[Chem. Pharm. Bull. 31(10)3411—3417(1983)]

Studies on the Terpenoids and Related Alicyclic Compounds. XXIX.[1,2] Chemical Transformations of α-Santonin into C-8 Lactonized Eudesmanolides: Telekin and Pinnatifidin

KOJI YAMAKAWA,* KIYOSHI NISHITANI, and AKIHIRO MURAKAMI

Faculty of Pharmaceutical Sciences, Science University of Tokyo, Ichigaya-funagawara-machi, Shinjuku-ku, Tokyo 162, Japan

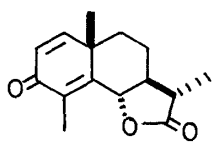
(Received January 20, 1983)

The chemical transformations of α-santonin (**1**), a C-6 lactonized eudesmanolide, into C-8 lactonized eudesmanolides, telekin (**4**) and pinnatifidin (**5**), are described. Desulfurization of the thio-ketal (**8**), derived from tetrahydroyomogin (**7**), with Raney Ni gave the 4-ene (**10**), which was converted into the α-epoxide (**12**). Ring-opening of the epoxy ring with $LiNEt_2$ afforded the allyl alcohol (**13**). Phenylselenenylation of **13** gave the selenide (**14**), and oxidative elimination then gave telekin (**4**). Bromination of 3-oxoeudesman-8,13-olide (**18**) gave the 2α-bromo-3-ketone (**19**). Reduction of **19** with $NaBH_4$ gave bromohydrins (**20** and **21**), which were treated with Zn dust to afford the olefin (**22**). Treatment of **22** with *N*-bromosuccinimide afforded the 2-hydroxy-3-bromide (**24**), which was oxidized to give the 2-oxo-3-bromide (**25**). Dehydrobromination of **25** afforded the 2-oxo-3-ene (**26**). Pinnatifidin (**5**) was synthesized from **26** by phenylselenenylation and deselenoxylation procedures.

Keywords——sesquiterpene lactone; α-methylene-γ-lactone; synthesis; α-santonin; telekin; pinnatifidin; bromohydrin; epoxide; transposition of lactone

In the preceding paper,[2] we described in detail the chemical transformations of α-santonin (**1**), a C-6 lactonized eudesmanolide, into C-8 lactonized eudesmanolides, *i.e.* yomogin (**2**) and four diastereoisomers of dihydrograveolide (**3**). The C-8 lactonized eudesmanolides are widely distributed in the family Compositae. The transposition of lactone from 6,13-olide to 8,13-olide *via* an allylic oxidation procedure had also been reported by us.[2]

We wish to report here the syntheses of C-8 lactonized eudesmanolides, telekin and pinnatifidin, from a C-8 lactonized enone (**7**).[2] Some regio- and stereoselective transformations of ring A were examined in the synthesis of telekin, and the transposition of the ketone group from C-3 to C-2 was achieved in the synthesis of pinnatifidin.



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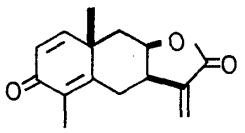

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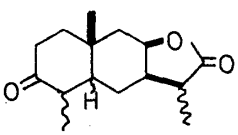

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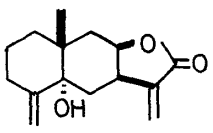

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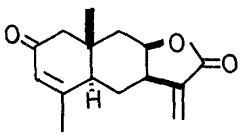

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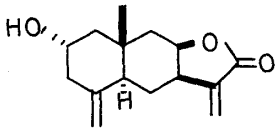

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Chemical Transformation of α-Santonin into Telekin

Telekin (**4**) was isolated from *Telekia speciosa* (SCHREB) BAUMG. and its structure was determined by Sörm *et al.*[3] Chemical transformation of α-santonin (**1**) into telekin (**4**) was investigated starting from the enone (**7**), which was a key intermediate in the synthesis of yomogin (**2**) as described in the preceding paper.[2]

Thio-ketalization of the enone (**7**) with ethanedithiol in the presence of boron trifluoride–ether complex gave a thioketal (**8**), mp 141—143 °C, in 74% yield. Desulfurization of **8** with Raney nickel in refluxing acetone provided diene (**9**) but not the expected compound (**10**). The structure of **9** was confirmed by its ^{1}H nuclear magnetic resonance (NMR) spectrum, in which two olefinic proton signals were seen at δ 5.68. Then, desulfurization was carried out in refluxing ethanol to give a mixture of **10** and **11** in a ratio of 4:1. Epoxidation of the above mixture with *m*-chloroperbenzoic acid in methylene chloride followed by separation of the reaction mixture gave unchanged **11** and an epoxide (**12**), mp 123—126 °C, in 19 and 41% yields from **8**, respectively. The stereoformula of **11** was consistent with that of authentic α-tetrahydroalantolactone[4] derived from isoalantolactone (**15**) by Nakazawa,[5] and thus the β-configuration of the C-11 methyl group of the enone lactone (**7**) is confirmed.

