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Studies on the Stereostructure of Eudesmanolides from *Umbelliferae*: Total Synthesis of (+)-Decipienin A

Francisco A. Macías,[a,*] José María Aguilar,[a] José María G. Molinillo,[a] Francisco Rodríguez-Luís,[a] Isidro G. Collado,[a] Guillermo M. Massanet[a,*] and Frank R. Fronczek[b]

[a]*Departamento de Química Orgánica, Facultad de Ciencias, Universidad de Cádiz, C/República Saharaui s/n, Apdo. 40, 11510-Puerto Real, Cádiz, Spain*

[b]*Department of Chemistry, Louisiana State University, Baton Rouge, LA 70803, USA*

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Abstract—The first total synthesis of (+)-decipienin A has been achieved in 4% overall yield in seven steps from (+)-dihydrocarvone, thus confirming the stereostructure proposed by Holub et al. (Holub, M.; Budesinsky, M. *Phytochemistry* **1986**, *25*, 2015–2026) for this lactone and the original assignments should be corrected as indicated in by formula (a) (6αH,7αH,10αmethyl-eudesman-6,12-olide). Two different strategies were used, the first one an attempt to build the α-hydroxy-γ-lactone moiety through functionalization of the C-6 position and the second involved the introduction of the C-11 hydroxyl group at the final steps of the synthetic scheme.

Introduction

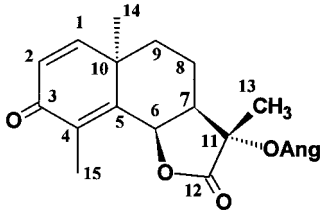
Sesquiterpene lactones constitute the most characteristic secondary metabolites isolated from *Compositae*.[1] This group of natural products shows a wide range of structural types and very interesting biological activities.[2,3]

Umbelliferae represent the second major source of natural sesquiterpene lactones. Holub showed that the majority of sesquiterpene lactones obtained from *Umbelliferae* have a different stereostructure than those isolated from *Compositae*. Based on spectroscopic grounds, he proposed that decipienin A and other eudesmanolides isolated from *Melanoselinum decipiens* (Schrader–Wendl.) Hoffm. (*Umbelliferae*, tribe *Laserpietieae*) have basic structure represented by formula (a) (6αH,7αH,10αmethyl-eudesman-6,12-olide) instead of formula (b) (6βH,7αH,10β-methyl-eudesman-6,12-olide)[4] (Fig. 1).

Previously we reported the synthesis of decipienin A (**1**) having the stereostructure **b**.[5] The observed differences between spectroscopic and physical data of this compound and those reported for the natural product led us to conclude that the original proposed stereostructure[6] is not correct. In order to confirm that a stereostructure type **a** should be assigned, here we report the preparation of decipienin A (**1a**) from (+)-dihydrocarvone (**2**).

Results and Discussion

The key intermediate in the synthesis was (−)-10-epi-α-



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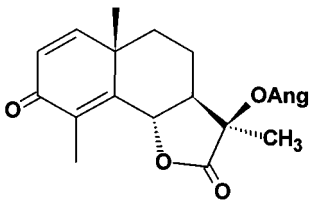

type b

Figure 1.

Keywords: terpenoids; enolates; annulation; stereocontrol.

* Corresponding authors.: Tel.: +34-956-016370; fax: +34-956-016288; e-mail: famacias@uca.es

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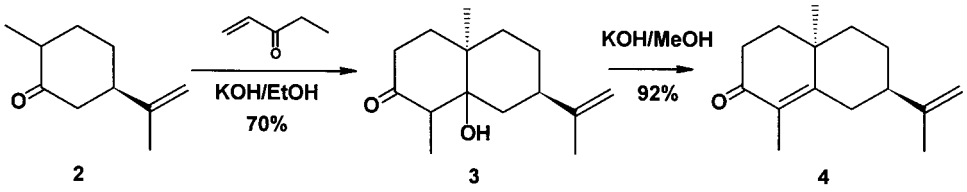


Scheme 1.

cyperon (**4**), which is readily available from Robinson annulation of (+)-dihydrocarvone (**2**) with ethylvinylketone.[7] The product of this reaction is known to be ketol **3**, which can be dehydrated by treatment with KOH in dry MeOH to give **4** in high yield (Scheme 1).

