Synthesis of (+)- and (−)-ferruginol *via* asymmetric cyclization of a polyene

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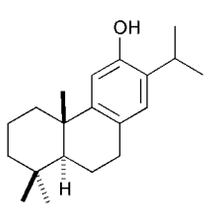
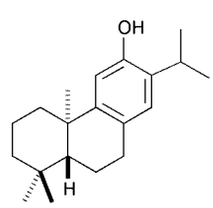
Stereoselectivity of modified polyenes which have a terminal benzene ring was found to be dependent on the size of substituent on the adjacent asymmetric carbon to the terminal benzene ring of the polyenes. (*R*)-(+)-2′-Hydroxy-1,1′-binaphthyl-2-yl (2*R*)-2-(4-methoxyphenyl)-5,9-dimethyldeca-4,8-dienoate gave (*R*)-(+)-2′-hydroxy-1,1′-binaphthyl-2-yl (4a*S*,9*R*,10a*S*)-1,2,3,4,4a,9,10,10a-octahydro-6-methoxy-1,1,4a-trimethylphenanthene-9-carboxylate stereoselectively by treatment with $BF_3{\cdot}Et_2O$ in nitromethane. The products were elaborated to (+)-ferruginol **1**. (−)-Ferruginol **2** and (±)-ferruginol **3** were also synthesized *via* a similar synthetic route.

Introduction

Abietane diterpenes are widely distributed natural products with various biological activities, *e.g.* ferruginol **1**,[1] 11-hydroxy-12-oxoabieta-7,9(11),13-triene,[2] 7a,11-dihydroxy-12-methoxy-abieta-8,11,13-triene,[2] forskalinone,[3] 16-acetoxy-7a,12-dihydroxyabieta-8,12-diene-11,14-dione,[4] 7-oxoroyleanone,[5] and many abietane diterpenes from *Salvia* species[6] with antibiotic activity, sageone[7] and 16-acetoxy-7a,12-dihydroxyabieta-8,12-diene-11,14-dione,[4] with antivirus activity, many catechol-type abietane diterpenes with antioxidant activity,[8] 3-*O*-benzoyl-hosloppone with antimalarial activity,[9] taxodone,[10] taxodione[10] and incanone[11] with cytotoxic activity. In the course of our investigation on the structure–activity relationship of abietane diterpenes, we planned to synthesize variously oxidized abietane diterpenes *via* asymmetric cyclization of polyenes. Polyene cyclization is one of the most effective synthetic reactions of terpenoids.[12] The difficulty is the introduction of chirality on the asymmetric carbon skeleton in the polyene cyclization step. Synthetic investigations of racemic abietanes *via* polyene cyclization have been reported;[13] asymmetric cyclization of polyenes, however, have not been adopted for the asymmetric synthesis of abietanes. We report herein total synthesis of (+)-ferruginol **1**,[1] (−)-ferruginol **2** and (±)-ferruginol **3** *via*



(+)-ferruginol: **1**



(−)-ferruginol: **2**

asymmetric cyclization of modified polyenes from biogenetic polyenes.

Results and discussion

In the polyene cyclization, the nucleophilic reactivity and the conformation of the terminal ring part are quite important in the control of product skeletons.[14] We planned, thus, to settle the conformation of the C-ring and the benzylic position of the starting material with modified polyenes **4** for our diterpene synthesis. The polyenes **4** which were synthesized from 4-methoxyphenylacetic acid **5** in 2 steps, were treated with boron trifluoride–diethyl ether ($BF_3{\cdot}Et_2O$) in nitromethane to give a mixture of compounds **6** and **7** (Scheme 1). The ratio of the products was dependent on the size of the alkoxy group of the ester **4** (see Table 1). The methyl ester **4b** gave a mixture of **6b** and **7b** (3:1) (62.9% yield), whereas isopropyl ester **4c** gave a mixture of **6c** and **7c** (10:1) (65.2%) by treatment with $BF_3{\cdot}Et_2O$ in nitromethane. Livinghouse reported that nitrile **4e** cyclized to form a mixture (1:1) of **6e** and **7e** without stereoselectivity under similar condition.[13] In our investigation into cyclization of these modified polyenes **4**, the bigger alkyl ester **4d** (diastereomeric mixture which was synthesized from racemic acid **4a** and (−)-menthol) gave only **6d** (1:1 diastereomeric mixture) (70.5%) whose 4a-methyl group is in a *trans* relationship to the 9-ester group. This selectivity was explained by the difference in stability between two transition states (**A** and **B**) to afford **6** and **7**, respectively. In the transition state **A**, which can transform into isomer **7**, the steric repulsion between the ester group and 8-H will be influenced by the size of alkyl group in the 9-ester, whereas the steric repulsion between the ester group and the other atoms of transition state **B** should be less. In the cyclization of the bigger alkyl ester **4c**, therefore, the transition state **B** should be much more stable than **A**, to give **6c**. The structures of **6** and **7** were certified by the splitting pattern of 9-H [**6b**: δ 3.85 (1H, doublet, $J = 7.3$ Hz); **7b**: δ 3.92 (1H, double doublet, $J = 3.4$, 10.8 Hz)] in the ^{1}H NMR spectra. These experiments showed that the stereochemistry at C-4a and C-10a of the product could be controlled by the stereochemistry at C-2 of the polyenes **4**.

Table 1 Products ratio in the cyclization of polyenes

Polyene	Products ratio (**6**:**7**)
4b	3:1
4c	10:1
4d	100: < 1
4e	1:1

The mixture (10:1) of tricyclic esters **6c** and **7c** was transformed to (±)-ferruginol **3** as shown in Scheme 2. The ester mixture (10:1) **6c** and **7c** was refluxed with KOH in ethanol–

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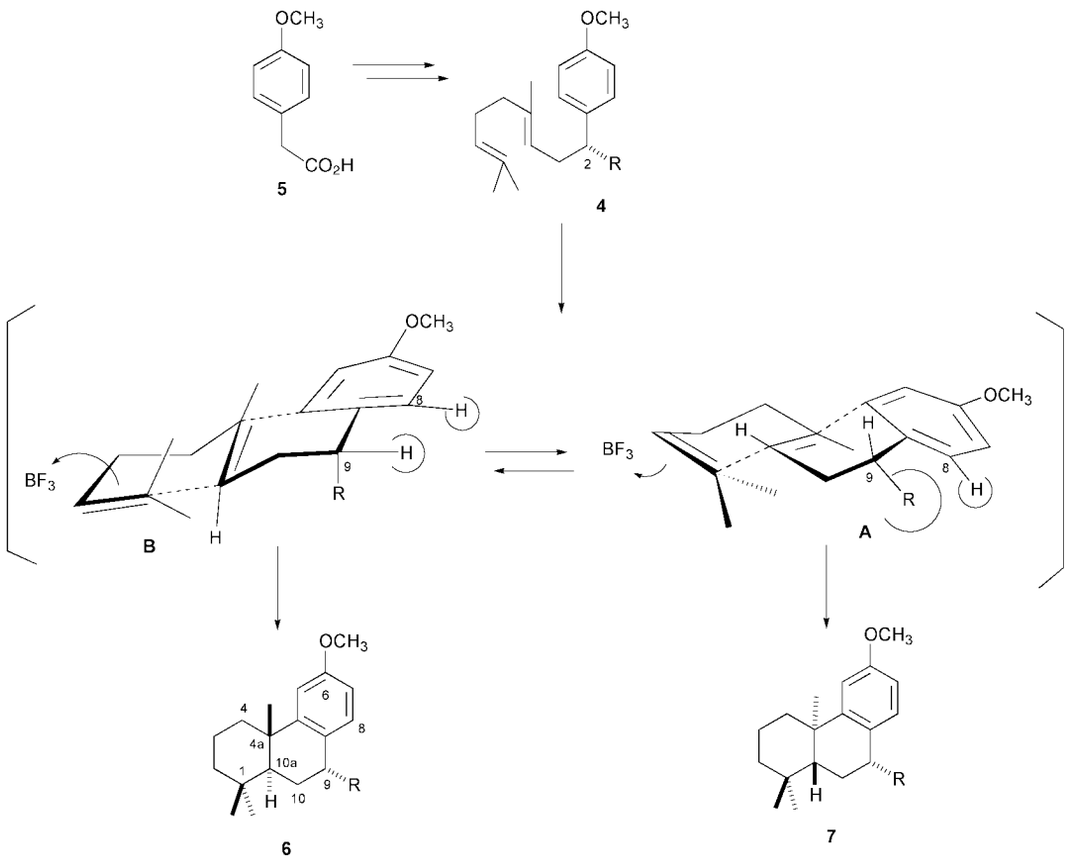
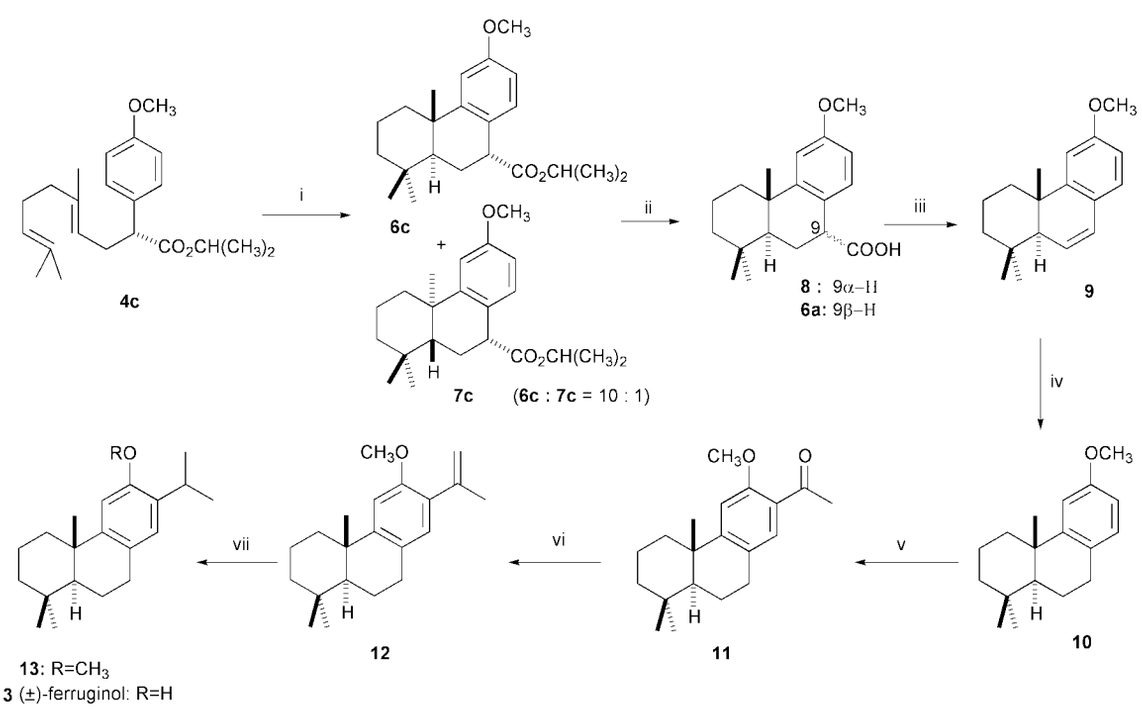


