Synthesis of 9-Deoxy-15-hydroxycotylenol and Its Germination-Stimulating Activity on Lettuce Seeds

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(Received November 27, 1997)

Cotylenins and fusicoccins, fungal diterpenoid glycosides, are know to have identical, yet unique, plant growth-regulating activities. These compounds widen the stomatal pore, stimulate cell enlargement, break seed dormancy, and stimulate rhizogenesis. Because of these plant-hormone like activities, fusicoccin, a representative of this family, has been widely utilized in plant physiology. During the course of our study on the structure-activity relationships of this class of compounds, 9-deoxy-15-hydroxycotylenol and its 15-methoxymethyl ether were synthesized in order to clarify the role of the 9α-hydroxy group of cotylenol, a common aglycon of cotylenins. Since these cotylenol analogs retained germination-stimulating activity on lettuce seeds, it has been clarified that the 9α-hydroxy group of cotylenol is not essential for its biological activities. This finding is informative in designing useful tools for targeting the 14-3-3 protein, which has recently been identified as the binding protein of fusicoccin.

Cotylenins (cotylenin A (**1**) is shown in Fig. 1 as a representative) were isolated as leaf-growth substances from an unidentified species of *Cladosporium*.[1] While fusicoccins (fusicoccin A (**2**) is shown in Fig. 1 as a representative) were originally isolated as phytotoxic substances responsible for a wilting decease of peach and almond trees caused by a phytopathogenic fungus, *Fusicoccum amygdali*.[2] In spite of these opposite effects on higher plants, their biological activities, i.e., stimulation of seed germination, cell enlargement, and stomatal opening, are regarded to be identical in principle.[3] Also, their aglycons, fusicoccane diterpenoids, having a 5-8-5-membered tricyclic skeleton, are closely related to each other. The mechanism of the biological actions has been intensively studied, and it has been clarified that most biological outcomes are the results of the promotion of H^+ extrusion, which is initiated with the activation of the plasma membrane-located H^+-ATPase, associated with the uptake of the K^+ in H^+/K^+ exchange system of higher plants. Because of these unique physiological activities and the mechanism of action, fusicoccin has been widely utilized in plant physiology. Also, more recently, the binding protein of fusicoccin has been clarified[4] as being a member of 14-3-3 proteins, which were originally identified as mammalian brain proteins. Since 14-3-3 proteins have been considered to take an important role in intracellular signal transductions,[5] cotylenins and fusicoccins have become more important as tools for studying biological regulatory pathways.[6] Furthermore, it has very recently been clarified that cotylenin A, a major constituent of cotylenins, produces functional and morphological differentiation in murine and human myeloid leukemia cells.[7] Therefore, studies on the derivatives of cotylenins and/or fusicoccins are important for understanding how this class of compounds triggers such responses, and also potentially to develop new tools for targeting 14-3-3 proteins.

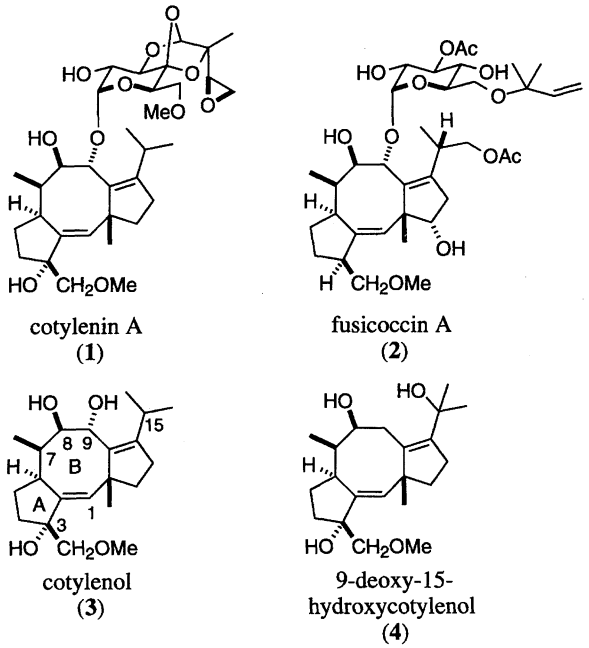


Fig. 1.

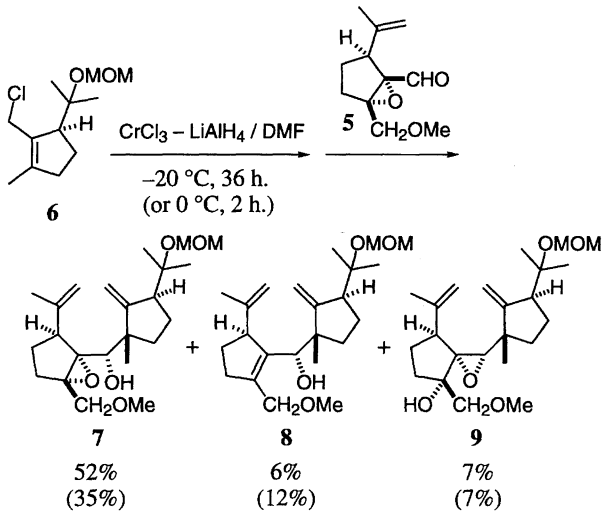
According to studies on structure–activity relationships, the structural requirements for biological activities in the diterpenoid portion of the fusicoccin molecule are: the β-hydroxy group at C-8, the configuration at C-3, and the chair-sofa conformation of the eight-membered ring. The importance of the sugar moiety is secondary to that of the

diterpenoid portion, since the aglycons retain most biological activities[8] and still compete with fusicoccin for binding to the receptor, the 14-3-3 protein.

As a part of our study[9] on the structure–activity relationships of this class of compounds, we postulated that the C-9 function is not essential for the bio-activities, since the C-9 hydroxy group of cotylenol (**3**),[10] a common aglycon of cotylenins, acts just as a linker for the sugar moiety in cotylenins. Thus, 9-deoxy-15-hydroxycotylenol (**4**) was chosen in this study to prove our hypothesis. The possibility that the hydroxy group or the sugar moieties located at the C-9α position in cotylenol or cotylenins contributes to the hydrophilicity on their neighboring circumstances let us put an additional hydroxy group at C-15, which was expected to take a similar role, since a substituent on C-15 must be located in the proximate position of the C-9α substituent based on the molecular model inspections.[11]

Results and Discussion

Synthetic Studies. As already reported,[12] the carbon framework of **4** can be constructed via an eight-membered ring formation by an ene reaction on an appropriately functionalized *B-seco*-fusicoccane derivative. Thus, similar to the first total synthesis of cotylenol (**3**),[13] the C_{10}-synthon for the A-ring (**5**)[13] was condensed with another C_{10}-synthon of the C-ring, (3*S*)-7-chloro-8-methoxymethoxyirid-1-ene (**6**)[14] by use of low-valent chromium species[15] in *N*,*N*-dimethylformamide (DMF) to give the desired condensate, 2α,3α-epoxy-16-methoxy-15-methoxymethoxy-8,9-*seco*-fusicocca-7,9-dien-1α-ol (**7**), only in moderate yield at 0 °C together with 16-methoxy-15-methoxymethoxy-8,9-*seco*-fusicocca-2,7,9-trien-1α-ol (**8**) and 1α,2α-epoxy-16-methoxy-15-methoxymethoxy-8,9-*seco*-fusicocca-7,9-dien-3α-ol (**9**) (Scheme 1). The by-product **8** must be derived from a deoxygenated unsaturated aldehyde, which must be formed reductively prior to the condensation reaction, while **9**, whose stereostructure was finally confirmed by an X-ray crystallographic analysis (see Experimental section) (Fig. 2),



Scheme 1.

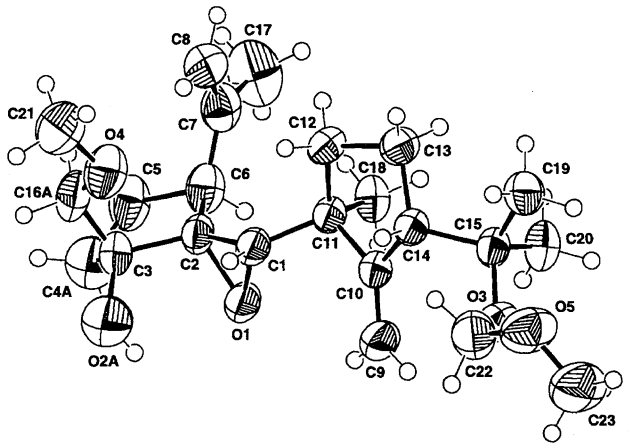
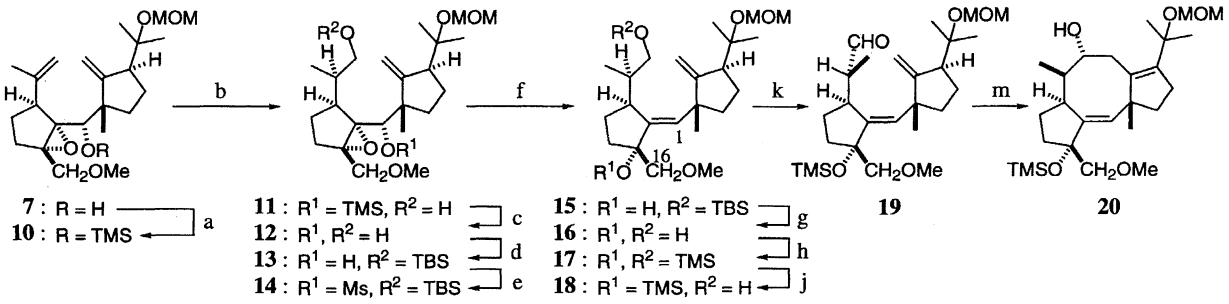


Fig. 2. Crystal structure of **9** showing 50% probability displacement ellipsoids. Although there are disordered contributions regarding to the conformation of A-ring (3 non-hydrogen sites, O2, C4, and C16, are involved), only the major contribution is shown for clarify.

must be derived from the Lewis acid-catalyzed isomerization of **7**. The ratio of **9** to **7** increased with elongating the reaction time and warming up the reaction mixture. It should be noted that the configuration of C-2 of **9** retained that of **7** during the isomerization. As an assumption, the formation of the by-product **8** should be suppressed if the reduction of allyl chloride **6** leading to the allylchromium species would be possible in the conditions that no electrophiles existed in the reaction medium. Although it had been well known in such conditions that the allylchromium species quickly gives a radical homo-coupling product at ambient temperature,[16] we finally found that this type of homo-coupling reaction was negligible below −20 °C. Thus, the pre-treatment of chloroiridene **6** by a low-valent chromium species at low temperature, before the addition of the epoxy-aldehyde **5**, remarkably improved the yield of the requisite product in the condensation reaction.

After protection of the secondary hydroxy group of **7** as a trimethylsilyl (TMS) ether **10**, the site and stereoselective hydroboration on C-8 was performed by 9-borabicyclo[3.3.1]-nonane (9-BBN) to afford **11** (Scheme 2). TMS protection of the 1α-hydroxy group of **11** was removed by a treatment with Bu_4NF to give a diol **12**. Then, the primary alcohol was selectively protected as a *t*-butyldimethylsilyl (TBS) ether, leading to **13**. A methanesulfonate **14**, derived from **13**, was reductively converted into **15** in moderate yield. In this Birch-type reduction step, the addition of iron(III) salt was indispensable to minimize any over-reduction. The requisite *E*-geometry of the C-1–C-2 double bond in **15** was confirmed by a nuclear Overhauser effect (NOE); a clear enhancement of the H-1 olefinic proton by the irradiation of C-16 methylene protons was diagnostic.