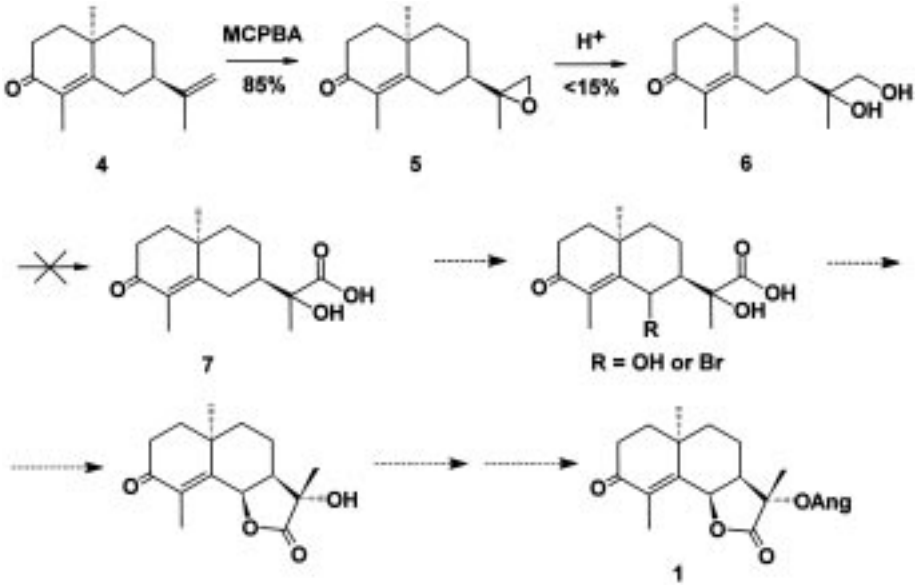
The first attempt to build the α-hydroxy-γ-lactone moiety through functionalization of the C-6 position in hydroxy acid **7** was planned as shown in Scheme 2.

Oxidation of **4** with *m*-chloroperbenzoic acid afforded epoxide **5** in 90% yield, which was converted to diol **6** by opening of the oxirane ring with different acids [$HClO_4$(3.0, 0.5, 0.25, 0.125 M)/THF, *p*-TsOH, H_2SO_4/$(CH_3)_2CO$] in a ca 10–20% yield. Attempted oxidation of **6** with chromium trioxide-pyridine, or pyridine chlorochromate, led to a mixture of products in a 15% overall yield. The major product isolated from these mixtures was the methyl ketone **8**, derived from the oxidative cleavage of the diol. Therefore, we explored the sequence outlined in Scheme 3, using this ketone **8** as starting material (Scheme 3).

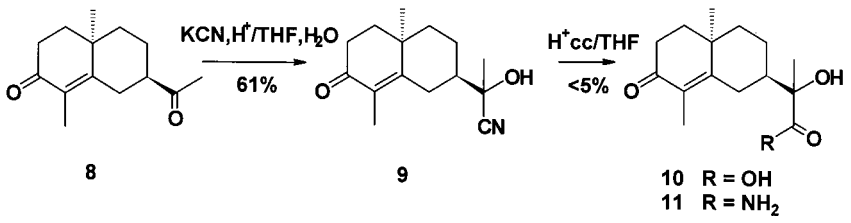
Cyanohydrin **9** was obtained in 60% yield from methylketone **4**. Hydrolysis of **9** gave the corresponding amide **11** in very low yield (below 5%), instead of the desired α-hydroxyacid **10**.

The second option consisted of different approach (Scheme 4) which involved the introduction of the C-11 hydroxyl group in the final steps of the sequence.

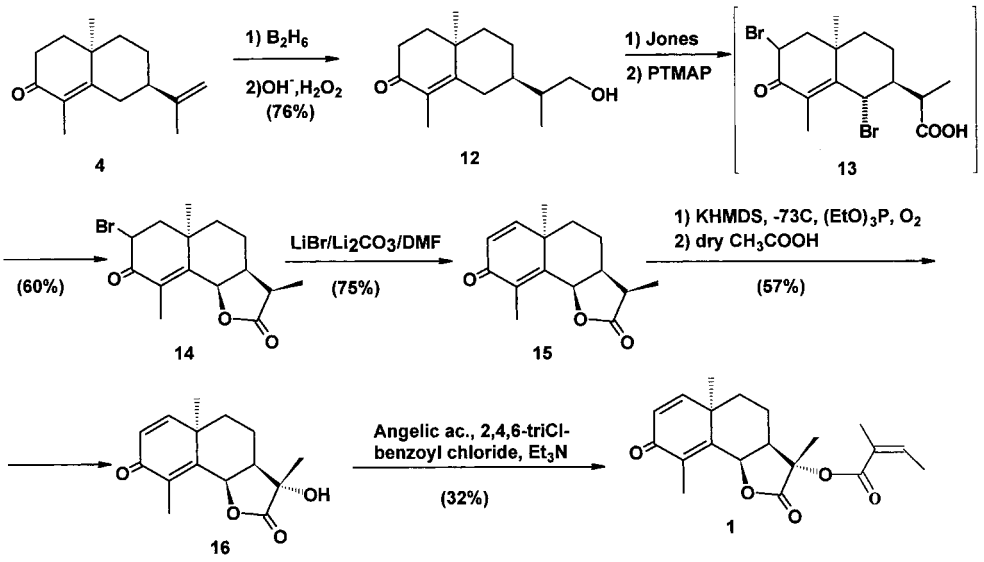
Hydroboration of **4** with B_2H_6 in THF under N_2 atmosphere gave the primary alcohol **12** in 76% yield which was treated with Jones reagent to afford a complex mixture from which the corresponding acid could not be isolated. However when oxidation with Jones reagent was followed by treatment with phenyltrimethylammonium bromide in dioxane, the dibromoacid derivative **13** was 'trapped' as the corresponding lactone **14** in 60% yield. In this case, dibromide intermediate **13** presents the correct configuration at C-6 to allow the obtention of the *cis*-lactone by nucleophilic displacement of the bromine atom.