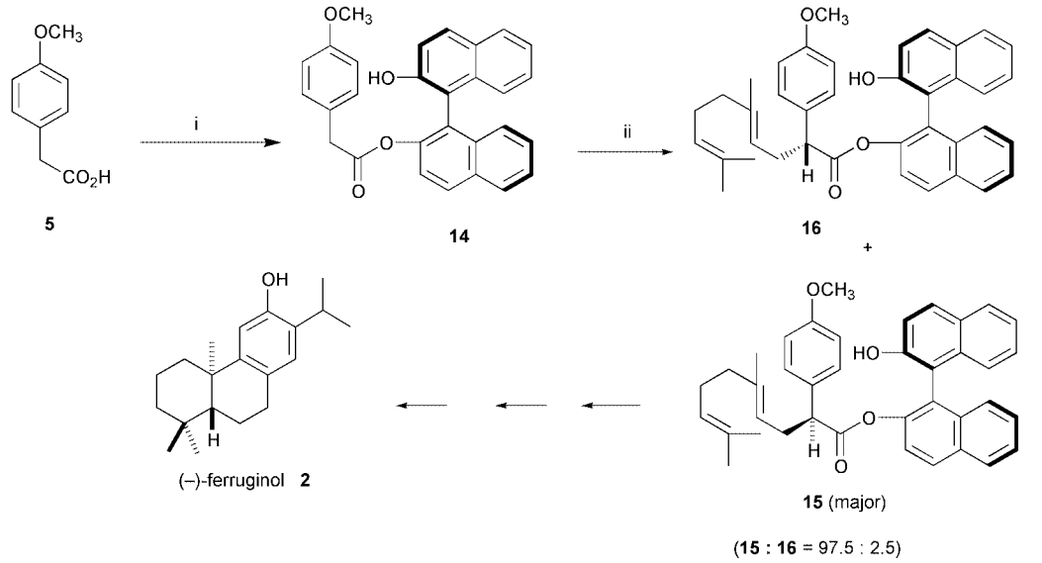
Scheme 1 **4a** R = CO_2H, **4b** R = CO_2CH_3, **4c** R = CO_2Pr^i, **4d** R = CO_2 menthyl, **4e** R = CN.



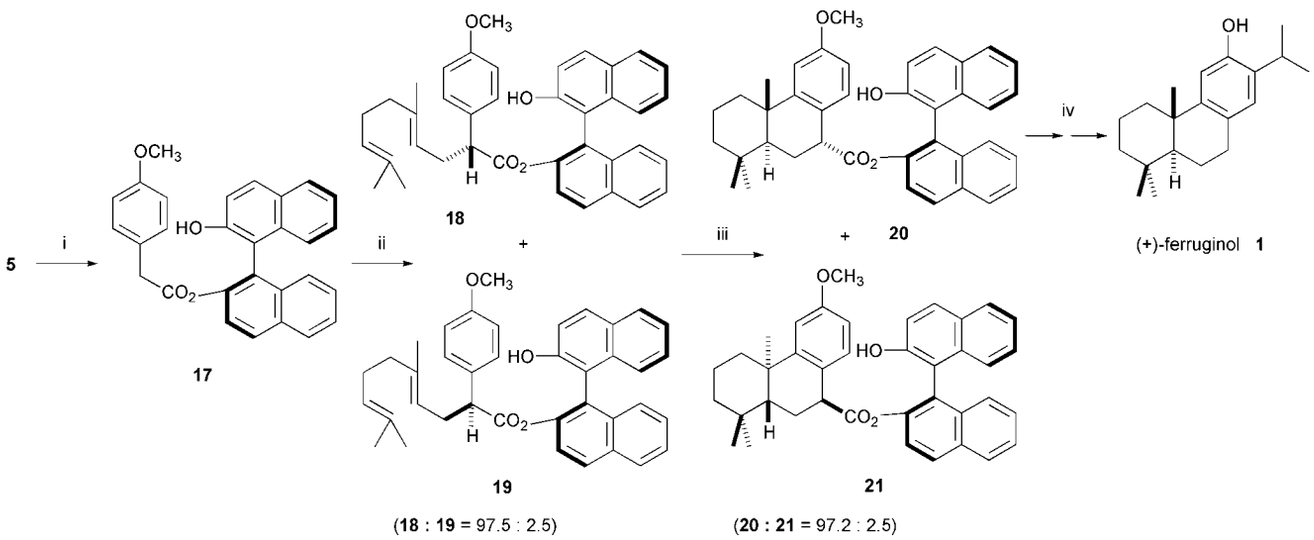
Scheme 2 *Reagents and conditions*: i, $BF_3{\cdot}Et_2O$, CH_3NO_2; ii, (a) aq. ethanol, KOH, reflux, 10 h, (b) HCl; iii, $Pb(OAc)_4$–$Cu(OAc)_2$, pyridine, reflux, 6 h; iv, H_2, 5% Pd/C, EtOAc, 16 h; v, CH_3COCl, $AlCl_3$, CH_2Cl_2; vi, Ph_3PCH_3Br, BuLi, THF; vii, (a) H_2, 5% Pd/C, EtOAc, 16 h, (b) EtSH, NaH, DMF, 120 °C, 48 h.

water for 10 h to give an acid (**8**) and its C-9-epimer (**6a**) (95%) which was decarboxylated by heating under reflux with $Pb(OCOCH_3)_4$ and $Cu(OCOCH_3)_2$ in pyridine for 6 h under Ar to give an olefin (**9**) (42%). Hydrogenation of **9** with H_2 and 5% Pd/C in ethyl acetate (EtOAc) gave methyl ether **10** (85%), which was acetylated with acetyl chloride (2.5 mol equiv.) and aluminium chloride (2.5 mol equiv.) in dichloromethane for 1.5 h to afford a ketone (**11**) (87%). Wittig reaction (47%) of **11** with methyltriphenylphosphonium bromide and butyllithium in tetrahydrofuran (THF), followed by hydrogenation of the olefin **12** with H_2 and 5% Pd/C in EtOAc, gave methyl ether **13** (quantitative yield). The methyl ether was treated with ethanethiol and sodium hydride in *N*,*N*-dimethylformamide (DMF) at 120 °C for 2 days to give (±)-ferruginol **3** (34%).[15]

Chiral polyenes **15** and **18** were then prepared for the asymmetric synthesis of (+)- and (−)-ferruginol. (*S*)-(−)-2′-



Scheme 3 *Reagents and conditions*: i, (*S*)-(−)-1,1′-bi-naphthol, CH_2Cl_2, DCC, DMAP; ii, LDA, geranyl chloride, THF–HMPA.



