Tetrahedron Letters, Vol.32, No.37, pp 4913-4916, 1991
Printed in Great Britain

0040-4039/91 $3.00 + .00
Pergamon Press plc

Anodic Oxidation of 2,3-Diarylbenzofurans : Different Reaction Pathways for the Cation Radical.

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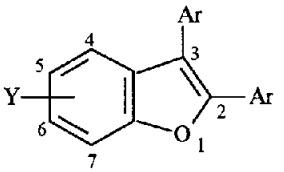
Key Words *: 2,3-diarylbenzofurans ; anodic oxidation ; rearrangement ; ring enlargement ; coupling.*

Abstract *The electrooxidation of 2,3-diarylbenzofurans leads to a rearrangement lactone, 3,3-diaryl-2(3H)-benzofuranone , together with a ring enlargement product, 9-aroyl-9-hydroxy-(9H)-xanthene . However, in some cases coupling products may be isolated in high yield.*

Previously[1], it was described that the electrooxidation of 1,2-dimethoxy-1,2-diphenylethylene gave benzil along with benzil dimethylmonoketal by migration of a methoxy group. Later[2], we established the fact that the anodic oxidation of aromatic enol ethers, such as 1-methoxy-1,2,2-triarylethylenes, gave a rearrangement product, 2-methoxy-1,2,2-triarylethanone .

This prompted us to study the anodic behaviour of benzofurans 1, derivatives possessing an ethylenic double bond with the same substituents but included in a cyclic structure :



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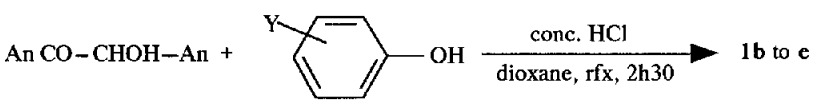
The same rearrangement could be expected and also other reactions, owing to the aromaticity of the furan ring. So far, the electrochemical oxidation of benzofurans (either unsubstituted or 2-phenyl,3-methyl and 2-ethoxycarbonyl-3-methyl substituted) was only carried out in methanol for the synthesis of 2,3-dimethoxy-2,3-dihydrobenzofurans [3].

Synthesis of benzofurans 1

Unsubstituted 2,3-diphenylbenzofuran **1a** was prepared by cyclisation of 1,2-diphenyl-2-phenoxy-1-ethanone by means of polyphosphoric acid (P.P.A.)[4] :

$$\text{Ph CO—CHCl—Ph} \xrightarrow[\text{acetone, rfx, 4h}]{\text{+ PhOH } (K_2CO_3)} \text{Ph CO—CH (OPh) Ph} \xrightarrow[\text{95°C, 3h}]{\text{P.P.A.}} \textbf{1a}$$

whereas 2,3-diparamethoxyphenyl-5 (or 6)-substituted-benzofurans **1b** to **e** were obtained, in a one-step procedure [5], by reaction of anisoin with the appropriate phenol (An = p-MeO-C_6H_4) :



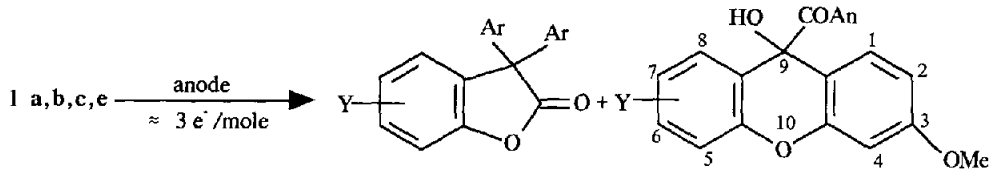
Cyclic voltammetry

In MeCN - $LiClO_4$, at a platinum microanode, with a sweep rate of 100 mV s^{-1}, benzofurans **1** exhibited fairly similar voltammograms : a first monoelectronic reversible (except for **1a**) oxidation peak followed by a second irreversible peak (reference electrode : Ag/Ag^+ 0.01 M) :

1	**1a**	**1b**	**1c**	**1d**	**1e**
Ar , Y	Ph , H	An , H	An, 5-Me	An, 5-OMe	An, 6-OMe
m.p. °C	123 (EtOH)	145 (iPr_2O-AcOEt)	122 (EtOH)	87 (MeOH)	90 (iPr_2O)
literature	references [4,6]	reference [5]	references [5,7]		reference [8]
Epa_1 V	+ 1.23	+ 0.91	+ 0.87	+ 0.88	+ 0.74
Epa_2V	+ 1.40	+ 1.09	+ 1.06	+ 1.23	+ 0.97

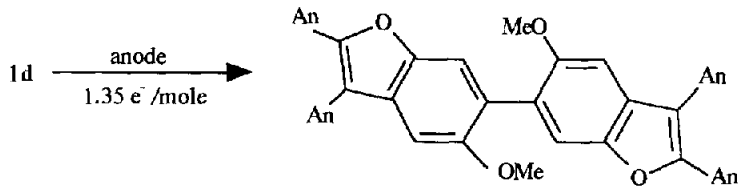
Controlled-potential electrolyses [1.40V (**1a**),1.05V (**1b**),1.00V (**1c** and **1d**), 0,86V (**1e**) versus S.C.E.]

