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Polymer 42 (2001) 2915–2939

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The antioxidant role of vitamin E in polymers. IV. Reaction products of DL-α-tocopherol with lead dioxide and with polyolefins

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Received 17 August 2000; accepted 31 August 2000

Abstract

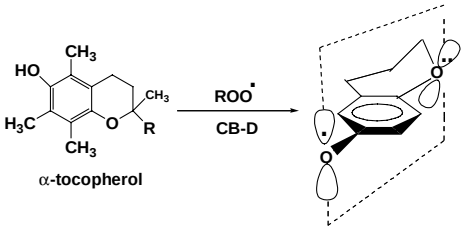
The reaction products of lead dioxide oxidation of the synthetic biological antioxidant DL-α-tocopherol in hexane were investigated at different molar ratios. Products were separated by normal phase high-performance liquid chromatography (HPLC) and isolated using semi-preparative HPLC. Four isomeric trimers and three isomeric spirodimers were obtained as the major reaction products in the presence of 10 and 40 molar excess of the oxidant PbO_2, respectively, whereas the aldehyde, 5-formyl-γ-tocopherol, was obtained as a minor product at 40 molar excess of PbO_2. Dihydroxydimers were formed as minor products at the stoichiometric ratio of tocopherol to PbO_2, and were also obtained as major products from a reaction of the spirodimer with $LiAlH_4$; three isomeric dihydroxydimers were obtained from both reactions. The structures of the different products were characterised by FTIR, UV–vis, ^{1}H-NMR, ^{13}C-NMR, EI-MS and FAB-MS, and based on these results possible structures of the isomeric forms of the products are suggested.

Characterisation of products obtained from the oxidation of DL-α-tocopherol in solution reported here has enabled the identification of a large number of oxidation products, including isomeric forms, detected and isolated from high-temperature melt reactions of the antioxidant DL-α-tocopherol in polyethylene and polypropylene.

Keywords: α-Tocopherol; Vitamin E; Polyolefins

1. Introduction

The biologically hindered phenol antioxidant α-tocopherol (the active form of vitamin E) is known to be one of the best chain breaking phenolic antioxidants. It reacts more rapidly with alkylperoxyl radicals than other similar phenolic antioxidants that lack the fused 6-membered heterocyclic ring. This high reactivity has been attributed to stereoelectronic effects conferred by the heterocyclic ring by the near configurational orthogonality of the oxygen lone electron pair of the chroman ring and the pi-electron of the aromatic ring leading to additional stabilisation of the resulting phenoxyl radical (see reaction 1) [1]:



(1)

Our studies on the antioxidant role of DL-α-tocopherol in polymers [2–5] have shown that it is one of the most powerful melt-stabilising antioxidants in polyethylene (PE) and polypropylene (PP) that outperforms the most effective synthetically hindered phenol antioxidants traditionally used for polymer melt stabilisation. It was further shown that its antioxidant effect is due to both the parent molecule and its oxidation products, which were found to include dimeric and trimeric products, as well as tocoquinones and aldehydes [4,5].

Dimers, trimers and aldehydes of DL-α-tocopherol have also been reported as products of reactions of tocopherol with inorganic oxidising agents, such as alkaline potassium ferricyanide, silver nitrate, ferric chloride, and free radical initiators such as peroxyl radicals [6–10]. However, very little has been reported on the reactions of DL-α-tocopherol with lead dioxide and the characterisation of the large number of stereoisomeric structures expected of the dimeric and trimeric oxidation products. This and the important antioxidant role played by both tocopherol and its oxidation products in polymers [4,5] has prompted our detailed studies on the exact nature of these products by studying solution oxidation reactions of the synthetic α-tocopherol using a mild oxidant (lead dioxide, PbO_2) in non-polar solvent,

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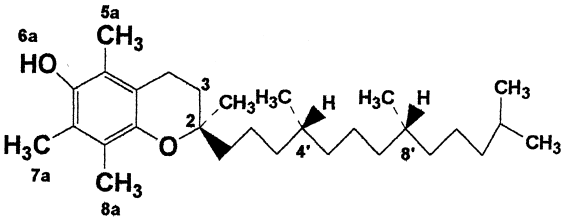
0032-3861/01/$ - see front matter
PII: S0032-3861(00)00653-4



Natural R,R,R α-tocopherol

Isomeric Structures of Synthetic dl-α-tocopherol:

1) 2R, 4'R, 8'R- and 2S, 4'S, 8'S-α-tocopherol
2) 2R, 4'R, 8'S- and 2S, 4'S, 8'R-α-tocopherol
3) 2R, 4'S, 8'R- and 2S, 4'R, 8'S-α-tocopherol
4) 2R, 4'S, 8'S- and 2S, 4'R, 8'R-α-tocopherol

Fig. 1. Structure of natural α-tocopherol.

with the aim of isolating and characterising the products, including the different isomeric forms, to help understand the nature of products formed during melt processing of polymers in the presence of tocopherol.

2. Experimental

2.1. Materials

Synthetic DL-α-tocopherol (Ronotec 202, min. 97%) (see Fig. 1) was kindly donated by Hoffmann–La Roche, Switzerland. Lead dioxide (min. 97%) and lithium aluminium hydride (min. 97%) were supplied by BDH and Aldrich, respectively. All solvents were HPLC grade and used without further purification. Low-density PE (pellets) and PP (granules) were unstabilised polymers supplied by BP chemicals, UK (as Novex) and Himont, USA (as Montell PH060), respectively.

2.2. Oxidation reactions of tocopherol with lead dioxide

α-Tocopherol (4.64 mmol) was dissolved in hexane and mixed with various amounts of lead dioxide (PbO_2) to prepare mixtures with different molar ratios up to 40 molar excess of the oxidant. The mixtures were stirred under continuous argon bubbling for 6 h at room temperature. Orange-brown to dark yellow-orange oils were collected after filtration (using microfibre filters to remove excess PbO_2) and solvent removal under vacuum. The crude oily products were purified by column chromatography. A neutral aluminium oxide column was prepared and eluted with petroleum ether to obtain successive fractions each of which was analysed first by thin layer chromatography and later by analytical normal-phase HPLC. The isomeric products were further purified and isolated using semi-preparative HPLC. The products were finally characterised by a range of spectroscopic techniques.

2.3. Synthesis of dihydroxydimer of tocopherol

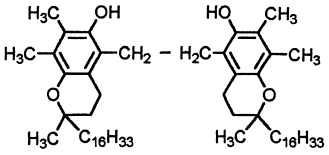
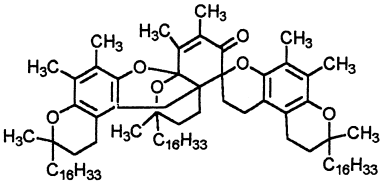
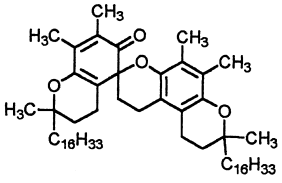
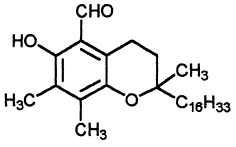
The dihydroxydimer (DHD) was prepared from the purified spirodimer (SPD) obtained from the reaction products of tocopherol with PbO_2 at a molar ratio of 1:40. The SPD (1.17 mmol) was dissolved in diethylether before the addition of lithium aluminium hydride (58.3 mmol) and the mixture was stirred and refluxed under argon for 2 h. Excess lithium aluminium hydride ($LiAlH_4$) was decomposed with water and the mixture was filtered under vacuum using a microfibre filter. The separated organic phase was washed twice with diethylether, dried over anhydrous sodium sulphate followed by solvent evaporation (under vacuum) giving a yellow oil obtained in 94% yield. This product was analysed and isolated by HPLC and characterised spectroscopically.

2.4. Chromatographic and spectroscopic analyses

Analytical HPLC was performed isocratically on Philips PU4100 liquid chromatograph and a PU4120 diode array detector (DAD) controlled by PU6003 chromoscan software. Spectral information from DAD enabled checks on the purity of chromatographic peaks and to finding optimum detection for each peak; peak areas were determined using the chromoscan integration software. A Gilson HPLC system was used for semi-preparative work for separation and collection of the different product fractions. The system comprised a Gilson 305 piston pump, a Gilson 806 manometric module, a Dynamax UV-1 variable wavelength UV/visible absorbance detector, and a Gilson FC203 fraction collector. Normal phase separation was achieved using Zorbax SIL columns (4.6 mm × 250 mm for analytical and 9.4 mm × 250 mm for semi-preparative HPLC) with mobile phase of varying ratios of hexane:1,4-dioxane at flow rates of 1 and 3.5 ml min^{-1} for analytical and semi-preparative HPLC, respectively, and UV-detection at 290 and 275 nm; the shorter wavelength was used to ascertain the presence or otherwise of tocoquinone. The concentration of the products was determined from their HPLC peak areas and their extinction coefficients at the respective wavelength used for detection.

Ultraviolet analysis was carried out on a Hewlett–Packard 8452A diode array spectrophotometer with HP 89532A DOS software. Infrared spectra were recorded on Perkin–Elmer 1710 Fourier Transform spectrophotometer run by IRDMS software. Proton and carbon nuclear magnetic resonance (^{1}H- and ^{13}C-NMR) spectra were recorded on Brucker spectrometer (300 and 100 or 75 MHz, respectively) using deuterated chloroform as solvent and internal standard. ^{13}C-NMR spectra were run using the *J*-modulated spin echo (JMOD) method, which provides a useful way of separating the methyl and tertiary carbon peaks (positive values) from the methylene and quaternary carbon peaks (negative values). ^{1}H, ^{13}C-NMR shift correlation spectra were used to assign the ^{13}C signals when the corresponding ^{1}H assignments are known, and vice versa. Electron impact ionisation mass spectra (EI-MS) were recorded on a Finnigan MAT

Table 1
Reaction yields (% weight) and major products of reactions of DL-α-tocopherol with PbO_2

Toc:PbO_2 ratio	Total % yield of reaction products	% Yield of major products	Isolated products	Structure of isolated products
1:1	98	Toc (75%), TRI (13%), DHD (10%)	DHD, E	
1:3	98	Toc (75%), TRI (23%)		
1:5	98	Toc (65%), TRI (33%)		
1:10	98	TRI (65%), Toc (33%)	TRI, A, B, C	
1:20	96	SPD (63%), TRI (33%)		
1:40	95	SPD (81%), TRI (13%)	SPD, D	
		ALD 1 (0.7%)	ALD 1, F	

CH7 using ethyl acetate as the solvent. Derivatisation of the Toc dimers (DHD and SPD) to form trimethylsilyl (TMS) ether enabled the distinction between the two dimers since their mass spectra were very similar ($M^+ = 858$, i.e. MM of DHD). Unlike SPD, silylation of DHD (containing two hydroxyl groups) was successful and confirmed its structure. Fast atom bombardment mass spectrometry (FAB-MS) was used to analyse the trimers.

3. Results

3.1. Oxidation reactions of tocopherol with lead dioxide (PbO_2)

The biologically active form of vitamin E occurs naturally in only one isomeric form as the *RRR*-α-tocopherol in spite of the fact that it has three stereocentres at carbon positions 2,4′,8′ (Fig. 1). On the other hand, the synthetic DL-α-tocopherol exists as a mixture of equal amounts of all eight possible optical isomers shown in Fig. 1 [11].

Oxidation of the synthetic DL-α-tocopherol with PbO_2 is expected, therefore, to result in a number of products having a complex mixture of stereoisomeric structures. Reactions carried out at six different molar ratios of the oxidant to tocopherol, ranging from stoichiometric to 40 molar excess, have resulted in different amounts of products, which were found (see later) to be based on four main structures, namely, DHD, SPD, trimer (TRI) and aldehyde (ALD). Table 1 shows the yield of the reactions and that of the major products formed in each case and the products isolated.

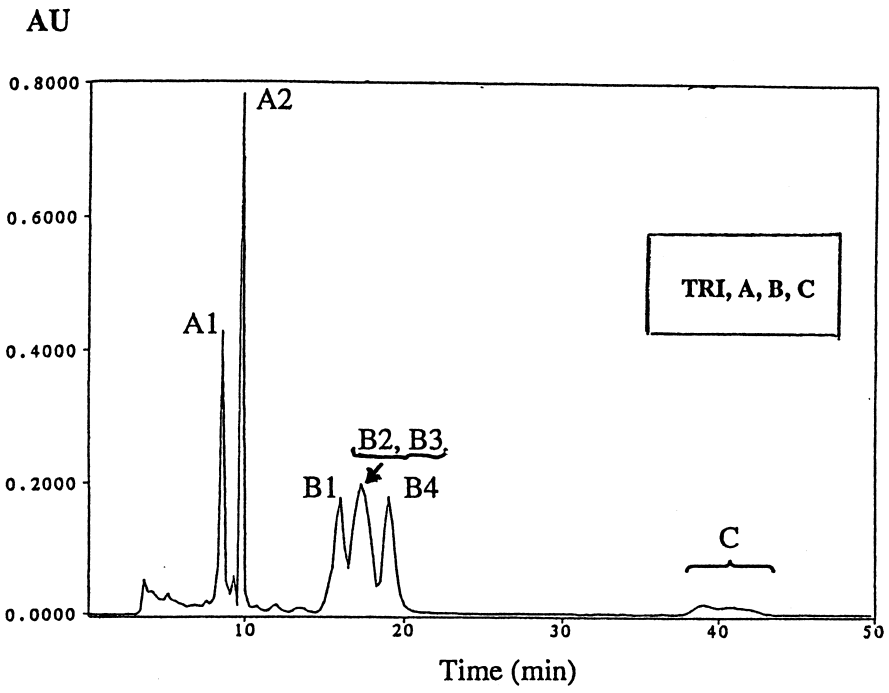


Fig. 2. HPLC chromatogram of the trimer obtained from reaction of tocopherol with PbO_2 at molar ratio of 1:10; detection wavelength of 290 nm and mobile phase ratio of 100:0.5.

