Synthetic Studies on Diterpenoid Quinones with Interleukin-1 Inhibitory Activity. Total Synthesis of (±)- and (+)-Triptoquinone A

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An efficient first total synthesis of (±)- and (+)-triptoquinone A (1), a novel diterpenoid quinone with significant inhibitory activity against interleukin-1 releases, has been completed. Birch reduction of tricyclic enone (±)-7, prepared from known 6-methoxy-2-isopropyl-1-naphthol (22), which is readily available in large quantities, was followed by immediate enolate trapping to provide silyl enol ether (±)-30. Compound 30 was converted into carboxylic acid (±)-4 via the corresponding enol triflate (±)-31 either by sequential palladium-catalyzed carbonylation and oxidation or by direct carboxylation. The total synthesis of (±)-1 was completed by oxidation of (±)-4 with CAN in 12 steps from 22 in 19 % overall yield at best. A second, enantioselective total synthesis of (+)-1 was accomplished via (+)-7, which was prepared by (−)-*N*-[4-(trifluoromethyl)benzyl]cinchonidinium bromide (33) catalyzed asymmetric Michael reaction of 6 with ethyl vinyl ketone and a subsequent aldol condensation. The absolute structures of triptoquinone B (2) and C (3), which were isolated concomitantly with triptoquinone A from the same plant sources, were established by a series of chemical reactions based on (+)-7.

During the course of our search for biologically active metabolites from plant sources, we found that the extracts of the *Tripterigium wilfordii* Hook fil var. *regelii* Makino, which has been used in China for the treatment of rheumatoid arthrites and spondylitis,[2] showed an inhibitory effect on interleukin-1 (IL-1) release.[3] Since IL-1 is believed to be intimately involved in rheumatoid arthritis, the development of drugs possessing this sort of activity seems to be significant for treatment of the disease. Bioassay-guided exploration led to the isolation of several structurally novel diterpenoid quinones. Several of these quinones (triptoquinone A,[4a] B,[4a] and C[4b] (1, 2, and 3)) proved to markedly inhibit the release of IL-1α and -1β from lipopolisaccaharide-stimulated human peripheral mononuclear cells. The structures of 1–3 (Figure 1) were elucidated on the basis of a series of NMR studies, and the absolute structure of 1 was established by X-ray analysis of the corresponding amide, which was derived from 1 and L-proline methyl ester. The most promising of these diterpenoids, from the standpoint of potential utility for treatment of rheumatoid arthritis, is triptoquinone A (1), which has progressed to further biological tests in vivo. Its promising activity makes 1 an attractive target for total synthesis.

In this paper we present an efficient first total synthesis of (±)-triptoquinone A (1) and an enantioselective total synthesis of (+)-1 via chiral tricyclic enone (+)-7. In addition, we also describe the determination of the absolute structures of the minor congeners triptoquinones B (2) and C (3).

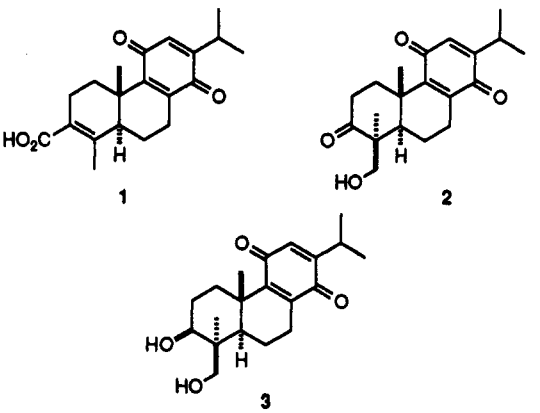

Figure 1.

Results and Discussion

Synthesis of (±)-Triptoquinone A (1). Scheme 1 outlines the key features of our synthetic approach to (±)-triptoquinone A (1). The pivotal step in this approach is the regioselective construction of the target molecule's α,β-unsaturated carboxylic acid moiety with a trans-fused AB ring juncture. We envisaged that carboxylic acid 4, which would readily be converted into 1, might be prepared from dienol ether 5 by acid hydrolysis and subsequent oxidation. We hoped that the acid hydrolysis would preferentially generate the AB trans-fused enal. Alternatively, we expected that enol ether 6, which already incorporates the necessary trans stereochemistry, could be transformed into 4 via the corresponding enol triflate with the aid of a transition-metal catalyst. Precursors 5 and 6 in turn might be constructed by standard manipulations from tricyclic enone 7, which could be derived from suitably functionalized tetralone 8 by a Robinson annulation reaction with ethyl vinyl ketone.

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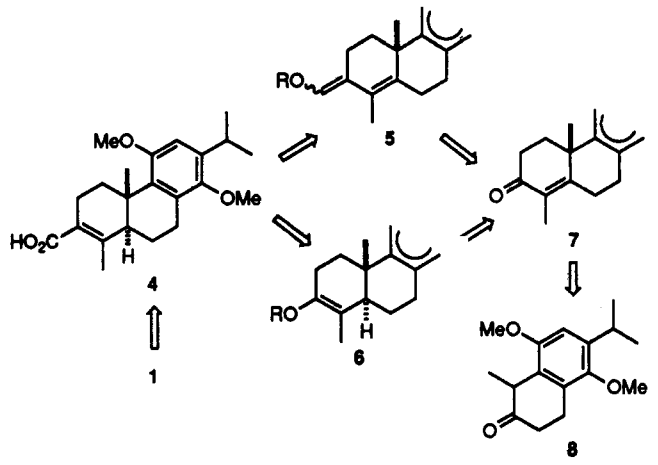
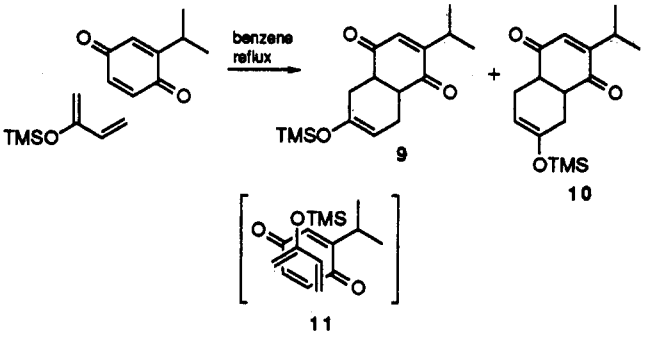
Scheme 1



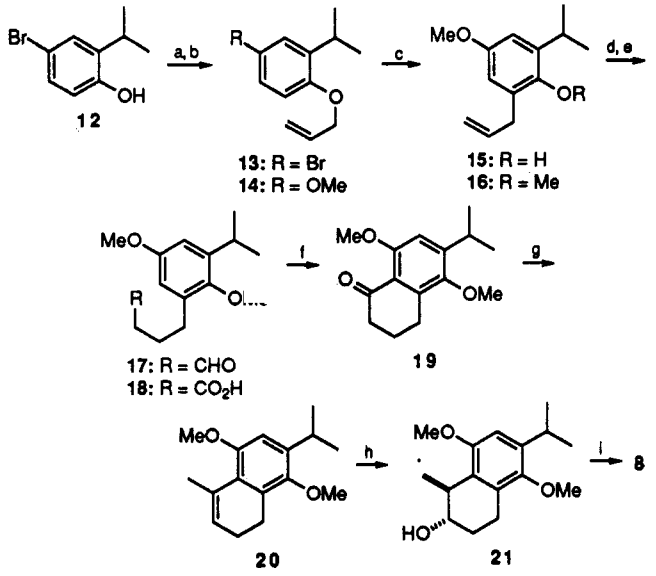
Scheme 2



The first phase of the synthesis required the efficient preparation of 8, and we initially examined the intermolecular Diels–Alder reaction of 2-(trimethylsilyl)-1,3-butadiene[5] and 2-isopropyl-1,4-benzoquinone.[6] The cycloaddition was expected to lead to the preferential formation of desired adduct 9 via transition state 11, which has fewer steric interactions (Scheme 2). Unexpectedly, however, when the reaction was conducted in refluxing toluene, a quantitative yield of an inseparable 1:1 mixture of the regioisomeric cycloadducts was obtained.[7] Consequently, a stepwise route was pursued.

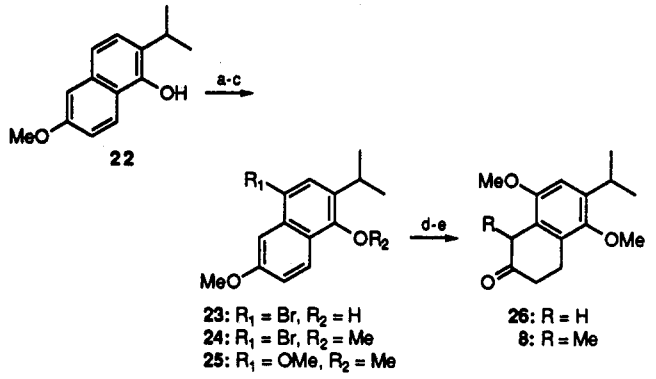
Thus, treatment of 4-bromo-2-isopropylphenol (12)[8] with allyl bromide and potassium carbonate followed by methoxylation of the resulting allyl ether 13 provided 14 (Scheme 3). Claisen rearrangement[9] of 14 at 200 °C afforded phenol 15, which was methylated to give 16. By means of the protocol of Brown,[10] 16 was treated with 9-BBN and lithium tri-*tert*-butoxyaluminum hydride under an atmosphere of carbon monoxide to give directly aldehyde 17 in 58% yield, after alkaline hydrogen peroxide treatment. Aldehyde 17 was then oxidized with sodium chlorite[11] in the presence of sulfamine to yield carboxylic acid 18. This sequence conveniently established the functionality for cyclization to α-tetralone 19; exposure of 18 to PPA, addition of methylmagnesium iodide to the resulting ketone 19, and acid-catalyzed dehydration provided 20. Conversion of 20 into desired β-tetralone 8 was executed in 78% overall yield by a hydroboration–oxidation sequence and Swern oxidation of the resulting alcohol 21. However, this approach required 12 steps (22% overall yield) from a commercial 2-isopropylphenol, and a more convenient route to 8 was investigated.

Scheme 3[a]



[a] (a) Allyl bromide, K_2CO_3, DMF, 78%; (b) NaOMe, CuI, MeOH, DMF, 92%; (c) (1) 200 °C, 91% (2) Me_2SO_4, K_2CO_3, acetone, 99%; (d) 9-BBN, CO, $LiAlH(^tBuO)_3$ then ^-OOH, 58%; (e) H_2NSO_3H, $NaClO_2$, aqueous dioxane, 97%; (f) PPA, 78%; (g) (1) MeMgI, benzene, Et_2O, (2) *p*-TsOH, benzene, 88%; (h) BH_3-Me_2S then ^-OOH, 87%; (i) $(COCl)_2$, DMSO, Et_3N, 90%.

