

ANODIC SYNTHESIS OF BUTENOLIDES FROM β -ETHYLENIC ESTERS DOUBLE CYCLIZATION IN THE PRESENCE OF OLEFINS

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Summary : Anodic oxidation of β -ethylenic esters yields butenolides **2**. In the presence of 1-phenyl-1-propene or α,β -disubstituted indenones a double cyclization takes place to yield more complex butenolides

INTRODUCTION

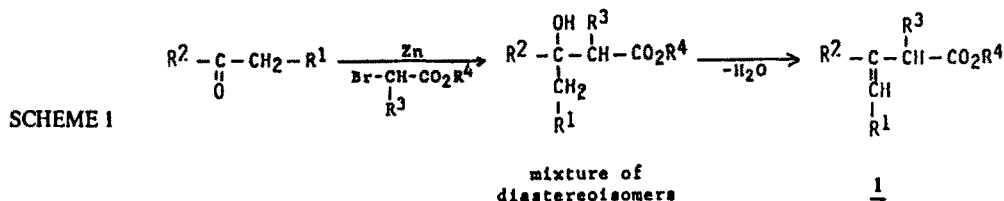
The anodic synthesis of $\Delta^{\alpha,\beta}$ butenolides (2(SH)-furanones) has been previously described by Torii's group¹⁻³. The method was based on oxidative decarboxylation of carboxylactones or oxidation of furoic acids.

The formation of the lactone ring can also be achieved by electrochemical oxidation of γ -ethylenic acids in acetonitrile or dichloromethane⁴. In methanol, competitive methoxylation of the side chain cannot be avoided⁵. A large number of chemical methods of synthesis of $\Delta^{\alpha,\beta}$ butenolides have also been described⁶⁻⁹.

An anodic one-step synthesis of butenolides has not been reported so far. In this paper we first describe the direct formation of $\Delta^{\alpha,\beta}$ butenolides from β,γ ethylenic esters. We also report on anodically induced [4+2] cycloadditions involving β -ethylenic esters and olefinic partners such as 1-phenyl-1-propene or derivatives of indenones.

RESULTS AND DISCUSSION

Unsaturated esters **1** were prepared by a classical sequence involving a Reformatsky reaction followed by dehydration of the resulting β -hydroxy esters. Mixtures of Z+E isomers **1** were used for electrolyses (Scheme 1, Table 1).



The anodic oxidation (see experimental) led to the formation of butenolides **2** in 20 to 83 % yield (Scheme 2, Table 2). The use of carefully dried $\text{Bu}_4\text{N}^+\text{BF}_4^-$ (0.2 molar) in methylene chloride clearly suppresses further reaction of the C-C double bond.

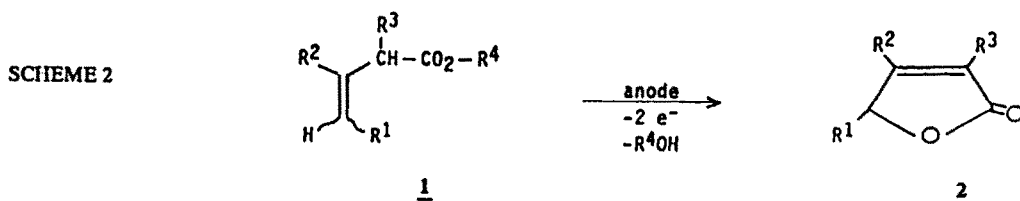
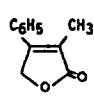
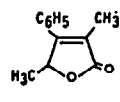
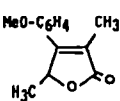
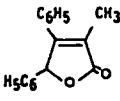


TABLE 1 - Physical constants of β ethylenic esters used as substrates in anodic formation of butenolides

