

Quinones. Part 2.† General Synthetic Routes to Quinone Derivatives with Modified Polyprenyl Side Chains and the Inhibitory Effects of these Quinones on the Generation of the Slow Reacting Substance of Anaphylaxis (SRS-A)

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General synthetic routes to quinone acids (8), quinone amides (9), quinone alcohols (10), and quinone methylketones (11) with polyprenyl side chains, in which allylic alcohols (3) are employed as the key intermediates, are described. The Claisen rearrangements and the Carrol reactions of the allylic alcohols (3) with ethyl orthoacetate and diketene produced the ethyl esters (4) and the methylketones (5), respectively. Quinone products (8), (10), and (11) were recovered by oxidative demethylation of hydroquinone dimethyl ethers (4), (5), and (7) or by acid hydrolysis of hydroquinone bis(methoxymethyl) ethers (4) and (5) followed by ferric chloride oxidation. Amidation of quinone acids (8) led to the formation of quinone amides (9). Inhibitory effects of these quinone derivatives on the generation of the slow reacting substance of anaphylaxis (SRS-A) in the lungs of sensitised guinea pigs are evaluated.

Quinone and hydroquinone compounds with polyprenyl side chains are widely distributed in the plant and animal kingdom.¹ Ubiquinones, phylloquinone (vitamin K₁), menaquinones (vitamin K₂), and plastoquinones are well known representatives. These compounds are present in high concentrations in mitochondria, microsomes, chloroplasts, chromatophores, and bacteria. In such organelle membranes, they play biologically important roles promoting electron transfer in photosynthesis and/or in respiratory chains, antioxidants, and fatty soluble vitamins. In the past ten years, there have also been a number of interesting articles²⁻⁸ which report that the fat-soluble vitamins, including tocopherol, phylloquinone, menaquinone, ubiquinone, and related quinone compounds, have various biological activities such as fertility factor, inhibition of human platelet aggregation, stabilisation of biological membranes, enhancement of humoral immune response to antigenic stimulation, and resistance to bacterial infection. The diversity of the pharmacological actions is still unclear at the molecular level.

Nevertheless, there are but few articles⁹ concerned with synthetic and biological studies of quinone and hydroquinone derivatives with modified polyprenyl side chains.

Imada *et al.*¹⁰ found that the metabolic degradation of ubiquinone-7 starts with oxidation of the terminal *trans*-methyl group in the heptaprenyl side chain. In the metabolism of ubiquinone-7 in the rat, 'Q-acid I' (8a) is one of the end products of the metabolic process. 'Q-Acid analogues' (8a-d) with longer polyprenyl side chains could be present as metabolites, but no such transient intermediates (8) have been isolated so far.

We have reported the regiospecific modification¹¹ of the terminal prenyl group in polyprenyl side chains of ubiquinone, menaquinone, and tocoquinone. In the course of our synthetic studies of quinone derivatives, convenient syntheses for quinone acids (8), quinone amides (9), quinone alcohols (10), and quinone methylketones (11) were needed to provide samples for bioassay. In this paper we report two related routes to quinone compounds (8), (9), (10), and (11), based on a stereoselective Claisen rearrangement¹² and Carrol

reaction,¹³ and discuss the inhibitory effects of these compounds on the SRS-A generation.¹⁴

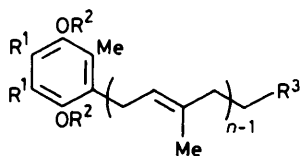
The allylic alcohols (3), which are the key intermediates for the preparation of the quinone derivatives in this work, were obtained by regiospecific epoxidation^{11a} of the terminal prenyl group in hydroquinone dimethyl ethers (1) and/or bis(methoxymethyl) ethers (1) with polyprenyl side chains, followed by thermal isomerisation of the resulting epoxides (2) with aluminium isopropoxide in refluxing toluene.^{11c} The Claisen rearrangements of the allylic alcohols (3) with ethyl orthoacetate were conducted under reflux in the presence of a small amount of propionic acid until ethanol was no longer distilled from the reaction mixture. The rearrangements made it possible to generate a series of ethyl esters of hydroquinone dimethyl ethers (4a-f) and/or bis(methoxymethyl)ethers (4g-k) readily and in good yields. Alkaline hydrolysis of the ethyl esters (4a-f) followed by oxidative demethylation of the resulting acids selectively at C-1 and -4 with ceric ammonium nitrate (CAN) in the presence of 2,6-dicarboxypyridine *N*-oxide¹⁵ and/or silver(II) oxide-nitric acid¹⁶ produced the quinone acids (8) in good yields. This type of oxidative demethylation is widely applicable to the selective formation of *p*-quinone derivatives from chemically stable and readily available hydroquinone dimethyl ethers. The quinone acids (8) were also produced by alkaline- or acid-hydrolysis of the bis(methoxymethyl) ethers followed by ferric chloride oxidation of the resulting hydroquinone acids. Analyses of the products (4) and (8) by high performance liquid chromatography (either normal or reverse phase) indicated essentially complete formation of the *trans*-isomers (>98%), based on product singularity and consideration of the reaction mechanism.¹²

It has been found that the Claisen rearrangement proceeds smoothly regardless of the number (*n*) of prenyl units in the side chain. By applying this rearrangement, a more facile and convenient synthesis, relative to earlier work,^{9c} of a series of quinone acids (8) has been developed.

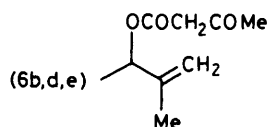
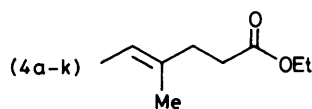
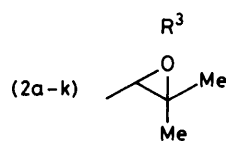
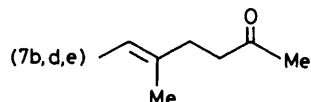
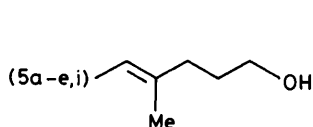
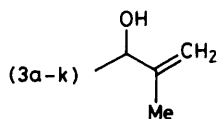
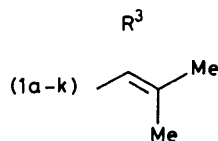
Amidation of the quinone acids (8) with amines was carried out by using either *N,N'*-dicyclohexylcarbodi-imide in the presence of *N*-hydroxysuccinimide or a mixed anhydride method to give a series of quinone amides (9).

Lithium aluminium hydride reduction of the ethyl esters (4) in absolute diethyl ether gave the corresponding alcohols (5),

† Part 1, S. Terao, K. Kato, M. Shiraishi and H. Morimoto, *J. Chem. Soc., Perkin Trans. I*, 1978, 1101.

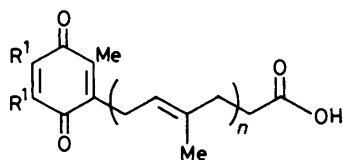


(1) - (7)



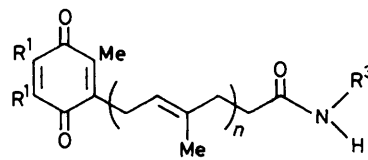
	<i>n</i>	R ¹	R ²
a;	1	OMe	Me
b;	2	OMe	Me
c;	2	Me	Me
d;	2	-CH:CHCH:CH-	Me
e;	3	-CH:CHCH:CH-	Me
f;	9	-CH:CHCH:CH-	Me

	<i>n</i>	R ¹	R ²
g;	1	OMe	CH ₂ OMe
h;	2	OMe	CH ₂ OMe
i;	3	OMe	CH ₂ OMe
j;	7	OMe	CH ₂ OMe
k;	2	Me	CH ₂ OMe



(8a-h)

	<i>n</i>	R ¹
a;	1	OMe
b;	2	OMe
c;	3	OMe
d;	7	OMe
e;	2	Me
f;	2	-CH:CHCH:CH-
g;	3	-CH:CHCH:CH-
h;	9	-CH:CHCH:CH-



(9a-i)

	<i>n</i>	R ¹	R ³
a;	3	-CH:CHCH:CH-	H
b;	2	OMe	H
c;	2	OMe	CH(Me) ₂
d;	7	OMe	3-pyridylmethyl
e;	2	-CH:CHCH:CH-	3-pyridylmethyl
f;	2	-CH:CHCH:CH-	Ph(Me)CH
g;	2	Me	3-pyridylmethyl
h;	2	OMe	<i>p</i> -hydroxyphenyl
i;	1	OMe	<i>p</i> -hydroxyphenyl

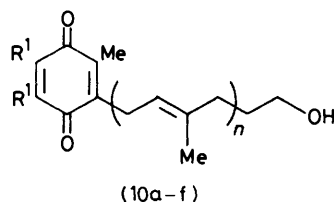
which were converted into the quinone alcohols (10) by the oxidative demethylation described above.

Reaction of the allylic alcohols (3b), (3d), and (3e) with diketene in the presence of sodium ethoxide or triethylamine as catalyst gave the corresponding acetoacetates (6b), (6d), and (6e), the structures of which were shown to be an equilibrium mixture of enol and keto forms by ¹H n.m.r. spectroscopy. The Carrol reaction of acetoacetates (6b), (6d), and (6e) was effected by heating the neat reactants up to 230 °C under an argon stream. The yields of the products were greatly improved by using aluminium isopropoxide as a catalyst. In general, this method for making protected methyl ketones (7)

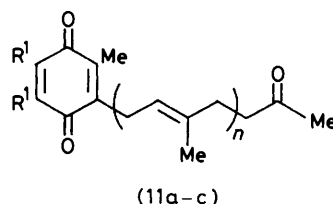
gave moderate yields (60–70%). Quinone methyl ketones (11) were obtained in an analogous manner by the conversion of the above hydroquinone dimethyl ethers (4) and (5). Since geometrical isomers formed from the Carrol reactions were neither observed in their ¹H n.m.r. spectra nor by high performance liquid chromatography, the newly formed trisubstituted olefin of the products (7) and (11) appears to have the *trans*-configuration.

The quinone compounds synthesised above were evaluated for their inhibitory effects on the SRS-A generation in the lung fragments of actively sensitised guinea pigs.

