Synthesis of torrentin, dihydrosantamarine, and saussurea lactone from santonin

GONZALO BLAY, LUZ CARDONA, BEGOÑA GARCÍA, AND JOSÉ R. PEDRO[1]

Department of Organic Chemistry, Faculty of Chemistry, University of Valencia, E-46100 Burjassot, Valencia, Spain

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The synthesis of the eudesmanolide torrentin (**1**) by sensitized photooxygenation of synthetic dihydrosantamarine (**3**) is reported. Both dihydrosantamarine and dihydroreynosin (**11**) were obtained from the 1,2-epoxide **9**, which, in turn, was prepared from the diselenide **7**. An improved procedure for the synthesis of the elemanolide saussurea lactone (**4**) is also reported.

Key words: eudesmanolide, elemanolide, santonin, torrentin, saussurea lactone.

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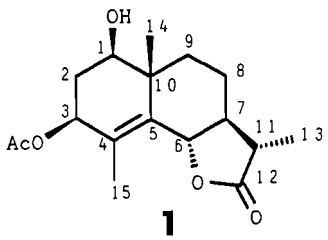
On rapporte la synthèse de l'eudesmolide de torrentine (**1**) par une photo-oxygénation de la dihydrosantamarine de synthèse (**3**). On a obtenu à la fois la dihydrosantamarine et la dihydroreynosine (**11**) à partir de l'époxyde **9** qui a par ailleurs été préparé à partir du disélénure **7**. On rapporte aussi une méthode améliorée de synthèse de l'élémanolide lactone de saussurea (**4**).

Mots clés : eudesmanolide, élémanolide, santonine, torrentine, lactone saussurea.

[Traduit par la rédaction]

Torrentin is an eudesmanolide isolated a few years ago (1) from *Artemisia herba-alba* subsp. *valentina,* and whose structure has been revised recently (2). This paper reports on the synthesis of torrentin (**1**) from santonin (**2**) via a multistep reaction sequence involving dihydrosantamarine (**3**) as an intermediate product. It also contributes an improved procedure for the synthesis of saussurea lactone (**4**) from santonin (**2**). The sesquiterpene lactones, which constitute an important group of natural compounds widely distributed in the family Compositae, have received much attention because of their biological activities (3).



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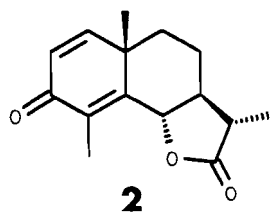

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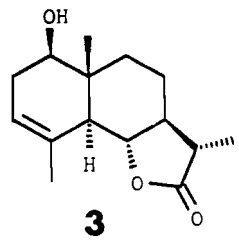

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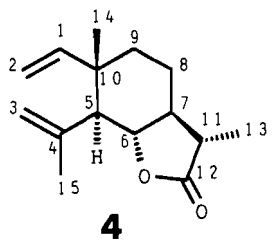

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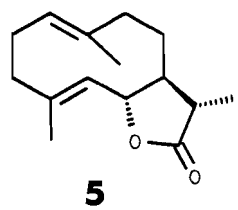

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Dihydrosantamarine (**3**) was synthesized previously (4) from the dihydrocostunolide (**5**) and, more recently, by an 11-step refunctionalization (5) of the A ring of santonin (**2**). We synthesized dihydrosantamarine (**3**) via a shorter synthetic pathway by applying a new selective transformation of diselenide **7** to the 1,2-epoxide **9**. The conversion of dihydrosantamarine (**3**) into torrentin (**1**) involved the sensitized photooxygenation of the 3,4-double bond of the former as a key step (6).

We used the diol-lactone **6** as starting product, which was prepared from santonin (**2**) according to Grieco (7), i.e., by hydrogenation and epimerization (8) at C4, formation of the corresponding tosylhydrazone and a Shapiro reaction (9), and, finally, the ozonolysis of the 2,3-double bond followed by reduction with sodium borohydride.

Our strategy was based on the synthesis of the 1,2-epoxide **9** from the diol **6** by oxidation–elimination of the diselenide **7** and the simultaneous epoxidation of the resulting double bond. Inasmuch as the elimination of the C2 selenoxide should be faster (10) than that of the C3 selenoxide, the yield of epoxide **9** must be more favourable than that of **10** in relation to those obtained by epoxidation (3) of saussurea lactone (**4**).

With the above ideas in mind, we addressed the synthesis

[1]Author to whom correspondence may be addressed.

