

## On the Preferential Oxidative Coupling at the 5- versus the 7-Position in Tocopherols and Related 6-Chromanols

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The structural requirements for the preferential oxidative coupling at the 5- versus the 7-position in tocopherols has been studied. During the investigation various methyl substituted 6-chromanols have been oxidized with *p*-benzoquinone. This has led to the characterization of nine new dimers of the chromanols.

When the chromanol has an unsubstituted 5-position, oxidative coupling takes place exclusively at that site regardless of whether the other *ortho* position is substituted or not and irrespective of whether a methyl group in the 8-position is present.

When the 6-chromanol carries a 5-methyl group, benzylic coupling occurs *via* this methyl group. The 7-methyl group, if present, does not participate in the coupling reaction and an 8-methyl group has no influence on the reaction pattern.

In the oxidation of  $\beta$ -tocopherol and 5-methyltocol models, benzylic coupling occurs *via* the 5-methyl group although there is an unsubstituted *ortho* position in the molecule. These compounds appear to be the first reported examples of phenols with free *ortho* positions forming oxidation products *via* benzylic coupling.

The observation that coupling occurs preferentially at the 5-position in the tocol series is interpreted as a result of the directing effect of the heterocyclic ring.

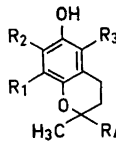
In previous publications we have described the isolation of tocopherol dimers from corn oil<sup>1,2</sup> and the syntheses of these dimers and of a number of other dimers and trimers,<sup>3</sup> formed from the different tocopherols under the influence of *p*-benzoquinone. This focused our attention to the marked preference for reaction at the 5-position *versus* the 7-position in the tocopherols. The aim of this investigation was therefore to establish the structural requirements for this enhanced reactivity at the 5-position. We wanted to determine whether

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the effect was due to the heterocyclic ring alone or if methyl groups in the aromatic ring exerted a directing influence that could explain the observations. We also wanted to ascertain if the greater reactivity includes both the 5-position of the ring and the 5-methyl group or if the effect is limited to the 5-methyl group, which would not be contradictory to previous data.<sup>3</sup>

Our previous experience<sup>3</sup> with benzoquinone as oxidizing agent suggested to us that it could be of use also in this investigation. We found that the oxidation products formed from the different 6-chromanols (1–8) were stable and non-polar compounds that could easily be separated and purified by preparative TLC. This is a great advantage over alkaline ferricyanide,<sup>4</sup> which in some cases gives rather complicated unstable products. In the previous study,<sup>3</sup> dimers and trimers were prepared from  $\alpha$ -,  $\beta$ -,  $\gamma$ -, and  $\delta$ -tocopherol and from their model compounds in which the isoprenoid side chain of the natural tocopherol had been replaced by a methyl group. In this study model compounds have been used.

In this paper and in the previous publication<sup>3</sup> are described the main oxidation products formed under the influence of benzoquinone from the  $\alpha$ -,  $\beta$ -,  $\gamma$ -, and  $\delta$ -tocopherol models 1–4 and from the models of some other non-naturally occurring tocol derivatives (5–8) of interest to the problem of the enhanced reactivity of the 5-position.

	1	R <sub>1</sub> CH <sub>3</sub>	R <sub>2</sub> CH <sub>3</sub>	R <sub>3</sub> CH <sub>3</sub>	$\alpha$ -tocopherol
	2	CH <sub>3</sub>	H	CH <sub>3</sub>	$\beta$ -tocopherol
	3	CH <sub>3</sub>	CH <sub>3</sub>	H	$\gamma$ -tocopherol
	4	CH <sub>3</sub>	H	H	$\delta$ -tocopherol
	5	H	CH <sub>3</sub>	CH <sub>3</sub>	5,7-dimethyltocol
	6	H	CH <sub>3</sub>	H	7-methyltocol
	7	H	H	CH <sub>3</sub>	5-methyltocol
	8	H	H	H	tocol

R<sub>4</sub> = –C<sub>16</sub>H<sub>33</sub> or –CH<sub>3</sub> (model compound)