3.2. Purification and isolation of synthesised trimers and spirodimers

The crude products of the oxidation reactions of DL-α-tocopherol with PbO_2 were purified and separated by column chromatography and HPLC. The pure products were isolated by semi-preparative HPLC with the major products comprising trimeric and dimeric compounds.

The trimeric products (see characterisation later) were obtained at high yield (about 65%) when using 10 molar excess PbO_2 and four products were isolated. The crude mixture of the trimeric compounds from this reaction was separated and purified by column chromatography on neutral aluminium oxide and fractionated with mixtures of petroleum ether and diethylether followed by semi-preparative HPLC. The first fraction (yellow oil), which was obtained (petroleum ether:diethyl ether = 9:1 v/v), in 63% yield gave an HPLC trace showing five major peaks (A1, A2, B1, B2, B3, B4), in addition to some minor peaks (C) (Fig. 2). Continued elution with diethylether yielded 23% tocopherol (second fraction) with an overall total column recovery of 86% of oily products. The mixture of trimers obtained from the first fraction was further purified by semi-preparative HPLC to give a purity of 100% (as determined from the concentrations of all products in the mixture from HPLC peak areas and extinction coefficients at the wavelength of detection of 290 nm). Four peaks (each representing a different trimeric isomer) were collected from separate chromatographic runs of given samples corresponding to compounds A1 (retention time $Rt = 9.50$ min), A2 ($Rt = 9.83$ min), B1–B4 (B1 $Rt = 14.50$; B2 + B3 $Rt = 15.67$; B4 $Rt = 17.50$ min; all collected and referred to as compound 'B'), and C1–C4 ($Rt = 30$–40 min; all collected and referred to as compound 'C'). The weight percent of each of the three types of trimeric compounds in the mixture was found to be as follows: compounds A = 30%, compounds B = 63% and compounds C = 7% (calculated from HPLC). The isolated individual products (A, B and C) were further analysed by HPLC and their structures determined spectroscopically as described later.

The dimeric compounds having the SPD structure (see characterisation later) were obtained in high yields (81%) at 40 molar excess PbO_2. Purification and separation of the different isomeric compounds of the SPD were carried out as above. The chromatographic column containing the crude SPD (from the above reaction) was eluted initially by petroleum ether:diethylether at 100:2 to yield 8% of a yellow oil (first fraction). Continuing elution with a 10:1 v/v solvent ratio yielded 11% of a yellow-orange oil (second fraction). Finally, elution with a further portion of diethylether gave 66% of a dark yellow-orange oil (third fraction) with a total column recovery of 85%. This third fraction which contained the SPD-isomers as major products (isolated as 93% pure, with 4% trimers and 3% tocopherol) was further purified by semi-preparative HPLC to give 100% pure 'spirodimeric' compounds. Three HPLC peaks of the SPD were separated using hexane: dioxane (100:3 v/v) (see Fig. 3) and collected from separate chromatographic runs (compounds D1, D2, D3, $Rt = 4.67$, 5.33 and 6.17 min, respectively).

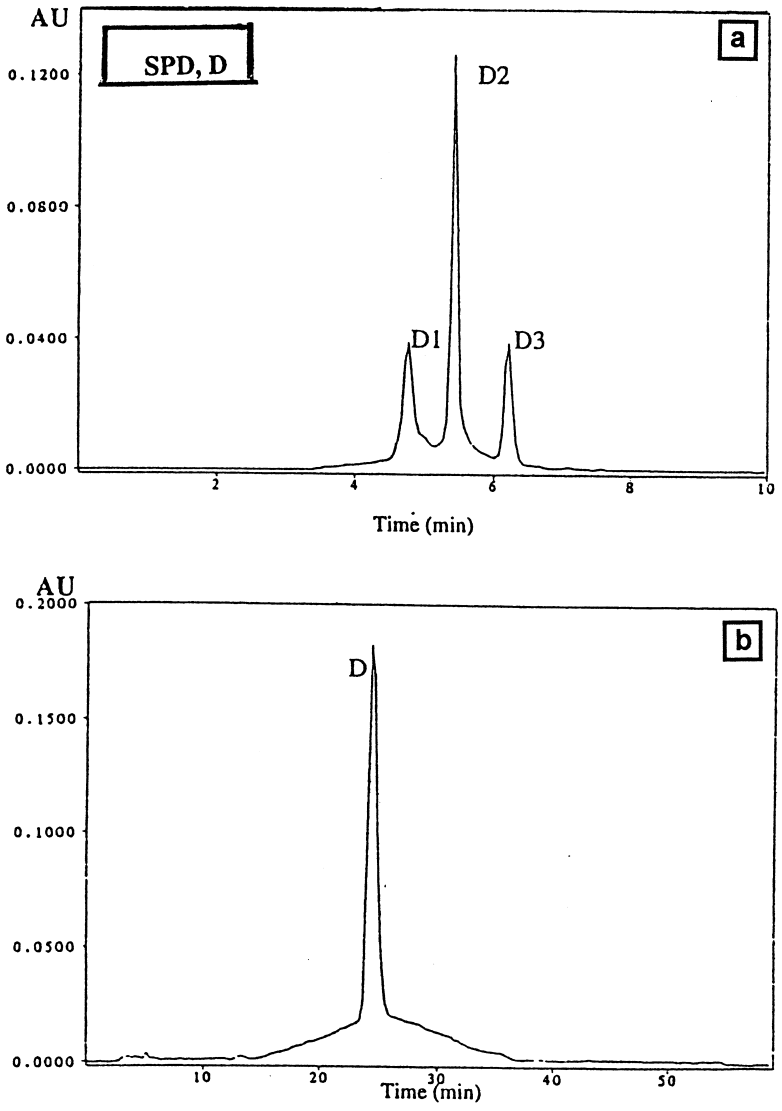


Fig. 3. HPLC chromatogram of the spirodimer obtained from reaction of tocopherol with PbO_2 at molar ratio of 1:40; detection wavelength of 300 nm and mobile phase ratio of 100:3 (a), and 100: 0.5 (b).

3.3. Synthesis and purification of dihydroxydimers

The DHD product was isolated from the stoichiometric reaction of tocopherol with PbO_2 in low yields (10%). The DHD was also synthesised from a reduction reaction of the SPD (which had 93% purity and was isolated by column chromatography from the reaction products of tocopherol with PbO_2; 40 molar excess) with $LiAlH_4$ resulting in a crude DHD product with purity of 56% (from HPLC). The impurities were found to be tocoquinone, TQ (20%), TRI (12%), SPD (9%), and tocopherol (3%). The crude DHD product was further purified by semi-preparative HPLC to yield 98% pure dihydroxydimeric compounds (sole impurity is the SPD, which is well separated with $Rt < 8$ min). The 'pure' DHD product gave three main HPLC peaks; the product corresponding to corresponding to each peak was collected individually from separate chromatographic runs (see Fig. 4) (compounds E1, E2, E3 + E4 with $Rt = 36.75$, 38.50, 41.0–45.0 min, respectively). The structures of the three isolated compounds were determined as described later.

4. Discussion

4.1. Effect of PbO_2 concentration on the distribution of oxidation products

The nature of the products formed from oxidation reactions of tocopherol with lead dioxide in hexane were found to be mainly of dimeric, trimeric and aldehydic structures based on the characterisation below and literature data [2,6–10]. The effect of the concentration of the oxidant on

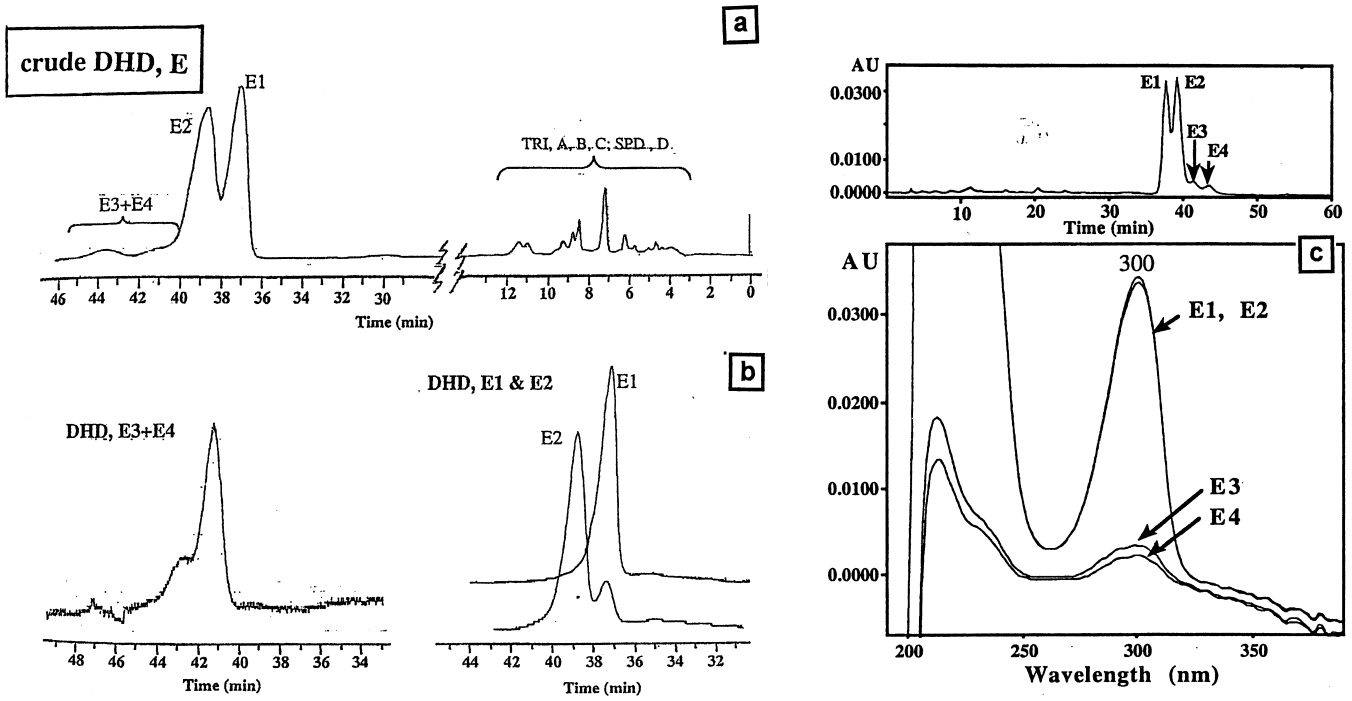


Fig. 4. HPLC chromatogram (a, b) and UV spectra (c) of the dihydroxydimer (DHD) obtained from reaction of spirodimer with $LiAlH_4$, as a crude product (a) and the purified isolated DHD products (b); HPLC detection wavelength of 290 nm and mobile phase ratio of 100:2.

the nature and distribution of each of the products (TRI, DHD, ALD and SPD) formed is shown in Fig. 5. It is clear that increasing the concentration of PbO_2 up to 10 molar excess is accompanied by a sharp decrease in the concentrations of tocopherol that is paralleled by a sharp increase in the concentration of the TRI. The latter becomes the major product (65% yield) of the reaction in the presence of 10 molar excess of the oxidant, whereas the SPD is completely absent at all molar ratios below 10. However, at higher concentrations of PbO_2 (>10 molar excess), SPD is formed and prevails at high oxidant concentrations, with up to 81% yield at a 40 molar excess, concomitant with a decreases in the amount of TRI formed. The DHD is mainly formed at low oxidant concentrations (up to 10% yield at the stoichiometric ratio). The formation of the ALD occurs probably through a side reaction as it is formed at only very low levels at all oxidant concentrations.

