ORGANIC LETTERS

2000
Vol. 2, No. 4
441−443

Ruthenium-Catalyzed Cyclic Carbonylation of Allenyl Alcohols. Selective Synthesis of γ- and δ-Lactones

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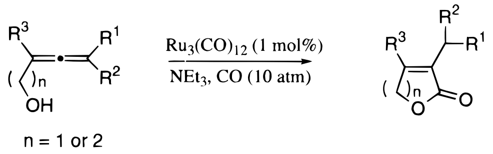
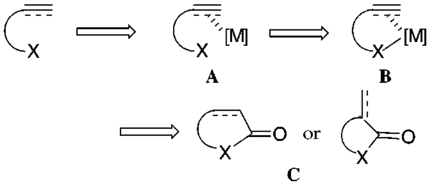
Received November 29, 1999

ABSTRACT



Ruthenium complex-catalyzed carbonylation of allenyl alcohols quantitatively gave cyclic carbonyl compounds, γ- and δ-lactones, in which the hydroxy group of allenyl alcohols participated in the cyclization. A wide variety of allenyl alcohols, such as mono-, di-, and trisubstituted alcohols, can be used in this reaction to produce 3- and 4-substituted γ-lactones. Similarly, the cyclic carbonylation of 3,4-pentadien-1-ol 10a and 2-methyl-4,5-hexadien-2-ol 11a gave δ-lactones, 5,6-dihydro-3-methyl-2*H*-pyran-2-one 10b, and 5,6-dihydro-6,6-dimethyl-3-methyl-2*H*-pyran-2-one 11b, respectively, in a quantitative yield.

Scheme 1



Much attention is being devoted to tandem carbonylation reactions of alkenes and alkynes catalyzed by transition-metal complexes in terms of the efficient syntheses of heterocyclic compounds such as lactones and lactams.[1] In such tandem carbonylation reactions, unsaturated substrates having a functional group adjacent to the C═C or C≡C bond initially coordinate to metal catalysts ([M]) to give intermediate **A**. Intramolecular interaction of the metal with the functional groups such as hydroxyl,[2] amino,[3] formyl,[4] and ester[5] results in the formation of metallacycle intermediate **B**, followed by insertion of carbon monoxide and then elimination of the metal to afford cyclic carbonyl compound **C** (Scheme 1). Among heterocyclic products from this type of tandem carbonylation, particularly γ-lactone is an important precursor for the synthesis of many natural and biologically active compounds.[6] Actually, the tandem reactions of alkenes and alkynes giving γ-lactones have been extensively studied,[2] whereas there are few examples of the cyclic carbonylation of allenes that have been investigated.[7] Very recently, Ma and co-workers have reported a synthetic method for γ-lactones by a Pd(0)-catalyzed intramolecular cyclization reaction of 2,3-allenecarboxylic acids with aryl or alkenyl halides, but the reaction gave γ-lactones in low yields.[8] Herein, we wish to report a new type of the tandem reaction

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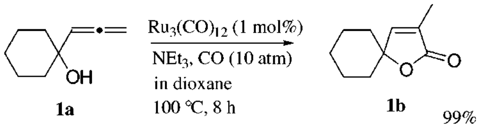
(1) For a review, see: (a) Schore N. E. *Chem. Rev.* **1988**, *88*, 1081. (b) Colquhoun, H. M.; Thompson, D. J.; Twigg, M. V. *Carbonylation: Direct Synthesis of carbonyl Compounds*; Plenum Press: New York, 1991. (c) Stille, J. K. In *Comprehensive Organic Synthesis*; Trost, B. M., Fleming, I., Eds.; Pergamon Press: New York, 1991; Vol. 4, p 913. (d) Ojima, I.; Tzamarioudaki, M.; Li, Z.; Donovan, R. J. *Chem. Rev.* **1996**, *96*, 635. (e) Ungvary, F. *Coord. Chem. Rev.* **1998**, *170*, 245.

