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$Mo(CO)_6$-Catalyzed oxidation of furan derivatives to *E*- and *Z*-enediones by cumyl hydroperoxide

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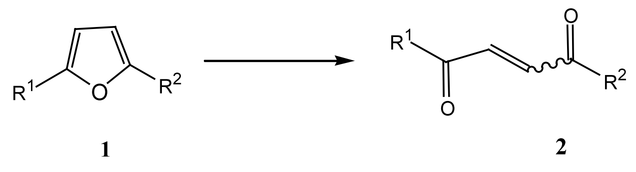
Abstract—*E*- and *Z*-Enediones are easily accessible by controlled oxidation of 2,5-disubstituted furans with $Mo(CO)_6$/cumyl hydroperoxide system. The use of *t*-butyl hydroperoxide, as oxygen donor, leads to the formation of 2*H*-pyran-3(6*H*)-one derivatives. © 2003 Elsevier Science Ltd. All rights reserved.

Furan derivatives represent important synthetic substrates because of their latent enedicarbonyl functionality that can be easily disclosed by a variety of oxidative photochemical,[1,2] electrochemical[3] and chemical methodologies. In particular, as regards the chemical conversion of furans **1** into products **2** very satisfactory results have been obtained by using epoxidizing agents (*m*-chloroperbenzoic acid,[4] dioxirane,[5] magnesium monoperoxyphtalate,[6] methyltrioxorhenium/urea-hydrogen peroxide adduct[7]), metal oxidants (pyridinium chlorochromate,[8] cerium(IV) ammonium nitrate[9]), or by a two step sequence involving the previous conversion of **1** into the corresponding 2,5-dialkoxy-2,5-dihydrofurans, followed by controlled hydrolysis to **2** under acidic conditions.[10] Furthermore, it is noteworthy that **2** can be obtained in the desired *E* or *Z* C=C geometry by a careful choice of the reagents and/or the experimental conditions (Scheme 1).

The wide availability of procedures can be surely attributed to the important synthetic value of compounds **2**, used as key-intermediates in the preparation of several classes of compounds, as cyclopentenone derivatives[11,12] (rethrolones,[3] prostaglandins[13]), chiral polyfunctional open-chain systems,[14] variously substituted furans,[15] 3(2*H*)-furanones,[16] 2(3*H*)-furanones,[17] 2,5-dihydrofurans.[18]



Scheme 1.

Now, we wish to report a very simple procedure, based on the employment of $Mo(CO)_6$/cumyl hydroperoxide (CHP) system as mild oxidant of 2,5-dialkyl furans of type **1**, that allows to get alternatively *E*- or *Z*-enediones **2** in satisfactory yields (Scheme 2).

In fact, when the starting materials **1** were submitted to treatment with CHP (1 equiv.) in $CHCl_3$ solution under the conditions reported in Scheme 2 and Table 1 (entries a–d), the formation of *E*-**2** was found to take place in a satisfactory way.

Since all the previously reported procedures involving the use of epoxidizing agents afforded exclusively *Z*-enediones **2**, we supposed that, under the conditions of Proc. A, a ready *Z*→*E* isomerization could be promoted by the slightly acidic reaction medium. In fact, when the same experiments were performed in the presence of anhydrous Na_2CO_3 (1 equiv.), Proc. B, products **2** could be isolated as *Z* geometrical isomers (entries e–h, Table 1).

