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Chemistry of Zamoranic Acid. Part IX[1] Homochiral Synthesis of Polygodial and Warburganal from 17-Acetoxy-7-labden-15-ol

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Abstract: 14,15-di*nor*-17-acetoxy-7-labden-13-one, **4** was prepared from zamoranic acid methyl ester **5**. Photochemical cleavage of **4** gave 12-acetoxy-7,9(11)-drimadiene, **3**, in 75% overall yield. The chemo- and diastereoselective epoxidation of **3** afforded 12-acetoxy-9α and 9β(11)-epoxy-7-drimene, **17** and **18** in 4:1 ratio. Ring-opening of **17** (or the mixture **17/18**) using BF_3•Et_2O or ring-opening of the mixture **17/18** lead to the synthetic precursor of polygodial: (9*R*)-12-acetoxy-drimen-11-al, **20**, with a 90% diastereoisomeric excess. The chemo- and diastereoselective *cis*-hydroxylation of diene **3** led to the synthetic precursor of warburganal 9α,11,12-trihydroxy-7-drimene, **29** with 47% yield. Polygodial and warburganal were prepared from zamoranic acid methyl ester in 55 and 27% overall yield, respectively.

INTRODUCTION

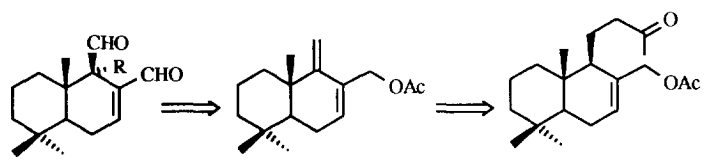
Much attention has been paid to the synthesis of active drimanes due to their wide range of biological activities and their possible industrial application.[2-7]

Many different precursors have been used so far as starting materials in the synthesis of drimanes, being these active or not, which include many tricyclic diterpenes (*e.g.*: abietic acid, levopimaric acid, royleanone, podocarpic acid and hispanolone) as well as bicyclic diterpenoids (*e.g.*: manool and communic acid).[8]

We have recently published the semisyntheses of polygodial **1** and warburganal **2**, two important antifeedant agents, from the bicyclic diterpene zamoranic acid methyl ester.[1e,1g]

In order to establish if the functionality of the biannular system is reponsible for the low-medium overall yield (caused by side reactions) in the synthesis of both active drimanes, we examined the use of methyl ketone **4**, as starting material, that possesses an acetoxymethylene group at C-17 instead of a carboxymethyl group. This change produced a considerable increase in the overall yield and a fruitful advantage in the synthetic strategies.

We report now the synthesis of polygodial **1**[9] and warburganal **2**[10] from **4** through the diene **3**.



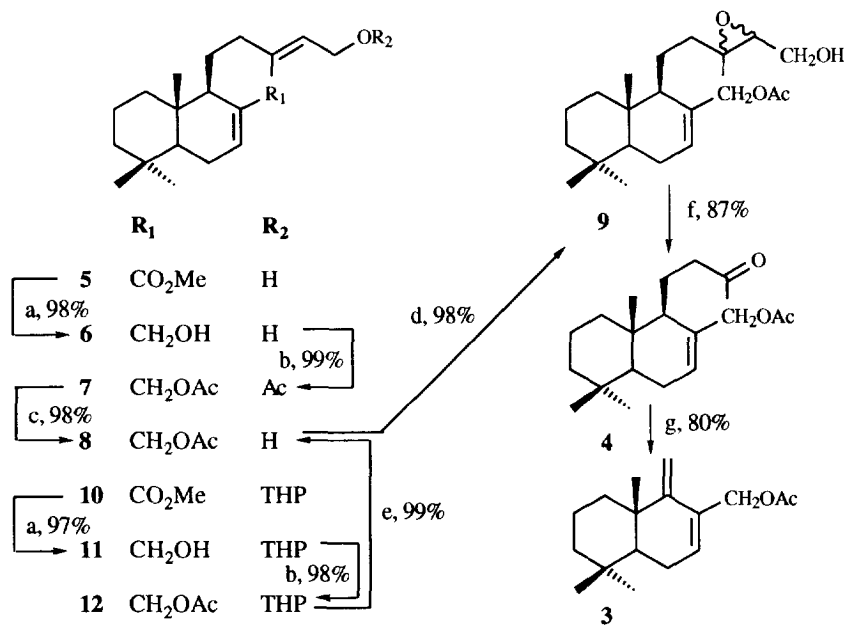
1 **R** = H, polygodial **3** **4**

2 **R** = OH, warburganal

Scheme 1. Retrosynthetic Analysis

RESULTS AND DISCUSSION

Methyl ketone **4** is prepared from zamoranic acid methyl ester **5** as depicted in Scheme 2. Reduction of **5** with LAH afforded diol **6**, whose diacetyl derivative **7** was chemoselectively hydrolyzed with K_2CO_3 to give the hydroxy derivative **8**. Treatment of the latter with MCPBA afforded a mixture of epoxides **9**. Cleavage of **9** with H_5IO_6[11] gave ketone **4**, as shown in Scheme 2, an alternative route uses tetrahydropyranyl derivative **10**, prepared from the natural mixture of zamoranic acid and its 13,14–dihydro derivative[1a] and separated by CC. Reduction of **10** with LAH afforded **11** and its acetylation gave monoacetyl derivative **12**, whose deprotection with TsOH also afforded **8**.



Scheme 2. a) LAH; b) Ac_2O/Py; c) K_2CO_3/MeOH; d) MCPBA; e) TsOH; f) H_5IO_6; g) hv.

Table 1 summarizes some of the results of Norrish II type photochemical cleavage of compound **4** to prepare diene **3**.[12]

Table 1. Norrish II Type Photochemical Cleavage

Lamp	Time (h)	3 (% Yield)
a	4.0	68
a	5.5	79
b	1.0	79
b	1.5	77
c	2.5	75
c	3.0	80

a. Hanau Q-81 (Hg, high pressure); b. Hanovia 450 W (Hg, medium pressure); c. Hanau TQ-150 (Hg, high pressure).

The best results are achieved using the high pressure lamp (Hanau TQ–150, 500 W), irradiating the solution for 3 hours. Irradiation couldn't be prolonged because the methyl ketone **4** decomposed and no more transformation is achieved.

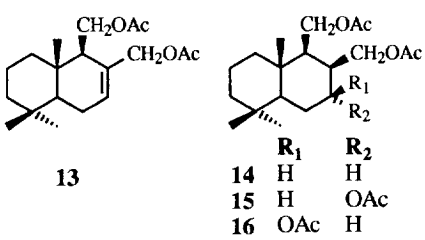
At first glance, the synthesis of polygodial from diene **3** will be straight forward by hydroboration of the exocyclic double bond. The stereospecificity of the reaction should be governed by the angular methyl group (Me–15) of the drimanic skeleton, allowing hydroboration only by the less hindered α-face of the molecule.

Table 2. Hydroboration Reaction

Entry	BH_3/3 ratio (mmol)	Solvent	Oxidant	3[a] %	13 %	14 %	15 %	16 %
1	1/3	THF	TAO[b]	60	8		–	–
2	1/1	THF	H_2O_2	47	18		6	1
3	5/3	THF	H_2O_2	–	25	35	17	3
4	10/3	THF	H_2O_2	–	–	25	28	5
5	5/3	Diglyme	TAO[b]	54	18		–	–
6	10/3	Diglyme	TAO[b]	20	52		–	–

a. Recovered starting material. b. Trimethyl amine N-oxide.

