

The Revised Structure of Dispermol and Total Synthesis of Maytenoquinone, Dispermol, and Dispermone

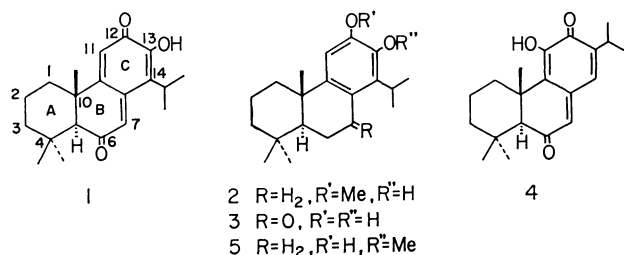
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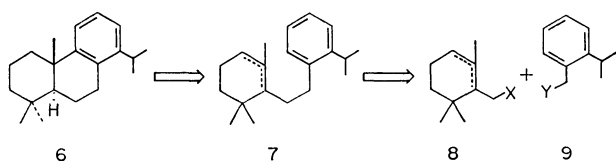
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Condensation of β -cyclocitral with 2-isopropyl-3,4-dimethoxybenzyl chloride afforded an alcohol (**15**) which was converted into ($\pm$)-12,13-dimethoxytotara-8,11,13-trien-6-one (**18**). Demethylation of ($\pm$)-**18** followed by air oxidation gave ($\pm$)-maytenoquinone. Reductive cleavage of the hydroxyl group in ($\pm$)-**15** produced a phenethyl derivative which was cyclized to give ($\pm$)-12,13-dimethoxytotara-8,11,13-triene (**23**) and its *cis*-isomer (**24**). Oxidation of ($\pm$)-**23** with chromium trioxide, followed by demethylation of the resulting 7-oxo compound (**25**), afforded ($\pm$)-dispermone. The Wittig reaction of (*R*)-(-)- α -cyclocitral with 2-isopropyl-3,4-dimethoxybenzyltriphenylphosphonium chloride yielded a styrene derivative. This was partially hydrogenated and then cyclized to give (+)-**23** and (-)-**24**. The *trans*-isomer (**23**) was converted into (-)-dispermone (**3**) via (-)-**25** and also partially demethylated to (+)-12-methoxytotara-8,11,13-trien-13-ol (**2**), the proposed structure for dispermol. Since the synthetic (+)-**2** was not identical with the natural compound, (-)-**3** was then converted into (+)-13-methoxytotara-8,11,13-trien-12-ol, which was identical with natural dispermol. (-)-**25** was also converted into (+)-maytenoquinone.

Recently, three new tricyclic diterpenes possessing a totarane skeleton, maytenoquinone, dispermol, and dispermone, have been isolated from *Maytenus dispermus* by Martin.¹⁾ Their structures were deduced to be **1**, **2**, and **3**, on the basis of chemical and spectroscopic studies. Among these natural diterpenes, maytenoquinone (**1**) is especially of interest, because it has a unique quinone-methide chromophore, such as that in taxodione (**4**)²⁻⁵⁾ which has shown a significant tumor-inhibiting activity. In connection with our synthetic studies on natural diterpenes, we attempted the syntheses of these natural compounds to confirm the proposed structures and to elaborate a new synthetic route for the tricyclic diterpenes with an aromatic C ring. This paper⁶⁾ describes the revision of the structure of dispermol and the total syntheses of maytenoquinone (**1**), dispermol (**5**), and dispermone (**3**) by the new route.



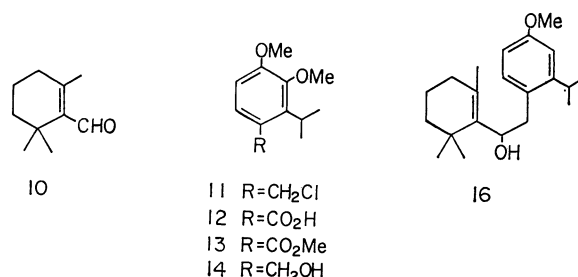
Our basic strategy for the synthesis of totara-8,11,13-triene skeleton (**6**) is shown in Scheme 1. That is, two C₁₀ units (**8** and **9**), including A and C rings of natural compounds, were first condensed to give a C₂₀ unit (**7**) and this, by intramolecular cyclization, was converted into an octahydrophenanthrene derivative (**6**) which was then transformed into the natural compounds.

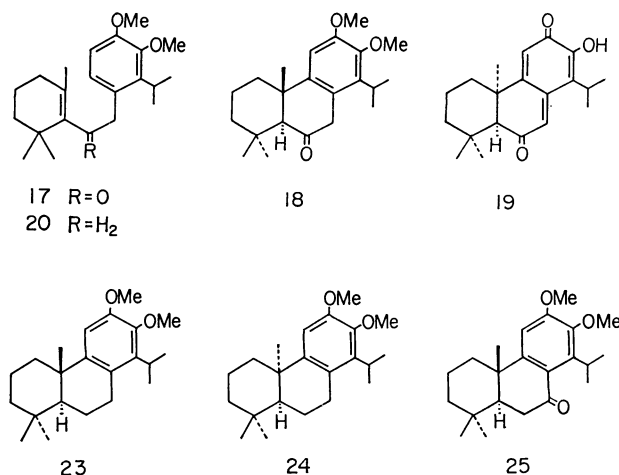


Scheme 1.

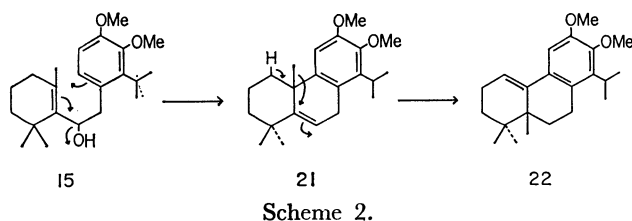
Syntheses of ($\pm$)-Maytenoquinone (**1**) and ($\pm$)-Dispermone (**3**).

β -Cyclocitral (**10**)^{7,8)} and 2-isopropyl-3,4-dimethoxybenzyl chloride (**11**),⁹⁾ prepared from 2-isopropyl-3,4-dimethoxybenzoic acid (**12**)⁹⁾ via three steps, were chosen as the starting materials. Condensation of **10** with **11** in the presence of lithium naphthalenide afforded the desired alcohol (**15**), together with a small amount of a demethoxylated alcohol (**16**). The alcohol (**15**) was oxidized with chromium trioxide-pyridine complex to yield the corresponding α,β -unsaturated ketone (**17**), which was then submitted to intramolecular cyclization with anhydrous aluminium chloride in refluxing toluene. Because of the formation of a phenolic by-product, the crude product was immediately methylated with methyl iodide and anhydrous potassium carbonate in refluxing methyl ethyl ketone to give ($\pm$)-12,13-dimethoxytotara-8,11,13-trien-6-one (**18**). Demethylation of ($\pm$)-**18** with boron tribromide in dichloromethane afforded ($\pm$)-13-hydroxytotara-7,9(11),13-triene-6,12-dione (**1**), whose spectral data were identical with those of natural maytenoquinone. On the other hand, the demethylation of ($\pm$)-**18** with hydrobromic acid in refluxing acetic acid yielded ($\pm$)-*cis*-maytenoquinone (**19**).¹⁰⁾ The *cis*-configuration of the A/B ring junction in ($\pm$)-**19** was supported by its NMR spectrum, which showed a signal due to one of the *gem*-dimethyl groups at the C-4 position in very high field (δ 0.62 ppm) owing to the shielding effect of the C ring.¹¹⁾





