Synthesis of (+)-Hanagokenol A, (+)-Fortunins E, G, H, and (–)-Sugikurojin A from Abietic Acid

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Abstract: A series of 12-hydroxy-substituted abietane diterpenes, functionalized on C19 or C18, have been synthesized starting from 18-hydroxyferruginol. The first synthesis of antibacterial hanagokenol A and fortunins E, G, and H, and a new procedure for preparing sugikurojin A and the immunosuppressive 19-hydroxyferruginol are reported.

Key words: antibiotics, diastereoselectivity, phenols, terpenoids, oxidation

Oxygenated abietane diterpenes, especially phenols and quinones, are interesting metabolites due to the wide range of valuable biological activity exhibited by some of them. Representative examples of such derivatives are taxodione[1] and salvinolone,[2] which are active against methicillin-resistant *Staphylococcus aureus* (MRSA) and vancomycin-resistant *Enterococcus* (VRE), two bacteria that are increasingly found in hospitals worldwide. Another significant oxidized abietane diterpene is 6α-hydroxysugiol, which strongly inhibits various human tumors and oncogen-transformed cells.[3] Abietane phenols functionalized at C19, even though they are not very abundant, have also been found in nature. Examples of these include lambertic acid (**1**)[4] and 12-hydroxyabieta-8,11,13-trien-19-al (**2**);[5] the isolation of 6,7-dehydro-19-hydroxyferruginol (sugikurojin A, **3**), a new diterpene from *Cryptomeria japonica*, was recently reported,[6] and very recent studies have revealed that 19-hydroxyferruginol (**4**)[7] is a target for tolerance after transplantation and in autoimmune diseases.[8] Abietane phenols bearing a functional group on C18 are most frequently found in natural sources, e.g. 12-hydroxydehydroabietic acid (**5**),[9] and the gastroprotective 18-hydroxyferruginol (**6**).[10] Recently, the MRSA and VRE antibacterial hanagokenol A (**7**) was isolated from *Cladonia rangiferina*.[11] More recently, fortunins E (**9**), G (**10**), and H (**8**) were isolated from the bark of *Cladonia fortunei*.[12] The biological activity of compounds **8**–**10** has not yet been investigated.

In spite of the interest of this type of compound, few syntheses have been reported, and most of these have been total syntheses, including polyene cascade cyclizations,[13] Diels–Alder cycloadditions,[14] electrophilic cyclizations,[15] Robinson annulations,[16] and domino acylation–cycloalkylations.[17] Diastereoselective syntheses of these compounds have also been reported, in most cases starting from podocarpic[18] and abietic acid. The introduction of an oxygenated function on C12 of the latter compound has been undertaken utilizing different procedures, such as the preparation of an iron complex,[19] the electrochemical oxidation of the methyl ester,[20] or the Baeyer–Villiger oxidation of the 12-acetyl derivative of dehydroabietic acid.[21] Our group has reported a new procedure for this purpose, which was used for the synthesis of compounds **5** and **6** and others.[22] The preparation of C19-functionalized abietane diterpenes, such as compounds **1**–**4**, has been achieved most frequently by starting from natural C19 functionalized precursors.[23] In a previous paper, we communicated the synthesis of sugikurojin A (**3**) and 19-hydroxyferruginol (**4**) from the labdane diterpene *trans*-communic acid, via manganese(III)-based oxidative free radical cyclization.[24]

The synthesis of the scarce C19-functionalized abietane diterpenes starting from the abundant C18-functionalized abietane diterpenes appears to be of interest. Only two

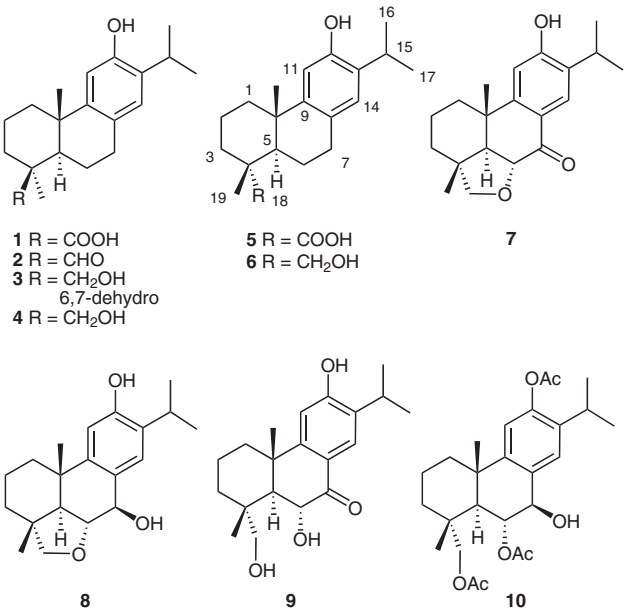

Figure 1 Bioactive abietane diterpenes and related compounds

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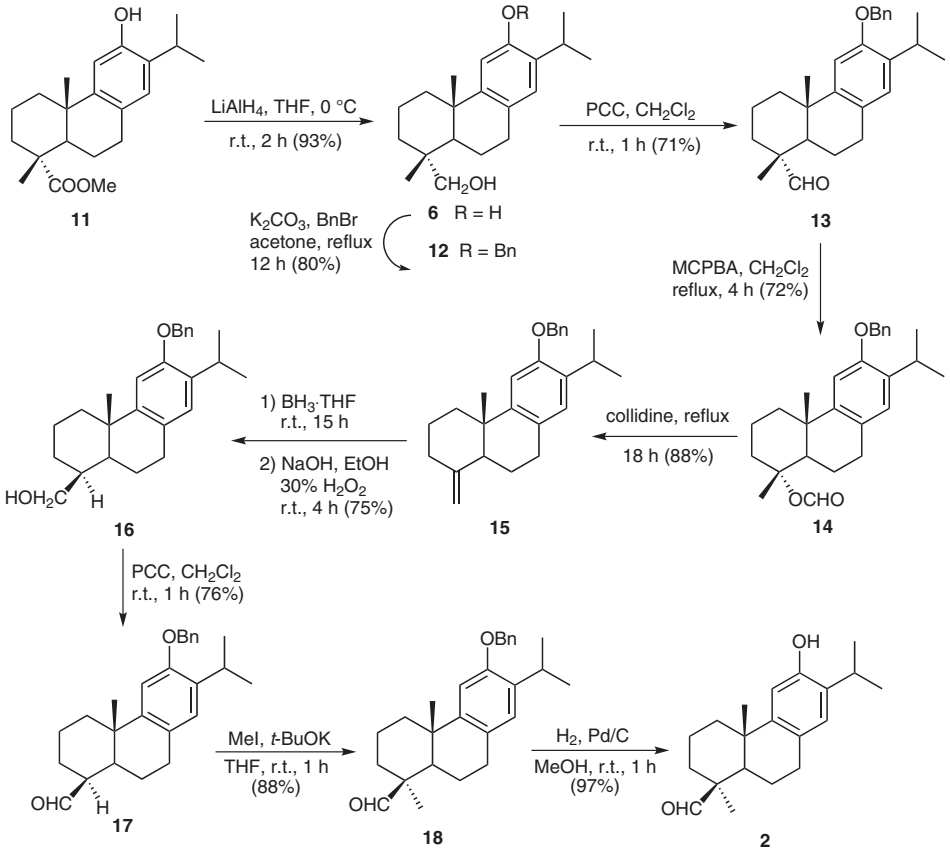
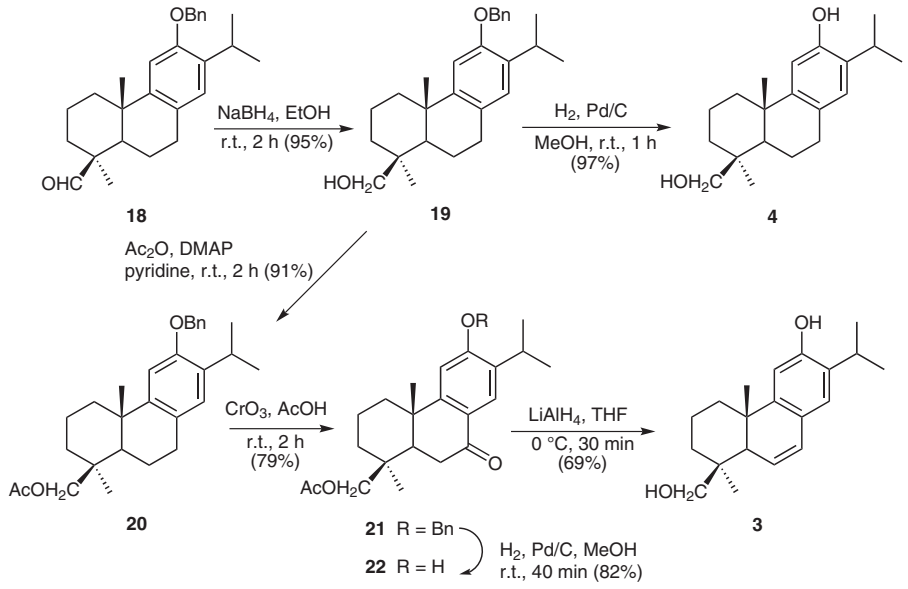


Scheme 1 Synthesis of aldehyde **2** from hydroxy ester **11**

procedures, based on oxidative decarboxylations, have been reported to achieve this goal; however, they exhibited low regioselectivity[25] or they were tedious and expensive.[26] We report in this paper a new procedure that avoids these problems starting from methyl 12-hydroxydehydroabietate (**11**), which is easily prepared from abietic acid,[21,22] utilizing methodology developed in our laboratory.[27] The key step is the transformation of a formate into an exocyclic alkene with complete regioselectivity.

The synthesis of 12-hydroxyabieta-8,11,13-trien-19-al (**2**) from hydroxy ester **11** is depicted in Scheme 1. Treatment of aldehyde **13** with *m*-chloroperoxybenzoic acid in refluxing dichloromethane for four hours gave formate **14**, which after heating at 170 °C in collidine for 18 hours was



Scheme 2 Synthesis of compounds **3** and **4** from aldehyde **18**

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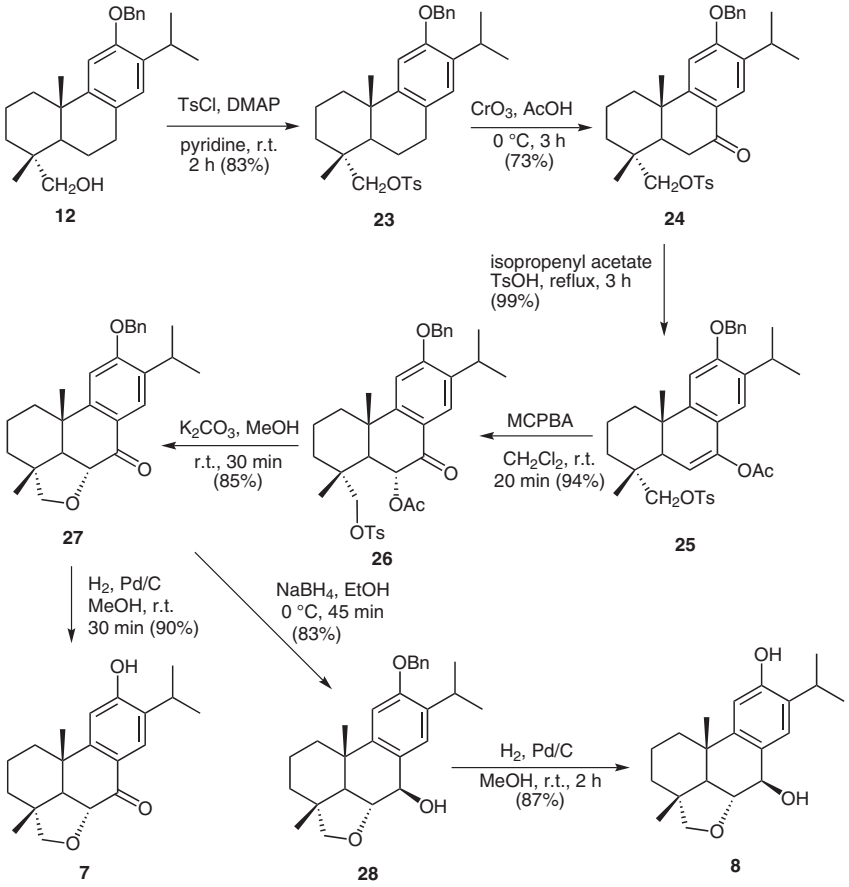

Scheme 3 Synthesis of hanagokenol A (**7**) and fortunin H (**8**) from alcohol **12**

transformed into exocyclic olefin **15**. Hydroboration–oxidation of this substrate afforded alcohol **16**, which was then oxidized to give intermediate aldehyde **17**. Treatment of this with iodomethane in the presence of potassium *tert*-butoxide led to aldehyde **18**, which was finally converted into aldehyde **2**.

