Photooxygenation of Chromone-2-carboxylic Acid: Identification of Ketohydroperoxide Using a Chemiluminescence Technique

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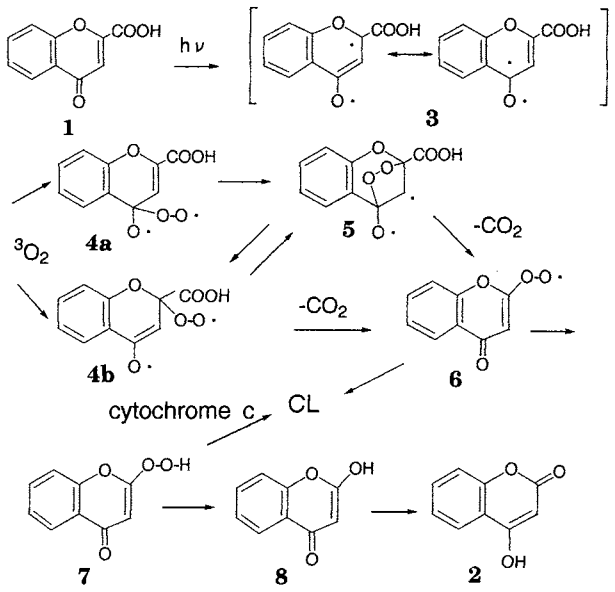
Irradiation of chromone-2-carboxylic acid in aerated ethanol solution gives 4-hydroxycoumarine with the quantum yield of 0.02. The reaction proceeds via the decarboxylation followed by the addition of the oxygen molecule. Chemiluminescence measuring was successfully applied to detect the ketohydroperoxide intermediate in the photoreaction.

The photoreactions[1,2] of the compounds having a chromone structure in deaerated alcohol solution proceed via a ketyl radical by the hydrogen abstraction from the solvent to give the reduced form, while some of them show the photooxygenation in oxygen saturated solutions.[3,4] In the latter, the reaction does not proceed without a sensitizer such as a rose bengal or a methylene blue. Chromone-2-carboxylic acid (**1**) shows the photooxygenation in aerated alcohol solution without a sensitizer. The photoproduct is 4-hydroxycoumarine (**2**). We now report the intriguing photooxygenation and decarboxylation of **1** and its reaction mechanism identified by the chemiluminescence detection applied to the photoreaction.

Irradiation (500 W Xe lamp with a pyrex filter) of **1** in air saturated ethanol (70 mg in 200 cm^3) for 6 hours gives the unique photoproduct **2**[5] of 41.8 mg and the recovery of **1** of 13.5 mg. The reaction was monitored by HPLC with methanol - water - acetic acid(60 : 40 : 3 in volume) solvent. The quantum yield for the disappearance of **1** with the 313 nm irradiation (a 150 W xenon lamp with an interference filter) was measured. Light intensity was determined by a potassium trioxalatoferrate (III) actinometer. The value is 0.02 at 20 °C. Quite the same photoreaction occurs in aerated methanol or 2-propanol. Upon irradiation of chromone itself and flavone in aerated ethanol solution, little changes in the absorption spectra are observed, though they show photoreaction in deaerated systems. Clearly, the carboxyl group at 2-position is prerequisite for the photoreaction. In spite of the decarboxylation product of **1**, the photoproduct **2** contains an extra oxygen atom. In addition, **2** was not generated by the photosensitized oxygenation reaction such as the excitation of a methylene blue or a rose bengal in oxygen saturated ethanol. These facts indicate the singlet oxygen does not take part in the photoreaction, though the oxygen molecule attacks **1**.

We propose Scheme 1 for the photoreaction of **1** initiated by the addition of oxygen molecule. Biradical **3**, which is assumed in the photorearrangement of cyclohexadienone and cyclohexenone,[6] is supposed first. Two pathways to **2** are considered; one is that the ground state oxygen molecule attacks the 2-position of biradical **3** generating peroxy radical **4a** and the other is the attack at C4-position giving peroxy radical **4b** followed by cyclization to endo-peroxide **5**.[7] Both the biradical **4b** and **5**, are precursors for the peroxy radical **6** and the ketoperoxide **7** by means of the homolytic decarboxylation under the irradiation conditions. The photooxygenation by a superoxide may be eliminated because of the absence of the sensitizer to form a superoxide in this system. Chromone **1** itself can not be an electron donor to the oxygen molecule due to the presence of the carboxyl group. Matsuura[3] and Chou[4] investigated the photosensitized oxygenation of 3-hydroxyflavone(3-HF). They postulated a hydroperoxide as an intermediate and concluded that the presence of a hydroxyl group is indispensable for the photooxygenation, because 3-methoxyflavone, which can not take an enol form, did not show the photooxygenation. Especially, the direct excitation of 3-HF in oxygen saturated nonpolar solvents gave the same product as that of the sensitization experiment.[4] The idea of the addition of oxygen molecule to 2-position of flavone ring is the same as ours.