Most of the quinone compounds tested in this study showed



	n	R ¹
a;	1	OMe
b;	2	OMe
c;	3	OMe
d;	2	Me
e;	2	-CH:CHCH:CH-
f;	3	-CH:CHCH:CH-



	n	R ¹
a;	2	OMe
b;	2	-CH:CHCH:CH-
c;	3	-CH:CHCH:CH-

more potent inhibitory effects on the SRS-A generation in the chopped lung preparations of actively sensitised guinea pigs in comparison with those of the reference compound, eicosa-5,8,11,14-tetraenoic acid (ETYA),^{17a,c} 3-amino-1-(*m*-trifluoromethylphenyl)-2-pyrazoline (BW-755c),^{17b} and nordihydroguaiaretic acid (NDGA)^{17d} which are known to act as both inhibitors of cyclo-oxygenase and lipoxygenase. The results will be published elsewhere.¹⁸

Experimental

Silica gel used for column chromatography was from Merck (silica gel 60, 70–230 mesh). Tetrahydrofuran (THF), diisopropyl ether (IPE), and diethyl ether (Et₂O) were distilled from calcium hydride before use. M.p.s are uncorrected. ¹H N.m.r. spectra were recorded for CDCl₃ solution with a Varian XL-100, EM-390 and/or T-60 spectrometer using internal Me₄Si (δ = 0) as the standard. Solutions were dried over magnesium sulphate.

General Procedure for Preparation of Hydroquinone Dimethyl Ethers (1a–f) and Bismethoxymethyl Ethers (1g–k).—

Method A. A solution of 2-bromo-1,4-dimethoxy-3-methylnaphthalene (9.45 g, 33.4 mmol) in dry THF (92 ml) was cooled to –50 °C under argon. To the solution was added *n*-butyl-lithium in hexane (15; 22.8 ml, 37 mmol) with stirring. After 5 min under the same conditions, cuprous bromide was added to the solution to form lithium di-(1,4-dimethoxy-3-methyl-2-naphthyl)cuprate. The bath temperature was raised to –40 °C, farnesyl bromide (9.6 g, 33.6 mmol) in dry THF (66 ml) was then added dropwise to the solution of the organocupper compound. After the addition of the reagent, the reaction mixture was brought to room temperature, stirred for 2 h, and then quenched with 4*M*-hydrochloric acid to isolate the product by extraction with hexane. The hexane layer was washed with water and dried. The crude product obtained upon solvent evaporation was chromatographed on silica gel using IPE–hexane (1 : 9) as eluant to give *all-trans* 1,4-dimethoxy-2-methyl-3-(3,7,11-trimethyldodeca-2,6,10-trienyl)naphthalene (1e) (10.6 g, 77.6%) as a colourless oil, δ 1.55 (s, 6 H, 2 Me), 1.63 (s, 3 H, Me), 1.82 (s, 3 H, Me), 1.85–2.20 (m, 8 H, 4 CH₂), 2.37 (s, 3 H, Me), 3.55 (d, 2 H, *J* 8 Hz, CH₂), 3.83 (s, 3 H, OMe), 3.85 (s, 3 H, OMe), 5.07 (s, 3 H, 3 CH=), 7.3–7.55 (m, 2 H, Arom-H), and 7.9–8.15 (m, 2 H, Arom-H) (Found: C, 82.6; H, 9.5. C₂₈H₃₆O₂ requires C, 82.7; H, 9.42%).

Method B. *trans*-6-(3,7-Dimethylocta-2,6-dienyl)-2,3-dimethoxy-5-methyl-1,4-benzoquinone (15.9 g, 50 mmol) in Et₂O (300 ml) was shaken with a solution of sodium hydrosulphite (17.4 g, 100 mmol) in water (250 ml) at room temperature until the reaction mixture became colourless. The

organic layer was separated, washed with saturated aqueous sodium chloride, and dried. After removal of the solvent under reduced pressure, the resulting hydroquinone was dissolved in dimethylformamide (100 ml) under nitrogen. Then chloromethyl methyl ether (10.1 g, 125 mmol) and potassium carbonate (18 g) were added to the solution during 10 min. After stirring for 20 min at room temperature, the product was isolated by addition of ice (150 g) and IPE (300 ml). The organic layer was washed with water, dried, and evaporated under reduced pressure. The residue was chromatographed on silica gel eluting with IPE–hexane (2 : 3) to give *trans*-6-(3,7-dimethylocta-2,6-dienyl)-2,3-dimethoxy-5-methyl-1,4-bis(methoxymethoxy)benzene (1h) (19.4 g, 95%) as a colourless oil; δ 1.58 (s, 3 H, Me), 1.67 (s, 3 H, Me), 1.77 (s, 3 H, Me), 1.9–2.3 (m, 4 H, 2 CH₂), 2.17 (s, 3 H, Me), 3.44 (d, *J* 8 Hz, 2 H, CH₂), 3.58 (s, 6 H, 2 OMe), 3.86 (s, 6 H, 2 OMe), 5.04 (s, 4 H, OCH₂O), and 5.0–5.3 (m, 2 H, 2 CH=) (Found: C, 67.8; H, 8.5. C₂₃H₃₀O₆ requires C, 68.0; H, 8.9%).

Table 1 lists the other hydroquinone dimethyl ethers (1a–d) and (1f) and bis(methoxymethyl) ethers (1g) and (1i–k) prepared as above by method A or B from the corresponding bromides or quinones.

General Preparation of Epoxides (2a–k).—Depending on whether the number (*n*) of the prenyl units in the side chains was less than 2 (*n* ≤ 2) or more than 3 (*n* ≥ 3), one of two general methods was employed.

Method A. 1,2,3,4-Tetramethoxy-5-methyl-6-(3-methylbut-2-enyl)benzene (1a) (28.0 g, 0.1 mol) and sodium acetate (8.0 g) were dissolved in a mixture of acetic acid (100 ml) and dichloromethane (50 ml) at –10 °C. 40% Peracetic acid (20 g) was added to the mixture with vigorous stirring. During the addition of the reagent, the reaction temperature was maintained below 0 °C. When the reaction was complete, the product was isolated by addition of water (50 ml) and IPE (100 ml). The organic layer was washed with saturated aqueous sodium hydrogen carbonate, water, dried, and evaporated under reduced pressure to dryness. The crude product was chromatographed on silica gel eluting with IPE to give 6-(2,3-epoxy-3-methylbutyl)-1,2,3,4-tetramethoxy-5-methylbenzene (2a) (28.6 g, 96.6%) as a colourless oil; δ 1.30 (s, 3 H, Me), 1.43 (s, 3 H, Me), 2.22 (s, 3 H, Me), 2.7–3.0 (m, 3 H, CHO and CH₂), 3.80 (s, 3 H, OMe), 3.84 (s, 3 H, OMe), and 3.92 (s, 6 H, 2 OMe) (Found: C, 64.7; H, 8.1. C₁₆H₂₄O₅ requires C, 64.8; H, 8.2%).

Method B.^{11a} *all-trans*-1,4-Dimethoxy-2-methyl-3-(3,7,11-trimethyldodeca-2,6,10-trienyl)naphthalene (1e) (10.35 g, 25.5 mmol) was dissolved in 20% aqueous 1,2-dimethoxyethane (500 ml) at –5 °C. *N*-Bromosuccinimide (5 g, 30.5 mmol) was added in portions to the solution during 1 h with stirring. The product was isolated by addition of ethyl acetate and water,

Table 1. Data for the hydroquinone dimethyl ethers and bis(methoxymethyl) ethers (1)

Compd. no. (1a)	Method B	Formula C ₁₆ H ₂₄ O ₄	% Found (Required)		¹ H N.m.r. δ (p.p.m.)
			C 68.6 (68.5)	H 8.6 (8.6)	
(1b)	A	C ₂₁ H ₃₂ O ₄	72.4 (72.4)	9.2 (9.3)	1.56 (s, 3 H, Me), 1.63 (s, 3 H, Me), 1.74 (s, 3 H, Me), 1.9—2.2 (m, 4 H, 2 CH ₂), 2.13 (s, 3 H, Me), 3.30 (d, J 8 Hz, 2 H, CH ₂), 3.78 (s, 6 H, 2 OMe), 3.89 (s, 6 H, 2 OMe), and 5.04 (m, 1 H, CH=)
(1c)	B	C ₂₁ H ₃₂ O ₂	79.8 (79.7)	10.2 (10.2)	1.56 (s, 3 H, Me), 1.62 (s, 3 H, Me), 1.75 (s, 3 H, Me), 2.16 (s, 9 H, 3Me), 1.9—2.2 (m, 4 H, 2 CH ₂), 3.23 (d, J 8 Hz, 2 H, CH ₂), 3.60 (s, 6 H, 2 OMe), and 4.89—5.14 (m, 2 H, 2 CH=)
(1d)	A	C ₂₃ H ₃₀ O ₂	81.4 (81.6)	8.8 (8.9)	1.55 (s, 3 H, Me), 1.60 (s, 3 H, Me), 1.80 (s, 3 H, Me), 1.9—2.2 (m, 4 H, 2 CH ₂), 2.35 (s, 3 H, Me), 3.51 (d, J 8 Hz, 2 H, CH ₂), 3.83 (s, 3 H, OMe), 3.85 (s, 3 H, OMe), 5.07 (m, 2 H, 2 CH=), 7.3—7.55 (m, 2 H, Arom-H), and 7.9—8.15 (m, 2 H, Arom-H)
(1f) ^a	A	C ₅₈ H ₈₆ O ₂	85.7 (85.6)	10.5 (10.5)	1.58 (s, 24 H, 8 Me), 1.66 (s, 3 H, Me), 1.80 (s, 3 H, Me), 2.00 (br s, 32 H, 16 CH ₂), 2.34 (s, 3 H, Me), 3.54 (d, J 8 Hz, 2 H, CH ₂), 3.83 (s, 3 H, OMe), 3.85 (s, 3 H, OMe), 5.10 (m, 9 H, 9 CH=), 7.3—7.55 (m, 2 H, Arom-H), and 7.90—8.15 (m, 2 H, Arom-H)
(1g)	B	C ₁₈ H ₂₈ O ₆	63.8 (63.5)	7.9 (8.3)	1.69 (s, 3 H, Me), 1.77 (s, 3 H, Me), 2.21 (s, 3 H, Me), 3.42 (d, J 8 Hz, 2 H, CH ₂), 3.56 (s, 6 H, 2 OMe), 3.85 (s, 6 H, 2 OMe), 5.0—5.3 (m, 1 H, CH=), and 5.09 (s, 4 H, CH ₂ O)
(1i)	B	C ₂₈ H ₄₄ O ₆	70.9 (70.6)	8.7 (9.3)	1.56 (s, 6 H, 2 Me), 1.67 (s, 3 H, Me), 1.77 (s, 3 H, Me), 1.9—2.3 (m, 8 H, 4 CH ₂), 2.18 (s, 3 H, Me), 3.43 (d, J 8 Hz, 2 H, CH ₂), 3.60 (s, 6 H, 2 OMe), 3.87 (s, 6 H, 2 OMe), 5.08 (s, 4 H, 2 OCH ₂ O), and 5.0—5.3 (m, 3 H, 3 CH=)
(1j)	B	C ₄₈ H ₇₆ O ₆	77.2 (77.0)	9.8 (10.2)	1.58 (s, 18 H, 6 Me), 1.67 (s, 3 H, Me), 1.74 (s, 3 H, Me), 1.8—2.3 (m, 24 H, 12 CH ₂), 2.16 (s, 3 H, Me), 3.37 (d, J 8 Hz, 2 H, CH ₂), 3.57 (s, 6 H, 2 OMe), 3.84 (s, 6 H, 2 OMe), 4.9—5.3 (m, 7 H, 7 CH=), and 5.02 (s, 4 H, 2 OCH ₂ O)
(1k)	B	C ₂₃ H ₃₆ O ₄	73.6 (73.4)	9.3 (9.6)	1.57 (s, 3 H, Me), 1.64 (s, 3 H, Me), 1.74 (s, 3 H, Me), 1.9—2.2 (m, 4 H, 2 CH ₂), 2.18 (s, 9 H, 3Me), 3.36 (d, J 8 Hz, 2 H, CH ₂), 3.58 (s, 6 H, 2 OMe), 4.9—5.2 (m, 2 H, 2 CH=), and 5.06 (s, 4 H, 2 OCH ₂ O)

