80), 201 (73), 172 (26), 171 (30), 142 (14), 127 (16), 126 (100), 125 (33), 114 (44), 113 (20).

2,3-Dinitronaphthalene: ^{1}H NMR (100 MHz, $CDCl_3$) δ 8.46 (br s, 2 H, H1), 7.97–8.18 (m, 2 H, H6), 7.65–7.95 (m, 2 H, H7); MS m/z (relative intensity) 218 (M^+, 100), 188 (14), 160 (4), 144 (19), 130 (27), 127 (7), 126 (63), 115 (9), 114 (88), 113 (22).

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Supplementary Material Available: Tables with full coordinates, bond distances, bond angles, and anisotropic thermal parameters for 2,3-dinitronaphthalene (8 pages). Ordering information is given on any current masthead page.

Synthesis and Kinetic Study of Antioxidant Activity of New Tocopherol (Vitamin E) Compounds

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New tocopherol (vitamin E) compounds (5,7-diethyltocol (**3**), 5,7-diisopropyltocol (**4**), 7-*tert*-butyl-5-methyltocol (**5**), and 8-*tert*-butyl-5-methyltocol (**6**)) have been synthesized by condensation of isophytol with the corresponding alkylhydroquinone. The second-order rate constants, k_s, for the reaction of 10 kinds of tocopherol derivatives including α-, β-, γ-, and δ-tocopherols with substituted phenoxyl radical in ethanol have been measured in the temperature range 10.0–35.0 °C, with a stopped-flow spectrophotometer, as a model reaction of tocopherols with unstable free radicals (LOO$^\bullet$, LO$^\bullet$, and HO$^\bullet$) in biological systems. The result indicates that the rate constants, k_s, increase as the total electron-donating capacity of the alkyl substituents on the aromatic ring increases. For the tocopherol derivatives, log k_s was found to correlate roughly with the sum of the Hammett's σ constants ($\Sigma\sigma$) or the Brown's σ^+ constants ($\Sigma\sigma^+$), but the two cases could not be distinguished. Half-peak oxidation potentials ($E_{p/2}$) for tocopherol compounds have also been measured by using a cyclic voltammetry technique. The log of the second-order rate constants, k_s, obtained for tocopherols was found to correlate with their half-peak oxidation potentials ($E_{p/2}$). The antioxidant activities of tocopherol derivatives **2**–**5** having two alkyl substituents, such as methyl, ethyl, isopropyl, and *tert*-butyl groups, at the ortho positions of the OH group are similar to each other, suggesting that the effect of steric hindrance on the reaction rate is small. Further, the reactivities of these tocopherols **2**–**5** are about half that of α-tocopherol. From detailed analysis of the temperature dependence of k_s values of the tocopherols, the activation energy, E_{act}, for the reaction has been determined. The observed activation energies were found to be related linearly to the half-peak oxidation potentials. From the results, the property of the transition state in the above free radical scavenging reaction by tocopherols has been discussed. Electron spin resonance measurements were performed for the tocopheroxyl radicals **3**–**6** in toluene, and the proton hyperfine coupling constants and g_{iso} values were determined.

Introduction

Vitamin E compounds (α-, β-, γ-, and δ-tocopherols) are well known as scavengers of active free radicals (LOO$^\bullet$, LO$^\bullet$, and HO$^\bullet$) generated in biological systems. Recently, several investigators have measured the second-order rate constants k_s for H atom abstraction by active free radicals from α-, β-, γ-, and δ-tocopherols in homogeneous solution, by using different experimental methods such as O_2 consumption,[1–3] ESR,[4] and stopped-flow spectrophotometry.[5] It was observed that the second-order rate constants, k_s, of tocopherols decrease in the order of $\alpha > \beta \sim \gamma > \delta$-tocopherol; further, the relative magnitudes of k_s, that is, the relative antioxidant activity of α-, β-, γ-, and δ-tocopherols, obtained from three different experimental methods agree well with each other.[5]

In order to obtain the tocopherol compounds having higher antioxidant activity than α-tocopherol and in order to clarify the structure–activity relationship in antioxidant action of tocopherols, several investigators, including the present authors, have prepared many tocopherol compounds.[2,3,6–15] It was found that a few tocopherols have

