values were obtained: **4**, 0.96; **6/7** (mixture), 0.54; **9**, 0.41; **11**, 0.32; and **10**, 0.12. These substances were separated by preparative TLC and also by column chromatography on alumina where the order of elution was now: **4**, **11**, **9**, **6/7**, and finally **10**. The relative amounts of these products depended very much on the exact conditions chosen: (A) Diene **3** (1.04 g, 7.0 mmol) was added to a stirred mixture of 98% sulfuric acid (1.0 mL), acetonitrile (5.0 mL), and glacial acetic acid (5.0 mL) at 0 °C. The reaction was worked up as described previously after 30 min. Major products: **4**, **6/7**, **9**, and **10**. (B) Diene **3** (1.58 g, 10.7 mmol) was added to a stirred mixture of 98% sulfuric acid (1.5 mL), acetonitrile (3.0 mL), and glacial acetic acid (15.0 mL) at 0 °C. The reaction was stirred for 30 min at 0 °C and then for 3 days at room temperature. The reaction was then worked up by the usual method. Major products: **9**–**11**.

2,6-Dimethylbicyclo[3.3.1]nona-2,6-diene (4). The diene was obtained as an oil, which was identical with authentic material:[16a] IR (liquid film) 3020 (w), 2990 (s), 1670 (w), 1200 (w), 1140 (w), 1020 (m), 930 (m), 910 (m), 800 (s) cm^{-1}; ^{13}C NMR ($CDCl_3$) δ 137.2 (C), 119.2 (CH), 32.4 (CH), 30.4 (CH_2), 29.6 (CH_2), 22.4 (CH_3).

endo**/*****exo*****-6-Acetamido-2,6-dimethylbicyclo[3.3.1]non-2-ene (6/7).** Roughly equal amounts of the two isomers were obtained as a mixture: mp 89–94 °C; IR (liquid film) 3320 (s), 3080 (m), 1645 (s), 1540 (s), 1305 (m), 1290 (w), 1230 (w), 1120 (w), 1030 (w) cm^{-1}; MS, *m/z* (>10%) 207 (M$^+$, 17), 149 (10), 148 (M – CH_3CONH_2, 77), 133 (18), 120 (27), 112 (49), 107 (30), 106 (12), 105 (19), 94 (13), 93 (33), 92 (21), 91 (16), 79 (10), 77 (10), 70 (100), 60 (16), 57 (11), 43 (16), 42 (10); ^{1}H NMR ($CDCl_3$) δ 5.40–5.34 (m, 2 H, =CH and NH), 2.18–1.80 (m, 3 H), 1.92 and 1.88 (2 s, 3 H, $C\mathit{H}_3CONH$), 1.76–1.21 (m, 7 H), 1.57 (br s, 6 H, CH_3C=), 1.47 and 1.33 (2 s, 3 H, $C\mathit{H}_3CNHCO$); ^{13}C NMR ($CDCl_3$) δ 169.5 (C), 169.1 (C), 135.7 (C), 135.6 (C), 121.9 (CH), 121.6 (CH), 57.4 (C), 57.3 (C), 33.6 (two superimposed CH, resolved if C_6D_6 was added), 33.1 (CH), 32.9 (CH), 31.2 (CH_2), 29.6 (CH_2), 28.05 (CH_2), 28.01 (CH_2), 27.25 (CH_2), 27.23 (CH_2), 25.0 (CH_3), 24.7 (CH_2), 24.5 (CH_3), 24.22 (CH_2), 24.20 (CH_3), 22.9 (CH_3), 21.94 (CH_3), 21.92 (CH_3). Anal. Calcd for $C_{13}H_{21}NO$: C, 75.32; H, 10.21; N, 6.76. Found: C, 75.04; H, 10.46; N, 6.73.