Scheme 4 *Reagents and conditions:* i, (*R*)-(+)-1,1′-bi-naphthol, CH_2Cl_2, DCC, DMAP; ii, LDA, geranyl chloride, THF–HMPA; iii, $BF_3{\cdot}OEt_2$, CH_3NO_2, 12 h; iv, see Scheme 5.

Hydroxy-1,1′-binaphthyl-2-yl ester **14** of 4-methoxyphenylacetic acid **5** was treated with lithium diisopropylamide (LDA) in THF–hexamethylphosphoric triamide (HMPA), and then alkylated with geranyl chloride (35 mol equiv.) to give a diastereomeric mixture of polyenes **15** and **16** (97.5 : 2.5) in 38% yield (Scheme 3).[16,17] The ratio of isomers was determined by ^{1}H NMR spectroscopy. The absolute stereochemistry of **15** and **16** was determined by the conversion of **15** to unnatural (−)-ferruginol **2**. Natural (+)-ferruginol **1** was then synthesized from (*R*)-(+)-2′-hydroxy-1,1′-binaphthyl-2-yl alcohol *via* a similar synthetic route as shown in Scheme 4. The mixture of esters **18** and **19** (97.5 : 2.5), which was synthesized from (*R*)-(+)-1,1′-binaphthyl-2-yl alcohol, was treated with $BF_3{\cdot}Et_2O$ in nitromethane at ambient temperature for 12 h to give tricyclic esters **20** (49%) and **21** which were separated by silica gel column chromatography.

The tricyclic ester **20** was refluxed with KOH in EtOH–H_2O for 24 h to afford C-9 epimerized carboxylic acid (+)-**8** (67%), which was decarboxylated with $Pb(OAc)_4$–$Cu(OAc)_2$ in quinoline to afford olefin (+)-**9** (68%) (Scheme 5). The double bond at C-9–C-10 was hydrogenated with H_2 and 5% Pd/C in EtOAc to give (+)-**10** (83%). Friedel–Crafts acylation of (+)-**10** with acetyl chloride and 4 molar equivalents of aluminium chloride in dichloromethane for 24 h gave deprotected ketophenol (+)-**22** directly (67%). Wittig reaction of (+)-**22** with methyltriphenylphosphonium bromide and *n*-butyllithium in THF afforded olefin (+)-**23**, which was hydrogenated with H_2 and 5% Pd/C in ethyl acetate to give (+)-ferrugiol **1** in quantitative yield.

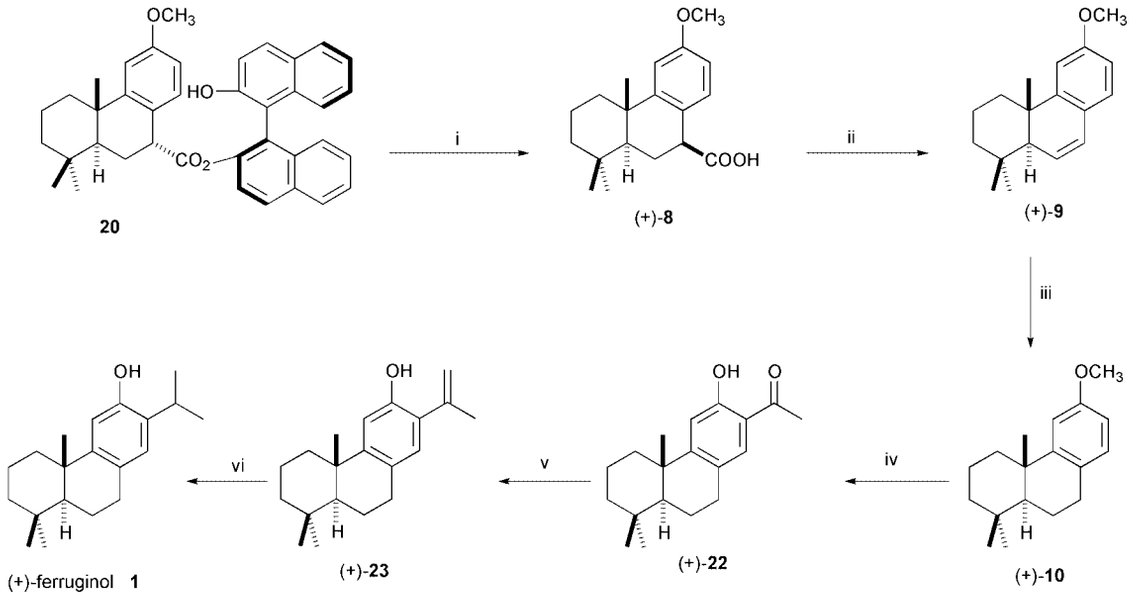
Evans reported the potent antimicrobial activity of ferruginol against methicillin-resistant *Staphylococcus aureus* (MRSA).[18] We evaluated the antimicrobial activities of three synthetic ferruginols (**1**, **2** and **3**) against MRSA and vancomycin-resistant *enterococcus* (VRE). It was found that unnatural (−)-ferruginol **2** showed the strongest activity against VRE and MRSA of the three ferruginols. Further results on antimicrobial activity will be reported, together with those of other abietane compounds, elsewhere in due course.

Conclusions. We have synthesized optical isomers of ferruginol *via* asymmetric cyclization of modified polyenes. This synthetic route should be useful for the synthesis of highly oxidized natural abietanes and their optical antipodes selectively.

Experimental

General

NMR spectra were measured on a JEOL ALPHA-400 (^{1}H: 400 MHz, ^{13}C: 100 MHz) for samples in $CDCl_3$ containing tetramethylsilane as internal standard. *J*-Values are in Hz. IR



Scheme 5 *Reagents and conditions*: i (a) aq. ethanol, KOH, reflux, 24 h; (b) HCl; ii, $Pb(OAc)_4$–$Cu(OAc)_2$, quinoline, reflux, 15 h, iii, H_2, 5% Pd/C, EtOAc, 24 h; iv, CH_3COCl, $AlCl_3$, CH_2Cl_2; v, Ph_3PCH_3Br, BuLi, THF; vi, H_2, 5% Pd/C, EtOAc, 24 h.

spectra were measured on a JEOL JIR-WINSPEC 50 IR spectrometer, UV spectra on a JASCO UVDEC-460 spectrometer, and optical rotations on a JASCO DIP-360 polarimeter, respectively. $[\alpha]_D$-Values are in units of 10^{-1} deg cm^2 g^{-1}. Mass spectra were recorded on a JEOL JMS-SX-102A spectrometer. Mps were measured on a MEL-TEMP (Laboratory Device) and were uncorrected; TLC was carried out on Kieselgel GF_{254} (0.25 mm thickness). Silica gel 60 (70–230 mesh ASTM) was used for column chromatography.

2-(4-Methoxyphenyl)-5,9-dimethyldeca-4,8-dienoic acid 4a

To a THF (20 ml) solution of diisopropylamine (1.48 ml, 10.5 mmol) and *n*-butyllithium in hexane (6.56 ml, 10.5 mmol), was added a solution of *p*-methoxyphenyl acetic acid (0.831 g, 5 mmol) in THF (5 ml) at −78 °C. The solution was stirred for 1 h and then a solution of geranyl chloride (0.949 g, 5.5 mmol) in THF (3 ml) was added. The solution was stirred for a further 1 h and was allowed to warm to ambient temperature, and the reaction was stopped with 1 M HCl. The mixture was extracted with EtOAc. The organic layer was washed with brine, dried over $MgSO_4$, and evaporated. The residue was chromatographed on a silica gel column with EtOAc–hexane (1 : 5) to give *2-(4-methoxyphenyl)-5,9-dimethyldeca-4,8-dienoic acid* **4a** (1.34 g, 89%) as a liquid (Found: M$^+$, 302.1871, $C_{19}H_{26}O_3$ requires *M*, 302.1882); *m*/*z* 302 (M$^+$, 8%), 256 (22), 178 (17), 166 (100), 137 (51), 121 (26), 95 (18); λ_{max}(EtOH)/nm 202 (ε/dm^3 mol^{-1} cm^{-1} 2.3×10^3), 228 (1.1×10^3), 275 (1.8×10^2); ν_{max}(film)/cm^{-1} 2914, 1703, 1610, 1583, 1512, 1446, 1377, 1300, 1252, 1180, 1109, 1037, 939, 831; δ_H 7.23 (2H, d, *J* 8.9), 6.84 (2H, d, *J* 8.9), 5.03 (2H, m), 3.78 (3H, s), 3.50 (1H, t, *J* 7.6), 2.74 (1H, m), 2.43 (1H, m), 1.95 (4H, m), 1.65 (3H, s), 1.56 (6H, s); δ_C 179.9, 158.7, 137.7, 131.3, 130.3, 129.0, 124.0, 120.6, 114.1, 113.9, 55.3, 51.0, 39.7, 31.8, 26.6, 25.8, 17.8, 16.2.