However, the reaction was not chemoselective, when stoichiometric quantities were used (entry 1),[14] low transformation of the substrate was observed and after acetylation of the reaction mixture and CC of the crude product, a not separable mixture of **13** and **14** was obtained. The former is the corresponding hydroborated exocyclic double bond, in which the addition had occurred, as expected, from the less hindered α-face, leading to a β-configuration of the acetoxymethylene group at C-9, and **14** is the reduction product of **13**. When the amount of borane was increased[15,16] other minor products of *bis*-hydroboration as **15** and **16** were formed. When the reaction was carried out in THF using a molar ratio 10:3 (entry 4) the reaction products were **14** (free of **13**), **15** and **16**. (Table 2 summarizes the reaction conditions and results of the hydroboration reaction).



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	R_1	R_2
14	H	H
15	H	OAc
16	OAc	H

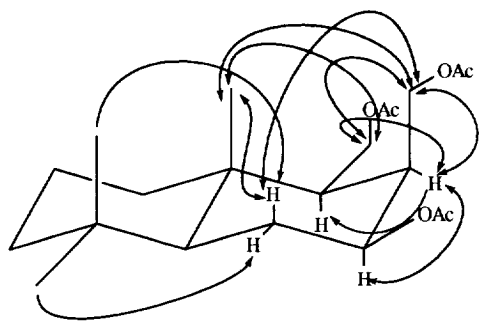
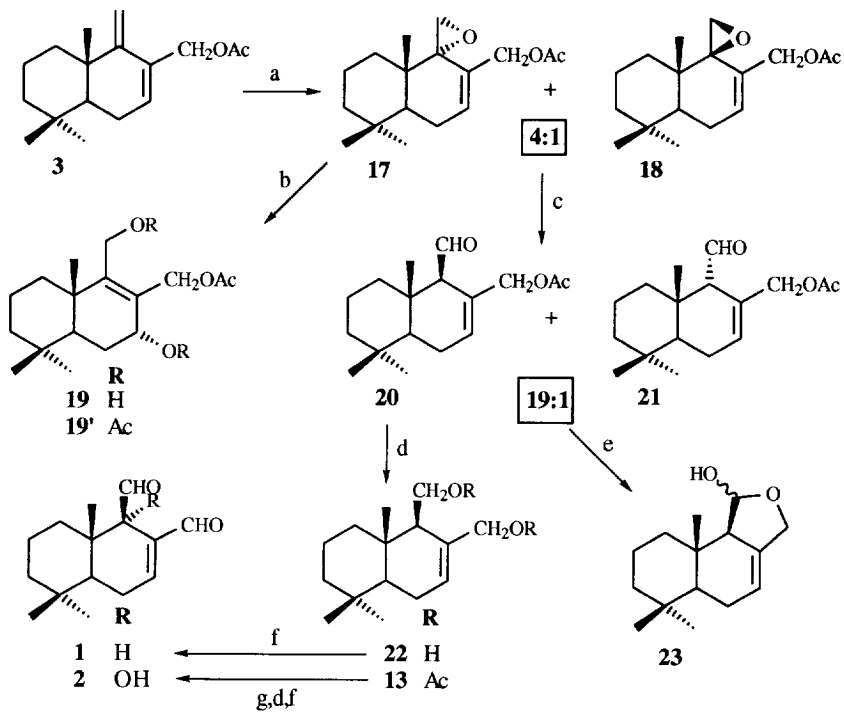


Figure 1. Nuclear Overhauser Effects observed for **16**.

Analysis of the ^1H NMR data of **15** indicates that the geminal hydrogen of the secondary acetoxy function corresponds to an α-configuration of the acetoxyl group (δ ppm 5.11), while in compound **16** the acetoxyl group

at C-7 (1H, ddd, δ ppm 4.85, J = 10.5, 5.6, 4.9 Hz) must be β, meaning that **16** is an epimer of **15** at C-7. The stereochemistry of **16** was confirmed by nOe experiments (Figure 1).

In order to functionalize C-11, an alternative route was planned (Scheme 3), in which upon reacting **3** with stoichiometric quantities of MCPBA, the epoxides **17** and **18** were isolated in 4:1 ratio. The major isomer **17**, separated by CC, led to an allylic rearranged product **19** under basic ring–opening conditions. The acetyl derivative of the latter, **19'**, provided ^{1}H NMR data useful to assign the α-configuration of the secondary hydroxyl group at C-7 according to the coupling constant of the *gem*-hydrogen. When **17** was treated with BF_3•Et_2O,[17] a mixture of aldehydes, **20** and **21**, was obtained diastereoselectively (19:1 ratio). Treatment of the mixture of **17** and **18** with BF_3•Et_2O under the same reaction conditions provided the same result as the previous reaction. According to these results, the mechanism of the reaction must be cationic and not a concerted one, meaning that the geometry of the intermediate carbocation, controlled by Me-10, guides hydride migration by the less hindered face.[17] When the mixture **20/21** was chromatographed on silica gel, only epimer **21** was separated. Reduction of **20** with LAH afforded **22** (5*S*,9*R*,10*S*–7–drimen–11,12–diol), precursor of polygodial and warburganal.[1e,18] Basic hydrolysis of **20** led to **23**, a mixture of drimeninol and isodrimeninol.[19]



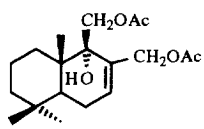
Scheme 3. a) MCPBA/CH_2Cl_2; b) NaOH/*t*–BuOH; c) BF_3•Et_2O, benzene; d) LAH, Et_2O; e) K_2CO_3/MeOH; f) Swern oxidation; g) SeO_2.

Preparation of warburganal from diene **3** could be carried out by selective *cis*–hydroxylation of the exocyclic double bond. Table 3 summarizes reaction conditions and results. Treatment of **3** with OsO_4[20] and acetylation afforded products hydroxylated at C–9/C–11, **24**, C–7/C–8, **25** and both, **26**.

Table 3. *Cis*–hydroxylation of compound **3**.

Entry	3	Solvent	OsO_4	Oxidant	Time	3[a]	24	25	26
	(mmol)				(h)	%	%	%	%
1	0.23	*t*-BuOH/THF/H_2O	b	NMO	52	16	42	12	–
2	0.23	*t*-BuOH/THF/H_2O	b	NMO	144	14	47	12	–
3	0.76	*t*-BuOH/THF/H_2O	b	NMO	168	33	31	29	–
4	0.34	*t*-BuOH	b	Et_4NOH/*t*–BuO_2H	72	28	13	–	–
5	0.14	Pyridine	c	–	120	10	–	9	13

a. Recovered starting material; b. Catalytic; c. Stoichiometric



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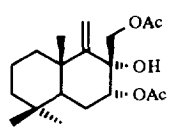

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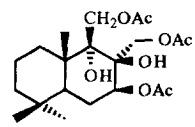

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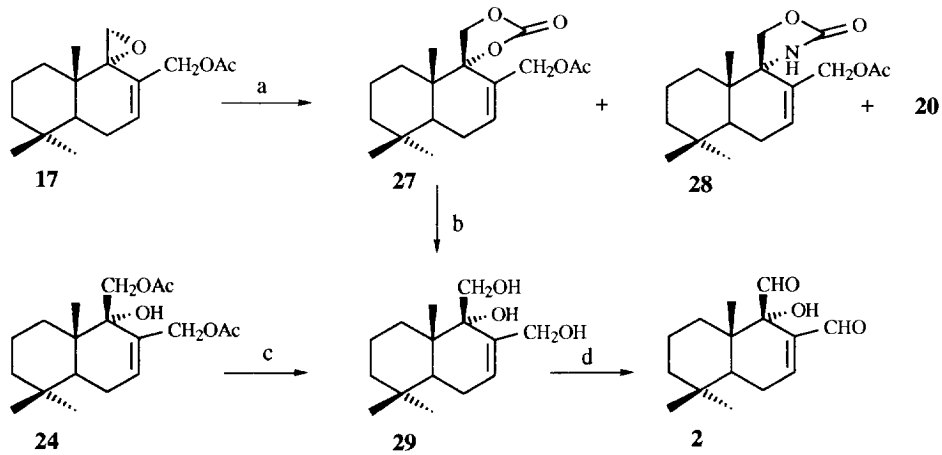
From these results the following conclusions were drawn: the desired product **24**, corresponding to the selective *cis*–hydroxylation of the exocyclic double bond from the less hindered α-face was prepared under catalytic conditions[16,21-23] but not under stoichiometric conditions (entry 5). The study of the NMR ^1H irradiations in compound **25** allows the determination of the acetoxy group stereochemistry as α, indicating also that the *cis*–hydroxylation of the annular double bond took place from the less hindered face. *Cis*–hydroxylation with OsO_4 under stoichiometric conditions afforded **25** and **26** (M^+ 414, $C_{21}H_{34}O_3$), a compound with two CH_2OAc groups, two tertiary hydroxyl groups and a β-secondary acetoxy group, resulting from the *cis*–hydroxylation of both double bonds; the exocyclic one from the less hindered face and the annular one from the β-face. These results indicate that the main product **24** came from a chemo– and stereoselective reaction, while **26** is the hydroxylated derivative of **24**, in which the reagent approached the substrate from the β-face due to steric hindrance or by extension of the Kishi rule, that is, the resulting stereochemistry either in acyclic or cyclic systems supposes an approach to the double bond from the opposite face of the pre–existing hydroxyl group.[24] Finally, reduction of **24** with LAH afforded **29**, precursor of warburganal,[1e,18] (Scheme 4).

