Epoxidation of an α-Tocopherol Model Compound, 2,2,5,7,8-Pentamethylchroman-6-ol, with Potassium Superoxide; *X*-Ray Crystal Structure of 4a,5;7,8-Diepoxy-4a,7,8,8a-tetrahydro-8a-hydroxy-2,2,5,7,8-pentamethylchroman-6(5*H*)-one

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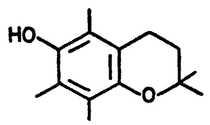
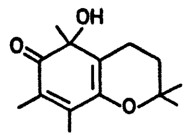
Summary An α-tocopherol model compound, 2,2,5,7,8-pentamethylchroman-6-ol, was oxidized in the presence of dicyclohexyl-18-crown-6 with KO_2 to give a diepoxide, whose structure was determined by spectroscopy and *X*-ray crystallography.

RECENTLY much attention has been given to the reaction of superoxide with organic compounds.[1] It is interesting to examine the reactivity of α-tocopherol (vitamin E), a naturally occurring antioxidant, towards superoxide since it is expected to have defence functions against oxidative and free-radical-induced damage in biological systems.[2] In fact, the α-tocopherol model compounds 6-hydroxy-2,5,7,8-tetramethylchroman-2-carboxylic acid[3] and 2,2,5,7,8-pentamethylchroman-6-ol (**1**)[4] react with superoxide anion (O_2^-) to afford 2-hydroxy-2-methyl-4-(3,5,6-trimethylbenzoquinon-2-yl)butanoic acid and 5-hydroxy-2,2,5,7,8-pentamethylchroman-6(5*H*)-one (**2**), respectively. We report here that the α-tocopherol model compound (**1**) is oxidized with potassium superoxide (KO_2) to give the diepoxide, 4a,5; 7,8-diepoxy-4a,7,8,8a-tetrahydro-8a-hydroxy-2,2,5,7,8-pentamethylchroman-6(5*H*)-one (**3**).

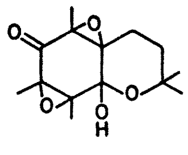
An acetonitrile solution of (**1**) (4 mmol) was added dropwise at 20 °C under oxygen to a solution of KO_2 (4 mmol) in acetonitrile and dicyclohexyl-18-crown-6 (6.8 mmol). The products were purified by silica gel column chromatography and by fractional crystallization. Compound (**3**), m.p. 89—90 °C, needles, was isolated in 23% yield; ν_{max} (KBr) 1725 (C=O) and 3445 cm^{-1} (OH); δ(^{1}H; CDCl$_3$) 1·27, 1·44, 1·47, 1·49, and 1·54 (all s, 3H), 1·58—2·16 (m, 4H), and 3·02 (s, 1H); δ(^{13}C; CDCl$_3$) 11·3 (q), 12·2 (q), 12·6 (q), 22·6 (t), 28·9 (q), 31·2 (q), 31·4 (t), 61·0 (s), 61·9 (s), 64·8 (s), 66·8 (s), 73·9 (s), 94·0 (s), and 200·1 p.p.m. (s); *m/e* 268 (M^+); satisfactory elemental analyses were obtained. Its spectral properties are in accordance with the assigned structure. To confirm its structure, a single crystal *X*-ray diffraction analysis was carried out. *Crystal data:* (**3**), $C_{14}H_{20}O_5$, space group *R*3c, lattice constants (hexagonal unit cell) $a = b = 26·577(15)$, $c = 10·423(6)$ Å, $\gamma = 120°$, $Z = 18$. The crystal structure was solved by the direct method and refined by the block-diagonal least-squares method including anisotropic thermal parameters.



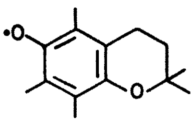
(1)



(2)



(3)



(4)

The final R value for 1042 observed structure factors (up to $2\theta = 138°$) was 0·07 without hydrogen atoms. The lattice constants and intensities were measured on a four-circle X-ray diffractometer using graphite monochromated Cu-K_α radiation, and an ORTEP drawing of the structure is in the Figure.†

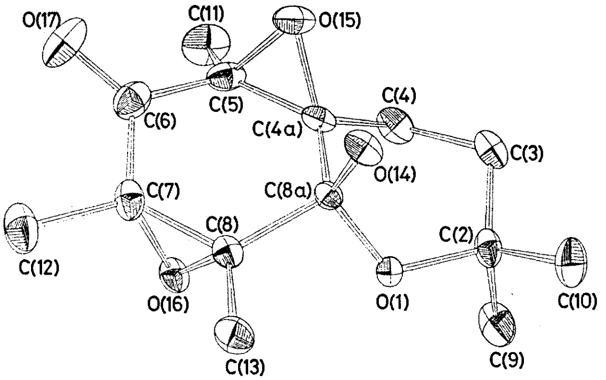


FIGURE. ORTEP plot of the molecular structure of the diepoxide (**3**) with thermal ellipsoids drawn at the 30% probability level.

Under the conditions employed here, five minor products were obtained. According to their n.m.r. data, two of them are known to be 1,1-dimethyl-3-(3,5,6-trimethylbenzoquinon-2-yl)propanol[6] and its corresponding 2,3-epoxide,[7] and the other compounds are suggested to be 4a,8a-dihydro-4a-hydroxy-2,2,6,7,8a-pentamethylchroman-5,8-dione, and its corresponding 6,7-epoxide, and an unknown epoxide.

Since (**3**) was also obtained in the presence of molecular oxygen (O_2) from the reaction of (**1**) in acetonitrile with O_2^- generated electrochemically by the method reported previously[8] (no data were given), O_2^- must be responsible for the formation of (**3**) from (**1**) and KO_2. However, the absence of O_2 markedly inhibited this reaction. Further, the chromanoxyl radical (**4**) was observed by e.s.r. spectrometry immediately after the addition of (**1**) to electrochemically generated O_2^-.[9] Presumably, (**3**) is produced from the reaction of a tautomer of the chromanoxyl radical (**4**) (*i.e.*, 6,8a-dihydro-6-oxochroman-8a-yl) with O_2. Very recently it was shown that solutions of O_2^- behave towards phenolic compounds as if they were strongly basic.[10] In addition, 2,3; 5,6-diepoxy-4-hydroxy-2,4,6-tri-t-butylcyclohexanones are formed by the action of O_2 in the base-catalysed oxygenation of t-butylphenols.[11] These data suggest that O_2^- acts as a base in the initial step of the oxidation of (**1**), and that (**4**) is formed from the chromanoxyl anion.

As described previously,[4] the reaction of (**1**) and KO_2 suspended in tetrahydrofuran gives (**2**), a completely different product from (**3**). In this case, O_2 seems to react specifically with a tautomer (5,6-dihydro-6-oxochroman-5-yl) of the radical (**4**). If O_2^- acts as a base, it is plausible that the formation of different products depends on the reaction conditions, because very selective reactions depending on solvent and temperature have been reported in the base-catalysed oxygenation of phenols.[12]

(*Received*, 19*th September* 1978; *Com.* 1011.)

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† 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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