Isopropyl 2-(4-methoxyphenyl)-5,9-dimethyldeca-4,8-dienoate 4c

To a solution of 2-(4-methoxyphenyl)-5,9-dimethyldeca-4,8-dienoic acid **4a** (302 mg, 1 mmol) and propan-2-ol (0.5 ml, 1 mmol) in CH_2Cl_2 (20 ml) were added dicyclohexylcarbodiimide (DCC) (225 mg, 1.11 mmol) and 4-(dimethylamino)pyridine (DMAP) (98 mg, 0.808 mmol) at 0 °C. The solution was stirred at ambient temperature for 2 h. The formed precipitate of DCU was filtered and the precipitate was washed with EtOAc. Combined organic solution was washed with brine, dried over $MgSO_4$ and evaporated. The residue was chromatographed on a silica gel column (EtOAc-hexane, 1 : 10) to give isopropyl *2-(4-methoxyphenyl)-5,9-dimethyldeca-4,8-dienoate* **4c** (234 mg, 68%) as a liquid (Found: M$^+$, 344.2353, $C_{22}H_{32}O_3$ requires *M*, 344.2351); *m*/*z* 344 (M$^+$, 45%), 257 (15), 220 (27), 207 (72), 187 (18), 166 (73), 137 (25), 121 (100), 109 (12); λ_{max}(EtOH)/nm 202 (ε/dm^3 mol^{-1} cm^{-1} 2.7×10^3), 228 (1.3×10^3), 275 (1.9×10^2); ν_{max}(film)/cm^{-1} 2979, 2931, 2854, 1732, 1610, 1512, 1452, 1371, 1300, 1252, 1174, 1109, 1037, 831; δ_H 7.23 (2H, d, *J* 8.9), 6.83 (2H, d, *J* 8.9), 5.06 (2H, m), 4.97 (1H, m), 3.78 (3H, s), 3.45 (1H, dd, *J* 7.0, 8.5), 2.73 (1H, m), 2.39 (1H, m), 1.96 (4H, m), 1.66 (3H, s), 1.57 (6H, s), 1.21 (3H, d, *J* 6.3), 1.14 (3H, d, *J* 6.3); δ_C 173.4, 158.4, 137.2, 131.2, 128.8, 124.1, 120.9, 113.7, 67.8, 55.2, 51.4, 39.8, 32.4, 26.7, 25.7, 21.9, 21.7, 17.7, 16.2.

Methyl ester **4b** and menthyl ester **4d** were synthesized by similar procedures to those described above.

Methyl 2-(4-methoxyphenyl)-5,9-dimethyldeca-4,8-dienoate 4b. A *liquid* (Found: M$^+$, 316.2007, $C_{20}H_{28}O_3$ requires *M*, 316.2038); *m*/*z* 316 (M$^+$, 16%), 257 (18), 180 (100), 179 (100), 165 (35), 151 (97), 135 (30), 121 (100); λ_{max}(EtOH)/nm 229 (ε/dm^3 mol^{-1} cm^{-1} 1.0×10^4), 274 (1.7×10^3), 280 (1.4×10^3); λ_{max}(film)/cm^{-1} 2973, 2937, 2865, 1731, 1511, 1245; δ_H 7.22 (2H, d, *J* 8.6), 6.84 (2H, d, *J* 8.6), 5.03 (2H, br t, *J* 6.9), 3.78 (3H, s), 3.64 (3H, s), 3.51 (1H, t, *J* 7.8), 2.73 (1H, ddd, *J* 7.7, 7.7, 15.4), 2.42 (1H, ddd, *J* 7.7, 7.7, 15.4), 1.95 (4H, m), 1.66 (3H, s), 1.57 (3H, s), 1.56 (3H, s); δ_C 174.2, 158.3, 137.3, 131.3, 131.1, 130.9, 128.8, 124.0, 120.9, 113.8, 113.3, 55.2, 51.8, 50.98, 39.7, 32.3, 26.6, 25.7, 17.7, 16.1.

Menthyl 2-(4-methoxyphenyl)-5,9-dimethyldeca-4,8-dienoate 4d, diastereomeric mixture. A liquid, ν_{max}(film)/cm^{-1} 2931, 2854, 1727, 1511, 1450, 1251, 1174, 1147, 1037; δ_H 7.24 (2H, m), 6.85 (2H, m), 5.06 (1H, m), 4.64 (1H, m), 3.79 (3H, s), 3.47 (1H, m), 2.74 (1H, m), 2.41 (1H, m), 1.96 (4H, m), 1.67 (3H, s), 1.58 (6H, s), 1.6–0.8 (6H, m), 0.88 (4.5H, m), 0.72 (3H, d, *J* 6.9), 0.55 (1.5H, d, *J* 6.9); δ_C 173.51, 173.48 158.42, 158.39, 137.34, 137.19, 131.42, 131.29, 131.27, 131.23, 130.09, 128.81, 128.71, 124.14, 124.04, 120.97, 120.92, 113.67, 113.62, 74.39, 74.32, 74.23, 74.17, 55.81, 55.29, 55.27, 51.52, 51.45, 51.37, 51.31, 47.16, 46.95, 40.97, 40.56, 39.78, 35.00, 34.35, 32.35, 32.10, 31.43, 26.70, 26.27, 26.18, 25.85, 25.81, 25.74, 25.54, 24.82, 23.28, 22.10, 20.81, 17.85, 17.75, 16.24, 16.00.

Isopropyl 1,2,3,4,4a,9,10,10a-octahydro-6-methoxy-1,1,4a-trimethylphenanthrene-9-carboxylate 6c and 7c

Isopropyl 2-(4-methoxyphenyl)-5,9-dimethyldeca-4,8-dienoate **4c** (244 mg, 0.71 mmol) as a solution in nitromethane (2 ml) was added to a nitromethane (10 ml) solution of $BF_3{\cdot}OEt_2$ (0.37 ml, 2.98 mmol) at ambient temperature and the solution was stirred for 4 h at ambient temperature. The reaction was stopped by addition of saturated aq. $NaHCO_3$ and the mixture was extracted with EtOAc. The solution was washed with brine, dried over $MgSO_4$, and evaporated. The residue was chromatographed on a silica gel column with EtOAc–hexane (1 : 10) to give a mixture (10 : 1) of phenanthrenes **6c** and **7c** (159 mg, 65.2%) as a liquid (Found: M^+, 344.2365. $C_{22}H_{32}O_3$ requires *M*, 344.2351); *m*/*z* 344 (M^+, 22%), 257 (100), 201 (14), 187 (12), 173 (23), 161 (11), 129 (15); λ_{max}(EtOH)/nm 202 (ε/dm^3 mol^{-1} cm^{-1} 4.8×10^3), 277 (3.3×10^2); ν_{max}(film)/cm^{-1} 2937, 1734, 1608, 1577, 1504, 1468, 1373, 1294, 1257, 1174, 1105, 1074, 1043, 864, 848, 808; δ_H 7.09 (1H, d, *J* 8.6), 6.82 (1H, d, *J* 2.1), 6.69 (1H, dd, *J* 2.6, 8.4), 5.01 (1H, septet, *J* 6.3), 3.79 (1H, d, *J* 7.3), 3.77 (3H, s), 2.25–1.27 (9H, m), 1.24 (6H, m), 1.18 (3H, s), 0.97 (3H, s), 0.92 (3H, s); δ_C 174.6, 158.4, 151.8, 130.9, 123.7, 110.8, 110.2, 67.9, 55.2, 46.3, 44.3, 41.5, 38.5, 38.1, 33.3, 33.1, 24.8, 22.6, 22.0, 21.9, 21.6, 19.4.

Methyl ester pair **6b**, **7b** and menthyl ester **6d** were synthesized by similar procedures to that described above.

Methyl 1,2,3,4,4a,9,10,10a-octahydro-6-methoxy-1,1,4a-trimethylphenanthrene-9-carboxylate 6b and 7b (mixture). A *liquid* (Found: M^+, 316.2021. $C_{20}H_{28}O_3$ requires *M*, 316.2038); *m*/*z* 316 (M^+, 44%), 273 (23), 257 (59), 192 (44), 180 (100), 179 (100), 151 (100), 135 (63), 121 (57), 69 (53); λ_{max}(EtOH)/nm 227 (ε/dm^3 mol^{-1} cm^{-1} 2.0×10^3), 275 (1.3×10^3), 282 (1.2×10^3); ν_{max}(film)/cm^{-1} 2948, 1737, 1610, 1573, 1255, 1160, 1039, 848; δ_H 7.11 (1H, d, *J* 8.3), 6.83 (1H, d, *J* 2.4), 6.69 (1H, dd, *J* 2.4, 8.4), 3.85 (1H, d, *J* 7.3), 3.77 (3H, s), 3.68 (3H, s), 2.19 (2H, m), 1.90 (1H, m), 1.8–1.2 (6H, m), 1.17 (3H, s), 0.95 (3H, s), 0.91 (3H, s); δ_C 175.3, 158.4, 151.6, 130.8, 123.2, 110.7, 110.2, 54.8, 51.8, 46.4, 44.0, 41.3, 38.4, 38.0, 33.1, 32.8, 24.7, 22.5, 21.5, 19.2.

