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LETTERS TO THE EDITOR

A SIMPLE METHOD FOR THE SYNTHESIS OF ESTERS OF 2-HYDROXY-3-OXO-2,3-DIHYDROFURAN-2-YLACETIC ACID

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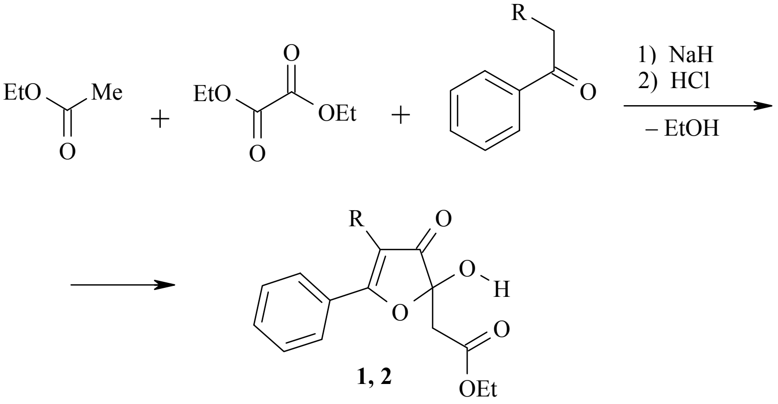
2-Hydroxy-2,3-dihydrofuran-3-ones are successfully used in organic synthesis, especially for the preparation of biologically active compounds [1-5]. The known methods for the synthesis of 5-aryl-2-hydroxyfuran-3(2H)-ones generally include several stages and are not suitable for preparation [4, 5]. We have developed a very simple and suitable one-step method for the synthesis of 2-hydroxy-3-oxo-2,3-dihydrofuran-2-ylacetate esters **1,2** by the reaction of ethyl acetate with diethyl oxalate and methyl ketones (for example, acetophenone or dibenzoylmethane) in the presence of sodium hydride with subsequent treatment of the mixture with hydrochloric acid:



1, 2

1 R = H, **2** R = PhCO

Apart from compound **1**, a secondary product – *Z*-2-hydroxy-4-oxo-4-phenyl-2-butenoic acid (benzoyltartaric acid) was isolated in 27% yield from the reaction mixture of ethyl acetate, diethyl oxalate, and acetophenone, which was identified by comparison with a known sample [6].

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In the ^{1}H NMR spectra of the hydroxyfuranones **1** and **2** there are two doublets of two interacting CH_2 groups at δ 2.94 and 2.98, and 3.16 and 3.28 respectively, corresponding to AB spin systems, and also the signal of the hydroxy group $C_{(2)}OH$ at δ7.58 and 8.36 ppm. The possible open chain forms of compounds **1** and **2** , suggested for analogs in [5], were not observed in the spectra.

Compounds **1** and **2** posses bacteriostatic activity against lines of *Staphylococcus aureus* and the intestinal bacteria *Eschericia coli,* effective on bacterial cultures with a minimum effective concentration of 250 μg/ml.

^{1}H NMR spectra of DMSO-d_6 solutions of compounds **1** and **2** with TMS as internal standard were recorded on a Bruker DRX-500 (500 MHz) machine and the ^{13}C NMR spectrum of a $CDCl_3$ solution with TMS as internal standard was recorded with a Gemini -300BB (75 MHz). IR spectra of nujol mulls were recorded with a Specord M-80 spectrometer.

Cyclocondensation of ethyl acetate with diethyl oxalate and methyl ketones. To a mixture of AcOEt (5.0 ml, 0.05 mol, diethyl oxalate (6.8 ml, 0.05 mol), and dioxin (40-50 ml), sodium hydride (60% suspension in mineral oil) (2.0 g, 0.05 ml) was added with stirring and cooling, then, after 10 min, acetophenone (6.0 ml, 0.05 mol) or 1,3-diphenylpropane-1,3-dione (dibenzoylmethane) (11.2 g, 0.05 mol) and NaH (2.0 g, 0.05 mol) were added with cooling. Cold water (100 ml) and 15% hydrochloric acid (20 ml) were added over 3-5 h and the mixture was extracted with ethyl acetate (150-200 ml). The solvent was evaporated, the residue was triturated with diethyl ether (20 ml) and recrystallized from MeCN or AcOEt to give compound **1** or **2.** Benzoylpyruvic acid was additionally isolated by fractional crystallization from AcOEt. Yield 2.60 g (27%); mp 156-157°C (dec. AcOEt) [6].

Ethyl 2-hydroxy-3-oxo-5-phenyl-2,3-dihydrofuran-2-ylacetate (1). Yield 5.68 (43%); mp 117-118°C (from MeCN) (112-114°C [5]). Spectra are not reported in [5], so we list them here. IR spectrum, ν, cm^{-1}: 3128 ($C_{(2)}OH$), 1742 (CO_{ester}), 1690 ($C_{(3)}O$), 1660, 1637, 1588 ($C_{(4)}=C_{(5)}$, $C=C_{arom}$). ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 1.02 (3H, t, $J = 6.9$, $^{gem}J = 11.5$, CH_3 in COOEt), 2.94, 2.98 (2H, 2 d, $^{gem}J = 16.2$, CH_2 in CH_2COOEt), 3.93 (2H, q, $J = 6.9$, $^{gem}J = 10.7$, CH_2 in COOEt); 6.38 (1H, s, $C_{(4)}H$); 7.56-8.08 (5H, m, C_6H_5); 7.58 (1H, s, $C_{(2)}OH$). Found, %: C 64.38, H 5.21. $C_{14}H_{14}O_5$. Calculated, %: C 64.12, H 5.38.

Ethyl 4-benzoyl-2-hydroxy-3-oxo-5-phenyl-2,3-dihydrofuran-2-ylacetate (2). Yield 11.50 g (63%); mp 124-125°C (from AcOEt). IR spectrum, ν, cm^{-1}: 3120 ($C_{(2)}OH$), 1736 (CO_{ester}), 1708 ($C_{(3)}O$), 1665 ($Ph\underline{CO}$), 1655, 1630, 1575 ($C_{(4)}=C_{(5)}$, $C=C_{arom}$). ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 1.05 (3H, t, $J = 6.9$, $^{gem}J = 11.5$, CH_3 in COOEt); 3.16, 3.28 (2H, 2 d, $^{gem}J = 17.4$, CH_2 in CH_2COOEt); 3.91 (2H, q, $J = 6.9$, $^{gem}J = 10.7$, CH_2 in COOEt); 7.25-7.90 (10H, m, $2C_6H_5$); 8.36 (1H, s, $C_{(2)}OH$). ^{13}C NMR spectrum, δ, ppm: 13.5 ($COOCH_2\underline{C}H_3$); 40.7 ($\underline{C}H_2COOEt$); 59.6 ($COO\underline{C}H_2CH_3$); 102.4 ($C_{(3)}$); 114.3 ($C_{(4)}$); 128.7, 128.8, 129.6, 133.9 ($\underline{C}_6H_5$); 130.4, 132.4, 133.6, 137.6 ($\underline{C}_6H_5$); 168.8 ($\underline{C}OOEt$); 184.3 ($C_{(5)}$), 190.2 ($C_6H_5\underline{C}O$); 195.8 ($C_{(3)}O$). Found, %: C 68.49, H 4.73. $C_{21}H_{18}O_6$. Calculated, %: C 68.85; H. 4.95.

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