Scheme 2.



Scheme 3.



Scheme 4.

The absolute configuration, established by the X-ray analysis[8] of **14** (Fig. 2), confirmed that configuration at the chiral centres C-6, C-7, and C-10 fit the stereochemical requirements proposed by Holub for the eudesmanolides isolated from plants of the *Umbelliferae* (6αH, 7αH, 14β-methyl). Elimination of the bromine atom at C-2 was accomplished by treatment with Li_2CO_3 in DMF to provide dienone **15** in 75% yield.

The introduction of the hydroxyl group at C-11 in lactone **15** presented several problems as we have described previously for related compounds.[9] Treatment with Vedejs' reagent[10] resulted in the formation of complex mixtures, and the use of a flow of molecular oxygen in THF and LDA effected lactone decarbonylation to give the corresponding methyl-ketone instead of the hydroxylation product.

In the course of our studies on chemical transformations of sesquiterpene lactones we have reported a new method for hydroxylation at the C-11 position,[11] where the enolate is generated by deprotonation with potassium hexamethyl-disilazide (KHMDS), trapped by using a flow of molecular oxygen in THF, and reduced 'in situ' with triethyl phosphite, that avoid the decarboxylation problems.[4,8] Hydroxylation of **15** using this procedure gave **16** in 57% yield. Esterification of **16** with angelic chloride in pyridine proceeded with isomerization of the double bond to give the tiglate derivative. When the reaction was carried out using the mixed anhydride obtained from angelic acid and 2,4,6-trichlorobenzoyl chloride, (+)-decipienin A (**1**) was obtained in 32% yield. The synthetic decipienin A was identical with the natural product isolated from *Melanoselinum decipiens*.[6]

In conclusion, the total synthesis of (+)-decipienin A (**1**) has been achieved for the first time in 6% overall yield in five steps from cyperon **4**, thus confirming the stereostructure proposed by Holub et al. for this lactone and that the original assignments should be corrected as indicated in Fig. 1a.

Experimental

Materials and general procedures

Infrared spectra were recorded on a Perkin–Elmer 257 spectrometer in film. ^{1}H NMR and ^{13}C NMR spectra were made

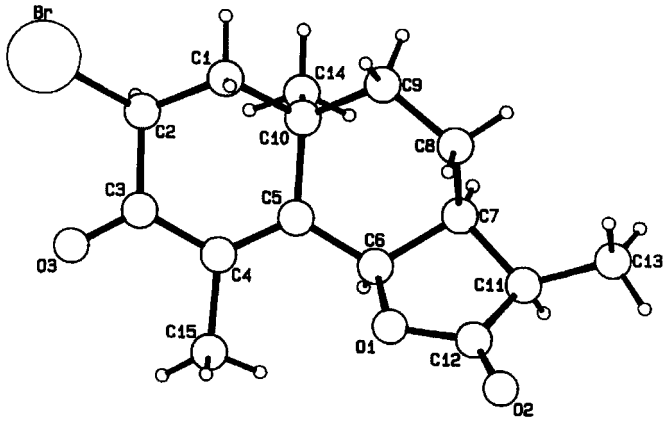


Figure 2. X-Ray structure of **14**.

on Varian Gemini-200 and Bruker AM-400 spectrometers, using $CDCl_3$ as internal standard. Mass spectra were recorded on a VG 12–250 spectrometer using 70 eV. Chromatographic separations were made on silica gel (Merck), employing hexane, ethyl acetate mixtures as eluent.