Menthyl 1,2,3,4,4a,9,10,10a-octahydro-6-methoxy-1,1,4a-trimethylphenanthrene-9-carboxylate 6d, diastereomeric mixture. A *liquid*, *m*/*z* 440 (M^+, 55%), 397 (23), 257 (100), 201 (22), 173 (46), 161 (57), 83 (27), 69 (23), 55 (23); ν_{max}(film)/cm^{-1} 2952, 2877, 1718, 1610, 1457, 1255, 1164, 1037; δ_H 7.07 (1H, m), 6.82 (1H, m), 6.68 (1H, m), 4.62 (1H, m), 3.83 (1H, d, *J* 7.3), 3.77 (3H, s), 2.2–1.1 (16H, m), 0.95, 0.65 (20H, m).

1,2,3,4,4a,9,10,10a-Octahydro-6-methoxy-1,1,4a-trimethylphenanthrene-9-carboxylic acid 8 and 6a

A mixture of isopropyl 1,2,3,4,4a,9,10,10a-octahydro-6-methoxy-1,1,4a-trimethylphenanthrene-9-carboxylate **6c** and **7c** (563 mg, 1.64 mmol) and KOH (920 mg) in EtOH (10 ml) and water (10 ml) was heated under reflux for 10 h. After cooling, the mixture was acidified with 6 M HCl and extracted with EtOAc. The organic layer was washed with brine, dried over $MgSO_4$ and evaporated to give a mixture (**8** : **6a**, 1 : 10) (470 mg, 95%) which was chromatographed on silica gel with EtOAc–hexane (1 : 10) to give *1,2,3,4,4a,9,10,10a-octahydro-6-methoxy-1,1,4a-trimethylphenanthrene-9-carboxylic acid* **8** and C-9 epimer **6a**.

Acid **8**, mp 175.8 °C (Found: M^+, 302.1876, $C_{19}H_{26}O_3$ requires *M*, 302.1882); *m*/*z* 302 (M^+, 77%), 257 (100), 201 (19), 187 (21), 173 (40), 161 (48), 149 (27); ν_{max}(film)/cm^{-1} 2941, 1699, 1610, 1574, 1502, 1464, 1404, 1284, 1252, 1207, 1022, 935; δ_H 7.13 (1H, d, *J* 8.7), 6.83 (1H, d, *J* 2.8), 6.70 (1H, dd, *J* 2.8, 8.7), 3.91 (1H, dd, *J* 8.4, 10.9), 3.78 (3H, s), 2.28–1.30 (9H, m), 1.27 (3H, s), 0.96 (3H, s), 0.95 (3H, s); δ_C 181.8, 158.5, 151.9, 129.5, 123.2, 111.0, 110.3, 55.2, 48.8, 46.1, 41.6, 38.8, 37.9, 33.6, 33.2, 24.8, 23.5, 21.6, 19.2.

Acid **6a**, mp 144–145 °C, ν_{max}(film)/cm^{-1} 6102, 1714, 1608, 1573, 1186, 1072, 798; δ_H 713 (1H, d, *J* 8.6), 6.82 (1H, d, *J* 2.7), 6.71 (1H, dd, *J* 2.7, 8.6), 3.87 (1H, br d, *J* 7.3), 3.78 (3H, s), 2.22 (2H, br d, *J* 13.8), 2.05–1.89 (1H, m), 1.77–1.22 (6H, m), 1.17 (3H, s), 0.95 (3H, s), 0.91 (3H, s); δ_C 181.5, 158.6, 151.8, 131.2, 122.7, 110.9, 110.4, 55.2, 46.6, 44.1, 41.1, 38.4, 38.1, 33.2, 30.0, 24.8, 22.4, 21.6, 19.3.

1,2,3,4,4a,10a-Hexahydro-6-methoxy-1,1,4a-trimethylphenanthrene 9

Lead(IV) acetate (643 mg, 1.45 mmol) and copper(II) acetate (116 mg, 0.57 mmol) were added to a solution of 1,2,3,4,4a,9,10,10a-octahydro-6-methoxy-1,1,4a-trimethylphenanthrene-9-carboxylic acid **8** (175 mg, 0.58 mmol) in pyridine (10 ml) and the mixture was heated at 150 °C for 6 h under Ar. The mixture was extracted with EtOAc and water, and the organic layer was washed with brine, dried over $MgSO_4$, and evaporated. The residue was chromatographed on a silica gel with EtOAc–hexane (1 : 10) to give an oily liquid, *1,2,3,4,4a,10a-hexahydro-6-methoxy-1,1,4a-trimethylphenanthrene* **9** (61 mg, 42%) (Found: M^+, 256.1823, $C_{18}H_{24}O$ requires *M*, 256.1827); *m*/*z* 256 (M^+, 73%), 255 (38), 185 (40), 174 (41), 149 (77), 137 (100), 121 (54), 95 (66); λ_{max}(EtOH)/nm 210 (ε/dm^3 mol^{-1} cm^{-1} 8.5×10^3), 272 (5.6×10^3); ν_{max}(film)/cm^{-1} 2931, 1736, 1604, 1568, 1485, 1395, 1306, 1279, 1246, 1213, 1174, 1076, 1037, 820; δ_H 6.98 (1H, d, *J* 8.4), 6.75 (1H, d, *J* 2.5), 6.65 (1H, dd, *J* 2.5, 8.4), 6.49 (1H, dd, *J* 3.1, 9.5), 5.88 (1H, dd, *J* 2.6, 9.5), 3.79 (3H, s), 2.1 (2H, m), 1.81–1.17 (5H, m), 1.04 (3H, s), 1.03 (3H, s), 0.97 (3H, s); δ_C 159.1, 150.1, 127.7, 127.3, 126.9, 126.2, 109.6, 108.9, 55.3, 50.9, 41.1, 38.2, 36.0, 33.0, 32.7, 22.7, 20.3, 19.1.

1,2,3,4,4a,9,10,10a-Octahydro-6-methoxy-1,1,4a-trimethylphenanthrene 10

A mixture of 1,2,3,4,4a,10a-hexahydro-6-methoxy-1,1,4a-trimethylphenanthrene **9** (5.0 mg, 0.02 mmol) and 5% Pd/C (1 mg) in EtOAc (3 ml) was stirred under H_2 at ambient temperature for 16 h. The mixture was filtered and the filtrate was evaporated. The residue was chromatographed on a silica gel column with EtOAc–hexane (1 : 10) to give *1,2,3,4,4a,9,10,10a-octahydro-6-methoxy-1,1,4a-trimethylphenanthrene* **10** (4.3 mg, 85%), a liquid (Found: M^+, 258.1975. $C_{18}H_{26}O$ requires *M*, 258.1984); *m*/*z* 258 (M^+, 100%), 243 (48), 187 (19), 173 (38), 161 (58), 147 (47), 121 (18); λ_{max}(EtOH)/nm 202 (ε/dm^3 mol^{-1} cm^{-1} 3.8×10^3), 280 (3.6×10^2), 282 (1.2×10^3); ν_{max}(film)/cm^{-1} 2941, 2908, 1736, 1610, 1577, 1502, 1458, 1288, 1252, 1174, 1070, 1043, 804; δ_H 6.95 (1H, d, *J* 8.4), 6.80 (1H, d, *J* 2.5), 6.65 (1H, dd, *J* 2.5, 8.3), 3.77 (3H, s), 2.90–2.73 (2H, m), 2.24 (1H, d, *J* 12.4), 1.88–1.20 (8H, m), 1.19 (3H, s), 0.94 (3H, s), 0.92 (3H, s); δ_C 157.5, 151.3, 129.7, 127.4, 110.6, 110.1, 55.3, 50.4, 41.7, 38.9, 38.1, 33.6, 33.4, 29.7, 24.9, 21.8, 19.4, 19.2.