Aldehyde **18** is also an adequate precursor for the synthesis of sugikurojin A (**3**) and 19-hydroxyferruginol (**4**) (Scheme 2). Reduction of the aldehyde group and deprotection of the phenol hydroxy group gave compound **4**. On the other hand, acetylation of alcohol **19** and subsequent treatment with chromium(VI) oxide gave ketone **21**, which after hydrogenation and reduction with lithium aluminum hydride afforded diol **3**.

Next, the synthesis of the recently reported antimicrobial hanagokenol A (**7**) and fortunins E (**9**), G (**10**), and H (**8**), which have not previously been synthesized, was undertaken. These C18 functionalized abietane diterpenes were synthesized from 18-hydroxyferruginol (**6**) or from its benzyl derivative **12**. Scheme 3 shows the synthesis of compounds **7** and **8** starting from alcohol **12**. The oxidation of tosylate **23** with chromium(VI) oxide in acetic acid gave ketone **24**, which was then converted into the enol acetate **25**. Treatment of this compound with *m*-chloroperoxybenzoic acid afforded acetoxy ketone **26**, which after treatment with potassium carbonate in methanol at room temperature and further hydrogenation led to hanagokenol A (**7**). The treatment of ketone **27** with sodium borohydride gave alcohol **28**, which after debenzylation afforded fortunin H (**8**); this compound was also directly obtained when hydrogenation of compound **27** was prolonged for four hours. Compounds **7** and **8** have spectroscopic properties identical to those reported in the literature.[11,12]

The synthesis of fortunins E (**9**) and G (**10**) is depicted in Scheme 4. The key intermediate was the triacetoxy ketone **32**, resulting from the treatment of enol acetate **31** with *m*-chloroperoxybenzoic acid. Saponification of compound **32** with potassium carbonate in methanol at room temperature afforded compound **9**. Treatment of triacetyl derivative **32** with sodium borohydride in ethanol at –20 °C gave fortunin G (**10**). The spectroscopic properties of compounds **9** and **10** were identical to those reported in the literature.[12]

In summary, a new and efficient procedure for this synthesis of C19-functionalized abietane diterpenes from the corresponding natural abundant C18-functionalized derivatives has been developed; utilizing this, sugikurojin A (**3**) and the immunosupressive **4** have been synthesized from abietic acid. Moreover, the first synthesis of antimicrobial hanagokenol A (**7**) and fortunins E (**9**), G (**10**), and H (**8**) starting from 18-hydroxyferruginol (**6**) has been achieved.

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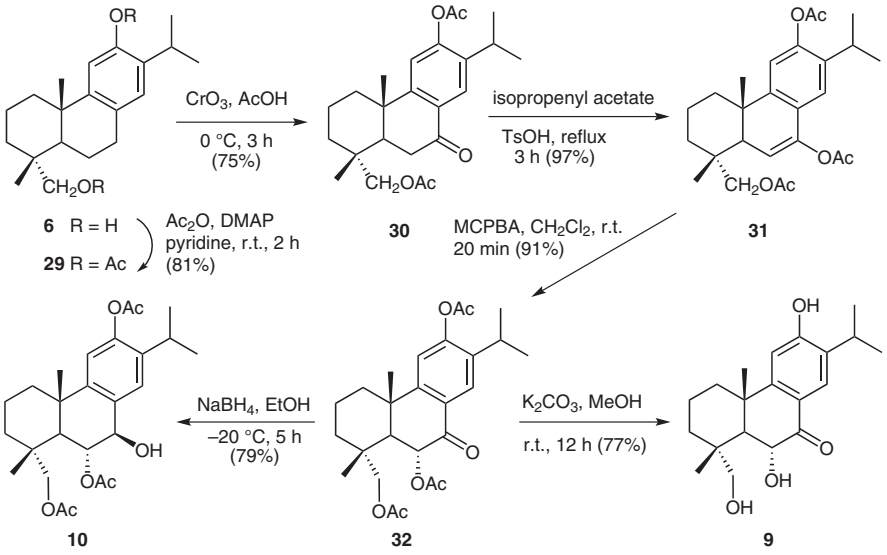

Scheme 4 Synthesis of fortunins E (**9**) and G (**10**) from phenol **6**

CH_2Cl_2 was dried over CaH_2. Toluene, THF, and benzene were dried over Na. MeOH was distilled from Mg at 1 bar. DMF and EtOH were dried over 4 Å molecular sieves. Reactions were monitored for the disappearance of starting material by TLC. Separations were carried out by conventional column chromatography on silica gel 60 (230–400 mesh) using hexane–*t*-BuOMe mixtures of increasing polarity. IR spectra were obtained using a Perkin Elmer Spectrum models 782 and 983G spectrophotometers with samples between NaCl plates or as KBr pellets. ^1H or ^{13}C NMR spectra were recorded on a Varian 500 spectrometer. The signals of the ^{13}C NMR were assigned utilizing DEPT experiments and on the basis of literature data. Interchangeable assignments are indicated by * or **. HRMS were obtained on a trisector WG AutoSpecQ spectrometer. FAB spectra acquisition was performed with a 10000 resolution and a relative error of 5 ppm. Microanalytical data for C and H were determined on a Fisons Carlo Erba EA 1108 analyzer.

18-Hydroxyferruginol (6)

$LiAlH_4$ (1.59 g, 39.7 mmol) was added at 0 °C to a stirred soln of **11** (11.3 g, 37.8 mmol) in anhyd THF (150 mL) and the mixture was stirred at r.t. under an argon atmosphere for 2 h. Then, 2 M HCl (50 mL) was added slowly at 0 °C and the solvent was removed. *t*-BuOMe (80 mL) was added and the layers were fractionated. The organic layer was washed with brine (3 × 30 mL), dried (anhyd Na_2SO_4), and concentrated to give **6** (10.6 g, 93%) as a colorless oil.

12-(Benzyloxy)abieta-8,11,13-trien-18-ol (12)

To a soln of **6** (9.48 g, 31.4 mmol) in acetone (100 mL) was added K_2CO_3 (6.49 g, 47.03 mmol) and the mixture was stirred at r.t. for 15 min. Then BnBr (7.4 mL, 47.03 mmol) was added and the mixture was stirred at reflux for 12 h. The solvent was evaporated and the crude mixture was poured into *t*-BuOMe–H_2O (5:1, 120 mL). The organic phase was washed with H_2O (2 × 30 mL) and brine (3 × 30 mL) and dried (Na_2SO_4). The solvent evaporated to give a crude product that was purified by flash chromatography (silica gel, 40% *t*-BuOMe–hexanes) to give pure **12** (9.85 g, 80%) as a yellow oil.

$[\alpha]_D^{25}$ +30.5 (*c* 0.03, $CHCl_3$).

IR (film): 3378, 2928, 2868, 1612, 1499, 1380, 1246, 1216, 1028, 756, 697 cm^{-1}.

^1H NMR (500 MHz, $CDCl_3$): δ = 0.89 (s, 3 H), 1.21 (d, *J* = 6.9 Hz, 3 H), 1.22 (s, 3 H), 1.23 (d, *J* = 6.9 Hz, 3 H), 1.36–1.54 (m, 4 H), 1.62–1.84 (m, 4 H), 2.21 (d, *J* = 12.5 Hz, 1 H), 2.82 (m, 2 H), 3.23 (d, *J* = 11.1 Hz, 1 H), 3.33 (h, *J* = 6.9 Hz, 1 H), 3.48 (d, *J* = 11.1 Hz, 1 H), 5.05 (s, 2 H), 6.79 (s, 1 H), 6.87 (s, 1 H), 7.31 (t, *J* = 7.3 Hz, 1 H), 7.39 (t, *J* = 7.52 Hz, 2 H), 7.45 (d, *J* = 7.2 Hz, 2 H).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 37.9 (C1), 19.1 (C2)*, 38.6 (C3), 49.5 (C4), 44.1 (C5), 18.8 (C6)*, 29.6 (C7), 134.7 (C8), 147.9 (C9), 37.1 (C10), 108.6 (C11), 154.1 (C12), 138.0 (C13), 126.6 (C14), 26.7 (C15), 22.8 (C16)**, 23.0 (C17)**, 72.3 (C18), 17.5 (C19), 25.3 (C20), 70.4 (CH_2OBn), 127.2 (COBn), 127.3 (2 CHOBn), 127.7 (CHOBn), 128.5 (2 CHOBn).

HRMS (FAB): *m*/*z* [M + Na]$^+$ calcd for $C_{27}H_{36}O_2Na$: 415.2613; found: 415.2605.

Anal. Calcd for $C_{27}H_{36}O_2$: C, 82.61; H, 9.24. Found: C, 82.35; H, 9.27.

12-(Benzyloxy)abieta-8,11,13-trien-18-al (13)

PCC (6.26 g, 29.04 mmol) was added to a stirred soln of **12** (6.26 g, 15.95 mmol) in anhyd CH_2Cl_2 (80 mL) and the mixture was stirred at r.t. under an argon atmosphere for 1 h (TLC monitoring). The reaction was worked up by the addition of CH_2Cl_2 (40 mL) and the resulting mixture was filtered through a silica gel pad and washed with hexane–*t*-BuOMe (1:4, 150 mL). Removal of the solvent under vacuum afforded **13** (4.42 g, 71%) as a yellow oil. Flash chromatography of **13** (131 mg) (silica gel, 15% *t*-BuOMe–hexanes) gave pure **13** (122 mg).

$[\alpha]_D^{25}$ +30.6 (*c* 0.1, $CHCl_3$).

IR (film): 1725, 1499, 1459, 1379, 1248, 1028, 696 cm^{-1}.

^1H NMR (500 MHz, $CDCl_3$): δ = 1.16 (s, 3 H), 1.19 (d, *J* = 6.9 Hz, 3 H), 1.20–1.30 (m, 2 H), 1.22 (d, *J* = 6.9 Hz, 3 H), 1.26 (s, 3 H), 1.43–1.50 (m, 2 H), 1.76–1.85 (m, 3 H), 1.90 (dd, *J* = 12.4, 1.8 Hz, 1 H), 2.26 (br d, *J* = 13.0 Hz, 1 H), 2.82 (d, *J* = 4.4 Hz, 1 H), 2.84 (d, *J* = 4.2 Hz, 1 H), 3.33 (h, *J* = 6.9 Hz, 1 H), 5.05 (s, 2 H), 6.77 (s, 1 H), 6.88 (s, 1 H), 7.32 (t, *J* = 7.2 Hz, 1 H), 7.39 (t, *J* = 7.6 Hz, 2 H), 7.45 (d, *J* = 7.1 Hz, 2 H), 9.26 (s, 1 H).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 32.1 (C1), 17.8 (C2), 38.0 (C3), 49.9 (C4), 43.0 (C5), 21.5 (C6), 29.8 (C7), 135.2 (C8), 146.7 (C9), 36.7 (C10), 108.0 (C11), 154.2 (C12), 137.8 (C13), 126.8 (C14), 26.7 (C15), 22.7 (C16)*, 22.9 (C17)*, 206.2 (C18), 14.0 (C19), 25.0 (C20), 70.3 (CH_2OBn), 126.8 (COBn), 127.2 (2 CHOBn), 127.6 (CHOBn), 128.5 (2 CHOBn).

HRMS (FAB): *m*/*z* [M + Na]$^+$ calcd for $C_{27}H_{34}O_2Na$: 413.2457; found: 413.2436.

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Anal. Calcd for $C_{27}H_{34}O_2$: C, 83.03; H, 8.77. Found: C, 83.35; H, 8.71.

12-(Benzyloxy)-4α-(formyloxy)-18-norabieta-8,11,13-triene (14)

Solid MCPBA (2.59 g, 10.45 mmol) and $NaHCO_3$ (874 mg, 10.45 mmol) in CH_2Cl_2 (170 mL) were added to a soln of **13** (2.04 g, 5.23 mmol) in CH_2Cl_2 (180 mL) and the mixture was stirred under reflux for 4 h. Removal of the solvent under vacuum afforded a crude product and *t*-BuOMe–H_2O (120: 40 mL) was added. The layers were fractionated, the organic phase was washed with sat. $NaHCO_3$ (10 × 30 mL) and brine (2 × 30 mL), dried (Na_2SO_4), and concentrated to give **14** (1.53 g, 72%) as yellow oil. Flash chromatography of **14** (200 mg) (silica gel, 15% *t*-BuOMe–hexanes) gave pure **14** (187 mg).

