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Photochemical Versus Aluminium Chloride-Catalyzed Fries Rearrangement of Aryl Hydrogen Succinates. Synthesis of 2(3*H*)-Furanones

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Summary. The photochemical and aluminium chloride-catalyzed Fries rearrangement of a series of aryl hydrogen succinates **3a–f** to the corresponding 4-oxoacids **1a–f** are compared. Both approaches are complementary: the photochemical process is more general and becomes the method of choice for the succinoylation of phenols supporting alkoxy or hydroxy substituents, while the classical rearrangement is superior in the presence of alkyl or halogen substituents. These results are applied to the preparation of the 2(3*H*)-furanones **2a–f**.

Keywords. Fries rearrangement; Photo-Fries rearrangement; Aryl hydrogen succinates; 4-Oxoacids; 2(3*H*)-Furanones.

Photochemische und Aluminiumchlorid-katalysierte Friessche Umlagerung von Bernsteinsäuremonoarylestern. Synthese von 2(3*H*)-Furanonen

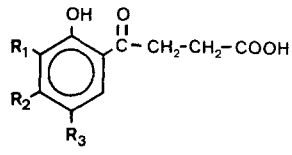
Zusammenfassung. Die photochemische und $AlCl_3$-katalysierte Friessche Umlagerung einer Reihe von Bernsteinsäuremonoarylestern **3a–f** zu den entsprechenden 4-Oxosäuren **1a–f** werden verglichen. Beide Methoden ergänzen einander: Der photochemische Prozeß ist breiter anwendbar und wird bei Phenolen mit Alkoxy- oder Hydroxy-Substituenten bevorzugt, während die klassische Umlagerung in Gegenwart von Alkyl- oder Halogen-Substituenten vorteilhafter ist. Diese Ergebnisse werden für die Synthese der 2(3*H*)-Furanone **2a–f** angewendet.

Introduction

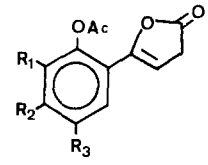
The introduction of a succinic acid-derived side chain in aromatic systems is a very interesting process from the synthetic point of view [2], since it constitutes the key carbon-carbon bond forming step in the Haworth [3] synthesis of polycyclic hydrocarbons. The process is also valuable because it affords 4-oxoacids, which are potentially applicable as antiinflammatory agents [4] and also as versatile intermediates for the synthesis of heterocycles [5].

In this context, we were interested in the preparation of a series of 4-(2-hydroxyaryl)-4-oxobutanoic acids **1** as precursors of 5-(2-acetoxyaryl)-2(3*H*)-furanones **2**, whose photochemistry is currently a matter of study in these

laboratories [6]. In principle two methods could be suitable to achieve the desired preparation of **1**: (i) the direct Friedel-Crafts acylation of phenols with reactive succinic acid derivatives and (ii) the Lewis acid-catalyzed Fries rearrangement of aryl hydrogen succinates **3**. Both methods are closely related from the mechanistic point of view and, as a consequence, they present analogous advantages and limitations. Among the latter, the acidic medium favours the formation of undesired byproducts through a variety of unwanted secondary reactions [2]. On the other hand, it has been reported that this type of approach fails completely in a number of cases, as, for example, in the succinoylation of hydroquinone or its monomethyl ether [7].



1



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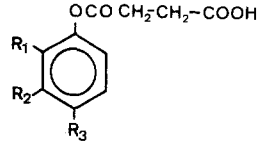

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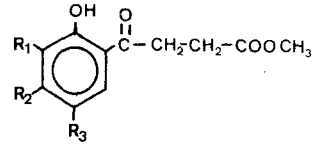

4

a: $R_1 = R_2 = H$; $R_3 = OCH_3$
b: $R_1 = R_2 = H$; $R_3 = OH$ (OAc)
c: $R_1 = R_2 = H$; $R_3 = CH_3$
d: $R_1 = R_3 = CH_3$; $R_2 = H$
e: $R_1 = R_2 = H$; $R_3 = Cl$
f: $R_1 = H$; $R_2 = CH_3$; $R_3 = Cl$
g: $R_1 = R_2 = R_3 = H$
h: $R_1 = R_3 = H$; $R_2 = CH_3$

As a possible alternative to synthesize the required oxoacids **1**, we decided to investigate the photo-Fries rearrangement [8–10] of aryl hydrogen succinates **3**, which would take place under neutral conditions and at room temperature. The results are reported in the present paper [11] and compared with those obtained by the classical Fries rearrangement of the same substrates with aluminium chloride.

