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A Further Selective Pathway in Thermal Conversion of 2,5-Epidioxy-2-alkoxy-2,5-dihydrofurans (2-Alkoxyfuran *endo*-Peroxides). Synthesis of the First 5-Hydroperoxyfuran-2(5*H*)-ones

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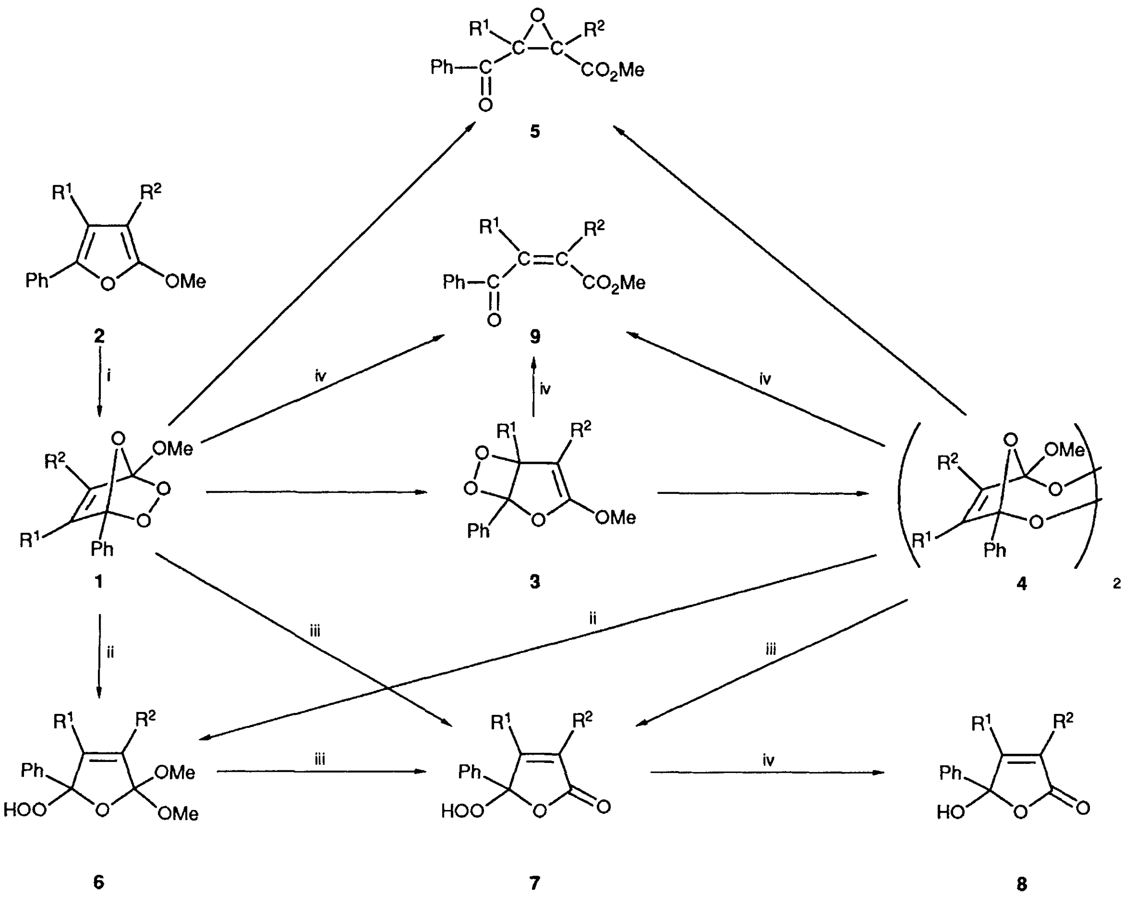
Thermal conversion of the epidioxydihydrofurans **1** leads, *via* dioxetanes **3**, to the stereoisomeric dimers **4** which have a structural relationship with antitumour cyclic peroxides and represent convenient starting materials for several multifunctional compounds; their mild acid hydrolysis provides a convenient entry to the synthesis of the furanone derivatives **7** and **8** which are structurally related to biologically active products.

The synthesis and the chemical behaviour of 2,5-epidioxy-2-alkoxy-2,5-dihydrofurans have been the subject of recent investigations.[1-5] These allowed it to be established that thermal rearrangement of 1-alkoxy-4-phenyl-2,3,7-trioxabicyclo[2.2.1]hept-5-enes leads to carbonyl oxides[1,3,4] and/or 3*H*-1,2-dioxoles[2,5] depending on the nature of the substituents



