Pergamon

Tetrahedron 57 (2001) 8425–8442

TETRAHEDRON

Common synthetic strategy for optically active cyclic terpenoids having a 1,1,5-trimethyl-*trans*-decalin nucleus: syntheses of (+)-acuminolide, (−)-spongianolide A, and (+)-scalarenedial

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Received 6 July 2001; accepted 6 August 2001

Abstract—We have developed a simple and practical method for providing enantiomerically pure bi-, tri-, and tetracyclic frameworks having a 1,1,5-trimethyl-trans-decalin nucleus, and demonstrated their utility for terpenoid synthesis. Thus, we achieved the stereocontrolled total syntheses of (+)-acuminolide as a bicyclic, (−)-spongianolide A as a tricyclic, and (+)-scalarenedial as a tetracyclic terpenoid from the corresponding optically pure cyclic β-ketoesters, which were obtained by repeating the same method of the ring construction, including the olefin cyclization with Lewis acid, followed by simple optical resolution using chiral auxiliaries for acetal formation, respectively. This is a general and valuable strategy for the synthesis of enantiomerically pure cyclic terpenoids having the 1,1,5-trimethyl-*trans*-decalin nucleus.

1. Introduction

The carbon skeleton consisting of a 1,1,5-trimethyl-*trans*-decalin nucleus is found in typical terpenoids such as drimane sesquiterpene and labdane diterpene, and some of them have been paid much attention because of their attractive biological activities represented by warburganal[1] and forskolin.[2] In addition to these terpenes, acuminolide,[3] spongianolide A,[4] and scalarenedial[5] can also be listed as biologically interesting bi-, tri-, and tetracyclic terpenes having a 1,1,5-trimethyl-*trans*-decalin nucleus (Fig. 1). Some methods for synthesis of optically active terpenoids having this nucleus have been developed including (1) the derivation of the commercially available natural terpenoids, (−)-sclareol[6] or (+)-sclareolide,[7] (2) biological resolution[8] by an enzyme or microorganism, and (3) enantio- or diastereoselective polyene cyclization.[9] Among them, biomimetic cyclization of polyenes bearing a chiral epoxide by treatment with Lewis acid or of *dl*-polyenes with a chiral Lewis acid are very attractive and efficient methods. It

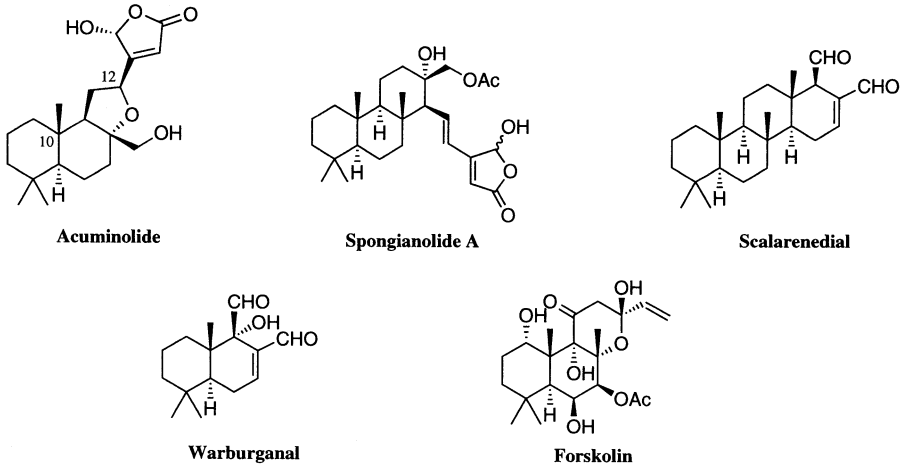

Figure 1. Natural terpenoids having 1,1,5-trimethyl-*trans*-decalin nucleus.

Keywords: terpenes and terpenoiods; biologically active compounds; common synthetic strategy; 1,1,5-trimethyl-*trans*-decalin nucleus.
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PII: S0040-4020(01)00825-0

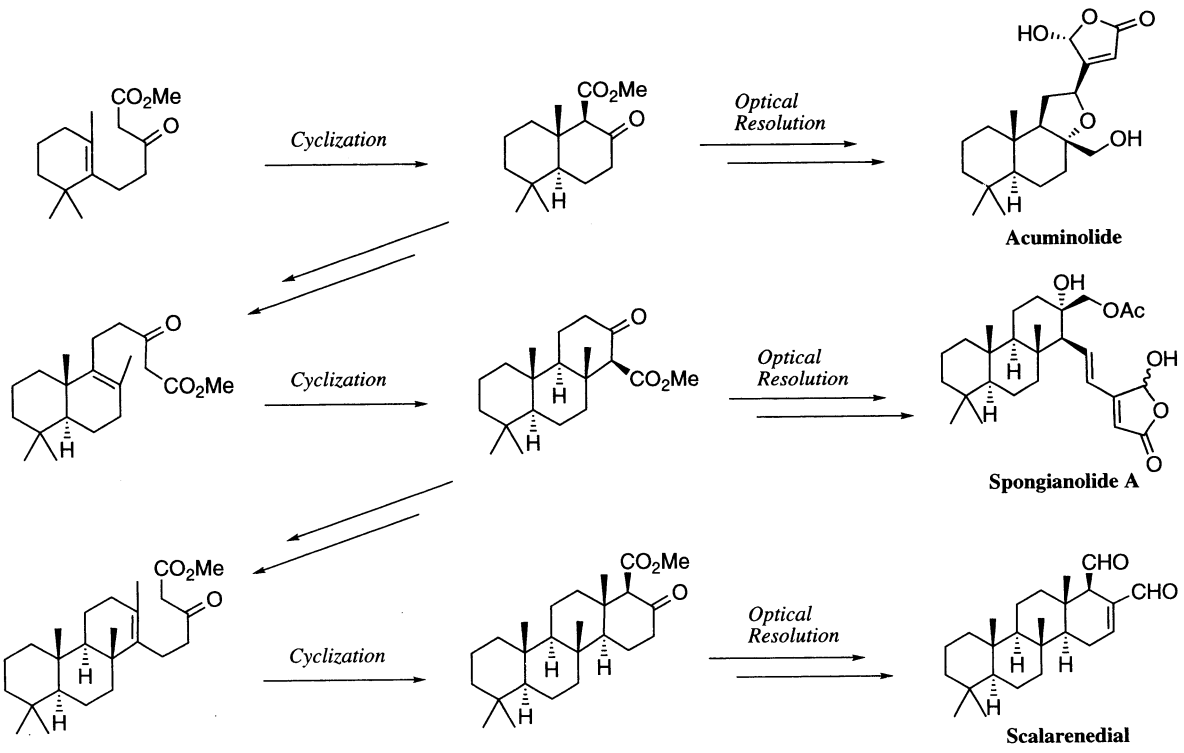


Figure 2. Synthetic strategy.

seems, however, that there is some limitation to application of this biomimetic cyclization to the syntheses of a wide variety of terpenoids having a 1,1,5-trimethyl-*trans*-decalin nucleus, because suitable polyene structures for the smooth cyclization are confined, and their synthesis is not necessarily simple.

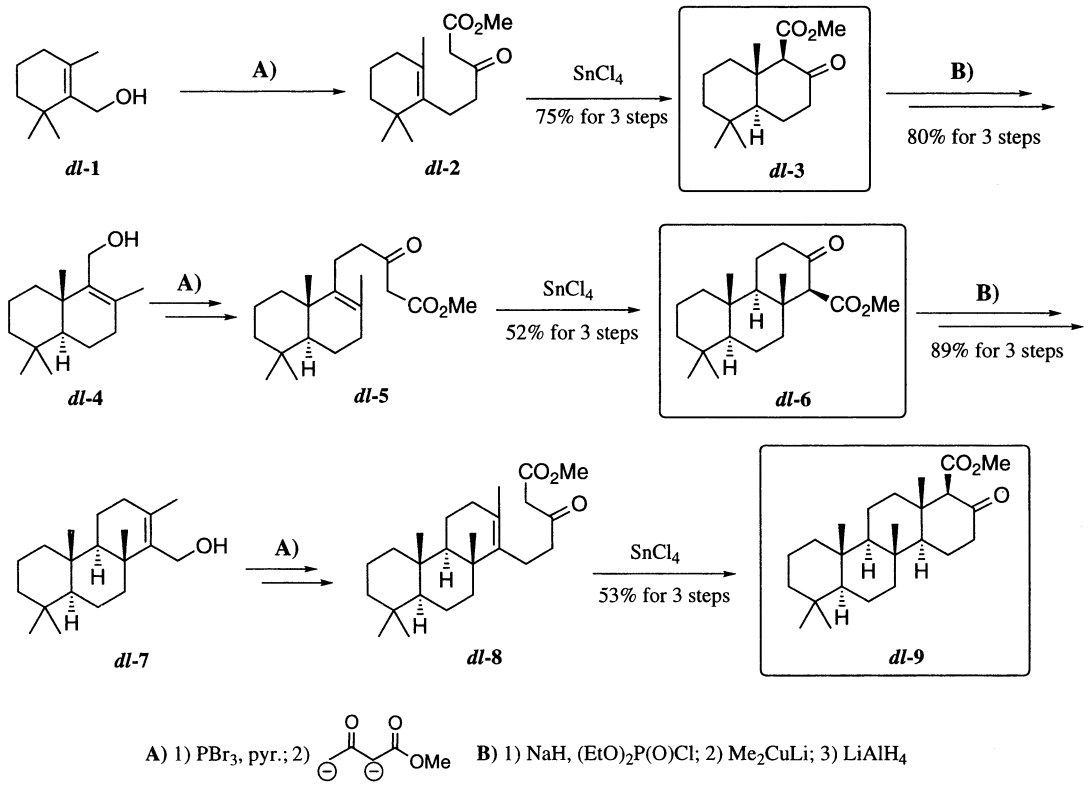
Our common strategy to synthesize the enantiomerically pure bi-, tri-, and tetracyclic skeleton bearing the 1,1,5-trimethyl-*trans*-decalin nucleus, is to repeat a sequence of the reactions for ring construction starting from cyclogeraniol via linear β-ketoester formation and then olefin cyclization with Lewis acid to yield the corresponding bicyclic β-ketoester. This method is easily applicable to the ring construction from the bicyclic to the tricyclic, and from the tricyclic to the tetracyclic β-ketoesters, with high stereoselectivity. Furthermore, the cyclic β-ketoesters thus obtained would be simply resolved by the same procedure using the same chiral auxiliaries for an acetal formation. In order to demonstrate the feasibility of this strategy, we planned to synthesize some biologically interesting di- and sesterterpenoids, and selected (+)-acuminolide, (−)-spongianolide A, and (−)-scalarenedial as the target molecules, which contain a bi-, tri-, and tetracyclic framework and an unsaturated aldehyde function, respectively (Fig. 2).

(+)-Acuminolide,[3] which is a highly oxidized diterpene possessing a γ-hydroxybutenolide function, was isolated from the stem bark of a tree, *Neouvaria acuminatissima*, and its two-dimensional structure was determined by X-ray crystallography, but its absolute configuration had not been confirmed. This terpene was reported to display cytotoxic activity in human cancer cell lines and cultured P388 cells, and the most potent activity was observed in melanoma (Me12) (ED_{50} 0.7 μg mL^{-1}) and prostate (LNCaP) (ED_{50} 0.8 μg mL^{-1}) cells.

(−)-Spongianolide A,[4] which was isolated along with spongianolide B–F from a marine sponge, *Spongia* sp., is a tricyclic sesterterpene, and was reported to inhibit proliferation of the mammary tumor cell line MCF-7 (IC_{50} 0.5–1.4 μM) and protein kinase C (PKC) (IC_{50} 20–30 μM). Thus, some terpenoids possessing a γ-hydroxybutenolide moiety represented by manoalide, which strongly inhibits phospholipase A_2 (PLA_2),[10] and dysidiolide,[11] which shows antimitotic activity, as well as in acuminolide and spongianolide A have been proposed to show quite attractive biological activities.

(−)-Scalarenedial,[5] which contains a 6/6/6/6 fused ring system, was isolated from a marine sponge, a specimen of *C. mollor*, and shows not only antitumor and anti-inflammatory but also fish antifeedant property (LD_{50} 0.77 μg mL^{-1} in the *Artemia salina* shrimp bioassay). (−)-Scalarenedial strongly inhibits the hydrolytic activity of the hydrolytic enzyme, phospholipase A_2 (PLA_2), as well as manoalide.[12] In connection with our interest in elucidating the inhibitory mechanism of PLA_2 by some aldehyde terpenoids represented by manoalide[10] or scalaradial,[12] the stereocontrolled simple synthesis of the enantiomerically pure tetracyclic scalarenedial is also a very attractive subject. In scalaradial, it was reported that the presence of a bulky group in the C-12 position, such as an acetoxy group, might decrease the inhibitory activity toward PLA_2.[5]

Herein, we report in detail the stereocontrolled total



Scheme 1.

syntheses of the optically active (+)-acuminolide,[14] (−)-spongianolide A,[15] and (+)-scalarenedial,[16] and the determination of the absolute configurations of the former two. In these syntheses, we demonstrate a simple, practical and efficient common strategy for the synthesis of optically active cyclic terpenoids bearing the 1,1,5-trimethyl-*trans*-decalin nucleus.

2. Results and discussion

2.1. Preparation of the bi-, tri-, and tetracyclic frameworks by means of Lewis acid-mediated olefin cyclization

As a basic intermediate for the synthesis of cyclic terpenoids bearing a 1,1,5-trimethyl-*trans*-decalin nucleus, we chose racemic bicyclic β-ketoester **3**,[17] which was simply prepared from cyclogeraniol **1** by a sequence of bromination, condensation with the dianion of methyl acetoacetate, and then cyclization by a tin tetrachloride treatment (Scheme 1). Use of tin tetrachloride in absolute dichloromethane substantially improved the yield of the cyclization. The bicyclic β-ketoester **3** was transformed into bicyclic allyl alcohol **4** by enol phosphonate formation with sodium hydride and diethylchlorophosphate, introduction of a methyl group with lithium dimethyl-cuprate, and then lithium aluminum hydride reduction of the ester group in 80% yield for three steps. Next, we applied the same sequence as that from **1** into **3**, to the allyl alcohol **4** and obtained tricyclic β-ketoester **6** through linear β-ketoester **5** by bromination, β-ketoester formation, and then cyclization, in 52% yield. Furthermore, by using the same procedure, efficient transformation of the tricyclic β-ketoester **6** into tetracyclic β-ketoester **9** was successfully realized through tricyclic allyl alcohol **7** and linear β-ketoester **8**. Initially, we anticipated a low cyclization yield because of the relatively low solubility of **8** in CH_2Cl_2 and the characteristic 6/6/6/6 fused ring system of **9**. Quite fortunately, no serious problems were incurred in the tetracyclic ring construction, and the tetracyclic **9** was easily obtained in 53% overall yield from **7**.

Thus, by using the same olefin cyclization procedure, we efficiently obtained bi-, tri-, and tetracyclic β-ketoesters **3**, **6**, and **9** as racemic forms.

2.2. Optical resolution for preparation of the enantiomerically pure cyclic β-ketoesters, and determination of their absolute configurations

Resolution of the enantiomers of β-ketoesters **3**, **6**, and **9** thus synthesized was achieved by utilization of a chiral auxiliary for acetal formation. We established two effective resolution methods using the chiral 1,2-diol derivatives, (2*R*,3*R*)-2,3-butanediol (**A**) and 1,4-di-*O*-benzyl-L-threitol (**B**)[18] (Fig. 3).