#### OXIDATION REACTIONS AND RESULTS

*$\beta$ -Tocopherol (2).* In the previous publication<sup>3</sup> we reported on the isolation of three compounds formed in the oxidation of the  $\beta$ -tocopherol model with benzoquinone in refluxing benzene. The main product was a trimer *9b* while the two minor products were characterized as the dimers *14a* and *15*. It was also predicted by analogy with the reaction pattern of  $\alpha$ -tocopherol that  $\beta$ -spiro dimer *10b* and  $\beta$ -tocopherylethane *11b* were probably also formed in this reaction, although they were not detected. This has now been confirmed in an oxidation experiment carried out at room temperature. Three oxidation products were isolated by preparative TLC, one of which was the previously identified trimer *9b*. The other two products were found to be the predicted  $\beta$ -spiro dimer *10b* and  $\beta$ -tocopherylethane *11b*. The compounds were identified by co-chromatography and spectral comparison with authentic materials.<sup>4</sup> The  $\beta$ -spiro model dimer *10b* is the main product in the oxidation of the  $\beta$ -model (2) with alkaline ferricyanide<sup>4</sup> and the  $\beta$ -tocopherylethane model

Table 1. Physical data for oxidation products of methyl substituted 6-hydroxychromans.

Compound	Yield %	Formula	Mol. wt. Found/ Calc.	Chroma- tography $R_F^a$	UV $\lambda_{\max}$ (hexane) ( $m\mu$ )	IR film ( $\text{cm}^{-1}$ )	NMR $\delta$ -values ppm <sup>b,c</sup>		
							Aromatic	OH	Aromatic methyl groups
$\gamma$ -Diphenyl ether dimer <i>12a</i>	25	$\text{C}_{26}\text{H}_{31}\text{O}_4$	398/410	0.90	297	3400	5.90 (s, 1)	4.70 (s, 1)	2.25 (s, 3) 2.05 (s, 3) 2.00 (s, 3)
$\gamma$ -Biphenyl ether dimer <i>13a</i>	8	$\text{C}_{26}\text{H}_{34}\text{O}_4$	395/410	0.76	300	3400	—	4.20 (s, 1)	2.13 (s, 6) 2.05 (s, 6)
$\delta$ -Diphenyl ether dimer <i>12b</i>	30	$\text{C}_{24}\text{H}_{30}\text{O}_4$	397/382	0.81	293 297	3400	6.59 (s, 1) 6.43 (d, 1) 6.26 (d, 1)	4.50 (s, 1)	2.10 (s, 3) 2.06 (s, 3)
7-Methyltolcol diphenyl ether dimer <i>12c</i>	36	$\text{C}_{24}\text{H}_{30}\text{O}_4$	384/382	0.69	296	3400	6.07 (s, 1) 6.37 (s, 1) 6.52 (s, 1)	4.80 (s, 1)	2.22 (s, 3) 2.30 (s, 3)
7-Methyltolcol biphenyl dimer <i>13b</i>	4	$\text{C}_{24}\text{H}_{30}\text{O}_4$	390/382	0.60	298	3400	6.58 (s, 2)	4.28 (s, 2)	2.20 (s, 6)
5-Methyltolcol diphenyl ether dimer <i>14b</i>	3 <sup>e</sup>	$\text{C}_{24}\text{H}_{30}\text{O}_4$	376/382	0.88	292	3400	6.70 (s, 2) 5.90 (s, 1)	4.40 (broad)	2.20 (s, 6)
5-Methyltolcol dihydroxydimer <i>11c</i> <sup>d</sup>	5 <sup>e</sup>	$\text{C}_{24}\text{H}_{30}\text{O}_4$	371/382	0.15	296	3400	6.61 (s, 4)	—	—
Tocol diphenyl ether dimer <i>12d</i>	13	$\text{C}_{22}\text{H}_{28}\text{O}_4$	348/354	0.64	294	3400	<i>f</i>	4.70 (broad)	—
Tocol biphenyl dimers <sup>g</sup> <i>13c</i>	1	$\text{C}_{22}\text{H}_{28}\text{O}_4$	—	0.55	297	3400	—	—	—