exo**-11-Acetoxy-2,4,*****endo*****-11-trimethyl-3-azatricyclo[5.3.1.0^{4,9}]undec-2-ene (9).** The acetate was obtained as a solid: mp 96–97 °C after purification by sublimation; IR (paraffin mull) 1730 (s), 1680 (m), 1260 (s), 1190 (m), 1105 (m), 1080 (m), 1045 (m), 1020 (m), 885 (m), 795 (m) cm^{-1}; MS, *m/z* (>10%) 249 (M$^+$, 17), 206 (10), 164 (12), 149 (27), 148 (100), 133 (33), 121 (10), 120 (57), 108 (12), 107 (27), 106 (27), 105 (16), 95 (16), 94 (20), 93 (34), 92 (22), 91 (14), 81 (10), 79 (10), 71 (14), 70 (10), 55 (10), 43 (46), 42 (10), 41 (13); ^{1}H NMR ($CDCl_3$) δ 3.12 (s, 1 H), 2.26–2.22 (d, 1 H), 2.13 (s, 3 H), 2.01 (s, 3 H), 1.80–1.27 (m, 8 H), 1.60 (s, 3 H), 1.30 (s, 3 H), 1.15–1.08 (m, 1 H); ^{13}C NMR ($CDCl_3$) δ 170.4 (C), 169.2 (C), 86.9 (C), 58.8 (C), 42.0 (CH), 36.1 (CH), 32.6 (CH_2), 31.9 (CH), 31.6 (CH_3), 29.0 (CH_3), 27.3 (CH_2), 27.1 (CH_2), 22.6 (CH_3), 22.3 (CH_3), 19.8 (CH_2). Anal. Calcd for $C_{15}H_{23}NO_2$: C, 72.25; H, 9.30; N, 5.62. Found: C, 72.45; H, 9.44; N, 5.72.

11-Methylene-2,4-dimethyl-3-azatricyclo[5.3.1.0^{4,9}]undec-2-ene (11). The alkene was obtained as a mobile oil: IR (liquid film) 3075 (w), 1670 (m), 1630 (m), 1300 (w), 1195 (w), 1115 (w), 1015 (w), 890 (s) cm^{-1}; MS, *m/z* (>5%) 189 (M$^+$, 5), 149 (13), 148 (M – CH_3CN, 100), 133 (25), 120 (15), 119 (20), 107 (14), 106 (27), 105 (31), 94 (11), 93 (35), 92 (32), 91 (33), 81 (9), 80 (19), 79 (25), 78 (7), 77 (14), 68 (6), 67 (6), 65 (7), 55 (6), 53 (9), 42 (11), 41 (16), 39 (13); ^{1}H NMR ($CDCl_3$) δ 4.66 (d, 1 H, J = 2.2 Hz), 4.64 (d, 1 H, J = 2.2 Hz), 2.87 (s, 1 H), 2.58–2.54 (d, 2 H), 2.01 (s, 3 H), 1.97–1.46 (m, 6 H), 1.34 (s, 3 H), 1.31–1.25 (m, 1 H), 1.04–0.96 (m, 1 H); ^{13}C NMR ($CDCl_3$) δ 170.4 (C), 152.8 (C), 108.6 (CH_2), 59.2 (C), 44.9 (CH), 35.8 (CH), 33.2 (CH_2), 32.5 (CH), 32.1 (CH_2), 31.8 (CH_3), 31.4 (CH_2), 26.3 (CH_2), 25.4 (CH_3). Anal. Calcd for $[C_{13}H_{19}N]^+$ *m/z* 189.1512, found *m/z* 189.1627; calcd for $[C_{11}H_{16}]^+$ *m/z* 148.1247, found *m/z* 148.1311.

Acknowledgment. We thank Dr. J. J. Brophy and Dr. I. Gregor (mass spectra) and H. Stender (NMR spectra) for their skillful assistance.

Registry No. **3**, 26069-13-6; **4**, 77452-58-5; **6**, 111935-65-0; **7**, 111935-66-1; **9**, 111935-67-2; **10**, 111935-64-9; **11**, 111935-68-3; CH_3CN, 75-05-8.