Reaction of the bicyclic β-ketoester **3** with commercially

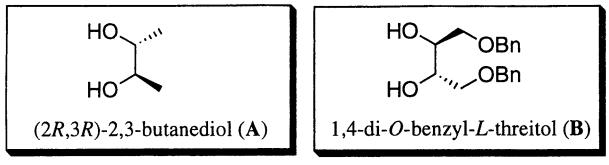
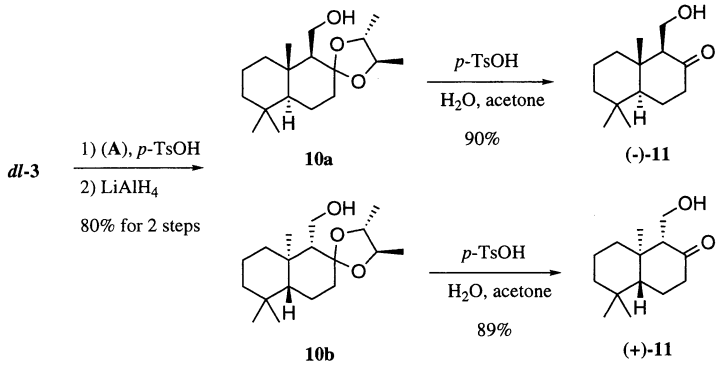


Figure 3. Optically active 1,2-diol derivatives as chiral auxiliaries.



Scheme 2.

available (**A**), gave the corresponding acetal as a diastereomeric mixture. Unfortunately, these diastereomers were not easily separated. A mixture of **10a** and **10b**, which were obtained by reduction of the ester group, however, was nicely separated by column chromatography on silica gel (eluted with hexane containing from 2 to 10% ethyl acetate). Thereafter, hydrolysis of the acetal by treatment with a catalytic amount of *p*-TsOH in acetone and water at room temperature gave the enantiomerically pure bicyclic β-ketoalcohol (+)- and (−)-**11** without dehydration, respectively (Scheme 2). Fortunately, the same procedure as that for **3** could be applied to the tricyclic β-ketoester **6** (Scheme 3). Thus, the enantiomerically pure tricyclic β-ketoalcohol **13** was readily obtained via the corresponding alcohol **12**. The absolute configurations of **11** and **13** obtained were identical with those reported, namely (−)-**11** was (5*S*,9*S*,10*S*)[19] and (+)-**13** was (5*S*,8*R*,9*R*,10*S*,14*S*),[20] respectively.

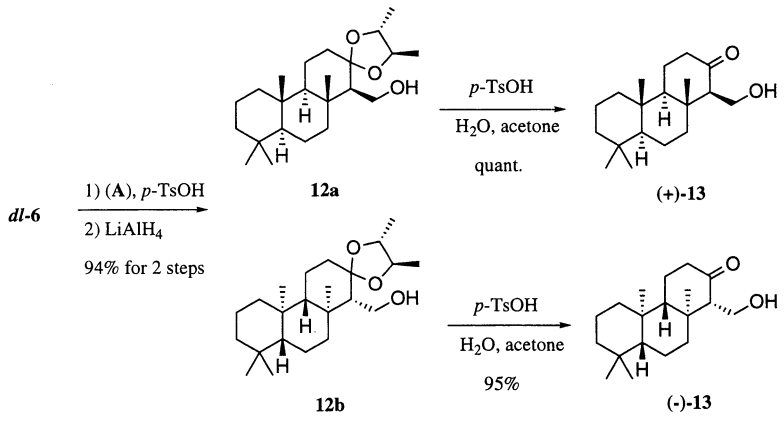
Furthermore, we also tried another route to obtain the enantiomerically pure cyclic β-ketoesters from the corresponding racemic forms by using the chiral auxiliary (**B**) (Scheme 4). Acetal formation of the bicyclic β-ketoester **3** with chiral 1,2-diol (**B**), and then removal of the benzyl group by hydrogenation produced diol **14**. The diastereomeric mixture of **14** was also nicely separated by column chromatography on silica gel (eluted with $CHCl_3$ containing from 1 to 6% CH_3OH). Then, acid treatment of each of them gave the enantiomerically pure bicyclic β-ketoesters (+)-, and (−)-**3**, respectively. By applying this resolution method to the tri-, and tetracyclic β-ketoesters **6** and **9**, we obtained the enantiomerically pure tri-, and tetracyclic β-ketoesters via the corresponding diols **15** and **16** (Scheme 4).

In order to determine the absolute configuration of the respective β-ketoesters, enantiomerically pure (−)-**3** was transformed into a sesquiterpene, albicanol, by a sequence of Wittig olefination and then reduction of the ester group. The spectral data of albicanol thus synthesized were in good agreement with those of (5*S*,9*S*,10*S*)-(+)-albicanol ($[\alpha]_D^{24}=+10.4$ (*c* 0.55, $CHCl_3$), literature[19] $[\alpha]_D^{20}=+13$ (*c* 0.6, $CHCl_3$)). Thus, the absolute configuration of (−)-**3** was determined as (5*S*,9*R*,10*S*). The optical rotation values of tri-, and tetracyclic β-ketoesters **6** and **9** thus resolved were identical with those of the corresponding compounds, which were derived from (−)-**3**, respectively. Accordingly, the absolute configurations of (+)-**6** and (−)-**9** were determined as (5*S*,8*R*,9*R*,10*S*,14*S*) and (5*S*,8*R*,9*R*,10*S*,13*S*, 14*S*,18*R*), respectively (Scheme 5).

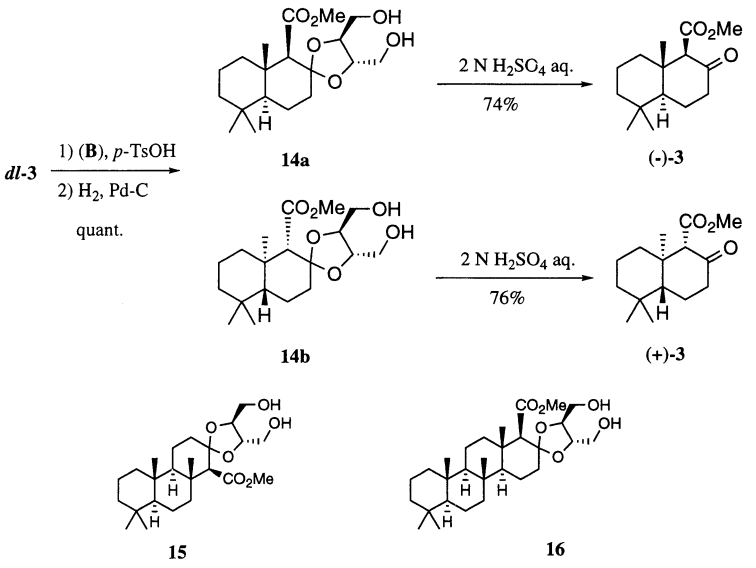
Thus, we succeeded in the preparation of enantiomerically homogeneous cyclic β-ketoesters **3**, **6**, and **9**, and β-ketoalcohols **11** and **13** via olefin cyclization and then simple optical resolution. These compounds would be important as chiral intermediates for the terpenoid synthesis.

2.3. Total synthesis of a bicyclic diterpene, (+)- and (−)-acuminolide, and determination of its absolute configuration

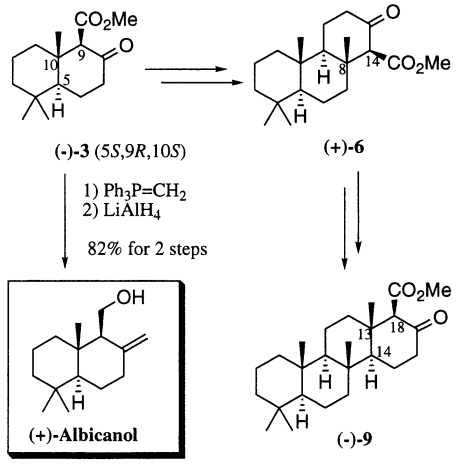
The first synthesis of acuminolide was reported in 1998 by Zoretic and co-workers starting from commercially



Scheme 3.



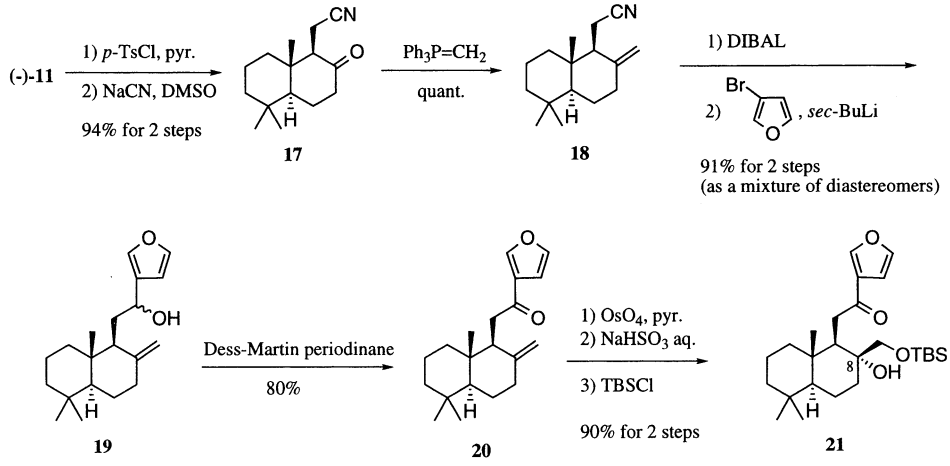
Scheme 4.



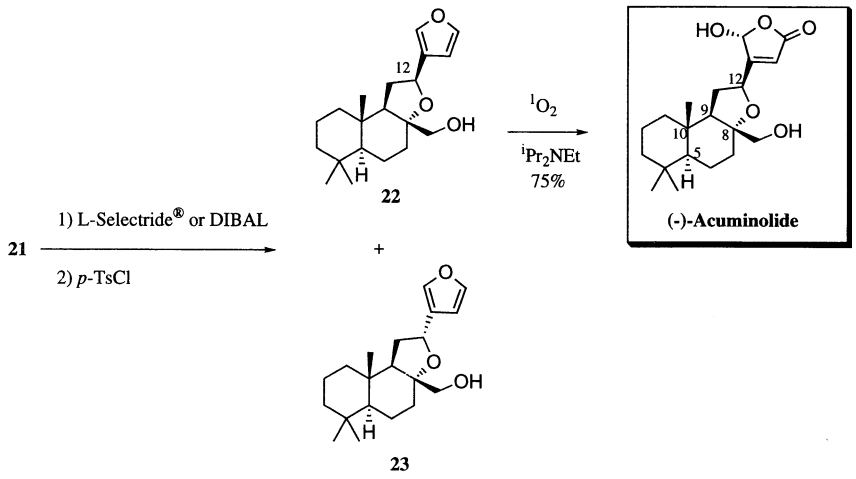
Scheme 5. Determination of the absolute configuration of β-ketoesters **3**, **6**, and **9**.

available (+)-sclareolide.[7] In that synthesis, the regioselectivity for the preparation of the desired intermediate was not controlled, and also the stereoselectivity for the construction of the C-12 asymmetric center was poor. In addition, the optical rotation value of the synthesized acuminolide was not mentioned at all; therefore, the absolute configuration of the natural (+)-acuminolide had not been determined yet.

For the total synthesis and determination of the absolute configuration of a bicyclic diterpene, (+)-acuminolide, we used the (−)-form of the bicyclic β-ketoalcohol **11** as the starting material, whose absolute configuration was already determined as mentioned previously,[19] because most natural terpenoids have *S* configuration at the C-10 position. The β-ketoalcohol (−)-**11** was transformed into exomethylene nitrile **18** by the known procedure;[21] thus, a sequence of tosylation, cyanation, and then the Wittig reaction with salt-free triphenylphosphonium methylide gave **18** in 94% yield for three steps (Scheme 6). DIBAL reduction of **18** yielded the corresponding aldehyde, which was reacted with 3-lithiofuran prepared from 3-bromofuran and *sec*-BuLi in



Scheme 6.



Scheme 7.

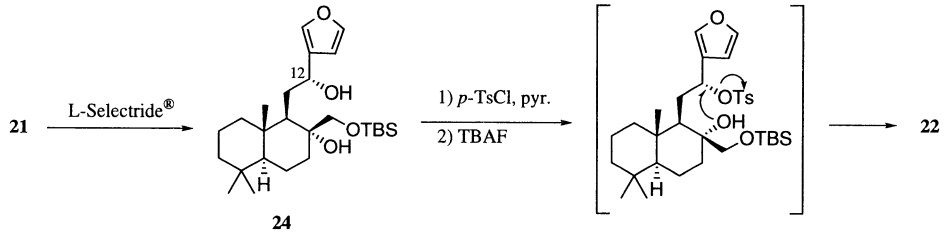
situ at −78°C, to produce secondary alcohol **19** in 91% yield for two steps as a mixture of diastereomers. Although the diastereomers of **19** were narrowly distinguishable by TLC, it could be used in the next oxidation without further purification. Although the oxidation of **19** with $BaMnO_2$,[22] MnO_2, PCC, PDC, and activated DMSO gave a poor yield of the desired ketone **20**, it was obtained in high yield by the oxidation with Dess–Martin periodinane.[23] The exomethylene group of **20** was oxidized with osmium tetraoxide to produce the corresponding diol as a single stereoisomer. The stereochemistry of the C-8 hydroxy group was tentatively assigned as α, because the attack of OsO_4 from the β face would be prevented by the presence of the axial methyl group at the C-10 position. Protection of the primary hydroxy group of the diol with a *tert*-butyldimethylsilyl group afforded ketone **21**. Then, the diastereoselective reduction of the carbonyl group of **21** was examined (Scheme 7). Reduction with sodium borohydride effected no stereoselectivity, and the obtained diols were unstable in silica gel column chromatography. Reduction of **21** with DIBAL followed by acid treatment gave **23** as a major product in the ratio of 5:1 by ^1H NMR in 40% yield, while L-Selectride® reduction followed by acid treatment produced cyclic ether **22** along with its C-12 stereoisomer **23** in the ratio of 15:1 by ^1H NMR, in 80% yield. The diastereomers of the alcohol resulting from the reduction of **21** were not distinguishable from one another by TLC. Tosylation of the crude alcohol with *p*-TsCl in pyridine followed by treatment of tetra-*n*-butylammonium fluoride gave the same result as that of the acid treatment; hence, we assumed that the reduction stereoselectively proceeded to exclusively produce the (12*R*)-stereoisomer **24** (Scheme 8).

The synthesis of acuminolide was achieved by photosensitized oxygenation of **22** in the presence of a catalytic amount of tetraphenylporphine (TPP) and excess amount of diisopropylethylamine in CH_2Cl_2 at −78°C in 75% yield (Scheme 7).[3,24] The spectral data and melting point of the synthesized acuminolide were in good agreement with those of the natural product.[3] However, to our surprise, the sign of the optical rotation value showed a minus ($[\alpha]_D^{23}=-33.2$ (*c* 1.25, $CHCl_3$)), which is contrary to that of the natural acuminolide ($[\alpha]_D^{20}=+36.2$ (*c* 1.34, $CHCl_3$)). Thus, the synthesized acuminolide was the antipode of natural (+)-acuminolide.