Scheme 1 shows a proposed mechanism for the formation of the different oxidation products of tocopherol. ESR measurements [12,13] have confirmed that the formation of α-tocopheroxyl radical (Toc·) is the first step in the oxidation of tocopherol (Scheme 1, rn a). At lower PbO_2 concentrations, the concentration of the initial Toc· radical produced is expected to be low, which explains the limited formation of DHD that occur via coupling of two Toc· radicals (Scheme 1, rn e). The Toc· radical produced under these conditions reacts further with PbO_2, at the expense of its coupling reaction, to form a biradical leading to the formation of quinone methide (QM) of Toc (Scheme 1, rn b). The study of the chemistry of simple *o*-quinone methides has shown [14] that trimerisation is a facile reaction that proceed through two successive Diels–Alder reactions (see reaction 2). Likewise, it is suggested here that the QM of tocopherol (formed at low PbO_2 concentrations) will react favourably with two further QM molecules in Diels–Alder-type reactions to produce the TRI through the intermediacy of SPD (Scheme 1, rn c and d). This is supported by the finding that the TRI is the major primary product of tocopherol oxidation at and below 10 molar excess of the oxidant (see Fig. 5):

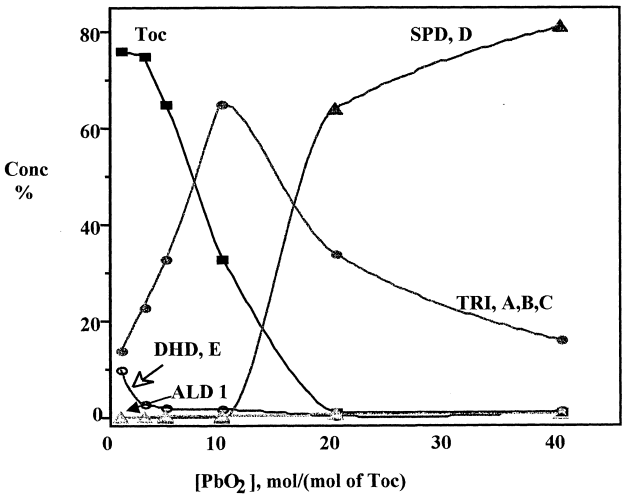
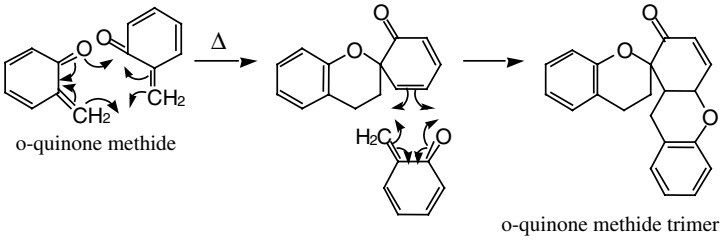


Fig. 5. Distribution of oxidation products formed from reactions of tocopherol with PbO_2 at different molar ratios.

product of tocopherol oxidation reaction (see Fig. 5). It has been reported [15] that alkaline ferricyanide oxidation of 2,2′-dihydroxy-3,5,3′,5′-tetramethyl dibenzyl yield a keto ether analogous to the SPD of tocopherol. Later literature work [16] has also suggested that DHD of tocopherol is oxidised further to SPD in the presence of oxidising conditions, by two one-electron oxidations followed by an intramolecular coupling reaction. In the light of this early literature it is proposed here that in the presence of high lead oxide concentration, SPD is formed, most likely, via the intermediacy of the DHD (see Scheme 1, rn e, f, g).

4.2. Characterisation of synthesised products based on the dihydroxydimer

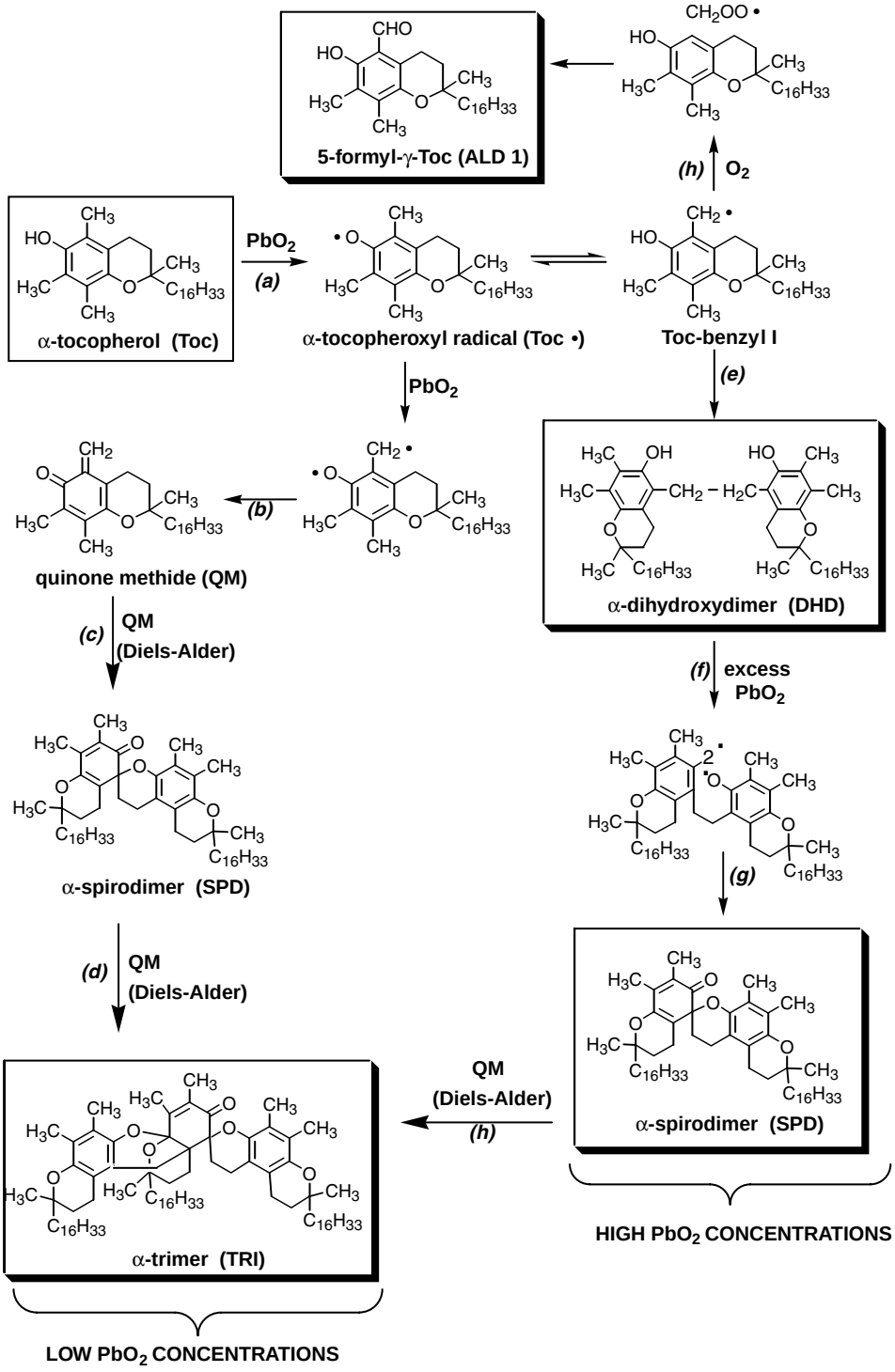
The structure of the symmetrical dimer of DL-α-tocopherol (DHD), isolated from extruded PE samples processed with tocopherol, was previously characterised and the different isomers, which were detected in the polymer were collected together and presented for spectral characterisation as a single entity [2]. The dimeric structure of



(2)

As the concentration of lead dioxide in the reactions is increased, the concentration of the initially formed Toc· radical also increases leading to the formation of higher levels of an intermediate dimer (DHD). At high lead dioxide concentrations (>10 molar) the SPD becomes a major

the DHD synthesised in this work (from the reduction of the corresponding SPD) was characterized by its ^{1}H and ^{13}C-NMR, FTIR and UV (λ_{max} at 300 nm) spectral data which were found to be almost identical to those of the DHD isolated from PE previously identified [2]. Further confirmation of the



Scheme 1.

structure of the synthesised DHD was sought from the $^{1}H-^{13}C$-NMR correlation spectrum (Fig. 6) its EI-MS spectrum showing a molecular ion peak M^{+} at 859 (MM of Toc = 430), as well as the EI-MS spectrum of a silylated-DHD showing a molecular ion peak at 1002 (mass of DHD − 2H + 2 × mass of TMS) (see Fig. 7) confirming further the presence of two hydroxyl groups.

In contrast to earlier work [17,18] which refers to the detection of only one HPLC peak for the DHD of tocopherol, the present work shows clearly the presence of three HPLC peaks (E1, E2, major, and E3 + E4, minor) (see Fig. 4). The corresponding compounds E1 and E2 were separated and isolated individually whereas compounds E3 and E4 were not well separated and were

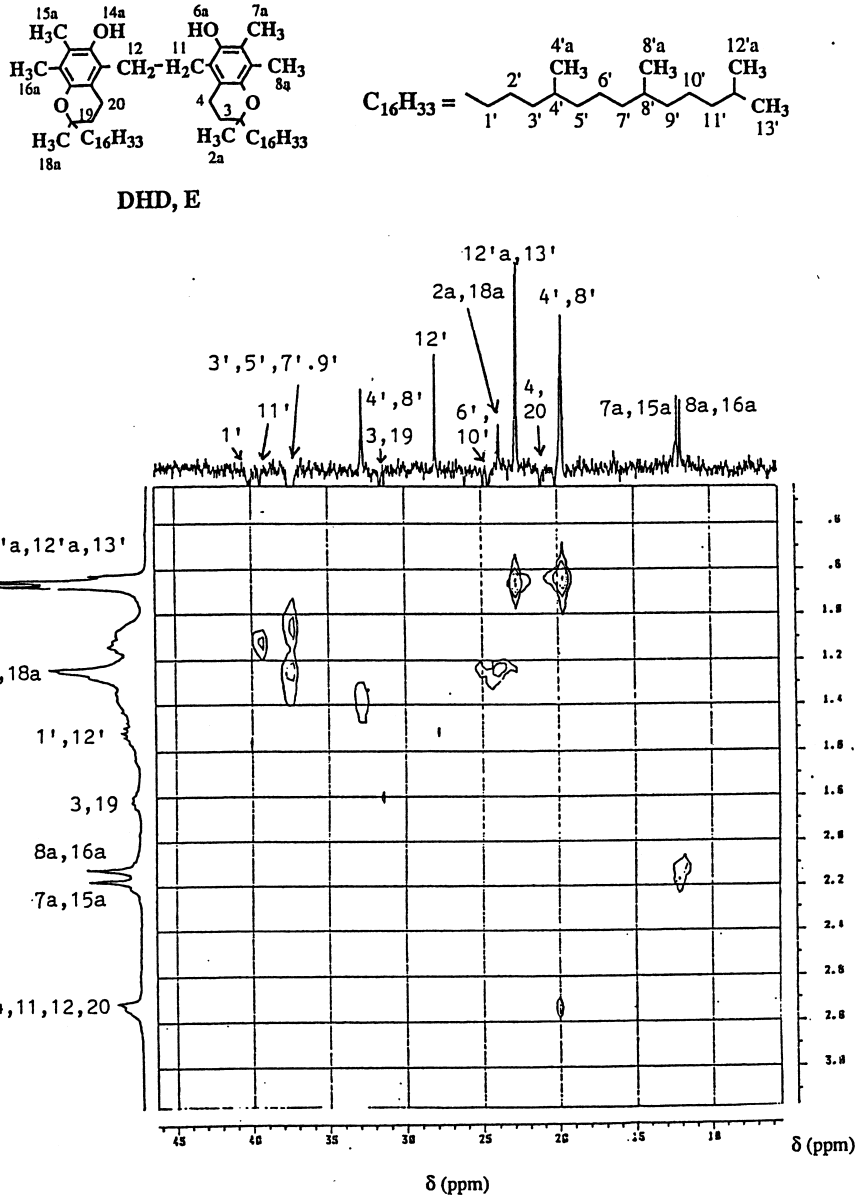


Fig. 6. $^{1}H-^{13}C$-NMR correlation spectrum of dihydroxydimer.

collected accordingly as a mixture of the two and presented for further analysis as the third compound. The three 'compounds' were found to have similar spectroscopic characteristics, see for e.g. their UV spectra (Fig. 4) and ^{1}H- and ^{13}C-NMR spectral data (Tables 2 and 3) suggesting that these compounds are stereoisomers of the DHD. The ^{1}H-NMR spectrum of any of the three isolated DHD isomers is shown to be almost identical to that of tocopherol (compare for example compound E1 and tocopherol, see Fig. 8) except that the DHD isomers have two aromatic methyl group signals (at 2.11 and 2.16 ppm) instead of the three signals observed for tocopherol (hydrogens 5a, 8a and 7a with chemical shifts at 2.16, 2.17 and 2.20 ppm, respectively) (see also Table 2). This confirms the symmetrical nature of the stereoisomeric structures of DHD as each of the two aromatic methyl signals corresponds to two identical methyl groups (hydrogens 7a, 15a and 8a,16a) and the single hydroxyl signal at 5.43 ppm corresponding to two identical groups (hydrogens 6a and 14a). A similar pattern was observed in ^{13}C-NMR, showing two aromatic methyl signals each corresponding to two identical methyl groups (carbons 16a, 8a and 7a, 15a) for the isomers of compound E (example for isomer E1) compared to three (carbons 5a, 7a, 8a) for tocopherol (Table 3 and Fig. 9). Table 3 shows also that ^{13}C-NMR spectra of E1 and E2 have very similar chemical shifts, and in the case of compounds E3 + E4 there is a small variation in chemical shifts for almost all the carbon positions (compared to E1 and E2) since the