^a M.p. 51—52 °C

and the organic layer was washed with water, and dried. The solvent was evaporated under reduced pressure to dryness. The residue was chromatographed on silica gel eluting with IPE-hexane (1:1) to give the bromohydrin (6.85 g, 13.6 mmol, 61.3%) which was dissolved in methanol (50 ml). To the methanolic solution was added sodium hydroxide (1.0 g, 25 mmol) at room temperature. When the reaction was com-

plete, the product was isolated by addition of water and hexane. The organic layer was worked up in the usual manner to give *all-trans-1,4-dimethoxy-2-methyl-3-(3,7,11-trimethyl-10,11-epoxydodeca-2,6-dienyl)naphthalene* (2e) (5.6 g, 97%) as a colourless oil; δ 1.18 (s, 3 H, Me), 1.23 (s, 3 H, Me), 1.57 (s, 3 H, Me), 1.4—1.6 (m, 2 H, CH₂), 1.80 (s, 3 H, Me), 2.03 (m, 6 H, 3 CH₂), 2.35 (s, 3 H, Me), 2.62 (m, 1 H, CHO),

Table 2. Data for the epoxides (2)

Compd. no.	Method	Formula	% Found (Required)		¹ H N.m.r. δ (p.p.m.)
			C	H	
(2b)	A	C ₂₁ H ₃₂ O ₅	69.4 (69.2)	8.8 (8.9)	1.24 (s, 6 H, 2 Me), 1.5—1.8 (m, 2 H, CH ₂), 1.78 (s, 3 H, Me), 2.0—2.3 (m, 2 H, CH ₂), 2.13 (s, 3 H, Me), 2.65 (m, 1 H, CHO), 3.31 (d, <i>J</i> 8 Hz, 2 H, CH ₂), 3.77 (s, 6 H, 2 OMe), 3.88 (s, 6 H, 2 OMe), and 5.08 (m, 1 H, CH=)
(2c)	A	C ₂₁ H ₃₂ O ₅	75.6 (75.9)	9.4 (9.7)	1.24 (s, 6 H, 2 Me), 1.5—1.8 (m, 2 H, CH ₂), 1.76 (s, 3 H, Me), 2.16 (s, 9 H, 3 Me), 3.23 (d, <i>J</i> 8 Hz, 2 H, CH ₂), 3.60 (s, 6 H, 2 OMe), and 5.08 (m, 1 H, CH=)
(2d)	A	C ₂₃ H ₃₀ O ₃	77.6 (77.9)	8.6 (8.5)	1.20 (s, 6 H, 2 Me), 1.63 (m, 2 H, CH ₂), 1.83 (s, 3 H, Me), 2.15 (m, 2 H, CH ₂), 2.35 (s, 3 H, Me), 2.62 (m, 1 H, CHO), 3.53 (d, <i>J</i> 8 Hz, 2 H, CH ₂), 3.85 (s, 6 H, 2 OMe), 5.12 (m, 1 H, CH=), 7.25—7.5 (m, 2 H, Arom-H), and 7.9—8.15 (m, 2 H, Arom-H)
(2f)	B	C ₅₈ H ₈₆ O ₃	83.7 (83.9)	10.4 (10.3)	1.23 (s, 3 H, Me), 1.27 (s, 3 H, Me), 1.60 (s, 23 H, 7 Me and CH ₂), 1.83 (s, 3 H, Me), 2.00 (br s, 30 H, 15 CH ₂), 2.37 (s, 3 H, Me), 2.68 (m, 1 H, CHO), 3.55 (d, <i>J</i> 8 Hz, 2 H, CH ₂), 3.87 (s, 6 H, 2 OMe), 5.10 (m, 8 H, 8 CH=), 7.3—7.55 (m, 2 H, Arom-H), and 7.9—8.1 (m, 2 H, Arom-H)
(2g)	A	C ₁₈ H ₂₈ O ₇	60.5 (60.7)	7.6 (7.9)	1.28 (s, 3 H, Me), 1.40 (s, 3 H, Me), 2.29 (s, 3 H, Me), 2.8—3.1 (m, 3 H, CH ₂ and CHO), 3.55 (s, 6 H, 2 OMe), 3.84 (s, 6 H, 2 OMe), 5.07 (s, 2 H, OCH ₂ O), and 5.12 (s, 2 H, OCH ₂ O)
(2h)	A	C ₂₃ H ₃₆ O ₇	65.3 (65.1)	8.2 (8.5)	1.24 (s, 6 H, 2 Me), 1.5—1.8 (m, 2 H, CH ₂), 1.81 (s, 3 H, Me), 2.0—2.3 (m, 2 H, CH ₂), 2.19 (s, 3 H, Me), 2.66 (m, 1 H, CHO), 3.42 (d, <i>J</i> 8 Hz, 2 H, CH ₂), 3.61 (s, 6 H, 2 OMe), 3.89 (s, 6 H, 2 OMe), 5.0—5.3 (m, 1 H, CH=), and 5.09 (s, 4 H, OCH ₂ O)
(2i)	B	C ₂₈ H ₄₄ O ₇	68.3 (68.3)	8.7 (9.0)	1.25 (s, 3 H, Me), 1.29 (s, 3 H, Me), 1.5—1.8 (m, 2 H, CH ₂), 1.63 (s, 3 H, Me), 1.79 (s, 3 H, Me), 1.9—2.3 (m, 6 H, 3 CH ₂), 2.19 (s, 3 H, Me), 2.69 (m, 1 H, CHO), 3.40 (d, <i>J</i> 8 Hz, 2 H, CH ₂), 3.59 (s, 6 H, 2 OMe), 3.88 (s, 6 H, 2 OMe), 5.08 (m, 4 H, 2 OCH ₂ O), and 5.0—5.3 (m, 2 H, 2 CH=)
(2j)	B	C ₄₈ H ₇₆ O ₇	75.4 (75.3)	9.9 (10.0)	1.24 (s, 3 H, Me), 1.27 (s, 3 H, Me), 1.5—1.7 (m, 2 H, CH ₂), 1.58 (s, 15 H, 5 Me), 1.74 (s, 3 H, Me), 1.8—2.3 (m, 22 H, 11 CH ₂), 2.16 (s, 3 H, Me), 2.67 (m, 1 H, CHO), 3.36 (d, <i>J</i> 8 Hz, 2 H, CH ₂), 3.56 (s, 6 H, 2 OMe), 3.84 (s, 6 H, 2 OMe), 4.9—5.3 (m, 6 H, 6 CH=), and 5.02 (s, 4 H, OCH ₂ O)
(2k)	A	C ₂₃ H ₃₆ O ₅	70.3 (70.4)	9.3 (9.2)	1.21 (s, 3 H, Me), 1.23 (s, 3 H, Me), 1.5—1.8 (m, 2 H, CH ₂), 1.76 (s, 3 H, Me), 2.0—2.3 (m, 2 H, CH ₂), 2.17 (s, 9 H, 3 Me), 2.64 (m, 1 H, CHO), 3.37 (d, <i>J</i> 8 Hz, 2 H, CH ₂), 3.55 (s, 3 H, OMe), 3.57 (s, 3 H, OMe), 5.0—5.2 (m, 1 H, CH=), and 5.07 (s, 4 H, 2 OCH ₂ O)

3.53 (d, *J* 8 Hz, CH₂), 3.85 (s, 6 H, 2 OMe), 5.10 (m, 2 H, 2-CH=), 7.25—7.5 (m, 2 H, Arom-H), and 7.9—8.15 (m, 2 H, Arom-H) (Found: C, 79.6; H, 9.1%).

Table 2 lists the other epoxides (2b—d) and (2f—k) pre-

pared as above by method A or B from the corresponding ethers.

