Reactivity of 5-Methyl-3(2*H*)-furanones toward Schiff Bases; Synthesis of 5-Styryl-3(2*H*)-furanone Derivatives

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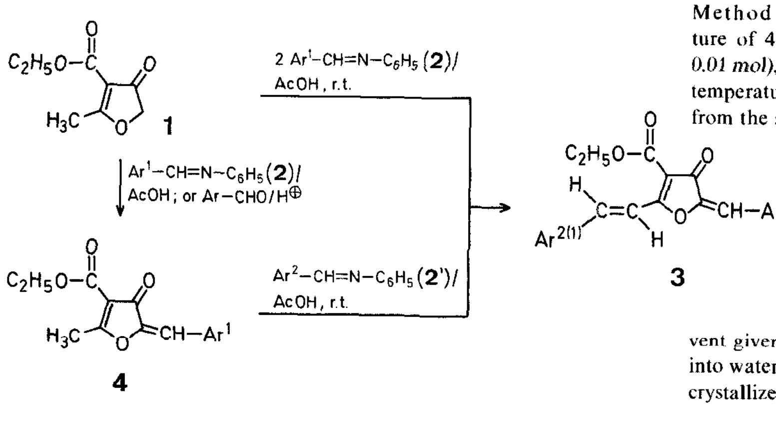
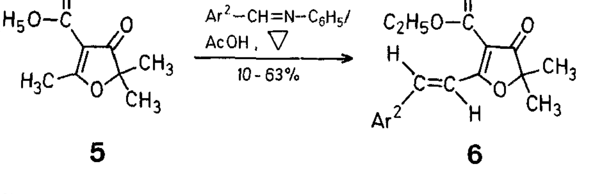
2-Benzylidene-3-oxo-2,3-dihydrofurans [**4**, 2-benzylidene-3(2*H*)-furanones] were first prepared a few years ago[1,2,3]. We now report a convenient preparation of the 5-styryl-3(2*H*)-furanone derivatives **3** and **6** by reaction of the 3(2*H*)-furanones **1**[1], **4**[1,3], and **5**[4] with Schiff bases (**2**). The synthesis of 2,2-dimethyl-3-oxo-5-styryl-2,3-dihydrofuran by a Claisen-type condensation from methyl cinnamate and 3-hydroxy-3-methylbutanone has recently been reported[5].



The reaction of two mol equivalents of imines **2** with 4-ethoxycarbonyl-5-methyl-3-oxo-2,3-dihydrofuran (**1**) in acetic acid at room temperature results in the stereospecific formation of (*Z*)-2-benzylidene-4-ethoxycarbonyl-3-oxo-5-(*E*)-styryl-2,3-dihydrofurans (**3**). This reaction proceeds via addition of the acidic methylene group of **1** to the protonated Schiff base **2** and deamination of the resultant intermediate to give the (*Z*)-2-benzylidene-4-ethoxycarbonyl-5-methyl-3-oxo-2,3-dihydrofuran **4**. Reaction of **4** with a second mol of Schiff base **2** then leads to the formation of the (*Z*)-2-benzylidene-4-ethoxycarbonyl-3-oxo-5-(*E*)-styryl-2,3-dihydrofuran **3** having identical aryl groups (Ar^1). The whole reaction is carried out as a one-step procedure. For the synthesis of compounds **3** having two different aryl groups (Ar^1, Ar^2), compound **4** is prepared from **1** using only one mol equivalent of **2**, isolated, and then submitted to the reaction with one mol equivalent of a second Schiff base **2'**. Compounds **4** prepared from **1** and **2** are identical with the products obtained from the acid-catalyzed condensation of compounds **1** with aromatic aldehydes[1,3].

In the case of 4-ethoxycarbonyl-3-oxo-2,2,5-trimethyl-2,3-dihydrofuran (**5**), the reaction (using only one mol equivalent of Schiff base) is carried out in boiling acetic acid because at room temperature only negligible conversion of **5** into **6** is observed even after 24 h.



5 **6**

A literature search showed that the reaction of Schiff bases with ketones is only of limited applicability[6]. In the present investigation, the use of Schiff bases in a reaction which is formally analogous to the aldol reaction deserves particular attention because this condensation cannot be achieved under basic conditions[1,7]. For related reactions under basic conditions, see Ref.[8].

