Tetrahedron Vol. 49, No. 12, pp. 2457-2468, 1993
Printed in Great Britain

0040-4020/93 $6.00+.00
Pergamon Press Ltd

SYNTHESIS OF AN ADVANCED FORSKOLIN INTERMEDIATE

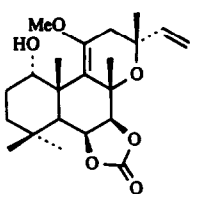
Stefan Bick, Silke Zimmermann, Heike Meuer, William S.Sheldrick, and Peter Welzel*
Fakultät für Chemie der Ruhr-Universität, Postfach 102148, D-4630 Bochum (Germany)

(*Received in Germany* 28 *December* 1992)

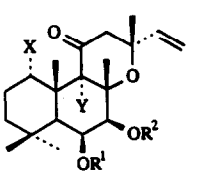
Abstract - The 8,13-epoxylabdane derivative *rac*-**19** was prepared in eight steps commencing from (E,E)-farnesol (**8**). Key reactions are the formation of **7** from drimenal (**9b**) and **6**, Sharpless I epoxidation (**7**→**11**), epoxy alcohol oxidation (**11**→**16**), reductive epoxide cleavage (**16**→**15**), peracid epoxidation (**15**→**18**), and the trimethylsilyl triflate-mediated conversion of **18** into **19**.

Introduction

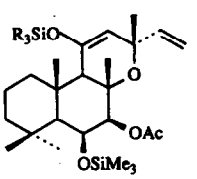
The unexpected and highly interesting direct stimulation of the enzyme adenylate cyclase by forskolin (**2a**)[1] and the rather complex structure of this labdane diterpene have provoced great efforts directed at its synthesis.[2] Three total syntheses of **2a** have been reported until now.[2] In contrast to the published total syntheses we planned to develop a synthetic approach towards **2a** making use of the fact that 1,9-dideoxyforskolin **2c** can be converted into **2a** by a combination of chemical and enzymatic steps.[3] Thus, 1α-hydroxylation of **2c** with *Neurospora crassa* furnished in about 20% yield 9-deoxyforskolin (**2b**)[4] which was chemically converted into **2a** via enol ether **1**.[5] Whereas in the 9-deoxy series (with the 1α-OH group) under basic conditions 9,11-enolate formation occurs (cf. **1**[5]) the 1,9-dideoxy compounds under the same conditions



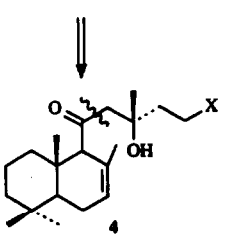
1



2	X	Y	R¹	R²
a	OH	OH	H	Ac
b	OH	H	H	Ac
c	H	H	H	Ac
d	H	OH	H	Ac

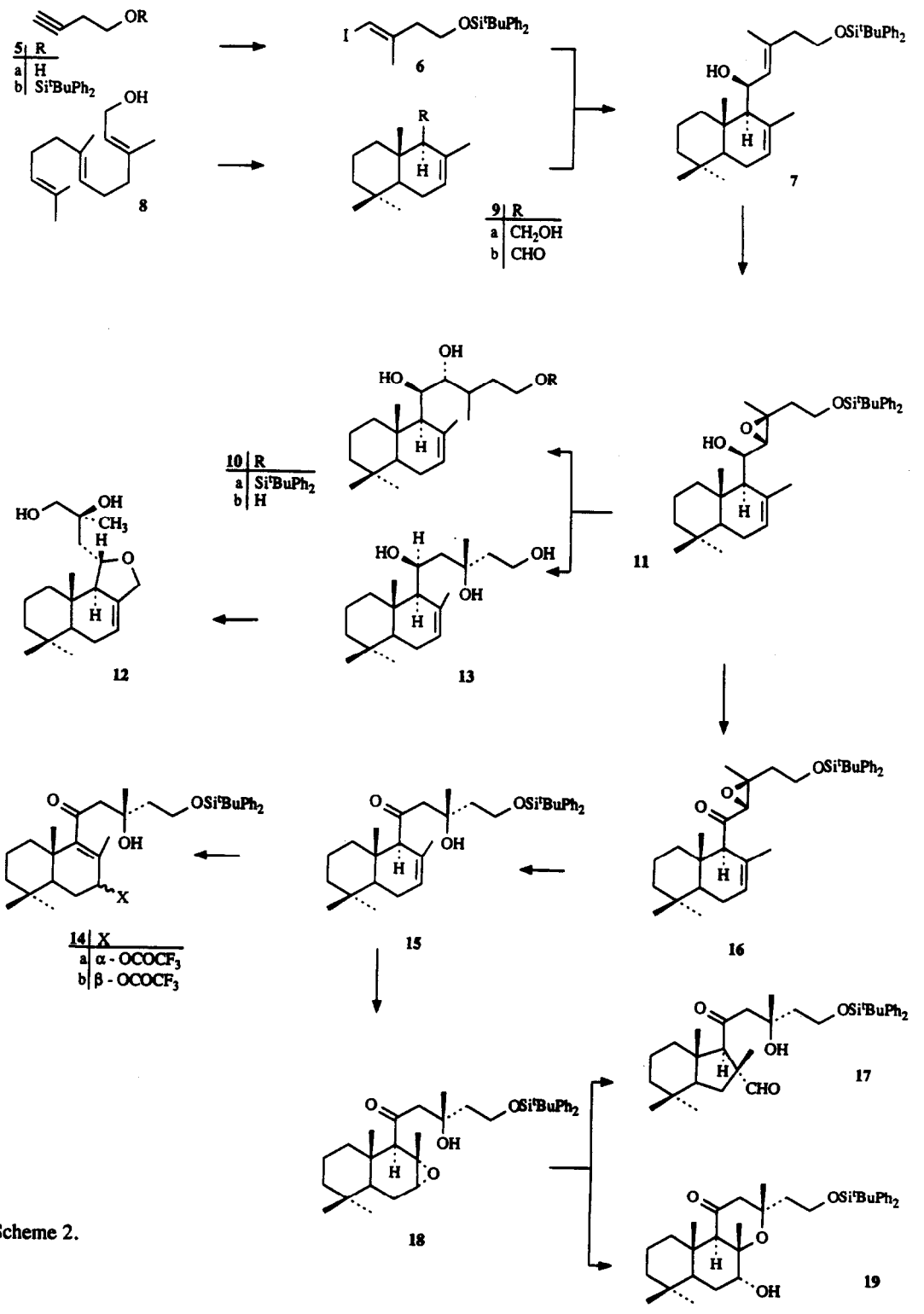


3



4

Scheme 1.


5 R
a H
b SitBuPh2
OR
OH
8
I
OSitBuPh2
6
R
H
9 R
a CH2OH
b CHO
HO
H
7
OH
HO
OR
10 R
a SitBuPh2
b H
HO
OH
CH3
H
O
12
H
HO
OH
OH
13
11
O
16
15
14 X
a α - OCOCF3
b β - OCOCF3
X
17
CHO
18
19

Scheme 2.

form the 11,12-enolates (cf. 3[6]). Allylic oxidation with selenium dioxide then allows introduction of the 9α-OH group to give a deoxyforskolin derivative of type 2d[7] which also can microbiologically be hydroxylated in the 1-position (*Neurospora crassa*).[4,8] Even the direct 1,9-dihydroxylation with *a Scopuloriopsis sp.* has been achieved albeit in low yield.[9]

What follows in this article is the description of a sequence of reactions leading from **8** to **19**, which is a potential intermediate on the way to **2c**. This work is based on the retrosynthetic analysis indicated in **2c** ⇒ **4**.

