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^{13}C Nuclear Magnetic Resonance Studies on α-Tocopherol and Its Derivatives

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The ^{13}C signal assignments of the aromatic carbon atoms in α-tocopherol were confirmed using [methyl-^{13}C]α-tocopherol. The ^{13}C-NMR spectra of α-tocopherol alkyl ethers and 5-alkyl-2,5,7,8-tetramethyl-2-(4,8,12-trimethyltridecyl)chroman-6(5H)-ones, which are formed in the radical scavenging reaction of α-tocopherol with alkyl radicals, were recorded and examined. In α-tocopherol and its alkyl ethers, C-5 is more shielded than nearly equivalent C-7. The chemical shift difference seems to be consistent with the reactivity difference between these carbon atoms, which is known as the "Mills-Nixon effect."

Keywords——α-tocopherol; vitamin E; [methyl-^{13}C]α-tocopherol; α-tocopherol alkyl ether; chroman-6(5H)-one; ^{13}C-NMR; ^{13}C chemical shift; ^{13}C-^{13}C coupling constant

The ^{13}C nuclear magnetic resonance (^{13}C-NMR) spectra of tocopherols (vitamin E) and their model compounds, 2,2-dimethylchromanols, have already been studied.[2] However, the ^{13}C signals due to C-5 or C-7 and due to C-4a or C-8 in the molecules were not definitively assigned. Here, we confirm the assignment of these signals in α-tocopherol (I) on the basis of studies on [methyl-^{13}C]α-tocopherol.

Recently, we reported that two types of products are obtained from the radical scavenging reaction of α-tocopherol with some alkyl radicals, *i. e.*, α-tocopherol alkyl ethers (II) and 5-alkyl-2,5,7,8-tetramethyl-2-(4,8,12-trimethyltridecyl)chroman-6(5H)-ones (III), as shown in Fig. 1.[3,4] ^{13}C-NMR spectroscopy was most useful for the structure determination of these compounds, since they are complex compounds with many carbon atoms. In the present paper, we assign the signals in the ^{13}C-NMR spectra of the products, II and III, and we also discuss the substituent effects on ^{13}C chemical shifts due to the introduction of some alkyl groups into α-tocopherol.

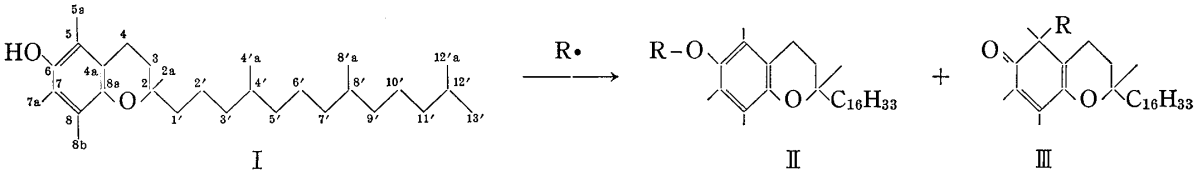


Fig. 1

Confirmation of the Assignment of Aromatic Carbon Signals of α-Tocopherol

The spectra of [methyl-^{13}C]α-tocopherol, IV, V and VI, derived from γ-tocopherol, β-tocopherol and 5,7-dimethyltocol, respectively (Fig. 2), show that the intensities of signals due to ^{13}C-enriched methyl carbon atoms are considerably enhanced, and signals showing

1) Location: *35-2 Sakae-cho, Itabashi-ku, Tokyo 173, Japan*; Contribution TMIG-I 26.
2) M. Matsuo and S. Urano, *Tetrahedron*, **32**, 229 (1976).
3) S. Urano and M. Matsuo, *Lipids*, **11**, 380 (1976).
4) S. Urano, Y. Hattori, S. Yamanoi, and M. Matsuo, *Lipids*, **12**, 105 (1977).

