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A CONVENIENT METHOD FOR THE SYNTHESIS OF γ-SUBSTITUTED-β-ACETYL-γ-BUTYROLACTONES

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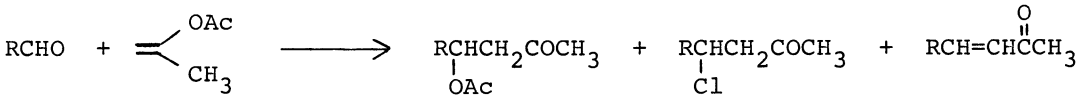
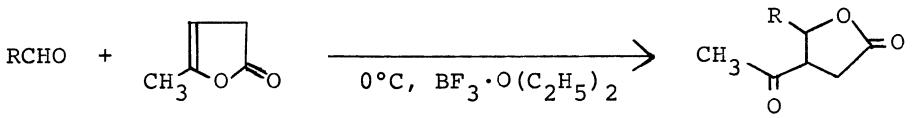
It was established that γ-substituted-β-acetyl-γ-butyrolactones are prepared in good yields by the reaction of α-angelicalactone with various aldehydes in the presence of $BF_3 \cdot O(C_2H_5)_2$.

Recently, it was found in our laboratory that trimethylsilyl enol ethers[1),2)] or isopropenylacetate[3)] reacts with various aldehydes, ketones, and acetals in the presence of $TiCl_4$ or other Lewis acids to afford the aldol type addition products in good yields. For example, isopropenylacetate reacts with aldehydes to give β-acetoxy methylketones (I) along with β-chloroketones (II) and α,β-unsaturated ketones (III). The latter two products are formed by the subsequent displacement or elimination reaction of I.



I II III

In the present experiment, it was established that β-acetyl-γ-butyrolactones were obtained in good yields by the reaction of α-angelicalactone with aldehydes in the presence of $BF_3 \cdot O(C_2H_5)_2$.



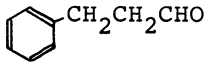
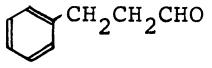
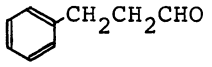
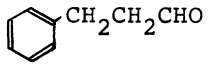
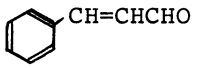
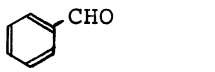
IV

In a typical procedure, $BF_3 \cdot O(C_2H_5)_2$ (0.142 g, 1 mmol) in 4 ml of methylene chloride was added slowly at 0°C into a mixture of α-angelicalactone (0.098 g, 1 mmol) and β-phenylpropionaldehyde (0.134 g, 1 mmol) in 6 ml of methylene chloride and the reaction mixture was stirred for 8 hr at 0°C. After being quenched with NaCl-saturated aqueous solution, it was extracted with benzene. β-Acetyl-γ-phenethyl-γ-butyrolactone was isolated in 94% yield by silica gel chromatography.

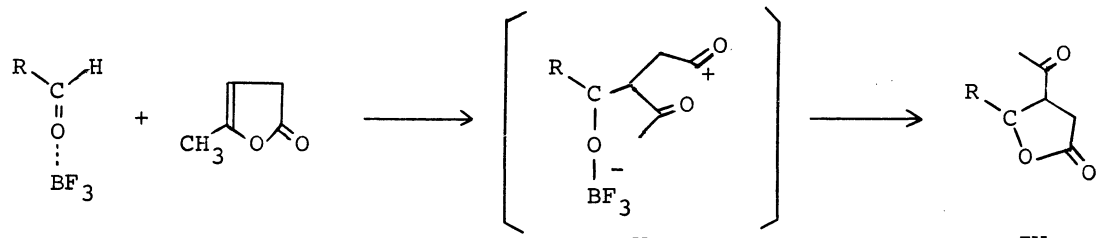
In a similar manner, various β-acetyl-γ-butyrolactones were obtained in good yields by the reaction of aldehydes, such as benzaldehyde, cinnamaldehyde, and

chloroacetaldehyde, with α-angelicalactone (see Table I).

Table I. The reactions of α-angelicalactone with aldehydes

Aldehydes	Amount of $BF_3 \cdot Et_2O$	Reaction conditions Solvent	Temp.	Time(hr)	γ-Butyrolactones Yield(%)
	1.0 eq.	CH_2Cl_2	0°C	8	94
	0.5 eq.	CH_2Cl_2	0°C	8	94
	1.0 eq.	CH_2Cl_2	r.t.	1	85
	1.0 eq.		r.t.	1	84
	1.0 eq.	CH_2Cl_2	0°C	12	79
	1.0 eq.	CH_2Cl_2	r.t.	24	62
$ClCH_2CHO$	1.0 eq.	CH_2Cl_2	0°C	1	84

The reaction may be explained by assuming an initial formation of aldehyde-$BF_3 \cdot O(C_2H_5)_2$ complex, which in turn reacts with α-angelicalactone to give an addi-



V IV

tion product of (V). The intermediate adduct V immediately cyclizes to form γ-butyrolactone (IV).

It was also found that benzene and methylene chloride were more suitable solvents than diethyl ether and carbon tetrachloride with respect to yield and reaction velocity. Examination of the effect of catalysts showed that the yield of β-acetyl-γ-phenethyl-γ-butyrolactone by the reaction of α-angelicalactone with β-phenylpropionaldehyde in the presence of $TiCl_4$ or $SnCl_4$ (40-50%) is lower than that of $BF_3 \cdot O(C_2H_5)_2$ (94%).

The application of this reaction to new synthesis of naturally occurring γ-butyrolactone derivatives is now in progress.

REFERENCES

1) T. Mukaiyama, K. Narasaka, and K. Banno, Chem. Lett., 1011 (1973).
2) T. Mukaiyama and M. Hayashi, Chem. Lett., 15 (1974).
3) T. Mukaiyama, T. Izawa, and K. Saigo, Chem. Lett., in press.

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