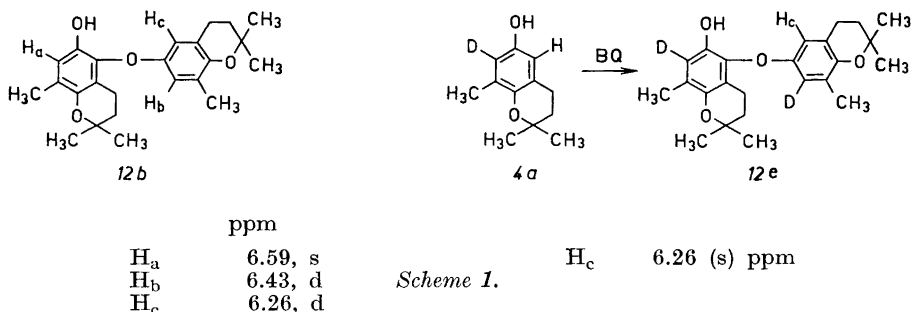
<sup>a</sup> On silica gel G developed in ether:light petroleum 1:4.<sup>b</sup> Sample in  $\text{CCl}_4$ -solution.<sup>c</sup> Aliphatic protons at ppm 1.35–1.10 and 1.70. Benzyllic protons usually not well resolved.<sup>d</sup> Benzyllic protons at ppm 2.78 (t, 8 H).<sup>e</sup> DDQ was used as oxidizing agent.<sup>f</sup> AB-pattern and multiplet, see text and Fig. 1.<sup>g</sup> The amount obtained did not allow a complete structure elucidation.

*11b* is formed by reduction of the spiro dimer with ascorbic acid.<sup>4</sup> The previously described dimers *14a* and *15* were not detected when the oxidation was carried out at room temperature.

*γ-Tocopherol (3)*. Oxidation of the *γ*-tocopherol model (*3*) with benzoquinone at room temperature afforded the *γ*-diphenyl ether model dimer \* *12a* and the *γ*-biphenyl model dimer \* *13a*, in analogy to the dimers formed from natural *γ*-tocopherol.<sup>3</sup> The compounds were identified by molecular weight determination and by IR-, UV-, and NMR-spectroscopy<sup>3</sup> (Table 1).

*δ-Tocopherol (4)*. From the oxidation of the *δ*-tocopherol model (*4*) with benzoquinone, only one reaction product was isolated. It was found to be a dimer (M.W. 397) analogous to the dimer formed from natural *δ*-tocopherol. The IR- and UV-spectra are very similar to those of the natural *δ*-dimer<sup>3</sup> and the NMR-spectra are identical except for signals due to aliphatic protons. The product is therefore assigned structure *12b*, a diphenyl ether dimer of the *δ*-model.

The structure of the natural *δ*-dimer as a compound formed by coupling at the 5-position of the chroman moiety was assigned on the basis of the strong preference for reaction at the 5-position *versus* the 7-position observed in other tocopherols.<sup>3</sup> By the study of the NMR-spectra of the dimer *12b* and of its partly deuterated analogue *12e*, we have now been able to obtain an unambiguous structural proof for the *δ*-model dimer. The spectrum of the *δ*-model dimer exhibits three peaks representing aromatic protons. Examination of these signals revealed that the peak at ppm 6.59 is a singlet while the two others are unsymmetrical doublets centered at ppm 6.43 and 6.26 ( $J \sim 3$  cps). The two doublets must thus be due to the two protons  $H_b$  and  $H_c$



(Scheme 1) at the *meta* position to each other, and the singlet represents the proton  $H_a$ . In order to determine unequivocally the structure of *12b*, dimerization of the 5-H-7-D-*δ*-tocopherol model<sup>5</sup> *4a* with benzoquinone was carried out as before. This afforded a compound having identical IR- and UV-spectra

\* The name *γ*-diphenyl ether model dimer is used for 2,2,7,8-tetramethyl-5-([2,2,7,8-tetramethyl-6-chroman]oxy)-6-chromanol and the name *γ*-biphenyl model dimer is used for 2,2,7,8-tetramethyl-5-(6-hydroxy-2,2,7,8-tetramethyl-5-chroman-1-yl)-6-chromanol. Analogous designations are used for the dimers of the other chromanols reported in this paper.

and chromatographical properties as *12b* and is therefore assigned structure *12e*. The NMR-spectrum of this dimer shows only one aromatic proton as a singlet at ppm 6.26, apparently representing proton  $H_c$  (Scheme 1). This is conclusive evidence that the two 7-positions are not involved in the dimerization and that the  $\delta$ -diphenyl ether model dimer is formed by coupling *via* the 5-position of the chromanol. This also shows that the previous structural assignment of the natural  $\delta$ -dimer<sup>3</sup> is correct.