Synthesis of Bicyclic Labdane Derivatives *rac*-13 and *rac*-15

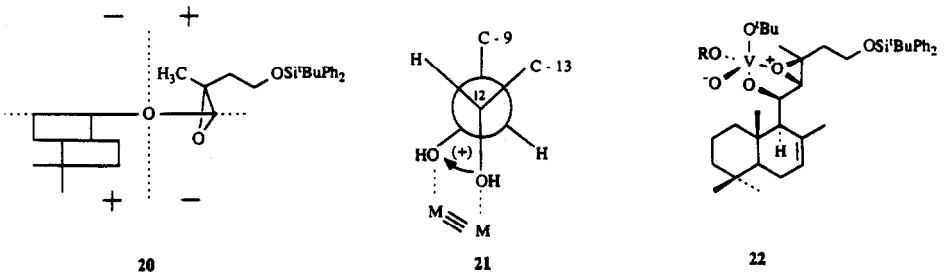
The labdane skeleton was constructed from aldehyde *rac*-**9b** and the C_5 building block **6**. *Rac*-**9b** was prepared making use of the excellent fluorosulfonic acid-mediated cyclization of trans,trans-farnesol (**8**) described by Vlad[10] which provided (±)-drimenol (*rac*-**9a**) in 52% yield, followed by pyridinium dichromate (PDC)[11] oxidation. Zirconocene-mediated carboalumination of **5b** with trimethylaluminum[12] and subsequent trapping of the intermediate organometallic with iodine gave vinyl iodide **6** (69%). Halogen-metal exchange with tert-butyllithium provided the corresponding vinyllithium reagent which reacted with *rac*-**9b** to furnish *rac*-**7** in a yield of 55%. A single (racemic) stereoisomer was formed the configuration of which at C-11 was determined at a later stage. Sharpless I epoxidation of *rac*-**7** with vanadyl acetylacetonate - tert-butyl hydroperoxide[13] was again stereoselective. The configurational assignment at the newly created stereogenic centres at C-12 and C-13 of *rac*-**11** will be discussed below. The reagent of choice for the opening of α-hydroxy epoxides to give 1,3 diols is REDAL.[14] However, this reagent failed completely in the present case. No reaction was observed even at 80°C. As expected,[14] lithium aluminum hydride opened the epoxide in both directions. Three products were obtained. Disappointingly, the desired 1,3 diol was a minor product: the ratio of the 1,2-diols *rac*-**10a** and *rac*-**10b** and the 1,3-diol *rac*-**13** was roughly 5:2. The 1,2-diols may be mixtures of 13-epimers, this point has, however, not been clarified. To overcome the problems associated with installing the oxygen functionalities properly at C-11 and C-13, epoxy alcohol *rac*-**11** was oxidized with PDC[11] to give *rac*-**16** (84% yield). For the conversion of α,ß-epoxy ketones to ß-hydroxy ketones exist two general approaches. One includes a nucleophilic substitution at the α-position by reagents such as iodide[15] or a selenide[16] followed by a redox process leading to the ketone enolate. The other methodology is based on electron transfer to the CO group either in the ground or in the excited state and subsequent epoxide opening. The first-mentioned procedure did not work in the present instance, neither with iodide nor with selenide.[17] In contrast, the second approach proved suitable for the conversion of *rac*-**16** into *rac*-**15**. Thus, irradiation of *rac*-**16** in the presence of triethylamine[18] led to the formation of *rac*-**15** in about 56% yield. The SmI_2-induced reaction[19] was even more effective and provided *rac*-**15** in 89% yield.

Configurational Assignments of 7, 10, 11, 13, 15, and 16

The result of an X-ray analysis of *rac*-**15** is depicted in Figure 1 demonstrating the desired (SR) configuration at C-13. From this result and the known configuration around the double bond in **7** the configuration at C-12 and C-13 of the epoxy ketone **16** could be assigned as well as the configuration at C-12 in **10a/10b** and at C-13 in **13**. The other stereochemical problems were solved using circular dichroism (CD). (+)-Drimenol (*ent*-**9a**)[20] was converted into *ent*-**10b** as described above for the racemic series. The Snatzke group has shown that optically active 1,2- (and 1,3-) diols react with $[Mo_2(OAc)_4]$ in DMSO

solution to form *in-situ* complexes the CD of which at around 300 nm can be correlated with the configuration of the diol. For open-chain vicinal sec,sec-glycols the sign of the torsional angle O-C-C-O is the same as that of the 300 nm band assuming a conformation of the complex in which each O-C-C-R moiety is antiperiplanar as indicated in formula **21** (Scheme 3).[21] For *ent*-**10b** the positive Cotton effect at 304 nm ($\Delta\varepsilon$ = + 1.1) is indicative of a positive torsional angle O-C-12-C-11-O corresponding to the (R)-configuration at C-11 in **10b**. From this result the relative configuration at C-11 of **7** and **13** can be deduced. Further, for the epoxidation of **7** to give **11** a transition state geometry as indicated in formula **22** can be assumed.[13]

With *ent*-**11** in hand we also tried to determine the preferred conformation of the epoxy ketone unit of **16** in solution. *Ent*-**11** was oxidized to give *ent*-**16** the CD of which at 311 nm was negative ($\Delta\varepsilon$ = -2.0). If it is the α,ß-epoxy ketone unit which determines the CD, then, based on the *reversed octant rule*,[22] a conformation as depicted in **20** can be assumed.



20 **21** **22**

Scheme 3.

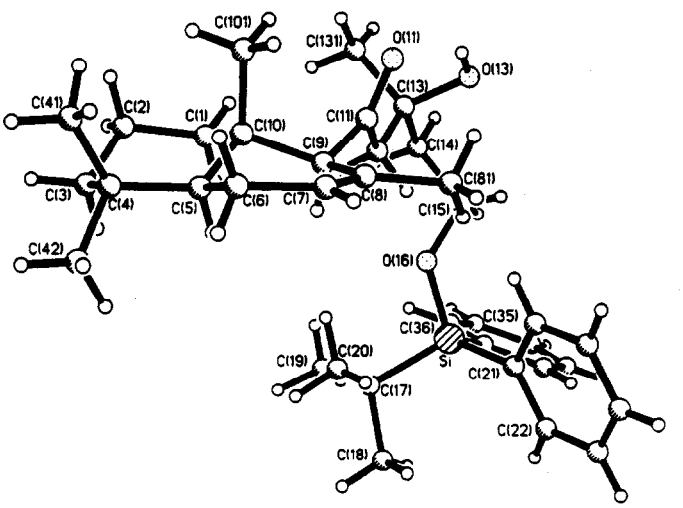
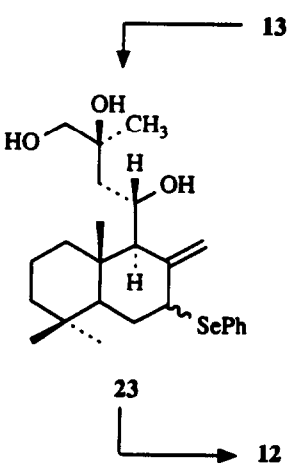


Figure 1. X-ray crystal structure of rac-**15**

Cyclization Studies

When compound *rac*-13 was treated with N-phenylselenophthalimide[23] in the presence of $SnCl_4$ 11,17-epoxide *rac*-12 rather than the desired 8,13-epoxide was obtained. An ene-type reaction to give an intermediate 23 followed by an S_N' reaction may explain the formation of this compound.