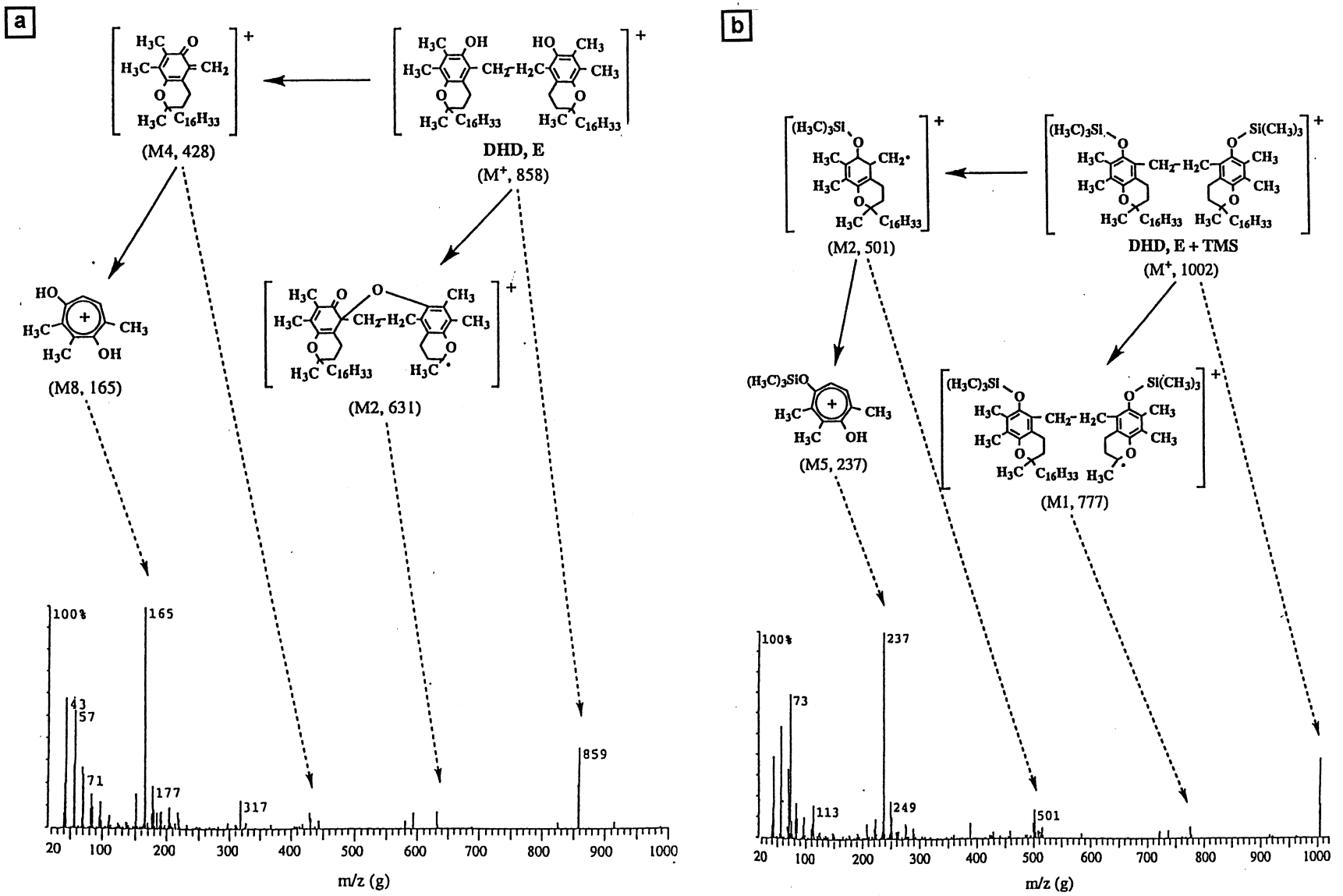
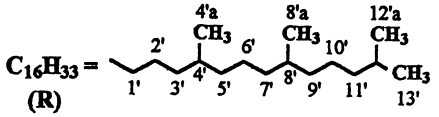


Fig. 7. EI-MS spectra of dihydroxydimer in acetate (a) and in acetate after silylation with TMS (b).

Table 2
[1]H-NMR characteristics of synthesised isomers of dihydroxydimer, DHD, and aldehyde, ALD, and that of α-tocopherol is also shown for comparison

δ (ppm) (multipicity) (s = singlet, m = multiplet)



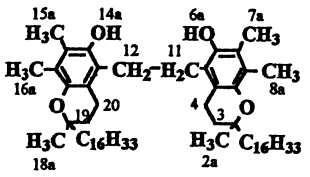
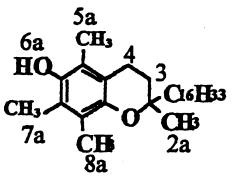
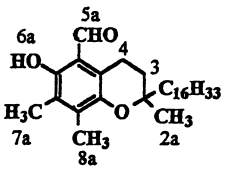
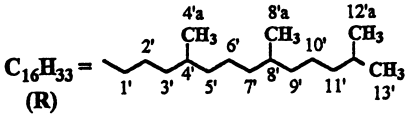
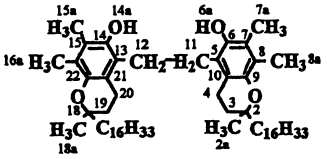
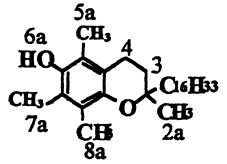
Group	Position							
		DHD			Tocopherol			
		E1	E2	E3 + E4	Toc	Position	ALD 1	Position
CH_3 of R	4′a, 8′a, 12′a, 13′	0.75–0.95	0.8–0.95 (broad)	0.75–0.95	0.85–1.0	4′a, 8′a, 12′a, 13′	0.7–0.9	4′a, 8′a, 12′a, 13′
CH_3, sat.	2a, 18a	1.22 (s)	1.22 (s)	1.22 (s)	1.27 (s)	2a	1.24 (s)	2a
CH_2 of R	3′, 5′, 7′, 9′	0.95–1.45	0.95–1.45	0.95–1.45	1.05–1.4	3′, 5′, 7′, 9′	– 0.95–1.45	18a 3′, 5′, 7′, 9′
	11′	0.95–1.15	0.95–1.15	0.95–1.15	1.05–1.25	11′	0.95–1.2	11′
	6′, 10′	1.15–1.3	1.15–1.3	1.15–1.3	1.3–1.4	6′, 10′	1.2–1.3	6′, 10′
CH_2, CH of R	2′, 4′, 8′	1.3–1.45	1.3–1.45	1.3–1.45	1.4–1.55	2′, 4′, 8′	1.3–1.45	2′, 4′, 8′
CH of R	1′, 12′	1.45–1.65	1.45–1.7	1.45–1.65	1.55–1.7	1′, 12′	1.45–1.65	1′, 12′
CH_2, β unsat.	3, 19	1.7–1.9 (m)	1.7–1.9 (m)	1.7–1.9 (m)	1.75–1.95 (m)	3	1.7–1.9 (m) –	3 19
CH_3, unsat. (aromatic)	16a 8a 7a 15a	2.11 (s) 2.16 (s) 	2.11 (s) 2.15 (s) 2.16 (s)	2.11 (s) 2.12 (s) 2.16 (s) 	2.16 (s) 2.20 (s) 2.17 (s) 	5a 7a 8a 	2.14 (s) – 2.15 (s) –	8a 16a 7a 15a
CH_2, α unsat.	4, 11, 20 12	2.65–2.8	2.65–2.75	2.65–2.8	2.6–2.7 (t)	4	2.95–3.1 (t) –	4 11, 20, 12
O–H	6a, 14a	5.43 (s)	5.46 (s)	5.43 (s)	4.3 (s)	6a	12.10 (s) –	6a 14a
CHO	–	–	–	–	–	–	10.18 (s)	5a

Table 3
^{13}C-NMR characteristics of α-tocopherol and synthesised DHD

δ (ppm) (multiplicity) (s = singlet, d = doublet, m = multiplet)



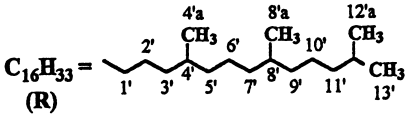


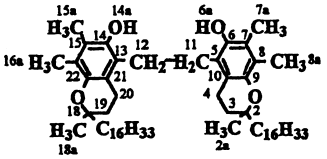
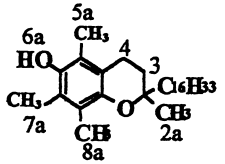


Group	Position C (sign) (+): 1°, 3°C (−): 2°, 4°	DHD			Tocopherol	
		E1	E2	E3 + E4	Toc	position (sign)
CH_3, arom.	16a (+)	11.90 (s)	11.90 (s)	11.06 (d)	11.23 (s)	5a (+)
	8a (+)				11.75 (s)	8a (+)
	7a (+)	12.12 (s)	12.12 (s)	11.62 (s)	12.16 (s)	7a (+)
	15a (+)			11.84 (s)		
R	4′a, 8′a(+)	19.67, 19.74 (≥d)	19.67, 19.73 (m)	19.40, 19.47, 19.73 (m)	19.58, 19.67, 19.73 (m)	4′a, 8′a (+)
	2′(−)	21.04 (s)	21.03 (s)	20.53, 20.79 (d)	21.03 (s)	2′(−)
	12′a, 13′(+)	22.62, 22.72 (d)	22.61, 22.71 (d)	22.35, 22.45 (d)	22.62, 22.71 (d)	12′a, 13′ (+)
	6′(−)	24.44 (s)	24.43 (s)	24.16 (s)	24.43 (s)	6′(−)
	10′(−)	24.80 (s)	24.80 (s)	24.52 (s)	24.80 (s)	10′(−)
	12′(+)	27.97 (s)	27.97 (s)	27.70 (s)	27.96 (s)	12′(+)
	4′, 8′ (+)	32.76 (s)	32.76 (s)	32.49 (≥d)	23.66, 32.76 (2)	4′, 8′(+)
	3′, 5′, 7′, 9′(−)	37.38 (m)	37.27, 37.38 (m)	36.99, 37.11 (m)	37.27, 37.32, 37.38, 37.44, 37.55 (m)	3′(−) 5′, 7′, 9′(−)
	11′(−)	39.35 (s)	39.35 (s)	39.07 (s)	39.35 (s)	11′(−)
	1′(−)	39.95, 40.07 (d)	39.97, 40.10 (d)	39.63 (d)	39.76, 39.84 (d)	1′(−)
CH_2, α and β unsat.	4(−)	20.07 (s)	20.07 (s)	20.51 (s)	20.73 (s)	4(−)
	20(−)					
	12(−)	25.99 (s)	26.00 (s)	25.91 (s)		
	11(−)					
	3(−)	31.53	31.55 (s)	31.26 (d)	31.46, 31.52 (d)	3(−)
	19(−)					
CH_3, sat	2a, 18a(+)	23.78 (s)	23.77 (s)	25.55 (s)	23.74 (s)	2a(+)
C,sat	2(−)	74.60 (s)	74.60 (s)	74.34 (s)	74.44 (s)	2(−)
	18(−)					

Table 3 (*continued*)

δ (ppm) (multiplicity) (s = singlet, d = doublet, m = multiplet)



Group	Position C (sign) (+): 1°, 3°C (−): 2°, 4°					
		DHD			Tocopherol	
		E1	E2	E3 + E4	Toc	position (sign)
C, unsat	7(−) 15(−)	116.31 (s)	116.31 (s)	116.11 (s)	118.54 (s)	7(−)
	8(−) 16(−)	121.40 (s)	121.40 (s)	121.00 (s), 121.41 (s)	121.09 (s)	8(−)
	5(−) 13(−)	122.73 (s)	122.73 (s)	122.51 (s)	117.25 (s)	5(−)
	10(−) 21(−)	123.36 (s)	123.36 (s)	123.03 (s)	122.53 (s)	10(−)
	6(−) 14(−)	144.80 (s)	144.80 (s)	144.40 (s) 144.50 (s)	144.49 (s)	6(−)
	9(−) 22(−)	145.58 (s)	145.58 (s)	145.33 (s)	145.51 (s)	9(−)