Alternatively, hydroxylation of $\Delta^{9,11}$ of compound **3** was carried out by treating epoxide **17** with Chlorosulfonyl isocyanate (CSI)[25] to afford **20** (38%), **27** (22%) and **28** (18%), (Scheme 4). Carbonate **27** shows nOe between he angular methyl group (Me–15) and the hydrogens of C–11 indicating that the stereochemistry of C–9 is the one depicted in the formula, and, more over, due to the regio– and stereospecific character of the reaction with CSI,[25] the stereochemistry for the epoxides **17** and **18** is unambiguously established. Basic hydrolysis of **27** afforded triol **29** (96%), being this a new synthetic route to the desired product.

Carbamate **28**, whose structure is in agreement with the spectroscopic properties, is now under study as synthetic intermediate in the preparation of active drimanes.



Scheme 4. a) CSI; b) NaOH/Dioxane; c) LAH; d) Swern oxidation.

CONCLUSIONS

When zamoranic acid methyl ester **5** was used as starting material, polygodial and warburganal were synthesized in 31 and 22% overall yield, respectively.[1e] Overall yield was dramatically influenced by one of the side chain degradation steps, that proceeded in low yield due to side reactions, the cleavage of epoxide with H_5IO_6, 53 % yield. However, functional group transformation, carboxymethyl group into acetoxymethylene group) increased overall yield considerably, especially in the preparation of polygodial, 55% yield, and up to 27% yield in the preparation of warburganal. In these cases the starting material is monoacetate **8** prepared in 94% yield from zamoranic acid methyl ester. Transformation of **8** into the respective precursors of **1** and **2** required, as key steps, the epoxide ring-opening with $BF_3 \cdot Et_2O$ for **1** and the *cis*-hydroxylation reaction for **2**.

EXPERIMENTAL PART

Unless otherwise stated, all chemicals were purchased as the highest purity commercially available and were used without further purification. Melting points were determined with a Kofler hot stage melting point apparatus and are uncorrected. IR spectra were recorded on a BOMEM 100 FT IR spectrophotometer. ^1H and ^{13}C NMR spectra were performed in deuterochloroform and referenced to the residual peak of $CHCl_3$ at δ 7.26 ppm and δ 77.0 ppm, for ^1H and ^{13}C, respectively in a Bruker WP-200 SY. Chemical shifts are reported in δ ppm and coupling constants (J) are given in Hz. MS spectra were performed in a VG-TS 250 spectrometer at 70 eV ionizing voltage. Mass Spectra are presented as m/z (% rel. int.) Optical Rotations were determined in a Perkin-Elmer 241 polarimeter in 1 dm cells. Diethyl ether, THF, benzene were distilled from sodium, and pyridine and dichloromethane were distilled from calcium hydride under Ar atmosphere.

Table 4. ^{13}C NMR data.

C	3	4	6	7	8	14	15	17	19	20	21	23	25	26	27	28
1	37.5	39.2	39.3	39.1	39.1	39.3	38.9	30.0	35.8	40.3	37.7	40.0	38.9	32.3	30.3	31.5
2	19.0	18.7	18.8	18.8	18.8	18.5*	18.4	18.0	18.7	18.3	18.6	18.5	19.1	18.2	17.8	18.1
3	42.2	42.2	42.4	42.3	42.3	41.9	41.7	41.6	41.4	42.0	42.4	42.6	41.6	41.3	41.1	41.6
4	33.4	33.1	33.0	33.0	33.0	33.5	32.6	33.0	33.0	33.1	33.1	33.0	33.2	33.4	32.9	33.1
5	48.1	49.7	50.1	49.8	49.8	35.0	40.4	45.8	45.3	49.0	44.7	50.1	45.3	43.1	42.4	44.3
6	24.3	23.8	23.8	23.9	23.9	29.2	22.6	24.2	28.2	23.7	24.3	23.8	24.4	23.9	24.0	23.9
7	130.5	129.8	125.6	129.2	129.0	17.7*	70.8	137.6	66.6	130.7	131.4	117.1	73.2	73.1	139.0	134.1
8	130.7	133.5	139.8	134.1	134.1	56.3#	48.2§	129.5	151.6	128.5	126.9	136.7	74.4	n.o.‡	128.5	132.1
9	154.9	51.8	51.9	51.9	52.1	51.6#	46.5§	62.6	131.2	64.9	64.3	61.9	158.9	76.0	86.8	65.0
10	37.7	36.9	36.7	36.6	36.9	37.3	36.9	36.0	39.4	37.1	36.6	33.5	39.4	43.6	39.6	39.6
11	104.3	20.4	25.2	25.0	25.1	62.8§	62.0#	48.2	57.5	204.4	202.2	99.5	110.4	62.3	65.6*	65.6*
12	66.0	44.9	41.2	41.4	41.2	64.1§	62.3#	63.8	63.4	66.9	67.3	69.0	67.9	64.9	66.1*	67.4*
13	32.8	208.3	140.3	142.5	139.7	33.3	33.1	32.5	33.0	33.2	32.8	33.1	32.9	33.6	32.4	32.9
14	22.1		123.7	118.8	123.9	21.6	20.9	20.9	21.7	22.0	21.9	21.5	22.4	21.2	21.8	21.7
15	20.8		59.2	61.3	59.3	16.5	15.7	18.4	18.8	15.6	20.8	14.1	20.9	16.1	14.7	15.4
16		30.0	16.4	16.5	16.3											
17		67.7	66.0	67.8	67.7											
18		33.1	33.1	33.0	33.0											
19		21.9	21.9	21.8	21.8											
20		13.6	13.7	13.8	13.8											
O<u>C</u>OMe	170.9	170.7		171.1	170.8	171.2	170.9	170.5	171.4	170.5	170.6		170.9	170.6	170.5	170.0
O<u>C</u>OMe				170.7		171.2	170.9						170.4	170.4		
O<u>C</u>OMe							170.1							169.8		
OCO<u>Me</u>	21.0	21.1		21.1	21.1	21.1	21.4	21.0	21.2	20.9	21.2		21.4	21.2	20.8	20.9
OCO<u>Me</u>				21.0		21.1	21.3						21.3	21.0		
OCO<u>Me</u>							20.9							20.9		
–C=O															154.5	159.8

*, #, §: values may be interchange in the same column. ‡: not observed in $CDCl_3$

REDUCTION OF **5** WITH LAH: *7,13E–labdadien–15,17–diol*, **6**.