8a-Hydroxy-4aα-methyl-7β-(propen-2-yl)-perhydronaphtalen-2-one (3)

A solution of dry ethanol (1.2 mL) and KOH (366 mg, 6.5 mmol) was added to a solution of dihydrocarvone (5 g, 32.9 mmol) in ethyl ether (10 mL) at 0°C under N_2 atmosphere. After the mixture has been stirred for 10 min a solution of ethylvinylketone (1.25 g, 14.9 mmol) in ethyl ether (7.2 mL) was introduced dropwise during one hour. The mixture was stirred for one hour, then it reached 30°C and allowed to stand for 1.5 h. The solution was neutralized with aq. HCl (5%) turning from orange to yellowish and then extracted with ethyl ether (5×10 mL). The ether layer was washed with brine and dried with Na_2SO_4. Then, the solvent was removed under reduced pressure. The residue was chromatographed (Hexane:AcOEt 4:1) to give **3** (2.46 g, 10.43 mmol, 70%) as colourless oil.

3: IR $(KBr)^{neat}$ ν_{max}: 3500 (hydroxyl group), 1694 (ketone), 1638 (C–C double bond) cm^{-1}; MS, *m/z* (relative intensity), $C_{15}H_{24}O_2$: 236 $[M]^+$ (13), 218 $[M-H_2O]^+$ (6), 109 $[C_8H_{13}]^+$ (100); δ_H (200 MHz, $CDCl_3$): 4.68–4.65 (1H, m, H-12), 4.64–4.62 (1H, m, H-12′), 2.83 (1H, dq, *J*=7, 1 Hz, H-4), 2.55 (1H, dddd, *J*=14, 14, 7, 1 Hz, H-2), 2.30 (1H, ddd, *J*=14, 5, 2 Hz, H-2′), 2.23–2.20 (1H, m, H-7), 1.85–1.70 (2H, m, H-6 and H-6′), 1.65 (3H, dd, *J*=1, 1 Hz, H-13), 1.58–1.20 (6H, m, H-1, H-8, H-9), 1.21 (3H, s, H-14), 1.01 (3H, s, H-15).

(−)-10-*epi*-α-Cyperon (4)

Alcohol **3** (1.3 g, 5.5 mmol) was dissolved in 20 mL of a solution of KOH (10%) in dry MeOH. The mixture was heated at reflux under N_2 atmosphere for 8 h, after which it was cooled, diluted with water (25 mL), and neutralized with aq. HCl (5%). The mixture was extracted with ethyl ether (5×15 mL), and the organic layer was washed with brine and dried with Na_2SO_4. Then, the solvent was removed under reduced pressure. The residue was chromatographed (Hexane:AcOEt 49:1) to give **4** (1.1 g, 5.05 mmol, 92%) as colourless oil.

4: $[\alpha]_D^{20}=-171.6$ (*c* 0.1, $CHCl_3$); IR $(KBr)^{neat}$ ν_{max}: 1654 (α,β-unsaturated ketone), 1603 (C–C double bond) cm^{-1}; MS, *m/z* (relative intensity), $C_{15}H_{22}O$: 218 $[M]^+$ (58), 203 $[M-CH_3]^+$ (36); δ_H (200 MHz, $CDCl_3$): 4.80 (1H, brs, H-12), 4.62 (1H, brs, H-12′), 2.89 (1H, ddd, *J*=16, 2, 2 Hz, H-2), 2.36 (1H, ddd, *J*=16, 6.5, 1.5 Hz, H-2′), 2.7–2.3 (3H, m, H-6, H-6′ and H-7α), 1.81 (3H, s, H-15), 1.72 (3H, dd, *J*=1, 1 Hz, H-13), 1.65–1.20 (6H, m, H-1, H-8, H-9), 1.24 (3H, s, H-14). HREIMS: M^+, found 218.1668. $C_{15}H_{22}O$ requires 218.1671.

11,12-Epoxycyperon (5)

Alkene **4** (80 mg, 0.37 mmol) was dissolved in 5 mL of a mixture of *i*-propanol and water (8:2) and MCPBA (200 mg, 1.16 mmol) was added. After 20 h the reaction mixture was neutralized with a solution of aq. NaOH (5%), and extracted with ethyl ether (5×5 mL). The organic layer was chromatographed (Hexane:Et_2O, 7:3) to yield 73 mg (0.31 mmol, 85%) of **5** as colourless oil. Different methods for opening the epoxide were tested, including $HClO_4$ (0.125, 0.25, 0.5, 3.0 M) in THF, *p*-toluensulfonic acid, H_2SO_4/acetone, obtaining low yields of **6** in all cases (ca 15% yield) as colourless oil. Subsequent oxidation of this compound with $KMnO_4$ afforded methylketone **8** (53%) as yellow oil, instead of the corresponding α-hydroxyacid **7**.

