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The Oxidative Dimerization of α-,β-,γ-, and δ-Tocopherols[1]

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A study of the oxidative dimerization of α-, β-, γ-, and δ-tocopherols and corresponding model compounds in the presence of *p*-benzoquinone has led to the synthesis and characterization of nine dimers and two trimers. Six of these dimers are new.

Mechanisms are formulated which give rise to these products. These mechanisms involve initial formation of phenoxy radicals which then react in two different ways: (1) two phenoxy radicals couple through oxygen or the *ortho* positions on the ring (β-, γ-, and δ-tocopherols); and (2) phenoxy radicals rearrange to benzyl radicals followed by coupling (α- and β-tocopherols). A strong preference was noted for reaction at the 5-position *versus* the 7-position regardless of whether the substituents in these positions were hydrogen or methyl. The electronic or steric factors underlying this preference are not readily apparent.

Four dimers of γ- and δ-tocopherol (*3a* and *4a*) have been obtained during the fractionation of freshly prepared corn oil.[2] The need for synthetic tocopherol dimers for structural comparison led us to undertake a study of the oxidative dimerization of the four tocopherols, α, β, γ, and δ (*1a—4a*, respectively). Since each of two of the isolated dimers [2] involve two different tocopherols (tocotrienols [1]), the oxidation of all possible binary mixtures of the tocopherols has also been carried out to study the formation of such "mixed" tocopherol dimers.

Nine dimers and two trimers of the tocopherols (*1a—4a*) or appropriate models (*1b—4b*) have been synthesized and characterized. Six of these dimers are new. It is now possible to formulate, in general terms, the mechanisms which lead to the four distinct structural types of dimers, and the factors that govern which dimerization pathway is preferred for a given tocopherol.

The oxidation of α-tocopherol (*1a*) has been extensively studied,[3] most recently by Skinner and Parkhurst.[4] Oxidations have been carried out using a variety of reagents, and a diversity of products are known. Among these

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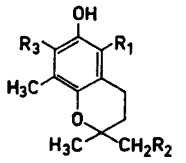
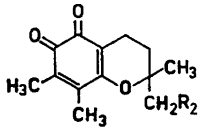


1, $R_1 = R_3 = CH_3$, α-tocopherol
2, $R_1 = CH_3$; $R_3 = H$, β-tocopherol
3, $R_1 = H$; $R_3 = CH_3$, γ-tocopherol
4, $R_1 = R_3 = H$, δ-tocopherol



a: $R_2 = -(CH_2CH_2\overset{CH_3}{\overset{|}{C}}HCH_2)_3H$, natural tocopherol
b: $R_2 = H$, tocopherol model compound

oxidation products of α-tocopherol (*1a*) are two dimers, spirodimer (*8a*)[4] and α-tocopherylethane (*10a*),[5] and one trimer (*6a*).[6] The oxidation reactions of β-, γ-, and δ-tocopherols (*2a*, *3a*, and *4a*) have been less studied. Boyer[7] reported the oxidation of each of the tocopherols (*1a*—*4a*) using ferric chloride in the presence of 2,2'-bipyridine. β-Tocopherylquinone has been prepared from β-tocopherol (*2a*) by oxidation with silver nitrate or ferric chloride.[8] Oxidation of γ-tocopherol with these reagents produces tocored (*5a*).[9] McHale and Green[10] prepared 5-(γ-tocopheryloxy)-γ-tocopherol[1] (*12a*) by heating equimolar portions of γ-tocopherol (*3a*) and *p*-benzoquinone in benzene under reflux. Prior to the present work, no dimers of β- or δ-tocopherol (*2a* or *4a*) have been characterized.

Oxidative dimerization of α-, β-, γ-, and δ-tocopherols (1a—4a) *and model compounds* (1b—4b). The synthesis of dimer *12a*,[10] one of the γ-tocopherol dimers discovered during the fractionation of corn oil,[2] by treatment of γ-tocopherol (*3a*) with *p*-benzoquinone, indicated to us that this reagent might be a general oxidizing agent for the preparation of other tocopherol dimers. Indeed, we have found that when each of the tocopherols (*1a*—*4a*) and/or their model compounds (*1b*—*4b*) was treated individually with one equivalent of benzoquinone in refluxing benzene, the corresponding reaction products were obtained by preparative thin layer chromatography. Equimolar quantities of all possible binary mixtures of the tocopherols were similarly treated.