$LiAlH_4$ (0.63 g, 0.02 mol) was added to a solution of **5** (10 g, 0.03 mol) in dry ether (50 ml), and the reaction mixture was stirred for 30 min at room temperature under Ar atmosphere. Then ether moistened with water was added and the reaction mixture dried (Na_2SO_4), filtered and evaporated to give **6** (9 g, 98% yield). $[\alpha]_D$ = –1.8 ($CHCl_3$, 0.9). IR (film) ν_{max} cm^{-1}: 3330 (broad), 1650, 1090, 990. ^1H δ: 5.76 (1H, m, H–7), 5.44 (1H, t, J = 7.3, H–14), 4.17 (1H, d, J = 12.2, H_a–17), 4.15 (2H, d, J = 7.3, H–15), 3.99 (1H, d, J =12.2, H_b–17), 1.69 (3H, s, Me–16), 0.88, 0.86, 0.74 (3H, s, ea, Me–19, Me–18, Me–20). ^{13}C δ: see Table 4; Found: C, 78.36; H, 11.18. $C_{20}H_{34}O_2$ requires C, 78.38; H, 11.18%.

ACETYLATION OF **6**: *15,17–diacetoxy–7,13E–labdadiene*, **7**.

6 (9.0 g, 0.03 mol) was acetylated with Ac_2O (6 ml) and pyridine (6 ml). The reaction mixture was left over night at room temperature, then poured into ice–water and extracted with ether. The ether extracts were combined and washed with 2N HCl, $NaHCO_3$ and water, dried with Na_2SO_4, filtered and evaporated to give **7** (11.4 g, 99% yield). $[\alpha]_D$ = –12.6 ($CHCl_3$, 1.1). IR (film) ν_{max} cm^{-1}: 1740, 1680, 1450, 1370, 1240, 1030, 960. ^1H δ: 5.81 (1H, m, H–7), 5.33 (1H, t, J = 7.3, H–14), 4.57 (2H, d, J = 7.3, H–15), 4.55, 4.46 (1H, d, ea, J = 12.2, H–17), 2.06, 2.05 (3H, s, ea, –OCO**Me**), 1.69 (3H, s, Me–16), 0.88, 0.86, 0.75 (3H, s, ea, Me–19, Me–18, Me–20). ^{13}C δ: see Table 4.

SELECTIVE HYDROLYSIS OF **7**: *17–acetoxy–7,13E–labdadien–15–ol*, **8**.

A solution of 3% K_2CO_3 in MeOH was added to compound **7** (9.0 g, 0.02 mol). The reaction was monitored by TLC and judged complete after 30 min. Water was added and the reaction mixture extracted with ether. The organic layer washed with 2N HCl and water, dried with Na_2SO_4, filtered and evaporated. The crude reaction product was chromatographed affording unreacted starting material **7** (2g, 22%, Hexane/EtOAc 4:1), **8** (5.4 g, 60%, Hexane/EtOAc 7:3) and **6** (1.5 g, 17%, Hexane/EtOAc 1:1). Compound **8**: IR (film) ν_{max} cm^{-1}: 3380, 1740, 1240, 1020. ^1H δ: 5.80 (1H, m, H–7), 5.40 (1H, t, J = 6.8, H–14), 4.58 (1H, d, J = 12.2, H_a–17), 4.44 (1H, d, J = 12.2, H_b–17), 4.14 (2H, d, J = 6.8, H–15), 2.08 (3H, s, –OCO**Me**), 1.67 (3H, s, Me–16), 0.88, 0.86, 0.75 (3H, s, ea, Me–19, Me–18, Me–20). ^{13}C δ: see Table 4; Found: C, 75.82; H, 10.42. $C_{20}H_{36}O_3$ requires C, 75.82; H, 10.41%.

TREATMENT OF **8** WITH MCPBA: *17–acetoxy–13,14–epoxy–7–labden–15–ol*, **9**.

MCPBA (6.5 g, 0.04 mol) was added to compound **8** (12.0 g, 0.03 mol) dissolved in CH_2Cl_2 (40 ml). The reaction mixture was stirred at room temperature for 50 min. The solvent was removed and the residue extracted with ether, washed with 10% $NaHCO_3$ and water, dried with Na_2SO_4, filtered and evaporated to afford **9** (12.3 g, 98% yield). IR (film) ν_{max} cm^{-1}: 3420, 1740, 1240, 1020. ^1H δ: 5.73 (1H, m, H–7), 4.46 (1H, d, J = 12.2, H_a–17), 4.32 (1H, d, J = 12.2, H_b–17), 3.64 (2H, m, H–15), 3.15 (1H, bs, –O**H**), 2.85 (1H, m, H–14), 1.97 (3H, s, –OCO**Me**), 1.19 (3H, s, Me–16), 0.79, 0.77, 0.67 (3H, s, ea, Me–18, Me–19, Me–20).

OXIDATION OF **9** WITH PERIODIC ACID: *14,15–dinor–17–acetoxy–7–labden–13–one*, **4**.

A solution of periodic acid (8.3 g, 0.03 mol) in water (27 ml) was added to compound **9** (12.0 g, 0.03 mol) dissolved in THF (40 ml). The reaction was stirred at room temperature for 2.5 h. The reaction mixture was extracted with ether, washed with 5% $Na_2S_2O_3$, 10% Na_2CO_3 and water. Removal of the solvent afforded **4** (11.4 g, 87%). $[\alpha]_D$ = –12.4 ($CHCl_3$, 1.4). IR (film) ν_{max} cm^{-1}: 2920, 1745, 1718, 1440, 1390, 1370, 1240. ^1H δ: 5.78 (1H, m, H–7), 4.41 (1H, d, J = 11.5, H_a–17), 4.40 (1H, d, J =11.5, H_b–17), 2.05 (3H, s, Me–16), 2.00 (3H, s, –OCO**Me**), 0.82, 0.79, 0.71 (3H, s, ea, Me–19, Me–18, Me–20). ^{13}C δ: see Table 4; MS: 302 ([M^+–18], 4), 278 (8), 260 (98), 245 (30), 227 (94), 202 (57), 189 (100), 159 (50), 133 (70), 119 (99), 93 (95), 81 (64), 69 (67), 55 (77); Found: M^+-H_2O, 302.2246 $C_{20}H_{30}O_2$ requires *M-H_2O*, 302.2246; Found: C, 74.95; H, 10.08. $C_{20}H_{32}O_3$ requires C, 74.96; H, 10.06%.

REDUCTION OF **10** WITH LAH: *15–tetrahydropyranyloxy–7,13E–labdadien–17–ol*, **11**.

$LiAlH_4$ (0.83 g, 0.02 mol) was added to a solution of **10** (16.5 g, 0.04 mol) in dry ether (50 ml), and the reaction mixture was stirred for 30 min at room temperature under Ar atmosphere. Then ether moistened with water was added and the reaction mixture dried (Na_2SO_4), filtered and evaporated to give **11** (15 g, 97% yield).

Compound **11**: IR (film) ν_{max} cm^{-1}: 3420, 1670, 1210, 1150, 1040, 920, 880. ^1H δ: 5.74 (1H, m, H–7), 5.37 (1H, t, J = 6.4, H–14), 4.61 (1H, m, H–2'), 1.68 (3H, s, Me–16), 0.87, 0.85, 0.74 (3H, s, ea, Me–19, Me–18, Me–20). ^{13}C δ: 39.1 (1), 18.8 (2), 42.3 (3), 33.0 (4), 50.1 (5), 23.7 (6), 125.1 (7), 139.5 (8), 51.7 (9), 36.8 (10), 25.1 (11), 41.3 (12), 140.8 (13), 121.0 (14), 62.2 (15), 16.6 (16), 65.7 (17), 33.1 (18), 21.9 (19), 13.7 (20), 97.9 (2'), 30.8 (3'), 25.6 (4'), 19.6 (5'), 63.8 (6').

ACETYLATION AND ACID HYDROLYSIS OF **11**: *17–acetoxy–7,13E–labdadien–15–ol*, **8**.

