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NEW REGIO- AND STEREOSELECTIVE PREPARATION OF TRICHLORINATED γ-BUTYROLACTONES BY COPPER CATALYZED CYCLIZATION OF ALLYL TRICHLOROACETATES

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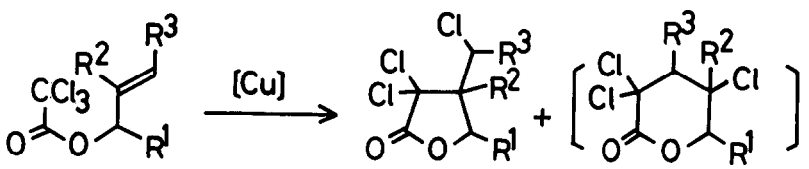
Summary: A novel synthetic method for γ-butyrolactones is presented. The process involves high regioselectivity to afford γ-lactones. In cases of trichloroacetates of secondary allylic alcohols, high *cis*-selective cyclization is accomplished.

An efficient construction of ring systems is one of the problems in modern organic chemistry. Recently, potential utility of free radical cyclizations for the preparation of five, six, or seven membered rings in complicated molecules was explored by Stork[1], Hart[2], Bachi[3], and Ueno[4] who claimed an effective synthesis of steroids, alkaloids, and other natural products. A widely used process for the free radical cyclizations is an intramolecular trap of reductively generated radical species with olefinic or acetylenic bonds.[5] In this paper, we wish to report a new type of radical cyclization involving simple addition of carbon-halogen bond to olefinic linkage, copper catalyzed cyclization of allyl trichloroacetates. The present cyclization is a novel and versatile preparative method for γ-lactones with high regio- and stereoselectivity.



As outlined in the scheme, we found that allyl trichloroacetates underwent intramolecualr addition involving carbon-halogen bond cleavage. This process is considered to be an intramolecular version of well-known addition reaction of

trichloroacetates to olefins.[6] Various transition metal salts and complexes reportedly showed catalytic activity in the intermolecular reaction[6], however, in the intramolecular reaction, an effective catalyst was limited to copper salts. The solvent was also rather limited, and CH_3CN was effective, but alcohols, benzene, and polar aprotic solvents such as DMF were not. The results using other catalysts and/or other solvents led to decomposition of the starting material to afford a complicated mixture of products.

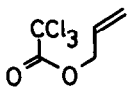
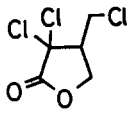
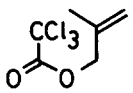
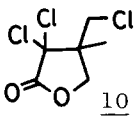
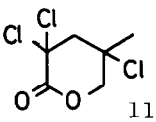
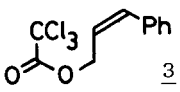
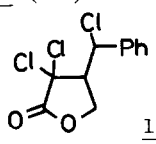
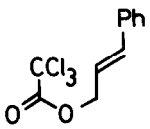
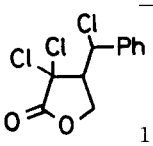
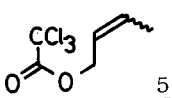
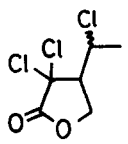
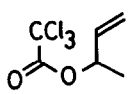
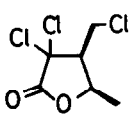
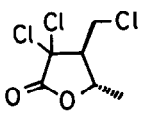
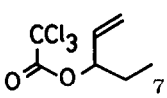
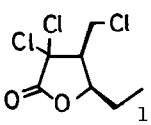
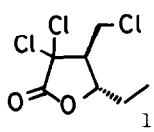
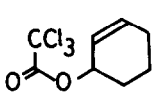
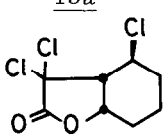
A typical procedure follows: a solution of allyl trichloroacetate (1) (2 mmol) in dry CH_3CN (16 mL) containing CuCl(0.6 mmol) was heated at 140°C for 1 h in a pressure bottle under argon atmosphere. The solution was cooled and passed through a short silica-gel column to remove the copper salts. After removal of the solvent, purification of the residue by column chromatography (silica-gel, hexane-ether) afforded the lactone 9 in 72% yield.[7] Other examples are summarized in Table. As a catalyst, Cu_2O, CuC_2Ph, and $Cu(NO_3)_2$ were also effective.