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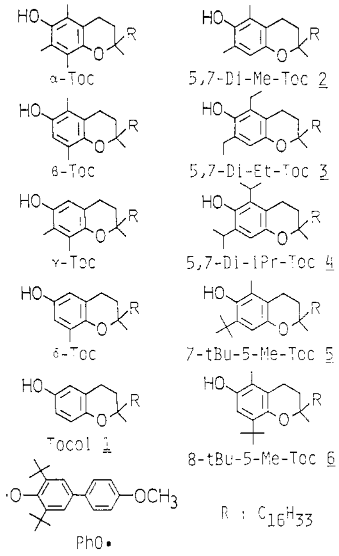

Figure 1. Molecular structures of tocopherols and substituted phenoxyl radical (PhO•).

higher antioxidant activity than α-tocopherol.[3,13,15] However, the number of the tocopherol compounds having a phytyl side chain at position 2 are very limited.[8,9,13,15] Although α-tocopherol and an α-tocopherol model, in which the phytyl side chain is replaced by a methyl group, have similar antioxidant activity,[3,14,16,17] the latter compound generally shows little or no vitamin E activity in vivo.[18,19] The phytyl chain appears to be necessary for the phospholipid penetration.

Therefore, in the present work, in order to obtain tocopherol compounds having higher in vivo biological activity than α-tocopherol, we have prepared several new tocopherol derivatives that have two alkyl substituents at ortho positions of the OH group and the phytyl side chain at position 2 (see Figure 1). We have measured the reaction rates k_s of tocopherol derivatives wtih 2,6-di-*tert*-butyl-4-(4-methoxyphenyl)phenoxyl (PhO•) (abbreviated to "substituted phenoxyl" hereafter) in ethanol solution, using stopped-flow spectrophotometry.[5,14] From the results, the structure–activity relationship in antioxidant action of tocopherol has been discussed. From detailed analysis of the temperature dependence of k_s values, activation energy for the reaction between tocopherols and substituted phenoxyl radical has been determined. ESR studies have also been performed with the tocopheroxyl radicals.

Results and Discussion

Measurement of the Second-Order Rate Constants, k_s, for the Reaction of Tocopherols with Substituted Phenoxyl Radical. The oxidation rates of tocopherol derivatives by substituted phenoxyl were studied spectrophotometrically with a stopped-flow technique in the presence of excess tocopherol in ethanol. The details of

$$\mathrm{PhO^\bullet} + \mathrm{TocH} \xrightarrow{k_s} \mathrm{PhOH} + \mathrm{Toc^\bullet} \qquad (1)$$

experiments are reported in a previous paper.[5] The rate was measured by following the decrease in absorbance at 376 and 580 nm of phenoxyl radical. The pseudo-first-order rate constants, k_{obsd}, observed at 376 and at 580 nm were linearly dependent on the concentration of tocopherol, and thus the rate law is expressed as

$$-\mathrm{d}[\mathrm{PhO^\bullet}]/\mathrm{d}t = k_{\mathrm{obsd}}[\mathrm{PhO^\bullet}] = k_s[\mathrm{TocH}][\mathrm{PhO^\bullet}] \qquad (2)$$

where k_s is the second-order rate constant for oxidation of tocopherol by phenoxyl radical. For each tocopherol, k_s was measured in 10 independent experiments. The experimental error in k_s value for each tocopherol was ±5% at maximum. The values k_s calculated from k_{obsd} are listed in Table I.

Table I. Second-Order Rate Constants (k_s) and Relative Rate Constants for Oxidation of Tocopherols by Substituted Phenoxyl in Ethanol at 25.0 °C and Half-Peak Oxidation Potentials ($E_{p/2}$) for Tocopherols

tocopherols	$10^{-3}k_s$,[a] $M^{-1}\ s^{-1}$	k_s(Toc)/ k_s(α-Toc)	$E_{p/2}$ vs SCE,[b] mV
α-tocopherol	5.12[c]	1.00	860
β-tocopherol	2.24[c]	0.44	920
γ-tocopherol	2.42[c]	0.47	930
δ-tocopherol	1.00[c]	0.20	990
tocol (1)	0.56	0.11	1050
5,7-di-Me-Toc (2)	2.39	0.47	890
5,7-di-Et-Toc (3)	1.97	0.38	890
5,7-di-iPr-Toc (4)	2.51	0.49	890
7-tBu-5-Me-Toc (5)	2.97	0.58	880
8-tBu-5-Me-Toc (6)	3.62	0.71	970

[a] Experimental errors <±5%. [b] Experimental errors <±20 mV. [c] These values are reported in a previous paper (ref 5).