A Kinetic Study of Reactions of Tocopherols with a Substituted Phenoxyl Radical

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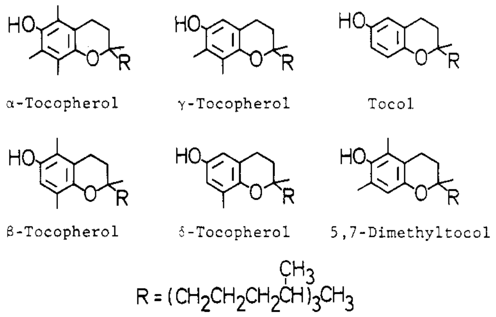
Vitamin E (α-, β-, γ-, and δ-tocopherols) is well-known to scavenge active free radicals (LOO$^\bullet$, LO$^\bullet$, and HO$^\bullet$) generated in biological systems. The above free radical scavenging actions by vitamin E have been ascribed to the initial reaction of the phenolic hydroxyl group with the production of a tocopheroxyl radical.[1,2] Recently, Burton et al. have reported absolute second-order rate constants, k_1, for the reaction of α-, β-, γ-, and δ-tocopherols with poly(peroxystyryl)peroxyl radicals using the inhibited autoxidation of styrene method (reaction 1).[3-5] In a



$R = (CH_2CH_2CH_2\overset{CH_3}{CH})_3CH_3$

$$LOO^\bullet + Toc \xrightarrow{k_1} LOOH + Toc^\bullet \qquad (1)$$

previous work, we have determined spectrophotometrically the rates of reaction of α-, β-, γ-, and δ-tocopherols with a stable substituted phenoxyl radical (2,6-di-*tert*-butyl-4-(4-methoxyphenyl)phenoxyl (ArO$^\bullet$)) in ethanol using stopped-flow technique as a model reaction of tocopherols with unstable free radicals (reaction 2).[6] The relative k_2

$$ArO^\bullet + Toc \xrightarrow{k_2} ArOH + Toc^\bullet \qquad (2)$$

values (α:β:γ:δ=100:44:47:20) obtained by the stopped-flow technique are in good agreement with the k_1 values (100:41:44:14) obtained by the inhibited autoxidation of styrene method, although the absolute values are about 600 times smaller than those for the reaction of tocopherols with the poly(peroxystyryl)peroxyl radical in chlorobenzene (see Table I).[6] The result suggests that the relative reactivities, that is, relative antioxidant activities, of tocopherols in homogeneous solution do not depend on the kinds of radicals (substituted phenoxyl and peroxyl radicals) used, while the absolute rates are considerably different from each other.

In the present work, we have measured the second-order rate constants, k_2, for the reaction of tocol and 5,7-di-

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Table I. Second-Order Rate Constants (k_1 and k_2) for Oxidation of Tocopherols and Half-Peak Oxidation Potentials ($E_{p/2}$) for Tocopherols

	$10^{-6}\ k_1$ ($M^{-1}\ s^{-1}$)	$10^{-3}k_2$ ($M^{-1}\ s^{-1}$)	$E_{p/2}$ vs SCE (mV)
α-tocopherol	3.20	5.12	859 ± 31
β-tocopherol	1.30	2.24	920 ± 26
γ-tocopherol	1.40	2.42	930 ± 16
δ-tocopherol	0.44	1.00	990 ± 6
tocol		0.56	1050 ± 11
5,7-dimethyltocol	1.80	2.39	893 ± 9
radical	poly(peroxystyryl) peroxyl	substituted phenoxyl	

methyltocol[7,8] with stable substituted phenoxyl radicals (ArO•) in ethanol at 25.0 °C. Half-peak oxidation potentials ($E_{p/2}$) for tocopherol compounds have also been measured, using cyclic voltammetry technique.