5: IR $(KBr)^{neat}$ ν_{max}: 1656 (α,β-unsaturated ketone) cm^{-1}; MS, *m/z* (relative intensity), $C_{15}H_{22}O_2$: 234 $[M]^+$ (20), 219 $[M-CH_3]^+$ (13), 203 $[M-CH_2O]^+$ (66), 176 $[M-C_3OH_6]$ (78); δ_H (200 MHz, $CDCl_3$): 2.85 (1H, ddd, *J*=15, 2, 2 Hz, H-2) 2.75–2.68 (3H, m, H-6, H-6′, H-7), 2.60 (1H, d, *J*=6 Hz, H-12), 2.48 (1H, d, *J*=6 Hz, H-12′), 2.33 (1H, ddd, *J*=15, 6.5, 1.5 Hz, H-2′), 1.81 (3H, s, H-15), 1.69–1.24 (6H, m, H-1, H-8, H-9), 1.36 (3H, s, H-13), 1.21 (3H, s, H-14). HREIMS: M^+, found 234.1620. $C_{15}H_{22}O_2$ requires 234.1620.

6: IR $(KBr)^{neat}$ ν_{max}: 3480 (hydroxyl group), 1650 (α,β-unsaturated ketone) cm^{-1}; MS, *m/z* (relative intensity) $C_{15}H_{24}O_3$: 252 $[M]^+$ (4), 234 $[M-H_2O]^+$ (17), 221 $[M-CH_3O]$ (21); δ_H (200 MHz, $CDCl_3$): 3.81 (1H, d, *J*=9.5 Hz, H-12), 3.62 (1H, d, *J*=9.5 Hz, H-12′), 2.87 (1H, ddd, *J*=15, 2, 2 Hz, H-2), 2.72-2.48 (3H, m, H-6, H-6′ and H-7), 2.39 (1H, ddd, *J*=15, 6, 2 Hz, H-2′), 1.99 (3H, brs, H-15), 1.70–1.28 (6H, m, H-1, H-8, H-9), 1.35 (3H, s, H-13), 1.18 (3H, s, H-14). HREIMS: M^+, found 252.1730. $C_{15}H_{24}O_3$ requires 252.1725.

8: IR $(KBr)^{neat}$ ν_{max}: 1714 (ketone), 1645 (α,β-unsaturated ketone), 1604 (C–C-double bond) cm^{-1}; MS, *m/z* (relative intensity), $C_{14}H_{20}O_2$: 220 $[M]^+$ (8), 205 $[M-CH_3]^+$ (4), 178 $[M-C_2HO]^+$ (23), 43 $[CH_3CO]^+$ (100); δ_H (200 MHz, $CDCl_3$): 2.74 (1H, ddd, *J*=16, 3, 2 Hz, H-2), 2.63–2.34 (3H, m, H-6, H-6′, H-7), 2.21 (1H, brdd, *J*=16, 6 Hz, H-2′), 2.16 (3H, s, H-13), 1.79 (3H, brs, H-15), 1.67–1.27 (6H, m, H-1, H-8, H-9), 1.23 (3H, s, H-14). HREIMS: M^+, found 220.1469. $C_{14}H_{20}O_2$ requires 220.1463.

2-[1,2,3,4,4a,5-Hexahydro-4aα,8-dimethyl-7(6H)-oxonapht-2-yl]-2-hydroxy-propanenitrile (9)

Ketone **8** (44 mg, 0.2 mmol) was dissolved in THF/H_2O (2.5 mL) and a few drops of $HClO_4$ and KCN (20 mg, 0.31 mmol) were added. The reaction was monitorized by TLC, and when it was complete was neutralized with a solution of aq. HCl (5%), and extracted with ethyl ether (5×5 mL). Chromatography (Hexane:AcOEt, 3:1) afforded **9** (30 mg, 0.12 mmol, 60%) as yellow oil.

Cyanohydrin **9** (10 mg, 0.04 mmol) was dissolved in THF (5 mL) and 2.0 mL of aq. H_2SO_4 (5%) were added. After 12 h it was neutralized with a solution of aq. NaOH (5%), and extracted with ethyl ether (5×5 mL). The organic layer was chromatographed (Hexane: Et_2O, 7:3) to give the corresponding amide **11** in very low yield (below 5%) as colourless oil, instead of the desired α-hydroxyacid **10**.

