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Side-chain migration reactions and ring B aromatization in labdanes: scope and limitations. Synthesis of isofregenedane type tetrahydronaphthalenic diterpenes

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Abstract—The reaction of bicyclic diterpenes with an allylic oxygenated function or an equivalent functionality on ring B in the presence of I_2/benzene afforded a simple and rapid synthesis of tetrahydronaphthalenic diterpenes of the isofregenedane class.

1. Introduction

All bicyclic diterpens with an aromatic ring are not prevalent in nature.[1] Until now only four compounds have been described and belong to two isomeric carbon skeleta: fregenedane, with one member: fregenedadiol,[2] and isofregenedane, with three members: isofregenedadiol,[3] chrysolic acid[4] and 14-isofregeneden-13-ol.[5] All of these structures have been determined spectroscopically (Fig. 1).

A new rearrangement reaction that allows accessibility to isofregenedane compounds and particularly to isofregenedadiol **1** is described.

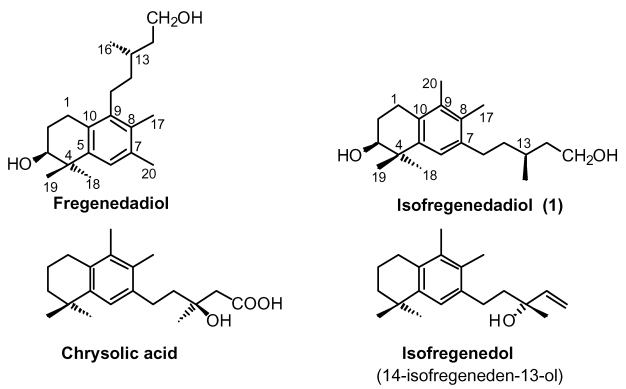
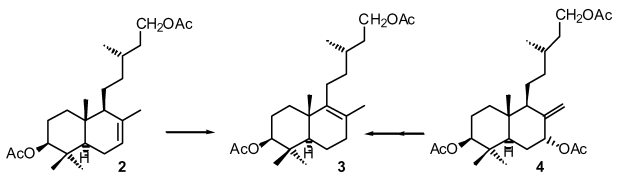


Figure 1.

2. Results and discussion

Our group has studied the double bond isomerization (Δ^7 to Δ^8) in the labdane class of compounds by heating the corresponding substrate in I_2/benzene solution.[3]

Compound **3** was obtained from **2**[6] (Scheme 1). However, this isomerization did not produce a good yield of **3** when substrate **4** was employed.



Scheme 1.

2.1. Reaction of compound 4 with I_2

Reflux of a benzene solution of **4**[7] (Scheme 2), in the presence of I_2, until all the starting material disappeared, afforded a major mixture of **5/6** (71%, 4/1) with four minor compounds **7**,[8] **8**, **9** and **10**.[8] Compounds **5** and **6** were separated by MPLC (Flash Silica gel) or by CC of its monoacetyl derivatives **11** and **12** (4/1) obtained from the selective hydrolysis of the mixture with K_2CO_3/MeOH.

The major compound **5** was identified as isofregenedadiol diacetate, isolated from *Halimium viscosum*.[3] The 2D heteronuclear correlation experiments (HMQC and HMBC, 500 MHz) of **11** confirmed the pentasubstituted

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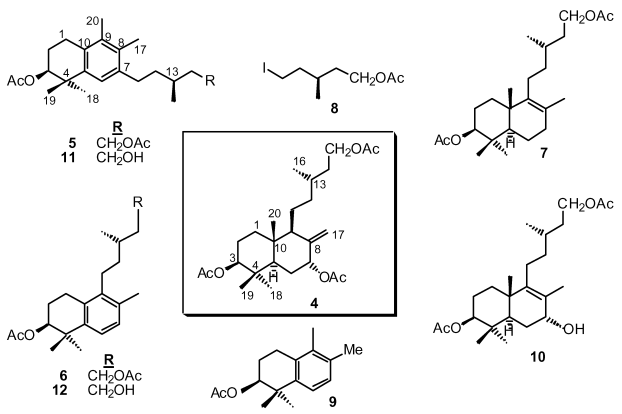


Scheme 2.

tetrahydronaphthalenic structure. Results are summarized in Table 1.

Monoacetyl derivative **12** is a bicyclic norditerpenoid (M^+ *m/z* 332, $C_{21}H_{32}O_3$) with a tetrasubstituted tetrahydronaphthalenic structure, formed by Me-20 loss and ring-B aromatization (two *ortho* aromatic proton signals are observed in ^{1}H NMR).

The structures of the remaining compounds are determined spectroscopically.

Due to the results observed with compound **4** in the isomerization reaction with Iodine, several assays have been carried out with labdanes having different side-chains: saturated **13**–**28**, unsaturated **29**–**31** or degradated **32**–**33** with allylic functions or equivalent functionalities on ring B, prepared from the major compounds: 7-labden-3β,15-diol, **34**,[7] 6-oxocativic acid, **39**,[9] dihidrozamoranic acid, **43**,[10] zamoranic acid **46**[11] isolated from the extracts of different Cistaceae (*Cistus ladaniferus* and *H. viscosum*) or the commercially available sclareol **54** (Fig. 2). The results obtained with each one of them are presented as follows.

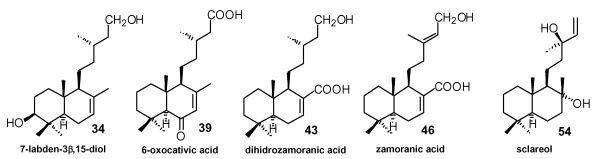
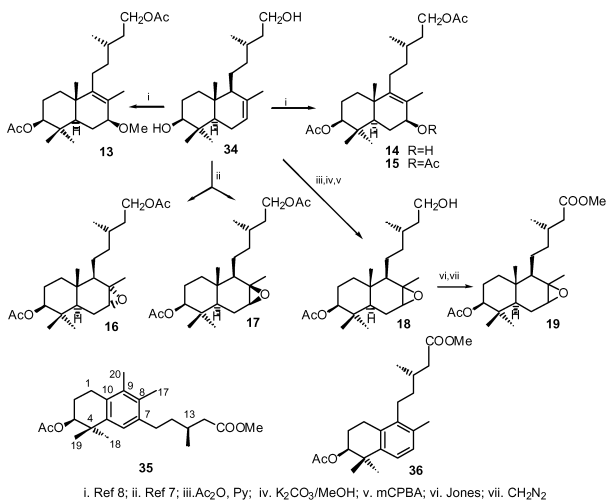


Figure 2. Starting material.

2.2. Preparation of compounds 13–19 and their reaction with I_2

Compounds **13**–**19** were synthesized from 7-labden-3β,15-diol, **34**, according to Scheme 3:

The reaction of compounds **13**–**17** with I_2/benzene/reflux

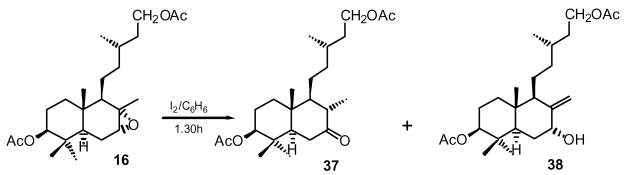


i. Ref 8; ii. Ref 7; iii.Ac_2O, Py; iv. K_2CO_3/MeOH; v. mCPBA; vi. Jones; vii. CH_2N_2

Scheme 3.

Table 1.

No	Compound	mg	C_6H_6	I_2	M 10^{-3} I_2/C_6H_6 reflux	h	Reaction products 4/1	%	Other products
1	**4**	470	25	140	22	6	**5/6**	71	**7**–**10**
2	**13**	229	20	45	9	5	**5/6**	70	
3	**14**	70	10	45	9	2	**5/6**	71	
4	**15**	54	10	45	9	1	**5/6**	72	
5	**16**	103	50	203	16	23	**5/6**	68	**7**–**10**
6	**17**	72	20	140	25	24	**5/6**	68	
7	**18**	107	25	150	24	6	**11/12**	65	
8	**19**	330	25	120	19	22	**35/36**	68	
9	**20**	90	15	130	34	23	**42**	70	
10	**21**	632	20	140	28	3	**41**	61	
11	**22**	87	5	230	90	16	**42**	60	
12	**23**	33	5	12	47	10	–	–	
13	**24**	33	5	12	47	4	**42**	30	
14	**25**	70	5	24	94	4	**42**	30	
15	**26**	34	5	12	47	2	**42**	51	**45**
16	**26**	30	5	12	47	42	–	–	
17	**27**	72	5	20	80	5	**51/52**	20	**53**
18	**28**	33	5	10	40	5	**51/52**	27	**53**
19	**29**	133	20	160	32	5	**50**	8	
20	**30**	77	15	160	42	70	**50**	8	
21	**31**	15	4	15	4	1	**50**	8	
22	**32**	146	20	130	26	3	**58**	58	
23	**33**	692	40	360	36	1	**58**	58	

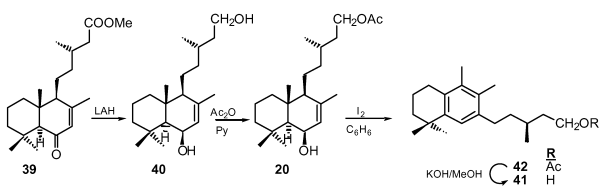


Scheme 4.

led to **5/6** as shown in Table 1. Compound **18** afforded **11/12** (4/1) and compound **19** gave the mixture **35/36** (4/1) (see Table 1).

If the reaction of **16** is quenched and analyzed after 1.5 h the major product is **38**[7] and **37** is just a minor reaction product (Scheme 4); indicating that if the reaction is continued **38** is the compound that is subsequently transformed into the mixture **5/6** (68%, 4/1) and the other minor reaction products **7**–**10**.

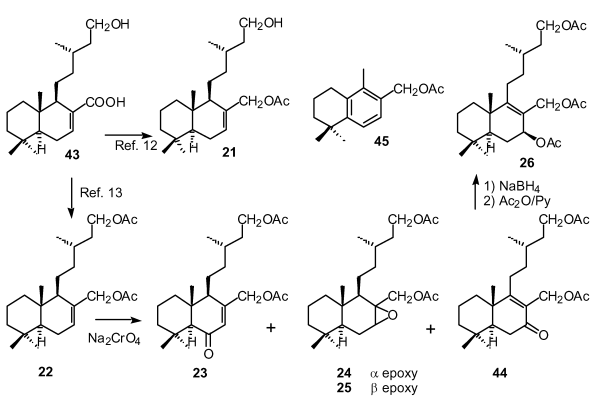
The availability of methyl-6-oxocativate **39** from *C. ladaniferus*[9a] allowed other assays with a different allylic system on ring B. Compound **20**, obtained according to the reaction scheme shown (Scheme 5) isomerized under the same reaction conditions to compound **42**, that is hydrolyzed to afford **41**.