Results and Discussion

As listed in Table I, 5,7-dimethyltocol 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 is ca. 11% as reactive as α-tocopherol. The result indicates that the antioxidant activity of these tocopherols varies depending on the number of methyl substitutions. Consequently, we can expect that the antioxidant activity of these tocopherol compounds relates to the total electron-donating character of the methyl group substituted to the aromatic ring.

The values of log k_2 for tocopherols have been plotted against both the sum of the Hammett's σ constants ($\sum\sigma$) and the Brown's σ^+ constants ($\sum\sigma^+$) for all the substituents on the tocopherols.[9] The logarithms of rate constants k_2 were found to roughly correlate with $\sum\sigma$ or $\sum\sigma^+$ substituent constants, but the two cases could not be distinguished. Howard and Ingold have measured the rate constants k_1 for the reaction of o-alkylphenols with poly(peroxystyryl)peroxyl radicals.[9] They reported that the steric effect due to o-alkyl substituents is important. However, the present result indicates that the steric effect on the reaction rate is not remarkable for the reactions of tocopherols with a substituted phenoxyl radical in ethanol. A similar trend was observed for the reaction of tocopherols with poly(peroxystyryl)peroxyl radical.

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, using 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. Cyclic voltammetry indicates that the tocopherol oxidations are not reversible and that subsequent reactions consume the oxidized tocopherols. Therefore, the experimental half-peak oxidation potentials ($E_{p/2}$) are used, which, in a series of similar compounds, should be linearly related to the half-wave oxidation potentials ($E_{1/2}$).[10] The observed half-peak oxidation potentials ($E_{p/2}$) are summarized in Table I.

The values of log k_2 for tocopherols have been plotted against $E_{p/2}$. As shown in Figure 1, a plot of log k_2 vs $E_{p/2}$ is linear over most of the range with a slope of $-4.8\ V^{-1}$ (correlation coefficient = 0.98). The same correlation is given for the reaction of tocopherols with peroxyl radical, showing a slope of $-6.4\ V^{-1}$ (correlation coefficient = 0.99) (see Figure 1). Foote et al. have extensively studied the reaction of $^1O_2$ with alkyl-substituted phenols.[10] 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-wave oxidation potentials ($E_{p/2}$). Matsuura et al.[11] and Foote et al.[10] 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. Svanholm et al. have proposed that in the first step of antioxidation tocopherol produces a cation radical by one-electron extraction.[12] The cation radicals are comparatively stable, and recently we have succeeded in measuring ESR and ENDOR spectra of cation radicals obtained by the oxidation of α-, β-, γ-, and δ-tocopherol model compounds in a $AlCl_3$–CH_2Cl_2 mixture.[13] These facts may suggest the existence of the charge-transfer intermediate in the above free radical scavenging reactions by tocopherols. However, Burton and Ingold reported that the reaction of α-tocopherol with peroxyls exhibits a substantial deuterium kinetic isotope effect ($k_1^H/k_1^D = 5.4 \pm 0.4$).[5] From the result, they indicated that H atom transfer (reaction 1) 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 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 at present why the log of the second-order rate constants (k_1 and k_2) obtained for tocopherols correlates 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 ($E_{p/2}$).

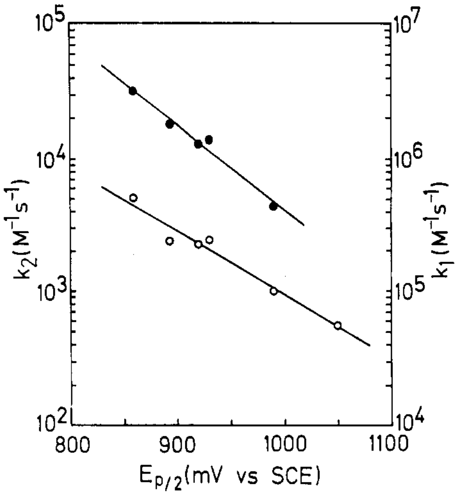

Figure 1. Plots of log k_1 (●) and log k_2 (○) vs $E_{p/2}$ for tocopherol compounds.