Scheme 4[a]



[a] (a) NBS, DMF, 85%; (b) Me_2SO_4, KOH, 96%; (c) NaOMe, CuI, MeOH, DMF, 92%; (d) (1) Na, EtOH, (2) $(CO_2H)_2$, aqueous MeOH, 100%; (e) pyrrolidine, benzene then MeI, dioxane, 81%.

Reaction of 2-isopropyl-6-methoxynaphthol (22),[12] which was prepared in 42% overall yield from a commercial 6-methoxy-1-tetralone via a five-step sequence, with NBS, methylation of the resulting bromide 23, and subsequent displacement of the bromine in 24 with methoxide in the presence of CuI provided 25 in 75% overall yield from 22 (Scheme 4). Exposure of 25 to sodium in ethanol led to a mixture of 3,4- and 1,4-dihydro-2,5,8-trimethoxy-6-isopropylnaphthalenes (3.4:1 by ^1H NMR), which upon acid hydrolysis with oxalic acid in aqueous methanol gave tetralone 26 quantitatively. Subsequent introduction of

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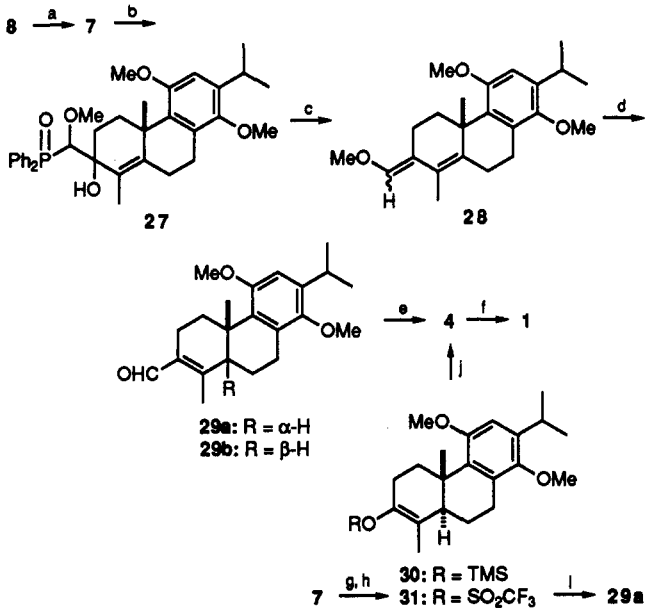
Scheme 5[a]



[a] (a) ethyl vinyl ketone, KOH, aqueous MeOH, 60%; (b) $Ph_2P(O)CH_2OMe$, LDA, THF, 100%; (c) KH, DMF, 98%; (d) $(CO_2H)_2$, aqueous MeOH, 89%; (e) H_2NSO_3H, $NaClO_2$, aqueous dioxane, 76%; (f) $(NH_4)_2Ce(NO_2)_6$, aqueous MeCN, 83%; (g) Li, liquid NH_3, ^tBuOH then TMSCl, Et_3N, THF; 94%; (h) MeLi, THF then $PhN(SO_2CF_3)_2$, 94%; (i) $Pd(Ph_3P)_4$, $^nBu_3SnH$, LiCl, CO, THF, 95%; (j) $Pd(OAc)_2$, DPPF, $^nBu_3N$, CO, DMF, H_2O, 53%.

the methyl group on the benzylic carbon via the enamine was achieved by treatment of **26** with pyrrolidine and methyl iodide to afford **8** in an 11-step sequence from a commercial 6-methoxy-1-tetralone in 26% overall yield. This second route to **8** appeared to be slightly advantageous.

With suitably functionalized β-tetralone **8** in hand, we focused our attention on the conversion of this substance into carboxylic acid **4**, the penultimate intermediate for triptoquinone A (Scheme 5). Robinson annulation of **8** with ethyl vinyl ketone afforded tricyclic enone **7**, which was initially converted into dienol ether **28**. It was anticipated that acid hydrolysis of **28** would lead to the preferential formation of desired AB trans-fused enal **29a**. Reaction of **7** with LDA and (methoxymethyl)diphenylphosphine oxide[13] followed by elimination of the elements of diphenylphosphinic acid with potassium hydride[14] yielded a mixture of stereoisomeric dienol ethers **28** (4.4:1 by ^1H NMR). Acid hydrolysis of the mixture furnished a chromatographically separable mixture of diastereomeric enals **29a,b** in 73 and 14% overall yield from **7**, respectively. However, 400-MHz ^1H NMR analysis of the diastereomers did not permit the complete assignment of the stereochemistries since the diagnostic allylic methine signal appeared in the same region as the other methylenes. Determination of the exact stereostructures of **29a,b** was made by independent conversion of both isomers into triptoquinone A. Unexpectedly, the minor diastereomer was found to be the desired one. Thus, oxidation of minor isomer **29a** with sodium chlorite smoothly provided the corresponding carboxylic acid **4**, and the stage was set for oxidation to (±)-**1**. Finally, **4** was oxidized with CAN in aqueous acetonitrile to give a quinone that exhibited spectroscopic data and TLC behavior fully in accord with those of natural triptoquinone A (**1**) (83% yield from **29a**). This completed total synthesis has a major problem: the desired enal was only obtained as a minor product of the acid hydrolysis of **28**. We thus set out to develop an alternate approach that would establish the AB trans stereochemistry in a highly diastereoselective manner. An adaptation of Stork's Birch reduction followed by an in situ enolate trapping process[15] seemed especially promising. Thus, reaction of **7** with lithium in ammonia in the presence of *tert*-butyl alcohol and subsequent trapping of the enolate with chlorotrimethylsilane produced silyl enol ether **30** as the only discernable stereoisomer in 94% yield after purification by silica gel chromatography. The stereochemistry of the ring juncture in **30** was assigned as trans on the basis of literature precedent.[15] The lithium enolate generated in situ by exposure of **30** to methyllithium was allowed to react with *N*-phenyltrifluoromethanesulfonimide[16] to yield the corresponding triflate **31** in 94% yield. Transformation of **31** into enal **29a** was cleanly accomplished in 94% yield by treatment of **31** with a catalytic amount of tetrakis(triphenylphoshine)palladium, tri-*n*-butyltin hydride, and lithium chloride in THF under an atmosphere of carbon monoxide.[17] The enal thus obtained was identical to the sample prepared from **28** as a minor product. Alternatively, triflate **31** could be directly converted into acid **4** in 58% yield by using the Murai[18] variant of the Orter[19] palladium-catalyzed carboxylation. Thus, the first total synthesis of (±)-triptoquinone A (**1**) was completed in 12 steps in 19% overall yield from known compound **22**, which is readily accessible in large quantities by means of the sequence **7** → **31** → **29a** → **4** → **1**.

Asymmetric Synthesis of (+)-Triptoquinone A. Given our successful synthesis of (±)-triptoquinone A, the lone stumbling block to be overcome prior to realizing a synthesis of (+)-**1** was the preparation of optically active (*S*)-**7**. To this end, we considered utilizing the asymmetric Michael reaction developed by Vandewalle[20] as perhaps the most likely route to yield quantities of material of sufficient optical purity. Treatment of **8** with 0.1 equiv of (−)-*N*-(*p*-trifluoromethyl)benzylcinchonidinium bromide (**33**) (Scheme 6), 1.5 equiv of ethyl vinyl ketone, and KOH in the presence of 0.2 equiv of 18-crown-6 in toluene at room temperature for 24 h produced annulated product (+)-**7** (20%) along with Michael adduct **32** (20%). The latter was converted into **7** in 82% yield by exposure to KOH in aqueous MeOH. The optical purity of (+)-**7** was determined as 100% ee by ^1H NMR with a chiral shift reagent ($Eu(hfc)_3$), and the absolute configuration of the quaternary stereogenic center was deduced to be the requisite *S* from the mechanistic rationale described by Vandewalle.

With the desired optically pure tricyclic enone (+)-**7** in hand, production of triptoquinone A in its natural dex-

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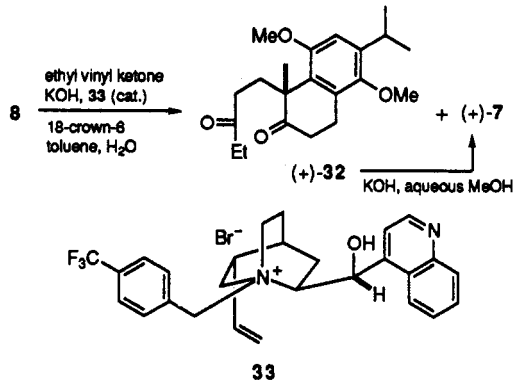
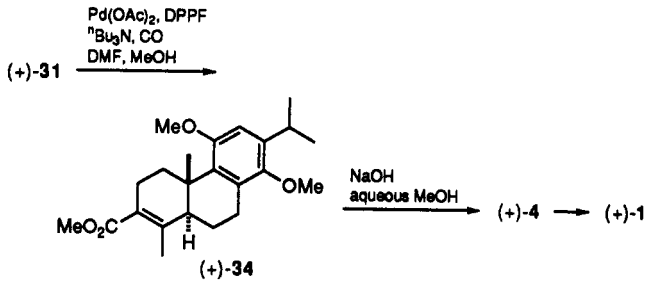
Scheme 6



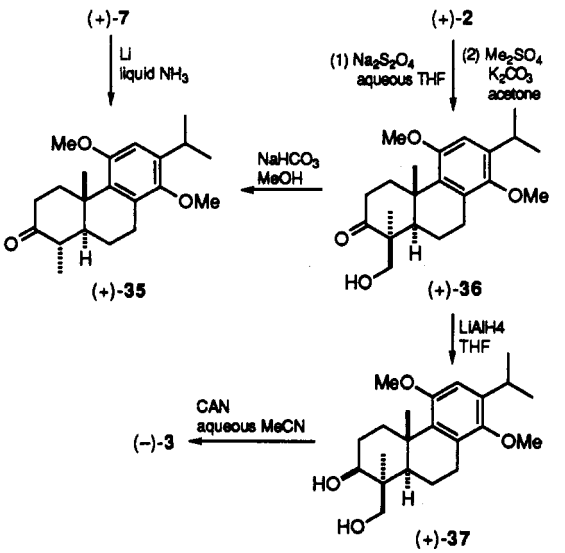
Scheme 7



trorotatory form was investigated. Transformation of (+)-7 thus obtained into chiral triflate (+)-31 was achieved uneventfully by a synthetic sequence parallel to that carried out the racemic series. Carbomethoxylation of 31 with 0.05 equiv of palladium acetate and 1.8 equiv of tri-*n*-butylamine in the presence of 0.06 equiv of DPPF in DMF–MeOH under an atmosphere of carbon monoxide at 90 °C for 1 h provided methyl ester (+)-34 in 99% yield (Scheme 7). Alkaline hydrolysis of (+)-34 occurred in nearly quantitative yield in methanolic NaOH solution at 60 °C to give carboxylic acid (+)-4. Final CAN oxidation of (+)-4 afforded (+)-triptoquinone A (1). The identity of our synthetic (+)-1 [mp 175 °C, $[\alpha]_D$ +125° (*c* 0.34, $CHCl_3$); lit.[4] mp 178–180 °C, $[\alpha]_D$ +128° (*c* 0.25, $CHCl_3$)] was confirmed by careful comparison of its IR, ^1H NMR, MS, and TLC behavior with those of the natural product. It is noteworthy that the two-step conversion of 31 into (+)-4 was a significant improvement over the previous route (72%) employed for the synthesis of the racemate.