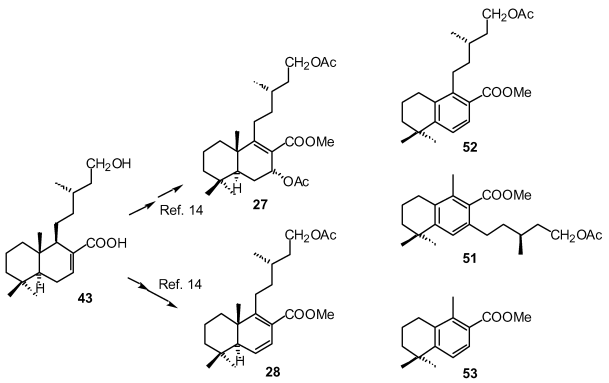
Scheme 5.

Compounds **21**–**26** synthesized from dihydrozamoranic acid, **43**,[12–14] isolated from *H. viscosum* and *Halimium verticilatum*[10] (Scheme 6) afforded the isomerization products **41** (from **21**) or **42** (from **22**–**26**) with some traces of **45**.

With a methoxycarbonyl at C-17, compounds **27** and **28**



Scheme 6.

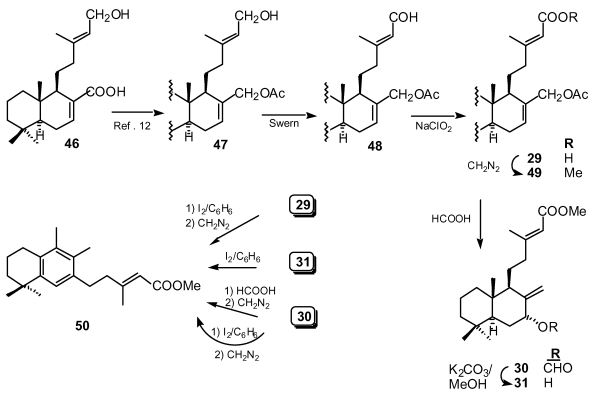


Scheme 7.

(Scheme 7), the reaction does not proceed as well and both **51** and **52** were obtained in low yield, and **53** in moderate yield.

2.3. Preparation and reaction with I_2 of compounds 29–31

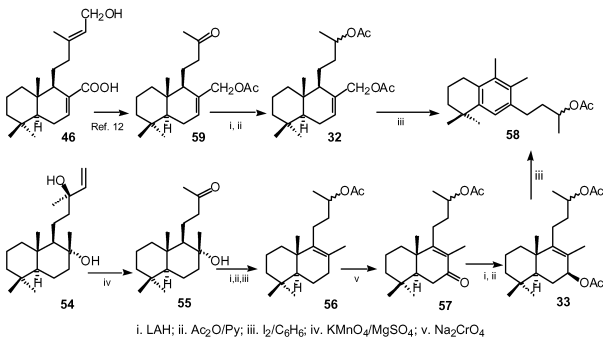
An unsaturated side-chain as in **29**–**31**, synthesized from zamoranic acid **46**[12] (Scheme 8) afforded complex mixtures from which the rearranged product **50** was isolated with low yield (8%, Table 1).



Scheme 8.

2.4. Preparation of compounds 32 and 33 and their reaction with I_2

Dinor derivatives **32** (obtained from zamoranic acid **46**,[12] Scheme 9) and **33** (from sclareol **54**) gave excellent yields of a rearranged product with aromatized ring B **58**.



Scheme 9.

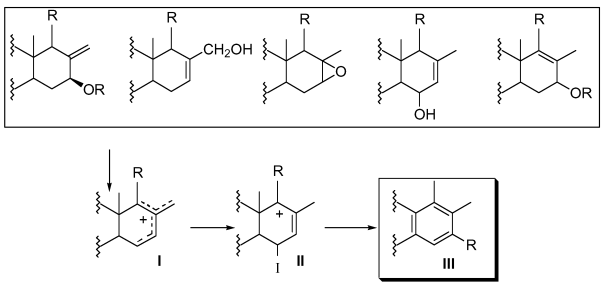
With substrates **4** (Scheme 2) and **16** (Scheme 3), in addition to the major reaction product, all the minor reaction products were separated and characterized. In all other assays, the components were identified by TLC and only the major products were separated and characterized: **45** (Scheme 6) and **58** (Scheme 9).

Substrate with the entire side-chain (entries 1–11, Table 1) leading to isofregenedane derivatives gave analog results and no-dependence was observed between concentration, Iodine amount and/or total reaction time.

Function requirements seems to be an allylic hydroxyl or acetoxyl group in any position of ring B or an oxiranic ring. Analog yields were observed when an acetoxyl group is the functionality at C-17 (compounds **21** and **22**, Scheme 6) but a yield drop in **42** (Scheme 5) was observed when there is an additional functional group **24**–**25**, (Scheme 6). A carbonyl group **23** (Scheme 6), or base (Et_3N) inhibited the reaction.

The presence of the complete side-chain indicated that the yields are independent from the functionality at C-15 (hydroxymethylene, acetoxymethylene, methoxycarbonyl) and only in the presence of a double bond Δ^{13}, the rearranged products (entries 19–21, Table 1) were obtained in less than 10% yield. When the substrate has a degraded side-chain (entries 22 and 23, Table 1, Scheme 9) aromatization and rearrangement proceed with good yields.

Considering that the reaction is inhibited by Et_3N, it could be supposed, that is an acid mediated reaction. The generation of HI in situ promotes the rearrangement to afford product III through intermediates I and iodide II by a mechanism described in Ref. 3 (Scheme 10).



Scheme 10.

3. Experimental

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 and 77.0 ppm, for ^1H and ^{13}C respectively, on a Bruker WP-200 SY and a BRUKER DRX 400 MHz. Chemical shifts are reported in δ ppm and coupling constants (J) are given in Hz. MS were performed at a VG-TS 250 spectrometer at 70 eV ionizing voltage. Mass Spectra are presented as m/z (% rel. int.). HRMS were recorded on a VG Platform (Fisons) spectrometer using Chemical Ionization (ammonia as gas). Optical rotations were determined on a Perkin–Elmer 241 polarimeter in 1 dm cells. Diethyl ether, THF and benzene were distilled from sodium, and pyridine and dichloromethane were distilled from calcium hydride under argon atmosphere.

3.1. General procedure of treatment with I_2 (C_6H_6)

To a solution of the compound in dry benzene was added I_2. The reaction mixture was refluxed for 6 h. After cooling and extraction with benzene, the organic phase was washed with 20% $NaHSO_3$ and water (until neutral), dried over anhydrous Na_2SO_4, filtered and evaporated to dryness. The crude product was chromatographed through silicagel.

3.2. Reaction of 4 with I_2

To a solution of **4** (6.0 g, 12.3 mmol) in dry benzene (25 mL) was added I_2 (140 mg, 0.55 mmol). The reaction mixture was refluxed during 6 h. After cooling and extraction with benzene, the organic phase was washed with 20% $NaHSO_3$ and water (until neutral), dried over anhydrous Na_2SO_4, filtered and evaporated to dryness. The crude product (5.98 g) was chromatographed through silicagel: eluted with hexane to afford **8** (390 mg, 7% yield), **9** (399 mg, 7% yield) and **7** (195 mg, 3% yield); with hexane/EtOAc 95/5 to afford a mixture of **5/6** (3.39 g, 71% yield); and with hexane/EtOAc 1/1 to afford **10** (89 mg, 2% yield). The mixture **5/6** was further chromatographed (MPLC, hexane/EtOAc 95/5) to give **5** (2.86 g, 60% yield) and **6** (334 mg, 7% yield).

3.2.1. 3β,15-Diacetoxy-isofregenedane: 5. $[\alpha]_D^{20°C}=+4.3$ (c=1.0, $CHCl_3$); IR ν_{max}^{film}: 1740, 1620, 1580, 1240 cm^{-1}. ^1H NMR ($CDCl_3$): 7.00 (1H, s, H-6), 4.96 (1H, dd, J_1=6.8 Hz, J_2=4.3 Hz, H-3), 4.15 (2H, t, J=6.8 Hz, H-15), 2.80–2.50 (2H, m, H-1), 2.70–2.50 (2H, m, H-11), 2.21 (3H, s, Me-17), 2.16 (3H, s, Me-20), 2.06 (3H, s, MeCOO–), 2.05 (3H, s, MeCOO–), 1.9–1.0 (7H, m), 1.31 (3H, s ea, Me-18 and Me-19), 1.02 (3H, d, J=6.4 Hz, Me-16) ppm. ^{13}C NMR ($CDCl_3$): 25.0 (C-1); 24.0 (C-2); 77.4 (C-3); 37.4 (C-4); 141.1 (C-5); 124.6 (C-6); 138.7 (C-7); 131.8 (C-8); 134.8 (C-9); 130.6 (C-10); 32.1 (C-11); 38.4 (C-12); 30.3 (C-13); 35.6 (C-14); 62.9 (C-15); 19.6 (C-16); 15.5 (C-17); 29.9 (C-18); 26.1 (C-19); 15.7 (C-20); 170.9 (Me*C*OO–); 170.7 (Me*C*OO–); 21.2 (*Me*COO–) and 20.9 (*Me*COO–). MS, m/z: 388 [M^+] (15), 328 (80), 316 (35), 253 (18), 200 (38), 187 (100), 157 (35), 131 (58), 119 (57), 83 (44), 13 (60). HRMS calcd for $C_{24}H_{36}O_4$: 388.2614; found: 388.2609.