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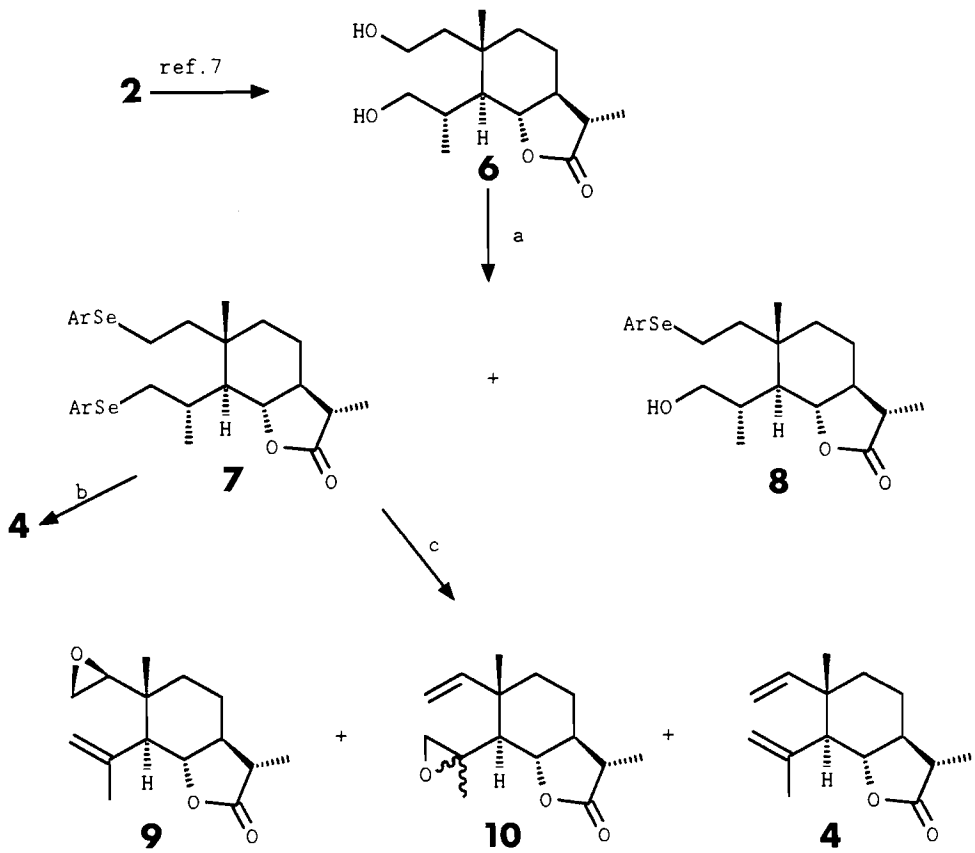


Reagents: (a) 4.8 eq. ArSeCN, *n*-Bu_3P; (b) 30% H_2O_2; (c) *m*-CPBA; Ar = *o*-$NO_2C_6H_4$-

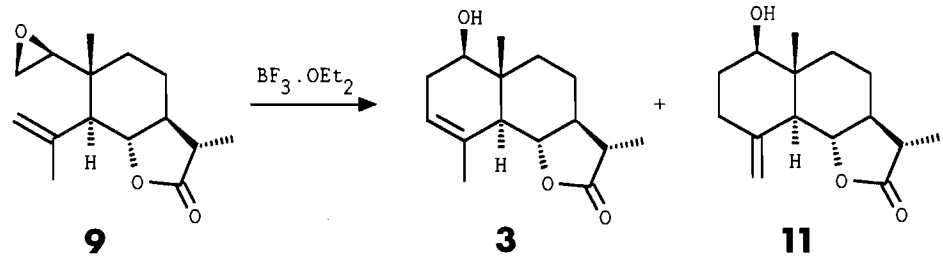
SCHEME 1

of the diselenide **7** from the diol **6** by reaction with *o*-nitrophenylselenocyanate-tri-*n*-butylphosphine. Despite Grieco's explicit claim that **7** cannot be synthesized (7), our past experience with similar substrates (11, 12) told us that the synthesis in question should pose no problem. In fact, the diselenide **7** was obtained with a yield of 72% by reaction of the diol **6** with 4.8 equivalents of *o*-nitrophenylselenocyanate–tri-*n*-butylphosphine in THF–pyridine. Diselenide **7** was subjected to various simultaneous oxidation–elimination and epoxidation procedures with epoxidizing reagents such as sodium perborate/acetic anhydride (13), *p*-nitroperoxybenzoic acid (14), trifluoroacetic anhydride/H_2O_2 (15), and trichloroacetonitrile/H_2O_2 (16) at temperatures between 0 and 4°C and for long reaction times (7 days), which yielded mainly the divinyl compound **4**. However, the use of hexafluoroacetone/H_2O_2 (17) under identical reaction conditions provided the 1,2-epoxide **9** with a yield of 25%, together with the 3,4-epoxide **10** (19%) and the divinyl compound **4** (34%), while shorter reaction times and room temperature conditions yielded preferentially the 3,4-epoxide **10**. Finally, the best yields of the 1,2-epoxide **9** were secured with *m*-chloroperoxybenzoic acid. After 8 days at 0–4°C, the said epoxide was obtained with a yield of 44%, together with 11% of the 3,4-epoxide **10** and 10% of the divinyl compound **4**. Even though the yield of the 1,2-epoxide **9** obtained by oxidation of the diselenide **7** was somewhat low, it is interesting to note the selectivity of the reaction, since the epoxides **9** and **10** were obtained in a 4:1 ratio, while direct epoxidation of divinyl compound **4** yielded the same epoxides in a 1:4 ratio (4) (Scheme 1).