$[\alpha]_D^{25}$ +19.6 (*c* 0.15, $CHCl_3$).

IR (film): 1719, 1499, 1459, 1381, 1249, 1201, 1182, 1131, 1102, 1027, 736 cm^{-1}.

^1H NMR (500 MHz, $CDCl_3$): δ = 1.18 (s, 3 H), 1.21 (d, *J* = 6.9 Hz, 3 H), 1.23 (d, *J* = 6.9 Hz, 3 H), 1.46 (m, 1 H), 1.57 (s, 3 H), 1.67–1.76 (m, 3 H), 1.80 (m, 1 H), 1.98 (dd, *J* = 12.4, 1.8 Hz, 1 H), 2.05 (br dd, *J* = 13.8, 6.5 Hz, 1 H), 2.17 (br d, *J* = 12.2 Hz, 1 H), 2.64 (dd, *J* = 8.4, 2.6 Hz, 1 H), 2.83–2.89 (m, 2 H), 3.33 (h, *J* = 6.9 Hz, 1 H), 5.05 (s, 2 H), 6.75 (s, 1 H), 6.89 (s, 1 H), 7.31 (t, *J* = 7.3 Hz, 1 H), 7.39 (t, *J* = 7.3 Hz, 2 H), 7.44 (t, *J* = 7.0 Hz, 2 H), 8.08 (s, 1 H).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 37.8 (C1), 18.7 (C2), 38.2 (C3), 87.2 (C4), 49.8 (C5), 20.2 (C6), 29.5 (C7), 135.4 (C8), 146.6 (C9), 38.8 (C10), 108.6 (C11), 154.5 (C12), 138.0 (C13), 126.9 (C14), 26.9 (C15), 22.8 (C16)*, 23.0 (C17)*, 20.1 (C19), 24.7 (C20), 160.5 (COCHO), 70.7 (CH_2OBn), 127.1 (COBn), 127.3 (2 CHOBn), 128.6 (2 CHOBn).

HRMS (FAB): *m*/*z* [M + Na]$^+$ calcd for $C_{27}H_{34}O_3Na$: 429.2406; found: 429.2418.

Anal. Calcd for $C_{27}H_{34}O_3$: C, 79.76; H, 8.43. Found: C, 79.92; H, 8.48.

12-(Benzyloxy)-4-methylene-18,19-dinorabieta-8,11,13-triene (15)

A soln of **14** (2.44 g, 6.0 mmol) in collidine (10 mL) was stirred under reflux for 18 h (TLC monitoring). The mixture was cooled to r.t. and *t*-BuOMe (80 mL) was added; the black soln was washed with 2 M HCl (5 × 25 mL) and brine. The organic layer was dried and concentrated under reduced pressure to afford **15** (1.91 g, 88%). Flash chromatography of **15** (83 mg) (silica gel, 5% *t*-BuOMe–hexanes) gave pure **15** (77 mg).

$[\alpha]_D^{25}$ +63.5 (*c* 0.21, $CHCl_3$).

IR (film): 1499, 1459, 1409, 1324, 1250, 1189, 1028, 887, 735 cm^{-1}.

^1H NMR (500 MHz, $CDCl_3$): δ = 1.00 (s, 3 H), 1.22 (d, *J* = 6.9 Hz, 3 H), 1.24 (d, *J* = 6.9 Hz, 3 H), 1.56 (ddd, *J* = 13.0, 13.0, 4.5 Hz, 1 H), 1.70–1.86 (m, 4 H), 2.06 (ddd, *J* = 13.4, 13.4, 5.5 Hz, 1 H), 2.17–2.22 (m, 2 H), 2.38 (br d, *J* = 12.8 Hz, 1 H), 2.84 (d, *J* = 4.4 Hz, 1 H), 2.86 (d, *J* = 4.0 Hz, 1 H), 3.34 (h, *J* = 6.9 Hz, 1 H), 4.60 (s, 1 H), 4.85 (s, 1 H), 5.06 (s, 2 H), 6.83 (s, 1 H), 6.92 (s, 1 H), 7.32 (t, *J* = 7.3 Hz, 1 H), 7.39 (t, *J* = 7.5 Hz, 2 H), 7.45 (d, *J* = 7.4 Hz, 2 H).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 36.4 (C1), 21.5 (C2), 38.5 (C3), 150.7 (C4), 47.9 (C5), 23.0 (C6), 29.3 (C7), 134.9 (C8), 145.2 (C9), 39.5 (C10), 109.1 (C11), 154.1 (C12), 137.9 (C13), 126.8 (C14), 23.8 (C15), 22.7 (C16)*, 22.8 (C17)*, 106.4 (C19), 22.9 (C20), 70.3 (CH_2OBn), 126.1 (COBn), 127.2 (2 CHOBn), 127.6 (CHOBn), 128.4 (2 CHOBn).

HRMS (FAB): *m*/*z* [M + Na]$^+$ calcd for $C_{26}H_{32}ONa$: 383.2351; found: 383.2346.

Anal. Calcd for $C_{26}H_{32}O$: C, 86.62; H, 8.95. Found: C, 86.39; H, 9.00.

12-(Benzyloxy)-18-norabieta-8,11,13-trien-19-ol (16)

1 M BH_3·THF (8 mL, 8 mmol) was added to a soln of **15** (1.57 g, 4.36 mmol) in anhyd THF (10 mL) at –10 °C under an argon atmosphere and the mixture was stirred at r.t. for 15 h (TLC monitoring). Then, EtOH (2 mL), 4 M NaOH in EtOH (2 mL), and 30% H_2O_2 (3 mL) were added and the mixture was stirred at r.t. for 4 h. The solvent was evaporated and *t*-BuOMe (120 mL) was added. The organic layer was washed with H_2O (3 × 20 mL) and brine (2 × 20 mL) and dried (anhyd Na_2SO_4). Removal of the solvent under vacuum afforded a crude product that was purified by flash chromatography column (silica gel, 30% *t*-BuOMe–hexanes), affording **16** (1.24 g, 75%) as a yellow colorless syrup. Flash chromatography of **16** (227 mg) (silica gel, 25% *t*-BuOMe–hexanes) gave pure **16** (213 mg).

$[\alpha]_D^{25}$ +71.2 (*c* 0.14, $CHCl_3$).

IR (film): 3374, 1611, 1499, 1458, 1406, 1319, 1241, 1168, 1027, 755, 696 cm^{-1}.

^1H NMR (500 MHz, $CDCl_3$): δ = 1.04 (s, 3 H), 1.22 (d, *J* = 6.9 Hz, 3 H), 1.23 (d, *J* = 6.9 Hz, 3 H), 1.30–1.45 (m, 3 H), 1.61–1.67 (m, 2 H), 1.72 (m, 1 H), 1.83 (m, 1 H), 1.89–1.95 (m, 2 H), 1.98 (br d, *J* = 13.1 Hz, 1 H), 2.19 (br d, *J* = 11.7 Hz, 1 H), 2.83–2.87 (m, 2 H), 3.33 (h, *J* = 6.9 Hz, 1 H), 3.72 (dd, *J* = 10.3, 3.0 Hz, 1 H), 3.77 (d, *J* = 10.3 Hz, 1 H), 5.05 (s, 2 H), 6.77 (s, 1 H), 6.88 (s, 1 H), 7.32 (t, *J* = 7.3 Hz, 1 H), 7.39 (t, *J* = 7.5 Hz, 2 H), 7.45 (t, *J* = 7.0 Hz, 2 H).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 38.7 (C1), 18.3 (C2), 27.7 (C3), 44.1 (C4), 44.6 (C5), 24.6 (C6), 29.9 (C7), 134.9 (C8), 146.7 (C9), 37.3 (C10), 108.5 (C11), 154.2 (C12), 137.9 (C13), 126.7 (C14), 26.7 (C15), 22.7 (C16)*, 22.9 (C17)*, 61.8 (C19), 25.1 (C20), 70.4 (CH_2OBn), 127.1 (COBn), 127.1 (2 CHOBn), 127.6 (CHOBn), 128.4 (2 CHOBn).

HRMS (FAB): *m*/*z* [M + Na]$^+$ calcd for $C_{26}H_{34}O_2Na$: 401.2457; found: 401.2433.

Anal. Calcd for $C_{26}H_{34}O_2$: C, 82.49; H, 9.05. Found: C, 82.62; H, 9.09.

12-(Benzyloxy)-18-norabieta-8,11,13-trien-19-al (17)

PCC (700 mg, 3.25 mmol) was added to a stirred soln of **16** (650 mg, 1.72 mmol) in anhyd CH_2Cl_2 (40 mL) and the mixture was stirred at r.t. under an argon atmosphere for 1 h (TLC monitoring). Following the same workup used for **13**, **17** (489 mg, 76%) was obtained as a colorless syrup. Flash chromatography of **17** (47 mg) (silica gel, 15% *t*-BuOMe–hexanes) gave pure **17** (39 mg).

$[\alpha]_D^{25}$ +108.6 (*c* 0.09, $CHCl_3$).

IR (film): 1716, 1501, 1455, 1315, 1251, 1235, 1205, 1028, 889, 737, 696 cm^{-1}.

^1H NMR (500 MHz, $CDCl_3$): δ = 1.03 (s, 3 H), 1.22 (d, *J* = 6.9 Hz, 3 H), 1.23 (d, *J* = 6.9 Hz, 3 H), 1.27–1.44 (m, 2 H), 1.64–1.79 (m, 2 H), 1.94 (m, 1 H), 2.11 (ddd, *J* = 11.3, 5.5, 2.0 Hz, 1 H), 2.18 (br d, *J* = 13.4 Hz, 1 H), 2.29 (m, 1 H), 2.39 (br d, *J* = 13.4 Hz, 1 H), 2.46 (t, *J* = 4.9 Hz, 1 H), 2.90–2.92 (m, 2 H), 3.34 (h, *J* = 6.9 Hz, 1 H), 5.05 (s, 2 H), 6.77 (s, 1 H), 6.91 (s, 1 H), 7.31 (t, *J* = 7.3 Hz, 1 H), 7.39 (t, *J* = 7.5 Hz, 2 H), 7.44 (d, *J* = 7.1 Hz, 2 H), 10.03 (s, 1 H).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 38.3 (C1), 19.2 (C2), 24.9 (C3), 52.4 (C4), 45.1 (C5), 24.4 (C6), 30.2 (C7), 135.4 (C8), 145.3 (C9), 37.9 (C10), 108.7 (C11), 154.4 (C12), 137.9 (C13), 126.9 (C14), 26.8 (C15), 22.7 (C16)*, 22.8 (C17)*, 204.5 (C19), 23.5 (C20), 70.5 (CH_2OBn), 126.8 (COBn), 127.3 (2 CHOBn), 127.7 (CHOBn), 128.5 (2 CHOBn).

HRMS (FAB): *m*/*z* [M + Na]$^+$ calcd for $C_{26}H_{32}O_2Na$: 399.2300; found: 399.2989.

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Anal. Calcd for $C_{26}H_{32}O_2$: C, 82.94; H, 8.57. Found: C, 83.06; H, 8.57.

12-(Benzyloxy)abieta-8,11,13-trien-19-al (18)

To a soln of **17** (685 mg, 1.82 mmol) in anhyd THF (60 mL) was added *t*-BuOK (267 mg, 2.38 mmol) and the resulting brown soln was stirred for 5 min. Then MeI (450 mg, 3.17 mmol) was added and the mixture was stirred for 1 h (TLC monitoring). The solvent was removed in vacuo and *t*-BuOMe–H_2O (70:25, 105 mL) was added to the crude product and the layers were fractionated. The organic phase was washed with H_2O and brine and dried (Na_2SO_4). Removal of the solvent under vacuum afforded **18** (624 mg, 88%) as a colorless syrup. Flash chromatography of **18** (92 mg) (silica gel, 15% *t*-BuOMe–hexanes) gave pure **18** (84 mg).

$[\alpha]_D^{25}$ +64.9 (*c* 0.1, $CHCl_3$).

IR (film): 1717, 1613, 1501, 1456, 1407, 1377, 1327, 1249, 1216, 1169, 1028, 897, 772, 736 cm^{-1}.

