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

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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.

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 ester⁵ 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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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.

A representative reaction procedure is as follows. A mixture of 1-propa-1,2-dienylcyclohexan-1-ol **1a** (1 mmol), Ru₃(CO)₁₂ (0.01 mmol), and Et₃N (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, ¹³C NMR, IR, and mass spectra. The formation of any other products was not recognized in the ¹H NMR and ¹³C 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

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Table 1. Carbonylation of Allenyl Alcohols^a



^{*a*} Reaction conditions: substrate (1 mmol), NEt₃ (1.5 mmol), CO (initial pressure 10 atm at 25 °C), Ru₃(CO)₁₂ (0.01 mmol) in doxane (15 ml) at 100 °C for 8 h in a 100 mL stainless autoclave. ^{*b*} Isolated yield.

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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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.

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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.