The Reactions of 2-(Trimethylsiloxy)furans with Orthocarboxylic Esters, Acetals, and Acylal in the Presence of Lewis Acids

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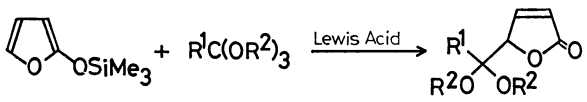
The reaction of 2-(trimethylsiloxy)furan (**1**) with orthocarboxylic esters, acetals, and acylal in the presence of Lewis acids afforded the corresponding 4-substituted 2-buten-4-olides. The reaction of 5-methyl-2-(trimethylsiloxy)furan with orthocarboxylic esters gave unstable 2-substituted 3-penten-4-olides as major products; these gave 2,5-alkanediones upon hydrolysis. The furan (**1**) also reacted with 1,1-diacetoxy-2-butene to give a mixture of 5-acetoxy-2,6-octadien-4-olide and 7-acetoxy-5-methyl-2,6-heptadien-4-olide. From the former compound, nigrosporalactone was synthesized.

In the preceding paper, we reported the synthesis of 2-(trimethylsiloxy)furans and their Diels-Alder reaction with maleic anhydride.[1] In the present paper, we will describe the reaction of some electrophiles with the furans in the presence of Lewis acids.

Results and Discussion

It was found that the reaction of 2-(trimethylsiloxy)-furan **1** with triethyl orthoacetate **2** (R^1=Me, R^2=Et) in dichloromethane, in the presence of catalytic amounts of a Lewis acid, afforded 5,5-diethoxy-2-hexen-4-olide **3** (R^1=Me, R^2=Et).



1 2 3

Scheme 1.

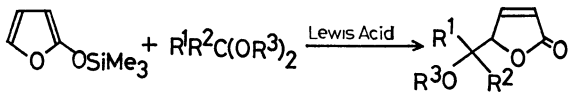
Among the Lewis acids examined, tin(IV) chloride and zinc chloride were found to be suitable catalysts for this reaction. That is, when the reaction was carried out at −40—10 °C for 2 h in the presence of tin(IV) chloride, **3** (R^1=Me, R^2=Et) was obtained in 71% yield, and **3** was obtained in 60% yield when the reaction was carried out at room temperature for 4.5 h in the presence of zinc chloride. But, when a stronger Lewis acid such as antimony(V) chloride or titanium(IV) chloride was used as a catalyst, the yield of **3** was low, probably because decomposition of **1** preferentially took place in contact with such a strong Lewis acid (Table 1). Next, we examined the reaction of **1** with various orthocarboxylic esters in the presence of zinc chloride or tin(IV) chloride. When triethyl orthocarboxylates were used, the yields of **3** decreased in the following order: R^1=H>Me>Et>Ph. When trimethyl orthoformate was used instead of triethyl orthoformate, **3** was obtained in higher yield. All these results suggest that the yields of **3** were markedly influenced by the size of the orthocarboxylic esters. These results are listed in Table 1.

Acetals also reacted with 2-(trimethylsiloxy)furan in the presence of tin(IV) chloride and afforded the corresponding 4-substituted 2-buten-4-olides in good yields.

Next, the reaction of 5-methyl-2-(trimethylsiloxy)-furan **6** with triethyl orthobenzoate was carried out. In this case, the formation of two compounds was confirmed by TLC, but the major product was found to be too unstable to isolate in a pure form. The acid hydrolysis of the reaction mixture afforded 1-phenyl-1,4-pentanedione as a major product and 4-benzoyl-2-penten-4-olide as a minor product. From this result, together with the NMR spectra of the crude mixture of the initially formed products, the major component of the unstable intermediate seems to possess the struc-