Determination of the Absolute Structures of Triptoquinone B and C. Since optically pure tricyclic enone (+)-7, whose absolute configuration at the quaternary stereogenic center was determined to be *S* by its eventual conversion into the structurally established (+)-triptoquinone A, was obtained, we next turned our attention to the determination of the absolute structures of triptoquinones B (2) and C (3), which were isolated concomitantly with triptoquinone A from *T. wilfordii* as minor components. We envisioned that (+)-7 would readily be reduced to 35, which could alternatively be derived from triptoquinone B (2) via 36 (Scheme 8). Comparison of the sign of optical rotation of the independently obtained 35 should firmly establish the absolute structure of natural 2. In addition, the absolute configuration of triptoquinone C (3) would be determined by the conversion of 36 into 3 by sequential stereoselective reduction and CAN oxidation of the resulting 1,3-diol 37. Thus, Birch reduction of (+)-7 with lithium in ammonia yielded 35 {$[\alpha]_D$ +150°}, the stereostructure of which was confirmed by a series of

Scheme 8



NOE experiments performed at 400 MHz. Natural triptoquinone B was reduced by sodium hydrosulfite, and subsequent methylation gave hydroxy ketone (+)-36, which was then treated with sodium bicarbonate in MeOH to produce, via a retro-aldol process, (+)-35 {$[\alpha]_D$ +151°}. The spectral properties of 35 showed it to be identical to the material derived from (+)-7. Reduction of (+)-36 with $LiAlH_4$ and subsequent oxidation of the resulting single diol (+)-37 with CAN led to (−)-3, which was also identical to the natural triptoquinone C in all respects. From these results, the absolute structures of 2 and 3 were convincingly established as shown in Figure 1.

In summary, an efficient first total synthesis of triptoquinone A, which exhibits a potent interleukin-1 inhibitory activity, has been accomplished in racemic and natural, optically active form. Furthermore, the absolute structures of the congeners, triptoquinone B and C, have been firmly established by chemical correlation with the chiral tricyclic enone used in the asymmetric synthesis.

Experimental Section

General. Melting points were measured on a Yamato MP-21 melting point apparatus and are uncorrected. IR were recorded on either a Perkin-Elmer 1720FT-IR or a Hitachi 270–30 spectrometer. NMR were recorded on either a JEOL GSX-400 (400 MHz) or a JEOL GX-270 (270 MHz) spectrometer. Chemical shifs are reported downfield from internal TMS on the δ scale. ^1H NMR coupling constants (*J*) are given in hertz (s, singlet; d, doublet; q, quartet; quint, quintet; sept, septet; m, multiplet; br, broadened). Mass spectra (MS) and exact mass determinations were obtained with a JEOL JMS-D300 or a Hitachi M-80A mass spectrometer. All optical rotations were measured at 24 °C in chloroform solution on a Union Giken PM-201 or a JASCO DIP-4 digital polarimeter. All reactions were performed under an inert atmosphere of argon. THF, diethyl ether, benzene, and toluene were distilled from sodium benzophenone ketyl under argon. Dichloromethane, chloroform, DMF, pyridine, diisopropylamine, and triethylamine were distilled from calcium hydride under argon. Methanol and ethanol were distilled from sodium. Analytical TLC was done on E. Merck silica gel GOF-254 (0.25 mm thickness). Column chromatography was carried out with E. Merck silica gel 60 (70–230 mesh).

Diels–Alder Reaction Leading to 9 and 10. A solution of 2-((trimethylsilyl)oxy)-1,3-butadiene (1.0 g, 7.0 mmol) and 2-isopropyl-1,4-benzoquinone (0.5 g, 3.3 mmol) in benzene (5 mL) was heated under reflux for 8 h. Evaporation of the solvent gave an inseparable mixture of 9 and 10 (1.5 g, 100%). The ^1H NMR

spectrum of the mixture showed diagnostic olefinic protons at δ 6.45 and 6.42 for **9** and **10**, respectively, as singlets in a ratio of 1:1.

Allyl 4-Bromo-2-isopropylphenyl Ether (13). A solution of allyl bromide (2.95 g, 24.4 mmol) in DMF (15 mL) was added to a suspension of 4-bromo-2-isopropylphenol (5.0 g, 23.3 mmol) and K_2CO_3 (3.37 g, 24.4 mmol) in DMF (70 mL), and the resulting mixture was heated at 80 °C for 3 h under vigorous stirring. After cooling, the mixture was diluted with water, extracted with Et_2O, washed with saturated brine, and dried over $MgSO_4$. The solvent was evaporated in vacuo, and the crude product was chromatographed on silica gel (hexane) to give **13** (4.6 g, 78%) as a colorless oil: IR (neat) 2963, 2360, 1486 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.20 (6H, d, J = 7.3 Hz), 3.32 (1H, sept, J = 7.3 Hz), 4.51 (2H, dt, J = 4.7, 1.5 Hz), 5.21–5.31 (1H, m), 5.35–5.45 (1H, m), 5.95–6.10 (1H, m), 6.68 (1H, d, J = 8.5 Hz), 7.22 (1H, dd, J = 8.5, 2.4 Hz), 7.29 (1H, d, J = 2.4 Hz); MS, m/z 256 (M^+ + 1), 254 (M^+ − 1). Anal. Calcd for $C_{12}H_{15}OBr$: C, 56.49; H, 5.93. Found: C, 56.30; H, 5.98.

Allyl 4-Methoxy-2-isopropylphenyl Ether (14). A solution of **13** (35 g, 0.14 mol) in DMF (58 mL) was added to a suspension of sodium methoxide (29.6 g, 0.55 mol) and cuprous iodide (26.4 g, 0.14 mol) in MeOH (140 mL)–DMF (80 mL) at 90 °C. After being refluxed for 8 h, the mixture was filtered, and the filtrate was extracted with Et_2O. The organic phase was washed (saturated brine) and dried ($MgSO_4$). Evaporation of the solvent gave a residue, which was chromatographed on silica gel (1:50 Et_2O/hexane) to afford **14** (26.1 g, 92%) as a colorless oil: IR (neat) 2961, 2361, 1500 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.21 (6H, d, J = 6.8 Hz), 3.34 (1H, sept, J = 6.8 Hz), 3.77 (3H, s), 4.47–4.50 (2H, m), 5.38–5.45 (1H, m), 6.01–6.11 (1H, m), 6.65 (1H, dd, J = 8.8, 3.0 Hz), 6.76 (1H, d, J = 8.8 Hz), 6.80 (1H, d, J = 3.0 Hz); MS, m/z 206 (M^+). Anal. Calcd for $C_{13}H_{18}O_2$: C, 75.69; H, 8.80. Found: C, 75.24; H, 9.35.

2-Allyl-4-methoxy-6-isopropylphenol (15). Allyl ether **14** (25.3 g, 0.12 mol) was heated at 200 °C for 3 h. The cooled mixture was chromatographed on silica gel (1:20 Et_2O/hexane) to leave **15** (23.1 g, 91%) as a colorless oil: IR (neat) 3522, 2836 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.22 (6H, d, J = 6.8 Hz), 3.22 (1H, sept, J = 6.8 Hz), 3.39 (2H, br d, J = 5.6 Hz), 3.76 (3H, s), 4.65 (1H, s), 5.17–5.23 (2H, m), 5.96–6.18 (1H, m), 6.52 (1H, d, J = 2.9 Hz), 6.68 (1H, d, J = 2.9 Hz); MS, m/z 206 (M^+). Anal. Calcd for $C_{13}H_{18}O_2$: C, 75.69; H, 8.80. Found: C, 75.33; H, 8.98.

1-Allyl-2,5-dimethoxy-3-isopropylbenzene (16). Dimethyl sulfate (30.9 g, 0.24 mol) was added to a suspension of **15** (11.3 g, 54.8 mmol) and K_2CO_3 (31.9 g, 0.23 mol) in acetone (400 mL), and the mixture was heated under reflux for 5 h. After the reaction mixture was cooled, water was added, and the mixture was extracted with Et_2O. The organic phase was washed (saturated brine), dried ($MgSO_4$), and evaporated to give a residue, which was chromatographed on silica gel (1:50 Et_2O/hexane) to afford **16** (11.95 g, 99%) as a colorless oil: IR (neat) 2963, 2359, 1605 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.22 (6H, d, J = 6.9 Hz), 3.31 (1H, sept, J = 6.9 Hz), 3.41 (1H, br d, J = 6.3 Hz), 3.68 (3H, s), 3.76 (3H, s), 5.07–5.15 (2H, m), 5.91–6.05 (1H, m), 6.56 (1H, d, J = 3.1 Hz), 6.66 (1H, d, J = 3.1 Hz); ^{13}C NMR (67.5 MHz, $CDCl_3$) δ 23.9 (q), 23.9 (q), 26.6 (d), 34.3 (t), 55.3 (q), 61.8 (q), 110.2 (d), 112.2 (d), 115.9 (t), 133.6 (s), 137.2 (d), 142.8 (s), 149.2 (s), 155.9 (s); MS, m/z 220 (M^+); HRMS calcd for $C_{14}H_{20}O_2$ 220.1465, found 220.1462. Anal. Calcd for $C_{14}H_{20}O_2 \cdot {}^1/_9H_2O$: C, 75.64; H, 9.17. Found: C, 75.67; H, 9.44.

