Platinum(0)-Catalyzed Carbonylative Lactonization of 5-Hydroxy-1-pentyne with Carbon Monoxide in the Presence of Thiols

Akiya Ogawa,* Ken-ichi Kawabe, Jun-ichi Kawakami, Masatoshi Mihara, and Toshikazu Hirao

Department of Applied Chemistry, Faculty of Engineering, Osaka University, Suita, Osaka 565-0871, Japan

Noboru Sonoda*

Department of Applied Chemistry, Faculty of Engineering, Kansai University, Suita, Osaka 564-0073, Japan

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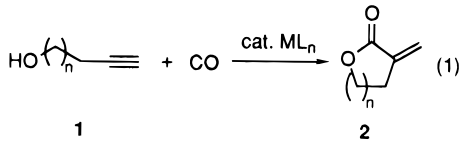
Summary: Tetrakis(triphenylphosphine)platinum(0) (Pt(PPh$_3$)$_4$) in the presence of aromatic thiols exhibits an excellent catalytic activity toward the carbonylative lactonization of 5-hydroxy-1-pentyne with carbon monoxide, which provides α-methylene-δ-lactone in good yield.

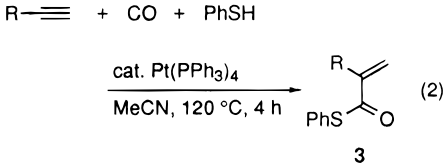
Introduction

The carbonylative cyclization of acetylenic alcohols with carbon monoxide is one of the most straightforward methods of obtaining α-methylenelactones (eq 1).[1] In



particular, the preparation of five-membered (γ) lactones (**2a**, $n = 1$) by the carbonylation of acetylenic alcohols has been studied intensively;[2] however, only very limited data are available for the carbonylative routes to six-membered (δ) lactone rings.[2a,c]

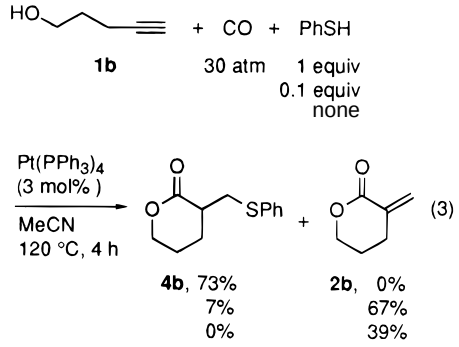
Recently we have developed a highly selective hydrothiocarboxylation of acetylenes with thiols and carbon monoxide catalyzed by Pt(PPh$_3$)$_4$ (eq 2).[3] Thus, if



acetylenic alcohols (**1**) are employed as substrates for this Pt(PPh$_3$)$_4$-catalyzed carbonylation with CO and thiols, carbonylative cyclization is expected to take place, providing the corresponding lactones. Described here is a catalytic cyclocarbonylation of 5-hydroxy-1-pentyne (**1b**, $n = 2$) to α-methylene-δ-lactone (**2b**, $n = 2$), which can be attained successfully by modifying the "hydrothiocarboxylation" procedure.

Results and Discussion

When the carbonylation of 5-hydroxy-1-pentyne (**1b**) was carried out in the presence of 1 equiv of benzenethiol and 1 mol % of platinum(0) catalyst under the pressure of carbon monoxide (30 atm) at 120 °C for 4 h, the desired cyclocarbonylation of 5-hydroxy-1-pentyne (**1b**) took place successfully to afford α-((phenylthio)-methyl)-δ-lactone (**4b**) selectively in good yield (eq 3).



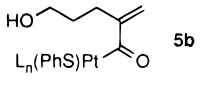
A possible reaction pathway for the formation of **4b** may include the following: (i) Pt(PPh$_3$)$_4$-catalyzed hydrothiocarboxylation of **1b** to give the α,β-unsaturated thiocarboxylate **3b** (**3**, R = HO(CH$_2$)$_3$), (ii) cyclization of **3b** to give α-methylene-δ-lactone (**2b**) with regeneration of PhSH, and (iii) the Michael addition of PhSH to **2b**, giving **4b**.[4] Thus, the Pt(PPh$_3$)$_4$-catalyzed carbonylation of **1b** with CO was conducted in the presence of

(1) Colquhoun, H. M.; Thompson, D. J.; Twigg, M. V. *Carbonylation: Direct Synthesis of Carbonyl Compounds*; Plenum Press: New York, 1991; pp 173−189.