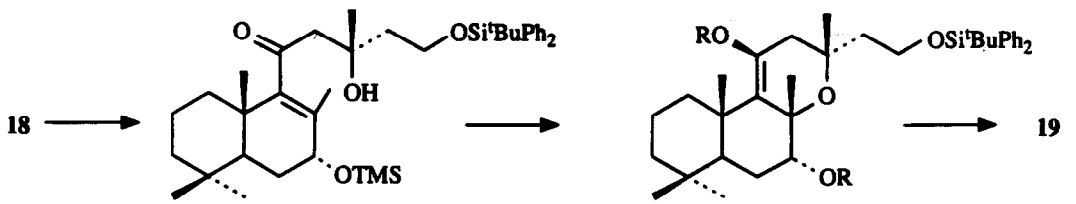


Scheme 4.

An attempted cyclization of *rac*-15 with mercury (II) trifluoroacetate was also unsuccessful. The epimeric allylic 7-trifluoroacetates *rac*-14a and *rac*-14b were formed probably via allylic organomercury intermediates.[24] The configurational assignment is based on the fact, that in *rac*-14b a NOE between 7-H and 5-H was observed.

Epoxidation of *rac*-15 with m-chloroperbenzoic acid yielded stereoselectively an 7,8-epoxide, *rac*-18, the α configuration of which was apparent from its $SnCl_4$-mediated rearrangement[25] which furnished *rac*-17.[26] The α configuration of the aldehyde group could be assigned on the basis of an NOE between the aldehyde proton and 9-H. When *rac*-18 was subjected to a trimethylsilyl triflate-mediated cyclization[27] a single cyclization product was formed which according to an X-ray analysis (see Figure 2) has structure *rac*-19. A NOE between the OH group and 9-H also indicated the axial orientation of the OH group. The configuration of *rac*-19 at C-7 and C-8 is a strong hint, that the cyclization is not a straightforward process.[28]

Probably the epoxide rearranges, triggered by the 11-keto group, to the allylic alcohol derivative *rac*-24 which on conjugate addition to the enone cyclizes to *rac*-25 the precursor of *rac*-19.



24 25

Scheme 5.

In conclusion: We have been able to synthesize the 8,13-epoxylabdane derivative *rac*-19 starting from trans,trans-farnesol (8) in eight steps. Further work on the conversion of rac-19 into *rac*-2c is in progress and will be reported in due time.

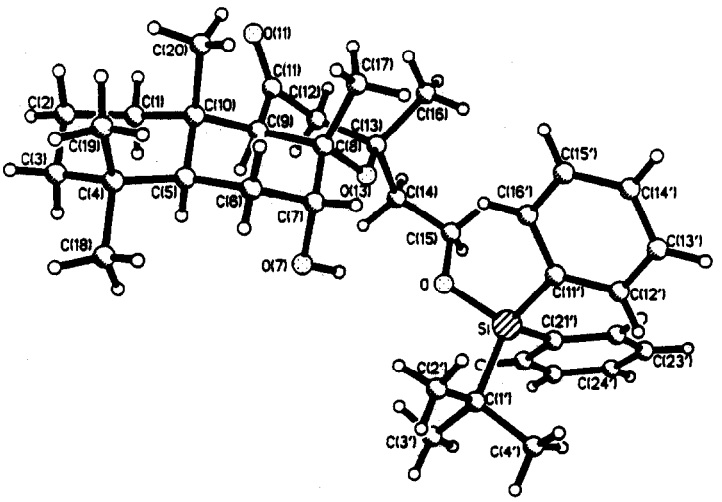


Figure 2. X-ray crystal structure of rac-19

EXPERIMENTAL

For general methods, instrumentation, and abbreviations, see ref.[29]; PG = protecting group

(±)-Drim-7-en-11-ol (*rac*-9a)

Fluorosulfonic acid (0.71 mL) was slowly added at -78° C to a stirred solution of t,t-farnesol (2.49g, 11.2 mmol) in 10:1 nitropropane - CH_2Cl_2 (190 mL). The reaction mixture was stirred at - 78° C for 1 h. After quenching with triethylamine (2.5 mL) usual work-up (CH_2Cl_2) followed by LC (petrol - ethyl acetate 8:1) gave *rac*-**9a** (1.3 g, 52%).

4-(tert-Butyl-diphenyl-silyloxy)-1-butyne (**5b**)

To a solution of 3-butyn-1-ol (1.12 g, 16 mmol), DMAP (0.5 g, 4 mmol), and triethylamine (2.6 g, 19 mmol) in CH_2Cl_2 (40 mL) ^{t}butyldiphenylsilyl chloride (5.4 mL, 20 mmol)[30] was added at 20°C. The mixture was left at 20°C for 2h. Usual work-up (CH_2Cl_2) and LC (petrol-ethyl acetate 10:1) furnished **5b** (5.54 g, 100%).- ^{1}H NMR (100 MHz, $CDCl_3$), δ = 1.08 (s, 9H, ^{t}butyl), 1.97 (t, 1H, 1-H), 2.48 (dt, 2H, CH_2-3), 3.81 (t, 2H, CH_2-4), 7.30-7.85 (10H, aromat. H), $J_{3,4}$ = 7 Hz, $J_{1,3}$ = 2.5 Hz.- IR (CCl_4): 3300 (C≡C-H), 1580 cm^{-1} (C=C).- $C_{20}H_{24}OSi$ (308.7), MS: m/z (%) = 251 (100), 221 (98), 211 (25), 105 (60).

(E)-4-(tert-Butyl-diphenyl-silyloxy)-1-iodo-2-methyl-1-butene (**6**)

To a solution of trimethylaluminum (2 mol/l solution in hexane, 2.3 mL, 6.4 mmol) and zirconocene dichloride (936.9 mg, 3.2 mmol) in CH_2Cl_2 (15 mL) a solution of **5b** (987.9 mg, 3.2 mmol) in CH_2Cl_2 (2 mL) was added at 0 °C. The mixture was stirred at 20°C for 14 h. At -23 °C a solution of I_2 (1035 mg, 4 mmol) in THF (10 mL) was added. Within 15 min the mixture was allowed to warm to 0°C. After addition of saturated aq. ammonium chloride (6 mL) and aq. saturated sodium thiosulfate (3 mL) usual work-up (CH_2Cl_2) followed by LC (petrol-ethyl acetate 40:1) provided **6** (998.2 mg, 69%).- ^{1}H NMR (80 MHz, $CDCl_3$), δ = 1.05 (s, 9H, ^{t}butyl), 1.68 (d, 3H, CH_3-5), 2.41 (dt, 2H, CH_2-2), 3.72 (t, 2H, CH_2-1), 5.91

(q, 1H, CH-4), 7.25-7.78 (10H, aromat. H).- IR ($CHCl_3$): 1120 cm^{-1} (C-O).- $C_{21}H_{27}OSiI$ (450.4), MS: m/z (%) = 393 (45), 235 (37), 183 (100), 105 (53).

(S,R)-15-(tert-Butyl-diphenyl-silyloxy)-*rac*-labd-7,12-dien-11-ol (*rac*-7)
A solution of **6** (214.1 mg, 0.47 mmol) in THF (4 mL) was cooled to -78 °C. tert-Butyllithium (1.7 mol/l in hexane, 0.205 mL, 0.35 mmol) was added and the reaction mixture was stirred at -78°C for 2 h. After slow addition of a solution of (±)-drimenal (*rac*-**9b**, 31.6 mg, 0.14 mmol) in THF (2 mL) the reaction mixture was stirred at -78°C for 1 h. Hydrolysis with saturated aq. ammonium chloride (-78°C→20°C), followed by usual work-up (CH_2Cl_2) and LC (petrol-ethyl acetate 30:1 + 1% NEt_3) yielded **7** (68.8 mg, 55%).- ^1H NMR (400 MHz, $CDCl_3$), δ = 0.84, 0.88, 0.99 (3s, 9H, CH_3-18, CH_3-19, CH_3-20), 1.02 (s, 9H, ^{t}butyl), 1.60 (d, J ≈ 2 Hz, 3H, CH_3-16), 1.82 (broad s, 3H, CH_3-17), 2.21 (m, 2H, CH_2-14), 3.73 (t, 2H, CH_2-15), 4.63 (dd, 1H, 11-H), 5.56-5.63 (2H, 7-H, 12-H), 7.31-7.68 (10H, aromat. H), $J_{11,12}$ = 3 Hz, $J_{11,12'}$ = 8 Hz, $J_{14,15}$ = 6.72 Hz.- IR (CCl_4): 3600 (OH), 1110 cm^{-1} (C-O).- MS: m/z (%) = 526 (2.2), 487 (2.0), 469 (8.3), 353 (20), 199 (100), 135 (59), 97 (97).- $C_{36}H_{52}O_2Si$ (544.8) calcd C 79.35, H 9.62, found C 79.28, H 9.61.