3.2.2. 3β,15-Diacetoxy-20-*nor*-fregenedane: 6. $[\alpha]_D^{20°C}=+6.8$ (c=0.8, $CHCl_3$); IR ν_{max}^{film}: 1740, 1620, 1580, 1380, 1360, 885 cm^{-1}. ^1H NMR ($CDCl_3$): 7.08 and 7.05 (1H, d ea, J=7.8 Hz, H-6 and H-7), 4.95 (1H, dd, J_1=6.8 Hz, J_2=4.3 Hz, H-3), 4.13 (2H, t, J=6.8 Hz, H-15), 2.90–2.70 (2H, m, H-1), 2.70–2.50 (2H, m, H-11), 2.30 (3H, s, Me-17), 2.10–1.90 (2H, m), 2.07 (3H, s, MeCOO–), 2.06 (3H, MeCOO–), 1.80–1.20 (5H, m), 1.31 (6H, s, Me-18 and Me-19), 1.05 (3H, d, J=6.4 Hz, Me-16). ^{13}C NMR ($CDCl_3$): 23.8 (C-1); 23.9 (C-2); 77.1 (C-3); 38.0 (C-4); 141.9 (C-5); 124.2 (C-6); 128.6 (C-7); 132.2 (C-8); 138.9 (C-9); 133.4 (C-10); 27.1 (C-11); 35.9 (C-12); 30.9 (C-13); 35.7 (C-14); 62.9 (C-15); 19.4 (C-16); 19.6 (C-17); 30.6 (C-18); 26.5

(C-19); 171.1 (Me*C*OO–); 170.9 (Me*C*OO–); 21.3 (*Me*COO–) and 21.0 (*Me*COO–). HRMS calcd for $C_{23}H_{34}O_4$: 374.2457; found: 374.2462.

3.2.3. 3*R*-1-Acetoxy-5-iodin-3-methylpentane: 8. IR ν_{max}^{film}: 2967, 1747, 1458, 1242, 1026 cm^{-1}. ^1H NMR ($CDCl_3$): 4.10 (2H, m, CH_2OAc), 3.20 (2H, m, CH_2I), 2.04 (3H, s, MeCOO–), 1.90–1.20 (5H, m), 0.92 (3H, d, J=6.1 Hz, *Me*–C-3). ^{13}C NMR ($CDCl_3$): 4.1 (C-1); 40.7 (C-2); 31.1 (C-3); 34.8 (C-4); 62.4 (C-5); 19.1 (C-6); 171.0 (Me*C*OO–) and 20.7 (*Me*COO–). MS, *m/z*: 270 [M^+] (<1), 210 (1), 143 (2), 127 (7), 83 (49), 55 (100).

3.2.4. 2β-Acetoxy-1,1,5,6-tetramethyl-1,2,3,4-tetrahidronaphthalene: 9. IR ν_{max}^{film}: 1740, 1500, 1240 cm^{-1}. ^1H NMR ($CDCl_3$): 7.16 and 7.06 (1H, d ea, J=7.8 Hz, H-7 and H-8), 4.87 (1H, dd, J_1=8.3 Hz, J_2=3.4 Hz, H-2), 2.90–2.70 (2H, m, H-4), 2.28 (3H, s, *Me*–C-5), 2.15 (3H, s, *Me*–C-6), 2.06 (3H, s, MeCOO–), 1.60–1.40 (2H, m), 1.31 (3H, s, *Me*–C-1) and 1.30 (3H, s, *Me*–C-1). ^{13}C NMR ($CDCl_3$): 37.9 (C-1); 77.4 (C-2); 23.8 (C-3); 24.7 (C-4); 134.3 (C-5); 132.9 (C-6); 128.0 (C-7); 123.8 (C-8); 141.6 (C-9); 133.9 (C-10); 19.6 (Me–C_6); 26.1 (Me–C_1); 20.5 (Me–C_1); 15.2 (Me–C_5); 21.0 (*Me*COO–) and 170.9 (Me*C*OO–). MS, *m/z*: 246 [M^+] (20), 87 (81), 73 (100), 159 (41), 145 (30), 133 (45), 115 (12), 105 (11), 91 (12).

3.3. Selective alkaline hydrolysis of 5/6: 11 and 12

To a mixture of **5/6** (382 mg, 0.98 mmol) in MeOH (7 mL), K_2CO_3 (138 mg, 1.0 mmol) was added. The reaction mixture was stirred at room temperature for 1.5 h. After addition of water, the mixture was extracted with ether. The organic phase was washed with HCl (2N) and water (until neutral), dried over anhydrous Na_2SO_4, filtered and evaporated to afford 290 mg of crude product that was chromatographed through deactivated silicagel. Elution with hexane/EtOAc 4/1 gave **11** (156 mg, 45%) and **12** (25 mg, 5%).

3.3.1. 3β-Acetoxy-isofregenedan-15-ol: 11. $[\alpha]_D^{20°C}$=−4.5 (c=0.9, $CHCl_3$); IR ν_{max}^{film}: 3500, 1740, 1240, 1500 cm^{-1}. ^1H NMR ($CDCl_3$): 7.03 (1H, s, H-6), 4.95 (1H, dd, J_1=6.8 Hz, J_2=4.3 Hz, H-3), 3.75 (2H, t, J=6.8 Hz, H-15), 2.78–2.50 (4H, m, H-1 and H-11), 2.22 (3H, s, Me-17), 2.17 (3H, s, Me-20), 2.07 (3H, s, MeCOO), 1.80–1.10 (7H, m), 1.32 (6H, s, Me-18 and Me-19), 1.02 (3H, d, J=6.4 Hz, Me-16). ^{13}C NMR ($CDCl_3$): 24.9 (C-1); 23.9 (C-2); 77.4 (C-3); 37.8 (C-4); 141.1 (C-5); 124.8 (C-6); 138.8 (C-7); 131.9 (C-8); 134.6 (C-9); 130.6 (C-10); 32.1 (C-11); 38.5 (C-12); 30.0 (C-13); 40.0 (C-14); 61.2 (C-15); 19.7 (C-16); 15.4 (C-17); 29.9 (C-18); 26.0 (C-19); 15.6 (C-20); 21.2 (*Me*COO–) and 170.9 (Me*C*OO). MS, *m/z*: 346 [M^+] (20), 286 (100), 200 (58), 185 (92), 183 (90), 157 (42), 119 (70), 83 (56), 69 (60). HRMS calcd for $C_{22}H_{34}O_3$: 346.2508; found: 346.2515.

3.3.2. 3β-Acetoxy-20-*nor*-fregenedan-15-ol: 12. $[\alpha]_D^{20°C}$=−3.4 (c=1.2, $CHCl_3$); IR ν_{max}^{film}: 3400, 1740, 1500, 1240 cm^{-1}. ^1H NMR ($CDCl_3$): 7.08 and 7.05 (1H, ea, d, J=7.8 Hz, H-6 and H-7), 4.95 (1H, dd, J_1=6.8 Hz, J_2=4.3 Hz, H-3), 3.75 (2H, t, J=6.8 Hz, H-15), 2.95–2.80 (2H, m, H-1), 2.70–2.50 (2H, m, H-11), 2.30 (3H, s, Me-17), 2.07 (3H, s, MeCOO–), 1.90–1.10 (7H, m), 1.31 (6H, s, Me-18 and Me-19), 1.05 (3H, d, J=6.4 Hz, Me-16). ^{13}C NMR ($CDCl_3$): 23.8 (C-1); 23.9 (C-2); 77.1 (C-3); 38.0 (C-4); 141.9 (C-5); 124.2 (C-6); 128.6 (C-7); 132.2 (C-8); 138.9 (C-9); 133.4 (C-10); 27.1 (C-11); 36.1 (C-12); 30.6 (C-13); 39.8 (C-14); 61.1 (C-15); 19.5 (C-16); 19.6 (C-17); 30.0 (C-18); 26.1 (C-19); 21.3 (*Me*COO–) and 171.1 (Me*C*OO). MS, *m/z*: 332 [M^+] (15), 272 (60), 169 (100), 143 (30), 115 (20), 83 (38), 69 (82). HRMS calcd for $C_{21}H_{32}O_3$: 332.2351; found: 332.2356.

3.4. Reaction of the compounds 13–17 with I_2

See Table 1.

3.5. Reaction of 16 with I_2 (1.5 h): 37 and 38

To a solution of **16** (103 mg, 0.25 mmol) in dry benzene (50 mL), I_2 (203 mg, 0.8 mmol) was added. The reaction was refluxed for 1.5 h. After cooling to room temperature, water was added and extracted with benzene. The benzene was washed with 20% $NaHSO_3$ and water (until neutral), dried over anhydrous Na_2SO_4, filtered and evaporated affording 84 mg of crude product. After column chromatography (hexane/EtOAc 4/1), were obtained **16** (26 mg, 25%), **37** (40 mg, 40%) and **38** (6 mg, 5%).

3.5.1. 8*S*-3β,15-Diacetoxy-labdan-7-one: 37. IR ν_{max}^{film}: 1740, 1712, 1240, 1040 cm^{-1}. ^1H NMR ($CDCl_3$): 4.49 (1H, dd, J_1=10.7 Hz, J_2=4.3 Hz, H-3), 4.10 (2H, t, J=6.4 Hz, H-15), 2.4–2.2 (3H, m), 2.06 and 2.05 (3H, s ea, MeCOO–), 1.90–1.20 (13H, m), 1.07 (3H, d, J=6.0 Hz, Me-17), 1.05, 0.91 and 0.89 (3H, s ea, Me-18, Me-19 and Me-20) 0.93 (3H, d, J=6.4 Hz, Me-16). ^{13}C NMR ($CDCl_3$): 36.0 (C-1); 27.2 (C-2); 80.2 (C-3); 38.1 (C-4); 47.7 (C-5); 35.1 (C-6); 218.4 (C-7); 57.7 (C-8); 53.2 (C-9); 38.0 (C-10); 23.5 (C-11); 38.3 (C-12); 30.5 (C-13); 39.1 (C-14); 62.9 (C-15); 19.4 (C-16); 12.8 (C-17); 27.5 (C-18); 15.9 (C-19); 13.7 (C-20); 21.2 (*Me*COO–); 21.0 (*Me*COO–); 171.2 (Me*C*OO) and 170.8 (Me*C*OO). HRMS calcd for $C_{24}H_{40}O_5$: 408.2876; found: 408.2872.