^1H NMR (500 MHz, $CDCl_3$): δ = 1.05 (s, 3 H), 1.11 (s, 3 H), 1.21 (d, *J* = 6.9 Hz, 3 H), 1.23 (d, *J* = 6.9 Hz, 3 H), 1.40 (ddd, *J* = 13.4, 13.4, 3.9, 1 H), 1.61–1.69 (m, 2 H), 1.75 (m, 1 H), 2.00 (ddd, *J* = 19.0, 12.8, 6.1 Hz, 1 H), 2.08–2.26 (m, 2 H), 2.83 (ddd, *J* = 16.5, 12.2, 6.5 Hz, 1 H), 2.92 (dd, *J* = 16.5, 5.1 Hz, 1 H), 3.33 (h, *J* = 6.9 Hz, 1 H), 5.04 (s, 2 H), 6.77 (s, 3 H), 6.90 (s, 1 H), 7.31 (t, *J* = 7.3 Hz, 1 H), 7.38 (t, *J* = 7.5 Hz, 2 H), 7.44 (t, *J* = 7.3 Hz, 2 H), 9.83 (s, 1 H).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 38.4 (C1), 19.0 (C2)*, 33.8 (C3), 48.6 (C4), 52.0 (C5), 19.2 (C6)*, 30.6 (C7), 135.1 (C8), 145.4 (C9), 38.1 (C10), 108.6 (C11), 154.2 (C12), 137.7 (C13), 126.6 (C14), 26.7 (C15), 22.7 (C16)**, 22.9 (C17)**, 24.0 (C18), 205.7 (C19), 24.2 (C20), 70.2 (CH_2OBn), 126.7 (COBn), 127.1 (2 CHOBn), 127.6 (CHOBn), 128.5 (2 CHOBn).

HRMS (FAB): *m*/*z* $[M + Na]^+$ calcd for $C_{27}H_{34}O_2Na$: 413.2457; found: 413.2461.

Anal. Calcd for $C_{27}H_{34}O_2$: C, 82.84; H, 8.77. Found: C, 82.99; H, 8.81.

12-Hydroxyabieta-8,11,13-trien-19-al (2)

To a soln of **18** (220 mg, 0.56 mmol) in anhyd MeOH (8 mL) was added 10% Pd/C (30 mg) and the mixture was stirred at r.t. under H_2 for 1 h. Filtration and concentration gave **2** (163 mg, 97%) as a colorless syrup.

12-(Benzyloxy)abieta-8,11,13-trien-19-ol (19)

$NaBH_4$ (70 mg, 1.84 mmol) was added to a stirred soln of **18** (380 mg, 0.97 mmol) in EtOH (10 mL) cooled at 0 °C and the mixture was stirred at r.t. for 2 h (TLC monitoring). The reaction was quenched with H_2O (5 mL) and the solvent was evaporated. The crude product was diluted with *t*-BuOMe (60 mL), washed with H_2O (2 × 20 mL) and brine (2 × 20 mL), and dried (Na_2SO_4). Removal of the solvent under vacuum afforded **19** (363 mg, 95%). Flash chromatography of **19** (64 mg) (silica gel, 25% *t*-BuOMe–hexanes) gave pure **19** (59 mg).

$[\alpha]_D^{25}$ +36.9 (*c* 0.07, $CHCl_3$).

IR (film): 3377, 1613, 1499, 1456, 1407, 1378, 1325, 1246, 1217, 1027, 890, 804, 756, 736, 696 cm^{-1}.

^1H NMR (500 MHz, $CDCl_3$): δ = 1.05 (s, 3 H), 1.17 (s, 3 H), 1.21 (d, *J* = 7.0 Hz, 3 H), 1.23 (d, *J* = 7.0 Hz, 3 H), 1.43 (ddd, *J* = 13.1, 13.1, 3.5 Hz, 1 H), 1.51 (br d, *J* = 12.6 Hz, 1 H), 1.60–1.73 (m, 4 H), 1.89 (br d, *J* = 13.6 Hz, 1 H), 1.97 (br dd, *J* = 13.0, 7.1 Hz, 1 H), 2.23 (br d, *J* = 12.6 Hz, 1 H), 2.74–2.85 (m, 2 H), 3.32 (h, *J* = 7.0 Hz, 1 H), 3.56 (d, *J* = 11.0 Hz, 1 H), 3.86 (d, *J* = 11.0 Hz, 1 H), 5.05 (s, 2 H), 6.80 (s, 1 H), 6.86 (s, 1 H), 7.31 (t, *J* = 7.1 Hz, 1 H), 7.38 (t, *J* = 7.6 Hz, 2 H), 7.45 (d, *J* = 7.3 Hz, 2 H).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 35.3 (C1), 19.1 (C2)*, 39.0 (C3), 38.7 (C4), 51.4 (C5), 19.4 (C6)*, 30.4 (C7), 134.8 (C8), 147.7 (C9), 37.8 (C10), 108.3 (C11), 154.2 (C12), 137.9 (C13), 126.5 (C14), 26.7 (C15), 22.7 (C16)**, 22.9 (C17)**, 26.8 (C18), 65.4 (C19), 25.6 (C20), 70.3 (CH_2OBn), 126.9 (COBn), 127.2 (2 CHOBn), 127.6 (CHOBn), 128.4 (2 CHOBn).

HRMS (FAB): *m*/*z* $[M + Na]^+$ calcd for $C_{27}H_{36}O_2Na$: 415.2613; found: 415.2607.

Anal. Calcd for $C_{27}H_{36}O_2$: C, 82.61; H, 9.24. Found: C, 82.40; H, 9.19.

19-Hydroxyferruginol (4)

To a soln of **19** (173 mg, 0.44 mmol) in anhyd MeOH (8 mL) was added 10% Pd/C (30 mg) and the mixture was stirred at r.t. under H_2 for 1 h. Filtration and concentration gave **4** (129 mg, 97%) as a colorless syrup.

19-Acetoxy-12-(benzyloxy)abieta-8,11,13-triene (20)

To a soln of **19** (352 mg, 0.9 mmol) in pyridine (3 mL) was added Ac_2O (1.5 mL) and DMAP (50 mg, 0.4 mmol) and the mixture was further stirred at r.t. for 2 h (TLC monitoring). The reaction was quenched with H_2O (5 mL) and the mixture was stirred for an additional 10 min. Then, it was diluted with *t*-BuOMe (50 mL), washed with H_2O (5 × 20 mL), 2 M HCl (5 × 20 mL), sat. $NaHCO_3$ (3 × 20 mL), and brine (3 × 20 mL), and dried (anhyd Na_2SO_4). Removal of the solvent under vacuum afforded **20** (355 mg, 91%) as a colorless oil. Flash chromatography of **20** (55 mg) (silica gel, 10% *t*-BuOMe–hexanes) gave pure **20** (48 mg).

$[\alpha]_D^{25}$ +47.0 (*c* 0.15, $CHCl_3$).

IR (film): 1736, 1647, 1500, 1458, 1376, 1242, 1029, 892, 847, 735, 696, 666 cm^{-1}.

^1H NMR (500 MHz, $CDCl_3$): δ = 1.04 (s, 3 H), 1.05 (m, 1 H), 1.20 (s, 3 H), 1.21 (d, *J* = 7.0 Hz, 3 H), 1.22 (d, *J* = 7.0 Hz, 3 H), 1.42 (ddd, *J* = 12.9, 12.9, 4.4 Hz, 1 H), 1.51 (br d, *J* = 12.5 Hz, 1 H), 1.61 (m, 1 H), 1.66–1.76 (m, 2 H), 1.79 (br d, *J* = 14.8 Hz, 1 H), 1.99 (dd, *J* = 12.9, 6.9 Hz, 1 H), 2.08 (s, 3 H), 2.24 (br d, *J* = 12.7 Hz, 1 H), 2.78 (ddd, *J* = 16.7, 11.7, 7.1 Hz, 1 H), 2.87 (dd, *J* = 16.7, 6.2 Hz, 1 H), 3.32 (h, *J* = 7.0 Hz, 1 H), 4.00 (d, *J* = 11.1 Hz, 1 H), 4.33 (d, *J* = 11.1 Hz, 1 H), 5.05 (s, 2 H), 6.79 (s, 1 H), 6.89 (s, 1 H), 7.31 (t, *J* = 7.3 Hz, 1 H), 7.38 (t, *J* = 7.5 Hz, 2 H), 7.44 (d, *J* = 7.6 Hz, 2 H).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 36.0 (C1), 19.0 (C2)*, 38.9 (C3), 37.7 (C4), 51.4 (C5), 19.4 (C6)*, 30.4 (C7), 134.9 (C8), 147.4 (C9), 37.2 (C10), 108.3 (C11), 154.2 (C12), 137.9 (C13), 126.5 (C14), 26.6 (C15), 22.7 (C16)**, 22.9 (C17)**, 27.3 (C18), 67.0 (C19), 25.6 (C20), 21.0 ($OCOCH_3$), 171.3 ($OCOCH_3$), 70.3 (CH_2OBn), 126.9 (COBn), 127.2 (2 CHOBn), 127.6 (CHOBn), 128.6 (2 CHOBn).

HRMS (FAB): *m*/*z* $[M + Na]^+$ calcd for $C_{29}H_{38}O_3Na$: 457.2719; found: 457.2721.

Anal. Calcd for $C_{29}H_{38}O_3$: C, 80.14; H, 8.81. Found: C, 79.98; H, 8.77.

19-Acetoxy-12-(benzyloxy)abieta-8,11,13-trien-7-one (21)

To a soln of **20** (348 mg, 0.8 mmol) in AcOH (8 mL) was added at 0 °C CrO_3 (160 mg, 1.6 mmol) and the mixture was stirred at r.t. for 2 h (TLC monitoring). Then *t*-BuOMe–H_2O (6:1, 70 mL) was added to the crude product and the phases were shaken and separated. The organic phase was washed with H_2O (10 × 15 mL) and brine (3 × 30 mL) and dried (anhyd Na_2SO_4). Removal of the solvent under vacuum afforded **21** (284 mg, 79%) as a yellow oil. Flash chromatography of **21** (82 mg) (silica gel, 20% *t*-BuOMe–hexanes) gave pure **21** (75 mg).

$[\alpha]_D^{25}$ +21.2 (*c* 0.15, $CHCl_3$).

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IR (film): 1737, 1673, 1601, 1498, 1457, 1374, 1259, 1242, 1178, 1029, 909, 850, 772, 697 cm^{-1}.

^1H NMR (500 MHz, $CDCl_3$): δ = 1.03 (s, 3 H), 1.06 (m, 1 H), 1.13 (ddd, *J* = 14.0, 14.0, 4.8 Hz, 1 H), 1.22 (d, *J* = 6.8 Hz, 3 H), 1.25 (d, *J* = 6.8 Hz, 3 H), 1.26 (s, 3 H), 1.54 (ddd, *J* = 12.9, 12.9, 4.1 Hz, 1 H), 1.64–1.83 (m, 2 H), 2.01 (dd, *J* = 14.4, 3.4 Hz, 1 H), 2.09 (s, 3 H), 2.30 (br d, *J* = 12.8 Hz, 1 H), 2.65 (dd, *J* = 17.8, 14.4 Hz, 1 H), 2.80 (dd, *J* = 17.8, 3.4 Hz, 1 H), 3.33 (h, *J* = 6.8 Hz, 1 H), 4.04 (d, *J* = 11.2 Hz, 1 H), 4.38 (d, *J* = 11.2 Hz, 1 H), 5.15 (s, 2 H), 6.82, (s, 1 H), 7.34 (t, *J* = 7.0 Hz, 1 H), 7.40 (t, *J* = 7.5 Hz, 2 H), 7.44 (d, *J* = 6.8 Hz, 2 H), 7.92 (s, 1 H).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 36.1 (C1), 18.6 (C2), 38.2 (C3), 38.0 (C4), 49.9 (C5), 35.9 (C6), 197.5 (C7), 135.8 (C8), 155.7 (C9), 36.8 (C10), 106.1 (C11), 160.8 (C12), 136.6 (C13), 125.8 (C14), 26.7 (C15), 22.4 (C16)*, 22.5 (C17)*, 26.8 (C18), 66.7 (C19), 23.8 (C20), 21.0 ($OCOCH_3$), 171.2 ($OCOCH_3$), 70.0 (CH_2OBn), 123.9 (COBn), 127.2 (2 CHOBn), 128.1 (CHOBn), 128.6 (2 CHOBn).