By comparing the second-order rate constants observed for 5,7-dimethyltocol (**2**) having two methyl groups at ortho positions with that of α-tocopherol, the former is only ca. 47% as reactive as the latter. On the other hand, the rate constants of tocopherol compounds **2**, **3**, **4**, and **5** having two alkyl substituents at a position ortho to the OH group are similar to each other. The result suggests that the effect of steric hindrance on the reaction rate is small.[14] Further, 5,7-dimethyltocol (**2**) has quite similar rate constants with those of β- and γ-tocopherols, whereas δ-tocopherol is only ca. 20% as reactive as α-tocopherol, and tocol (**1**) is only ca. 11% as reactive as α-tocopherol. The result indicates that the antioxidant activity of these tocopherols varies, depending on the number of alkyl substituents. Consequently, we can expect that the antioxidant activity of these tocopherol compounds relates to the total electron-donating character of the alkyl group substituents on the aromatic ring.[3,14,20] However, 8-*tert*-butyl-5-methyltocol (**6**) shows 62% higher antioxidant activity than that of β-tocopherol, against our expectation. The electronic interaction between the bulky *tert*-butyl group at the C-8 position and the oxygen in position 1 may induce the change in the extent of orbital overlap between the 2p type lone pair on the para oxygen atom and the aromatic π electron system and, thus, the change in the second-order rate constants.[1-3,21]

Howard and Ingold have measured the rate constants, k_1, for the reaction of *o*-alkylphenols with poly(peroxystyryl)peroxyl radicals.[22] They found that the logarithms of rate constants correlate with the sum of the Brown's σ^+ constants for all the substituents on the phenols ($\Sigma\sigma^+$). In the present work, the values of log k_s for tocopherols have

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Table II. Summary of k_s Values of α-, β-, γ-, and δ-Tocopherols in Ethanol

	$10^{-3}k_s$, M^{-1} s^{-1}					
tocopherols	10.0 °C	15.0 °C	20.0 °C	25.0 °C	30.0 °C	35.0 °C
α-Toc	3.55	4.10	4.64	5.34	6.02	6.77
β-Toc		1.91	2.14	2.46	2.93	3.33
γ-Toc		1.92	2.21	2.55	2.94	3.50
δ-Toc		0.80	0.95	1.15	1.35	

Table III. Summary of Activation Parameters for Reactions of Tocopherols with Substituted Phenoxyl in Ethanol

	E_{act},[a] kJ mol^{-1}	A_0, M^{-1} s^{-1}
α-tocopherol	18.7[b]	1.01×10^7
β-tocopherol	21.1	1.25×10^7
γ-tocopherol	22.2	2.03×10^7
δ-tocopherol	25.6	3.44×10^7
tocol (**1**)	27.1	2.43×10^7
5,7-di-Me-Toc (**2**)	17.5	3.00×10^6
5,7-di-Et-Toc (**3**)	18.7	4.23×10^6
5,7-di-iPr-Toc (**4**)	18.5	5.13×10^6
7-tBu-5-Me-Toc (**5**)	17.8	3.88×10^6
8-tBu-5-Me-Toc (**6**)	16.1	2.41×10^6

[a] For each tocopherol, experimental error in E_{act} was <±5%. For a plot of ln k_s vs $1/T$, correlation coefficient was <–0.997. [b] 4.47 kcal mol^{-1}.

been plotted against both the sum of the Hammett's σ constants ($\Sigma\sigma$) and the Brown's σ^+ constants ($\Sigma\sigma^+$) for all the substituents on the tocopherols. The logarithms of rate constants k_s were found to correlate roughly with $\Sigma\sigma$ or $\Sigma\sigma^+$ substituent constants. The correlation coefficients are –0.95 for log k_s – $\Sigma\sigma$ plot and –0.90 for log k_s – $\Sigma\sigma^+$ plot, except for tocopherol **6**. Thus, the two cases could not be distinguished.[20]

Temperature Dependence of the Second-Order Rate Constants k_s. We obtained k_s values as a function of the temperature between 10 and 35 °C in ethanol. The results obtained for α-, β-, γ-, and δ-tocopherols are listed in Table II. The k_s values increased depending on the temperature. Further, the relative k_s values ($k_s/k_s(\alpha\text{-Toc})$), that is, relative antioxidant activities, obtained for α-, β-, γ-, and δ-tocopherols increased slightly depending on the temperature. However, the order of the antioxidant activity in α-, β-, γ-, and δ-tocopherols was unchanged in this temperature range, and was $\alpha > \beta \sim \gamma > \delta$-tocopherols.