Conversions of the protecting groups of the 3α- and 8-hydroxy groups were then carried out; **15** was treated with Bu_4NF to give a diol **16**, which was converted into a bis-TMS ether **17**; then, the selective deprotection of the primary TMS

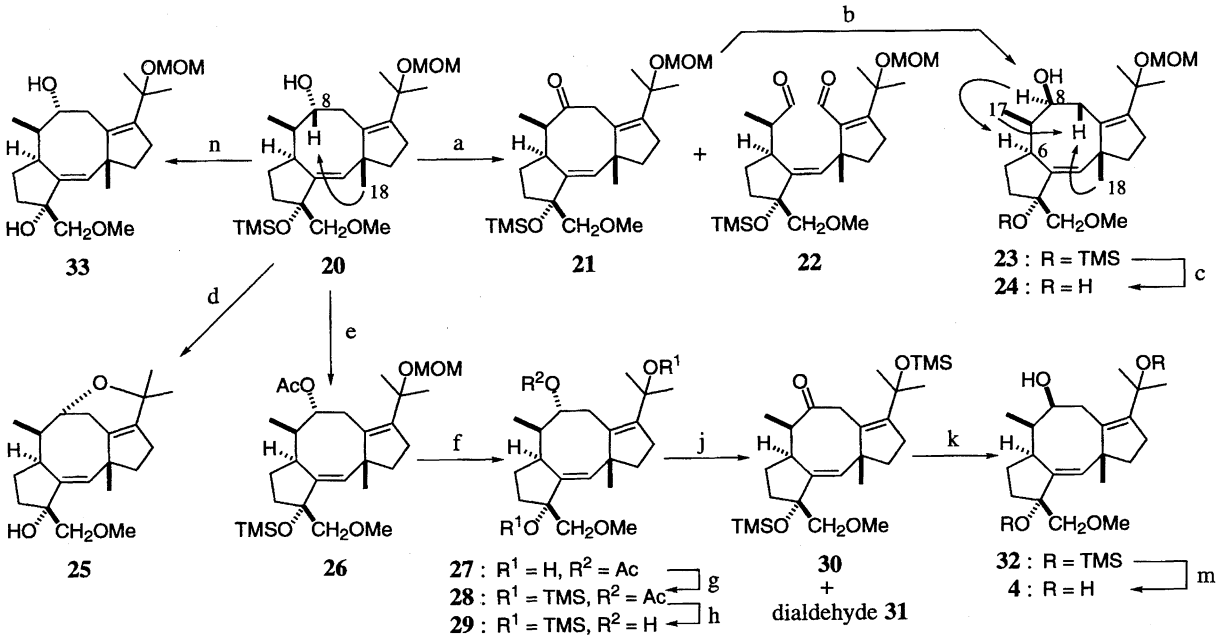


Scheme 2. [reagents (yields)]. a: TMSCl/pyridine (91%), b: i) 9-BBN; ii) H_2O_2, ^-OH (89%), c: Bu_4NF/THF (97%), d: TBSCl-imidazole/DMF (97%), e: MsCl/pyridine, f: Ca ($FeCl_3$)/liq NH_3 (45% from **13**), g: Bu_4NF/THF (93%), h: TMSCl/pyridine (94%), j: PPTS/aq THF (86%), k: PDC/CH_2Cl_2 (82%), m: 160 °C/xylene (86%).

ether of **17** was achieved to afford **18**. Subsequently, the aldehyde **19**, the precursor for the ene reaction, was obtained by pyridinium dichromate (PDC)-oxidation. The thermally-induced ene reaction of **19** occurred in a xylene solution to give a cyclizate, 16-methoxy-15-methoxymethoxy-3α-(trimethylsilyloxy)fusicocca-1,10(14)-dien-8α-ol (**20**) in good yield. The α-orientation of the C-8 hydroxy group was clarified by an NOE experiment; an enhancement of 8β-H was observed by irradiation of the C-18-Me signal.

For epimerization of the hydroxy group of **20** to the requisite 8β-configuration, **20** was oxidized with PDC to the corresponding ketone **21** in moderate yield, together with a dialdehydic by-product **22** (Scheme 3). Then, ketone **21** was stereoselectively reduced with diisobutylaluminum hydride (DIBALH, diisobutylalane) to give **23**. The stereochemistry of **23** was confirmed again by NOE experiments; NOE's from H-8α to H-6 and C-17-Me to H-9β indicated the β-configuration of the C-8 hydroxy group and the chair-sofa conformation of the eight-membered ring, respectively. Both the configuration and conformation had been reported to be inevitable for being biologically active.[17] The desilylation of **23** afforded **24**, a methoxymethyl ether of the final target **4**.

We set our next goal to synthesize triol **4**. Since the 8β-hydroxy group of cotylenol (**3**) tends to attack the C1–C2 double bond under acidic conditions,[10] deprotection of the methoxymethyl (MOM) group on the synthetic intermediate **20** was investigated. First, it had been hoped that the MOM group of **20** could be removed without protecting the C-8 hydroxy group. Unfortunately, the treatment of **20** with aqueous AcOH gave rise to a cyclic ether **25**, while the MOM group of the acetate **26** derived from **20** was removed by an acetic acid-treatment to afford **27**. The formation of the cyclic ether **25** suggested that this deprotection had proceeded not through the normal hydrolysis of the MOM group, but via an allylic cation formation at C-15. Both of the tertiary hydroxy groups of **27** were protected with TMS groups to give **28**; then, a reductive deprotection of the acetate gave an alcohol **29**. As before, the oxidation-reduction process was



Scheme 3. [reagents (yields)]. a: PDC/CH_2Cl_2 (**21**, 52%; **22**, 13%), b: DIBALH/hexane (82%), c: Bu_4NF/THF (96%), d: aq AcOH/THF (59%), e: Ac_2O/pyridine (84%), f: aq AcOH/THF (82%), g: TMSCl/pyridine (90%), h: $LiAlH_4$/THF (78%), j: PDC/CH_2Cl_2 (**30**, 46%; **31**, 9%), k: DIBALH/hexane (86%), m: Bu_4NF/THF (95%), n: Bu_4NF/THF (91%); Arrows in **20** and **23** are observed NOE's.

Table 1.[a] Stimulating Activity on Germination of Lettuce Seeds[b] (Germination Ratio/%) in the Presence of (±)-Abscisic Acid (2 ppm)[c]

Time	Compounds and concentrations [ppm (nM)]						
	4		**24**		**33**		
h	50 (143)	100 (275)	50 (127)	100 (253)	50 (127)	100 (253)	None
24	0	0	2.5	7.5	0	0	0
48	0	7.5	2.5	12.5	0	0	0
72	2.5	37.5	15	25	0	0	0
96	2.5	50	30	52.5	0	0	0
120	2.5	90	67.5	95	0	0	0

a) Experiments were carried out at 25 °C in the dark using 40 seeds. b) 'Mamma lettuce', Nakahara Seed Production Co. c) Without (±)-abscisic acid, 100% germination was observed within 48 h.

employed to invert the 8α-hydroxy group in **29**. The PDC-oxidation of **29** gave the kitone **30** together with the dial **31** as a by-product. Then, **30** was reduced with DIBALH to give the 8α-hydroxy derivative **32** stereoselectively. Removal of the silyl-protections was then effected with a fluoride ion to afford the triol **4**.

Biological Activities. Evaluation of the biological activities of the thus-obtained 9-deoxycotylenol derivatives, **4** and **24**, was carried out by checking the germination-stimulating activity using lettuce seeds. For confirming the importance of the 8β-hydroxy group, 8-*epi*-9-deoxy-15-methoxymethoxy-cotylenol (**33**) was derived from **20** simply by desilylation of the TMS protecting group. The antagonistic nature of these compounds toward (±)-abscisic acid was evaluated; the results are summarized in Table 1. The fact that **4** and **24** retained germination-stimulating activity clearly suggested that the 9α-hydroxy group of cotylenol (**3**) and/or the sugar moiety of cotylenins are not essential for the physiological activities of this class of compounds. On the other hand, **33**, 8-*epi*-**24**, completely lost its stimulating activity; this finding again confirmed the importance of the configuration of the 8-hydroxy group. The triol **4** is somewhat less active than the corresponding MOM derivative **24**. This fact might correlate with the higher polarity in **4**.[18]

Concluding Remarks. A total synthesis of 9-deoxy-15-hydroxycotylenol derivatives has been achieved. This methodology featured applications of a Cr(II) mediated lower temperature coupling reaction of two parts of appropriately functionalized iridoid synthons, and an eight-membered ring formation by an intramolecular ene reaction. The retention of the activity in 9-deoxycotylenol derivatives, **4** and **24**, clearly suggested that the 9α-hydroxyl is not essential for the biological activities of this class of compounds. Further studies, including clarification of the role of 15-oxygen functions in **4** and **24**, are now proceeding.

Experimental

The melting points were measured with a Yanagimoto micro melting-point apparatus, and are uncorrected. Elemental analyses were performed by the Institute of Central Analysis and the Institute of Advanced Material Study, Kyushu University. The NMR spectra were recorded on JEOL GSX 270H, LA 400 and/or LA 600 in $CDCl_3$ unless otherwise noted. The mass spectra were measured with a JEOL 01SG-2 or JMS-70 spectrometer at the Institute of Advanced Material Study, Kyushu University; among the data, only the molecular ion peak or the nearest peak as the alternative, and the base were recorded. The IR spectra were measured as KBr disks for crystalline compounds or as liquid films inserted between NaCl plates for oily compounds, using a JASCO IR-A 102 spectrometer. Optical rotations were measured with a Union PM-101 apparatus. All of the solvents were pre-dried by standard methods unless otherwise stated. All reactions involving nonaqueous solutions were performed under an inert atmosphere. The stationary phase for column chromatography was a Wakogel C-300, and the eluent was a mixture of hexane and ethyl acetate. The organic extracts were dried over anhydrous magnesium sulfate, unless otherwise stated.

Condensation of (1*R*,2*S*,3*S*)-1,2-Epoxy-6-methoxyirid-8-en-7-al (5) and (3*S*)-7-Chloro-8-methoxymethoxyirid-1-ene (6) into 2α,3α-Epoxy-16-methoxy-15-methoxymethoxy-8,9-*seco*-fusicocca-7,9-dien-1α-ol (7), 16-Methoxy-15-methoxymethoxy-8,9-*seco*-fusicocca-2,7,9-trien-1α-ol (8), and 1α,2α-Epoxy-16-methoxy-15-methoxymethoxy-8,9-*seco*-fusicocca-7,9-dien-3α-ol (9). To a suspension of $CrCl_3$ (20.4 g, 129 mmol) in anhydrous THF (200 cm^3) was added $LiAlH_4$ (2.28 g, 60.1 mmol) at 0 °C and the mixture was stirred for 1 h. THF was removed from the mixture by evaporation, and the residue was dissolved in anhydrous DMF (600 cm^3). After 30 min of vigorous stirring, the mixture was cooled to −20 °C, to which **6** (17.5 g, 75.2 mmol) dissolved in anhydrous DMF (30 cm^3) was introduced. Stirring was maintained at this temperature for 4 d prior to the addition of **5** (9.0 g, 45.9 mmol) in DMF (25 cm^3). The reaction mixture was stirred for 2 h and at 0 °C for further 12 h. The reaction was quenched with water and the mixture was extracted with ether. The combined organic layers were washed with brine, dried, and concentrated under reduced pressure. Flash chromatography of the residue on silica gel gave a mixture of **7** and **8**, and pure **9** (1.2 g, 7%) as colorless plates. The above mixture of **7** and **8** was subjected again to chromatography on silica gel to give **7** (9.6 g, 52%) and **8** (1.0 g, 6%), both as colorless needles.

