; Okano, T.; Kometani, S.; Iwasa, A. *Chem. Lett.* **1987**, 313.
7. Zargarian, D.; Alper, H. *Organometallics*, **1991**, *10*, 2914.; Huh, K. -T.; Orita, A.; Alper, H. *J. Org. Chem.* **1993**, *58*, 6956.
8. (a) Davies, H. M. L.; Hu, B. *J. Org. Chem.* **1992**, *57*, 4309. and references cited therein.; (b) Burke, S. D.; Pacofsky, G. J.; Piscopio, A. D. *J. Org. Chem.* **1992**, *57*, 2228.; (c) de Azevedo, M. B. M.; Murta, M. M.; Greene, A. E. *J. Org. Chem.* **1992**, *57*, 4567.
9. Koller,M.; Karpf, M.; Dreiding, A. S. *Helv. Chim. Acta.* **1986**, *69*, 560.
10. Maitlis, P. M. ; Espinet, P.; Russell, M. J. H. in *Comprehensive Organometallic Chemistry*; Wilkinson, G.; Stone, F. G. A.; Abel, E. W. Eds.; Pergamon Press: Oxford. **1982**; vol. *6*, pp. 459.
11. Huggins, J. M.; Bergman, R. G. *J. Am. Chem. Soc.* **1981**, *103*, 3002.; Rice, C.; Oliver, J. D. *J. Organomet. Chem.* **1978**, *145*, 121.; Otsuka, S.; Nakamura, A. *Adv. Organomet. Chem.* **1976**, 245.
12. Blackmore, T.; Bruce, M. I.; Stone, F. G. A. *J. Chem. Soc., Dalton Trans.* **1974**, 106.
13. Hart, D. W.; Schwartz, J. *J. Organomet. Chem.* **1975**, *87*, C11.
14. (a) Waegell, B. in *Organomtallics in Organic Synthesis*; de Meijere, A.; tom, Dieck, H. Eds.; Springer-Verlag: Berlin. **1987**, pp. 203.; (b) Heuman, A. in *Metal Promoted Selectivity in Organic Synthesis*; Nobel, A. F.; Graziani, M.; Hubert, A. J. Eds.; Kluwer Academic Publisher: Dordrecht. **1991**; pp. 133.
15. (a) Maitlis, P. M.; Espinet, P.; Russell, M. J. H. in *Comprehensive Organometallic Chemistry*; Wilkinson, G.; Stone, F. G. A.; Abel, E. W. Eds.; Pergamon Press: Oxford. **1982**; vol. *6*, pp. 326.; (b) Maitlis, P. M. *Acc. Chem. Res.* **1976**, *9*, 93.
16. Kaneda, K.; Uchiyama, T. Fujiwara, Y.; Imanaka, T.; Teranishi, S. *J. Org. Chem.* **1979**, *44*, 55.; Maitlis, P. M. *J. Organomet. Chem.* **1980**, *200*, 161.
17. Tsuji, J.; Morikawa, M.; Kiji, J. *J. Am. Chem. Soc.* **1964**, *86*, 8451.
18. (a) Fujiwara, Y.; Jintoku, T.; Takaki, K. *Chemtech.* **1990**, 636.; (b) Jintoku, T.; Fujiwara, Y.; Kawata, J.; Kawauchi, T.; Taniguchi, H. *J. Organomet. Chem.* **1990**, *385*, 427.

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