*5,7-Dimethyltocol (5)*. Oxidation of the 5,7-dimethyltocol model (*5*) by the method described for the  $\beta$ -model yielded the spiro dimer *10c* as the main product, identified by co-chromatography and spectral comparison with authentic material.<sup>4</sup> Several other minor products were formed but not further investigated.

*7-Methyltocol (6)*. Treatment of the 7-methyltocol model with benzoquinone as described for the  $\beta$ -model produced two phenolic compounds isolated by preparative TLC. The molecular weight of the main product was determined to be 384 revealing that the product is a dimer of the 7-methyltocol model. Its IR- and UV-spectra are very similar to those of the  $\gamma$ -diphenyl ether model dimer (Table 1) and the product is assigned structure *12c*. The NMR-spectrum, which is consistent with this structure, exhibits one-proton singlets at ppm 6.07, 6.37, and 6.52 representing aromatic protons. The hydroxyl group appears as a broad singlet at ppm 4.80, and the two singlets at ppm 2.22 and 2.30 (3H each) represent aromatic methyl groups.

The other isolated oxidation product was also found to be a dimer (M.W. 390) of the 7-methyltocol model. The IR- and UV-spectra are very similar to those of the  $\gamma$ -biphenyl model dimer (Table 1). The NMR-spectrum shows two-proton singlets at ppm 6.58 (Ar-H) and 4.28 (OH). Two aromatic methyl groups appear as a singlet at ppm 2.20. These data are consistent with the formulation of this compound as the 7-methyltocol biphenyl model dimer *13b*.

*5-Methyltocol (7)*. When the 5-methyltocol model (*7*) was treated with benzoquinone as described for the  $\beta$ -model, no reaction took place. The reaction mixture was therefore refluxed for 24 h and worked up, whereupon two phenolic products, both less polar than the parent chromanol, were detected by TLC. The amounts formed were too small to allow structural determination (<1 % yield). Oxidation of the 5-methyltocol model with 2,3-dichloro-5,6-dicyanobenzoquinone (DDQ) was therefore attempted. One equivalent of DDQ was used and the reaction was carried out in refluxing toluene for 24 h. TLC revealed a number of reaction products, most of them formed in small amounts. The two main products (both phenolic dimers, IR-stretching band at  $3400\text{ cm}^{-1}$ ) and unchanged starting material (30 %) were isolated by preparative TLC. The least polar of the products (3 % yield, M.W. 376) exhibits  $\lambda_{\text{max}}$  (hexane)  $292\text{ m}\mu$ , and in the NMR-spectrum aromatic protons appear as two singlets at ppm 6.70 (2H) and 5.90 (1H) and two aromatic methyl groups form a singlet at ppm 2.20. On the basis of these data, the compound is assigned structure *14b*, a diphenyl ether of the 5-methyltocol model formed by phenolic coupling at the 7-position. The more polar product (5 % yield, M.W. 371) exhibits  $\lambda_{\text{max}}$  (hexane)  $296\text{ m}\mu$  and NMR-signals at ppm 6.61 (s,4H,Ar-H) and 2.78 (t,8H,Ar-CH<sub>2</sub>-). The data are consistent with

structure *11c* a dihydroxydimer of the 5-methyltocol model *7*. This dimer is analogous to  $\beta$ -tocopherylethane model *11b* formed from the  $\beta$ -model (*2*) upon oxidation with benzoquinone.

*Tocol (8)*. Oxidation of the tocol model (*8*) with benzoquinone yielded two phenolic compounds (IR-stretching bands at  $3400\text{ cm}^{-1}$ ) both less polar than the starting material. The main product (13 % yield) was found to have a molecular weight of 348 indicating that the compound is a dimer of the tocol model. The UV-spectrum exhibits  $\lambda_{\text{max}}$  (hexane)  $294\text{ m}\mu$  and in the NMR-spectrum the signals due to the aromatic protons form two separate patterns. One of these is a multiplet (ppm 6.50–6.30, 3H) identical in shape with the spectrum of the aromatic protons in the tocol model compound.<sup>5</sup> This multiplet is apparently due to the three aromatic protons in the right part of the dimer (Fig. 1).