Our next effort was directed toward the syntheses of $(\pm)$ -**2** and $(\pm)$ -**3**. For reductive cleavage of the hydroxyl group, the alcohol (**15**) was treated at room temperature with dichloroaluminum hydride¹² in dry ether. Since the crude product contained a significant amount of diene compounds, it was hydrogenated over Pd-C in acetic acid to give the desired phenethyl derivative (**20**). In contrast to this result, when triethylsilane¹³ was used at 0 °C in the presence of boron trifluoride etherate, the alcohol (**15**) was smoothly converted into **20** together with a small amount of $(\pm)$ -12,13-dimethoxytotara-5,8,11,13-tetraene (**21**). The tetraene $(\pm)$ -**21** was also obtained in moderate yield by treatment of $(\pm)$ -**15** with boron trifluoride etherate at 0 °C. However, when the reaction of $(\pm)$ -**15** with boron trifluoride etherate was carried out at room temperature, a rearranged product (**22**) was produced. This compound was also obtained by the similar treatment of $(\pm)$ -**21**. Therefore, it is suggested that this rearrangement proceeded through the intermediate $(\pm)$ -**21**. The NMR spectrum of $(\pm)$ -**22** showed signals of an aromatic proton (δ 6.85), two methoxyl groups (δ 3.77 and 3.80), and an isopropyl group [δ 1.28 ppm (d, $J=7$ Hz)], suggesting the retention of the aromatic C ring. The compound, $(\pm)$ -**22**, also showed a signal at δ 6.00 ppm (t, $J=4$ Hz) due to a vinylic proton attached to a trisubstituted double bond and signals at δ 0.90 (3H) and 0.93 ppm (6H) due to three tertiary methyl groups. The appearance of three tertiary methyl signals in the higher field, and of vinylic and aromatic protons in the lower field, than those in $(\pm)$ -**21** suggested that the angular methyl group at the C-10 position rearranged to the C-5 position, resulting in the formation of a new trisubstituted double bond, as in Scheme 2. Thus, the structure



of $(\pm)$ -**22** was tentatively assigned as 12,13-dimethoxy-5-methyl-10-nortotara-1(10),8,11,13-tetraene. Intra-

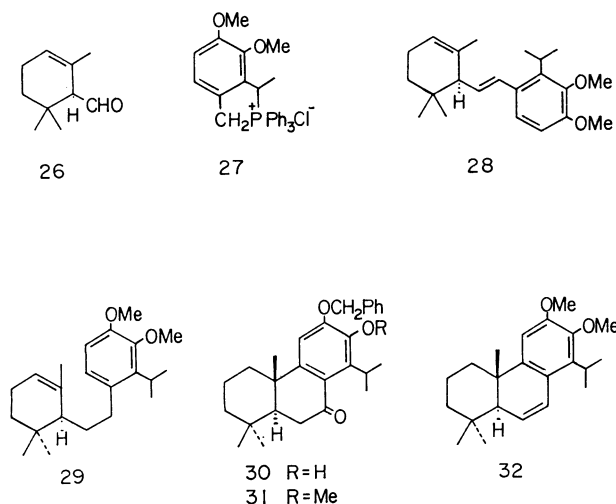
molecular cyclization of **20** with boron trifluoride etherate in dichloromethane afforded $(\pm)$ -12,13-dimethoxytotara-8,11,13-triene (**23**) as a major product and its *cis*-isomer (**24**) as a minor one. When the cyclization was carried out with anhydrous aluminium chloride in refluxing benzene, **20** gave $(\pm)$ -12-methoxytotara-8,11,13-trien-13-ol (**2**) in addition to the dimethoxy compounds, $(\pm)$ -**23** and $(\pm)$ -**24**. The phenol $(\pm)$ -**2** was also obtained by partial demethylation of $(\pm)$ -**23** with anhydrous aluminium chloride under similar conditions, and the methylation of $(\pm)$ -**2** with methyl iodide and anhydrous potassium carbonate yielded $(\pm)$ -**23**. The presence of a phenolic hydroxyl group at the C-13 position in $(\pm)$ -**2** was supported by pyridine-induced solvent shifts¹⁴ of the C-16 and C-17 methyls ($\Delta=-0.28$ ppm) and an aromatic proton ($\Delta=-0.12$ ppm) in its NMR spectrum, which was different from that of natural dispermol. This was further confirmed by the synthesis of optically active $(+)$ -**2**, which is described later. Thus, the proposed structure (**2**) for dispermol should now be revised. Since the conversion of the optically active tetraene (**21**) into the trienes (**23** and **24**) by catalytic hydrogenation had already been reported,¹ $(\pm)$ -**21** was also a useful intermediate for the present synthesis. The dimethyl ether $(\pm)$ -**23** was oxidized with chromium trioxide in acetic acid to give the corresponding 7-oxo compound (**25**) and this was then demethylated with boron tribromide in dichloromethane to afford $(\pm)$ -12,13-dihydroxytotara-8,11,13-trien-7-one (**3**), whose spectral data were identical with those of natural dispermone.

*Syntheses of $(+)$ -Maytenoquinone (**1**), $(+)$ -Dispermol (**5**), and $(-)$ -Dispermane (**3**).* Subsequently, our attention was directed toward the total syntheses of the optically active natural maytenoquinone, dispermol, and dispermane. The starting materials chosen for these syntheses were (R) - $(-)$ - α -cyclocitral (**26**)^{15,16} and 2-isopropyl-3,4-dimethoxybenzyltriphenylphosphonium chloride (**27**), which was prepared from **11** and triphenylphosphine in refluxing benzene. The Wittig reaction of $(-)$ -**26** with **27** in dry hexane in the presence of *n*-butyllithium gave the desired styrene derivative (**28**). In the NMR spectrum of $(-)$ -**28** the vicinal coupling constant ($J=15$ Hz) of vinylic protons suggested the presence of a *trans* disubstituted double bond. Partial hydrogenation of $(-)$ -**28** in ethanol over Pd-C afforded a phenethyl derivative (**29**), which was submitted to the intramolecular cyclization using anhydrous aluminium chloride in benzene. The crude product was then purified by column chromatography on silica gel to give $(+)$ -**23**, $[\alpha]_D +50.2^\circ$, along with $(-)$ -**24**. The conversion of $(+)$ -**23** into $(-)$ -dispermane (**3**) *via* the 7-oxo compound (**25**) was achieved by a method similar to that for the racemate.

$(+)$ -**23** was partially demethylated to give $(+)$ -**2**, mp 87–88.5 °C. The melting point of the synthetic $(+)$ -**2** was quite different from that of natural dispermol (mp 164–166 °C). From the comparison of the NMR spectra of $(+)$ -**2** and dispermol, the structure of natural product is expected to be 13-methoxytotara-8,11,13-trien-12-ol (**5**); this was successfully synthesized in the following manner. Partial benzylation of $(-)$ -**3** with benzyl chloride in the presence of potassium iodide

and anhydrous potassium carbonate produced the corresponding 12-benzyl ether (**30**). The presence of a phenolic hydroxyl group at the C-13 position in (–)-**30** was supported by the solvent shifts¹⁴ of the C-16 and C-17 methyls ($\Delta = -0.42$ ppm)¹⁷ in its NMR spectrum. Methylation of (–)-**30** with methyl iodide and anhydrous potassium carbonate gave the 13-methyl ether (**31**) which, on hydrogenolysis over PtO₂ in ethanol containing a small amount of perchloric acid, afforded (+)-**5**, mp 166.5–167.5 °C, whose physical and spectral data were identical with those of natural dispermol. Thus, the structure of dispermol could be determined to be **5**.