α-Tocopherol. McHale and Green[10] reported, without experimental details, that the oxidation of α-tocopherol (*1a*) with *p*-benzoquinone in benzene yielded α-tocopherylethane (*10*) as the major product. Our experiments using a model compound (*1b*) for α-tocopherol (*1a*) produced different results. The α-model compound *1b* was heated with one equivalent of *p*-benzoquinone in refluxing benzene for 24 h, and the resulting reaction mixture was separated by thin layer chromatography. Unchanged starting material (47 %) was recovered, and three previously recognized oxidation products, trimer *6b*[6] (24 %), spirodimer *8b*[4,11] (7.5 %), and the α-tocopherylethane model compound *10b*[5,11] (3 %), were obtained. The isolated products were characterized by comparison with authentic samples.[5,6,11] Treatment of α-tocopherol (*1a*) with benzoquinone under the same conditions produced similar products. Several additional, minor products were observed as dark-colored polar bands

on the thin layer plates. These products appear to be quinones (positive reaction with leucomethylene blue) but were not characterized.

β-Tocopherol. Treatment of the β-model compound (*2b*) with *p*-benzoquinone in refluxing benzene for 24 h produced three products and 57 % of recovered starting material. One product (9 % yield) possesses UV and IR spectra (Table 1) very similar to those of the α-model trimer *6b*, and is assigned structure *7b*. The NMR spectrum of this β-model trimer *7b* exhibits one-proton singlets at τ 3.51 and 3.67 representing aromatic protons. A one-proton signal at τ 4.20 (quartet, $J \cong 1.5$ cps) coupled with a three-proton signal at τ 8.05 are due to the vinyl proton and the methyl group present in the α,β-unsaturated ketone moiety.

Two other products, each of which accounted for about 2 % of the starting material, are both phenolic (IR stretching bands at 3500 cm^{-1}, Table 1). The least polar of these products exhibits λ_{max}^{hexane} at 295 mμ and NMR signals at τ 4.02 (1H, aromatic), τ 5.30 (—OH), and τ 7.77, 7.91, 8.05, and 8.22 (aromatic methyl) consistent with structure *17b*, β-diphenylether model dimer. The more polar product exhibits λ_{max}^{hexane} 300, 293 (sh) mμ. The NMR spectrum shows a two-proton signal at τ 5.82 and signals representing aromatic methyl groups at τ 7.91 ($2CH_3$); 8.00 ($1CH_3$); and 8.25 ($1CH_3$). No signals due to aromatic protons are observed. These data allow the formulation of this product as the β-diphenyl model dimer *18b*. No spirodimer (*9b*) or β-tocopherylethane model *11b* were detected in the reaction mixture.

γ-Tocopherol (3a). Treatment of γ-tocopherol (*3a*) with an equivalent of *p*-benzoquinone in refluxing benzene for 30 min produced two dimeric products, accounting for 38 % of the starting material. The IR spectra of both dimers show OH— stretching bands at ~3500 cm^{-1}. Their UV spectra are very similar to the spectra of the tocopherols and exhibit two absorption bands in the region 290—300 mμ (Table 1). The NMR spectra (Table 1) have been described,[2] and are consistent with the formulation of the compounds as 5-(γ-tocopheryloxy)-γ-tocopherol (*12a*),[10] 34 % yield, and 5-(γ-tocopheryl)-γ-tocopherol (*16a*), 4 % yield. Similar dimers have been reported by Hewgill *et al.*[12–15] in the oxidation of *p*-alkoxyphenols with potassium ferricyanide or silver oxide. Synthetic dimers *12a* and *16a* from γ-tocopherol proved to be indistinguishable chromatographically and spectrally from two nonpolar phenolic products, which were obtained in the fractionation of lipid extracts of fresh corn.[2]

δ-Tocopherol (4a). δ-Tocopherol (*4a*) was oxidized by *p*-benzoquinone somewhat more slowly than γ-tocopherol (*3a*). When the oxidation was terminated after 30 min, very little reaction had occurred. When the reaction was allowed to continue for 2 h, one major product was formed (23 % isolated yield). In the NMR spectrum of this product, two distinct aromatic methyl groups appear as singlets at τ 7.92 and 7.96, and the appearance of one-proton singlets at τ 3.46, 3.61, 3.78, and 5.52 indicate the presence of three aromatic ring protons and one OH-functionality. Formulation of the compound as 5-(δ-tocopheryloxy)-δ-tocopherol (*13a*) is consistent with these data.