7: Mp 77.5—78.0 °C. Found: C, 69.81; H, 9.63%. Calcd for $C_{23}H_{38}O_5$: C, 70.02; H, 9.71%. $[\alpha]_D^{16}$ +64.0 (*c* 1.00, $CHCl_3$); MS *m/z* 394 (M^+; 0.38) and 95 (base peak); IR (KBr) ν 3444, 2946, 2878, 2822, 1641, 1455, 1379, 1366, 1254, 1110, 1068, 1048, 840, and 750 cm^{-1}; ^{1}H NMR (600 MHz) δ = 1.11 (3H, s), 1.23 (3H, s), 1.26 (3H, s), 1.36—1.41 (1H, m), 1.44 (1H, m), 1.63 (1H, ddd, *J* = 13.0, 8.1, 3.3 Hz), 1.66 (3H, dd, *J* = 0.9, 0.4 Hz), 1.72—1.79 (2H, m), 1.96 (1H, dddd, *J* = 13.0, 9.5, 8.1, 1.5 Hz), 2.34 (1H, ddd, *J* = 16.1, 9.5, 3.3 Hz), 2.49 (1H, ddd, *J* = 16.1, 8.1, 0.9 Hz), 2.69 (1H, m), 3.06 (1H, d, *J* = 4.0 Hz), 3.34 (1H, m), 3.37 (3H, s), 3.38 (3H, s), 4.00 (1H, dd, *J* = 4.0, 1.5 Hz), 4.07 (1H, d, *J* = 11.9 Hz), 4.36 (1H, d, *J* = 11.9 Hz), 4.68 (1H, dd, *J* = 1.6, 0.7 Hz), 4.72 (1H, d, *J* = 7.3 Hz), 4.73 (1H, m), 4.78 (1H, d, *J* = 7.1 Hz), 5.08 (1H, dd, *J* = 2.7, 0.9 Hz), and 5.38 (1H, m); ^{13}C NMR (100 MHz) δ = 21.63, 21.65, 24.9, 25.5, 26.65, 26.69, 28.4, 33.0, 51.7, 52.3, 52.9, 55.5, 59.2, 71.0, 72.3, 72.8, 74.5, 78.7, 90.9, 109.3, 111.9, 146.7, and 157.9.

8: Mp 73—74 °C. Found: C, 73.10; H, 10.35%. Calcd for $C_{23}H_{38}O_4$: C, 72.98; H, 10.12%. $[\alpha]_D^{26}$ +165 (*c* 1.00, $CHCl_3$); MS *m/z* 225 (M^+ − 153; 5.3) and 121 (base peak); IR(KBr) ν 3448, 3066, 2962, 2828, 1641, 1460, 1378, 1366, 1148, 1037, 1148, 1037, and 892 cm^{-1}; ^{1}H NMR (400 MHz) δ = 1.16 (3H, s), 1.23 (3H, s), 1.28 (3H, s), 1.30 (1H, m), 1.38—1.48 (2H, m), 1.63 (1H, ddm,

J = 12.3, 8.5 Hz), 1.72 (3H, s), 1.78 (1H, ddm, J = 15.9, 8.2 Hz), 1.88—1.92 (2H, m), 2.07 (1H, m), 2.77 (1H, d, J = 8.2 Hz), 2.82 (1H, d, J = 5.3 Hz), 2.92 (1H, m), 3.38 (3H, s), 3.42 (3H, s), 3.88 (1H, d, J = 11.1 Hz), 3.91 (1H, d, J = 10.9 Hz), 4.10 (1H, d, J = 5.3 Hz), 4.72 (1H, d, J = 7.0 Hz), 4.73 (1H, d, J = 1.5 Hz), 4.79 (1H, d, J = 1.5 Hz), 4.81 (1H, d, J = 7.2 Hz), 5.06 (1H, m), and 5.42 (1H, dd, J = 2.4, 1.0 Hz); ^{13}C NMR (150 MHz) δ = 19.7, 22.0, 24.3, 26.3, 26.8, 28.0, 33.7, 35.3, 52.3, 53.2, 55.5, 58.4, 58.7, 70.6, 76.1, 78.7, 90.9, 109.5, 111.0, 138.5, 141.6, 147.8, and 157.4.

9: Mp 104—105 °C. Found: C, 70.31; H, 9.79%. Calcd for $C_{23}H_{38}O_5$: C, 70.02; H, 9.71%. $[\alpha]_D^{17}$ −63.4 (c 1.01, $CHCl_3$); MS m/z 394 (M^+; 0.2) and 103 (base peak); IR (KBr) ν 3468, 3090, 2988, 2964, 2882, 2056, 1820, 1639, 1471, 1455, 1368, 1182, 1140, 1039, and 907 cm^{-1}; ^{1}H NMR (600 MHz) δ = 0.90 (3H, s), 1.22 (3H, s), 1.27 (3H, s), 1.42—1.50 (2H, m), 1.56—1.59 (2H, m), 1.66 (1H, ddd, J = 13.2, 8.1, 7.9 Hz), 1.71 (3H, s), 1.77 (1H, m), 1.87 (1H, dt, J = 13.4, 6.8 Hz), 2.18—2.23 (1H, m), 2.71 (1H, dd, J = 9.3, 4.2 Hz), 2.82 (1H, ddt, J = 8.1, 7.9, 2.7 Hz), 2.85 (1H, s), 3.23 (1H, s), 3.34 (3H, s), 3.39 (3H, s), 3.41 (1H, d, J = 10.1 Hz), 3.42 (1H, dd, J = 10.1, 0.9 Hz), 4.74 (1H, d, J = 7.1 Hz), 4.79 (1H, d, J = 7.1 Hz), 4.80 (1H, d, J = 1.8 Hz), 4.85 (1H, s), 5.23 (1H, d, J = 2.7 Hz), and 5.35 (1H, d, J = 1.8 Hz); ^{13}C NMR (150 MHz) δ = 21.3, 21.8, 22.8, 26.2, 27.1, 27.2, 34.0, 34.4, 46.6, 48.4, 52.9, 55.5, 59.2, 68.3, 70.8, 75.4, 78.40, 78.44, 90.9, 109.6, 111.4, 146.5, and 159.1.

TMS Protection of 1α-Hydroxy Group of 7. Formation of 2α,3α-Epoxy-16-methoxy-15-methoxymethoxy-1-trimethylsilyloxy-8,9-*seco*-fusicocca-7,9-diene (10). A solution of **7** (2.6 g, 6.6 mmol) in anhydrous pyridine (30 cm^3) was treated with TMSCl (4.0 cm^3) and stirred for 20 h. The mixture was then diluted with aqueous $NaHCO_3$ and extracted with ether. The organic extract was washed with aqueous $KHSO_4$, aqueous $NaHCO_3$, and brine, dried, and evaporated in vacuo. Chromatography of the residue on silica gel gave **10** (2.8 g, 91%) as colorless crystals.

10: Mp 53—54 °C. Found: C, 67.08; H, 9.94%. Calcd for $C_{26}H_{46}O_5Si$: C, 66.91; H, 9.93%. $[\alpha]_D^{17}$ and +48.5 (c 0.99, $CHCl_3$); MS m/z 301 (M^+ − 165; 0.9) and 119 (base peak); IR (KBr) ν 3440, 3076, 2946, 2906, 2878, 2822, 1640, 1455, 1379, 1253, 1111, 1068, 1048, 905, 884, 864, 840, and 750 cm^{-1}; ^{1}H NMR (600M Hz) δ = 0.12 (9H, s), 1.08 (3H, s), 1.17 (1H, ddd, J = 12.5, 7.5, 1.8 Hz), 1.22 (3H, s), 1.28 (3H, s), 1.25—1.32 (2H, m), 1.58 (1H, ddm, J = 13.0, 10.4 Hz), 1.72 (3H, s), 1.74 (1H, m), 1.78 (1H, ddm, J = 10.4, 8.4 Hz), 2.07 (1H, dd, J = 14.1, 8.4 Hz), 2.35 (1H, td, J = 11.9, 7.1 Hz), 2.85 (1H, d, J = 8.4 Hz), 3.20 (1H, ddd, J = 11.5, 7.7, 2.7 Hz), 3.42 (3H, s), 3.43 (3H, s), 3.85 (1H, d, J = 11.9 Hz), 3.91 (1H, d, J = 11.9 Hz), 4.24 (1H, s), 4.69 (1H, d, J = 6.8 Hz), 4.74 (1H, d, J = 1.1 Hz), 4.82 (1H, d, J = 6.8 Hz), 4.82—4.83 (1H, m), 4.86 (1H, d, J = 2.2 Hz), and 5.47 (1H, dd, J = 1.6 Hz); ^{13}C NMR (150 MHz) δ = 1.1 (3C), 21.7 (2C), 25.9, 26.8, 26.9, 28.3, 28.7, 32.3, 52.0, 52.3, 53.7, 55.5, 59.0, 72.5, 73.2, 75.7, 76.1, 78.3, 90.9, 108.7, 112.7, 146.8, and 156.9.

Hydroboration of 10. Formation of 2α,3α-Epoxy-16-methoxy-15-methoxymethoxy-1-trimethylsilyloxy-8,9-*seco*-fusicocc-9-en-8-ol (11). To an anhydrous THF solution (350 cm^3) of **10** (7.0 g, 15 mmol) was added 9-BBN (14.0 g, 61 mmol), and the mixture was stirred for 12 h. The mixture was then treated with 3 M NaOH (70 cm^3) (1 M = 1 mol dm^{-3}) and 35% H_2O_2 (55 cm^3) at 40 °C for 1 h. The mixture was extracted with ether and the combined organic layers were dried and concentrated under reduced pressure. The residue was purified by flash chromatography, affording **11** (6.5 g, 89%) as a colorless oil.

11: HRFABMS Found: m/z 485.3281. Calcd for $C_{26}H_{49}O_6Si$: $[M+H]^+$, m/z 485.3298. $[\alpha]_D^{18}$ +24.8 (c 1.05, $CHCl_3$); MS m/z 333 (M^+ − 151; 0.3) and 197 (base peak); IR (NaCl) ν 3480, 2956, 2818, 1640, 1461, 1367, 1251, 1070, 1040, and 842 cm^{-1}; ^{1}H NMR (600 MHz) δ = 0.17 (9H, s), 0.98 (3H, d, J = 6.8 Hz), 1.13 (3H, s), 1.19 (1H, ddd, J = 12.5, 7.5, 2.0 Hz), 1.23 (3H, s), 1.28 (3H, s), 1.31 (1H, ddm, J = 11.7, 7.7 Hz), 1.33—1.38 (1H, m), 1.43 (1H, ddm, J = 13.6, 9.5 Hz), 1.73 (1H, ddm, J = 11.9, 7.0 Hz), 2.02 (1H, ddm, J = 13.6, 9.5 Hz), 2.12—2.18 (1H, m), 2.23 (1H, dm, J = 7.0 Hz), 2.39 (1H, ddm, J = 7.5 Hz), 3.18 (1H, ddm, J = 11.4, 7.9 Hz), 3.31 (1H, m), 3.37 (3H, s), 3.41 (3H, s), 3.57 (1H, m), 3.82 (1H, d, J = 11.7 Hz), 3.87 (1H, d, J = 11.7 Hz), 4.40 (1H, s), 4.68 (1H, d, J = 6.8 Hz), 4.82 (1H, d, J = 6.8 Hz), 4.83 (1H, d, J = 2.2 Hz), and 5.34 (1H, d, J = 1.8 Hz); ^{13}C NMR (150 MHz) δ = 1.07 (3C), 17.0, 20.1, 21.7, 26.8, 26.9, 28.9 (2C), 32.4, 36.1, 49.7, 52.2, 52.5, 55.5, 59.1, 64.1, 72.8, 73.1, 74.9, 75.5, 78.4, 90.8, 108.3, and 157.2.

