Potassium *tert*-Butoxide-catalysed Oxygenations of Vitamin E and its Model Compound 2,2,5,7,8-Pentamethylchroman-6-ol

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Oxygenation of vitamin E [**1a**, (*RRR*)-α-tocopherol] in tetrahydrofuran in the presence of potassium *tert*-butoxide under oxygen gave products **2a**, **3a**, **4a**, **5a** and **6a** arising from oxidation of the aromatic moiety. Under similar conditions, a vitamin E model compound, 2,2,5,7,8-pentamethylchroman-6-ol **1b**, gave the analogous products **2b**, **3b**, **4b**, **5b** and **6b**. Initial attack at the 5 position leads to the acyloin **6b**, which is converted into the isomer **5b**. The hydroperoxide **7b** is derived from the acyloin **5b** and transformed into the 7-methylene compound **3b**. The 8-methylene compound **2b** is converted into the carbolactone **4b**. The molecular structures of compounds **2b**, **3b**, **4b** and **7b** were confirmed by X-ray crystallographic analysis. Possible reaction pathways for the product formation and relationships between the product distribution and the basicity of reaction media are discussed.

It is believed that the importance of vitamin E, a main component of which is (*RRR*)-α-tocopherol **1a**, is to function as a biological antioxidant against lipid peroxidation *in vivo*.[1,2] It is certain that α-tocopherol is an efficient chain-breaking antioxidant which traps the peroxyl radical, the chain carrier of lipid peroxidation, and terminates its chain reaction.[3]

There is the possibility, however, that vitamin E plays an important role in scavenging not only the peroxyl radical[4–7] but also a variety of reactive species resulting in oxidative stress in biological systems. For example, α-tocopherol reacts with various types of radicals such as alkyl,[8–11] alkoxyl,[12] phenoxyl,[13] benzoyloxyl,[14,15] and superoxide.[16–24] α-Tocopherol quenches singlet molecular oxygen into triplet molecular oxygen[25–27] and also reacts chemically with singlet molecular oxygen to give a hydroperoxide[28–30] and other products.[31–34] Further, α-tocopherol is easily oxidized by ozone to give a unique spiro compound[35] and other products.[35,36] Presumably, the wide reactivity of α-tocopherol is one of the reasons it is an excellent biological protector against oxidative stress. Its antioxidant mechanism, however, is not fully understood. Extensive studies of its oxidation reactions are necessary for the elucidation of vitamin E's functions.

α-Tocopherol is oxidized at a slow rate in air. Previously, we reported that a vitamin E model compound, 2,2,5,7,8-pentamethylchroman-6-ol **1b**, was oxygenated in the presence of potassium *tert*-butoxide (Bu^{t}OK).[37] We have extensively studied the Bu^{t}OK-catalysed oxygenations of compounds **1a** and **1b**. We report here that in tetrahydrofuran (THF) in the presence of Bu^{t}OK, α-tocopherol **1a** is converted into three novel, unique compounds, dihydroxy-8-methylene-6-oxo compound **2a**, dihydroxy-7-methylene-5-oxo compound **3a**, and 8-methylenecarbolactone **4a**, in addition of two known compounds, the 6-hydroxy-5-oxo compound **5a** and 5-hydroxy-6-oxo compound **6a**, and that, under similar reaction conditions, compound **1b** is also converted into products **2b**, **3b**, **4b**, **5b** and **6b**, corresponding to the above compounds, as well as the hydroxyhydroperoxy-7-methylene-5-oxo compound **7b**. Further, we propose possible reaction pathways for the formation of the products and discuss relationships between the product distribution and the basicity of the reaction media.

Results

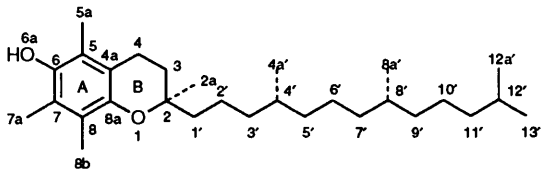
Oxygenation of a Vitamin E Model Compound **1b** *in Tetrahydrofuran in the Presence of Potassium* tert-*Butoxide*.—A solution of Bu^{t}OK in THF was added dropwise to a stirred solution of the model compound **1b** in THF on an ice–water-bath under oxygen. When an equimolar amount of Bu^{t}OK to that of the substrate was used, four products, **2b**, **4b**, **5b** and **6b**, were isolated by silica gel column chromatography. The yields of **2b**, **4b**, **5b** and **6b** were 4, 17, 16 and 8%, respectively (Table 1). When the oxygenation was carried out with a four-fold molar amount of Bu^{t}OK to that of the substrate, compounds **2b**, **3b**, **4b**, **6b** and **7b** were produced in 2, 5, 37, 9 and 4% yield, respectively (Table 1).

The elemental analysis and high-resolution mass (MS) spectral data indicated that compound **2b** had a molecular formula of $C_{14}H_{20}O_4$ corresponding to that of substrate **1b** with two additional oxygen atoms. The proton and carbon-13 nuclear magnetic resonance (^{1}H and ^{13}C NMR), infrared (IR), and ultraviolet (UV) spectra revealed that compound **2b** had four methyl groups, an exocyclic methylene group, a ketonic group, two hydroxy groups, two adjacent methylene groups, three quaternary sp^3 carbon atoms each bonded to one oxygen atom, three sp^2 carbon atoms bearing no hydrogen atoms, and a conjugated diene. These results suggest that compound **2b** is 7,8-dihydro-5,7-dihydroxy-2,2,5,7-tetramethyl-8-methylenechroman-6(5*H*)-one.

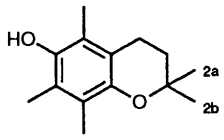
The structure of compound **2b** was confirmed by X-ray crystallographic analysis as has been communicated.[37] Fig. 1 shows the molecular structure. The crystal data are given in the Experimental section. Interestingly, the crystal of compound **2b** consists of only pairs of the enantiomers having the hydroxy groups at the 5 and 7 positions in a *cis* configuration (see Fig. 1).

The high-resolution MS spectral data indicated that compound **3b** had a structure, with formula $C_{14}H_{20}O_4$, isomeric with that of compound **2b**. The ^{1}H and ^{13}C NMR, IR and UV spectra revealed that compound **3b** had four methyl groups, an exocyclic methylene group, a ketonic group, two hydroxy groups, two adjacent methylene groups, three quaternary sp^3 carbon atoms each bonded to one oxygen atom, three sp^2 carbon atoms bearing no hydrogen atoms, and a conjugated enone. These results are consistent with the presumption that compound **3b** is 7,8-dihydro-6,8-dihydroxy-2,2,6,8-tetramethyl-7-methylenechroman-5(6*H*)-one.

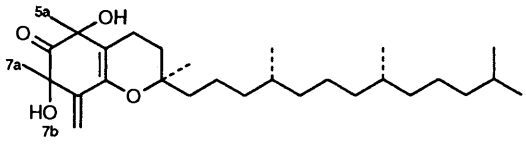
The structure **3b** was confirmed by X-ray crystallographic analysis. Fig. 2 shows the molecular structure. The crystal data are given in the Experimental section. The crystal of **3b** also