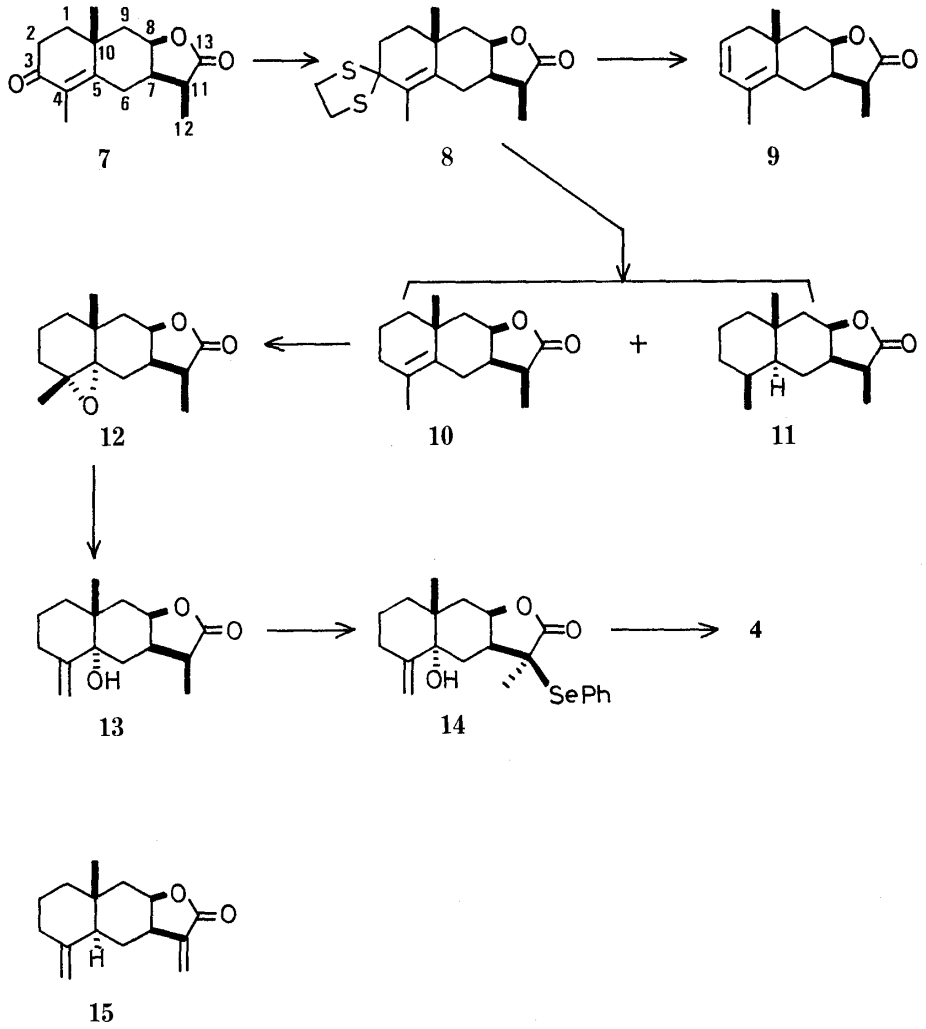

Chart 1

Treatment of the epoxide (**12**) with lithium diisopropylamide (LDA) in tetrahydrofuran at −78 °C afforded the allyl alcohol (**13**) in a low yield (11%). However, **12** was treated with lithium diethylamide in refluxing ether for 3 h to give **13**, mp 192—193 °C, in 57% yield. The

compound (**13**) showed an absorption band due to the hydroxyl group at 3435 cm^{-1} in its infrared (IR) spectrum and olefinic proton signals due to the C-4 exo-methylene moiety at δ 4.77 and 4.88 in its NMR spectrum. Phenylselenenylation of **13** gave a phenyl selenide (**14**), mp 217—219 °C. A singlet signal at δ 1.57 is attributable to the C-11 methyl protons. The phenylselenyl group should be in the *anti* relationship to the C-7 hydrogen, because the 7(11)-dehydrolactone compound could not be detected after oxidative *syn* elimination of **14** as described below. Therefore, the configuration of the benzeneselenyl group was assumed to be β. Treatment of **14** with hydrogen peroxide under the same conditions as used for the synthesis of yomogin[2] gave an exo-methylene-γ-lactone (**4**), mp 156—158 °C. The NMR spectrum of **4** was in good agreement with that of telekin reported by Sŏrm *et al.*[3]

Chemical Transformation of α-Santonin into Pinnatifidin

Herz *et al.* isolated some 2-oxo and 2-hydroxy C-8 lactonized eudesmanolides, *i.e.*, pinnatifidin (**5**)[6] and ivalin (**6**).[7] In this laboratory, the transposition of the ketone group in ring A of α-tetrahydrosantonin (**16**) to 2-oxosantanolide (**17**) had been achieved.[8]