Scheme 1 A proposed mechanism.

Chemiluminescence (CL) is observed as is often the case when the peroxides such as 1,2-dioxetane or hydroperoxide decomposes. Therefore the CL method can be used for the detection of the peroxide intermediates in the reaction. The CL is measured with a chemiluminescence detector model CLD-110 (Tohoku Electronic Industrial Co., Ltd) based on a single photon counting method. The amount detected corresponds to the total photons over the wavelength region between 300 and 650 nm. We could successfully detect the hydroperoxide **7** (or peroxy radical **6**) posturated in the photoreaction of **1** as in Scheme 1. The weak CL was observed immediately after the irradiation of **1** (1.0×10^{-3} mol dm^{-3}) in the course of the reaction. The decay

of the CL intensities is single exponential with the rate constant of 4.2 x 10^{-4} s^{-1}. In blank tests, all samples before irradiation as well as the irradiated ethanol show no CL.

Cytochrome c is known to be a good CL catalyst in the hydroperoxide assay.[8] It cleaves -C-O-OH to -CO*, which emits CL. Figure 1(a) shows the CL time profile of the solution to which cytochrome c was added at the downward arrow point after the weak CL species had completely disappeared in the course of the photoreaction. The CL intensities are about 30 times strong compared with those of the weak, and that, both the formation and the decay processes of emissive species are observed with their first order rate constants of 1.0 x 10^{-2} and 2.5 x 10^{-3} s^{-1}, respectively. Non-irradiated sample containing cytochrome c does not emit CL as shown in Figure 1(b). Unfortunately, we could not detect the trace of the emissive species or a new product in HPLC formed by the irradiation of **1** containing cytochrome c.

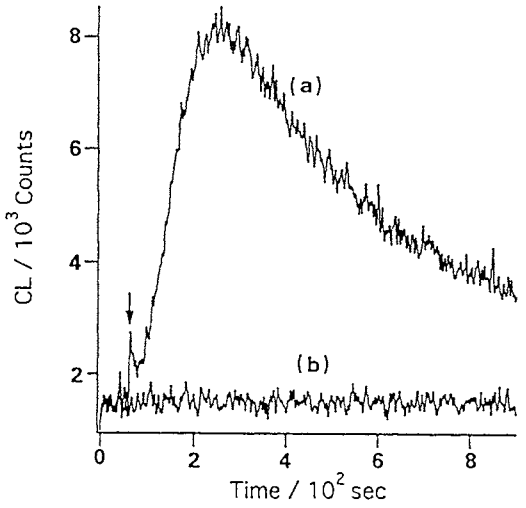


Figure 1. Time profile of CL intensities with an addition (downward arrow point) of cytochrome c to; (a) the solution in the course of the photoreaction; (b) a non-irradiated solution of **1**.

Evidently, there exist two emissive peroxide species in the photoreaction and we conclude the weak CL is from the radical **6** and the strong CL with the addition of cytochrome c is from the ketohydroperoxide **7**. It may be relatively stable in the solution, but during the separation, it goes to **8** through a silica gell colum or TLC plates. Therefore, we get only **2** as an end-product.

References and Note

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5 **2** : Mp 216 - 217 °C (colorless powder). Anal : Found: C, 66.61; H, 3.86%. Calcd for $C_9H_6O_3$:C, 66.67;H, 3.73%; HR Mass :162.0267 (Calcd for $C_9H_6O_3$; 162.0317) ; IR (KBr); 3083, 3059, 1648, 1614, 1543 cm^{-1}: ^1H NMR(DMSO - d_6, 600 M Hz); 5693 (H4, s), 7.440 (H6, dd, J = 7.8, 7.5 Hz), 7.464 (H8, d, J = 8.5 Hz), 7.737 (H7, dd, J = 8.5, 7.5 Hz), 7.916 (H5, d, J = 7.8 Hz), 12.03 (OH): ^{13}C NMR(DMSO - d_6, 150 M Hz) ; 90.996(C3), 115.806(C4a), 116.391 (C8), 123.225 (C5), 123.952 (C6), 132.734 (C7), 153.537(C1a), 161.922 (C3 and C4), 165.710 (C2).

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