(R)-15-(tert-Butyl-diphenyl-silyloxy)-*ent*-labd-7,12-dien-11-ol (*ent*-7)
Prepared from **6** and (-)-drimenal as decribed above. $[\alpha]_D$ = 7.5 (c 1.12 in $CHCl_3$).

(11RS, 12RS, 13SR)-15-(tert-Butyl-diphenyl-silyloxy)-12,13-epoxy-*rac*-labd-7-en-11-ol (*rac*-11)
To a solution of *rac*-**7** (15.3 mg, 0.028 mmol) in benzene (1 mL) vanadyl acetylacetonate (0.11 mg, 0.4 μmol) was added at 20°C. On addition of tert-butyl hydroperoxide (≈ 80 per cent in di-tert-butyl peroxide, dried over 4Å molecular sieves, according to iodometric titration 3.6 mol/l , 0.4 μl, 0.062mol) the colour of the solution turned from pink to colourless and then to yellow. Addition of water, usual work-up (CH_2Cl_2), and LC (petrol-ethyl acetate 30:1 + 0.1% NEt_3) yielded *rac*-**11** (11.8 mg, 75%)- ^1H NMR (400 MHz, $CDCl_3$), δ = 0.84, 0.88, 0.99 (3s, 9H, CH_3-18, CH_3-19, CH_3-20), 1.02 (s, 9H, ^{t}butyl), 1.38 (s, 3H, CH_3-16), 1.82 (s, $W_{1/2}$ = 6 Hz, 3H, CH_3-17), 3.18 (d, 1H, 12-H), 3.73 (t, 2H, CH_2-15), 3.88 (d, 1H, 11-H), 5.59-5.63 (1H, 7-H), 7.31-7.68 (10H, aromat. H), $J_{11,12}$ = 7 Hz, $J_{14,15}$ = 6Hz.- IR (CCl_4): 3500 (OH), 1100 cm^{-1} (C-O).- MS: m/z (%) = 542 (0.5), 503 (1), 473 (2), 425 (4.0), 269 (77), 199 (100), 109 (77).- $C_{36}H_{52}O_3Si$ (560.8) calcd C 77.09, H 9.35, found C 76.96, H 9.54.

(11S, 12S, 13R)-15-(tert-Butyl-diphenyl-silyloxy)-12,13-epoxy-*ent*-labd-7-en-11-ol (*ent*-11)
Prepared from *ent*-**7** as described above. $[\alpha]_D$ = 25.3 (c 1.04 in $CHCl_3$).

Opening of Epoxide 11 with $LiAlH_4$.
a) A solution of *rac*-**11** (58.0 mg, 0.1 mmol) in THF (3 mL) was added to $LiAlH_4$ (47.0 mg, 0.24 mmol) partially dissolved in THF (1.0 mL). After stirring at 20°C for 24 h H_2O (1 mL) was added. Usual work-up (CH_2Cl_2) and LC (petrol-ethyl acetate 5:1, then petrol-ethyl acetate 1:2) furnished *rac*-**10a** (12.5 mg, 22%) and a mixture of *rac*-**10b** und *rac*-**13** (26 mg) which was separated by preparative HPLC (5 μm Si 100 (Merck), toluene-acetone-triethylamine 15:1:1) to give *rac*-**13** (6.6 mg, 20%) and *rac*-**10b** (10.1 mg, 31%).
b) Using the same procedure *ent* -**10a**, *ent*-**10b**, and *ent*-**13** were prepared from *ent*-**11**.

(11RS, 12RS,13Ξ)-15-(tert-Butyl-diphenyl-silyloxy)-*rac*-labd-7-ene-11,12-diol (*rac*-**10a**)
^1H NMR (400 MHz, $CDCl_3$), δ = 0.82, 0.86, 0.89, 1.01 (4s, 12H, CH_3-16, CH_3-18, CH_3-19, CH_3-20), 1.08 (s, 9H, ^{t}butyl), 1.82 (s, 3H, CH_3-17), 2.22 (s, $W_{1/2}$ = 6 Hz, OH), 2.95 (s, $W_{1/2}$ = 8 Hz, OH), 3.65-3.72 (1H, 15-H), 3.74-3.82 (2H, 12-H, 15-H), 3.83-3.90 (d, 1H, 11-H), 5.10-5.15 (1H, 7-H), 7.31-7.69 (10H, aromat. H), $J_{11,12}$ = 10 Hz, $J_{14,15}$ = 6 Hz.- IR (CCl_4): 3640 (OH), 3600-3220 cm^{-1} (OH).- $C_{36}H_{54}O_3Si$ (562.8), MS: m/z (%) = 544 (0.2), 487 (3), 371 (15), 283 (15), 235 (30), 199 (40), 115 (100).

(11S, 12S,13Ξ)-15-(tert-Butyl-diphenyl-silyloxy)-*ent*-labd-7-ene-11,12-diol (*ent*-**10a**)
$[\alpha]_D$ = -3.7 (c 1.02 in $CHCl_3$).- CD of the *in-situ* complex with $Mo_2(OAc)_4$ (for details, see under *ent*-**10b**): λ_{max} ($\Delta\varepsilon$) = 310 nm (+ 1.3).

(11RS, 13SR)-*rac*-Labd-7-en-11,13,15-triol (*rac*-**13**)
^1H NMR (400 MHz, $CDCl_3$, H,H COSY), δ = 0.84, 0.88, 0.99 (3s, 9H, CH_3-18, CH_3-19, CH_3-20), 1.24 (dd, 1H, 12-H), 1.38 (s, 3H, CH_3-16), 1.69 (t, CH_2-14), 1.89 (s, 3H, CH_3-17), 2.41 (dd, 1H, 12-H), 3.88 (m, 2H, CH_2-15), 4.49 (dd, 1H, 11-H), 5.56-5.63 (1H, 7-H), $J_{11,12}$ = 12 Hz, $J_{11,12'}$ = 3 Hz, $|J_{12,12'}|$ = 14.5 Hz, $J_{14,15}$ = 6 Hz.- ^{13}C NMR (100.6 MHz, $CDCl_3$, DEPT), δ = 14.73 (CH_3-20) 18.94 (CH_2-2), 22.52 (CH_3-19), 23.61 (CH_2-6), 25.15 (CH_3-17), 26.19 (CH_3-16), 33.09 (Cq-4/10), 33.62 (CH_3-18), 37.48 (Cq-4/10), 40.31 (CH_2-3), 42.31 (CH_2-1), 44.04 (CH_2-14), 48.05 (CH_2-12), 50.13 (CH-5), 59.88 (CH_2-15), 60.71 (CH-9), 67.53 (CH-11), 75.00 (Cq-13), 127.47 (CH-7), 132.13 (Cq-8).- IR (CCl_4): 3620 (OH), 3580-3080 cm^{-1} (OH).- $C_{20}H_{36}O_3$ (324.5), MS: m/z (%) = 233 (1.9), 115 (100), 109 (35), 43 (43).