In this paper, we describe the synthesis of pinnatifidin (**5**) starting from hexahydroyomogin (**18**), which was prepared from α-santonin as described in the preceding paper.[2] Bromination of **18** gave a bromoketone (**19**), mp 163—165 °C, in 92% yield. The stereoformula of the bromoketone was confirmed by analysis of the IR (1725 cm^{-1}) and the NMR spectra. The NMR spectrum of **19** showed the C-2 proton signals as a double doublet at δ 4.92

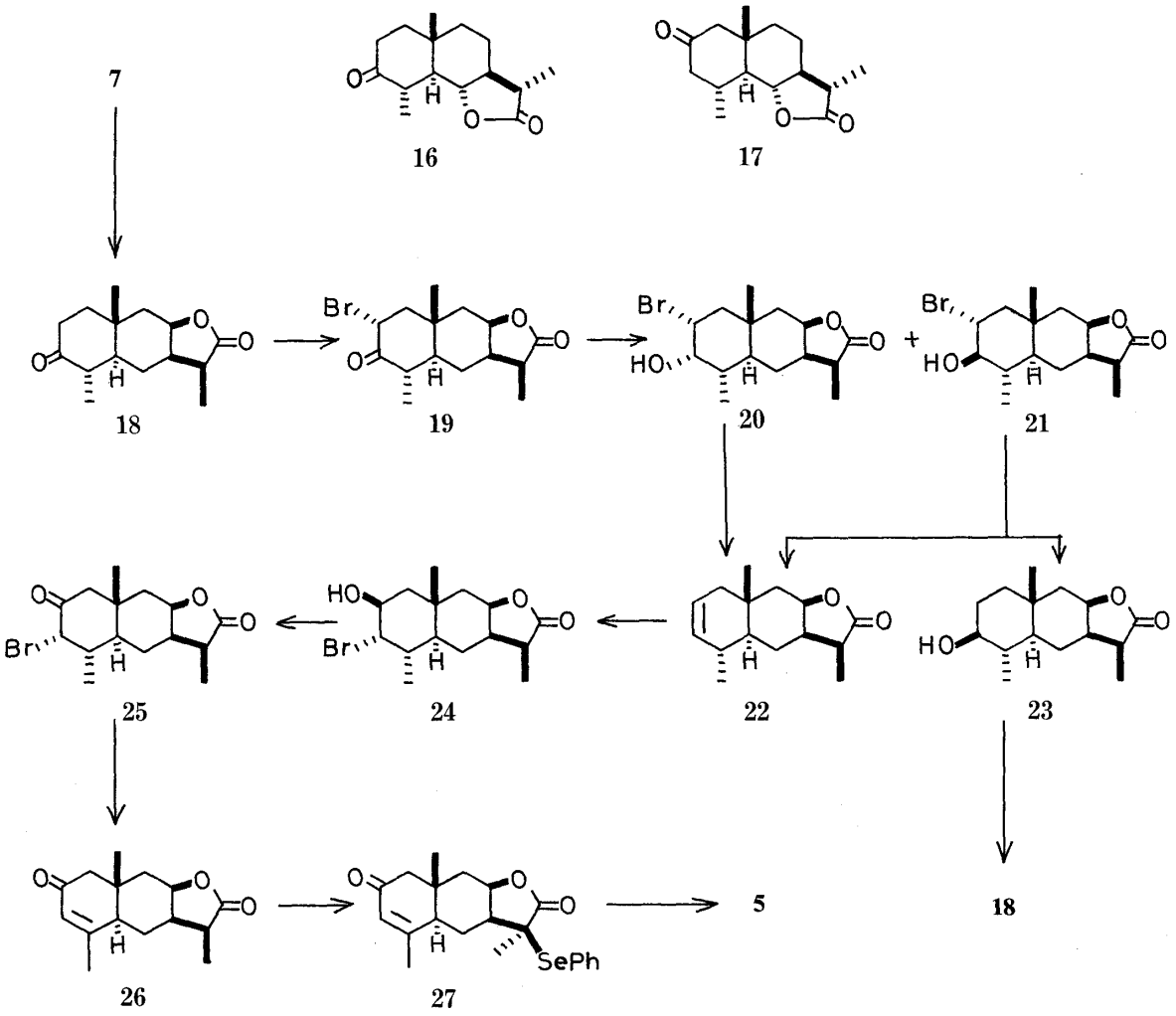

Chart 2

($J=15$ and 7 Hz). Reduction of **19** with sodium borohydride afforded two bromohydrins, the *cis*-isomer (**20**), mp 197—200 °C, in 47% yield and the *trans*-isomer (**21**), mp 159—162 °C, in 48% yield. In their NMR spectra, the C-3 proton signals of **20** and **21** appeared as a broad singlet at δ 3.85 and a triplet at δ 3.25 ($J=9$ Hz), respectively. Treatment of the *cis*-bromohydrin (**20**) with zinc dust in acetic acid gave an olefin (**22**), mp 107.5—109.5 °C, in 82% yield, whereas the *trans*-bromohydrin (**21**) gave the olefin (**22**) in 56% yield together with an alcohol, the 3β-hydroxy compound (**23**), mp 178—180 °C, in 19% yield. Jones oxidation of **23** gave the known ketone (**18**).