Results and Discussion

The starting aryl hydrogen succinates **3** were prepared in very good yields by reaction of the corresponding sodium phenolates with succinic anhydride in water, following a known procedure [12]. The reaction was completed within a few minutes at room temperature, and the products were easily isolated by acidification of the resulting solutions and subsequent filtration of the precipitates.

The photo-Fries rearrangement of **3** was carried out using a quartz immersion well photoreactor, provided with a 125 W medium pressure mercury lamp. In order

Table 1. Rearrangement of the aryl hydrogen succinates **3a–f**

Substrate	Product	% Irradiation		% $AlCl_3$	
		NMR	Isolated	NMR	Isolated
3a	**1a**	—	60	—	—[a]
3b	**1b**	—	55	—	—[b]
3c	**1c**	45	18	48	35[c]
3d	**1d**	60	25	50	40
3e	**1e**	57	20	25	12[d]
	1g		2	—	—
3f	**1f**	40	7	40	27
	1h		4	—	—

[a] The only isolated product was *p*-methoxyphenol
[b] The only isolated product was hydroquinone
[c] 40% in Ref. [13]
[d] 7% in Ref. [14]

to make a correct evaluation of this process, we also proceeded to duplicate the analogous reaction catalyzed by aluminium chloride, both to obtain data for comparison and to confirm that these were not affected by substantial variations with respect to literature.

The results of the two series of experiments are given in Table 1. The irradiations were first performed in ethanol. In the case of **3a** and **3b**, concentration of the irradiated solutions led to crystallization of the photo-Fries products **1a** and **1b** with nearly 60% yield. However, irradiation of the chloro derivatives **3e** and **3f** afforded crude photomixtures which were shown to contain two different 4-oxoacids (whose separation was achieved by column chromatography via the corresponding methyl esters **4**). This procedure allowed to isolate the expected products **1e** and **1f** together with the corresponding dehalogenated compounds **1g** and **1h** (yields given in Table 1). Based on the NMR-spectra of the residues obtained after elimination of the solvent, before esterification and chromatography, it could be established that the total amount of 4-oxoacids present in the reaction mixture was about 50%, as indicated by the intensities of the signal corresponding to the α-carbonyl protons.

In the photo-Fries rearrangement phenols are usually obtained as byproducts, their formation being explained by hydrogen abstraction by the primary phenoxy radicals before the in cage recombination with the accompanying acyl radicals. In fact, minor amounts of phenols were also found among the photoproducts of **3a**, **3b**, **3e**, and **3f** (data not given). Surprisingly, in the case of the methyl substituted analogues **3c** and **3d**, the formation of phenols became the almost exclusive reaction pathway when the irradiations were carried out in ethanol. Therefore, we attempted the photo-Fries rearrangement of **3c** and **3d** in dimethylsulfoxide, whose higher viscosity would be expected to enhance in cage recombination, to the detriment of phenol formation. The irradiation of the compounds **3c** and **3d** in dimethylsulfoxide led to the formation of the corresponding 4-oxoacids **1c** and **1d** (ca. 20% yield),

whose separation was also carried out by column chromatography of the corresponding methyl esters **4**.

Thus, the light-induced Fries rearrangement appears to be more general than its $AlCl_3$-catalyzed counterpart, since the latter fails with the esters of *p*-methoxyphenol and hydroquinone (**3 a** and **3 b**). This fact can be explained by the different reaction mechanisms. The classical reaction is electrophilic in nature and involves the generation of an acyl cation after coordination of the ester group with the Lewis acid, which in the case of esters **3 a** and **3 b** must compete with coordination of the more basic —OR group with the same reagent, thus rendering the aromatic nucleus deactivated.