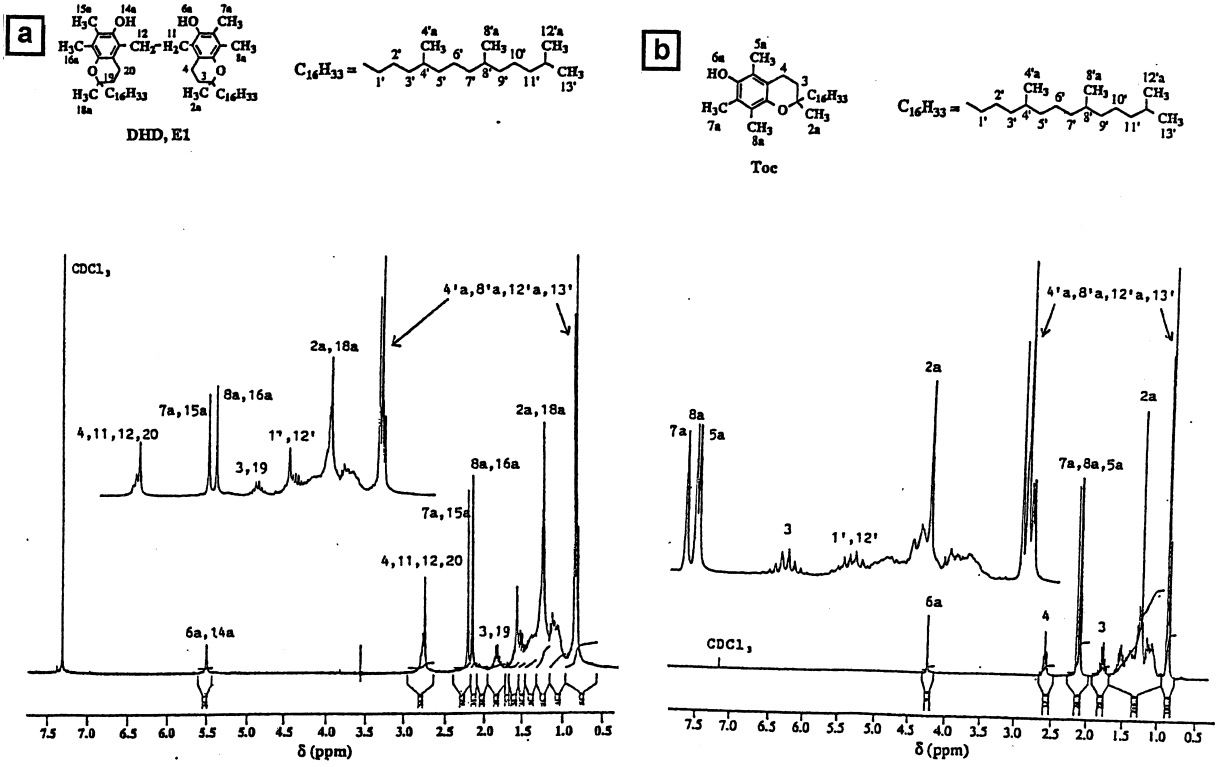


Fig. 8. ^{1}H-NMR spectra of the isolated dihydroxydimer product E1 (a) and that of tocopherol (b).

compounds corresponding to peaks E3 and E4 were collected together and are less pure than either of compounds E1 or E2.

The similarity in the structural characteristics of compounds E1, E2, E3 + E4, along with the differences observed in their HPLC retention times, confirm that these compounds are stereoisomeric forms of the DHD. The three stereoisomeric compounds of the DHD isolated in this work may have resulted from the different configurations at the chiral centres 2 and 18 (supporting the phytyl chain) (see Fig. 10). Different positions of the two phenolic hydroxyls caused by the rotation of the ethyl bond (positions 11 and 12), could also result in the differences observed in the HPLC retention times of the three different dihydroxy-dimeric compounds. It is also important to point out that the DHD compounds isolated from the oxidation reaction of tocopherol with PbO_2 (obtained as a minor product at a stoichiometric ratio) were also analysed and found to be identical in all their spectral and HPLC characteristics to that of the synthesised DHD characterised above.

4.3. Characterisation of synthesised products based on the spirodimer

The SPD was synthesised in a high yield from a reaction of tocopherol with 40 molar excess of PbO_2. The conjugated dimeric structure of SPD, which was isolated from extruded PE processed with tocopherol, was previously characterised but the different isomers, which were detected in the polymer were collected together and characterised as single 'compound' [2]. Literature findings [7,18,19] have shown that using non-optically active HPLC columns gave only one HPLC peak for the tocopherol-spirodimer. In the case of the SPD synthesised in this work, the use of a non-optically active column has also resulted in one broad peak at an eluent (hexane: dioxane) ratio of 100:0.5 v/v, but changing the ratio to 100:3 v/v resulted into three well separated HPLC peaks (D1, D2 and D3) having identical UV spectral characteristics (see Figs. 3 and 11). Compared to tocopherol, the presence of a new long wavelength absorption at 339 nm confirms the presence of conjugated carbonyl group in the SPD which is further supported by the infrared absorption at 1677 cm^{-1} as well as absorptions due to unsaturation at 1657 and 1598 cm^{-1} (note also the absence of a hydroxyl group absorption) (see Fig. 11). Examination of ^{13}C-NMR, ^{1}H–^{13}C-NMR correlation (Fig. 12) and EI-MS (molecular ion at 856) (Fig. 13) spectra of the SPD further confirm its structure.

It is tempting to suggest that in view of the identical areas of the two HPLC peaks D1 and D3, their identical UV spectra, and the doubling of the resonances of the chiral carbon at position 13 (at 115.57 and 115.77 ppm) and of carbons 14 and 15 (at 202.35, 202.49 and 145.79, 145.88 ppm, respectively), that two groups of stereoisomers; *R* and *S* configurations at position 13, represent the structure of compounds D1 and D3. It is tempting to suggest too that compound D2, which has an HPLC peak

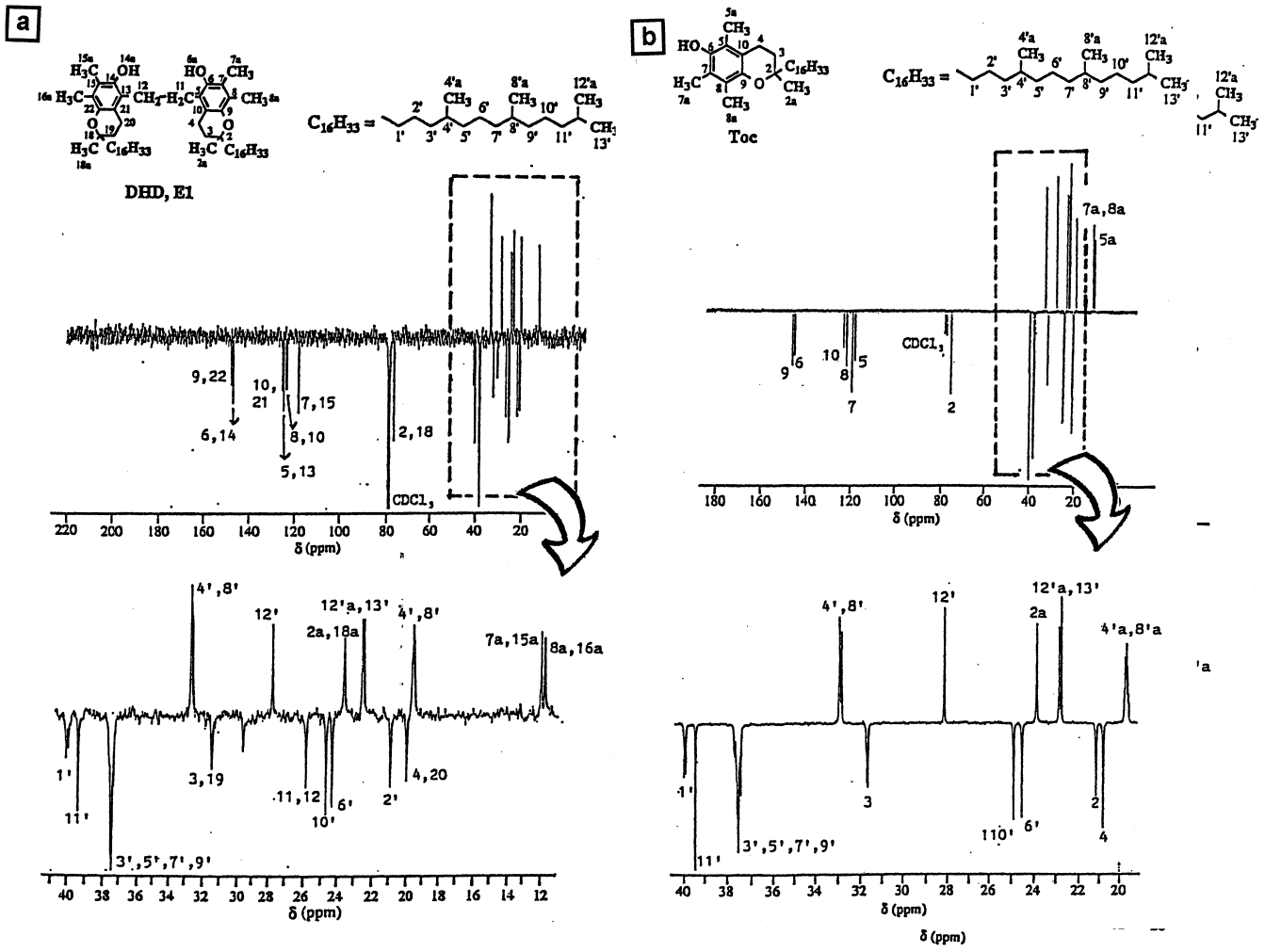


Fig. 9. ^{13}C-NMR spectra of the isolated dihydroxydimer product E1 (a) and that of tocopherol (b).

area about twice as large as that of D1 and D3 but with identical UV spectrum (see Fig. 11) is a racemic mixture of the *R* and *S* forms (see Fig. 14). However, earlier work [14] involving an α-tocopherol model (2,2,5,7,8-pentamethyl-6-chromanol) has shown that the separation of the

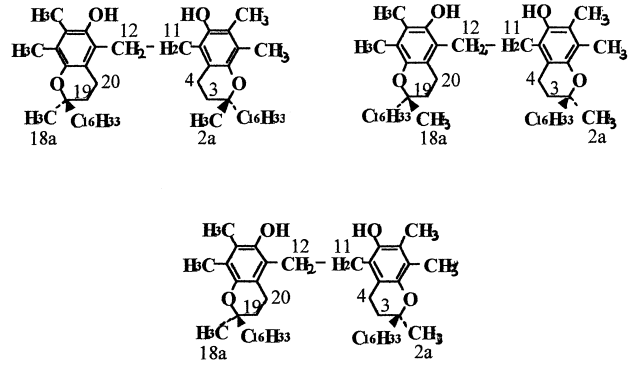


Fig. 10. Possible isomeric structures of dihydroxydimer products.

R and *S* configurations of the corresponding SPD formed from the model compound was only possible using an optically active column. Thus the above suggestions are tentatively made with caution pending further work.

4.4. Characterisation of synthesised products based on the trimer

The trimers of α-tocopherol have been previously isolated from polyolefins melt processed with DL-α-tocopherol and characterised in our laboratory [2]. However, in our previous work with the polymers, where analytical and preparative HPLC were used to separate and isolate the compounds for characterisation, three groups of HPLC peaks with different retention times were recognised to represent isomeric forms of trimers of tocopherol. The compounds corresponding to two of those peaks which were not very well separated (designated B and C) were collected together and characterised as a single 'compound' and identified as the trimer whereas the corresponding compound of the third peak which was well separated and

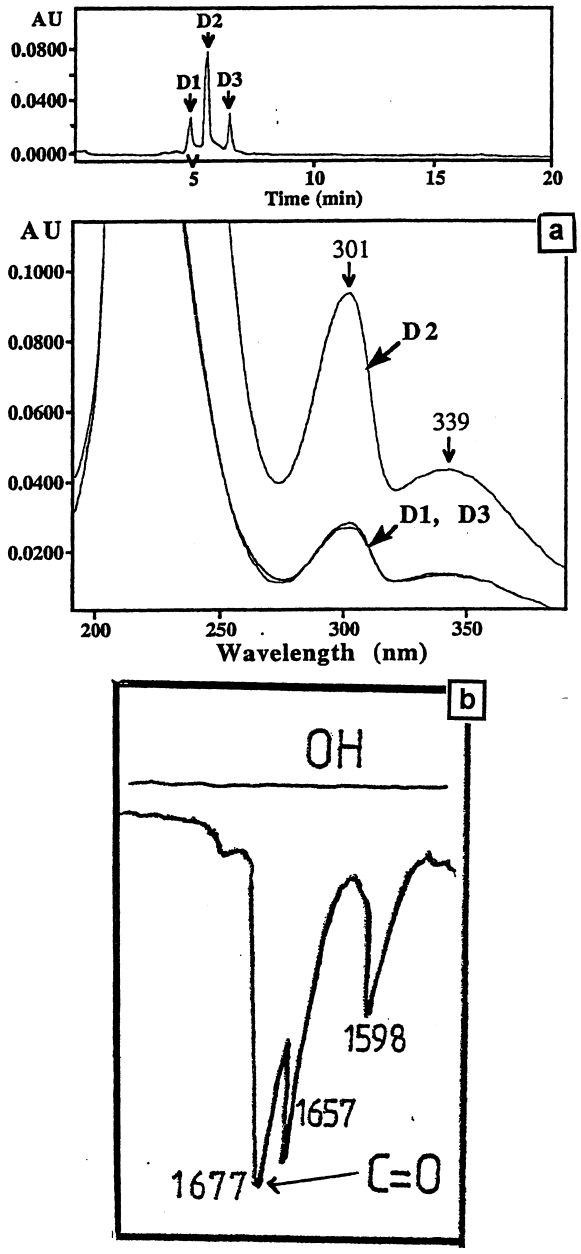


Fig. 11. UV (a) and FTIR (b) spectra of spirodimer products.