Hydroxybromination of the olefin (**22**) with *N*-bromosuccinimide in aq. dimethylsulfoxide at room temperature for 20 min gave a bromohydrin (**24**). This reaction may involve electrophilic attack from the α-side of the olefin to form an α-bromonium ion, and the hydroxy ion would attack the C-2 positive carbon to give a *trans* diaxial bromohydrin, 2β-hydroxy-3α-bromide (**24**). Oxidation of **24** (without purification) with the Jones reagent gave a bromoketone (**25**), mp 184—186 °C, in 80% yield from **22**. In the NMR spectrum of **25**, the C-3 proton signal appeared at δ 4.23 ($W_{1/2}=5$ Hz), and the IR spectrum showed absorption bands at 1754 and 1729 cm^{-1} due to the γ-lactone and the cyclohexanone, respectively. From these data, the stereoformula of the bromoketone (**25**) was concluded to be 2-oxo-3α(axial)-bromide. A benzene solution of **25** containing diazabicyclo[5,4,0]undecene (DBU) was refluxed for 2.5 h to furnish an enone (**26**), mp 187—189 °C, in 81% yield. All physical and spectral properties (mp, $[\alpha]_D$, IR and NMR) of **26** were in good agreement with those of dihydropinnatifidin derived from natural pinnatifidin, as reported by Herz *et al.*[6]

Phenylselenenylation of **26** under the same conditions as described for the synthesis of yomogin (**2**)[2] afforded a phenylselenide (**27**), mp 216—217 °C, in 84% yield. Treatment of **27** with H_2O_2 furnished (+)-pinnatifidin (**5**), mp 160—162 °C, quantitatively. All physical and spectral properties (mp, $[\alpha]_D$ and NMR) of **5** were in good agreement with those of (+)-pinnatifidin isolated from *Helenium pinnatifidum* (NUTT.) by Herz *et al.*[6]

Experimental[9]

3,3-Ethanedithio-11α(*H*)-eudesm-4,5-dien-8,13-olide (8)——Ethanedithiol (135 mg) and BF_3–OEt_2 (0.5 ml) were added to a solution of **7** (250 mg) in 10 ml of MeOH. The mixture was stirred at 0 °C for 6 h, then 10% $NaHCO_3$ was added, and the MeOH was removed by evaporation. The residue was extracted with EtOAc and the extract was washed with H_2O and brine, then dried. Evaporation of the EtOAc gave a crude product, which was purified by preparative thin-layer chromatography (TLC) with hexane–EtOAc (3 : 1) to give 273 mg (74%) of the thioketal (**8**). Recrystallization from hexane–EtOAc gave colorless needles, mp 141—143 °C. $[\alpha]_D^{23}$ +50.3° ($c=1.3$); IR cm^{-1}: 1760, 1750; NMR δ: 1.16 (3H, s, 10-CH_3), 1.23 (3H, d, $J=7$ Hz, 11-CH_3), 1.94 (3H, d, $J=1$ Hz, 4-CH_3), 3.34 (4H, m, $\diagup SCH_2$), 4.45 (1H, m, $W_{1/2}=9$ Hz, 8-H); MS *m/z* (% rel. int.): 324 (M^+, 56), 264 (100). *Anal.* Calcd for $C_{17}H_{24}O_2S_2$: $\diagdown SCH_2$

C, 69.92; H, 7.46; S, 19.76. Found: C, 62.90; H, 7.41; S, 19.81.

Reductive Desulfurization of 8——a) An acetone solution of **8** (109 mg in 10 ml) with W-2 Raney Ni (1 g) was heated at 50 °C for 80 min, then cooled. The Ni was filtered off, and the filtrate was concentrated. The product was purified by preparative TLC with hexane–EtOAc (3 : 1) to give 39.4 mg (50%) of the 2,4-diene (**9**) as an oil. NMR (60 MHz) δ: 1.02 (3H, s, 10-CH_3), 1.34 (3H, d, $J=7$ Hz, 11-CH_3), 1.76 (3H, s, 4-CH_3), 4.51 (1H, m, $W_{1/2}=10$ Hz, 8-H), 5.68 (2H, s, 2,3-H's).

b) An EtOH solution of **8** (400 mg in 10 ml) with W-2 Raney Ni (3 g) was heated at 40 °C for 25 min. Afrer work-up, the product was purified by preparative TLC using hexane–EtOAc (5 : 2) to give a mixture of **10** and **11** (4 : 1) as determined by NMR and gas-liquid chromatography (GLC) analyses. This mixture was subjected to epoxidation without separation.