Anodic oxidation of benzofurans **1** (4 mmol) in a three-compartment H-shaped cell (useful volume : 60 mL), at a platinum foil (A = 16 cm^2), in acetonitrile containing 0.3 M $LiClO_4$, in the presence of a soluble base such as 2,6-lutidine, led, in any case, to a rearrangement lactone, 3,3-diaryl-2 (3H)-benzofuranone **2**, along with, when Ar = An, a ring enlargement tricyclic product, 9-aroyl-9-hydroxy-3-methoxy-(9H)-xanthene **3**, except for **1d** which gave exclusively a coupling product, bis (2,3-diparamethoxyphenyl-5-methoxy-6-benzofuranyl) **4d** :



2a (17%)
2b (12%)
2c (15%)
2e (31%)

3b (15%)
3c (3%) + **4c** (2%)
3e (30%)

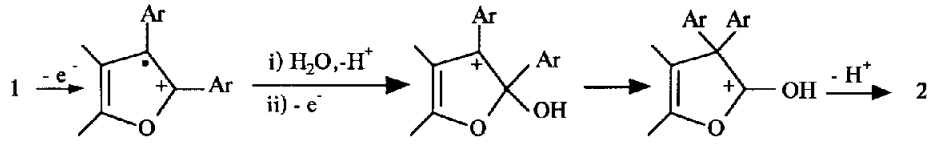


[+ corresponding monolactone (8%)]

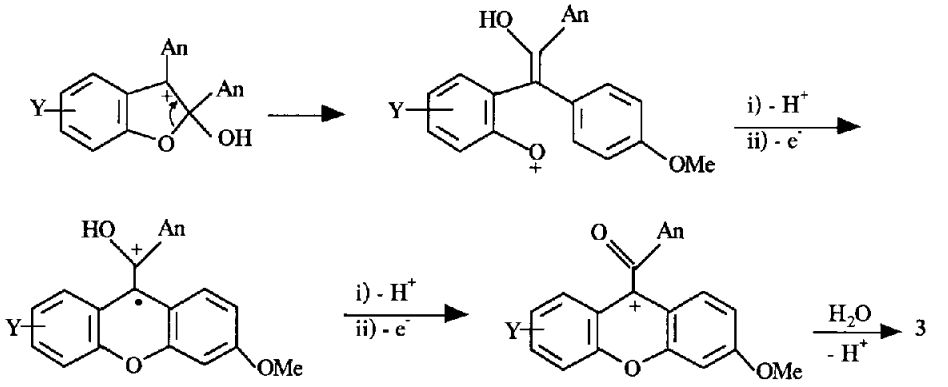
4d (78%)

Lactones **2** have a characteristic infrared absorption band (about 1800 cm^{-1}). Xanthene structure **3** was determined by an X-Ray analysis in the case of **3e**. Structure **4d** was demonstrated, after mass spectrometry, by 300 MHz ^1H NMR spectroscopy : the emergence of the aromatic protons as two singlets (δ 7.475 and 6.975), without the slightest perceptible coupling, implies that each proton is in para position to the other. See note[9] for physical and spectroscopic data of compounds **2**, **3** and **4d**.

For formation of lactones **2**, a likely mechanism implies the migration of the 2-aryl group after reaction of residual water of acetonitrile with the electrogenerated cation radical and further oxidation into a cation :

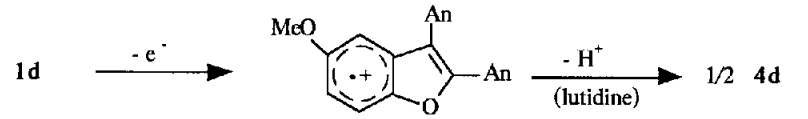


To account for ring enlargement into xanthenes **3**, one must propose a more complex mechanism in which the above cation, instead of undergoing an aryl migration, opens into an aryloxenium ion recyclising with the nearby benzene ring :



It is worth noting that this oxidation can proceed further because trace amounts of xanthones were detected by mass spectrometry.