(-)-(11S, 13R)-*ent*-Labd-7-en-11,13,15-triol (*ent*-**13**)
$[\alpha]_D$ = -2.9 (c 1.17 in $CHCl_3$).

(11RS, 12RS, 13Ξ)-*rac*-Labd-7-ene-11,12,15-triol (*rac*-**10b**)
^1H NMR (400 MHz, $CDCl_3$), δ = 0.84, 0.88 (2s, 6H, CH_3-18, CH_3-19), 0.91 (d, J = 7 Hz, 3H, CH_3-16), 0.99 (s, 3H, CH_3-20), 1.61 (m, 2H, CH_2-14), 1.82 (s, 3H, CH_3-17), 3.68 (m, 1H, 15-H), 3.73-3.82 (2H, 12-H, 15-H´), 3.88 (dd, 1H, 11-H), 5.56-5.63 ($W_{1/2}$ = 10 Hz, 1H, 7-H), $J_{11,12}$ = 10 Hz, $J_{14,15}$ = 6 Hz.- ^{13}C NMR (100.6 MHz, $CDCl_3$, DEPT), δ = 11.17 (CH_3-16), 15.00 (CH_3-20), 18.76 (CH_2-2), 22.27 (CH_3-19), 23.46 (CH_2-6), 25.01 (CH_3-17), 30.58 (CH-13), 32.90 (Cq-4 or Cq-10), 33.38 (CH_3-18), 37.10 (Cq-4 oder Cq-10), 38.27 (CH_2-1), 40.49 (CH_2-3), 42.03 (CH_2-14), 49.94 (CH-5), 55.74 (CH-9), 59.59 (CH_2-15), 69.84 (CH-11/12), 75.51 (CH-11/12), 127.40 (CH-7), 131.55 (Cq-8).- IR (CCl_4): 3680-3080 cm^{-1} (OH).- $C_{20}H_{36}O_3$ (324.5), MS: m/z (%) = 291 (1.0), 279 (0.8), 218 (15), 192 (20), 177 (30), 115 (100), 97 (67), 69 (85).

(-)-(11S, 12S, 13Ξ)-*ent*-Labd-7-ene-11,12,15-triol (*ent*-**10b**)
$[\alpha]_D$= -7.2 (c 0.69 in $CHCl_3$).- For the configurational assignment at C-11 *ent*-**10b** (2.7 mg) was treated with $Mo_2(OAc)_4$, and from the in situ complex the CD was measured as descibed in ref.[21], solvent DMSO (c 0.877 mmol/l), path length: 0.2 cm, λ_{max} ($\Delta\varepsilon$) = 304 nm (+ 1.13).

(12RS,13SR)-15-(tert-Butyl-diphenyl-silyloxy)-12,13-epoxy-*rac*-labd-7-en-11-one (*rac*-**16**)
A solution of *rac*-**11** (41.2 mg, 0.073 mmol) in 4 mL CH_2Cl_2 was added to a stirred suspension of pyridinum dichromate (221 mg, 0.588 mmol) in CH_2Cl_2 (3 mL). The mixture was stirred for 8 h at 20°C and then filtered through Florisil (elution with ether, 80 mL). LC (petrol-ethyl acetate 15:1) furnished *rac*-**16** (34.4mg, 84%).- ^1H NMR (400 MHz, $CDCl_3$), δ = 0.84, 0.85, 0.86 (3s, 9H, CH_3-18, CH_3-19, CH_3-20), 1.02 (s, 9H, ^{t}butyl), 1.32 (s, 3H, CH_3-16), 1.57 (s, 3H, CH_3-17), 3.39 (s, 1H, 9-H), 3.47 (s, 1H 12-H), 3.78 (dt, 2H, CH_2-15), 5.52-5.59 (m, 1H, 7-H), 7.32-7.63 (10 H, aromat. H), $J_{14,15}$ = 6.5 Hz.- IR (CCl_4): 1700 cm^{-1} (C=O).- MS: m/z (%) = 558 (1), 501 (12), 471 (11), 423 (10), 377 (10), 199 (100), 135 (38), 95 (54).- $C_{36}H_{50}O_3Si$ (558.8) calcd C 77.37, H 9.02, found C 77.35, H 9.13.

(12S,13R)-15-(tert-Butyl-diphenyl-silyloxy)-12,13-epoxy-*ent*-labd-7-en-11-one (*ent*-**16**)
Ent-**16** was prepared from *ent*-**11** as described for *rac*-**16**.- CD (c 1.14 mol/l in acetonitrile): λ_{max} ($\Delta\varepsilon$) = 311 (- 2.0), 237 nm (- 2.9).

(13SR)-15-(tertButyl-diphenyl-silyloxy)-13-hydroxy-*rac*-labd-7-en-11-one (*rac*-**15**)
A stream of argon was passed through a solution of *rac*-**16** (30 mg, 0.054 mmol) in acetonitrile (10 mL).

Then triethylamine (41 µl, 0.27 mmol) was added and the solution was irradiated (254 nm, Rayonet reactor) under argon for 20 min with 254 nm light (quartz vessel). Solvent evaporation and subsequent LC (petrol-ethyl acetate 15:1) provided *rac*-**15** (16.7 mg, 56%).
b) To a solution of *rac*-**16** (63 mg, 0.11 mmol) in 2:1 THF - methanol (6 mL), cooled to -90 °C, were added two portions of 0.1 mol/l SmI_2 in THF [a) 5.5 mL, 0.55 mmol, b) 2.2 mL, 0.22 mmol] until a slightly blue colour persisted. At -70°C saturated aq. K_2CO_3 (5 mL) was added and the mixture was allowed to warm to 20°C. Usual work-up (CH_2Cl_2) and LC (petrol-ethyl acetate 10:1) provided *rac*-**15** (54.7 mg, 89%).- M.p.113°C (CH_2Cl_2/hexane).- ^{1}H NMR (400 MHz, C_6D_6), δ = 0.82 (s, 6H) 1.08 (s, 3H) (CH_3-18, CH_3-19, CH_3-20), 1.19 (s, 9H, ^{t}butyl), 1.37 (s, 3H, CH_3-16), 1.60 (s, 3H, CH_3-17), 2.69, 2.74 (2d, 2H, CH_2-12), 2.98 (s, $W_{1/2}$ = 7.5 Hz, 1H, 9-H), 3.90-4.07 (2H, CH_2-15), 4.37 (s, $W_{1/2}$ = 6 Hz, 1H, OH), 5.45 (m, $W_{1/2}$ = 11 Hz, 1H, 7-H), 7.24-7.83 (10H, aromat. H), $|J_{12,12'}|$ = 18.5 Hz, $J_{14,15}$ = 6 Hz.- ^{13}C NMR (100.6 MHz, C_6D_6, DEPT), δ = 14.85 (CH_3-20), 19.00 (CH_2-2), 19.36 (Cq-PG), 21.75 (CH_3-19), 21.92 (CH_3-16), 24.08 (CH_2-6), 27.10 (CH_3-PG), 27.56 (CH_3-17), 33.08 (Cq-4/10), 33.49 (CH_3-18), 37.61 (Cq-4/10), 41.38 (CH_2-1), 42.28 (CH_2-3), 43.99 (CH_2-14), 49.60 (CH-5), 58.45 (CH_2-12), 61.33 (CH_2-15), 67.97 (CH-9), 71.51 (Cq-13), 124.42 (CH-7), 128.12 (CH-PG), 130.04 (CH-PG), 130.79 (Cq-8), 133.87 (Cq-PG), 135.96 (CH-PG), 214.03 (Cq-11).-IR (CCl_4): 3520 (OH), 1700 cm^{-1} (C=O).- MS: m/z (%) = 560 (7), 369 (45), 269 (30), 218 (30), 191 (100).- $C_{36}H_{52}O_3Si$ (560.8) calcd C 77.09, H 9.35, found C 77.19, H 9.50.

