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2,5-Dimethoxy-2,5-dihydrofuran and vinyl ethers in the synthesis of functionalised 2-alkylfurans

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Abstract—2,5-Dimethoxy-2,5-dihydrofuran reacts, in the presence of a catalytic amount of $MgBr_2{\cdot}Et_2O$ with the appropriate vinyl ether, to give functionalised 2-alkylfurans with good yield and mild reaction conditions, this represents a useful synthetic approach to 2-(2-furo)tetrahydro -furanic or -pyranic moieties. The reaction fails on using deactivated or α-substituted vinyl ethers. © 2001 Elsevier Science Ltd. All rights reserved.

2,5-Dimethoxy-2,5-dihydrofuran (**1**) represents a useful C_4 polyfunctionalized building block for organic reactions.[1] Our recent studies[2] in the synthesis of furofuranic structures[2c] gave evidence of the chemical reactivity of this allylic acetal. The rigidity of the unsaturated ring and the absence of stabilising anomeric effects present in its saturated 2,5-dimethoxytetrahydrofuran analogues are responsible for this reactivity.[3]

The reaction of **1** with several Lewis acids and vinyl ethers gave either no reaction (Lewis acid = $ZnCl_2$, $ZnBr_2$, $MgCl_2$, $CuBr{\cdot}Me_2S$) or polymerisation (Lewis acid = $AlCl_3$, $TiCl_4$, $SnCl_4$), in Et_2O or CH_2Cl_2 as solvents. However, an equimolecular amount of **1** and ethyl vinyl ether (**2a**) in the presence of a catalytic amount of $MgBr_2{\cdot}Et_2O$ in diethyl ether at room temperature gave unexpectedly after a few minutes, the 2-furylacetaldehyde diethyl acetal (**3a**) in 50% overall yield.

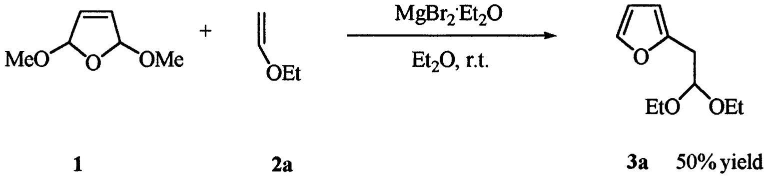
The reaction described in Scheme 1, represents a formal condensation between an acetal and the ethyl vinyl ether,[4] followed by aromatization.

The results obtained with several vinyl ethers characterised by different steric and electronic properties are collected in Table 1.

The reaction is independent of the configuration of the double bond (see Table 1, runs 2, 3, 8 and 10), but depends strictly on the steric hindrance at C_1 of the vinyl ether (see Table 1, run 9). Deactivated vinyl ethers are not reactive (see Table 1, runs 5, 6 and 7). The structure of the acetal obtained (symmetric or nonsymmetric) is dependent on the number of the ethoxy groups present in the reaction medium.[9] Cyclic acetals never give ring-opened products.

The reaction may proceed through the concerted mechanism shown in Scheme 2 in accordance with the reactivity of the intermediate complex **4** (Scheme 2) and the data reported in Table 1.

In fact, the instability of the non planar carbenium ion **6**[10] and the result showed in Table 1 (run 9) agree with the participation of the cyclic intermediate **7** (Fig. 1),



Scheme 1.

Keywords: vinyl ethers; allyl acetals; aldol condensation; Lewis acids.

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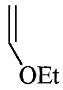
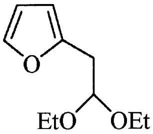
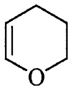
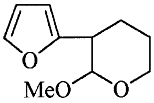
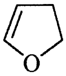
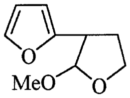
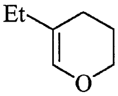
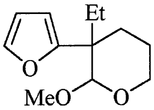
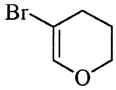
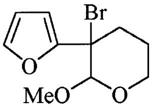
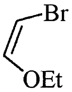
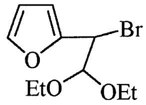
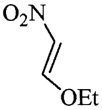
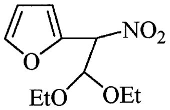
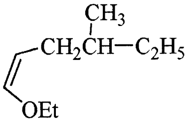
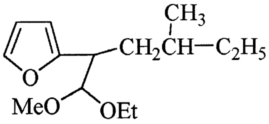
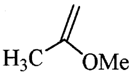
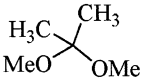
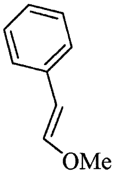
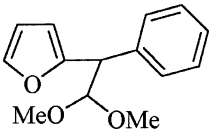
Table 1. Reaction of **1** and vinyl ethers, in the presence of a catalytic amount of magnesium bromide etherate[a]