General Procedure for Allylic Alcohols (3a—k).^{11b}—all-*trans*-1,4-Dimethoxy-2-methyl-3-(3,7,11-trimethyl-10,11-

Table 3. Data for the allylic alcohols (3)

Compd.	Formula	% Found (Required)		¹ H N.m.r. δ (p.p.m.)
		C	H	
(3a)	C ₁₆ H ₂₄ O ₅	64.6 (64.8)	8.4 (8.2)	1.84 (s, 3 H, Me), 2.19 (s, 3 H, Me), 2.56 (s, 1H, OH), 2.82 (m, 2 H, CH ₂), 3.79 (s, 3 H, OMe), 3.86 (s, 3 H, OMe), 3.92 (s, 6 H, 2 OMe), 4.14 (m, 1 H, CHO), and 4.95 (m, 2 H, =CH ₂)
(3b)	C ₂₁ H ₃₂ O ₅	69.2 (69.2)	8.8 (8.9)	1.5—1.8 (m, 3 H, CH ₂ and OH), 1.69 (s, 3 H, Me), 1.76 (s, 3 H, Me), 1.9—2.2 (m, 2 H, CH ₂), 2.12 (s, 3 H, Me), 3.30 (d, <i>J</i> 8 Hz, 2 H, CH ₂), 3.76 (s, 6 H, 2 OMe), 3.88 (s, 6 H, 2 OMe), 3.99 (m, 1 H, CHO), 4.82 (m, 2 H, =CH ₂), and 5.06 (m, 1 H, CH=)
(3c)	C ₂₁ H ₃₂ O ₃	75.9 (75.9)	9.5 (9.7)	1.5—1.8 (m, 3 H, CH ₂ and OH), 1.68 (s, 3 H, Me), 1.77 (s, 3 H, Me), 1.9—2.2 (m, 2 H, CH ₂), 3.34 (d, <i>J</i> 8 Hz, 2 H, CH ₂), 3.62 (s, 6 H, 2 OMe), 3.99 (m, 1 H, CHO), 4.82 (m, 2 H, =CH ₂), and 5.0—5.2 (m, 1 H, CH=)
(3d)	C ₂₃ H ₃₀ O ₃	77.8 (77.9)	8.4 (8.5)	1.45—1.65 (m, 2 H, CH ₂), 1.67 (s, 3 H, Me), 1.60—1.80 (m, 1 H, OH), 1.83 (s, 3 H, Me), 1.90—2.20 (m, 2 H, CH ₂), 2.37 (s, 3 H, Me), 3.53 (d, <i>J</i> 8 Hz, 2 H, CH ₂), 3.85 (s, 6 H, 2 OMe), 3.97 (m, 1 H, CHO), 4.82 (m, 2 H, =CH ₂), 5.15 (m, 1 H, CH=), 7.25—7.55 (m, 2 H, Arom-H), and 7.90—8.15 (m, 2 H, Arom-H)
(3f)	C ₅₈ H ₈₆ O ₃	83.6 (83.9)	10.2 (10.3)	1.60 (s, 24 H, 7 Me, OH, and CH ₂), 1.72 (br s, 3 H, Me), 1.82 (s, 3 H, Me), 1.9—2.2 (m, 30 H, 15 CH ₂), 2.37 (s, 3 H, Me), 3.55 (d, <i>J</i> 8 Hz, 2 H, CH ₂), 3.87 (s, 6 H, 2 OMe), 4.00 (m, 1 H, CHO), 4.87 (m, 2 H, =CH ₂), 5.10 (m, 8 H, 8 CH=), 7.30—7.55 (m, 2 H, Arom-H), and 7.9—8.15 (m, 2 H, Arom-H)
(3g)	C ₁₈ H ₂₈ O ₇	61.0 (60.7)	7.5 (7.9)	1.84 (s, 3 H, Me), 2.22 (s, 3 H, Me), 2.7—3.1 (m, 3 H, CH ₂ and OH), 3.56 (s, 6 H, 2 OMe), 3.85 (s, 6 H, 2 OMe), 3.8—4.0 (m, 1 H, CHO), 4.95 (m, 2 H, =CH ₂), 5.04 (s, 2 H, OCH ₂ O), and 5.08 (s, 2 H, OCH ₂ O)
(3h)	C ₂₃ H ₃₆ O ₇	65.3 (65.1)	8.2 (8.5)	1.5—1.8 (m, 3 H, CH ₂ and OH), 1.71 (s, 3 H, Me), 1.78 (s, 3 H, Me), 1.9—2.2 (m, 2 H, CH ₂), 2.19 (s, 3 H, Me), 3.39 (d, <i>J</i> 8 Hz, 2 H, CH ₂), 3.60 (s, 6 H, 2 OMe), 3.88 (s, 6 H, 2 OMe), 3.9—4.1 (m, 1 H, CHO), 4.86 (m, 2 H, =CH ₂), 5.0—5.2 (m, 1 H, CH=), and 5.06 (s, 4 H, 2 OCH ₂ O)
(3i)	C ₂₈ H ₄₄ O ₇	68.2 (68.3)	8.8 (9.0)	1.5—1.8 (m, 3 H, CH ₂ and OH), 1.57 (s, 3 H, Me), 1.69 (s, 3 H, Me), 1.9—2.2 (m, 6 H, 4 CH ₂), 2.15 (s, 3 H, Me), 3.36 (d, <i>J</i> 8 Hz, 2 H, CH ₂), 3.54 (s, 3 H, OMe), 3.56 (s, 3 H, OMe), 3.83 (s, 6 H, 2 OMe), 3.98 (m, 1 H, CHO), 4.84 (m, 2 H, =CH ₂), 4.9—5.2 (m, 2 H, 2 CH=), and 5.02 (s, 4 H, 2 OCH ₂ O)
(3j)	C ₄₈ H ₇₆ O ₇	75.8 (75.3)	9.8 (10.0)	1.5—1.8 (m, 3 H, CH ₂ and OH), 1.57 (s, 15 H, 5 Me), 1.72 (s, 3 H, Me), 1.73 (s, 3 H, Me), 1.8—2.2 (m, 22 H, 11 CH ₂), 2.16 (s, 3 H, Me), 3.36 (d, <i>J</i> 8 Hz, 2 H, CH ₂), 3.56 (s, 6 H, 2 OMe), 3.83 (s, 6 H, 2 OMe), 4.00 (m, 1 H, CHO), 4.86 (m, 2 H, =CH ₂), 4.9—5.6 (m, 6 H, 6 CH=), and 5.02 (s, 4 H, 2 OCH ₂ O)
(3k)	C ₂₃ H ₃₆ O ₅	70.1 (70.4)	9.4 (9.2)	1.5—1.8 (m, 3 H, CH ₂ and OH), 1.69 (s, 3 H, Me), 1.75 (s, 3 H, Me), 1.9—2.2 (m, 2 H, CH ₂), 2.18 (s, 9 H, 3 Me), 3.37 (d, <i>J</i> 8 Hz, 2 H, CH ₂), 3.56 (s, 3 H, Me), 3.58 (s, 3 H, OMe), 3.98 (m, 1 H, CHO), 4.7—4.9 (m, 2 H, =CH ₂), 5.02 (s, 4 H, 2 OCH ₂ O), and 4.9—5.2 (m, 1 H, CH=)

epoxydodeca-2,6-dienyl)naphthalene (2e) (5.6 g, 12.96 mmol) and aluminium isopropoxide (6.2 g, 30.4 mmol) were dissolved in toluene (50 ml), and heated under reflux for 20 h. After the reaction mixture had cooled to room temperature, the product was isolated by addition of 2M-hydrochloric acid (150 ml) and IPE (200 ml). The organic layer was washed with water, and dried, and evaporated under reduced pressure to dryness. The residue was chromatographed on silica gel eluting with hexane-IPE (9 : 1) to give *all-trans*-3-(10-hydroxy-3,7,11-trimethyldodeca-2,6,11-trienyl)-1,4-dimethoxy-2-methylnaphthalene (3e) (5.3 g, 94.6%) as a colourless oil; δ 1.55 (s, 3 H, Me), 1.40–1.60 (m, 2 H, CH₂), 1.65 (s, 3 H, Me), 1.60–1.70 (m, 1 H, OH), 1.80 (s, 3 H, Me), 1.8–2.2 (m, 6 H, 3 CH₂), 2.35 (s, 3 H, Me), 3.53 (d, *J* 8 Hz, 2 H, CH₂), 3.85 (s, 6 H, 2 OMe), 3.93 (m, 1 H, CHO), 4.80 (m, 2 H, =CH₂), 5.07 (m, 2 H, 2 CH=), 7.25–7.5 (m, 2 H, Arom-H), and 7.90–8.15 (m, 2 H, Arom-H) (Found: C, 79.4; H, 9.3. C₂₈H₃₈O₃ requires C, 79.6; H, 9.1%).

Table 3 lists the other allylic alcohols (3a–d) and (3f–k), prepared in the same manner from the corresponding epoxides.

Preparation of Ethyl Esters (4a–k) by Claisen Rearrangements of Allylic Alcohols (3a–k).—A mixture of *all-trans*-3-(10-hydroxy-3,7,11-trimethyldodeca-2,6,11-trienyl)-1,4-dimethoxy-2-methylnaphthalene (3e) (18.65 g, 44.2 mmol), ethyl orthoacetate (53 ml), and propionic acid (0.17 ml) was heated in a flask equipped with a Claisen adapter under reflux until ethanol no longer distilled from the reaction mixture. Upon cooling, the solvent was removed under reduced pressure and the residue was chromatographed on silica gel eluting with IPE-hexane (1 : 4) to give *all-trans*-3-(13-ethoxycarbonyl-3,7,11-trimethyltrideca-2,6,10-trienyl)-1,4-dimethoxy-2-methylnaphthalene (4e) (17.3 g) as a colourless oil; δ 1.20 (t, *J* 7.5 Hz, 3 H, Me), 1.55 (s, 6 H, 2 Me), 1.82 (s, 3 H, Me), 1.85–2.2 (m, 10 H, 5 CH₂), 2.30 (m, 2 H, CH₂), 2.35 (s, 3 H, Me), 3.53 (d, *J* 8 Hz, 2 H, CH₂), 3.85 (s, 6 H, 2 OMe), 4.08 (q, 7.5 Hz, 2 H, CH₂), 5.10 (m, 3 H, 3 CH=), 7.25–7.5 (m, 2 H, Arom-H), and 7.9–8.15 (m, 2 H, Arom-H) (Found: C, 78.2; H, 9.3. C₃₂H₄₄O₄ requires C, 78.9; H, 8.0%).

Table 4 gives details of the other ethyl ester (4a–d) and (4f–k), prepared in the same manner from the corresponding allylic alcohols.

Preparation of the Alcohols (5a–e) and (5i). General Procedure for the Reduction of the Ethyl-esters (4a–e) and (4i) with Lithium Aluminium Hydride.—To a stirred mixture of lithium aluminium hydride (0.23 g, 6.04 mmol) in dry Et₂O (930 ml), kept at 0–5 °C under nitrogen, was added slowly a solution of 6-(9-ethoxycarbonyl-3,7-dimethylnona-2,6-dienyl)-1,2,3,4-tetramethoxy-5-methylbenzene (4b) (2.62 g, 6.04 mmol) in dry Et₂O (10 ml) during 5 min. The reaction mixture was stirred for 1 h at room temperature. The stirred mixture was then treated slowly and cautiously with an aqueous solution of THF (10 ml) and 1M-hydrochloric acid (30 ml). The resulting product was extracted 3 times with Et₂O. The combined ether layer was washed with saturated aqueous sodium chloride, and dried. After removal of the solvent, the residue was chromatographed on silica gel eluting with IPE to give *all-trans*-6-(10-hydroxy-3,7-dimethyldodeca-2,6-dienyl)-1,2,3,4-tetramethoxy-5-methylbenzene (5b) (2.25 g, 95%) as a colourless oil; δ 1.4–1.7 (m, 3 H, CH₂ and OH), 1.57 (s, 3 H, Me), 1.74 (s, 3 H, Me), 1.9–2.2 (m, 6 H, 3 CH₂), 2.12 (s, 3 H, Me), 3.29 (d, *J* 8 Hz, 2 H, CH₂), 3.55 (m, 2 H, CH₂O), 3.77 (s, 6 H, 2 OMe), 3.88 (s, 6 H, 2 OMe), 4.9–5.2 (m, 2 H, 2 CH=) (Found: C, 70.2; H, 9.4. C₂₃H₃₀O₅ requires C, 70.4; H, 9.2%).