Binary mixtures of tocopherols. A product obtained during the fractionation of extracts of corn oil was shown to be 5-(δ-tocopheryloxy)-γ-tocopherol

(*15a*), a "mixed" dimer of γ- and δ-tocopherol (*3a* and *4a*).[2] This dimer was synthesized by treatment of an equimolar mixture of γ- and δ-tocopherol (*3a* and *4a*) with *p*-benzoquinone. In order to investigate the possibility of preparing other "mixed" tocopherol dimers, all possible binary mixtures of tocopherols (*1a*—*4a*) were heated with equimolar portions of benzoquinone in refluxing benzene for 30 min, and the resulting reaction mixtures were separated by thin layer chromatography. The results obtained are summarized in Table 2. Under the conditions used, no spiro- (*8a*) or tocopherylethane- (*10a*) dimers of α- or β-tocopherol (*1a* or *2a*) were formed. However, "mixed" dimers of β- and γ-tocopherols (*2a* and *3a*) and of γ- and δ-tocopherols (*3a* and *4a*) were isolated. Thus, when a mixture of β- and γ-tocopherol (*2a* and *3a*) was oxidized with benzoquinone in refluxing benzene for 30 min, a mixture of the γγ-dimers, 5-(γ-tocopheryloxy)-γ-tocopherol (*12a*) and 5-(γ-tocopheryl)-γ-tocopherol (*16a*) and the βγ-dimer, 5-(β-tocopheryloxy)-γ-tocopherol (*14a*) were formed. Similarly, codimerization of γ- and σ-tocopherol yielded the two γγ-dimers (*12a* and *16a*) and the γδ-dimer, 5-(δ-tocopheryloxy)-γ-tocopherol (*15a*).

The structure assignments of these mixed dimers are based on an analysis of their NMR spectra (Table 1). The spectrum of the βγ-dimer (*14a*) and that of the γδ-dimer (*15a*) exhibit singlets corresponding to one proton at τ 5.33 and 5.34, respectively, due to phenolic hydroxyls. These spectra are consistent only with diphenylether-type dimeric structures, since the isomeric biphenyl dimers possess *two* phenolic hydroxyls which appear as signals at higher field. For example, γ-diphenylether dimer, *12a*, shows a hydroxyl signal (1H, singlet) at τ 5.34, and the isomeric γ-biphenyl dimer, *16a*, shows a hydroxyl signal (2H, singlet) at τ 5.80 (Table 1).

Having established that both the βγ-dimer (*14a*) and the γδ-dimer (*15a*) are of the diphenylether-type, it was necessary to establish which of the isomeric diphenylether dimers were produced. In the case of the βγ-dimer, two structures are possible: a dimer produced by coupling of β-tocopheryloxy radical (*19a*, R = H) on the unsubstituted 5-position of γ-tocopherol (*3a*), or a dimer formed by attachment of γ-tocopheryloxy radical (*24a*, R = CH_3) at position-7 of β-tocopherol (*2a*). Three isomeric diphenylether dimers of δ- and γ-tocopherol are possible: a dimer produced by attachment of δ-tocopheryloxy radical (*24a*, R = H) at the 5-position of γ-tocopherol (*3a*), or attachment of a γ-tocopheryloxy radical (*24a*, R = CH_3) at either of positions-5 or -7 of δ-tocopherol (*4a*). That the diphenylether dimers formed possess structures *14a* and *15a* — products formed, in each case, by attack of a β- or δ-tocopheryloxy radical (*19a*, R = H, and *24a*, R = H, respectively) on the 5-position of γ-tocopherol (*3a*) — was established by the following comparisons.

In the NMR spectrum of the βγ-diphenylether dimer (*14a*), the aromatic proton appears as a singlet at τ 3.99 and in the spectrum of the γ-diphenylether dimer (*15a*) corresponding one-proton singlets appear at τ 3.61 and 3.78. These signals are identical to those observed in the β-diphenylether dimer *17a* (τ 3.99) and the δ-diphenylether dimer *13a* (τ 3.46, 3.61, and 3.78). In contrast, the aromatic proton in the γ-diphenylether dimer *12a* appears at τ 4.10, indicating that this is the aromatic proton which is absent in the "mixed" dimers *14a* and *15a*.

Table 1. Chromatographic and spectral data for the tocopherols and their dimers and trimers.