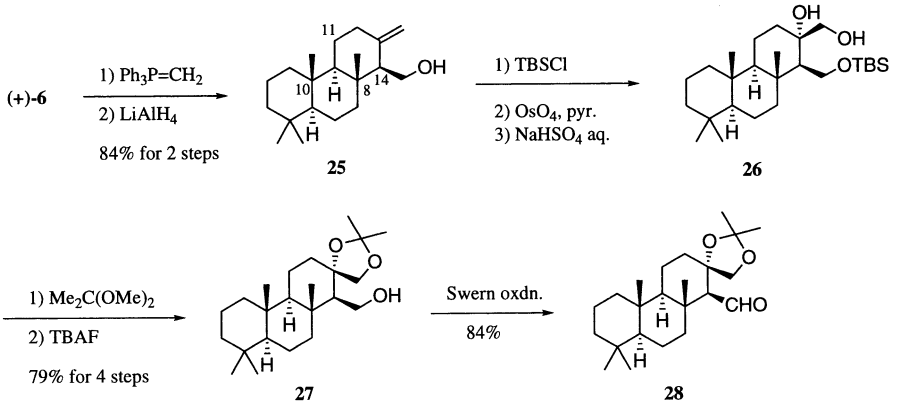
We synthesized (+)-acuminolide starting from (+)-**11** by the same procedure. The physical and spectral data, including the optical rotation value ($[\alpha]_D^{22}=+34.6$ (*c* 0.85, $CHCl_3$)) of the synthesized acuminolide, were in good agreement with those reported.[3] Furthermore, the melting point of a mixture of synthesized (+)-acuminolide (mp 207.5–208.5°C) and natural acuminolide (mp 207–208°C) showed no decrease. Thus, the absolute configuration of the (+)-acuminolide was determined as (5*R*,8*S*,9*S*,10*R*,12*R*), which is *ent*-form against the usual labdane diterpene. Thus, we achieved the stereoselective total synthesis of natural (+)-acuminolide and determination of the absolute configuration by the present synthesis.[14]

2.4. Total synthesis of a tricyclic sesterterpene, (−)-spongianolide A, and determination of its absolute configuration

Synthesis of tricyclic sesterterpene, (−)-spongianolide A, had not been reported and its absolute configuration had



Scheme 8.

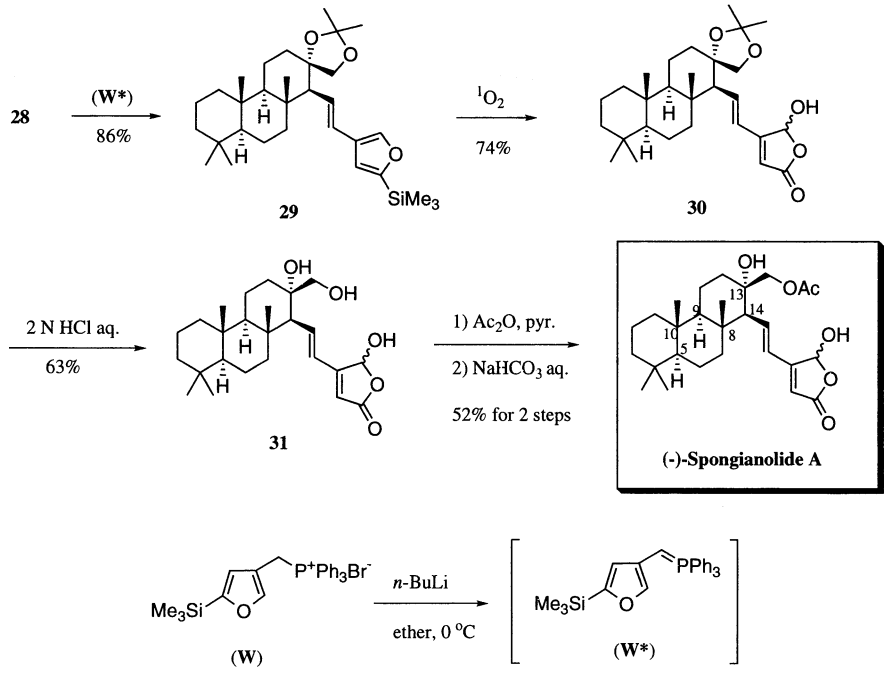


Scheme 9.

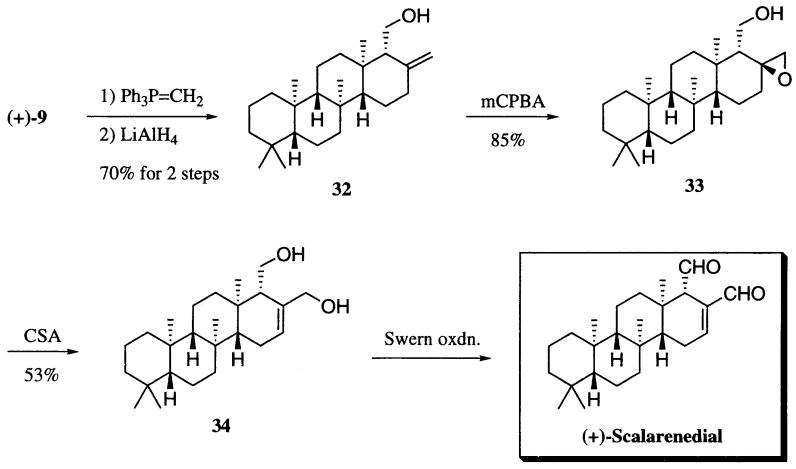
not been determined yet. In our synthetic study of this tricyclic sesterterpene, first, we started the synthesis from the optically pure tricyclic β-ketoalcohol (+)-**13** (Scheme 3). However, transformation from **13** into the corresponding *exo*methylene compound by the Wittig reaction with triphenylphosphonium methylide unfortunately proceeded only in poor yield. Then, we adopted the enantiomerically pure tricyclic β-ketoester (+)-**6** as the starting material (Scheme 9).

The Wittig reaction of the β-ketoester (+)-**6** with the crude solution of triphenylphosphonium methylide under the coexisting metal salt for 3 h caused severe epimerization at the C-14 position (14α:14β=1:4). However, the desired exomethylene compound was obtained stereoselectively (14α:14β=1:11) within 30 min by using excess salt-free Wittig ylide. The exomethylene compound thus obtained was followed by reduction with lithium aluminum hydride to yield alcohol **25**. The C-14 stereoisomer was easily separated by column chromatography on silica gel. After protection of the hydroxy group of **25** with a *tert*-butyldimethylsilyl group, oxidation of the *exo*methylene moiety with osmium tetraoxide stereoselectively produced the corresponding diol **26** as a single isomer, the diol moiety of which was protected by an acetonide formation with 2,2-dimethoxypropane, and then tetra-*n*-butylammonium fluoride treatment followed by Swern oxidation of the resulting hydroxy group produced aldehyde **28** in excellent yield.

Elongation of the five-carbon unit containing the γ-hydroxybutenolide moiety was efficiently achieved by our own method utilizing the Wittig reagent, 2-trimethylsilyl-4-furyltriphenylphosphonium methylide (**W***),[25] followed by photosensitized oxygenation.[26] Thus, reaction of aldehyde **28** with furanmethylide (**W***), which was prepared from the Wittig salt (**W**) by treatment with *n*-BuLi in dry THF, nicely produced conjugated furan **29** in 86% yield as a single geometrical isomer (Scheme 10). Photosensitized oxygenation of silylfuran **29** chemoselectively proceeded



Scheme 10.



Scheme 11.

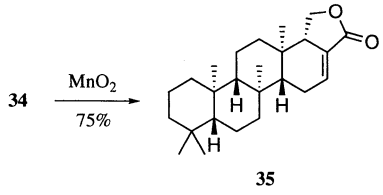
and the corresponding γ-hydroxybutenolide was regiospecifically generated to produce **30** as a 1:1 mixture of stereoisomers at the hydroxy group in the butenolide ring.

Synthesis of spongianolide A was achieved by treatment of **30** with acid to yield **31**, which was followed by acetylation and then chemoselective hydrolysis of the acetyl group in the butenolide moiety by treatment with aqueous sodium hydrogen carbonate in methanol. The spectral and physical data of the synthesized spongianolide A were in good agreement with those reported [mp 224.5–225.5°C, $[\alpha]_D^{24}=-31.2$ (*c* 0.58, CH_3OH), literature,[4] $[\alpha]_D=-31.9$ (*c* 1.4, CH_3OH)]. Thus, we achieved the first synthesis of (−)-spongianolide A and also determined its absolute configuration as (5*S*,8*R*,9*R*,10*S*,13*S*,14*S*) by the present synthesis.[15]

2.5. Formal synthesis of a tetracyclic sesterterpene, (+)-scalarenedial

As a demonstration of our method for the construction of a characteristic 6/6/6/6 fused ring system and in connection with our interest in elucidating the inhibitory mechanism of PLA_2 by some unsaturated aldehyde terpenoids,[13] we undertook a synthetic study of (+)-scalarenedial (Scheme 11). The synthesis of (−)-scalarenedial was reported in 1997 by Corey's group via a biomimetic route involving the enantiospecific tetracyclization reaction.[27]

The Wittig olefination of (+)-**9** with excess triphenylphosphonium methylide at room temperature for 10 min, followed by reduction of the ester group successfully produced alcohol **32**. Use of one equivalent of the Wittig reagent required longer reaction time, and caused severe isomerization of the ester group. Epoxidation of the exomethylene moiety in **32** with *m*-chloroperbenzoic acid stereoselectively produced the corresponding epoxide **33** as a single isomer. Among various trials to open the epoxide ring in **33** into the corresponding allyl alcohol, camphorsulfonic acid treatment in THF–water at 80°C successfully yielded the desired diol **34** in 53% yield, the enantiomer of which was transformed into (−)-scalarenedial by Corey's group.[27] The melting point and ^1H NMR of thus-synthesized **34** were in good agreement with those reported. In the ^{13}C NMR of our synthesized **34**, the chemical shifts of 23 peaks of the 24 signals were in good agreement with those reported, and the signal at 127.5 ppm of our compound was different from that reported at 141.6 ppm.[27] Our synthesized diol **34** was transformed into lactone **35** by using MnO_2 oxidation (Scheme 12). In this case, all of the spectral data of **35** thus obtained were in good agreement with those reported. Consequently, the formal synthesis of (+)-scalarenedial was thus achieved.[16]



Scheme 12.

3. Conclusion

We have established a simple and practical method for providing enantiomerically pure bi-, tri-, and tetracyclic frameworks having a 1,1,5-trimethyl-*trans*-decalin nucleus, and demonstrated their utility for terpenoid synthesis. Thus, we achieved the stereocontrolled total or formal syntheses of (+)-, and (−)-acuminolide as a bicyclic, (−)-spongianolide A as a tricyclic, and (+)-scalarenedial as a tetracyclic terpene from the corresponding optically pure bi-, tri-, and tetracyclic β-ketoesters or β-ketoalcohols, which were obtained by repeating the same method for the ring construction and the simple optical resolution. A widely applicable and efficient method for the synthesis of optically active cyclic terpenoids having a 1,1,5-trimethyl-*trans*-decalin nucleus was thus established.

4. Experimental

4.1. General

All commercially available reagents were used without further purification. All solvents were used after distillation. Tetrahydrofuran (THF), diethyl ether, benzene and toluene

were refluxed over and distilled from sodium. Dichloromethane was refluxed over and distilled from CaH_2. Dimethylformamide (DMF) and dimethyl sulfoxide (DMSO) were distilled from CaH_2 under reduced pressure. Methanol was refluxed over and distilled from magnesium. Triethylamine, diisopropylamine and diisopropylethylamine were refluxed over and distilled from KOH. Preparative separation was usually performed by column chromatography on silica gel (FUJI silysia Ltd., BW-200). IR spectra were recorded on a JASCO FT/IR-8000 MCT-5E spectrometer. ^{1}H- and ^{13}C NMR spectra were recorded at JEOL α-400 spectrometer and chemical shifts were represented as δ values relative to the internal standard TMS. Melting points were uncorrected.

4.2. Common procedure to prepare bicyclic (3), tricyclic (6) and tetracyclic β-ketoesters (9)

To a solution of allyl alcohol **1**, **4** or **7** (32 mmol) and pyridine (2.05 mL, 25 mmol) in diethyl ether (100 mL) was added phosphorus tribromide (3.6 mL, 38 mmol) at 0°C. After the reaction mixture was stirred at room temperature for 1 h, ice chips were added, and then the resulting mixture was extracted with diethyl ether. The organic layers were combined, washed with water, brine, dried over $MgSO_4$, filtered and concentrated in vacuo to give the corresponding bromide, which was used without further purification.

To a suspension of sodium hydride (1.9 g, 48 mmol, 60% in mineral oil) in THF (100 mL) was added methyl acetoacetate (4.4 mL, 41 mmol) at 0°C. After the reaction mixture was stirred at the same temperature for 10 min, *n*-BuLi (1.5 M in hexane, 32 mL, 48 mmol) was added dropwise. After the reaction mixture was stirred for an additional 10 min, a solution of the crude bromide in THF (10 mL) was added at the same temperature. After the resulting mixture was stirred at room temperature for 1 h, ice chips were added, and then the resulting mixture was extracted with diethyl ether. The organic layers were combined, washed with a saturated aqueous NH_4Cl solution, brine, dried over $mgSO_4$, filtered and concentrated in vacuo to give the corresponding linear β-ketoester **2**, **5** or **8**, which was used without further purification.

To a solution of crude linear β-ketoester **5** or **8** in dichloromethane (100 mL) was added tin tetrachloride (6.3 mL, 54 mmol) at −10°C. After being stirred at the same temperature for 30 min, the reaction mixture was warmed to room temperature, and stirred for an additional 20 h. The reaction mixture was poured into a 2N aqueous HCl solution, and then extracted with ethyl acetate. The organic layers were combined, washed with brine, dried over $mgSO_4$, filtered and concentrated in vacuo. Purification by silica gel column chromatography (from 2 to 20% ethyl acetate in hexane) followed by recrystallization from ethyl acetate–hexane gave the corresponding cyclic β-ketoester **3**, **6** or **9** (52–75% for 3 steps).

To a suspension of sodium hydride (1.75 g, 44 mmol, 60% in mineral oil) in THF (120 mL) was added a solution of cyclic β-ketoester **3** or **6** (40 mmol) in THF (10 mL) at 0°C. The reaction mixture was stirred at room temperature for 1 h, and diethyl chlorophosphonate (7.5 mL, 52 mmol) was added dropwise at 0°C. After the reaction mixture was stirred at room temperature for an additional 10 min, water was added at this temperature, and then the resulting mixture was extracted with ethyl acetate. The organic layers were combined, washed with water, brine, dried over $MgSO_4$, filtered and concentrated in vacuo, to give the corresponding enol phosphonate, which was used without further purification.

To a suspension of copper iodide (15.5 g, 80 mmol) in diethyl ether (100 mL) was added methyl lithium (1.5 M in diethyl ether, 107 mL, 160 mmol) at −50°C. After the mixture was stirred at −40°C for 10 min, a solution of the crude enol phosphonate in diethyl ether (10 mL) was added dropwise at −50°C. After the reaction mixture was stirred at 0°C for 1 h, water was added, and the resulting mixture was filtered through a pad of Celite, and then the filtrate was extracted with diethyl ether. The organic layers were combined, washed with a saturated aqueous NH_4Cl solution, brine, dried over $MgSO_4$, filtered and concentrated in vacuo to give the corresponding methylester, which was used without further purification.