(+)-Maytenoquinone (**1**) was synthesized as follows. The 7-oxo compound (–)-**25** was reduced with lithium aluminium hydride in dry ether and the resulting mixture of epimeric alcohols was dehydrated with dilute hydrochloric acid to give (–)-12,13-dimethoxytota-6,8,11,13-tetraene (**32**). Oxidation of (–)-**32** with *m*-chloroperbenzoic acid in dichloromethane, followed by treatment with dilute hydrochloric acid in refluxing methanol, gave (+)-**18** which, on demethylation with boron tribromide in dichloromethane and subsequent oxidation with silver oxide in refluxing chloroform, afforded (+)-maytenoquinone (**1**).



Experimental

All melting points are uncorrected. The IR spectra and optical rotations were measured in chloroform, and the NMR spectra in carbon tetrachloride at 60 MHz, with tetramethylsilane as an internal standard, unless otherwise stated. The chemical shifts are presented in terms of δ values; s: singlet, bs: broad singlet, d: doublet, bd: broad doublet, dd: double doublet, t: triplet, m: multiplet. Column chromatography was performed using Merck silica gel (0.063 mm).

Methyl 2-Isopropyl-3,4-dimethoxybenzoate (13). 2-Isopropyl-3,4-dimethoxybenzoic acid (**12**)⁹ was methylated with diazomethane in ether to give **13**, IR: 1710 cm⁻¹; NMR: 1.31 (6H, d, $J=7$ Hz, $-\text{CH}(\text{CH}_3)_2$), 3.80 (6H, s) and 3.83 (3H, s) (2-OCH₃ and $-\text{CO}_2\text{CH}_3$), 6.61 and 7.24 (each 1H, d, and $J=9$ Hz, aromatic protons).

2-Isopropyl-3,4-dimethoxybenzyl Alcohol (14). A solution of **13** (38.34 g) in dry ether (40 ml) was added to a stirred suspension of lithium aluminium hydride (6.11 g)

in dry ether (150 ml) with cooling in an ice-water bath. The mixture was then refluxed for 2 h, cooled, poured into a mixture of ice and dilute hydrochloric acid, and extracted with ether. The ether extract was washed with brine, dried over sodium sulfate, and evaporated *in vacuo* to give **14** (33.21 g: 98%); IR: 3600, 3400 cm⁻¹; NMR: 1.29 (6H, d, $J=7$ Hz, $-\text{CH}(\text{CH}_3)_2$), 1.87 (1H, s, $-\text{OH}$), 3.23 (1H, m, $-\text{CH}(\text{CH}_3)_2$), 3.77 (6H, s, 2-OCH₃), 4.43 (2H, s, $-\text{CH}_2\text{OH}$), 6.55 and 6.83 (each 1H, d, and $J=9$ Hz, aromatic protons).

2-Isopropyl-3,4-dimethoxybenzyl Chloride (11). A solution of thionyl chloride (17 ml) in dry ether (10 ml) was added at 5 °C to a stirred solution of **14** (33.21 g) in dry ether (40 ml) over a 30 min period. The solution was further stirred at room temperature for 1 h, diluted with dry benzene, and then evaporated *in vacuo* to give **11** (35.00 g: 97%); NMR: 1.35 (6H, d, $J=7$ Hz, $-\text{CH}(\text{CH}_3)_2$), 3.23 (1H, m, $-\text{CH}(\text{CH}_3)_2$), 3.81 (6H, s, 2-OCH₃), 4.51 (2H, s, $-\text{CH}_2\text{Cl}$), 6.57 and 6.83 (each 1H, d, and $J=8$ Hz, aromatic protons).

Condensation of β -Cyclocitral (10) and 2-Isopropyl-3,4-dimethoxybenzyl Chloride (11). A mixture of naphthalene (4.00 g) and small pieces of lithium (247 mg) in dry tetrahydrofuran (20 ml) was stirred at room temperature for 1 h in a stream of nitrogen. Into the above mixture a solution of β -cyclocitral^{7,8} (1.36 g) and 2-isopropyl-3,4-dimethoxybenzyl chloride (2.250 g) in dry tetrahydrofuran (10 ml) was added at 0–5 °C over a 45 min period. The mixture was further stirred at 0–5 °C for 2 h in a stream of nitrogen diluted with ether, poured into dilute hydrochloric acid, and extracted with ether. The ether extract was washed with brine, dried over sodium sulfate, and evaporated *in vacuo*. The residue was chromatographed on silica gel (400 g) using ether–benzene (1 : 99) as the eluent to give phenolic fractions (463 mg). Further elution with ether–benzene (1 : 99 and then 3 : 97) gave an oily alcohol (**15**) (1.496 g: 48%) which was crystallized from hexane: mp 72–72.5 °C; IR: 3560 cm⁻¹; NMR: 0.94 and 1.08 (each 3H and s, $-\text{C}(\text{CH}_3)_2$), 1.32 (6H, d, $J=7$ Hz, $-\text{CH}(\text{CH}_3)_2$), 1.89 (3H, s, $=\text{CCH}_3$), 3.23 (1H, m, $-\text{CH}(\text{CH}_3)_2$), 3.77 and 3.79 (each 3H and s, 2-OCH₃), 4.24 (1H, dd, $J=4$ and 9 Hz, $-\text{CHOH}$), 6.60 and 6.72 (each 1H, d, and $J=9$ Hz, aromatic protons). Found: C, 76.41; H, 9.86%. Calcd for C₂₂H₃₄O₃: C, 76.26; H, 9.89%.

The above phenolic fractions (463 mg) were combined and methylated for 6 h with methyl iodide (1.0 ml) and anhydrous potassium carbonate (3.0 g) in refluxing methyl ethyl ketone (10 ml). The mixture was filtered and the filtrate was evaporated *in vacuo*. The residue was dissolved in ether, washed with brine, dried over sodium sulfate, and then evaporated to give a crude product which was purified by column chromatography on silica gel (50 g) using benzene as the eluent to yield a demethoxylated alcohol (**16**) (227 mg: 8%); IR: 3560 cm⁻¹; NMR: 0.95 and 1.09 (each 3H and s, $-\text{C}(\text{CH}_3)_2$), 1.22 and 1.24 (each 3H, d, and $J=7$ Hz, $-\text{CH}(\text{CH}_3)_2$), 1.90 (3H, s, $=\text{CCH}_3$), 3.73 (3H, s, $-\text{OCH}_3$), 4.30 (1H, dd, $J=4$ and 9 Hz, $-\text{CHOH}$), 6.57 (1H, dd, $J=2$ and 8 Hz), 6.68 (1H, d, $J=2$ Hz), and 6.98 (1H, d, $J=8$ Hz) (aromatic protons). Further elution gave an additional alcohol (**15**) (168 mg: 5%).

