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LIPOXYGENASE-CATALYZED DEHYDRATION OF FURYLHYDROPEROXIDES

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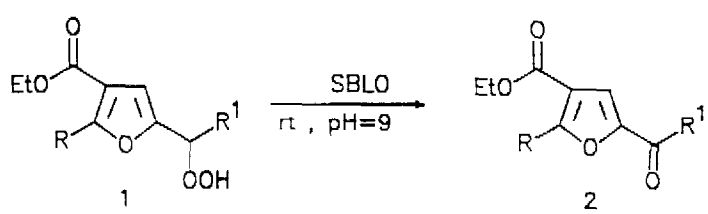
Abstract: *3-alkoxycarbonyl-5(1-hydroperoxyalkyl)-furans **1** are changed into the corresponding 5-acyl and 5-formyl derivatives **2** by a lipoxygenase-catalyzed process. The conversion shows to proceed in enantioselective way leading to chiral furylhydroperoxides and furylalcohols.*

Lypoxygenase plays a fundamental role in the enzymatic conversion of polyunsaturated fatty acids into physiologically important compounds, such as prostaglandins and leukotrienes[1] Nevertheless, in spite of the ever increasing importance of enzymes in organic synthesis, oxidative processes based on the employment of lipoxygenase have been only occasionally reported in the literature[2] and they usually involve lipid-like substances bearing one or more (Z,Z)-1,4-pentadienyl moieties.[3,4]

In the course of investigations on the reactivity of furylhydroperoxides, easily available by auto-oxidation of 5-alkylidene-4,5-dihydrofuran derivatives,[5] we have found that lipoxygenase shows a very good specificity of action on substrates of type 1

In fact, submitted to treatment with catalytic amounts of soybean lipoxygenase (SBLO) in buffer solution (pH=9) at room temperature, starting materials 1 undergo a Kornblum-DeLa Mare-type reaction leading in very satisfactory way to the corresponding 5-formyl- or 5-acylfuran derivatives **2**.



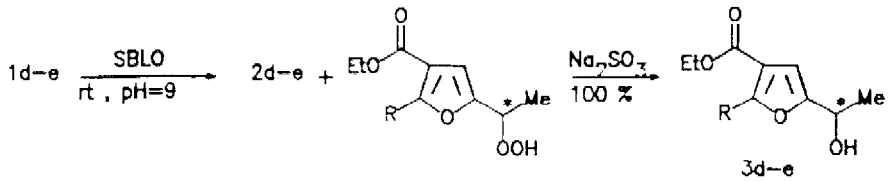
1 2

Table - Lipoxygenase-catalyzed formation of products 2

Entry	R	R^1	Product	React Time/h	Yield/%[a]	Recovered 1/%
a	-Me	-H	**2a**	2h	82	---
b	-Et	-H	**2b**	3h	88	---
c	-i-Pr	-H	**2c**	3h	86	---
d	-Me	-Me	**2d**	20h	56	42
e	-Et	-Me	**2e**	2h	51	34
f	-i-Pr	-Me	**2f**	48h	--	>98

[a] *All the yields refer to isolated chromatographically pure compounds and the assigned structures have been confirmed by IR, ^{1}H-NMR, MS data* [7]

It has to be noted that although the above procedure proves to be more efficient with primary hydroperoxides (entries a-c), the extension to secondary hydroperoxides has afforded interesting results. In particular, in this case the enzymatic conversion can be completely inhibited by steric effects (for ex., the presence of a branched side chain in 2 position of the furan ring of **2**, entry f) while it shows to proceed in enantioselective way in the remaining entries d and e. In fact starting materials **1**d-e,



recovered after the usual treatment and submitted to reduction with sodium thiosulfate, are quantitatively changed into chiral furylalcohols **3**d (R=Me, 44% e.e) and **3**e (R=Et, 35% e.e.).[8] The proposed procedure is of synthetic value since, besides representing one of the first applications of lipoxygenase with non lipid-like substrates, allows an easy approach to chiral building blocks in particular intermediates of type **3** have been widely used in the synthesis of important classes of natural products as carbohydrates, C-glycosides, manolides [9]

In a typical experimental procedure a mixture of **1**d, (0.5 mmol), commercial lipoxygenase (200 mg), 0.2 M borate buffer solution (200 ml) is stirred overnight at room temperature After the usual work-up the resulting crude product is purified by silica gel flash chromatography the elution with n-hexane-ethyl acetate mixtures affords pure **1** (0.021 mmol, 42%) and **2** (0 028 mmol, 56%). Then, **1** (0.021 mmol), dissolved in water (15 ml), is submitted to treatment with solid sodium thiosulfate (0.03 mmol) for 1h. After the usual procedure pure **3** is obtained in almost quantitative yield.

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7) For ex. **2**d; IR(1%,CCl_4)· 1720,1690 cm^{-1} H^1-NMR ($CDCl_3$) δ 7 40(s,1H), 4.28(q,2H, J=7Hz), 2.62 (s,3H), 2 42(s,3H), 1.33(t,3H, J=7Hz). MS(m/z). 196(M^+) **3**d, IR (1%,CCl_4): 3610-3500,1720,1610 cm^{-1} H^1-NMR ($CDCl_3$): δ 6 44(s,1H), 4 80(q,1H; J=7Hz), 4 24 (q,2H; J=7Hz), 2 52(s,3H), 2 20-1 80 (broad s, 1H), 1.49(d,3H, J=7Hz), 1.30 (t,3H, J=7Hz). MS(m/z). 198(M^+)

8) The enantiomeric excesses of alcohols 3 have been determined by ^{1}H-NMR analysis in the presence of Eu(hfc)$_3$

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