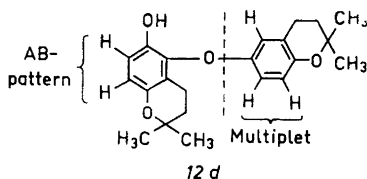


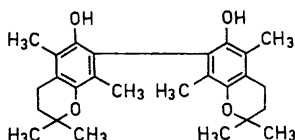
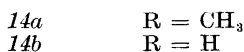
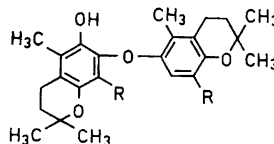
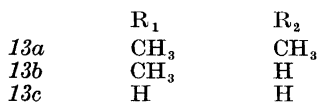
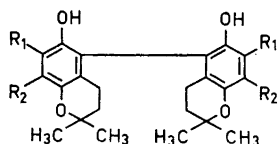
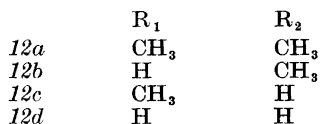
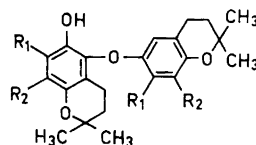
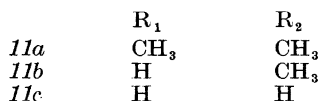
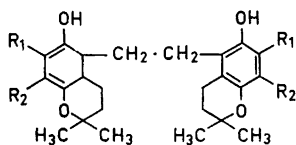
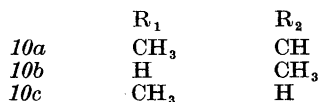
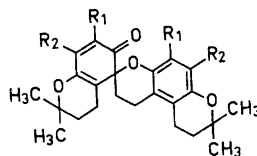
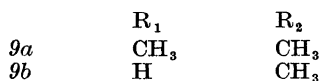
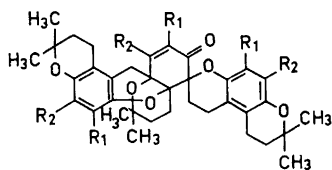
Fig. 1.

The other part of the dimer has two protons which appear in the spectrum as an AB-pattern centered at ppm 6.55 ( $\delta_{\text{A}}=6.64\text{ ppm}$ ;  $\delta_{\text{B}}=6.46\text{ ppm}$ ;  $J=9\text{ cps}$ ). One of the centre peaks of the AB-pattern is partly overlapping with one of the peaks in the multiplet. These data, which are consistent with the structure *12d*, show that the dimer is formed by coupling at the 5-position. Protons in a compound formed by coupling at the 7-position cannot give rise to an AB-pattern with a coupling constant as large as 9 cps.

The other product was obtained in only 1 % yield. Chromatographic data together with the IR- and UV-spectra indicate that the compound is the biphenyl dimer *13c*.

#### DISCUSSION OF THE RESULTS

The initial step in the homolytic oxidation of monohydric phenols is formation of a mesomeric phenoxy radical. Abundant data in the literature support this mechanism although<sup>7-9</sup> other possibilities have been discussed.<sup>9</sup> The subsequent fate of the phenoxy radical depends on the aromatic substitution pattern, but formation of dimers by the combination of two radicals is an important reaction pathway. This dimerization occurs *via* C—C or C—O coupling, while O—O coupling does not occur or gives unstable products.<sup>9</sup> The observed coupling takes place *ortho* and *para* to the hydroxyl group, which is an indication of the high density of unpaired electrons at these positions of the mesomeric radical. In this dimerization C—C coupling to biphenyl dimers is reported to be dominating.<sup>9</sup> When all the *ortho* and *para* positions are substituted with inert groups like tertiary butyl, the free phenoxy



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radical is comparatively stable. However, if one or more of the substituents are methyl groups, benzylic coupling can occur through benzyl radicals<sup>10</sup> or by dimerization of quinone methides,<sup>11</sup> yielding diarylethane dimers.