Table 5 gives details of the other alcohols (5a), (5c–e), and

(5i), prepared in the same manner from the corresponding esters.

Preparation of Acetoacetates (6b), (6d), and (6e).—*trans*-3-(6-Hydroxy-3,7-dimethylocta-2,7-dienyl)-1,4-dimethoxy-2-methylnaphthalene (3d) (4.0 g, 11.28 mmol) and sodium ethoxide (20 mg) were dissolved in toluene (4 ml). The solution was cooled with an ice-water bath, and diketene (1 ml, 12.76 mmol) was added dropwise while the reaction temperature was kept below 30 °C. Stirring was continued for 12 h at room temperature. The product was isolated by addition of 1M-hydrochloric acid (1 ml), water, and IPE. The organic layer was washed with saturated aqueous sodium hydrogen carbonate, and water. After drying (MgSO₄) the solvent was removed and the residue was chromatographed on silica gel, eluting with hexane-IPE (1 : 1), to give *trans*-3-(6-acetoacetoxy-3,7-dimethylocta-2,7-dienyl)-1,4-dimethoxy-2-methylnaphthalene (6d) (3.84 g, 77%) as a colourless oil; δ 1.66 (s, 3 H, Me), 1.81 (s, 3 H, Me), 1.7–2.2 (m, 4 H, 2 CH₂), 2.14 (s, 3 H, Me), 2.33 (s, 3 H, Me), 3.33 (d, *J* 8 Hz, 2 H, CH₂), 3.50 (s, 2 H, CH₂CO), 3.81 (s, 6 H, 2 OMe), 4.7–5.3 (m, 4 H, 2 CH=, =CH₂, and CHO), and 7.2–8.2 (m, 4 H, Arom-H) (Found: C, 74.2; H, 7.6. C₂₇H₃₄O₅ requires C, 73.9; H, 7.8%).

Table 6 gives details of the other acetoacetates prepared in the same manner from the corresponding allylic alcohols.

Preparation of the Methyl Ketones (7b), (7d), and (7e). General Procedure for the Carrol Reactions of the Acetoacetates (6b), (6d), and (6e).—A stirred mixture of the acetoacetate (6d) (3.84 g, 8.69 mmol) and aluminium isopropoxide (57 mg, 0.28 mmol) was heated at 230 °C under an argon stream for 3 h. The resulting product was cooled, dissolved in hexane-IPE (1 : 1) and then chromatographed on silica gel eluting with the same solvent to give *all-trans*-1,4-dimethoxy-2-methyl-3-(3,7-dimethyl-10-oxoundeca-2,6-dienyl)naphthalene (7d) (2.45 g, 71%) as a colourless oil; δ 1.55 (s, 3 H, Me), 1.83 (s, 3 H, Me), 2.10 (s, 3 H, Me), 2.33 (s, 3 H, Me), 3.36 (d, *J* 8 Hz, 2 H, CH₂), 3.50 (m, 2 H, CH₂CO), 3.81 (s, 6 H, 2 OMe), 1.9–2.2 (m, 4 H, 2 CH₂), 5.05 (m, 2 H, 2 CH=), and 7.2–8.2 (m, 4 H, Arom-H) (Found: C, 79.5; H, 8.8. C₂₆H₃₄O₃ requires C, 79.2; H, 8.7%).

Table 6 gives details of the other methyl ketones prepared in the same manner from the corresponding acetoacetates.

Formation of Quinone Derivatives.—Method A. *all-trans*-3-(13-Ethoxycarbonyl-3,7,11-trimethyltrideca-2,6,10-trienyl)-1,4-dimethoxy-2-methylnaphthalene (4e) (17.0 g 37 mmol) and sodium hydroxide (3.5 g) were dissolved in aqueous ethanol (150 ml) at room temperature. The reaction mixture was stirred for 2 h. The product was isolated by addition of 2M-hydrochloric acid (20 ml), ethyl acetate (300 ml), and water (200 ml). The organic layer was washed with water, dried, and evaporated under reduced pressure to give the corresponding acid (15.8 g, 98.5%). The acid (15.8 g, 36.6 mmol) and silver-(ii) oxide (17.01 g, 0.173 mol) were mixed in dioxan (300 ml) at 0 °C. 6M-Nitric acid (33.8 ml) was added and the reaction mixture was stirred until complete dissolution had occurred (30 min). The quinone product was isolated by addition of water (300 ml) and ethyl acetate (300 ml). The organic layer was washed with saturated aqueous sodium chloride, dried, and evaporated under reduced pressure to dryness. The residue was crystallised from IPE-hexane (1 : 2) to give 3-(13-carboxy-3,7,11-trimethyltrideca-2,6,10-trienyl)-2-methyl-1,4-naphthoquinone (8g) (3.23 g, 71%) as yellow needles, m.p. 74–75 °C; δ 1.58 (s, 6 H, 2 Me), 1.89 (s, 3 H, Me), 1.9–2.20 (m, 8 H, 4 CH₂), 2.20 (s, 3 H, Me), 2.34 (m, 4 H, CH₂CH₂CO), 3.37 (d, *J* 8 Hz, 2 H, CH₂), 4.9–5.3 (m, 3 H, 3 CH=), 7.6 CO), 3.37 (d, *J* 8 Hz, 2 H, CH₂), 4.9–5.3 (m, 3 H, 3 CH=),

Table 4. Data for the ethyl esters (4)

Compd. no.	Formula	% Found (Required)		¹ H N.m.r. δ (p.p.m.)
		C	H	
(4a)	C ₂₀ H ₃₀ O ₆	65.4 (65.6)	8.0 (8.3)	1.20 (t, <i>J</i> 7.5 Hz, 3 H, Me), 1.76 (s, 3 H, Me), 2.14 (s, 3 H, Me), 2.32 (m, 4 H, 2 CH ₂), 3.33 (d, <i>J</i> 8 Hz, 2 H, CH ₂), 3.77 (s, 6 H, 2 OMe), 3.89 (s, 6 H, 2 OMe), 4.08 (q, <i>J</i> 7.5 Hz, 2 H, OCH ₂), and 5.02 (m, 1 H, CH=)
(4b)	C ₂₅ H ₃₈ O ₆	69.3 (69.1)	8.6 (8.8)	1.22 (t, <i>J</i> 7.5 Hz, 3 H, Me), 1.58 (s, 3 H, Me), 1.75 (s, 3 H, Me), 1.9—2.2 (m, 4 H, 2 CH ₂), 2.13 (s, 3 H, Me), 2.30 (m, 4 H, 2 CH ₂), 3.29 (d, <i>J</i> 8 Hz, 2 H, CH ₂), 3.77 (s, 6 H, 2 OMe), 3.88 (s, 6 H, 2 OMe), 4.08 (q, <i>J</i> 7.5 Hz, 2 H, OCH ₂), and 4.9—5.2 (m, 2 H, 2 CH=)
(4c)	C ₂₅ H ₃₈ O ₄	74.3 (74.6)	9.7 (9.5)	1.22 (t, <i>J</i> 7.5 Hz, 3 H, Me), 1.57 (s, 3 H, Me), 1.76 (s, 3 H, Me), 1.9—2.2 (m, 4 H, 2 CH ₂), 2.17 (s, 9 H, 3 Me), 2.29 (m, 4 H, 2 CH ₂), 3.34 (d, <i>J</i> 8 Hz, 2 H, CH ₂), 3.62 (s, 6 H, 2 OMe), 4.08 (q, <i>J</i> 7.5 Hz, 2 H, OCH ₂), and 4.9—5.2 (m, 2 H, 2 CH=)
(4d)	C ₂₇ H ₃₆ O ₄	76.5 (76.4)	8.7 (8.5)	1.20 (t, <i>J</i> 7.5 Hz, 3 H, Me), 1.57 (s, 3 H, Me), 1.80 (s, 3 H, Me), 2.00 (m, 4 H, 2 CH ₂), 2.27 (m, 4 H, 2 CH ₂), 2.35 (s, 3 H, Me), 3.53 (d, <i>J</i> 8 Hz, 2 H, CH ₂), 3.85 (s, 6 H, 2 OMe), 4.07 (q, <i>J</i> 7.5 Hz, 2 H, OCH ₂), 5.08 (m, 3 H, 3 CH=), 7.25—7.50 (m, 2 H, Arom-H), and 7.9—8.15 (m, 2 H, Arom-H)
(4f)	C ₆₂ H ₉₂ O ₄	82.4 (82.6)	10.3 (10.3)	1.20 (t, <i>J</i> 7.5 Hz, 3 H, Me), 1.60 (s, 24 H, 8 Me), 1.72 (s, 3 H, Me), 2.37 (s, 3 H, Me), 3.55 (d, <i>J</i> 8 Hz, 2 H, CH ₂), 3.87 (s, 6 H, 2 OMe), 4.07 (q, <i>J</i> 7.5 Hz, 2 H, OCH ₂), 5.10 (m, 9 H, 9 CH=), 7.3—7.55 (m, 2 H, Arom-H), and 7.9—8.15 (m, 2 H, Arom-H)
(4g)	C ₂₂ H ₃₄ O ₈	62.0 (62.0)	7.8 (8.0)	1.18 (t, <i>J</i> 7.5 Hz, 3 H, Me), 1.76 (s, 3 H, Me), 2.14 (s, 3 H, Me), 2.34 (m, 4 H, 2CH ₂), 3.36 (d, <i>J</i> 8 Hz, 2 H, CH ₂), 3.54 (s, 3 H, Me), 3.56 (s, 3 H, Me), 3.84 (s, 6 H, 2 OMe), 4.15 (q, <i>J</i> 7.5 Hz, 2 H, OCH ₂), 4.9—5.2 (m, 1 H, CH=), and 5.02 (s, 4 H, 2 OCH ₂ O)
(4h)	C ₂₇ H ₄₂ O ₈	65.7 (65.6)	8.2 (8.6)	1.25 (t, <i>J</i> 7.5 Hz, 3 H, Me), 1.61 (s, 3 H, Me), 1.77 (s, 3 H, Me), 1.9—2.2 (m, 4 H, 2 CH ₂), 2.19 (s, 3 H, Me), 2.34 (m, 4 H, 2 CH ₂), 3.38 (d, <i>J</i> 8 Hz, 2 H, CH ₂), 3.62 (s, 6 H, 2 OMe), 3.90 (s, 6 H, 2 OMe), 4.15 (q, <i>J</i> 7.5 Hz, 2 H, OCH ₂), 5.11 (s, 4 H, OCH ₂ O), and 5.0—5.3 (m, 2 H, 2 CH=)
(4i)	C ₃₂ H ₅₀ O ₈	68.2 (68.3)	9.1 (9.0)	1.23 (t, <i>J</i> 7.5 Hz, 3 H, Me), 1.57 (s, 6 H, 2 Me), 1.74 (s, 3 H, Me), 1.8—2.2 (m, 8 H, 4 CH ₂), 2.16 (s, 3 H, Me), 2.33 (m, 4 H, 2 CH ₂), 3.36 (d, <i>J</i> 8 Hz, 2 H, CH ₂), 3.54 (s, 3 H, OMe), 3.56 (s, 3 H, OMe), 3.84 (s, 6 H, 2 OMe), 4.09 (q, <i>J</i> 7.5 Hz, 2 H, OCH ₂), 4.9—5.2 (m, 3 H, 3 CH=), and 5.02 (s, 4 H, 2 OCH ₂ O)
(4j)	C ₅₂ H ₈₂ O ₈	74.9 (74.8)	9.6 (9.9)	1.23 (t, <i>J</i> 7.5 Hz, 3 H, Me), 1.57 (s, 18 H, 7 Me), 1.74 (s, 3 H, Me), 1.8—2.2 (m, 24 H, 12 CH ₂), 2.16 (s, 3 H, Me), 2.33 (m, 4 H, 2 CH ₂), 3.36 (d, <i>J</i> 8 Hz, 2 H, CH ₂), 3.56 (s, 6 H, 2 OMe), 3.83 (s, 6 H, 2 OMe), 4.09 (q, <i>J</i> 7.5 Hz, 2 H, OCH ₂), 4.9—5.2 (m, 7 H, 7 CH=), and 5.02 (s, 4 H, 2 OCH ₂ O)
(4k)	C ₂₇ H ₄₂ O ₆	70.4 (70.1)	9.2 (9.2)	1.21 (t, <i>J</i> 7.5 Hz, 3 H, Me), 1.57 (s, 3 H, Me), 1.73 (s, 3 H, Me), 1.9—2.2 (m, 4 H, 2 CH ₂), 2.19 (s, 9 H, 3 Me), 2.28 (m, 4 H, 2 CH ₂), 3.35 (d, <i>J</i> 8 Hz, 2 H, CH ₂), 3.55 (s, 3 H, OMe), 3.57 (s, 3 H, OMe), 4.08 (q, <i>J</i> 7.5 Hz, 2 H, CH ₂ O), 5.12 (s, 4 H, 2 CH ₂ O), and 4.9—5.2 (m, 2 H, 2 CH=)