This cyclization provides unique features in the regio- and stereoselectivity. First, only five-membered ring was obtained in most cases shown in Table, though both five- and six-membered rings should be formed according to the scheme. Exception is the formation of δ-lactone 11 which can be explained by the fact that bulky methyl group is present at the position to prevent the γ-lactone formation. Second, stereochemical relationship between dichloroacetyl group and chlorine introduced was independent on the *cis/trans* ratio of the starting olefins. As shown in entries 3 and 4, only one diastereomer was obtained from either *cis*- or *trans*-cinnamyl trichloroacetate, 3 or 4.[8] Furthermore, crotyl trichloroacetate (*cis/trans* < *1/9*) was converted to a mixture of diastereomers in a ratio of 7 : 3.[9] (entry 5)

Third, as the most unique feature of this cyclization, remarkably high *cis*-selectivity was observed in the reaction of trichloroacetates of secondary allylic alcohols. In acyclic systems (entries 6 and 7), stereochemistry between alkyl substituents and introduced chloromethyl group in the lactones (14 and 15) was predominantly *cis*.[10] The *cis*-selectivity was also observed in a cyclic system (entry 8), and only *cis*-fused isomer 16 was obtained exclusively from 2-cyclohexenyl trichloroacetate (8).[11] In these cases, stereochemical relationship was determined by comparison of spectral data of reductively dechlorinated lactones with authentic samples.[12]

The present cyclization is a simple method for the preparation of γ-butyrolactones from easily available allyl trichloroacetates. The trichlorinated lactones are easily dechlorinated with excess Bu_3SnH in the presence of AIBN. The high regio- and stereoselectivity of this cyclization realizes induction of a new chiral center at β-position of the lactones from secondary allylic alcohols. From the view of relative asymmetric induction, it classifi-

Table.

	Substrates	Products (%)[a]	Diastereomer ratio
1.	 1	 9 (72)	
2.	 2	 10 (38)  11 (29)	
3.	 3	 12 (61)	
4.	 4	 12 (63)	
5.	 5	 13 (78)[b]	7 : 3
6.	 6	 14a  14b (62)[b]	9 : 1
7.	 7	 15a  15b (68)[b]	9 : 1
8.	 8	 16 (38)[c]	

a) Figures in parentheses are isolated yields.

b) Combined yields of diastereomers.

c) 100 mol% of CuCl was used.

es as a rare example of 1,2-asymmetric induction involving carbon-carbon bond formation.[13)]

Further extension and mechanistic studies on this highly regio- and stereoselective reactions are in progress.

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   d. Pd; J. Tsuji, K. Sato, and H. Nagashima, Chem. Lett., 1169 (1981)
7) 9; NMR ($CDCl_3$, 90MHz), δ 3.1-3.5 (m, 1H, C<u>H</u>CCl_2), 3.73 (dd, 1H, J = 9, 13 Hz, C<u>H</u>Cl), 3.97 (dd, 1H, J = 5, 13 Hz, C<u>H</u>Cl), 4.21 (dd, 1H, J = 9, 10 Hz, C<u>H</u>O), 4.65 (dd, 1H, J = 7, 10 Hz, C<u>H</u>O), IR ($CHCl_3$), 1810, 700 cm^{-1}, mp. 71.6 -72.0°C, Anal. ($C_5H_5Cl_3O_2$) C, H; calcd. 29.52, 2.48; found 29.46, 2.69
8) 12; NMR ($CDCl_3$, 90MHz), $Jc\underline{H}CCl_2$-$C\underline{H}Cl$ = 9.5 Hz
9) 13-major isomer; NMR ($CDCl_3$, 90MHz), $Jc\underline{H}CCl_2$-$C\underline{H}Cl$ = 9.5 Hz, minor isomer; $Jc\underline{H}CCl_2$-$CHCl$ = 7.7 Hz.
10) $Jc\underline{H}O$-$C\underline{H}CCl_2$ values of these lactones were confirmed by decoupling experiments. 14a; 10.0 Hz, 14b; 7.2 Hz, 15a; 9.1 Hz; 15b; 7.1 Hz. These compounds are unequivocally determined by selective reduction of chlorine group. See, footnote 12.
11) The coupling constant of 16, $Jc\underline{H}O$-$CHCCl_2$ = 5.1 Hz and $Jc\underline{H}CCl_2$-$C\underline{H}Cl$ = 7.7 Hz, indicate that the protons, C<u>H</u>Cl and C<u>H</u>CCl_2 are *trans*, whereas angular protons are *cis*.
12) The reduction was carried out with excess Bu_3SnH in the presence of AIBN at 140°C for 3 h. Spectral data of the reduced lactones are reported in the following papers: β,γ-dimethyl-γ-butyrolactones, H. Kanetsuna and T. Nonaka, Denki Kagaku, 47, 422 (1979); β-methyl-γ-ethyl-γ-butyrolactones, M. Tokuda, Y. Yokayama, T. Taguchi, A. Suzuki, and M. Itoh, J. Org. Chem., 37, 1859 (1972); the cyclic lactones, H. O. House, *ibid.*, 27, 4141 (1962)
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