HRMS (FAB): *m*/*z* [M + Na]$^+$ calcd for $C_{29}H_{36}O_4Na$: 471.2511; found: 471.2502.

Anal. Calcd for $C_{29}H_{36}O_4$: C, 77.64; H, 8.09. Found: C, 77.85; H, 8.14.

19-Acetoxy-12-hydroxyabieta-8,11,13-trien-7-one (22)

To a soln of **21** (269 mg, 0.6 mmol) in anhyd MeOH (10 ml) was added 10% Pd/C (60 mg) and the mixture was stirred at r.t. under H_2 for 40 min. Filtration and evaporation of the solvent yielded **22** (176 mg, 82%). Flash chromatography of **22** (35 mg) (silica gel, 35% *t*-BuOMe–hexanes) gave pure **22** (28 mg).

$[\alpha]_D^{25}$ +20.1 (*c* 0.2, $CHCl_3$).

IR (film): 3283, 1737, 1655, 1596, 1571, 1459, 1374, 1303, 1267, 1177, 1035, 758 cm^{-1}.

^1H NMR (500 MHz, $CDCl_3$): δ = 1.02 (s, 3 H), (ddd, *J* = 13.4, 13.4, 3.4 Hz, 1 H), 1.20 (s, 3 H), 1.24 (d, *J* = 6.8 Hz, 3 H), 1.25 (d, *J* = 6.8 Hz, 3 H), 1.54 (ddd, *J* = 13.0, 13.0, 3.9 Hz, 1 H), 1.63–1.74 (m, 2 H), 1.79 (br d, *J* = 14.6 Hz, 1 H), 2.00 (dd, *J* = 14.3, 3.4 Hz, 1 H), 2.09 (s, 3 H), 2.25 (br d, *J* = 12.5 Hz, 1 H), 2.66 (dd, *J* = 17.8, 14 Hz, 1 H), 2.80 (dd, *J* = 17.8, 3.4 Hz, 1 H), 3.17 (h, *J* = 6.8 Hz, 1 H), 4.03 (d, *J* = 11.1 Hz, 1 H), 4.37 (d, *J* = 11.1 Hz, 1 H), 6.47 (br s, 1 H), 6.74 (s, 1 H), 7.91 (s, 1 H).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 36.1 (C1), 18.6 (C2), 37.9 (C3), 37.8 (C4), 49.9 (C5), 35.9 (C6), 197.9 (C7), 133.2 (C8), 156.5 (C9), 36.8 (C10), 110.1 (C11), 158.9 (C12), 124.0 (C13), 126.7 (C14), 26.7 (C15), 22.3 (C16)*, 22.4 (C17)*, 27.0 (C18), 66.8 (C19), 23.6 (C20), 21.0 ($OCOCH_3$), 171.3 ($OCOCH_3$).

HRMS (FAB): *m*/*z* [M + Na]$^+$ calcd for $C_{22}H_{30}O_4Na$: 381.2042; found: 381.2029.

Anal. Calcd for $C_{22}H_{30}O_4$: C, 73.71; H, 8.44. Found: C, 73.58; H, 8.43.

Sugikurojin A (3)

$LiAlH_4$ (120 mg, 3.158 mmol) was added to a stirred soln of **22** (135 mg, 0.377 mmol) in anhyd THF (15 mL) at 0 °C and the mixture was kept stirred under an argon atmosphere for 30 min. 2 M HCl (0.5 mL) was added slowly at 0 °C and the mixture was stirred for an additional 10 min. The solvent was removed in vacuo and the crude product obtained was diluted with *t*-BuOMe–H_2O (3:1, 40 mL), and the phases were shaken and separated. The organic phase was washed with H_2O and brine and dried (anhyd Na_2SO_4). Removal of the solvent under vacuum afforded **3** (78 mg, 69%).

12-(Benzyloxy)-18-(tosyloxy)abieta-8,11,13-triene (23)

To a soln of **12** (9.8 g, 25 mmol) in pyridine (40 mL) at 0 °C was added TsCl (7.18 g, 37.65 mmol) and DMAP (100 mg, 0.8 mmol) and the mixture was stirred at r.t. for 2 h (TLC monitoring). The mixture was cooled at 0 °C, H_2O (20 mL) was added to quench the reaction and *t*-BuOMe (100 mL) was added. The organic layer was washed with 2 M HCl (5 × 20 mL), H_2O (1 × 20 mL), and brine (2 × 20 mL) and dried (Na_2SO_4). The solvent evaporated to give a crude product which was purified by flash chromatography (silica gel, 25% *t*-BuOMe–hexanes) to give pure **23** (11.39 g, 83%) as a colorless oil.

$[\alpha]_D^{25}$ +46.3 (*c* 0.3, $CHCl_3$).

IR (film): 1599, 1499, 1360, 1248, 1177, 1098, 1028, 966, 847, 759 cm^{-1}.

^1H NMR (500 MHz, $CDCl_3$): δ = 0.89 (s, 3 H), 1.18 (s, 3 H), 1.22 (d, *J* = 6.9 Hz, 3 H), 1.23 (d, *J* = 6.9 Hz, 3 H), 1.34–1.48 (m, 3 H), 1.50–1.78 (m, 5 H), 2.19 (br d, *J* = 12.6 Hz, 1 H), 2.47 (s, 3 H), 2.68–2.81 (m, 2 H), 3.34 (h, *J* = 6.9 Hz, 1 H), 3.63 (d, *J* = 9.3 Hz, 1 H), 3.83 (d, *J* = 9.3 Hz, 1 H), 5.04 (s, 2 H), 6.76 (s, 1 H), 6.86 (s, 1 H), 7.33 (d, *J* = 7.3 Hz, 1 H), 7.36 (d, *J* = 8.2 Hz, 2 H), 7.39 (t, *J* = 7.3 Hz, 2 H), 7.45 (d, *J* = 7.2 Hz, 2 H), 7.79 (d, *J* = 8.2 Hz, 2 H).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 35.1 (C1), 18.4 (C2), 37.2 (C3), 38.1 (C4), 43.9 (C5), 19.2 (C6), 29.3 (C7), 134.9 (C8), 147.3 (C9), 37.7 (C10), 108.1 (C11), 154.2 (C12), 137.9 (C13), 126.6 (C14), 26.7 (C15), 22.8 (C16)*, 23.0 (C17)*, 77.8 (C18), 17.2 (C19), 25.2 (C20), 70.4 (CH_2OBn), 126.9 (COBn), 127.2 (2 CHOBn), 127.7 (CHOBn), 128.0 (2 CHOBn), 133.1 (COTs), 128.5 (2 CHOTs), 129.9 (2 CHOTs), 144.7 (COTs), 21.7 (CH_3-OTs).

HRMS (FAB): *m*/*z* [M + Na]$^+$ calcd for $C_{34}H_{42}O_4SNa$: 569.2702; found: 569.2694.

Anal. Calcd for $C_{34}H_{42}O_4S$: C, 74.69; H, 7.74. Found: C, 74.90; H, 7.70.

12-(Benzyloxy)-18-(tosyloxy)abieta-8,11,13-trien-7-one (24)

To a soln of **23** (8.26 g, 15.13 mmol) in AcOH (30 mL) at 0 °C was added CrO_3 (3.02 g, 30.22 mmol), and the mixture was stirred for 3 h (TLC monitoring). The mixture was poured into *t*-BuOMe–H_2O (6: 1, 140 mL). The organic layer was washed with H_2O (10 × 40 mL), aq $NaHCO_3$ (2 × 20 mL), and brine (2 × 20 mL), dried (Na_2SO_4), and evaporated to give **24** (6.19 g, 73%) as a yellow oil. Flash chromatography of **24** (282 mg) (silica gel, 25% *t*-BuOMe–hexanes) gave pure **24** (271 mg).

$[\alpha]_D^{25}$ +27.8 (*c* 0.14, $CHCl_3$).

IR (film): 2930, 1670, 1599, 1497, 1360, 1258, 1176, 1097, 969, 846, 756, 666 cm^{-1}.

^1H NMR (500 MHz, $CDCl_3$): δ = 0.94 (s, 3 H), 1.19 (s, 3 H), 1.23 (d, *J* = 6.9 Hz, 3 H), 1.25 (d, *J* = 6.9 Hz, 3 H), 1.42–1.81 (m, 6 H), 2.11 (dd, *J* = 14.6, 3.7 Hz, 1 H), 2.20 (m, 1 H), 2.21 (dd, *J* = 17.8, 3.7 Hz, 1 H), 2.46 (s, 3 H), 3.34 (h, *J* = 6.9 Hz, 1 H), 3.59 (d, *J* = 9.7 Hz, 1 H), 3.64 (d, *J* = 9.7 Hz, 1 H), 5.15 (s, 2 H), 6.78 (s, 1 H), 7.45 (d, *J* = 8.3 Hz, 2 H), 7.34–2.46 (m, 5 H), 7.72 (d, *J* = 8.3 Hz, 2 H), 7.87 (s, 1 H).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 35.4 (C1), 18.0 (C2), 37.1 (C3), 37.9 (C4), 42.6 (C5), 34.8 (C6), 196.9 (C7), 135.9 (C8), 155.5 (C9), 37.1 (C10), 105.8 (C11), 160.8 (C12), 136.7 (C13), 125.9 (C14), 26.8 (C15), 22.4 (C16)*, 22.6 (C17)*, 76.6 (C18), 17.1 (C19), 23.8 (C20), 70.1 (CH_2OBn), 124.2 (COBn), 127.3 (2 CHOBn), 127.9 (CHOBn), 128.1 (2 CHOBn), 132.6 (COTs), 128.7 (2 CHOTs), 130.1 (2 CHOTs), 145.1 (COTs), 21.8 (CH_3-OTs).

HRMS (FAB): *m*/*z* [M + Na]$^+$ calcd for $C_{34}H_{40}O_5SNa$: 583.2494; found: 583.2503.

Anal. Calcd for $C_{34}H_{40}O_5S$: C, 72.83; H, 7.19. Found: C, 72.68; H, 7.26.

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7-Acetoxy-12-(benzyloxy)-18-(tosyloxy)abieta-6,8,11,13-tetraene (25)

To a soln of **24** (950 mg, 1.69 mmol) in isopropenyl acetate (8 mL) was added $TsOH·H_2O$ (cat., 20 mg) and he mixture was refluxed for 3 h (TLC monitoring). The mixture was cooled to r.t. and quenched with sat. aq $NaHCO_3$ (1 mL) and extracted with *t*-BuOMe (3 × 60 mL). The combined organic layers were washed with sat. aq $NaHCO_3$ (3 × 10 mL) and brine (2 × 15 mL) and dried (Na_2SO_4). The solvent was removed in vacuo to give a crude product that was purified by flash chromatography to afford **25** (1.01 g, 99%) as a yellow oil.

$[\alpha]_D^{25}$ +42.1 (*c* 0.1, $CHCl_3$).

IR (film): 3005, 2928, 2856, 1760, 1602, 1499, 1462, 1362, 1210, 1176, 967, 846, 757, 697, 667 cm^{-1}.

^1H NMR (500 MHz, $CDCl_3$): δ = 1.02 (s, 3 H), 1.16 (s, 3 H), 1.21 (d, *J* = 6.9 Hz, 3 H), 1.22 (d, *J* = 6.9 Hz, 3 H), 1.25–1.80 (m, 5 H), 2.07 (br d, *J* = 12.6 Hz, 1 H), 2.28 (s, 3 H), 2.39 (d, *J* = 2.8 Hz, 1 H), 2.45 (s, 3 H), 3.33 (h, *J* = 6.9 Hz, 1 H), 3.66 (d, *J* = 9.7 Hz, 1 H), 3.68 (d, *J* = 9.7 Hz, 1 H), 5.06 (d, *J* = 12.1 Hz, 1 H), 5.08 (d, *J* = 12.1 Hz, 1 H), 5.22 (d, *J* = 2.8 Hz, 1 H), 6.72 (s, 1 H), 6.78 (s, 1 H), 7.29 (d, *J* = 8.2 Hz, 2 H), 7.31 (d, *J* = 7.3 Hz, 1 H), 7.38 (t, *J* = 7.3 Hz, 2 H), 7.45 (d, *J* = 7.2 Hz, 2 H), 7.73 (d, *J* = 8.2 Hz, 2 H).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 34.4 (C1), 17.9 (C2), 35.3 (C3), 38.4 (C4), 44.6 (C5), 111.6 (C6), 146.1 (C7), 134.5 (C8), 147.3 (C9), 36.7 (C10), 106.3 (C11), 156.6 (C12), 137.4 (C13), 119.6 (C14), 26.8 (C15), 22.4 (C16)*, 22.9 (C17)*, 77.5 (C18), 18.0 (C19), 21.8 (C20), 70.3 (CH_2OBn), 122.1 (COBn), 127.3 (2 CHOBn), 127.9 (CHOBn), 128.1 (2 CHOBn), 129.9 (2 CHOTs), 132.8 (COTs), 132.8 (2 CHOTs), 144.7 (COTs), 21.8 (CH_3-OTs), 20.7 (OCO*C*H_3), 169.3 (O*C*OCH_3).