Empirically the temperature dependence of the rate constant k_s for such a reaction is given by the Arrhenius equation:

$$k_s = A_0 \exp(-E_{act}/kT) \qquad (3)$$

where k_s is the reaction rate of eq 1. From the Arrhenius plots of ln k_s vs $1/T$ for α-, β-, γ-, and δ-tocopherols, E_{act} and A_0 were determined. Similarly, the temperature dependence of k_s values of tocopherol derivatives **1**–**6** has been observed, and E_{act} and A_0 were determined. The obtained values are listed in Table III. From the Eyring theory of the activated transition state, on the other hand, one obtains

$$k_s = (kT/h) \exp(\Delta S^{\ddagger}/R) \exp(-\Delta H^{\ddagger}/RT) \qquad (4)$$

where $\Delta H^{\ddagger}$ is the activation enthalpy and $\Delta S^{\ddagger}$ is the activation entropy. The thermodynamic quantities $\Delta H^{\ddagger}$ and $\Delta S^{\ddagger}$ were deduced from plots of ln k_s/T vs $1/T$, which yielded straight lines according eq 4.

In the present work, we have measured the temperature dependence of the rate constants k_s for the reaction of α-, β-, γ-, and δ-tocopherols with substituted phenoxyl radical in ethanol and have succeeded in obtaining the activation energy E_{act} for the reaction. As expected from the relative k_s values (α:β:γ:δ = 1.00:0.44:0.47:0.20), the activation energy E_{act} increases in the order of $\alpha < \beta \sim \gamma < \delta$-tocopherol. On the other hand, the order of magnitude of frequency factor A_0 value ($\alpha < \beta < \gamma < \delta$) is different from that of the k_s value ($\alpha > \beta \sim \gamma > \delta$). The activation energies E_{act} of α-tocopherol and tocopherols **2**–**5** having two alkyl substituents at positions ortho to the OH group are similar to each other; however, the k_s values of tocopherols **2**–**5** are about half that of α-tocopherol. All the $\Delta S^{\ddagger}$ values of tocopherols are negative, and the change in $\Delta S^{\ddagger}$ values is very small.

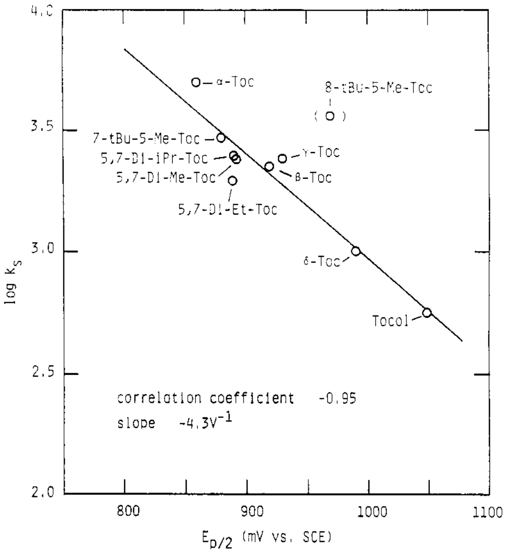

Figure 2. Plot of log k_s vs $E_{p/2}$ for tocopherol compounds.

The Correlation between E_{act} and $E_{p/2}$. Measurement of half-peak oxidation potentials ($E_{p/2}$) of tocopherols has been reported in a previous paper.[20] The observed values are listed in Table I. The values of log k_s for tocopherols have been plotted against $E_{p/2}$. As shown in Figure 2, a plot of log k_s vs $E_{p/2}$ is linear over most of the range with a slope of –4.3 V^{-1} (correlation coefficient = –0.95). Recently, Burton et al. have reported the k_1 values for the reaction of α-, β-, γ-, and δ-tocopherols, tocol, and 5,7-dimethyltocol with peroxyl radical.[1-3] As reported in a previous work, we have found that the same correlation exists for the reaction of tocopherols with peroxyl radical, showing a slope of –6.4 V^{-1} (correlation coefficient = –0.99).[20]

In the present work, the activation energy E_{act} for the reaction of tocopherols with phenoxyl has been obtained from the measurement of the temperature dependence of the second-order rate constants k_s. Therefore, the values of E_{act} have been plotted against half-peak oxidation potentials $E_{p/2}$. As shown in Figure 3, the E_{act} values were found to correlate with the $E_{p/2}$ values (correlation coefficient = 0.96), except for tocopherol **6**.