3α,4α-Epoxy-11β(*H*)-eudesman-8,13-olide (12)——A solution of the above mixture of **10** and **11** (4 : 1) in 10 ml of CH_2Cl_2 was treated with 220 mg of *m*-chloroperbenzoic acid. The mixture was stirred at room temperature for 10 h. The CH_2Cl_2 layer was washed with 10% $NaHCO_3$, 10% Mohr solution, and H_2O, then dried. Evaporation of the solvent followed by separation by preparative TLC with hexane–EtOAc (5 : 2) gave 55 mg (19% from **8**) of 4α,5α,11α(*H*)-eudesman-8,13-olide (**11**) and 126.4 mg (41% from **8**) of the epoxide (**12**). Recrystallization of **11** from hexane gave colorless needles, mp 140—142 °C. IR cm^{-1}: 1655. NMR δ: 0.90 (3H, d, $J=7$ Hz, , 4-CH_3), 0.99 (3H, s,

10-CH_3), 1.21 (3H, d, $J=7$ Hz, 11-CH_3), 4.44 (1H, m, $W_{1/2}=9$ Hz, 8-H); MS *m/z* (% rel. int.): 236 (M^+, 4), 177 (69), 44 (100). *Anal.* Calcd for $C_{15}H_{22}O_3$: C, 76.22; H, 10.23. Found: C, 76.26; H, 9.94. Recrystallization of **12** from hexane gave colorless needles, mp 123—126 °C. $[\alpha]_D^{24}$ +55.7° ($c=0.47$); IR cm^{-1}: 1765, 1754; NMR δ: 1.28 (3H, s, 10-CH_3), 1.28 (3H, d, $J=7$ Hz, , 11-CH_3), 1.31 (3H, s, 4-CH_3), 4.54 (1H, m, $W_{1/2}=12$ Hz, 8-H); MS *m/z* (% rel. int.): 250 (M^+, 5), 207 (36), 119 (69), 107 (100). *Anal.* Calcd for $C_{15}H_{24}O_2$: C, 71.97; H, 8.86. Found: C, 71.73; H, 8.72.

Dihydrotelekin (13)——The epoxide (**12**) (65 mg, 0.26 mmol in ether 1.5 ml) was added dropwise to a solution of $LiNEt_2$ (1.8 mmol [prepared from 0.16 ml of Et_2NH and 15% solution of *n*-BuLi (1.15 ml) in hexane under N_2 at 0 °C]) over a period of 30 min. The mixture was refluxed for 3 h. After cooling, the mixture was acidified with 10% HCl and extracted with ether. Evaporation of the ether followed by purification of the residue by preparative TLC with hexane–EtOAc (5:2) gave 37.1 mg (57%) of **13**. Recrystallization from hexane–EtOAc afforded colorless needles, mp 192—193 °C (reported[3] mp 189.5 °C). High-resolution MS: mol. wt. 250.1567 $C_{15}H_{22}O_3$ Found: M^+, 250.1532. $[\alpha]_D^{22}$ +117.3° ($c=0.37$); IR cm^{-1}: 3435, 1744, 1640; NMR δ: 0.95 (3H, s, 10-CH_3), 1.22 (3H, d, $J=7$ Hz, 11-CH_3), 4.54 (1H, m, $W_{1/2}=6$ Hz, 8-H), 4.74, 4.88 (each 1H, m, $=CH_2$); MS *m/z* (% rel. int.): 250 (M^+, 29), 232 (M^+-H_2O, 7), 177 (83), 121 (89), 41 (100).

Telekin (4)——**13** (22.5 mg, 0.09 mmol) in tetrahydrofuran (THF) was treated with LDA (0.45 mmol) at −78 °C for 1 h and then with PhSeSePh (56 mg) in THF (0.2 ml) containing 0.03 ml of hexamethylphosphoramide (HMPA) at −78—−50 °C for 2.5 h. Work-up as usual gave a solid, which was purified by preparative TLC with hexane–EtOAc (5:2) to give 6.2 mg (17%) of the phenylselenide (**14**). Recrystallization from hexane–EtOAc afforded colorless prisms, mp 217—219 °C. High-resolution MS: mol. wt. 406.1045 $C_{21}H_{26}O_3Se$ Found: M^+, 406.1044. IR cm^{-1}: 3470, 1758, 1732; NMR δ: 0.95 (3H, s, 10-CH_3), 1.57 (3H, s, 11-CH_3), 4.71, 4.88 (each 1H, br s, $W_{1/2}=4$ Hz, $=CH_2$), 5.12 (1H, m, $W_{1/2}=11$ Hz, 8-H), 7.3—7.70 (5H, m, PhSe); MS *m/z* (% rel. int.): 406 (M^+, 53), 231 (77), 230 (M^+-H_2O-PhSeH, 92), 95 (100).