(2) (a) Murray, T. F.; Samsel, E. G.; Varma, V.; Norton, J. R. *J. Am. Chem. Soc.* **1981**, *103*, 7520. (b) Murray, T. F.; Norton, J. R. *J. Am. Chem. Soc.* **1979**, *101*, 4107. (c) Murray, T. F.; Varma, V.; Norton, J. R. *J. Org. Chem.* **1978**, *43*, 353. (d) Murray, T. F.; Varma, V.; Norton, J. R. *J. Am. Chem. Soc.* **1977**, *99*, 8085. (e) Norton, J. R.; Shenton, K. E.; Schwartz, J. *Tetrahedron Lett.* **1975**, 51. (f) Tsuji, Y.; Kondo, T.; Watanabe, Y. *J. Mol. Catal.* **1987**, *40*, 295.

(3) Ogawa, A.; Kawakami, J.; Mihara, M.; Ikeda, T.; Sonoda, N.; Hirao, T. *J. Am. Chem. Soc.* **1997**, *119*, 12380.

(4) The other explanation is suggested to involve the formation of an acylplatinum intermediate (**5b**), followed by cyclization of **5b** to the δ-lactone (**2b**).



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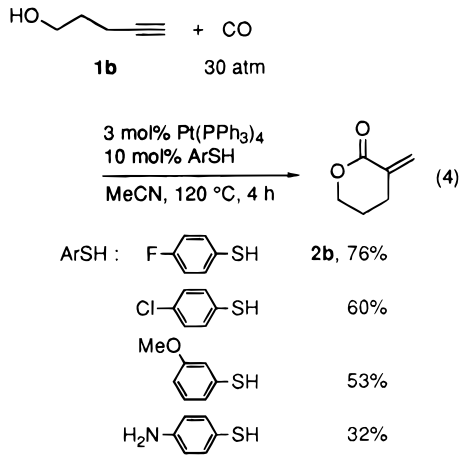
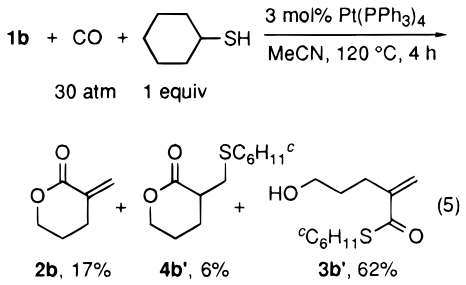
0.1 equiv of PhSH, resulting in the formation of α-methylene-δ-lactone (**2b**)[5] as the major product in good yield. In the absence of benzenethiol, **2b** was formed in only 39% yield along with a few byproducts. These results strongly suggest that $Pt(PPh_3)_4$ catalyst in the presence of a catalytic amount of PhSH is effective for the carbonylative lactonization leading to α-methylene-δ-lactone (**2b**).

The influence of the substituents on the aromatic thiols was demonstrated, as shown in eq 4. The yield of **2b** increased in the case of electron-withdrawing groups exhibiting no reactivity toward the platinum catalyst, such as the *p*-fluoro group.



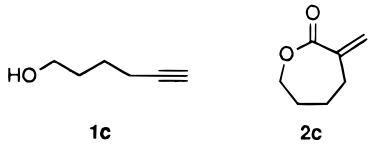
On the other hand, when a similar reaction of 5-hydroxy-1-pentyne (**1b**) with CO was conducted by using 1 equiv of an aliphatic thiol such as cyclohexanethiol in place of aromatic thiols, the desired δ-lactone derivatives (**2b** and **4b′**) were formed only in 17% and 6% yields, respectively. Instead, the hydrothiocarboxylation



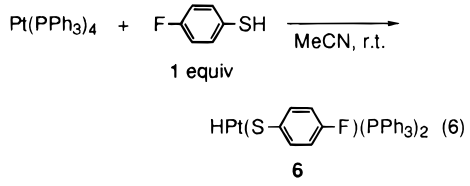
product (**3b′**) was obtained as the major product (62%). Heating the isolated **3b′** at 120 °C in the absence of the catalyst gradually produced the corresponding δ-lactone **2b**. The decreased ability of the cyclohexanethiolate group to act as a leaving group, compared with the phenylthiolate group, may contribute to the inefficiency of the cyclization step in the reaction using cyclohexanethiol.