Our results demonstrate the high reactivity of the 5-methyl H-atoms in the 5-methyl-3(2*H*)-furanone system. It appears that the present reaction provides the first example of reactive γ-hydrogen atoms in β-alkoxy-α,β-unsaturated carbonyl compounds with respect to the reaction with Schiff bases under acidic conditions.

The structure of compounds **3** and **6** are in agreement with their microanalyses as well as their I.R.-, U.V.-, and ^{1}H-N.M.R.-spectral data.

(*Z*)-2-Benzylidene-4-ethoxycarbonyl-3-oxo-5-(*E*)-styryl-2,3-dihydrofurans (3); General Procedures:

Method A: One-Step Procedure for Identical Aryl Groups Ar^1: A mixture of 4-ethoxycarbonyl-5-methyl-3-oxo-2,3-dihydrofuran (**1**; 1.702 g, 0.01 mol), an imine **2** (0.02 mol), and acetic acid (10 ml) is stirred at room temperature for 3 h. The solid product (which in most cases precipitates from the solution) is isolated by suction and recrystallized from the solvent given in Table 1. In the case of **3f**, the reaction mixture is poured into water (100 ml), the precipitated product isolated by suction, and recrystallized from ethanol.

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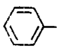
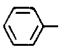
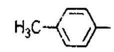
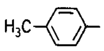
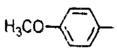
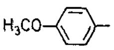
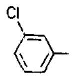
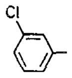
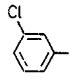
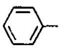
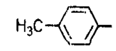
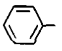
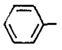
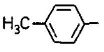
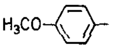
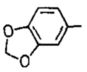
Table 1. Compounds 3 and 6 prepared

Product	Ar^1	Ar^2 (Ar^1)	Method	Yield [%]	m.p. [°C] (solvent)	Molecular Formula^a
3a			A	72	160–161° (ethyl acetate)	$C_{22}H_{18}O_4$ (346.4)
3b			A	83	165–166° (ethyl acetate)	$C_{24}H_{22}O_4$ (374.2)
3c			A	91	204° (acetonitrile)	$C_{24}H_{22}O_6$ (406.4)
3d			A	40	206° (chloroform)	$C_{22}H_{16}Cl_2O_4$ (415.3)
3e			B	66^b	183–184° (ethyl acetate)	$C_{22}H_{17}ClO_4$ (380.8)
3f			B	68^c	144° (ethanol)	$C_{23}H_{20}O_4$ (360.4)
6a			C	<10	87° (ethanol)	$C_{17}H_{18}O_4$ (286.3)
6b			C	63	106° (ethanol)	$C_{18}H_{20}O_4$ (300.3)
6c			C	60	123° (ethanol)	$C_{18}H_{20}O_5$ (316.3)
6d			C	57	159° (ethanol)	$C_{18}H_{18}O_6$ (330.3)

[a] The microanalyses of all products were in satisfactory agreement with the calculated values: C, ±0.28; H, ±0.11; Cl, ±0.07.

[b] Based on **4e**. Yield of **4e**: 34%; m.p. 127–128 °C.

$C_{15}H_{13}ClO_4$	calc.	C 61.54	H 4.48	Cl 12.11
(292.7)	found	61.62	4.41	12.41

[c] Based of **4f**. Yield of **4f**: 44%; m.p. 129 °C (Ref.[1], m.p. 130 °C).