Table 5. Data for the alcohols (5)

Compd. no.	Formula	% Found (Required)		¹ H N.m.r. δ (p.p.m.)
		C	H	
(5a)	C ₁₈ H ₂₈ O ₅	66.8 (66.6)	8.8 (8.7)	1.3—1.7 (m, 3 H, CH ₂ and OH), 1.76 (s, 3 H, Me), 1.9—2.1 (m, 2 H, CH ₂), 2.12 (s, 3 H, Me), 3.33 (d, <i>J</i> 8 Hz, 2 H, CH ₂), 3.56 (m, 2 H, CH ₂ O), 3.77 (s, 6 H, 2 OMe), 3.88 (s, 6 H, 2 OMe), and 5.00 (m, 1 H, CH=)
(5c)	C ₂₃ H ₃₆ O ₅	76.3 (76.6)	10.0 (10.1)	1.4—1.7 (m, 3 H, CH ₂ and OH), 1.57 (s, 3 H, Me), 1.76 (s, 3 H, Me), 1.9—2.2 (m, 6 H, 3 CH ₂), 2.17 (s, 9 H, 3 Me), 3.34 (d, <i>J</i> 8 Hz, 2 H, CH ₂), 3.54 (m, 2 H, CH ₂ O), 3.63 (s, 6 H, 2 OMe), and 4.9—5.2 (m, 2 H, 2 CH=)
(5d)	C ₂₅ H ₃₄ O ₅	78.2 (78.5)	9.2 (9.0)	1.4—1.7 (m, 3 H, CH ₂ and OH), 1.55 (s, 6 H, 2 Me), 1.77 (s, 3 H, Me), 2.17 (s, 3 H, Me), 1.9—2.1 (m, 6 H, 3 CH ₂), 3.35 (d, <i>J</i> 8 Hz, 2 H, CH ₂), 3.53 (m, 2 H, CH ₂ O), 3.80 (s, 6 H, 2 OMe), 5.0—5.1 (m, 2 H, 2 CH=), and 7.2—8.2 (m, 4 H Arom-H)
(5e)	C ₃₀ H ₄₂ O ₅	79.8 (80.0)	9.2 (9.4)	1.4—1.7 (m, 3 H, CH ₂ and OH), 1.53 (s, 6 H, Me), 1.77 (s, 3 H, Me), 2.17 (s, 3 H, Me), 1.9—2.1 (m, 10 H, 5 CH ₂), 3.35 (d, <i>J</i> 8 Hz, 2 H, CH ₂), 3.58 (m, 2 H, CH ₂ O), 3.80 (s, 6 H, 2 OMe), 5.0—5.1 (m, 3 H, 3 CH=), and 7.2—8.2 (m, 4 H, Arom-H)
(5i)	C ₃₀ H ₄₈ O ₇	69.0 (69.2)	8.7 (9.3)	1.4—1.7 (m, 3 H, CH ₂ and OH), 1.60 (s, 3 H, Me), 1.62 (s, 6 H, 2 Me), 1.74 (s, 3 H, Me), 1.9—2.2 (m, 10 H, 5 CH ₂), 2.22 (s, 3 H, Me), 3.44 (d, <i>J</i> 8 Hz, 2 H, CH ₂), 3.55 (m, 2 H, CH ₂ O), 3.56 (s, 6 H, 2 OMe), 3.85 (s, 6 H, 2 OMe), 5.0—5.3 (m, 3 H, 3 CH=), and 5.04 (s, 4 H, 2 OCH ₂ O)

Table 6. Data for the acetoacetates (6) and methyl ketones (7)

Compd.	Formula	% Found (Required)		¹ H N.m.r. δ (p.p.m.)
		C	H	
(6b)	C ₂₅ H ₃₆ O ₇	66.7 (66.9)	8.0 (8.1)	1.70 (s, 3 H, Me), 1.77 (s, 3 H, Me), 1.8—2.0 (m, 4 H, 2 CH ₂), 2.13 (s, 3 H, Me), 2.23 (s, 3 H, Me), 3.30 (d, <i>J</i> 8 Hz, 2 H, CH ₂), 3.39 (s, 2 H, CH ₂ CO), 3.78 (s, 6 H, 2 OMe), 3.88 (s, 6 H, 2 OMe), 4.90 (m, 2 H, CH ₂), and 5.0—5.2 (m, 2 H, CHO and CH=)
(6e)	C ₃₂ H ₄₂ O ₅	76.2 (75.9)	8.5 (8.4)	1.56 (s, 3 H, Me), 1.67 (s, 3 H, Me), 1.9—2.2 (m, 8 H, 4 CH ₂), 1.82 (s, 3 H, Me), 2.13 (s, 3 H, Me), 2.35 (s, 3 H, Me), 3.37 (d, <i>J</i> 8 Hz, 2 H, CH ₂), 3.52 (s, 2 H, CH ₂ CO), 3.81 (s, 3 H, OMe), 3.83 (s, 3 H, OMe), 4.75—5.30 (m, 5 H, =CH ₂ , CHO and 2 CH=), 7.15—8.20 (m, 4 H, Arom-H)
(7b)	C ₂₄ H ₃₆ O ₅	71.2 (71.3)	8.9 (9.0)	1.56 (s, 3 H, Me), 1.75 (s, 3 H, Me), 2.0—2.5 (m, 8 H, 4 CH ₂), 2.10 (s, 3 H, Me), 2.13 (s, 3 H, Me), 3.30 (d, <i>J</i> 8 Hz, 2 H, CH ₂), 3.77 (s, 6 H, 2 OMe), 3.88 (s, 6 H, 2 OMe), 5.03 (m, 1 H, CH=), and 5.07 (m, 1 H, CH=)
(7e)	C ₃₁ H ₄₂ O ₅	80.3 (80.5)	9.2 (9.2)	1.56 (s, 3 H, Me), 1.62 (s, 3 H, Me), 1.83 (s, 3 H, Me), 2.10 (s, 3 H, Me), 2.37 (s, 3 H, Me), 3.37 (d, <i>J</i> 8 Hz, 2 H, CH ₂), 3.56 (m, 2 H, CH ₂ CO), 3.87 (s, 6 H, 2 OMe), 5.10 (m, 3 H, 3 CH=), and 7.2—8.2 (m, 4 H, Arom-H)

7.6—7.75 (m, 2 H, Arom-H), 8.0—8.15 (m, 2 H, Arom-H), and 9.72 (s, 1 H, CO₂H) (Found: C, 77.3; H, 7.8. C₂₈H₃₄O₄ requires C, 77.4; H, 7.9%).