HRMS (FAB): *m*/*z* [M + Na]$^+$ calcd for $C_{36}H_{42}O_6SNa$: 625.2600; found: 625.2610.

Anal. Calcd for $C_{36}H_{42}O_6$: C, 71.73; H, 7.02. Found: C, 71.56; H, 6.98.

6α-Acetoxy-12-(benzyloxy)-18-(tosyloxy)abieta-8,11,13-trien-7-one (26)

To a soln of **25** (400 mg, 0.66 mmol) in CH_2Cl_2 (10 mL) at 0 °C was added MCPBA (115 mg, 0.67 mmol) (previously treated with sat. aq $NaHCO_3$ to remove 3-chlorobenzoic acid) and the mixture was stirred at r.t. for 20 min (TLC monitoring). The mixture was cooled to 0 °C, quenched with sat. aq Na_2SO_3 (1 mL), and stirred for an additional 15 min. The solvent was evaporated and the crude product was poured into *t*-BuOMe–H_2O (60:15, 75 mL). The organic phase was washed with sat. aq $NaHCO_3$ (7 × 15 mL) and brine (2 × 15 mL), dried (Na_2SO_4), and concentrated to give **26** (382 mg, 94%) as a yellow oil. Flash chromatography of **26** (59 mg) (silica gel, 20% *t*-BuOMe–hexanes) gave pure **26** (51 mg).

$[\alpha]_D^{25}$ +43.7 (*c* 0.1, $CHCl_3$).

^1H NMR (500 MHz, $CDCl_3$): δ = 1.03 (s, 3 H), 1.21 (d, *J* = 6.9 Hz, 3 H), 1.22 (d, *J* = 6.9 Hz, 3 H), 1.38 (s, 3 H), 1.49–1.61 (m, 3 H), 1.70–1.77 (m, 2 H), 1.97 (s, 3 H), 2.24 (br d, *J* = 12.3 Hz, 1 H), 2.39 (d, *J* = 13.1 Hz, 1 H), 2.42 (s, 3 H), 3.32 (h, *J* = 6.9 Hz, 1 H), 3.79 (d, *J* = 9.0 Hz, 1 H), 3.91 (d, *J* = 9.0 Hz, 1 H), 5.15 (s, 2 H), 5.81 (d, *J* = 13.1 Hz, 1 H), 6.79 (s, 1 H), 7.32 (d, *J* = 8.3 Hz, 2 H), 7.33–7.45 (m, 5 H), 7.74 (d, *J* = 8.3 Hz, 2 H), 7.89 (s, 1 H).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 36.0 (C1), 17.7 (C2), 37.4 (C3), 39.7 (C4), 46.5 (C5), 78.9 (C6), 191.6 (C7), 136.5 (C8), 154.5 (C9), 37.8 (C10), 105.9 (C11), 161.3 (C12), 136.7 (C13), 126.6 (C14), 26.7 (C15), 22.3 (C16)*, 22.5 (C17)*, 74.6 (C18), 17.3 (C19), 25.3 (C20), 70.2 (CH_2OBn), 122.3 (COBn), 127.2 (2 CHOBn), 128.0 (CHOBn), 128.2 (2 CHOBn), 128.8 (2 CHOTs), 129.9 (2 CHOTs), 133.3 (COTs), 144.7 (COTs), 21.6 (CH_3-OTs), 20.9 (OCO*C*H_3), 170.2 (O*C*OCH_3).

HRMS (FAB): *m*/*z* [M + Na]$^+$ calcd for $C_{36}H_{42}O_7SNa$: 641.2549; found: 641.2561.

Anal. Calcd for $C_{36}H_{42}O_7S$: C, 69.88; H, 6.84. Found: C, 70.01; H, 6.88.

18-(Benzyloxy)-6α,18-epoxyabieta-8,11,13-trien-7-one (27)

To a soln of **26** (332 mg, 0.537 mmol) in anhyd MeOH (10 mL) was added K_2CO_3 (175 mg, 1.26 mmol) and the mixture was stirred at r.t. for 30 min (TLC monitoring). MeOH was evaporated in vacuo and the crude product was poured into *t*-BuOMe–H_2O (3:1, 40 mL) and washed with H_2O (2 × 10 mL) and brine (10 mL). The organic layer was dried (Na_2SO_4) and evaporated to give **27** (184 mg, 85%) as a colorless syrup. Flash chromatography of **27** (42 mg) (silica gel, 25% *t*-BuOMe–hexanes) gave pure **27** (35 mg).

$[\alpha]_D^{25}$ +27.2 (*c* 0.2, $CHCl_3$).

IR: 1693, 1600, 1492, 1465, 1251, 1176, 1082, 1024, 1008, 849, 755, 666, 755 cm^{-1}.

^1H NMR (500 MHz, $CDCl_3$): δ = 1.22 (s, 3 H), 1.23 (d, *J* = 6.9 Hz, 3 H), 1.24 (d, *J* = 6.9 Hz, 3 H), 1.29 (s, 3 H), 1.40 (m, 1 H), 1.79–1.9 (m, 4 H), 2.02 (d, *J* = 14.4 Hz, 1 H), 2.17 (br d, *J* = 13.3 Hz, 1 H), 3.33 (h, *J* = 6.9 Hz, 1 H), 3.5 (d, *J* = 7.4 Hz, 1 H), 3.81 (d, *J* = 7.4 Hz, 1 H), 4.43 (d, *J* = 14.4 Hz, 1 H), 5.15 (s, 2 H), 6.74 (s, 1 H), 7.32–7.43 (m, 5 H), 7.97 (s, 1 H).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 34.9 (C1), 19.8 (C2), 38.3 (C3), 40.2 (C4), 56.6 (C5), 76.6 (C6), 196.2 (C7), 136.4 (C8), 154.8 (C9), 38.3 (C10), 107.1 (C11), 160.5 (C12), 136.6 (C13), 126.7 (C14), 26.9 (C15), 22.4 (C16)*, 22.6 (C17)*, 84.4 (C18), 18.4 (C19), 22.0 (C20), 70.1 (CH_2OBn), 124.3 (COBn), 127.2 (2 CHOBn), 127.9 (CHOBn), 128.1 (2 CHOBn).

HRMS (FAB): *m*/*z* [M + Na]$^+$ calcd for $C_{27}H_{32}O_3Na$: 427.2249; found: 427.2242.

Anal. Calcd for $C_{27}H_{32}O_3$: C, 80.16; H, 7.97. Found: C, 80.35; H, 8.00.

Hanagokenol A (7)

To a soln of **27** (73 mg, 0.18 mmol) in anhyd MeOH (6 mL) was added 10% Pd/C (30 mg) and the mixture was stirred at r.t. under H_2 for 30 min. Filtration and concentration gave **7** (51 mg, 90%) as a white solid. Flash chromatography of **7** (22 mg) (silica gel, 40% *t*-BuOMe–hexanes) gave pure **7** (15 mg).

$[\alpha]_D^{25}$ +78.2 (*c* 0.15, MeOH) [Lit.[11] +186 (*c* 0.18, MeOH)].

IR (KBr): 3374, 1761, 1709, 1613, 1588, 1032 cm^{-1}.

^1H NMR (500 MHz, $CDCl_3$): δ = 1.23 (s, 3 H), 1.25–1.40 (m, 2 H), 1.26 (d, *J* = 6.9 Hz, 3 H), 1.263 (d, *J* = 6.9 Hz, 3 H), 1.31 (s, 3 H), 1.44 (ddd, *J* = 12.9, 12.9, 3.0 Hz, 1 H), 1.77–1.92 (m, 2 H), 2.02 (d, *J* = 14.5 Hz, 1 H), 2.16 (m, 1 H), 3.14 (h, *J* = 6.9 Hz, 1 H), 3.5 (d, *J* = 7.4 Hz, 1 H), 3.82 (d, *J* = 7.4 Hz, 1 H), 4.43 (d, *J* = 14.5 Hz, 1 H), 5.53 (br s, 1 H), 6.64 (s, 1 H), 7.97 (s, 1 H).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 34.9 (C1), 19.8 (C2), 38.3 (C3), 40.1 (C4), 56.5 (C5), 72.8 (C6), 195.9 (C7), 133.5 (C8), 154.8 (C9), 37.9 (C10), 111.0 (C11), 158.1 (C12), 124.6 (C13), 127.5 (C14), 26.9 (C15), 22.3 (C16)*, 22.4 (C17)*, 84.3 (C18), 18.4 (C19), 22.0 (C20).

HRMS (FAB): *m*/*z* [M + Na]$^+$ calcd for $C_{20}H_{26}O_3Na$: 337.1780; found: 337.1769.

Anal. Calcd for $C_{20}H_{26}O_3$: C, 76.40; H, 8.33. Found: C, 76.22; H, 8.36.

12-(Benzyloxy)-6α,18-epoxyabieta-8,11,13-trien-7β-ol (28)

$NaBH_4$ (32 mg, 0.84 mmol) was added to a soln of **27** (135 mg, 0.334 mmol) in EtOH (5 mL) and the mixture was stirred at 0 °C for 45 min (TLC monitoring). The reaction was quenched with H_2O (1

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mL) and *t*-BuOMe (20 mL) was added. The organic layer was washed with H_2O (3 × 8 mL) and brine (8 mL), dried (Na_2SO_4), and concentrated to give **28** (112 mg, 83%) as a colorless oil. Flash chromatography of **28** (29 mg) (silica gel, 30% *t*-BuOMe–hexanes) gave pure **28** (21 mg).

$[\alpha]_D^{25}$ +70.1 (*c* 0.2, $CHCl_3$).

IR: 1498, 1456, 1255, 1175, 1089, 1028, 986, 903, 847, 759 cm^{-1}.

^1H NMR (500 MHz, $CDCl_3$): δ = 1.18 (s, 3 H), 1.19 (s, 3 H), 1.23 (d, *J* = 6.9 Hz, 3 H), 1.24 (d, *J* = 6.9 Hz, 3 H), 1.33 (m, 1 H), 1.34 (ddd, *J* = 13.0, 13.0, 3.9 Hz, 1 H), 1.60 (d, *J* = 12.6 Hz, 1 H), 1.65–1.95 (m, 3 H), 2.09 (br d, *J* = 12.8 Hz, 1 H), 3.35 (h, *J* = 6.9 Hz, 1 H), 3.45 (d, *J* = 7.3 Hz, 1 H), 3.74 (d, *J* = 7.3 Hz, 1 H), 3.97 (dd, *J* = 12.6, 7.1 Hz, 1 H), 4.70 (d, *J* = 7.1 Hz, 1 H), 5.07 (s, 2 H), 6.67 (s, 1 H), 7.32 (d, *J* = 7.3 Hz, 1 H), 7.38 (t, *J* = 7.3 Hz, 2 H), 7.45 (d, *J* = 7.2 Hz, 2 H), 7.47 (s, 1 H).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 35.2 (C1), 20.0 (C2), 38.6 (C3), 40.0 (C4), 54.7 (C5), 78.7 (C6), 72.8 (C7), 136.0 (C8), 146.8 (C9), 38.0 (C10), 108.0 (C11), 155.6 (C12), 137.6 (C13), 125.7 (C14), 27.0 (C15), 22.7 (C16)*, 22.8 (C17)*, 84.0 (C18), 19.0 (C19), 23.9 (C20), 70.1 (CH_2OBn), 127.3 (2 CHOBn), 127.8 (CHOBn), 128.6 (2 CHOBn), 130.0 (COBn).

HRMS (FAB): *m*/*z* [M + Na]$^+$ calcd for $C_{27}H_{34}O_3Na$: 429.2406; found: 429.2401.

Anal. Calcd for $C_{27}H_{34}O_3$: C, 79.76; H, 8.43. Found: C, 79.91; H, 8.39.