3.5.2. 3β,15-Diacetoxy-8(17)-labden-7α-ol: 38. IR ν_{max}^{film}: 3340, 3080, 1740, 1640, 1240, 1040, 890 cm^{-1}. ^1H NMR ($CDCl_3$): 5.04 (1H, s, H-17), 4.62 (1H, s, H-17), 4.53 (1H, d, J_1=11.2 Hz, J_2=4.4 Hz, H-3) 4.37 (1H, t, J=2.4 Hz, H-7), 4.08 (2H, t, J=6.8 Hz, H-15), 2.04 (6H, s, MeCOO–), 1.90–1.01 (15H, m), 0.90 (3H, d, J=6.4 Hz, Me-16), 0.87, 0.84 and 0.68 (3H, s ea, Me-18, Me-19 and Me-20). ^{13}C NMR ($CDCl_3$): 36.7 (C-1); 24.3 (C-2); 80.8 (C-3); 39.5 (C-4); 47.1 (C-5); 30.5 (C-6); 73.8 (C-7); 144.5 (C-8); 51.1 (C-9); 37.6 (C-10); 20.7 (C-11); 35.3 (C-12); 30.7 (C-13); 35.7 (C-14); 63.0 (C-15); 19.8 (C-16); 110.0 (C-17); 28.2 (C-18); 16.4 (C-19); 13.6 (C-20); 21.0 (*Me*COO–); 21.2 (2x*Me*COO–); 170.8 (Me*C*OO) and 171.8 (Me*C*OO). MS, *m/z*: 408 [M^+] (8), 390 (6), 366 (7), 348 (52), 330 (100), 315 (25), 265 (48), 187 (25), 136 (43), 121 (64), 107 (38), 95 (50).

3.6. Preparation of 18

To a solution of the diacetylderivative of **34** (21.05 g, 53.7 mmol) in MeOH (20 mL), K_2CO_3 (2.5 g, 18.3 mmol) was added. The reaction mixture was stirred at room

temperature for 1.0 h. After addition of water, the mixture was extracted with ether, the organic phase was washed with HCl (2N) and water (until neutral), dried over anhydrous Na_2SO_4, filtered and evaporated to afford 18.0 g of crude product.

To a solution of monoacetylderivative of the reaction product (6.17 g, 17.6 mmol) in CH_2Cl_2 (100 mL) *m*-CPBA (4.25 g, 27.1 mmol) was added and the solution was stirred at room temperature for 4 h. A solution of Na_2SO_3 10% aq. was added and the resulting solution was stirred for 5 min; the mixture was diluted and extracted with Et_2O. The organic phase was washed with $NaHCO_3$ 10%, water and brine, dried (Na_2SO_4) and the solvent evaporated in vacuum to give the epoxide **18** (5.47 g, 85%).

3.6.1. 3β-Acetoxy-7,8-epoxy-labdan-15-ol: 18. IR ν_{max}^{film}: 3340, 1740, 1240 cm^{-1}. ^1H NMR ($CDCl_3$): 4.30 (1H, dd, J_1=11.2 Hz, J_2=4.6 Hz, H-3); 3.70–3.50 (2H, m, H-15); 2.89 (1H, s, H-7); 1.94 (3H, s, MeCOO–); 1.90–1.01 (15H, m), 1.22 (3H, s, Me-17); 0.82 (3H, d, J=6.4 Hz, Me-16); 0.81, 0.73 and 0.67 (3H, s ea, Me-18, Me-19 and Me-20). ^{13}C NMR ($CDCl_3$): 36.4 (C-1); 23.2 (C-2); 80.7 (C-3); 37.5 (C-4); 45.8 (C-5); 22.6 (C-6); 60.1 (C-7); 58.7 (C-8); 55.7 (C-9); 36.4 (C-10); 22.9 (C-11); 39.4 (C-12); 30.2 (C-13); 39.6 (C-14); 60.7 (C-15); 19.7 (C-16); 22.7 (C-17); 27.3 (C-18); 16.3 (C-19); 14.3 (C-20); 21.2 (*Me*COO–) and 170.8 (Me*C*OO). HRMS calcd for $C_{22}H_{38}O_4$: 366.2770; found: 366.2768.

3.7. Jones oxidation of 18 and esterification: 19

To a solution of **18** (453 mg, 1.29 mmol) in acetone distilled over $KMnO_4$ (8 mL) Jones' reagent (2.5 mL) was added dropwise. After 20 min with stirring, some drops of isopropenal and water were added. After evaporation of solvent, the residue was extracted with ether and washed with 10% $NaHCO_3$. The alkaline solution was acidified with concentrated HCl and extracted with ether. The organic phase was washed with water (until neutral). After drying with anhydrous Na_2SO_4, filtered and evaporated, the concentrated reaction product (335 mg) was esterified with ethereal diazomethane solution affording **19** (345 mg, 71%).

3.7.1. Methyl 3β-acetoxy-7,8-epoxy-labdane-15-oate: 19. IR ν_{max}^{film}: 1740, 1620, 1240 cm^{-1}. ^1H NMR ($CDCl_3$): 4.35 (1H, dd, J_1=10.7 Hz, J_2=4.3 Hz, H-3); 3.60 (3H, s, COO*Me*); 2.91 (1H, s, H-7); 2.25 (1H, dd, J_1=14.6 Hz, J_2=6.8 Hz, H-14), 2.08 (1H, dd, J_1=14.6 Hz, J_2=6.4 Hz, H-14), 1.98 (3H, s, MeCOO), 1.90–1.01 (13H, m), 1.25 (3H, s, Me-17); 0.90 (3H, d, J=6.4 Hz, Me-16); 0.85, 0.77 and 0.71 (3H ea, s, Me-18, Me-19 and Me-20). ^{13}C NMR ($CDCl_3$): 36.2 (C-1); 23.0 (C-2); 80.2 (C-3); 37.1 (C-4); 45.2 (C-5); 22.8 (C-6); 60.3 (C-7); 58.1 (C-8); 55.1 (C-9); 36.2 (C-10); 24.2 (C-11); 39.0 (C-12); 31.1 (C-13); 41.2 (C-14); 173.0 (C-15); 19.9 (C-16); 22.5 (C-17); 27.4 (C-18); 16.0 (C-19); 14.2 (C-20); 51.2 (–COO*Me*). HRMS calcd for $C_{23}H_{38}O_5$: 394.2719; found: 394.2722.

3.8. Reaction of 18 and 19 with I_2

See Table 1.

3.8.1. Methyl 3β-acetoxy-isofregenedane-15-oate: 35. $[\alpha]_D^{20°C}$=+10.9 (c=1.17, $CHCl_3$); IR ν_{max}^{film}: 1740, 1720, 1620, 1240 cm^{-1}. ^1H NMR ($CDCl_3$): 7.03 (1H, s, H-6), 4.95 (1H, dd, J_1=6.8 Hz, J_2=4.3 Hz, H-3), 3.68 (3H, s, COOMe), 2.80–2.30 (6H, m), 2.23 (3H, s, Me-17), 2.22 (3H, s, Me-20), 2.07 (3H, s, MeCOO–), 1.70–1.20 (5H,m), 1.32 (6H, s, Me-18 and Me-19), 1.05 (3H, d, J=6.4 Hz, Me-16). ^{13}C NMR ($CDCl_3$): 24.9 (C-1); 23.9 (C-2); 77.3 (C-3); 37.8 (C-4); 141.1 (C-5); 124.6 (C-6); 138.0 (C-7); 131.9 (C-8); 135.3 (C-9); 130.8 (C-10); 32.2 (C-11); 38.1 (C-12); 30.7 (C-13); 41.6 (C-14); 173.6 (C-15); 19.8 (C-16); 15.5 (C-17); 30.0 (C-18); 26.1 (C-19); 15.7 (C-20); 21.3 (*Me*COO–); 172.0 (Me*C*OO–) and 51.4 (–COO*Me*). HRMS calcd for $C_{23}H_{34}O_4$: 374.2457; found: 374.2462.

3.8.2. Methyl 3β-acetoxy-20-*nor*-fregenedane-15-oate: 36. $[\alpha]_D^{20°C}$=+9.3 (c=0.8, $CHCl_3$); IR ν_{max}^{film}: 1740, 1720, 1620, 1240 cm^{-1}. ^1H NMR ($CDCl_3$): 7.12 and 7.05 (1H, d ea, J=8.5 Hz, H-6 and 7), 4.97 (1H, dd, J_1=6.8 Hz, J_2=4.3 Hz, H-3), 3.68 (3H, s, COOMe), 2.80–2.30 (6H, m), 2.29 (3H, s, Me-17), 2.07 (3H, s, MeCOO–), 1.80–1.10 (5H, m), 1.31 (3H, s, Me-18), 1.30 (3H, s, Me-19), 1.03 (3H, d, J=6.4 Hz, Me-16). HRMS calcd for $C_{22}H_{32}O_4$: 360.2301; found: 374.2308.

3.9. Reduction of 39 and acetylation of 40: 20

To a solution of **39** (122 mg, 0.37 mmol) in dry ether (6 mL), $LiAlH_4$ (40 mg, 1.05 mmol) was added. After stirring for 2 h at room temperature and usual work-up **40** (97 mg, 81%) was obtained. Compound **40** (90 mg) was acetylated at room temperature (1 mL Ac_2O, 1 mL Py, 12 h) and after usual work-up afforded **20** (90 mg, 85%).

3.9.1. 7-Labden-6β,15-diol: 40. IR ν_{max}^{film}: 3300, 1460, 1380, 1060 cm^{-1}. ^1H NMR ($CDCl_3$): 5.60–5.56 (1H, m, H-7), 4.40–4.34 (1H, m, H-6), 3.68 (2H, t, J=6.8 Hz, H-15), 2.10–1.10 (15H, m), 1.72 (3H, s, Me-17), 1.29 (3H, s, Me-20), 1.03 and 1.00 (3H, s ea, Me-18 and Me-19), 0.90 (3H, d, J=6.5 Hz, Me-16). ^{13}C NMR ($CDCl_3$): 40.1 (C-1); 19.1 (C-2); 44.9 (C-3); 34.2 (C-4); 56.4 (C-5); 66.3 (C-6); 125.6 (C-7); 138.4 (C-8); 54.6 (C-9); 36.8 (C-10); 24.7 (C-11); 39.7 (C-12); 30.6 (C-13); 41.5 (C-14); 61.2 (C-15); 19.8 (C-16); 22.0 (C-17); 32.7 (C-18); 24.8 (C-19); 16.3 (C-20). HRMS calcd for $C_{20}H_{36}O_2$: 308.2715; found: 308.2721.

3.9.2. 15-Acetoxy-7-labden-6β-ol: 20. IR ν_{max}^{film}: 3500, 1740, 1240, 1010 cm^{-1}. ^1H NMR ($CDCl_3$): 5.61–5.57 (1H, m, H-7), 4.42–4.36 (1H, m, H-6), 4.12 (2H, t, J=6.8 Hz, H-15), 2.10–1.10 (15H, m), 2.04 (3H, s, MeCOO–), 1.78 (3H, s, Me-17), 1.28 (3H, s, Me-20), 1.03 and 1.01 (3H, s ea, Me-18 and Me-19), 0.93 (3H, d, J=6.4 Hz, Me-16). MS, m/z: 350 [M^+] (12), 332 (18), 226 (9), 207 (8), 189 (22), 151 (33), 109 (63), 95 (58), 81 (71), 69 (100).