Deprotection of a TMS Ether of 11. Formation of 2α,3α-Epoxy-16-methoxy-15-methoxymethoxy-8,9-*seco*-fusicocc-9-ene-1α,8-diol (12). To an anhydrous THF solution (120 cm^3) of **11** (3.5 g, 7.2 mmol) was added Bu_4NF (1 M solution in THF; 10 cm^3) and the mixture was stirred for 6 h. The mixture was then treated with aqueous $NaHCO_3$ and extracted with ether. The combined ethereal layers were washed with brine, dried, and evaporated to provide **12** (2.9 g, 97%) as a colorless oil. A small sample was chromatographed on silica gel for spectroscopic and analytical purposes.

12: Found: C, 66.76; H, 9.75%. Calcd for $C_{23}H_{40}O_6$: C, 66.96; H, 9.77%. $[\alpha]_D^{18}$ +20.4 (c 1.08, $CHCl_3$). HRFABMS Found: m/z 413.2892. Calcd for $C_{23}H_{41}O_6$: $[M+H]^+$, m/z 413.2903. MS m/z 321 (M^+ − 91; 0.4) and 137 (base peak); IR (NaCl) ν 3414, 2960, 2820, 1640, 1459, 1381, 1366, 1260, 1204, 1179, 1144, 1100, 1042, 914, and 856 cm^{-1}; ^{1}H NMR (600M Hz) δ = 0.84 (3H, d, J = 7.0 Hz), 1.18 (3H, s), 1.24 (3H, s), 1.28 (3H, s), 1.37—1.47 (2H, m), 1.55 (1H, ddd, J = 12.3, 7.1, 2.0 Hz), 1.73—1.79 (2H, m), 1.90 (1H, dd, J = 13.6, 8.6 Hz), 1.97 (1H, ddd, J = 11.9, 7.1, 7.1 Hz), 2.12 (1H, d, J = 8.2 Hz), 2.39 (1H, qm, J = 7.0 Hz), 2.97 (1H, dm, J = 2.2 Hz), 2.98 (1H, ddm, J = 11.2, 7.9 Hz), 3.39 (3H, s), 3.40 (3H, s), 3.48 (2H, dm, J = 8.2 Hz), 3.58 (1H, d, J = 2.9 Hz), 3.82 (1H, d, J = 9.9 Hz), 3.94 (1H, d, J = 9.9 Hz),4.34 (1H, d, J = 2.6 Hz), 4.73 (1H, d, J = 7.1 Hz), 4.82 (1H, d, J = 7.1 Hz), 5.13 (1H, dd, J = 2.9, 1.1 Hz), and 5.38 (1H, dd, J = 2.2, 1.1 Hz); ^{13}C NMR (150 MHz) δ = 17.1, 19.4, 21.6, 25.2, 26.7, 26.9, 29.6, 33.2, 35.4, 49.2, 50.7, 52.9, 55.5, 59.1, 64.9, 71.1, 71.7, 73.3, 76.0, 78.6, 99.9, 108.5, and 158.8.

Protection of the Primary Alcohol of 12. Formation of 8-(*t*-Butyldimethylsilyloxy)-2α,3α-epoxy-16-methoxy-15-methoxymethoxy-8,9-*seco*-fusicocc-9-en-1α-ol (13). To an anhydrous DMF solution (100 cm^3) of **12** (2.9 g, 7.0 mmol) was added imidazole (1.8 g, 26 mmol) and TBSCl (2.0 g, 13 mmol) and the mixture was stirred for 1 h. The reaction mixture was treated with aqueous $NaHCO_3$, and extracted with ether. The combined organic layers were washed with aqueous $KHSO_4$ and aqueous $NaHCO_3$, dried, and concentrated in vacuo to give **13** (3.6 g, 97%) as colorless crystals. A small sample was further purified by flash chromatography on silica gel for analytical data.

13: Mp 57—58 °C. Found: C, 66.08; H, 10.14%. Calcd for $C_{29}H_{54}O_6Si$: C, 66.12; H, 10.33%. $[\alpha]_D^{26}$ +7.8 (c 1.03, $CHCl_3$). HRFABMS Found: m/z 527.3778. Calcd for $C_{29}H_{55}O_6Si$: $[M+H]^+$, m/z 527.3768. MS m/z 521 (M^+ + 1; 0.5) and 135 (base peak); IR (KBr) ν 3454, 2954, 2852, 2822, 2778, 1641, 1462, 1364, 1248, 1092, 1040, 926, 860, and 778 cm^{-1}; ^{1}H NMR (400 MHz) δ = 0.07$_1$ (3H, s), 0.07$_4$ (3H, s), 0.91 (9H, s), 0.92 (3H, d, J = 7.0 Hz), 1.21 (3H, s), 1.23 (3H, s), 1.28 (3H, s), 1.37—1.47 (3H, m), 1.51 (1H, ddd, J = 12.3, 7.2, 2.4 Hz), 1.63 (1H, ddm, J = 13.8, 8.9 Hz), 1.74—1.81 (1H, m), 1.91 (1H, ddd, J = 13.8, 7.2, 2.2 Hz), 2.03 (1H, ddd,

J = 12.1, 11.4, 7.5 Hz), 2.15 (1H, dm, J = 7.5 Hz), 2.16 (1H, m), 2.94 (1H, ddm, J = 10.4, 7.7, 2.6 Hz), 2.98 (1H, d, J = 3.6 Hz), 3.32 (1H, dd, J = 9.9, 7.0 Hz), 3.38 (3H, s), 3.40 (3H, s), 3.61 (1H, dd, J = 9.9, 5.6 Hz), 3.86 (2H, s), 4.23 (1H, d, J = 3.6 Hz), 4.72 (1H, d, J = 7.0 Hz), 4.81 (1H, d, J = 7.0 Hz), 5.13 (1H, br), and 5.38 (1H, br); ^{13}C NMR (100 MHz) δ = −5.4, −5.3, 17.3, 18.6, 20.1, 21.7, 25.0, 26.1 (3C), 26.6, 26.8, 29.7, 33.2, 36.3, 48.6, 51.3, 53.0, 55.5, 59.1, 64.8, 71.7, 72.5, 72.6, 75.0, 78.6, 90.9, 108.8, and 158.6.

Formation of 8-(*t*-Butyldimethylsilyloxy)-16-methoxy-15-methoxymethoxy-8,9-*seco*-fusicocca-1,9-dien-3α-ol (15) via 8-(*t*-Butyldimethylsilyloxy)-2α,3α-epoxy-16-methoxy-15-methoxymethoxy-8,9-*seco*-fusicocc-9-en-1α-yl Trifluorometanesulfonate (14). An anhydrous pyridine solution (10 cm^3) of **13** (335 mg, 0.64 mmol) was treated with MsCl (0.5 cm^3, excess) and stirred for 5 h at 0 °C for 6 h. The mixture was then treated with aqueous $NaHCO_3$ and extracted with ether. The combined organic layers were washed with aqueous $KHSO_4$ and aqueous $NaHCO_3$, and dried. Solvent removal provided crude **14** as a yellowish oil, which was used without further purification.

To liquid NH_3 (60 cm^3) was added Na (60 mg, 2.6 mmol) and $FeCl_3$ (cat. amount) at −78 °C. After the resultant blue resultant coloration was fade away, the solution was treated with Ca (120 mg, 3.0 mmol) while stirring. The solution was diluted with THF (40 cm^3) and a solution of the above **14** in THF (1.0 cm^3) was added dropwise in 10 min. The reaction mixture was stirred for 5 min before being treated with $PhCO_2Na$ to destroy any exess Ca. From the mixture, most of the NH_3 was removed by vaporization, and the residue was diluted with aqueous $NaHCO_3$ and extracted with ether. The organic extract was washed with aqueous K_2CO_3 and brine, dried, and concentrated. The residue was chromatographed on silica gel to give **15** (147mg, 45% from **13**) as a colorless oil.

15: Found: C, 67.82; H, 10.48%. Calcd for $C_{29}H_{54}O_5Si$: C, 68.19; H, 10.66%. $[\alpha]_D^{17}$ +25.0 (c 1.00, $CHCl_3$); MS m/z 493 ($M^+ - 17$; 28) and 227 (base peak); IR (NaCl) ν 3468, 2954, 2882, 1641, 1462, 1383, 1365, 1254, 1143, 1105, 1043, 836, 775, and 666 cm^{-1}; ^{1}H NMR (600 MHz) δ = 0.02$_7$ (3H, s), 0.02$_9$ (3H, s), 0.89 (9H, s), 0.93 (3H, d, J = 7.0 Hz), 1.21 (3H, s), 1.23 (3H, s), 1.28 (3H, s), 1.47 (1H, dm, J = 11.9 Hz), 1.60 (1H, dm, J = 12.3 Hz), 1.63—1.67 (2H, m), 1.70—1.73 (2H, m), 1.75—1.81 (2H, m), 1.89 (1H, m), 2.83 (1H, ddd, J = 11.0, 8.2, 2.7 Hz), 3.08 (1H, m), 3.29 (1H, d, J = 9.3 Hz), 3.30 (1H, d, J = 9.2 Hz), 3.38 (3H, s), 3.39 (1H, dd, J = 9.5, 4.6 Hz), 3.40 (3H, s), 3.53 (1H, dd, J = 9.5, 3.5 Hz), 4.73 (1H, d, J = 7.3 Hz), 4.80 (1H, d, J = 7.1 Hz), 4.93 (1H, d, J = 2.2 Hz), 5.29 (1H, d, J = 1.6 Hz), and 5.65 (1H, d, J = 2.2 Hz); ^{13}C NMR (150 MHz) δ = −5.43, −5.37, 16.4, 18.4, 22.0, 25.95, 25.97, 26.0 (3C), 26.2, 26.8, 35.4, 38.1 (2C), 42.5, 49.3, 52.4, 55.4, 59.4, 65.8, 78.6, 79.7, 81.5, 90.9, 108.9, 135.8, 145.5, and 160.8.

Deprotection of TBS Ether of 15. Formation of 16-Methoxy-15-methoxymethoxy-8,9-*seco*-fusicocca-1,9-diene-3α,8-diol (16). An anhydrous THF (30 cm^3) solution of **15** (0.80 g, 1.6 mmol) was treated with Bu_4NF (1 M solution in THF; 2.5 cm^3) at room temperature for 6 h. Chromatography of the mixture on silica gel provided **16** (0.58 g, 93%) as a colorless oil.

