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Synthesis of 2-Furylcarbinol Derivatives by an Acid-Catalysed Rearrangement of 2,5-Dimethoxy-2,5-Dihydrofurans

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Abstract 2,5-Dimethoxy-2,5-dihydrofurans **1** undergo an acid-catalysed rearrangement to 2-furylcarbinol derivatives **2** The reaction shows to be highly regioselective The diene **3** is found to be the key-intermediate, and its formation can be utilized for the one-pot preparation of 2-methoxy-1,6-dioxaspiro[4 4]non-3-en **5**

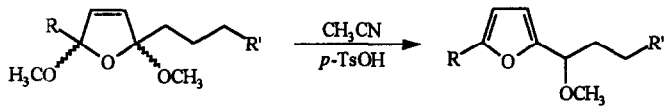
2,5-Dialkoxy-2,5-dihydrofurans have gained remarkable attention in synthetic organic chemistry during the past decade [1] They can be considered as synthetic equivalent of the cyclic acetal of malohaldehyde and have found a wide use for syntheses, consisting of intermolecular or intramolecular condensations, leading to pyridazines, tropinones, pyridinols, hexenuloses and benzenoid compounds [2] In addition, several authors have shown their utility in the cyclopent-2-enone synthesis, as precursor of *cis*-enedicarbonyl compounds [3,1b]

However, their chemical reactivity has been not much exploited up to now. As a part of our continuing interest in the reactivity of 2,5-dialkoxy-2,5-dihydrofurans,[4] we report a new and original application of 2,5-dimethoxy-2,5-dihydrofurans **1** as valuable starting materials for a facile and convenient synthesis of functionalised 2-furylcarbinol derivatives **2** 2-Furylcarbinols are key intermediates in organic synthesis for many purposes, especially in cyclopentenone and carbohydrate chemistry [2b,5] They have been hitherto prepared by condensation of 2-furyllithium with carbonyl compounds or by addition of a Grignard reagent to 2-formylfuran.[6]

Both methods are usually ineffective for a preparation of 2-furylcarbinols bearing additional functional groups The lack of more effective procedures caused these compounds to be sparely employed, in spite of their importance as intermediates

We have found that **1**, by treatment in acetonitrile and *p*-TsOH as catalyst at 0°C for 24h, underwent a rearrangement directly to 2-furylcarbinol derivatives **2** in good yields

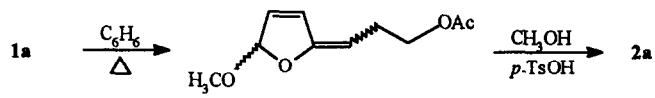
Acid-sensitive groups, such as acetoxy groups, were stable under the reaction conditions Then, the rearrangement showed a good regioselectivity, being the compound **1b** converted only into **2b** in 93% yield



1 2

a R=H, R'=OAc
b R=CH3; R'=OAc
c R=H, R'=C9H19

The unusual outcome of this reaction can tentatively be ascribed to the capability of the starting material to undergo an acid-catalysed elimination of methanol, giving rise to the formation of a reactive diene intermediate

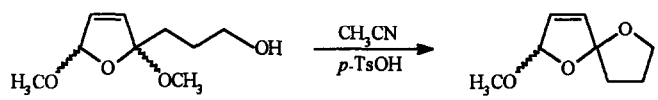


3

The compound **3**, obtained by heating in benzene, was quantitatively and rapidly converted into **2a** by reaction with methanol and *p*-TsOH as catalyst.[7]

The crucial role played by the formation of a diene intermediate, such as **3**, was witnessed by a parallel experiment which was carried out using the dihydrofuran **4**.

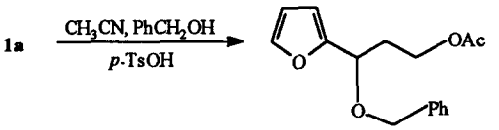
In this case, the reaction led to the formation of 2-methoxy-1,6-dioxaspiro[4 4]non-3-ene **5**, as a 1:1 mixture of stereoisomers in 90% yield



4 5

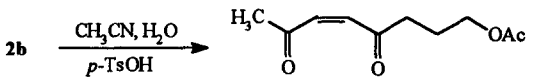
With the aim of exploiting the synthetic utility of this reaction, we have investigated the reactivity of **1** in presence of an alcohol, such as benzylic alcohol

Interestingly, the reaction of **1a**, effected in presence of a large excess of benzylic alcohol, afforded the corresponding benzyloxy derivative **6**, in 70% yield



6

It is worth noting that the reaction of **2b** in acetonitrile, *p*-TsOH and water as nucleophile gave only the corresponding *cis*-enedicarbonyl compound **7** in 90% yield [8]



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In conclusion, the success of this procedure broadens the field of application of 2-furylcarbinols. Then, the very simple conditions required could represent a substantial improvement of other previously described methods [6]