7-Acetyl-1,2,3,4,4a,9,10,10a-octahydro-6-methoxy-1,1,4a-trimethylphenanethrene 11

A mixture of $AlCl_3$ (133 mg, 1 mmol) and CH_3COCl (0.07 ml, 0.96 mmol) in dry CH_2Cl_2 (5 ml) was stirred at ambient temperature for 30 min under Ar, and then a CH_2Cl_2 (2 ml) solution of 1,2,3,4,4a,9,10,10a-octahydro-6-methoxy-1,1,4a-trimethylphenanthrene **10** (98 mg, 0.38 mmol) was added to the mixture. After stirring of the mixture at ambient temperature for 1.5 h, the reaction was stopped with water and the mixture was extracted with EtOAc. The organic layer was washed with brine, dried over $MgSO_4$, and evaporated. The residue was chromatographed on a silica gel column with EtOAc–hexane (1 : 5) to give *7-acetyl-1,2,3,4,4a,9,10,10a-octahydro-6-methoxy-1,1,4a-trimethylphenanthrene* **11** (100 mg, 87%), a liquid (Found: M^+, 300.2104, $C_{20}H_{28}O_2$ requires *M*, 300.2089); *m*/*z* 300 (M^+, 100%), 285 (76), 217 (30), 203 (38), 189 (30), 149 (37), 137 (15); λ_{max}(EtOH)/nm 218 (ε/dm^3 mol^{-1} cm^{-1} 1.9×10^3), 258 (1.0×10^3), 320 (3.8×10^2); ν_{max}(film)/cm^{-1} 2941, 1676, 1496, 1464, 1404, 1354, 1267, 1207, 1180, 1037; δ_H 7.44 (1H, s), 6.83 (1H, s), 3.87 (3H, s), 2.87 (2H, m), 2.58 (3H, s), 2.26 (1H, br d, *J* 12.7),

1.92–1.22 (8H, m), 1.20 (3H, s), 0.95 (3H, s), 0.93 (3H, s); δ_C 199.3, 157.1, 156.3, 130.8, 127.5 125.4, 107.4, 55.5, 50.1, 41.6, 38.9, 38.6, 33.6, 33.3, 31.9, 29.3, 24.7, 21.8, 19.3, 19.1.

1,2,3,4,4a,9,10,10a-Octahydro-7-isopropenyl-6-methoxy-1,1,4a-trimethylphenanthrene 12

To a solution of methyltriphenylphosphonium bromide (93 mg, 0.26 mmol) in THF (10 ml) was added a hexane solution of *n*-butyllithium (0.16 ml, 0.24 mmol) at −78 °C. The solution was stirred for 30 min at −78 °C and then a THF (1 ml) solution of 7-acetyl-1,2,3,4,4a,9,10,10a-octahydro-6-methoxy-1,1,4a-trimethylphenanthrene **11** (26 mg, 0.087 mmol) was added. The solution was stirred for 1 h at 0 °C and the reaction was stopped with saturated aq. NH_4Cl. The mixture was extracted with EtOAc and the organic layer was washed with brine, dried over $MgSO_4$, and evaporated. The residue was chromatographed on silica gel with EtOAc–hexane (1 : 10) to give *1,2,3,4,4a,9,10,10a-octahydro-7-isopropenyl-6-methoxy-1,1,4a-trimethylphenanthrene* **12** (12 mg, 47%) as a liquid (Found: M^+, 298.2304. $C_{21}H_{30}O$ requires *M*, 298.2297); *m*/*z* 298 (M^+, 100%), 283 (42), 213 (21), 201 (28), 187 (28), 161 (8), 129 (8); λ_{max}(EtOH)/nm 205 (ε/dm^3 mol^{-1} cm^{-1} 3.4×10^4), 287 (3.2×10^3); ν_{max}(film)/cm^{-1} 2925, 2844, 1610, 1496, 1458, 1404, 1371, 1246, 1207, 1103, 1070, 1043, 891; δ_H 6.85 (1H, s), 6.76 (1H, s), 5.10 (1H, s), 5.05 (1H, s), 3.79 (3H, s), 2.81 (2H, m), 2.26 (1H, br d, *J* 13.2), 2.10 (3H, s), 1.90–1.31 (8H, m), 1.21 (3H, s), 0.94 (3H, s), 0.93 (3H, s); δ_C 154.6, 150.0, 143.9, 129.9, 129.6, 127.0, 114.6, 107.1, 55.7, 50.47, 41.7, 39.0, 38.1, 33.6, 33.4, 29.7, 24.9, 23.4, 21.8, 19.4, 19.3.

(±)-Ferruginol methyl ether 13

A mixture of 1,2,3,4,4a,9,10,10a-octahydro-7-isopropenyl-6-methoxy-1,1,4a-trimethylphenanthrene **12** (31 mg, 0.10 mmol) and 5% Pd/C (3 mg) in EtOAc (2 ml) was stirred under H_2 for 16 h at ambient temperature. The mixture was filtered through Celite and the solution was evaporated. The residue was chromatographed on a silica gel column with EtOAc–hexane (1 : 10) to give (±)-*ferruginol methyl ether* **13**, in quantitative yield, as a liquid (Found: M^+, 300.2443. $C_{21}H_{32}O$ requires *M*, 300.2453); *m*/*z* 300 (M^+, 100%), 285 (64), 243 (9), 215 (14), 203 (19), 189 (23), 173 (7), 163 (13), 121 (7); λ_{max}(EtOH)/nm 205 (ε/dm^3 mol^{-1} cm^{-1} 4.2×10^3), 280 (3.6×10^2); ν_{max}(film)/cm^{-1} 2931, 1736, 1610, 1502, 1458, 1377, 1321, 1252, 1207, 1163, 1064, 1043, 891, 847; δ_H 6.83 (1H, s), 6.72 (1H, s), 3.78 (3H, s), 3.21 (1H, septet, *J* 6.9), 2.82 (2H, m), 2.25 (1H, br d, *J* 11.6), 1.90–1.31 (8H, m), 1.20 (3H, s), 1.19 (3H, d, *J* 7.0), 1.17 (3H, d, *J* 7.0), 0.94 (3H, s), 0.92 (3H, s); δ_C 154.9, 148.0, 134.0, 126.8, 126.3, 106.5, 55.6, 50.6, 41.8, 39.0, 37.9, 33.6, 33.4, 29.9, 26.6, 24.9, 23.0, 22.8, 21.8, 19.5, 19.4.

(±)-Ferruginol 3

A DMF (2 ml) solution of (±)-ferruginol methyl ether **13** (22 mg, 0.073 mmol) was added to a DMF (2 ml) solution of ethanethiol (0.15 ml, 2.03 mmol) and sodium hydride (78 mg, 1.96 mmol). The solution was refluxed at 120 °C for 48 h under Ar, and the reaction was stopped by adding saturated aq. NH_4Cl. The mixture was extracted with EtOAc. The organic layer was washed with brine, dried over $MgSO_4$, and evaporated. As the ^{1}H NMR spectrum of the residue showed the formation of dehydrogenated compounds, the residue was hydrogenated with 5% Pd/C (2 mg) in EtOAc (5 ml) for 16 h without separation. The product was filtered through Celite and evaporated. The residue was chromatographed over a silica gel column with EtOAc–hexane (1 : 5) to give (±)-ferruginol **3** (7 mg, 34%) as a liquid (Found: M^+, 286.2301. $C_{20}H_{30}O$ requires *M*, 286.2297); *m*/*z* 286 (M^+, 63%), 271 (44), 256 (40), 242 (20), 228 (50), 207 (30), 203 (29), 189 (47), 185 (42), 149 (49), 129 (75), 111 (65), 97 (100); λ_{max}(EtOH)/nm 203 (ε/dm^3 mol^{-1} cm^{-1} 3.1×10^3), 282 (2.8×10^2); ν_{max}(film)/cm^{-1} 3400, 2958, 1714, 1616, 1583, 1458, 1414, 1377, 1327, 1261, 1234, 1192, 1003; δ_H 6.83 (1H, s), 6.63 (1H, s), 4.45 (1H, s), 3.10 (1H, septet, *J* 7.0), 2.87–2.76 (2H, m), 2.17 (1H, br d, *J* 13.5), 1.88–1.29 (8H, m), 1.20 (6H, t, *J* 7.0), 1.17 (3H, s), 0.94 (3H, s), 0.91 (3H, s); δ_C 150.6, 148.6, 131.3, 127.2, 126.5, 110.9, 50.4, 41.7, 38.9, 37.6, 33.5, 33.4, 29.8, 26.8, 24.8, 22.8, 22.6, 21.7, 19.4, 19.3.