Recently, Burton et al. reported that the reaction of α-tocopherol with peroxyls exhibits a substantial deuterium kinetic isotope effect (k_1^H/k_1^D = 5.4 ± 0.4).[3] From the result, they indicated that H atom transfer is rate controlling, as with other phenols. The excellent correlations between the log k_1 of the peroxyl system and the half-peak oxidation potentials $E_{p/2}$ and the similar good

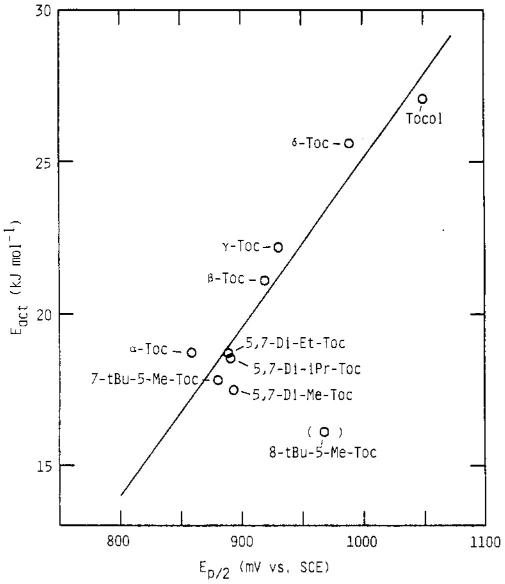

Figure 3. Plot of E_{act} vs $E_{p/2}$ for tocopherol compounds.

relationship for the present substituted phenoxyl system suggest a similar transition state for both the reactions; that is, the transition state involves breaking of the hydrogen–oxygen bond. However, it is not clear why both the logarithms of the second-order rate constants (k_l and k_s) and E_{act} obtained for tocopherols correlate well with their half-peak oxidation potentials $E_{p/2}$, if the simple hydrogen atom transfer from the tocopherols to the peroxyl or substituted phenoxyl radicals is rate-controlling. Bond energy D[ArO–H] in tocopherol derivatives may correlate with their half-peak oxidation potentials $E_{p/2}$. Mahoney and DaRooge have in fact suggested that the strengths of the O–H bonds in ring-substituted phenols depend on the nature of the remote substituent.[23] That is, the strengths of the O–H bonds depend on the extent to which the phenol is substituted on the ring by electron-donating or -withdrawing groups. On the other hand, Foote et al.[24] have extensively studied the reaction of $^1O_2$ with alkyl-substituted phenols. They have found that para-substituted 2,6-di-*tert*-butylphenols show a linear correlation between the log of the total rate of $^1O_2$ removal and their half-peak oxidation potentials $E_{p/2}$. Matsuura et al.[25] and Foote et al.[24] suggested that the most plausible scheme is a charge-transfer reaction between $^1O_2$ and phenol, leading to products by means of superoxide and phenol radical cation. In the present work, the log of the second-order rate constants, k_s, obtained for tocopherols was found to correlate with their half-peak oxidation potentials $E_{p/2}$. Further, it was found that the activation energies E_{act} for the reaction of tocopherols with substituted phenoxyl correlate well with their half-peak oxidation potentials $E_{p/2}$. These facts suggest that the transition state in the above free radical scavenging reaction by tocopherols has the property of the charge-transfer intermediate to some extent. Further study will be necessary to clarify the contribution of the charge-transfer intermediate in the above reaction.

ESR Studies of the Tocopheroxyl Radicals. The tocopherols **3**–**6** were oxidized with PbO_2 in toluene under vacuum. The well-resolved ESR hyperfine patterns were observed for these solutions, and the spectra were assigned to the primary tocopheroxyl-type radicals formed from the parent tocopherols by abstraction of a phenolic hydrogen atom. The similar ESR spectra were obtained by the reaction of tocopherol (5.00 mM) with substituted phenoxyl radical (2.50 mM) in toluene under vacuum, as reported before.[5] The assignment of the hyperfine splittings has been performed by a comparison of experimentally obtained couplings with reported ones for tocopheroxyl radicals, including α-, β-, γ-, and δ-tocopheroxyls.[26] All the hyperfine splittings and g_{iso} values obtained for these new tocopheroxyl radicals are summarized in Table 1S (supplementary material), together with those of α-tocopheroxyl radical.