In summary, both approaches are complementary. Thus, the photochemical process becomes the method of choice for the nuclear succinoylation of phenols supporting alkoxy or hydroxy substituents, while the classical rearrangement in acidic media seems superior in presence of alkyl or halogen substituents.

In the final stage of our work, as an application of the above results, we undertook the preparation of the 2(3*H*)-furanones **2 a–f**. Treatment of the 4-oxoacids **1 a–f** with acetic anhydride in the presence of sulfuric acid [5] afforded the desired products with nearly 80% yield. Current work is directed to study the photochemical behavior of these compounds and related enol lactones.

Experimental

Melting points were measured with a Kofler apparatus and are uncorrected. IR spectra were obtained in CCl_4 solutions with a Perkin-Elmer 577 spectrometer; absorptions ($\bar{\nu}$, cm^{-1}) are given only for the main bands. ^{1}H-NMR spectra were recorded on a 60 MHz Hitachi Perkin-Elmer R-24-B instrument in CCl_4 or $CDCl_3$ solutions unless otherwise specified; chemical shifts are reported as δ values (ppm) using Me_4Si as internal standard. Elemental analyses were performed at the Instituto de Química Orgánica of C.S.I.C. in Madrid.

Preparation of the Esters 3

To a solution of 2 g (0.05 mol) of NaOH in 100 ml of water were added under continuous magnetic stirring 0.05 mol of the corresponding phenol and then 5 g (0.05 mol) of succinic anhydride. After 10 min the resulting solution was acidified with concentrated HCl and the precipitate was filtered in vacuo, washed with water and dried, to give the esters **3**, which were purified by recrystallization.

Irradiation of the Esters 3

Procedure A. A solution of 2 g of ester **3** in 300 ml of dimethylsulfoxide was irradiated for 20 h at room temperature with a 125 W medium pressure mercury lamp inside a quartz immersion well photoreactor. The irradiated solution was poured into ice-water and subsequently submitted to continuous liquid-liquid extraction with ethyl ether. After removal of the solvent, 100 ml of methanol and 0.5 ml of H_2SO_4 were added and the mixture was refluxed during 4 h. Then it was concentrated in vacuo and the residue purified with silica-gel column chromatography (eluent hexane/ethyl ether 3/1), affording the esters **4**. The latter compounds were saponified with a solution of 2 g of NaOH in a mixture of 25 ml of water and 25 ml of ethanol. After 30 min the mixture was neutralized precipitating the corresponding acids **1**, which were filtered in vacuo and recrystallized.

Procedure B. A solution of 2 g of ester **3** in 300 ml of ethanol was irradiated for 20 h as described in Procedure A. Then, the solvent was concentrated in vacuo and the residue was treated as described in Procedure A, after continuous liquid-liquid extraction.

In the case of the esters **3a** and **3b**, the partial elimination of the solvent until a final volume of 15 ml led to the precipitation of the photoproducts **1a** and **1b**. Their methyl esters **4a** and **4b** were prepared by treatment with methanol and sulfuric acid, in the usual way.

Treatment of the Esters **3** *with* $AlCl_3$

A mixture of 2 mmol of ester **3** with 0.5 g (4 mmol) of anhydrous $AlCl_3$ was heated for 1 h at 170°C with magnetic stirring. Then, 50 ml of concentrated HCl and 50 ml of water were added and the precipitate was filtered in vacuo, dried and submitted to purification by recrystallization giving the acids **1**.

Preparation of the Lactones **2**

A mixture of 1 g of the acids **1** with 50 ml of acetic anhydride and 0.5 ml of H_2SO_4 was stirred for 1 h at room temperature and then poured into 200 ml ice-water under magnetic stirring. The resulting precipitate was filtered in vacuo, dried and purified by recrystallization leading to the lactones **2**.