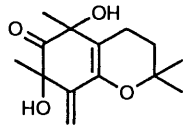
1a



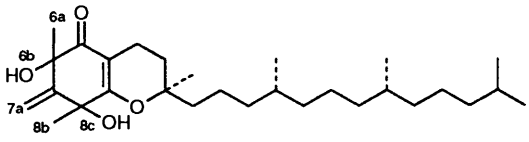
1b



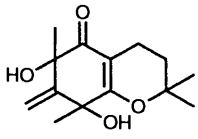
2a



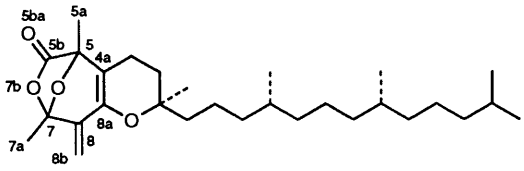
2b



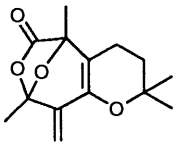
3a



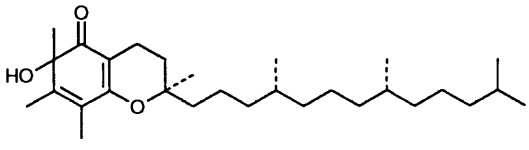
3b



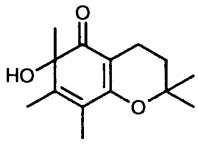
4a



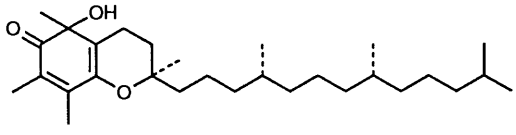
4b



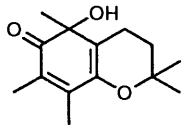
5a



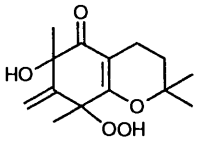
5b



6a



6b



7b

consists of only pairs of the enantiomers having two hydroxy groups at the 6 and 8 positions in a *cis* configuration.

The high-resolution MS spectral data indicated that compound **4b** had a molecular formula of $C_{14}H_{18}O_4$ corresponding to that of compound **2b** or **3b** minus two hydrogen atoms. The ^1H and ^{13}C NMR, IR and UV spectra revealed that compound **4b** had four methyl groups, an exocyclic methylene group, a cyclic lactone group, two adjacent methylene groups, three

Table 1 Reactions of compounds **1**, **2**, **5** and **7** in the presence of potassium *tert*-butoxide

Comp.	Molar quotient Bu^{t}OK/comp.	Reaction conditions		Recovery (%) starting material	Yield (%)										
		T/°C	t/h		**2a**	**3a**	**4a**	**5a**	**6a**	**2b**	**3b**	**4b**	**5b**	**6b**	**7b**
1a	1	5	1.25				4	16[c]	28[e]						
1a	4	5	1.25		3	16[a]	15	10[d]							
5a	2	5	1.5	29		20–22[b]									
1b	1	0	1.25							4		17	16	8	
1b	4	0	1.25							2	5	37		9	4
2b	2	5	1.5									26			
5b	2	7	1.0	15							13				16
7b	2	0	2.0	46							28				

[a] The total yield of **3aα** (8%) and **3aβ** (8%). [b] The yield of **3aα** (20%) or **3aβ** (22%). [c] The total yield of **5aα** (5%) and **5aβ** (11%). [d] The total yield of **5aα** (5%) and **5aβ** (5%). [e] The total yield of **6aα** (14%) and **6aβ** (14%).

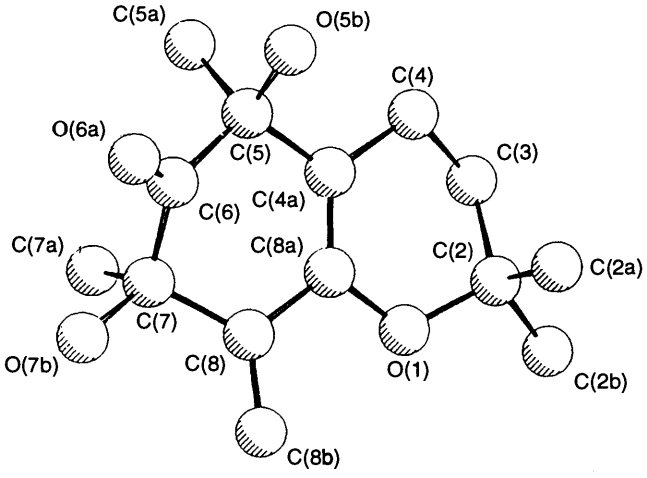


Fig. 1 X-Ray molecular structure of compound **2b**

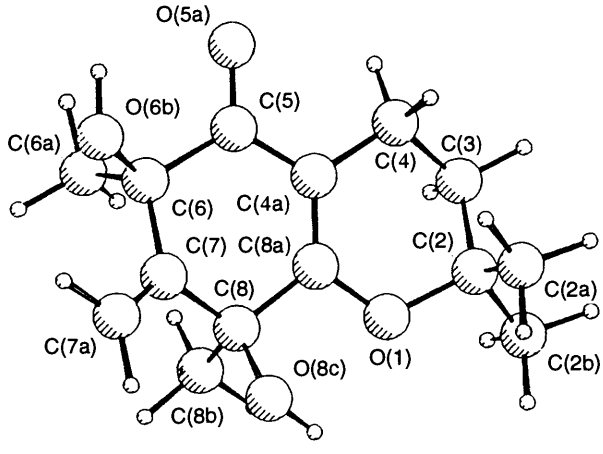


Fig. 2 X-Ray molecular structure of compound **3b**

quaternary sp^3 carbon atoms each bonded to one or two oxygen atoms, three sp^2 carbon atoms bearing no hydrogen atoms, and a conjugated diene. These data suggested that compound **4b** was 5,6,7,8-tetrahydro-2,2,5,7-tetramethyl-8-methylene-6-oxachromane-5,7-carbolactone.

The structure of compound **4b** was conclusively determined by X-ray crystallographic analysis. Fig. 3 shows the molecular structure. The crystal data are given in the Experimental section. The crystal of compound **4b** consists of pairs of the enantiomers on the molecular plane.

The high-resolution MS spectral data indicated that compound **7b** had a molecular formula of $C_{14}H_{20}O_5$ corresponding to that of compound **2b** or **3b** with an additional oxygen atom.

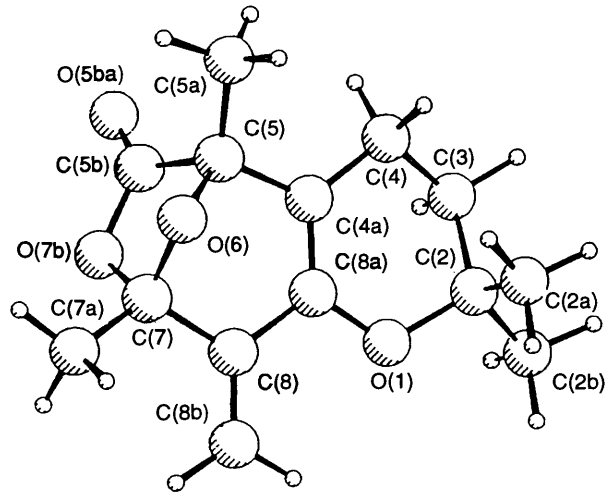


Fig. 3 X-Ray molecular structure of compound **4b**

The ^{1}H and ^{13}C NMR, IR and UV spectra revealed that compound **7b** has four methyl groups, an exocyclic methylene group, a ketonic group, a hydroxy group, a hydroperoxy group, two adjacent methylene groups, three quaternary sp^3 carbon atoms each bonded to one or two oxygen atoms, three sp^2 carbon atoms bearing no hydrogen atoms, and a conjugated enone. These results indicated that compound **7b** was 7,8-dihydro-8-hydroperoxy-6-hydroxy-2,2,6,8-tetramethyl-7-methylenechroman-5(6*H*)-one corresponding to that of compound **3b**, a hydroxy group of which was substituted for a hydroperoxy group. The structure of compound **7b** differs from that of compound **3b** only in a substituent at C-8; at that position, compound **7b** has a hydroperoxy group and compound **3b** has a hydroxy group.

The structure **7b** was confirmed by X-ray crystallographic analysis. Fig. 4 shows the molecular structure. The crystal data are given in the Experimental section. Interestingly, the crystal of compound **7b** consists of only pairs of the enantiomers having a hydroxy group at the 6 position and a hydroperoxy group at the 8 position in a *cis* configuration.