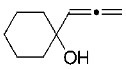
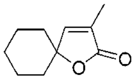
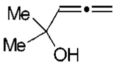
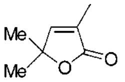
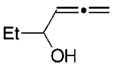
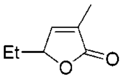
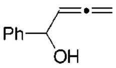
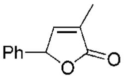
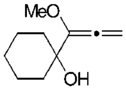
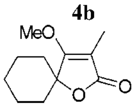
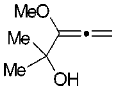
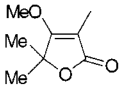
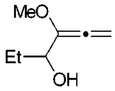
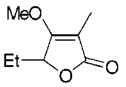
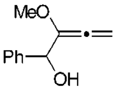
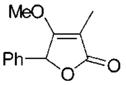
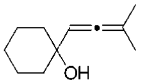
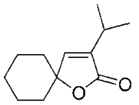
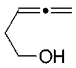
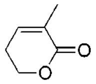
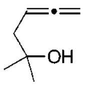
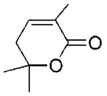
10.1021/ol990377d CCC: $19.00

of allenyl alcohols with carbon monoxide using a ruthenium complex as a catalyst. This carbonylation of allenyl alcohols directly gives γ- and δ-lactones in excellent yields. Although there are some examples on carbonylation of allenes leading to unsaturated carboxylic acids,[9] to our knowledge, the present reaction is the first catalytic cyclocarbonylation of allenyl alcohols.



1a **1b** (eq. 1)

Table 1. Carbonylation of Allenyl Alcohols[a]

run	substrate	product	yield[b](%)
1	 **1a**	 **1b**	99
2	 **2a**	 **2b**	95
3	 **3a**	 **3b**	96
4	 **4a**	 **4b**	98
5	 **5a**	 **5b**	98
6	 **6a**	 **6b**	95
7	 **7a**	 **7b**	91
8	 **8a**	 **8b**	93
9	 **9a**	 **9b**	98
10	 **10a**	 **10b**	95
11	 **11a**	 **11b**	98

[a] Reaction conditions: substrate (1 mmol), NEt_3 (1.5 mmol), CO (initial pressure 10 atm at 25 °C), $Ru_3(CO)_{12}$ (0.01 mmol) in doxane (15 ml) at 100 °C for 8 h in a 100 mL stainless autoclave. [b] Isolated yield.

A representative reaction procedure is as follows. A mixture of 1-propa-1,2-dienylcyclohexan-1-ol **1a** (1 mmol), $Ru_3(CO)_{12}$ (0.01 mmol), and Et_3N (1.5 mmol) in 1,4-dioxane (15 mL) was stirred at 100 °C for 8 h under 10 atm of carbon monoxide (eq 1). The gas chromatographic analysis of the reaction mixture showed that the carbonylation reaction selectively yielded a sole product. Simple removal of the catalyst by silica gel column chromatography gave 3-methyl-1-oxaspiro[4.5]dec-3-en-2-one **1b** in 99% yield, which was identified by the ^1H NMR, ^{13}C NMR, IR, and mass spectra. The formation of any other products was not recognized in the ^1H NMR and ^{13}C NMR. When the reaction was carried out at lower temperature (50 °C), **1b** was obtained only in 17% yield, and 80% of starting substrate **1a** was recovered. When the reaction temperature was increased to 80 °C, the reaction gave **1b** in 75% yield, and 20% of **1a** was recovered. Even under atmospheric pressure of carbon monoxide, the carbonylation took place at 100 °C to give **1b**, though the yield decreased to 62%. As the catalyst for the present carbonylation, ruthenium complexes such as $RuCl_3 \cdot xH_2O$ and $RuCl_2(PPh_3)_3$ showed a definite activity to give **1b** in 82 and 41% yield, respectively; however, $RuCl_2(dppe)_2$ is inactive. Complexes such as $Co_2(CO)_8$, $Fe_2(CO)_{10}$, and $Rh_6(CO)_{16}$ are not effective for the present reaction. In an investigation on the effect of additives, the lack of Et_3N reduced the yield of **1b** to 62% yield. On the basis of the above results, the carbonylation of several allenyl alcohols was examined under