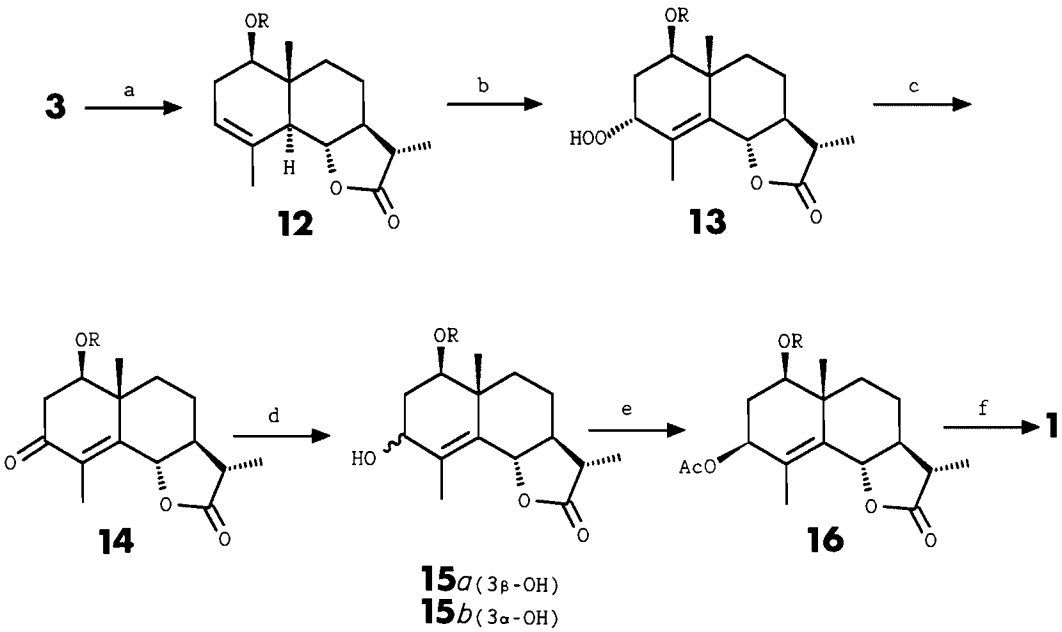
On the other hand, by oxidation of the diselenide **7** with H_2O_2/THF (18) saussurea lactone (**4**) was obtained with a yield of 90%. This synthesis of saussurea lactone (**4**) from santonin (**2**), through the diselenide **7**, improves remarkably those previously reported (7).

On treatment with boron trifluoride etherate, the compound **9** underwent an intramolecular Prins reaction, through the nucleophilic attack of the olefin on the coordinate form of the epoxide, and yielded a mixture of two eudesmanolides that were resolved by column chromatography (Scheme 2). The less polar compound was obtained with a yield of 59% and was identified as dihydrosantamarine (**3**) consistent with its ^1H NMR spectrum (δ_H 5.30 (brs, 3-H), 3.93 (dd, J = 9.8 and 11.1 Hz, 6-H), 3.62 (dd, J = 6.7 and 9.8 Hz, 1α-H), 1.79 (brs, 15-H)). The more polar component, which was obtained with a yield of 25%, was identified as dihydroreynosin **11**. Its ^1H NMR spectrum included two broad singlets (δ_H 4.95 and 4.80) corresponding to the protons of the exocyclic methylene group, in addition to the signals corresponding to 6-H (δ_H 4.03, t, J = 10.5 Hz) and 1α-H (δ_H 3.48, dd, J = 4.6 and 11.4 Hz).

Once dihydrosantamarine (**3**) had been synthesized it was transformed into torrentin (**1**). The introduction of an oxygenated function at C3 was thought to be feasible by sensitized photooxygenation of the 3,4-double bond (6). However, as such an oxygenated function of torrentin was an acetate



SCHEME 2



SCHEME 3

group, it required the hydroxyl group at C1 to be protected. Therefore, the first reaction involved was the treatment of dihydrosantamarine (**3**) with *tert*-butyldimethylsilyl chloride in DMF/imidazole (19) in order to protect the hydroxyl function as a silyl ether. Protected dihydrosantamarine, **12**, was converted into the corresponding 3α-hydroperoxide **13**, by bubbling oxygen through an ethanol solution sensitized by means of methylene blue and irradiated with two 400-W lamps. On treatment with acetic anhydride in pyridine (20), the hydroperoxide **13** yielded the α,β-unsaturated ketone **14**, which, by reduction with $LiAlH(O\text{-}t\text{-}Bu)_3$ in THF at 0°C, provided a mixture of the desired 3β-alcohol **15***a* (65%) and its 3α-epimer **15***b* (26%). Finally, on acetylation of **15***a* and cleavage of the silyl ether with $n\text{-}Bu_4NF$, torrentin (**1**) was obtained and was found to be identical with its natural counterpart (2) (Scheme 3).

Experimental

Melting points were determined in capillary tubes with a Büchi melting point apparatus and were used uncorrected. IR spectra were recorded on a Perkin–Elmer 281 spectrometer. ^1H and ^{13}C NMR were run on a Bruker AC-200 instrument (200.1 MHz for ^1H NMR and 50.3 MHz for ^{13}C) by using $CDCl_3$ solutions (Tables 1 and 2). Mass spectra were recorded at 70 eV on a Hewlett–Packard GC/MS system 5988A, with an ULTRA-2 GC column (25 m, cross-linked diphenyl 5% phenylmethyl silicone gum phase). Optical

TABLE 1. ^{13}C NMR data of compounds **4**, **6–10** (50.3 MHz, $CDCl_3$, δ)