4-(2,5-Dimethoxy-3-isopropylphenyl)butyraldehyde (17). 9-BBN (0.5 M in THF, 67 mL, 33.5 mmol) was added to a stirred 0 °C solution of **16** (7.0 g, 31.1 mmol) in THF (12.7 mL) over a period of 20 min, and the mixture was stirred for 20 min at rt. To the solution at −20 to −25 °C was added LiAl(t-BuO)$_3$H (1.0 M in THF, 33.4 mL, 33.4 mmol) dropwise over a period of 45 min. After being stirred at the same temperature for 1.5 h, the solution was allowed to warm to rt over 1 h, and a solution of NaH_2PO_4 (26.2 g, 0.22 mol) and $K_2HPO_4 \cdot 2H_2O$ (29.3 g, 0.16 mol) in water (76.4 mL) was added. Then 30% H_2O_2 (13.4 mL) was added, and the mixture was stirred at rt for 1 h and diluted with water. The resulting mixture was extracted with Et_2O, and the organic extracts were washed (saturated brine) and dried ($MgSO_4$). The solvent was evaporated, and the crude residue was purified by column chromatography on silica gel (1:50 Et_2O/hexane) to give recovered **16** (2.3 g) as a colorless oil. From the fractions eluted with Et_2O/hexane = 1/5, **17** (3.1 g, 39%, 58% based on the amount of **16** consumed) was obtained as a colorless oil: IR (neat) 2961, 1724 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.22 (6H, d, J = 6.9 Hz), 1.90–2.03 (2H, m), 2.48 (2H, td, J = 7.1, 1.5 Hz), 2.65 (2H, t, J = 7.6 Hz), 3.29 (1H, sept, J = 6.9 Hz), 3.67 (3H, s), 3.77 (3H, s), 6.54 (1H, d, J = 3.2 Hz), 6.65 (1H, d, J = 3.2 Hz), 9.77 (1H, t, J = 1.5 Hz); MS, m/z 250 (M^+). Anal. Calcd for $C_{15}H_{22}O_3$: C, 71.97; H, 8.86. Found: C, 71.67; H, 9.08.

4-(2,5-Dimethoxy-3-isopropylphenyl)butyric Acid (18). A solution of sulfamic acid (1.5 g, 15.5 mmol) in water (150 mL) was added to a solution of **17** (2.9 g, 11.6 mmol) in dioxane (150 mL). To the mixture at rt was added a solution of sodium chlorite (1.4 g, 20.7 mmol) in water (25 mL), and the mixture was stirred for 3 min and extracted with Et_2O. The organic extracts were washed (saturated brine), dried ($MgSO_4$), and concentrated. The crude product was chromatographed on silica gel (30:1 $CHCl_3$/MeOH) to give **18** (3.0 g, 97%) as a colorless oil: IR (neat) 2963, 1708 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.22 (6H, d, J = 6.8 Hz), 1.96 (2H, quint, J = 7.4 Hz), 2.42 (2H, t, J = 7.4 Hz), 2.68 (2H, t, J = 7.4 Hz), 3.29 (1H, sept, J = 6.8 Hz), 3.68 (3H, s), 3.77 (3H, s), 6.56 (1H, d, J = 3.1 Hz), 6.65 (1H, d, J = 3.1 Hz); MS, m/z 266 (M^+). Anal. Calcd for $C_{15}H_{22}O_4$: C, 66.15; H, 8.39. Found: C, 66.09; H, 8.23.

5,8-Dimethoxy-6-isopropyl-1-tetralone (19). A mixture of **18** (2.9 g, 10.9 mmol) and PPA (45 g) was heated at 80 °C for 1 h. The mixture was poured into ice–water and extracted with Et_2O. The ethereal extracts were washed (saturated brine) and dried ($MgSO_4$), and the solvent was evaporated to give a residure, which was chromatographed on silica gel (20:1 $CHCl_3$/AcOEt) to afford **19** (2.1g, 78%) as colorless prisms, mp 60–61.5 °C, after recrystallization from hexane: IR (KBr) 2954, 1673 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.22 (6H, d, J = 6.9 Hz), 2.03 (2H, quint, J = 6.4 Hz), 2.60 (2H, t, J = 6.4 Hz), 2.93 (2H, t, J = 6.4 Hz), 3.37 (1H, sept, J = 6.9 Hz), 3.69 (3H, s), 3.89 (3H, s), 6.71 (1H, s); MS, m/z 248 (M^+). Anal. Calcd for $C_{15}H_{20}O_3$: C, 72.55; H, 8.12. Found: C, 72.55; H, 8.44.

1,4-Dimethoxy-5-methyl-2-isopropyl-7,8-dihydronaphthalene (20). MeMgI (3.0 M in Et_2O, 2.98 mL, 8.9 mmol) was added dropwise to an ice-cooled solution of **19** (1.9 g, 7.7 mmol) in benzene (15 mL)–Et_2O (21 mL). After the solution was stirred at rt for 3 h, saturated aqueous NH_4Cl was added, the resulting mixture was extracted with Et_2O, and the organic phase was washed (saturated brine), dried ($MgSO_4$), and concentrated. The residue was taken up into benzene (45 mL), p-TsOH (20 mg) was added, and the resulting solution was heated under reflux with a Dean–Stark trap for 45 min. The mixture was diluted with water, the organic phase was separated, the aqueous phase was extracted with Et_2O, the combined organic phases were washed (saturated brine) and dried ($MgSO_4$), and the solvent was removed to give a residue, which was purified by column chromatography on silica gel (1:15 Et_2O/hexane) to afford **20** (1.66g, 88%) as a colorless oil: IR (neat) 2960, 1599 cm^{-1}; ^{1}H NMR (270 MHz, $CDCl_3$) δ 1.24 (6H, d, J = 6.9 Hz), 2.03–2.10 (2H, m), 2.19 (3H, d, J = 1.4 Hz), 2.68 (2H, t, J = 7.5 Hz), 3.33 (1H, sept, J = 6.9 Hz), 3.65 (3H, s), 3.78 (3H, s), 5.81 (1H, tq, J = 4.9, 1.4 Hz), 6.55 (1H, s); MS, m/z 246 (M^+). Anal. Calcd for $C_{16}H_{22}O_2$: C, 78.01; H, 9.00. Found: C, 77.71; H, 9.19.

6-Hydroxy-1,4-dimethoxy-5-methyl-2-isopropyl-5,6,7,8-tetrahydronaphthalene (21). $BH_3 \cdot SMe_2$ (0.33 mL, 3.5 mmol) was added dropwise to a stirred solution of **20** (1.5 g, 6.1 mmol) in THF (20 mL) at 0 °C. After being stirred at rt for 3 h, the mixture was successively treated with water (16 mL), 2 N NaOH (4.1 mL), and 30% H_2O_2 (0.78 mL) at 0 °C and stirred at rt for 2.5 h. It was then diluted with water, extracted with Et_2O, washed (saturated brine), and dried ($MgSO_4$). Removal of the solvent gave a residue, which was chromatographed on silica gel (15:1 $CHCl_3$/AcOEt) to provide **21** (1.4 g, 87%) as colorless prisms, mp 92–94 °C, after recrystallization from Et_2O and hexane: IR (KBr) 3345, 2958, 1604 cm^{-1}; ^{1}H NMR (270 MHz, $CDCl_3$) δ 1.16 (6H, d, J = 7.1 Hz), 1.22 (6H, d, J = 6.9 Hz), 1.88–1.96 (2H, m), 2.70–2.86 (2H, m), 3.08 (1H, qd, J = 7.1, 2.6 Hz), 3.33 (1H, sept, J = 6.9 Hz), 3.69 (3H, s), 3.80 (3H, s), 3.97–4.03 (1H, m), 6.57 (1H, s); MS, m/z 264 (M^+). Anal. Calcd for $C_{16}H_{24}O_3$: C, 72.69; H, 9.15. Found: C, 72.31; H, 9.58.

4-Bromo-2-isopropyl-6-methoxy-1-naphthol (23). A solution of NBS (4.03 g, 23.1 mmol) in DMF (50 mL) was added to a stirred solution of **22** (5.0 g, 23.1 mmol) in DMF (100 mL) at 0 °C. After being stirred at 0 °C for 3 h, the mixture was diluted with water and extracted with AcOEt. The extracts were washed (saturated brine), dried ($MgSO_4$), and concentrated to give a residue, which was chromatographed on silica gel (10:50:1 Et_2O/hexane/$CHCl_3$) to afford **23** (5.8 g, 85%) as pale yellow prisms, mp 81.5–83.5 °C, after recrystallization from Et_2O and hexane: IR (KBr) 3528 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 1.33 (6H, d, J = 6.8 Hz), 3.20 (1H, sept, J = 6.8 Hz), 3.96 (3H, s), 5.18 (1H, br s), 7.16 (1H, dd, J = 8.8, 2.4 Hz), 7.41 (1H, d, J = 2.4 Hz), 7.58 (1H, s), 8.06 (1H, d, J = 8.8 Hz); MS, m/z 296 (M^+ + 1), 294 (M^+ − 1). Anal. Calcd for $C_{14}H_{15}O_2Br$: C, 56.97; H, 5.12. Found: C, 56.89; H, 5.17.

4-Bromo-2-isopropyl-1,6-dimethoxynaphthalene (24). Dimethyl sulfate (1.47 g, 11.6 mmol) was added to a stirred solution of **23** (1.0 g, 3.39 mmol) in 1 N KOH (1.7 mL) at 0 °C, and the resulting mixture was stirred at the same temperature for 45 min. The reaction mixture was diluted with water and extracted with AcOEt, and the organic phase was washed (saturated brine), dried ($MgSO_4$), and concentrated to give a crude residue, which was chromatographed on silica gel (5:100:2 Et_2O/hexane/$CHCl_3$) to provide **24** (1.0 g, 96%) as colorless prisms, mp 108–110 °C, after recrystallization from hexane: IR (KBr) 2964 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 1.28 (6H, d, J = 7.3 Hz), 3.50 (1H, sept, J = 7.3 Hz), 3.95 (3H, s), 7.18 (1H, dd, J = 9.0, 2.3 Hz), 7.43 (1H, d, J = 2.3 Hz), 7.65 (1H, s), 7.99 (1H, d, J = 9.0 Hz); MS, m/z 310 (M^+ + 1), 308 (M^+ − 1). Anal. Calcd for $C_{15}H_{17}O_2Br$: C, 58.27; H, 5.54. Found: C, 58.28; H, 5.65.