Compound	Chromatography (R_F)	UV λ_{max}^{hexane} (mμ)	IR in CCl_4 (cm^{-1})	NMR τ-values [a,b]				Mass spectra m/e for M^+ [c] m/e
				Aromatic	OH	Benzylic	Aromatic methyl groups	
α-Tocopheryl-ethane *10b*	0.31 [d]	297 293(sh)	3500	—	5.00	7.40	7.94; 8.00	438
α-Spirodimer *8b*	0.57 [d]	292 298 337	1685	—	—	7.50	8.00 [e]	
α-Trimer *6b*	0.65 [d]	293 297(sh)	1690	—	—	7.50	7.86; 7.90 [f]; 7.93; 8.01	654
α-Tocopherol *1a*	0.37 [d]	293 297(sh)	3500	—	6.16	7.49	7.94; 8.00	
β-Trimer *7b*	0.37 [d]	292 297(sh)	1690	3.51 3.67	—	7.50	7.94; 7.97 [g]	
β-Biphenyl-dimer *18b*	0.25 [d]	300 293(sh)	3500	—	5.82	7.36	7.91; 8.00; 8.25	
β-Diphenyl-etherdimer *17b*	0.72 [d]	295	3500	3.99	5.30	7.40	7.77; 7.92; 8.05; 8.22	
β-Tocopherol *2a*	0.40 [d]	293 297	3500	3.76	6.11	7.46	8.00	
γ-Biphenyl-dimer *16a*	0.67 [h]	300 292(sh)	3500	—	5.80	7.50	7.87; 7.94	830
γ-Diphenyl-etherdimer *12a*	0.80 [h]	297 292(sh)	3500	4.10	5.34	7.50	7.75; 7.87; 7.93; 7.97	830
γ-Tocopherol *3a*	0.30 [h]	294 300	3500	3.90	5.90	7.43	7.96; 7.99	
δ-Diphenyl-etherdimer *13a*	0.72 [h]	293 297	3500	3.46 3.61 3.78	5.52	7.40	7.92; 7.96	
δ-Tocopherol *4a*	0.22 [h]	295 298(sh)	3500	3.74 3.84	5.37	7.43	7.99	
βγ-Diphenyl-etherdimer *14a*	0.63 [h]	295 291(sh)	3500	3.99	5.33	7.40	7.79; 7.87; 7.97; 8.05	
γδ-Diphenyl-etherdimer *15a*	0.60 [h]	296	3500	3.62 3.79	5.34	7.40	7.88; 7.96	

[a] Sample in CCl_4 solution.
[b] Alkyl protons at τ 8.40, 8.80, and 9.15.
[c] A detailed description of the mass spectra of this series of compounds will be reported elsewhere.[29]
[d] Silica gel G developed in ether:hexane (3:7).
[e] Vinylic methyl groups at τ 8.10 and 8.21.
[f] Vinylic methyl groups at τ 8.10 and 8.34.
[g] Vinylic proton at τ 4.20, and vinylic methyl group at τ 8.05.
[h] Silica gel G developed in ether:hexane (1:9).