2,6,6-Trimethyl-1-cyclohexenyl 2-Isopropyl-3,4-dimethoxybenzyl Ketone (17). A solution of ($\pm$)-**15** (1.500 g) in pyridine (3.0 ml) was added at 5–10 °C to a stirred chromium trioxide–pyridine complex prepared from chromium trioxide (2.17 g) and pyridine (30 ml). The mixture was stirred at 5–10 °C for 2 h, poured into a mixture of ice

and dilute hydrochloric acid, and filtered. The filtrate was extracted with ether and the extract was washed with brine, dried over sodium sulfate, and then evaporated *in vacuo*. The residue was chromatographed on silica gel (150 g) using benzene as the eluent to give an α,β -unsaturated ketone (**17**) (200 mg: 13%) which was recrystallized from hexane: mp 81–82.5 °C; IR: 1690 cm^{-1} ; NMR: 1.07 (6H, s, $-\dot{\text{C}}(\text{CH}_3)_2$), 1.30 (6H, d, $J=7$ Hz, $-\text{CH}(\text{CH}_3)_2$), 1.60 (3H, s, $=\dot{\text{C}}\text{CH}_3$), 3.73 (2H, s, $-\text{COCH}_2-$), 3.82 and 3.84 (each 3H and s, 2-OCH₃), 6.58 (2H, s, aromatic protons). Found: C, 76.88; H, 9.53%. Calcd for $\text{C}_{22}\text{H}_{32}\text{O}_3$: C, 76.70; H, 9.36%. Further elution with ether–benzene (1:99) afforded the starting alcohol (**15**) (1.020 g: 68%).

($\pm$)-12,13-Dimethoxytotara-8,11,13-trien-6-one (**18**). A mixture of **17** (93 mg) and anhydrous aluminium chloride (72 mg) in dry toluene (10 ml) was refluxed for 6 h. The mixture was diluted with ether, washed successively with dilute hydrochloric acid and water, dried over sodium sulfate, and then evaporated *in vacuo* to give a crude product, whose IR spectrum showed a band at 3540 cm^{-1} due to a phenolic hydroxyl group.

The above crude product was refluxed for 6 h with methyl iodide (0.5 ml) and anhydrous potassium carbonate (3.0 g) in methyl ethyl ketone (5.0 ml). After the usual work-up, the product was purified by column chromatography on silica gel (10 g) using hexane–benzene (1:4) as the eluent to give ($\pm$)-**18** (49 mg: 53%) which was recrystallized from hexane: mp 144–145 °C; IR: 1710 cm^{-1} ; NMR: 1.05 and 1.12 (each 3H and s, $-\dot{\text{C}}(\text{CH}_3)_2$), 1.29 (3H, s, $\text{C}_{10}-\text{CH}_3$), 1.29 (6H, d, $J=7$ Hz, $-\text{CH}(\text{CH}_3)_2$), 2.35 (1H, s, C_5-H), 3.06 (1H, m, $-\text{CH}(\text{CH}_3)_2$), 3.41 (2H, d, $J=5$ Hz, $-\text{COCH}_2-$), 3.78 and 3.80 (each 3H and s, 2-OCH₃), 6.66 (1H, s, $\text{C}_{11}-\text{H}$). Found: C, 76.69; H, 9.33%. Calcd for $\text{C}_{22}\text{H}_{32}\text{O}_3$: C, 76.70; H, 9.36%. Further elution with benzene gave the starting ketone **17** (29 mg: 31%).

($\pm$)-Maytenoquinone (**1**). A mixture of ($\pm$)-**18** (100 mg) and boron tribromide (1.0 g) in dichloromethane (10 ml) was stirred at 0–5 °C for 1 h and then at room temperature for 30 min. The mixture was poured into ice–water, extracted with ether, and the extract was washed successively with aqueous sodium thiosulfate and brine. The dried solution was evaporated to dryness. The residue was purified by repeated column chromatography on silica gel using hexane–benzene (1:1) as the eluent and then recrystallized from hexane to give ($\pm$)-maytenoquinone (**1**) (63 mg: 69%), mp 173–174 °C; IR: 3370, 1660, 1630 cm^{-1} ; NMR (CDCl_3): 1.17 and 1.26 (each 3H and s, $-\dot{\text{C}}(\text{CH}_3)_2$), 1.26 (3H, s, $\text{C}_{10}-\text{CH}_3$), 1.31 and 1.37 (each 3H, d, and $J=7$ Hz, $-\text{CH}(\text{CH}_3)_2$), 2.48 (1H, s, C_5-H), 3.06 (1H, m, $-\text{CH}(\text{CH}_3)_2$), 6.37 and 6.59 (each 1H, d, and $J=2$ Hz, C_7-H and $\text{C}_{11}-\text{H}$), 7.12 (1H, s, $-\text{OH}$). Found: C, 76.22; H, 8.42%. Calcd for $\text{C}_{20}\text{H}_{26}\text{O}_3$: C, 76.40; H, 8.34%.

($\pm$)-cis-Maytenoquinone (**19**). A mixture of ($\pm$)-**18** (44.2 mg) and 47% hydrobromic acid (2.0 ml) in acetic acid (10 ml) was refluxed for 2.5 h and then evaporated *in vacuo*. The residue was extracted with ether and the extract was washed successively with aqueous sodium hydrogen-carbonate and water, dried over sodium sulfate, and then evaporated. The crude product was purified by column chromatography on silica gel (10 g) using ether–benzene (1:99) to give ($\pm$)-**19** (33.9 mg: 82%) which was recrystallized from hexane: mp 184–187 °C (sintered at ca. 160 °C); IR: 3370, 1650, 1630 cm^{-1} ; NMR (CDCl_3): 0.62 and 0.97 (each 3H and s, $-\dot{\text{C}}(\text{CH}_3)_2$), 1.18 (3H, s, $\text{C}_{10}-\text{CH}_3$), 1.31 and 1.37 (each 3H, d, and $J=7$ Hz, $-\text{CH}(\text{CH}_3)_2$), 2.26 (1H, s, C_5-H), 6.45 and 6.64 (each 1H, d, and $J=2$ Hz,

C_7-H and $\text{C}_{11}-\text{H}$), 7.23 (1H, s, $-\text{OH}$). Found: C, 76.68; H, 8.61%. Calcd for $\text{C}_{20}\text{H}_{26}\text{O}_3$: C, 76.40; H, 8.34%.

Reductive Cleavage of a Hydroxyl Group in the Alcohol (15). With Triethylsilane in the Presence of Boron Trifluoride Etherate: A solution of boron trifluoride etherate (3.34 ml) in dichloromethane (5.0 ml) was added at $-10-0$ °C to a stirred solution of ($\pm$)-**15** (1.830 g) and triethylsilane (1.230 g) in dichloromethane (50 ml). The mixture was further stirred at this temperature for 1 h, diluted with ether, and then washed with water. The dried solution was evaporated *in vacuo* and the residue was chromatographed on silica gel (100 g) using hexane–benzene (7:3) as the eluent to give 2-(2,6,6-trimethyl-1-cyclohexenyl)-1-(2-isopropyl-3,4-dimethoxyphenyl)ethane (**20**) (1.560 g: 89%); NMR: 1.04 (6H, s, $-\dot{\text{C}}(\text{CH}_3)_2$), 1.34 (6H, d, $J=7$ Hz, $-\text{CH}(\text{CH}_3)_2$), 1.68 (3H, s, $=\dot{\text{C}}\text{CH}_3$), 3.18 (1H, m, $-\text{CH}(\text{CH}_3)_2$), 3.78 and 3.80 (each 3H and s, 2-OCH₃), 6.56 and 6.74 (each 1H, d, and $J=8$ Hz, aromatic protons). Found: C, 80.15; H, 10.53%. Calcd for $\text{C}_{22}\text{H}_{34}\text{O}_2$: C, 79.95; H, 10.37%. Further elution with hexane–benzene (1:1) afforded ($\pm$)-12,13-dimethoxytotara-5,8,11,13-tetraene (**21**) (132 mg: 8%); NMR: 1.16 and 1.22 (each 3H and s, $-\dot{\text{C}}(\text{CH}_3)_2$), 1.26 (3H, s, $\text{C}_{10}-\text{CH}_3$), 1.27 and 1.32 (each 3H, d, and $J=7$ Hz, $-\text{CH}(\text{CH}_3)_2$), 3.78 (6H, s, 2-OCH₃), 5.83 (1H, dd, $J=2.5$ and 5.5 Hz, C_6-H), 6.68 (1H, s, $\text{C}_{11}-\text{H}$). Found: C, 80.67; H, 9.94%. Calcd for $\text{C}_{22}\text{H}_{32}\text{O}_2$: C, 80.44; H, 9.83%.

