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A DYNAMIC CHEMILUMINESCENT PROCESS. CYCLIC AND ACYCLIC PATHWAYS IN THE PHOTOOXIDATIVE DECARBONYLATION OF 5-METHYLFURFURAL

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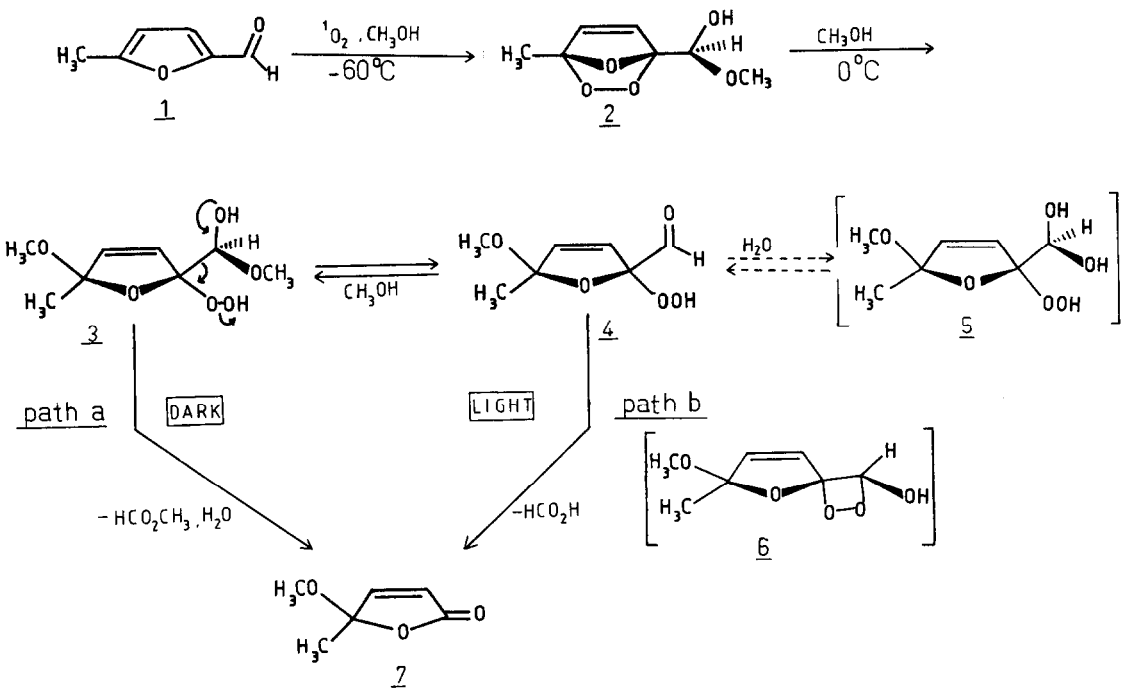
The photooxidative decarbonylation of 5-methylfurfural was found to proceed via an α-hydroperoxyhemiacetal intermediate or via a cyclic chemiluminescent pathway.

The α-hydroperoxycarbonyl structure plays a central role in important metabolic processes such as dioxygenase (e.g. phenol ring cleavage)[1-3] and indole-3-acetic acid decarboxylation mechanisms[4] and bioluminescence[1,2,4,5] (luciferin oxygenation). The base-catalysed decomposition of several α-hydroperoxyketones has been studied in detail and the α-cleavage has been explained by a predominant acyclic carbonyl addition mechanism and a minor cyclic 1,2-dioxetane pathway[1b,6,7]. We here report on the dynamic chemiluminescent decarbonylation of 5-methylfurfural, a reaction which can be mildly and selectively directed to proceed via an acyclic (dark) and a cyclic (chemiluminescent) pathway, and the isolation of an α-hydroperoxyhemiacetal intermediate of the acyclic pathway.

Photooxidation of 5-methylfufural (1) dissolved in dry methanol containing rose bengal for 3 h at 40 °C resulted in its quantitative conversion into methyl formate, water and lactone 7[8]. The mechanism of the photooxidative decarbonylation is outlined in Scheme 1.