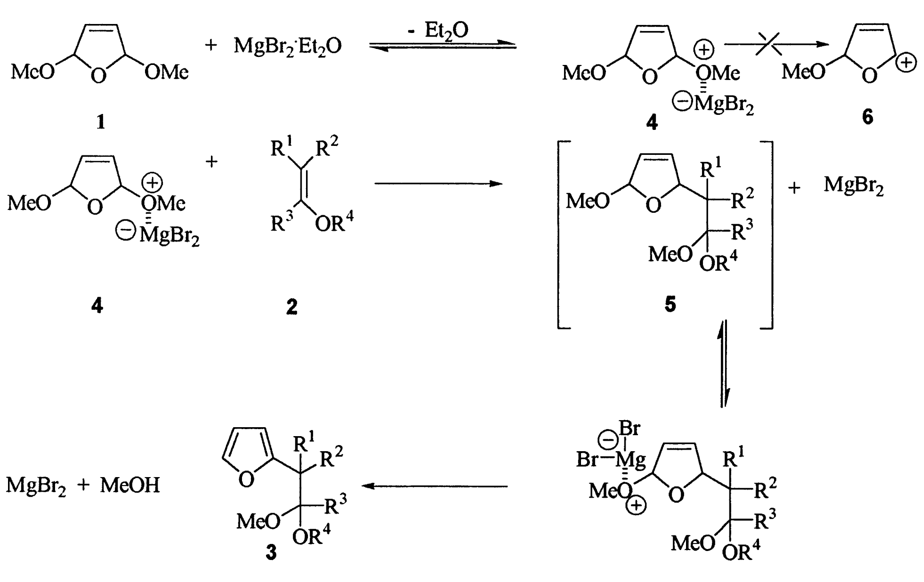
Run	*Vinyl Ether (2)*	*Product (3)*	*Reaction time*[b]	*1/2*	*Yield*[c]
1			15 min.	2	90%
2			15 min.	1,5	70%[d]
3			15 min.	1,5	75%[d]
4[e]			30 min.	1,5	65%[d]
5[f]			10 h.	1	-
6[g]			10 h.	1	-
7[h]			10 h.	1	-
8[i]			30 min.	1	80%[d]
9			10 h.	1	-
10[l]			1 h.	1	50%

[a] The ^1H and ^{13}C NMR, FT-IR and mass-spectroscopic analyses were in accordance with the proposed structures. [b] The reaction was stopped when **1** was completely reacted (g.c. analysis). [c] The yields were based on the product recovered. [d] Mixture of diastereomers. [e] The vinyl ether was prepared in quantitative yield, starting from the corresponding bromide and EtMgBr in anhydrous THF in the presence of a catalytic amount of Ni(diphenylphosphinoethane)dichloride [Ni(dppe)Cl_2]. [f] The vinyl ether was prepared via our procedure.[5] [g] The *cis* vinyl ether was prepared by the procedure of Lou.[6] [h] The *trans* vinyl ether was prepared by the procedure of Kogan.[7] [i] The *cis* vinyl ether was prepared starting from the *cis* 2-bromovinyl ethyl ether employing the same experimental procedure reported in note (e). [l] The *cis* vinyl ether was prepared from 2-phenylacetaldehyde dimethyl acetal via the Miginiac procedure.[8]

that appears sterically forbidden for 2-methoxypropene as estimated by HyperChem© Program (PC version), at room temperature, by using the molecular mechanics force field (MM+) model.[10]

In a typical run, the vinyl ether **2** (0.01 mol), dissolved in 30 ml of anhydrous diethyl ether, was dropped slowly into an ethereal solution (100 ml) of **1** (Aldrich©) (see Table 1), containing 200 mg of $MgBr_2{\cdot}Et_2O$ (Aldrich©) at room temperature. After the time required (see Table 1), the volatile compounds were eliminated under reduced pressure and the brown oil so obtained was dissolved in anhydrous benzene. After filtration of the solution, the solvent was evaporated under reduced pressure giving chemically pure **3**.

The reaction described herein allows us to obtain, in a single step and with good yields, 2-furylacetaldehyde



Scheme 2.

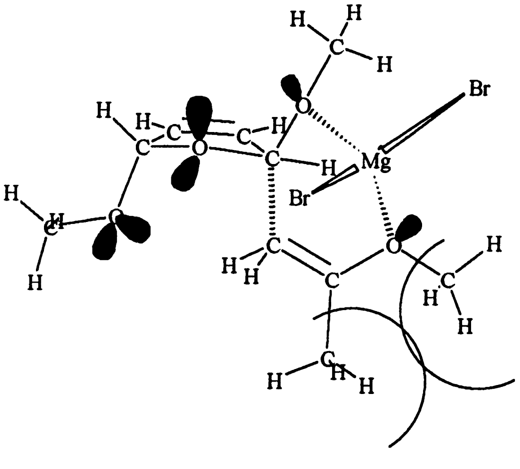


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Figure 1.

acetals, 2-(2-furo)tetrahydrofuranic or 2-(2-furo)tetrahydropyranic structures of interest in the organic chemistry field.

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5. Bromine in CH_2Cl_2 was added dropwise to an equimolecular amount of vinyl ether at −78°C. A mixture of Et_3N (2 molar equivalents) in CH_2Cl_2 were added to the stirred solution at room temperature and after the removal of the solvent, pentane was added and the solution filtered off. The chemically pure 2-bromodihydro-2*H*-pyran was obtained, after distillation (80°C/0.02 mmHg), in 85% overall yield.
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