C	6	7[a]	8[a]	9	10	4
1	45.5	37.9[b]	37.7[b]	58.8	147.9	147.8
2	58.8	20.0	19.9	44.6[b]	111.7	111.3
3	69.1	35.3	68.2	116.1	52.5	115.1
4	35.0	29.9	33.5	140.4	55.5	140.9
5	48.0	49.6	45.2	53.5[c]	54.5[b]	55.7
6	83.3	81.4	81.7	80.8	80.6	81.2
7	53.7	52.2	52.2	51.8[c]	52.1[b]	52.2
8	24.4	23.4	23.4	22.9	23.5	23.5
9	39.6	39.7[b]	40.0[b]	34.1[b]	40.8	39.4
10	40.0	40.5	40.4	39.3	42.3	42.6
11	41.8	40.7	40.8	41.4	41.2	41.6
12	182.0	179.2	179.5	178.9	178.8	179.1
13	12.7	12.4	12.4	12.5	12.5	12.5
14	13.7[b]	17.7[c]	13.1[c]	23.2[d]	18.3[c]	23.9[b]
15	22.1[b]	21.3[c]	21.9[c]	15.3[d]	21.8[c]	18.3[b]

[a]Aromatic carbons for compound 7: 125.4, 125.5, 126.4, 126.6, 128.7, 128.8, 132.6, 133.6, 133.7, 146.4, and 146.7; compound **8**: 125.3, 126.3, 129.1, 133.6, and 146.6;

[b–d]The signals with these superscripts may be interchanged within the corresponding spectrum.

TABLE 2. ^{13}C NMR of compounds **1**, **3**, **11–16** (50.3 MHz, $CDCl_3$, δ)

C	3	11	12	13	14	15*a*	15*b*	16[a]	1[a]
1	75.0	78.2	75.6	73.2	74.8	75.2	73.2	74.7	74.1
2	32.6[b]	31.2[b]	33.7[b]	31.0	43.1	36.6	36.3	33.4	32.9
3	121.1	36.0[b]	121.6	86.0	197.4	71.0	71.9	72.8	72.8
4	133.3	142.8	133.3	121.6	129.4	128.1[b]	126.2[b]	124.8[b]	125.0[b]
5	53.5[c]	52.4[c]	53.7[c]		152.8	132.0[b]	134.2[b]	134.1[b]	133.9[b]
6	81.2	79.3	81.5	82.6	82.0	82.7	82.5	82.7	82.5
7	50.4[c]	52.3[c]	50.7[c]	52.6	52.0	52.8	52.6	52.4	52.5
8	22.7	23.0	22.9	24.3	24.4	24.6	24.3	24.5	24.5
9	34.4[b]	33.5[b]	35.3[b]	38.4	38.3	38.5	38.5	38.6	38.1
10	40.6	42.8	41.2	42.9	44.2	43.4	42.9	43.1	42.6
11	40.5	41.2	40.7	41.0	41.1	41.3	41.0	41.1	41.1
12	179.6	179.3	179.7	178.5	177.6	178.6	178.6	178.4	178.3
13	12.3	12.5	12.5	12.4	12.4	12.4	12.4	12.3	12.4
14	10.9[d]	11.6	11.3[d]	18.4[b]	11.1[b]	14.6[c]	17.6[c]	14.2[c]	14.4[c]
15	23.1[d]	110.3	23.3[d]	18.0[b]	17.8[b]	19.0[c]	17.8[c]	18.5[c]	18.4[c]
MeSi			−4.8	−4.8	−5.0	−4.9	−4.8	−5.0	
MeSi			−4.0	−4.0	−4.0	−4.1	−3.9	−4.0	
Me_3CSi			18.0	17.7	17.9	18.0	18.0	18.0	
Me_3CSi			25.8	25.8	25.7	25.8	25.8	25.7	

[a]Acetate carbons 21.1 and 170.8.
[b–d]The signals with these superscripts may be interchanged within the corresponding spectrum.

rotations were taken on a Perkin–Elmer 241 polarimeter. Reaction solvents were purified and dried by standard methods (20). THF was distilled from Na–benzophenone prior to use. *o*-Nitrophenylselenocyanate was prepared by Bauer's procedure as described by Hori and Sharples (21) and had a melting point of 140–142°C.