Method B.¹⁵ 6-(10-Hydroxy-3,7-dimethyldeca-2,6-dienyl)-1,2,3,4-tetramethoxy-5-methylbenzene (5b) (7.8 g, 20 mmol) and 2,6-dicarboxypyridine *N*-oxide (14.6 g, 80 mmol) were dissolved in 30% aqueous acetonitrile (180 ml) with stirring. To the solution was added dropwise a cold solution of ceric

ammonium nitrate (43.8 g, 80 mmol) in 50% aqueous acetonitrile (180 ml) during 40 min. The reaction was stirred under the same conditions for an additional 20 min. Precipitates appeared as the reaction proceeded. When the reaction was complete, the precipitates were filtered, and the filtrate was concentrated under reduced pressure. The product was isolated by addition of IPE (500 ml) and water (200 ml). The organic layer was washed with saturated aqueous sodium

Table 7. Data for the quinone derivatives (8), (10), and (11)

Compd no.	Method	Formula M.p. (°C)	% Found (Required)		¹ H N.m.r. δ (p.p.m.)
(8a)	B, C	C ₁₆ H ₂₀ O ₆	62.1 (62.3)	6.6 (6.5)	1.75 (s, 3 H, Me), 1.98 (s, 3 H, Me), 2.35 (m, 4 H, CH ₂ CH ₂ CO), 3.16 (d, <i>J</i> 8 Hz, 2 H, CH ₂ O), 3.96 (s, 6 H, 2 OMe) 4.99 (m, 1 H, CH=), and 10.63 (s, 1 H, CO ₂ H)
(8b)	B, C	C ₂₁ H ₂₈ O ₆ 54—56	66.8 (67.0)	7.6 (7.5)	1.60 (s, 3 H, Me), 1.75 (s, 3 H, Me), 1.8—2.2 (m, 4 H, 2 CH ₂) 2.02 (s, 3 H, OMe), 2.34 (m, 4 H, CH ₂ CH ₂ CO), 3.20 (d, <i>J</i> 8 Hz, 2 H, CH ₂), 3.97 (s, 3 H, OMe), 3.99 (s, 3 H, OMe), 4.8—5.3 (m, 2 H, CH=), and 10.83 (s, 1 H, CO ₂ H)
(8c)	C	C ₂₆ H ₃₆ O ₆	70.3 (70.2)	8.2 (8.2)	1.60 (s, 6 H, 2 Me), 1.75 (s, 3 H, Me), 1.9—2.2 (m, 11 H, 4 CH ₂ and Me), 2.34 (m, 4 H, CH ₂ CH ₂ CO), 3.18 (d, <i>J</i> 8 Hz, 2 H, CH ₂), 3.97 (s, 3 H, OMe), 3.99 (s, 3 H, OMe), 4.8—5.3 (m, 3 H, CH=), and 10.52 (d, 1 H, CO ₂ H)
(8e)	A	C ₂₁ H ₂₈ O ₄ 65—67	73.4 (73.2)	8.3 (8.2)	1.60 (s, 3 H, Me), 1.76 (s, 3 H, Me), 2.01 (s, 9 H, 3 Me), 1.9—2.2 (m, 4 H, 2 CH ₂), 2.34 (m, 4 H, CH ₂ CH ₂ CO), 3.24 (d, <i>J</i> 8 Hz, 2 H, CH ₂), 5.12 (m, 2 H, CH=), and 10.23 (m, 1 H, CO ₂ H)
(8f)	A	C ₂₃ H ₂₆ O ₄ 94.5—95	75.3 (75.4)	7.3 (7.2)	1.57 (s, 3 H, Me), 1.89 (s, 3 H, Me), 1.9—2.2 (m, 4 H, CH ₂), 2.20 (s, 3 H, Me), 2.34 (m, 4 H, CH ₂ CH ₂ CO), 3.37 (d, <i>J</i> 8 Hz, 2 H, CH ₂), 4.9—5.3 (m, 2 H, CH=), 7.6—7.75 (m, 2 H, Arom-H), 8.0—8.15 (m, 2 H, Arom-H), and 10.86 (s, 1 H, CO ₂ H)
(8h)	A	C ₃₈ H ₈₂ O ₄ 31—32	82.7 (82.6)	9.9 (9.8)	1.61 (s, 24 H, 8 Me), 1.89 (s, 3 H, Me), 1.9—2.2 (br s, 32 H, 16 CH ₂), 2.20 (s, 3 H, Me), 2.34 (m, 4 H, CH ₂ CH ₂ CO), 3.37 (d, <i>J</i> 8 Hz, 2 H, CH ₂), 4.9—5.3 (m, 9 H, 9 CH=), 7.6—7.75 (m, 2 H, Arom-H), 8.0—8.15 (m, 2 H, Arom-H), and 10.56 (s, 1 H, CO ₂ H)
(10a)	B	C ₁₆ H ₂₂ O ₅	65.3 (65.3)	7.6 (7.5)	1.5—1.8 (m, 3 H, CH ₂ and OH), 1.77 (s, 3 H, Me), 1.9—2.2 (m, 2 H, CH ₂), 2.02 (s, 3 H, Me), 3.22 (d, <i>J</i> 8 Hz, 2 H, CH ₂), 3.63 (m, 2 H, CH ₂ O), 4.01 (s, 6 H, 2 OMe), and 4.9—5.2 (m, 1 H, CH=)
(10c)	C	C ₂₆ H ₃₈ O ₅	72.6 (72.5)	8.8 (8.9)	1.4—1.7 (m, 3 H, CH ₂ and OH), 1.56 (s, 3 H, Me), 1.58 (s, 3 H, Me), 1.72 (s, 3 H, Me), 1.8—2.2 (m, 10 H, 5 CH ₂), 2.00 (s, 3 H, Me), 3.16 (d, <i>J</i> 8 Hz, 2 H, CH ₂), 3.59 (m, 2 H, CH ₂ O), 3.97 (s, 6 H, 2 OMe), and 4.8—5.2 (m, 3 H, 3CH=)
(10d)	B	C ₂₁ H ₃₀ O ₃	76.3 (76.3)	9.1 (9.2)	1.5—1.8 (m, 3 H, CH ₂ and OH), 1.57 (s, 3 H, Me), 1.72 (s, 3 H, Me), 1.9—2.2 (m, 6 H, 3 CH ₂), 2.00 (s, 9 H, 3 Me), 3.18 (d, <i>J</i> 8 Hz, 2 H, CH ₂), 3.57 (m, 2 H, CH ₂ O), and 4.8—5.2 (m, 2 H, 2 CH=)
(10e)	A	C ₂₃ H ₂₈ O ₃ 40	78.6 (78.4)	7.7 (8.0)	1.55 (s, 3 H, Me), 1.6—1.8 (m, 3 H, CH ₂ and OH), 1.77 (s, 3 H, Me), 1.9—2.2 (m, 6 H, 3 CH ₂), 2.17 (s, 3 H, Me), 3.55 (d, <i>J</i> 8 Hz, 2 H, CH ₂), 3.53 (m, 2 H, CH ₂ O), 5.00 (m, 2 H, 2 CH=), 7.5—8.2 (m, 4 H, Arom-H)
(10f)	A	C ₂₈ H ₃₆ O ₃	80.4 (80.0)	8.8 (8.6)	1.53 (s, 6 H, 2Me), 1.77 (s, 3 H, Me), 1.6—1.8 (m, 3 H, CH ₂ and OH), 1.9—2.2 (m, 10 H, 5 CH ₂), 2.17 (s, 3 H, Me), 3.35 (d, <i>J</i> 8 Hz, 2 H, CH ₂), 3.58 (m, 2 H, CH ₂ O), 5.00 (m, 3 H, 3 CH=), 7.5—8.2 (m, 4 H, Arom-H)
(11a)	B	C ₂₂ H ₃₀ O ₅	70.5 (70.6)	8.3 (8.1)	1.57 (s, 3 H, Me), 1.72 (s, 3 H, Me), 2.0—2.5 (m, 8 H, 4 CH ₂), 2.01 (s, 3 H, Me), 2.12 (s, 3 H, COMe), 3.17 (d, <i>J</i> 8 Hz, 2 H, CH ₂), 3.98 (s, 6 H, 2 OMe), 4.92—5.03 (m, 2 H, 2 CH=)
(11b)	A	C ₂₄ H ₂₈ O ₃	78.8 (79.1)	7.6 (7.7)	1.56 (s, 3 H, Me), 1.78 (s, 3 H, Me), 1.9—2.2 (m, 4 H, 2 CH ₂), 2.08 (s, 3 H, COMe), 2.15 (s, 3 H, Me), 2.34 (m, 4 H, CH ₂ CH ₂ CO), 3.23 (d, <i>J</i> 8 Hz, 2 H, CH ₂), 5.00 (m, 2 H, 2 CH=), 7.4—8.2 (m, 4 H, Arom-H)
(11c)	A	C ₂₉ H ₃₆ O ₃	80.2 (80.5)	8.5 (8.4)	1.56 (s, 3 H, Me), 1.62 (s, 3 H, Me), 1.78 (s, 3 H, Me), 1.9—2.2 (m, 8 H, 4 CH ₂), 2.10 (s, 3 H, COMe), 2.16 (s, 3 H, Me), 2.35 (m, 4 H, CH ₂ CH ₂ CO), 3.23 (d, <i>J</i> 8 Hz, 2 H, CH ₂), 5.1 (m, 3 H, 3 CH=), 7.4—8.2 (m, 4 H, Arom-H)

Table 8. Data for the quinone amides (9)