In order to determine the positions of the exocyclic methylene groups in compounds **2b**, **3b**, **4b** and **7b**, we performed oxygenations of [5a-$^2H_3$]**1b** and [7a-$^2H_3$]**1b** in THF with a three-fold molar amount of Bu^{t}OK to that of each substrate. The oxygenations of [5a-$^2H_3$]**1b** and [7a-$^2H_3$]**1b** did not result in loss of the methylene signals in the ^{1}H NMR spectra of compounds **2b** and **4b**, while the oxygenation of [7a-$^2H_3$]**1b** resulted in loss of the methylene signals in the ^{1}H NMR spectra of compounds **3b** and **7b**. Therefore, the methylene groups are assigned to the 8 positions of compounds **2b** and **4b** and the 7 positions of compounds **3b** and **7b**.

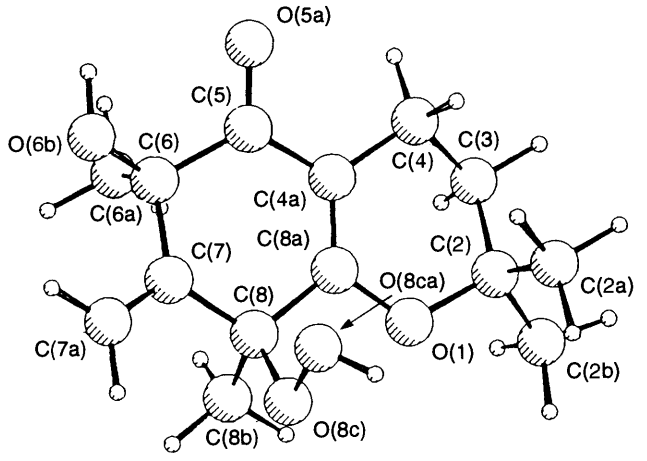


Fig. 4 X-Ray molecular structure of compound **7b**

The ^{13}C chemical shifts of the methylene carbon atoms at C-3 and -4 are 32.2–32.4 and 17.1–18.1, respectively, for compounds **2b**, **4b** and **6b**, and 31.5–31.7 and 15.5–16.6, respectively, for compounds **3b**, **5b** and **7b** (see the Experimental section). The methylene carbon atoms of compounds **3b**, **5b** and **7b** resonate upfield from those of compounds **2b**, **4b** and **6b**. Presumably, the former carbon atoms may receive some shielding effect due to the adjacent α,β-unsaturated ketonic groups.

Intermediacy of Compounds **2b**, **5b** *and* **7b** *in the Formation of Products.*—In order to ascertain whether or not compounds **2b**, **3b**, **4b**, **5b**, **6b** and **7b** are end-products in the oxygenation of substrate **1b**, we examined their fate under the reaction conditions described above. When allowed to stand in THF in the presence of a two-fold molar amount of Bu^{t}OK to each substrate at 5 °C under oxygen for 1.5 h, compound **2b** gave lactone **4b** in 26% yield (Table 1). Further, under similar reaction conditions, compound **5b** gave both diol **3b** and hydroperoxide **7b** in 13 and 16% yield, respectively, while hydroperoxide **7b** gave diol **3b** in 28% yield (Table 1). These results showed that compound **2b** was a precursor of lactone **4b**, and that compound **5b** was a precursor of hydroperoxide **7b**, which in turn was a precursor of diol **3b**.

Uptake of Oxygen by Products **2b** *and* **5b**.—During conversion into compound **4b**, 0.041 mmol of diol **2b** absorbed 0.014 mmol of molecular oxygen. During conversion into compounds **7b** and **3b**, 0.042 mmol of the acyloin **5b** absorbed 0.03 mmol of molecular oxygen. These results showed that these conversions were oxygenations.

Oxygenation of (RRR)-α-*Tocopherol* **1a** *in Tetrahydrofuran in the Presence of Potassium* tert-*Butoxide.*—A solution of Bu^{t}OK in THF was added dropwise to a stirred solution of compound **1a** in THF at 5 °C under oxygen. When an equimolar amount of Bu^{t}OK to that of the substrate was used, five products, **4a**, **5aα**, **5aβ**, **6aα** and **6aβ**, were isolated by silica gel column chromatography. The yields of compounds **4a**, **5aα**, **5aβ**, **6aα** and **6aβ** were 4, 5, 11, 14 and 14%, respectively (Table 1). When oxygenation of compound **1a** was carried out with a four-fold molar amount of Bu^{t}OK to that of the substrate as described above, six products, **2a**, **3aα**, **3aβ**, **4a**, **5aα** and **5aβ**, were obtained in 3, 8, 8, 15, 5 and 5% yield, respectively (Table 1).

It was found that compounds **5aα** and **5aβ** were identical with previously reported (2*R*,6*S*,4′*R*,8′*R*)- and (2*R*,6*R*,4′*R*,8′*R*)-6-hydroxy-2,6,7,8-tetramethyl-2-(4′,8′,12′-trimethyltridecyl)-chroman-5(6*H*)-one, respectively, and that compounds **6aα** and **6aβ** were identical with (2*R*,5*R*,4′*R*,8′*R*)- and (2*R*,5*S*,4′*R*,8′*R*)-5-hydroxy-2,5,7,8-tetramethyl-2-(4′,8′,12′-trimethyltridecyl)-chroman-6(5*H*)-one, respectively.[19]

The spectral data indicated that the partial structures of compounds **2a**, **3a** and **4a** without an isoprenoid side-chain were identical with those of compounds **2b**, **3b** and **4b**, respectively, without a methyl group at the 2-position: that is, compound **2a** is 7,8-dihydro-5,7-dihydroxy-2,5,7-trimethyl-8-methylene-2-(4′,8′,12′-trimethyltridecyl)chroman-6(5*H*)-one, compound **3a** is 7,8-dihydro-6,8-dihydroxy-2,6,8-trimethyl-7-methylene-2-(4′,8′,12′-trimethyltridecyl)chroman-5(6*H*)-one, and lactone **4a** is 5,6,7,8-tetrahydro-2,5,7-trimethyl-8-methylene-2-(4′,8′,-12′-trimethyltridecyl)-6-oxachromane-5,7-carbolactone.

From an analogy to the structure of the model compound **2b**, compound **2a** may have two hydroxy groups at C-5 and -7 in a *cis* configuration. Compound **2a** exhibits a Cotton effect in its circular dichroism (CD) spectrum (see the Experimental section). Presumably, compound **2a** may be either (2*R*,5*S*,7*R*,4′*R*,8′*R*)- or (2*R*,5*R*,7*S*,4′*R*,8′*R*)-7,8-dihydro-5,7-dihydroxy-2,5,7-trimethyl-8-methylene-2-(4′,8′,12′-trimethyltridecyl)chroman-6(5*H*)-one.

Compounds **3aα** and **3aβ** both are 7,8-dihydro-6,8-dihydroxy-2,6,8-trimethyl-7-methylene-2-(4′,8′,12′-trimethyltridecyl)-chroman-5(6*H*)-one. From an analogy to the structure of model compound **3b**, compound **3a** also may have two hydroxy groups at C-6 and -8 in a *cis* configuration. Compounds **3aα** and **3aβ** exhibit Cotton effects in their CD spectrum (see the Experimental section). Furthermore, compounds **3aα** and **3aβ** were found to be derived from dienones **5aα** and **5aβ**, respectively, as shown below. Since these configurations at the 6-position are presumed to remain unchanged during the conversion of acyloin **5a** into diol **3a**, it follows that compound **3aα** has the 6*S* configuration and its isomer **3aβ** has the 6*R* configuration. Thus, isomers **3aα** and **3aβ** may be (2*R*,6*S*,8*R*,4′*R*,8′*R*)- and (2*R*,6*R*,8*S*,4′*R*,8′*R*)-7,8-dihydro-6,8-dihydroxy-2,6,8-trimethyl-7-methylene-2-(4′,8′,12′-trimethyltridecyl)chroman-5(6*H*)-one, respectively.