3.10. Reaction of 20 and 21 with I_2

See Table 1.

3.10.1. Isofregenedane-15-ol: 41. IR ν_{max}^{film}: 3500, 1470, 1370, 1150 cm^{-1}. ^1H NMR ($CDCl_3$): 7.03 (1H, s, H-6), 3.72 (2H, t, J=6.8 Hz, H-15), 2.8–2.5 (3H, m), 2.25 (1H, m),

2.21 (3H, s, Me-17), 2.17 (3H, s, Me-20), 1.80–1.10 (9H, m), 1.30 (6H, s, Me-18 and Me-19), 1.02 (3H, d, J=6.4 Hz, Me-16). ^{13}C NMR ($CDCl_3$): 28.5 (C-1); 19.8 (C-2); 39.0 (C-3); 33.8 (C-4); 143.1 (C-5); 125.0 (C-6); 138.6 (C-7); 132.2 (C-8); 134.7 (C-9); 131.2 (C-10); 32.1 (C-11); 38.6 (C-12); 30.1 (C-13); 40.0 (C-14); 61.2 (C-15); 19.7 (C-16); 15.4 (C-17); 32.1 (C-18); 32.1 (C-19); 15.6 (C-20). HRMS calcd for $C_{20}H_{32}O$: 288.2453; found: 288.2459.

3.10.2. 15-Acetoxy-isofregenedane: 42. IR ν_{max}^{film}: 1740, 1470, 1360, 1120 cm^{-1}. ^{1}H NMR ($CDCl_3$): 7.02 (1H, s, H-6), 4.15 (2H, t, J=6.8 Hz, H-15), 2.80–2.50 (3H, m), 2.25 (1H, m), 2.20 and 2.15 (3H, s ea, Me-17 and Me-20), 2.05 (3H, s, MeCOO–), 1.80–1.10 (9H, m), 1.29 (6H, s, Me-18 and Me-19), 1.02 (3H, d, J=6.5 Hz, Me-16). ^{13}C NMR ($CDCl_3$): 28.4 (C-1); 19.7 (C-2); 38.7 (C-3); 33.7 (C-4); 143.1 (C-5); 124.9 (C-6); 137.9 (C-7); 132.3 (C-8); 134.9 (C-9); 131.3 (C-10); 29.7 (C-11); 38.4 (C-12); 30.1 (C-13); 35.4 (C-14); 63.0 (C-15); 19.4 (C-16); 15.5 (C-17); 32.0 (C-18); 32.0 (C-19); 15.7 (C-20); 21.1 (*Me*COO–); 171.3 (Me*C*OO–). MS, *m/z*: 330 [M$^+$] (60), 315 (58), 302 (8), 274 (12), 255 (25), 200 (48), 185 (100), 157 (27), 133 (91), 105 (19), 83 (38), 69 (48). HRMS calcd for $C_{22}H_{34}O_2$: 330.2559; found: 330.2564.

3.11. Oxidation of 22: 23, 24, 25 and 44

To a mixture of Na_2CrO_4 anhydrous (433 mg, 2.67 mmol) in dry C_6H_6 (4.0 mL), stirred at room temperature for 15 min. Sodium acetate (345 mg, 4.20 mmol), Ac_2O (4.0 mL) and AcOH (2.5 mL) were added. A solution of compound **22** (550 mg, 1.40 mmol) in dry benzene (3.0 mL) was added to the oxidant mixture with stirring and heated at 40°C. After 48 h water was added (2.0 mL), ice and stirred during 35 min. After removal of the solvent, the residue was extracted with ether several times, the combined organic layer was washed with $NaHCO_3$, water and dried over Na_2SO_4, and the solvent removed under vacuum. Column chromatography (hexane and mixtures hexane/EtOAc) afford: **25** (35 mg, 6%), **24** (44 mg, 8.0%), **23** (60 mg, 11%) and **44** (300 mg, 55%).

3.11.1. 15,17-Diacetoxy-7-labden-6-one: 23. $[\alpha]_D^{20°C}$= +9.0 (c=0.8, $CHCl_3$); IR ν_{max}^{film}: 2930, 2872, 1740, 1676, 1462, 1238, 1047 cm^{-1}. ^{1}H NMR ($CDCl_3$): 5.86 (1H, s, H-7), 4.65 (2H, s, H-17), 4.11–4.03 (2H, m, H-15), 2.07 (3H, s, Me–COO), 2.00 (3H, s, Me–COO), 2.11–0.98 (15H, m), 1.11 (3H, s, Me-19), 1.06 (3H, s, Me-18), 0.90 (3H, d, J=6.1 Hz, Me-16) and 0.83 (3H, s, Me-20). ^{13}C NMR ($CDCl_3$): 39.3 (C-1); 18.0 (C-2); 42.9 (C-3); 32.2 (C-4); 63.5 (C-5); 199.7 (C-6); 126.0 (C-7); 154.5 (C-8); 54.5 (C-9); 43.4 (C-10); 23.8 (C-11); 35.0 (C-12); 30.4 (C-13); 38.5 (C-14); 62.7 (C-15); 19.3 (C-16); 63.3 (C-17); 32.6 (C-18); 21.4 (C-19); 14.6 (C-20); 20.9 (*Me*COO–); 20.7 (*Me*COO–); 170.2 (Me*C*OO–) and 171.1 (Me*C*OO–). MS, *m/z*: 406 [M$^+$] (1), 365 (6), 347 (7), 332 (4), 291 (5), 264 (4), 240 (100), 204 (21), 180 (20), 162 (21), 147 (22), 135 (75), 121 (20), 109 (30), 95 (16), 81 (26), 69 (26), 55 (35).

3.11.2. 7α,8α-Epoxy-15,17-diacetoxylabdane: 24. IR ν_{max}^{film}: 2928, 2872, 1742, 1462, 1236, 1036, 756 cm^{-1}. ^{1}H NMR ($CDCl_3$): 4.29 (1H, d, J=11.9 Hz, H_A-17), 4.06 (2H, t, J=7.1 Hz, H-15), 3.96 (1H, d, J=11.9 Hz, H_B-17), 3.16 (1H, s br, H-7), 2.05 (3H, s, Me–COO–), 2.03 (3H, s, Me–COO–), 2.10–0.91 (17H, m), 0.88 (3H, d, J=6.5 Hz, Me-16), 0.85 (3H, s, Me-19); 0.84 (3H, s, Me-18) and 0.75 (3H, s, Me-20). ^{13}C NMR ($CDCl_3$): 39.2 (C-1); 18.6 (C-2); 42.0 (C-3); 33.2 (C-4); 48.2 (C-5); 22.7 (C-6); 57.7 (C-7); 59.1 (C-8); 54.9 (C-9); 35.7 (C-10); 21.4 (C-11); 38.6 (C-12); 30.1 (C-13); 35.1 (C-14); 63.0 (C-15); 19.4 (C-16); 66.8 (C-17); 32.6 (C-18); 21.9 (C-19); 14.2 (C-20); 21.1 (*Me*COO–); 20.7 (*Me*COO–); 170.4 (Me*C*OO–) and 171.2 (Me*C*OO–). HRMS calcd for $C_{24}H_{40}O_5$: 408.2876; found: 408.2881.

3.11.3. 7β,8β-Epoxy-15,17-diacetoxylabdane: 25. IR ν_{max}^{film}: 2926, 2854, 1742, 1462, 1234, 1038, 756 cm^{-1}. ^{1}H NMR ($CDCl_3$): 4.27 (1H, d, J=11.8 Hz, H_A-17), 3.84 (1H, d, J=11.8 Hz, H_B-17), 4.08 (2H, t, J=6.8 Hz, H-15), 3.21 (1H, d, J=6.4 Hz, H-7), 2.08 (3H s, MeCOO–), 2.04 (3H s, MeCOO–), 2.11–0.95 (17H, m), 0.93 (3H, d, J=6.5 Hz, Me-16), 0.87 (3H, s, Me-19), 0.85 (3H, s, Me-18) and 0.82 (3H, s, Me-20). ^{13}C NMR ($CDCl_3$): 39.2 (C-1); 18.3 (C-2); 41.8 (C-3); 33.2 (C-4); 48.2 (C-5); 22.7 (C-6); 57.7 (C-7); 59.1 (C-8); 50.2 (C-9); 35.3 (C-10); 21.5 (C-11); 38.9 (C-12); 30.1 (C-13); 35.1 (C-14); 63.0 (C-15); 19.4 (C-16); 66.8 (C-17); 33.9 (C-18); 21.8 (C-19); 15.3 (C-20); 21.0 (*Me*COO–); 20.8 (*Me*COO–); 170.5 (Me*C*OO–) and 171.2 (Me*C*OO–). HRMS calcd for $C_{24}H_{40}O_5$: 408.2876; found: 408.2883.

3.11.4. 15,17-Diacetoxy-8-labden-7-one: 44. $[\alpha]_D^{20°C}$= +12.2 (c=0.4, $CHCl_3$); IR ν_{max}^{film}: 2930, 2872, 1740, 1676, 1605, 1462, 1238, 1047 cm^{-1}. ^{1}H NMR ($CDCl_3$): 4.73 (1H, d, J=11.5 Hz, H_A-17), 4.66 (1H, d, J=11.5 Hz, H_B-17), 4.01 (2H, t, J=6.7 Hz, H-15), 2.42–2.14 (4H,m), 1.97 (3H, s, MeCOO–), 1.96 (3H, s, MeCOO–), 1.90–0.98 (12H, m), 1.05 (3H, s, Me-20), 0.87 (3H, d, J=7.6 Hz, Me-16), 0.85 (3H, s, Me-19) and 0.82 (3H, s, Me-18). ^{13}C NMR ($CDCl_3$): 37.3 (C-1); 18.3 (C-2); 40.9 (C-3); 33.1 (C-4); 49.5 (C-5); 35.0 (C-6); 198.4 (C-7); 128.8 (C-8); 175.1 (C-9); 41.1 (C-10); 26.5 (C-11); 35.3 (C-12); 30.7 (C-13); 35.0 (C-14); 62.3 (C-15); 18.8 (C-16); 57.6 (C-17); 32.2 (C-18); 21.2 (C-19); 18.3 (C-20); 21.2 (*Me*COO–); 20.8 (*Me*COO–); 170.8 (Me*C*OO) and 170.9 (Me*C*OO). MS, *m/z*: 406 [M$^+$] (1), 365 (9), 347 (12), 331 (5), 290 (7), 263 (4), 240 (91), 204 (32), 180 (23), 147 (20), 135 (100), 121 (25), 111 (52), 109 (57), 95 (23), 81 (22), 69 (20).