With Dichloroaluminium Hydride: Lithium aluminium hydride (33 mg) was added to a solution of anhydrous aluminium chloride (345 mg) in dry ether (20 ml), and the mixture was stirred at room temperature for 1 h. To the above solution was added dropwise a solution of ($\pm$)-**15** (150 mg) in dry ether (4.0 ml). The mixture was further stirred at room temperature for 1 h, poured into a mixture of ice and dilute hydrochloric acid, and extracted with ether. The ether extract was washed with brine, dried over sodium sulfate, and evaporated *in vacuo*. The residue was chromatographed on silica gel (16 g) using hexane–benzene (4:1) as the eluent to give an oil (121 mg: 86%), which was hydrogenated at room temperature for 6 h with 5% Pd–C (130 mg) in acetic acid (10 ml) in an atmosphere of hydrogen. After the usual work-up, the crude product was purified by column chromatography on silica gel (15 g) using hexane–benzene (4:1) as the eluent to afford **20** (85 mg: 60%).

($\pm$)-12,13-Dimethoxytotara-5,8,11,13-tetraene (**21**). Boron trifluoride etherate (0.18 ml) was added at $-10-0$ °C to a solution of ($\pm$)-**15** (98 mg) in dichloromethane (10 ml). The mixture was stirred at this temperature for 1 h, poured into water, and extracted with ether. The ether extract was washed with water, dried over sodium sulfate, and then evaporated *in vacuo*. The crude product was purified by column chromatography on silica gel (10 g) to give ($\pm$)-**21** (55 mg: 60%), whose IR and NMR spectra were identical with those of the sample described above.

($\pm$)-12,13-Dimethoxy-5-methyl-10-nortotara-1(10),8,11,13-tetraene (**22**). From the Alcohol (**15**): A solution of ($\pm$)-**15** (75 mg) and boron trifluoride etherate (0.14 ml) in dichloromethane (10 ml) was stirred at room temperature for 2 h, and then poured into water. The mixture was extracted with ether, dried over sodium sulfate, and evaporated *in vacuo*. The crude product was chromatographed on silica gel (10 g) using hexane–benzene (4:1) as the eluent to give ($\pm$)-**22** (33 mg: 45%); NMR: 0.90 (3H, s) and 0.93 (6H, s) ($-\dot{\text{C}}(\text{CH}_3)_2$ and C_5-CH_3), 1.28 (6H, d, $J=7$ Hz, $-\text{CH}(\text{CH}_3)_2$), 3.77 and 3.80 (each 3H and s, 2-OCH₃), 6.00 (1H, t, $J=4$ Hz, C_1-H), 6.85 (1H, s, $\text{C}_{11}-\text{H}$). Found: C, 80.31; H, 9.98%. Calcd for $\text{C}_{22}\text{H}_{32}\text{O}_2$:

C, 80.44; H, 9.83%.

From the Tetraene (21): A solution of ($\pm$)-**21** (105 mg) and boron trifluoride etherate (0.20 ml) in dichloromethane (5.0 ml) was stirred at room temperature for 1 h. After a similar treatment to that described above, the crude product was purified by column chromatography on silica gel to give ($\pm$)-**22** (54 mg).

Intramolecular Cyclization of 20. With Boron Trifluoride Etherate: A solution of **20** (313 mg) and boron trifluoride etherate (0.60 ml) in dichloromethane (5.0 ml) was allowed to stand at room temperature for 13.5 h, and then poured into water. The mixture was extracted with ether and the extract was washed with water, dried over sodium sulfate, and evaporated *in vacuo*. The crude product was purified by column chromatography on silica gel (30 g) using hexane-benzene (4 : 1) as the eluent to give the *cis*-isomer (**24**) (81 mg; 26%); NMR: 0.43 and 0.94 (each 3H and s, $-\dot{\text{C}}(\text{CH}_3)_2$), 1.15 (3H, s, $\text{C}_{10}-\text{CH}_3$), 1.22 and 1.30 (each 3H, d, and $J=7$ Hz, $-\text{CH}(\text{CH}_3)_2$), 3.80 (6H, s, $2-\text{OCH}_3$), 6.66 (1H, s, $\text{C}_{11}-\text{H}$). Found: C, 79.87; H, 10.53%. Calcd for $\text{C}_{22}\text{H}_{34}\text{O}_2$: C, 79.95; H, 10.37%. Further elution gave ($\pm$)-12,13-dimethoxytara-8,11,13-triene (**23**) (222 mg; 71%) which was recrystallized from methanol: mp 133.5–134 °C; NMR: 0.92 and 0.94 (each 3H and s, $-\dot{\text{C}}(\text{CH}_3)_2$), 1.19 (3H, s, $\text{C}_{10}-\text{CH}_3$), 1.26 (6H, d, $J=7$ Hz, $-\text{CH}(\text{CH}_3)_2$), 3.73 (6H, s, $2-\text{OCH}_3$), 6.58 (1H, s, $\text{C}_{11}-\text{H}$). Found: C, 80.22; H, 10.51%. Calcd for $\text{C}_{22}\text{H}_{34}\text{O}_2$: C, 79.95; H, 10.37%.

With Anhydrous Aluminium Chloride: A mixture of **20** (111 mg) and anhydrous aluminium chloride (51 mg) in dry benzene (4.0 ml) was refluxed for 4 h. The mixture was poured into ice-water and extracted with ether. The ether extract was washed with brine, dried over sodium sulfate, and then evaporated *in vacuo*. The crude product was chromatographed on silica gel (10 g) using hexane-benzene (4 : 1) as the eluent to give ($\pm$)-12-methoxytara-8,11,13-trien-13-ol (**2**) (34 mg; 34%), which was recrystallized from hexane: mp 125–126 °C; IR: 3538 cm^{-1} ; NMR (CDCl_3): 0.92 and 0.95 (each 3H and s, $-\dot{\text{C}}(\text{CH}_3)_2$), 1.20 (3H, s, $\text{C}_{10}-\text{CH}_3$), 1.34 (6H, d, $J=7$ Hz, $-\text{CH}(\text{CH}_3)_2$), 3.84 (3H, s, $-\text{OCH}_3$), 5.62 (1H, s, $\text{C}_{13}-\text{OH}$), 6.70 (1H, s, $\text{C}_{11}-\text{H}$).