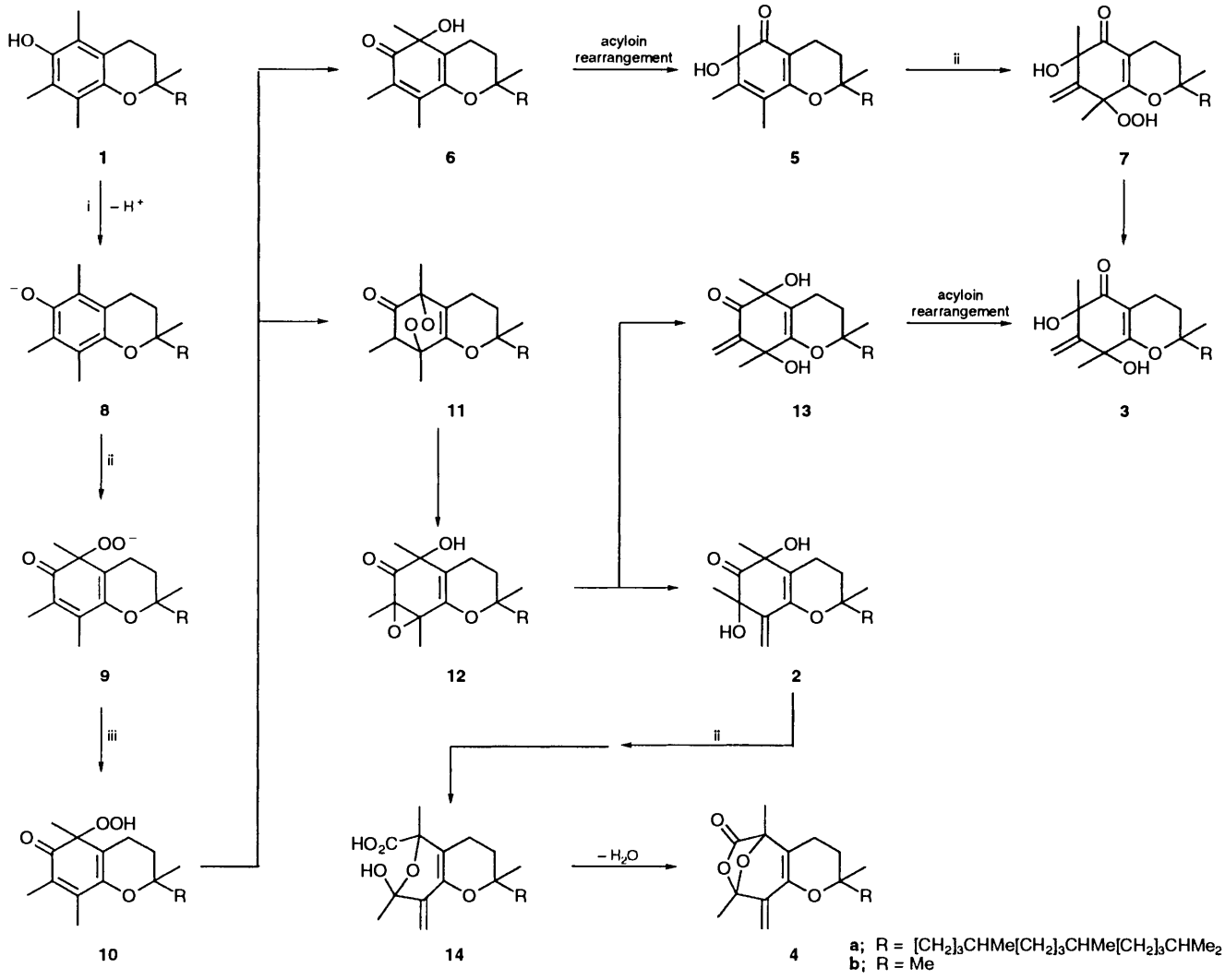
As described above, lactone **4a** is assigned to be 5,6,7,8-tetrahydro-2,5,7-trimethyl-8-methylene-2-(4′,8′,12′-trimethyltridecyl)-6-oxachromane-5,7-carbolactone. However, compound **4a** is presumed to be a mixture of a pair of epimers, because it exhibits several coupled signals in the ^{13}C NMR spectrum (see the Experimental section). This suggests that compound **4a** is a 1:1 mixture of (2*R*,5*R*,7*R*,4′*R*,8′*R*)- and (2*R*,5*S*,7*S*,4′*R*,8′*R*)-5,6,7,8-tetrahydro-2,5,7-trimethyl-8-methylene-2-(4′,8′12′-trimethyltridecyl)-6-oxachromane-5,7-carbolactone, whose structures without both an isoprenoid side-chain and a methyl group at the 2-position are a pair of antipodes.

Intermediacy of Acyloin **5a** *in the Formation of Products.*—When stored in THF in the presence of a two-fold molar amount of Bu^{t}OK to that of each substrate at 5 °C under oxygen for 1.5 h, acyloin **5aα** gave diol **3aα** in 20% yield and acyloin **5aβ** gave diol **3aβ** in 22% yield. These results indicated that compounds **5aα** and **5aβ** are precursors of diols **3aα** and **3aβ**, respectively.

Discussion

According to the observations described above, we propose possible reaction pathways for the Bu^{t}OK-catalysed oxygenations of α-tocopherol and the model compound in aprotic solvents as shown in Scheme 1.

Under the basic requirement that Bu^{t}OK be solubilized in an aprotic solvent, substrates are converted into the chromanolate anions **8**. One molecule of molecular oxygen is added to the anions at the 5-position to give 6-oxo-5-peroxide anions **9** which are convertible into the 6-oxo-5-hydroperoxides **10**. However, there is another possibility, that electron transfer takes place from the chromanolate anions **8** to molecular oxygen, leading to the superoxide radical and the corresponding



Scheme 1 Possible reaction pathways for the formation of reaction products. *Reagents:* i, base; ii, O_2; iii, H^+.

chromanoxyl radical, which combine to give 6-oxo-5-peroxide anions **9**.

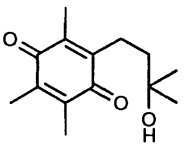
The hydroperoxides **10** give rise to the 5-hydroxy-6-oxo compounds **6**, which are transformed into the 6-hydroxy-5-oxo compounds **5** through an acyloin rearrangement. The oxygenation of the acyloins **5** gives the 8-hydroperoxy-6-hydroxy-7-methylene-5-oxo compounds **7**, which are converted into the 6,8-dihydroxy-7-methylene-5-oxo compounds **3**.

On the other hand, the hydroperoxides **10** could be cyclized to give the 5,8-epidioxides **11**, which are transformed into the 7,8-epoxy-5-hydroxy compounds **12**. Compounds **12** could rearrange to form both the 5,7-dihydroxy-8-methylene compounds **2** and the 5,8-dihydroxy-7-methylene compounds **13**, each of which has two hydroxy groups in a *cis* configuration. Acyloin rearrangement of the compounds **13** may give rise to the 7-methylene-5-oxo compounds **3** having two hydroxy groups in a *cis* configuration, because the migration of a methyl group in acyloin rearrangements occurs only on one side of the molecular plane.[19] Thus, this may be an additional possible pathway for the formation of the 7-methylene-5-oxo compounds **3**.

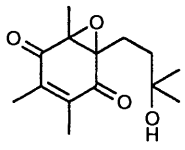
Interestingly, either 5,7-dihydroxy-8-methylene-6-oxo compound **2b** or 6,8-dihydroxy-7-methylene-5-oxo compound **3b** has two hydroxy groups in a *cis* configuration, and 8-hydroperoxy-6-hydroxy-7-methylene-5-oxo compound **7b** also has hydroxy and hydroperoxy groups in a *cis* configuration. As discussed above, on the basis of the assumption that compounds **2** may be derived from the epoxides **12** *via* the epidioxides **11**, it is plausible that the configuration of the two hydroxy groups in compound **2b** is *cis* (Fig. 1). In addition, it is quite reasonable that diol **3b** has two hydroxy groups in a *cis* configuration, because this compound is derived from hydroperoxide **7b** also having two hydroxy groups in a *cis* configuration. It is unknown, however, why only compound **7b** having hydroxy and hydroperoxy groups in a *cis* configuration is formed and not that having hydroxy and hydroperoxy groups in a *trans* configuration. In addition, 6-hydroxy-5-oxo compounds **5aα** and **5aβ** are stereospecifically converted into diols **3aα** and **3aβ**, respectively. Thus, it is evident that the conversion of hydroperoxides **7** into diols **3** proceeds stereospecifically.