*2,3-Di-*o*-nitrophenylseleno-5,7*α*H,4,6,11*β*H-eleman-6,12-olide* **7**

To a solution of diol **6** (35 mg, 0.127 mmol) and *o*-nitrophenylselenocyanate (141 mg, 0.62 mmol) in THF–pyridine 1:1 (1.4 mL) at room temperature under argon, was added, via syringe, tri-*n*-butylphosphine (195 μL, 0.778 mmol) and the mixture stirred for 5 h. To this reaction mixture was added, also via syringe, the resulting solution from *o*-nitrophenylselenocyanate (35 mg, 0.15 mmol), pyridine (0.5 mL), and tri-*n*-butylphosphine (48 μL, 0.19 mmol). Then the reaction mixture was stirred for 20 h. After solvent removal, the residue was chromatographed on silica gel (dichloromethane–methanol 100:1). The first eluted product was diselenide **7** (60 mg, 72%) and the second one was the monoselenide **8** (13 mg, 23%). Compound **7** was a yellow solid, mp 157–158°C (hexane–acetone); ν_{max} (KBr)/cm^{-1}: 3080, 3060, 1770, 1590, 1560, 1505, 1330, 1000, and 735; δ_H: 8.26(1H, dd, *J* 1.4 and 8.3, Ar-H), 8.14(1H, d, *J* 8.0, Ar-H), 7.50–7.20(6H, m, Ar-H), 4.04(1H, t, *J* 10.7, 6-H), 3.10–3.00(2H, m, 3-H), 2.94 (1H, td, *J* 5.5 and 12.0, 2-H), 2.75(1H, td, *J* 4.7 and 12.0, 2′-H), 2.26(1H, 2q, *J* 6.9 and 12.2, 11-H), 1.26 and 1.23 (6H, two d, *J* 6.9, 13-H and 15-H), and 1.00(3H, s, 14-H) Anal. calcd. for $C_{27}H_{32}N_2O_6Se_2$: C 50.79, H 5.05; found: C 50.8, H 5.0. Compound **8** was a yellow oil; ν_{max}/cm^{-1} (NaCl): 3540–3300, 1760, 1580, 1555, 1500, 1330, 1000, and 725; δ_H: 8.24(1H, dd, *J* 1.5 and 8.0, Ar-H), 7.56 (1H, dd, *J* 1.5 and 8.0, Ar-H), 7.49(1H, td, *J* 1.5 and 8.0, Ar-H), 7.27(1H, td, *J* 1.5 and 8.0, Ar-H), 3.99(1H, t, *J* 10.7, 6-H), 3.60–3.50(2H, m, 3-H), 3.16 (1H, td, *J* 4.5 and 12.0, 2-H), 2.82(1H, td, *J* 4.3 and 12.0, 2′-H), 2.25(1H, dq, *J* 6.9 and 12.1, 11-H), 1.20(3H, d, *J* 6.9, 13-H), 1.00(3H, s, 14-H), and 0.99(3H, d, *J* 7.0, 15-H).

*1,2β-Epoxy-5,7*α*H,6,11*β*H-elem-3-en-6,12-olide* **9** *from* **7**

To a solution containing diselenide **7** (184 mg, 0.288 mmol) in CH_2Cl_2 (7 mL), 85% *m*-chloroperbenzoic acid (439 mg, 2.16 mmol) was added at 0°C and the resulting mixture stirred at 0–4°C for 9 days. The product was treated by the usual procedure and chromatographed on silica gel (increasing polarity of hexane–ether) to afford compound **4** (7 mg, 10%), compound **9** (32 mg, 44%), and compound **10** (9 mg, 11%). Their physical and spectral features were as follows: compound **9**, mp 145–147°C (hexane–dichloromethane); ν_{max} (KBr)/cm^{-1}: 3060, 1765, 1630, 1010, 890, 860, and 800; δ_H: 5.07(1H, brs, 3-H), 4.83(1H, brs, 3′-H), 4.04(1H, dd, *J* 10.2 and 11.6, 6-H), 2.86(1H, t, *J* 3.5, 1-H), 2.64 (2H, m, 2-H), 2.42(1H, d, *J* 11.6, 5-H), 2.31(1H, dq, *J* 6.9 and 12.1, 11-H), 1.82(3H, s, 15-H), 1.20(3H, d, *J* 6.9, 13-H), and 0.86(3H, s, 14-H); *m/z* (EI): 250 (M^+, 1%), 235 ($M^+ - CH_3$, 5), 219 (2), 151 (10), 149 (21), 147 (11), 137 (15), 121 (30), 107 (38), 93 (43), 83 (58), and 55 (100). Compound **10**, mp 109–110°C (hexane–dichloromethane); ν_{max}(KBr)/cm^{-1}: 3100, 1770, 1015, 995, and 810; δ_H: 5.81(1H, dd, *J* 10.8 and 17.5, 1-H), 5.04(1H, d, *J* 17.5, 2-H), 5.02(1H, d, *J* 10.8, 2′-H), 4.01(1H, t, *J* 10.9, 6-H), 2.73(1H, d, *J* 4.4, 3-H), 2.50(1H, d, *J* 4.4, 3′-H), 2.31(1H, dq, *J* 7.0 and 12.0, 11-H), 1.37(3H, s, 15-H), 1.21(3H, d, *J* 7.0, 13-H), and 1.19(3H, s, 14-H); *m/z* (EI): 250 (M^+, 1%), 235 ($M^+ - CH_3$, 15), 221 (3), 207 (3), 193 (7), 181 (12), 167 (16), 149 (27), 137 (20), 123 (33), 109 (54), 93 (57), and 55 (100).