To a suspension of lithium aluminum hydride (3.1 g, 80 mmol) in diethyl ether (100 mL) was added dropwise a solution of the crude methylester in diethyl ether (10 mL) at 0°C. After the reaction mixture was stirred at room temperature for 12 h, water was added, and the precipitate was filtered through a pad of Celite, and then the filtrate was concentrated in vacuo. Purification by silica gel column chromatography (from 3 to 10% ethyl acetate in hexane) gave the corresponding allyl alcohol **4** or **7** (80–89% for 3 steps).

4.2.1. (4a*S,8a*S**)-3,4,4a,5,6,7,8,8a-Octahydro-2,5,5,8a-tetra-methyl-*trans*-naphthalene-1-methanol (*dl*-4).** Mp 90.0–91.0°C; IR (KBr, cm^{-1}) 3368, 1458, 1435, 1375; ^{1}H NMR (400 MHz, $CDCl_3$) δ 4.20 (d, 1H, *J*=11.6 Hz), 4.04 (d, 1H, *J*=11.6 Hz), 2.07 (m, 2H), 1.89 (m, 1H), 1.72 (s, 3H), 1.56 (m, 5H), 1.20 (m, 3H), 0.96 (s, 3H), 0.89 (s, 3H), 0.84 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 140.91, 132.43, 77.19, 58.27, 51.64, 41.62, 38.00, 36.75, 33.64, 33.22, 21.54, 20.64, 19.26, 18.90, 18.83; FAB^+ HRMS Found *m/z* 222.1983, Calcd for $C_{15}H_{26}O$ M^+ 222.1984.

4.2.2. (1*R,4a*S**,4b*R**,8a*R**,10a*S**)-3,4,4a,4b,5,6,7,8,8a,9,10,10a-Dodecahydro-1-methoxycarbonyl-4b,8,8,10a-tetra-methyl-*trans*-*anti*-*trans*-phenanthrene-2(1*H*)-one (*dl*-6).** Mp 150.0–151.0°C; IR (KBr, cm^{-1}) 1746, 1714; ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.68 (s, 3H), 3.24 (s, 1H), 2.48 (ddd, 1H, *J*=14.6, 5.6, 2.0 Hz), 2.31 (dddd, 1H, *J*=14.6, 12.9, 7.6, 1.0 Hz), 2.00 (m, 1H), 1.70 (m, 5H), 1.40 (m, 5H), 1.17 (s, 3H), 0.94 (s, 3H), 0.90 (s, 3H), 0.88 (s, 3H), 0.83 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 205.60, 168.59, 69.98, 57.86, 56.61, 51.42, 42.57, 41.84, 40.81, 40.35, 40.10, 37.95, 33.38, 33.22, 21.91, 21.49, 18.42, 16.05, 15.43; Anal. found: C, 75.00; H, 10.09%. Calcd for $C_{20}H_{32}O_3$: C, 74.96; H, 10.06%.

4.2.3. (4a*S,4b*R**,8a*R**,10a*S**)-3,4,4a,4b,5,6,7,8,8a,9,10,10a-Dodecahydro-4b,8,8,10a-tetramethyl-*trans*-*anti*-*trans*-phenanthrene-1-methanol (*dl*-7).** Mp 127.0–129.0°C; IR

(KBr, cm^{-1}) 3380, 2926, 2361, 2344, 1460, 1387; ^1H NMR (400 MHz, $CDCl_3$) δ 4.18 (d, 1H, J=11.5 Hz), 4.04 (d, 1H, J=11.5 Hz), 2.04 (m, 2H), 1.97 (m, 1H), 1.71 (m, 3H), 1.61 (m, 2H), 1.39 (m, 5H), 1.11 (m, 3H), 0.97 (s, 3H), 0.85 (s, 6H), 0.82 (s, 3H), 0.81 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 140.97, 132.28, 58.14, 56.42, 56.35, 42.11, 39.67, 38.28, 37.36, 34.01, 33.26, 21.73, 21.32, 19.16, 18.63, 18.59, 17.71, 16.37; FAB$^+$ HRMS Found m/z 290.2598, Calcd for $C_{20}H_{34}O$ M^+ 290.2609.

4.2.4. (1*R,4a*S**,4b*R**,6a*S**,10a*S**,10b*R**,12a*S**)-3,4,4a,4b,5,6,6a,7,8,9,10,10a,10b,11,12,12a-Hexadecahydro-1-metho-xycarbonyl-4b,7,7,10a,12a-pentamethyl-*trans*]-*anti-trans-anti-trans*-chrysene-2(1*H*)-one (*dl*-9).** Mp 207.0–208.0°C; IR (KBr, cm^{-1}) 1746, 1719; ^1H NMR (400 MHz, $CDCl_3$) δ 3.68 (s, 3H), 3.21 (s, 1H), 2.47 (ddd, 1H, J=14.6, 5.2, 1.7 Hz), 2.29 (m, 1H), 1.98 (m, 1H), 0.70–1.85 (m, 18H), 1.16 (s, 3H), 0.90 (s, 3H), 0.86 (s, 3H), 0.83 (s, 3H), 0.81 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 205.57, 168.59, 70.02, 61.20, 58.32, 56.55, 51.41, 42.40, 42.05, 41.99, 40.87, 40.49, 39.90, 38.28, 37.50, 33.27, 21.85, 21.30, 18.59, 18.19, 17.26, 17.22, 16.31, 15.35; Anal. found: C, 77.19; H, 10.43%. Calcd for $C_{25}H_{40}O_3$: C, 77.27; H, 10.37%.

4.3. General procedure for the optical resolution using the chiral auxiliary (A)

To a solution of β-ketoester **3** or **6** (10 mmol) in benzene (50 mL) was added (2*R*,3*R*)-(−)-2,3-butanediol (**A**) (1.0 g, 11 mmol) and a catalytic amount of *p*-toluenesulfonic acid. After the reaction mixture was stirred under reflux condition for 2 h, a saturated aqueous $NaHCO_3$ solution was added, and then the resulting mixture was extracted with ethyl acetate. The organic layers were combined, washed with brine, dried over $MgSO_4$, filtered and concentrated in vacuo to give the corresponding acetal, which was used without further purification.

To a suspension of lithium aluminum hydride (700 mg, 18.5 mmol) in diethyl ether (40 mL) was added dropwise a solution of the crude acetal in diethyl ether (5 mL) at 0°C. After the reaction mixture was stirred at room temperature for 12 h, water was added, and the precipitate was filtered through a pad of Celite, and then the filtrate was concentrated in vacuo to give crude methylester (80–94% for 2 steps). Purification by silica gel column chromatography (from 2 to 10% ethyl acetate in hexane) gave acetal **10a** and its diastereomer **10b**, or **12a** and its diastereomer **12b**, respectively.

To a solution of the acetal (3.4 mmol) in acetone (30 mL) was added a catalytic amount of *p*-toluenesulfonic acid and water at room temperature. After the reaction mixture was stirred for 12 h, a saturated aqueous $NaHCO_3$ solution was added, and then the resulting mixture was extracted with ethyl acetate. The organic layers were combined, washed with brine, dried over $MgSO_4$, filtered and concentrated in vacuo. Purification by silica gel column chromatography (from 10 to 30% ethyl acetate in hexane) followed by recrystallization from ethyl acetate–hexane gave the corresponding optically active β-ketoalcohol **11** or **13** (89–100%).

4.3.1. (1*S*,4a*S*,8a*S*)-1,2,3,4,4a,5,6,7,8,8a-Decahydro-5,5,8a-tri-methyl-2-oxo-*trans*-naphthalene-1-methanol-2-[((1*R*,2*R*)-dimethyl)ethylene acetal] (10a) (slower moving diastereomer). Mp 122.5–123.0°C; $[\alpha]_D^{24}$=−15.9 (*c* 1.00, $CHCl_3$); IR (KBr, cm^{-1}) 3517, 1146, 1115, 1084, 1020; ^1H NMR (400 MHz, $CDCl_3$) δ 3.91 (dd, 1H, J=10.8, 7.2 Hz), 3.80 (m, 1H), 3.63 (m, 1H), 3.55 (m, 1H), 3.00 (d, 1H, J=8.4 Hz), 1.93 (m, 1H), 1.82 (m, 1H), 1.30 (d, 3H, J=6.1 Hz), 1.23 (d, 3H, J=6.1 Hz), 1.0–1.7 (m, 9H), 0.87 (s, 3H), 0.86 (s, 3H), 0.81 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 111.83, 77.88, 77.78, 59.67, 58.84, 54.97, 41.86, 39.49, 38.41, 37.67, 33.65, 33.24, 21.66, 20.07, 18.59, 18.37, 16.46, 15.68; Anal. found: C, 72.72; H, 10.90%. Calcd for $C_{18}H_{31}O_3$: C, 72.91; H, 10.89%.

4.3.2. (1*R*,4a*R*,8a*R*)-1,2,3,4,4a,5,6,7,8,8a-Decahydro-5,5,8a-tri-methyl-2-oxo-*trans*-naphthalene-1-methanol-2-[((1*R*,2*R*)-dimethyl) ethylene acetal] (10b) (faster moving diastereomer). Mp 78.5–79.5°C; $[\alpha]_D^{24}$=−4.18 (*c* 1.03, $CHCl_3$); IR (KBr, cm^{-1}) 3551, 1188, 1157, 1123, 1092, 1032; ^1H NMR (400 MHz, $CDCl_3$) δ 3.82 (ddd, 1H, J=11.2, 8.4, 0.8 Hz), 3.73 (m, 2H), 3.61 (m, 1H), 3.25 (d, 1H, J=10.0 Hz), 1.96 (m, 1H), 1.82 (m, 1H), 1.29 (d, 3H, J=2.0 Hz), 1.27 (d, 3H, J=2.0 Hz), 1.0–1.7 (m, 9H), 0.88 (s, 3H), 0.84 (s, 3H), 0.82 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 111.83, 81.03, 76.36, 59.35, 58.87, 55.05, 41.82, 39.53, 38.94, 38.34, 33.71, 33.29, 21.78, 20.07, 19.31, 18.61, 18.59, 16.51, 15.54; Anal. found: C, 72.84; H, 10.92%. Calcd for $C_{18}H_{32}O_3$: C, 72.93; H, 10.88%.

4.3.3. (1*S*,4a*S*,8a*S*)-1,2,3,4,4a,5,6,7,8,8a-Decahydro-5,5,8a-tri-methyl-2-oxo-*trans*-naphthalene-1-methanol ((−)-11).[19] Mp 68.0–69.0°C; $[\alpha]_D^{24}$=−38.3 (*c* 0.99, $CHCl_3$); IR (KBr, cm^{-1}) 3262, 1709, 1146, 1046; ^1H NMR (400 MHz, $CDCl_3$) δ 3.96 (dd, 1H, J=11.2, 9.5 Hz), 3.60 (brd, 1H, J=10.7 Hz), 2.47 (ddd, 1H, J=14.4, 5.1, 2.0 Hz), 2.32 (m, 2H,), 2.05 (m, 1H), 1.69 (m, 2H), 1.50 (m, 4H), 1.28 (m, 2H), 0.98 (s, 3H), 0.87 (s, 3H), 0.81 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 214.77, 65.33, 57.72, 53.45, 42.01, 41.66, 41.09, 39.02, 33.53, 23.23, 21.76, 18.73, 15.82.

4.3.4. (1*R*,4a*R*,8a*R*)-1,2,3,4,4a,5,6,7,8,8a-Decahydro-5,5,8a-tri-methyl-2-oxo-*trans*-naphthalene-1-methanol ((+)-11). Mp 67.5–68.5°C; $[\alpha]_D^{24}$=+38.5 (*c* 1.00, $CHCl_3$).

4.3.5. (1*R*,4a*S*,4b*R*,8a*R*,10a*S*)-1,2,3,4,4a,4b,5,6,7,8,8a,9,10,10a-Tetradecahydro-4b,8,8,10a-tetramethyl-2-oxo-*trans-anti-trans*-phenanthrene-1-methanol-2-[(1*R*,2*R*)-dimethylethylene acetal] (12a) (faster moving diastereomer). Mp 140.0–140.5°C; $[\alpha]_D^{23}$=−4.45 (*c* 1.00, $CHCl_3$); IR (KBr, cm^{-1}) 3536, 2936, 2876, 2856, 1142, 1086, 1022; ^1H NMR (400 MHz, $CDCl_3$) δ 3.81 (dd, 1H, J=10.4, 8.4 Hz), 3.72 (m, 2H), 3.60 (ddd, 1H, J=10.8, 10.8, 1.6 Hz), 3.25 (d, 1H, J=10.4 Hz), 1.88 (m, 2H), 1.60 (m, 5H), 1.40 (m, 3H), 1.28 (d, 3H, J=5.6 Hz), 1.27 (d, 3H, J=5.6 Hz), 1.26 (m, 1H), 1.14 (m, 1H), 0.85 (s, 3H), 0.85 (m, 4H), 0.83 (s, 3H), 0.82 (s, 3H), 0.80 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 111.70, 81.00, 76.38, 59.70, 59.25, 59.21, 56.40, 42.00, 41.15, 40.12, 38.83, 38.68, 37.55, 33.26, 21.33, 18.60, 18.32, 18.11, 16.84, 16.51, 16.45; Anal. found: C, 75.90; H, 11.10%. Calcd for $C_{23}H_{40}O_3$: C, 75.78; H, 11.06%.

4.3.6. (1*S*,4a*R*,4b*S*,8a*S*,10a*R*)-1,2,3,4,4a,4b,5,6,7,8,8a,9,10,10a-Tetradecahydro-4b,8,8,10a-tetramethyl-2-oxo-*trans-anti-trans*-phenanthrene-1-methanol-2-[(1*R*,2*R*)-dimethylethylene acetal] (12b) (slower moving diastereomer). Mp 207.5–208.0°C; $[\alpha]_D^{24}=-9.20$ (*c* 0.08, $CHCl_3$); IR (KBr, cm^{-1}) 3512, 2968, 2940, 2852, 1142, 1076, 1020, 1000; ^1H NMR (400 MHz, $CDCl_3$) δ 3.89 (ddd, 1H, *J*=10.8, 7.6, 2.0 Hz), 3.78 (dq, 1H, *J*=8.4, 6.0 Hz), 3.62 (ddd, 1H, *J*=9.6, 9.6, 1.6 Hz), 3.54 (dq, 1H, *J*=8.4, 6.0 Hz), 3.00 (dd, 1H, *J*=9.6, 1.6 Hz), 1.90 (m, 2H), 1.60 (m, 5H), 1.42 (m, 11H), 1.29 (d, 3H, *J*=6.0 Hz), 1.22 (d, 3H, *J*=6.0 Hz), 1.26 (m, 1H), 0.85 (s, 6H), 0.83 (m, 4H), 0.81 (s, 3H), 0.80 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 111.70, 77.86, 77.77, 59.96, 59.58, 58.73, 56.44, 42.00, 41.09, 40.08, 38.74, 37.55, 37.50, 34.95, 33.27, 21.34, 18.87, 18.58, 18.34, 16.95, 16.44, 16.33; Anal. found: C, 75.87; H, 11.07%. Calcd for $C_{23}H_{40}O_3$: C, 75.78; H, 11.06%.