Products

4-Methoxyphenyl Hydrogen Succinate (**3a**). Yield 97%; recrystallized from benzene; m.p. 116–117°C (lit. [12] 117–118°C); IR: 1760 (C=O, ester), 1705 (C=O, acid); NMR: 7.20–6.80 (m, 4H, *Ar*-H), 3.80 (s, 3H, OCH_3), 2.84 (s, 4H, CH_2—CH_2).

4-Hydroxyphenyl Hydrogen Succinate (**3b**). Yield 90%; recrystallized from water; m.p. 171–173°C (lit. [12] 174–175°C); IR: 1750 (C=O, ester), 1710 (C=O, acid); NMR: 7.10–6.70 (m, 4H, *Ar*-H), 2.77 (m, 4H, CH_2—CH_2).

4-Methylphenyl Hydrogen Succinate (**3c**). Yield 99%; recrystallized from cyclohexane; m.p. 103–105°C (lit. [15] 105–106°C); IR: 1760 (C=O, ester), 1720 (C=O, acid); NMR: 7.00 (AA'BB', 4H, *Ar*-H), 2.80 (s, 4H, CH_2—CH_2), 2.35 (s, 3H, CH_3).

2,4-Dimethylphenyl Hydrogen Succinate (**3d**). Yield 81%; recrystallized from hexane, m.p. 76–77°C; IR: 1760 (C=O, ester), 1720 (C=O, acid); NMR: 6.82 (m, 3H, *Ar*-H), 2.80 (s, 4H, CH_2—CH_2), 2.37 (s, 3H, C_4—CH_3), 2.11 (s, 3H, C_2—CH_3). Anal. calcd. for $C_{12}H_{14}O_4$: C 64.86, H 6.35; found: C 64.71, H 6.34.

4-Chlorophenyl Hydrogen Succinate (**3e**). Yield 82%; recrystallized from cyclohexane; m.p. 113–117°C (lit. [12] 115–115.5°C); IR: 1760 (C=O, ester), 1720 (C=O, acid); NMR: 7.10 (AA'BB', 4H, *Ar*-H), 2.75 (s, 4H, CH_2—CH_2).

4-Chloro-3-methylphenyl Hydrogen Succinate (**3f**). Yield 84%; recrystallized from cyclohexane; m.p. 110–113°C; IR: 1760 (C=O, ester), 1720 (C=O, acid); NMR: 7.25 (d, $J = 8$, H-5), 6.87 (d, $J = 2$, H-2), 6.80 (dd, H-6), 2.80 (s, 4H, CH_2—CH_2), 2.35 (s, 3H, CH_3). Anal. calcd. for $C_{11}H_{11}ClO$: C 54.55, H 4.57, Cl 14.61; found: C 54.23, H 4.57, Cl 14.33.

4-(2-Hydroxy-5-methoxyphenyl)-4-oxobutanoic Acid (**1a**). Yield 60%; procedure B; recrystallized from benzene; m.p. 142.5–143.5°C; IR: 1690 (C=O, acid), 1640 (C=O, ketone); NMR: 11.70 (s, 1H, chelated OH), 7.30–7.00 (m, 3H, *Ar*-H), 3.83 (s, 3H, OCH_3), 3.38 (t, $J = 7$, 2H, *Ar*$COCH_2$), 2.82 (t, 2H, CH_2COOCH_3). Anal. calcd. for $C_{11}H_{12}O_5$: C 58.92, H 5.39; found: C 58.98, H 5.13.

4-(2,5-Dihydroxyphenyl)-4-oxobutanoic Acid (**1b**) [16]. Yield 55%; procedure B; recrystallized from water; m.p. 183.5–184.5°C; IR: 1705 (C=O, acid), 1640 (C=O, ketone); NMR: 11.60 (s, 1H, chelated OH), 7.50–6.70 (m, 3H, *Ar*-H), 3.38 (t, $J = 7$, 2H, *Ar*$COCH_2$), 2.72 (t, 2H, CH_2COOCH_3). Anal. calcd. for $C_{10}H_{10}O_5$: C 57.14, H 4.79; found: C 57.01, H 4.67.