Acetylation of **11** with Ac_2O (4 ml) and pyridine (4 ml) afforded after usual work–up **12** (16.3 g, 98%). TsOH (489 mg, 0.003 mol) was added to a solution of compound **12** (16.0 g, 0.04 mol) in MeOH (60 ml). The reaction was monitored by TLC and judged complete after 1 hour. Water was added and the reaction mixture was extracted with ether. The organic layers were combined and washed with 10% Na_2CO_3 and water, dried (Na_2SO_4), filtered and evaporated to afford **8** (13 g, 99%).

NORRISH II CLEAVAGE OF **4**: *12–acetoxy–7,9–drimadiene*, **3**.

In a 250 ml quartz flask was poured **4** (131 mg, 0.4 mmol) dissolved in hexane (250 ml) and dry N_2 was bubbled through the solution. The solution was irradiated for 3 h with a UV lamp (Hanau, 500 W, Hg vapour, high pressure). The solvent was removed and the residue (130 mg) chromatographed over SiO_2 (8 g) affording **3** (81 mg, 80%, hexane/EtOAc, 9:1) and **4** (40 mg, 13%, hexane/EtOAc, 4:1).

Compound **3**: $[\alpha]_D$ = –88.4 ($CHCl_3$, 1.1). IR (film) ν_{max} cm^{-1}: 3080, 1745, 1470, 1380, 1240, 1005, 890; ^1H δ: 5.96 (1H, m, H–7), 4.89 (1H, s, H_a–11), 4.81 (1H, s, H_b–11), 4.73 (1H, d, J = 12.2, H_a–12), 4.64 (1H, d, J = 12.2, H_b–12), 2.06 (3H, s, –OCO**Me**), 0.96, 0.93, 0.87 (3H, s, ea, Me–15, Me–14, Me–13). ^{13}C δ: see Table 4; MS: 262 ([M^+], 38), 220 (20), 202 (80), 187 (81), 159 (80), 133 (100), 119 (90), 105 (70), 91 (73), 69 (72). Found: C, 77.79; H, 9.98. $C_{17}H_{26}O_2$ requires C, 77.82; H, 9.99%.

HYDROBORATION OF **3**

A. BH_3 (1:3) in THF

A solution of **3** (51 mg, 0.18 mmol) in THF (7 ml) was cooled at 0 °C under Ar atmosphere and BH_3 (1M in THF, 0.06 ml) was added. The reaction was monitored by TLC and stirred for 24 h at room temperature, then, trimethylamine N–oxide (TAO, 22 mg, 0.19 mmol) was added and the mixture heated for 1 h at 50 °C. The mixture was cooled to room temperature, extracted with ether, washed with brine and dried (Na_2SO_4). After removal of solvent, the crude reaction product was acetylated with Ac_2O (0.5 ml) and pyridine (1.0 ml). CC of the crude acetylation product, eluting with hexane/EtOAc 9:1, afforded unreacted **3** (30 mg, 60%) and a mixture of **13/14** (5 mg, 8%). IR (film) ν_{max} cm^{-1}: 2925, 1745, 1380, 1365, 1240. ^1H δ: 5.87 (1H, m, H–7), 4.52 (1H, m), 4.28 (1H, dd, J = 11.3 and 5.2), 4.15 (5H, m), 2.06, 2.04 (3H, s, ea, –OCO**Me**), 0.90, 0.88, 0.86, 0.84, 0.81 (3H, s, ea).

B. BH_3 (1:1) in THF

A solution of **3** (160 mg, 0.61 mmol) in THF (15 ml) was cooled at 0 °C under Ar atmosphere and BH_3 (1M in THF, 0.61 ml) was added. The reaction was monitored by TLC and stirred for 24 h at room temperature, then, the mixture was cooled at 0 °C and EtOH (2.3 ml), 6N NaOH (0.4 ml) and 33% H_2O_2 (0.7 ml, dropwise) were added sequentially, warmed to 50 °C and stirred for 1 h. The mixture was then cooled to room temperature, and a saturated solution of K_2CO_3 (15 ml) was added. The mixture was extracted with ether, washed with brine and dried (Na_2SO_4). After removal of solvent, the crude reaction product was acetylated with Ac_2O (0.5 ml) and pyridine (1.0 ml). CC of the crude acetylation product, eluting with hexane/EtOAc 9:1, afforded unreacted **3** (75 mg, 47%), a mixture of **13/14** (36 mg, 18%), **15** (13 mg, 6%) and **16** (3 mg, 1%).

Compound **15**: *8S,9S–7α–11,12–triacetoxydrimane*. $[\alpha]_D$ = –5.9 ($CHCl_3$, 1.6). IR (film) ν_{max} cm^{-1}: 2925, 1745, 1380, 1365, 1240; ^1H δ: 5.11 (1H, m, H–7), 4.25 (1H, dd, J = 10.7 and 4.9, H_a–11), 4.12 (1H, dd, J = 11.0 and 3.4, H_a–12), 4.03 (1H, dd, J = 10.7 and 6.3, H_b–11), 3.97 (1H, dd, J = 11.0 and 7.3, H_b–12), 2.08 (3H, s, –OCO**Me**), 2.06 (6H, s, –OCO**Me**), 0.84 (3H, s), 0.81 (6H, s). ^{13}C δ: see Table 4; MS: 382 ([M^+], 2), 322 (3), 307 (3), 262 (37), 220 (100), 187 (42), 133 (53), 109 (57), 95 (40), 81 (51), 69 (75), 55 (62).

Compound **16**: *8S,9S–7β–11,12–triacetoxydrimane*. IR (film) ν_{max} cm^{-1}: 1745, 1470, 1380, 1360, 1240. ^1H δ: 4.85 (1H, ddd, J = 10.5, 5.6 and 4.9, H–7), 4.28 (1H, dd, J = 11.5 and 4.9, H_a–11), 4.21 (1H, dd, J = 11.5 and 6.5, H_a–12), 4.19 (1H, dd, J = 11.5 and 3.1, H_b–12), 4.11 (1H, dd, J = 11.3 and 9.5, H_b–11), 2.65 (1H, m, H–8), 2.03 (6H, s, –OCO**Me**), 1.99 (3H, s, –OCO**Me**), 1.77 (1H, ddd, J = 15.8, 4.9 and 2.7, H_α–6), 0.88, 0.83, 0.82 (3H, s, ea, Me–13, Me–14, Me–15); MS: 382 ([M^+], 4), 322 (6), 307 (5), 262 (67), 220 (90), 187 (100), 133 (56), 109 (67), 95 (44), 81 (51), 69 (77), 55 (88).

C. BH_3 (5:3) in THF

A solution of **3** (168 mg, 0.64 mmol) in THF (15 ml) was cooled at 0 °C under Ar atmosphere and BH_3 (1M in THF, 1.06 ml) was added. The reaction was monitored by TLC and stirred for 24 h at room temperature, then, the mixture was cooled at 0 °C and EtOH (2.3 ml), 6N NaOH (0.4 ml) and 33% H_2O_2 (0.7 ml, dropwise) were added sequentially, warmed to 50 °C and stirred for 1 h. The mixture was then cooled to room temperature, and a saturated solution of K_2CO_3 (15 ml) was added. The mixture was extracted with ether, washed with brine and dried (Na_2SO_4). After removal of solvent, the crude reaction product was acetylated with Ac_2O (0.5 ml) and pyridine (1.0 ml). CC of the crude acetylation product, eluting with hexane/EtOAc 9:1, afforded unreacted **3** (41 mg, 25%), a mixture of **13/14** (70 mg, 35%), **15** (40 mg, 17%) and **16** (7 mg, 3%).