4.3.7. (1*R*,4a*S*,4b*R*,8a*R*,10a*S*)-1,2,3,4,4a,4b,5,6,7,8,8a,9,10,10a-Tetradecahydro-4b,8,8,10a-tetramethyl-2-oxo-*trans-anti-trans*-phenanthrene-1-methanol ((+)-13).[20] Mp 136.0–137.0°C; $[\alpha]_D^{24}=+25.9$ (*c* 1.12, $CHCl_3$); IR (KBr, cm^{-1}) 3404, 1716, 1378, 1030; ^1H NMR (400 MHz, $CDCl_3$) δ 3.97 (ddd, 1H, *J*=11.4, 9.6, 4.0 Hz), 3.58 (ddd, 1H, *J*=11.2, 10.2, 3.6 Hz), 2.48 (dd, 1H, *J*=10.4, 4.4 Hz), 2.44 (ddd, 1H, *J*=14.0, 5.2, 2.0 Hz), 2.30 (m, 1H), 2.01 (m, 1H), 1.68 (m, 5H), 1.31 (m, 6H), 0.90 (m, 2H), 0.89 (s, 3H), 0.87 (s, 3H), 0.82 (s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 214.68, 65.56, 58.19, 57.62, 56.28, 41.81, 41.73, 41.62, 40.50, 40.11, 37.94, 33.33, 33.19, 22.11, 21.46, 18.55, 18.45, 16.67, 16.18.

4.3.8. (1*S*,4a*R*,4b*S*,8a*S*,10a*R*)-1,2,3,4,4a,4b,5,6,7,8,8a,9,10,10a-Tetradecahydro-4b,8,8,10a-tetramethyl-2-oxo-*trans-anti-trans*-phenanthrene-1-methanol ((−)-13). Mp 131.5–133.0a°C; $[\alpha]_D^{24}=-25.9$ (*c* 1.30 $CHCl_3$).

4.4. General procedure for the optical resolution using the chiral auxiliary (B)

To a solution of β-ketoester **3**, **6**, or **9** (24 mmol) in benzene (100 mL) was added 1,4-di-*O*-benzyl-L-threitol (**B**) (7.9 g, 26 mmol) and a catalytic amount of *p*-toluenesulfonic acid. After the reaction mixture was stirred under reflux condition for 2 h, a saturated aqueous $NaHCO_3$ solution was added, and then the resulting mixture was extracted with ethyl acetate. The organic layers were combined, washed with brine, dried over $MgSO_4$, filtered and concentrated in vacuo to give the corresponding acetal, which was used without further purification.

To a solution of the crude acetal in ethyl acetate (100 mL) was added Pd–C (4.8 g), and the mixture was stirred at room temperature for 48 h under hydrogen atmosphere. The reaction mixture was filtered and concentrated in vacuo to give crude alcohol (90–100% for 2 steps). Purification by silica gel column chromatography (from 1 to 6% methanol in chloroform) gave acetal **14a** and **14b**, **15a** and **15b**, or **16a** and **16b**, respectively.

To a solution of the acetal (5.6 mmol) in methanol (50 mL) was added a catalytic amount of a 2N aqueous H_2SO_4 solution at room temperature. After the reaction mixture was stirred for 48 h under reflux condition, a saturated aqueous $NaHCO_3$ solution was added, and then the resulting mixture was extracted with ethyl acetate. The organic layers were combined, washed with brine, dried over $MgSO_4$, filtered and concentrated in vacuo. Purification by silica gel column chromatography (from 10 to 30% ethyl acetate in hexane) followed by recrystallization from ethyl acetate–hexane gave the corresponding optically active β-ketoester **3**, **6**, or **9** (74–80%).

4.4.1. (1*R*,4a*S*,8a*S*)-3,4,4a,5,6,7,8,8a-Octahydro-1-methoxy-carbonyl-5,5,8a-trimethyl-*trans*-naphthalene-2(1*H*)-one-2-[((1*S*,2*S*)-di(hydroxymethyl))ethylene acetal] (14a) (slower moving diastereomer). Mp 123.0–124.0°C; $[\alpha]_D^{21}=+10.4$ (*c* 1.18, $CHCl_3$); IR (KBr, cm^{-1}) 3476, 3447, 3285, 1716, 1207, 1155, 1126, 1034; ^1H NMR (400 MHz, $CDCl_3$) δ 4.09 (ddd, 1H, *J*=8.8, 4.4, 3.6 Hz), 4.00 (ddd, 1H, *J*=8.8, 4.9, 4.0 Hz), 3.81 (dd, 1H, *J*=12.0, 3.6 Hz), 3.73 (dd, 1H, *J*=11.6, 4.0 Hz), 3.66 (dd, 1H, *J*=12.0, 3.6 Hz), 3.64 (s, 3H), 3.62 (dd, 1H, *J*=12.0, 4.0 Hz), 2.49 (s, 1H), 1.91 (dd, 1H, *J*=9.0, 3.0 Hz), 1.52 (m, 6H), 1.21 (m, 3H), 1.18 (m, 3H), 0.91 (m, 1H), 0.89 (s, 3H), 0.86 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 171.82, 109.51, 79.15, 76.38, 63.09, 61.87, 61.63, 54.89, 51.09, 41.80, 39.91, 39.63, 39.19, 33.58, 33.19, 21.60, 19.64, 18.31, 14.88; Anal. found: C, 64.19; H, 9.11%. Calcd for $C_{19}H_{32}O_6$: C, 64.02; H, 9.05%.

4.4.2. (1*S*,4a*R*,8a*R*)-3,4,4a,5,6,7,8,8a-Octahydro-1-methoxy-carbonyl-5,5,8a-trimethyl-*trans*-naphthalene-2(1*H*)-one-2-[((1*S*,2*S*)-di(hydroxymethyl)) ethylene acetal] (14b) (faster moving diastereomer). Mp 127.0–127.5°C; $[\alpha]_D^{24}=-28.1$ (*c* 1.18, $CHCl_3$); IR (KBr, cm^{-1}) 3500, 3440, 3328, 3000, 1716, 1212, 1154, 1076, 1052; ^1H NMR (400 MHz, $CDCl_3$) δ 4.12 (ddd, 1H, *J*=8.6, 2.4, 0.8 Hz), 4.07 (ddd, 1H, *J*=12.4, 2.4, 0.8 Hz), 4.03 (ddd, 1H, *J*=8.4, 3.6, 3.6 Hz), 3.88 (d, 1H, *J*=10.4 Hz), 3.78 (ddd, 1H, *J*=10.4, 4.8, 3.6 Hz), 3.66 (s, 3H), 3.55 (m, 1H), 2.53 (s, 1H), 1.96 (dd, 1H, *J*=8.0, 4.8 Hz), 1.90 (ddd, 1H, *J*=12.8, 3.2, 3.2 Hz), 1.54 (m, 5H), 1.24 (m, 3H), 1.17 (s, 3H), 0.89 (s, 3H), 0.85 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 172.23, 109.14, 77.60, 75.50, 62.90, 61.60, 59.79, 54.47, 51.44, 41.80, 39.90, 39.31, 38.25, 33.50, 33.19, 21.45, 20.11, 18.36; Anal. found: C, 64.28; H, 9.08%. Calcd for $C_{19}H_{32}O_6$: C, 64.02; H, 9.05%.

4.4.3. (1*R*,4a*S*,8a*S*)-3,4,4a,5,6,7,8,8a-Octahydro-1-methoxy-carbonyl-5,5,8a-trimethyl-*trans*-naphthalene-2(1*H*)-one ((−)-3).[17] Mp 103.0–104.0°C; $[\alpha]_D^{22}=-54.3$ (*c* 0.82, $CHCl_3$).

4.4.4. (1*S*,4a*R*,8a*R*)-3,4,4a,5,6,7,8,8a-Octahydro-1-methoxy-carbonyl-5,5,8a-trimethyl-*trans*-naphthalene-2(1*H*)-one ((+)-3). Mp 103.0–104.0°C; $[\alpha]_D^{22}=+55.0$ (*c* 1.05, $CHCl_3$).

4.4.5. (1*R*,4a*S*,4b*R*,8a*R*,10a*S*)-3,4,4a,4b,5,6,7,8,8a,9,10,10a-Dodecahydro-1-methoxycarbonyl-4b,8,8,10a-tetramethyl-*trans-anti-trans*-phenanthrene-2(1*H*)-one-2-[((1*S*,2*S*)-di(hydroxymethyl))ethylene acetal] (15a) (faster moving diastereomer). Mp 223.0–225.0°C; $[\alpha]_D^{24}=-45.1$ (*c* 1.16, $CHCl_3$); IR (KBr, cm^{-1}) 3483, 2940, 1730, 1200, 1148, 1132, 1046; ^1H NMR (400 MHz, $CDCl_3$) δ 4.06 (m, 3H), 3.90 (d, 1H, *J*=10.8 Hz), 3.77 (ddd, 1H, *J*=12.4,

4.8, 3.6 Hz), 3.65 (s, 3H), 3.55 (m, 1H), 2.53 (s, 1H), 1.97 (dd, 1H, *J*=8.0, 4.8 Hz), 1.88 (ddd, 1H, *J*=8.4, 3.6, 3.6 Hz), 1.51 (m, 10H), 1.18 (m, 1H), 1.17 (s, 3H), 0.85 (s, 6H), 0.84 (s, 3H), 0.81 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 172.21, 109.02, 77.60, 75.53, 63.11, 61.61, 59.80, 59.01, 56.68, 51.41, 41.99, 41.34, 40.01, 39.70, 38.02, 37.57, 33.27, 21.34, 18.97, 18.50, 18.08, 16.21, 15.98; Anal. found: C, 67.44; H, 9.49%. Calcd for $C_{24}H_{40}O_6$: C, 67.89; H, 9.50%.

4.4.6. (1*S*,4a*R*,4b*S*,8a*S*,10a*R*)-3,4,4a,4b,5,6,7,8,8a,9,10,10a-Dodecahydro-1-methoxycarbonyl-4b,8,8,10a-tetramethyl-*trans*-*anti*-*trans*-phenanthrene-2(1*H*)-one-2-[((1*S*, 2*S*)-di(hydroxymethyl))ethylene acetal] (15b) (slower moving diastereomer). Mp 171.0–172.0°C; $[\alpha]_D^{21}$=+20.6 (*c* 0.92, $CHCl_3$); IR (KBr, cm^{-1}) 3483, 2940, 1730, 1200, 1148, 1132, 1046; ^{1}H NMR (400 MHz, $CDCl_3$) δ 4.10 (dt, 1H, *J*=8.8, 4.0 Hz), 4.00 (dt, 1H, *J*=8.8, 4.0 Hz), 3.81 (brm, 1H), 3.73 (brm, 1H), 3.64 (s, 3H), 3.58 (m, 2H), 2.50 (s, 1H), 2.18 (m, 1H), 1.88 (m, 1H), 1.49 (m, 10H), 1.20 (s, 3H), 1.14 (ddd, 1H, *J*=13.6, 13.6, 4.0 Hz), 0.86 (s, 3H), 0.85 (s, 3H), 0.85 (m, 3H), 0.81 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 172.07, 109.70, 79.04, 77.64, 63.60, 62.12, 61.99, 59.79, 56.99, 51.37, 42.32, 41.67, 40.39, 39.93, 39.70, 37.91, 33.60, 21.67, 18.83, 18.34, 16.66, 16.41; Anal. found: C, 67.42; H, 9.44%. Calcd for $C_{24}H_{40}O_6$: C, 67.89; H, 9.50%.

4.4.7. (1*R*,4a*S*,4b*R*,8a*R*,10a*S*)-3,4,4a,4b,5,6,7,8,8a,9,10,10a-Dodecahydro-1-methoxycarbonyl-4b,8,8,10a-tetramethyl-*trans*-*anti*-*trans*-phenanthrene-2(1*H*)-one ((+)-6). Mp 170.0–172.0°C; $[\alpha]_D^{24}$=+29.1 (*c* 1.02, $CHCl_3$).

4.4.8. (1*S*,4a*R*,4b*S*,8a*S*,10a*R*)-3,4,4a,4b,5,6,7,8,8a,9,10,10a-Dodecahydro-1-methoxycarbonyl-4b,8,8,10a-tetramethyl-*trans*-*anti*-*trans*-phenanthrene-2(1*H*)-one ((−)-6). Mp 165.0–166.0°C; $[\alpha]_D^{23}$ −29.4 (*c* 0.86, $CHCl_3$).

4.4.9. (1*R*,4a*S*,4b*R*,6a*S*,10a*S*,10b*R*,12a*S*)-3,4,4a,4b,5,6,6a,7,8,9,10,10a,10b,11,12,12a-Hexadecahydro-1-methoxycarbonyl-4b,7,7,10a,12a-pentamethyl-*trans*-*anti*-*trans*-*anti*-*trans*-chrysene-2(1*H*)-one-2-[((1*S*,2*S*)-di(hydroxymethyl))ethylene acetal] (16a) (slower moving diastereomer). Mp 262.0–264.0°C; $[\alpha]_D^{26}$=+14.1 (*c* 0.17, $CHCl_3$); IR (KBr, cm^{-1}) 3474, 3403, 2944, 1717; ^{1}H NMR (400 MHz, $CDCl_3$) δ 4.11 (dt, 1H, *J*=8.8, 3.9 Hz), 4.00 (1H, *J*=8.8, 3.9 Hz), 3.83 (brm, 1H), 3.75 (brm, 1H), 3.64 (s, 3H), 3.60 (m, 2H), 2.47 (s, 1H), 1.88 (m, 1H), 1.77 (m, 1H), 0.75–1.70 (m, 19H), 1.19 (s, 3H), 0.86 (s, 3H), 0.83 (s, 3H), 0.81 (s, 3H), 0.80 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 171.74, 109.43, 78.91, 77.20, 76.18, 63.29, 61.68, 61.57, 61.19, 59.88, 56.56, 51.06, 42.10, 41.98, 41.46, 39.80, 39.44, 37.88, 37.53, 33.28, 21.31, 18.63, 18.43, 18.24, 17.58, 16.86, 16.16, 16.00; Anal. found: C, 70.53; H, 10.09%. Calcd for $C_{29}H_{48}O_6$: C, 70.70; H, 9.82%.

4.4.10. (1*S*,4a*R*,4b*S*,6a*R*,10a*R*,10b*S*,12a*R*)-3,4,4a,4b,5,6,6a,7,8,9,10,10a,10b,11,12,12a-Hexadecahydro-1-methoxycarbonyl-4b,7,7,10a,12a-pentamethyl-*trans*-*anti*-*trans*-*anti*-*trans*-chrysene-2(1*H*)-one-2-[((1*S*,2*S*)-di(hydroxymethyl))ethylene acetal] (16b) (faster moving diastereomer). Mp 258.0–260.0°C; $[\alpha]_D^{26}$=−24.3 (*c* 0.15, $CHCl_3$); IR (KBr, cm^{-1}) 3424, 2924, 2847, 1717; ^{1}H NMR (400 MHz, $CDCl_3$) δ 4.06 (m, 3H), 3.87 (d, 1H, *J*=10.7 Hz), 3.78 (ddd, 1H, *J*=12.0, 4.2, 3.9 Hz), 3.65 (s, 3H), 3.54 (m, 1H), 2.51 (s, 1H), 0.80–2.00 (m, 21H), 1.15 (s, 3H), 0.85 (s, 3H), 0.83 (s, 3H), 0.81 (s, 3H), 0.80 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 172.24, 109.11, 77.53, 77.21, 75.54, 63.12, 61.57, 61.20, 60.69, 59.77, 59.42, 56.57, 51.44, 42.10, 41.93, 41.45, 39.81, 39.54, 38.06, 37.53, 33.28, 21.31, 18.90, 18.64, 18.24, 17.45, 16.91, 16.16, 15.88; Anal. found: C, 70.44; H, 9.78%. Calcd for $C_{29}H_{48}O_6$: C, 70.70; H, 9.82%.