2-Isopropyl-1,4,6-trimethoxynaphthalene (25). CuI (559 mg, 2.93 mmol) was added to a solution of NaOMe (631 mg, 11.7 mmol) in MeOH (3mL)–DMF (1.7 mL), and the mixture was heated at 90 °C. To the solution was added dropwise a solution of **24** (901 mg, 2.91 mmol) in DMF (1.17 mL), and the resulting mixture was heated under reflux for 2 h. Once the mixture cooled, the resulting solid was filtered off, and the filtrate was diluted with water and extracted with AcOEt. The extract was washed (saturated brine), dried ($MgSO_4$), and concentrated to give a residue, which was chromatographed on silica gel (5:100:2 Et_2O/hexane/$CHCl_3$) to afford **25** (700 mg, 92%) as colorless plates, mp 80–81.5 °C, after recrystallization from hexane: IR (KBr) 2963 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 1.29 (6H, d, J = 7.3 Hz), 3.57 (1H, sept, J = 7.3 Hz), 3.85 (3H, s), 3.92 (3H, s), 3.99 (3H, s), 6.67 (1H, s), 7.16 (1H, dd, J = 9.3, 2.5 Hz), 7.48 (1H, d, J = 2.5 Hz), 7.93 (1H, d, J = 9.3 Hz); MS, m/z 260 (M^+). Anal. Calcd for $C_{16}H_{20}O_3$: C, 73.82; H, 7.74. Found: C, 73.56; H, 7.81.

5,8-Dimethoxy-6-isopropyl-2-tetralone (26). Na (10.3 g, 0.45 gatm) was added by portions over 45 min to a stirred solution of **25** (16.0 g, 61.5 mmol) in EtOH (100 mL) at 50 °C. After the mixture refluxed for 30 min, EtOH (17 mL) was added, and the mixture was allowed to cool to rt, diluted with water, and extracted with Et_2O. The ethereal extract was washed (saturated brine), dried ($MgSO_4$), and concentrated to leave a residue, which was taken up into MeOH (170 mL). To the MeOH solution was added a solution of oxalic acid (7.3 g, 57.9 mmol) in water (30 mL), and the mixture was then refluxed for 21 h. After the mixture was diluted with water, it was extracted with Et_2O, and the organic phases were washed (saturated brine) and dried ($MgSO_4$). Evaporation of the solvent followed by column chromatography on silica gel (5:140:3 Et_2O/hexane/$CHCl_3$) provided **26** (14.5 g, 95%) as a colorless oil. The oil was not stable, so it was immediately used for the next reaction: IR (neat) 1713 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 1.25 (6H, d, J = 7.3 Hz), 2.55 (2H, dd, J = 7.3, 6.8 Hz), 3.11 (2H, dd, J = 7.3, 6.8 Hz), 3.36 (1H, sept, J = 7.3 Hz), 3.48 (2H, s), 3.70 (3H, s), 3.81 (3H, s), 6.64 (1H, s); MS, m/z 248 (M^+); HRMS calcd for $C_{15}H_{20}O_3$ 248.1412, found 248.1406. Anal. Calcd for $C_{15}H_{20}O_3 \cdot {}^1/_7\ H_2O$: C, 71.81; H, 8.15. Found: C, 71.84; H, 8.37.

5,8-Dimethoxy-6-isopropyl-1-methyl-2-tetralone (8). (a) From 21. A solution of DMSO (0.17 mL, 2.3 mmol) was added to a stirred solution of oxalyl chloride (0.1 mL, 1.1 mmol) in CH_2Cl_2 (2.5 mL) at −50 °C. To the cooled solution was added a solution of **21** (264 mg, 1.0 mmol) in CH_2Cl_2 (1 mL). After being stirred at the same temperature for 15 min, the mixture was treated with Et_3N (0.7 mL, 5.0 mmol) and stirred at −50 °C for 5 min. It was then allowed to warm to rt over 1 h, diluted with water, extracted with $CHCl_3$, washed (saturated brine), and dried ($MgSO_4$). Removal of the solvent gave a residue, which was chromatographed on silica gel (1:5 Et_2O/hexane) to provide **8** (235 mg, 90%) as a pale yellow oil: IR (neat) 1713 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 1.23 (3H, d, J = 6.8 Hz), 1.27 (3H, d, J = 6.8 Hz), 1.35 (3H, d, J = 7.3 Hz), 2.40 (1H, ddd, J = 16.4, 12.3, 6.3 Hz), 2.73 (1H, ddd, J = 16.4, 4.9, 3.7 Hz), 2.91 (1H, ddd, J = 16.0, 12.3, 4.9 Hz), 3.28 (1H, ddd, J = 16.0, 6.3, 3.7 Hz), 3.36 (1H, sept, J = 6.8 Hz), 3.69 (3H, s), 3.75 (1H, q, J = 7.3 Hz), 3.81 (3H, s), 6.65 (1H, s); MS, m/z 262 (M^+); HRMS calcd for $C_{16}H_{22}O_3$ 262.1568, found 262.1577. Anal. Calcd for $C_{16}H_{22}O_3$: C, 73.25; H, 8.45. Found: C, 73.09; H, 8.71.

(b) From 26. Pyrrolidine (5.1 g, 71.8 mmol) and 3-Å molecular sieves (12.6 g) were added to a solution of **26** (15.3 g, 61.7 mmol) in benzene (91 mL), and the mixture was stirred at rt for 4.5 h. After the solvent was evaporated, a solution of MeI (90 g, 10.6 mmol) in dioxane (100 mL) was added to the residue, and the resulting mixture was heated under reflux for 45 h. Then, 5% aqueous HCl (45 mL) was added, and the solution was refluxed for 3 h. It was diluted with water, extracted with Et_2O, washed (saturated brine), dried ($MgSO_4$), and concentrated to give a residue, which was purified by column chromatography on silica gel (20:140:3 Et_2O/hexane/$CHCl_3$) to afford **8** (13.1 g, 81%), a pale yellow oil, which was identical to the material prepared from **21**.

5,8-Dimethoxy-1,4a-dimethyl-7-isopropyl-4,4a,9,10-tetrahydro-2(3*H*)-phenanthrenone ((±)-7). A solution of **8** (6.3 g, 24.0 mmol) in MeOH (9 mL) was added to a stirred solution of KOH (1.51 g, 27.0 mmol) in water (4 mL)–MeOH (45 mL) at 0 °C. The mixture was allowed to cool to −20 °C, ethyl vinyl ketone (2.0 g, 24.0 mmol) was added, and the resulting solution was stirred at −20 °C for 1 h and then at rt for 15 h. The reaction mixture was then acidified with 10% HCl, diluted with water, and extracted with $CHCl_3$. The organic phase was washed (saturated brine), dried ($MgSO_4$), and evaporated to leave a residue, which was chromatographed on silica gel (25:125:3 Et_2O/hexane/$CHCl_3$) to afford **7** (4.7 g, 60%) as colorless needles, mp 135–137 °C, after recrystallization from Et_2O and hexane: IR (KBr) 1657 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 1.22 (3H, d, J = 7.0 Hz), 1.24 (3H, d, J = 7.0 Hz), 1.65 (3H, s), 1.76–1.88 (1H, m), 1.87 (3H, s), 2.20–2.29 (1H, m), 2.41-2.53 (2H, m), 2.67 (1H, ddd, J = 18.1, 14.7, 5.1 Hz), 2.95 (1H, ddd, J = 12.5, 3.5, 3.5 Hz), 3.03 (1H, ddd, J = 13.3, 5.1, 2.5 Hz), 3.25–3.36 (2H, m), 3.65 (3H, s), 3.82 (3H, s), 6.65 (1H, s); MS, m/z 328 (M^+). Anal. Calcd for $C_{21}H_{28}O_3$: C, 76.79; H, 8.58. Found: C, 76.42; H, 8.91.

2-Hydroxy-5,8-dimethoxy-1,4a-dimethyl-7-isopropyl-2-(1-methoxy-1-(diphenylphosphoryl)methyl)-2,3,4,4a,9,10-hexahydrophenanthrene (27). A solution of (methoxymethyl)diphenylphosphine oxide (1.15 g, 4.67 mmol) was added to a stirred THF solution (13.5 mL) of LDA, prepared from diisopropylamine (0.65 mL, 4.63 mmol) and *n*-BuLi (1.6 M in hexane, 3.0 mL, 4.80 mmol), at −78 °C. After the mixture stirred at the same temperature for 25 min, a solution of (±)-**7** (750 mg, 2.29 mmol) in THF (6 mL) was added, and the resulting mixture was stirred at -78 °C for 2.5 h. It was quenched with 10% aqueous citric acid solution (19 mL) at -10 °C and extracted with AcOEt, and the organic extract was washed (saturated brine), dried ($MgSO_4$), and concentrated. The crude residue was chromatographed on silica gel (10:1 $CHCl_3$/AcOEt) to give **27** (1.1 g, 84%) as a colorless crystalline powder, mp 95 °C dec, after recrystallization from Et_2O and hexane: IR (KBr) 3308, 2961, 1603 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 1.21 (3H, d, J = 6.8 Hz), 1.25 (3H, d, J = 6.8 Hz), 1.45 (3H, s), 1.70–1.80 (1H, m), 1.88 (3H, s), 1.80–2.13 (3H, m), 2.23 (1H, ddd, J = 13.1, 3.4, 3.4 Hz), 2.35–2.45 (1H, m), 2.73–2.80 (1H, m), 3.07 (3H, s), 3.03–3.13 (1H, m), 3.28 (1H, sept, J = 6.8 Hz), 3.61 (3H, s), 3.68 (3H, s), 4.16 (1H, d, J = 9.1 Hz), 5.41 (1H, s), 6.60 (1H, s), 7.41–7.57 (6H, m), 7.78–7.85 (2H, m), 8.10-8.17 (2H, m); MS, m/z 574 (M^+). Anal. Calcd for $C_{35}H_{43}O_5P$: C, 73.15; H, 7.54. Found: C, 72.87; H, 7.85. From the later fractions, another diastereoisomer (210 mg, 16%) was obtained as a colorless crystalline powder, mp 196–197 °C dec: IR (KBr) 3316, 2968, 1604 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 1.21 (6H, d, J = 6.9 Hz), 1.50 (3H, s), 1.71–1.81 (2H, m), 1.83 (3H, s), 1.82–1.96 (1H, m), 2.30–2.40 (2H, m), 2.73–2.87 (2H, m), 2.95 (3H, s), 3.06–3.10 (1H, m), 3.28 (1H, sept, J = 6.9 Hz), 3.58 (3H,

s), 3.77 (3H, s), 3.92 (1H, d, J = 9.3 Hz), 6.60 (1H, s), 7.26–7.53 (6H, m), 7.77–7.81 (2H, m), 8.02–8.08 (2H, m); MS, m/z 574 (M^+). Anal. Calcd for $C_{35}H_{43}O_5P \cdot {}^1/_2H_2O$: C, 72.26; H, 7.62. Found: C, 71.90; H, 7.60.