16: Found: C, 69.32; H, 10.08%. Calcd for $C_{23}H_{40}O_5$: C, 69.66; H, 10.17%. $[\alpha]_D^{12}$ +50.5 (c 1.07, $CHCl_3$). HRFABMS Found: m/z 397.2920. Calcd for $C_{23}H_{41}O_5$: $[M+H]^+$, m/z 397.2954. MS m/z 289 ($M^+ - 107$; 52) and 103 (base peak); IR (NaCl) ν 3432, 2960, 2876, 2820, 1641, 1460, 1382, 1366, 1258, 1179, 1142, 1105, 1042, and 902 cm^{-1}; ^{1}H NMR (400 MHz) δ = 0.95 (3H, d, J = 7.0 Hz), 1.227 (3H, s), 1.232 (3H, s), 1.28 (3H, s), 1.45—1.65 (4H, m), 1.78—1.88 (2H, m), 1.90—2.04 (3H, m), 2.17 (1H, s), 2.88 (1H, ddm, J = 10.9, 8.0, 2.9 Hz), 3.06 (1H, ddm, J = 10.1, 2.4 Hz), 3.29 (1H, d, J = 9.2 Hz), 3.30 (1H, dm, J = 7.2 Hz), 3.37 (1H, d, J = 9.4 Hz), 3.38 (3H, s), 3.39 (3H, s), 3.55 (1H, ddm, J = 10.1, 6.5 Hz), 4.93 (1H, dd, J = 2.9, 1.0 Hz), 5.33 (1H, d, J = 1.2 Hz), and 5.70 (1H, d, J = 2.4 Hz); ^{13}C NMR (100 MHz) δ = 16.6, 21.8, 24.0, 26.2, 26.9, 27.1, 35.6, 37.2, 38.8, 43.1, 48.9, 52.5, 55.5, 59.3, 65.4, 77.9, 78.7, 81.6, 91.0, 108.8, 135.6, 145.9, and 161.4.

Formation of 3α,8-Bis(trimethylsilyloxy)-16-methoxy-15-methoxymethoxy-8,9-*seco*-fusicocca-1,9-diene (17). An anhydrous pyridine solution (8.0 cm^3) of **16** (0.58 g, 1.5 mmol) and TMSCl (2.5 cm^3, excess) was stirred at room temperature for 12 h; the mixture was extracted with ether and chromatographed on silica gel to give **17** (0.74 g, 94%) as a colorless oil.

17: Found: C, 64.41; H, 10.36%. Calcd for $C_{29}H_{56}O_5Si_2$: C, 64.39; H, 10.44%. $[\alpha]_D^{13}$ −6.6 (c 1.06, $CHCl_3$); MS m/z 496 ($M^+ - 44$; 6.6) and 103 (base peak); IR (NaCl) ν 2956, 2882, 2820, 1641, 1460, 1382, 1367, 1250, 1144, 1109, 1076, 1042, 877, 839, and 754 cm^{-1}; ^{1}H NMR (400 MHz) δ = 0.07 (9H, s), 0.09 (9H, s), 0.93 (3H, d, J = 6.8 Hz), 1.19 (3H, s), 1.23 (3H, s), 1.28 (3H, s), 1.44—1.62 (4H, m), 1.68—1.81 (3H, m), 1.87 (1H, m), 1.98 (1H, dt, J = 12.8, 6.8 Hz), 2.84 (1H, m), 2.97 (1H, m), 3.12 (1H, d, J = 9.8 Hz), 3.21 (1H, d, J = 10.0 Hz), 3.26 (1H, dd, J = 9.5, 7.8 Hz), 3.35 (3H, s), 3.39 (3H, s), 3.51 (1H, dd, J = 9.5, 3.4 Hz), 4.74 (1H, d, J = 7.1, 7.3 Hz), 4.80 (1H, d, J = 7.3 Hz), 4.94 (1H, dd, J = 2.7, 1.0 Hz), 5.27 (1H, dd, J = 2.2, 1.0 Hz), and 5.64 (1H, d, J = 2.2 Hz); ^{13}C NMR (100 MHz) δ = −0.5 (3C), 2.3 (3C), 16.4, 22.2, 25.3, 25.8, 26.1, 26.9, 34.4, 37.7, 37.9, 42.2, 48.9, 52.3, 55.4, 59.2, 64.9, 78.7, 79.0, 85.0, 90.9, 108.6, 135.3, 145.4, and 161.3.

Selective Deprotection of the Primary TMS Ether of 17. Formation of 16-Methoxy-15-methoxymethoxy-3α-trimethylsilyloxy-8,9-*seco*-fusicocca-1,9-dien-8-ol (18). A moistened THF solution (50 cm^3) of **17** (0.74 g, 1.4 mmol) and PPTS (a catalytic amount) was stirred at 0 °C for 5 h. Chromatographic purification of the mixture through silica gel afforded **18** (0.55 g, 86%) as a colorless oil.

18: Found: C, 66.74; H, 10.25%. Calcd for $C_{26}H_{48}O_5Si$: C, 66.62; H, 10.32%. $[\alpha]_D^{26}$ +14.3 (c 1.12, $CHCl_3$); MS m/z 423 ($M^+ - 45$; 12), 225 (base peak); IR (NaCl) ν 3446, 2956, 2878, 2820, 1640, 1459, 1382, 1366, 1248, 1144, 1107, 1042, 839, and 753 cm^{-1}; ^{1}H NMR (600 MHz) δ = 0.09 (9H, s), 0.94 (3H, d, J = 7.0 Hz), 1.22 (3H, s), 1.23 (3H, s), 1.27 (3H, s), 1.45 (1H, ddm, J = 13.0, 6.4 Hz), 1.46 (1H, m), 1.57 (1H, ddm, J = 12.8, 7.5 Hz), 1.59, (1H, m), 1.76—1.85 (2H, m), 1.87 (1H, dm, J = 12.1 Hz), 1.99 (1H, ddd, J = 13.2, 6.8, 6.4 Hz), 2.15 (1H, m), 2.22 (1H, br), 2.90 (1H, ddm, J = 10.9, 8.4 Hz), 2.95 (1H, m), 3.18 (1H, d, J = 9.7 Hz), 3.23 (1H, m), 3.30 (1H, d, J = 9.9 Hz), 3.35 (3H, s), 3.38 (3H, s), 3.55 (1H, dd, J = 10.8, 5.7 Hz), 4.87 (2H, s), 4.96 (1H, d, J = 1.8 Hz), 5.32 (1H, d, J = 0.9 Hz), and 5.68 (1H, d, J = 2.7 Hz); ^{13}C NMR (150 MHz) δ = 2.3 (3C), 16.7, 21.7, 23.3, 26.2, 27.0, 27.3, 35.2, 36.6, 38.5, 43.1, 48.5, 52.4, 55.5, 59.1, 65.1, 77.6, 78.8, 85.1, 90.9, 108.6 135.3, 145.3, and 161.9.

PDC Oxidation of 18. Formation of 16-Methoxy-15-methoxymethoxy-3α-trimethylsilyloxy-8,9-*seco*-fusicocca-1,9-dien-8-al (19). To an anhydrous CH_2Cl_2 solution (50 cm^3) of **18** (0.55 g, 1.2 mmol) was added Molecular Sieves (4 Å, 2.0 g) and PDC (1.2 g, 1.3 mmol), and the mixture was stirred for 3 h. The mixture was then diluted with ether and filtered through a short Florisil column, and the filtrate was evaporated in vacuo. The residue was chromatographed on silica gel to give **19** (0.45 g, 82%) as a colorless oil.

19: HRFABMS Found: m/z 467.3201. Calcd for $C_{26}H_{47}O_5Si$: $[M+H]^+$, m/z 467.3193. $[\alpha]_D^{16}$ −38.2 (c 1.63, $CHCl_3$); MS m/z 421 ($M^+ - 45$; 8) and 183 (base peak); IR (NaCl) ν 2956, 2882,

2820, 2718, 1722, 1640, 1459, 1382, 1366, 1248, 1144, 1107, 1040, and 839 cm^{-1}; ^1H NMR (400 MHz) δ = 0.09 (9H, s), 1.01 (3H, d, J = 7.0 Hz), 1.24 (3H, s), 1.25 (3H, s), 1.28 (3H, s), 1.32 (1H, dm, J = 12.8 Hz), 1.48—1.64 (3H, m), 1.89—1.91 (3H, m), 1.97 (1H, dt, J = 13.0, 6.6 Hz), 2.82 (1H, ddd, J = 10.6, 8.0, 2.7 Hz), 2.95 (1H, qm, J = 7.0 Hz), 3.15 (1H, d, J = 9.9 Hz), 3.17 (1H, m), 3.19 (1H, d, J = 9.7 Hz), 3.32 (3H, s), 3.37 (3H, s), 4.75 (1H, d, J = 7.2 Hz), 4.76 (1H, d, J = 7.2 Hz), 4.96 (1H, dd, J = 2.9, 1.0 Hz), 5.31 (1H, dd, J = 2.4, 1.0 Hz), 5.78 (1H, d, J = 2.4 Hz), and 9.60 (1H, d, J = 1.0 Hz); ^{13}C NMR (150 MHz) δ = 2.3 (3C), 12.3, 21.9, 24.9, 26.1, 26.8, 27.7, 34.7, 36.5, 41.8, 48.6, 48.7, 52.7, 55.5, 59.1, 78.3, 78.7, 84.7, 91.0, 109.2, 136.1, 144.2, 160.7, and 206.4.

Thermally Induced ene Reaction of 19 to a Cyclizate, 16-Methoxy-15-methoxymethoxy-3α-(trimethylsilyloxy)fusicocca-1,10(14)-dien-8α-ol (20). A xylene solution (4.0 cm^3) of **19** (22 mg, 0.047 mmol) was degassed and sealed in a glass tube containing Na_2CO_3 (34 mg) and heated in an autoclave at 160 °C for 24 h. The mixture was then chromatographed on silica gel to give **20** (19 mg, 86%) as colorless oil.

20: Found: C, 66.73; H, 9.90%. Calcd for $C_{26}H_{46}O_5Si$: C, 66.91; H, 9.93%. $[\alpha]_D^{26}$ +31.4 (c 1.02, $CHCl_3$); MS m/z 421 ($M^+ - 45$; 7.2) and 135 (base peak); IR (NaCl) ν 3416, 2950, 2882, 1454, 1379, 1362, 1247, 1145, 1107, 1085, 1037, 920, 864, 839, and 753 cm^{-1}; ^1H NMR (600 MHz) δ = 0.08 (9H, s), 0.84 (3H, d, J = 7.1 Hz), 1.18 (3H, s), 1.38 (1H, ddm, J = 13.0, 7.1 Hz), 1.40 (3H, s), 1.43 (3H, s), 1.58 (1H, ddd, J = 13.0, 7.3, 7.3 Hz), 1.64 (1H, dm, J = 7.0 Hz), 1.66 (1H, m), 1.78 (1H, ddd, J = 11.7, 7.9, 3.5 Hz), 1.90 (1H, dddd, J = 13.0, 9.2, 7.3, 3.5 Hz), 2.00 (1H, ddd, J = 13.0, 7.1, 7.0 Hz), 2.13 (1H, m), 2.26 (1H, d, J = 14.3 Hz), 2.27 (1H, m), 3.08 (1H, dd, J = 14.3, 9.0 Hz), 3.16 (1H, d, J = 10.3 Hz), 3.33 (1H, d, J = 10.3 Hz), 3.37 (3H, s), 3.41 (3H, s), 3.43 (1H, dm, J = 8.7 Hz), 3.63 (1H, dm, J = 9.0 Hz), 4.75 (1H, d, J = 7.3 Hz), 4.81 (1H, d, J = 7.3 Hz), and 5.46 (1H, d, J = 2.4 Hz); ^{13}C NMR (150 MHz) δ = 2.4 (3C), 13.4, 26.5, 27.1, 27.9, 29.5, 31.5, 31.8, 35.5, 36.3, 40.8, 44.8, 54.5, 55.7, 59.3, 73.3, 78.5, 79.0, 85.3, 91.5, 134.1, 137.3, 140.7, and 141.8.