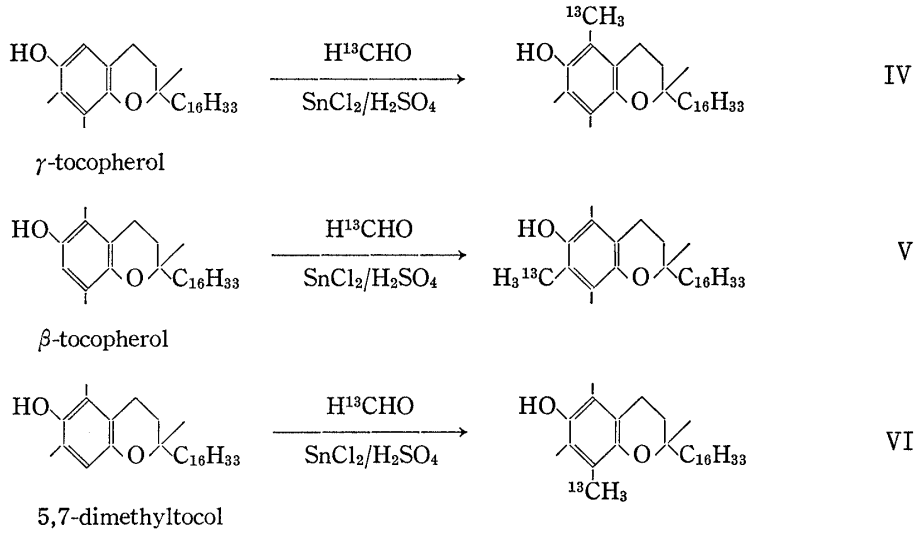


Fig. 2

^{13}C-^{13}C coupling are observed with each ^{13}C-labeled compound. The ^{13}C-^{13}C coupling pattern enables us to assign unambiguously the aromatic carbon signals of α-tocopherol, because a signal due to an aromatic carbon atom adjacent to a ^{13}C-enriched methyl carbon atom is split with a large coupling constant ($^1J_{C-C}$=about 45 Hz). In the spectrum of [5-$^{13}CH_3$]α-tocopherol, the intensity of a signal at 11.2 ppm, which is assigned to a ^{13}C-enriched methyl carbon atom attached to C-5, is enhanced, and signals at 118.5 and 145.4 ppm are split with coupling constants of 46.7 and 3.5 Hz, respectively. The signal having the large coupling constant corresponds to the aromatic carbon atom (C-5) attached to the ^{13}C-enriched methyl carbon atom. Since the signal at 145.4 ppm has already been assigned to C-8a,[2] the small coupling constant of 3.5 Hz is determined to be $^3J_{C-C}$. Similarly, $^1J_{C-C}$'s between C-7 and C-7a and between C-8 and C-8b are 45.9 and 46.1 Hz, and $^3J_{C-C}$'s between C-8a and C-7a and between C-6 and C-8b are 3.8 and 3.6 Hz, as observed in the spectra of [7-$^{13}CH_3$]- and [8-$^{13}CH_3$]α-tocopherol. Although the other coupling constants were too small to be determined, the trend of the magnitudes of these coupling constants is quite similar to that observed for mono-substituted benzenes.[5] For toluene, the ^{13}C-^{13}C coupling constants decrease in the following order: $^1J_{C-C} \gg {}^3J_{C-C} > {}^2J_{C-C} > {}^4J_{C-C}$.[6] On the basis of the ^{13}C-^{13}C coupling pattern, the signals of the aromatic carbon atoms in α-tocopherol are assigned as follows: 117.0 (C-4a), 118.5 (C-5), 144.4 (C-6), 121.0 (C-7), 122.3 (C-8), and 145.4 ppm (C-8a) (Table I).

