

FACILE OXIDATIVE CYCLIZATION AND CARBONYLATION OF ALLYLIC ALCOHOLS

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Summary: Palladium chloride catalyzed reaction [room temperature, one atmosphere] of primary, secondary, and tertiary allylic alcohols with carbon monoxide and oxygen, hydrochloric acid, and cupric chloride in tetrahydrofuran affords five-membered ring lactones.

Attempts to effect the metal catalyzed carbonylation reaction of allyl alcohols to form lactones have met with mixed success. The cobalt carbonyl or rhodium chloride catalyzed carbonylation of allyl alcohol at 240° and 300 atmospheres, afforded γ -butyrolactone in only 2% yield, the major product (50%) being propanal. However, one can isolate the lactone in 60% yield using carbon monoxide and hydrogen in acetonitrile². The same lactone was obtained in 68% yield by rhodium carbonyl catalyzed reaction of allyl alcohol with carbon monoxide and water, in the presence of 4-dimethylaminopyridine, at elevated temperatures and pressures [50°C, 10 atm.]³. Use of allylic secondary alcohols as substrates gave lactones in poor yields [the main process is isomerization to carbonyl compounds]⁴. All of these methods require the use of stringent conditions, and none are of general applicability.

Recently, we described the conversion of γ,δ - and δ,ϵ -unsaturated alcohols to five and six membered ring lactones using carbon monoxide and oxygen in acidic tetrahydrofuran with palladium chloride as catalyst and cupric chloride as reoxidant⁵. In light of the above reports it seemed, a priori, that the application of the acidic palladium catalyzed reaction to allylic alcohols would have little probability of success as a general route to lactones [competing reactions such as isomerization and carbonium ion generation appeared likely]. However, we were gratified to learn that a variety of allylic alcohols do undergo regiospecific carbonylation and cyclization, at room temperature and atmospheric pressure, to give butyrolactones in fair to good yields. We now describe the results of this investigation⁶.

Treatment of an acidic tetrahydrofuran solution (60-70 ml.) of 2-buten-1-ol [crotyl alcohol] with carbon monoxide, oxygen, cupric chloride, and palladium chloride as the catalyst

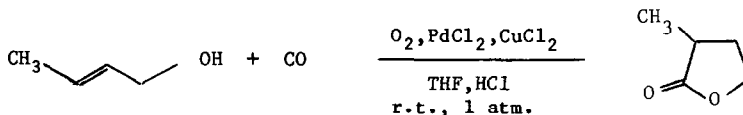

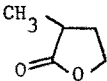
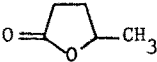
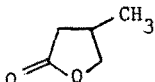
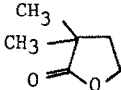
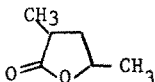
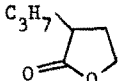
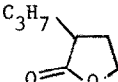
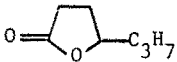


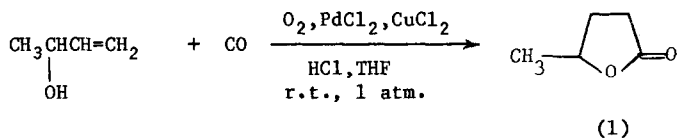
Table 1

Palladium Catalyzed Cyclization of Allylic Alcohols to Lactones

Substrate	Product ^a	Yield, % ^b
$\text{CH}_2=\text{CHCH}_2\text{OH}$		35
<i>trans</i> - $\text{CH}_3\text{CH}=\text{CHCH}_2\text{OH}$		50
$\text{CH}_3\underset{\text{OH}}{\text{CH}}\text{CH}=\text{CH}_2$		70
$\text{CH}_2=\text{C}(\text{CH}_3)\text{CH}_2\text{OH}$		15
$(\text{CH}_3)_2\text{C}=\text{CHCH}_2\text{OH}$		45
$\text{CH}_3\underset{\text{OH}}{\text{CH}}\text{CH}=\text{CHCH}_3$		65 ^c
<i>trans</i> - $\text{C}_3\text{H}_7\text{CH}=\text{CHCH}_2\text{OH}$		35
<i>cis</i> - $\text{C}_3\text{H}_7\text{CH}=\text{CHCH}_2\text{OH}$		60
$\text{C}_3\text{H}_7\underset{\text{OH}}{\text{CH}}\text{CH}=\text{CH}_2$		40