Further, acyloins **2** are converted into carbolactones **4** by oxidative ring cleavage followed by dehydrative recyclization. Details of the mechanism of oxygenation of compounds **2** are unclear, although hydroxy acids **14** are believed to be formed as intermediates. It seems reasonable that the final step in the formation of lactones **4** should be recyclization of hydroxy acids **14** by standard esterification, because lactone **4b** can be extracted with diethyl ether from an acidic aqueous reaction mixture but not from a basic aqueous reaction mixture. The structure of lactones **4** is unique. Details of the mechanism of their formation still remain to be clarified.

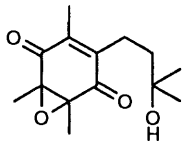
We have already reported that α-tocopherol **1a**, as well as the model compound **1b**, is oxygenated in an aprotic solvent with potassium superoxide and that the superoxide radical acts in this oxygenation as a base.[19,21] It has been observed that in



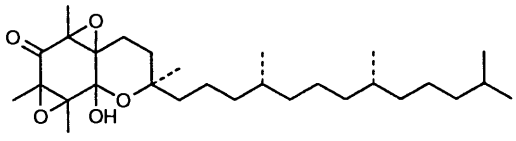
15b



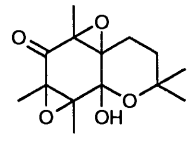
16b



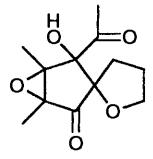
17b



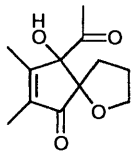
18a



18b



19b



20b

an aprotic solvent in the presence of suspended potassium superoxide, α-tocopherol **1a** gives products **4a**, **5a** and **6a**, and model compound **1b** gives compounds **5b** and **6b**.[19] In a previous paper, compound **4a** was referred to as the unknown compound **7**.[19] On the other hand, it has been found that in an aprotic solvent in the presence of potassium superoxide solubilized with dicyclohexano-18-crown-6, α-tocopherol **1a** gives a diepoxide, 4a,5;7,8-diepoxy-4a,7,8,8a-tetrahydro-8a-hydroxy-2,5,7,8-tetramethyl-2(4′,8′,12′-trimethyltridecyl)chroman-6(5*H*)-one **18a**, and compound **1b** gives a ring-opened compound, 2-(3-hydroxy-3-methylbutyl)-3,5,6-trimethyl-*p*-benzoquinone **15b**, two ring-opened epoxides, 2,3-epoxy-2-(3-hydroxy-3-methylbutyl)-3,5,6-trimethyl-*p*-benzoquinone **16b** and 2,3-epoxy-5-(3-hydroxy-3-methylbutyl)-2,3,6-trimethyl-*p*-benzoquinone **17b**, a diepoxide, 4a,5;7,8-diepoxy-4a,7,8,8a-tetrahydro-8a-hydroxy-2,2,5,7,8-pentamethylchroman-6(5*H*)-one **18b**, and two recyclized spiro compounds, 9-acetyl-7,8-epoxy-9-hydroxy-2,2,7,8-tetramethyl-1-oxaspiro[4.4]nonan-6-one **19b** and 9-acetyl-9-hydroxy-2,2,7,8-tetramethyl-1-oxaspiro[4.4]non-7-en-6-one **20b** (and not the [4.5] structures as erroneously stated in a previous paper[21]).

These results taken together, it seems that the reaction pathways of the oxygenation of substrates **1a** and **1b** change in relation to the polarity and basicity of the reaction medium. In THF containing suspended potassium superoxide, oxygenation and acyloin rearrangement take place. In THF containing Bu^{t}OK, oxygenation, acyloin rearrangement, ring cleavage in ring A, and recyclization take place (see structures **1a** and **1b** for rings A and B). In acetonitrile containing potassium superoxide chelated by dicyclohexano-18-crown-6, oxygenation, ring cleavage in rings A and B, recyclization, and epoxidation take place.

In basic media, compounds **1** were found to be very sensitive to ground-state molecular oxygen. As shown in Scheme 1, the base-catalysed oxygenation of compounds **1** appears to proceed by an ionic mechanism to give stable products. Thus, vitamin E may function as an oxygen trap under basic conditions.

Experimental

General.—All m.p.s are uncorrected and were determined with a Yanagimoto microapparatus (Yanagimoto Seisakusho, Kyoto, Japan). UV spectra were measured on a Cary 119 spectrometer (Varian Associates, Palo Alto, CA, USA). IR and CD spectra were recorded on JASCO IR-2 and JASCO J-500A spectrometers (Japan Spectroscopic Company, Tokyo, Japan), respectively. ^{1}H and ^{13}C NMR spectra were taken on a Varian VXR-400S spectrometer (Varian Associates), using 99.8% $CDCl_3$ as both solvent and internal standard (trace $CHCl_3$: δ_H 7.24 for ^{1}H, and δ_C 77.0 for ^{13}C). *J*-Values are given in Hz. ^{13}C NMR measurements were carried out under the broad-band proton-decoupling mode and by means of DEPT pulse sequences for the determination of multiplicities of ^{13}C signals. Mass spectra were taken on a JEOL JMS-DX303 spectrometer (Japan Electron Optical Laboratories, Oome, Japan). Analytical and preparative high-performance liquid chromatography (HPLC) were performed on a Varian 5560 high-performance liquid chromatograph (Varian Associates, Walnut Creek, CA, USA) and a Waters PrepLC System 500A equipped with a PrepPAK-500 silica column (Waters Chromatography Corporation, Milford, MA, USA), respectively. For the assay of oxygen uptake, a pressure change in a sealed flask containing a reaction mixture were measured with a pressure-sensing apparatus[5] composed of a model PLC pressure transducer (Celesco Transducer Product Inc., Canoga Park, CA, USA) and a model SPX-A DC amplifier (Tsukasa Sokken Co., Ltd., Tokyo, Japan). (*RRR*)-α-Tocopherol **1a** was purified, by HPLC, from a mixture of the isomers obtained from Sigma Chemical Company (St. Louis, MO, USA). A vitamin E model compound, 2,2,5,7,8-pentamethylchroman-6-ol **6b**, was synthesized by the method of Nilsson *et al.*[38] and was recrystallized from hexane. The [5a-$^2H_3$]- and [7a-$^2H_3$]-vitamin E model compounds were prepared as described previously.[19] Silica gel (Wakogel C-200 for column chromatography), Bu^{t}OK, and THF were purchased from Wako Pure Chemical Industries (Osaka, Japan). For purification, Bu^{t}OK was sublimed, while THF was stored over sodium hydroxide pellets for several days, was distilled, and then was dried over sodium wire before use.

X-Ray Crystallography.—The crystal structures were solved by the direct methods (MULTAN) and refined by block-diagonal-matrix least-squares. Intensities were collected on a Philips PW1100 diffractometer using graphite-monochromated

Cu-Kα radiation. The perspective views of the molecular structures were drawn by the PLUTO program.[39]

For compound **2b**, a total of 2479 reflections were observed in the 2θ range 6–156° above the 2σ(*I*) level. No appreciable decrease in intensity was found. The final *R*-value was 0.098 without hydrogen-atom contributions. The 14 carbon and 4 oxygen atoms were refined with the assumption of anisotropic thermal vibrations. The perspective view of the molecule is shown in Fig. 1. Crystal data: $C_{14}H_{20}O_4$; M = 252.3; crystal habit: thick plates; triclinic; space group $P\bar{1}$; $Z = 2$; D_{calc} = 1.216 g cm^{-3}; a = 13.135(8), b = 9.167(6), c = 6.226(4) Å; α = 106.08(6), β = 102.35(6), γ = 97.65(6)°; V = 689 Å^3.