It is very interesting that C-5 and C-4a are more shielded than C-7 and C-8. This may indicate that the electron densities at C-5 and C-4a are higher than those at C-7 and C-8. The 6-hydroxychroman nucleus is known to show a remarkable regiospecificity towards oxidation,[7] electrophilic substitution[8] and radical alkylation[3,4]; *i. e.*, the C-5 position of the nucleus is much more active than the nearly equivalent C-7 position (the Mills–Nixon effect).[9,10] Although the orientational preference has been discussed in terms of strain,[11] hybridization,[12] and cross-conjugation effects in the transition states,[13] the chemical shift difference between

5) E. Breitmaier and W. Voelter, "^{13}C NMR Spectroscopy," Verlag Chemie, Weinheim, 1974, pp. 101—103.
6) A.M. Ihrig and J.L. Marshall, *J. Am. Chem. Soc.*, **94**, 1756 (1972).
7) J.L.G. Nilsson, G.D. Daves, Jr. and K. Folkers, *Acta Chem. Scand.*, **22**, 207 (1968).
8) K.G. Svensson, H. Selander, M. Karlsson, and J.L.G. Nilsson, *Tetrahedron*, **29**, 1115 (1973).
9) W.H. Mills and I.G. Nixon, *J. Chem. Soc.*, **1930**, 2510.
10) J.L.G. Nilsson, H. Selander, H. Sievertsson, and I. Skanberg, *Tetrahedron*, **26**, 879 (1970).
11) J. Vaughan, G.J. Welch, and G.J. Wright, *Tetrahedron*, **21**, 1665 (1965).
12) A.R. Bassindale, C. Eaborn, and D.R.M. Walton, *J. Chem. Soc.*, **B 1969**, 12.
13) J.M. Behan, F.M. Dean, and R.A.W. Johnstone, *Tetrahedron*, **32**, 167 (1976).

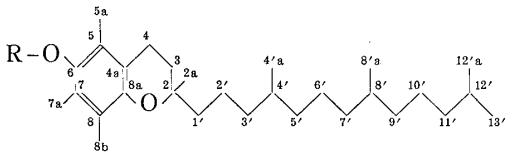
C-5 and C-7 seems to cast new light on the reactivity difference between these carbon atoms. Presumably, hyperconjugation to the benzylic methylene group of C-4[13] may be responsible for the shielding effect at C-5.

^{13}C Chemical Shifts of α-Tocopherol Alkyl Ethers

The ^{13}C-NMR spectra of six α-tocopherol alkyl ethers (the methyl, ethyl, *n*-propyl, isopropyl, *n*-butyl and *sec*-butyl ethers) were recorded (Tables I and II). For α-tocopherol methyl ether, the ^{13}C signals of C-2, C-2a, C-3, C-4 and the carbon atoms in the isoprenyl moiety were assigned by comparison with the ^{13}C chemical shifts of the corresponding carbon atoms in α-tocopherol.[2] The signal of a methoxy carbon atom in the methyl ether was easily identified on the basis of its chemical shift value (67.2 ppm) and the quartet splitting pattern in the off-resonance spectrum. The signals due to the methyl carbon atoms bonded to the aromatic ring and due to the aromatic carbon atoms in the methyl ether were assigned by the ^{13}C labeling technique; [5-$^{13}CH_3$]- and [8-$^{13}CH_3$]α-tocopherol methyl ethers were prepared by the reaction of either IV or VI with methyl iodide in the presence of sodium hydride. The enhanced signals in the spectra of [5-$^{13}CH_3$]- and [8-$^{13}CH_3$]α-tocopherol methyl ethers show that the signals at 11.6 and 11.8 ppm are due to C-5a and C-8b. The residual methyl carbon signal at 12.5 ppm is known to be due to C-7a. The signals at 125.5 and 147.6 ppm are split with coupling constants of 45.2 and 3.4 Hz in the spectrum of [5-$^{13}CH_3$]α-tocopherol methyl ether, and the signals at 122.7 and 149.3 ppm are split with coupling constants of 46.2 and 3.4 Hz in the spectrum of [8-$^{13}CH_3$]α-tocopherol methyl ether. These data show that the signals at 122.7, 125.5, 147.6 and 149.3 ppm are due to C-8, C-5, C-8a and C-6, respectively. The signals at 117.3 and 127.5 ppm can be assigned to C-4a and C-7 by analogy with the chemical shift values of C-4a (117.0 ppm) and C-7 (121.0 ppm) of α-tocopherol.[2]