2-(Methoxymethylene)-5,8-dimethoxy-1,4a-dimethyl-7-isopropyl-2,3,4,4a,9,10-hexahydrophenanthrene (28). A solution of **27** (1.53 g, 2.7 mmol) in DMF (19.6 mL) was added to a stirred suspension of KH (930 mg, 23.2 mmol) in DMF (19.6 mL) at −10 °C. After being stirred at 0 °C for 1 h, the reaction mixture was treated with 10% aqueous citric acid (40 mL), extracted with AcOEt, washed (saturated brine), and dried ($MgSO_4$). The organic phase was evaporated, and the residue was chromatographed on silica gel (5:50:1 Et_2O/hexane/$CHCl_3$) to afford an inseparable 3:1 mixture of E/Z isomers **28** (923 mg, 98%) as a colorless oil: IR (neat) 2953, 1646, 1602 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 1.18–1.28 (3H, d, J = 6.8 Hz), 1.50 ($^3/_4$H, s), 1.51 ($^3/_4$H, s), 1.91–2.11 (1H, m), 1.80 ($^3/_4$H, s), 2.08 ($^3/_4$H, s), 2.23–2.48 (2H, m), 2.61–2.71 (1H, m), 2.78–2.93 (2H, m), 3.06–3.17 (1H, m), 3.25–3.36 (1H, m), 3.55 ($^3/_4$H, s), 3.63 ($^3/_4$H, s), 3.63 ($^3/_4$H, s), 3.68 ($^3/_4$H, s), 3.78 ($^3/_4$H, s), 3.80 ($^3/_4$H, s), 5.71 ($^1/_4$H, s), 6.10 ($^3/_4$H, s), 6.60 ($^1/_4$H, s), 6.61 ($^3/_4$H, s); MS, m/z 356 (M^+); HRMS calcd for $C_{23}H_{32}O_3$ 356.2351, found 356.2348. Anal. Calcd for $C_{23}H_{32}O_3 \cdot {}^1/_2H_2O$: C, 75.58; H, 9.10. Found: C, 76.30; H, 9.06.

(4a*S,10a*R**)-5,8-Dimethoxy-1,4a-dimethyl-7-isopropyl-3,4,4a,9,10,10a-hexahydrophenanthrene-2-carbaldehyde ((±)-29a) and (4a*S**,10a*S**)-5,8-Dimethoxy-1,4a-dimethyl-7-isopropyl-3,4,4a,9,10,10a-hexahydrophenanthrene-2-carbaldehyde ((±)-29b).** A mixture of **28** (2.1 g, 5.9 mmol, mixture of E/Z isomers) and oxalic acid (690 mg, 5.5 mmol) in degassed MeOH (45 mL)–water (7 mL) was heated under reflux for 4.5 h. The reaction mixture was diluted with water, extracted with AcOEt, washed (saturated brine), dried ($MgSO_4$), and concentrated to leave a residue, which was chromatographed on silica gel (20:300:3 Et_2O/hexane/$CHCl_3$) to give **29b** (1.45 g, 72%) as colorless prisms, mp 137–139 °C, after recrystallization from Et_2O and hexane: IR (KBr) 1665, 1637 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 1.21 (3H, d, J = 6.8 Hz), 1.23 (3H, d, J = 6.8 Hz), 1.35 (3H, s), 1.55–1.65 (1H, m), 1.75–1.85 (1H, m), 2.01–2.23 (5H, m), 2.26 (3H, s), 2.65 (1H, ddd, J = 16.8, 11.0, 4.4 Hz), 2.95 (1H, ddd, J = 17.5, 5.3, 1.5 Hz), 3.30 (1H, sept, J = 6.8 Hz), 3.66 (3H, s), 3.80 (3H, s), 6.60 (1H, s), 10.18 (1H, s); MS, m/z 342 (M^+). Anal. Calcd for $C_{22}H_{30}O_3$: C, 77.16; H, 8.83. Found: C, 77.41; H, 8.93. From the later fractions, 350 mg (17%) of **29a** was obtained as colorless prisms, mp 102–104 °C, after recrystallization from Et_2O and hexane: IR (KBr) 1670, 1633 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 1.12 (3H, s), 1.22 (3H, d, J = 6.8 Hz), 1.23 (3H, d, J = 6.8 Hz), 1.25–1.68 (3H, m), 2.23 (3H, d, J = 1.5 Hz), 2.18–2.31 (1H, m), 2.41–2.53 (2H, m), 2.68 (1H, ddd, J = 17.5, 12.7, 6.6 Hz), 3.03 (1H, ddd, J = 13.5, 7.5, 3.3 Hz), 3.11 (1H, ddd, J = 17.5, 5.3, 1.5 Hz), 3.31 (1H, sept, J = 6.8 Hz), 3.70 (3H, s), 3.80 (3H, s), 6.61 (1H, s), 10.21 (1H, s); ^{13}C NMR (67.5 MHz, $CDCl_3$) δ 15.0 (q), 18.5 (q), 19.4 (t), 20.9 (t), 23.7 (q), 23.8 (q), 26.3 (t), 26.4 (d), 32.0 (t), 37.6 (s), 49.4 (d), 55.2 (q), 60.6 (q), 107.1 (d), 130.5 (s), 132.9 (s), 134.2 (s), 138.8 (s), 148.7 (s), 155.1 (s), 157.5 (s), 190.7 (s); MS, m/z 342 (M^+); HRMS calcd for $C_{22}H_{30}O_3$ 342.2194, found 342.2172.

(4a*S,10a*R**)-5,8-Dimethoxy-1,4a-dimethyl-7-isopropyl-2-((trimethylsilyl)oxy)-3,4,4a,9,10,10a-hexahydrophenanthrene ((±)-30).** Li (4.43 g, 0.63 g atom) was added to liquid NH_3 (1 L), which had been rigorously distilled over Na, at −78 °C. After the mixture stirred at the same temperature for 15 min, a solution of **7** (34.9 g, 0.1 mmol) and t-BuOH (15.7 g, 0.21 mol) in THF (245 mL) was added, and the mixture was stirred for 30 min, treated with isoprene (47.8 mL), and concentrated to leave a residue, which was taken up into THF (280 mL). To the ice–water-cooled THF solution was added a solution of chlorotrimethylsilane (68.1 g, 0.62 mmol) and Et_3N (86.2 g, 0.85 mmol) in THF (245 mL), and the resulting solution was stirred at 0 °C for 30 min. The mixture was diluted with saturated aqueous $NaHCO_3$, extracted with Et_2O, washed (saturated brine), dried ($MgSO_4$), concentrated, and chromatographed on silica gel (1:20 Et_2O/hexane) to afford **30** (40.1 g, 94%) as colorless prisms, mp 124–125 °C, after recrystallization from hexane: IR (KBr) 2839, 1681 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 0.19 (9H, s), 1.16 (3H, s), 1.22 (6H, d, J = 6.8 Hz), 1.41–1.53 (2H, m), 1.63 (3H, m), 1.98–2.13 (2H, m), 2.21–2.40 (2H, m), 2.26 (1H, ddd, J = 17.5, 12.2, 6.8 Hz), 2.97–3.06 (1H, m), 3.10–3.18 (1H, m), 3.30 (1H, sept, J = 6.8 Hz), 3.68 (3H, s), 3.78 (3H, s), 6.58 (1H, s); MS, m/z 402 (M^+). Anal. Calcd for $C_{24}H_{38}O_3Si$: C, 71.59; H, 9.51. Found: C, 71.40; H, 9.30.

(4a*S,10a*R**)-5,8-Dimethoxy-1,4a-dimethyl-7-isopropyl-2-(trifluoromethanesulfonyloxy)-3,4,4a,9,10,10a-hexahydrophenanthrene ((±)-31).** MeLi (1.4 M in Et_2O, 57.7 mL, 80.7 mmol) was added dropwise to a stirred solution of **30** (27.0 g, 67.2 mmol) in THF (380 mL) at 0 °C. After being stirred at rt for 30 min, the mixture was allowed to cool to −78 °C. A solution of *N*-phenyltrifluoromethanesulfonimide (25.6 g, 71.7 mmol) in THF (380 mL) was added, and the mixture was stirred at 0 °C for 9.5 h. It was then diluted with water, extracted with Et_2O, washed (saturated brine), dried ($MgSO_4$), and concentrated to give a residue, which was chromatographed on silica gel (1:50 Et_2O/hexane) to provide **31** (29.1 g, 94%) as a colorless powder, mp 132.5–133.5 °C: IR (KBr) 2841, 1699, 1603 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 1.21 (3H, s), 1.22 (6H, d, J = 6.8 Hz), 1.48–1.63 (2H, m), 1.81 (3H, d, J = 0.9 Hz), 2.03–2.11 (1H, m), 2.31–2.65 (3H, m), 2.68 (1H, ddd, J = 17.8, 12.2, 6.5 Hz), 3.03–3.11 (1H, m), 3.25–3.37 (2H, m), 3.68 (3H, s), 3.79 (3H, s), 6.60 (1H, s); ^{13}C NMR (67.5 MHz, $CDCl_3$) δ 13.9 (q), 17.1 (q), 19.8 (t), 23.7 (q), 23.8 (q), 26.0 (t), 26.4(t), 26.4 (d), 32.1 (t), 37.3 (s), 47.2 (d), 55.2 (q), 60.6 (q), 107.1 (d), 118.3 (q), 127.2 (s), 130.8 (s), 131.8 (s), 139.1 (s), 143.6 (s), 149.0 (s), 155.1 (s); MS, m/z 462 (M^+); HRMS calcd for $C_{22}H_{29}O_5SF_3$ 462.1688, found 462.1701.