PDC-Oxidation of 20 to 16-Methoxy-15-methoxymethoxy-3α-(trimethylsilyloxy)fusicocca-1,10(14)-dien-8-one (21) and 16-Methoxy-15-methoxymethoxy-3α-trimethylsilyloxy-8,9-*seco*-fusicocca-1,10(14)-diene-8,9-dial (22). A CH_2Cl_2 solution (20 cm^3) of **20** (0.13 g, 0.28 mmol) with Molecular Sieves (4 Å, 0.26 g) was treated with PDC (0.22 g, 0.57 mmol) and stirred for 2 h. The mixture was then diluted with ether and filtered through a short Florisil column. The filtrate was evaporated in vacuo, and the residue was chromatographed on silica gel to give **21** (67 mg, 52%) and **22** (17 mg, 13%) as colorless oils.

21: HRMS Found: m/z 464.2984. Calcd for $C_{26}H_{44}O_5Si$: $[M]^+$, m/z 464.2958. $[\alpha]_D^{26}$ −11.6 (c 1.13, $CHCl_3$); MS m/z 420 ($M^+ - 44$; 13) and 73 (base peak); IR (NaCl) ν 2952, 2884, 2822, 1707, 1455, 1376, 1364, 1314, 1248, 1201, 1145, 1099, 1033, 920, 867, 839, and 754 cm^{-1}; ^1H NMR (600 MHz) δ = 0.08 (9H, s), 0.96 (3H, d, J = 6.8 Hz), 1.11 (3H, s), 1.38 (3H, s), 1.39 (3H, s), 1.44—1.49 (2H, m), 1.77 (1H, m), 1.81 (1H, ddd, J = 12.1, 7.3, 2.6 Hz), 1.87 (1H, ddd, J = 12.1, 8.8, 8.6 Hz), 2.15 (1H, m), 2.36 (1H, ddd, J = 16.3, 8.6, 2.0 Hz), 2.43 (1H, dddd, J = 16.3, 8.2, 8.1, 2.4 Hz), 2.62 (1H, d, J = 17.2 Hz), 2.93 (1H, dd, J = 10.4, 0.9 Hz), 3.00 (1H, d, J = 10.6 Hz), 3.00 (1H, ddm, J = 7.1, 2.7 Hz), 3.34 (3H, s) 3.35 (3H, s), 3.80 (1H, dm, J = 7.1 Hz), 3.87 (1H, d, J = 17.2 Hz), 4.57 (1H, d, J = 7.3 Hz), 4.70 (1H, d, J = 7.1 Hz), and 5.47 (1H, d, J = 2.9 Hz); ^{13}C NMR (150 MHz) δ = 2.3 (3C), 12.8, 24.9, 26.8, 27.5, 27.6, 32.0, 33.8, 41.9, 42.9, 42.0, 42.6, 52.9, 55.4_{87}, 55.4_{93}, 59.2, 77.6, 78.2, 85.0, 91.8, 132.7, 140.6, 140.7, 145.4, and 213.9.

22: ^1H NMR (270 MHz) δ = 0.10 (9H, s), 1.00 (3H, d, J = 7.0 Hz), 1.29 (1H, m), 1.42 (3H, s), 1.45 (3H, s), 1.46 (3H, s), 16.1 (1H, m), 1.72 (1H, ddd, J = 12.8, 8.4, 2.6 Hz), 1.86 (1H, ddd, J = 12.8, 8.1, 4.8 Hz), 2.02 (1H, ddd, J = 12.1, 6.6, 4.8 Hz), 2.31 (1H, ddd, J = 12.8, 9.5, 9.2 Hz), 2.54 (1H, ddd, J = 18.7, 9.2, 2.6 Hz), 2.69 (1H, ddd, J = 18.7, 9.9, 8.8 Hz), 2.96 (1H, m), 3.12, (1H, d, J = 9.5 Hz), 3.14 (1H, m), 3.19 (1H, d, J = 9.5 Hz), 3.31 (3H, s), 3.34 (3H, s), 4.66 (1H, d, J = 7.3 Hz), 4.72 (1H, d, J = 7.3 Hz), 5.89 (1H, d, J = 2.6 Hz), 9.48 (1H, d, J = 0.7 Hz), and 10.4 (1H, s); ^{13}C NMR (67.5 MHz) δ = 2.3 (3C), 12.4, 24.9, 27.2, 27.7, 28.1, 34.0, 34.2, 34.8, 42.5, 48.5, 50.5, 55.7, 59.1, 78.3, 78.5, 84.9, 91.8, 134.2, 143.6, 146.5, 162.8, 191.3, and 205.9.

DIBALH-Reduction of 21. Formation of 16-Methoxy-15-methoxymethoxy-3α-(trimethylsilyloxy)fusicocca-1,10(14)-dien-8β-ol (23). To a solution of **21** (67 mg, 0.14 mmol) in hexane (2.0 cm^3) at −78 °C was added DIBALH (0.17 cm^3 of 1 M solution in toluene). After 10 min of stirring, the reaction was quenched with aqueous NH_4Cl, and the mixture extracted with ether. The organic phase was dried and evaporated. Chromatography of the residue on silica gel gave **23** (55 mg, 82%) as colorless oil.

23: Found: C, 66.87; H, 9.91%. Calcd for $C_{26}H_{46}O_5Si$: C, 66.91; H, 9.93%. $[\alpha]_D^{25}$ +8.0 (c 1.00, $CHCl_3$); FABMS: m/z 421 ($M^+ - 45$; 64 and 73 (base peak); IR (NaCl) ν 3432, 2952, 2882, 2820, 1669, 1451, 1380, 1362, 1314, 1248, 1204, 1145, 1105, 1073, 1037, 919, 864, 840, and 755 cm^{-1}; ^1H NMR (600 MHz) δ = 0.08 (9H, s), 0.84 (3H, d, J = 7.0 Hz), 1.15 (3H, s), 1.32 (1H, m), 1.40 (3H, s), 1.45 (3H, s), 1.46 (1H, dm, J = 13.2 Hz), 1.64 (1H, ddm, J = 11.9, 8.1 Hz), 1.74 (1H, ddd, J = 11.7, 7.5, 3.8 Hz), 1.84 (1H, m), 1.89 (1H, m), 2.07 (1H, m), 2.13 (1H, dd, J = 13.2, 10.4 Hz), 2.14 (1H, m), 2.19 (1H, ddd, J = 15.6, 7.5, 1.8 Hz), 2.65 (1H, d, J = 12.8 Hz), 2.79 (1H, dd, J = 9.0, 9.0 Hz), 3.01 (1H, d, J = 10.3 Hz), 3.34 (1H, d, J = 10.3 Hz), 3.37 (3H, s), 3.41 (3H, s), 4.09 (1H, d, J = 10.4 Hz), 4.72 (1H, d, J = 6.6 Hz), 4.73 (1H, d, J = 6.6 Hz), and 5.48 (1H, d, J = 2.6 Hz); ^{13}C NMR (150 MHz) δ = 2.3 (3C), 8.5, 26.7, 26.8, 27.5, 29.9, 30.8, 31.0, 34.2, 40.3, 41.0, 42.9, 54.5, 55.5, 59.3, 77.2, 77.9, 78.5, 85.3, 91.9, 134.5 137.9, 140.4, and 141.6.

Desilylation of 23. Formation of 9-Deoxy-15-methoxymethoxycotylenol (24). A solution of **23** (16 mg, 0.034 mmol) in anhydrous THF (2.0 cm^3) was treated with Bu_4NF (1 M solution in THF; 0.20 cm^3) at room temperature for 6 h. The mixture was then diluted with aqueous $NaHCO_3$ and extracted with ether. The organic extract was washed with brine, dried, and evaporated in vacuo. Silica-gel chromatography of the residue afforded **24** (13 mg, 96%) as a colorless oil.

24: $[\alpha]_D^{27}$ +42.9 (c 0.63, $CHCl_3$); FABMS: m/z 377 ($M^+ - 17$; 6) and 154 (base peak); IR (NaCl) ν 3450, 2948, 2882, 2820, 1451, 1380, 1362, 1300, 1192, 1144, 1099, 1035, 951, and 920 cm^{-1}; ^1H NMR (600 MHz) δ = 0.84 (3H, d, J = 7.0 Hz), 1.23 (3H, s), 1.36 (1H, m), 1.39 (3H, s), 1.45 (3H, s), 1.50 (1H, ddd, J = 13.4, 10.4, 7.5 Hz), 1.70 (1H, dm, J = 12.3 Hz), 1.85—1.88 (2H, m), 1.96—2.04 (2H, m), 2.13 (1H, dd, J = 12.8, 10.6 Hz), 2.16—2.23 (2H, m), 2.44 (1H, s), 2.61 (1H, d, J = 13.0 Hz), 2.93 (1H, m), 3.22 (1H, dd, J = 9.5, 0.7 Hz), 3.41 (3H, s), 3.42 (3H, s), 3.44 (1H, d, J = 9.5 Hz), 4.14 (1H, dm, J = 10.8 Hz), 4.73 (1H, d, J = 6.4 Hz), 4.74 (1H, d, J = 6.4 Hz), and 5.63 (1H, d, J = 2.4 Hz); ^{13}C NMR (150 MHz) δ = 8.5, 26.56, 26.58, 27.0, 29.8, 31.0, 31.8, 36.1, 40.6, 41.7, 43.8, 54.8, 55.5, 59.4, 77.2, 77.9, 78.4, 82.0, 91.9, 135.5, 138.2, 140.4, and 141.3.

Attempted Hydrolysis of the MOM Group in 24. Formation of 8α,15-Epoxy-16-methoxyfusicocca-1,10(14)-dien-3α-ol (25). A moistened solution of **24** (50 mg, 0.11 mmol) in THF (2.0 cm^3)

and acetic acid (1.5 cm^3) was stirred at room temperature for 6 h. The mixture was then treated with aqueous $NaHCO_3$ and extracted with ethyl acetate, which was washed with brine, dried, and evaporated. The residue was chromatographed on silica gel to give **25** (21 mg, 59%) as a colorless oil.

25: ^{1}H NMR (600 MHz) δ = 0.69 (3H, d, J = 7.3 Hz), 1.19 (3H, s), 1.27 (1H, m), 1.28 (3H, s), 1.39 (3H, s), 1.48 (1H, dddd, J = 12.6, 9.3, 7.7, 0.9 Hz), 1.66—1.71 (2H, m), 1.87 (1H, m), 1.93—1.97 (2H, m), 2.12 (1H, d, J = 14.6 Hz), 2.23 (1H, dm, J = 15.6 Hz), 2.23—2.27 (2H, m), 2.48 (1H, s), 3.05 (1H, m), 3.12 (1H, dd, J = 9.5, 0.9 Hz), 3.36 (1H, d, J = 9.5 Hz), 3.40 (3H, s), 3.96 (1H, m), and 5.53 (1H, d, J = 2.6 Hz); ^{13}C NMR (67.5 MHz) δ = 13.1, 21.5, 25.9, 27.4, 29.0, 30.5, 31.1, 35.7, 37.0, 40.0, 45.2, 50.7, 59.3, 74.7, 75.9, 77.6, 82.5, 133.6, 137.4, 141.0, and 142.5.

Protection of 8α-Hydroxyl of 24. Formation of 8α-Acetoxy-15-methoxymethoxy-3α-(trimethylsilyloxy)fusicocca-1,10(14)-diene (26). A solution of **20** (0.38 g, 0.81 mmol) in pyridine (10 cm^3) was treated with acetic anhydride (1.5 cm^3, excess). The reaction mixture was stirred at room temperature for 12 h, and treated with a saturated $NaHCO_3$ solution, washed with brine, dried, and evaporated. Chromatography of the residue on silica gel gave **26** (0.35 g, 84%) as a colorless oil.

