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LETTERS TO THE EDITOR

A NEW METHOD FOR THE SYNTHESIS OF $\Delta^{\alpha,\beta}$-BUTENOLIDES. EFFECTIVE SYNTHESIS OF 3-(6-CARBOMETHOXYHEXYL)-5-METHYLFURAN-2(5H)-ONE – A SYNTHON FOR 10-OXAPROSTANOIDS

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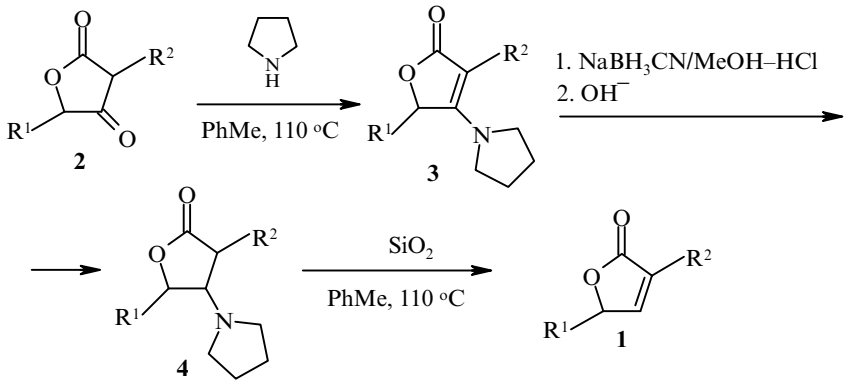
The development of effective methods for the synthesis of 2(5H)-furanones ($\Delta^{\alpha,\beta}$-butenolides) is of great practical value. $\Delta^{\alpha,\beta}$-Butenolides are structural components of a series of natural compounds such as acetogenines, muconolactones, etc. [1-4]. 2(5H)-Furanones are suitable intermediates in the synthesis of natural products and their analogs, which include γ-butyrolactone rings in their structures, among which are the biologically active heteroanalogs of prostaglandins, the 10-oxaprostanoids [5, 6].

During an investigation of the synthesis based on tetronic acids we have developed an effective method for the synthesis of 3-(6-carbomethoxyhexyl)-5-methylfuran-2(5H)-one (**1a**), a synthon for 11-desoxy-11-methyl-10-oxaprostanoids, containing the natural α-chain of prostaglandin. The proposed route for the synthesis of 2(5H)-furanones is based on the selective reduction of enamines **3** prepared from 3-alkyltetronic acids **2**. It is a new method for the preparation of 3-alkyl- and 3,5-dialkyl-2(5H)-furanones, including enantiomerically pure products, from the corresponding 3-alkyl- and 3,5-dialkyltetronic acids.



2 **3** **4** **1**

1a R^1 = Me, R^2 = $(CH_2)_6CO_2Me$

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Enamino lactone **3**, obtained in yields of 80-90% from the corresponding tetronic acid **2** by reacting with 1.2 equiv. of pyrrolidine, was reduced with sodium cyanoborohydride in methanolic HCl. We found that amino lactone **4**, formed as a result of reduction, when purified on a silica gel column underwent partial retro-Michael elimination of pyrrolidine to give 2(5H)-furanone **1**. If the mixture of reduction products, without purification, was boiled in toluene in the presence of silica gel the required 2(5H)-furanone **1** was formed in 55-75% yield (based on **3**).

3-(6-Carbomethoxyhexyl)-5-methyl-4-N-pyrrolidinofuran-2(5H)-one (3). Pyrrolidine (1.2 equiv.) was added with stirring to a suspension of tetronic acid **2** (1 mmol) in toluene (the starting acid **2** was synthesized from Meldrum's acid by a modification of a known method [7]). The obtained pyrrolidine salt of the β-dicarbonyl compound was boiled with a Dean–Stark trap for 5-6 h. The reaction mixture was filtered, toluene was evaporated and, after column chromatography of the reaction mixture, enamine **3** was isolated in 90% yield. IR spectrum, ν, cm^{-1} (film): 1640, 1745, 2940. ^1H NMR spectrum ($CDCl_3$), δ, ppm: 1.36 (6H, m); 1.48 (3H, d, 5-Me); 1.64 (2H, m, CH_2); 1.92 (4H, m, CH_2); 2.32 (4H, t, CH_2); 3.50 (4H, m, $N(CH_2)_2$); 3.67 (3H, s, OMe); 4.80 (1H, q, HCMe). Found, %: C 66.12; H 8.81; N 4.54. $C_{17}H_{27}NO_4$. Calculated, %: C 65.99; H 8.80; N 4.53.

3-(6-Carbomethoxyhexyl)-5-methylfuran-2(5H)-one (1). Dry $NaBH_3CN$ (2 equiv.) and 6 M solution of hydrogen chloride in MeOH (an arbitrary amount to maintain the acid medium) was added in portions to a solution of compound **3** (1 mmol) in a small quantity of methanol. The mixture was stirred until the starting enamino lactone had disappeared (monitored by TLC) and, after evaporation of methanol, careful basification, and extraction with ether, the separated diastereomeric mixture of aminolactone **4** was boiled in toluene in the presence of silica gel (2 g) without purification for 6-12 h until it was completely converted to compound **3** (monitored by TLC). After normal workup and column chromatography furanone **1a** was obtained in 55% yield. IR spectrum, ν, cm^{-1} (film): 1660, 1745-1760, 2940. ^1H NMR spectrum ($CDCl_3$), δ, ppm, *J*, Hz: 1.41 (3H, d, *J* = 7.0, Me); 1.59, 2.30 (8H, m, CH_2); 3.66 (3H, s, OMe); 5.00 (1H, q, *J* = 7.0, HCMe); 7.11 (1H, m, HC=). Found, %: C 65.14; H 8.37; M^+ 240. $C_{13}H_{20}O_4$. Calculated, %: C 64.98; H 8.39; M 240.

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