For compound **3b**, a total of 2188 reflections (out of a possible 3137 reflections) were measured in the 2θ range 6–156° above 2σ(*I*). The structure was refined to an *R*-value of 0.056. The 14 carbon and 4 oxygen atoms were refined with the assumption of anisotropic thermal vibrations. The 20 hydrogen atoms were refined with the assumption of isotropic thermal vibrations. The hydrogen atoms were found on the difference electron-density map and were located at calculated positions. The maximum residual electron density found on the final difference electron-density map was 0.4 e Å^{-3}. The perspective view of the molecule is shown in Fig. 2. The crystal data are given below: $C_{14}H_{20}O_4$; M = 252.3; crystal habit: prisms; crystal size 0.18 × 0.15 × 0.65 mm; monoclinic; space group $P2_1/a$; $Z = 4$; D_{calc} = 1.272 g cm^{-3}; a = 11.485(6), b = 15.812(8), c = 7.511(5) Å; β = 105.08(6)°; V = 1317 Å^3; μ for Cu-Kα = 7.18 cm^{-1}.

For compound **4b**, a total of 2044 reflections (out of a possible 2909 reflections) were measured in the 2θ range 6–156° above 2σ(*I*). Intensities decreased upon X-ray exposure. The decrease in *F* during a 25 h measurement was 10.5%, but it was calibrated on the basis of the intensities of three standard reflections measured at every 60 min. The structure was refined to an *R*-value of 0.059. The number of reflections used for the refinement was 2049. The 14 carbon and 4 oxygen atoms were refined with the assumption of anisotropic thermal vibrations. The 18 hydrogen atoms were refined with the assumption of isotropic thermal vibrations. The hydrogen atoms were found on the difference electron-density map and were located at calculated positions. The maximum residual electron density found on the final difference electron-density map was 0.12 e Å^{-3}. The perspective view of the molecule is shown in Fig. 3. Crystal data are given below: $C_{14}H_{18}O_4$; M = 250.3; crystal habit: plates; crystal size 0.6 × 0.09 × 0.03 mm; monoclinic; space group $C2/c$; $Z = 8$; D_{calc} = 1.261 g cm^{-3}; a = 25.332(18), b = 5.735(4), c = 18.200(13) Å; β = 94.26(7)°; V = 2637 Å^3; μ for Cu-Kα = 7.2 cm^{-1}.

For compound **7b**, a total of 2615 reflections (out of a possible 2978 reflections) were measured in the 2θ range 6–156° above 2σ(*I*). The structure was refined to an *R*-value of 0.068. The 14 carbon and 5 oxygen atoms were refined with the assumption of anisotropic thermal vibrations. The 20 hydrogen atoms were refined with the assumption of isotropic thermal vibrations. The hydrogen atoms were found on the difference electron-density map and were located at calculated positions. The maximum residual electron density found on the final difference electron-density map was 0.15 e Å^{-3}. The perspective view of the molecule is shown in Fig. 4. The crystal data are given below: $C_{14}H_{20}O_5$; M = 268.3; crystal habit: thick plates; crystal size 0.10 × 0.20 × 0.50 mm; triclinic; space group $P\bar{1}$; $Z = 2$; D_{calc} = 1.276 g cm^{-3}; lattice constants a = 9.404(5), b = 12.543(7), c = 6.219(4) Å; α = 89.71(5), β = 100.59(5), γ = 104.21(5)°; V = 698.4 Å^3; μ for Cu-Kα = 7.61 cm^{-1}.

Additional crystallographic data are available as supplementary material.*

Oxygenation of the Vitamin E Model Compound **1b**.—(a) *With an equimolar amount of potassium* tert-*butoxide to that of the substrate.* To a stirred solution of compound **1b** (440 mg, 2 mmol) in THF (100 cm^3) on an ice–water-bath was added a solution of Bu^{t}OK (224 mg, 2 mmol) in THF (20 cm^3) dropwise over a period of *ca.* 15 min under oxygen. After addition of Bu^{t}OK was complete, the mixture was stirred for 1 h. The reaction was quenched by addition of brine and the reaction mixture was extracted with diethyl ether. The extract was dried over anhydrous sodium sulfate. After filtration, the solvent was evaporated off under reduced pressure. The residue is referred to as fraction B. The alkaline aqueous phase, from which fraction B had been extracted, was acidified with a small amount of conc. hydrochloric acid and then was extracted with diethyl ether. The extract was dried over anhydrous sodium sulfate. After filtration, the solvent was evaporated off under reduced pressure. The residue is referred to as fraction A.

From fraction B, three oxidation products were isolated by silica gel column chromatography. First, compound **6b** was eluted in 8% yield with a 4:1 mixture of hexane and diethyl ether; secondly, compound **5b** in 16% yield with a 2:1 mixture of hexane and diethyl ether; and thirdly, compound **2b** in 4% yield with a 1:1 mixture of hexane and diethyl ether. For *compound* **2b**: m.p. 92–93 °C (from hexane) (Found: C, 66.2; H, 8.0. $C_{14}H_{20}O_4$ requires C, 66.65; H, 7.99%); λ_{max}(MeCN)/nm 246 (ε/dm^3 mol^{-1} 8000); ν_{max}(KBr)/cm^{-1} 1739 (CO) and 3420 (OH); δ_H($CDCl_3$) 1.22 (3 H, s, 2a-H_3), 1.33 (3 H, s, 2b-H_3), 1.55 (3 H, s, 5a-H_3), 1.60 (3 H, s, 7a-H_3), 1.71–1.78 (2 H, m, 3-H_2), 2.20–2.50 (2 H, m, 4-H_2), 3.33 (1 H, s, OH), 3.76 (1 H, s, OH), 5.45–5.47 (1 H, m, 8b-H) and 5.51–5.53 (1 H, m, 8b-H); δ_C($CDCl_3$) 17.1 (t, C-4), 25.1 (q, C-2a), 25.4 (q, C-5a), 27.4 (q, C-2b), 29.2 (q, C-7a), 32.3 (t, C-3), 74.0, 74.6 and 78.0 (s, C-2, -5 and -7), 110.0 (t, C-8b), 110.3 (s, C-4a), 143.1 and 145.0 (s, C-8 and -8a) and 213.0 (s, C-6).

From fraction A, compound **4b** was purified in 17% yield by silica gel column chromatography using a 4:1 mixture of hexane and diethyl ether as eluent. For *compound* **4b**: m.p. 76–77 °C (from hexane) (Found: M$^+$, 250.1205. $C_{14}H_{18}O_4$ requires M, 250.1189); λ_{max}(MeCN)/nm 271 (ε 7800); ν_{max}(KBr)/cm^{-1} 1790 (CO); δ_H($CDCl_3$) 1.22 (3 H, s, 2a-H_3), 1.24 (3 H, s, 2b-H_3), 1.56 (3 H, s, 5a-H_3), 1.56–1.72 (2 H, m, 3-H_2), 1.79 (3 H, s, 7a-H_3), 2.04–2.12 (1 H, m, 4-H), 2.20–2.30 (1 H, m, 4-H), 5.24 (1 H, s, 8b-H) and 5.59 (1 H, s, 8b-H); δ_C($CDCl_3$) 16.0 (q, C-5a), 18.1 (t, C-4), 20.4 (q, C-7a), 24.9 (q, C-2a), 27.4 (q, C-2b), 32.4 (t, C-3), 74.5 and 78.3 (s, C-2 and -5), 107.1 and 107.3 (s, C-4a and -7), 109.8 (t, C-8b), 136.2 and 143.7 (s, C-8 and -8a) and 172.6 (s, C-5b).