26: HRFABMS Found: m/z 509.3289. Calcd for $C_{28}H_{49}O_6Si$: $[M+H]^+$, m/z 509.3298. $[\alpha]_D^{12}$ −25.2 (c 1.23, $CHCl_3$); MS m/z 507 ($M^+ - 1$; 1.6) and 297 (base peak); IR (NaCl) ν 2976, 2948, 2882, 2820, 1735, 1657, 1459, 1376, 1245, 1145, 1105, 1086, 1036, 839, and 753 cm^{-1}; ^{1}H NMR (400 MHz) δ = 0.06 (9H, s), 0.75 (3H, d, J = 6.8 Hz), 1.37 (3H, s), 1.38 (3H, s), 1.43 (3H, s), 1.53 (1H, m), 1.65—1.71 (2H, m), 1.73—1.83 (2H, m), 1.86—1.95 (2H, m), 2.03 (3H, s), 2.18—2.25 (2H, m), 2.32 (1H, dd, J = 15.0, 3.6 Hz), 3.27 (1H, dd, J = 15.0, 11.8 Hz), 3.29 (1H, d, J = 10.1 Hz), 3.35 (1H, d, J = 10.1 Hz), 3.36 (3H, s), 3.39 (3H, s), 3.62 (1H, m), 4.59 (1H, d, J = 7.0 Hz), 4.70 (1H, d, J = 7.0 Hz), 4.87 (1H, ddd, J = 11.8, 10.6, 3.6 Hz), and 5.50 (1H, d, J = 2.2 Hz); ^{13}C NMR (100 MHz) δ = 2.3 (3C), 13.4, 21.3, 27.5, 27.6, 27.7, 27.9, 31.9, 32.9, 36.5, 37.7, 40.5, 42.8, 54.8, 55.2, 59.2, 76.2, 77.5, 79.3, 85.0, 92.2, 135.3, 138.6, 139.2, 142.4, and 170.7.

Deprotection of the MOM Group of 26. Formation of 8α-Acetoxy-16-methoxyfusicocca-1,10(14)-diene-3α,15-diol (27). A moistened solution of **26** (0.27 g, 0.53 mmol) in THF (5.0 cm^3) and acetic acid (3.0 cm^3) was stirred at room temperature for 16 h. The mixture was then treated with aqueous $NaHCO_3$ and extracted with ethyl acetate, which was washed with brine, dried, and evaporated. The residue chromatographed on silica gel to give **27** (0.17 g, 82%) as colorless crystals.

27: Mp 117—118.5 °C. Found: C, 70.34; H, 9.43%. Calcd for $C_{23}H_{36}O_5$: C, 70.38; H, 9.24%. $[\alpha]_D^{12}$ −32.7 (c 1.01, $CHCl_3$); MS m/z 375 ($M^+ - 17$; 2) and 270 (base peak); IR (KBr) ν 3528, 3402, 2968, 2950, 2924, 2864, 1736, 1715, 1659, 1459, 1371, 1258, 1241, 1088, 1022, 938, and 897 cm^{-1}; ^{1}H NMR (600 MHz) δ = 0.74 (3H, d, J = 6.8 Hz), 1.37 (3H, s), 1.375 (3H, s), 1.377 (3H, s), 1.55 (1H, dddd, J = 13.0, 7.5, 1.6, 1.5 Hz), 1.60 (1H, br), 1.68 (1H, ddd, J = 12.6, 9.2, 9.0 Hz), 1.69 (1H, m), 1.79 (1H, ddd, J = 12.5, 7.9, 2.2 Hz), 1.82—1.89 (2H, m), 1.98 (1H, m) 2.04 (3H, s), 2.17 (1H, ddm, J = 15.6, 9.0 Hz), 2.18 (1H, br), 2.27 (1H, m), 2.37 (1H, dd, J = 14.8, 3.5 Hz), 3.39 (1H, d, J = 9.3 Hz), 3.42 (3H, s), 3.46 (1H, d, J = 9.5 Hz), 3.49 (1H, dd, J = 14.8, 11.4 Hz), 3.79 (1H, m), 4.86 (1H, ddd, J = 11.4, 10.1, 3.7 Hz), and 5.65 (1H, d, J = 2.2 Hz); ^{13}C NMR (150 MHz) δ = 13.7, 21.3, 27.0, 28.1, 29.6, 30.5, 31.5, 32.4, 37.7, 38.2, 41.1 42.9, 54.7, 59.4, 72.5, 76.2, 79.2, 81.9, 135.9, 137.1, 141.5, 142.4, and 170.7.

TMS Protection of the Diol 27. Formation of 8α-Acetoxy-16-methoxy-3α,15-bis(trimethylsilyloxy)fusicocca-1,10(14)-diene (28). An anhydrous pyridine solution (5.0 cm^3) of **27** (0.15 g, 0.38 mmol) and TMSCl (0.8 cm^3, excess) was stirred at room temperature for 12 h. Then the mixture was diluted with aqueous $NaHCO_3$ and extracted with ether. The organic phase was dried, concentrated, and chromatographed on silica gel to give **28** (185 mg, 90%) as colorless crystals.

28: Mp 75.5—76.5 °C. Found: C, 64.64; H, 9.73%. Calcd for $C_{29}H_{53}O_5Si_2$: C, 64.88, H, 9.76%. $[\alpha]_D^{16}$ −35.7 (c 1.06, $CHCl_3$); MS m/z 449 ($M^+ - 97$; 10) and 73 (base peak); IR (NaCl) ν 2952, 2888, 1735, 1656, 1459, 1377, 1247, 1188, 1052, 1024, 968, 865, 839, and 753 cm^{-1}; ^{1}H NMR (600 MHz) δ = 0.06 (9H, s), 0.13 (9H, s), 0.13 (9H, s), 0.74 (3H, d, δ = 6.8 Hz), 1.36 (3H, s), 1.36_8 (3H, s), 1.37_2 (3H, s), 1.49—1.53 (1H, m), 1.64 (1H, ddd, J = 12.5, 9.2, 9.2 Hz), 1.66 (1H, m), 1.75—1.82 (2H, m), 1.87—1.93 (2H, m), 2.03 (3H, s), 2.12 (1H, m), 2.24, (1H, m), 2.28 (1H, dd, J = 14.8, 3.7 Hz), 3.29 (1H, d, J = 10.0 Hz), 3.34 (1H, d, J = 10.0 Hz) 3.36 (3H, s), 3.51 (1H, dd, J = 14.7, 11.9 Hz), 3.77 (1H, m), 4.86 (1H, ddd, J = 11.9, 10.4, 3.7 Hz), and 5.47 (1H, d, J = 2.2 Hz); ^{13}C NMR (150 MHz) δ = 2.3 (3C), 2.4 (3C), 13.6, 21.3, 27.0, 27.6, 30.1, 30.7, 31.6, 32.8, 36.5, 37.5, 40.7, 42.9, 54.5, 59.2, 74.8, 76.6, 79.5, 85.2, 135.4, 137.0, 141.3, 142.7, and 170.8.

Reductive Removal of the Acetate in 28. Formation of 16-Methoxy-3α,15-bis(trimethylsilyloxy)fusicocca-1,10(14)-dien-8α-ol (29). To a solution of **28** (0.18 g, 0.34 mmol) in THF (10 cm^3) at 0 °C was added $LiAlH_4$ (0.2 g, excess). After 15 min of stirring, the reaction quenched with water and the mixture extracted with ether. The combined ethereal layers were washed with brine, dried, and evaporated. The residue was purified by chromatography on silica gel to give **29** (0.13 g, 78%) as colorless crystals.

29: Mp 58—59 °C. HRFABMS Found: m/z 495.3323. Calcd for $C_{27}H_{51}O_4Si_2$: $[M+H]^+$. m/z 495.3326. MS m/z 359 ($M^+ - 135$; 70) and 73 (base peak); $[\alpha]_D^{17}$ +35.1 (c 1.05, $CHCl_3$); IR (KBr) ν 3442, 3330, 2954, 2890, 2824, 1460, 1360, 1314, 1250, 1105, 1048, 996, 841, and 752 cm^{-1}; ^{1}H NMR (600 MHz) δ = 0.08 (9H, s), 0.24 (9H, s), 0.79 (3H, d, J = 7.1 Hz), 1.13 (3H, s), 1.27 (1H, qdm, J = 7.1, 5.5 Hz), 1.42 (3H, s), 1.45 (3H, s), 1.52 (1H, ddd, J = 12.1, 8.8, 8.2 Hz), 1.63 (1H, ddd, J = 11.7, 8.2, 7.8 Hz), 1.69—1.75 (2H, m), 1.91 (1H, m), 1.99—2.08 (2H, m), 2.11 (1H, d, J = 14.5 Hz), 2.23 (1H, m), 3.08 (1H, d, J = 11.6 Hz), 3.11 (1H, dd, J = 14.5, 7.5 Hz), 3.34 (1H, d, J = 10.4 Hz), 3.38 (3H, s), 3.60 (1H, dm, J = 5.5 Hz), 4.56 (1H, br), and 5.46 (1H, d, J = 2.6 Hz); ^{13}C NMR (150 MHz) δ = 2.4 (3C), 2.6 (3C), 13.3, 27.7, 28.1, 29.8, 30.2, 30.6, 31.8, 35.0, 35.2, 40.9, 44.1, 54.2, 59.3, 73.1, 77.8, 78.1, 85.5, 133.9, 134.6, 141.1, and 143.1.

PDC-Oxidation of 29. Formation of 16-Methoxy-3α,15-bis(trimethylsilyloxy)fusicocca-1,10(14)-dien-8-one (30) and 16-Methoxy-3α,15-bis(trimethylsilyloxy)-8,9-*seco*-fusicocca-1,10(14)-diene-8,9-dial (31). A CH_2Cl_2 solution (10 cm^3) of **29** (0.10 g, 0.20 mmol) with Molecular Sieves (4 Å, 0.20 g) was treated with PDC (0.18 g, 0.46 mmol) and stirred for 3 h. The mixture was then diluted with ether and filtered through a short Florisil column. The filtrate was evaporated in vacuo, and the residue was chromatographed on silica gel to give **30** (45 mg, 46%) and **31** (8.7 mg, 8.5%), both as colorless crystals.

30: Mp 86—87 °C. Found: C, 65.74; H, 9.79%. Calcd for $C_{27}H_{48}O_4Si_2$: C, 65.80; H, 9.82%. $[\alpha]_D^{17}$ −17.5 (c 1.20, $CHCl_3$); FABMS m/z 477 ($M^+ - 15$; 8.4) and 73 (base peak); IR (KBr) ν 3448, 2935, 2956, 1706, 1459, 1378, 1360, 1316, 1252, 1172, 1026, 894, 869, 838, 758, and 686 cm^{-1}; ^{1}H NMR (400 MHz) δ = 0.08 (9H, s), 0.12 (9H, s), 0.96 (3H, d, J = 7.0 Hz), 1.36 (3H, s), 1.40 (3H, s), 1.42—1.52 (2H, m), 1.73—1.80 (2H, m), 1.84 (1H, ddd,

J = 12.1, 8.5, 8.5 Hz), 2.13 (1H, m), 2.31—2.37 (2H, m), 2.57 (1H, d, J = 16.9 Hz), 2.95 (1H, d, J = 10.6 Hz), 3.02 (1H, d, J = 10.4 Hz), 3.24 (1H, m), 3.34 (3H, s), 3.76 (1H, m), 4.15 (1H, d, J = 16.9 Hz), and 5.46 (1H, d, J = 2.9 Hz); ^{13}C NMR (100 MHz) δ = 2.3 (3C), 2.5 (3C), 12.7, 25.1, 27.1, 30.1, 30.2, 31.7, 34.0, 38.8, 41.5, 42.5, 42.7, 52.9, 59.2, 75.7, 78.2, 85.1, 133.1, 137.9, 142.9, 145.3, and 214.4.