$ \begin{array}{c} \text{R}^1-\text{CH}=\text{C} \begin{array}{l} \text{Ar} \\ \text{CH}-\text{CO}_2 \text{C}_2\text{H}_5 \\ \text{R}^3 \end{array} \\ \end{array} \quad 1 \quad \left(\begin{array}{l} \text{R}^2 = \text{Ar} \\ \text{R}^4 = \text{C}_2\text{H}_5 \end{array} \right) $						
	R ¹	R ³	Ar	+ E _p ^a (v)	I. R. cm ⁻¹	N. M. R. ppm/TMS
1a	H	CH ₃	C ₆ H ₅	1.75	$\nu_{\text{C}=\text{O}} = 1730$ $\nu_{\text{C}=\text{C}} = 1620$	1.13 (t, CH ₃), 1.37 (d, CH ₃) 3.63 (q, CH), 4.06 (q, CH ₂) 5.17 and 5.30 (2s, =CH ₂)
1b (E + Z)	CH ₃	CH ₃	C ₆ H ₅	1.46 1.59	$\nu_{\text{C}=\text{O}} = 1730$ $\nu_{\text{C}=\text{C}} = 1600$	1.23 (t, CH ₃), 1.26 (d, CH ₃) 1.5 and 1.8 (2d, CH ₃) 3.76 (q, CH), 4.05 (q, CH ₂) 5.66 (q, =CH)
1c (E + Z)	CH ₃	CH ₃	4 MeO-C ₆ H ₄ -	1.10 1.24	$\nu_{\text{C}=\text{O}} = 1730$ $\nu_{\text{C}=\text{C}} = 1600$	1.17 (t, CH ₃), 1.26 (d, CH ₃) 1.5 and 1.75 (2d, CH ₃) 3.73 (s, OCH ₃), 3.83 (q, CH) 4.03 (q, CH ₂), 5.6 (q, =CH)
1d	H	C ₂ H ₅	C ₆ H ₅	1.75	$\nu_{\text{C}=\text{O}} = 1730$ $\nu_{\text{C}=\text{C}} = 1620$	0.9 (t, CH ₃), 1.17 (t, CH ₃) 1.8 (m, CH ₂), 3.40 (t, CH) 4.10 (q, CH ₂), 5.25 and 5.35 (2s, =CH ₂)
1e (E + Z)	C ₆ H ₅	CH ₃	C ₆ H ₅	1.33	$\nu_{\text{C}=\text{O}} = 1720$ $\nu_{\text{C}=\text{C}} = 1590$	1.0-1.42 (m, 6H, 2 CH ₃) 3.43 (q, CH) 4.07 (q, CH ₂) 6.5 and 6.7 (2s, =CH, E + Z)

^a Potential of the corresponding anodic step measured versus a Ag/Ag⁺ 0.01 M reference-electrode

TABLE 2 - Results of anodic electrolyses for compound 1

ENTRY	E _{ox} ^a Total Electricity consumption	Main isolated electrolysis product	Isolat. Yield %	m.p. °C	I. R. cm ⁻¹	N. M. R. ppm/TMS
1a	+ 1.9 V 3 F.M ⁻¹	 2a	20	124	$\nu_{\text{C}=\text{O}} 1740$ $\nu_{\text{C}=\text{C}} 1645$	2.10 (t, CH ₃ , ⁵ J = 1.6 Hz) 5.00 (q, CH ₂ , ⁵ J = 1.6 Hz) 7.40 (s, 5H arom.)
1b (E + Z)	+ 1.8 V 2 F.M ⁻¹	 2b	70	68	$\nu_{\text{C}=\text{O}} 1750$ $\nu_{\text{C}=\text{C}} 1650$	1.37 (d, CH ₃), 2.03 (s, CH ₃) 5.30 (q, CH), 7.36 (5H arom.)
1c (E + Z)	+ 1.3 V 2 F.M ⁻¹	 2c	34	103	$\nu_{\text{C}=\text{O}} 1750$ $\nu_{\text{C}=\text{C}} 1650$	1.4 (d, CH ₃), 2.03 (s, CH ₃) 3.83 (s, OCH ₃), 5.23 (q, CH) 6.86 and 7.23 (4H arom.)
1e (E + Z)	+ 1.5 V 2 F.M ⁻¹	 2e	83	90	$\nu_{\text{C}=\text{O}} 1730$ $\nu_{\text{C}=\text{C}} 1630$	2.13 (d, CH ₃ , ⁵ J = 1.8 Hz) 6.18 (q, 1H, ⁵ J = 1.8 Hz) 7.23 and 7.30 (2s, 10H, Ar)

^a Working potential versus a Ag/Ag⁺ 0.01 M reference-electrode

When the anodic oxidation of **1a** and **1b** was effected in the presence of 1-phenyl-1-propene or 2,3-disubstituted indenones (**3**) in methylene chloride, two consecutive reactions took place in the electrolytic cell. A [4+2] cycloaddition leading to a new β -ethylenic ester **4** is followed by an oxidative cyclization yielding polycyclic butenolides **5** (Scheme 3, Table 3). Yields are rather low. The structure of **5c** was confirmed by X-ray diffraction analysis: we note that the lactonic ring is in endo position (Figure 1).