(4a*S,10a*R**)-5,8-Dimethoxy-1,4a-dimethyl-7-isopropyl-3,4,4a,9,10,10a-hexahydrophenanthrene-2-carbaldehyde ((±)-29a).** A mixture of **31** (11.4 g, 24.6 mmol), $(Ph_3P)_4Pd$ (28.5 g, 23.0 mmol), and LiCl (2.1 g, 50.3 mmol) in THF (570 mL) was stirred at rt for 15 min, and then the mixture was allowed to warm to 50 °C. After the mixture was stirred at the same temperature for 2 h under an atmosphere of carbon monoxide, a solution of *n*-Bu_3SnH (8.4 g, 28.8 mmol) in THF (355 mL) was added over 3.5 h, and the mixture was stirred at 50 °C for 21 h. It was then diluted with water, extracted with Et_2O, washed (saturated brine), dried ($MgSO_4$), and concentrated. Chromatographic purification on silica gel (20:300:3 Et_2O/hexane/$CHCl_3$) gave **29a** (8.0 g, 95%) as colorless prisms, mp 137–139 °C. Compound **29a** thus obtained was completely identical in all respects to the authentic material prepared from **28**.

(4a*S,10a*R**)-5,8-Dimethoxy-1,4a-dimethyl-7-isopropyl-3,4,4a,9,10,10a-hexahydrophenanthrene-2-carboxylic Acid ((±)-4). (a) From 29a.** Sulfamic acid (3.7 mg, 0.038 mmol) and sodium chlorite (3.5 mg, 0.038 mmol) were successively added to a solution of **29a** (9.9 mg, 0.03 mmol) in 50% aqueous dioxane (1.4 mL), and the resulting mixture was stirred at rt for 30 min. It was then diluted with water, extracted with $CHCl_3$, washed (saturated brine), dried ($MgSO_4$), and concentrated to give a residue, which was chromatographed on silica gel (20:1 $CHCl_3$/MeOH) to afford (±)-**4** (7.0 mg, 68%) as a yellowish orange crystalline powder, mp 224–225 °C, after recrystallization from $CHCl_3$ and hexane: IR (KBr) 2943, 1675, 1606 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 1.15 (3H, s), 1.22 (3H, d, J = 6.8 Hz), 1.23 (3H, d, J = 6.8 Hz), 1.53–1.66 (2H, m), 2.17 (3H, m), 2.15–2.25 (1H, m), 2.33–2.43 (2H, m), 2.55–2.75 (2H, m), 2.93 (1H, ddd, J = 13.1, 7.5, 3.7 Hz), 3.05–3.15 (1H, m), 3.31 (1H, sept, J = 6.8 Hz), 3.70 (3H, s), 3.80 (3H, s), 6.60 (1H, s); MS, m/z 358 (M^+). Anal. Calcd for $C_{22}H_{30}O_4$: C, 73.71; H, 8.44. Found: C, 74.02; H, 8.31.

From 31. A mixture of **31** (200 mg, 0.4 mmol), *n*-Bu_3N (160 mg, 0.8 mmol), $Pd(OAc)_2$ (2.6 mg, 0.012 mmol), and DPPF (14.4 mg, 0.026 mmol) in DMF (1.73 mL)–water (0.78 mL) was heated at 95 °C for 3.5 h under an atmosphere of carbon monoxide. The reaction mixture was diluted with water, extracted with Et_2O, washed (saturated brine), and dried ($MgSO_4$). Evaporation of the solvent followed by column chromatography on silica gel (20:1 $CHCl_3$/MeOH) and subsequent recrystallization from $CHCl_3$/hexane provided (±)-**4** (83 mg, 54%), which was identical to the authentic material prepared above.

(±)-Triptoquinone A ((±)-1). A solution of CAN (18.6 g, 33.9 mmol) in water (110 mL) was added to a stirred solution of (±)-**4** (5.5 g, 15.4 mmol) in MeCN (440 mL) at rt. After being stirred at the same temperature for 35 min, the mixture was diluted with water, extracted with $CHCl_3$, washed (saturated brine), and dried ($MgSO_4$). Removal of the solvent gave a residue, which was chromatographed on silica gel (30:1 $CHCl_3$/MeOH) to afford (±)-**1** (4.2 g, 83%) as a yellowish-orange solid, mp 208–209

°C: IR (KBr) 2967, 1648 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.11 (3H, d, J = 6.8 Hz), 1.12 (3H, d, J = 6.8 Hz), 1.18 (3H, s), 1.41–1.56 (2H, m), 2.11 (3H, d, J = 1.4 Hz), 2.21–2.30 (2H, m), 2.39 (1H, ddd, J = 20.3, 11.5, 6.8 Hz), 2.41–2.61 (2H, m), 2.75–2.83 (2H, m), 3.01 (1H, sept d, J = 6.8, 1.0 Hz), 6.38 (1H, s); ^{13}C NMR (67.5 MHz, $CDCl_3$) δ 18.4 (q), 18.7 (t), 19.1 (q), 21.3 (q), 21.4 (q), 24.4 (t), 25.1 (t), 26.3 (d), 31.8 (t), 36.5 (s), 47.3 (d), 124.6 (s), 131.7 (d), 142.4 (s), 148.0 (s), 148.6 (s), 153.1 (s), 174.4 (s), 187.4 (s), 187.7 (s); MS, m/z 328 (M$^+$); HRMS calcd for $C_{20}H_{24}O_4$ 328.1674, found 328.1674. Anal. Calcd for $C_{20}H_{24}O_4 \cdot {}^1/_3H_2O$: C, 71.83; H, 7.43. Found: C, 71.94; H, 7.51.

(+)-(4a*S*)-5,8-Dimethoxy-1,4a-dimethyl-7-isopropyl-4,4a,9,-10-tetrahydro-2(3*H*)-phenanthrenone ((+)-7) and (+)-(1*R*)-5,8-Dimethoxy-6-isopropyl-1-methyl-(3-oxopentyl)-2-tetralone ((+)-32). Aqueous (60%) KOH (13.5 mL) was added to a solution of **8** (7.0 g, 26.7 mmol) and (−)-*N*-(*p*-trifluoromethyl)-benzylcinchonidinium bromide (**33**) (1.42 g, 2.67 mmol) in toluene (500 mL) at 0 °C. After the mixture stirred at −45 °C for 30 min, ethyl vinyl ketone (3.37 g, 40.0 mmol) was added, and the mixture was stirred at the same temperature for 1 h and then at rt for 16 h. To the mixture was added 18-crown-6 (1.46 g, 5.54 mmol), and the resulting solution was stirred at rt for 24 h. It was then treated with an aqueous solution (12 mL) of citric acid (2.57 g, 13.3 mmol), extracted with Et_2O, washed (saturated brine), dried ($MgSO_4$), and concentrated to leave a residue, which was chromatographed on silica gel (1:5 Et_2O/hexane) to afford (+)-**7** (2.0 g, 23%) as colorless prisms, mp 174 °C, after recrystallization from EtOH. The spectral data of this material were consistent with those of the racemate: $[\alpha]_D$ +360° (*c* 0.60). From the later fractions, (+)-**32** (1.8 g, 19%) was obtained as a colorless oil: $[\alpha]_D$ +213° (*c* 0.75); IR (film) 2964, 1714, 1604 cm^{-1}; ^{1}H NMR (270 MHz, $CDCl_3$) δ 0.92 (3H, t, J = 7.3 Hz), 1.23 (3H, d, J = 7.0 Hz), 1.24 (3H, d, J = 7.0 Hz), 1.53 (3H, s), 1.71–1.89 (1H, m), 2.05–2.60 (6H, m), 2.65–2.91 (2H, m), 3.22–3.42 (2H, m), 3.66 (3H, s), 3.80 (3H, s), 6.65 (1H, s); ^{13}C NMR (67.5 MHz, $CDCl_3$) δ 7.7 (q), 23.3 (t), 23.6 (q), 23.8 (q), 25.1 (q), 26.5 (d), 29.7 (t), 35.4 (t), 36.9 (t), 39.2 (t), 51.2 (s), 55.2 (q), 61.1 (q), 107.9 (d), 127.6 (s), 130.9 (s), 140.2 (s), 147.9 (s), 154.8 (s), 211.1 (s), 214.0 (s); MS, m/z 346 (M$^+$); HRMS calcd for $C_{21}H_{30}O_4$ 346.2143, found 346.2152.

Conversion of (+)-32 into (+)-7. KOH (70 mg, 1.25 mmol) was added to a solution of (+)-**32** (400 mg, 1.16 mmol) in 93% aqueous MeOH (2.7 mL). After being stirred at rt for 24 h, the mixture was acidified with 10% HCl, extracted with Et_2O, washed (saturated brine), and dried ($MgSO_4$). Evaporation of the solvent followed by column chromatography on silica gel (1:5 Et_2O/hexane) gave (+)-**7** (310 mg, 82%) as a colorless oil, whose optical rotation and spectral properties were identical to the authentic material.

(+)-(4a*S*,10a*R*)-5,8-Dimethoxy-1,4a-dimethyl-7-isopropyl-2-((trimethylsilyl)oxy)-3,4,4a,9,10,10a-hexahydrophenanthrene ((+)-30). By means of the procedure described for the preparation of (±)-**30**, (+)-**7** was converted into (+)-**30** (as colorless prisms, mp 78 °C) after recrystallization from hexane: $[\alpha]_D$ +120° (*c* 0.60).

(+)-(4a*S*,10a*R*)-5,8-Dimethoxy-1,4a-dimethyl-7-isopropyl-2-(trifluoromethanesulfonyloxy)-3,4,4a,9,10,10a-hexahydrophenanthrene ((+)-31). By means of the procedure described for the preparation of (±)-**31**, (+)-**30** was converted into (+)-**31** (as colorless prisms, mp 136–136.5 °C; $[\alpha]_D$ +122° (*c* 0.46)).