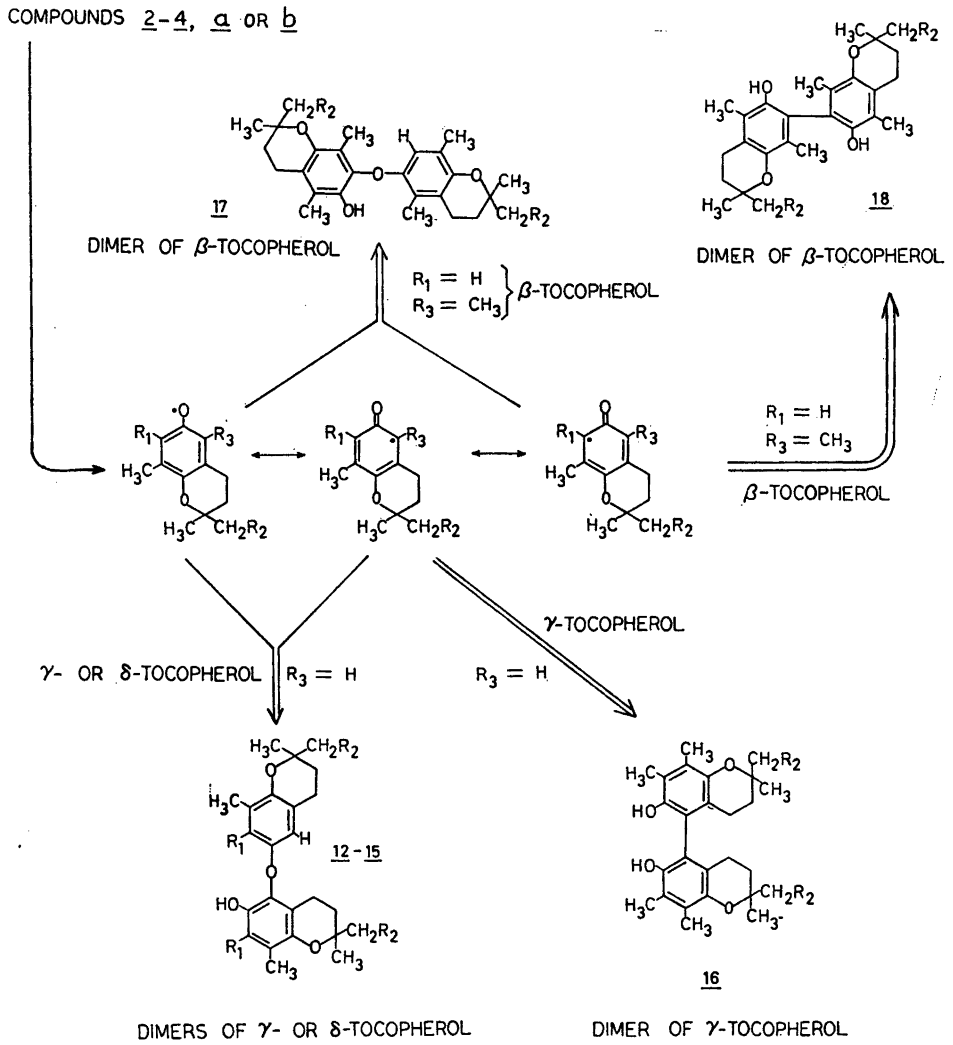
Mechanisms of dimerization. Abundant data in the literature indicate that the initial step in the oxidation of phenols is the removal of the phenolic hydrogen with formation of a phenoxy radical.[16] The stability of phenoxy radicals is dependent, primarily, on the number and orientation of ring substituents,[17] 2,4,6-trisubstituted phenols produce particularly stable phenoxy radicals.[18] The order of stability of the tocopheryloxy radicals predicted by these principles is $\alpha > \beta \cong \gamma > \delta$. This order is in accord with the observation that the vitamin E activity of the tocopherols is: $\alpha > \beta > \gamma > \delta$.[19] In the present study, reaction times of 12—24 h were necessary to achieve appreciable dimerization of α- and β-tocopherol (*1a* and *2a*); under similar conditions, γ- and δ-tocopherol (*3a* and *4a*) were significantly dimerized in periods of 30 min or less. These large differences in reactivity reflect the modes of reaction available to the different tocopheryloxy radicals. These pathways are outlined in Schemes 1 and 2.

The favored reaction pathway of many phenoxy radicals,[20] and one which is of great importance in the biogenesis of many phenolic alkaloids,[21] involves the coupling through the *ortho-* or *para*-positions of two such phenoxy radicals to produce dimers, or the coupling of a phenoxy radical with another radical species, to form a substitution product.[12,15,17] The dimerization of γ- and δ-tocopherols (*3a* and *4a*) exemplifies this process (Scheme 1). β-Tocopherol (*2a*) also dimerizes similarly although, in this case, this pathway is not the major one.

The bulky substituents present in the tocopherols apparently preclude coupling of radicals at ring positions bearing substituents; consequently, α-tocopherol (*1a*), and to a large extent β-tocopherol (*2a*), dimerize in an alternative way (*Scheme 2*). α- and β-Tocopherols (*1a* and *2a*) appear to dimerize *via* a coupling reaction between two benzyl radicals (*20*) to produce tocopherylethanes (*10*, *11*). Benzyl radical intermediates (*20*) have been suggested by Inglett and Mattill [9] in the benzoyl peroxide oxidation of α-tocopherol. Schudel *et al.*[11] have shown that α-tocopherylethane (*10a*) can be oxidized to the α-spirodimer (*8a*) presumably *via* two one-electron oxidations followed by an intramolecular radical coupling (21 → 22 → 8). Recent work by Boguth *et al.*[22] supports this mechanism. Formation of trimer (*6*) is most easily formulated as involving a Diels-Alder reaction with a quinone methide (*24*) as suggested by Skinner and Parkhurst.[6] From the oxidation of the model compound for α-tocopherol (*1b*), the tocopherylethane dimer (*10b*), the spirodimer (*8b*), and the trimer (*6b*) have been isolated. From the oxidation of the model compound for β-tocopherol (*2b*), only the trimer (*7b*) was isolated; however, it is probable that β-tocopherylethane dimer *11b* and the spirodimer *9b* were formed as intermediates.