The experimental values of spin densities (ρ_i^π) were estimated by using the relations $a_i^H = 27\rho_i^\pi$, $a_i^{CH_3} = 27\rho_i^\pi$, and $a_4^{CH_2} = 54 \cos^2 30° \times \rho_{4a}^\pi$, as performed for α-, β-, γ-, and δ-tocopheroxyl radicals.[26] All the experimental spin densities (ρ_i^π) calculated from the ESR hyperfine splittings are summarized in Table 1S.

Recently, Burton et al. have reported absolute rate constants, k_l, for the reaction of α-tocopherol and some related phenols (for example, 4-methoxy-2,3,5,6-tetramethylphenol) with peroxyl radicals (LOO•).[1-3] By comparing the k_l value for α-tocopherol with those found for structurally related phenols that lacked the 6-membered heterocyclic ring, they suggested that the structure of this ring was largely responsible for the high reactivity of α-tocopherol. That is, the high reactivity of α-tocopherol has been attributed to stereoelectric factors relating to the orientation of the p-type lone pair on the oxygen in position 1 with respect to the aromatic ring. Burton et al. have also reported that for 2-substituted 6-hydroxy-2,5,7,8-tetramethylchromans and for some 2,6-dimethylphenols log k_l can be correlated with the extent of stabilization of corresponding phenoxyl radicals as measured by the unpaired spin density at the two ortho methyl groups. There is, in fact, a rough correlation between log k_l and ($a_5^{CH_3}$ + $a_7^{CH_3}$).[3] As described in a previous section, we can expect that tocopherol **6** and β-tocopherol have similar electronic structure. In fact, in tocopherol **6** and β-tocopherol, ($a_5^{CH_3}$ + $a_7^{CH_3}$) values (10.64 G for **6** and 10.70 G for β-tocopherol) are similar to each other. However, the k_s value of tocopherol **6** (3.62×10^3 M^{-1} s^{-1}) is larger than that of β-tocopherol (2.24×10^3 M^{-1} s^{-1}). The reason is not clear at present.

Experimental Section

Measurements. The stopped-flow data were obtained on a UNISOKU stopped-flow spectrophotometer Model RS-450 by mixing equal volumes of ethanol solutions of substituted phenoxyl and tocopherol. The oxidation reactions were studied under pseudo-first-order conditions, and the observed rate constants, k_{obsd}, were calculated in the usual way by using a standard least-squares analysis.[5]

Cyclic voltammetry was performed at 20 °C under an atmosphere of nitrogen with a platinum electrode and a saturated calomel reference electrode in acetonitrile (dried over P_2O_5) containing 40 mM tetrabutylammonium perchlorate, with a Yanaco cyclic voltammetric analyzer Model P-1000H. Under these conditions, ferrocene as a standard sample has a half-wave potential ($E_{1/2}$) of +400 mV. The observed half-peak oxidation potentials ($E_{p/2}$) are summarized in Table I. The experimental error in $E_{p/2}$ values was ±20 mV at maximum.

The ESR measurements were carried out using a JES-FE-2XG spectrometer equipped with a Takeda-Riken microwave frequency counter. The g values were measured relative to the value of Li-TCNQ powder, calibrated with $(KSO_3)_2NO$ (g = 2.0054). All

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the ESR spectra have been measured in a sealed, degassed system.