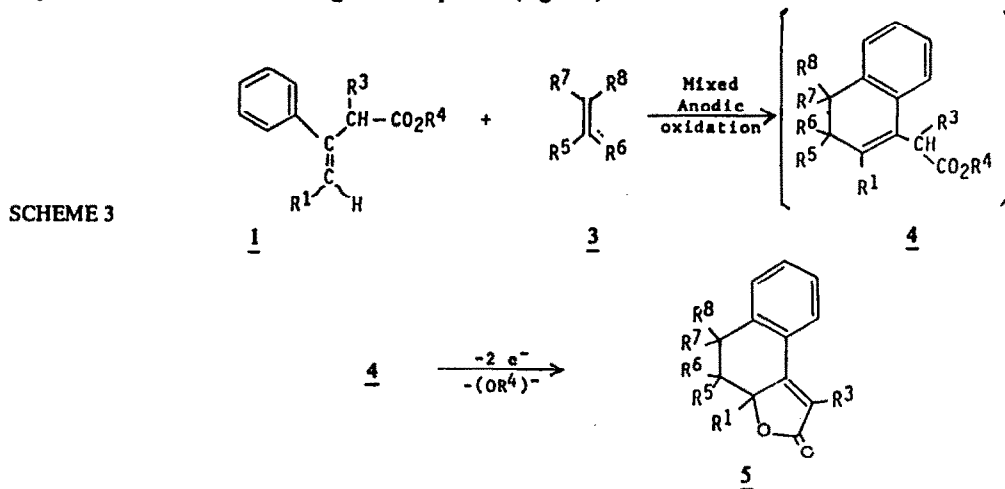


TABLE 3. Results of mixed electrolyses and concomitant cyclization

Mixed electrolysis of	$E_{ox}(V)$	Quantity of electricity	PRODUCED BUTENOLIDE	Yield %	m.p., °C	I.R. (in KBr) cm^{-1}	N.M.R. (in $CDCl_3$) ppm/TMS
1a + $C_6H_5-CH=CH-CH_3$ (E)	+ 1.5	2.3 F. \cdot M $^{-1}$	 5a *	16	165	$\nu_{C=O}$ 1740 $\nu_{C=C}$ 1645	1.14(d, CH_3), 2.08(m, CH^b) 2.24(d, CH_3 , $5J = 1.75$ Hz) 3.86(d, CH^a , $3J_{H^a, H^b} = 11$ Hz) 4.76(dq, HC , $3J_{HC, H^b} = 11.75$ Hz)
1a +	+ 1.6	2.5 F. \cdot M $^{-1}$	 5b	16	211	$\nu_{C=O}$ 1742 1712 $\nu_{C=C}$ 1645	1.52 (s, CH_3), 1.9 (s, CH_3) 2.08 (d, CH_3 , $5J = 1.7$ Hz) 5.1 (q, CH)
1a +	+ 1.6	2 F. \cdot M $^{-1}$	 5c **	23	262	$\nu_{C=O}$ 1740 1710 $\nu_{C=C}$ 1660	1.00 (s, CH_3), 2.09 (d, CH_3 , $5J = 1.7$ Hz) 5.11 (q, CH)
1d +	+ 1.6	3 F. \cdot M $^{-1}$	 5d	16	256	$\nu_{C=O}$ 1740 1705 $\nu_{C=C}$ 1660	1.02 (s, CH_3), 1.2 (t, CH_3) 2.6 (q, CH_2), 5.12 (s, CH)