Product **4d** forms by mere coupling of cation radical **1**$^{\bullet+}$ whose positive charge is localized on the fused benzene ring thanks to the stabilizing effect of the electron-donating methoxy group :



Under these conditions, the same coupling was expected for 6-methoxybenzofuran **1e**, whereas only lactone **2e** and xanthene **3e** were isolated ; this is probably due to the steric hindrance which would exist between 6-methoxy group and 3'-anisyl ring in the coupling product.

These mechanisms emphasize the great versatility of the behaviour of 2,3-diarylbenzofuran **1** cation radical whose reactivity can localize on :

. the ethylenic double bond , and lead either to rearrangement lactone **2**, or to xanthene **3** after ring opening.

. the benzene ring and give coupling product **4**.

Moreover this electrosynthesis constitutes the first general preparation of benzofuranones **2**, because only **2a** was reported in literature [10] and the procedure was repeated [11] with a yield lower than 2% .

In conclusion, note that the anodic oxidation of 2,3-diarylbenzofurans, which themselves show physiological activities[12], leads to potentially anti-inflammatory 2(3H)-benzofuranones[13], and to xanthenes whose structure is encountered in naturally occurring compounds with many biological properties[14].

References and notes

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9. **2a** : m.p. 118°C (iPr_2O) [lit. [12] :118°C] ; NMR ($CDCl_3$) δ Ph 7.27(peak) ; M.S. m/z 286 ($C_{20}H_{14}O_2$) - **2b** : m.p. 148°C (iPr_2O) ; NMR ($CDCl_3$) δ OMe 3.76 (s, 6 H), δ Ph 7.27 - 7.12 - 6.88 - 6.73 (AA'BB' system) and 7.22 (12 H) ; M.S. m/z 346 ($C_{22}H_{18}O_4$) - **2c** : m.p. 115°C (iPr_2O - AcOEt 90-10) ; NMR ($CDCl_3$) δ Me 2.33 (s, 3 H), δ OMe 3.78 (s,6 H), δ Ph 6.78 - 6.91 - 7.15 - 7.28 and 7.12 (m) (11 H) ; M.S. m/z 360 ($C_{23}H_{20}O_4$) - **2e** : gum ; NMR ($CDCl_3$) δ OMe 3.78 (s,6 H) 3.82 (s,3 H) δ Ph 6.75 - 6.90 - 7.12 - 7.27 (AA'BB' system) and 6.78, 7.08, 7.22 (11 H) ; M.S. m/z 376 ($C_{23}H_{20}O_5$).
   3b: m.p.140°C (iPr_2O);IR (KBr) ν OH 3390, ν CO 1640; NMR ($CDCl_3$) δ OMe 3.78 (s,3H) 3.66 (s,3H) , δ Ph and OH 6.25 to 7.68 (multiplet,12 H) ; M.S.m/z 362 ($C_{22}H_{18}O_5$).
   3c : gum ; IR (KBr) ν OH 3430, ν CO 1650 .
   3e : m.p.179°C (iPr_2O - AcOEt 50-50) ; IR (KBr) : νOH 3425, νCO 1650 ; NMR ($CDCl_3$) δ OMe 3.72 (s, 3 H), δ OMe 3.82 (s, 6 H), δ OH 6.20 (s, 1 H), δ Ar 6.50 to 6.83-7.02-7.15-7.55-7.72 (m, 10 H) ; M.S. m/z 392 ($C_{23}H_{20}O_6$) ; X-Ray analysis : $C_{23}H_{20}O_6$.
   4c : m.p. 325°C ($CHCl_3$) ; IR (KBr) ν Ar 1605 ; NMR ($CDCl_3$) δ Me 2.10 (s, 6 H), δ OMe 3.83 (s, 6 H), δ OMe 3.92 (s, 6 H), δ Ar 6.80 - 7.70 (m, 20 H) ; M.S. m/z 686 ($C_{46}H_{38}O_6$) - **4d** : m.p. 170 - 190°C (cyclohexane - Ac OEt 35-65 : crystals solvated by cyclohexane) ; IR (KBr) νAr 1605 ; 300 MHz NMR ($CDCl_3$) δ cyclohexane 1.42 , δ OMe 3.76 (s,6 H) , 3.80 (s,6 H), 3.89 (s,6 H), δ Ar 6.975 (s,2 H), 7.475 (s,2 H) and δ Ar 7.02-7.05-7.43-7.46, 6.83-6.86-7.57-7.60 (two AA'BB' systems, 16 H) ; M.S. m/z 718 ($C_{46}H_{38}O_8$).
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(Received in France 11 June 1991)