Summary. A kinetic study of reactions of tocopherols with a substituted phenoxyl radical has been performed,

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using stopped-flow technique. The log of the second-order rate constants (k_2) obtained for tocopherols was found to correlate with their half-wave oxidation potentials ($E_{p/2}$); the same correlation was found for the reaction of tocopherols with peroxyl radical.

Acknowledgment. We are very grateful to Eisai Co. for the generous gift of α-, β-, γ-, and δ-tocopherols. We are also very grateful to Prof. Yoichi Kitamura for use of the stopped-flow spectrophotometer and his helpful discussions.

Registry No. α-Tocopherol, 59-02-9; γ-tocopherol, 7616-22-0; tocol, 119-98-2; β-tocopherol, 148-03-8; δ-tocopherol, 119-13-1; 5,7-dimethyltocol, 493-35-6.

Deoxygenation of Tertiary Alcohols Using Raney Nickel[†]

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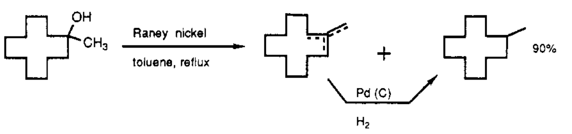
Introduction

Tertiary alcohols have been deoxygenated by using a variety of different routes.[1,2] These include reduction of tertiary alcohol thioformates using tributylstannane,[3] acid-catalyzed hydrogenolysis using palladium or platinum catalysts in the presence of hydrogen,[4] benzylic hydrogenolysis under dissolving metal conditions,[5] ionic deoxygenations using silanes and Lewis acids,[6] and the use of transition-metal catalysts.[7] During the course of our investigation of the oxidation of secondary alcohols to ketones using Raney nickel,[8] we found that tertiary alcohols were easily deoxygenated by Raney nickel under similar reaction conditions. Raney nickel has previously been used in reductive desulfurization reactions or as a hydrogenation catalyst in the reduction of nitro groups,[9] isoxazolidines,[10] and olefins.

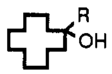
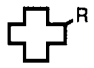
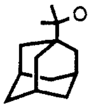
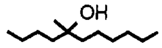
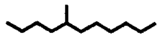
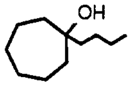
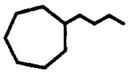
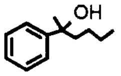
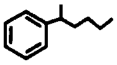
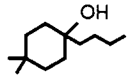
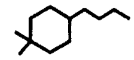
Results and Discussion

We report that the use of Raney nickel in toluene provides a mild and inexpensive means of efficiently deoxygenating tertiary alcohols under neutral conditions. Heating a toluene solution of 1-methyl-1-cyclododecanol with washed[11] Raney nickel for 40 min resulted in the formation of a mixture[12a] of methylcyclododecenes and methylcyclododecane (eq 1). Subsequent hydrogenation of the olefins [Pd(C), H_2, EtOH, EtOAc] gave a 90% yield of methylcyclododecane.[12b] The deoxygenation and olefin reduction sequence could also be carried out in one step. For example, reaction of 1-methyl-1-cyclododecanol with a large excess of Raney nickel yielded exclusively methylcyclododecane in 90% yield after 12 h in refluxing toluene.[12c] We found that with other tertiary alcohols the reduction proceeded cleanly and in high yield as is illustrated by the results in Table I.



(1)

Table I

entry	alcohol	product(s)[a]	yield (%)[b]
			
1	$R = CH_3$		90
2	R = n-Bu		89
3	R = t-Bu		91[c]
4			90
			
5	R = TBDMS		86
6	R = Ac		90
7			80
8			83
9			94
10		 	71 13
11			90
12			99

[a] Products obtained after hydrogenation of the olefins. [b] All yields refer to isolated materials. [c] Yield of olefins.

tert-Butyldimethylsilyl ethers and acetates were stable to the reaction conditions as is demonstrated by entries

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[†] Dedicated to Professor Gilbert Stork on the occasion of his 65th birthday.

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