*5,7*α*H,6,11*β*H-Elema-1,3-dien-6,12-olide* **4** *from* **7**

A solution of diselenide **7** (26 mg, 0.041 mmol) in THF (0.3 mL) was treated with 30% aqueous hydrogen peroxide (45 μL, 0.04 mmol) at 0°C for 20 h. The reaction mixture was extracted with ethyl acetate and filtered through a short plug of silica gel to afford compound **4** (8.8 mg, 90%) with the following features: mp 149–152°C (hexane–dichloromethane); ν_{max}(KBr)/cm^{-1}: 3090, 1765, 1640, 1005, 1000, 910, and 890, δ_H: 5.78(1H, dd, *J* 10.9 and 17.3, 1-H), 5.01(1H, m, 3-H), 4.96(1H, dd, *J* 0.8 and 10.9, 2-H), 4.92(1H, dd, *J* 0.8 and 17.3, 2′-H), 4.67(1H, brs, 3′-H), 4.10(1H, dd, *J* 10.2 and 11.5, 6-H), 2.31(1H, dq, *J* 7.0 and 12.0 11-H), 2.21(1H, d, *J* 11.5, 5-H), 1.76(3H, s, 15-H), 1.21(3H, d, *J* 7.0, 13-H), and 1.06(3H, s, 14-H); *m/z* (EI): 234 (M^+, 4%), 220 (2), 219 ($M^+ - CH_3$, 11), 206 (1), 199 (1), 177 (11), 167 (16), 156 (74), 149 (48), 141 (33), and 139 (100).

*1β-Hydroxy-5,7*α*H,6,11*β*H-eudesm-3-en-6,12-olide* **3** *and 1β-hydroxy-5,7*α*H,6,11*β*H-eudesm-4(15)-en-6,12-olide* **11** *from* **9**

To a solution of epoxide **9** (71 mg, 0.287 mmol) in benzene (4 mL), $BF_3 \cdot OEt_2$ (81 μL, 0.287 mmol) was added. The mixture was stirred at room temperature for 30 min, after which it was worked up in the usual manner. By flash chromatography (increasing polarity of hexane – ethyl acetate), compounds **3** (43 mg, 59%) and **11** (18 mg, 25%) were separated. Compound **3** was a

solid melting at 130–132°C (hexane–dichloromethane); ν_{max}(KBr)/cm^{-1}: 3500, 3020, 1745, 1180, 1125, 1040, and 850; δ_H: 5.30 (1H, brs, 3-H), 3.93 (1H, dd, *J* 9.8 and 11.1, 6-H), 3.62 (1H, dd, *J* 6.7 and 9.8, 1-H), 2.50–2.30 (1H, m, 2-H), 2.27 (1H, dq, *J* 6.8 and 12.2, 11-H), 2.19(1H, brd, *J* 11.1, 5-H), 1.79(3H, brs, 15-H), 1.20(3H, d, *J* 6.8, 13-H), and 0.86(3H, s, 14-H); *m/z* (EI): 250 (M^+, 14%), 235 ($M^+ - CH_3$, 1), 232 ($M^+ - H_2O$, 1), 222 (1), 217 (1), 167 (35), and 149 (100). Compound **11** was a solid melting at 138–139°C; ν_{max}(KBr)/cm^{-1}: 3490, 3090, 1750, 1650, 1150, 1135, 1045, 995, and 890; δ_H: 4.95(1H, brs, 15-H), 4.80(1H, brs, 15′-H), 4.03(1H, t, *J* 10.5, 6-H), 3.48(1H, dd, *J* 4.6 and 11.4, 1-H), 2.40–2.25(2H, m, 3-H and 11-H, overlapped signals), 2.02(1H, brd, *J* 10.5, 5-H), 1.20(3H, d, *J* 6.9, 13-H), and 0.80(3H, s, 14-H); *m/z* (EI): 250 (M^+, 1.4%), 233 (M^+ − OH, 3), 232 ($M^+ - H_2O$, 19) 217 (2), 206 (2), 191 (3), 177 (5), 165 (23), 147 (14), 121 (33), 107 (32), and 55 (100).

*1*β-tert-*Butyldimethylsilyloxy-5,7*α*H,6,11*β*H-eudesm-3-en-6,12-olide* ***12*** *from* ***3***

To a solution of dihydrosantamarine **3** (70 mg, 0.28 mmol) in DMF (2.4 mL), *tert*-butyldimethylsilyl chloride (182 mg, 1.17 mmol) and imidazol (229 mg, 3.37 mmol) were added. The temperature of the reaction was raised to 35–40°C, with stirring for 24 h. The reaction product, extracted with ethyl acetate, was chromatographed on silica gel, from which hexane – ethyl acetate (9:1) eluted compound **12** (90 mg, 88%), mp 123–126°C from hexane–ether; ν_{max}(KBr)/cm^{-1}; 3025, 1775, 1250, 1175, 1090, 860, 830, and 770; δ_H: 5.28(1H, brs, 3-H), 3.91(1H, dd, *J* 9.8 and 11.0, 6-H), 3.55(1H, dd, *J* 6.7 and 9.4, 1-H), 2.25(1H, dq, *J* 6.7 and 12.1, 11-H), 2.15(1H, brd, *J* 11.0, 5-H), 2.35–2.10(1H, m, 2-H, overlapped with 11-H and 5-H), 2.1–1.8(3H, m, 2′-H, 8-H, and 9-H), 1.77(3H, brs, 15-H), 1.65–1.40(2H, m, 7-H and 8′-H), 1.20(3H, d, *J* 6.7, 13-H), 1.12(td, 1H, *J* 3.7, 13.0, 9′-H), and 0.85 (12H, s, 14-H and Me-C-Si); *m/z* (CI, methane): 365 [$(M + H)^+$, 19%)], 307 [$(M + H)^+ - C_4H_{10}$, 39], 233 (100), 187 (27), 158 (12), and 157 (74). Anal. calcd. for $C_{21}H_{36}O_3Si$: C 69.18, H 9.95; found: C 69.2, H 9.9.