NMR ($\text{C}_6\text{D}_6\text{N}$): 0.90 and 0.93 (each 3H and s, $-\dot{\text{C}}(\text{CH}_3)_2$), 1.21 (3H, s, $\text{C}_{10}-\text{CH}_3$), 1.61 and 1.63 (each 3H, d, and $J=7$ Hz, $-\text{CH}(\text{CH}_3)_2$), 3.72 (3H, s, $-\text{OCH}_3$), 6.82 (1H, s, $\text{C}_{11}-\text{H}$). Found: C, 79.78; H, 10.38%. Calcd for $\text{C}_{21}\text{H}_{32}\text{O}_2$: C, 79.70; H, 10.19%. Further elution gave ($\pm$)-**24** (11 mg; 9%) and ($\pm$)-**23** (41 mg; 36%).

Partial Demethylation of 23. A mixture of ($\pm$)-**23** (102 mg) and anhydrous aluminium chloride (60 mg) in dry benzene (20 ml) was refluxed for 3 h. After the work-up described above, the crude product was chromatographed on silica gel (10 g) using hexane-benzene (4 : 1) as the eluent to give ($\pm$)-**2** (27 mg; 28%), whose IR and NMR spectra were identical with those of the sample described above. Further elution gave the starting ($\pm$)-**23** (44 mg).

Methylation of 2. A mixture of ($\pm$)-**2** (60 mg), methyl iodide (1.0 ml), and anhydrous potassium carbonate (3.0 g) in methyl ethyl ketone (10 ml) was refluxed for 14 h. After the usual work-up, the product was chromatographed on silica gel (6.0 g) using hexane-benzene (1 : 1) as the eluent to give ($\pm$)-**23** (51 mg; 82%), whose IR and NMR spectra were identical with those of the sample described above.

($\pm$)-12,13-Dimethoxytara-8,11,13-trien-7-one (25). A mixture of ($\pm$)-**23** (209 mg) and chromium trioxide (190 mg) in acetic acid (20 ml) was stirred at room temperature for 2 h and then diluted with ether. The ether solution

was washed successively with water, aqueous sodium hydrogencarbonate, and water. The dried solution was then evaporated *in vacuo* and the residue was chromatographed on silica gel (20 g) using hexane-benzene (1 : 4) as the eluent to give ($\pm$)-**25** (118 mg; 54%), which was recrystallized from methanol: mp 129–130 °C; IR: 1660 cm^{-1} ; NMR (90 MHz): 0.93 and 1.02 (each 3H and s, $-\dot{\text{C}}(\text{CH}_3)_2$), 1.12 (3H, s, $\text{C}_{10}-\text{CH}_3$), 1.23 and 1.31 (each 3H, d, and $J=7$ Hz, $-\text{CH}(\text{CH}_3)_2$), 3.76 and 3.83 (each 3H and s, $2-\text{OCH}_3$), 6.58 (1H, s, $\text{C}_{11}-\text{H}$). Found: C, 76.98; H, 9.27%. Calcd for $\text{C}_{22}\text{H}_{32}\text{O}_3$: C, 76.70; H, 9.36%.

($\pm$)-Dispermone (3). Boron tribromide (0.1 ml) was added at 0–5 °C to a solution of ($\pm$)-**25** (47 mg) in dichloromethane (2.0 ml). The mixture was allowed to stand at room temperature for 4 h, poured into ice-water, and extracted with ether. The ether extract was washed successively with aqueous sodium thiosulfate and water, dried over sodium sulfate, and then evaporated *in vacuo*. The crude product was chromatographed on silica gel (5.0 g) using chloroform as the eluent to give ($\pm$)-dispermone (**3**) (38 mg; 88%), which was recrystallized from ether-hexane: mp 242–245 °C (sintered at ca. 230 °C); IR: 3595, 3540, 3200, 1655 cm^{-1} ; NMR (90 MHz: $(\text{CD}_3)_2\text{CO}$): 0.92, 1.01, and 1.08 (each 3H and s, $-\dot{\text{C}}(\text{CH}_3)_2$ and $\text{C}_{10}-\text{CH}_3$), 1.30 and 1.38 (each 3H, d, and $J=7$ Hz, $-\text{CH}(\text{CH}_3)_2$), 3.86 (1H, m, $-\text{CH}(\text{CH}_3)_2$), 6.73 (1H, s, $\text{C}_{11}-\text{H}$). Found: C, 75.61; H, 8.72%. Calcd for $\text{C}_{20}\text{H}_{28}\text{O}_3$: C, 75.91; H, 8.92%.

2-Isopropyl-3,4-dimethoxybenzyltriphenylphosphonium Chloride (27). A mixture of the benzyl chloride (**11**) (35.0 g) and triphenylphosphine (40.1 g) in dry benzene (35 ml) was refluxed for 5 min. The precipitated salt (**27**) (mp 243–245 °C, 29.0 g) was collected by filtration and the filtrate was further refluxed for 6 h to give some additional salt (38.5 g).

(-)-3-(2-Isopropyl-3,4-dimethoxystyryl)-2,4,4-trimethyl-1-cyclohexene (28). A solution of *n*-butyllithium in dry hexane (15%: 2.1 ml) was added at room temperature to a stirred suspension of **27** (2.010 g) in dry hexane (6.0 ml) in a stream of nitrogen, and the mixture was stirred for 1 h. To the above mixture a solution of (*R*)-(-)- α -cyclocitral (**26**), $[\alpha]_D -712^\circ$ (EtOH), (390 mg) in dry hexane (3.0 ml) was added at 8–10 °C over a 5 min period. The mixture was further stirred at this temperature for 4 h, exposed to air for a few min until the red solution turned yellow, then poured into dilute hydrochloric acid and extracted with ether. The ether extract was washed with brine, dried over sodium sulfate, and evaporated *in vacuo*. The residue was triturated with hexane, and the precipitated triphenylphosphine oxide was removed by filtration. The filtrate was evaporated *in vacuo*. The crude product was chromatographed on silica gel (40 g) using hexane-benzene (7:3) as the eluent to give (-)-**28** as an oil (647 mg; 77%), $[\alpha]_D -258^\circ$; NMR: 0.91 and 0.96 (each 3H and s, $-\dot{\text{C}}(\text{CH}_3)_2$), 1.32 (6H, d, $J=7$ Hz, $-\text{CH}(\text{CH}_3)_2$), 1.67 (3H, bs, $=\dot{\text{C}}\text{CH}_3$), 3.37 (1H, m, $-\text{CH}(\text{CH}_3)_2$), 3.77 and 3.80 (each 3H and s, $2-\text{OCH}_3$), 5.42 (1H, m, $-\text{CH}=\dot{\text{C}}-$), 5.55 (1H, dd, $J=9$ and 15 Hz, $-\dot{\text{C}}\text{H}-\text{CH}=\text{CH}-$), 6.61 (1H, d, $J=15$ Hz, $-\dot{\text{C}}\text{H}-\text{CH}=\text{CH}-$), 6.58 and 6.90 (each 1H, d, and $J=9$ Hz, aromatic protons). Found: C, 80.46; H, 9.93%. Calcd for $\text{C}_{22}\text{H}_{32}\text{O}_3$: C, 80.44; H, 9.83%.