Table 1. YIELDS OF 5-SUBSTITUTED 5,5-DIALKOXY-2-PENTEN-4-OLIDES

	R^1	R^2	Lewis acid	Reaction conditions: Temp (°C)	Reaction conditions: Time (h)	Yield **3** (%)
3a	Me	Et	$SnCl_4$	r. t.	1	20
3a	Me	Et	$ZnCl_2$	r. t.	4.5	60
3a	Me	Et	$SnCl_4$	−40—10	2	71
3a	Me	Et	$ZnCl_2$	−40—10	2	56
3a	Me	Et	$SbCl_5$	−40—10	2	57
3a	Me	Et	$TiCl_4$	−40—10	2	30
3a	Me	Et	$BF_3 \cdot Et_2O$	−40—10	2	38
3b	Et	Et	$SnCl_4$	−40—10	2	63
3b	Et	Et	$ZnCl_2$	r. t.	4.5	63
3c	Ph	Et	$SnCl_4$	−40—10	2	48
3c	Ph	Et	$ZnCl_2$	r. t.	4.5	44
3d	H	Et	$SnCl_4$	−40—10	2	72
3e	H	Me	$SnCl_4$	−40—10	2	91

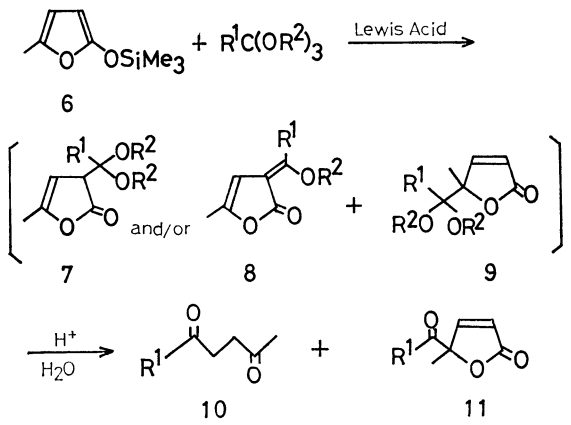


1 4 5

Scheme 2.

Table 2. YIELDS OF 5-SUBSTITUTED 5-ALKOXY-2-PENTEN-4-OLIDES

	R^1	R^2	R^3	Yield **5** (%)
5a	H	C_6H_5	C_2H_5	77
5b	H	p-$CH_3C_6H_4$	C_2H_5	65
5c	H	n-C_9H_{19}	C_2H_5	61
5d	CH_3	CH_3	CH_3	52
5e	C_2H_5	C_2H_5	CH_3	68
5f	$-(CH_2)_4-$		C_2H_5	77
5g	$-(CH_2)_5-$		C_2H_5	38
5h	$-(CH_2)_{11}-$		CH_3	50

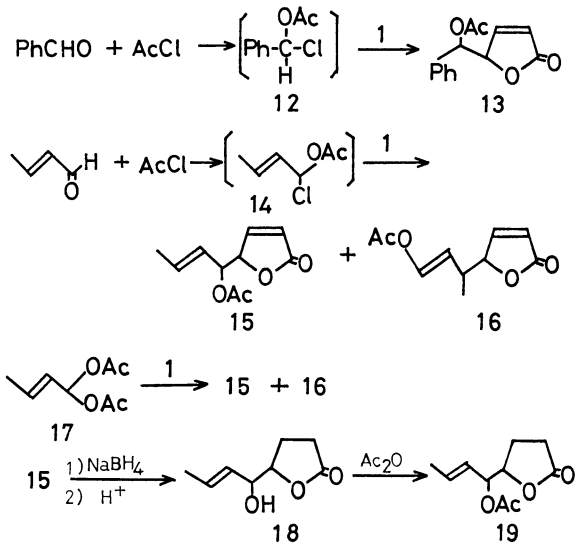


Scheme 3.

Table 3. Yields of 1,4-diketones

R^1	R^2	Lewis acid	Reaction conditions Temp(°C)	Time(h)	Yield **10** (%)
Ph	Et	$SnCl_4$	r. t.	0.5	32
Ph	Et	$SnCl_4$	−5	5.5	32
Ph	Et	$ZnCl_2$	r. t.	4.5	20
Ph	Et	$SbCl_5$	r. t.	1.0	55
n-C_6H_{13}	Me	$SbCl_5$	r. t.	2.0	37

ture of **7** and/or **8**.[2] In contrast to the reaction of **1**, it is to be noted that the electrophile attacked preferentially at the 3-position of **6**. This fact can be explained by considering the steric repulsion between the methyl group at 5-position of the siloxyfuran and the electrophile. The effects of the reaction conditions, especially on the solvents and catalysts, were then examined. In this case, tin(IV) chloride was not a good catalyst. When the reaction was carried out in the presence of tin(IV) chloride, triethyl orthobenzoate still remained even after 24 h, though the other starting material, **6**, had disappeared. This suggests that the decomposition of **6** took place under the reaction conditions. When antimony(V) chloride was used instead of tin(IV) chloride, the yield was improved.