(b) *With a four-fold molar amount of potassium* tert-*butoxide over that of the substrate.* The oxygenation of compound **1b** (440 mg, 2 mmol) was carried out with Bu^{t}OK (900 mg, 8 mmol) as described above. From fraction A was obtained compound **4b** in 37% yield. Fraction B was fractionated to give four products by silica gel column chromatography. First, compound **6b** was eluted in 9% yield with a 3:1 mixture of hexane and diethyl ether; secondly, compound **2b** in 2% yield with a 2:1 mixture of hexane and diethyl ether; thirdly, compound **7b** in 4% yield with a 1:1 mixture of hexane and diethyl ether; and fourthly, compound **3b** in 5% yield with a 2:3 mixture of hexane and diethyl ether. The product **3b** was further purified by recrystallization from a mixture of hexane and diethyl ether.

For *compound* **3b**: m.p. 149–151 °C (from a mixture of hexane and diethyl ether) (Found: M$^+$, 252.1372. $C_{14}H_{20}O_4$ requires M, 252.1362); λ_{max}(MeCN)/nm 260 (ε 19 000); ν_{max}(KBr)/cm^{-1} 1603 (CO) and 3420 (OH); δ_H($CDCl_3$) 1.30 (3

* Atomic coordinates, bond lengths and angles, and thermal parameters for model compounds **2b**, **3b**, **4b** and **7b** have been deposited at the Cambridge Crystallographic Data Centre.

For details of the deposition scheme, see 'Instructions for Authors,' *J. Chem. Soc., Perkin Trans. 1*, 1993, issue 1.

H, s, 2a-H_3), 1.35 (3 H, s, 2b-H_3), 1.45 (3 H, s, 6a-H_3), 1.63 (3 H, s, 8b-H_3), 1.65–1.75 (2 H, m, 3-H_2), 2.12–2.20 (1 H, m, 4-H), 2.42–2.50 (2 H, m, 4-H and OH), 3.87 (1 H, s, OH), 5.57 (1 H, d, *J* 1.4, 7a-H) and 5.62 (1 H, d, *J* 1.4, 7a-H); $\delta_C(CDCl_3)$ 16.1 (t, C-4), 25.6, 27.1, 28.3 and 31.3 (q, C-2a, -2b, -6a and -8b), 31.5 (t, C-3), 71.7, 75.3 and 78.2 (s, C-2, -6 and -8), 105.8 (s, C-4a), 110.4 (t, C-7a), 152.0 (s, C-7), 168.7 (s, C-8a) and 198.5 (s, C-5).

For *compound* **7b**: m.p. 132–134 °C (from a mixture of hexane and diethyl ether) (Found: M^+, 268.1272. $C_{14}H_{20}O_5$ requires M, 268.1301); λ_{max}(MeCN)/nm 260 (ε 19 300); ν_{max}(KBr)/cm^{-1} 1620 (CO) and 3420 (OH); $\delta_H(CDCl_3)$ 1.34 (3 H, s, 2a-H_3), 1.38 (3 H, s, 2b-H_3), 1.43 (3 H, s, 6a-H_3), 1.53 (3 H, s, 8b-H_3), 1.70–1.74 (2 H, m, 3-H_2), 2.13–2.21 (1 H, m, 4-H), 2.46–2.54 (1 H, m, 4-H), 3.95 (1 H, br s, OH), 5.49 (1 H, s, 7a-H), 5.74 (1 H, s, 7a-H) and 7.85 (1 H, br s, OOH); $\delta_C(CDCl_3)$ 16.6 (t, C-4), 24.3, 26.1, 26.8 and 32.4 (q, C-2a, -2b, -6a and -8b), 31.5 (t, C-3), 75.5, 78.4 and 83.4 (s, C-2, -6 and -8), 109.5 (s, C-4a), 110.3 (t, C-7a), 149.5 (s, C-7), 165.9 (s, C-8a) and 198.0 (s, C-5).

Oxygenation of [5a-$^2H_3$]- *and* [7a-$^2H_3$]**1b**.—The oxygenation of [5a-$^2H_3$]**1b** or [7a-$^2H_3$] **1b** (150 mg) was carried out in THF with a three-fold molar amount of Bu^{t}OK (235 mg) to each substrate. Labelled products **2b**, **3b**, **4b** and **7b** were isolated as described above.

Intermediacy of Compounds **2b**, **5b** *and* **7b** *in the Formation of Products*.—(a) *Conversion of diol* **2b** *into lactone* **4b**. A solution of diol **2b** (74 mg, 0.3 mmol) in THF (20 cm^3) was added to a stirred solution of Bu^{t}OK (66 mg, 0.6 mmol) in THF (100 cm^3) at 5 °C under oxygen. The mixture was stirred for 1.5 h. The reaction was quenched by addition of brine. After extraction with diethyl ether, the mixture was acidified with a small amount of conc. hydrochloric acid. The acidified solution was extracted with diethyl ether. This extract was dried over anhydrous sodium sulfate, filtered, and concentrated to dryness. From the residue thus obtained, compound **4b** was isolated in 26% yield.

(b) *Conversion of acyloin* **5b** *into diol* **3b** *and hydroperoxide* **7b**. A solution of Bu^{t}OK (160 mg, 1.4 mmol) in THF (20 cm^3) was added to a stirred solution of compound **5b** (200 mg, 0.85 mmol) in THF (100 cm^3) at 7 °C under oxygen. The reaction mixture was stirred for 1 h. After addition of water, the reaction mixture was extracted with diethyl ether. The extract was washed with brine, dried over anhydrous sodium sulfate, and filtered. The solvent was evaporated off under reduced pressure. The resulting residue was chromatographed on a silica gel column. The starting material **5b** was eluted in 15% recovery, and then hydroperoxide **7b** in 16% yield with a 1:1 mixture of hexane and diethyl ether. Furthermore, diol **3b** was eluted in 13% yield with a 2:3 mixture of hexane and diethyl ether.

(c) *Conversion of hydroperoxide* **7b** *into diol* **3b**. A solution of Bu^{t}OK (17 mg, 0.15 mmol) in THF (10 cm^3) was added to a stirred solution of hydroperoxide **7b** (20 mg, 0.07 mmol) in THF (20 cm^3) on an ice–water-bath under oxygen. The mixture was stirred for 2 h. The reaction was quenched by addition of water and the reaction mixture was extracted with diethyl ether. The extract was dried over sodium sulfate. After filtration, the extract was concentrated to dryness. On the basis of the intensities of signals in the ^1H NMR spectrum of the residue obtained, the yield of diol **3b** and the recovery of substrate **7b** were estimated to be 28 and 46%, respectively.

Uptake of Oxygen by Products **2b** *and* **5b**.—Absorption of oxygen in a stirred solution of compound **2b** (10.3 mg, 0.041 mmol) or compound **5b** (10.0 mg, 0.042 mmol) in THF (1 cm^3) with Bu^{t}OK (12 mg, 0.11 mmol) at 5.3 °C under air was followed by measurement of the pressure change in a sealed flask.[5] Substrates **2b** and **5b** absorbed 0.014 and 0.030 mmol of molecular oxygen, respectively, over a period of 2 h.

Oxygenation of (RRR)-α-*Tocopherol* **1a**.—(*a*) *With an equimolar amount of potassium* tert-*butoxide to that of the substrate*. A solution of Bu^{t}OK (224 mg, 2 mmol) in THF (20 cm^3) was added to a stirred solution of α-tocopherol **1a** (860 mg, 2 mmol) in THF (100 cm^3) dropwise over a period of *ca.* 15 min at 5 °C under oxygen. The reaction mixture was stirred for 1 h. After the reaction had been quenched by addition of water, reaction products were extracted with diethyl ether. The extract was dried over sodium sulfate, filtered, and concentrated under reduced pressure. An oily residue was obtained which was chromatographed on silica gel. First, lactone **4a** was eluted in 4% yield with a 5:1 mixture of hexane and diethyl ether; secondly, isomers **6aα** and **6aβ** as two yellow eluates in 14 and 14% yield, respectively, with a 3:1 mixture of hexane and diethyl ether; and thirdly, isomers **5aα** and **5aβ** in 5 and 11% yield, respectively, with a 2:1 mixture of hexane and diethyl ether.