3.12. Reduction of 44 and acetylation: 26

To a solution of **44** (450 mg, 1.11 mmol) in MeOH (7.0 mL), $NaBH_4$ (35.0 mg, 0.91 mmol) was added at room temperature. The mixture was stirred for 25 h, then HCl 2N (0.5 mL) and water (5.0 mL) were added. The mixture was extracted with ether, washed with water and dried over Na_2SO_4. After filtration, the solvent was concentrated under vacuum giving 388 mg (86%) of the reduction product, that was acetylated with Ac_2O/Py in the usual conditions (1 mL/1 mL) and extracted with ether, chromatographed (Hex./EtOAc) to afford as a colorless oil **26** (300 mg, 77%).

3.12.1. 7β,15,17-Triacetoxy-8-labdene: 26. $[\alpha]_D^{20°C}$= +16.7 (c=0.8, $CHCl_3$); IR ν_{max}^{film}: 2963, 2871, 1740, 1648,

1466, 1242, 1026 cm^{-1}. ^1H NMR ($CDCl_3$): 5.42 (1H, t, J=8.4 Hz, H-7), 4.63 (1H, d, J=12.0 Hz, H_A-17), 4.45 (1H, d, J=12.0 Hz, H_B-17), 4.04 (2H, t, J=6.7 Hz, H-15), 2.01 (3H s, MeCOO–), 2.00 (3H s, MeCOO–), 1.99 (3H s, MeCOO–), 2.10–0.95 (16H, m), 1.01 (3H, s, Me-20), 0.89 (3H, d, J=6.6 Hz, Me-16), 0.85 (3H, s, Me-19) and 0.80 (3H, s, Me-18). ^{13}C NMR ($CDCl_3$): 36.0 (C-1); 18.5 (C-2); 41.2 (C-3); 33.0 (C-4); 49.0 (C-5); 25.3 (C-6); 71.5 (C-7); 124.2 (C-8); 153.7 (C-9); 39.8 (C-10); 25.1 (C-11); 37.9 (C-12); 30.7 (C-13); 35.2 (C-14); 62.6 (C-15); 19.0 (C-16); 60.9 (C-17); 21.2 (C-18); 32.2 (C-19); 20.1 (C-20); 21.2 (*Me*COO–); 21.0 (*Me*COO–) 20.9 (*Me*COO–) 171.1 (Me*C*OO–) 170.9 (Me*C*OO–) and 170.7 (Me*C*OO–). MS, *m*/*z*: 450 [M^+] (1), 416 (2), 394 (2), 362 (2), 345 (2), 330 (5), 320 (2), 285 (2), 270 (2), 234 (2), 229 (2), 201 (11), 187 (100), 163 (5), 133 (24), 131 (18), 119 (38), 105 (20), 91 (15), 69 (13), 58 (10).

3.13. Treatment of compounds 22–26 with I_2

See Table 1. The main compound obtained was **42** has been already described and traces of **45** were obtained in the reaction of **26**.

3.13.1. 1,5,5-Trimethyl-2-acetoxymethyl-5,6,7,8-tetrahydronaphthalene: 45. IR ν_{max}^{film}: 2960, 2925, 1740, 1632, 1597, 1235, 1026, 860, 818 cm^{-1}. ^1H NMR ($CDCl_3$): 7.23 and 7.14 (1H, d ea, J=8.4 Hz, H-3 and H-4), 5.09 (2H, s, CH_2OAc), 2.64 (2H, t, J=6.3 Hz, H-8), 2.18 (3H, s, *Me*–C-1), 2.07 (3H, s, MeCOO–), 1.90–1.22 (4H, m) and 1.27 (6H, s, *Me*–C-5). ^{13}C NMR ($CDCl_3$): 135.4 (C-1); 130.9 (C-2); 127.2 (C-3); 124.3 (C-4); 34.3 (C-5); 38.4 (C-6); 19.4 (C-7); 28.1 (C-8); 128.8 (C-8a); 146.6 (C-4a); 65.6 (–*C*H_2OAc); 31.9 (*Me*–C-5); 31.9 (*Me*–C-5); 14.9 (*Me*–C-1); 21.0 (*Me*COO–); 171.0 (Me*C*OO–). MS, *m*/*z*: 246 [M^+] (1), 231 (51), 187 (22), 186 (89), 172 (18), 171 (100), 156 (10), 143 (20), 128 (17), 115 (9), 105 (8), 91 (6), 77 (5).

3.14. Treatment of compounds 27 and 28 with I_2

See Table 1.

3.14.1. Methyl 15-acetoxy-isofregenedan-17-oate: 51. IR ν_{max}^{film}: 2932, 1752, 1718, 1596, 1464, 1242, 1139 cm^{-1}. ^1H NMR ($CDCl_3$): 7.63 (1H, s, H-6), 4.14–4.08 (2H, m, H-15), 3.87 (3H, s, COOMe), 2.95–2.41 (4H, m), 2.18 (3H, s, Me-20), 2.05 (3H, s, MeCOO–), 1.98–1.04 (9H, m), 1.25 (6H, s, Me-18 and Me-19), 0.95 (3H, d, J=6.5 Hz, Me-16). ^{13}C NMR ($CDCl_3$): 25.9 (C-1); 28.9 (C-2); 38.4 (C-3); 34.6 (C-4); 150.2 (C-5); 126.1 (C-6); 134.9 (C-7); 127.7 (C-8); 138.5 (C-9); 131.5 (C-10); 27.6 (C-11); 38.7 (C-12); 30.6 (C-13); 37.1 (C-14); 63.0 (C-15); 19.3 (C-16); 169.0 (C-17); 31.7 (C-18); 31.7 (C-19); 14.1 (C-20); 51.8 (COO*Me*); 21.0 (*Me*COO–); 171.4 (Me*C*OO). MS, *m*/*z*: 374 [M^+] (<1%), 343 (27), 342 (65), 283 (22), 282 (21), 267 (22), 255 (24), 245 (45), 229 (31), 228 (31), 227 (100), 215 (42), 199 (26), 171 (26), 157 (22), 141 (21), 129 (27), 73 (21), 55 (37).

3.14.2. Methyl 15-acetoxy-20-*nor*-fregenedan-17-oate: 52. IR ν_{max}^{film}: 2932, 1753, 1717, 1597, 1464, 1242, 1140 cm^{-1}. ^1H NMR ($CDCl_3$): 7.58 (1H, d, J=8.4 Hz, H-6), 7.24 (1H, d, J=8.4 Hz, H-7), 4.16–4.08 (2H, m, H-15), 3.85 (s, COOMe), 2.95–2.41 (4H, m), 2.05 (3H, s, MeCOO–), 1.87–1.03 (9H, m), 1.28 (6H, s, Me-18 and Me-19) 1.02 (3H, d, J=6.6 Hz, Me-16). ^{13}C NMR ($CDCl_3$): 27.1 (C-1); 27.4 (C-2); 38.3 (C-3); 34.5 (C-4); 150.1 (C-5); 124.4 (C-6); 127.4 (C-7); 127.6 (C-8); 141.9 (C-9); 135.2 (C-10); 29.6 (C-11); 38.3 (C-12); 30.7 (C-13); 37.2 (C-14); 63.0 (C-15); 19.3 (C-16); 168.9 (C-17); 31.8 (C-18); 31.8 (C-19); 51.8 (COO*Me*); 21.0 (*Me*COO–); 171.2 (Me*C*OO). MS, *m*/*z*: 360 [M^+] (<1%), 328 (25), 286 (12), 269 (17), 268 (12), 253 (20), 242 (22), 231 (15), 214 (27) 213 (100), 201 (15), 157 (25), 129 (18), 115 (15), 91 (8), 69 (13).

3.14.3. 1,5,5-Trimethyl-2-methoxycarbonil-5,6,7,8-tetrahidronaphthalene: 53. IR ν_{max}^{film}: 3075, 3037, 2944, 1711, 1591, 1254, 668 cm^{-1}. UV (Ethanol) λ_{max}: 211 nm (ε=16840), 242 nm (ε=11471) and 283 nm (ε=1350). ^1H NMR ($CDCl_3$): 7.56 (1H, d, J=8.2 Hz, H-4), 7.25 (1H, d, J=8.2 Hz, H-3), 3.87 (3H, s, –COOMe), 2.65 (2H, t, J=6.3 Hz, H-8), 2.41 (3H, s, *Me*–C-1), 1.86–1.82 (2H, m, H-7), 1.65–1.61 (2H, m, H-6), 1.29 (6H, s, *Me*–C-4). ^{13}C NMR ($CDCl_3$): 136.0 (C-1); 128.1 (C-2); 126.9 (C-3); 124.0 (C-4); 34.3 (C-5); 38.2 (C-6); 19.4 (C-7); 28.1 (C-8); 137.4 (C-8a); 149.7 (C-14a); 16.5 (*Me*–C-1); 31.7 (*Me*–C-5); 31.7 (*Me*–C-5); 51.8 (–COO*Me*) 169.3 (*C*OOMe). MS, *m*/*z*: 232 [M^+] (23), 217 (100), 185 (29), 158 (23), 143 (37), 128 (62), 115 (46), 91 (15), 77 (14), 59 (25), 51 (12).

3.15. Swern oxidation of 47: 48

To a solution of freshly distilled $(ClCO)_2$ (0.9 mL, 0.31 mmol) in dry CH_2Cl_2 (10 mL) under argon atmosphere, cooled at −78°C, 1.4 mL of DMSO (19.76 mmol), was carefully added. After stirring for 15 min at −78°C a solution of **47** (2.19 g, 6.29 mmol) in dry CH_2Cl_2 (10 mL) was added. The reaction mixture was kept at −78°C for 45 min. After that, 6 mL of Et_3N was added and the reaction mixture was left to reach room temperature and some drops of water were added. The reaction mixture was extracted with EtOAc. The organic phase was washed with HCl (2N) and water, dried over anhydrous Na_2SO_4. After evaporation of the solvent 1.88 g of crude product was obtained and chromatographed. Elution with CH_2Cl_2/ether 49/1 gave 1.64 g (75%) of **48**.

