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NEW SYNTHETIC METHOD OF 5- AND 2,5-SUBSTITUTED 3-FUROATES, AND 1,4-DICARBONYL COMPOUNDS FROM UNSATURATED LACTONES

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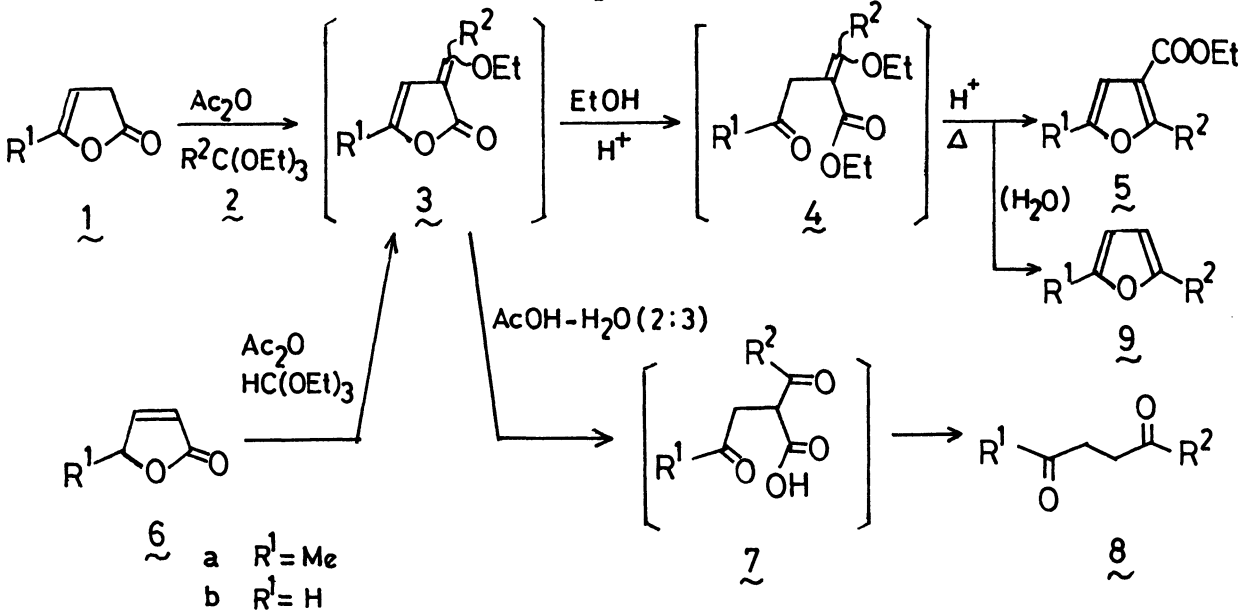
The title compounds were synthesized from 4-substituted 2-(1'-ethoxyalkylidene)-3-buten-4-olides 3 obtained by the reaction of 4-substituted 2- or 3-buten-4-olides with ortho esters and acetic anhydride.

The utility of 1,4-dicarbonyl compounds and furans as synthetic intermediates to heterocycles and cyclopentenones is now well recognized, and extensive studies on the synthesis of these compounds have been made by many groups.[1,2] Among these studies we paid much attention to the fact that certain 2-acylbutenolides yielded the corresponding furans or 1,4-diketones on treatment with acid,[2] though synthesis of 2-acylbutenolides having certain substituents was rather difficult. Therefore, easy conversion of readily available butenolides to their 2-acyl derivatives will provide a useful synthetic method of these compounds. In this communication we wish to report a new synthetic method of furan derivatives and 1,4-dicarbonyl compounds from various butenolides via their 2-acyl derivatives.[3]

First we examined acylation of unsaturated lactones, such as 3-penten-4-olide and 2-buten-4-olide, under various basic conditions, but all attempts were failed probably because of their instability under such conditions. Next we tried the introduction of acyl equivalent at 2-position of unsaturated lactones under rather acidic conditions. When 3-penten-4-olide 1 (R^1=Me, 0.1 mol), ethyl orthoformate (0.15 mol), and acetic anhydride (0.3 mol) were refluxed for 3 h, almost pure 2-ethoxymethylene derivative 3 (R^1=Me, R^2=H, Bp 122~124°C/15 mmHg) was obtained by