While the general features concerning the various modes of oxidative dimerization of the tocopherols are readily rationalized as shown in Schemes 1 and 2, certain selective reactions in this study and by previous workers[*e.g.*,4,11] are not clearly explicable, but deserve comment. Although little difference in either electronic or steric environments are apparent, a very strong preference exists for reaction at the 5-position *versus* the 7-position of the tocopherols. This preference is observed regardless of whether the substituents in the 5- and 7-positions are hydrogen or methyl, as shown by the following observations.

SCHEME 1



$R_1 = H$, $R_3 = CH_3$, β-TOCOPHEROL

$R_1 = CH_3$, $R_3 = H$, γ-TOCOPHEROL

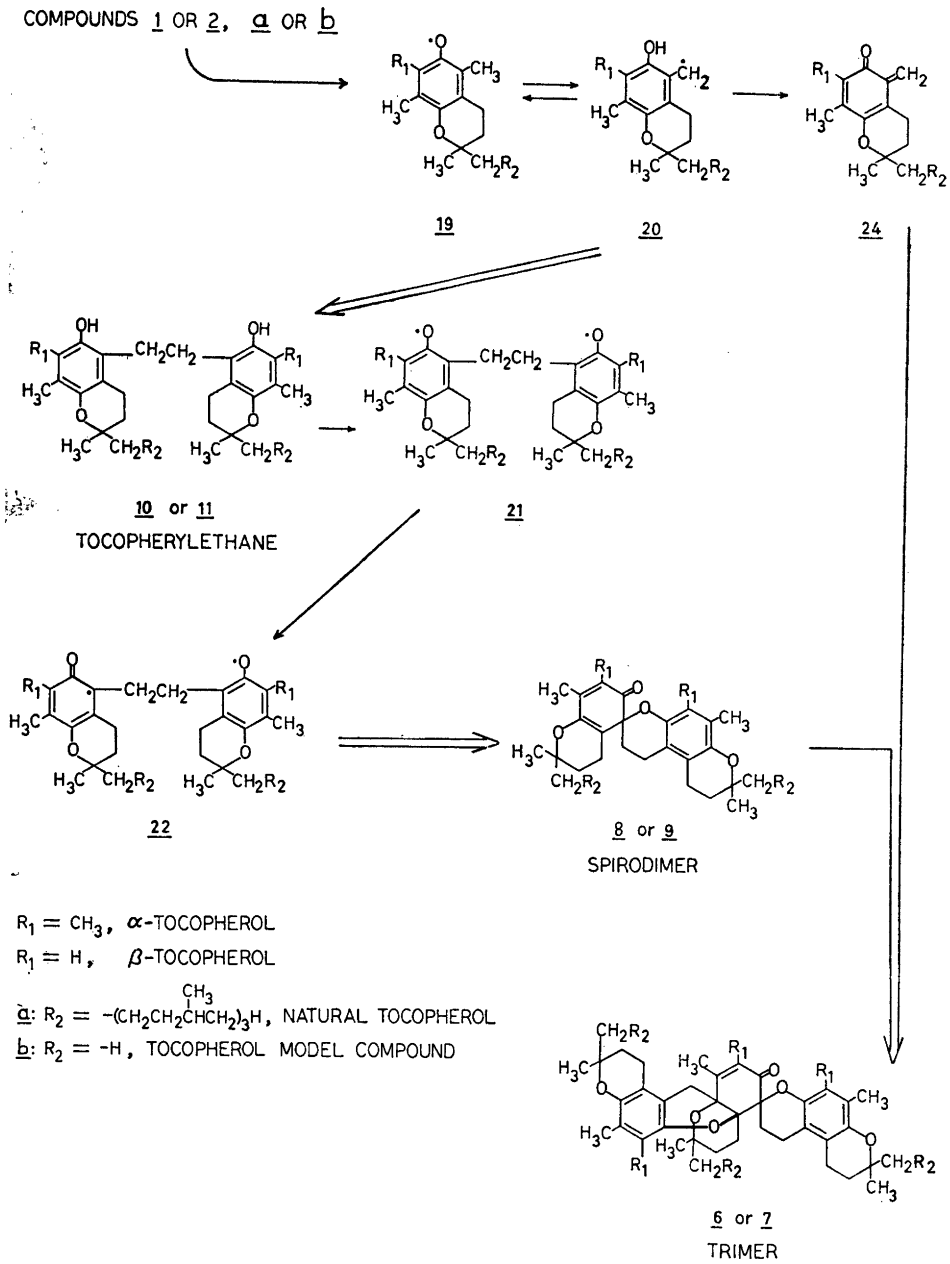
$R_1 = R_3 = H$, δ-TOCOPHEROL

a: $R_2 = -(CH_2CH_2\underset{\displaystyle CH_3}{\underset{|}{C}}HCH_2)_3H$, NATURAL TOCOPHEROL

b: $R_3 = -H$, TOCOPHEROL MODEL COMPOUND

Scheme 1. Dimerization of tocopherols *via* phenoxy radical intermediates; major dimerization pathway for γ- and δ-tocopherols, minor pathway for β-tocopherol.