D. BH_3 (10:3) in THF

A solution of **3** (160 mg, 0.61 mmol) in THF (15 ml) was cooled at 0 °C under Ar atmosphere and BH_3 (1M in THF, 2.03 ml) was added. The reaction was monitored by TLC and stirred for 24 h at room temperature, then, the mixture was cooled at 0 °C and EtOH (2.3 ml), 6N NaOH (0.4 ml) and 33% H_2O_2 (0.7 ml, dropwise) were added sequentially, warmed to 50 °C and stirred for 1 h. The mixture was then cooled to room temperature, and a saturated solution of K_2CO_3 (15 ml) was added. The mixture was extracted with ether, washed with brine and dried (Na_2SO_4). After removal of solvent, the crude reaction product was acetylated with Ac_2O (0.5 ml) and pyridine (1.0 ml). CC of the crude acetylation product, eluting with hexane/EtOAc 9:1, **14** (49 mg, 25%), **15** (66 mg, 28%) and **16** (12 mg, 5%).

Compound **14**: $[\alpha]_D$ = 27.2 ($CHCl_3$, 1.7). IR (film) ν_{max} cm^{-1}: 1745, 1470, 1380, 1360, 1240. MS: 324 ([M^+], 3), 309 (10), 264 (6), 249 (6), 231 (8), 204 (100), 189 (47), 123 (63), 81 (53), 69 (68), 55 (53). ^1H δ: 4.28 (1H, dd, J = 11.3 and 5.2, H_a–11), 4.14 (1H, t, J = 10.4, H_a–12), 4.07 (2H, m, H_b–11 and H_b–12), 2.04, 2.03 (3H, s, ea, –OCO**Me**), 0.86, 0.83, 0.81 (3H, s, ea, Me–15, Me–14, Me–13). ^{13}C δ: see Table 4.

E. BH_3 (5:3) in Diglyme

A solution of **3** (136 mg, 0.52 mmol) in diglyme (2 ml) was cooled at 0 °C under Ar atmosphere and BH_3 (1M in THF, 0.86 ml) was added. The reaction was monitored by TLC and stirred for 24 h at room temperature, then, trimethylamine N–oxide (TAO, 59 mg, 0.53 mmol) was added and the mixture heated for 1 h at 50 °C. The mixture was cooled to room temperature, extracted with ether, washed with brine and dried (Na_2SO_4). After removal of solvent, the crude reaction product was acetylated with Ac_2O (0.5 ml) and pyridine (1.0 ml). CC of the crude acetylation product, eluting with hexane/EtOAc 9:1, afforded unreacted **3** (61 mg, 54%) and a mixture of **13/14** (52 mg, 18%).

F. BH_3 (10:3) in Diglyme

A solution of **3** (113 mg, 0.43 mmol) in diglyme (2 ml) was cooled at 0 °C under Ar atmosphere and BH_3 (1M in THF, 1.44 ml) was added. The reaction was monitored by TLC and stirred for 24 h at room temperature, then, trimethylamine N–oxide (49 mg, 0.44 mmol) was added and the mixture heated for 1 h at 50 °C. The mixture was cooled to room temperature, extracted with ether, washed with brine and dried (Na_2SO_4). After removal of solvent, the crude reaction product was acetylated with Ac_2O (0.5 ml) and pyridine (1.0 ml). CC of the crude acetylation product, eluting with hexane/EtOAc 9:1, afforded unreacted **3** (18 mg, 20%) and a mixture of **13/14** (56 mg, 52%).

TREATMENT OF **3** WITH MCPBA: *12–acetoxy–9α(11)–epoxy–7–drimen*, **17** and *12–acetoxy–9β(11)–epoxy–7–drimen*, **18**.

MCPBA (265 mg, 1.5 mmol) was added to compound **3** (367 mg, 1.4 mmol) dissolved in CH_2Cl_2 (10 ml). The reaction mixture was stirred at room temperature for 50 min. The solvent was removed and the residue extracted with ether, washed with 10% $NaHCO_3$ and water, dried with Na_2SO_4, filtered and evaporated to afford a yellow oil corresponding to the mixture of epoxides **17/18** (360 mg, 4:1 ratio). IR (film) ν_{max} cm^{-1}: 1750, 1675, 1470, 1380, 1360, 1270, 1240, 840. ^1H δ: 6.26 (1H, dd, J = 6.4 and 2.9, H–7), 6.15 (1H, m, H–7'), 4.45 (1H, d, J = 12.2, H_a–12), 4.21 (1H, d, J = 12.2, H_b–12), 3.27 (1H, d, J = 4.0, H_a–11'), 2.91 (1H, d, J = 3.8, H_a–11), 2.86 (1H, d, J = 3.8, H_b–11), 2.67 (1H, d, J = 4.0, H_b–11'), 2.02 (3H, s, –OCO**Me**), 0.99, 0.91, 0.89 (3H, s, ea, Me–15, Me–14, Me–13).

Column chromatography of the oil on SiO_2 (30 g) washed with 5% Et_3N in hexane and eluting with

hexane:EtOAc 95:5, afforded **17** (285 mg, 78%). $[\alpha]_D$ = -50.3 ($CHCl_3$, 0.4). IR (film) ν_{max} cm^{-1}: 1750, 1675, 1470, 1380, 1360, 1270, 1240, 840; ^1H δ: 6.26 (1H, dd, J = 6.4 and 2.9, H–7), 4.45 (1H, d, J = 12.2, H_a–12), 4.21 (1H, d, J = 12.2, H_b–12), 2.91 (1H, d, J = 3.8, H_a–11), 2.86 (1H, d, J = 3.8, H_b–11), 2.02 (3H, s, –OCO**Me**), 0.99, 0.91, 0.89 (3H, s, ea, Me–15, Me–14, Me–13). ^{13}C δ: see Table 4; MS: 278 ([M^+], 5), 263 (7), 235 (55), 218 (27), 203 (33), 189 (27), 133 (41), 119 (55), 105 (81), 109 (75), 91 (80), 69 (81), 55 (100); Found: C, 73.32; H, 9.43. $C_{18}H_{26}O_5$ requires C, 73.35; H, 9.41%.

TREATMENT OF **3** WITH MCPBA AND FLUORIDES: *12–acetoxy–9α(11)–epoxy–7–drimen*, **17** and *12–acetoxy–9β(11)–epoxy–7–drimen*, **18**.

Potassium fluoride (6 mg, 0.1 mmol), sodium fluoride (14 mg, 0.3 mmol) and MCPBA (40 mg, 0.23 mmol) were dissolved in CH_2Cl_2 (1.2 ml), chilled in an ice–bath and purged with a stream of Ar. Compound **3** (54 mg, 0.21 mmol) dissolved in CH_2Cl_2 (3 ml) was added to the solution, the resulting mixture was stirred for 45 min. The solvent was removed and ether was added, the reaction mixture was washed with 10% Na_2CO_3 and water, dried with Na_2SO_4, filtered and evaporated to afford a yellow oil corresponding to the mixture of epoxides **17/18** (54 mg, 98%, 4:1 ratio).

BASIC HYDROLYSIS OF **17**: *12–acetoxy–8–drimen–7α,11–diol*, **19**.

A solution of 0.5 N NaOH (10 ml) in *t*–BuOH (5:1) was added to a mixture of **17/18** (310 mg, 1.2 mmol). The reaction mixture was stirred for 24 h at room temperature and was then heated to 40 °C for 8 h. Water was added and the mixture was extracted with ether, washed with 2N HCl and water, dried (Na_2SO_4), filtered and evaporated to give a crude reaction product (305 mg) that was chromatographed affording, with hexane/EtOAc 95:5, **17/18** (200 mg, 65%) and, with hexane/EtOAc 9:1, **19** (70 mg, 23%). IR: ν_{max} (film) cm^{-1}: 3400, 1740, 1240. ^1H δ: 4.86 (1H, d, J = 12.2, H_a–12), 4.81 (1H, d, J = 12.2, H_b–12), 4.20 (3H, m, H–7 and H–11), 2.09 (3H, s, –OCO**Me**), 0.99, 0.94, 0.91 (3H,s, ea, Me–15, Me–14, Me–13). ^{13}C δ: see Table 4.