(5) For the synthesis of α-methylene-δ-lactone (**2b**), see: (a) Paterson, I. *Tetrahedron* **1988**, *44*, 4207. (b) Murray, A. W.; Reid, R. G. *J. Chem. Soc., Chem. Commun.* **1984**, 132. (c) Mori, M.; Washioka, Y.; Urayama, T.; Yoshiura, K.; Chiba, K.; Ban, Y. *J. Org. Chem.* **1983**, *48*, 4058. (d) Semmelhack, M. F.; Brickner, S. J. *J. Org. Chem.* **1981**, *46*, 1723. (e) Paterson, I.; Fleming, I. *Tetrahedron Lett.* **1979**, 993. (f) Ksander, G. M.; McMurry, J. E.; Johnson, M. *J. Org. Chem.* **1977**, *42*, 1180. (g) Harmon, A. D.; Hutchinson, C. R. *J. Org. Chem.* **1975**, *40*, 3474. (h) Harmon, A. D.; Hutchinson, C. R. *Tetrahedron Lett.* **1973**, 1293.

Next, we examined the carbonylative lactonization of some other acetylenic alcohols by the use of the catalytic $Pt(PPh_3)_4$/CO/*p*-F-C_6H_4SH system. The $Pt(PPh_3)_4$-catalyzed reaction of 4-hydroxy-1-butyne (**1a**) with CO in the presence of 10 mol % of *p*-F-C_6H_4SH at 120 °C afforded α-methylene-γ-lactone (**2a**) in 69% yield, whereas the same reaction in the absence of *p*-F-C_6H_4SH provided 75% of **2a**. On the other hand, a similar carbonylative lactonization of 6-hydroxy-1-hexyne (**1c**) in the presence and absence of *p*-F-C_6H_4SH gave rise to 30% and 23% of α-methylene-ε-lactone (**2c**), respectively. These results indicate that the presence of thiols is ineffective when the cyclization is very fast (in the case of **1a**) or very slow (in the case of **1c**).



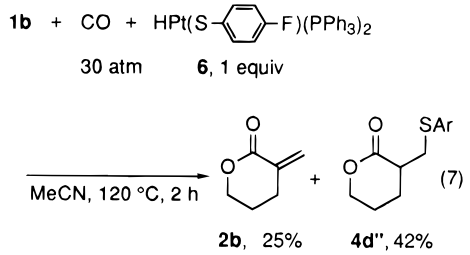
To gain insight into the reaction pathway, the stoichiometric reaction of $Pt(PPh_3)_4$ with *p*-F-C_6H_4SH was examined, as indicated in eq 6. The equimolar reaction



pale yellow solid (mp 144 °C)
^{1}H NMR ($CDCl_3$) δ −10.16 (Pt-H)
Anal. Calcd. for $C_{42}H_{35}PtFP_2S$: C, 59.49; H, 4.16.
Found: C, 59.17; H, 4.27.

of $Pt(PPh_3)_4$ with *p*-F-C_6H_4SH afforded a pale yellow solid which can be identified as a platinum sulfide complex (**6**) on the basis of the spectral and elemental analyses.