At -60 °C singlet oxygen reacted rapidly with 1 to give the bicyclic ozonide 2[9-12], in which the aldehyde moiety was unexpectedly found to be completely in the hemiacetal form. The facile hemiacetal formation is attributed to the influence of the two α-oxy substituents on the aldehyde function (comparable to hemiketal formation in α-ketoesters[7]). At 0 °C a quantitative stereoselective methanol addition generates the α-hydroperoxyhemiacetal compound 3, isolated in the pure form below 10 °C (oil; mixture of two diastereoisomers)[12].

SCHEME 1

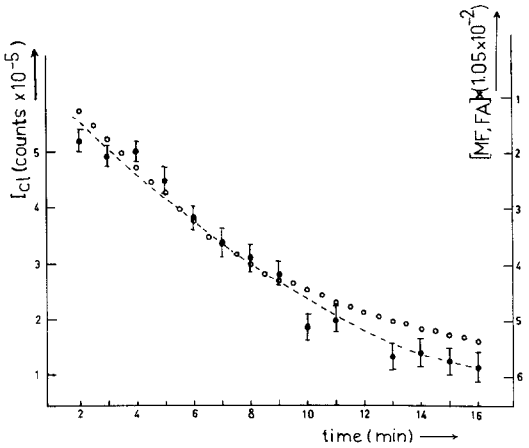


To our knowledge compound 3 is the first isolated and characterized intermediate of the proposed acyclic decarbonylation mechanism of α-hydroperoxycarbonyl compounds[1b,6,7]. In accordance with this mechanism, 3 decomposes at more elevated temperatures (> 20 °C) quantitatively into 7, methyl formate and water (Scheme 1, path a) with first-order kinetics (k_1 = 1.34 x 10^{-4} s^{-1} at 40 °C).

Surprisingly, when methanol was carefully removed from the methanolic solution of 3 at 0-5 °C and the residue subsequently dissolved in dry chloroform, the α-hydroperoxyaldehyde 4 was formed[12] (3/4 ≈ 7/3 at 22 °C). The equilibrium (Scheme 1) strongly depended upon solvent, temperature and the concentration of methanol. When the temperature was increased above 15 °C, 4 decomposed quantitatively into 7 and formic acid. The ratio of methyl formate to formic acid was constant during the decomposition of the mixture of 3 and 4 at a given temperature; however, an enhanced formation of formic acid is observed during the period of temperature increase. The decarbonylation of 4 can be explained via cyclization to an intermediate hydroxydioxetane 6 (not detected as a stable intermediate), followed by a fast cleavage to 7 (Scheme 1, path b).

The formation of 7 and formic acid cannot be attributed to decomposition of the hydrate 5 under the reaction conditions as we confirmed independently. In conformity with the decomposition of 4 via the hydroxydioxetane 6 we observed the formation of chemiexcitated lactone 7 during the slow decomposition of the equilibrium mixture of 3 and 4 in $CHCl_3$ at 22 °C. The chemiluminescence was measured during the decomposition of 4 in the presence of added fluorescers 9,10-diphenylanthracene (DPA) and 9,10-dibromoanthracene (DBA).