ACETYLATION OF **19**: *7α,11,12–triacetoxy–8–drimene*, **19'**.

19 (70 mg) was acetylated with Ac_2O (1 ml) and pyridine (1 ml). The reaction mixture was left over night at room temperature, then poured into ice–water and extracted with ether. The ether extracts were combined and washed with 2N HCl, $NaHCO_3$ and water, dried with Na_2SO_4, filtered and evaporated to give **19'** (70 mg, 80%). IR (film) ν_{max} cm^{-1}: 1750, 1740, 1680, 1370, 1240, 1230. ^1H δ: 5.41 (1H, d, J = 3.9, H–7), 4.68 (1H, d, J = 12.2, H_a–11), 4.62 (2H, s, H–12), 4.54 (1H, d, J = 12.2, H_b–11), 2.06, 2.05, 2.04 (3H, s, ea, –OCO**Me**), 0.99, 0.86, 0.85 (3H, s, ea, Me–15, Me–14, Me–13). ^{13}C δ: 35.4 (1), 18.7 (2), 41.3 (3), 32.8 (4), 46.0 (5), 25.6 (6), 68.2 (7), 147.8 (8), 130.8 (9), 39.2 (10), 58.9 (11), 61.2 (12), 32.7 (13), 21.4 (14), 20.3 (15), 170.6, 170.5, 170.4 (OCOMe), 21.2, 20.9, 20.8 (OCO**Me**).

TREATMENT OF **17** WITH BF_3: **20** AND **21**.

Freshly distilled BF_3•Et_2O (one drop) was added to a solution of **17** (141 mg, 0.5 mmol) in dry benzene and stirred for 5 min. Water was added and the mixture extracted with ether. The organic layer was washed with 10% Na_2CO_3 and water, dried, filtered and evaporated to give **20/21** (138 mg, 98%). IR (film) ν_{max} cm^{-1}: 2840, 2760, 1745, 1720, 1470, 1380, 1365, 1240. ^1H δ: 9.76 (1H, d, J = 5.3, H–11), 9.64 (1H, d, J = 5.3, H–11'), 6.01 (1H, m, H–7), 4.57 (1H, d, J = 12.3, H_a–12), 4.43 (1H, d, J = 12.3, H_b–12), 2.84 (1H, m, H–

9), 2.01 (3H, s, –OCOMe), 1.04, 0.93, 0.88 (3H, s,ea). The integral of peaks H–11 and H–11' indicates that **20/21** are present in a 98:2 ratio.

EPIMERIZATION OF **20**: *9S–12–acetoxy–7–drimen–11–al*, **21**.

Compound **20** (60 mg) was passed through a Silica gel column (6 g) affording **21** (55 mg). IR (film) ν_{max} cm^{-1}: 2840, 2760, 1745, 1720, 1470, 1380, 1365, 1240. MS: 278 ([M^+], 3), 249 (4), 234 (13), 217 (21), 189 (100), 119 (48), 109 (64), 91 (56), 81 (47), 69 (82), 55 (73). ^1H δ: 9.64 (1H, d, J = 5.3, H–11), 6.09 (1H, m, H–7), 4.45 (1H, d, J = 12.3, H_a–12), 4.28 (1H, d, J = 12.3, H_b–12), 2.47 (1H, d, J = 5.3, H–9), 2.01 (3H, s, –OCOMe), 0.94, 0.92, 0.91 (3H, s, ea, Me–15, Me–14, Me–13). ^{13}C δ: see Table 4.

REDUCTION OF **20** WITH LAH: *9R–7–drimen–11,12–diol*, **22**.

$LiAlH_4$ (10 mg, 0.3 mmol) was added to a solution of **20** (133 mg, 0.5 mmol) in dry ether (5 ml), and the reaction mixture was stirred for 1 h at room temperature under Ar atmosphere. Then ether moistened with water was added and the reaction mixture dried (Na_2SO_4), filtered and evaporated to give **22** (104 mg, 92% yield). $[\alpha]_D$ –6.4 ($CHCl_3$, c 1.0). IR (film) ν_{max} cm^{-1}: 3340, 1465, 1390, 1365, 1036. MS: 218 ([M^+-18], 21), 190 (17), 137 (10), 123 (50), 109 (83), 95 (30), 81 (41), 69 (70), 55 (74), 41 (100).^1H δ: 5.81 (1H, m, H-7), 4.38 (1H, d, J = 12.1, H_a-12), 3.99 (1H, d, J = 12.1, H_b-12), 3.92 (1H, dd, J = 11.9 and 2.1, H_a-11), 3.69 (1H, dd, J = 11.9 and 7.5, H_b-11), 0.89, 0.87, 0.77 (3H, s,ea).

BASIC HYDROLYSIS OF **20**: **23**.

A solution of 3% K_2CO_3 in MeOH was added to compound **7** (84 mg, 0.3 mmol). The reaction was monitored by TLC and judged complete after 30 min. Water was added and the reaction mixture extracted with ether. The organic layer washed with 2N HCl and water, dried with Na_2SO_4, filtered and evaporated. The crude reaction product was chromatographed affording unreacted starting material **20** (15 mg, 24%, hexane/EtOAc 97:3) and **23** (35 mg, 56%, Hexane/EtOAc 95:5). IR (film) ν_{max} cm^{-1}: 3400, 1470, 1400, 1380, 1020, 930, 830. ^1H δ: 5.51 (1H, m, H–7), 5.27 (1H, t, J = 4.4, H–11), 4.48 (1H, d, J = 11.2, H_a–12), 4.19 (1H, d, J = 11.2, H_b–12), 1.58 (1H, s, –OH), 0.92, 0.89, 0.82 (3H, s, ea). ^{13}C δ: see Table 4.

CIS–HYDROXYLATION OF **3**.

A. CATALYTIC WITH NMO AS COOXIDANT.

N–Methylmorpholine–N–oxide (31 mg, 0.23 mmol) and OsO_4 (1M in *t*–BuOH, 0.05 ml) were added to compound **3** (60 mg, 0.23 mmol) dissolved in a mixture of *t*–BuOH/THF/H_2O (10:3:1, 3.7 ml) and stirred at room temperature for 52 h. The mixture was cooled at 0 °C and a saturated solution of Na_2SO_3 (2 ml) was added. The mixture was stirred at room temperature for 16 h, filtered through a Celite pad, washed with CH_2Cl_2 and the filtrate evaporated to give a yellow oil (63 mg), which was acetylated with Ac_2O (1 ml) and pyridine (1 ml), extracted, evaporated and chromatographed to give **3** (9 mg, 29%, hexane/EtOAc, 9:1), **24** (32 mg, 42%, hexane/EtOAc 4:1) and **25** (9 mg, 12%, hexane/EtOAc 4:1).

Compound **24**: $[\alpha]_D$ –37.5 ($CHCl_3$, 4.0). IR (film) ν_{max} cm^{-1}: 3340, 1750, 1470, 1380, 1240, 1100; ^1H

δ: 6.04 (1H, dd, J = 5.4 and 2.4, H-7), 4.60 (1H, d, J = 11.6, H_a-12), 4.59 (1H, d, J = 11.6, H_b-12), 4.28 (1H, d, J = 11.7, H_a-11), 4.19 (1H, d, J = 11.7, H_b-11), 2.05, 2.04 (3H, s, ea, –OCO**Me**), 0.93 (3H, s), 0.90 (6H, s); MS: 338 ([M^+], 2), 278 (13), 265 (48), 214 (42), 205 (29), 154 (100), 109 (85), 81 (72), 69 (71), 55 (65).