A solution of **14** (4.6 mg) was treated with 35% H_2O_2 in THF at 0 °C for 30 min. Extraction with ether followed by purification by preparative TLC with hexane–EtOAc (1:1) afforded 1.8 mg (64%) of (+)-telekin (**4**). Recrystallization from hexane–EtOAc yielded colorless needles, mp 156—158 °C (reported[3] mp 159.5—160 °C). High-resolution MS: mol. wt. 248.1410 $C_{15}H_{20}O_3$ Found: M^+, 248.1385. $[\alpha]_D^{22}$ +183.3° ($c=0.06$); NMR δ: 0.98 (3H, s, 10-CH_3), 4.57 (1H, m, $W_{1/2}=12$ Hz, 8-H), 4.72, 4.89 (each 1H, m, C(4)=CH_2), 5.60, 6.17 (each 1H, d, $J=1$ Hz, C(11)=CH_2); MS *m/z* (% rel. int.): 248 (M^+, 42), 230 (M^+-H_2O, 20), 192 (24), 124 (88), 41 (100).

3-Oxo-2α-bromoeudesman-8,13-olide (19)——**18**[2] (100 mg, 0.4 mmol) was stirred with Br_2 (90 mg, 0.5 mmol) in $CHCl_3$ at 0 °C until the red color of the mixture disappeared. After usual work-up, removal of the solvent gave a crude solid, which was purified by preparative TLC with benzene–EtOAc (8:1) to afford 120.5 mg (92%) of the 2α-bromide (**19**), mp 161—164 °C. Recrystallization from hexane–EtOAc afforded colorless prisms, mp 163—165 °C. High-resolution MS: mol. wt. 330.0673. $C_{15}H_{21}BrO_3$ Found: M^+, 330.0676. $[\alpha]_D^{23}$ −11.3° ($c=0.79$); IR cm^{-1}: 1757, 1752, 1732; NMR δ: 1.15 (3H, d, $J=7$ Hz, 4-CH_3), 1.22 (3H, d, $J=7$ Hz, 11-CH_3), 1.27 (3H, s, 10-CH_3), 4.50 (1H, m, $W_{1/2}=10$ Hz, 8-H), 4.86 (1H, ddd, $J=14$, 6, 2 Hz, 2-H); MS *m/z* (% rel. int.): 330, 328 (M^+-Br, 9), 122 (100).

$NaBH_4$ Reduction of the 2α-Bromide (19)——An EtOH solution of **19** (100 mg in 15 ml) was reduced with 15 mg of $NaBH_4$ at 0 °C for 3 h. The mixture was extracted with EtOAc, and the extract was concentrated to give a crude product, which was purified by preparative TLC with benzene–EtOAc (8:1) to give 47 mg (49%) of the 3α-hydroxy-2α-bromide (**20**) and 48 mg (49%) of the 3β-hydroxy-2α-bromide (**21**). Recrystallization of **20** from hexane–EtOAc gave colorless needles, mp 197.5—200 °C. $[\alpha]_D^{23}$ −3.75° ($c=0.8$). IR cm^{-1}: 3510, 1743; NMR δ: 0.98 (3H, s, 10-CH_3), 1.08 (3H, d, $J=7$ Hz, 4-CH_3), 1.19 (3H, d, $J=7$ Hz, 11-CH_3), 3.84 (1H, br d, $W_{1/2}=5$ Hz, 3-H), 4.38—4.58 (2H, m, 2,8-H); MS *m/z* (% rel. int.): 331, 329 (M^+, 1), 288, 286 (26), 251 (M^+-Br, 20), 233 (97), 189 (62), 159 (100). *Anal.* Calcd for $C_{15}H_{23}BrO_3$: C, 54.39; H, 7.00: Br, 24.12. Found: C, 54.44; H, 7.05; Br, 24.25. Recrystallization of **21** from hexane–EtOAc afforded colorless prisms, mp 159—162 °C. $[\alpha]_D^{20}$ −83.3° ($c=0.06$). IR cm^{-1}: 3510, 1735; NMR δ: 1.00 (3H, s, 10-CH_3), 1.16 (3H, d, $J=7$ Hz, 4-CH_3), 1.20 (3H, d, $J=7$ Hz, 11-CH_3), 3.25 (1H, t, $J=9$ Hz, 3-H), 4.10—4.59 (1H, m, 2-H), 4.46 (1H, m, $W_{1/2}=11$ Hz, 8-H); MS *m/z* (% rel. int.): 331, 329 (M^+, 2), 288 (21), 286 (22), 251 (M^+-Br, 47), 233 (100), 159 (81).