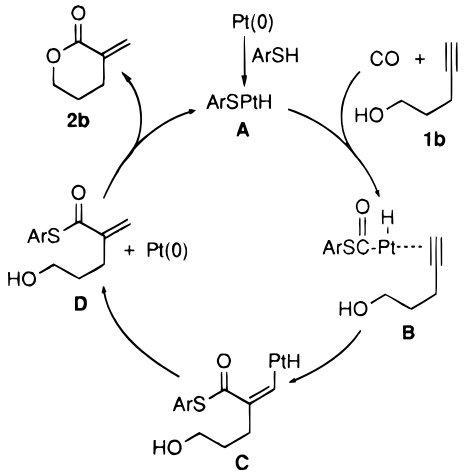
When the carbonylation of 5-hydroxy-1-pentyne (**1b**) was conducted by using stoichiometric amounts of the complex **6** in the presence of CO (30 atm), α-methylene-δ-lactone (**2b**) and α-{((*p*-fluorophenyl)thio)methyl}-δ-lactone (**4b″**) were obtained in 25% and 42% yields, respectively (eq 7).



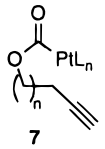
The result suggests that the complex **6** can act as a reagent for the carbonylative lactonization of **1b** with CO.

On the other hand, the stoichiometric reaction of 5-hydroxy-1-pentyne (**1b**) with $Pt(PPh_3)_4$ in the absence of thiol at 120 °C gave a yellow solution with a yellow precipitate. The yellow precipitate was identified as the starting platinum(0) complex, indicating the recovery

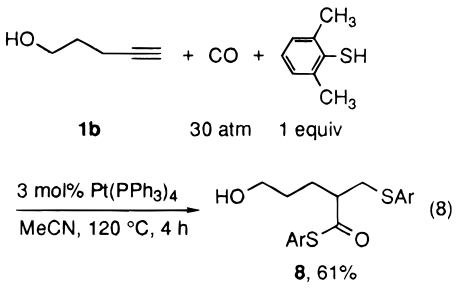
Scheme 1



of most of $Pt(PPh_3)_4$. The measurement of the yellow solution by ^1H NMR indicated the formation of a trace amount of a platinum hydride complex (δ −6.53, J_{Pt-H} = 648 Hz). The result suggests the possibility that, in the absence of thiols, the carbonylation proceeds via oxidative addition of the acetylenic alcohol (**1b**) to Pt(0), followed by CO insertion leading to an acylplatinum intermediate (**7**), similar to the cyclocarbonylation of acetylenic alcohols using the $PdCl_2/SnCl_2/PR_3$ system.[2b,d]



Next, we examined the reaction of **1b** with CO by using a sterically hindered aromatic thiol such as 2,6-dimethylbenzenethiol (eq 8). Although the carbonylation of **1b** using the usual aromatic thiols afforded δ-lactone derivatives without formation of acyclic carbonylating products, the reaction using 2,6-dimethylbenzenethiol provided **8** as the major carbonylating product selectively. The result suggests that the carbonylative lactonization of **1b** proceeds via the hydrothiocarboxylation of the acetylenic moiety.



On the basis of the mechanistic experiments mentioned above, a possible reaction pathway for the present carbonylative lactonization using the catalytic $Pt(PPh_3)_4$/CO/ArSH system can be depicted as shown in Scheme 1: (i) oxidative addition of ArSH to low-valent platinum to generate an ArS-[Pt]-H species (**A**), which undergoes coordination of hydroxyacetylene (**1b**) and insertion of carbon monoxide to form species **B**, (ii) regioselective acylplatination leading to species **C**, followed by reductive elimination to produce α,β-unsaturated thioester **D** and Pt(0), and (iii) intramolecular cyclization of **D** to provide α-methylene-δ-lactone (**2b**) and ArSH, the latter of which adds oxidatively to Pt(0), regenerating catalyst **A**.

In summary, the carbonylative lactonization of 5-hydroxy-1-pentyne to give α-methylene-δ-lactone has been found to proceed efficiently by using catalytic $Pt(PPh_3)_4$ in the presence of small amounts of aromatic thiols. We are currently examining the applicability of this methodology to a variety of different classes of substrates.