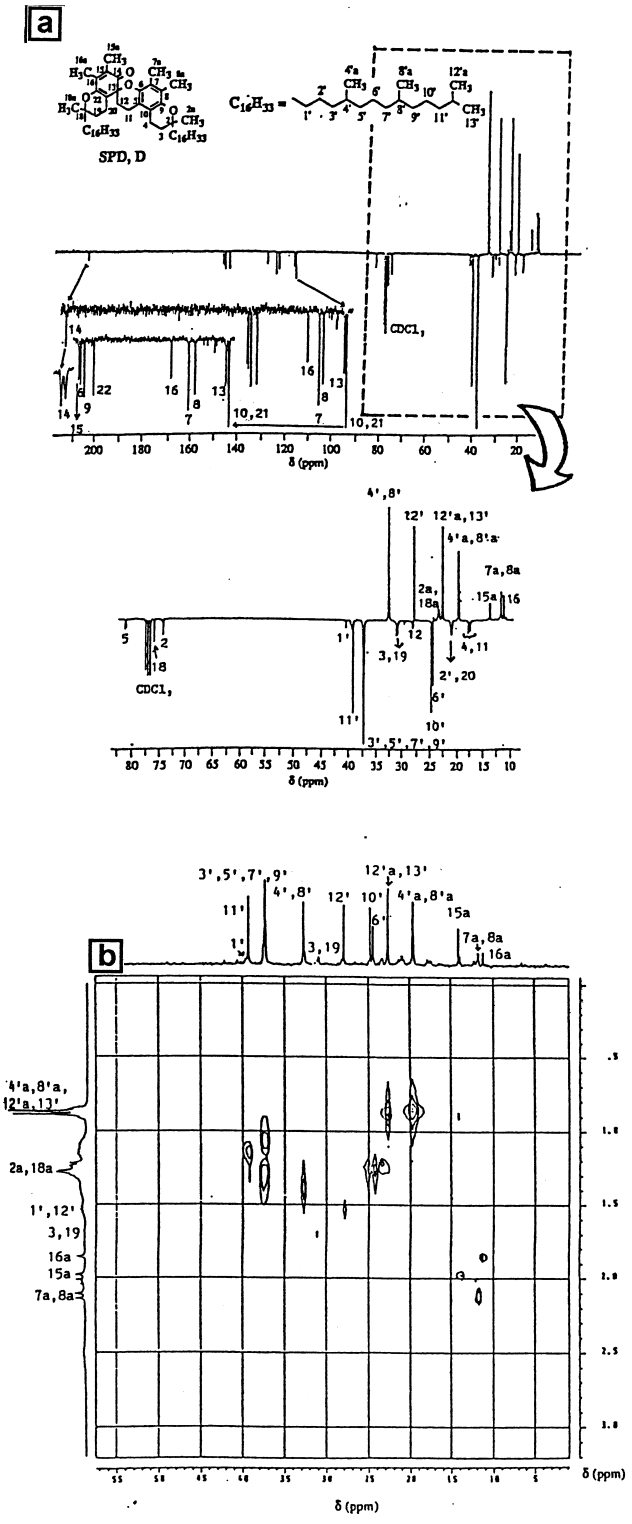


Fig. 12. ^{13}C-NMR (a) and ^{1}H–^{13}C-NMR correlation (b) spectra of spirodimer.

found to have similar overall spectral behaviour (designated trimer A), was not fully characterised and was not reported. In this work, we have synthesised, from oxidation reaction of tocopherol with 10-molar excess PbO2, the trimer which was purified to obtain 100% purity. This trimer gave rise to an HPLC chromatogram with features corresponding to three separate groups of isomeric trimers (see Fig. 2), which were found to occur at a ratio of 30% A (A1 and A2), 63% B (B1–B4) and 7% C (C1–C4). The identity of the synthesised trimeric group of compounds A, B, and C is supported by their FTIR spectrum (1693 and 1648 cm^{-1} for >C=O and >C=C<, respectively) and FAB-MS spectrum with a molecular ion peak of the trimer at 1285 [(3 times molar mass of Toc) − 6H) and initial fragmentation to SPD ($m/z = 857$) and a QM ($m/z = 428$) (see Fig. 15).

In the case of the trimers of natural *RRR*-α-tocopherol, at least four structures could be expected as all the chiral

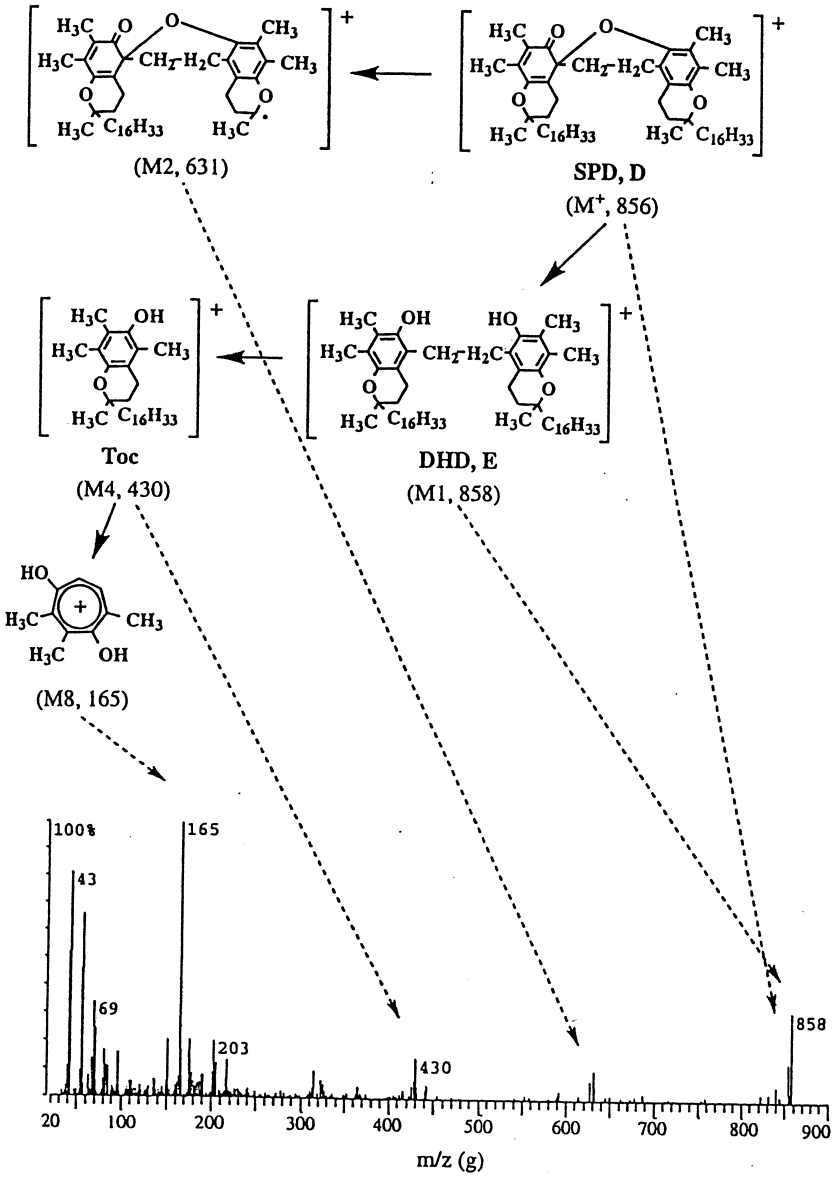


Fig. 13. EI-MS spectrum of spirodimer in acetate.

centres including the ones in the phytyl chain have the *R*-configuration. However, only two trimers of *RRR*-Toc were reported [20], which were separated by HPLC and shown to differ in the configuration at the chiral centres 21 and 22 (though no comment was made about the configuration at position 13). As for trimers formed from DL-α-tocopherol, the picture is much more complex as a very large number of stereoisomers can form since, even if the chiral centres in the phytyl chain are not taken into account, there are still six chiral centres with 64 possible isomers. In the work reported

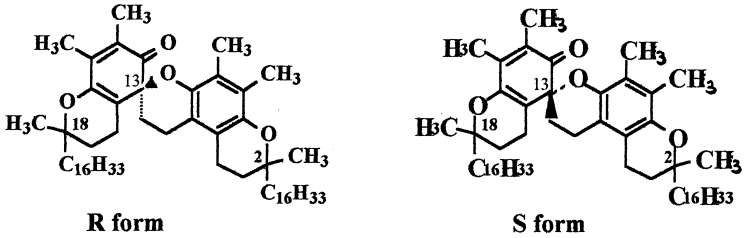


Fig. 14. Possible isomeric structures of spirodimer products.

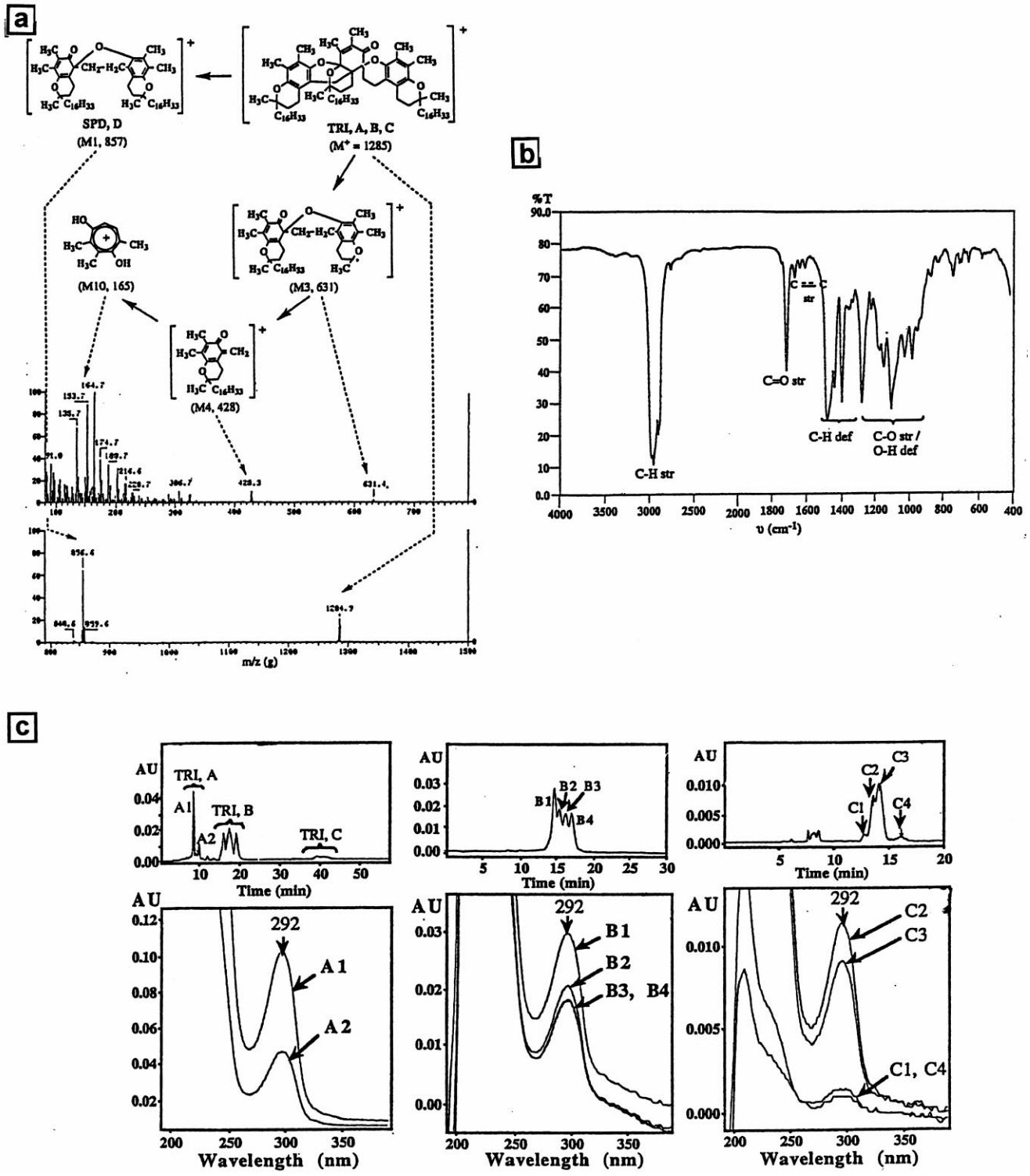


Fig. 15. Spectral characteristics of the trimer: (a) FAB-MS in acatate; (b) FTIR; (c) UV spectra of the different isolated isomeric trimer products.