The assignment of the resonances in the other alkyl ethers was based on a comparison with chemical shifts in α-tocopherol methyl ether. However, the chemical shift difference between the signals of C-6 and C-8a in α-tocopherol isopropyl ether is too small for them to

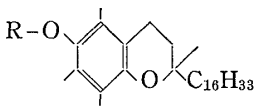
Table I. ^{13}C Chemical Shifts of α-Tocopherol Alkyl Ethers[a]



No.	R					
	Me	Et	*n*-Pr	iso-Pr	*n*-Bu	*sec*-Bu
2	74.6	74.7	74.6	74.6	74.7	74.7
2a	23.9	23.6	23.9	23.9	23.9	23.9
3	31.3	31.4	31.4	31.5	31.5	31.4
4	20.7	20.7	20.7	20.8	20.7	20.7
4a	117.3	117.3	117.3	117.3	117.4	117.4
5	125.5	125.7	125.7	126.3	125.8	125.7
5a	11.6	11.8	11.8	13.0	11.8	11.8
6	149.3	148.5	148.3	147.2	148.5	148.2
7	127.5	127.8	127.7	128.3	127.8	127.8
7a	12.5	12.8	12.7	13.8	12.7	12.6
8	122.7	122.7	122.6	122.7	122.7	122.8
8a	147.6	147.6	147.5	147.3	147.6	147.6
8b	11.8	11.8	11.8	11.8	11.8	11.8
1'	40.1	40.2	40.1	40.1	40.1	40.1

a) In ppm relative to tetramethylsilane. The ^{13}C chemical shifts of C-2' to C-13" are not listed because they are similar to the corresponding shifts of an isoprenyl side chain in α-tocopherol.[2]

Table II. ^{13}C Chemical Shifts of Alkyl Carbon Atoms in α-Tocopherol Alkyl Ethers[a)]



R	α $-OCH_3$	α β $-OCH_2CH_3$	α β γ $-OCH_2CH_2CH_3$	α β $-OCH(CH_3)_2$	α β γ δ $-OCH_2CH_2CH_2CH_3$	α β γ $-OCH_2CH(CH_3)_2$
α	67.2	68.4	74.5	74.9	72.8	79.3
β	—	15.6	23.5	22.4	32.5	29.3
γ	—	—	10.7	—	19.5	19.5
δ	—	—	—	—	14.0	—

a) In ppm relative to tetramethylsilane.

be assigned by the above method. Thus, the spectrum of [5-$^{13}CH_3$]α-tocopherol isopropyl ether was examined. A signal at 147.3 ppm is split with a coupling constant of 3.8 Hz. This indicates that C-8a resonates at 147.3 ppm, and C-6 at 147.2 ppm. The signals due to the alkoxy carbon atoms were assigned by reference to the chemical shift data for various ethers.[14] The chemical shifts for α-tocopherol alkyl ethers are shown in Tables I and II.

Figure 3 shows the magnitudes of the substituent effects on the aromatic carbon atoms, produced by the formation of alkyl ethers. Marked changes in the shieldings are apparent for C-5, C-6, C-7 and C-8a. The alkylation of a phenolic hydroxyl group of α-tocopherol produces a downfield shift of the carbon atoms (Fig. 3).