SCHEME 2



Scheme 2. Dimerization of tocopherols *via* benzyl radical intermediates; major dimerization pathway for α- and β-tocopherols.

(1) Both the dimers (*8a, b* and *10a, b*) and the trimers (*6a,b*) formed by oxidation of α-tocopherol (*1a*) or its model (*1b*) involved reaction at the 5-methyl group; no product involving the 7-methyl group was observed. Similar results have been obtained by treatment of α-tocopherol (*1a*) with nitric acid,[23] silver nitrate,[24] ferric chloride,[24] benzoyl peroxide,[4] or alkaline potassium ferricyanide;[6] in none of these cases was a product involving substitution of the 7-methyl group observed.

(2) Oxidation of γ- and δ-tocopherol (*3a* and *4a*) with *p*-benzoquinone proceeded rapidly (30 min) to produce dimers involving coupling of the tocopheryloxy radicals (Scheme 1) in contrast to the very slow (12—24 h) formation of α-tocopherol dimers *via* initial rearrangement to the benzyl-type radical, *20*. However, β-tocopherol (*2a*), which differs from γ-tocopherol (*3a*) only in that the 5- and 7-substituents are reversed, is oxidized only very slowly as is α-tocopherol (*1a*), and the major product is derived from the benzylic radical, *19*.

(3) Oxidation of δ-tocopherol (*4a*) yielded only a single diphenylether dimer, *13a*. While the structure of this dimer as a product involving coupling at the 5-position is assigned by a consideration of the reaction selectivities observed for β- and γ-tocopherols (*2a* and *3a*), it is nonetheless striking that only a single product was formed in detectable quantities and is an impressive demonstration of the great differences in reactivity of the 5- and 7-positions of the tocopherols.

EXPERIMENTAL

General comments. The UV, IR, and NMR spectra were measured as previously described.[2] Thin layer chromatography (TLC) was carried out using silica gel G plates prepared as described.[2] Freshly distilled hexane was used throughout. Commercially available tocopherols were used after purification by preparative TLC in hexane/ether (5:1). Reagent grade *p*-benzoquinone was used without further purification. 6-Hydroxy-2,2,5,7,8-pentamethylchroman (α-model compound, *1b*)[25] and 6-hydroxy-2,2,5,8-tetramethylchroman (β-model compound, *2b*)[26] were synthesized as described previously. *Oxidation of γ-tocopherol* (3a). A solution of 374 mg (0.87 mM) of γ-tocopherol (*3a*) and 94 mg (0.87 mM) of *p*-benzoquinone in 25 ml of benzene was heated under reflux for 30 min. The solvent was evaporated *in vacuo*, and the residue was triturated with 20 ml of hexane and filtered. A thin layer chromatogram of the filtrate developed in hexane/ether (9:1) showed 3 phenolic components (Emmerie-Engel[27] and Gibb's[28] positive spots at R_F 0.8, 0.7, and 0.3). Nearer the origin, several reddish-brown spots were observed. The phenolic material, $R_F = 0.3$, was shown to be unchanged γ-tocopherol (*3a*) by chromatographic comparison. The product mixture was chromatographed on preparative thin layer plates developed in hexane/ether (9:1), and the two upper phenolic bands were removed from the plates separately and eluted. Each of these two products was further purified by TLC using hexane/ether (100:1) as the developing solvent system. Plates were developed 5 times in this system. The compound of higher R_F (127 mg, 34 % yield) was identified as 5-(γ-tocopheryloxy)-γ-tocopherol (*12a*), and the compound of lower R_F (15 mg, 4 % yield) was identified as 5-(γ-tocopheryl)-γ-tocopherol (*16a*) by analysis of their UV, IR, and NMR spectra (Table 1). Both of these compounds were shown to be indistinguishable from the products obtained during the fractionation of lipids from corn.[2]

Oxidation of δ-tocopherol (4a). When δ-tocopherol (*4a*) was treated with *p*-benzoquinone in refluxing benzene for 30 min, as described for γ-tocopherol (*3a*), very little reaction occurred. When the reflux time was extenbed to 2 h, 5-(δ-tocopheryloxy)-δ-tocopherol (*13a*) was isolated in 23 % yield as the only detected phenolic reaction product.