3.15.1. 17-Acetoxy-7,13*E*-labdadien-15-al: 48. IR ν_{max}^{film}: 2710, 1740, 1670, 1252, 1028 cm^{-1}. ^1H NMR ($CDCl_3$): 9.97 (1H, d, J=8.2 Hz, H-15), 5.87 (1H, d, J=8.2 Hz, H-14), 5.86–5.82 (1H, m, H-7), 4.54 (1H, d, J=12.3 Hz, H-17), 4.45 (1H, d, J=12.3 Hz, H-17), 2.40–1.95 (4H, m), 2.15 (3H, s, Me-16), 2.05 (3H, s, MeCOO–), 1.93–0.90 (10H, m), 0.87 (3H, s, Me-19), 0.85 (3H, s, Me-18), 0.75 (3H, s, Me-20). ^{13}C NMR ($CDCl_3$): 39.1 (C-1); 18.7 C-2; 42.1 C-3; 33.0 (C-4); 49.9 (C-5); 23.9 (C-6); 130.1 (C-7); 133.4 (C-8); 51.6 (C-9); 36.8 (C-10); 24.5 (C-11); 42.0 (C-12); 163.5 (C-13); 127.5 (C-14); 191.1 (C-15); 17.6 (C-16); 67.7 (C-17); 33.0 (C-18); 21.6 (C-19); 13.6 (C-20); 21.6 (*Me*COO–); 170.6 (Me*C*OO). HRMS calcd for $C_{22}H_{34}O_3$: 346.2508; found: 346.2502.

3.16. Oxidation of 48 with $NaClO_2$: 29

To a solution of **48** (600 mg, 1.72 mmol) in *t*-BuOH (16 mL) were added successively, 2-methyl-2-butene

(4.5 mL), a solution of $NaH_2PO_4 \cdot 2H_2O$ (1.7 g), 12 mL $NaClO_2$ and 19 mL of H_2O. After 22 h at room temperature, the reaction mixture was extracted with ether, dried over anhydrous Na_2SO_4, filtered and evaporated to give **29** (438 mg, 70%).

By treatment of **29** with diazomethane led to **49** (438 mg, 100%)

3.16.1. 17-Acetoxy-7,13*E*-labdadien-15-oic: 29. IR ν_{max}^{film}: 3600–2800, 1740, 1690, 1242, 1022 cm^{-1}. ^1H NMR ($CDCl_3$): 5.86–5.82 (1H, m, H-7), 5.69 (1H, s, H-14), 4.55 (1H, d, *J*=12.3 Hz, H-17), 4.46 (1H, d, *J*=12.2 Hz, H-17), 2.30–2.02 (4H, m), 2.16 (3H, s, Me-16), 2.07 (3H, s, MeCOO–), 2.00–1.01 (10H, m), 0.87, 0.86 and 0.75 (3H, s ea, Me-19, Me-18 and Me-20). ^{13}C NMR ($CDCl_3$): 39.1 (C-1); 18.7 (C-2); 42.1 (C-3); 33.0 (C-4); 49.9 (C-5); 23.9 (C-6); 129.9 (C-7); 133.6 (C-8); 51.6 (C-9); 36.9 (C-10); 24.8 (C-11); 42.2 (C-12); 162.8 (C-13); 115.5 (C-14); 171.8 (C-15); 19.2 (C-16); 67.6 (C-17); 33.0 (C-18); 21.8 (C-19); 13.6 (C-20); 21.1 (*Me*COO–); 170.8 (Me*C*OO–). HRMS calcd for $C_{22}H_{34}O_4$: 362.2457; found: 362.2461.

3.16.2. Methyl 17-acetoxy-7,13*E*-labdadien-15-oate: 49. IR ν_{max}^{film}: 1740, 1721, 1649, 1435, 1240, 1020 cm^{-1}. ^1H NMR ($CDCl_3$): 5.82–5.78 (1H, m, H-7), 5.63 (1H, s, H-14), 4.53 (1H, d, *J*=12.3 Hz, H-17), 4.42 (1H, d, *J*=12.2 Hz, H-17), 3.64 (3H, s, COOMe), 2.30–1.94 (4H, m), 2.13 (3H, s, Me-16), 2.03 (3H, s, MeCOO), 1.92–0.90 (10, H), 0.85, 0.83 and 0.72 (3H, s ea, Me-19, Me-18 and Me-20). ^{13}C NMR ($CDCl_3$): 39.0 (C-1); 18.7 (C-2); 42.1 (C-3); 33.0 (C-4); 49.6 (C-5); 23.7 (C-6); 129.9 (C-7); 133.7 (C-8); 50.8 (C-9); 36.6 (C-10); 24.8 (C-11); 42.4 (C-12); 160.4 (C-13); 115.5 (C-14); 167.1 (C-15); 18.9 (C-16); 67.8 (C-17); 33.0 (C-18); 21.8 (C-19); 13.6 (C-20); 50.8 (–COO*Me*); 21.1 (*Me*COO–); 170.8 (Me*C*OO). MS, *m/z*: [M^+] (8), 330 (12), 316 (12), 301 (15), 285 (10), 262 (100), 248 (28), 221 (32), 202 (95), 189 (20), 133 (52), 124 (62), 109 (100), 91 (50), 79 (52), 69 (76), 55 (78).

3.17. Reaction of 29 with HCOOH and esterification: 30

Compound **29** (160 mg, 0.44 mmol) was dissolved in HCOOH (5 mL). After 15 h at room temperature the mixture was extracted with ether. The ether solution was washed with water, dried over anhydrous Na_2SO_4, filtered and evaporated to yield 148 mg of crude mixture that was esterified with an ethereal solution of CH_2N_2. After evaporation of the solvent **30** (150 mg, 97%) was obtained.

3.17.1. Methyl 7α-formiloxy-8(17),13*E*-labdadien-15-oate: 30. IR ν_{max}^{film}: 1723, 1651, 1435, 1227, 1148 cm^{-1}. ^1H NMR ($CDCl_3$): 8.05 (1H, s, OOCH), 5.60 (1H, s, H-14), 5.52 (1H, s, H-7), 5.24 (1H, s, H-17), 4.78 (1H, s, H-17), 3.70 (3H, s, –COOMe), 2.30–1.80 (3H, m), 2.16 (3H, s, Me-16), 1.80–0.90 (11H, m), 0.90, 0.85 and 0.70 (3H, s ea, Me-18, Me-19 and Me-20). ^{13}C NMR ($CDCl_3$): 38.9 (C-1); 19.8 (C-2); 42.0 (C-3); 33.1 (C-4); 48.6 (C-5); 20.9 (C-6); 76.4 (C-7); 144.5 (C-8); 51.0 (C-9); 39.5 (C-10); 29.0 (C-11); 38.8 (C-12); 160.3 (C-13); 115.5 (C-14); 167.2 (C-15); 18.7 (C-16); 112.7 (C-17); 33.1 (C-18); 21.4 (C-19); 13.6 (C-20); 50.7 (–COO*Me*); 160.4 (–OOCH). HRMS calcd for $C_{22}H_{34}O_4$: 362.2457; found: 362.2461.

3.18. Hydrolysis of 30: 31

To a solution of **30** (71 mg, 0.2 mmol) in MeOH (5 mL) K_2CO_3 (180 mg, 1.31 mmol) was added. The reaction mixture was stirred at room temperature for 4 h, after that time was extracted with ether. The organic phase was washed with HCl (2N), 6% $NaHCO_3$ and water, dried over anhydrous Na_2SO_4, filtered and evaporated. The residue (74 mg) was chromatographed on silicagel and eluted with hexane/EtOAc 9/1 affording **31** (51 mg, 82% yield).

3.18.1. Methyl 7α-hydroxy-8(17),13*E*-labdadien-15-oate: 31. IR ν_{max}^{film}: 3500, 2900–2800, 1738, 1227, 1150 cm^{-1}. ^1H NMR ($CDCl_3$): 5.70 (1H, s, H-14), 5.10 (1H, s, H-17), 4.62 (1H, s, H-17), 4.40 (1H, s, H-7), 3.70 (3H, s, –COOMe), 2.30–180 (3H, m), 2.17 (3H, s, Me-16), 1.80–0.90 (11H, m), 0.89, 0.81 and 0.70 (3H, s ea, Me-18, Me-19 and Me-20). HRMS calcd for $C_{21}H_{34}O_3$: 334.2508; found: 334.2512.

3.19. Reaction of 29 and 30 with I_2 and esterification: 50

See Table 1.

3.20. Reaction of 31 with I_2: 50

See Table 1.

3.21. Reaction of 30 with HCOOH and esterification: 50

The compound **30** (100 mg, 0.28 mmol) was dissolved in HCOOH (5 mL), and refluxed for 22 h. After cooling and addition of water, the reaction mixture was worked-up as usual, to afford a residue (70 mg) that was esterified with an ethereal solution of diazometane. Evaporation of the solvent and column chromatography on silicagel of the residue **50** (11 mg, 10%) was isolated.

3.21.1. Methyl 13*E*-isofregeneden-15-oate: 50. IR ν_{max}^{film}: 1723, 1647, 1223, 1146 cm^{-1}. ^1H NMR ($CDCl_3$): 7.01 (1H, s, H-6), 5.75 (1H, s, H-14), 3.70 (3H, s, –COOMe), 2.86–2.50 (5H, m), 2.40–2.20 (1H, m), 2.26, 2.21 and 2.16 (3H, s ea, Me-16, Me-17 and Me-20), 1.92–0.90 (4H, m), 1.28 (6H, s, Me-18 and Me-19). ^{13}C NMR ($CDCl_3$): 28.5 (C-1); 19.8 (C-2); 38.8 (C-3); 33.8 (C-4); 143.6 (C-5); 125.0 (C-6); 136.6 (C-7); 132.9 (C-8); 135.4 (C-9); 131.4 (C-10); 32.8 (C-11); 42.2 (C-12); 159.7 (C-13); 115.5 (C-14); 167.2 (C-15); 19.0 (C-16); 15.4 (C-17); 32.0 (C-18); 32.0 (C-19); 15.6 (C-20); 50.7 (–COO*Me*). MS, *m/z*: 314 [M^+] (18), 301 (12), 284 (4), 273 (7), 225 (3), 213 (4), 201 (100), 190 (54), 185 (58), 172 (28), 145 (30), 119 (48), 105 (40), 91 (38), 81 (30), 69 (50), 55 (70).

3.22. Reduction of 59 with $LiAlH_4$ and acetylation: 32

To a solution of **59** (585 mg, 1.91 mmol) in dry ether (20 mL), $LiAlH_4$ (100 mg, 2.63 mmol) was added. The mixture was stirred at room temperature for 1 h. After usual work-up, the crude product (450 mg) was acetylated with Ac_2O (1 mL) and pyridine (1 mL). After 12 h at room temperature and usual work-up **32** (450 mg, 75%) was obtained.