Experimental Section

General Comments. Acetylenic alcohols, thiols, and tetrakis(triphenylphosphine)platinum(0) were obtained commercially, and the alcohols were purified by distillation if necessary. Acetonitrile was purified by distillation from phosphorus pentoxide before use. ^1H NMR spectra of $CDCl_3$ solutions were recorded on a JEOL JNM-GSX-270 (270 MHz) spectrometer. ^{13}C NMR spectra of $CDCl_3$ solutions were also recorded on a JEOL JNM-GSX-270 (68 MHz) spectrometer. Chemical shifts in the ^1H NMR and ^{13}C NMR spectra were determined relative to Me_4Si. IR spectra were recorded on a Perkin-Elmer Model 1600 spectrometer. Mass spectra were recorded on a JEOL JMS-DX303 apparatus. Purification of products was performed by using MPLC with Merck 25−40 μm mesh silica gel (Art 9390, length 350 mm, i.d. 30 mm) or recycling preparative HPLC (Japan Analytical Industry Co., Ltd., Model LC-908, JAIGEL-1H and −2H (GPC), length 600 mm, i.d. 20 mm, eluent $CHCl_3$). High-resolution mass spectra (HRMS) and combustion analyses were performed at the Instrumental Analysis Center of the Faculty of Engineering, Osaka University.

Platinum(0)-Catalyzed Carbonylative Lactonization of 5-Hydroxy-1-pentyne (1b) with CO in the Presence of 10 mol % of *p*-F-C_6H_4SH: General Procedure. In a 50 mL stainless steel autoclave equipped with a magnetic stirring bar were placed tetrakis(triphenylphosphine)platinum ($Pt(PPh_3)_4$; 0.15 mmol, 3 mol %), acetonitrile (5 mL), 5-hydroxy-1-pentyne (**1a**; 5 mmol), and *p*-fluorobenzenethiol (0.5 mmol, 10 mol %). The apparatus was charged with carbon monoxide at 30 atm, and the mixture was heated at 120 °C for 11 h with magnetic stirring. The resulting brown precipitate was removed by filtration through Celite, and the filtrate was concentrated under reduced pressure. The crude mixture was analyzed by using a ^1H and ^{13}C NMR spectrometer, and then the purification was conducted by MPLC, followed by recycling preparative HPLC. α-Methylene-δ-lactone (**2b**): pale yellow oil; ^1H NMR (270 MHz, $CDCl_3$) δ 1.96 (quint, 2 H, J = 5.9 Hz), 2.68 (t, 2 H, J = 6.1 Hz), 4.38 (t, 2 H, J = 5.1 Hz), 5.57 (s, 1 H), 6.41 (s, 1 H); ^{13}C NMR (68 MHz, $CDCl_3$) δ 23.0, 27.9, 66.9, 127.9, 134.1, 165.3; IR (NaCl) 2961, 1719, 1625, 1479, 1439, 1400, 1297, 1150, 1072, 1020, 950, 913, 806, 669, 616 cm^{-1}; MS (EI) m/z 112 (M^+, 100). Anal. Calcd for $C_6H_8O_2$: C, 64.27; H, 7.19. Found: C, 63.88; H, 7.14.

Platinum(0)-Catalyzed Carbonylative Lactonization of 5-Hydroxy-1-pentyne (1b) with CO in the Presence of Stoichiometric Amounts of *p*-F-C_6H_4SH. The carbonylation was performed by using *p*-fluorobenzenethiol (5 mmol), as indicated in the above general procedure (reaction conditions: **1b** (5 mmol), CO (30 atm), $Pt(PPh_3)_4$ (0.15 mmol, 3 mol %), CH_3CN (5 mL), 120 °C, 11 h). After the same workups as mentioned above, the crude product was purified by column chromatography on silica gel (length 180 mm, i.d. 15 mm, eluent hexane/Et_2O (1:1)), yielding 0.80 g (67%) of α-(*p*-fluorophenylthio)methyl-δ-lactone (**4b″**): yellow oil; ^1H NMR (270 MHz, $CDCl_3$) δ 1.61−1.73 (m, 1 H), 1.87−1.94 (m, 2 H), 2.26−2.34 (m, 1 H), 2.59−2.70 (m, 1 H), 2.89−2.97 (dd, 1 H, J = 12.1, 9.4 Hz), 3.52−3.58 (dd, 1 H, J = 13.6, 3.9 Hz), 4.30 (t,