4-(2-Hydroxy-5-methylphenyl)-4-oxobutanoic Acid (**1c**). Yield 18%; procedure A; recrystallized from cyclohexane; m.p. 131–134°C; IR: 1705 (C=O, acid), 1655 (C=O, ketone); NMR: 11.84 (s, 1H, chelated OH), 7.46 (d, $J < 2$, H-6), 7.22 (dd, H-4), 6.80 (d, $J = 9$, H-3), 3.30 (t, $J = 7$, 2H, $ArCOCH_2$), 2.75 (t, 2H, CH_2COOCH_3), 2.30 (s, 3H, CH_3). Anal. calcd. for $C_{11}H_{12}O_4$: C 63.46, H 5.81; found: C 63.23, H 6.13.

4-(2-Hydroxy-3,5-dimethylphenyl)-4-oxobutanoic Acid (**1d**). Yield 25%; procedure A; recrystallized from cyclohexane; m.p. 149–151°C; IR: 1695 (C=O, acid), 1640 (C=O, ketone); NMR: 12.20 (s, 1H, chelated OH), 7.32 (d, $J < 2$, H-6), 7.10 (d, H-4), 3.30 (t, $J = 6$, 2H, $ArCOCH_2$), 2.75 (t, 2H, CH_2COOCH_3), 2.27 and 2.25 (s + s, 2× 3H, 2× CH_3). Anal. calcd. for $C_{12}H_{14}O_4$: C 64.86, H 6.35; found: C 64.51, H 6.34.

4-(5-Chloro-2-hydroxyphenyl)-4-oxobutanoic Acid (**1e**). Yield 20%; procedure B; recrystallized from cyclohexane; m.p. 178–180°C (lit. [14] 180–181°C); IR: 1690 (C=O, acid), 1640 (C=O, ketone); NMR (*DMSO-d_6*): 7.78 (d, $J = 2$, H-6), 7.50 (dd, H-4), 6.95 (d, $J = 10$, H-3), 3.33 (t, $J = 6$, 2H, $ArCOCH_2$), 2.59 (t, 2H, CH_2COOCH_3).

4-(5-Chloro-2-hydroxy-4-methylphenyl)-4-oxobutanoic Acid (**1f**). Yield 7%; procedure B; recrystallized from chloroform; m.p. 178–182°C; IR: 1700 (C=O, acid), 1650 (C=O, ketone); NMR (Acetone-d_6): 7.89 (s, 1H, H-6), 6.88 (s, 1H, H-3), 3.39 (t, $J = 7$, 2H, $ArCOCH_2$), 2.70 (t, 2H, CH_2COOCH_3), 2.39 (s, 3H, CH_3). Anal. calcd. for $C_{11}H_{11}ClO_4$: C 54.45, H 4.57, Cl 14.61; found: C 54.58, H 4.89, Cl 14.69.

4-(2-Hydroxyphenyl)-4-oxobutanoic Acid (**1g**). Yield 2%; procedure B; recrystallized from water; m.p. 127–130°C (lit. [17] 145–146°C); IR: 1720 (C=O, acid), 1640 (C=O, ketone); NMR (Acetone-d_6): 7.95 (dd, $J_1 = 8$, $J_2 < 2$, H-6), 7.40 (m, H-4), 7.10–6.60 (m, H-3 + H-5), 3.35 (t, $J = 6$, 2H, $ArCOCH_2$), 2.75 (t, 2H, CH_2COOCH_3). Anal. calcd. for $C_{10}H_{10}O_4$: C 61.85, H 5.15; found: C 61.86, H 5.25.

4-(2-Hydroxy-4-methylphenyl)-4-oxobutanoic Acid (**1h**). Yield 4%; procedure B; recrystallized from water; m.p. 154–157°C; IR: 1690 (C=O, acid), 1640 (C=O, ketone); NMR (Acetone-d_6): 7.75 (d, $J = 9$, H-6), 6.72 (dd, H-5), 6.68 (d, $J = 2$, H-3), 3.35 (t, $J = 6$, 2H, $ArCOCH_2$), 2.70 (t, 2H, CH_2COOCH_3), 2.33 (s, 3H, CH_3). Anal. calcd. for $C_{11}H_{12}O_4$: C 63.46, H 5.81; found: C 63.16, H 5.86.