9: IR (KBr)^{neat} ν_{max}: 3400 (hydroxyl group), 2245 (nitrile), 1640 (α,β-unsaturated ketone) cm^{-1}; MS, *m/z* (relative intensity), $C_{15}H_{21}NO_2$: 247 $[M]^+$ (3), 221 $[M-CN]^+$ (4), 229 $[M-H_2O]^+$ (24); δ_H (200 MHz, $CDCl_3$): 2.65 (1H, ddd, *J*=16, 2, 1 Hz, H-2), 2.54–2.30 (3H, m, H-6, H-6′, H-7), 2.15 (1H, ddd, *J*=16, 7, 1 Hz, H-2′), 1.80 (3H, brs, H-15), 1.71–1.28 (6H, m, H-1, H-8, H-9), 1.35 (3H, s, H-13), 1.21 (3H, s, H-14). HREIMS: M^+, found 247.1570. $C_{15}H_{21}NO_2$ requires 247.1572.

11: IR (KBr)^{neat} ν_{max}: 3450 (hydroxyl group), 3330, 3150 (H–N, amide), 1650 (α,β-unsaturated ketone and amide) cm^{-1}. MS, *m/z* (relative intensity), $C_{15}H_{23}NO_3$: 265 $[M]^+$ (10), 247 $[M-H_2O]^+$ (23); δ_H (200 MHz, $CDCl_3$): 2.68 (1H, ddd, *J*=15, 2, 1 Hz, H-2), 2.62–2.30 (3H, m, H-6, H-6′, H-7), 2.20 (1H, ddd, *J*=15, 6, 2 Hz, H-2′), 1.78 (3H, s, H-15) 1.73–1.30 (6H, m, H-1, H-8, H-9), 1.34 (3H, s, H-13), 1.24 (3H, s, H-14). HREIMS: M^+, found 265.1681. $C_{15}H_{23}NO_3$ requires 265.1678.

1,8a,4,4a,5,6,7,8-Octahydro-7β-(2-hydroxy-isopropyl)-1,4aα-dimethyl-naphtalen-2(3H)-one (12)

3.7 mL of borane tetrahydrofuran complex solution (1 M) were added to a solution of alkene **4** (436 mg, 2 mmol) in dry THF (10 mL) under N_2 atmosphere and allowed to stand for 1 h. Then, 0.3 mL of water, 1.0 mL of NaOH 3N, and 1.0 mL of H_2O_2 (30%) were added. The mixture was stirred during 1 h, and then NaCl was added until the solution was saturated. The mixture was extracted with AcOEt (5×10 mL), and the organic layer washed with brine. Chromatography (Hexane:AcOEt, 3:1) afforded alcohol **12** (359 mg, 1.52 mmol, 76%) as colourless gum.

12: $[\alpha]_D^{20}=-160.3$ (*c* 0.12, $CHCl_3$); IR (KBr)^{neat} ν_{max}: 3440 (hydroxyl group), 1640 (α,β-unsaturated ketone), 1600 (double bond) cm^{-1}; MS, *m/z* (relative intensity), $C_{15}H_{24}O_2$: 236 $[M]^+$ (11), 221 $[M-CH_3]^+$ (13), 218 $[M-H_2O]^+$ (2), 203 $[M-H_2O-CH_3]^+$ (9), 177 $[M-C_3H_7O]^+$ (100); δ_H (200 MHz, $CDCl_3$): 3.67 (1H, dd, *J*=10.5, 3.5 Hz, H-12), 3.45 (1H, dd, *J*=10.5, 3.5 Hz, H-12′), 2.72 (1H, ddd, *J*=15, 3, 2 Hz, H-2), 2.62–2.35 (3H, m, H-6, H-6′, H-11), 2.19 (1H, brdd, *J*=15, 7 Hz, H-2′), 1.76 (3H, d, *J*=1 Hz, H-15), 1.69–1.26 (7H, m, H-1, H-7α, H-8, H-9), 1.21 (3H, s, H-14), 0.95 (3H, d, *J*=7 Hz, H-13). HREIMS: M^+, found 236.1781. $C_{15}H_{24}O_2$ requires 236.1776.

(2*S*)-Bromo-1,2-dehydro-6β, 10α, 11β-α-santonin (14)

Alcohol **12** (800 mg, 3.39 mmol) was dissolved in acetone (40.3 mL) and then Jones' reagent (5.7 mL; 63% CrO_3/H_2SO_4 cc) was added. After 1 h, water, AcOEt and Na_2CO_3 were added until the pH was approximately 4. The mixture was extracted with AcOEt (5×25 mL), the organic layer washed with brine, dried with Na_2SO_4 and the solvent evaporated under reduced pressure. The mixture was dissolved in dioxan (30 mL) and small portions of phenyltrimethylammonium perbromide (2.5 g) and an excess of Na_2CO_3 (until an amount is deposited at the bottom) were added. After 1.5 h, an excess of $Na_2S_2O_3$ was added and stirred for 30 min. The reaction was neutralized with a solution of aq. HCl (5%), and extracted with $CHCl_3$ (5×25 mL) and AcOEt (5×20 mL). After chromatography an epimeric mixture of bromolactone **14** was obtained (659 mg, 2.02 mmol, 60%) as yellow crystals.