4.4.11. (1*R*,4a*S*,4b*R*,6a*S*,10a*S*,10b*R*,12a*S*)-3,4,4a,4b,5,6,6a,7,8,9,10,10a,10b,11,12,12a-Hexadecahydro-1-methoxycarbonyl-4b,7,7,10a,12a-pentamethyl-*trans*-*anti*-*trans*-*anti*-*trans*-chrysene-2(1*H*)-one ((−)-9). Mp 223.0–225.0°C; $[\alpha]_D^{26}$=−19.3 (*c* 0.20, $CHCl_3$).

4.4.12. (1*S*,4a*R*,4b*S*,6a*R*,10a*R*,10b*S*,12a*R*)-3,4,4a,4b,5,6,6a,7,8,9,10,10a,10b,11,12,12a-Hexadecahydro-1-methoxycarbonyl-4b,7,7,10a,12a-pentamethyl-*trans*-*anti*-*trans*-*anti*-*trans*-chrysene-2(1*H*)-one ((+)-9). Mp 220.0–221.0°C; $[\alpha]_D^{26}$=+20.2 (*c* 0.31, $CHCl_3$).

4.4.13. (+)-Albicanol[19] from bicyclic β-ketoester (−)-3. To a suspension of methyltriphenylphosphonium bromide (2.12 g, 5.94 mmol) in THF (8 mL) was added sodium amide (231 mg, 5.94 mmol) at room temperature. After being stirred for 40 min at 40°C, the mixture was left to stand at room temperature for 1 h. The resulting supernatant, which contained the salt-free Wittig reagent, was slowly added to a solution of bicyclic β-ketoester (−)-**3** (300 mg, 1.19 mmol) in THF (4 mL) at 0°C, and the resulting mixture was stirred at 30°C for 3 h. After water was added, the mixture was extracted with hexane. The organic layers were combined, washed with brine, dried over $MgSO_4$, filtered and concentrated in vacuo to give the corresponding exomethylene compound, which was used without further purification.

To a suspension of lithium aluminum hydride (90 mg, 2.38 mmol) in diethyl ether (3 mL) was added dropwise a solution of the crude exomethylene compound obtained in diethyl ether (2 mL) at 0°C. After the reaction mixture was stirred at room temperature for 12 h, water was added, and the precipitate was filtered through a pad of Celite, and then the filtrate was concentrated in vacuo. Purification by silica gel column chromatography (from 10 to 20% ethyl acetate in hexane) followed by recrystallization from ethyl acetate–hexane gave (+)-albicanol (217 mg, 82% for 2 steps), as colorless crystals: mp 69.0–71.0°C; $[\alpha]_D^{24}$=+10.4 (*c* 0.55, $CHCl_3$); IR (KBr, cm^{-1}) 3384, 3080, 2868, 2856, 1644, 1464, 1390, 1026; ^{1}H NMR (400 MHz, $CDCl_3$) δ 4.94 (d, 1H, *J*=1.6 Hz), 4.64 (d, 1H, *J*=1.6 Hz), 3.84 (brdd, 1H, *J*=11.2, 3.2 Hz), 3.76 (dd, 1H, *J*=10.8, 10.0 Hz), 2.43 (ddd, 1H, *J*=12.8, 4.4, 2.4 Hz), 2.01 (m, 2H), 1.71 (m, 2H), 1.34 (m, 8H), 0.88 (s, 3H), 0.81 (s, 3H), 0.72 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 147.84, 106.25, 59.14, 58.71, 55.13, 41.94, 38.96, 37.84, 33.60, 33.44, 24.17, 21.71, 19.19, 15.26.

4.5. Total synthesis of (+)-, and (−)-acuminolide

4.5.1. 1-(3-Furyl)-2-[(1*S*,4a*S*,8a*S*)-1,2,3,4,4a,5,6,7,8,8a-decahydro-5,5,8a-trimethyl-2-methylene-1-*trans*-naphthyl]-methylketone (20). To a solution of nitrile **18**[21] (1.3 g,

5.60 mmol) in toluene (40 mL) was added diisobutylaluminum hydride (1.0 M in toluene, 11.2 mL, 11.2 mmol) at 0°C. After the reaction mixture was stirred at room temperature for 2 h, a 2N aqueous HCl solution was added, and then the resulting mixture was extracted with ethyl acetate. The organic layers were combined, washed with brine, dried over $MgSO_4$, filtered and concentrated in vacuo to give the corresponding aldehyde, which was used without further purification.

To a solution of 3-bromofuran (1.23 g, 8.37 mmol) in diethyl ether (15 mL) was added dropwise *sec*-BuLi (1.0 M in cyclohexane, 7.30 mL, 7.30 mmol) over 10 min at −78°C. After the reaction mixture was stirred for 30 min, a solution of the crude aldehyde in diethyl ether (25 mL) was added dropwise. After the reaction mixture was stirred at −78°C for 30 min, a saturated aqueous NH_4Cl solution was added, and then the resulting mixture was extracted with diethyl ether. The organic layers were combined, washed with brine, dried over $MgSO_4$, filtered and concentrated in vacuo to give coupling product **19** (1.51 g as a mixture of diastereomer, 91% for 2 steps), which was used without further purification.

To a solution of the crude product **19** in dichloromethane (25 mL) was added Dess–Martin periodinane (3.56 g, 8.39 mmol) at 0°C. After the reaction mixture was stirred at room temperature for 2 h, a saturated aqueous $NaHCO_3$ solution was added. After being stirred for an additional 15 min, the resulting mixture was extracted with ethyl acetate. The organic layers were combined, washed with a saturated aqueous NH_4Cl solution and brine, dried over $MgSO_4$, filtered and concentrated in vacuo. Purification by silica gel column chromatography (5% ethyl acetate in hexane) gave ketone **20** (1.21 g, 80%): mp 99.0–100.0°C; $[\alpha]_D^{24}=-22.8$ (*c* 0.96, $CHCl_3$); IR (NaCl, cm^{-1}) 3137, 1659, 1559, 1512, 1429, 1165; ^1H NMR (400 MHz, $CDCl_3$) d 8.08 (dd, 1H, *J*=1.5, 0.98 Hz), 7.43 (dd, 1H, *J*=2.0, 1.5 Hz), 6.78 (dd, 1H, *J*=2.0, 0.98 Hz), 4.72 (d, 1H, *J*=1.2 Hz), 4.37 (d, 1H, *J*=1.2 Hz), 2.94 (dd, 1H, *J*=16.6, 9.8 Hz), 2.76 (dd, 1H, *J*=16.6, 3.7 Hz), 2.65 (dd, 1H, *J*=9.8, 2.9 Hz), 1.1–2.2 (m, 11H), 0.90 (s, 3H), 0.83 (s, 3H), 0.76 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 194.57, 149.25, 146.63, 144.06, 128.12, 108.79, 106.38, 55.03, 51.11, 41.99, 39.25, 38.95, 37.49, 36.39, 33.54, 33.50, 23.94, 21.75, 19.26, 14.75; EI^+ HRMS Found *m/z* 300.2094, Calcd for $C_{20}H_{28}O_2$ M^+ 300.2082.

4.5.2. 1-(3-Furyl)-2-[(1*R*,2*R*,4a*S*,8a*S*)-1,2,3,4,4a,5,6,7,8,8a-decahydro-5,5,8a-trimethyl-2-hydroxy-2-*tert*-butyldimethylsiloxymethyl-1-*trans*-naphthyl]methylketone (21). To a solution of osmium tetraoxide (1.0 g, 3.93 mmol) in pyridine (15 mL) was added dropwise a solution of ketone **20** (1.07 g, 3.57 mmol) in pyridine (10 mL) at 0°C. After being stirred for 3 h at room temperature, the reaction mixture was poured into an aqueous $NaHSO_3$ (6.77 g, 56.43 mmol) solution (50 mL). After an additional 18 h, the resulting mixture was extracted with ethyl acetate. The organic layers were combined, washed with a saturated aqueous $CuSO_4$ solution and brine, dried over $MgSO_4$, filtered and concentrated in vacuo to give the corresponding diol, which was used without further purification.

To a solution of the crude diol in DMF (25 mL) was added *tert*-butyldimethylsilyl chloride (915 mg, 6.07 mmol) and imidazole (486 mg, 7.14 mmol) at 0°C. The reaction mixture was stirred at room temperature for 1.5 h, a saturated aqueous $NaHCO_3$ solution was added, and then the resulting mixture was extracted with diethyl ether. The organic layers were combined, washed with brine, dried over $MgSO_4$, filtered and concentrated in vacuo. Purification by silica gel column chromatography (20% ethyl acetate in hexane) gave silyl ether **21** (1.52 g, 90% for 2 steps): mp 124.5–126.0°C; $[\alpha]_D^{23}=-4.50$ (*c* 0.63, $CHCl_3$); IR (KBr, cm^{-1}) 3530, 3125, 1672, 1512, 1462, 1254, 1088; ^1H NMR (400 MHz, $CDCl_3$) δ 8.23 (s, 1H), 7.41 (brs, 1H), 6.81 (brs, 1H), 3.65 (d, 1H, *J*=9.8 Hz), 3.41 (dd, 1H, *J*=9.8, 1.5 Hz), 3.17 (s, 1H), 3.08 (dd, 1H, *J*=16.1, 3.0 Hz), 2.40 (dd, 1H, *J*=7.6, 3.0 Hz), 2.11 (dt, 1H, *J*=12.7, 3.0 Hz), 1.1–1.7 (m, 10H), 0.91 (s, 3H), 0.86 (s, 3H), 0.79 (s, 3H), 0.09 (s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 195.94, 147.45, 143.66, 127.40, 109.08, 73.24, 64.20, 55.69, 54.06, 41.58, 39.53, 37.75, 36.92, 33.28, 33.15, 25.86, 21.45, 19.96, 18.33, 18.25, 15.72, −5.40; EI^+ HRMS Found *m/z* 488.2984, Calcd for $C_{26}H_{44}O_4Si$ M^+ 448.3009.

4.5.3. (2*S*,3a*R*,5a*S*,9a*S*,9b*R*)-2-(3-Furyl)-1,2,3a,4,5,5a,6,7,8,9,9a,9b-dodecahydro-3a-hydroxymethyl-6,6,9a-trimethy-*trans*-naphtho[2,1-*b*]furan (22) and (2*R*,3a*R*,5a*S*,9a*S*, 9b*R*)-2-(3-furyl)-1,2,3a,4,5,5a,6,7,8,9,9a,9b-dodecahydro-3a-hydroxymethyl-6,6,9a-trimethy-*trans*-naphtho[2,1-*b*]furan (23). To a solution of silyl ether **21** (300 mg, 0.67 mmol) in THF (6 mL) was added dropwise a solution of L-Selectride® (1.0 M in THF, 2.0 mL, 2.00 mmol) at −78°C. The reaction mixture was stirred for 30 min at −78°C, water was added, and then the resulting mixture was extracted with ethyl acetate. The organic layers were combined, washed with a saturated aqueous NH_4Cl solution and brine, dried over $MgSO_4$, filtered and concentrated in vacuo to give the corresponding alcohol, as a mixture of diastereomers.

To a dichloromethane (6 mL) solution of the crude compound was added *p*-toluenesulfonyl chloride (126 mg, 0.67 mmol). After the reaction mixture was stirred for 2 h at 40°C, a saturated aqueous NH_4Cl solution was added, and then the resulting mixture was extracted with ethyl acetate. The organic layers were combined, washed with brine, dried over $MgSO_4$, filtered and concentrated in vacuo to give a mixture of **22** and **23** (170 mg, 80% for 2 steps, the ratio was 15:1 by ^1H NMR). Purification by silica gel column chromatography (from 7 to 25% ethyl acetate in hexane) gave cyclic ether **22** (faster moving diastereomer) and **23** (slower moving diastereomer).

Data for **22**: Mp 100.0–101.0°C; $[\alpha]_D^{23}=+10.6$ (*c* 0.96, $CHCl_3$); IR (KBr, cm^{-1}) 3555, 2998, 1503, 1462, 1053, 1028; ^1H NMR (400 MHz, $CDCl_3$) δ 7.402 (s, 1H), 7.398 (s, 1H), 6.43 (t, 1H, *J*=1.4 Hz), 5.02 (m, 1H), 3.59 (d, 1H, *J*=10.7 Hz), 3.40 (dd, 1H, *J*=10.7, 2.1 Hz), 2.1–2.4 (m, 3H), 1.0–2.0 (m, 12H), 0.98 (s, 3H), 0.96 (s, 3H), 0.95 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 143.89, 139.17, 127.87, 108.90, 83.26, 72.99, 62.91, 61.16, 57.14, 42.31, 39.76, 36.45, 34.77, 33.47, 33.08, 30.16, 21.01, 20.35, 18.41, 15.41; FAB^+ HRMS Found *m/z* 319.2239, Calcd for $[C_{20}H_{30}O_3+H]^+$ 319.2273.

Data for **23**: $[\alpha]_D^{22}=-8.32$ (*c* 1.16, $CHCl_3$); IR (NaCl, cm^{-1}) 3349, 2129, 1508, 1458, 1157, 1026; ^1H NMR (400 MHz, $CDCl_3$) δ 7.39 (s, 1H), 7.37 (s, 1H), 6.34 (s, 1H), 5.10 (dd, 1H, *J*=9.3, 2.2 Hz), 3.55 (s, 2H), 2.39 (dt, 1H, *J*=11.6, 3.0 Hz), 2.17 (ddd, 1H, *J*=13.5, 11.5, 9.3 Hz), 1.0–2.0 (m, 14H), 0.89 (s, 3H), 0.84 (s, 3H), 0.79 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 143.61, 139.06, 128.83, 108.49, 83.89, 71.16, 61.20, 59.37, 57.37, 42.36, 39.68, 36.36, 34.44, 33.54, 33.12, 31.02, 21.02, 20.25, 18.41, 15.08; FAB^+ HRMS Found *m/z* 319.2287, Calcd for $[C_{20}H_{30}O_3+H]^+$ 319.2273.