(11RS, 13SR)-11,17-Epoxy-*rac*-labd-7-ene-13,15-diol (*rac*-**12**)
To a solution of *rac*-**13a** (29.8 mg, 0.09 mmol) in CH_2Cl_2 (500 µl), cooled to -78 °C, a solution of N-phenylselenophthalimide (42.3 mg, 0.14 mmol) in CH_2Cl_2 (250 µl) and a 10 per cent solution of $SnCl_4$ in CH_2Cl_2 (85 µl, 0.07 mmol) were added. A slightly yellow precipitate was formed. The stirred reaction mixture was allowed to warm to 20°C within 3 h. At about -10°C the precipitate dissolved and a clear yellow solution resulted. TLC indicated that *rac*-**13a** was not completely consumed, therefore a further portion of each N-phenylselenophthalimide (42.3 mg, 0.14 mmol) and $SnCl_4$ (85 µl of the 10 per cent solution, 0.07 mmol) was added and the mixture was stirred at 20°C for another 30 min. After solvent evaporation and LC (petrol-ethyl acetate 10:1 + 0,1 % NEt_3) *rac*-**12** (slightly impure, 11.4 mg, 40 %) was obtained.- ^{1}H NMR (400 MHz, $CDCl_3$, H,H COSY), δ = 0.81, 0.89, 0.91 (3s, 9H, CH_3-18, CH_3-19, CH_3-20), 1.32 (s, 3H, CH_3-16), 3.75 (s, $W_{1/2}$ = 10 Hz, 1H, 15-OH), 3.83 ($W_{1/2}$ = 13 Hz, 2H, CH_2-15), 4.07 (mk, 1H, 11-H), 4.13 (m, 1H, 17-H), 4.34 (m, 1H, 17-H), 4.51 (s, $W_{1/2}$ = 3 Hz, 1H, OH), 5.50 (m, $W_{1/2}$ = 9 Hz, J = 2 Hz, 1H, 7-H), $|J_{17,17'}|$ = 12 Hz.- ^{13}C NMR (100.6 MHz, $CDCl_3$, DEPT), δ = 14.16 (CH_3-20), 18.54 (CH_2-2), 21.63 (CH_3-19), 23.79 (CH_2-6), 26.42 (CH_3-16), 32.90 (Cq-4 oder 10), 33.31 (CH_3-18), 34.27 (Cq-4 oder 10), 40.64 (CH_2-1), 42.15 (CH_2-3), 43.73 (CH_2-12), 46.44 (CH_2-14), 49.96 (CH-5), 59.51 (CH_2-15), 60.72 (CH-9), 69.19 (CH_2-17), 74.18 (Cq-13), 77.32 (CH-11), 116.36 (CH-7), 123.53 , 134.23, 137.31 (Cq-8).

Treatment of *rac*-**15** with Mercuric Trifluoroacetate
A solution of $Hg(OCOCF_3)_2$ (160.7 mg, 0.376 mmol) and *rac*-**15** (105.5 mg, 1.188 mmol) in benzene (3 mL) was stirred at 20°C for 6 h. Saturated aq NaCl (2 mL) was added. Usual work-up (CH_2Cl_2) and LC (petrol-ethyl acetate 40:1 + 0.1 % NEt_3) yielded *rac*-**14b** (18.8 mg, 15%) and *rac*-**14a** (19.4 mg, 15%) .

(7RS, 13SR)-15-(tert-Butyl-diphenyl-silyloxy)-13-hydroxy-7-trifluoracetoxy-*rac*-labd-8-en-11-one (*rac*-**14a**)
^{1}H NMR (400 MHz, C_6D_6), δ = 0.58, 0.67, 1.11 (3s, 9H, CH_3-18, CH_3-19, CH_3-20), 1.15 (s, 9H, ^{t}butyl), 1.32, 1.38 (2s, 6H, CH_3-16, CH_3-17), 1.88-2.06 (3H multiplet containing the CH_2-14 signals), 2.65, 2.81 (2d, 2H, CH_2-12), 3.89-4.02 (2H, CH_2-15), 5.28 (t, J = 3 Hz, 1H, 7-H), 7.19-7.26 (6H, aromat. H), 7.72-7.80 (4H, aromat. H), $|J_{12,12'}|$ = 19 Hz.- ^{13}C NMR (100.6 MHz, C_6D_6, DEPT), δ = 15.17 (CH_3-20), 18.53 (CH_2-2), 19.29 (Cq-PG), 20.78 (CH_3-19), 21.31 (CH_3-16), 25.27 (CH_2-6), 27.04 (CH_3-PG), 27.41 (CH_3-17), 32.70 (CH_3-18), 32.93 (Cq-4 or Cq-10), 36.93 (CH_2-1), 38.21 (Cq-4 or Cq-10), 41.20 (CH_2-3), 43.67 (CH_2-14), 49.34 (CH-5), 56.25 (CH_2-12), 61.27 (CH_2-15), 71.36 (Cq-13),

79.20 (CH-7), 123.86 (Cq-8), 127.73 (CH-PG), 130.06 (CH-PG), 133.79 (Cq-9), 135.90 (CH-PG), 152.78 (Cq-21), 208.98 (Cq-11).- IR (CCl_4): 3500 (OH), 1775 (C=O), 1680 cm^{-1} (C=O).- $C_{38}H_{51}O_5F_3Si$ (672.9), MS: m/z (%) = 597 (13), 558 (4), 483 (25), 331 (100), 269 (68), 199 (90), 119 (81).- ^{19}F NMR (75 MHz, $CDCl_3$, $CFCl_3$ as external standard), δ = -75.8 (s).

(7SR, 13SR)-15-(tert-Butyl-diphenyl-silyloxy)-13-hydroxy-7-trifluoracetoxy-*rac*-labd-8-en-11-one (*rac*-14b)
^1H NMR (400 MHz, C_6D_6, NOE), δ = 0.58, 0.70, 1.02 (3s, 9H, CH_3-18, CH_3-19, CH_3-20), 1.17 (s, 9H, ^{t}butyl), 1.19 (m, 1H, 6α-H), 1.31, 1.33 (2 s, 6H, CH_3-16, CH_3-17), 1.40 (m, 1H, 6ß-H), 1.63 (doublet structure, 1H, 5-H), 1.85-2.05 (2H, CH_2-14), 2.67/2.83 (2 d, 2H, CH_2-12), 3.89-4.01 (2H, CH_2-15), 5.10 (d, 1H, 7-H), 7.20-7.28 (6H, aromat. H), 7.72-7.80 (4H, aromat. H), $J_{5,6\beta}$ = 15 Hz, $|J_{6\alpha,6\beta}|$ = ca. 13 Hz, $J_{6\beta,7}$ = 4.5 Hz, $|J_{12,12'}|$ = 19.5 Hz.- ^{13}C NMR (100.6 MHz, C_6D_6, DEPT), δ = 17.05 (CH_3-20), 18.63 (CH_2-2), 18.75 (CH_3-19), 19.30 (Cq-PG), 21.20 (CH_3-16), 25.77 (CH_2-6), 27.05 (CH_3-PG), 27.41 (CH_3-17), 32.41 (CH_3-18), 32.52 (Cq-4 or 10), 36.93 (CH_2-1), 38.51 (Cq-4 or 10), 41.19 (CH_2-3), 43.84 (CH_2-14), 45.61 (CH-5), 56.07 (CH_2-12), 61.17 (CH_2-15), 71.37 (Cq-13), 77.28 (CH-7), 122.42 (Cq-8), 127.73 (CH-PG), 130.06 (CH-PG), 133.75 (Cq-PG), 133.87 (CH-9), 135.91 (CH-PG), 153.77 (Cq-21), 209.65 (C-11).- IR (CCl_4): 3520 (OH), 1780 (C=O), 1680 cm^{-1} (C=O).- $C_{38}H_{51}O_5F_3Si$ (672.9).- MS: m/z (%) = 597 (M- ^{t}butyl-H_2O, 3), 558 (11), 483 (40), 434 (30), 377 (35), 351 (20), 269 (100), 199 (87), 119 (83).- ^{19}F NMR (75 MHz, $CDCl_3$, $CFCl_3$ as external standard), δ = -75.8 (s).