Scheme 4.

When trimethyl orthoheptanoate was used instead of orthobenzoate, 2,5-undecanedione **10**(R=C_6H_{13}), which is known to be an important intermediate for the synthesis of dihydrojasmone,[3] was obtained in 37% yield. These results are summarized in Table 3.

Aldehydes are known to form adducts with acyl chloride.[4] So the reaction of **1** with such adducts was examined. Namely, the reaction of **1** with the mixture of benzaldehyde and acetyl chloride in the presence of a Lewis acid afforded 5-acetoxy-5-phenyl-2-penten-4-olide **13** in 57% yield. Similarly, the reaction of **1** with the mixture of crotonaldehyde and acetyl chloride afforded a 1:1 mixture of 5-acetoxy-2,6-octadien-4-olide **15** and 7-acetoxy-5-methyl-2,6-heptadien-4-olide **16** in 57% yield. When 1,1-diacetoxy-2-butene **17** was used instead of haloacetate **14**, a 1:1 mixture of **15** and **16** was obtained in 86% yield. Sodium borohydride reduction followed by acid hydrolysis of the mixture afforded threo and erythro isomers of **18** in over-all yields of 14 and 16%, respectively. The NMR spectrum of acetyl derivative of the erythro isomer

Table 4. Analytical data of 5-substituted 5,5-dialkoxy-2-penten-4-olides

Product	IR, cm^{-1}	NMR, δ	Formula	Found (Calcd), % C	H
3a	1750—1800(C=O) 1600(C=C)	1.14(3H, t), 1.06(3H, s), 1.18(3H, t), 3.50(2H, q), 3.56(2H, q), 4.98—5.06(1H, m) 6.06(1H, dd), 7.44(1H, dd)	$C_{10}H_{16}O_4$	60.12 (59.98	8.14 8.05)
3b	1755—1795(C=O) 1600(C=C)	0.84(3H, t), 1.12(3H, t), 1.18(3H, t), 1.64(2H, q), 3.44(2H, q), 3.54(2H, q), 4.96—5.10(1H, m), 6.02(1H, dd), 7.56(1H, dd)	$C_{11}H_{18}O_4$	61.47 (61.66	8.43 8.47)
3c	1760—1790(C=O) 1600(C=C)	1.12(3H, t), 1.30(3H, t), 3.54(2H, q), 3.70(2H, q), 5.18—5.30(1H, m), 5.66(1H, dd), 7.22(5H, s), 7.34(1H, dd)	$C_{15}H_{18}O_4$	68.83 (68.68	6.90 6.92)
3d	1760—1800(C=O) 1605(C=C)	1.16(3H, t), 1.24(3H, t), 3.70(2H, q), 3.74(2H, q), 4.48(1H, d), 4.86—5.03(1H, m), 6.10(1H, dd), 7.46(1H, dd)	$C_9H_{14}O_4$	58.13 (58.05	7.68 7.58)
3e	1760—1800(C=O) 1605(C=C)	3.40(3H, s), 3.44(3H, s), 4.34(1H, d), 6.12(1H, dd), 4.92—5.06(1H, m), 7.48(1H, dd)	$C_7H_{10}O_4$	53.11 (53.16	6.39 6.37)