In anisole the *ortho* and *para* carbon atoms are shielded by 1.0—2.9 ppm relative to the corresponding carbon atoms of phenol.[15] The *ortho* and *para* carbon atoms of 2,6-dimethylanisole, however, are more deshielded than those of 2,6-dimethylphenol. This deshielding effect in 2,6-dimethylanisole can be explained in terms of a substantial reduction of electron release from the oxygen into the aromatic ring due to steric interference of the *ortho* substituents with a methoxy group.[15] The deshielding effect at C-5, C-7 and C-8a of α-tocopherol alkyl ether is probably similar to the above effect in 2,6-dimethylanisole. In α-tocopherol alkyl ethers, the substituent effect of an isopropyl group seems to be somewhat different from those of other alkyl groups. It is interesting that the methyl carbon atoms, C-5a and C-7a, in the isopropyl ether are deshielded relative to those in the other alkyl ethers, because this trend is opposite to that expected for a usual steric interaction between the isopropyl group and the methyl groups. The reason for the deshielding effect at C-5a and C-7a is unclear at present. However, it may be some kind of steric deshileding effect on the basis of the finding

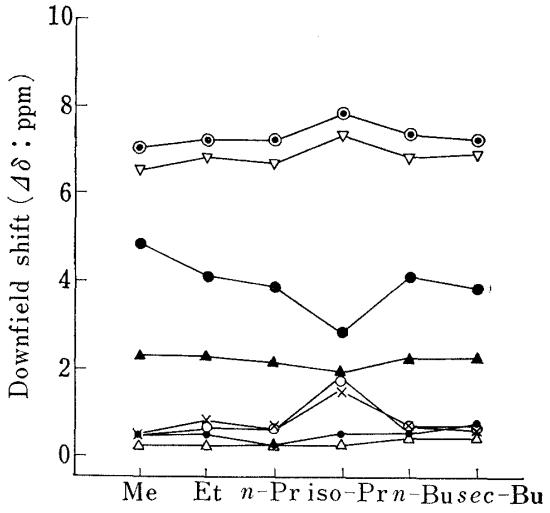


Fig. 3. Substituent Effects in α-Tocopherol Alkyl Ethers due to Alkoxy Groups; ^{13}C Chemical Shift Differences between the Corresponding Carbon Atoms of α-Tocopherol and Its Alkyl Ethers

⊙: C-5, ▽: C-7, ●: C-6, ▲: C-8a, ○: C-5a, ×: C-7a, •: C-8, △: C-4a.

14) J.B. Stothers, "Carbon-13 NMR Spectroscopy," Academic Press, New York, 1972, pp. 139—144.
15) G.W. Buchanan, G.M. Montaudo, and P. Finocchiaro, *Can. J. Chem.*, **52**, 767 (1974).

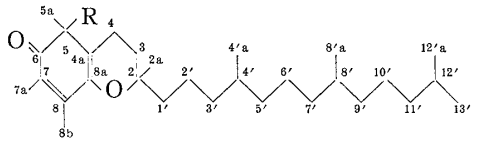
that the methyl carbon atoms of 1,8-dimethylnaphthalene[16] and 2,6-diisopropylanisole[15] are unusually deshielded as compared with those of methylnaphthalene and 2-isopropylanisole, respectively.

^{13}C Chemical Shifts of 5-Alkyl-2,5,7,8-tetramethyl-2-(4,8,12-trimethyltridecyl)chroman-6(5H)-ones

Cyclohexadienone derivatives, 5-alkyl-2,5,7,8-tetramethyl-2-(4,8,12-trimethyltridecyl)-chroman-6(5H)-ones (III), are obtained by the reaction of α-tocopherol with alkyl radicals.[3,4] Their ^{13}C chemical shifts have been reported in part.[3,4] This paper describes all the ^{13}C chemical shifts of these compounds and the assignments of the resonances of their aromatic carbon atoms. These were confirmed by studies of [7-$^{13}CH_3$]- and [8-$^{13}CH_3$]2,5,5,7,8-pentamethyl-2-(4,8,12-trimethyltridecyl)chroman-6(5H)-one (X and XI). On the basis of the signal enhancement of the ^{13}C-enriched C-7a and C-8b and the coupling constants of 45.9 (^1J between C-7 and C-7a), 42.5 (^1J between C-8 and C-8b) and 3.8 Hz (^3J between C-7 and C-8a), the following signal assignments of III (R=Me) are reasonable: 11.4 (C-7a), 14.1 (C-8b), 118.1 (C-4a), 127.7 (C-7), 146.8 (C-8) and 141.1 ppm (C-8a).