(7RS, 8SR, 13SR)-15-(tert-Butyl-diphenyl-silyloxy)-7,8-epoxy-13-hydroxy-*rac*-labdan-11-one (*rac*-18)
A solution of commercial 55 per cent m-chloroperbenzoic acid (142.2 mg, 0.453 mmol) and *rac*-15 (140.0 mg, 0.266 mmol) in $CHCl_3$ (6 mL) was stirred at 20°C for 90 min. After addition of saturated aq. $NaHCO_3$ (10 mL) usual work-up (CH_2Cl_2) and LC (petrol-ethyl acetate 10:1) furnished *rac*-18 (155.7 mg, 99%).- ^1H NMR (400 MHz, $CDCl_3$, NOE), δ = 0.84, 0.88, 1.00 (3s, 9H, CH_3-18, CH_3-19, CH_3-20), 1.04 (s, 9H, ^{t}butyl), 1.19, 1.27 (2s, 6H, CH_3-16, CH_3-17), 1.68 (dt, J = 2.5 Hz, 2H, 6ß-H), 1.78-1.95 (2H, CH_2-14), 2.09 (dd, 1H, 1α-H), 2.67 (s, 1H, 9-H), 2.76, 2.88 (2d, 2H, CH_2-12), 2.97 (m, $W_{1/2}$ = 5 Hz, 1H, 7-H), 3.73-3.91 (2H, CH_2-15), 7.32-7.48 (6H, aromat. H), 7.60-7.69 (4H, aromat. H), $J_{1ß,2}$ = 4.5 and 1 Hz, $|J_{1ß,1\alpha}|$ = 15 Hz, $|J_{6\alpha,6ß}|$ = 15 Hz, $J_{6ß,5}$ = 13 Hz, $J_{6ß,7}$ = 3 Hz, $|J_{12,12'}|$ = 18.5 Hz, $J_{14,15}$ = 6 Hz.- ^{13}C NMR (100.6 MHz, $CDCl_3$, assignment by comparison with *rac*-19), δ = 14.86 (CH_3-20), 18.52 (CH_2-2), 19.32 (Cq-PG), 22.30 (CH_3-19), 23.12 (CH_3-16), 23.15 (CH_2-6), 27.10 (CH_3-PG), 27.22 (CH_3-17), 33.09 (Cq-4 or Cq-10), 33.12 (CH_3-18), 37.46 (Cq-4 or Cq-10), 39.77 (CH_2-1), 42.07 (CH_2-3), 42.73 (CH_2-14), 45.38 (CH-5), 57.59 (Cq-8), 59.06 (CH_2-12), 60.56 (CH-7), 61.27 (CH_2-15), 67.22 (CH-9), 71.84 (Cq-13), 127.99 (CH-PG), 130.03 (CH-PG), 133.38 (Cq-PG), 135.78 (CH-PG), 213.45 (Cq-11).- IR (CCl_4): 3500 (OH), 1700 cm^{-1} (C=O).- MS: m/z (%) = 501 (8), 269 (100), 235 (60), 199 (85).- $C_{36}H_{52}O_4Si$ (576.8), calcd C 74.95, H 9.09, found C 75.09, H 9.21.

(1RS, 2RS, 3aSR, 7aSR)-1-((3SR)-5-tert-Butyl-diphenyl-silyloxy-3-hydroxy-3-methyl-pentan-1-oyl)-2-formyl-2,4,4,7a-tetramethyl-hexahydro-indan (*rac*-17)
To a solution of *rac*-17 (26.5 mg, 0.05 mmol) in CH_2Cl_2 (7 mL), cooled to -78°C , $SnCl_4$ (13 µl, 0.05 mmol) was added. The stirred reaction mixture was allowed to warm to 20°C within 1 h and was left at 20°C for 25 h. H_2O (2 mL) was added. Usual work-up (CH_2Cl_2) followed by LC (petrol-ethyl acetate = 20:1) provided *rac*-17 (7 mg, 26%).- ^1H NMR (400 MHz, $CDCl_3$, NOE, labdane numbering), δ = 0.81, 0.85, 0.98 (3s, 9H, CH_3-18, CH_3-19, CH_3-20), 1.03 (s, 9H, ^{t}butyl), 1.18, 1.26 (2s, 6H, CH_3-16, CH_3-17), 1.96 (dd, J = 13 Hz, J = 6 Hz, 1H, 5-H), 2.53, 2.64 (2d, 2H, CH_2-12), 3.02 (s, 1H, 9-H), 3.71-3.88 (2H, CH_2-15), 4.21 (s, 1H, OH), 7.25-7.78 (10H, aromat. H), 9.38 (s, 1H, CH=O), $|J_{12,12'}|$ = 17 Hz, $J_{14,15}$ = 6 Hz.- IR (CCl_4): 3500 (OH), 1725 (C=O), 1700 cm^{-1} (C=O).- $C_{36}H_{52}O_4Si$ (576.8), MS: m/z (%) = 548 (0.5), 519 (3.5), 501 (3.5),269 (100), 235 (95), 199 (75).

(7RS, 8RS, 13SR)-15-(tert-Butyl-diphenyl-silyloxy)-8,13-epoxy-7-hydroxy-*rac*-labdan-11-one (*rac*-19)
To a solution of *rac*-18 (82.1 mg, 0.14 mmol) in toluene (15 mL) trimethylsilyl triflate (30.5 µl, 0.16 mmol) was added at 0°C. The mixture was left at 20°C for 10 min. H_2O (2 mL) was added. Usual work-up and subsequent LC (petrol-ethyl acetate 15:1) yielded *rac*-19 (46.7 mg, 57%).- M.p. 118°C (petrol).- ^1H NMR (400 MHz, C_6D_6, NOE, H,H COSY), δ = 0.75, 0.92, 1.01 (3s, 9H, CH_3-18, CH_3-19, CH_3-20), 1.08, 1.16 (2s, 6H, CH_3-16, CH_3-17), 1.18 (s, 9H, ^{t}butyl), 1.50-1.71 (4H, containing the CH_2-14 signals), 1.79-1.88 (dt, 1H, 6α-H), 2.19, 2.47 (2d, CH_2-12), 2.54 (dt, 1H, 1ß-H), 2.80 (s, 1H, 9-H), 3.45 (bs, 1H, OH), 3.58 (t, 1H, 7-H), 3.67-3.82 (CH_2-15), 7.19-7.32 (6H, aromat. H), 7.72-7.83 (4H, aromat. H), $|J_{1ß,1α}|$ = 13 Hz, $J_{5,6α}$ = 3 Hz, $|J_{6ß,6α}|$ = 14.5 Hz, $J_{6α,7}$ = 3 Hz, $J_{7,6ß}$ = 3 Hz, $|J_{12,12'}|$ = 14.5 Hz.- ^{13}C NMR (100.6 MHz, $CDCl_3$, DEPT), δ = 15.44 (CH_3-20), 18.55 (CH_2-2), 19.32 (Cq-PG), 21.75 (CH_3-19), 24.93 (CH_2-6), 25.83 (CH_3-16), 27.09 (CH_3-PG), 29.47 (CH_3-17), 32.90 (CH_3-18), 33.45 (Cq-4 or Cq-10), 36.75 (Cq-4 or Cq-10), 38.82 (CH_2-1), 42.22 (CH_2-3), 46.60 (CH-5), 47.71 (CH_2-14), 53.55 (CH_2-12), 60.27 (CH_2-15), 63.15 (CH-9), 73.05 (CH-7), 77.99 (Cq-8), 80.80 (Cq-13), 127.97 (CH-PG), 130.00 (CH-PG), 133.70 (Cq-PG), 135.80 (CH-PG), 208.86 (Cq-11).- IR (CCl_4): 3560 (OH), 1700 cm^{-1} (C=O).- MS: m/z (%) = 519 (M-^{t}butyl, 8), 501 (4), 433 (8), 269 (100), 235 (20), 199 (30).- $C_{36}H_{52}O_4Si$ (576.9), calcd C 74.95, H 9.10, found C 74.86, H 9.15.