General Procedure for the synthesis of compounds 2. 2,5-dimethoxy-2,5-dihydro-2-(3-acetoxypropyl)-furan **1a** (230 mg, 1mmol), prepared following the published procedures,[9] was dissolved in 10 ml of acetonitrile at rt, then, 5 mg of *p*-TsOH were added under stirred. After 20 min , the reaction mixture was poured into 50 ml of diethyl ether and washed with aq sat NaCl until neutrality The crude product, after evaporation of the solvent, was chromathographed on SiO_2. Eluition with 4:1 *n*-hexane-diethyl ether gave **2a**, as oil (0 85 mmol, 85%) **2a** ^{1}H-NMR ($CDCl_3$, δ). 2 01 (s, 3H), 2 0-2 3 (m, 2H), 3 23 (s, 3H), 4 0-4 2 (m, 2H), 4.27 (dd, 1H, J_1=7 9Hz, J_2=6.1Hz), 6 27 (dd, 1H, J_1=3 2Hz, J_2=0 8Hz), 6 32 (dd, 1H, J1=3 2Hz, J2=1 8Hz), 7.38 (dd, 1H, J_1=1.8Hz, J_2=0 8Hz); IR ($CHCl_3$, cm^{-1}) 1735, MS· m/z 198

General Procedure for the synthesis of 2-methoxy-1,6-dioxaspiro[4.4]non-3-ene (5). The reaction was carried out as above, starting from 100 mg of 2,5-dimethoxy-2,5-dihydro-2-(3-hydroxypropyl)-furan **4** After chromathography, 90 mg of pure **5** were obteined as oil (90%) ^{1}H-NMR ($CDCl_3$, δ) 1 9-2 3 (m, 4H), 3 34 (s, 3H), 3 8-4 0 (m, 1H), 4 0-4 2 (m, 1H), 5 59 (s, 1H), 5.95 (d, 1H, J=6.0Hz), 5.99 (d, 1H, J=6.0Hz); MS: m/z 156.

General Procedure for the synthesis of 2-(1-benzyloxy-3-acetoxypropyl)-5-methylfuran (6). 100 Mg of **2a** were dissolved in 4 ml of acetonitrile, then 1 8 mol of $PhCH_2OH$ and 2 mg of *p*-TsOH were added at 0°C under stirring The cooling bath was removed, and the reaction mixture was stirred for 24h at rt. After the usual

work-up and chromatography, 85 mg of pure **6** were obtained as oil (70%) ^{1}H-NMR ($CDCl_3$, δ) 1 95 (s, 3H), 2 0-2 3 (m, 2H), 4 0-4 2 (m, 2H), 4 31 (d, 1H, J=11 9Hz), 4 44 (dd, 1H, J_1=8.4Hz, J_2=5 5Hz), 4 52 (d, 1H, J=11 9Hz), 6 29 (dd, 1H, J1=3 2Hz, J_2=0 8Hz), 6 35 (dd, 1H, J_1=3 2Hz, J_2=1 8Hz), 7 2-7 4 (m, 5H), 7 41 (dd, 1H, J1=1 8Hz, J_2=0 8Hz), MS m/z 274

Reference and Notes

1. (a) Dean, F M ; *Adv. Heterocyclic Chemistry* **1982**, *30*, 167, *31*, 237; (b) Lipshutz, B M ; *Chem.Rev.* **1986**, *86*, 795
2. (b) Elming *Advances in Organic Chemistry*, *2*, Interscience, New York, **1960**, p 67; (b) Holder, N.L., *Chem. Rev.* **1982**, *82*, 287
3. (a) Ellison, R A , *Synthesis* **1973**, 397, (b) Kametani, T , Fukumoto, K , *Heterocycles* **1978**, *10*, 498, (c) Jurczack, J , Pikul, S , *Tetrahedron Letters* **1985**, *26*, 3039
4. Cecchini, C., De Mico, A., D'Onofrio, F , Piancatelli, G , Tofani, D , *Tetrahedron Letters* **1993**, in press.
5. (a) Denmark, S E , *Comprehensive Organic Synthesis*, *5*, Pergamon Press, Oxford, **1991**, pp.771-772; (b) Ley, S V , Madin, A.; *ibid.*, *7*, pp 260-263
6. Piancatelli, G , *Heterocycles* **1982**, *19*, 1735 and the references therein
7. Data of **3**. ^{1}H-NMR ($CDCl_3$, δ) 2.05 (s, 3H), 2 51 (dt, 2H, J_1=J_2=7 0Hz), 3 43 (s, 3H), 4 09 (t, 2H, J=7 0Hz), 4 49 (t, 1H, J=7.0Hz), 6 00 (m, 2H), 6 30 (dd, 1H, J_1=7.0Hz, J_2=1.3Hz); IR ($CHCl_3$, cm^{-1}). 1738, 1676, MS m/z 198
8. Data of 7 ^{1}H-NMR ($CDCl_3$, δ) 1 8-2 2 (m, 2H), 2 00 (s, 3H), 2 26 (s, 3H), 2.62 (t, 2H, J=7.0Hz), 4.08 (t, 2H, J=7 0Hz), 6 28 (s, 2H), IR ($CHCl_3$, cm^{-1}) 1730, 1698, 1610; MS: m/z 198
9. Yur'ev, Y K , Zefirov, N S , Shteinman, A. A , *Zh. Obshch. Khim.* **1963**, *33*, 1150; [*C.A.* **1963**, *59*, 11395c]

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