14: IR (KBr)^{neat} ν_{max}: 1762 (γ-lactone), 1650 (ketone α,β-unsaturated) cm^{-1}; MS, *m/z* (relative intensity), $C_{15}H_{19}BrO_3$: 326 $[M]^+$ (8), 328 $[M+2]^+$ (8), 247 $[M-Br]^+$ (80), 233 $[M-Br-CH_3]^+$ (14), 219 $[M-Br-CO]^+$ (40); δ_H (400 MHz, $CDCl_3$): 5.17 (1H, d, *J*=5 Hz, H-6), 4.94 (1H, dd, *J*=9.5, 9.5 Hz, H-2), 2.88 (1H, dq, *J*=7, 7 Hz, H-11), 2.59 (1H, dd, *J*=14, 9.5 Hz, H-1), 2.38 (1H, dd, *J*=14, 9.5 Hz, H-1′), 1.94 (3H, s, H-15), 1.62–1.38 (5H, m, H-7α, H-8α, H-8β, H-9α, H-9β), 1.28 (3H, s, H-14), 1.24 (3H, d, *J*=7 Hz, H-13). HREIMS: M^+, found 326.0522. $C_{15}H_{19}BrO_3$ requires 326.0518.

Isomer of α-santonin 15

To a suspension of dry LiBr (64 mg, 0.74 mmol) and Li_2CO_3 (84 mg, 1.14 mmol) in dry DMF (20 mL) at 120°C under nitrogen atmosphere was added **14** (120 mg, 0.37 mmol). After the mixture was stirred for 75 min at 120–125°C, it was cooled and aq. acetic acid (5%) was added. The reaction mixture was extracted with AcOEt (5×20 mL), and the organic layer concentrated under reduced pressure. Chromatography (Hexane:AcOEt, 1:1) yielded 64 mg (0.26 mmol, 70%) of lactone **15** as colourless oil.

15: $[\alpha]_D^{20}=-69.8$ (*c* 0.2, $CHCl_3$); IR (KBr)^{neat} ν_{max}: 1755 (γ-lactone), 1640 (ketone α,β-unsaturated) cm^{-1}. MS, *m/z* (relative intensity), $C_{15}H_{18}O_3$: 246 $[M]^+$ (15), 231 $[M-CH_3]^+$ (21), 218 $[M-CO]^+$ (32); δ_H (200 MHz, $CDCl_3$): 6.72 (1H, d, *J*=10 Hz, H-1), 6.23 (1H, d, *J*=10 Hz, H-2), 5.21 (1H, d, *J*=5 Hz, H-6), 2.90 (1H, dq, *J*=7, 7 Hz, H-11), 2.02 (3H, s, H-15), 1.75–1.46 (5H, m, H-7α, H-8α, H-8β, H-9α, H-9β), 1.30 (3H, s, H-14), 1.25 (3H, d, *J*=7 Hz, H-13). HREIMS: M^+, found 246.1253. $C_{15}H_{18}O_3$ requires 246.1256.

6β,10α-α-Santonin (16)

Lactone **15** (75 mg, 0.30 mmol) was dissolved in dry THF (15 mL). A 0.4 M solution of KHMDS (1.5 mL, 0.4 mmol) in THF was added at −73°C with continuous stirring. The solution immediately turned red. Triethyl phosphite (1.5 mL) was added and the mixture was stirred for 1 h. Then, a current of oxygen was bubbled through the solution for 1 h and the system was warmed to −20°C. Neutralization was carefully accomplished by addition of 30% solution of dry acetic acid in THF (until the colour turned to yellowish). A Sorensen buffer solution (pH=7) was added and organic solvents and water evaporated under reduced pressure. The solid was extracted with AcOEt (5×10 mL) at 50°C. The crude extract was chromatographed (Hexane:AcOEt, 4:1) to give **16** (46 mg, 0.18 mmol, 57%) as colourless oil.