X-ray Structural Analyses of *rac*-15 and *rac*-19
rac-15 crystallizes in the monoclinic space group C2/c with a = 21.987(6), b = 9.941(3), c = 30.840(7) Å, ß = 101.69(2)°, V = 6601(2) $Å^3$, Z = 8. The structure was refined to R = 0.053, wR = 0.042 for 3609 independent reflections [$M_oK_α$, 20 ≤ 50°, $F_o^2 > 1.5\ σ\ (F_o^2)$]. rac-19 crystallizes in the monoclinic space group C2/c with a = 29.480(5), b = 7.707(2), c = 29.025(5) Å, ß = 93.08(3)°, V = 6585(3) $Å^3$, Z = 8. The structure was refined to R = 0.073, wR = 0.070 for 1623 independent reflections [$M_oK_α$, 20 ≤ 45°, $F_o^2 > 2.0\ σ\ (F_o^2)$]. Further details of the structure investigation may be obtained from Fachinformationszentrum Energie, Physik, Mathematik GmbH, D-7514 Eggenstein-Leopoldshafen 2 (Germany) on quoting the deposition number CSD - 56873. Any request should be accompanied by the full literature citation of this paper.

Acknowledgements - We wish to thank Dr.D.Müller, Dr.W.Dietrich, and their colleagues for the MS and NMR spectra, and U.Wagner for the CD spectra. Financial support by the Deutsche Forschungsgemeinschaft and the Fonds der Chemischen Industrie is gratefully acknowledged.

REFERENCES AND NOTES

Dedicated with appreciation to Professor Meinhart Zenk on the occasion of his 60th birthday.

[1] For leading references, see Robbins, J.D.; Laurenza, A.; Kosley Jr., R.W.; O´Malley, G.J.; Spahl, B.; Seamon, K.B. *J.Med.Chem.* **1991**, *34*, 3204-3212.
[2] Colombo M.I.; Zinczuk, J.; Ruveda, E.A. *Tetrahedron* **1992**, *48*, 963-1037.
[3] cf. Scherkenbeck, J.; Dietrich, W.; Müller, D.; Böttger, D.; Welzel, P. *Tetrahedron*, **1986**, *42*, 5949-5959.
[4] Aretz, W.; Böttger, D.; Sauber, K. EP 212293 (4.3.1987) , C.A. **1987**, *106*, 212559w.
[5] Hrib, N.J. *Tetrahedron Lett.* **1987**, *28*, 19-22.
[6] Scherkenbeck, J.; Böttger, D.; Welzel, P. *Tetrahedron*, **1987**, *43*, 3797-3802.
[7] Khandelwal, Y.; Jotwani, B.R.; Inamdar, P.K.; de Souza, N.J.; Rupp, R.H. *Tetrahedron* **1989**, *45*, 763-766.
[8] Aretz, W.; Böttger, D.; Sauber, K. *Biol.Chem. Hoppe-Seyler* **1986**, *367 suppl.*, 213.
[9] Nadkarni, S.R.; Akut, P.M.; Ganguli, B.N.; Khandelwal, Y.; de Souza, N.J.; Rupp, R.H.; Fehlhaber, H.W. *Tetrahedron Lett.* **1986**, *27*, 5265-5268.
[10] Polovinka, M.P.; Unzur, N.D.; Peruttskii, V.B.; Korchagina, D.V.; Gatilov, Y.V.; Bagryanskaya, Y.; Mamatyuk, V.A.; Sal'nikov, G.E.; Vlad, P.V.; Barakhash, V.A. *Zh. Org. Khim.* **1991**, *27*, 2116-2131.
[11] Corey, E.J.; Schmidt, G. *Tetrahedron Lett.* **1979**, 399-402.

[12]Rand, C.L.; van Horn, D.E.; Moore, M.W.; Negishi, E. *J.Org. Chem.* **1981**, *46*, 4093-4096.
[13]Narula, A.S. *Tetrahedron Lett.* **1982**, *23*, 5579-5582, and references therein.
[14]Finan, J.M.; Kishi, Y. *Tetrahderon Lett.* **1982**, *23*, 2719-2722.
[15]Paulsen, H.; Eberstein, K.; Koebernick, W. *Tetrahedron Lett.* **1974**, 4377-4380.
[16]Miyashita, M.; Suzuki, T.; Yoshikoshi, A. *Tetrahedron Lett.* **1987**, *28*, 4293-4296 , and references therein.
[17]Bick, St., Dissertation, Ruhr-Universität Bochum, 1992.
[18]Cossy, J.; Bouzide, A.; Ibhi,S.; Aclinou, P. *Tetrahedron* **1991**, *37*, 7775-7782, and references therein.
[19]Review: Molander, G.A.; *Chem. Rev.* **1992**, *92*, 29-68.
[20]The preparation of this compound will be reported in a forthcoming publication.
[21]Frelek, J.; Majer, Zs.; Perkowska, A.; Snatzke, G.; Vlahov, I.; Wagner, U. *Pure Appl.Chem.* **1985**, *57*, 441-451.
[22]Djerassi, C.; Klyne, W.; Norin, T.; Ohloff, G.; Klein, E. *Tetrahedron* **1965**, *21*, 163-178; Schaffner K., Snatzke ,G. *Helv.Chim.Acta* **1965**, *48*, 347-361; see also Tocanne, J.F. *Tetrahedron* **1972**, *28*, 389-416.
[23]Nicolaou, K.C.; Petasis, N.A.; Claremon, D.A. *Tetrahedron* **1985**, *41*, 4835-4841, and references therein.
[24]Review: Arzoumanian, H.; Metzger, J. *Synthesis* **1971**, 527- 536; Rappoport, Z.; Winstein, S.; Young, W.G. *J.Am.Chem.Soc.*. **1972**, *94*, 2320- 2329.
[25]Kirk, D.N.; Hartshorn, M.P. *Steroid Reaction Mechanisms*, p. 352ff., Elsevier Publishing Company, Amsterdam 1968.
[26]For a retro-aldol reaction of **18**, see ref. [17]
[27]Noyori, R.; Murata, S.; Suzuki, M. *Tetrahedron*, **1981**, *37*, 3899-3910.
[28]cf. for example the synthesis of (-)-borjatriol by Abad, A.; Agulló, M.; Arnó, M.; Cuñat, A. C.; Zaragozá, R.J. *J.Org. Chem.* **1992**, *57*, 50-54. Shirahama, H.; Hayano, K.; Kanemoto, Y.; Misumi, S.; Ohtsuka, T.; Hashiba, N.; Furusaki, A.; Murata, S.; Noyori, R.; Matsumoto, T. *Tetrahedron Lett.* **1980**, *21*, 4835-4838.
[29]Metten, K.H.; Welzel, P. *Tetrahedron*, **1990**, *46*, 5145-5154.
[30]Chaudary, S: K.; Hernandez, O. *Tetrahedron Lett*, **1979**, 99-102.