According to the chemical shift data reported previously for some cyclohexadienones, sp^2 carbon atoms at the β- and δ-positions with respect to ketone groups are greatly deshielded (140—155 ppm).[17] This can be explained in terms of the electron-withdrawing effect of the ketonic oxygen atoms. However, C-4a in III, which is in the δ-position relative to a ketone

Table IIIa. ^{13}C Chemical Shifts of 5-Alkyl-2,5,7,8-tetramethyl-2-(4,8,12-trimethyltridecyl)chroman-6(5H)-ones[a]

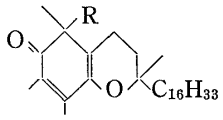


No.	R					
	Me	Et	*n*-Pr	iso-Pr	*n*-Bu	*sec*-Bu
2	74.8	74.9	74.9	74.9	74.9	75.0
2a	23.3	23.2 23.7[c]	23.3	23.6	23.2	23.2
3	31.2	31.1 31.2[c]	31.1	31.3	31.1	31.2
4	18.5	18.2	18.3	18.3	18.3	18.7
4a	118.1	116.3	116.9	117.2	116.8	117.5
5	46.7	51.5	51.0	53.5	51.0	50.5
5a	25.2 or 25.7[b]	26.2 26.5[c]	26.8	24.8	26.9	26.2
6	204.6	204.5	204.5	204.5	204.5	204.1
7	127.7	128.9	128.6	129.9	129.6	128.7
7a	11.4	11.2	11.2	11.2	11.1	11.4
8	146.8	147.4	147.5	147.1	147.5	147.0
8a	141.1	142.5	142.4	143.1	142.5	142.3
8b	14.1	14.3	14.3	14.2	14.2	14.3
1′	39.7	40.2	40.1	40.2	40.2	39.8
2′	20.8	20.8	20.8	20.9	20.8	20.9

a) In ppm relative to tetramethylsilane. The ^{13}C chemical shifts of C-3′ to C-13″ are not listed because they are similar to the corresponding shifts of an isoprenyl side chain in α-tocopherol.[2]
b) Assignable to either C-5a or C-5b.
c) See the text.

16) S.H. Grover, J.P. Guthrie, J.B. Stothers, and C.T. Tan, *J. Magn. Res.*, **10**, 227 (1973).
17) R. Hollenstein and W. von Philipsborn, *Helv. Chim. Acta*, **55**, 2030 (1972).

Table IIIb. ^{13}C Chemical Shifts of Alkyl Carbon Atoms in 5-Alkyl-2,5,7,8-tetramethyl-2-(4,8,12-trimethyltridecyl)chroman-6(5H)-ones[a]



R	α $-CH_3$	α β $-CH_2CH_3$	α β γ $-CH_2CH_2CH_3$	α β $-CH(CH_3)_2$	α β γ δ $-CH_2CH_2CH_2CH_3$	α β γ $-CH_2CH(CH_3)_2$
α	25.2 or 25.7[b]	18.2	41.9	22.5	39.2	48.6
β	—	9.4 9.6[c]	18.6	16.7 19.2	26.9	28.5
γ	—	—	14.5	—	23.1	23.7 24.2
δ	—	—	—	—	14.3	—

a) In ppm relative to tetramethylsilane.
b) Assignable to either C-5a or C-5b.
c) See the text.

group, is abnormally shielded (116—118 ppm). Presumably, the shielding may be due to hyperconjugation to a methylene group (C-4), similar to that in the 6-hydroxychroman nucleus.[13] The ^{13}C chemical shifts of III are shown in Tables III a and b. The signal assignments were made by reference to the chemical shift data for III (R=Me), α-tocopherol[2] and alkanes.[18] In the case of III (R=Et), the signals of C-2a, C-3, C-5a and an ethylene carbon atom attached to C-5 were observed as doublets. This is in accord with the view that epimers differing in configuration at C-5 may be produced by the non-stereoselective attack of an ethyl radical at C-5 in α-tocopherol,[3] although such doublets were not found in the spectra of III (R=Pr or Bu) (Table III).