2 H, J = 5.8 Hz), 6.97−7.03 (t, 2 H), 7.35−7.40 (q, 2 H); ^{13}C NMR (68 MHz, $CDCl_3$) δ 21.8, 24.0, 36.6, 39.7, 68.6, 115.9, 116.3, 130.3, 132.3, 132.4, 160.6, 163.6, 172.8; IR (NaCl) 2957, 1732, 1589, 1490, 1224, 1155, 828 cm^{-1}; MS (EI) m/z 240 (M^+, 90.8); HRMS calcd for $C_{12}H_{13}O_2FS$ 240.0620, found 240.0628.

Platinum(0)-Catalyzed Hydrothiocarboxylation of 5-Hydroxy-1-pentyne (1b) with CO and Cyclohexanethiol. $Pt(PPh_3)_4$ (3 mol %) catalyzed the carbonylation of **1b** (1 mmol) in CH_3CN (1 mL) at 120 °C. After the same workups as mentioned above, the crude product was purified by MPLC, followed by recycling preparative HPLC. α-((Cyclohexylthio)-methyl)-δ-lactone (**3b′**): pale brown oil; ^{1}H NMR (270 MHz, $CDCl_3$) δ 1.26−1.93 (m, 12 H), 2.21 (s, 1 H), 2.42 (t, 2 H, J = 7.5 Hz), 3.54 (m, 1 H), 3.62 (t, 2 H, J = 6.3 Hz), 5.59 (s, 1 H), 6.10 (s, 1 H); ^{13}C NMR (68 MHz, $CDCl_3$) δ 25.4, 25.9, 27.7, 31.4, 32.9, 42.2, 61.5, 122.4, 148.0, 194.0; IR (NaCl) 2931, 2853, 1658, 977, 939 cm^{-1}; MS (EI) m/z 228 (M^+, 27.0); HRMS calcd for $C_{12}H_{21}O_2S$ 229.1262, found 229.1283.

Platinum(0)-Catalyzed Carbonylative Lactonization of 6-Hydroxy-1-hexyne (1c) with CO in the Presence of 10 mol % of *p*-F-C$_6$H$_4$SH. According to the general procedure, the carbonylative lactonization of 6-hydroxy-1-hexyne (**1c**) was carried out and the purification by MPLC, followed by recycling preparative HPLC, provided α-methylene-ϵ-lactone (**2c**) and 2-{(*p*-fluorothiophenoxy)carbonyl}-6-hydroxy-1-hexene. Former product: ^{1}H NMR (270 MHz, $CDCl_3$) δ 1.79 (m, 2 H), 1.87 (m, 2 H), 2.39 (br t, 2 H), 4.19 (br t, 2 H, J = 4.8 Hz), 5.43 (s, 1 H), 5.64 (s, 1 H); ^{13}C NMR (68 MHz, $CDCl_3$) δ 27.4, 28.3, 31.6, 69.1, 122.4, 142.8, 173.0; IR (NaCl) 2938, 2862, 1727, 1304, 1253, 1222, 1160, 1142, 1080, 1043, 926 cm^{-1}; MS (EI) m/z 126 (M^+, 25.8); HRMS calcd for $C_7H_{10}O_2$ 126.0681, found 126.0708. Latter product: ^{1}H NMR (270 MHz, $CDCl_3$) δ 1.50 (s, OH), 1.58 (quint, 4 H, J = 3.3 Hz), 2.37 (br t, 2 H), 3.64 (t, 2 H, J = 5.9 Hz), 5.71 (s, 1 H), 6.24 (s, 1 H), 7.11 (t, 2 H, J = 11.2 Hz), 7.37−7.42 (q, 2 H, J = 3.8 Hz); ^{13}C NMR (68 MHz, $CDCl_3$) δ 24.4, 31.6, 32.0, 62.4, 116.2, 116.5, 122.9, 123.4, 136.8, 137.0, 147.7, 161.6, 165.3, 191.7; HRMS calcd for $C_{13}H_{16}O_2FS$ 255.0855, found 255.0838.

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