Materials. *d*-α, *d*-β-, *d*-γ, and *d*-δ-tocopherol were kindly supplied from Eisai Co., Ltd. *dl*-Tocol (**1**) and *dl*-5,7-dimethyltocol (**2**) were prepared according to the method of Nilsson et al.[6] 5,7-Diethyltocol (**3**) and 5,7-diisopropyltocol (**4**) were synthesized by condensation of isophytol with the corresponding alkylhydroquinone, according to a procedure similar to that used by Nilsson et al. to prepare α-, β-, γ-, and δ-tocopherol models. On the other hand, 5,7-di-*tert*-butyltocol (**7**) could not be prepared by condensation of 2,6-di-*tert*-butylhydroquinone with isophytol, because of large steric repulsion between the bulky *tert*-butyl group at the C-5 position and the β-methylene protons at the C-4 position in **7**. In fact, condensation of 2-*tert*-butyl-6-methylhydroquinone with isophytol gave only 7-*tert*-butyl-5-methyltocol (**5**), and the isomeric 5-*tert*-butyl-7-methyltocol (**5′**) has not been obtained in the reaction. Similarly, condensation of 2-*tert*-butyl-5-methylhydroquinone with isophytol gave only 8-*tert*-butyl-5-methyltocol (**6**), which is one of the two possible isomers. The result of the analysis of hyperfine splitting constants of tocopheroxyl radicals **5** and **6** obtained by the PbO_2 oxidation of the corresponding tocopherols supports the above structures (see Table 1S).

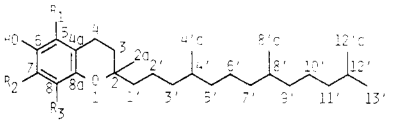
The 2,6-di-*tert*-butyl-4-(4-methoxyphenyl)phenoxyl (abbreviated to "substituted phenoxyl" (PhO•)) was prepared according to the method of Müller et al.[27] Radical concentration of substituted phenoxyl was obtained from the results of the paramagnetic susceptivility measurements at 20 °C, after correcting for the diamagnetic contribution ($\chi_{dia} = -0.22 \times 10^{-3}$ emu/mol) calculated by Pascal's method. The value was 100% for substituted phenoxyl, assuming the Curie law.

5-7-Diethyltocol (3). 2,6-Diethylhydroquinone (9.6 g, 58 mmol) was dissolved in formic acid (99%) (75 mL) and THF (tetrahydrofuran) (20 mL), and the solution was heated to reflux. A THF (5 mL) solution of isophytol (17.2 g, 58 mmol) was added dropwise slowly during 1 h, and the refluxing was continued for an additional 3 h with stirring. The reaction mixture was poured onto crushed ice (200 g) and extracted with diethyl ether (5 × 50 mL). Petroleum ether (bp 40–50 °C) (50 mL) was added to the combined diethyl ether extracts, and the mixture was washed with water (5 × 50 mL). After removal of the solvent, the residue was dissolved in methanol (75 mL), 1 mL of concentrated HCl was added, and the solution was refluxed for 20 min to hydrolyze the formate of **3** produced. The methanol was then evaporated, and the residue was taken up in diethyl ether (50 mL) and washed with $NaHCO_3$ solution and with water, and the solution was dried over anhydrous sodium sulfate. The solvent was evaporated, and the residual oil was extracted three times with hot petroleum ether (bp 40–50 °C) (2 × 100 mL). Removal of the solvent gave 28 g of viscous oil, which was purified by distillation under reduced pressure to give a thin yellow viscous oil of **3** (12 g, 47%): bp 190–205 °C (0.03 mmHg); ^1H NMR ($CDCl_3$, 60 MHz) δ 0.81 (s, 6 H, 4′a- and 8′a-CH_3), 0.89 (s, 6 H, 12′a- and 13′-CH_3), 0.90–1.60 (m, 21 H, 1′–12′-H), 1.13 (t, 3 H, 5b- or 7b-CH_3), 1.21 (t, 3 H, 5b- or 7b-CH_3), 1.22 (s, 3 H, 2a-CH_3), 1.77 (t, 2 H, J = 7.2 Hz, 3-CH_2), 2.49 (t, 2 H, J = 7.2 Hz, 4-CH_2), 2.61 (q, 4 H, J = 6.8 Hz, 5a- and 7a-CH_2), 4.20 (s, 1 H, 6-OH), 6.48 (s, 1 H, 8-H);[28,29] UV spectrum λ_{max} = 294.3 nm (log ϵ = 3.55 in ethanol). Anal. Calcd for $C_{30}H_{52}O_2$: C, 81.03; H, 11.79. Found: C, 80.95; H, 11.91.