Fortunin H (8)

To a soln of **28** (219 mg, 0.54 mmol) in distilled MeOH (10 mL) was added 10% Pd/C (150 mg) and the mixture was stirred at r.t. under H_2 for 2 h. Filtration and concentration gave **8** (148 mg, 87%) as a yellow amorphous solid. Flash chromatography of **8** (32 mg) (silica gel, 50% *t*-BuOMe–hexanes) gave pure **8** (25 mg).

$[\alpha]_D^{25}$ +114.1 (*c* 0.15, $CHCl_3$) [Lit.[12] +108 (*c* 0.29, MeOH)].

^1H NMR (500 MHz, $CDCl_3$): δ = 1.21 (s, 3 H), 1.25 (s, 3 H), 1.25–1.40 (m, 2 H), 1.25 (d, *J* = 6.8 Hz, 3 H), 1.26 (d, *J* = 6.8 Hz, 3 H), 1.60 (d, *J* = 12.6 Hz, 1 H), 1.66–1.92 (m, 3 H), 2.08 (br d, *J* = 12.7 Hz, 1 H), 3.13 (h, *J* = 6.8 Hz, 1 H), 3.46 (d, *J* = 7.2 Hz, 1 H), 3.76 (d, *J* = 7.2 Hz, 1 H), 3.99 (dd, *J* = 12.6, 7.1 Hz, 1 H), 4.69 (d, *J* = 7.1 Hz, 1 H), 6.56 (s, 1 H), 7.44 (s, 1 H).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 35.2 (C1), 20.0 (C2), 38.6 (C3), 40.0 (C4), 54.6 (C5), 78.8 (C6), 76.6 (C7), 133.0 (C8), 147.2 (C9), 37.7 (C10), 111.2 (C11), 152.7 (C12), 1128.6 (C13), 126.1 (C14), 27.1 (C15), 22.6 (C16)*, 22.7 (C17)*, 83.9 (C18), 19.0 (C19), 23.9 (C20).

Anal. Calcd for $C_{20}H_{28}O_3$: C, 75.91; H, 8.92. Found: C, 76.07; H, 8.86.

12,18-Diacetoxyabieta-8,11,13-triene (29)

To a soln of **6** (6.83, 22.6 mmol) in pyridine (40 ml) at 0 °C was added Ac_2O (20 mL) and DMAP (100 mg, 0.8 mmol) and the mixture was stirred at r.t. for 2 h (TLC monitoring). The mixture was cooled to 0 °C, H_2O (15 mL) was added to quench the reaction, and the mixture was stirred for an additional 20 min. Then it was diluted with *t*-BuOMe (100 mL) and washed with 2 M HCl (5 × 20 mL), H_2O (1 × 20 mL), sat. aq $NaHCO_3$ (5 × 20 mL), and brine (2 × 20 mL). The organic layer was dried (Na_2SO_4), and the solvent evaporated to give **29** (7.07 g, 81%) as a colorless syrup. Flash chromatography of **29** (640 mg) (silica gel, 15% *t*-BuOMe–hexanes) gave pure **29** (626 mg).

$[\alpha]_D^{25}$ +21.2 (*c* 0.17, $CHCl_3$).

IR (film): 1739, 1498, 1463, 1369, 1239, 1219, 1037, 914, 757 cm^{-1}.

^1H NMR (500 MHz, $CDCl_3$): δ = 0.93 (s, 3 H), 1.18 (d, *J* = 6.8 Hz, 3 H), 1.19 (d, *J* = 6.8 Hz, 3 H), 1.21 (s, 3 H), 1.6–1.81 (m, 8 H), 2.04 (s, 3 H), 2.19 (br d, *J* = 12.6 Hz, 1 H), 2.30 (s, 3 H), 2.70–2.88 (m, 2 H), 2.91 (h, *J* = 6.8 Hz, 1 H), 3.67 (d, *J* = 11.1 Hz, 1 H), 3.98 (d, *J* = 11.1 Hz, 1 H), 6.83 (s, 1 H), 6.94 (s, 1 H).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 35.5 (C1), 18.5 (C2), 36.8 (C3), 38.3 (C4), 43.7 (C5), 19.0 (C6), 29.8 (C7), 133.0 (C8), 146.3 (C9), 37.6 (C10), 118.0 (C11), 148.4 (C12), 136.9 (C13), 127.1 (C14), 27.3 (C15), 23.08 (C16)*, 23.09 (C17)*, 72.3 (C18), 17.6 (C19), 25.3 (C20), 21.0 (2 OCO*C*H_3), 171.1 (O*C*OCH$_3$), 171.4 (O*C*OCH$_3$).

HRMS (FAB): *m*/*z* [M + Na]$^+$ calcd for $C_{24}H_{34}O_4Na$: 409.2355; found: 409.2361.

Anal. Calcd for $C_{24}H_{34}O_4$: C, 74.58; H, 8.87. Found: C, 74.74; H, 8.92.

12,18-Diacetoxyabieta-8,11,13-trien-7-one (30)

To a soln of **29** (6.9 g, 17.87 mmol) in AcOH (30 mL) at 0 °C, was added CrO_3 (3.66 g, 36.6 mmol), and the mixture was stirred for 3 h (TLC monitoring). The mixture was poured into *t*-BuOMe–H_2O (5:1, 120 mL). The organic phase was washed with H_2O (10 × 40 mL), aq $NaHCO_3$ (2 × 20 mL), and brine (2 × 20 mL), dried (Na_2SO_4), and evaporated to give **30** (5.36 g, 75%) as a yellow oil. Flash chromatography of **30** (352 mg) (silica gel, 20% *t*-BuOMe–hexanes) gave pure **30** (341 mg).

$[\alpha]_D^{25}$ +17.3 (*c* 0.2, $CHCl_3$).

IR (film): 1740, 1681, 1609, 1561, 1463, 1369, 1237, 1201, 1117, 1039, 909, 756 cm^{-1}.

^1H NMR (500 MHz, $CDCl_3$): δ = 0.97 (s, 3 H), 1.17 (d, *J* = 7.0 Hz, 3 H), 1.19 (d, *J* = 7.0 Hz, 3 H), 1.23 (s, 3 H), 1.39–1.56 (m, 3 H), 1.68–1.79 (m, 2 H), 1.99 (s, 3 H), 2.19–2.21 (m, 2 H), 2.31 (s, 3 H), 2.60–2.61 (m, 2 H), 2.96 (h, *J* = 7.0 Hz, 1 H), 3.67 (d, *J* = 11.3 Hz, 1 H), 3.80 (d, *J* = 11.3 Hz, 1 H), 6.97 (s, 1 H), 7.96 (s, 1 H).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 35.8 (C1), 18.0 (C2), 37.2 (C3), 37.7 (C4), 42.9 (C5), 35.1 (C6), 197.7 (C7), 128.9 (C8), 152.7 (C9), 36.6 (C10), 117.8 (C11), 154.7 (C12), 138.6 (C13), 126.5 (C14), 27.3 (C15), 22.73 (C16)*, 22.74 (C17)*, 71.3 (C18), 17.2 (C19), 23.8 (C20), 20.9 (2 OCO*C*H_3), 169.9 (O*C*OCH$_3$), 171.0 (O*C*OCH$_3$).

HRMS (FAB): *m*/*z* [M + Na]$^+$ calcd for $C_{24}H_{32}O_5Na$: 423.2147; found: 423.2156.

Anal. Calcd for $C_{24}H_{32}O_5$: C, 71.97; H, 8.05. Found: C, 72.23; H, 8.11.

7,12,18-Triacetoxyabieta-6,8,11,13-tetraene (31)

To a soln of **30** (791 mg, 1.98 mmol) in isopropenyl acetate (8 mL) was added TsOH·H_2O (cat. 20 mg). The mixture was refluxed for 3 h, cooled to r.t., and quenched with sat. $NaHCO_3$. The mixture was extracted with *t*-BuOMe (3 × 60 mL) and the combined organic layers were washed with sat. aq $NaHCO_3$ (3 × 10 mL), brine (2 × 15 mL), and dried (Na_2SO_4). The soln was evaporated in vacuo and the residue was purified by flash chromatography to afford **31** (848 mg, 97%) as yellow oil.

$[\alpha]_D^{25}$ +25.6 (*c* 0.2, $CHCl_3$).

IR (film): 1761, 1739, 1656, 1491, 1464, 1369, 1205, 1103, 1038, 912, 757 cm^{-1}.

^1H NMR (500 MHz, $CDCl_3$): δ = 1.05 (s, 3 H), 1.17 (d, *J* = 7.0 Hz, 3 H), 1.19 (d, *J* = 7.0 Hz, 3 H), 1.22 (s, 3 H), 1.42 (m, 1 H), 1.45 (dd, *J* = 9.8, 3.7 Hz, 1 H), 1.61 (ddd, *J* = 12.3, 12.3, 3.7 Hz, 1 H), 1.69–1.85 (m, 2 H), 2.03 (s, 3 H), 2.09 (br d, *J* = 12.6 Hz, 1 H), 2.28 (s, 3 H), 2.31 (s, 3 H), 2.59 (d, *J* = 2.8 Hz, 1 H), 2.96 (h, *J* = 7.0 Hz, 1 H), 3.74 (d, *J* = 11.3 Hz, 1 H), 3.86 (d, *J* = 11.3 Hz, 1 H), 5.6 (d, *J* = 2.8 Hz, 1 H), 6.79 (s, 1 H), 7.06 (s, 1 H).

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^{13}C NMR (125 MHz, $CDCl_3$): δ = 34.6 (C1), 18.0 (C2), 35.2 (C3), 38.2 (C4), 44.5 (C5), 115.1 (C6), 145.4 (C7), 127.5 (C8), 147.4 (C9), 36.1 (C10), 116.6 (C11), 148.3 (C12), 137.2 (C13), 119.8 (C14), 27.3 (C15), 22.7 (C16)*, 22.9 (C17)*, 71.5 (C18), 18.4 (C19), 21.0 (C20), 20.8 (OCO*C*H$_3$), 20.9 (2 OCO*C*H$_3$), 169.1 (O*C*OCH$_3$), 169.6 (O*C*OCH$_3$), 171.0 (O*C*OCH$_3$).

HRMS (FAB): *m*/*z* [M + Na]$^+$ calcd for $C_{26}H_{34}O_6Na$: 465.2253; found: 465.2248.

Anal. Calcd for $C_{26}H_{34}O_6$: C, 70.56; H, 7.74. Found: C, 70.35; H, 7.73.

6α,12,18-Triacetoxyabieta-8,11,13-trien-7-one (32)

To a soln of **31** (800 mg, 1.81 mmol) in CH_2Cl_2 (10 mL) at 0 °C was added MCPBA (331 mg, 1.93 mmol), previously treated with $NaHCO_3$, and the mixture was stirred at r.t. for 20 min (TLC monitoring). The mixture was cooled at 0 °C and quenched with sat. aq Na_2SO_3 (5 mL) and stirred for an additional 5 min. The CH_2Cl_2 was evaporated and the mixture was poured into *t*-BuOMe–H_2O (4:1, 75 mL). The organic phase was washed with sat. aq $NaHCO_3$ (3 × 15 mL) and brine (5 × 15 mL), dried (Na_2SO_4), and concentrated to give **32** (754 mg, 91%) as a yellow oil. Flash chromatography of **32** (91 mg) (silica gel, 20% *t*-BuOMe–hexanes) gave pure **32** (84 mg).

$[\alpha]_D^{25}$ +57.6 (*c* 0.2, $CHCl_3$).

IR (film): 3016, 2964, 2937, 2874, 1746, 1695, 1612, 1566, 1467, 1372, 1236, 1199, 117, 1041, 926, 907, 756 cm^{-1}.

^{1}H NMR (500 MHz, $CDCl_3$): δ = 1.06 (s, 3 H), 1.19 (d, *J* = 6.8 Hz, 3 H), 1.21 (d, *J* = 6.8 Hz, 3 H), 1.43 (m, 1 H), 1.43 (s, 3 H), 1.58–1.82 (m, 4 H), 2.01 (s, 3 H), 2.21 (s, 3 H), 2.26 (br d, *J* = 12.3 Hz, 1 H), 2.34 (s, 3 H), 2.59 (d, *J* = 13.2 Hz, 1 H), 2.98 (h, *J* = 6.8 Hz, 1 H), 3.65 (d, *J* = 10.9 Hz, 1 H), 4.12 (d, *J* = 10.9 Hz, 1 H), 5.87 (d, *J* = 13.2 Hz, 1 H), 7.03 (s, 1 H), 7.99 (s, 1 H).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 36.7 (C1), 17.8 (C2), 37.8 (C3), 39.3 (C4), 45.7 (C5), 74.6 (C6), 192.6 (C7), 139.4 (C8), 153.2 (C9), 36.7 (C10), 117.8 (C11), 153.7 (C12), 127.3 (C13), 127.3 (C14), 27.3 (C15), 22.7 (C16), 22.7 (C17), 73.3 (C18), 17.7 (C19), 25.5 (C20), 20.95 (OCO*C*H$_3$), 20.98 (OCO*C*H$_3$), 21.0 (OCO*C*H$_3$), 169.1 (O*C*OCH$_3$), 170.4 (O*C*OCH$_3$), 171.0 (O*C*OCH$_3$).