4.5.4. (−)-Acuminolide. A solution of cyclic ether **22** (220 mg, 0.69 mmol), diisopropylethylamine (1.20 mL, 6.90 mmol), and a catalytic amount of 5,10,15,20-tetraphenyl-21*H*,23*H*-porphine in dichloromethane (5 mL) was irradiated with halogen–tungsten lamp under oxygen atmosphere for 1.5 h at −78°C. After the reaction mixture was allowed to warm to room temperature, a saturated aqueous oxalic acid solution was added, and then the resulting mixture was extracted with dichloromethane–methanol (3:1). The organic layers were combined, dried over $MgSO_4$, filtered and concentrated in vacuo. Purification by silica gel column chromatography (from 50 to 70% ethyl acetate in hexane) followed by recrystallization from ethyl acetate–hexane gave (−)-acuminolide (181 mg, 75%), as colorless crystals: mp 207.0–208.0°C; $[\alpha]_D^{23}=-33.2$ (*c* 1.25, $CHCl_3$); IR (KBr, cm^{-1}) 3503, 3355, 2946, 2897, 2872, 1752, 1653, 1468, 1142, 1053; ^1H NMR (400 MHz, $CDCl_3+CD_3OD$ (9:1)) δ 6.13 (s, 1H), 6.09 (s, 1H), 4.93 (brs, 1H), 3.67 (d, 1H, *J*=11.1 Hz), 3.31 (d, 1H, *J*=11.1 Hz), 2.39 (brd, 1H, *J*=8.8 Hz), 2.21 (m, 1H), 1.0–2.0 (m, 14H), 0.90 (s, 3H), 0.83 (s, 3H), 0.80 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3+CD_3OD$ (9: 1)) δ 171.15, 170.14, 116.24, 98.09, 84.28, 74.13, 62.02, 60.92, 56.91, 41.94, 39.53, 36.14, 33.99, 33.03, 32.78, 28.86, 20.59, 20.09, 18.08, 15.23; Anal. found: C, 68.38; H, 8.59%. Calcd for $C_{20}H_{30}O_3$: C, 68.55; H, 8.63%.

4.5.5. (+)-Acuminolide.[3] Mp 207.5–208.5°C; $[\alpha]_D^{23}=+34.6$ (*c* 0.85, $CHCl_3$); Anal. found: C, 68.18; H, 8.65%. Calcd for $C_{20}H_{30}O_3$: C, 68.55; H, 8.63%. [lit.[3] mp 207–208°C; $[\alpha]_D^{20}=+36.2$ (*c* 1.34, $CHCl_3$)].

4.6. Total synthesis of (−)-spongianolide A

4.6.1. (1*R*,4a*S*,4b*R*,8a*R*,10a*S*)-1,2,3,4,4a,4b,5,6,7,8,8a,9,10,10a-Tetradecahydro-4b,8,8,10a-tetramethyl-2-methylene-*trans*-*anti*-*trans*-phenanthrene-1-methanol (25). To a suspension of methyltriphenylphosphonium bromide (5.57 g, 15.60 mmol) in THF (40 mL) was added sodium amide (609 mg, 15.60 mmol) at room temperature. After being stirred for 40 min at 40°C, the mixture was left to stand at room temperature for 1 h. The resulting supernatant, which contained the salt-free Wittig reagent, was slowly added to a solution of tricyclic β-ketoester (+)-**6** (1.10 g, 3.45 mmol) in THF (10 mL) at room temperature. After the reaction mixture was stirred at 30°C for 3 h, water was added, and then the resulting mixture was extracted with hexane. The organic layers were combined, washed with brine, dried over $MgSO_4$, filtered and concentrated in vacuo to give the corresponding exomethylene compound, which was used without further purification.

To a suspension of lithium aluminum hydride (262 mg, 6.90 mmol) in diethyl ether (20 mL) was added dropwise a solution of the crude exomethylene compound in diethyl ether (5 mL) at 0°C. After reaction mixture was stirred at room temperature for 12 h, water was added, and the precipitate was filtered through a pad of Celite, and then the filtrate was concentrated in vacuo. Purification by silica gel column chromatography (from 10 to 20% ethyl acetate in hexane) gave alcohol **25** (844 mg, 84% for 2 steps): mp 99.0–100.0°C; $[\alpha]_D^{24}=-11.7$ (*c* 1.05, $CHCl_3$); IR (KBr, cm^{-1}) 3300, 1644, 1464, 1444; ^1H NMR (400 MHz, $CDCl_3$) δ 4.93 (d, 1H, *J*=1.6 Hz), 4.64 (d, 1H, *J*=1.6 Hz), 3.79 (m, 2H), 2.41 (ddd, 1H, *J*=12.8, 4.4, 2.4 Hz), 2.00 (m, 2H), 1.66 (m, 5H), 1.36 (m, 6H), 0.86 (m, 2H), 0.86 (s, 3H), 0.81 (s, 3H), 0.80 (s, 3H), 0.72 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 147.79, 105.95, 59.83, 59.49, 58.68, 56.42, 41.97, 40.61, 40.04, 39.30, 37.80, 33.32, 33.23, 23.01, 21.43, 18.93, 18.56, 16.28, 16.25; EI^+ HRMS Found *m/z* 290.2592, Calcd for $C_{20}H_{34}O$ M^+ 290.2610.

4.6.2. (1*R*,2*S*,4a*R*,4b*S*,8a*S*,10a*R*)-1,2,3,4,4a,4b,5,6,7,8,8a,9,10,10a-Tetradecahydro-1-hydroxymethyl-4b,8,8,10a-tetra-methyl-2,2′-di-*O*-isopropylidene-*trans*-*anti*-*trans*-phenanthrene (27). To a solution of alcohol **25** (258 mg, 0.89 mmol) in DMF (8 mL) was added *tert*-butyldimethylsilyl chloride (174 mg, 1.16 mmol), 4-(dimethylamino)pyridine (22 mg, 0.18 mmol) and triethylamine (0.19 mL, 1.33 mmol) at 0°C. After the reaction mixture was stirred at room temperature for 1.5 h, a saturated aqueous $NaHCO_3$ solution was added, and then the resulting mixture was extracted with diethyl ether. The organic layers were combined, washed with brine, dried over $MgSO_4$, filtered and concentrated in vacuo to give the corresponding silyl ether, which was used without further purification.

To a solution of osmium tetraoxide (248 mg, 0.98 mmol) in pyridine (8 mL) was added dropwise a solution of crude silyl ether in pyridine (3 mL) at 0°C. After being stirred for 4 h at room temperature, the reaction mixture was poured into an aqueous $NaHSO_3$ (1.64 g, 13.66 mmol) solution (6 mL). The resulting mixture was stirred for an additional 18 h, and extracted with ethyl acetate. The organic layers were combined, washed with a saturated aqueous $CuSO_4$ solution and brine, dried over $MgSO_4$, filtered and concentrated in vacuo to give the corresponding diol **26**, which was used without further purification.

To a solution of the crude diol **26** in acetone (12 mL) was added 2,2-dimethoxypropane (1.09 mL, 8.88 mmol) and a catalytic amount of pyridinium *p*-toluenesulfonate at room temperature. After the reaction mixture was stirred at the same temperature, a saturated aqueous $NaHCO_3$ solution was added, and then the resulting mixture was extracted with ethyl acetate. The organic layers were combined, washed with brine, dried over $MgSO_4$, filtered and concentrated in vacuo to give the corresponding acetonide, which was used without further purification.

To a solution of the crude acetonide in THF (10 mL) was added tetra-*n*-butylammonium fluoride (581 mg,

2.22 mmol) at room temperature. After the reaction mixture was stirred for 3 h at 60°C, water was added, and then the resulting mixture was extracted with ethyl acetate. The organic layers were combined, washed with brine, dried over $MgSO_4$, filtered and concentrated in vacuo. Purification by silica gel column chromatography (from 5 to 20% ethyl acetate in hexane) gave alcohol **27** (256 mg, 79% for 4 steps): mp 187.0–188.0°C; $[\alpha]_D^{24}=-3.47$ (*c* 1.01, $CHCl_3$); IR (KBr, cm^{-1}) 3552, 3492, 3456, 1056, 1026; ^1H NMR (400 MHz, $CDCl_3$) δ 3.82 (m, 4H), 3.14 (dd, 1H, *J*=10.0, 1.6 Hz), 2.11 (ddd, 1H, *J*=12.4, 3.2, 3.2 Hz), 1.87 (dd, 1H, *J*=5.2, 1.6 Hz), 1.65 (m, 5H), 1.44 (s, 3H), 1.39 (s, 3H), 1.27 (m, 7H), 0.95 (dd, 1H, *J*=12.0, 2.4 Hz), 0.85 (s, 3H), 0.81 (m, 2H), 0.79 (s, 3H), 0.78 (s, 3H), 0.66 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 106.97, 86.12, 67.99, 59.57, 59.39, 56.22, 41.90, 40.60, 39.90, 38.87, 38.42, 37.44, 33.22, 28.56, 26.55, 21.31, 19.44, 18.54, 18.33, 17.03, 16.10; Anal. found: C, 75.80; H, 11.04%. Calcd for $C_{23}H_{40}O_3$: C, 75.78; H, 11.06%.

4.6.3. (1*S*,2*S*,4a*R*,4b*S*,8a*S*,10a*R*)-1,2,3,4,4a,4b,5,6,7,8,8a,9,10, 10a-Tetradecahydro-1-formyl-4b,8,8,10a-tetramethyl-2,2′-di-*O*-isopropylidene-*trans*-*anti*-*trans*-phenanthrene (28). To a solution of oxalyl chloride (0.14 mL, 1.576 mmol) in dichloromethane (5 mL) was added dropwise DMSO (0.13 mL, 1.89 mmol) at −78°C. After the mixture was stirred for 10 min at the same temperature, a solution of alcohol **27** (228 mg, 0.63 mmol) in dichloromethane (2 mL) was added. The resulting reaction mixture was stirred for 40 min at −78°C, and triethylamine (0.44 mL, 3.14 mmol) was added. After the mixture was stirred for 10 min at room temperature, water was added, and then the resulting mixture was extracted with diethyl ether. The organic layers were combined, washed with brine, dried over $MgSO_4$, filtered and concentrated in vacuo. Purification by silica gel column chromatography (from 3 to 10% ethyl acetate in hexane) gave aldehyde **28** (190 mg, 84%): mp 195.0–196.0°C; $[\alpha]_D^{24}=-13.3$ (*c* 1.07, $CHCl_3$); IR (KBr, cm^{-1}) 1712, 1052, 1032; ^1H NMR (400 MHz, $CDCl_3$) δ 9.98 (d, 1H, *J*=4.0 Hz), 4.30 (dd, 1H, *J*=8.8, 2.0 Hz), 3.93 (d, 1H, *J*=8.8 Hz), 2.49 (d, 1H, *J*=4.0 Hz), 2.08 (ddd, 1H, *J*=8.4, 3.2, 3.2 Hz), 1.63 (m, 6H), 1.40 (s, 3H), 1.28 (m, 6H), 1.22 (s, 3H), 1.03 (s, 3H), 0.85 (s, 3H), 0.82 (m, 3H), 0.80 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 205.29, 107.38, 82.78, 68.67, 67.70, 59.15, 56.43, 41.90, 40.65, 39.86, 39.69, 39.26, 37.57, 33.22, 28.25, 26.20, 21.34, 19.39, 18.44, 17.86, 17.11, 16.24; Anal. found: C, 76.18; H, 10.61%. Calcd for $C_{23}H_{38}O_3$: C, 76.20; H, 10.56%.

4.6.4. 4-[2-((1*S*,2*S*,4a*R*,4b*S*,8a*S*,10a*R*)-1,2,3,4,4a,4b,5,6,7,8,8a,9, 10,10a-Tetradecahydro-4b,8,8,10a-tetramethyl-2,2′-di-*O*-isopropylidene-*trans*-*anti*-*trans*-phenanthyl)-(*E*)-ethynyl]-2-trimethylsilylfuran (29). To a solution of 2-trimethylsilyl-4-furyltriphenylphosphonium methylide (**W***), which was prepared from the silylfuran–Wittig salt (**W**) (320 mg, 0.65 mmol) and *n*-BuLi (1.5 M in hexane, 0.43 mL, 0.65 mmol) in THF (6 mL), was added dropwise a solution of aldehyde **28** (194 mg, 0.54 mmol) in THF (3 mL) at 0°C. After the reaction mixture was stirred for 10 min at 0°C, water was added, and then the resulting mixture was extracted with diethyl ether. The organic layers were combined, washed with brine, dried over $MgSO_4$, filtered and concentrated in vacuo. Purification by silica gel column chromatography (from 5 to 20% ethyl acetate in hexane) gave silylfuran **29** (225 mg, 86%): mp 112.0–113.0°C; $[\alpha]_D^{24}=-16.4$ (*c* 0.97, $CHCl_3$); IR (KBr, cm^{-1}) 1685, 1636, 1252; ^1H NMR (400 MHz, $CDCl_3$) δ 7.53 (s, 1H), 6.70 (s, 1H), 6.31 (d, 1H, *J*=15.2Hz), 5.84 (dd, 1H, *J*=15.2, 10.0 Hz), 3.90 (dd, 1H, *J*=8.4, 2.0 Hz), 3.82 (d, 1H, *J*=8.4 Hz), 2.14 (d, 1H, *J*=10.0 Hz), 2.09 (ddd, 1H, *J*=12.4, 3.2, 3.2 Hz), 1.38 (s, 3H), 1.35 (m, 12H), 1.13 (s, 3H), 0.86 (m, 3H), 0.85 (s, 3H), 0.83 (s, 3H), 0.82 (s, 3H), 0.79 (s, 3H), 0.27 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 161.21, 143.85, 124.86, 124.78, 124.45, 117.20, 107.10, 83.86, 68.39, 62.17, 59.72, 56.51, 42.03, 39.99, 39.74, 38.60, 37.54, 33.27, 33.25, 28.37, 26.49, 21.40, 19.44, 18.57, 18.14, 16.41, 16.31, −1.68; EI^+ HRMS Found *m/z* 498.3527, Calcd for $C_{31}H_{50}O_2Si$ M^+ 498.3529.

4.6.5. 2-Hydroxy-3-[2-((1*S*,2*S*,4a*R*,4b*S*,8a*S*,10a*R*)-1,2,3,4,4a,4b,5,6,7,8,8a,9,10,10a-Tetradecahydro-4b,8,8,10a-tetramethyl-2,2′-di-*O*-isopropylidene-*trans*-*anti*-*trans*-phenanthyl)-(*E*)-ethynyl]-5-butenolide (30). A solution of silylfuran **29** (117 mg, 0.24 mmol) and a catalytic amount of 5,10,15,20-tetraphenyl-21*H*,23*H*-porphine in dichloromethane (3 mL) was irradiated with halogen–tungsten lamp under oxygen atmosphere for 1.5 h at −78°C. After being allowed to warm to room temperature, the reaction mixture was concentrated in vacuo to remove of the solvents. Purification by silica gel column chromatography (50% ethyl acetate in hexane) gave butenolide **30** (74 mg, 74%), as a mixture of stereoisomers at the hydroxy group in the butenolide ring: mp 203.0–205.0°C; $[\alpha]_D^{24}=-18.5$ (*c* 0.96, $CHCl_3$); IR (KBr, cm^{-1}) 3384, 3284, 1760, 1738, 1642, 1194, 1166, 1156; ^1H NMR (400 MHz, $CDCl_3$) δ 6.49 (dd, 1H, *J*=15.6, 9.6 Hz), 6.41 (dd, 1H, *J*=15.6, 1.2 Hz), 6.23 (brdd, 1H, *J*=10.8, 7.6 Hz), 5.86 (s, 1H), 4.55 (brdd, 1H, *J*=15.2, 8.0 Hz), 3.84 (m, 2H), 2.23 (dd, 1H, *J*=10.0, 6.4 Hz), 2.11 (m, 1H), 1.50 (m, 9H), 1.38 (s, 3H), 1.14 (d, 3H, *J*=15.6 Hz), 1.10 (m, 2H), 0.87 (s, 3H), 0.86 (m, 4H), 0.84 (s, 3H), 0.83 (d, 3H, *J*=1.6 Hz), 0.80 (d, 1H, *J*=0.8 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ (171.18, 171.14), (141.31, 140.76), (125.69, 125.47), 115.79, (107.34, 107.20), (97.50, 97.49), (83.75, 83.71), (68.37, 68.10), (62.87, 62.68), 59.46, 56.51, (42.23, 42.09), 41.94, 39.95, (39.63, 39.38), (38.97, 38.83), 37.58, (33.27, 33.23), (28.29, 28.06), (26.45, 26.26), 21.36, 19.33, 18.50, 18.09, 16.41; Anal. found: C, 73.18; H, 9.41%. Calcd for $C_{28}H_{42}O_5$: C, 73.33; H, 9.23%.