Experimental

^{13}C-NMR Measurements——^{13}C-NMR spectra were recorded on a Varian XL-100-12 WG NMR spectrometer equipped with a Varian 620/L computer, operating at 25.16 MHz at about 30°. Each sample was dissolved in $CDCl_3$ containing tetramethylsilane as an internal standard. Ten-mm sample tubes were used for all the measurements.

^{13}C-Labeled Compounds

[5-$^{13}CH_3$]α-Tocopherol (IV)——Stannous chloride (3 g) was added with stirring to a solution of γ-tocopherol (0.7 g) in a mixture of isopropyl ether (70 ml) and conc. hydrochloric acid (10 ml). Next, ^{13}C-paraformaldehyde (50 mg: 90 atom %, Merck Sharp and Dohm, Quebec, Canada) was added. The mixture was refluxed with stirring for 1.5 hr. The suspension was poured into ice-water (30 ml) and extracted with isopropyl ether. The organic phase was separated and washed with water. The isopropyl ether solution was dried over sodium sulfate. After filtration, the solution was concentrated *in vacuo* to give an oily residue (0.76 g). The residue was charged on a silica gel column (100 g) and eluted with a mixture of *n*-hexane and ether (20: 1 v/v). Each fraction collected was analyzed by gas–liquid and thin–layer chromatography. The fractions containing α-tocopherol were combined and concentrated to afford pure IV (0.31 g, 44.2%). TLC: $Rf=0.54$ (silica gel G, benzene: *n*-hexane/7: 1); UV; $\lambda_{max}^{n\text{-hexane}}$ nm (ε) 291 (3000), 298 (3200); ^1H-NMR: $\delta_{TMS}^{CDCl_3}$ 4.16 (s, 1H, –OH), 2.60 (t, 2H, $J=6.5$ Hz, Ar–C$\underline{H}_2$–), 2.15 (s, 3H, Ar–C$\underline{H}_3$), 200 (s, 6H, 2×Ar–C$\underline{H}_3$), 1.78 (t, 2H, $J=6.5$ Hz, Ar–CH_2–C$\underline{H}_2$–); ^{13}C-NMR: $\delta_{TMS}^{CDCl_3}$ *in* Table I.

[7-$^{13}CH_3$]α-Tocopherol (V)——Compound V (0.35 g, 48.4%) was prepared from β-tocopherol (0.7 g) and ^{13}C-paraformaldehyde (50 mg) by the same method.

[8-$^{13}CH_3$]α-Tocopherol (VI)——Compound VI (0.28 g, 38.7%) was synthesized from 5,7-dimethyltocol (0.7 g) and ^{13}C-paraformaldehyde (50 mg).

[5-$^{13}CH_3$]α-Tocopherol Methyl Ether (VII)——Sodium hydride (10 mg) was added with stirring to a solution of IV (0.15 g) in a mixture of tetrahydrofuran (10 ml) and dimethyl sulfoxide (5 ml). After 10 min,

18) G.C. Levy and G.L. Nelson, "Carbon-13 Nuclear Magnetic Resonance for Organic Chemists," Wiley-Interscience, New York, 1972, pp. 38—43.