Compd. no.	Method	Formula M.p. (°C)	% Found (Required)			¹ H N.m.r. δ (p.p.m.)
			C	H	N	
(9b)	A	C ₂₁ H ₂₉ NO ₅ 88—89	67.1 (67.2)	7.8 (7.8)	3.7 (3.7)	1.59 (s, 3 H, Me), 1.71 (s, 3 H, Me), 1.9—2.1 (m, 4 H, 2 CH ₂), 2.00 (m, 3 H, Me), 2.27 (m, 4 H, CH ₂ CH ₂ CO), 3.16 (d, <i>J</i> 8 Hz, 2 H, CH ₂), 3.97 (s, 6 H, 2 OMe), 4.9—5.1 (m, 2 H, CH=), and 5.67 (m, 2 H, NH ₂)
(9c)	A	C ₂₄ H ₃₅ NO ₅ 88—89	69.0 (69.0)	8.5 (8.4)	3.5 (3.5)	1.13 (d, <i>J</i> 6 Hz, 6 H, 2 Me), 1.58 (s, 3 H, Me), 1.71 (s, 3 H, Me), 1.9—2.1 (m, 4 H, 2 CH ₂), 2.00 (s, 3 H, Me), 2.22 (m, 4 H, CH ₂ CH ₂ CO), 3.16 (d, <i>J</i> 8 Hz, 2 H, CH ₂), 3.97 (s, 6 H, 2 OMe), 4.01 (m, 1 H, NCH), 4.9—5.1 (m, 2 H, 2 CH=), and 5.41 (m, 1 H, NH)
(9d)	A	C ₅₂ H ₇₄ N ₂ O ₅ 56—58	77.5 (77.4)	9.1 (9.2)	3.6 (3.5)	1.58 (s, 18 H, 6 Me), 1.72 (s, 3 H, Me), 1.9—2.2 (m, 27 H, 12 CH ₂ and Me), 2.32 (m, 4 H, CH ₂ CH ₂ CO), 3.16 (d, <i>J</i> 8 Hz, 2 H, CH ₂), 3.96 (s, 6 H, 2 OMe), 4.43 (s, 2 H, CH ₂), 4.0—5.2 (m, 7 H, 7 CH=), 5.91 (m, 1 H, NH), 7.24 (m, 1 H, Arom-H), 7.61 (m, 1 H, Arom-H), and 8.50 (m, 2 H, Arom-H)
(9e)	A	C ₂₉ H ₃₂ N ₂ O ₃ 113—114	76.3 (76.3)	7.1 (7.1)	6.1 (6.1)	1.56 (s, 3 H, Me), 1.75 (s, 3 H, Me), 1.9—2.2 (m, 4 H, 2 CH ₂), 2.17 (s, 3 H, Me), 2.31 (m, 4 H, CH ₂ CH ₂ CO), 3.35 (d, <i>J</i> 8 Hz, 2 H, CH ₂), 4.43 (s, 2 H, CH ₂), 5.00 (m, 2 H, CH=), 6.35 (m, 1 H, NH), and 7.1—8.9 (m, 8 H, Arom-H)
(9f)	A	C ₃₁ H ₃₅ NO ₃ 108—109	69.3 (79.3)	7.6 (7.5)	3.0 (3.0)	1.55 (s, 3 H, Me), 1.76 (s, 3 H, Me), 1.9—2.2 (m, 4 H, 2 CH ₂), 2.17 (s, 3 H, Me), 2.4—2.8 (m, 8 H, CH ₂ CH ₂ CO and CH ₂ CH ₂ N), 3.35 (d, <i>J</i> 8 Hz, 2 H, CH ₂), 5.00 (m, 2 H, 2 CH=), 6.20 (m, 1 H, NH), 7.21 (s, 5 H, Arom-H), and 7.4—8.1 (m, 4 H, Arom-H)
(9g)	A	C ₂₇ H ₃₄ N ₂ O ₃ 94—97	74.5 (74.6)	7.9 (7.9)	6.5 (6.5)	1.56 (s, 3 H, Me), 1.70 (s, 3 H, Me), 1.98 (s, 9 H, 3 Me), 2.0—2.2 (m, 4 H, 2CH ₂), 2.29 (m, 4 H, CH ₂ CH ₂ CO), 3.16 (d, <i>J</i> 8 Hz, 2 H, CH ₂), 4.42 (s, 2 H, CH ₂), 4.9—5.1 (m, 2 H, CH ₂), 6.42 (m, 1 H, NH), and 7.2—8.6 (m, 4 H, Arom-H)
(9i)	B	C ₂₂ H ₂₅ NO ₆	65.9 (66.2)	6.3 (6.3)	3.2 (3.5)	1.78 (s, 3 H, Me), 1.97 (s, 3 H, Me), 2.38 (m, 4 H, CH ₂ CH ₂ CO), 3.17 (d, <i>J</i> 8 Hz, 2 H, CH ₂), 3.94 (s, 6 H, 2 OMe), 5.05 (m, 1 H, CH=), 6.50 (br s, 1 H, NH), 6.72 (d, <i>J</i> 9 Hz, 2 H, Arom-H), 7.16 (s, 1 H, OH), and 7.32 (d, <i>J</i> 9 Hz, 2 H, Arom-H)

chloride, and dried. After removal of the solvent, the residue was chromatographed on silica gel eluting with IPE-ethyl acetate (9 : 1) to give *all-trans*-6-(10-hydroxy-3,7-dimethyldeca-2,6-dienyl-2,3-dimethoxy-5-methyl-1,4-benzoquinone (10b) 5.87 g, 81%) as an orange coloured oil; δ 1.5—1.8 (m, 3 H, CH₂ and OH), 1.57 (s, 3 H, Me), 1.72 (s, 3 H, Me), 1.9—2.2 (m, 6 H, 3 CH₂), 2.00 (s, 3 H, Me), 3.16 (d, *J* 8 Hz, 2 H, CH₂), 3.57 (m, 2 H, CH₂O), 3.97 (s, 6 H, 2 Me), and 4.8—5.2 (m, 2 H, 2 CH=) (Found: C, 69.7; H, 8.3. C₂₁H₃₀O₅ requires C, 69.6; H, 8.3%).

Method C. A solution of 6-(29-ethoxycarbonyl-3,7,11,15,19,23,27-heptamethylnonacosyl-2,6,10,14,18,22,26-heptenyl-2,3-dimethoxy-1,4-bis(methoxymethoxy)-5-methylbenzene (4j) (0.83 g, 1.0 mmol) in THF (10 ml) was hydrolysed with 1M aqueous sodium hydroxide (1.4 ml) at 50 °C for 3 h with stirring. After cooling, the solution was concentrated under reduced pressure and the residue was acidified with dilute hydrochloric acid. The resulting product, isolated in the usual manner, in 1,2-dimethoxyethane (10 ml) was treated with 2M aqueous sulphuric acid (1.0 ml) at 70 °C under nitrogen with stirring for 2 h. The reaction mixture was cooled, and an excess of 10% aqueous ferric chloride solution (2 ml) was added. The reaction was stirred for 30 min, the organic solvent

was removed under reduced pressure and the product was isolated by addition of IPE (20 ml) and water (10 ml). The organic layer was washed with water, dried, and evaporated under reduced pressure to dryness. The residue was chromatographed on silica gel, eluting with IPE, to give *all-trans*-2,3-dimethoxy-5-methyl-6-(29-carboxy-3,7,11,15,19,23,27-heptamethylnonacosyl-2,6,10,14,18,22,26-heptenyl)-2,3-dimethoxy-5-methyl-1,4-benzoquinone (8d), as orange needles (from hexane), m.p. 32—34 °C; δ 1.61 (s, 18 H, 6 Me), 1.76 (s, 3 H, Me), 2.2 (m, 27 H, 12 CH₂ and Me), 2.34 (m, 4 H, CH₂CH₂CO), 3.18 (d, *J* 8 Hz, 2 H, CH₂), 3.97 (s, 3 H, OMe), 3.99 (s, 3 H, OMe), 4.9—5.3 (m, 7 H, 7 CH=), and 10.22 (s, 1 H, CO₂H) (Found: C, 77.3; H, 9.7. C₄₆H₆₈O₆ requires C, 77.1; H, 9.6%).

Table 7 lists the other quinone derivatives prepared as above by method A, B or C.

Preparation of Quinone Amides (9a—g).—**Method A.** To a stirred mixture of *all-trans*-3-(13-carboxy-3,7,11-trimethyltrideca-2,6,10-trienyl)-2-methyl-1,4-naphthoquinone (8g) (1.5 g, 3.5 mmol) and *N*-hydroxysuccinimide (480 mg, 4.2 mmol) in dichloromethane (10 ml) at 0 °C was added *N,N'*-dicyclohexylcarbodi-imide (860 mg). The reaction mixture was stirred for 1.5 h under the same conditions, and 30% ammonia

water (0.58 ml) was then added to the stirred solution. The reaction was allowed to continue for 1 h. Dicyclohexylurea deposited during the reaction was filtered off. The filtrate was evaporated under reduced pressure to dryness. The residue was chromatographed on silica gel eluting with IPE-ethyl acetate (1 : 1) to give 3-(13-aminocarbonyl-3,7,11-trimethyltrideca-2,6,10-trienyl)-2-methyl-1,4-naphthoquinone (9a) (1.2 g, 80%) as yellow needles (from ethyl acetate), m.p. 90–91 °C; δ 1.55 (s, 6 H, 2 Me), 1.78 (s, 3 H, Me), 2.17 (s, 3 H, Me), 3.35 (d, J 8 Hz, 2 H, CH₂), 5.05 (m, 3 H, 5 CH=), 5.55 (m, 2 H, NH₂), and 7.5–8.2 (m, 4 H, Arom-H) (Found: C, 77.5; H, 8.1; N, 3.2. C₂₈H₃₅NO₃ requires C, 77.3; H, 8.1; N, 3.5%).

Method B. To a solution of all-*trans*-6-(9-carboxy-3,7-dimethylnona-2,6-dienyl)-2,3-dimethoxy-5-methyl-1,4-benzoquinone (8b) (1.50 g, 40 mmol) and ethyl chloroformate (0.43 g, 4.0 mmol) in dry THF (15 ml) was added a solution of triethylamine (0.56 ml, 4.0 mmol) in dry THF at –5 °C with stirring under nitrogen. After 5 min, a solution of *p*-aminophenol (0.44 g, 4.0 mmol) in dimethylformamide (10 ml) was added and the reaction mixture was stirred for 1 h. When the reaction was complete, the solvent was concentrated under reduced pressure. The product was isolated in the usual manner and was chromatographed on silica gel, using IPE-ethyl acetate (1 : 1) as eluant, to give all-*trans*-6-(9-*p*-hydroxyphenylaminocarbonyl-2,3-dimethylnona-2,6-dienyl)-2,3-dimethoxy-5-methyl-1,4-benzoquinone (9h) (1.42 g, 76%) as orange needles from IPE-ethyl acetate (4 : 1), m.p. 67–69 °C; δ 1.60 (s, 3 H, Me), 1.70 (s, 3 H, Me), 1.9–2.2 (m, 4 H, 2 CH₂), 2.00 (s, 3 H, Me), 2.36 (m, 4 H, CH₂CH₂CO), 3.16 (d, 2 H, J 8 Hz, CH₂), 3.94 (s, 6 H, 2 OMe), 4.87–5.1 (m, 2 H, 2 CH=), 6.53 (m, 1 H, NH), and 6.73–7.90 (m, 5 H, Arom-H) (Found: C, 69.2; H, 7.0; N, 2.8. C₂₇H₃₃NO₆ requires C, 69.4; H, 7.1; N, 3.0%).

Table 8 lists the other quinone amides prepared as above by method A or B from the corresponding quinone carboxylic acids.

Bioassay.—Guinea pig (Hartley strain, female and male, body weight 300–350 g) were sensitised with egg albumin as an antigen according to the method of Orange *et al.*^{14a} The amount of SRS-A generated by immunological reaction in the lung fragments of sensitised guinea pigs was assayed using the guinea pig ileum preparations by the method of Brocklehurst.^{14b} The quinone compounds tested were added simultaneously with antigen.

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