Eudesm-2-en-8β,13-olide (22)——a) Reduction of the *cis*-Bromohydrin (**20**): Zn dust (80 mg) was added to a solution of **20** (37.8 mg) in 1 ml of AcOH, and the mixture was refluxed for 3 h. The Zn was filtered off, and the filtrate was concentrated. The residue was extracted with EtOAc, and the extract was concentrated *in vacuo* to give a solid, which was purified by preparative TLC with hexane–EtOAc (3:1) to give 21.8 mg (82%) of the 2,3-dehydro compound (**22**). Recrystallization from hexane afforded colorless needles, mp 107.5—109.5 °C. $[\alpha]_D^{23}$ −62.5° ($c=0.8$). IR cm^{-1}: 1765, 1755, 1651; NMR δ: 0.92 (3H, s, 10-CH_3), 1.02 (3H, d, $J=7$ Hz, 4-CH_3), 1.21 (3H, d, $J=7$ Hz, 11-CH_3), 4.45 (1H, m, $W_{1/2}=10$ Hz, 8-H), 5.48 (2H, s, 2,3-H); MS *m/z* (% rel. int.): 234 (M^+, 48), 219 (100), 145 (90). *Anal.* Calcd for $C_{15}H_{22}O_2$: C, 76.88; H, 9.46. Found: C, 76.40; H, 9.39.

b) Reduction of the *trans*-Bromohydrin (**21**): **21** (117 mg) in 4 ml of AcOH was treated with 250 mg of Zn dust at reflux temperature for 2.5 h. Work-up in the same manner as described above gave the 2,3-dehydro compund (**22**) (46 mg, 55.5%) and the 3β-hydroxy derivative (**23**) (17 mg; 19%). Recrystallization of **23** from hexane–EtOAc gave colorless prisms, mp 178—180 °C. $[\alpha]_D^{24}$ −29.1° ($c=0.45$); IR cm^{-1}: 3505, 1764, 1755; NMR δ: 0.95 (3H, s, 10-CH_3), 1.02 (3H, d, $J=6$ Hz, 4-CH_3), 1.20 (3H, d, $J=7$ Hz, 11-CH_3), 3.13 (1H, td, $J=9$, 5 Hz, 3-H), 4.45 (1H, m, $W_{1/2}=$

10 Hz, 8-H); MS *m/z* (% rel. int.): 252 (M^+, 4), 234 ($M^+ - H_2O$, 7), 208 (38), 161 (36), 122 (100). *Anal.* Calcd for $C_{15}H_{24}O_3$: C, 71.39; H, 9.59. Found: C, 71.53; H, 9.71.

Oxidation of **23** (10.4 mg) with the Jones reagent in acetone (3 ml) afforded the known ketone (**18**) quantitatively.

3α-Bromo-2β-hydroxyeudesman-8,13-olide (24)——Four drops of H_2O and 240 mg (1.35 mmol) of *N*-bromosuccinimide (NBS) were added to a solution of **22** (157 mg, 0.48 mmol) in 2 ml of dimethylsulfoxide (DMSO), and the mixture was stirred at room temperature for 20 min under an N_2 atmosphere. After addition of 5% $NaHCO_3$ followed by extraction with EtOAc, the extract was washed and dried. Evaporation of the solvent gave a colorless solid (**24**) (134.6 mg, 61%). Recrystallization from MeOH gave colorless needles, mp 122—124 °C. $[\alpha]_D^{24}$ −2.6° (*c*=0.16); IR cm^{-1}: 3410, 1735, 1730; NMR δ: 1.03 (3H, d, *J*=7 Hz, 4-CH_3), 1.17 (3H, s, 10-CH_3), 1.21 (3H, d, *J*=7 Hz, 11-CH_3), 4.27 (2H, m, $W_{1/2}$=9 Hz, 2,3-H), 4.47 (1H, m, $W_{1/2}$=9 Hz, 8-H); MS *m/z* (% rel. int.): 333, 331 (M^+, 1), 315, 313 ($M^+ - H_2O$, 3), 233 ($M^+ - Br - H_2O$, 100). *Anal.* Calcd for $C_{15}H_{23}BrO_3$: C, 54.39; H, 7.00; Br, 24.12. Found: C, 54.57; H, 7.26; Br, 24.49.

