Polish J. Chem., **77**, 369–371 (2003) **COMMUNICATION**

Synthesis of 1-(2,5-Dimethoxy-2,5-dihydrofuran-2-yl)ethanol from 2-Acetylfuran

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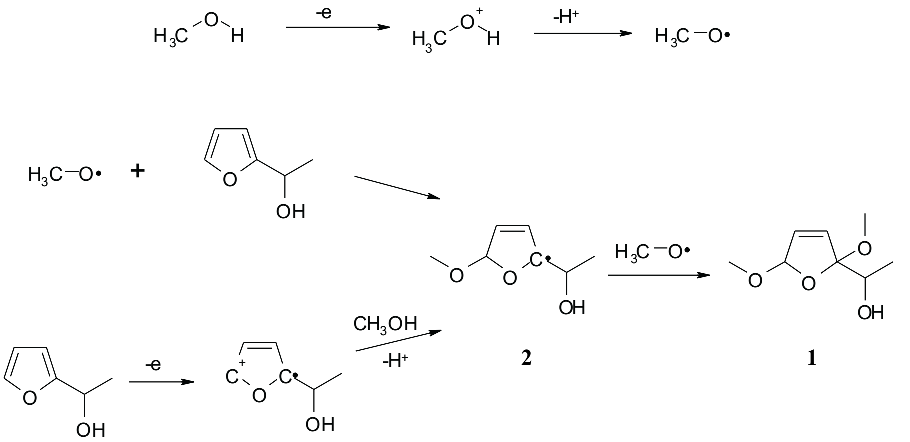
1-(2,5-Dimethoxy-2,5-dihydrofuran-2-yl)ethanol (**1**) is used as a starting material in the synthesis of numerous natural products such as carbohydrates, macrolides, pheromones and alkaloids [1,2]. Depending on absolute (R) or (S) configuration of the stereogenic centre at C-1, deoxyaminosugars of the D- or L-series respectively (*e.g.* daunosamine, ristosamine) [3] can be prepared from **1**. Diastereoselective resolution of **1** for mixtures of (1R)- and (1S)-diastereoisomers is possible by enzymatic acylation [4]. According to literature, **1** has been previously synthesized from pure 1-(furan-2-yl)ethanol either by an one-pot two step chemical method [5] – bromination (Br_2, MeOH, –40°C), then methoxylation (MeOH, NH_3, pH 8, –40°C to RT), or by an electrochemical methoxylation (MeOH, NH_4Br, Pt-electrode) [6–9]. The first method requires a stoichiometric quantity of bromine and gives stoichiometric amount of ammonium bromide as side product, what is a serious drawback, especially for multigram scale preparations. The electrochemical process [6–9] was carried out under acidic conditions (NH_4Br) on platinum electrode starting from pure 1-(furan-2-yl)ethanol. It is noteworthy that alcohol is much less stable than ketone and much more expensive. Because reduction is usually performed in methanol, we decided to reduce 2-acetylfuran to alcohol and to carry out the electrolysis of the whole mixture without 1-(furan-2-yl)ethanol isolation.