Table 2. Spectral Data of Compounds 3 and 6

Product	I.R. ($CHCl_3$) $\nu_{C=O}$ [cm^{-1}]	U.V. (ethanol) λ_{max} [nm] (ε)	^{1}H-N.M.R. ($CDCl_3$)^a δ [ppm]
3a	1740, 1705	380 (42400), 284 (14900)	1.44 (t, 3H, J=7.5 Hz); 4.52 (q, 2H, J=7.5 Hz); 5.34 (s, 1H); 8.00, 8.18 (2H, AB system, J_{AB}=18.5 Hz)
3b	1730, 1700	392 (36100), 291 (14500), 253 (11300)	1.47 (t, 3H, J=7 Hz); 2.42 (s, 6H); 4.52 (q, 2H, J=7 Hz); 6.90 (s, 1H); 7.87, 8.02 (2H, AB system, J_{AB}=18 Hz)
3c	1730, 1700	416 (33500), 300 (16300), 264 (14800)	1.45 (t, 3H, J=7 Hz); 3.97 (s, 6H); 4.53 (q, 2H, J=7 Hz); 6.98 (s, 1H); 8.00 (s, 2H)
3d	1735, 1705	371 (38500), 285 (12100)	1.46 (t, 3H, J=7 Hz); 4.55 (q, 2H, J=7 Hz); 6.92 (s, 1H); 7.94, 8.17 (2H, AB system, J_{AB}=17 Hz)
3e	1735, 1705	378 (39600), 284 (13100)	1.43 (t, 3H, J=7 Hz); 4.49 (q, 2H, J=7 Hz); 6.86 (s, 1H); 7.97, 8.12 (2H, AB system, J_{AB}=19 Hz)
3f	1730, 1700	382 (44100), 287 (18000)	1.45 (t, 3H, J=7 Hz); 2.45 (s, 3H); 4.55 (q, 2H, J=7 Hz); 7.02 (s, 1H); 8.04, 8.18 (2H, AB system, J_{AB}=17 Hz)
6a	1740, 1705	344 (18500), 228 (10000)	1.44 (t, 3H, J=7.5 Hz); 1.51 (s, 6H); 4.51 (q, 2H, J=7.5 Hz); 8.00, 8.22 (2H, AB system, J_{AB}=16 Hz)
6b	1740, 1705	354 (22500), 229 (11200)	1.45 (t, 3H, J=7.5 Hz); 1.52 (s, 6H); 2.47 (s, 3H); 4.51 (q, 2H, J=7.5 Hz); 7.98, 8.12 (2H, AB system, J_{AB}=17 Hz)
6c	1740, 1705	376 (26800), 235 (12100)	1.45 (t, 3H, J=7.5 Hz); 1.52 (s, 6H); 3.98 (s, 3H); 4.51 (q, 2H, J=7.5 Hz); 8.05 (s, 2H)
6d	1740, 1705	385 (22800), 260 (7900)	1.45 (t, 3H, J=7 Hz); 2.45 (s, 3H); 4.55 (q, 2H, J=7 Hz); 7.98 (s, 2H)

[a] Aromatic protons are not listed.

Method B: Two-Step Procedure for Two Different Aryl Groups Ar^1 and Ar^2:

(Z)-2-Benzylidene-4-ethoxycarbonyl-5-methyl-3-oxo-2,3-dihydrofurans **(4e, f)**: A mixture of 4-ethoxycarbonyl-5-methyl-3-oxo-2,3-dihydrofuran (**1**; 3.4 g, 0.02 mol), an imine **2** (0.01 mol), and acetic acid (20 ml) is stirred at room temperature. The addition product precipitates after about 0.5-1 h and stirring is confinued until complete dissolution (3-5 h) by subsequent deamination. The reaction mixture is then poured into 5% hydrochloric acid (100 ml) and the resultant solid product is isolated by suction, washed with water, and recrystallized twice from ethanol.

(Z)-2-Benzylidene-4-ethoxycarbonyl-3-oxo-5-(E)-styryl-2,3-dihydrofurans **(3)**: A mixture of compound **4** (0.01 mol), an imine **2′** (0.01 mol), and acetic acid (10 ml) is stirred at room temperature for 3 h. The product is isolated as in Method A.

2,2-Dimethyl-4-ethoxycarbonyl-3-oxo-5-(*E*)-styryl-2,3-dihydrofurans (6); General Procedure:

Method C: A mixture of 4-ethoxycarbonyl-3-oxo-2,2,5-trimethyl-2,3-dihydrofuran (**5**; 1.982 g, 0.01 mol), an imine **2′** (0.01 mol), and acetic acid (10 ml) is refluxed for 8 h, then allowed to cool, and poured into water (100 ml). The resultant mixture is allowed to stand overnight, the precipitated solid product is isolated by suction, and recrystallized from ethanol.

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