(*R*)-(+)-2′-Hydroxy-1,1′-binaphthyl-2-yl 4-methoxyphenylacetate 17

To a solution of 4-methoxyphenylacetic acid **5** (665 mg, 4 mmol) and (*R*)-(+)-1,1′-binaphthol (1.14 g, 4 mmol) in CH_2Cl_2 (50 ml) were added DCC (908 mg, 4.4 mmol) and DMAP (391 mg, 3.2 mmol) at 0 °C. The solution was stirred at ambient temperature for 15 h. The precipitate of dicyclohexylurea was filtered off and washed with EtOAc. The combined solution was washed with brine, dried over $MgSO_4$, and evaporated. The residue was chromatographed on a silica gel column (EtOAc–hexane, 1 : 5) to give oily *(R)-(+)-2′-hydroxy-1,1′-binaphthyl-2-yl 4-methoxyphenylacetate* **17** (1.63 g, 94%) (Found: M^+, 434.1505. $C_{29}H_{22}O_4$ requires *M*, 434.1518); *m*/*z* 434 (M^+, 56%), 369 (19), 368 (46), 287 (21), 286 (92), 236 (18), 200 (12), 148 (66), 122 (12), 121 (100), 111 (14), 97 (22), 96 (12), 95 (15), 83 (23), 82 (27), 81 (15), 71 (14), 69 (19), 67 (15), 57 (14); $[\alpha]_D$ +45.4 (*c* 5.0, $CHCl_3$); ν_{max}(film)/cm^{-1} 3415, 3234, 1754, 1712, 1619, 1596, 1513, 1120, 1033; δ_H 8.05–7.18 (12H, m), 6.63 (2H, d, *J* 8.7), 6.54 (2H, d, *J* 8.7), 3.75 (3H, s), 3.35 (2H, s); δ_C 171.0, 158.3, 147.9, 133.4, 133.3, 132.1, 130.7, 130.2, 129.7, 128.2, 127.9, 127.3, 126.5, 126.2, 125.6, 124.5, 123.4, 121.5, 118.2, 113.8, 113.7, 55.1, 21.2.

(*R*)-(+)-2′-Hydroxy-1,1′-binaphthyl-2-yl (2*R*)- and (2*S*)-2-(4-methoxyphenyl)-5,9-dimethyldeca-4,8-dienoate 18 and 19

To a THF (10 ml) solution of n-BuLi hexane solution (3 ml, 4.2 mmol) was added diisopropylamine (0.6 ml, 4.2 mmol) at −78 °C under Ar. The solution was stirred for 30 min at −78 °C and then a solution of (*R*)-(+)-2′-hydroxy-1,1′-binaphthyl-2-yl 4-methoxyphenylacetate **17** (868 mg, 2 mmol) in THF (20 ml) was added. After stirring of the mixture for 1 h, HMPA (3.5 ml, 20 mmol) and geranyl chloride (12.7 ml, 68.6 mmol) were added (neat). After being stirred at −78 °C for a further 5 h, the solution was allowed to warm to ambient temperature and then the reaction was stopped with 1 M HCl. The mixture was extracted with EtOAc. The solution was washed with brine, dried over $MgSO_4$, and evaporated. The residue was chromatographed on a silica gel column with EtOAc–hexane (1 : 5) to give *(R)-(+)-2′-hydroxy-1,1′-binaphthyl-2-yl (2R)-2-(4-methoxyphenyl)-5,9-dimethyldeca-4,8-dienoate* **18** and (*R*)-(+)-2′-hydroxy-1,1′-binaphthyl-2-yl (2*S*)-2-(4-methoxyphenyl)-5,9-dimethyldeca-4,8-dienoate **19** (97.5 : 2.5) (436 mg, 38%).

Compound **18** was a liquid (Found: M^+, 570.2761. $C_{39}H_{38}O_4$ requires *M*, 570.2770); *m*/*z* 570 (M^+, 59%), 287 (22), 286 (96), 285 (25), 284 (35), 257 (24), 256 (24), 239 (18), 202 (26), 187 (69), 173 (14), 148 (24), 123 (38), 122 (14), 121 (100), 120 (10), 81 (11), 69 (47); $[\alpha]_D$ +28.1 (*c* 0.5, $CHCl_3$); ν_{max}(film)/cm^{-1} 3646, 3627, 3565, 2966, 2836, 1749, 1704, 1621, 1515; δ_H 8.03–6.95 (12H, m), 6.66 (2H, d, *J* 8.9), 6.48 (2H, d, *J* 8.9), 5.00 (1H, t, *J* 6.6), 4.89 (1H, t, *J* 7.2), 3.77 (3H, s), 3.38 (1H, t, *J* 7.9), 2.22 (1H, m), 2.16 (1H, m), 1.90–1.66 (4H, m), 1.65 (3H, s), 1.57 (3H, s), 1.41 (3H, s); δ_C 173.2, 158.2, 151.2, 147.8, 137.5, 133.4, 133.3, 132.1, 131.3, 130.6, 130.2, 129.3, 128.9, 128.4, 128.1, 127.8, 127.3, 126.4, 126.1, 125.5, 124.3, 124.1, 124.0, 123.3, 123.2, 121.6, 120.4, 120.3, 118.2, 113.8, 113.5, 55.1, 50.7, 39.6, 31.6, 26.7, 25.7, 17.8, 16.1.

(*R*)-(+)-2′-Hydroxy-1,1′-binaphthyl-2-yl (4a*S*,9*R*,10a*S*)-1,2 3,4,4a,9,10,10a-octahydro-6-methoxy-1,1,4a-trimethylphenanthrene-9-carboxylate 20

A solution of (*R*)-(+)-2′-hydroxy-1,1′-binaphthyl-2-yl (2*R*)- and (2*S*)-2-(4-methoxyphenyl)-5,9-dimethyldeca-4,8-dienoate

18 and **19** (97.5 : 2.5) (495 mg, 0.87 mmol) in nitromethane (5 ml) was added to a nitromethane (11 ml) solution of BF_3·OEt_2 (0.46 ml, 3.65 mmol) at ambient temperature and the solution was stirred for 12 h at ambient temperature. The reaction was stopped by addition of saturated aq. $NaHCO_3$ and the mixture was extracted with EtOAc. The organic layer was washed with brine, dried over $MgSO_4$, and evaporated. The residue was chromatographed on a silica gel column with EtOAc–hexane (1 : 5) to give *(R)-(+)-2′-hydroxy-1,1′-binaphthyl-2-yl (4aS,9R,10aS)-1,2,3,4,4a,9,10,10a-octahydro-6-methoxy-1,1,4a-trimethylphenanthrene-9-carboxylate* **20** (243 mg, 49%) as a liquid (Found: M^+, 570.2796. $C_{39}H_{38}O_4$ requires *M*, 570.2770); *m/z* 570 (M^+, 3%), 393 (11), 368 (13), 302 (44), 286 (14), 258 (18), 257 (100), 256 (10), 205 (10), 201 (16), 187 (23), 185 (12), 173 (34), 171 (19), 161 (36), 159 (13), 158 (12), 147 (10), 129 (11), 121 (16), 115 (10), 83 (10), 69 (16); $[\alpha]_D$ +88.0 (*c* 1.0, $CHCl_3$); ν_{max}(film)/cm^{-1} 3621, 3068, 2950, 1621, 1506, 1363, 1211, 1118, 1037; δ_H 8.05–7.00 (12H, m), 7.00 (1H, d, *J* 8.2), 6.64 (1H, d, *J* 2.4), 6.32 (1H, dd, *J* 2.4, 8.2), 5.19 (1H, s), 3.75 (3H, s), 3.59 (1H, d, *J* 7.2), 2.11–1.18 (9H, m), 1.04 (3H, s), 0.83 (3H, s), 0.82 (3H, s); δ_C 174.5, 158.3, 151.6, 151.4, 148.1, 133.5, 133.4, 132.1, 130.8, 130.7, 130.2, 128.1, 127.9, 127.3, 126.6, 126.1, 125.7, 124.5, 123.4, 123.2, 121.9, 121.4, 118.4, 114.1, 110.7, 109.7, 55.0, 46.3, 43.7, 41.3, 38.2, 37.9, 33.1, 32.7, 24.7, 22.1, 21.5, 19.2.

(4a*S*,9*S*,10a*S*)-1,2,3,4,4a,9,10,10a-Octahydro-6-methoxy-1,1,4a-trimethylphenanthrene-9-carboxylic acid (+)-8

A mixture of (*R*)-(+)-2′-hydroxy-1,1′-binaphthyl-2-yl (4a*S*,9*R*,10a*S*)-1,2,3,4,4a,9,10,10a-octahydro-6-methoxy-1,1,4a-trimethylphenanthrene-9-carboxylate **20** (290 mg, 0.52 mmol) and KOH (146 mg) in EtOH (7 ml) and water (7 ml) was heated under reflux for 24 h. After cooling, the mixture was acidified with 1 M HCl and extracted with EtOAc. The organic layer was washed with brine, dried over $MgSO_4$, and evaporated to give a mixture (261 mg, 2 : 1) of (4a*S*,9*S*,10a*S*)-1,2,3,4,4a,9,10,10a-octahydro-6-methoxy-1,1,4a-trimethylphenanthrene-9-carboxylic acid (+)-**8** (175 mg, 67%) and (*R*)-(+)-1,1′-binaphthyl-2-yl alcohol (86 mg).