Oxidation of tocopherols produces different products depending on the oxidation agent.<sup>12</sup> Dimers and trimers have been isolated from *in vitro* oxidation<sup>12</sup> and also from biological material,<sup>2,13-15</sup> where they have been suggested as metabolites formed when the tocopherols served as non-specific biological

antioxidants.<sup>16</sup> In addition to dimer formation, the heterocyclic ring may open to form tocoquinone.<sup>12</sup>

$\alpha$ -Tocopherol (*1*) represents the type of phenol where the *ortho* and *para* positions are substituted. Numerous reports in the literature<sup>3,12</sup> indicate that this compound forms adducts only by benzylic coupling. Only the 5-methyl group is involved in this reaction; no coupling at the 7-methyl group has been observed. Two dimers *10a* and *11a* and a trimer *9a* have been isolated from the oxidation with benzoquinone.<sup>3</sup> In this study we show that the 5,7-dimethyltolcol model (*5*) reacts like  $\alpha$ -tocopherol, yielding a spiro dimer by coupling *via* the 5-methyl group. Similar benzylic coupling is seen in the oxidation of  $\beta$ -tocopherol (*2*) and 5-methyltolcol (*7*). Both these compounds have a 5-methyl group and an unsubstituted position *ortho* to the hydroxyl group. They would therefore be expected to form oxidation products by C—C and C—O coupling at that position. Although this coupling does occur, it is only a minor reaction pathway. Oxidation of the  $\beta$ -tocopherol model with benzoquinone in refluxing benzene<sup>3</sup> yielded the diphenyl ether dimer *14a* and the biphenyl dimer *15* as minor products, the main product being a trimer *9b*. When we repeated the oxidation at room temperature, the same trimer was obtained together with two dimers *10b* and *11b*, all three compounds being formed by reactions involving the 5-methyl group. No adducts formed *via* the 7-position were detected in this reaction. 5-Methyltolcol was oxidized only very sluggishly with benzoquinone. DDQ was therefore used and two products were identified. The main component, the dihydroxy dimer *11c* was formed *via* benzylic coupling while the minor product, the diphenyl ether dimer *14b* was formed by coupling at the 7-position.

The data show that 6-chromanols with a methyl group in the 5-position form coupling products preferentially *via* this methyl group irrespective of whether a methyl group in the 8-position is present, and regardless of whether the other *ortho* position (the 7-position) is substituted or not. The same phenomenon is apparent in the oxidation of such 6-chromanols with alkaline ferricyanide.<sup>4</sup>  $\beta$ -Tocopherol and 5-methyltolcol models appear to be the first reported examples of phenols with a free *ortho* position forming oxidation products *via* benzylic coupling.

The mechanism of the benzylic coupling has been studied for  $\alpha$ -tocopherol. This compound apparently forms a quinone methide as a reaction intermediate when oxidized with benzoquinone<sup>17</sup> or alkaline ferricyanide.<sup>18</sup> Only the 5-methyl group is involved in the formation of the quinone methide, as apparent from the specific coupling at that position. Quinone methides are probably intermediates also in the oxidation of the other 5-methyl-6-chromanols studied here (*2,5,7*). The observation that benzylic coupling is the main reaction route in compounds with a 5-methyl group indicates that the quinone methide is the prevailing intermediate and not the mesomeric phenoxy radical.

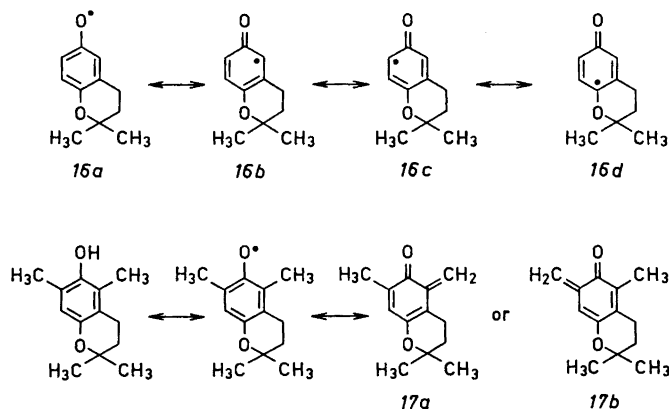
The oxidative coupling pattern for 6-chromanols unsubstituted at the 5-position has also been studied. Oxidation of the tocol model *8* with benzoquinone yielded a diphenyl ether dimer *12d* as the main product, formed by coupling at the 5-position. Related compounds have been studied by Hewgill *et al.*<sup>19,20</sup> in their oxidation of 3-alkyl-4-alkoxyphenols with alkaline ferricyanide. The products obtained were spiroketals formed by C—C and C—O



coupling *para* to the alkyl group. Analogous coupling of the tocol model would have formed dimers *via* the 7-position, appears to be the least sterically hindered. The observation that coupling only occurs at the 5-position must thus be interpreted as a result of the directing effect of the heterocyclic ring. The same phenomenon can be observed in the oxidation of the  $\delta$ -tocopherol model (4), which also forms coupling products only *via* the 5-position, although the compound has two free positions *ortho* to the hydroxyl group. The  $\delta$ -model seems to be more easily oxidized than the tocol model as judged from the yields of the diphenyl ether dimers (30 and 13 %, respectively). The 7-methyltocol 6 and  $\gamma$ -tocopherol 3 models also give dimers by reaction at the 5-position, but this is in accord with normal oxidative coupling.