Compound **25**: *7α,12-diacetoxy-9-drimen-8α-ol.* $[\alpha]_D$ -42.0 ($CHCl_3$, c 0.3).IR (film) ν_{max} cm^{-1}: 3800 (broad), 3500, 1745, 1470, 1380, 1240, 1100; ^1H δ: 5.46 (1H, s, H_a-11), 5.14 (1H, s, H_b-11), 5.14 (1H, m, H-7), 4.50 (1H, d, J = 11.7, H_a-12), 3.95 (1H, d, J = 11.7, H_b-12), 2.12, 2.09 (3H, s, ea, –OCO**Me**), 1.10, 0.84, 0.81 (3H, s, ea, Me–15, Me–14, Me–13). ^{13}C δ: see Table 4; MS: 278 ([M^+]-60, 10), 265 (100), 236 (10), 223 (48), 205 (41), 109 (35), 81 (32), 69 (55), 55 (53).

B. CATALYTIC WITH *t*-BuOOH AS COOXIDANT.

Et_4NOH (0.12 ml), *t*-BuOOH (0.07 ml) and OsO_4 (1M in *t*-BuOH, 0.01 ml) were added to a solution of **3** (90 mg, 0.34 mmol) in *t*-BuOH (0.07 ml) pre–cooled at 0 °C, under Ar atmosphere and stirred for 3 days at room temperature. A saturated solution of Na_2SO_3 (2 ml) was added and stirring was continued for 1 h. The mixture was filtered through a Celite pad, washed with ether and the filtrate dried with Na_2SO_4 and evaporated to give a yellow oil (80 mg) which was acetylated with Ac_2O (0.5 ml) and pyridine (1 ml) to give a mixture of diacetates (90 mg). CC on a silica gel column gave **3** (21 mg, 23%, hexane/EtOAc 9:1) and **24** (10 mg, 13%, hexane/EtOAc 4:1).

C. STOICHIOMETRIC

Compound **3** (38 mg, 0.14 mmol) in dry pyridine (1.2 ml) was added to a solution of OsO_4 (44 mg, 0.17 mmol) dissolved in dry pyridine (1.2 ml) and stirred for 5 days. A 40 % solution of $NaHSO_3$ (0.9 ml) was added and stirring was continued for 1.5 h. Water (5 ml) was added and the reaction mixture extracted with $CHCl_3$ and EtOAc, dried with Na_2SO_4 and evaporated to afford a crude product (40 mg) which was acetylated with Ac_2O/Py, after usual work–up and chromatography **3** (4 mg, 1%, hexane/EtOAc 9:1), **25** (7 mg, 9%, hexane/EtOAc 7:3) and **26** (8 mg, 13%, hexane/EtOAc 7:3) were separated.

Compound **26**: *7β,11,12-triacetoxi-8β,9α-drimanediol.* $[\alpha]_D$ +26.1 ($CHCl_3$, c 0.8).IR (film) ν_{max} cm^{-1}: 3450, 1745, 1460, 1370, 1240, 114o; ^1H δ: 5.19 (1H, m, H-7), 4.44 (1H, d, J = 11.7, H_a–11), 4.35 (1H, d, J = 11.7, H_b–11), 4.22 (1H, d, J = 11.5, H_a–12), 4.17 (1H, d, J = 11.5, H_b–12), 2.09, 2.08, 2.06 (3H, s, ea, –OCO**Me**), 1.08, 0.91, 0.84 (3H, s, ea, Me–15, Me–14, Me–13). ^{13}C δ ($CDCl_3$): see Table 4.^{13}C (C_6D_6) δ: 32.5 (1), 18.5 (2), 41.6 (3), 33.4 (4), 44.0 (5), 24.2 (6), 72.9 (7), 78.2 (8), 76.4 (9), 43.3 (10), 62.3 (11), 64.8 (12), 33.5 (13), 22.0 (14), 16.2 (15), 170.0, 169.2 , 169.1 (–OCOMe), 20.7, 20.4, 20.2 (–OCO**Me**); MS: 414 ([M^+], 4), 400 (5), 358 (10), 341 (9), 323 (57), 294 (53), 276 (80), 263 (60), 251 (98), 234 (12), 221 (20), 137 (22), 123 (40), 109 (60), 95 (40), 81 (53), 69 (100).

SYNTHESIS OF THE CYCLIC CARBONATE **27**.

Chlorosulfonyl isocyanate (CSI, 0.04 ml, 0.44 mmol) in C_6H_6/CH_2Cl_2 (5:1, 1.2 ml) was added dropwise to a solution of **17** (100 mg, 0.4 mmol) in C_6H_6/CH_2Cl_2 (5:1, 1.2 ml) precooled at – 10 °C. The mixture was stirred for 10 min, and the solvent evaporated under reduced pressure. The residue was dissolved in

acetone/water (95:5, 2.4 ml) and the resulting acid solution was neutralized with 5% KOH and stirred for 30 min, extracted with ether, washed, evaporated and chromatographed to give **20** (36 mg, 38%, hexane:EtOAc 9:1), **27** (26 mg, 22%, hexane/EtOAc 4:1) and **28** (9 mg, 8%, hexane/EtOAc 4:1).

Compound **27**: $[\alpha]_D$ -102.2 ($CHCl_3$, c 1.1). IR (film) ν_{max} cm^{-1}: 2940, 1800, 1740, 1675, 1380, 1365, 1240, 1200; ^1H δ: 6.30 (1H, m, H-7), 4.76 (1H, d, J = 12.7, H_a-12), 4.58 (1H, d, J = 12.7, H_b-12), 4.38 (2H, s, H-11), 2.06 (3H, s, –OCO**Me**), 0.92, 0.91 (3H, s, ea), 0.81 (3H, s, Me-15). ^{13}C δ: see Table 4; MS: 322 ([M^+], 5), 262 (11), 218 (18), 124 (100), 109 (99), 81 (84), 69 (99), 55 (80); Found: M^+, 322.1779 $C_{18}H_{26}O_5$ requires *M* 322.1780; Found: C, 67.05; H, 8.12. $C_{18}H_{26}O_5$ requires C, 67.06; H, 8.13%.

28: IR (film) ν_{max} cm^{-1}: 3220, 2850, 1745, 1380, 1365, 1240, 1200; ^1H δ: 6.03 (1H, m, H-7), 4.75 (1H, d, J = 12.7, H_a-12), 4.50 (1H, d, J = 12.7, H_b-12), 4.31 (2H, s, H-11), 2.04 (3H, s, –OCO**Me**), 0.90 (6H, s, Me-13, Me-14), 0.80 (3H, s, Me-15). ^{13}C δ: see Table 4; MS: 321 ([M^+], 36), 278 (30), 261 (80), 246 (60), 218 (82), 202 (99), 124 (22), 109 (37), 95 (28), 81 (60), 69 (100), 55 (60).

HYDROLYSIS OF **27**: *7-drimen-9α,11,12-triol* , **29**.

A solution of 4% NaOH in 1,4–dioxane (2 ml) was added to **27** (25 mg, 0.8 mmol) and stirred at room temperature for 30 min. The reaction mixture was extracted with ether, washed with 2N HCl and water. Removal of solvent afforded **29** (19 mg, 96%). $[\alpha]_D$ -83.0 ($CHCl_3$, c 0.3). IR (film) ν_{max} cm^{-1}: 3380, 2920, 1460, 1380, 1360, 1150, 1070; ^1H δ: 5.91 (1H, dd, J = 4.7 and 2.3, H-7), 4.32 (1H, d, J = 12.2, H_a-12), 4.14 (1H, d, J = 12.2, H_b-12), 3.76 (1H, d, J = 11.5, H_a-11), 3.75 (1H, d, J = 11.5, H_b-11), 0.93, 0.91, 0.82 (3H, s, ea, Me–15, Me–14, Me–13); MS: 254 ([M^+], 3), 236 (3), 223 (60), 219 (6), 205 (38), 149 (28), 130 (68), 112 (57), 109 (80), 91 (34), 81 (63), 69 (83), 55 (79), 41 (100).

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