Methyl 4-(2-Hydroxy-5-methoxyphenyl)-4-oxobutanoate (**4a**). Oil; IR: 1750 (C=O, ester), 1640 (C=O, ketone); NMR: 11.70 (s, 1H, chelated OH), 7.30–7.00 (m, 3H, *Ar*-H), 3.83 (s, 3H, OCH_3), 3.70 (s, 3H, $COOCH_3$), 3.38 (t, $J = 6$, 2H, $ArCOCH_2$), 2.82 (t, 2H, CH_2COOCH_3). Anal. calcd. for $C_{12}H_{14}O_5$: C 60.49, H 5.92; found: C 60.28, H 6.07.

Methyl 4-(2,5-Dihydroxyphenyl)-4-oxobutanoate (**4b**). Recrystallized from water; m.p. 129–130°C; IR: 1715 (C=O, ester), 1660 (C=O, ketone); NMR (*DMSO-d_6*): 7.10 (d, $J = 3$, H-6), 7.00–6.40 (m, H-3 + H-4), 3.50 (s, 3H, $COOCH_3$), 3.20 (t, $J = 6$, $ArCOCH_2$), 2.55 (t, 2H, CH_2COOCH_3). Anal. calcd. for $C_{11}H_{12}O_5$: C 58.93, H 5.34; found: C 58.97, H 5.43.

Methyl 4-(2-Hydroxy-5-methylphenyl)-4-oxobutanoate (**4c**). Recrystallized from water; m.p. 52–53°C; IR: 1755 (C=O, ester), 1660 (C=O, ketone); NMR: 11.44 (s, 1H, chelated OH), 7.24 (d, $J < 2$, H-6), 7.00 (dd, H-4), 6.55 (d, $J = 8$, H-3), 3.51 (s, 3H, $COOCH_3$), 3.11 (t, $J = 6$, 2H, $ArCOCH_2$), 2.53 (t, 2H, CH_2COOCH_3), 2.20 (s, 3H, CH_3). Anal. calcd. for $C_{12}H_{14}O_4$: C 64.85, H 6.35; found: C 64.71, H 6.34.

Methyl 4-(2-Hydroxy-3,5-dimethylphenyl)-4-oxobutanoate (**4d**). Recrystallized from cyclohexane; m.p. 60–65°C; IR: 1750 (C=O, ester), 1650 (C=O, ketone); NMR: 11.65 (s, 1H, chelated OH), 7.25 (d, $J < 2$, H-6), 7.00 (d, H-4), 3.65 (s, 3H, $COOCH_3$), 3.25 (t, $J = 6$, 2H, $ArCOCH_2$), 2.65 (t, 2H, CH_2COOCH_3), 2.23 and 2.17 (s + s, 2× 3H, 2× CH_3). Anal. calcd. for $C_{13}H_{16}O_4$: C 66.10, H 6.78; found: C 66.08, H 6.88.

Methyl 4-(5-Chloro-2-hydroxyphenyl)-4-oxobutanoate (**4e**). Recrystallized from cyclohexane; m.p. 44–49°C; IR: 1755 (C=O, ester), 1665 (C=O, ketone); NMR: 12.17 (s, 1H, chelated OH), 7.65 (d, $J = 2$, H-6), 7.25 (dd, H-4), 6.80 (d, $J = 10$, H-3), 3.65 (s, 3H, $COOCH_3$), 3.25 (t, $J = 6$, 2H, $ArCOCH_2$), 2.65 (t, 2H, CH_2COOCH_3). Anal. calcd. for $C_{11}H_{11}ClO_4$: C 54.43, H 4.54, Cl 14.13; found: C 54.35, H 4.73, Cl 14.64.