HRMS (FAB): *m*/*z* [M + Na]$^+$ calcd for $C_{26}H_{34}O_7Na$: 481.2202; found: 481.2198.

Anal. Calcd for $C_{26}H_{34}O_7$: C, 68.10; H, 7.47. Found: C, 67.91; H, 7.51.

Fortunin E (9)

To a soln of **32** (140 mg, 0.3 mmol) in distilled MeOH (8 mL) was added K_2CO_3 (169 mg, 1.2 mmol) and the mixture was stirred at r.t. for 12 h (TLC monitoring). The reaction was quenched by slow addition of 2 M HCl (3 mL) at 0 °C, then MeOH was evaporated and the crude product was poured into MEK–H_2O (5:1, 60 mL). The organic layer was washed with H_2O (4 × 15 mL) and brine (2 × 15 mL), dried (Na_2SO_4), and evaporated to give **9** (76 mg, 77%) as an amorphous solid. Flash chromatography of **9** (32 mg) (silica gel, 70% *t*-BuOMe–hexanes) gave pure **9** (26 mg).

$[\alpha]_D^{25}$ +18.1 (*c* 0.15, $CHCl_3$) [Lit.[12] +17 (*c* 0.29, $CHCl_3$)].

IR (KBr): 3386, 1661, 1600, 1508, 1463, 1267, 1114, 1036, 757 cm^{-1}.

^{1}H NMR (500 MHz, $CDCl_3$): δ = 1.14 (s, 3 H), 1.20 (d, *J* = 7.0 Hz, 3 H), 1.22 (d, *J* = 7.0 Hz, 3 H), 1.30 (s, 3 H), 1.32–1.46 (m, 3 H), 1.63 (m, 1 H), 1.77 (m, 1 H), 2.04 (br d, *J* = 12.8 Hz, 1 H), 2.17 (d, *J* = 12.6 Hz, 1 H), 3.19 (h, *J* = 7.0 Hz, 1 H), 3.23 (d, *J* = 11.4 Hz, 1 H), 3.57 (d, *J* = 11.4 Hz, 1 H), 4.52 (d, *J* = 12.8 Hz, 1 H), 6.76 (s, 1 H), 7.94 (s, 1 H).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 38.2 (C1), 18.3 (C2), 37.7 (C3), 38.8 (C4), 52.6 (C5), 72.2 (C6), 198.2 (C7), 134.5 (C8), 156.4 (C9), 37.5 (C10), 110.0 (C11), 161.1 (C12), 120.4 (C13), 127.1 (C14), 26.9 (C15), 22.1 (C16)*, 22.3 (C17)*, 74.6 (C18), 17.4 (C19), 25.0 (C20).

HRMS (FAB): *m*/*z* [M + Na]$^+$ calcd for $C_{20}H_{28}O_4Na$: 355.1885; found: 355.1883.

Anal. Calcd for $C_{20}H_{28}O_4$: C, 72.26; H, 8.49. Found: C, 72.40; H, 8.51.

Fortunin G (10)

To a soln of **32** (100 mg, 0.218 mmol) in anhyd EtOH (10 mL), at –20 C was added $NaBH_4$ (25 mg, 0.6 mmol) and the mixture was stirred at –20 °C for 5 h (TLC monitoring). The reaction was quenched with H_2O (3 mL) and the solvent was evaporated to give a crude product that was diluted with *t*-BuOMe and washed with H_2O (3 × 15 mL) and brine (2 × 15 mL). The organic layer was dried (Na_2SO_4), and concentrated to give **10** (79 mg, 79%) as a yellow amorphous solid. Flash chromatography of **10** (28 mg) (silica gel, 50% *t*-BuOMe–hexanes) gave pure **10** (19 mg).

$[\alpha]_D^{25}$ +36.5 (*c* 0.2, $CHCl_3$) [Lit.[12] +38 (*c* 0.18, $CHCl_3$)].

IR (KBr): 3460, 1738, 1605, 1469, 1372, 1238, 1040, 913, 757 cm^{-1}.

^{1}H NMR (500 MHz, $CDCl_3$): δ = 0.99 (s, 3 H), 1.18 (d, *J* = 6.5 Hz, 3 H), 1.19 (d, *J* = 6.5 Hz, 3 H), 1.35 (s, 3 H), 1.39–1.74 (m, 7 H), 2.04 (s, 3 H), 2.12 (d, *J* = 11.8 Hz, 1 H), 2.15 (s, 3 H), 2.30 (s, 3 H), 2.93 (h, *J* = 6.9 Hz, 1 H), 3.55 (d, *J* = 10.8 Hz, 1 H), 4.15 (d, *J* = 10.8 Hz, 1 H), 4.59 (d, *J* = 5.1 Hz, 1 H), 5.39 (dd, *J* = 11.8, 5.2 Hz, 1 H), 6.83 (s, 1 H), 7.37 (s, 1 H).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 37.1 (C1), 17.8 (C2), 38.2 (C3), 39.2 (C4), 45.3 (C5), 78.4 (C6), 76.2 (C7), 133.0 (C8), 147.4 (C9), 36.4 (C10), 117.1 (C11), 147.9 (C12), 138.3 (C13), 127.2 (C14), 27.3 (C15), 22.9 (C16)*, 23.0 (C17)*, 73.7 (C18), 17.9 (C19), 26.0 (C20), 20.8 (OCO*C*H$_3$), 20.9 (OCO*C*H$_3$), 21.5 (OCO*C*H$_3$), 169.6 (O*C*OCH$_3$), 170.1 (O*C*OCH$_3$), 172.5 (O*C*OCH$_3$).

HRMS (FAB): *m*/*z* [M + Na]$^+$ calcd for $C_{26}H_{36}O_7Na$: 483.2359; found: 483.2366.

Anal. Calcd for $C_{26}H_{36}O_7$: C, 67.80; H, 7.88. Found: C, 68.02; H, 7.84.

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References

(1) (a) Kupchan, S. M.; Karim, A.; Marcks, C. *J. Org. Chem.* **1969**, *34*, 3912. (b) Kupchan, S. M.; Karim, A.; Marcks, C. *J. Am. Chem. Soc.* **1968**, *90*, 5923.
(2) (a) Gil, R. R.; Cordell, G. A. *J. Nat. Prod.* **1994**, *57*, 181. (b) Lin, L. Z.; Blasko, G.; Cordell, G. A. *Phytochemistry* **1989**, *28*, 177.
(3) Son, K.-H.; Oh, H.-M.; Choi, S.-K.; Han, D.-C.; Kwon, B.-M. *Bioorg. Med. Chem. Lett.* **2005**, *15*, 2019.
(4) Campello, J. de P..; Fonseca, S. F.; Cnag, C.-J.; Wenkert, E. *Phytochemistry* **1975**, *14*, 243.
(5) Machida, K.; Shioda, K.; Yapita, Y.; Kakuda, R.; Kikuchi, M. *Nat. Med.* **2001**, *55*, 147.
(6) Arihara, S.; Umeyama, A.; Bando, S.; Imoto, S.; Ono, M.; Tani, M.; Yoshikawa, K. *Chem. Pharm. Bull.* **2004**, *52*, 354.
(7) Cambie, R. C.; Cox, R. E.; Sidwell, D. *Phytochemistry* **1984**, *23*, 333.

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(8) Takei, M.; Umeyama, A.; Arihara, S. *Biochem. Biophys. Res. Commun.* **2005**, *337*, 730.
(9) Kinouchi, Y.; Ohtsu, H.; Tokuda, H.; Nishino, H.; Matsunaga, S.; Tanaka, R. *J. Nat. Prod.* **2000**, *63*, 817.
(10) (a) Fukushima, I.; Sayama, Y.; Kyogoku, K.; Murayama, H. *Agric. Biol. Chem.* **1968**, *32*, 1103. (b) Harrison, L. J.; Asakawa, Y. *Phytochemistry* **1987**, *26*, 1211.
(11) Yoshikawa, K.; Kokudo, N.; Tanaka, M.; Nakano, T.; Shibata, H.; Haragaki, N.; Higuchi, T.; Hashimoto, T. *Chem. Pharm. Bull.* **2008**, *56*, 89.
(12) Yao, S.; Tang, C.-P.; Ke, C.-Q.; Ye, Y. *J. Nat. Prod.* **2008**, *71*, 1242.
(13) Harring, S. R.; Livinghouse, T. *Tetrahedron Lett.* **1989**, *30*, 1499.
(14) (a) Engler, T. A.; Sampath, U.; Naganathan, S.; Vander Velde, D.; Takusagawa, F. *J. Org. Chem.* **1989**, *54*, 5712. (b) Zambrano, J. L.; Rosales, V.; Nakano, T. *Tetrahedron Lett.* **2003**, *44*, 1859.
(15) (a) Banik, B. K.; Ghosh, S.; Ghatak, V. R. *Tetrahedron* **1988**, *44*, 6947. (b) Majetich, G.; Siesel, D. *Synlett* **1995**, 559. (c) Majetich, G.; Liu, S.; Fang, J.; Siesel, D.; Zhang, Y. *J. Org. Chem.* **1997**, *62*, 6928. (d) Tada, M.; Nishiiri, S.; Zhixiang, Y.; Imai, Y.; Tajima, S.; Okazaki, N.; Kitano, Y.; Chiba, K. *J. Chem. Soc., Perkin Trans. 1* **2000**, 2657.
(16) Shishido, K.; Got, K.; Miyoshi, S.; Takaishi, Y.; Shibuya, M. *J. Org. Chem.* **1994**, *59*, 406.
(17) Bhar, S. S.; Ramana, M. M. V. *J. Org. Chem.* **2004**, *69*, 8935.
(18) (a) Huffman, J. W. *J. Org. Chem.* **1970**, *35*, 3154. (b) Banerjee, A. K.; Acevedo, J. C.; Canudes-Gonzalez, N. *Bull. Soc. Chim. Belg.* **1990**, *99*, 9. (c) Cambie, R. C.; Rutledge, P. S.; Woodgate, P. D. *Aust. J. Chem.* **1993**, *46*, 1447. (d) Burnell, R. H.; Cote, C.; Girard, M. *J. Nat. Prod.* **1993**, *56*, 461.
(19) Haslinger, E.; Michl, G. *Tetrahedron Lett.* **1988**, *29*, 5754.
(20) Takemura, S.; Matsubara, Y.; Obata, T.; Zhou, Z.; Fujiwara, Y. *Nippon Kagaku Kaishi* **1994**, 545.
(21) (a) Cambie, R. C.; Franich, R. A. *Aust. J. Chem.* **1971**, *24*, 134. (b) Akita, H.; Oishi, T. *Chem. Pharm. Bull.* **1981**, *29*, 1579.
(22) Alvarez-Manzaneda, E.; Chaboun, R.; Cabrera, E.; Alvarez, E.; Alvarez-Manzaneda, R.; Lachkar, M.; Messouri, I. *Tetrahedron Lett.* **2007**, *48*, 989.
(23) Carman, R. M.; Deeth, H. C.; Marti, R. A.; Mori, K.; Matsui, M. *Tetrahedron Lett.* **1968**, *9*, 3359.
(24) Alvarez-Manzaneda, E.; Chahboun, R.; Cabrera, E.; Alvarez, E.; Alvarez-Manzaneda, R.; Lachkar, M.; Messouri, I. *Synlett* **2007**, 2425.
(25) Pelletier, S. W.; Herald, D. L. Jr. *J. Chem. Soc., Chem. Commun.* **1971**, 10.
(26) Tagat, J. R.; Nazareno, D. V.; Puar, M. S.; McCombie, S. W.; Ganguly, A. K. *Bioorg. Med. Chem. Lett.* **1994**, *4*, 1101; and references cited therein.
(27) Barrero, A. F.; Alvarez-Manzaneda, E.; Alvarez-Manzaneda, R.; Chahboun, R.; Meneses, R.; Aparicio, M. B. *Synlett* **1999**, 713.

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