*1*β-tert-*Butyldimethylsilyloxy-3*α*-hydroperoxy-7*α*H,6,11*β*H-eudesm-4-en-6,12-olide* ***13*** *from* ***12***

Compound **12** (102 mg, 0.281 mmol) was dissolved in absolute ethanol (23 mL) and methylene blue (2.3 mg) was added. Oxygen was gently bubbled through the solution. The reaction tube was submerged in a water bath (17°C) thermostated by an external flow of cold methanol and irradiated by two lamps (HOSRAM HQL, 400 W each) for 7 h. The product was isolated by evaporating the solution to dryness, then dissolving the residue in dichloromethane and passing it through a short column of silica gel using ethyl acetate as solvent. After solvent removal, the residue was chromatographed on silica gel (increasing polarity of hexane – ethyl acetate) to afford unreacted starting material (6 mg, 6%), compound **14** (5 mg, 5%), and compound **13** (65 mg, 58%); ν_{max}(KBr)/cm^{-1}: 3500–3120, 1790, 1745, 1100, 1030, 985, 830, and 775; δ_H: 8.24(1H, s, OOH), 4.54 (1H, brd, *J* 10.5, 6-H), 4.20(1H, brs, 3-H), 3.72(1H, dd, *J* 3.6 and 12.5 Hz, 1-H), 2.3–2.2(2H, m, 2-H and 11-H), 1.95(3H, s, 15-H), 1.18(3H, d, *J* 6.8, 13-H), 1.03(3H, s, 14-H), 0.87(9H, s, Me-C-Si), 0.10(3H, s, Me-Si), and 0.03(3H, s, Me-Si).

*1*β-tert-*Butyldimethylsilyloxy-3-oxo-7*α*H,6,11*β*H-eudesm-4-en-6,12-olide* ***14*** *from* ***13***

A solution of hydroperoxide **13** (58 mg, 0.147 mmol) in pyridine (0.6 mL) was treated with acetic anhydride (3 drops) for 1 h. The reaction mixture was dissolved in ethyl acetate (100 mL), washed with diluted aqueous HCl and brine, and dried. Evaporation of the solvent yielded pure ketone **14** (55 mg, 99%), mp 146–148°C from hexane–ether; ν_{max}(KBr)/cm^{-1}: 1775, 1660, 1610, 1090, 1020, 980, 830, and 770; δ_H: 4.72(1H, dd, *J* 1.5 and 11.6, 6-H), 3.77(1H, t, *J* 8.8, 1-H), 2.53(2H, d, *J* 8.8, 2-H), 2.32(1H, dq, *J* 7.0 and 11.6, 11-H), 2.12(1H, dt, *J* 3.0 and 13.5, 9-H), 2.1–1.9(1H, m, 8-H), 1.96(3H, d, *J* 1.5, 15-H), 1.85(1H, qd, *J* 3.0 and 12.3, 8′-H), 1.29(1H, td, *J* 4.4 and 13.3, 9′-H), 1.23(3H, d, *J* 7.0, 13-H), 1.22(3H, s, 14-H), 0.86(9H, s, Me-C-Si), 0.05(3H, s, Me-Si), and 0.02(3H, s, Me-Si); *m/z* (CI, methane): 379 [$(M + H)^+$, 39%], 321 [$(M + H)^+ - C_4H_{10}$, 60], and 247 (100). Anal. calcd. for $C_{21}H_{34}O_4Si$: C 66.62, H 9.05; found: C 66.6, H 9.0.

*1*β-tert-*Butyldimethylsilyloxy-3*β*-hydroxy-7*α*H,6,11*β*H-eudesm-4-en-6,12-olide* ***15****a from* ***14***

A solution of compound **14** (38 mg, 0.101 mmol) in THF (1.3 mL) was treated at 0°C with LiAlH(O-*t*-Bu)$_3$ (142 mg, 0.50 mmol) in THF (1.3 mL) for 2 h. The reaction mixture was worked up in the usual way. Two products were separated by flash chromatography: the 3α-alcohol ***15****b* (9.9 mg, 26%) and the 3β-alcohol ***15****a* (24.9 mg, 65%). Compound ***15****b*, an oil; ν_{max} (NaCl)/cm^{-1}: 3520–3300, 1760, 1250, 1100, 1025, 980, 830, and 770; δ_H: 4.55(1H, brd, *J* 11.3, 6-H), 3.94(1H, brs, 3-H), 3.76(1H, dd, *J* 4.8 and 11.4, 1-H), 2.25(1H, dq, *J* 6.8 and 11.8, 11-H), 1.97(3H, s, 15-H), 1.03(3H, s, 14-H), 1.46(1H, qd, *J* 3.4 and 12.2, 8-H), 1.20(1H, d, *J* 6.8, 13-H), 1.03(3H, s, 14-H), 0.87(9H, s, Me-C-Si), 0.08(3H, s, Me-Si), and 0.04(3H, s, Me-Si); *m/z* (CI, methane): 363 [$(M + H)^+ - H_2O$, 16], 277 (9), 249, (100), 231 (35), 175 (15). Anal. calcd. for $C_{21}H_{36}O_4Si$: C 66.27, H 9.53; found: C 66.3, H 9.5. Compound ***15****a*, mp 155–157°C (hexane–ether); ν_{max}(KBr)/cm^{-1}: 3500, 1760, 1085, 1030, 1010, 980, 830, and 730; δ_H: 4.58(1H, dt, *J* 1.3 and 10.9, 6-H), 4.03(1H, ddd, *J* 1.3, 6.3 and 8.4, 3-H), 3.47(1H, dd, *J* 3.1 and 11.4, 1-H), 2.24(1H, dq, *J* 7.0 and 11.8, 11-H), 2.03(1H, ddd, *J* 3.1, 6.3, and 12.6, 2-H), 1.93(3H, s, 15-H), 2.00–1.60(1H, m, 7-H), 1.74(1H, ddd, *J* 8.4, 11.4, and 12.6, 2′-H), 1.49(1H, qd, *J* 3.2 and 12.0, 8′-H), 1.21(3H, d, *J* 7.0, 13-H), 1.12(3H, s, 14-H), 0.87(9H, s, Me-C-Si), 0.07(3H, s, Me-Si), and 0.03(3H, s, Me-Si); *m/z* (CI, methane): 3.63 [$(M + H)^+ - H_2O$, 19%], 277 (9), 249, (100), 231 (29), and 175 (20). Anal. calcd. for $C_{21}H_{36}O_4Si$: C 66.27, H 9.53; found: C 66.3, H 9.4.