Table 5. Analytical data of 5-substituted 5-alkoxy-2-penten-4-olides

Products	IR, cm^{-1}	NMR, δ	Formula	Found(Calcd), % C	Found(Calcd), % H	Mp, °C
5a	1765—1780(C=O) 1600(C=C)	1.02—1.36(3H, m), 3.20—3.62(2H, m), 4.40(1H, d), 4.80—5.12(1H, m), 5.76—6.04(1H, m), 7.00—7.38(1H, m), 7.14—7.30(5H, m)	$C_{13}H_{14}O_3$	71.38 (71.54	6.52 6.47)	oil
5b	1755—1780(C=O) 1605(C=C)	0.98—1.32(3H, m), 2.30(3H, s), 3.14—3.56(2H, m), 4.34(1H, d), 4.76—5.10(1H, m), 5.70—6.02(1H, m), 6.92—7.40(1H, m), 7.00—7.16(4H, m)	$C_{14}H_{16}O_3$	72.29 (72.39	6.96 6.94)	oil
5c	1760—1790(C=O) 1600(C=C)	0.68—1.82(22H, m), 3.16—3.70(3H, m), 4.64—5.04(1H, m), 5.98(1H, dd), 7.40(1H, dd)	$C_{16}H_{28}O_3$	71.62 (71.60	10.62 10.52)	oil
5d	1750—1770(C=O) 1600(C=C)	1.00(3H, s), 1.28(3H, s), 3.22(3H, s), 4.64—4.80(1H, m), 6.00(1H, dd), 7.44(1H, dd)	$C_8H_{12}O_3$	61.89 (61.52	7.84 7.75)	oil
5e	1755—1770(C=O) 1785(C=O) 1600(C=C)	0.82(3H, t), 0.92(3H, t), 1.52(2H, q), 1.64(2H, q), 3.20(3H, s), 5.98(1H, dd), 4.84—4.96(1H, m), 7.54(1H, dd)	$C_{10}H_{16}O_3$	65.01 (65.19	8.75 8.75)	oil
5f	1755—1775(C=O) 1795(C=O) 1600(C=C)	1.10(3H, t), 1.36—1.90(8H, m), 3.40(2H, q), 4.90—5.02(1H, m), 5.98(1H, dd), 7.42(1H, dd)	$C_{11}H_{16}O_3$	67.39 (67.32	8.26 8.22)	oil
5g	1750—1790(C=O) 1600(C=C)	1.00—2.10(10H, m), 1.16(3H, t), 3.48(2H, q), 4.90—5.02(1H, m), 6.10(1H, dd), 7.46(1H, dd)	$C_{12}H_{18}O_3$	68.58 (68.54	8.66 8.63)	56— 57.5
5h	1750, 1790(C=O) 1600(C=C)	1.08—1.86(22H, m), 3.24(3H, s), 4.90—5.02(1H, m), 6.12(1H, dd), 7.62(1H, dd)	$C_{17}H_{28}O_3$	73.01 (72.82	10.03 10.06)	108

agreed with that of nigrosporalactone reported in the literature.[5] Thus, the natural nigrosporalactone was proved to be the erythro isomer.

In conclusion, 2-(trimethylsiloxy)furans reacted with various electrophiles similar to the silyl enol ethers[6] and afforded various substituted unsaturated lactones, which can be regarded as useful synthetic intermediates.

Experimental

A Typical Example of the Reaction of 2-(Trimethylsiloxy)-furan with Orthocarboxylates or Acetals. Triethyl orthoacetate (179 mg, 1.1 mmol) in dichloromethane (2 ml) was added to 2-(trimethylsiloxy)furan (172 mg, 1.1 mmol) and cooled to −40 °C. The reaction temperature was gradually raised to 10 °C after the addition of a few drops of tin(IV) chloride. Separation of the reaction mixture by silica gel TLC afforded 5,5-diethoxy-2-hexen-4-olide (155 mg, 71%).

1-Phenyl-1,4-pentanedione: To a solution of triethyl orthobenzoate (224 mg, 1 mmol) and 5-methyl-2-(trimethylsiloxy)furan (208 mg, 1.3 mmol) in dry dichloromethane (2.5 ml), was added one drop of antymony(V) chloride at room temperature. The reaction mixture was stirred at room temperature for 0.5 h, and the solvent was removed under reduced pressure. To the residue 5 ml of 40% of aqueous acetic acid was added and the resulting solution was refluxed for 45 min. After cooling to room temperature, the reaction mixture was extracted with three portions of ether. Removal of the solvent under reduced pressure gave a brownish oil, from which 1-phenyl-1,4-pentanedione was isolated in 55% yield by silica gel TLC (hexane–ether).

2,5-Undecanedione: The reaction of trimethyl orthoheptanoate with 5-methyl-2-(trimethylsiloxy)furan and the hydrolysis of the reaction products were carried out in a procedure similar to that mentioned above, and the isolation by TLC (hexane R_f=0.5) afforded 2,5-undecanedione in 37% yield.