Furthermore, it has to be noted that when *t*-butyl hydroperoxide (TBHP) was used in substitution of CHP, very complex mixtures of products were obtained in consequence of the unexpected high reactivity of compounds **2** under the standard conditions. However, under more controlled conditions involving treatment

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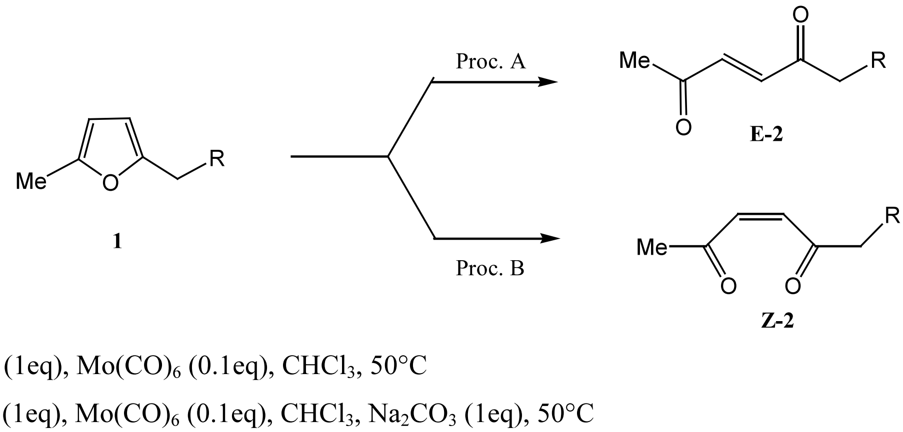


Scheme 2.

Table 1. Mo(CO)$_6$-catalyzed oxidation of 2,5-dialkyl furans **1** with CHP

Entry	R	Reac. time (h)	Procedure	Product	Yield (%)[a]
a	n-C_4H_9	20	A	*E*-**2a**	65
b	n-C_7H_{15}	16	A	*E*-**2b**	67
c	n-C_9H_{19}	20	A	*E*-**2c**	63
d	-H	24	A	*E*-**2d**	93
e	n-C_4H_9	20	B	*Z*-**2a**	64
f	n-C_7H_{15}	20	B	*Z*-**2b**	61
g	n-C_9H1_9	24	B	*Z*-**2c**	63
h	-H	12	B	*Z*-**2d**	53

[a] All the yields refer to isolated chromatographically pure compounds whose structures were confirmed by IR and ^{1}H NMR data and by comparison with authentic samples prepared through known procedures.[4,8]

with TBHP (1 equiv.), in CHCl$_3$ solution at 40°C, in the presence of a very reduced amount of Mo(CO)$_6$ (0.01 equiv.), the formation of *E*-**2** enediones was again found to occur in appreciable yields (Table 2) although incomplete conversion was required in order to minimize the formation of the additional reaction products **4** (Scheme 3).

It is noteworthy that, when 3 equiv. of TBHP were used in order to get the complete conversion of the starting material (entry d, Table 2) the corresponding products *E*-**2b** and **4b** were obtained in 45 and 55% yield, respectively.

A set of experiments has then allowed to disclose an unprecedented reactivity both of *Z*- and *E*-**2** and furthermore, to obtain useful information on the reaction pathway leading to compounds **4**. In fact, irrespective

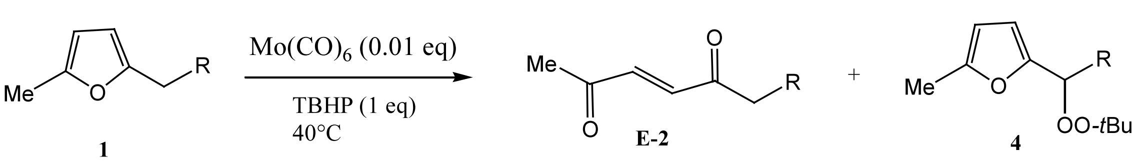
Table 2. Mo(CO)$_6$-catalyzed oxidation of dialkyl furans **1** with TBHP

Entry	R	Reac. time (h)	Conv. (%)	*E*-**2** Yield (%)[a]	**4** Yield(%)[b]
a	n-C_4H_9	24	80	52	10
b	n-C_7H_{15}	24	82	50	4
c	n-C_9H_{19}	32	83	52	10
d	n-C_7H_{15}	8	100[c]	45[b]	55[b]