2-Oxo-3α-bromoeudesman-8β,13-olide (25)——A DMSO solution of **22** (89 mg, 0.38 mmol in 1 ml) containing 2 drops of H_2O was treated with 135 mg (0.76 mmol) of NBS at room temperature for 10 min. Work-up in the same manner as described above gave the crude bromohydrin, which was oxidized with the Jones reagent in acetone at room temperature. After evaporation of the solvent, the residue was chromatographed on a silica gel column. Elution with hexane–EtOAc (2:1) gave 100.2 mg (80% from **22**) of **25** as colorless crystals. Recrystallization from hexane–EtOAc gave colorless needles, mp 184—186 °C. $[\alpha]_D^{24}$ +16.6° (*c*=0.56). IR cm^{-1}: 1754, 1729; NMR δ: 0.89 (3H, s, 10-CH_3), 1.13 (3H, d, *J*=6 Hz, 4-CH_3), 1.22 (3H, d, *J*=7 Hz, 11-CH_3), 3.08 (1H, d, *J*=14 Hz, 1α-H), 4.23 (1H, m, $W_{1/2}$=5 Hz, 3-H), 4.49 (1H, m, $W_{1/2}$=10 Hz, 8-H); MS *m/z* (% rel. int.): 330, 328 (M^+, 12), 249 ($M^+ - Br$, 87), 101 (100). *Anal.* Calcd for $C_{15}H_{21}BrO_3$: C, 54.72; H, 6.43; Br, 24.27. Found: C, 54.80; H, 6.51; Br, 24.10.

Dihydropinnatifidin (26)——A benzene solution of **25** (42.6 mg in 3 ml) was treated with 30 mg of DBU, and the mixture was refluxed for 1.5 h. The benzene layer was washed and dried. Evaporation of the benzene gave a brown residue, which was purified by preparative TLC with benzene–EtOAc (3:1) to give 27 mg (81%) of **26**. Recrystallization from benzene afforded colorless crystals, mp 187—189 °C (reported[6] mp 189.5—190.5 °C). $[\alpha]_D^{23}$ +125.9° (*c*=0.41, EtOH). UV nm (ε): 239 (13800); IR cm^{-1}; 1763, 1672, 1621; NMR δ: 0.99 (3H, s, 10-CH_3), 1.26 (3H, d, *J*=7 Hz, 11-CH_3), 1.96 (3H, t, *J*=1 Hz, 4-CH_3), 4.52 (1H, m, $W_{1/2}$=7 Hz, 8-H), 5.94 (1H, m, 3-H); MS *m/z* (% rel. int.): 248 (M^+, 28), 175 (60), 69 (100). *Anal.* Calcd for $C_{15}H_{20}O_3$: C, 72.55; H, 8.12. Found: C, 72.23; H, 7.96.

Pinnatifidin (5)——**26** (14 mg, 0.056 mmol) was treated with LDA (0.17 mmol) in THF at −78 °C for 1.5 h. When the enolate formation was complete, a solution of PhSeSePh (37.5 mg, 0.12 mmol) in THF (0.3 ml) containing HMPA (0.02 ml) was added at −78 °C. The mixture was stirred at −70——−50 °C for 2.5 h, then extracted with ether. The ether layer was washed and dried. Evaporation of the ether gave a crude solid, which was purified by preparative TLC with hexane–EtOAc (1:1) to give 19.2 mg (84%) of the phenylselenide (**27**). Recrystallization from hexane–EtOAc gave colorless needles, mp 216—217 °C. NMR (60 MHz) δ: 0.90 (3H, s, 10-CH_3), 1.51 (3H, s, 11-CH_3), 1.88 (3H, d, *J*=2 Hz, 4-CH_3) 5.05 (1H, m, 8-H), 5.90 (1H, m, 3-H), 7.20—7.70 (5H, m, PhSe).

A solution of the phenylselenide (**27**) (12.5 mg) in 0.5 ml of THF was treated with 35% H_2O_2 (0.04 ml) at 0° for 30 min. The organic layer was washed and dried. Removal of the solvent *in vacuo* gave 7.8 mg (quantitative) of colorless crystals (**5**) mp 160—162 °C. (reported[6] mp 164—165 °C). The physical and spectral data of **5** were consistent with those of natural (+)-pinnatifidin reported by Herz *et al.*[6] $[\alpha]_D^{22}$ +286.4° (*c*=0.15, EtOH); IR ($CHCl_3$) cm^{-1}: 1755, 1650, 1610; NMR δ: 0.91 (3H, s, 10-CH_3), 1.95 (3H, t, *J*=1 Hz, 4-CH_3), 4.55 (1H, m, $W_{1/2}$=8 Hz, 8-H), 5.68, 6.21 (each 1H, d, *J*=1 Hz, =CH_2), 5.94 (1H, m, 3-H).

Acknowledgement The authors wish to thank Dr. Kamiya of Fujisawa Pharmaceutical Industry Ltd. for providing α-santonin. Thanks are also to Dr. Saito of Tanabe Seiyaku Co., Ltd. for microanalyses, and to Mrs. Toshioka, Mrs. Takayama, Mrs. Hasegawa and Miss Sawabe of this laboratory for mass and NMR spectral measurements.

References and Notes

1) A part of this work was presented at the ACS/CSJ Chemical Congress, Honolulu, Hawaii, U.S.A., April 1—6, 1979, and a part is taken from Murakami, Master's Thesis, Sci. Univ. Tokyo, 1979.
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9) Experimental conditions were the same as described in the preceding paper, see ref. 2.