Potassium t-Butoxide-catalysed Oxygenation of an α-Tocopherol Model Compound 2,2,5,7,8-Pentamethylchroman-6-ol

By SHIGENOBU MATSUMOTO and MITSUYOSHI MATSUO*

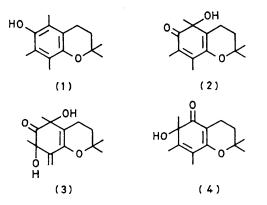
(Tokyo Metropolitan Institute of Gerontology, 35-2 Sakaecho, Itabashiku, Tokyo 173, Japan)

and YOICHI IITAKA

(Faculty of Pharmaceutical Sciences, University of Tokyo, Bunkyoku, Tokyo 113, Japan)

Summary The potassium t-butoxide-catalysed oxygenation of an α -tocopherol model compound, 2,2,5,7,8-pentamethylchroman-6-ol, gave 5-hydroxy-2,2,5,7,8-pentamethylchroman-6(5H)-one (2) and 7,8-dihydro-5,7-dihydroxy-8-methylene-2,2,5,7-tetramethylchroman-6(5H)one, and 6-hydroxy-2,2,6,7,8-pentamethylchroman-5(6H)one which was found to be formed as the result of the acyloin rearrangement of (2).

The importance of α -tocopherol, vitamin E, as a biological antioxidant is widely recognized.¹ Its antioxidant mechanisms have, however, been understood only in part. Extensive studies of its oxidation reactions are necessary for the elucidation of vitamin E functions.²

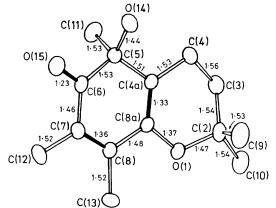


We report here that Bu^tOK-catalysed oxygenation of 2,2,5,7,8-pentamethylchroman-6-ol (1), an α -tocopherol model compound, gave two novel oxidation products,

5-hydroxy-2,2,5,7,8-pentamethylchroman-6(5H)-one (2) and 7,8-dihydro-5,7-dihydroxy-8-methylene-2,2,5,7-tetramethyl -chroman-6(5H)-one (3), and 6-hydroxy-2,2,6,7,8-pentamethylchroman-5(6H)-one (4), previously assumed to be (2) and whose structure was revised recently.³

Bu^tOK (1 mmol) in tetrahydrofuran (THF) was added dropwise to a stirred solution of (1) (1 mmol) in THF at 0 °C under an oxygen atmosphere. Three oxidation products [(2), (3), and (4)] were obtained in yields of 8·3, 4·1, and 16·3%, respectively, and were purified by silica gel column chromatography.

Compound (4) was identified on the basis of its spectral data and arises from the reaction of (1) with potassium superoxide $(\mathrm{KO}_2)^{.3,4}$ Mass spectroscopy and elemental



analysis revealed that both (2) and (4) had the same molecular formula, $C_{14}H_{20}O_3$. In addition, the spectral data of (2) were similar to those of (4)⁴ [(2), m.p. 75-76 °C; m/e 236 (*M*⁺); λ_{max} (MeCN) 378 nm; ν_{max} (KBr) 1641, 3470 cm⁻¹] which suggest that (2) may be isomeric to (4) positionally. An X-ray crystallographic analysis of (2) was carried out and its structure is shown in Figure 1.

Crystal data: (2), $C_{14}H_{20}O_3$, M = 236.3, pale yellow, thick plates, monoclinic, space group $P2_1/n$, Z = 4, $D_{calc} = 1.166$ g cm⁻³, a = 16.456(8), b = 9.473(5), c = 8.656(4) Å, $\beta = 94.04(6)^{\circ}$, U = 1346 Å³. A total of 1641 reflections with $I > 2\sigma(I)$ were measured within the range $6 < 2\theta <$ 120° using graphite-monochromated Cu- K_{α} radiation. The specimen deteriorated slightly under X-ray irradiation. The structure was solved by direct methods and refined by blockdiagonal least-squares to an R value of 0.118. Further refinement was not attempted owing to the rather poor quality of the intensity data.[†]

Recently, (2) has been implicated as a necessary precursor to (4), and the mechanism for the conversion of (2) into (4)has been presumed to involve an acyloin rearrangement. In order to determine whether it is actually converted into (4), (2) (1 mmol) was treated with either KO₂ (1 mmol) or Bu^tOK (0.4 mmol) under conditions similar to those for the production of (4), and gave (4) quantitatively. This indicates clearly that the base-catalysed acyloin rearrangement of (2) gives (4) exclusively.

The structure of (3) was determined by spectroscopy and by X-ray crystallography [m.p. 92–93 °C; m/e 252 (M^+); λ_{max} (MeCN) 246 nm; ν_{max} (KBr) 1739, 3420 cm⁻¹].

Crystal data: (3), $C_{14}H_{20}O_4$, M = 252.3, colourless, thick plates, triclinic, space group $P\overline{1}$, Z = 2, $D_{calc} = 1.126$ g cm⁻³, a = 13.135(8), b = 9.167(6), c = 6.229(4) Å, $\alpha =$ 106.08(6), $\beta = 102.35(6)$, $\gamma = 97.65(6)^{\circ}$, $U = 689 \text{ Å}^3$. A total of 2479 reflections with $2\theta \leq 156^\circ$ were measured as for (2). No appreciable decrease in intensity was noticed. The determination and refinement were carried out as before. The final R value was 0.098 without hydrogen atom contributions.[†] As shown in Figure 2, the structure of (3) is

unique, a cyclohexenone derivative with an exocyclic methylene. The mechanism for the formation of (3) is not clear.

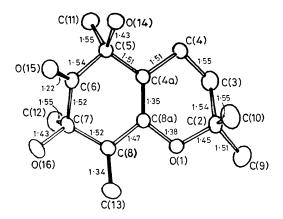


FIGURE 2. The molecular structure of (3) together with bond lengths (Å) for non-hydrogen atoms (mean e.s.d. 0.006 Å). The black bonds represent double bonds.

From the above observations, the following conclusions may reasonably be drawn. In the base-catalysed oxygenation of (1), the acyloin rearrangement of intermediate (2)gives (4).³ As has been suggested previously,³⁻⁵ the superoxide anion acts as a base since the common product (4) is obtained from oxygenation of (1) catalysed by KO_2 or $Bu^{\dagger}OK$. The attack of molecular oxygen following the carbanion formation at C(5) in (1) may initiate the base-catalysed oxygenation.⁴ Molecular oxygen is efficiently trapped in the presence of a base by α -tocopherol⁶ and its model compound (1). This may account for some of their antioxidant effects.

We thank the Ministry of Education, Science, and Culture of Japan for Grants-in-Aid for Scientific Research.

(Received, 20th July 1981; Com. 861.)

[†] The atomic co-ordinates are available on request from the Director of the Cambridge Crystallographic Data Centre, University Chemical Laboratory, Lensfield Road, Cambridge CB2 1EW. Any request should be accompanied by the full literature citation for this communication.

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