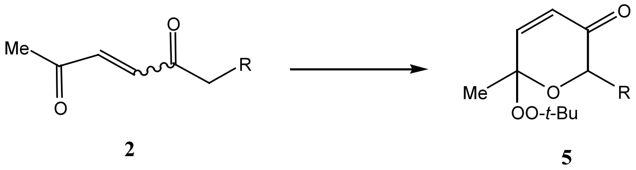
[a] All the yields refer to isolated chromatographically pure compounds whose structures were confirmed by IR and ^{1}H NMR data and by comparison with authentic samples obtained by previously reported procedures.[8,19]

[b] In this entry the yields were calculated by ^{1}H NMR analysis on the crude reaction mixture.

[c] In this entry 3 equiv. of TBHP were used.



Scheme 3.



Scheme 4.

Table 3. $Mo(CO)_6$-catalyzed oxidation of **2** to **5** with TBHP

Entry	Substrate	Reac. time (h)	Conversion (%)	**5** Yield (%)[a]
a	*Z*-**2b**	62	91	58
b	*E*-**2b**	60	88	57
c	*E*-**2c**	64	87	59
d	*E*-**2d**	64	90	63

[a] All the yields refer to isolated chromatographically pure compounds and are calculated on the starting materials. Structural determination is based on IR, ^1H and ^{13}C NMR and by comparison with authentic samples obtained by a previously reported procedure.[19] In all entries mixed peroxides of type **4** were obtained as less abundant products (8–10% yields).

of the C=C bond geometry, enediones **2** were smoothly converted into the peroxypyranone derivatives **5** under the usual oxidative conditions [TBHP (3 equiv.), $Mo(CO)_6$ (0.01 equiv.) in $CHCl_3$ solution at rt for 72 h] (Scheme 4, Table 3).

Although the mechanistic aspects have not been fully clarified, the involvement of intermediates **3b** and **4b** in the oxidative conversion of *Z*-**2b** (chosen as representative substrate) into **5b** has been supported by the achievement of the synthetic sequence reported in Scheme 5.

In conclusion, both *E*- and *Z*-enediones are readily accessible by a simple and convenient procedure and, furthermore, products **2** prove to be useful intermediates in the preparation of furan and 2*H*-pyran-3(6*H*)-one derivatives.

Typical procedure for the oxidation of 1 to enediones 2 by CHP

A mixture of **1** (2 mmol), $Mo(CO)_6$ (0.2 mmol), CHP (2 mmol), anhydrous Na_2CO_3 (2 mmol) (required for the synthesis of *Z*-**2**) $CHCl_3$ (4 ml) was stirred at 50°C for the time reported in Table 1. Then, a 0.1N aqueous solution of $Na_2S_2O_3$ (15 ml) was added and the mixture was stirred at rt for 1 h. The absence of unreacted hydroperoxide was established with acidified starch–iodide test paper, according to Sharpless' report.[20] Then, diethyl ether (50 ml) was added and the organic phase was washed with brine (3×10 ml) until neutrality. After drying over anhydrous Na_2SO_4, the solvent was removed under a reduced pressure and the resulting crude product **2** was purified by silica gel column chromatography by elution with *n*-hexane–diethyl ether mixtures.

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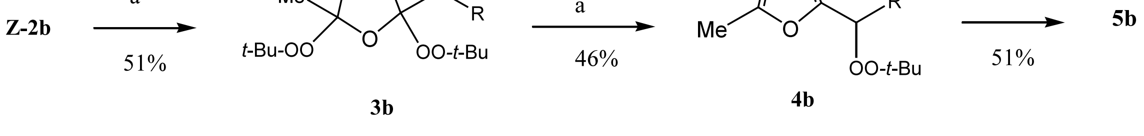

Scheme 5. *Reagents and conditions*: (a) TBHP (3 equiv.), $Mo(CO)_6$ (0.01 equiv.), $CHCl_3$, 24 h, rt.