(-)-2-(2,6,6-Trimethyl-2-cyclohexenyl)-1-(2-isopropyl-3,4-dimethoxyphenyl)ethane (29). A suspension of (-)-**28** (2.012 g) and 5% Pd-C (1.0 g) in ethanol (20 ml) was stirred at room temperature in an atmosphere of hydrogen. After

one mole equivalent of hydrogen had been absorbed (*ca.* 1.5 h), the mixture was filtered. The filtrate was evaporated *in vacuo* and the residue was purified by column chromatography on silica gel (200 g) using hexane–benzene (7:3) as the eluent to afford (–)-**29** as an oil (1.705 g; 84%), $[\alpha]_D -90.3^\circ$; NMR: 0.91 and 1.01 (each 3H and s, $-\dot{\text{C}}(\text{CH}_3)_2$), 1.34 (6H, d, $J=7$ Hz, $-\text{CH}(\text{CH}_3)_2$), 1.73 (3H, bs, $=\dot{\text{C}}\text{CH}_3$), 3.24 (1H, m, $-\text{CH}(\text{CH}_3)_2$), 3.80 (6H, s, 2-OCH₃), 5.30 (1H, m, $-\text{CH}=\dot{\text{C}}-$), 6.53 and 6.69 (each 1H, d, and $J=9$ Hz, aromatic protons). Found: C, 80.21; H, 10.11%. Calcd for C₂₂H₃₄O₂: C, 79.95; H, 10.37%.

Intramolecular Cyclization of (–)-29. A mixture of (–)-**29** (1.705 g) and anhydrous aluminium chloride (690 mg) in dry benzene (17 ml) was stirred at 25–30 °C for 30 min and then poured into a mixture of ice and dilute hydrochloric acid. The mixture was extracted with ether. The ether extract was washed with brine, dried over sodium sulfate, and evaporated *in vacuo*. The residue was chromatographed on silica gel (170 g) using hexane–benzene (4:1) as the eluent to give (–)-**24** (581 mg; 34%), $[\alpha]_D -36.4^\circ$, whose IR and NMR spectra were identical with those of (±)-**24**. Found: C, 79.77; H, 10.63%. Calcd for C₂₂H₃₄O₂: C, 79.95; H, 10.37%. Further elution gave (+)-**23** as a solid (739 mg; 43%), $[\alpha]_D +32.4^\circ$, which was recrystallized from methanol: mp 89–91 °C, $[\alpha]_D +50.2^\circ$ (lit.¹⁾ mp 89–90 °C, $[\alpha]_D +35^\circ$). The IR and NMR spectra were identical with those of (±)-**23**. Found: C, 79.93; H, 10.67%. Calcd for C₂₂H₃₄O₂: C, 79.95; H, 10.37%.

(+)-12-Methoxytotara-8,11,13-trien-13-ol (2). A mixture of (+)-**23** (93 mg) and anhydrous aluminium chloride (40 mg) in dry benzene (4.0 ml) was refluxed for 3 h with stirring. After the usual work-up, the crude product was purified by column chromatography on silica gel (15 g) using hexane–benzene (9:1) as the eluent to give (+)-**2** (68 mg; 77%), which was recrystallized from methanol: mp 87–88.5 °C, $[\alpha]_D +50.2^\circ$, whose IR and NMR spectra were identical with those of (±)-**2**. Found: C, 79.87; H, 10.32%. Calcd for C₂₁H₃₂O₂: C, 79.70; H, 10.19%.

(–)-12,13-Dimethoxytotara-8,11,13-trien-7-one (25). A solution of (+)-**23** (124 mg) in acetone (3.0 ml) was oxidized at 16–20 °C for 30 min with Jones reagent (8N: 0.20 ml) and then diluted with ether. The ether solution was washed with water, dried over sodium sulfate, and evaporated *in vacuo*. The crude product was purified by column chromatography on silica gel (15 g) using hexane–benzene (1:4) as the eluent to give the starting (+)-**23** (14 mg; 11%). Further elution gave (–)-**25** (95 mg; 74%), $[\alpha]_D -19.2^\circ$, NMR (CDCl₃): 0.92 and 1.01 (each 3H and s, $-\dot{\text{C}}(\text{CH}_3)_2$), 1.13 (3H, s, C₁₀–CH₃), 1.29 and 1.38 (each 3H, d, and $J=7$ Hz, $-\text{CH}(\text{CH}_3)_2$), 3.67 (1H, m, $-\text{CH}(\text{CH}_3)_2$), 3.83 and 3.89 (each 3H and s, 2-OCH₃), 6.72 (1H, s, C₁₁–H). NMR (C₆D₆N): 0.81 and 0.89 (each 3H and s, $-\dot{\text{C}}(\text{CH}_3)_2$), 1.03 (3H, s, C₁₀–CH₃), 1.46 and 1.60 (each 3H, d, and $J=7$ Hz, $-\text{CH}(\text{CH}_3)_2$), 3.85 (6H, s, 2-OCH₃), 4.17 (1H, m, $-\text{CH}(\text{CH}_3)_2$), 6.81 (1H, s, C₁₁–H). The IR and NMR spectra were identical with those of (±)-**25**.

(–)-Dispermone (3). A solution of (–)-**25** (95 mg) and boron tribromide (0.10 ml) in dichloromethane (1.0 ml) was allowed to stand at 0–5 °C for 2 h and then treated as described for the preparation of (±)-**3**. The crude product was purified by column chromatography on silica gel using chloroform as the eluent to give (–)-dispermone (**3**) (80 mg; 92%), which was recrystallized from acetone–hexane: mp 262–267 °C, $[\alpha]_D -47.3^\circ$ (EtOH) (lit.¹⁾ mp 263–265 °C,

$[\alpha]_D -48^\circ$, whose IR and NMR spectra were identical with those published.¹⁾ Found: C, 75.75; H, 8.92%. Calcd for C₂₀H₂₈O₃: C, 75.91; H, 8.92%.

(–)-12-Benzyloxy-13-hydroxytotara-8,11,13-trien-7-one (30). A mixture of (–)-**3** (204 mg), benzyl chloride (90 mg), potassium iodide (110 mg), and anhydrous potassium carbonate (1.0 g) in methyl ethyl ketone (10 ml) was refluxed for 5.5 h with stirring. After the usual work-up, the product was purified by column chromatography on silica gel (30 g) using benzene as the eluent to give (–)-**30** (260 mg; 99%), $[\alpha]_D -17.8^\circ$; IR: 3540, 1660 cm^{–1}; NMR (CDCl₃): 0.93 and 1.01 (each 3H and s, $-\dot{\text{C}}(\text{CH}_3)_2$), 1.11 (3H, s, C₁₀–CH₃), 1.33 and 1.44 (each 3H, d, and $J=7$ Hz, $-\text{CH}(\text{CH}_3)_2$), 3.86 (1H, m, $-\text{CH}(\text{CH}_3)_2$), 5.15 (2H, s, $-\text{OCH}_2-$), 5.81 (1H, s, C₁₃–OH), 6.77 (1H, s, C₁₁–H), 7.42 (5H, s, aromatic protons). NMR (C₆D₆N): 0.81 and 0.90 (each 3H and s, $-\dot{\text{C}}(\text{CH}_3)_2$), 1.07 (3H, s, C₁₀–CH₃), 1.74 and 1.87 (each 3H, d, and $J=7$ Hz, $-\text{CH}(\text{CH}_3)_2$), 4.44 (1H, m, $-\text{CH}(\text{CH}_3)_2$), 5.25 (2H, s, $-\text{OCH}_2-$), 6.93 (1H, s, C₁₁–H). Found: C, 79.75; H, 8.44%. Calcd for C₂₇H₃₄O₃: C, 79.76; H, 8.43%.