* Structure established from 250 MHz 1H NMR measurements

** Structure determined by means of X Ray analysis.

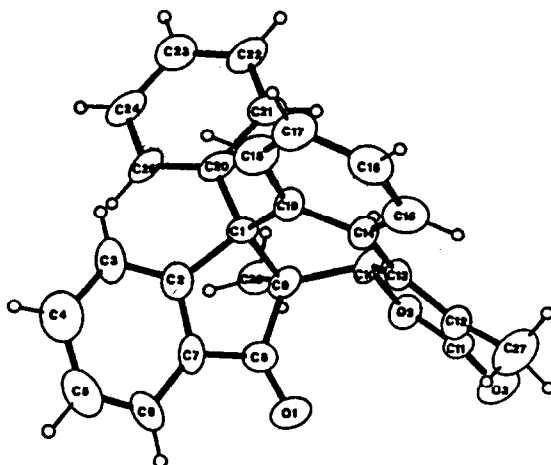
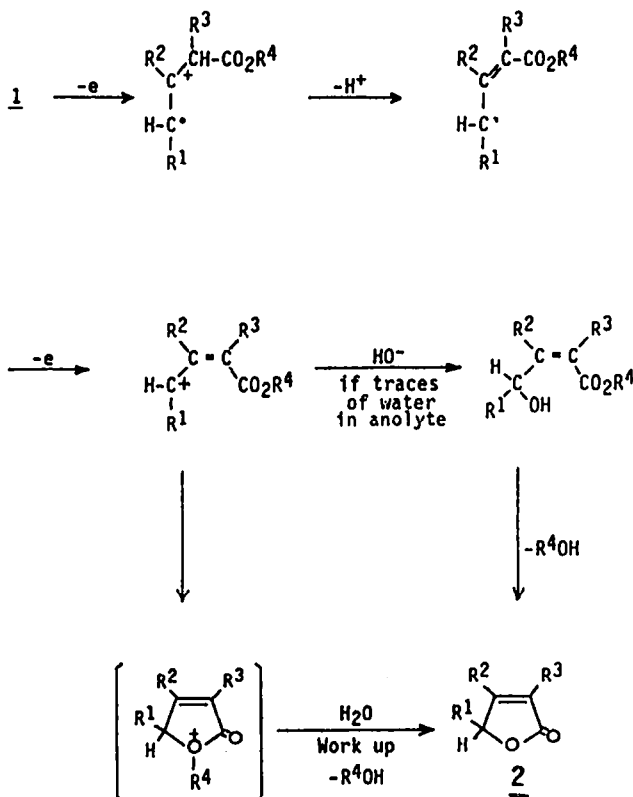


FIGURE 1 : Perspective view of the molecular structure of **5c**

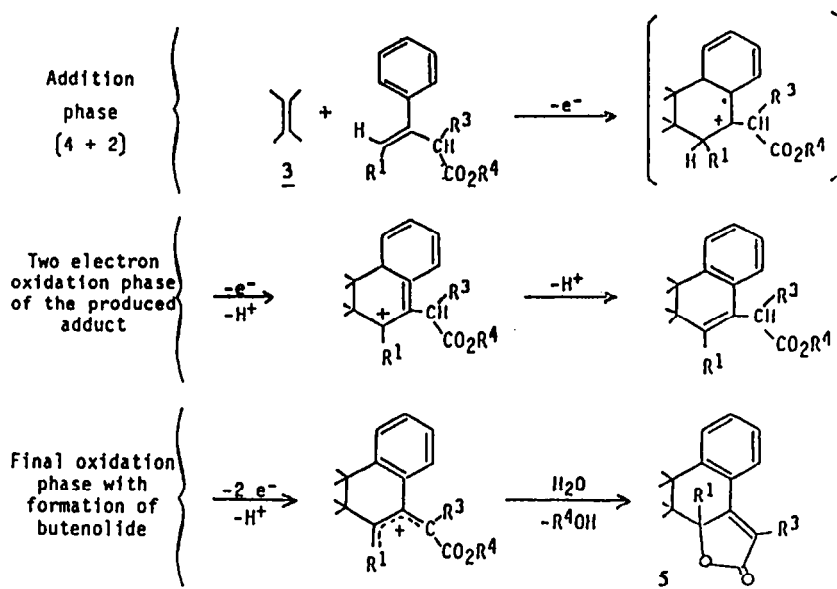
The proposed mechanism involves the formation of an allylic cation by the sequence shown in Scheme 4. In the absence of any nucleophile, a cyclization could take place followed by an elimination of R^4OH upon work-up. Alternatively, traces of water in the anolyte could lead to a γ -hydroxy-ester which would cyclise to **2**. It is notable that when R^1 is a phenyl group, the yield of **2** is much higher. This probably results from the greater stabilisation of the allylic cation.



SCHEME 4

A possible mechanism for the reaction in the presence of an olefinic partner is shown in Scheme 5. It was experimentally established that the olefin **3** was more readily oxidized than the unsaturated ester which therefore behaves in the donor. The oxidation process could occur in three steps. The first would be a [4+2] addition of the type already described by us in the case of purely catalytic systems¹⁰. Due to the high tendency of a six membered ring radical to undergo a deprotonation and therefore a further oxidation process one may observe a two-electron oxidation affording, in a second phase, the formation of a new β -ethylenic ester (which can be isolated when electrooxidations are conducted in acetonitrile as solvent). The last phase of the process should, of course, proceed according to the already given Scheme 4.

It remains to show that such a reaction can be extended to other systems possessing a double bond β to an electron-withdrawing group. A "one pot" electrochemical reaction combining a [4+2] cycloaddition catalyzed by a one electron transfer, and an oxidation of the so created double bond is of interest and we are motivated to focus work in that direction in order to generalize such processes.