16: $[\alpha]_D^{20}=-20.4$ (*c* 0.1, $CHCl_3$); IR (KBr)^{neat} ν_{max}: 3450 (hydroxyl group), 1790 (γ-lactone), 1650 (α,β-unsaturated ketone) cm^{-1}; MS, *m/z* (relative intensity), $C_{15}H_{18}O_4$: 262 $[M]^+$ (3), 247 $[M-CH_3]^+$ (3), 244 $[M-H_2O]^+$ (10), 218 $[M\text{-}CO_2]^+$ (1), 123 (11), 69 (72), 55 (100); δ_H (200 MHz, $CDCl_3$): 6.75 (1H, d, *J*=10 Hz, H-1), 6.21 (1H, d, *J*=10 Hz,

H-2), 5.62 (1H, dq, *J*=7, 1.5 Hz, H-6), 2.92 (1H, ddd, *J*=7, 7, 7 Hz, H-7), 2.05 (3H, d, *J*=1.5 Hz, H-15), 1.81–1.79 (1H, m, H-8α), 1.70–1.48 (3H, m, H-8β, H-9α, H-9β), 1.33 (3H, s, H-13), 1.28 (3H, s, H-14); δ_C (100 MHz, $CDCl_3$): 188.3 (s, C-3), 179.6 (s, C-12), 158.0 (d, C-1), 153.6 (s, C-5), 136.8 (s, C-4), 127.2 (d, C-2), 78.5 (d, C-6), 76.8 (s, C-11, 47.4 (d, C-7), 41.4 (s, C-10), 34.6 (t, C-9), 28.9 (q, C-14), 22.2 (q, C-13), 20.1 (t, C-8), 14.4 (q, C-15); HREIMS: M^+, found 262.1201. $C_{15}H_{18}O_4$ requires 262.1205.

(+)-Decipienin A (1)

To a stirred solution of angelic acid (25 mg, 0.25 mmol) in dry toluene:DCM (1:1; 3 mL) under argon was added 2,4,6-trichlorobenzoyl chloride (38.6 μL, 0.25 mmol) and triethylamine (34.9 μL, 0.25 mmol). The resulting mixture was stirred for 2 h at 20°C and then treated with **16** (10 mg, 0.038 mmol). The mixture was stirred for 4 days at room temperature and was then diluted with ether (2 mL) and filtered. The filtrate was concentrated under reduced pressure and the resulting crude mixture purified by HPLC using a silica gel column (Hexane:AcOEt, 6:4) to give **1** (4.2 mg, 0.012 mmol, 32%).

1: Colourless crystals, mp 182–184°C; $[\alpha]_D^{20}=+54.3$ (*c* 0.1, $CHCl_3$) [lit.[6] $[\alpha]_D^{25}=+54.9$ (*c* 0.2, $CHCl_3$)]; IR $(KBr)^{neat}$ ν_{max}: 2945, 1776 (γ-lactone), 1725 (α,β-unsaturated ester), 1650 (α,β-unsaturated ketone) cm^{-1}; MS, *m/z* (relative intensity): 244 $[M-HOAng]^+$ (45), 229 $[244-CH_3]^+$ (28), 216 (20), 201 (18), 83 (100), 55 (86); δ_H (400 MHz, $CDCl_3$): 6.74 (1H, d, *J*=10 Hz, H-1), 6.23 (1H, d, *J*=10 Hz, H-2), 6.20 (1H, qq, *J*=7, 1.5 Hz, H-3′), 5.62 (1H, dq, *J*=8, 1.5 Hz, H-6), 3.59 (1H, ddd, *J*=8, 7, 7 Hz, H-7), 2.09 (3H, d, *J*=1.5, H-15), 1.98 (1H, dq, *J*=7, 1.5 Hz, H-4′), 1.95–1.93 (1H, m, H-8α), 1.88 (1H, dq, *J*=1.5, 1.5 Hz, H-5′), 1.72–1.69 (1H, m, H-9β), 1.68–1.48 (2H, m, H-8β, H-9α), 1.43 (3H, s, H-13), 1.28 (3H, s, H-14); δ_C (100 MHz, $CDCl_3$): 185.3 (s, C-3), 174.6 (s, C-12), 166.0 (s, C-1′), 156.0 (d, C-1), 152.6 (s, C-5), 140.5 (d, C-3′), 134.1 (s, C-4), 127.1 (s, C-2′), 126.5 (d, C-2), 79.0 (s, C-11), 76.5 (d, C-6), 47.5 (d, C-7), 41.2 (s, C-10), 34.3 (t, C-9), 27.4 (q, C-14), 21.6 (t, C-8), 20.1 (q, C-13), 18.9 (q, C-5′), 15.9 (q, C-4′), 13.1 (q, C-15); HREIMS: $[M-HOAng]^+$, found 244.1091. $C_{15}H_{16}O_3$ requires 244.1089.

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