4.6.6. 2-Hydroxy-3-[2-((1*S*,2*S*,4a*R*,4b*S*,8a*S*,10a*R*)-1,2,3,4,4a,4b, 5,6,7,8,8a,9,10,10a-Tetradecahydro-2-hydroxy-2-hydro-xymethyl-4b,8,8,10a-tetramethyl-*trans*-*anti*-*trans*-phenanthyl)-(*E*)-ethynyl]-5-butenolide (31). To a solution of butenolide **30** (63 mg, 0.14 mmol) in THF (2 mL) was added a catalytic amount of a 2N aqueous HCl solution at room temperature. After being stirred for 48 h at 60°C, the reaction mixture was filtered to remove solvents, and then the diol **31** was obtained as a white solid (32 mg, 63%): mp 238°C (decompose); $[\alpha]_D^{24}=+2.28$ (*c* 0.57, DMSO); IR (KBr, cm^{-1}) 3536, 3388, 3176, 2932, 2872, 2848, 1742, 1638, 1304, 1140, 1070; ^1H NMR (400 MHz, DMSO-d_6) d 7.81 (s, 1H), 6.54 (brdd, 1H, *J*=14.8, 10.8 Hz), 6.27 (d, 1H, *J*=15.6 Hz), 6.23 (s, 1H),

6.01 (s, 1H), 4.32 (brs, 1H), 3.92 (brs, 1H), 3.49 (m, 1H), 2.50 (m, 1H), 2.09 (brs, 1H), 1.96 (d, 1H, J=10.4 Hz), 1.38 (m, 11H), 0.90 (s, 3H), 0.86 (m, 4H), 0.82 (s, 3H), 0.79 (s, 3H), 0.78 (s, 3H); ^{13}C NMR (100 MHz, DMSO-d_6) d 171.17, 162.41, (142.35, 141.81), 124.03, 114.18, 97.83, 74.16, 66.39, 63.80, (63.10, 62.96), 59.86, 56.06, 42.34, 41.67, 38.45, 37.83, 37.16, 33.12, 32.95, 21.24, 18.41, 18.12, 17.68, 17.11, 16.10; FAB$^+$ HRMS Found m/z 441.2651, Calcd for $[C_{25}H_{38}O_5+Na]^+$ 441.2619.

4.6.7. (−)-Spongianolide A.[4] To a solution of diol **39** (49 mg, 0.12 mmol) in pyridine (2 mL) was added acetic anhydride (0.03 mL, 0.35 mmol) at room temperature. After the reaction mixture was stirred for 3 h at 50°C, a saturated aqueous $CuSO_4$ solution was added, and then the resulting mixture was extracted with ethyl acetate. The organic layers were combined, washed with brine, dried over $MgSO_4$, filtered and concentrated in vacuo to give the corresponding diacetate, which was used without further purification.

To a solution of the crude diacetate obtained in methanol (1 mL) was added a catalytic amount of a saturated aqueous $NaHCO_3$ solution at room temperature. After the reaction mixture was stirred for 30 h at the same temperature, a saturated aqueous NH_4Cl solution was added, and then the resulting mixture was extracted with ethyl acetate. The organic layers were combined, washed with brine, dried over $MgSO_4$, filtered and concentrated in vacuo. Purification by silica gel column chromatography (50% ethyl acetate in hexane) followed by recrystallization from ethyl acetate–hexane gave (−)-spongianolide **A** (28 mg, 52% for 2 steps), as colorless crystals: mp 224.5–225.5°C; $[\alpha]_D^{24}=-31.2$ (c 0.60, $CHCl_3$); IR (KBr, cm^{-1}) 3428, 3408, 3300, 3268, 1740, 1726, 1642, 1196, 1142, 1040; ^{1}H NMR (400 MHz, acetone-d_6) δ 6.71 and 6.70 (brdd, 1H, J=16.0, 10.4 Hz), 6.46 (d, 1H, J=15.6 Hz), 6.39 and 6.37 (s, 1H), 5.97 and 5.94 (s, 1H), 4.40 (d, 1H, J=11.6 Hz), 4.05 (dd, 1H, J=20.0, 11.6 Hz), 2.13 (d, 1H, J=10.4 Hz), 2.06 (s, 3H), 1.54 (m, 9H), 1.10 (m, 3H), 1.05 (s, 3H), 0.88 (s, 3H), 0.87 (m, 4H), 0.86 (s, 3H), 0.83 (s, 3H); ^{13}C NMR (100 MHz, acetone-d_6) δ 171.71, (171.43, 171.16), (162.72, 162.55), (141.41, 141.01), (126.22, 126.07), (116.18, 116.05), (98.64, 98.60), (73.68, 73.58), (68.12, 68.05), (67.97, 67.85), 61.19, 57.40, 43.52, 42.82, 40.58, 39.01, 38.38, 38.29, 33.89, 33.67, 21.70, 20.86, 19.42, 19.24, 18.87, 17.76, 16.73; FAB$^+$ HRMS Found m/z 443.2802, Calcd for $[C_{25}H_{38}O_5-OH]^+$ 443.2619.

4.7. Formal synthesis of (+)-scalarenedial

4.7.1. (1*S*,4a*R*,4b*S*,6a*R*,10a*R*,10b*S*,12a*R*)-1,2,3,4,4a,4b,5,6,6a,7,8,9,10,10a,10b,11,12,12a-Octadecahydro-4b,7,7,10a,12a-pentamethyl-2-methylene-*trans*-*anti*-*trans*-*anti*-*trans*-chrysene-1-methanol (32). To a suspension of methyltri-phenylphosphonium bromide (2.78 g, 7.78 mmol) in THF (12 mL) was added sodium amide (304 mg, 7.78 mmol) at room temperature. After being stirred for 40 min at 40°C, the mixture was left to stand at room temperature for 1 h. The supernatant, which contained the salt-free Wittig reagent, was slowly added to a solution of tetracyclic β-ketoester (+)-**9** (200 mg, 0.52 mmol) in THF (5 mL) at room temperature. After the reaction mixture was stirred at room temperature for 15 min, water was added, and then the resulting mixture was extracted with ethyl acetate. The organic layers were combined, washed with a saturated aqueous $NaHCO_3$ solution and brine, dried over $MgSO_4$, filtered and concentrated in vacuo to give the corresponding exomethylene compound, which was used without further purification.

To a suspension of lithium aluminum hydride (79 mg, 2.07 mmol) in THF (2 mL) was added dropwise a solution of the crude exomethylene compound obtained in THF (2 mL) at 0°C. After the reaction mixture was stirred at room temperature for 24 h, water and a 2N aqueous HCl solution were added, and then the resulting mixture was extracted with ethyl acetate. The organic layers were combined, washed with brine, dried over $MgSO_4$, filtered and concentrated in vacuo. Purification by silica gel column chromatography (from 1 to 10% ethyl acetate in hexane) gave alcohol **32** (130 mg, 70% for 2 steps): mp 170.0–171.0°C; $[\alpha]_D^{22}=+6.28$ (c 0.11, $CHCl_3$); IR (KBr, cm^{-1}) 3509, 2928, 2845, 1647; ^{1}H NMR (400 MHz, $CDCl_3$) δ 4.92 (d, 1H, J=1.5 Hz), 4.62 (d, 1H, J=1.2 Hz), 3.82 (dd, 1H, J=11.0, 3.7 Hz), 3.77 (dd, 1H, J=10.7, 9.5 Hz), 2.41 (ddd, 1H, J=12.8, 4.3, 2.4 Hz), 1.90–2.04 (m, 2H), 1.20–1.80 (m, 13H), 1.05–1.18 (m, 2H), 0.94 (m, 1H), 0.75–0.85 (m, 3H), 0.84 (s, 3H), 0.804 (s, 6H), 0.798 (s, 3H), 0.70 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 147.86, 105.95, 61.02, 60.27, 59.50, 58.73, 56.48, 42.13, 41.99, 40.72, 39.84, 39.14, 38.10, 37.78, 37.48, 33.28, 22.96, 21.33, 18.65, 18.29, 17.77, 17.49, 16.21, 16.14; Anal. found: C, 83.55; H, 12.05%. Calcd for $C_{25}H_{42}O$: C, 83.73; H, 11.80%.

4.7.2. (1*S*,2*S*,4a*R*,4b*S*,6a*R*,10a*R*,10b*S*,12a*R*)-2-Epoxymethylene-1,2,3,4,4a,4b,5,6,6a,7,8,9,10,10a,10b,11,12,12a-octa-decahydro-4b,7,7,10a,12a-pentamethyl-*trans*-*anti*-*trans*-*anti*-*trans*-chrysene-1-methanol (33). To a solution of alcohol **32** (30 mg, 0.08 mmol) and a 0.5 M aqueous $NaHCO_3$ solution (0.35 mL, 0.17 mmol) in dichloro-methane (2 mL) was added *m*-chloroperbenzoic acid (17 mg, 0.10 mmol) at 0°C. After the reaction mixture was stirred at room temperature for 40 min, a saturated aqueous $NaHSO_3$ solution was added, and then the resulting mixture was extracted with diethyl ether. The organic layers were combined, washed with a saturated aqueous $NaHCO_3$ solution and brine, dried over $MgSO_4$, filtered and concentrated in vacuo. Purification by silica gel column chromatography (from 6 to 10% ethyl acetate in hexane) gave epoxide **33** (27 mg, 85%): mp 235.0–237.0°C; $[\alpha]_D^{21}=+2.87$ (c 0.73, $CHCl_3$); IR (KBr, cm^{-1}) 3509, 2932, 2845, 1701; ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.61 (ddd, 1H, J=11.0, 11.0, 3.2 Hz), 3.40 (dd, 1H, J=11.5, 10.3 Hz), 3.20 (dd, 1H, J=3.7, 2.2 Hz), 3.10 (d, 1H, J=10.7 Hz), 2.71 (d, 1H, J=3.7 Hz), 1.20–2.00 (m, 18H), 1.14 (td, 1H, J=13.2, 3.9 Hz), 1.04 (dd, 1H, J=12.4, 2.9 Hz), 0.96 (td, 1H, J=13.2, 4.2 Hz), 0.85 (s, 3H), 0.832 (s, 3H), 0.827 (s, 3H), 0.81 (s, 3H), 0.80 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 61.86, 60.84, 59.69, 58.91, 56.42, 54.58, 51.76, 42.08, 41.96, 40.55, 39.80, 37.96, 37.46, 36.16, 33.27, 21.33, 20.41, 18.62, 18.28, 17.49, 17.26, 16.61, 16.19; FAB$^+$ HRMS Found m/z 375.3279, Calcd for $[C_{25}H_{42}O_2+H]^+$ 375.3263.

4.7.3. (1*S*,4a*R*,4b*S*,6a*R*,10a*R*,10b*S*,12a*R*)-1,4,4a,4b,5,6,6a,7,8,9,10,10a,10b,11,12,12a-Hexadecahydro-1,2-di-(hydroxymethyl)-4b,7,7,10a,12a-pentamethyl-*trans-anti-trans-anti-trans*-chrysene (34).[27] To a solution of epoxide **33** (45 mg, 0.12 mmol) in THF (4 mL) and water (1 mL) was added a catalytic amount of 10-camphorsulfonic acid at room temperature. After the reaction mixture was stirred under reflux condition for 3 h, a saturated aqueous $NaHCO_3$ solution was added, and then the resulting mixture was extracted with ethyl acetate. The organic layers were combined, washed with brine, dried over $MgSO_4$, filtered and concentrated in vacuo. Purification by silica gel column chromatography (from 3 to 10% ethyl acetate in hexane) followed by recrystallization from ethyl acetate–hexane gave diol **34** (24 mg, 53%), whose spectral data were in good corresponding with those reported[27]: mp 214.0–216.0°C; $[\alpha]_D^{21}=-6.80$ (*c* 0.20, $CHCl_3$); IR (KBr, cm^{-1}) 3360, 2920, 2845, 1721, 1672; ^1H NMR (400 MHz, $CDCl_3$) δ 5.78 (m, 1H), 4.35 (d, 1H, *J*=12.0 Hz), 3.98 (d, 1H, *J*=12.0 Hz), 3.90 (dd, 1H, *J*=10.8, 2.0 Hz), 3.69 (dd, 1H, *J*=10.8, 8.5 Hz), 0.75–2.20 (m, 20H), 0.89 (s, 3H), 0.87 (s, 3H), 0.84 (s, 3H), 0.83 (s, 3H), 0.72 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 136.64, 127.55, 67.45, 61.51, 60.79, 56.42, 54.95, 54.70, 42.13, 41.73, 41.06, 39.86, 37.58, 37.39, 35.57, 33.29, 22.50, 21.37, 18.61, 18.15, 17.63, 16.78, 16.42, 15.31.

4.7.4. (1*S*,4a*R*,4b*S*,6a*R*,10a*R*,10b*S*,12a*R*)-1,4,4a,4b,5,6,6a,7,8,9,10,10a,10b,11,12,12a-Hexadecahydro-4b,7,7,10a,12a-pentamethyl-*trans-anti-trans-anti-trans*-chryseno [2,1-*c*] dihydro-2(3*H*)-furanone (35).[27] To a solution of diol **34** (8 mg, 0.02 mmol) in dichloromethane (3.0 mL) was added manganese dioxide (240 mg) at room temperature. After being stirred for 15 min at the same temperature, the reaction mixture was filtered through a pad of Celite, and then the filtrate was concentrated in vacuo. Purification by silica gel column chromatography (from 2 to 8% ethyl acetate in hexane) gave lactone **35** (6 mg, 75%), whose IR, ^1H-, and ^{13}C NMR were in good corresponding with those of reported[27]: IR (KBr, cm^{-1}) 2931, 1766; ^1H NMR (400 MHz, $CDCl_3$) δ 6.85 (m, 1H), 4.34 (t, 1H, *J*=9.3 Hz), 4.02 (t, 1H, *J*=9.2 Hz), 2.75 (m, 1H), 2.35 (m, 1H), 2.10 (m, 1H), 0.75–2.20 (m, 15H), 0.90 (s, 3H), 0.84 (s, 6H), 0.80 (s, 3H), 0.75 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 170.23, 136.43, 126.93, 67.25, 61.34, 56.42, 54.84, 51.16, 42.07, 41.71, 40.84, 39.90, 37.62, 37.52, 34.29, 33.27, 24.10, 21.34, 18.57, 18.03, 17.16, 16.41, 14.01.

Acknowledgements

We are grateful to Professor A. Douglas Kinghorn of Department of Medicinal Chemistry and Pharmacognosy, University of Illinois at Chicago for providing his natural acuminolide. We thank Mr Yu Yamamoto and his co-workers of the Institute for Life Science Research at Asahi Chemical Industry Co., Ltd. for their high-resolution mass spectra measurements and elemental analyses. This work was partially supported by a Grant-in-Aid for Scientific Research 09480415 from the Ministry of Education, Science, Sports and Culture of Japan.

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