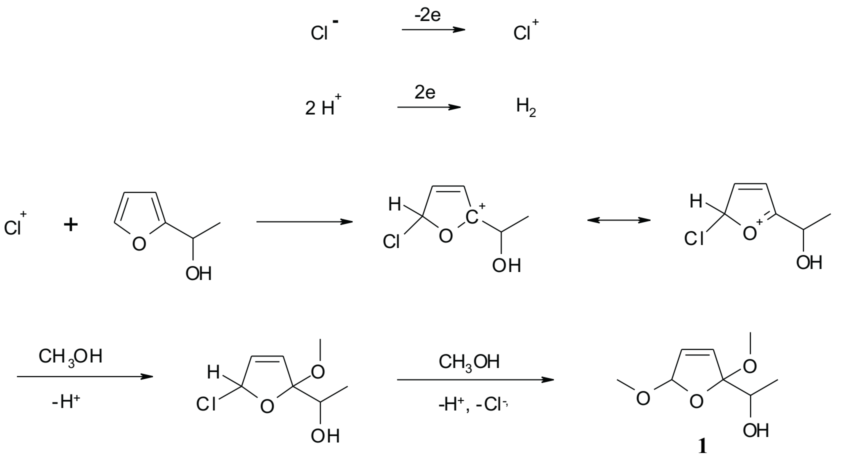
Herein we report a convenient synthetic route to **1** directly from 2-acetylfuran. Starting ketone (0.1 M) in methanol (20 mL) was reduced with $NaBH_4$ [10] at 0–5°C to 1-(2-furyl)ethanol and the whole mixture was subjected to electrolysis without isolation of alcohol. The electrolyser without diaphragme was charged with reaction mixture (pH 10–11) directly or after pH lowering to 8 (addition of 36% aq. HCl, precipitate filtration and washing with MeOH), and diluted with methanol to 100 mL. Methoxylation process (carbon electrodes, distance 5 mm, current density 3 A/dm^2, temp. –10°C, magnetic stirring) was continued up to delivery electric charge of 2.1 F/mol (100% starting alcohol conversion by GC). Presumed mechanism of methoxylation process is shown in Scheme 1.

Scheme 1



Transient radical **2** possibly arises in electrode process directly from 1-(furan-2-yl)ethanol or as a result of reaction between alcohol and methoxyl radical formed in anodic process. In solutions of pH 8 attained by addition of hydrochloric acid another mechanism can operate (Scheme 2). This hypothesis is confirmed by the observation that after delivery of 1 F/mol electric charge, the quantity of product **1** is two times larger for electrolysis at pH 8 than for electrolysis at pH 10–11. However, after supplying 2.1 F/mol the quantities of **1** are similar, what indicates that the increase in radical **2** concentration retards the anodic process of Cl^+ formation and the mechanism shown in Scheme 1 is predominating. Nevertheless the pH of the range investigated does not affect the product yield, but the workup procedure is less troublesome for solutions of lower pH, because an emulsion has not been formed during the extraction step.

Scheme 2



Compound **1** can be isolated from the mixture by a careful distillation under reduced pressure. It is thermally stable to 100℃ – after 2 h heating decomposition products have not been found, however, isomerization occurs, because the diastereoisomers ratio has been changed (GC-CARLO ERBA Instruments: column: RTx-1, 30 m×0.32 mm, 0.25μm, temp.: 50°÷250℃, 4°/min., carrier gas: N_2). When heating was continued for 2 h at 130℃, thermal decomposition of 65% of **1** to 2-acetylfuran (26%) and some other lower molecular weight products (39%) have been observed (GC;GC/MS-FISONS Instruments, GC 8000, detector MD 800, temp. 60°÷250°C, 4°/min., carrier gas: He, EI = 70 eV). From the mixture after methoxylation 75% of methanol was evaporated and the residue was extracted continuously with 100 mL of boiling dichloromethane. When methoxylation was carried out at pH 10–11, the decreasing of pH to 7.5–8 before extraction by addition of concentrated hydrochloric acid was necessary. After solvent evaporation the residue was distilled under reduced pressure with temperature control in distillation flask (below 130°C). The product was collected at b.p. 64–66°C/0.3 Tr (n_D^{20} = 1.4520). Usually 10–20% of **1** has been recovered from freezing condenser cooled with a dry ice – methanol bath. Overall yield of 1-(2,5-dimethoxy-2,5-dihydrofuran-2-yl)ethanol for two steps (reduction, methoxylation) was 55–65%. The scaling-up procedure to 1 mole of 2-acetylfuran resulted in *ca.* 5% higher overall yield. Moreover, the advantage of our procedure is the full recycling of solvents (methanol and dichloromethane evaporated from mixtures were reused in several subsequent preparations) and the absence of any waste side-products. The method is in align with current trends for "green solutions " of synthetic problems [11].

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