Methyl 4-(5-Chloro-2-hydroxy-4-methylphenyl)-4-oxobutanoate (**4f**). Recrystallized from cyclohexane; m.p. 95–97°C; IR: 1755 (C=O, ester), 1660 (C=O, ketone); NMR: 11.62 (s, 1H, chelated OH), 7.57 (s, 1H, H-6), 6.70 (s, 1H, H-3), 3.62 (s, 3H, $COOCH_3$), 3.20 (t, $J = 6$, 2H, $ArCOCH_2$), 2.62 (t, 2H, CH_2COOCH_3), 2.35 (s, 3H, $ArCH_3$). Anal. calcd. for $C_{12}H_{13}ClO_4$: C 56.14, H 5.07, Cl 14.13; found: C 56.19, H 5.15, Cl 13.84.

Methyl 4-(2-Hydroxyphenyl)-4-oxobutanoate (**4g**). Recrystallized from cyclohexane; m.p. 33–34°C; IR: 1755 (C=O, ester), 1650 (C=O, ketone); NMR: 12.50 (s, 1H, chelated OH), 7.60 (dd, $J_1 = 8$, $J_2 < 2$, H-6), 7.22 (m, H-4), 6.27 (m, H-3 + H-5), 3.57 (s, 3H, $COOCH_3$), 3.20 (t, $J = 6$, 2H, $ArCOCH_2$), 2.60 (t, 2H, CH_2COOCH_3). Anal. calcd. for $C_{11}H_{12}O_4$: C 63.46, H 5.81; found: C 63.43, H 5.73.

Methyl 4-(2-Hydroxy-4-methylphenyl)-4-oxobutanoate (**4h**). Recrystallized from cyclohexane; m.p. 59–61°C; IR: 1750 (C=O, ester), 1655 (C=O, ketone); NMR: 11.80 (s, 1H, chelated OH), 7.42 (d, $J = 8$, H-6), 6.50 (m, H-3 + H-5), 3.62 (s, 3H, $COOCH_3$), 3.17 (t, $J = 6$, 2H, $ArCOCH_2$), 2.57 (t, 2H, CH_2COOCH_3), 2.30 (s, 3H, CH_3). Anal. calcd. for $C_{12}H_{14}O_4$: C 64.85, H 6.34; found: C 64.62, H 6.71.

5-(2-Acetoxy-5-methoxyphenyl)-2(3H)-furanone (**2a**). Yield 60%; recrystallized from benzene/*n*-heptane; m.p. 93°C; IR: 1780 (C=O, lactone), 1750 (C=O, acetate); NMR: 7.30–6.80 (m, 3H, *Ar*-H), 5.80 (t, $J = 3$, 1H, $CHCH_2$), 3.82 (s, 3H, OCH_3), 3.38 (d, 2H, $CHCH_2$), 2.32 (s, 3H, $OCOCH_3$). Anal. calcd. for $C_{13}H_{12}O_5$: C 62.89, H 4.87; found: C 62.85, H 5.09.

5-(2,5-Diacetoxyphenyl)-2(3H)-furanone (**2b**). Yield 58%; recrystallized from cyclohexane/benzene 9/1; m.p. 110°C; IR: 1800 (C=O, lactone), 1760 (C=O, acetate); NMR: 7.60–7.20 (m, 3H, *Ar*-H), 5.92 (t, $J = 3$, 1H, $CHCH_2$), 3.42 (d, 2H, $CHCH_2$), 2.36 and 2.31 (s + s, 2 × 3H, 2 × $OCOCH_3$). Anal. calcd. for $C_{14}H_{12}O_6$: C 60.86, H 4.37; found: C 60.63, H 4.46.

5-(2-Acetoxy-5-methylphenyl)-2(3H)-furanone (**2c**) [18]. Yield 79%; recrystallized from cyclohexane; m.p. 117–121°C; IR: 1795 (C=O, lactone), 1750 (C=O, acetate); NMR: 7.40–6.90 (m, 3H, *Ar*-H), 5.75 (t, $J = 3$, 1H, $CHCH_2$), 3.35 (d, 2H, $CHCH_2$), 2.37 (s, 3H, CH_3), 2.35 (s, 3H, $OCOCH_3$). Anal. calcd. for $C_{13}H_{12}O_4$: C 67.24, H 5.21; found: C 67.05, H 5.33.