EXPERIMENTAL

IR spectra were recorded in CHCl_3 or KBr, on a Perkin-Elmer instrument model 1320, the ^1H NMR spectra on a JEOL PMX 60 SI (60 MHz) or BRUKER WH 250 (250 MHz).

High resolution mass spectra were recorded using a VARIAN MAT 311 (70eV). Crystal data were collected on an automatic Enraf-Nonius CAD-4 diffractometer of the "Centre de diffraction" of the University of Rennes.

Melting points are uncorrected (Reichert-Kofler hot-stage apparatus)

Preparation of β -hydroxy esters :

A solution of ketone (M/20) and ethyl 2-bromo alkanonate (M/20) in benzene was added dropwise to 5 g of zinc powder and the mixture heated at 80° C under a nitrogen atmosphere. After hydrolysis, the solvent was removed and the crude product was purified by distillation (80 % yield).

Preparation of β -ethylenic esters :

The mixture of diastereoisomers of β -hydroxy esters was heated in toluene (100 ml) containing 1 g of p-toluene sulfonic acid for 2 hours.

β -ethylenic esters obtained were purified (**1a** and **1d**), E and Z isomers (**1b**, **1c** and **1e**) were separated with SiO_2 column chromatography using cyclohexane-ethyl acetate (90/10) as eluents. Physical constants of **1** are given in the Table I.

Ethyl 2-methyl-3-phenyl-3-butenolate **1a**, 72 % yield, $\text{C}_{14}\text{H}_{16}\text{O}_2$ *m/z* 204

Ethyl 2-methyl-3-phenyl-3-pentenoate **1b**, 80 % yield, $\text{C}_{14}\text{H}_{18}\text{O}_2$ *m/z* 218

Ethyl 2-methyl-3-(4-methoxyphenyl)-pentenoate **1c**, 70 % yield, $\text{C}_{15}\text{H}_{20}\text{O}_3$ *m/z* 248

Ethyl 2-ethyl-3-phenyl-3-butenolate **1d**, 70 % yield, $\text{C}_{14}\text{H}_{18}\text{O}_2$ *m/z* 218

Ethyl 3,4-diphenyl-2-methyl-3-phenyl-3-butenolate **1e**, 92 %, $\text{C}_{19}\text{H}_{20}\text{O}_2$ *m/z* 280

Trans- β -methylstyrene is a commercial product (Aldrich)

Indenones **3** were obtained according to literature ¹¹.

Preparative electrolyses :

Controlled potential macroelectrolyses were performed with a potentiostat (PRT 40-1X Tacussel) and a current integrator (model IG5 Tacussel).

Preparative electrolyses were carried out in a three compartment H cell with $2 \cdot 10^{-3}$ mole of **1** (or **1+3**) in 50 ml of anolyte.

A 0.2 molar solution of Bu_4NBF_4 in methylene chloride was used as electrolyte. The working electrode (anode) was a platinum sheet (area : 16 cm^2) and cathode a graphite rod.

Oxidations were performed under a potentiostatic control ; the reference electrode was the Ag/Ag^+ 0.01 M system .

Tables 2 and 3 give the total electricity consumption.

The reaction mixture was purified by SiO_2 chromatography (eluent : Cyclohexane 70-Ethyl acetate 30).

Electrooxidations were carried out on the mixture of E and Z isomers for **1b**, **1c** and **1e** esters, but the yields of the reactions were the same when isomers were treated separately.

3-methyl-4-phenyl-2(5H)-furanone **2a**: $\text{C}_{11}\text{H}_{10}\text{O}_2$ *m/z* 174 ; this compound was prepared before : see reference 12.

3,5-dimethyl-4-phenyl-2(5H)-furanone **2b** : $\text{C}_{12}\text{H}_{12}\text{O}_2$ *m/z* 188

3,5-dimethyl-4-(4-methoxyphenyl)-2(5H)-furanone **2c** : $\text{C}_{13}\text{H}_{14}\text{O}_3$ *m/z* 218

4,5-diphenyl-3-methyl-2(5H)-furanone **2d** : $\text{C}_{17}\text{H}_{14}\text{O}_2$ *m/z* 250

Butenolide **2a** $\text{C}_{20}\text{H}_{18}\text{O}_2$ *m/z* 290

Butenolide **2b** $\text{C}_{22}\text{H}_{18}\text{O}_3$ *m/z* 330

Butenolide **2c** $\text{C}_{27}\text{H}_{20}\text{O}_3$ *m/z* 392

Butenolide **2d** $\text{C}_{28}\text{H}_{22}\text{O}_3$ *m/z* 406

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