FIGURE 1

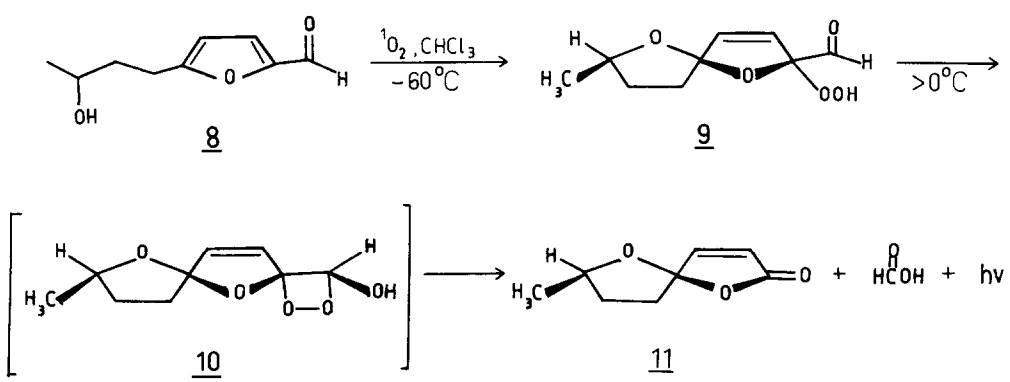


DPA fluorescence (I_{Cl}) decay curve (0) and methyl formate (MF), formic acid (FA) concentration vs time (- - • - -) for decomposition of 3 + 4 in $CDCl_3$ at 50 °C (3 + 4, 6.15 x 10^{-2} M; DPA, 2.0 x 10^{-2} M)

Figure 1 shows the time-dependent DPA fluorescence and the conversion of 4 as detected by NMR during decomposition in $CHCl_3$. In methanol as the solvent, where no 4 was present, chemiluminescence in the presence of fluorescers DPA or DBA, was essentially zero. Addition of methanol to the chloroform solution of 3 and 4 also resulted in a non-chemiluminescent decomposition upon heating. This means that the oxidative decarbonylation represents a very mild (neutral medium, room temperature) dynamic system in which the selection of a dark or a chemiluminescent pathway, solely depends on, and can be directed by, the hemiacetalization equilibrium.

As the preparation of 3 and 4 requires the use of a hydroxylic solvent, it was not possible to completely suppress the dark decomposition (path a). Such a pathway is avoided with the furfural derivative 8[12,13], which contains an internal hydroxyl group (Scheme 2). In agreement with previous observations[10], 8 yielded the spiro-α-hydroperoxyaldehyde 9[12], which decomposed into lactone 11 and formic acid[14].

SCHEME 2



DPA- and DBA-enhanced chemiluminescence was observed during decomposition of 9 in agreement with a hydroxydioxetane intermediate 10, thus confirming a predominantly cyclic decomposition pathway (path b) for 9. Mild ways of chemiexcitation such as the one reported in this paper deserve consideration in the elucidation of in vivo mechanisms of chemiexcitation[2,4] resulting in several pathological effects.

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8. No other products were observed in the NMR spectra.Lactone 7, isolated by distillation in 90 % yield (bp 40-42 °C, 0.05 mm Hg), was prepared independently from 2-methylfuran[9,10].

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12. All new compounds showed spectral and physical data consistent with the structures indicated. Some representative NMR data are: 2 ^{1}H NMR ($CDCl_3$)δ 2.02 (s, 3H), 4.95, 4.99 (2s, 1H) 5.32 (br.s, 1H), 6.55, 6.75 (2 AB systems, J = 5,8 Hz, J = 6.0 Hz, 2H); ^{13}C NMR (CD_3OD)δ 12.0, 92.2, 112.0, 112.2, 112.5, 130.7, 131.0, 133.3; 3 ^{1}H NMR (CD_3OD)δ 1.51, 1.54 (2s, 3H), 3.31 (br.s, 3H), 3.45, 3.49 (2s, 3H), 4.75 (br.s, 2H), 4.97, 5.05 (2 s, 1H), 6.08, 6.10 (2 AB systems, J = 6.0 Hz, 2H); ^{13}C NMR (CD_3OD) 23.9, 94.8, 95.6, 112.6, 114.2, 114.4, 126.0, 126.2, 135.6, 136.3; 4 ^{1}H NMR ($CDCl_3$)δ 1.58 (s, 3H), 3.23 (s, 3H), 5.35 (br.s, 1H) 5.93, 6.30 (AB system, J = 5.5 Hz, 2H), 9.66 (s, 1H).

13. Furfural derivative 8 is conveniently prepared by Vilsmeyer formylation of 4-(2-furyl)-butanol-2 followed by acid hydrolysis of the formic acid ester of 8.

14. The selectivity towards 9 was 80 % at 65 % conversion of 8; unidentified by-products, probably the results of radical reactions in $CHCl_3$, were observed. These products, however remained unchanged during the quantitative conversion of 9 to 11.

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