(+)-(4a*S*,10a*R*)-Methyl 5,8-Dimethoxy-1,4a-dimethyl-7-isopropyl-3,4,4a,9,10,10a-hexahydrophenanthrene-2-carboxylate ((+)-34). *n*-Bu_3N (160 mg, 0.44 mmol) was added to a mixture of (+)-**31** (110 mg, 0.24 mmol), $Pd(OAc)_2$ (1.43 g, 0.012 mmol), and DPPF (14.4 mg, 0.014 mmol) in DMF (0.95 mL)–MeOH (0.43 mL), and the mixture was stirred at 90 °C for 1 h under an atmosphere of carbon monoxide. The mixture was then diluted with water, extracted with Et_2O, washed (saturated brine), dried ($MgSO_4$), and concentrated to leave a residue, which was chromatographed on silica gel (1:10 Et_2O/hexane) to afford (+)-**34** (88 mg, 99%) as colorless prisms, mp 83–85 °C: $[\alpha]_D$ +179° (*c* 0.30); IR (film) 2960, 1712 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.15 (3H, s), 1.22 (3H, d, J = 6.8 Hz), 1.23 (3H, d, J = 6.8 Hz), 1.50–1.63 (2H, m), 2.06 (3H, d, J = 1.5 Hz), 2.14–2.22 (1H, m), 2.29–2.39 (2H, m), 2.48–2.71 (2H, m), 2.97 (1H, ddd, J = 13.0, 7.5, 3.6 Hz), 3.05–3.11 (1H, m), 3.31 (1H, sept, J = 6.8 Hz), 3.69 (3H, s), 3.75 (3H, s), 3.79 (3H, s), 6.60 (1H, s); ^{13}C NMR (67.5 MHz, $CDCl_3$) δ 18.3 (q), 18.6 (q), 19.8 (t), 23.8 (q), 23.9 (q), 25.1 (t), 26.4 (t), 26.4 (d), 32.6 (t), 37.4 (s), 48.4 (d), 51.1 (q), 55.2 (q), 60.6(q), 107.1 (d), 125.1 (s), 130.8 (s), 133.3 (s), 138.7 (s), 146.4 (s), 148.8 (s), 155.1 (s), 169.8 (s); MS, m/z 372 (M$^+$); HRMS calcd for $C_{23}H_{32}O_4$ 372.2300, found 372.2268.

(+)-(4a*S*,10a*R*)-5,8-Dimethoxy-1,4a-dimethyl-7-isopropyl-3,4,4a,9,10,10a-hexahydrophenanthrene-2-carboxylic Acid ((+)-4). A solution of 0.9 N NaOH (1.6 mL) was added to a solution of (+)-**34** (85 mg, 0.23 mmol) in MeOH (7 mL), and the solution was stirred at 60 °C for 3 d. The mixture was acidified with 10% HCl and extracted with $CHCl_3$. The extracts were washed (saturated brine), dried ($MgSO_4$), and concentrated. Column chromatography on silica gel (30:1 $CHCl_3$/MeOH) of the crude product gave (+)-**4** (81 mg, 99%), whose spectral data are consistent with those of the racemate, as colorless prisms, mp 182–185 °C: $[\alpha]_D$ +198° (*c* 0.30).

(+)-Triptoquinone A ((+)-1). By means of the procedure described for the preparation of (±)-**1**, (+)-**4** was converted into (+)-**1**, as a yellowish crystalline powder, mp 175 °C: $[\alpha]_D$ +125° (*c* 0.34).

(+)-(1*S*,4a*S*,10a*R*)-3,4,4a,9,10,10a-Hexahydro-1-(hydroxymethyl)-1,4a-dimethyl-5,8-dimethoxy-7-isopropyl-2(1*H*)-phenanthrenone ((+)-36). A solution of $Na_2S_2O_4$ (450 mg, 2.6 mmol) was added to a solution of triptoquinone B ((+)-**2**) (45 mg, 0.14 mmol) in THF (2 mL) at rt. After being stirred for 30 min, the mixture was diluted with water, extracted with Et_2O, washed (saturated brine), dried ($MgSO_4$), and concentrated to give a residue, which was taken up into acetone (2 mL). To the solution were added K_2CO_3 (159 mg, 1.2 mmol) and dimethyl sulfate (154 mg, 1.2 mmol). The resulting mixture was heated under reflux for 3 h, acidified with 10% HCl, and extracted with Et_2O. The ethereal extract was washed (saturated brine), dried ($MgSO_4$), concentrated, and chromatographed on silica gel (20:1 $CHCl_3$/AcOEt) to afford (+)-**36** (43 mg, 88%) as colorless prisms, mp 133–134 °C: $[\alpha]_D$ +226° (*c* 0.70); IR (film) 3496, 2964, 1694, 1648, 1604 cm^{-1}; ^{1}H NMR (270 MHz, $CDCl_3$) δ 1.21 (3H, d, J = 6.9 Hz), 1.23 (3H, d, J = 6.9 Hz), 1.26 (3H, s), 1.41 (3H, s), 1.40–1.55 (1H, m), 1.18–2.08 (2H, m), 2.15–2.26 (1H, m), 2.36 (1H, ddd, J = 14.7, 9.0, 4.0 Hz), 2.48–2.65 (1H, m), 2.75 (1H, ddd, J = 14.7, 10.9, 6.9 Hz), 3.00 (1H, ddd, J = 13.7, 9.0, 6.9 Hz), 3.05–3.15 (1H, m), 3.30 (1H, sept, J = 6.9 Hz), 3.43 (1H, d, J = 11.3 Hz), 3.67 (3H, s), 3.78 (3H, s), 4.18 (1H, d, J = 11.3 Hz), 6.60 (1H, s); MS, m/z 360 (M$^+$). Anal. Calcd for $C_{22}H_{32}O_4$: C, 73.30; H, 8.95. Found: C, 73.13; H, 9.13.

(+)-(1*S*,4a*S*,10a*R*)-3,4,4a,9,10,10a-Hexahydro-1,4a-dimethyl-5,8-dimethoxy-7-isopropyl-2(1*H*)-phenanthrenone ((+)-35). From (+)-7. Li (7.6 mg, 1.1 mg atm) was added in portions to liquid NH_3 (5 mL), which had been distilled over Na, at -78 °C, and the solution was stirred at the same temperature for 10 min. A solution of (+)-**7** (60 mg, 0.18 mmol) in THF (1 mL) was added at −78 °C, and the resulting mixture was stirred for 2 h and treated with isoprene (2.0 mg, 0.03 mmol). The solvent was removed under a stream of nitrogen to leave a residue, which was then diluted with 10% HCl. It was then extracted with Et_2O, and the organic phases were washed (saturated brine), dried ($MgSO_4$), and concentrated to give an oily residue, which was chromatographed on silica gel (10:100:1 Et_2O/hexane/$CHCl_3$) to provide (+)-**35** (1.8 mg, 3%) as a colorless oil: $[\alpha]_D$ +150° (*c* 0.02); IR (neat) 2964, 1710 cm^{-1}; ^{1}H NMR (270 MHz, $CDCl_3$) δ 1.13 (3H, d, J = 6.6 Hz), 1.22 (3H, d, J = 6.9 Hz), 1.24 (3H, d, J = 6.9 Hz), 1.42 (3H, s), 1.41–1.71 (3H, m), 1.87–1.98 (1H, m), 2.38–2.58 (4H, m), 2.98–3.11 (2H, m), 3.25–3.37 (2H, m), 3.68 (3H, s), 3.80 (3H, s), 6.61 (1H, s); ^{13}C NMR (67.5 MHz, $CDCl_3$) δ 12.3 (q), 17.4 (q), 21.5 (t), 23.7 (q), 23.8 (q), 26.2 (t), 26.3 (d), 35.6 (t), 37.9 (t), 38.1 (s), 44.6 (d), 51.4 (d), 55.1 (q), 60.6 (q), 107.1 (d), 131.2 (s), 132.3 (s), 138.9 (s), 148.8 (s), 155.0 (s), 213.7 (s); MS, m/z 330 (M$^+$); HRMS calcd for $C_{21}H_{30}O_3$ 330.2195, found 330.2186.

From (+)-36. A solution of (+)-**36** (1.4 g, 3.9 mmol) and $NaHCO_3$ (1.6 g, 19.6 mmol) in MeOH (70 mL) was heated under reflux for 14.5 h. The solvent was evaporated to leave a residue, which was diluted with water and extracted with Et_2O. The ethereal extract was washed (saturated brine), dried ($MgSO_4$), concentrated, and chromatographed on silica gel (1:5 Et_2O/hexane) to give (+)-**35** (470 mg, 37%) as a colorless oil, which was identical to the authentic material derived from (+)-**7**: $[\alpha]_D$ +151° (*c* 1.00)

(+)-(1*S*,2*S*,4a*S*,10a*R*)-1,2,3,4,4a,9,10,10a-Octahydro-2-hydroxy-1-(hydroxymethyl)-1,4a-dimethyl-5,8-dimethoxy-7-isopropylphenanthrene ((+)-37). A solution of (+)-**36** (116 mg, 0.32 mmol) in THF (3 mL) was added to a suspension of $LiAlH_4$ (41 mg, 1.1 mmol) in THF (1 mL) at 0 °C. After being stirred at 0 °C for 1 h, the mixture was carefully quenched with water and extracted with Et_2O. The organic phases were washed (saturated brine), dried ($MgSO_4$), concentrated, and chromatographed on silica gel (3:1 $CHCl_3$/AcOEt) to give (+)-**37** (90 mg, 77%) as colorless prisms, mp 177–179 °C, after recrystallization from Et_2O and hexane: $[\alpha]_D$ +105° (*c* 0.36); IR (KBr) 3381, 2961, 1601 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 1.20 (3H, d, *J* = 6.8 Hz), 1.21 (3H, d, *J* = 6.8 Hz), 1.23 (3H, s), 1.23–1.28 (1H, m), 1.31 (3H, s), 1.33 (1H, d, *J* = 12.7 Hz), 1.38–1.51 (1H, m), 1.75–1.83 (1H, m), 1.88–2.01 (2H, m), 2.61 (1H, ddd, *J* = 17.5, 12.3, 6.3 Hz), 3.02 (1H, dd, *J* = 17.5, 4.2 Hz), 3.15 (1H, ddd, *J* = 13.7, 3.7, 3.7 Hz), 3.27 (1H, sept, *J* = 6.8 Hz), 3.38 (1H, d, *J* = 11.3 Hz), 3.51 (1H, dd, *J* = 12.0, 4.7 Hz), 3.67 (3H, s), 3.77 (3H, s), 4.32 (1H, d, *J* = 11.3 Hz), 6.57 (1H, s); MS, *m/z* 362 (M^+); HRMS calcd for $C_{22}H_{34}O_4$ 362.2458, found 362.2474. Anal. Calcd for $C_{22}H_{34}O_4$: C, 72.89; H, 9.45. Found: C, 72.68; H, 9.66.

(−)-Triptoquinone C ((−)-3). A solution of CAN (255 mg, 0.46 mmol) in water (3.5 mL) was added to a solution of (+)-**37** (80 mg, 0.22 mmol) in MeCN (12 mL) at rt. After being stirred at rt for 20 min, the mixture was diluted with water, extracted with Et_2O, washed (saturated brine), dried ($MgSO_4$), and concentrated. Chromatographic purification of the crude material on silica gel (3:1 $CHCl_3$/AcOEt) afforded (−)-**3** (57 mg, 78%) as a yellowish crystalline powder, mp 176-178 °C, after recrystallization from hexane. The material thus obtained was completely identical in all respects to the natural product: $[\alpha]_D$ −63° (*c* 0.13).

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