5-Acetoxy-5-phenyl-2-penten-4-olide: Benzaldehyde (318 mg, 3 mmol) and acetyl chloride (238 mg, 3.03 mmol) were dissolved in 4 ml of dry dichloromethane, and the solution was stirred at room temperature for 15 min. Then the solution was cooled to −78 °C. 2-(Trimethylsiloxy)furan (515 mg, 3.3 mmol) was added to the solution and catalytic amounts of tin(IV) chloride were subsequently added. The mixture was allowed to warm to room temperature for 20 h with stirring. Ten ml of phosphate buffer (pH 7) was then added and the mixture was extracted with ethyl acetate. The organic layer was washed with water and dried over sodium sulfate. Ethyl acetate was removed under reduced pressure, and the residue was separated by silica gel column chromatography to give 5-acetoxy-5-phenyl-2-pentene-4-olide in 57% yield. IR (NaCl): 1750—1790 cm^{-1} (C=O), 1610 cm^{-1} (C=C); NMR($CDCl_3$): δ=2.10 (3H, s), 5.16—5.34 (1H, m), 5.86 (1H, d), 5.98—6.18 (1H, m), 7.10—7.60 (6H, m). Found: C, 67.24; H, 5.22%. Calcd for $C_{13}H_{12}O_4$: C, 67.23; H, 5.21%.

5-Hydroxy-6-octen-4-olide (Nigrosporalactone): To a solution of 2-(trimethylsiloxy)furan (2.43 g, 15.6 mmol) and 1,1-diacetoxy-2-butene (2.58 g, 15 mmol) in 20 ml of dry dichloromethane was added a catalytic amount of tin(IV) chloride at −40 °C. The mixture was allowed to warm to room temperature for 2 h, and was then stirred for 1 h at room temperature. Phosphate buffer (pH 7) was added to the mixture and the mixture was extracted with ethyl acetate. Ethyl acetate was removed under reduced pressure. Separation of the residue by column chromatography on silica gel gave 2.54 g of the mixture of 5-acetoxy-

2,6-octadien-4-olide and 7-acetoxy-5-methyl-2,6-heptadien-4-olide. This mixture was dissolved in 20 ml of methanol and cooled to 0 °C. Sodium borohydride(737 mg) was added to the solution in small portions and stirred for 0.5 h after the completion of the addition. The resulted mixture was acidified with 1 M hydrochloric acid (50 ml), and was stirred for 5 days. Methanol was removed under reduced pressure and the resulting mixture was extracted with ethyl acetate. The organic layer was washed with water and dried on sodium sulfate. After the removal of ethyl acetate under reduced pressure, the separation of the residue by TLC afforded erythro isomer (16%) and threo isomer (14%) of 5-hydroxy-6-octen-4-olide. Each of these were acetylated using an excess of triethyl amine and acetic anhydride. 5-Acetoxy-6-octen-4-olide (erythro): IR (NaCl): 1750 cm^{-1}, 1790 cm^{-1} (C=O); NMR ($CDCl_3$): δ=1.74 (3H, d), 2.04 (3H, s), 2.20—2.54 (4H, m), 4.48 (1H, dq), 5.28 (1H, dd), 5,50 (1H, dd), 5.84 (1H, dq). Found: C, 60.10; H, 7.09%. Calcd for $C_{10}H_{14}O_4$: C, 60.59, H, 7.12%. 5-Acetoxy-6-octen-4-olide (threo); IR (NaCl): 1750 cm^{-1}, 1790 cm^{-1} (C=O); NMR ($CDCl_3$): δ=1.76 (3H, d), 2.02 (3H, s), 2.00—2.54 (4H, m), 4.50 (1H, dq), 5.28 (1H, dd), 5.44(1H, dd), 5.82 (1H, dq). Found: C, 60.08; H, 6.95%. Calcd for $C_{10}H_{14}O_4$: C, 60.59; H, 7.12%.

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2) The NMR spectra of the crude mixture showed complex signals in which some signals probably due to **7** and **8** were observed. **7**: ($CDCl_3$) 1.70 (3H, s, $-CH_3$), 5.05 (1H, s, C=CH). **8**: 2.00 (3H, s, $-CH_3$), 6.00 (1H, s, C=CH), 4.33 (2H, q, C=C–OCH_2–). For the synthesis of 2,5-alkanediones *via* 2-ethoxyalkylidene 3-buten-4-olides, see: M. Asaoka, N. Sugimura, and H. Takei, *Chem. Lett.*, **1977**, 171.

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