3.22.1. 13,17-Diacetoxy-14,15-dinor-7-labdene: 32. IR

ν_{max}^{film}: 1742, 1458, 1370, 1240 cm^{-1}. ^1H NMR ($CDCl_3$): 5.60–5.56 (1H, m, H-7), 4.88–4.82 (1H, m, H-13), 4.55 (1H, d, J=11.5 Hz, H_A-17), 4.35 (1H, d, J=11.5 Hz, H_B-17), 2.03 (3H, s, MeCOO–), 2.00 (3H, s, MeCOO–), 2.25–0.90 (14H, m), 1.18 (3H, d, J=6.5 Hz, Me-16), 0.85 and 0.83 (3H, s ea, Me-18 and Me-19), 0.72 (3H, s, Me-20). ^{13}C NMR ($CDCl_3$): 37.5 (C-1); 18.8 (C-2); 42.3 (C-3); 33.0 (C-4); 49.9 (C-5); 23.9 (C-6); 129.0 (C-7); 134.0 (C-8); 52.5 (C-9); 36.7 (C-10); 22.0 (C-11); 39.2 (C-12); 71.2 (C-13); 19.8 (C-16); 67.6 (C-17); 33.0 (C-18); 20.9 (C-19); 13.7 (C-20); 21.1 (*Me*COO–); 21.0 (*Me*COO–); 170.7 (Me*C*OO–) and 170.6 (Me*C*OO–). HRMS calcd for $C_{22}H_{36}O_4$: 364.2614; found: 364.2619.

3.23. Oxidation of 54 with $KMnO_4/MgSO_4$: 55

To a solution of **54** (4.54 g, 14.73 mmol) in acetone (250 mL) $KMnO_4$ (91.07 g, 53.0 mmol) and $MgSO_4$ (9.17 g, 76.4 mmol) were added. The reaction mixture was stirred at room temperature for 6 h and then filtered through Florisil (60–100 mesh ASTM) and celite and washed with acetone/isopropanol (50/2 mL). After evaporation of the solvent **55** (2.93 g, 71%) was obtained.

3.23.1. 8-Hydroxy-14,15-dinor-labdan-13-one: 55. $[\alpha]_D^{20°C}$=+6.7 (c=1.0, $CHCl_3$); IR ν_{max}^{film}: 3500, 1700, 1450, 1100 cm^{-1}. ^1H NMR ($CDCl_3$): 2.72–2.00 (3H, m), 2.13 (3H, s, MeCO–), 1.90–1.10 (14H, m), 1.15 (3H, s, Me-17), 0.86, 0.80 and 0.78 (3H, s ea, Me-20, Me-18 and Me-19). ^{13}C NMR ($CDCl_3$): 40.2 (C-1); 18.5 (C-2); 42.1 (C-3); 33.4 (C-4); 56.6 (C-5); 19.0 (C-6); 44.8 (C-7); 73.8 (C-8); 60.9 (C-9); 39.2 (C-10); 20.6 (C-11); 46.3 (C-12); 210.6 (C-13); 29.6 (C-16); 24.2 (C-17); 33.4 (C-18); 21.5 (C-19); 15.2 (C-20). HRMS calcd for $C_{18}H_{32}O_2$: 280.2402; found: 280.2410.

3.24. Preparation of 56

To a solution of **55** (2.93 g, 10.46 mmol) in dry ether (100 mL) $LiAlH_4$ (300 mg) was added. After stirring 1 h at room temperature, the reaction mixture was worked-up as usual. The crude product (2.72 g, 92%) was acetylated with Ac_2O (4 mL), pyridine (4 mL) and left at room temperature for 12 h. To a solution of acetylderivative (2.40 g, 7.41 mmol) in dry benzene (60 mL) I_2 (650 mg, 2.56 mmol) was added. The reaction was heated to 80°C for 2.5 h, cooled and extracted with benzene. The organic phase was washed with 20% $NaHSO_3$ and water, dried over anhydrous Na_2SO_4, filtered and evaporated to afford **56** (2.06 g, 91%).

3.24.1. 13-Acetoxy-14,15-dinor-8-labdene: 56. IR ν_{max}^{film}: 1744, 1459, 1377, 1257, 1131 cm^{-1}. ^1H NMR ($CDCl_3$): 4.93–4.80 (1H, m, H-13), 2.03 (3H, s, MeCOO–), 1.55 (3H, s, Me-17), 2.10–1.00 (15H, m), 1.21 (3H, d, J=6.2 Hz, Me-16), 0.92, 0.87 and 0.82 (3H, s ea, Me-20 and Me-19). ^{13}C NMR ($CDCl_3$): 37.2 (C-1); 19.2 (C-2); 42.0 (C-3); 33.2 (C-4); 52.1 (C-5); 19.2 (C-6); 33.7 (C-7); 126.0 (C-8); 140.1 (C-9); 39.1 (C-10); 23.5 (C-11); 36.7 (C-12); 71.5 (C-13); 19.8 (C-16); 20.2 (C-17); 33.3 (C-18); 21.7 (C-19); 19.3 (C-20); 21.2 (*Me*COO–); 170.6 (Me*C*OO). HRMS calcd for $C_{20}H_{34}O_2$: 306.2559; found: 306.2566.

3.25. Oxidation of 56 with Na_2CrO_4: 57

To a solution of **56** (2.06 g, 6.73 mmol) in dry benzene, NaOAc (3.34 g, 34.3 mmol), Na_2CrO_4 (5.98 g, 29.6 mmol), AcOH (28 mL) and Ac_2O (28 mL) were added. The reaction mixture was stirred and heated to 60°C for 2 h. After cooling, ice-crushed was added and left for 1 h. The mixture was extracted with ether to yield a crude mixture (2.47 g). Column chromatography on silicagel eluting with hexane/EtOAc 95/5 afforded **57** (1.31 g, 61%).

3.25.1. 13-Acetoxy-14,15-dinor-8-labden-7-one: 57. IR ν_{max}^{film}: 1740, 1670, 1460, 1370, 1240 cm^{-1}. UV (EtOH) λ_{max}: 249 nm (ε=12000). ^1H NMR ($CDCl_3$): 5.10–4.84 (1H, m, H-13), 2.55–2.10 (4H, m), 2.03 (3H, s, MeCOO–), 1.92–1.02 (9H, m), 1.70 (3H, s, Me-17), 1.22 (3H, d, J=6.2 Hz, Me-16), 1.03, 0.87 and 0.84 (3H, s ea, Me-20, Me-18 and Me-19). ^{13}C NMR ($CDCl_3$): 36.2 (C-1); 18.7 (C-2); 41.0 (C-3); 32.5 (C-4); 50.4 (C-5); 35.0 (C-6); 199.7 (C-7); 130.3 (C-8); 166.9 (C-9); 41.4 (C-10); 25.1 (C-11); 35.3 (C-12); 70.9 (C-13); 19.7 (C-16); 11.7 (C-17); 33.0 (C-18); 19.6 (C-19); 18.3 (C-20); 21.3 (*Me*COO–); 170.5 (Me*C*OO). HRMS calcd for $C_{20}H_{32}O_3$: 320.2351; found: 320.2356.

3.26. Reduction of 57 with $LiAlH_4$ and acetylation: 33

To a solution of **57** (1.08 g, 3.37 mmol) in dry ether (20 mL) $LiAlH_4$ (180 mg, 4.70 mmol) was added. The reaction mixture was stirred at room temperature for 1 h. After usual work-up (947 mg, 100%) were obtained and after acetylation (Ac_2O, 4 mL and Pyridine, 4 mL) and work-up as usual yielded **33**, 1.19 g (97%).

3.26.1. 7β,13-Diacetoxy-14,15-dinor-8-labdene: 33. IR ν_{max}^{film}: 1736, 1450, 1370, 1240 cm^{-1}. ^1H NMR ($CDCl_3$): 5.30 (1H, t, J=6.5 Hz, H-7), 4.69–4.45 (1H, m, H-13), 2.03 (3H, s, MeCOO–), 2.01 (3H, s, MeCOO–), 2.20–1.00 (13H, m), 1.55 (3H, s, Me-17), 1.22 (3H, d, J=6.2 Hz, Me-16), 1.03, 0.87 and 0.84 (3H, s ea, Me-20, Me-18 and Me-19). ^{13}C NMR ($CDCl_3$): 36.9 (C-1); 18.7 (C-2); 41.6 (C-3); 36.0 (C-4); 49.8 (C-5); 23.6 (C-6); 88.7 (C-7); 125.3 (C-8); 146.5 (C-9); 39.7 (C-10); 25.9 (C-11); 36.0 (C-12); 71.3 (C-13); 19.7 (C-16); 20.1 (C-17); 33.0 (C-18); 19.8 (C-19); 14.7 (C-20); 21.6 (*Me*COO–); 21.2 (*Me*COO–); 170.5 (Me*C*OO–) and 171.0 (Me*C*OO–). HRMS calcd for $C_{22}H_{36}O_4$: 364.2614; found: 346.2611.

3.27. Reaction of 32 and 33 with I_2: 58

See Table 1.

3.27.1. 13-Acetoxy-14,15-dinor-isofregenedane: 58. IR ν_{max}^{film}: 1740, 1244, 1128, 1045, 955 cm^{-1}. ^1H NMR ($CDCl_3$): 7.03 (1H, s, H-6), 5.11–4.86 (1H, m, H-13), 2.78–2.54 (3H, m), 2.30–2.20 (1H, m), 2.18 (3H, s, Me-17), 2.14 (3H, s, Me-20), 2.07 (3H, s, MeCOO–), 1.98–1.10 (6H, m), 1.27 (6H, s ea, Me-18 and Me-19), 1.26 (3H, d, J=6.2 Hz, Me-16). ^{13}C NMR ($CDCl_3$): 28.5 (C-1); 19.8 (C-2); 38.9 (C-3); 33.9 (C-4); 143.3 (C-5); 124.9 (C-6); 136.9 (C-7); 132.5 (C-8); 134.8 (C-9); 131.2 (C-10); 30.3 (C-11); 37.2 (C-12); 70.9 (C-13); 19.9 (C-16); 15.3 (C-17); 32.0 (C-18); 32.0 (C-19); 15.8 (C-20); 21.2 (*Me*COO–); 170.5

(Me*C*OO–). HRMS calcd for $C_{20}H_{30}O_2$: 302.2246; found: 302.2251.

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