(–)-12-Benzyloxy-13-methoxytotara-8,11,13-trien-7-one (31). A mixture of (–)-**30** (182 mg), methyl iodide (0.10 ml), and anhydrous potassium carbonate (500 mg) in methyl ethyl ketone (5.0 ml) was refluxed for 33 h. After the usual work-up, the crude product was purified by column chromatography on silica gel (20 g) using hexane–benzene (1:1) as the eluent to give (–)-**31** (177 mg; 94%), $[\alpha]_D -15.1^\circ$, IR: 1660 cm^{–1}, NMR: 0.94 and 1.02 (each 3H and s, $-\dot{\text{C}}(\text{CH}_3)_2$), 1.10 (3H, s, C₁₀–CH₃), 1.28 and 1.35 (each 3H, d, and $J=7$ Hz, $-\text{CH}(\text{CH}_3)_2$), 3.83 (3H, s, $-\text{OCH}_3$), 5.10 (2H, s, $-\text{OCH}_2-$), 6.69 (1H, s, C₁₁–H), 7.38 (5H, s, aromatic protons). Found: C, 80.23; H, 8.61%. Calcd for C₂₈H₃₆O₃: C, 79.96; H, 8.63%.

(+)-Dispermol (5). A mixture of (–)-**31** (101 mg), PtO₂ (40 mg), and 60% perchloric acid (4 drops) in ethanol (10 ml) was stirred at room temperature for 2.5 h in an atmosphere of hydrogen. After the usual work-up, the crude product was chromatographed on silica gel (15 g) using benzene as the eluent to give (+)-dispermol (**5**) (50 mg; 66%), which was recrystallized from hexane: mp 166.5–167.5 °C, $[\alpha]_D +43.5^\circ$ (lit.¹⁾ mp 164–166 °C, $[\alpha]_D +37^\circ$; IR: 3550, 3360 cm^{–1}; NMR (CDCl₃): 0.95 (6H, s, $-\dot{\text{C}}(\text{CH}_3)_2$), 1.19 (3H, s, C₁₀–CH₃), 1.34 (6H, d, $J=7$ Hz, $-\text{CH}(\text{CH}_3)_2$), 3.37 (1H, m, $-\text{CH}(\text{CH}_3)_2$), 3.79 (3H, s, $-\text{OCH}_3$), 5.2 (1H, br, C₁₂–OH), 6.80 (1H, s, C₁₁–H). NMR (C₆D₆N): 0.88 and 0.94 (each 3H and s, $-\dot{\text{C}}(\text{CH}_3)_2$), 1.20 (3H, s, C₁₀–CH₃), 1.49 (6H, d, $J=7$ Hz, $-\text{CH}(\text{CH}_3)_2$), 3.43 (1H, m, $-\text{CH}(\text{CH}_3)_2$), 4.05 (3H, s, $-\text{OCH}_3$), 7.13 (1H, s, C₁₁–H). Found: C, 79.44; H, 10.25%. Calcd for C₂₁H₃₂O₂: C, 79.70; H, 10.19%.

(–)-12,13-Dimethoxytotara-6,8,11,13-tetraene (32). A mixture of (–)-**25** (250 mg) and lithium aluminium hydride (30 mg) in dry ether (5.0 ml) was refluxed for 2 h. The mixture was poured into dilute hydrochloric acid, extracted with ether, and the ether extract was washed with brine, dried over sodium sulfate, and then evaporated. The residue was recrystallized from methanol to give (–)-**32** (174 mg; 73%), mp 96–97 °C, $[\alpha]_D -100^\circ$; NMR: 0.99 and 1.01 (each 3H and s, $-\dot{\text{C}}(\text{CH}_3)_2$), 1.06 (3H, s, C₁₀–CH₃), 1.33 (6H, d, $J=7$ Hz, $-\text{CH}(\text{CH}_3)_2$), 3.46 (1H, m, $-\text{CH}(\text{CH}_3)_2$), 3.73 and 3.81 (each 3H and s, 2-OCH₃), 5.83 (1H, dd, $J=3$ and 10 Hz, C₆–H), 6.54 (1H, s, C₁₁–H), 6.76 (1H, dd, $J=3$ and 10 Hz, C₇–H). Found: C, 80.19; H, 9.95%. Calcd for C₂₂H₃₂O₂: C, 80.44; H, 9.83%. The mother

liquor of crystallization was evaporated and the residue was chromatographed on silica gel (25 g) using hexane-benzene (1:1) as the eluent to give some additional (–)-**32** (29 mg; 12%).

(+)-12,13-Dimethoxytotara-8,11,13-trien-6-one (**18**). A solution of (–)-**32** (202 mg) and 70% *m*-chloroperbenzoic acid (170 mg) in dichloromethane (5.0 ml) was allowed to stand at 5–7 °C for 1.5 h and then diluted with ether. The solution was washed successively with aqueous potassium iodide, aqueous sodium thiosulfate, aqueous sodium hydrogencarbonate, and water. After the solvent had been removed *in vacuo*, the residue was dissolved in methanol (5.0 ml) containing dilute hydrochloric acid (10%: 0.5 ml). The solution was refluxed for 30 min in an atmosphere of nitrogen, cooled, and extracted with ether. The ether extract was washed with water, dried over sodium sulfate, and then evaporated *in vacuo*. The crude product was chromatographed on silica gel (20 g) using benzene as the eluent to give (+)-**18** (146 mg; 69%), $[\alpha]_D +117^\circ$, whose IR and NMR spectra were identical with those of (±)-**18**. Found: C, 76.91; H, 9.28%. Calcd for $C_{22}H_{32}O_3$: C, 76.70; H, 9.36%.

(+)-Maytenoquinone (**1**). A mixture of (+)-**18** (146 mg) and boron tribromide (0.14 ml) in dichloromethane (3.0 ml) was stirred at 0–5 °C for 1 h, poured into ice-water, and extracted with ether. The ether extract was washed successively with aqueous sodium thiosulfate and water, dried over sodium sulfate, and then evaporated *in vacuo*. The residue was chromatographed on silica gel (30 g) using benzene as the eluent to give (+)-maytenoquinone (**1**) (12.2 mg; 9.1%). Further elution with ether-benzene (1:9) afforded 12,13-dihydroxytotara-8,11,13-trien-6-one (117 mg; 87%); IR: 3540, 3250, 1705 cm^{-1} ; NMR ($CDCl_3$): 1.10 (6H, s, $-C(CH_3)_2$), 1.35 (3H, s, $C_{10}-CH_3$), 1.36 (6H, d, $J=7$ Hz, $-CH(CH_3)_2$), 2.50 (1H, s, C_5-H), 3.10 (1H, m, $-CH(CH_3)_2$), 3.55 (2H, bd, $J=2$ Hz, $-COCH_2-$), 5.54 (s) and 6.21 (bs) (each 1H, $C_{12}-OH$ and $C_{13}-OH$), 6.80 (1H, s, $C_{11}-H$).

The above phenol (117 mg) was stirred and refluxed for 1 h with silver oxide (170 mg) in chloroform (10 ml). The mixture was then filtered and the filtrate was evaporated *in vacuo*. The residue was purified by column chromatography on silica gel (20 g) using benzene as the eluent to give (+)-maytenoquinone (**1**) (60 mg; 51%) (total 72.2 mg; 54% overall yield from (+)-**18**), which was recrystallized from methanol: mp 156–158 °C, $[\alpha]_D +407^\circ$ (lit.¹⁾ mp 158–160 °C, $[\alpha]_D +298^\circ$. Found: C, 76.48; H, 8.63%. Calcd for $C_{20}H_{26}O_3$: C, 76.40; H, 8.34%. The IR and NMR

spectra were identical with those of (±)-**1**.

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