a; R¹ = Me, R² = CO_2Me
b; R¹ = Ph, R² = CO_2Et

Scheme 1 *Reagents*: i, $^1O_2$; ii, MeOH; iii, H_3O^+; iv, Et_2S

at C-5 and C-6. In contrast neither carbonyl oxide nor dioxole is generated by thermal rearrangement of **1a**, an example of the series substituted at C-5 with an electron-donating group and at C-6 with an electron-withdrawing substituent, obtained by dye-sensitized photo-oxygenation of the furan **2a** at −75 °C.[5] We have now shown by NMR spectroscopy that **1a** at −50 °C rearranges quantitatively into the dioxetane **3a**[†][‡] (Scheme 1) which represents the first example of a furanodioxetane. The dioxetane **3a** at −50 °C, within 30 h, leads to the dimeric peroxides **4a**[‡] in high yield.[§] The presence of complex patterns of resonances in the NMR spectra of the dimers **4a** is due to different stereoisomeric and conformational forms;[8] the presence of a mixture of stereoisomers explains the wide melting range of compounds **4**. The separation of the stereoisomers is very difficult owing to their thermal instability and ready hydrolysis. The dimers **4a** lead almost quantitatively to the epoxide **5a**[5] on heating at 70 °C in inert solvents and react with methanol to give nearly quantitatively the 2,5-dihydrofuran **6a**, which was obtained previously from the monomeric peroxide **1a** by addition of methanol.[5] Both the monomeric **1a** and dimeric **4a** peroxides as well as the 2,5-dihydrofuran **6a** quantitatively undergo mild acid hydrolysis into the hydroperoxylactone **7a**,[‡] which is reduced readily and quantitatively by diethyl sulphide to the hydroxylactone **8a**.[¶] Solutions of the monomeric **1a** and dimeric **4a** peroxides and of the dioxetane **3a** are reduced by diethyl sulphide to the ethylene **9a**.[¶] The dioxetane **3a** at −60 °C does not react with methanol or with dilute acid.

Similar results were obtained when the furan **2b** was used as starting material.[¶]

It is noteworthy that the dimeric peroxides **4** are structurally related to antitumour constituents of marine sponges.[9] Moreover, they are stable at room temperature, and their behaviour with the reagents studied is very similar to that of the thermally unstable peroxides **1**; they can therefore be used as key intermediates in the synthesis of several classes of multifunctional compounds. In particular, the good yields together with mild reaction conditions make the conversion of the dimers **4** and the 2,5-dihydrofurans **6**[||] into lactones **7** and of **7** in turn into compounds **8** convenient entries to the synthesis of functionalized furan-2(5*H*)-ones. These lactones have a structural relationship with compounds which play a significant role in biochemistry and/or phytochemistry;[10] also, compounds **7** are the first examples of 5-hydroperoxyfuran-2(5*H*)-ones.

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[†] The rearrangement of epidioxy compounds into dioxetanes was recently observed in the alkoxyoxazole series.[6]

[‡] NMR spectra were recorded at 200 MHz (^{1}H) in CDCl$_3$ except for **3a** (CDCl$_3$–CFCl$_3$, 3 : 1 v/v, at −60 °C).

3a, ^{1}H: δ 1.57 (s, 3H, Me), 3.76 (s, 3H, CO$_2$Me), 4.26 (s, 3H, OMe), 7.20–7.70 (m, 5H, Ph); ^{13}C: δ 19.4 (q, Me), 51.4 (q, CO$_2$*Me*), 58.4 (q, OMe), 83.9 (s, *C*=C–OMe), 97.9 (s, *C*–Me), 116.9 (s, *C*–Ph), 126.8, 128.9 and 131.0 (3d, CH of Ph), 130.3 (s, C-1 of Ph), 164.0 and 172.2 (2s, CO$_2$ and C=*C*–OMe).

4a, melting range 90–105 °C; M_r (benzene f.p. depression) 602 (required 556); IR (CHCl$_3$) ν/cm^{-1} 1720; the ^{1}H NMR spectrum shows three complex patterns of resonances in the three reported ranges with relative areas 3 : 6 : 5 respectively: δ 1.80–2.30 (Me), 3.40–4.00 (OMe), 7.20–7.70 (Ph); the ^{13}C NMR spectrum shows complex patterns of resonances centred at the values reported: δ 11.7 (Me), 51.6 (OMe), 114.2 (*C*–Ph), 122.3 (*C*–OMe), 126.4 and 128.4 (CH of Ph), 131.3 (C=*C*–CO$_2$Me), 135.7 (C-1 of Ph), 152.1 (*C*=C–CO$_2$Me), 162.7 (CO$_2$); satisfactory C, H and O$_{act}$ analyses.

7a, IR (CCl$_4$) ν/cm^{-1} 3510, 3300, 1794, 1728 and 1671; ^{1}H: δ 2.33 (s, 3H, Me), 3.86 (s, 3H, OMe), 7.43 (m, 5H, Ph), 10.52 (br, 1H, OOH); ^{13}C: δ 13.2 (q, Me), 52.3 (q, OMe), 110.9 (s, C-5), 119.9 (s, C-3), 125.8, 128.8 and 130.3 (3d, CH of Ph), 131.8 (s, C-1 of Ph), 161.2 and 166.8 (2s, 2CO$_2$), 174.5 (s, C-4); satisfactory C, H and O$_{act}$ analyses.

[§] The monomeric peroxide **1a**, on rapid heating at room temperature, leads to the epoxide **5a**, by the direct rearrangement previously observed,[7] and to polymeric materials.[5]

[¶] All new compounds obtained exhibited satisfactory analytical and/or spectral data.

[||] The use of the 2,5-dihydrofurans **6** which, as well as compounds **1** and **4**, include an orthoester function, offers experimental advantages and a wide range of applicability since compounds such as **6** can be obtained by direct dye-sensitized photooxygenation in methanol of the 2-alkoxyfurans with the sole exception of those unsubstituted at C-4.[1,5]