distillation in 55% yield. The structure was confirmed by NMR and IR spectra. NMR ($CDCl_3$): δ 1.38 (t, 3H), 2.05 (s, 3H), 4.25 (q, 2H), 5.75 (s, 1H), 7.18 (s, 1H), IR (NaCl): 1760 (C=O), 1655 (C=C). This compound, however, polymerized easily on exposure to air and was difficult to handle in a pure state. So, it was decided to use this compound without purification for the next step. After the reaction of 3-penten-4-olide, ethyl orthoformate, and acetic anhydride was carried out as described above, excess reactants and low boiling products were removed by distillation under reduced pressure and the residue was heated in absolute ethanol in the presence of a catalytic amount of Amberlyst 15 at 75°C for 0.5 h. After removal of excess ethanol, the residue was heated at 120°C for 3 h. From the reaction mixture ethyl 5-methyl-3-furoate was isolated by distillation (Bp 87~89°C/16 mmHg) in 52% yield.[4] When p-toluenesulfonic acid was used instead of Amberlyst 15 in the above reaction, the yield was decreased to 36%. Thus, Amberlyst 15 was used as a catalyst for further studies. By this method various ethyl 5-substituted-3-furoates were prepared in moderate yields starting from 4-substituted-3-buten-4-olides and ethyl orthoformate.



When ethyl orthoacetate was used instead of ethyl orthoformate, 4-aryl-3-buten-4-olides afforded corresponding furan derivatives in moderate yields. But in the case of less reactive 3-penten-4-olide the reaction proceeded very slowly and the side reaction between orthoacetate and acetic anhydride to form 10 became prevailing. Consequently, the yield of furan derivative was very poor.

$$CH_3C(OEt)_3 + Ac_2O \longrightarrow CH_3COCH{=}C(OEt)_2 \quad \underset{\sim}{10}$$

When triethyl orthobenzoate was used, the reaction with butenolide was very slow even when 4-substituent was aryl, and none of furan derivative was obtained. In some cases, corresponding 2,5-disubstituted furan $\underset{\sim}{9}$, probably produced by contaminated water, was isolated. These results are summarized in Table 1.

Table 1. Synthesis of 3-Furoate Derivatives

R^1	R^2	Isolated Yield (%)[b] $\underset{\sim}{5}$	Mp (°C)	$\underset{\sim}{9}$
C_2H_5	H	38[a]	—	—
C_6H_5	H	50[a]	55∿56	—
p-$CH_3OC_6H_4$	H	11[a]	74.5	—
CH_3	CH_3	7	—	—
C_6H_5	CH_3	57[a]	—	—
p-$CH_3OC_6H_4$	CH_3	58[a]	64	13
C_6H_5	C_2H_5	64[a]	—	12
p-$CH_3OC_6H_4$	C_2H_5	45[a]	45∿46	9
C_6H_5	C_6H_5	0[a]	—	—

a) Toluene was used as a solvent in the last step.
b) Reaction was carried out using 2 mmol of unsaturated lactone, 2.4-3.0 mmol of orthocarboxylic ester, and 5.5-10 mmol of acetic anhydride and yields were calculated based on unsaturated lactone $\underset{\sim}{1}$. All these compounds were isolated by TLC and comfirmed by their elemental analyses and spectral data.

Next we applied this method to 2-penten-4-olide $\underset{\sim}{6a}$. The formation of the intermediate $\underset{\sim}{3}$ (R^1=Me, R^2=H) was detected by TLC and $\underset{\sim}{5}$ (R^1=Me, R^2=H) was successfully obtained in 40% yield. Then we tried the reaction of 2-buten-4-olide $\underset{\sim}{6b}$. In this case, the formation of the intermediate $\underset{\sim}{3}$ (R^1, R^2=H) was also detected, but at the last step, complex side reaction took place and only tarry material resulted.

Intermediate $\underset{\sim}{3}$ can be regarded as a derivative of 2-acylated butenolide and is expected to afford the corresponding 1,4-dicarbonyl compound by acid hydrolysis. This assumption was realized when a mixture of acetic acid-water (2:3) and crude $\underset{\sim}{3}$ (R^1=Ph, R^2=CH_3) was refluxed for 1 h (Method A), expected diketone was isolated in 51% yield. Similarly, various 1,4-dicarbonyl compounds were successfully obtained. When catalytic amount of p-toluenesulfonic acid was used instead of acetic acid

(Method B), the yield of diketone was poor. These results are summarized in Table 2.

Table 2. Synthesis of 1,4-Dicarbonyl Compounds

R^1	R^2	Method	Isolated Yield (%)* 8	Mp(°C)
C_6H_5	CH_3	A	51	—
C_6H_5	CH_3	B	5	—
C_6H_5	C_2H_5	A	73	—
C_6H_5	C_6H_5	A	12	143
p-$CH_3OC_6H_4$	CH_3	A	83	58
p-$CH_3OC_6H_4$	C_2H_5	A	80	77

* Reaction was carried out using 1 mmol of unsaturated lactone, 1.2-1.5 mmol of orthocarboxylic ester, and 2.5 mmol of acetic anhydride and yields were calculated based on unsaturated lactone 1. All these compounds were isolated by TLC and confirmed by their elemental analyses and spectral data.

References and Notes

1) See the following reviews and references cited therein.
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