^aProducts were identified by comparison of physical data [b.p., gc retention times, ir, nmr (¹H¹³C), ms] with those for authentic materials. ^bYields were not optimized. ^c1:1 *cis-trans*.

afforded α -methyl- γ -butyrolactone in 30% yield. This reaction is sensitive to the concentration of acid and the amount of solvent [also a concentration effect]. Reduction of the acid concentration by a factor of two gave the lactone in only 10% yield. More fruitful results were obtained by using half (30-35 ml.) the amount of tetrahydrofuran [50% lactone isolated]. Note that a further reduction in the volume of THF (to 15-20 ml) gives the lactone in significantly lower yield (28%). This concentration effect was also observed with other substrates such as 3-buten-2-ol where use of half the amount of THF [i.e., 30-35 ml. vs 60-70



ml.] resulted in an increase in the yield of 1 from 10 to 70%. No lactone was formed in the absence of oxygen.

The palladium catalyzed carbonylation and cyclization of allylic alcohols to lactones is a general process (see Table 1 for results). It is applicable to primary, secondary and tertiary alcohols and to cis and trans isomers. Although the yields are modest in some instances, this reaction constitutes a simple method for the construction of lactones from allylic alcohols. Furthermore, it occurs under exceptionally mild conditions, particularly when one compares the present reaction with previous methodology²⁻⁴.

The following procedure was used: to PdCl₂ [0.140 g., 0.78 mmol] in dry THF [30-35 ml.] was added HCl (0.5 ml.) and CuCl₂ [0.21 g., 1.56 mmol]. Carbon monoxide was bubbled through THF during this time. Then oxygen was bubbled through THF (together with carbon monoxide), the allylic alcohol (7.8 mmol) was added, and the reaction mixture was stirred at room temperature for 15-18 hours. The mixture was filtered, the filtrate was concentrated and the lactone was purified by preparative thin layer chromatography [silica gel, 3:1 ether-hexane].

Acknowledgement

We are indebted to British Petroleum and to the Natural Sciences and Engineering Research Council of Canada for support of this research.

References

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6. Very recently the synthesis of *cis*-3-hydroxy tetrahydrofuran 2-acetic acid lactones was described by means of the palladium catalyzed oxycarbonylation of 4-penten-1,3-diols [Tamaru, Y.; Kobayashi, T.; Kawamura, S.I.; Ochiai, H.; Hojo, M.; Yoshida, Z., Tetrahedron Lett. 1985, 26, 3207]. The authors did not discuss the utilization of their reaction to simple allylic alcohols, or to diols containing an allylic primary or tertiary alcohol unit. Interestingly, while their procedure (no oxygen, acetic acid) is not applicable to systems containing a 2-buten-1-ol type moiety [e.g., 1-phenyl-4-hexen-1,3-diol or 2-benzyl-4-hexen-1,3-diol; an exception is lg which affords a lactone in only 24% yield], the reaction described above proceeds in quite good yields for these, as well as for other kinds of allylic alcohols. Finally, Semmelhack and co-workers have shown that allylic secondary alcohols [ortho-disubstituted arenes] are convertible to lactones using stoichiometric quantities of palladium acetate, but not palladium chloride, in tetrahydrofuran under an atmosphere of carbon monoxide [Semmelhack, M.F.; Bodurow, C.; Baum, M. Tetrahedron Lett. 1984, 25, 3171].

(Received in USA 22 July 1985)