This dimer was isolated and purified by the techniques described above, and the structure was assigned on the basis of its characteristic spectral properties (Table 1).

Oxidation of α- and β-tocopherols (1a *and* 2a) *and their model compounds* (1b *and* 2b). When α- and β-tocopherols (*1a* and *2a*) or their model compounds (*1b* and *2b*) were treated with *p*-benzoquinone in benzene under reflux for 2 h, very little reaction was evident (TLC analysis). When the reflux period was extended to 24 h, several products were produced. The model compounds (*1b* and *2b*), without side chains, were studied more extensively, but it was shown that the parent tocopherols (*1a* and *2a*) yielded similar product distributions.

6-Hydroxy-2,2,5,7,8-pentamethylchroman (1b) (*α-model compound*). A solution of 440 mg (2 mM) of 6-hydroxy-2,2,5,7,8-pentamethylchroman [25] (α-model compound, *1b*) and 216 mg (2 mM) of *p*-benzoquinone in 25 ml of benzene was heated under reflux for 24 h. The solvent was removed, and the residue was triturated with 25 ml of hexane and filtered. The solvent was evaporated from the filtrate, and the resulting product mixture was shown to consist of four Emmerie-Engel positive compounds (one of which was unchanged starting material, 47%). The 3 phenolic products were isolated by preparative TLC in hexane/ether (7:3). Each compound was further purified by TLC using benzene as the developing solvent. In this way, there were obtained α-trimer *6b*[6] (24 % yield), spirodimer *8b*[4,11] (7.5 % yield), and α-tocopherylethane model dimer *10b*[5,11] (3 % yield), identical in all respects with authentic samples.[5,6,11] Spectral data (UV, IR, and NMR) are recorded in Table 1.

Table 2. Formation of dimers and trimers from the different tocopherols.

Tocopherol	δ	γ	β	α
α	No αδ-dimer isolated [a]	No αγ-dimer isolated [a]	No αβ-dimer isolated [a]	Trimer *6b* 70 % [b,c] Spirodimer *8b* 20 % Tocopherylethane *10b* 10 %
β	No βδ-dimer isolated [a]	Diphenylether-type mixed dimer *14a* [a]	Trimer *7b* 70 % [b,c] Biphenyldimer *18b* 20 % Diphenylether dimer *17b* 10 %	
γ	Diphenylether-type mixed dimer *15a* [a]	Diphenylether dimer *12a* 90 % Biphenylether dimer *16a* 10 % [a,b]		
δ	Diphenylether dimer *13a* [d]			

[a] Reflux in benzene with one equivalent of *p*-benzoquinone for 30 min.

[b] The percentages shown indicate the relative amounts of each compound in the product mixture.

[c] Reflux in benzene with one equivalent of *p*-benzoquinone for 24 h.

[d] Reflux in benzene with one equivalent of *p*-benzoquinone for 2 h.

6-Hydroxy-2,2,5,8-tetramethylchroman (2b) (*β-model compound*). Treatment of 220 mg (1 mM) of 6-hydroxy-2,2,5,8-tetramethylchroman [26] (*β*-model compound, *2b*) with 108 mg (1 mM) of *p*-benzoquinone followed by work-up and product isolation as described for α-model compound, *1b*, yielded *β*-tirmer *7b* (9 % yield), diphenylether dimer *17b* (2 % yield), and biphenyl dimer *18b* (2 % yield). Characteristic spectra which establish the assigned structures are reported in Table 1.

Oxidation of binary mixtures of tocopherols. Equimolar mixtures of each possible pair of the 4 tocopherols (6 pairs in all, see Table 2) were treated with the stoichiometric amount of *p*-benzoquinone in refluxing benzene for 30 min. The reaction mixtures were worked up as described for the oxidation of *γ*-tocopherol. In all cases in which *γ*-tocopherol (*3a*) was present, the *γγ*-dimers *12a* and *16a* were formed. Under the reaction conditions used, only *βγ*- and *γδ*-"mixed" dimers were formed. Spectral data (UV, IR, and NMR) which characterize these products as 5-(*β*-tocopheryloxy)-*γ*-tocopherol (*14a*) and 5(*δ*-tocopheryloxy)-*γ*-tocopherol (*15a*) are recorded in Table 1. Compound *15a* was shown to be identical to a "mixed" dimer of *γ*- and *δ*-tocopherols (*3a* and *4a*) which had been obtained in the fractionation lipids from corn oil.[2]

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