(4a*S*,10a*S*)-1,2,3,4,4a,10a-Hexahydro-6-methoxy-1,1,4a-trimethylphenanthrene (+)-9

(4a*S*,9*S*,10a*S*)-1,2,3,4,4a,9,10,10a-Octahydro-6-methoxy-1,1,4a-trimethylphenanthrene-9-carboxylic acid (+)-**8** (105 mg, 0.35 mmol) was heated with lead(IV) acetate (466 mg, 1.05 mmol) and copper(II) acetate (64 mg, 0.35 mmol) in quinoline (3 ml) at 130 °C for 15 h under Ar. The mixture was extracted with EtOAc and water, and the organic layer was washed with brine, dried over $MgSO_4$, and evaporated. The residue was chromatographed on a silica gel column with EtOAc–hexane (1 : 10) to give oily (4a*S*,10a*S*)-1,2,3,4,4a,10a-hexahydro-6-methoxy-1,1,4a-trimethylphenanthrene (+)-**9** (61 mg, 68%), $[\alpha]_D$ +32.6 (*c* 1.0, $CHCl_3$).

(4a*S*,10a*S*)-1,2,3,4,4a,9,10,10a-Octahydro-6-methoxy-1,1,4a-trimethylphenanthrene (+)-10

A mixture of (4a*S*,10a*S*)-1,2,3,4,4a,10a-hexahydro-6-methoxy-1,1,4a-trimethylphenanthrene (+)-**9** (61 mg, 0.24 mmol) and 5% Pd/C (6 mg) in EtOAc (3 ml) was stirred under H_2 at ambient temperature for 24 h. The mixture was filtered and the filtrate was evaporated. The residue was chromatographed on a silica gel column with EtOAc–hexane (1 : 10) to give (4a*S*,10a*S*)-1,2,3,4,4a,9,10,10a-octahydro-6-methoxy-1,1,4a-trimethylphenanthrene (+)-**10** (52 mg, 83%) as a liquid, $[\alpha]_D$ +64.0 (*c* 1.0, $CHCl_3$).

(4a*S*,10a*S*)-7-Acetyl-1,2,3,4,4a,9,10,10a-octahydro-6-hydroxy-1,1,4a-trimethylphenanthrene (+)-22

A mixture of $AlCl_3$ (128 mg, 0.96 mmol) and CH_3COCl (0.07 ml, 0.96 mmol) in dry CH_2Cl_2 (2 ml) was stirred at ambient temperature for 30 min under Ar, and then a CH_2Cl_2 (2 ml) solution of (4a*S*,10a*S*)-1,2,3,4,4a,9,10,10a-octahydro-6-methoxy-1,1,4a-trimethylphenanthrene (+)-**10** (49 mg, 0.19 mmol) was added to the mixture. After stirring of the mixture at ambient temperature for 24 h, the reaction was stopped with 1 M HCl and the mixture was extracted with EtOAc. The organic layer was washed with brine, dried over $MgSO_4$, and evaporated. The residue was chromatographed on a silica gel column with EtOAc–hexane (1 : 3) to give *(4aS,10aS)-7-acetyl-1,2,3,4,4a,9,10,10a-octahydro-6-hydroxy-1,1,4a-trimethylphenanthrene* (+)-**22** (36 mg, 67%) as a liquid (Found: M^+, 286.1890. $C_{19}H_{26}O_2$ requires *M*, 286.1933); *m/z* 287 (M^+, 42), 286 (100), 272 (12), 271 (61), 229 (17), 215 (23), 204 (12), 203 (75), 202 (12), 201 (46), 189 (81), 187 (24), 175 (43), 163 (20), 159 (13), 157 (10), 149 (10), 145 (10), 129 (11), 128 (11), 115 (13), 83 (10), 69 (20); $[\alpha]_D$ +75.2 (*c* 1.0, $CHCl_3$); λ_{max}(EtOH)/nm 201 (ε/dm^3 mol^{-1} cm^{-1} 1.4×10^4), 217 (1.5×10^3), 262 (2.5×10^3), 340 (6.6×10^2); ν_{max}(film)/cm^{-1} 3646, 3565, 2885, 2842, 1652, 1373, 1265; δ_H 11.78 (1H, s), 7.38 (1H, s), 6.86 (1H, s), 2.96–2.72 (2H, m), 2.57 (3H, s), 2.22 (1H, br d, *J* 11.6), 1.93–1.19 (8H, m), 1.17 (3H, s), 0.95 (3H, s), 0.93 (3H, s); δ_C 203.6, 159.9, 130.7, 126.0, 117.5, 113.4, 49.7, 41.5, 38.6, 38.5, 33.6, 33.3, 29.4, 26.5, 24.3, 21.7, 19.2, 19.0.

(4a*S*,10a*S*)-1,2,3,4,4a,9,10,10a-Octahydro-6-hydroxy-7-isopropenyl-1,1,4a-trimethylphenanthrene (+)-23

To a solution of methyltriphenylphosphonium bromide (217 mg, 0.61 mmol) in THF (2 ml) was added a hexane solution of *n*-butyllithium (0.40 ml, 0.61 mmol) at −10 °C. The solution was stirred for 30 min at −10 °C and then a THF (1 ml) solution of (4a*S*,10a*S*)-7-acetyl-1,2,3,4,4a,9,10,10a-octahydro-6-hydroxy-1,1,4a-trimethylphenanthrene (+)-**22** (35 mg, 0.12 mmol) was added. The solution was stirred for 4 h and the reaction was stopped with 1 M HCl. The mixture was extracted with EtOAc and the organic layer was washed with brine, dried over $MgSO_4$, and evaporated. The residue was chromatographed on silica gel with EtOAc–hexane (1 : 5) to give *(4aS,10aS)-1,2,3,4,4a,9,10,10a-octahydro-6-hydroxy-7-isopropenyl-1,1,4a-trimethylphenanthrene* (+)-**23** (18 mg, 54%) as a liquid (Found: M^+, 284.2164. $C_{20}H_{28}O$ requires *M*, 284.2140); *m/z* 284 (M^+, 100%), 283 (24), 271 (59), 270 (25), 269 (83), 243 (41), 242 (32), 241 (68), 228 (35), 226 (24), 215 (22), 213 (34), 203 (25), 201 (49), 199 (32), 189 (26), 187 (45), 185 (23), 175 (21), 173 (35), 171 (40); $[\alpha]_D$ +28.7 (*c* 0.5, $CHCl_3$); λ_{max}(EtOH)/nm 202 (ε/dm^3 mol^{-1} cm^{-1} 2.8×10^4), 217 (7.2×10^3), 229 (3.1×10^3); ν_{max}(film)/cm^{-1} 3446, 2925, 1710, 1637, 1496, 1473, 1373, 1267, 1228, 1201, 1002, 892, 771; δ_H 6.82 (1H, s), 6.81 (1H, s), 5.47 (1H, s), 5.34 (1H, s), 5.11 (1H, s), 2.84–2.76 (2H, m), 2.21 (1H, br d, *J* 12), 2.09 (3H, d, *J* 1), 1.85–1.20 (8H, m), 1.18 (3H, s), 0.94 (3H, s), 0.92 (3H, s); δ_C 150.8, 149.8, 142.1, 127.8, 126.6, 126.0, 114.9, 111.1, 50.3, 41.7, 38.5, 37.8, 33.5, 33.3, 29.6, 24.7, 24.3, 21.7, 19.3, 19.2.

(+)-Ferruginol 1

A mixture of (4a*S*,10a*S*)-1,2,3,4,4a,9,10,10a-octahydro-6-hydroxy-7-isopropenyl-1,1,4a-trimethylphenanthrene (+)-**23** (6 mg, 0.02 mmol) and 5% Pd/C (0.7 mg) in EtOAc (2 ml) was stirred under H_2 for 24 h at ambient temperature. The mixture was filtered through Celite and the solution was evaporated. The residue was chromatographed on a silica gel column with EtOAc–hexane (1 : 5) to give (+)-ferruginol **1** in quantitative yield as a liquid, $[\alpha]_D$ +55.7 (*c* 0.5, $CHCl_3$).

(−)-Ferruginol **2** was synthesized by similar procedures as described above for (+)-ferruginol **1**.

(4a*R*,10a*R*)-1,2,3,4,4a,10a-Hexahydro-6-methoxy-1,1,4a-trimethylphenanthrene (−)-9. $[\alpha]_D$ −30.6 (*c* 1.0, $CHCl_3$).

(4a*R*,10a*R*)-1,2,3,4,4a,9,10,10a-Octahydro-6-methoxy-1,1,4a-trimethylphenanthrene (−)-10. $[\alpha]_D$ −64.5 (*c* 10.0, $CHCl_3$).

(4a*R*,10a*R*)-7-Acetyl-1,2,3,4,4a,9,10,10a-octahydro-6-hydroxy-1,1,4a-trimethylphenanthrene (−)-22. $[\alpha]_D$ −75.6 (*c* 10.0, $CHCl_3$).

(4a*R*,10a*R*)-1,2,3,4,4a,9,10,10a-Octahydro-6-hydroxy-7-isopropenyl-1,1,4a-trimethylphenanthrene (−)-23. $[\alpha]_D$ −29.5 (*c* 1.0, $CHCl_3$).

(−)-Ferriginol 2. $[\alpha]_D$ −57.1 (*c* 1.0, $CHCl_3$).

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