5,7-Diisopropyltocol (4). Compound **4** was prepared by the reaction of isophytol with 2,6-diisopropylhydroquinone according to the procedure described above: bp 180–190 °C (0.04 mmHg); ^1H NMR ($CDCl_3$) δ 0.80 (s, 6 H, 4′a- and 8′a-CH_3), 0.86–1.51 (m, 21 H, 1′–12′-H), 0.90 (s, 6 H, 12′a- and 13′-CH_3), 1.21 (d, 6 H, J = 6.8 Hz, 5- or 7-$CH(CH_3)_2$), 1.23 (s, 3 H, 2a-CH_3), 1.36 (d, 6 H, J = 6.8 Hz, 5- or 7-$CH(CH_3)_2$), 1.74 (t, 2 H, J = 6.5 Hz, 3-CH_2), 2.65 (t, 2 H, J = 6.5 Hz, 4-CH_2), 3.11 (sep, 2 H, J = 6.8 Hz, 5- and 7-$CH(CH_3)_2$), 4.26 (s, 1 H, 6-OH), 6.48 (s, 1 H, 8-H); UV spectrum λ_{max} = 294.0 nm (log ϵ = 3.61 in ethanol). Anal. Calcd for $C_{32}H_{56}O_2$: C, 81.29; H, 11.94. Found: C, 81.33; H, 12.15.

7-*tert*-Butyl-5-methyltocol (5). Compound **5** was prepared by the reaction of isophytol with 2-*tert*-butyl-6-methylhydroquinone according to the procedure described above: bp 192–197 °C (0.06 mmHg); ^1H NMR ($CDCl_3$) δ 0.81 (s, 6 H, 4′a- and 8′a-CH_3), 0.87–1.56 (m, 21 H, 1′–12′-H), 0.91 (s, 6 H, 12′a- and 13′-CH_3), 1.23 (s, 3 H, 2a-CH_3), 1.38 (s, 9 H, 7-$C(CH_3)_3$), 1.75 (t, 2 H, J = 6.8 Hz, 3-CH_2), 2.07 (s, 3 H, 5-CH_3), 2.55 (t, 2 H, J = 6.8 Hz, 4-CH_2), 4.30 (s, 1 H, 6-OH), 6.56 (s, 1 H, 8-H); UV spectrum λ_{max} = 292.5 nm (log ϵ = 3.54 in ethanol). Anal. Calcd for $C_{31}H_{54}O_2$: C, 81.16; H, 11.86. Found: C, 80.90; H, 12.07.

8-*tert*-Butyl-5-methyltocol (6). Compound **6** was prepared by the reaction of isophytol with 2-*tert*-butyl-5-methylhydroquinone according to the procedure described above: bp 172–186 °C (0.20 mmHg); ^1H NMR ($CDCl_3$) δ 0.82 (s, 6 H, 4′a- and 8′a-CH_3), 0.88–1.48 (m, 21 H, 1′–12′-H), 0.91 (s, 6 H, 12′a- and 13′-CH_3), 1.23 (s, 3 H, 2a-CH_3), 1.35 (s, 9 H, 8-$C(CH_3)_3$), 1.72 (t, 2 H, J = 6.8 Hz, 3-CH_2), 2.07 (s, 3 H, 5-CH_3), 2.61 (t, 2 H, J = 6.8 Hz, 4-CH_2), 4.64 (s, 1 H, 6-OH), 6.59 (s, 1 H, 7-H); UV spectrum λ_{max} = 295.6 nm (log ϵ = 3.58 in ethanol). Anal. Calcd for $C_{31}H_{54}O_2$: C, 81.16; H, 11.86. Found: C, 80.90; H, 12.12



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Registry No. 1, 119-98-2; 2, 17976-95-3; 3, 118112-45-1; 3 (formate), 118112-48-4; 4, 118142-12-4; 4 (formate), 118112-50-8; 5, 118112-46-2; 5 (formate), 118112-49-5; 6, 118112-47-3; 6 (formate), 118112-51-9; 7, 70285-32-4; α-toc, 59-02-9; β-toc, 148-03-8; γ-toc, 7616-22-0; δ-toc, 119-13-1; isophytol, 505-32-8; 2,6-diethylhydroquinone, 7330-81-6; 2,6-diisopropylhydroquinone, 1988-10-9; 2-*tert*-butyl-6-methylhydroquinone, 2349-84-0; 2-*tert*-butyl-5-methylhydroquinone, 2349-76-0; 2,6-di-*tert*-butylhydroquinone, 2444-28-2.

Supplementary Material Available: Table with hyperfine couplings (a_i^H), g_{iso} values, and spin densities (ρ_i^π) of the tocopheroxyl radicals derived from tocopherol compounds in toluene at 20 °C (1 page). Ordering information is given on any current masthead page.

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