The enhanced reactivity at the 5-position of the tocopherols has been previously observed in both oxidation<sup>12</sup> and substitution<sup>21,22</sup> reactions. The present study gives conclusive evidence that in oxidation reactions the increased reactivity includes both the 5-carbon of the aromatic ring and the 5-methyl group. This is also observed when alkaline ferricyanide is the oxidizing agent.<sup>4</sup> The reaction specificity is apparently to be ascribed solely to the heterocyclic ring, aromatic methyl groups do not seem to have any significant influence. Electrophilic substitution reactions in the tocopherols studied by Green *et al.*<sup>21,22</sup> take place preferentially at the 5-position, although some substitution seems to occur also at the 7-position.<sup>21</sup> No substitution reactions at the 5- and the 7-methyl groups have been studied.

The radical initially formed in the oxidation of tocol have the mesomeric forms 16a–d (Scheme 2) where 16a–c would most easily form dimers.



Scheme 2

When adduct formation occurs *via* benzylic coupling a quinone methide is apparently an intermediate in the reaction.<sup>17,18</sup> The most likely reaction pathway<sup>11</sup> for the formation of this quinone methide is illustrated in Scheme 2.

Although the energetic states of the two structural forms 16b and 16c are expected to be similar, the products obtained on oxidative coupling indicate

that *16b* is overwhelmingly predominant. Similarly, it was found that *17a* predominates over *17b* although considerations of the energetic states would lead us to expect reaction products from both forms. An analogous phenomenon is found in electrophilic substitution of 5-hydroxyindane and 6-hydroxytetralin, both showing enhanced reactivity at one *ortho* position to the hydroxyl group versus the other.<sup>23</sup> This observation has later been referred to as the Mills-Nixon effect. This result of electrophilic substitutions in these ring systems has been extensively studied<sup>21,24-28</sup> since it was first reported in 1930, but the phenomenon is not fully understood as yet. Recent investigations by Meier *et al.*<sup>29</sup> indicate that the condensation of small saturated rings (6-membered or smaller) to the benzene molecule always causes a distortion of the geometry of the aromatic ring and thus induces a certain strain into the system. This effect may favour reaction at one position over another, as indicated in the MO-calculations on 5-hydroxyindane performed by Longuet-Higgins and Coulson.<sup>24</sup>

## EXPERIMENTAL

*General comments.* Melting points were determined with calibrated Anschütz thermometers in an electrically heated metal block. Infrared absorption spectra were measured with a Perkin-Elmer 237 spectrophotometer, and ultraviolet absorption spectra were measured with a Bausch & Lomb Spectronic 505 spectrophotometer. Nuclear magnetic resonance spectra were measured in CCl<sub>4</sub>-solutions with a Varian Associates A 60 instrument. Chemical shifts are expressed in ppm relative to tetramethylsilane ( $\delta_{\text{TMS}}=0.00$  ppm). Molecular weight determinations were performed using a Hitachi Perkin-Elmer Model 115 Molecular Weight Apparatus with benzene as solvent. Thin layer chromatography was performed using silica gel G plates of 0.3 mm (analytical) and 1 mm (preparative) thickness, prepared and stored as previously described.<sup>4</sup> Redistilled light petroleum, b.p. 40–60°, was used throughout. The 6-chromanols were prepared as previously described.<sup>6</sup> Reagent grade *p*-benzoquinone and DDQ were used without further purifications. The structure of each compound described is assigned on the basis of its molecular weight and its characteristic spectral properties (Table 1).