5-(2-Acetoxy-3,5-dimethylphenyl)-2(3H)-furanone (**2d**). Yield 82%; recrystallized from cyclohexane; m.p. 139–145°C; IR: 1790 (C=O, lactone), 1760 (C=O, acetate); NMR: 7.20–7.00 (m, 2H, *Ar*-H), 5.65 (t, $J = 3$, 1H, $CHCH_2$), 3.30 (d, 2H, $CHCH_2$), 2.32 (s, 6H, 2 × CH_3), 2.10 (s, 3H, $OCOCH_3$). Anal. calcd. for $C_{14}H_{14}O_4$: C 68.29, H 5.73; found: C 68.12, H 5.90.

5-(2-Acetoxy-5-chlorophenyl)-2(3H)-furanone (**2e**). Yield 80%; recrystallized from cyclohexane; m.p. 112–120°C; IR: 1815 (C=O, lactone), 1765 (C=O, acetate); NMR: 7.47–6.87 (m, 3H, *Ar*-H), 5.73 (t, $J = 3$, 1H, $CHCH_2$), 3.30 (d, 2H, $CHCH_2$), 2.27 (s, 3H, $OCOCH_3$). Anal. calcd. for $C_{12}H_9ClO_4$: C 57.05, H 3.59, Cl 14.03; found: C 56.87, H 3.65, Cl 14.22.

5-(2-Acetoxy-5-chloro-4-methylphenyl)-2(3H)-furanone (**2f**). Yield 79%; recrystallized from cyclohexane; m.p. 113–118°C; IR: 1785 (C=O, lactone), 1765 (C=O, acetate); NMR: 7.57–6.93 (s, 2H, *Ar*-H), 5.72 (t, $J = 3$, 1H, $CHCH_2$), 3.35 (d, 2H, $CHCH_2$), 2.37 (s, 3H, CH_3), 2.32 (s, 3H, $OCOCH_3$). Anal. calcd. for $C_{13}H_{11}ClO_4$: C 58.55, H 4.16, Cl 13.29; found: C 58.81, H 4.55, Cl 13.49.

References and Notes

[1] Deceased, Fall 1987
[2] Berliner E. (1949) Org. Reactions **5**: 229
[3] March J. (1985) Advanced Organic Chemistry, 3rd edn. McGraw-Hill, New York, p. 486
[4] Bucloxic acid, fenbufen and furobufen are three examples: Shen T. Y. (1980) Nonsteroidal Antiinflammatory Agents. In: Wolff E. M. (ed.) Burger's Medicinal Chemistry, Vol. 3. Wiley-Interscience, New York, p. 1205
[5] See, for example: Rao Y. S. (1976) Chem. Rev. **76**: 625
[6] Martínez-Utrilla R., Miranda M. A. (1981) Tetrahedron **37**: 2111
[7] Dalal G. A., Nargud K. S. (1937) J. Indian Chem. Soc. **14**: 406
[8] Bellus D., Hrdlovic P. (1967) Chem. Rev. **67**: 599
[9] Bellus D. (1971) Adv. Photochem. **8**: 109
[10] Pfau M., Julliard M. (1977) Bull. Soc. Chim. France: 785
[11] Part of this work has appeared as a preliminary communication: Martínez-Utrilla R., Miranda M. A. (1980) Tetrahedron Lett.: 2281
[12] Gaetjens E., Morawetz H. (1960) J. Amer. Chem. Soc. **82**: 5328
[13] Awad W. I., Baddar F. G., Marei A. E. (1954) J. Chem. Soc.: 4538
[14] Baddar F. G., Enayat I., Abdel-Wahab S. M. (1967) J. Chem. Soc. C: 343
[15] Baddar F. G., Wahhab S. A., Awad B. M., Guindy N. M., Wahba M., Malek B. A. A. (1970) J. Chem. Soc. B: 739
[16] Coillard J., Mentzer C. (1953) Bull. Soc. Chim. France **20**: 171
[17] Baddar F. G., El-Assal L. S. (1950) J. Chem. Soc.: 3606
[18] Zymalkosky F. (1951) Arch. Pharm. **284**: 292

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