For *compound* **4a** (a mixture of the two epimers) (Found: M^+, 460.3523. $C_{29}H_{48}O_4$ requires M, 460.3552); λ_{max}(hexane)/nm 269 (ε 7300); ν_{max}(neat)/cm^{-1} 1795 (CO); $\delta_H(CDCl_3)$ 1.17 (3 H, s, 2a-H_3), 1.55 (3 H, s, 5a-H_3), 1.78 (3 H, s, 7a-H_3), 5.22 (1 H, s, 8b-H), and 5.56/5.57 (1 H, s, 8b-H, twin signals of the epimers); $\delta_C(CDCl_3)$ 15.9/16.1 (q, C-5a, twin signals of the epimers), 17.8/17.9 (t, C-4, twin), 19.6 and 19.7 (q, C-4′a and -8′a), 20.4 (q, C-7a), 20.7/20.9 (t, C-2′, twin), 22.0/24.1 (q, C-2a, twin), 22.6 and 22.7 (q, C-12′a and -13′), 24.4 and 24.8 (t, C-6′ and -10′), 28.0 (d, C-12′), 30.7/30.8 (t, C-3, twin), 32.6 and 32.8 (d, C-4′ and -8′), 37.26, 37.34, 37.37 and 37.42 (t, C-3′, -5′, -7′ and -9′), 38.14/40.89 (t, C-1′, twin), 39.3 (t, C-11′), 76.6/76.7 and 78.2/78.3 (s, C-2 and -5, twin), 107.10/107.22 and 107.25/107.33 (s, C-7 and -4a, twin), 109.64/109.70 (t, C-8b, twin), 136.2 and 143.5 (s, C-8 and -8a) and 175.52/175.55 (s, C-5b, twin).

(b) *With a four-fold molar amount of potassium* tert-*butoxide over that of the substrate*. Oxygenation of compound **1a** (860 mg, 2 mmol) was carried out with excess of Bu^{t}OK (896 mg, 8 mmol) as described above. Oily reaction products were fractionated by silica gel chromatography. First, lactone **4a** was eluted in 15% yield with a 5:1 mixture of hexane and diethyl ether; secondly, isomers **5aα** and **5aβ** in turn in 5 and 5% yield, respectively, with a 2:1 mixture of hexane and diethyl ether; thirdly, a mixture of compounds **3aα** and **2a** with a 1:1 mixture of hexane and diethyl ether; and fourthly, compound **3aβ** in 8% yield with a 1:2 mixture of hexane and diethyl ether. The mixture of compounds **3aα** and **2a** was further fractionated on another silica gel column using a 2:1 mixture of hexane and diethyl ether and compounds **3aα** and **2a** were obtained in 8 and 3% yield, respectively.

For *compound* **2a**: oil (Found: M^+, 462.3713. $C_{29}H_{50}O_4$ requires, M, 462.3709); λ_{max}(hexane)/nm 246 (ε 8600); CD λ(hexane)/nm 292 ($\Delta\varepsilon$ −1.64); ν_{max}(neat)/cm^{-1} 1721 (CO) and 3445 (OH); $\delta_H(CDCl_3)$ 1.56 (3 H, s, 5a-H_3), 1.61 (3 H, s, 7a-H_3), 3.23 (1 H, s, OH), 3.70 (1 H, s, OH), 5.45 (1 H, m, 8b-H) and 5.51 (1 H, m, 8b-H); $\delta_C(CDCl_3)$ 16.9 (t, C-4), 19.6 and 19.7 (q, C-4′a and -8′a), 20.9 (t, C-2′), 22.0 (q, C-2a), 22.7 and 22.9 (q, C-12′a and -13′), 24.5 and 24.8 (t, C-6′ and -10′), 25.4 (q, C-5a), 28.0 (d, C-12′), 29.2 (q, C-7a), 30.9 (t, C-3), 32.7 and 32.8 (d, C-4′ and -8′), 37.3 (×2) and 37.4 (×2) (t, C-3′, -5′, -7′ and -9′), 39.4 (t, C-11′), 40.9 (t, C-1′), 74.6, 75.9 and 77.8 (s, C-2, -5 and -7), 109.9 (t, C-8b), 110.4 (s, C-4a), 142.8 and 145.0 (s, C-8 and -8a) and 212.9 (s, C-6).

For *compound* **3aα**: oil; (Found: M^+, 462.3703); λ_{max}(hexane)/nm 255 (ε 8000); CD λ(hexane)/nm 301 ($\Delta\varepsilon$ −0.61); ν_{max}(neat)/cm^{-1} 1660 (CO) and 3420 (OH); $\delta_H(CDCl_3)$ 1.47 (3 H, s, 6a-H_3), 1.63 (3 H, s, 8b-H_3), 2.59 (1 H, s, OH), 3.91 (1 H, s, OH), 5.59 (1 H, d, *J* 1.3, 7a-H) and 5.65 (1 H, d, *J* 1.3, 7a-H); $\delta_C(CDCl_3)$ 15.9 (t, C-4), 19.6 and 19.8 (q, C-4′a and -8′a), 21.0 (t, C-2′), 22.6 and 22.7 (q, C-12′a and -13′), 23.0 (q, C-2a), 24.5 and 24.8 (t, C-6′ and -10′), 28.0 (d, C-12′), 28.5 and 31.4 (q, C-6a

and -8b), 29.7 (t, C-3), 32.7 and 32.9 (d, C-4′ and -8′), 37.3 (×2) and 37.4 (×2) (t, C-3′, -5′, -7′ and -9′), 39.4 (t, C-11′), 40.5 (t, C-1′), 71.9, 75.4 and 80.5 (s, C-2, -6 and -8), 106.0 (s, C-4a), 110.4 (t, C-7a), 152.2 (s, C-7), 168.8 (s, C-8a) and 198.4 (s, C-5).

For *isomer* **3αβ**: oil (Found: M^+, 462.3704); CD λ_{max}-(hexane)/nm 255 (ε 8200); λ(hexane)/nm 307 ($\Delta\varepsilon$ +2.55); ν_{max}(neat)/cm^{-1} 1660 (CO) and 3420 (OH); δ_H($CDCl_3$) 1.47 (3 H, s, 6a-H_3), 1.65 (3 H, s, 8b-H_3), 2.55 (1 H, s, OH), 3.92 (1 H, s, OH), 5.59 (1 H, d, *J* 1.1, 7a-H) and 5.64 (1 H, d, *J* 1.1, 7a-H); δ_C($CDCl_3$) 15.9 (t, C-4), 19.6 and 19.7 (q, C-4′a and -8′a), 20.9 (t, C-2′), 22.6 and 22.7 (q, C-12′a and -13′), 24.4 (×2) (t, C-6′ and q, -2a), 24.8 (t, C-10′), 27.9 (d, C-12′), 28.4 and 31.1 (q, C-6a and -8b), 29.8 (t, C-3), 32.7 and 32.8 (d, C-4′ and -8′), 37.4 (×4) (t, C-3′, -5′, -7′ and -9′), 39.0 (t, C-1′), 39.4 (t, C-11′), 71.8, 75.3 and 80.6 (s, C-2, -6 and -8), 106.0 (s, C-4a), 110.5 (t, C-7a), 152.1 (s, C-7), 168.9 (s, C-8a) and 198.4 (s, C-5).

Intermediacy of Acyloin **5a** *in the Formation of Products.*—Compound **5aα** (200 mg, 0.45 mmol) was kept in THF (10 cm^3) in the presence of Bu^{t}OK (100 mg, 0.89 mmol) at 5 °C under oxygen for 1.5 h. The products were purified by silica gel chromatography using a mixture of hexane and diethyl ether as eluent. The starting material was eluted in 29% recovery. Compound **3aα** was isolated in 20% yield. Under the same reaction conditions acyloin **5aβ** was transformed into diol **3aβ** in 22% yield.

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