a solution of methyl iodide (50 mg) in tetrahydrofuran (3 ml) was added dropwise. The mixture was stirred for 3 hr, then poured onto crushed ice (30 g) and extracted with ether. The combined ether extract was washed with water and dried over sodium sulfate. After concentration, the residual oil was applied to a silica gel column (50 g) and eluted with a mixture of *n*-hexane and ether (20: 1). The yield of VII was 0.11 g (70.4%). IR: ν_{max}^{neat} cm^{-1} 1015 (C–O–C); UV: $\lambda_{max}^{n\text{-hexane}}$ nm (ε) 281 (2200), 287 (2500), 290 (2400); MS: *m/e* 445; ^{1}H-NMR: $\delta_{max}^{CDCl_3}$ 3.64 (s, 3H, –O–CH_3), 2.59 (t, 2H, J=6.5 Hz, Ar–C$\underline{H}_2$–), 2.20, 2.15, 2.11 (each s, 3H, Ar–C$\underline{H}_3$), 1.80 (t, 2H, J=6.5 Hz, Ar–CH_2–C$\underline{H}_2$).

[**8-$^{13}CH_3$]α-Tocopherol Methyl Ether (VIII)**——Compound VIII (0.1 g, 64.6%) was obtained by the reaction of VI (0.15 g) with methyl iodide (50 mg) in the presence of sodium hydride (10 mg).

[**5-$^{13}CH_3$]α-Tocopherol Isopropyl Ether (IX)**——Compound IX (90 mg, 54.7%) was prepared by the reaction of IV (0.15 g) with isopropyl iodide (60 mg) in the presence of sodium hydride (10 mg). IR: ν_{max}^{neat} cm^{-1} 1015; UV: $\lambda_{max}^{n\text{-hexane}}$ nm (ε) 283 (2500), 288 (2700), 291 (2500); MS: *m/e* 473; TLC: *Rf*=0.65 (silica gel G, *n*-hexane: ether/4: 1); ^{1}H-NMR: $\delta_{TMS}^{CDCl_3}$ 3.94 (m, 1H, –O–C$\underline{H}$–Me_2), 2.54 (t, 2H, Ar–C$\underline{H}_2$–), 2.06, 2.08, 2.13 (each s, 3H, Ar–C$\underline{H}_3$), 1.76 (t, 2H, J=6.5 Hz, Ar–CH_2–C$\underline{H}_2$–).

[**7-$^{13}CH_3$]2,5,5,7,8-Pentamethyl-2-(4,8,12-trimethyltridecyl)chroman-6(5H)-one (X)**——Ferrous sulfate (50 mg) was dissolved with stirring at 60° in dimethyl sulfoxide (3 ml) containing V (0.43 g). Hydrogen peroxide (30%, 0.4 g) in dimethyl sulfoxide (2 ml) was added dropwise to the mixture with stirring at 60° for 15 min. The stirring was continued for another 15 min. The reaction mixture was poured into ice-water and extracted with chloroform. The extract was washed with water and dried over sodium sulfate. After concentration, the residual oil was charged on a silica gel column and eluted with benzene. The yield of X was 50 mg (11.3%). TLC: *Rf*=0.27 (silica gel G, benzene: methylene chloride/4: 1); UV: $\lambda_{max}^{n\text{-hexane}}$ nm (ε) 334 (5300); IR: ν_{max}^{neat} cm^{-1} 1640; MS: *m/e* 445; ^{1}H-NMR: $\delta_{TMS}^{CDCl_3}$ 2.14 (t, 2H, J=6.5 Hz, C=C–C$\underline{H}_2$–), 1.99 (s, 3H, C=C–C$\underline{H}_3$), 1.86 (d, 3H, J=125 Hz, ^{13}C–CH_3), 1.65 (t, 2H, J=6.5 Hz, –CH_2–C$\underline{H}_2$–).

[**8-$^{13}CH_3$]2,5,5,7,8-Pentamethyl-2-(4,8,12-trimethyltridecyl)chroman-6(5H)-one (XI)**——Compound XI (80 mg, 17.2%) was obtained by the methylation of VI (0.45 g) using the above method.

Tocopherols——DL-Tocopherols were used in all the experiments.