*Oxidation with benzoquinone* and detection and purification of the oxidation products from the different chromanols were all performed by the same procedure, illustrated by the oxidation of the  $\beta$ -tocopherol model (2). A solution of 6-hydroxy-2,2,5,7-tetramethylchroman ( $\beta$ -model, 2) (0.5 g, 2.42 mmole) and *p*-benzoquinone (0.26 g, 2.42 mmole) in benzene (200 ml) was stood at room temperature for 24 h. The benzene was then evaporated *in vacuo* and the residue dissolved in light petroleum (50 ml). Undissolved black material was filtered off and the filtrate was evaporated to a small volume. TLC of a small aliquot of this solution was run with starting material (2) and the previously described compounds *9b* (trimer),<sup>3</sup> *10b* (spirodimer),<sup>4</sup> *11b* ( $\beta$ -tocopherylethane),<sup>4</sup> *14a* (diphenyl ether dimer),<sup>3</sup> and *15* (biphenyl dimer)<sup>3</sup> as references. When the plate was sprayed with Gibbs' reagent,<sup>30</sup> spots corresponding to 2, *9b*, *10b*, and *11b* were detected. No spots with the same  $R_F$ -value as *14a* and *15* were observed.

The products were purified by chromatography on five preparative TLC-plates developed in ether:light petroleum (2:3). The edges of the plates were sprayed with Gibbs' reagent,<sup>30</sup> the bands were removed separately from the plates and eluted with ether. The ether was then removed under a stream of nitrogen. Yields: *9b*, 50 mg; *10b*, 26 mg, and *11b*, 25 mg. (60 % of the starting material was recovered unchanged). Several dark-coloured bands appeared near the origin of the plates. These products gave a positive reaction with leucomethylene blue indicating that they are quinones, but they were not further investigated.

$\gamma$ -Tocopherol. Benzoquinone oxidation of 6-hydroxy-2,2,7,8-tetramethylchroman ( $\gamma$ -model, 3) yielded two crystalline oxidation products together with recovered starting material (25 %). The least polar of the products, obtained in 24 % yield, was identified

as the diphenyl ether *12a*, m.p. 185–188° (from light petroleum). (Found: C 75.8; H 8.58; M.W. 398. Calc. for  $C_{26}H_{34}O_4$ : C 76.1; H 8.35; M.W. 410). The more polar product, obtained in 8 % yield, was identified as the biphenyl dimer *13a*, m.p. 192–194° (from light petroleum). (Found: C 76.3; H 8.43; M.W. 395. Calc. for  $C_{26}H_{34}O_4$ : C 76.1; H 8.35; M.W. 410).

$\delta$ -Tocopherol model (4) treated with benzoquinone afforded the diphenyl ether dimer *12b* as an oil in 30 % yield. Similarly, the diphenyl ether dimer *12d* was prepared in the same yield from the 5-H-7-D- $\delta$ -tocopherol model.<sup>5</sup> Elucidation of the structure was based mainly on a combination of the NMR-spectra of the two dimers, as discussed above.

5,7-Dimethyltolcol model (5) afforded the spirodimer *10c* in 10 % yield, 42 % of the starting material was recovered unchanged.

7-Methyltolcol model (6) reacted analogously to the  $\gamma$ -model (3) affording two products. The least polar compound, isolated as an oil in 36 % yield, exhibits spectral data consistent with the structure *12c* a diphenyl ether dimer. The more polar compound was obtained as an oil in 4 % yield and was identified as the biphenyl dimer *13b*.

5-Methyltolcol model (7) treated with benzoquinone as described for the  $\beta$ -model (2), or in refluxing benzene for 24 h, yielded only very small amounts of oxidation products, hence oxidation with DDQ was attempted.

5-Methyltolcol model (7) (250 mg, 1.31 mmole) and DDQ (320 mg, 1.31 mmole) in toluene (25 ml) were refluxed for 24 h. After filtration, the solvent was evaporated *in vacuo* and the two main oxidation products were isolated by preparative TLC as described for the  $\beta$ -model (2) (30 % of the starting material was recovered unchanged). The least polar of the products (3 % yield) was identified as the diphenyl ether dimer *12d*. The more polar compound (5 % yield) was found to be the dihydroxydimer *11d*. Both compounds were obtained as viscous colourless oils.

The tocol model (8) formed two main products on oxidation with benzoquinone. The main product (13 % yield) was identified as the diphenyl ether dimer *12d* obtained as a dark oil. The other product was obtained in only 1 % yield. Although this amount was too little for a complete structure elucidation, the compound is assumed to be the biphenyl dimer *13c*. This assignment is based on its chromatographic properties and its UV- and IR-spectra.

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