*1*β-tert-*Butyldimethylsilyloxy-3*β*-acetoxy-7*α*H,6,11*β*H-eudesm-4-en-6,12-olide* ***16*** *from* ***15****a*

Compound ***15****a* (28 mg, 0.074 mmol) was treated with acetic anhydride (0.18 mL) in pyridine (0.25 mL) containing a catalytic amount of 4-dimethylaminopyridine for 3 h. Usual work-up yielded compound **16** (28 mg, 89%) as a colorless oil; ν_{max}(NaCl)/cm^{-1}: 1780, 1740, 1250, 1235, 1020, 835, and 770; δ_H 5.31(1H, brt, *J* 8.5, 3-H), 4.57(1H, dt, *J* 1.4 and 11.0, 6-H), 3.47(1H, dd, *J* 3.3 and 12.7, 1-H), 2.24(1H, dq, *J* 7.0 and 11.8, 11-H), 2.05(3H, s, MeCOO-), 2.1–1.9 (1H, m, 2-H), 1.75(3H, s, 15-H), 1.8–1.6 (2H, m, 2′-H and 7-H), 1.47(1H, qd, *J* 3.2 and 12.7, 8′-H), 1.20(3H, d, *J* 7.0, 13-H), 1.12(3H, s, 14-H), 0.85(9H, s, Me-C-Si), 0.05(3H, s, Me-Si), and 0.01(3H, s, Me-Si); *m/z* (CI, methane): 363 [$(M + H)^+ - CH_3COOH$, 42%], 277 (11), 249 (100), 231 (40), 185 (17), 157 (29), and 117 (32). Anal. calcd. for $C_{23}H_{38}O_5Si$: C 65.36, H 9.06); found: C 65.4, H 9.0.

*1*β-*Hydroxy-3*β*-acetoxy-7*α*H,6,11*β*H-eudesm-4-en-6,12-olide (torrentin)* ***1*** *from* ***16***

Compound **16** (20 mg, 0.048 mmol), dissolved in THF (0.35 mL), was treated for 5 min with *n*-$Bu_4NF \cdot 3H_2O$ (57 mg, 0.18 mmol), dried overnight *in vacuo*, then over P_2O_5. The reaction mixture was worked up in the usual way and chromatographed on silica gel (flash, hexane–ether 4:6) affording torrentin (**1**) (14 mg, 92%) as a solid of melting point 202–204°C (hexane–ether); $[\alpha]_D^{24}$ +36.0 (*c* 0.67, $CHCl_3$); ν_{max}(KBr)/cm^{-1}: 3500, 3300–3200, 1780, 1760, 1705, 1660, 1260, 1240, 1170, 1020, and 980; δ_H: 5.31(1H, brt, *J* 8.2, 3-H), 4.60(1H, dt, *J* 1.5 and 11.1, 6-H), 3.53 (1H, brd, *J* 3.0 and 12.3, 1-H), 2.26 (1H, dq, *J* 7.0 and 11.8, 11-H), 2.16(1H, ddd, *J* 3.0, 6.7, and 12.0, 2α-H), 2.06(3H, s, CH_3COO-), 2.1–2.0(1H, m, 9β-H), 2.0–1.8(1H, m, 8α-H), 1.78(3H, s, 15-H), 1.8–1.6(2H, m, 2β-H and 7-H, overlapped signals), 1.53(1H, qd, *J* 3.4 and 12.1, 8β-H), 1.25(1H, td, *J* 3.8 and 13.2, 9α-H), 1.21(3H, d, *J* 6.9, 13-H), and 1.16(3H, s, 14-H); *m/z* (EI): 308 (M^+, 2%), 290 ($M^+ - H_2O$, 0.1), 266 (1.2), 248 ($M^+ - CH_3COOH$, 100), and 233 (16). Anal. calcd. for $C_{17}H_{24}O_5$: C 66.21, H 7.84); found: C 66.2, H 7.8.

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