31: $[\alpha]_D^{17}$ −119.5 (c 0.435, $CHCl_3$); ^{1}H NMR (400 MHz) δ = 0.10 (9H, s), 0.13 (9H, s), 0.99 (3H, d, J = 6.8 Hz), 1.22—1.28 (1H, m), 1.41 (3H, s), 1.44 (3H, s), 1.46 (3H, s), 1.55—1.63 (1H, m), 1.69 (1H, ddd, J = 12.8, 8.7, 2.4 Hz), 1.88 (1H, dm, J = 12.8 Hz), 2.01 (1H, ddd, J = 12.8, 7.7, 6.7 Hz), 2.31 (1H, ddm, J = 13.0, 9.4 Hz), 2.48 (1H, ddd, J = 18.6, 9.4, 2.4 Hz), 2.63 (1H, ddd, J = 18.6, 9.2, 8.9 Hz), 2.99 (1H, m), 3.11 (1H, d, J = 9.9 Hz), 3.14 (1H, ddm, J = 5.3, 2.9 Hz), 3.19 (1H, d, J = 9.7 Hz), 3.31 (3H, s), 5.91 (1H, d, J = 2.9 Hz), 9.48 (1H, s), and 10.4 (1H, s); ^{13}C NMR (100 MHz) δ = 2.3 (3C), 2.4 (3C), 12.4, 24.9, 27.7, 30.6, 31.1, 33.8, 34.3, 34.7, 42.5, 48.4, 50.3, 59.1, 75.9, 78.4, 84.9, 134.6, 143.4, 145.4, 165.1, 191.8, and 205.8.

DIBALH-Reduction of the ketone 30. Formation of 16-Methoxy-3α,15-bis(trimethylsilyloxy)fusicocca-1,10(14)-dien-8β-ol (32). To a solution of **30** (35 mg, 0.071 mmol) in hexane (2.0 cm^3) at −78 °C was added DIBALH (0.06 cm^3 of 1 M solution in toluene). After 10 min of stirring, the reaction was quenched with water, and the mixture was extracted with ether. The organic phase was dried and evaporated. Chromatography of the residue on silica gel gave **32** (31 mg, 86%) as a colorless oil.

32: Found: C, 65.55; H, 10.14%. Calcd for $C_{27}H_{50}O_4Si_2$: C, 65.53; H, 10.18%. $[\alpha]_D^{26}$ +14.3 (c 1.05, $CHCl_3$); MS m/z 449 ($M^+ - 45$; 19) and 359 (base peak); IR (NaCl) ν 3390, 2952, 2890, 2876, 2820, 1452, 1377, 1360, 1312, 1250, 1203, 1165, 1149, 1106, 1077, 1030, 981, 865, 839, 753, and 684 cm^{-1}; ^{1}H NMR (600 MHz) δ = 0.08 (9H, s), 0.20 (9H, s), 0.81 (3H, d, J = 7.0 Hz), 1.15 (3H, s), 1.26 (1H, m), 1.39 (3H, s), 1.41 (3H, s), 1.44 (1H, dtd, J = 12.1, 8.8, 1.3 Hz), 1.60 (1H, ddd, J = 11.7, 9.5, 8.2 Hz), 1.73 (1H, ddd, J = 11.7, 7.3, 2.4 Hz), 1.80 (1H, m), 1.91 (1H, ddm, J = 12.8, 6.4 Hz), 2.01 (1H, dd, J = 12.5, 10.6 Hz), 2.02 (1H, m), 2.08 (1H, ddd, J = 12.1, 6.4, 2.4 Hz), 2.16, (1H, ddm, J = 15.0, 7.5 Hz), 2.81—2.84 (2H, m), 2.98 (1H, dd, J = 10.4, 1.1 Hz), 3.32 (1H, d, J = 10.3 Hz), 3.37 (3H, s), 4.14, (1H, dm, J = 10.1 Hz), and 5.44 (1H, J = 2.7 Hz); ^{13}C NMR (600 MHz) δ = 2.3 (3C), 2.8 (3C), 8.4, 27.2, 29.5, 20.1, 30.2, 31.0, 31.4, 34.1, 40.0, 41.9, 43.3, 54.1, 59.3, 76.5, 76.7, 77.8, 85.3, 134.2, 134.3, 140.4, and 144.2.

Deprotection of the Silyl Ethers of 32. Formation of 9-Deoxy-15-hydroxycotylenol (4). A solution of **32** (21 mg, 0.042 mmol) in anhydrous THF (2.0 cm^3) was treated with Bu_4NF (1 M solution in THF; 0.2 cm^3) at room temperature for 6 h. The mixture was then diluted with aqueous $NaHCO_3$ and extracted with ether. The organic extract was washed with brine, dried, and evaporated in vacuo. Silica-gel chromatography of the residue afforded **4** (14 mg, 95%) as colorless crystals.

4: 134—135 °C (decomp). Found: C, 71.97; H, 9.76%. Calcd for $C_{21}H_{34}O_4$: C, 71.96; H, 9.78%. $[\alpha]_D^{26}$ +28.2 (c 0.71, $CHCl_3$); MS m/z 332 ($M^+ - 18$; 9.8) and 269 (base peak); IR (KBr) ν 3416, 2968, 2938, 2870, 2838, 1659, 1477, 1360, 1259, 1181, 1116, 1061, 1042, 1013, 979, 945, and 895 cm^{-1}; ^{1}H NMR (600 MHz) δ = 0.83 (3H, d, J = 7.1 Hz), 1.13 (3H, s), 1.35 (1H, m), 1.39 (6H, s), 1.48 (1H, dddd, J = 13.0, 8.8, 7.1, 0.9 Hz), 1.68 (1H, ddd, J = 12.1, 8.1, 7.3 Hz), 1.73 (1H, ddd, J = 12.1, 7.9, 4.9 Hz), 1.86 (1H, qdm, J = 7.0, 4.2 H), 1.97—2.03 (2H, m), 2.10 (1H, m), 2.12 (1H, dd, J = 12.8 10.8 Hz), 2.20 (1H, dddd, J = 15.2, 7.9, 7.3, 2.0 Hz), 2.46 (1H, br), 2.70 (1H, d, J = 12.3 Hz), 2.95 (1H, ddm, J = 7.8, 7.4 Hz), 3.20 (1H, dd, J = 9.5, 0.9 Hz), 3.42 (3H, s), 3.43 (1H, d, J = 9.5 Hz), 4.24 (1H, ddd, J = 11.7, 4.0, 3.1 Hz), and 5.61 (1H, d, J = 2.4 Hz); ^{13}C NMR (150 MHz) δ = 8.3, 27.0, 29.9, 30.1, 30.5, 31.4, 31.9, 35.9, 40.6, 41.2, 43.8, 54.4, 59.4, 73.4, 77.6, 77.7, 82.0, 135.4, 135.9, 140.2, and 142.5.

Deprotection of the Silyl Ether of 20. Formation of 8-*epi*-9-Deoxy-15-methoxymethoxycotylenol (33). A solution of **20** (18 mg, 0.039 mmol) in anhydrous THF (2.0 cm^3) was treated with Bu_4NF (1 M solution in THF; 0.2 cm^3) at room temperature for 12 h. The mixture was then diluted with aqueous $NaHCO_3$ and extracted with ether. The organic extract was washed with brine, dried and evaporated in vacuo. Silica-gel chromatography of the residue afforded **33** (14 mg, 91%) as a colorless oil.

33: $[\alpha]_D^{28}$ +73.9 (c 0.69, $CHCl_3$); MS m/z 394 (M^+; 0.6) and 190 (base peak); ^{1}H NMR (600 MHz) δ = 0.85 (3H, d, J = 7.0 Hz), 1.19 (3H, s), 1.38 (3H, s), 1.43 (3H, s), 1.46 (1H, dm, J = 12.6 Hz), 1.61—1.66 (1H, m), 1.68—1.75 (2H, m), 1.92 (1H, ddd, J = 13.4, 10.4, 7.1 Hz), 1.99 (1H, m), 2.17 (1H, m), 2.26 (1H, dd, J = 14.8, 2.2 Hz), 2.26—2.31 (2H, m), 3.13 (1H, dd, J = 14.8, 9.5 Hz), 3.17 (1H, br), 3.36 (1H, d, J = 9.3 Hz), 3.40 (3H, s), 3.41 (1H, d, J = 9.4 Hz), 3.42 (3H, s), 3.57 (1H, dm, J = 2.2 Hz), 3.61 (1H, m), 4.72 (1H, d, J = 7.3 Hz), 4.79 (1H, d, J = 7.3 Hz), and 5.62 (1H, d, J = 2.2 Hz); ^{13}C NMR (150 MHz) δ = 14.0, 26.7, 27.1, 27.4, 29.8, 31.7, 32.4, 37.3, 37.5, 40.6, 45.6, 54.8, 55.7, 59.4, 73.2, 78.66, 78.7, 81.9, 91.6, 135.0, 137.9, 140.3, and 142.3.

Crystallographic Structure Determination of 9. The crystal of **9** was obtained as a colorless prism by recrystallization of the compound from a mixture of hexane and ethyl acetate. The measurement was made on an Enraf–Nonius FR 590 diffractometer with graphite monocromated Cu $K\alpha$ radiation (λ = 1.54184 Å). The data were collected at a temperature 23±2 °C using the ω–2θ scan technique to a maximum 2θ value of 139.9°. The structure was solved by a direct method (SIR92[19]), and was refined using full-matrix least squares (SHELXL93[20]) based on F^2 of all independent measured reflections. All H atoms were located at ideal positions and were included in the refinement, but restrained to ride on the atom to which they were bonded. Isotropic thermal factors of H atoms were held fixed to 1.2 times or 1.5 times (for methyl groups) U_{eq} of the riding atoms. The crystallographic data are listed in Table 2. Others have been deposited as Document No. 71021 at the

Table 2. Crystallographic Data for **9**

Formula	$C_{23}H_{38}O_5$
Formula weight	M_r = 394.55
Crystal color	Colorless
Crystal size/mm	0.50 × 0.30 × 0.25
Crystal system	Monoclinic
Space group	$P2_1$
a/Å	12.816(3)
b/Å	10.8610(10)
c/Å	8.138(2)
β/deg	95.79(2)
V/Å^3	1127.0(4)
Z	2
D_{calcd}/g cm^{-3}	1.163
μ/mm^{-1}	0.641
No. of reflections	2256
No. of obsd refl. [$I > 2\sigma(I)$]	2022
Refined parameters	284
Refinement	F^2(SHELXL93)
$R[F^2 > 2\sigma(F^2)]$	0.0628
$wR(F^2)$	0.2075

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The crystal structure of the compound showed disordered contributions regarding the conformation of the A-ring (C4-down for the major and C4-up for the minor). Only the major conformer is shown in Fig. 2 for clarity. The ratio of the populations of two disordered contributions was calculated normally by SHELXL93 to be 64 : 36.

Germination Tests. The effect of compounds **4**, **24**, and **33** on the germination of lettuce seeds was studied in the presence of 2 ppm of (±)-abscisic acid at 25 °C in the dark. The number of germinated seeds was counted after the indicated period of time, and the value was expressed as a percentage based on the number of seeds tested (40 seeds were used in each experiment). Without abscisic acid, a germination inhibitor, 100% of germination was observed within 48 h. The results are summarized in Table 1.

This work was supported in part by a Grant-in-Aid for Scientific Research No. 07680633 from the Ministry of Education, Science, Sports and Culture.

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