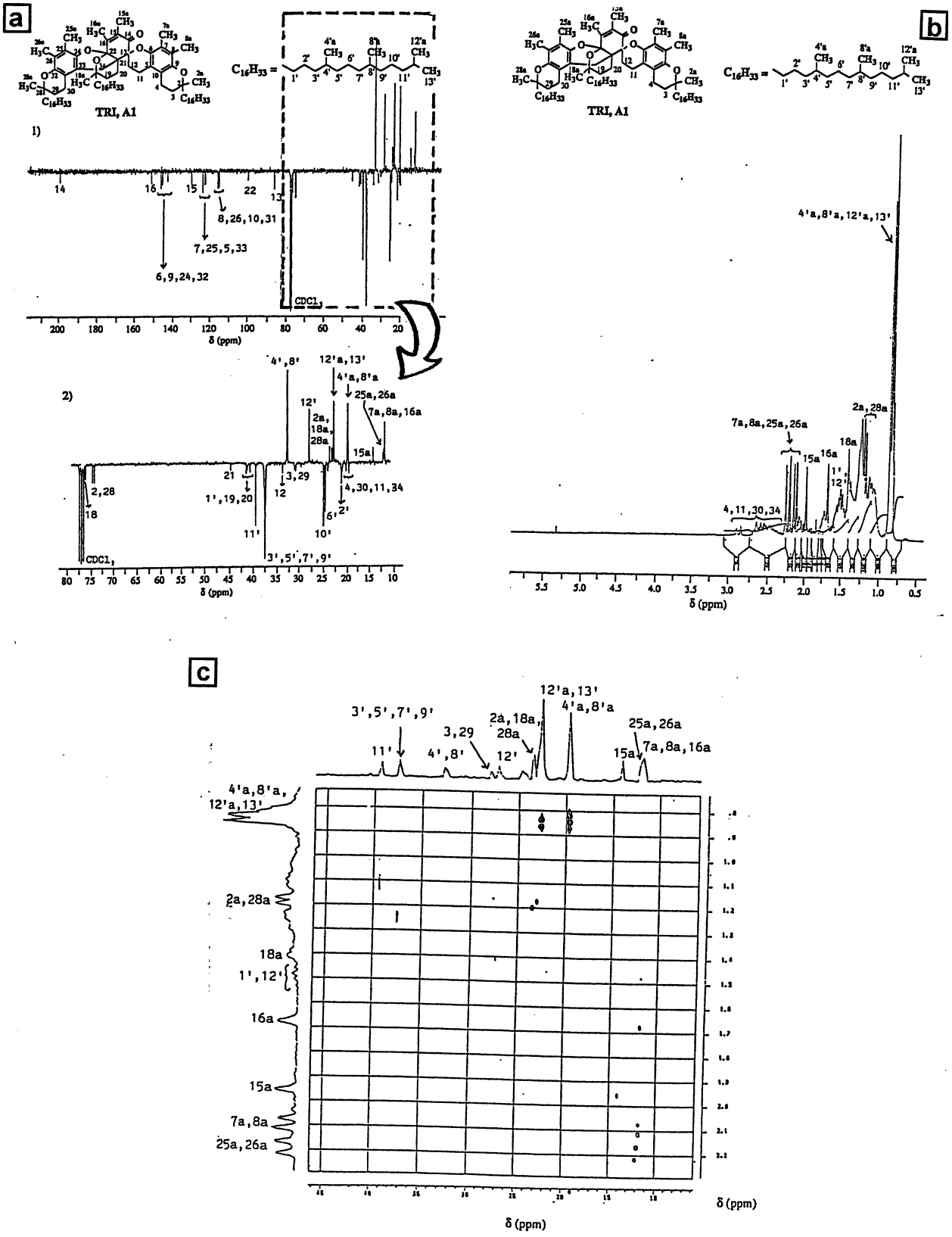
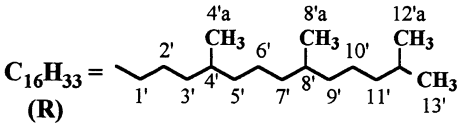


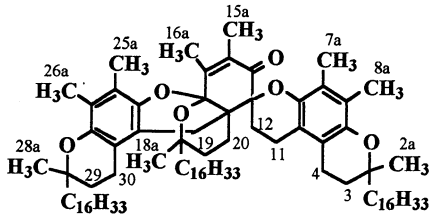
Fig. 16. NMR spectral characteristics of the isolated trimeric isomer A1: (a) ^{13}C-NMR; (b) ^{1}H-NMR, (c) ^{1}H–^{13}C-NMR correlation spectrum.

Table 4
^{1}H-NMR characteristics of synthesised trimers, A1, A2, B and C

δ, ppm (multiplicity) (s = singlet)



Group Position



		A1	A2	B	C
CH_3 of R	4–a, 8–a, 12–a, 13–	0.8–0.9	0.8–0.95	0.8–0.9	0.8–0.95
CH_3, sat	**2a, 28a**	**1.17 (s), 1.20 (s)**	**1.18 (s), 1.20 (s)**	**1.19 (s), 1.21 (s)**	**1.19 (s)**
	18a	**1.43 (s)**	**1.25 (s)**	**1.26 (s), 1.43 (s)**	**1.25 (s), 1.43 (s)**
	3′, 5′, 7′, 9′	1.0–1.45	1.0–1.45	1.0–1.45	1.0–1.45
	11′	1.0–1.15	1.0–1.15	1.0–1.2	1.0–1.2
	6′, 10′	1.15–1.3	1.15–1.3	1.2–1.35	1.2–1.35
CH_2, CH of R	2′, 4′, 8′	1.3–1.4	1.3–1.4	1.35–1.45	1.35–1.45
CH of R	1′, 12′	1.45–1.65	1.45–1.65	1.45–1.65	1.45–1.6
CH_2, β unsat.	3, 12, 29	1.7–1.8	1.7–1.8	1.7–1.9	1.65–1.85
CH_3, unsat.	**16a**	**1.67 (s)**	**1.66 (s)**	**1.67, 1.68**	**1.66 (s), 1.68 (s)**
	15a	**1.99 (s)**	**1.98 (s)**	**1.97, 1.98**	**1.96 (s), 1.97 (s)**
	7a, 8a	2.07 (s), 2.11 (s)	2.08 (s), 2.11 (s)	2.09 (s), 2.13 (s)	2.09 (s), 2.12 (s)
	25a, 26a	2.16 (s), 2.21 (s)	2.17 (s), 2.21 (s)	2.17 (s), 2.23 (s)	2.18 (s), 2.22 (s)
CH_2, α unsat.	4, 11, 30, 34	2.25–2.9	2.3–2.95	2.3–2.95	2.3–2.95

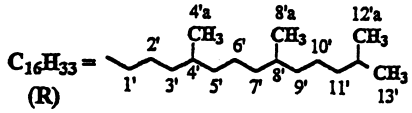
here using non-optically active HPLC column, we observe at least 10 peaks (compounds) with different retention times representing the trimeric stucture though we have isolated and characterised only four compounds: A1, A2, B1–B4, C1–C4 (see Fig. 2). The isomeric structures of the isolated trimeric compounds is confirmed by the similarity in all their spectral characteristics (IR, UV, NMR). For example, Fig. 15 shows that all the different HPLC peaks corresponding to the trimers A1, A2, B, and C have identical UV spectra with an absorption maximum at 292 nm. Fig. 16 shows the ^{1}H-, the ^{13}C-NMR and the ^{1}H–^{13}C-NMR correlation spectra which identify the structure of the isolated and purified trimer A1 and similar spectra were obtained for the other trimeric isomers isolated in this work.

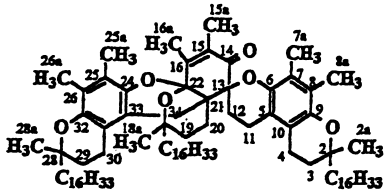
It is important to point out here that in spite of the overall similarities in the ^{1}H- and ^{13}C-NMR spectral data of the four isolated trimeric isomers shown in Tables 4 and 5, there are some subtle differences in their chemical shifts and multiplicity. For example, it is clear that whereas each of the trimers A1 and A2 represent one specific stereoisomer, the other trimers B (compounds B1–B4; four HPLC peaks, see Fig. 2) and C (compounds C1–C4, at least four HPLC peaks) are themselves mixtures of stereoisomers as indicated by the doubling of the ^{1}H-resonances at positions 15a and 16a (conjugated methyls) as well as doubling of the ^{13}C-resonances at positions 15a (conjugated methyl), 2, 18, 28, 21 (chiral centres), 14 (carbonyl), 15 and 16 (conjugated carbons) and trebling of the ^{13}C-resonances at position 22 (chiral centre).

The ^{1}H-NMR spectra differentiates further between the trimers A1 and A2, B and C. It has been shown [20] from ^{1}H-NMR of the *RRR*-TRI derived from *RRR*-α-tocopherol that when the third chroman moiety is positioned *trans* with respect to the 18a methyl group, the latter is placed in a shielding environment above the plane of the enone system, in contrast to a *cis* conformer where deshielding of the 18a proton was observed. Closer examination of the ^{1}H-NMR chemical shifts of the methyl groups 2a, 18a and 28a for the trimers A1, A2, B and C (Table 4) indicates clearly that the trimer A1 must have a *cis* structure with respect to the third

Table 5
^{13}C-NMR characteristics of synthesised TRI, A, B and C

δ (ppm) (multiplicity) (s = singlet, d = doublet, t = triplet, m = multiplet)



Group	Position (sign) (+): 1°, 3°C (−): 2°, 4°C			
		A1	A2	B
CH_2, arom. + α, β unsat.	16a(+)	11.71 (s)	11.71 (s)	11.70 (s)
	7a, 8a(+)			
	25a, 26a(+)	11.90, 12.07 (d)	12.07 (s)	11.89, 12.06 (d)
	15a(+)	**14.07 (s)**	**14.34 (s)**	**14.06, 14.32 (d)**
R	4′a, 8′a(+)	19.66 (s)	19.66 (s)	19.66, 19.72 (d)
	2′(−)	20.99 (s)	20.99 (s)	21.00, 21.22 (≥d)
	12′a, 13′(+)	22.61, 22.70 (d)	22.62, 22.71 (d)	22.61, 22.70 (d)
	6′(−)	24.45 (s)	24.44 (s)	24.43 (s)
	10′(−)	24.79 (s)	24.80 (s)	24.79 (s)
	12′(+)	27.96 (s)	27.96 (s)	27.95 (s)
	4′, 8′(+)	32.76 (s)	32.76, 32.97 (d)	32.75 (s)
	3′, 5′, 7′, 9′(−)	37.27, 37.39 (≥d)	37.40 (≥d)	37.26, 37.37, 37.56 (≥d)
	11′(−)	39.35 (1)	39.34 (s)	39.34 (1)
	1′(−)	40.62, 41.19 (d)	40.60, 41.15 (d)	40.60, 41.19 (d)
CH_3, α and β unsat.	4, 30, 11, 34(−)	19.35, 19.99 (d)	19.35, 21.63 (≥d)	19.35, 19.99 (d)
	3.29(−)	30.87, 31.13 (d)	30.88, 31.10 (d)	30.86, 31.10 (≥d)
CH_2, sat.	12(−)	33.65 (s)	34.03 (s)	33.60 (s)
	19(−)	41.43 (s)	42.45 (s)	41.44, 42.47 (d)
	20(−)			
CH_3, sat.	**2a, 18a, 28a(+)**	**23.05, 23.55 (d)**	**23.07, 23.51, 27.14 (t)**	**23.07, 23.54, 24.01 (t)**
C, sat	**21(−)**	**44.88 (1)**	**44.07 (1)**	**44.07, 44.89 (d)**
	2, 28(−)	74.31,74.71 (d)	74.32, 74.74 (d)	74.29, 74.43, 74.69, 74.73 (m)
	18(−)	76.16 (s)	77.13 (s)	76.15, 77.12 (d)
	13(−)	85.51 (s)	85.54 (s)	85.48 (s)
	22(−)	**99.25 (s)**	**100.05 (s)**	**99.24, 100.07, 100.18 (t)**
C, unsat	8, 26, 10, 31(−)	114.84, 115.13, 115.56, 115.75 (m)	115.16, 115.51, 115.78 (m)	114.84, 114.93, 115.12, 115.47, 115.62, 115.74 (m)
	7, 25, 5, 33(−)	121.91, 122.24, 123.51 (t)	121.92, 122.26, 123.51 (t)	121.90, 122.25, 123.47 (t)
	15(−)	**129.23 (s)**	**129.69 (s)**	**129.26, 129.72 (d)**
	6, 9, 24, 32(−)	141.98, 144.68, 145.56 (≥t)	142.37, 144.71, 145.44, 145.69 (m)	141.96, 142.01, 142.37, 142.43, 144.68, 145.48, 145.54, 145.68 (m)
	16(−)	**150.64 (s)**	**150.28 (s)**	**150.19, 150.60 (d)**
	14(−)	**198.75 (s)**	**198.90 (s)**	**198.70, 198.80 (d)**

