Oxidation of a Vitamin E Model Compound, 2,2,5,7,8-Pentamethylchroman-6-ol, with the t-Butylperoxyl Radical

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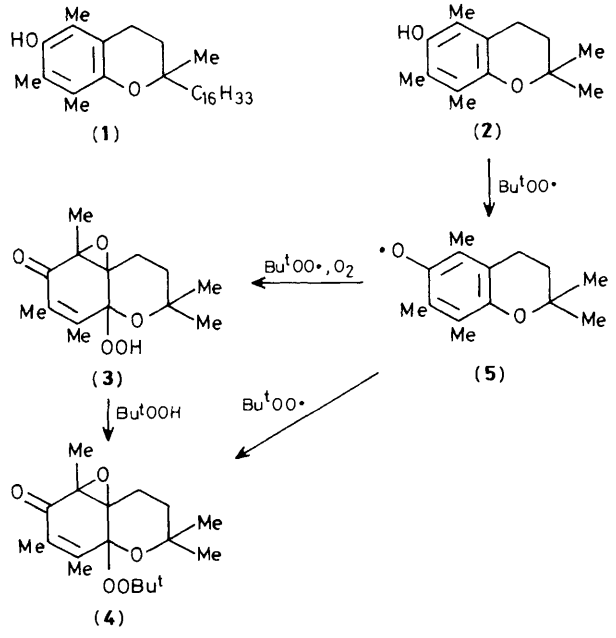
In a t-butylperoxyl radical-generating system, a vitamin E model compound, 2,2,5,7,8-pentamethylchroman-6-ol, was converted into 4a,5-epoxy-4a,5-dihydro-8a-hydroperoxy-2,2,5,7,8-pentamethylchroman-6(8a*H*)-one (**3**), the structure of which has been determined by *X*-ray crystallography, and 8a-t-butyldioxy-4a,5-epoxy-4a,5-dihydro-2,2,5,7,8-pentamethylchroman-6(8a*H*)-one (**4**).

Vitamin E, mainly α-tocopherol (**1**), is believed to be an important biological antioxidant against lipid peroxidation *in vivo*,[1] which is suspected to be responsible for ageing and some serious diseases, such as arteriosclerosis and cancer.[2,3]



Scheme 1. Possible pathways for the formation of (**3**) and (**4**).

However, details of its antioxidant mechanism are not fully understood. Although a molecule of vitamin E is kinetically thought to scavenge two molecules of peroxyl radicals in chain-breaking reactions against lipid peroxidation,[4] there are few reports on the analysis of reaction products from vitamin E in peroxyl radical-generating systems.[5]

We report here that in a t-butylperoxyl radical-generating system, in which the t-butyoxyl radical from the thermal decomposition of di-t-butyl peroxyoxalate (DBPO) reacts with t-butyl hydroperoxide to generate the t-butylperoxyl radical quantitatively,[6] the vitamin E model compound 2,2,5,7,8-pentamethylchroman-6-ol (**2**) was converted into the epoxychromanones (**3**) and (**4**).

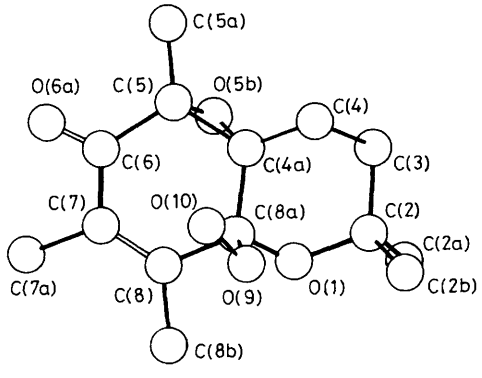


Figure 1. The *X*-ray crystal structure of (**3**). Double bonds are shown by double lines.

When (**2**) (50 μmol) was set aside at 50 °C for 5 h in benzene (1 ml) containing DBPO (22 μmol) and Bu^{t}OOH (1.0 mmol), (**3**) was obtained in 26% yield after purification by silica gel column chromatography. After reaction for 48 h, (**4**) was obtained in 44% yield.

The structure of (**3**) was determined by its spectral data and elemental analyses and confirmed by *X*-ray crystallographic analysis: $C_{14}H_{20}O_5$ (M_r 268.3); m.p. 84—85 °C; $\lambda_{max.}$ (MeCN) 246 nm (ε 6300); $\nu_{max.}$ (KBr) 1671 (C=O) and 3345 cm^{-1} (OOH); δ (^{1}H, $CDCl_3$) 1.36 (s, 3H), 1.47 (s, 6H), 1.54—1.64 (m, 1H), 1.82 (s, 3H), 1.92 (s, 3H), 1.96—2.04 (m, 1H), 2.50—2.65 (m, 2H), and 7.71 (s, 1H); δ (^{13}C, $CDCl_3$) 10.2 (q), 12.4 (q), 13.9 (q), 20.7 (t), 28.5 (q), 30.9 (q), 34.0 (t), 61.6 (s), 63.2 (s), 75.9 (s), 101.8 (s), 129.7 (s), 145.7 (s), and 196.2 (s).† The *X*-ray crystal structure of (**3**) is shown in Figure 1.

The structure of (**4**) (colourless oil) was determined by spectroscopic comparison with (**3**). Data were analogous, except for replacement of the ^{1}H n.m.r. singlet at δ 7.71 in (**3**) by a singlet (9H) at δ 1.03, and additional ^{13}C n.m.r. signals at 26.1 (3C, q) and 78.9 (s).

† *Crystal data:* Space group $P2_1/a$; a = 14.134(8), b = 17.867(11), c = 11.439(9) Å, β = 101.50(6) °, U = 2832 Å^3. The intensities of 985 reflections with $I \geq 2\sigma(I)$ were measured using graphite-monochromated Cu-K_α radiation, for $2\theta \leq 120°$. The structure was solved by the direct method and refined by block-diagonal least-squares to an R value of 0.098. Atomic co-ordinates, bond lengths and angles, and thermal parameters have been deposited at the Cambridge Crystallographic Data Centre. See Notice to Authors, Issue No. 1, 1986.

E.s.r. spectroscopy showed the presence of the 2,2,5,7,8-pentamethylchroman-6-oxyl radical (**5**) in the reaction mixture. Under degassed conditions in the reaction system (**2**) afforded (**4**) without (**3**). When DBPO was omitted, small amounts of (**3**) and (**4**) were obtained under aerobic conditions, but no products were detected after degassing the system. When Bu^{t}OOH was omitted, neither (**3**) nor (**4**) was obtained. When (**3**) was heated at 50 °C for 20 h in benzene containing Bu^{t}OOH (**4**) was obtained in almost quantitative yield. These findings suggest that the products are formed *via* pathways such as those shown in Scheme 1. Because the antioxidant behaviour of (**2**) is known to be quite similar to that of vitamin E,[4] (**1**) is expected to react with the peroxyl radical similarly to (**2**). The products obtained from (**1**) in this system are currently being studied.

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