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(2) (a) Urata, H.; Yugari, H.; Fuchikami, T. *Chem. Lett.* **1987**, 833. (b) Ohe, K.; Takahashi, H.; Uemura, S.; Sugita, N. *J. Org. Chem.* **1987**, *52*, 4859. (c) Matsuda, I.; Ogiso, A.; Sato, S. *J. Am. Chem. Soc.* **1990**, *112*, 6120. (d) Ali, E. B.; Alper, H. *J. Org. Chem.* **1991**, *56*, 5357. (e) Matsushita, K.; Komori, T.; Oi, S.; Inoue, Y. *Tetrahedron Lett.* **1994**, *35*, 5889. (f) Ali, E. B.; Okuro, K.; Vasapollo, G. Alper, H. *J. Am. Chem. Soc.* **1996**, *118*, 4264. (g) Xiao, W.; Alper, H. *J. Org. Chem.* **1997**, *62*, 3422. (h) Yu, W.; Alper, H. *J. Org. Chem.* **1997**, *62*, 5684. (i) Gabriele, B.; Salerno, G.; De Pascali, F.; Costa, M. Chiusoli, G. P. *J. Chem. Soc., Perkin Trans. 1* **1997**, 147. (j) Ogawa, A.; Kawabe, K.; Kawakami, J.; Mihara, M.; Hirao, T.; Sonoda, N. *Organometallics* **1998**, *17*, 3111. (k) Yoneda, E.; Sugioka, T.; Hirao, K.; Zhang, S.; Takahashi, S. *J. Chem. Soc., Perkin Trans. 1* **1998**, 477. (l) Yoneda, E.; Kaneko, T.; Zhang, S.; Takahashi, S. *Tetrahedron Lett.* **1998**, *39*, 5061. (m) Zhang, X.; Cao, P. *J. Am. Chem. Soc.* **1999**, *121*, 7708.

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(7) (a) *The Chemistry of Ketenes, Allenes, and Related Compounds*; Patai, S., Ed.; John Wiley & Sons: New York, 1980; Part 1. (b) Schuster, H. F.; Coppola, G. M. *Allenes in Organic Synthesis*; John Wiley & Sons: New York, 1988.

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the following conditions: substrate (1 mmol); catalyst, $Ru_3(CO)_{12}$ (1 mol %); additive, Et_3N (1.5 mmol); solvent, dioxane (15 mL), CO 10 atm, 100 °C.

The results obtained are summarized in Table 1.[10] The cyclic carbonylations of allenyl alcohols in Table 1 proceeded smoothly to give the corresponding γ- or δ-lactones in excellent yields. For example, the reaction of 1,1-disubstituted 2,3-allenyl alcohol **2a** gave the corresponding γ-lactone, **2b**, with a high selectivity (run 2). 2,3-Allenyl alcohols **3a** and **4a**, which have an alkyl or an aryl substituent at the 1-position of allenyl alcohols, gave the corresponding γ-lactones, **3b** and **4b**, in quantitative yields (runs 3 and 4). 2-Methoxy-2,3-allenyl alcohols such as **5a**, **6a**, **7a**, and **8a** gave tri- or tetrasubstituted-γ-lactones **5b**, **6b**, **7b**, and **8b** (runs 5−8). These compounds cannot be prepared by the cyclic carbonylation of propargyl alcohols using a Pd catalyst.[2h] The cyclic carbonylation of **9a**, which is a trisubstituted allene, also gave the corresponding γ-lactone, **9b**, quantitatively (run 9). Furthermore, the cyclic carbonylation of **10a** and **11a**, which contain a dimethylene spacer between the hydroxyl and allenyl groups, similarly took place to give δ-lactones **10b** and **11b** in 95 and 98% yield, respectively (runs 10 and 11).

In conclusion, we have found that ruthenium complexes catalyze the novel cyclic carbonylation of allenyl alcohols to give lactones with a high selectivity. This intramolecular tandem reaction provides a new and efficient method for the selective synthesis of γ- and δ-lactones simply from allenyl alcohols with carbon monoxide.

Acknowledgment. We thank the technical staff in the Material Analysis Center of ISIR, Osaka University, for mass spectrometric and elemental analyses. E.Y. is grateful for a JSPS Fellowship for Japan Junior Scientists

Supporting Information Available: Experimental details. This material is available free of charge via the Internet at http://pubs.acs.org.

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[10] All new compounds were identified by NMR, IR, mass spectral analyses, and elemental analyses. See the Supporting Information.