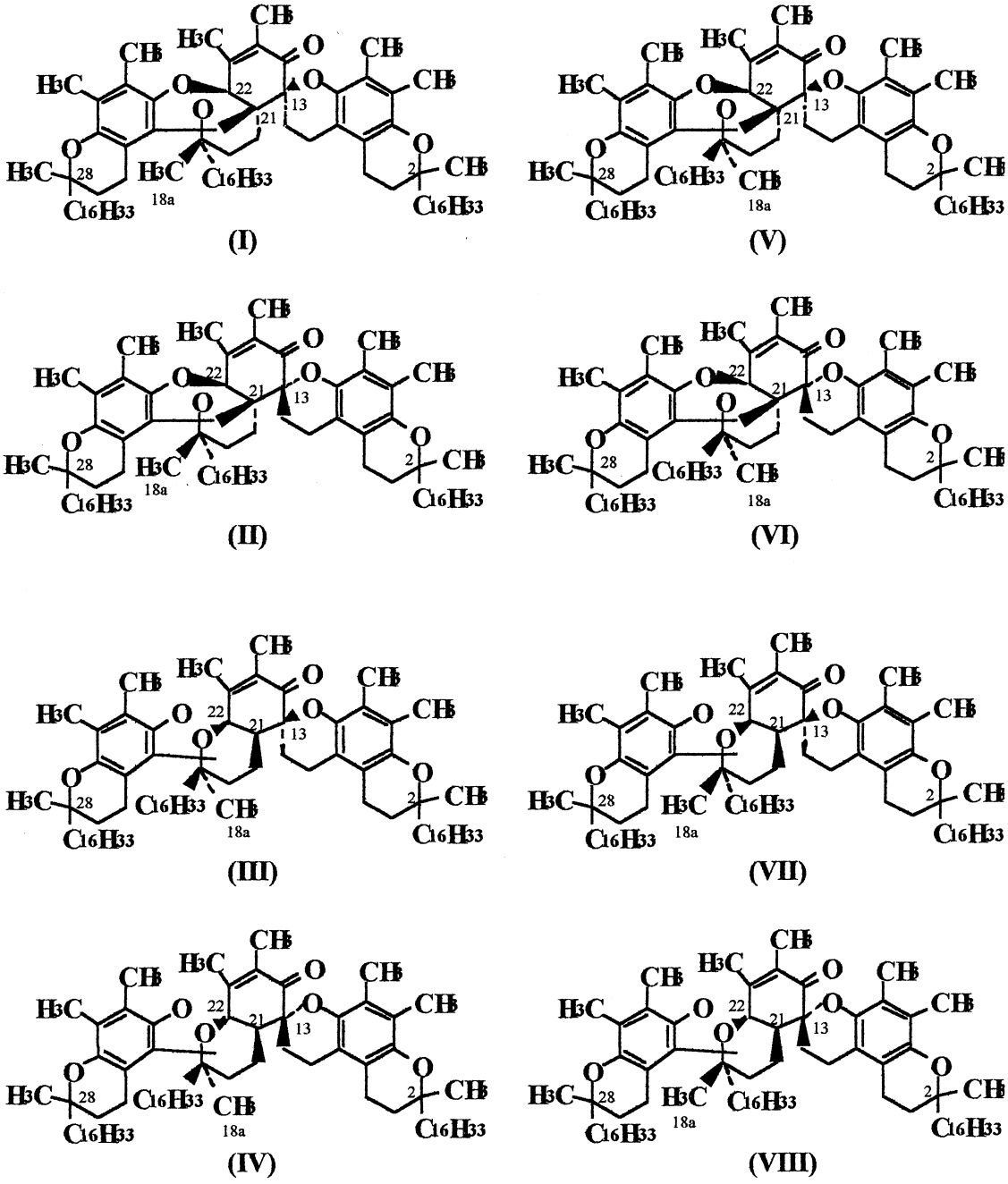


Fig. 17. Possible isomeric structures of trimer products.

chroman moiety and methyl 18a (methyl 18a, $\delta = 1.43$ ppm), e.g. structures III and IV in Fig. 17, whereas the trimer A2 must have a *trans* structure (methyl 18a, $\delta = 1.25$ ppm), e.g. structures V and VI. On the other hand, it is suggested here that trimers B and C, which are both mixtures of stereoisomers, contain both *trans* and *cis* structures (methyl 18a, $\delta = 1.25$ and 1.43 ppm). It is very difficult to justify labelling the exact isomeric structure to each individual isolated trimer without further work, which involves labelling or derivatisation of the pure individual isomers, e.g. through degradation studies on each pure isomer followed by derivatising the fragments with compounds, which posses a chiral centre of known configuration. Although it is possible to suggest that based on the spectral evidence given above it is quite likely that the isomers isolated in this work differ mainly in their configuration at

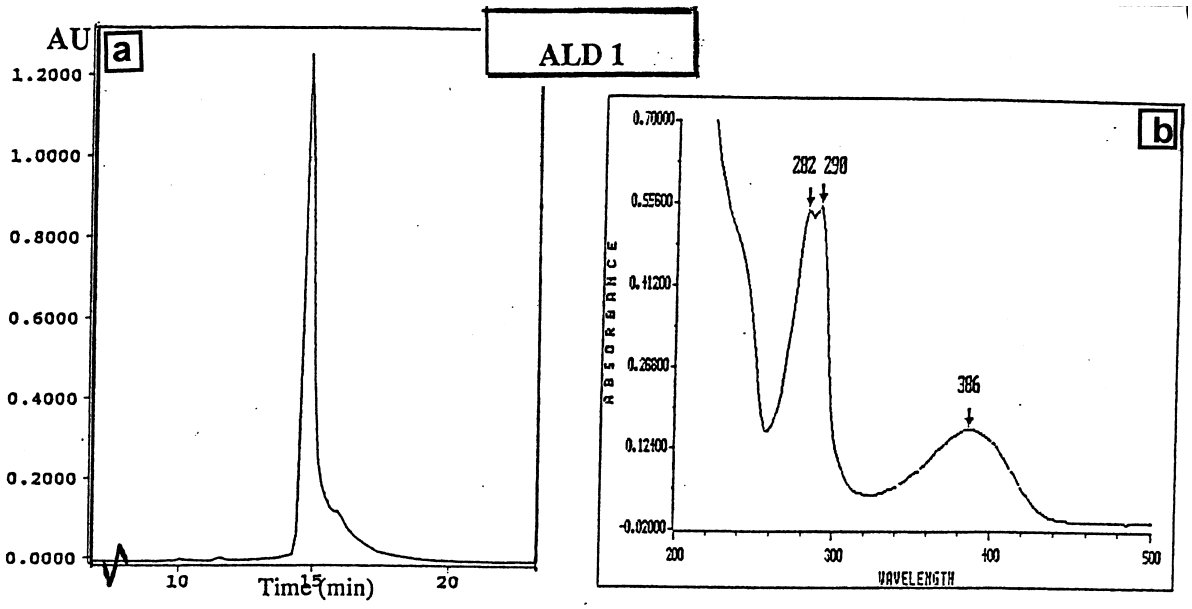


Fig. 18. HPLC chromatogram (a) and UV-spectrum (b) of the aldehyde; HPLC detection wavelength of 290 nm and mobile phase ratio of 100:0.5.

the chiral centres 13, 18, 21 and 22 and the *cis* and *trans* configurations discussed above, giving rise to the eight main structures as shown in Fig. 17.

4.5. Aldehyde isolated from PbO_2 oxidation reaction (ALD-1)

The ALD was formed as a minor product in the oxidation reaction of tocopherol with PbO_2 and was isolated from the products obtained at a ratio of 40 molar excess oxidant at a yield of 0.7% only (see Table 1). HPLC analysis revealed only one peak for the ALD, which was isolated by semi-preparative HPLC and was shown to have a UV spectrum with a long wavelength absorption maximum at 386 nm (see Fig. 18) (compared to tocopherol $\lambda_{max} = 298$ nm) attributed to the presence of aryl aldehyde group. This ALD was subjected to further spectroscopic examinations, see for example Table 2 for the ^{1}H-NMR of the isolated ALD from the PbO_2 oxidation reaction (note in particular the aldehydic proton chemical shift at 10.18 ppm and the down-field shift of the OH proton 6a to 12.09 compared to that of tocopherol at 4.3 ppm), and was found to be identical to both a synthesised ALD [21] and an ALD, which was isolated from a melt processed PE containing tocopherol [2] confirming its identity as the 5-formyl-γ-tocopherol shown (see Table 2 for structure).

4.6. Tocopherol products formed during processing of PP and PE

Synthetic α-tocopherol was used as an antioxidant in PE and PP where it was compounded in the polymers at different concentrations during processing using in the case of PE a single screw extruder at 180°C and for PP an internal mixer at 200°C. The processed polymers were extracted in dichloromethane (a solvent for both the parent antioxidant and its oxidation products) and the extracts were analysed by HPLC. Fig. 19 shows a typical example of HPLC traces (run at two wavelengths of detection of 275 nm, to detect the tocoquinone, and 290 nm for all other products) from each of the two polymers which were processed initially with 0.2% DL-α-tocopherol. The work discussed above on the PbO_2 oxidation of tocopherol in solution and the characterisation of the different products has helped us to identify the corresponding chromatographic peaks of the various oxidation products formed during melt processing of polymers. It is clear that, similar to the solution experiments, polymers containing tocopherol result also in products with different stereoisomeric forms, e.g. trimers A, B, and C. In contrast to the solution oxidation, however, the use of the polymers give rise to more than one ALD and a small amount of tocoquinone which are not formed in the PbO_2 reactions. Full characterisation of each of the isomeric products isolated from the polymers will be discussed elsewhere [21].

5. Conclusions

The nature of the products formed from oxidation reactions of DL-α-tocopherol with PbO_2 in hexane, examined at different ratios, was investigated and found to be based on dimeric, trimeric and aldehydic structures and were found to be similar to those obtained during melt processing of PE or PP with the tocopherol. Different isomeric

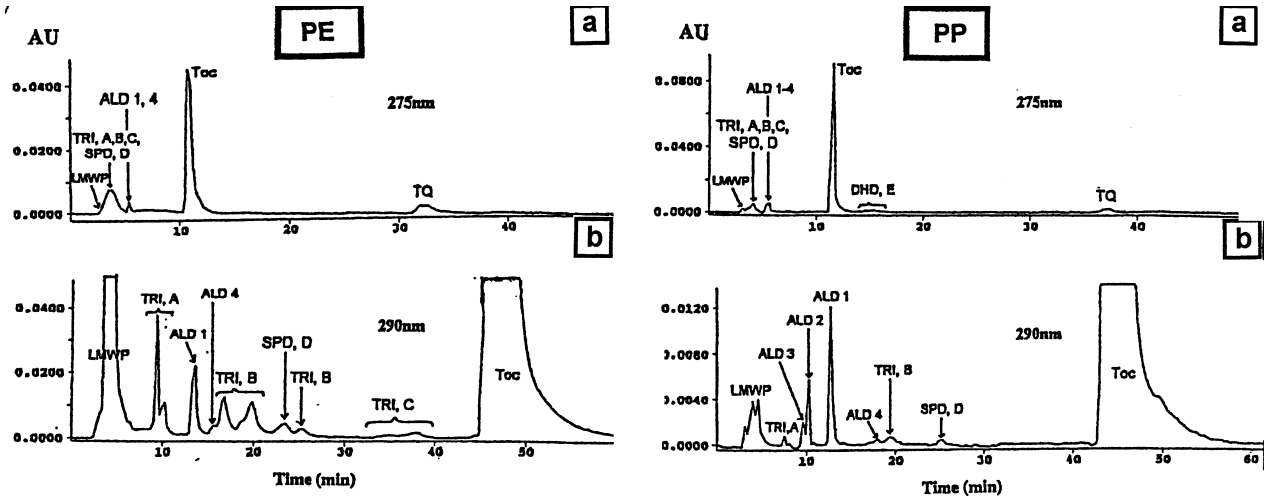


Fig. 19. HPLC chromatograms of tocopherol products extracted from PE and PP processed with 0.2% DL-α-tocopherol; HPLC detection wavelengths shown and mobile phase ratio of 100:4 (a) and 100:0.5 (b).

forms of each of the synthesised products were separated and characterized and the main conclusions of the work are as follows:

1. *Products from PbO_2 reactions*:
   - At least 10 stereoisomeric forms of the trimers of tocopherol were separated on an HPLC column from a reaction of tocopherol with 10 molar excess of PbO_2. Out of these, four isomers were isolated and characterised with two found to be pure compounds (A1 and A2) and further two (B and C) with each found to be containing mixed isomeric compounds. These were suggested to have configurational differences at chiral centres 13, 18, 21 and 22, giving rise to 8 main structures. Trimer A1, and some of the trimers B and C, were found to have a *cis* structure, whereas trimer A2 and the other part of trimers B and C were shown to have a *trans* structure with respect to methyl position 18a and the third chroman moiety in the trimeric structure.
   - Three isomeric forms of the SPD were separated and characterised.
   - Four isomeric forms of the DHD were separated and three were isolated and characterised. The different stereoisomeric structures are suggested to be due to the presence of the chiral centres at positions 2 and 18.
   - Only one aldehydic structure was obtained. It was isolated as a minor product from the oxidations of tocopherol with 40 molar excess of PbO_2 and was identified and characterized as 5-formyl-γ-tocopherol.
2. *Products formed during polymer processing*:
   - Overall, the products formed in PE and PP are similar to those isolated from the PbO_2 reactions but in the case of polymers more than one ALD was formed in addition to the formation of tocoquinone which is normally observed in polymer melt reactions but not in solution reactions.

Acknowledgements

We are grateful to Hoffmann la-Roche (Switzerland and USA) for financial support of this work. Special thanks are due to M. Gmunder for help with the mass spectroscopy, to D. Burdick and T. Young for useful discussions and C. St Porcain for valuable comments. Thanks are also due to M. Perry for running the NMR spectra.

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